Effect of Violent Exercise Upon Fibrinogen Level

C. Paul Hodgkinson

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EFFECT OF VIOLENT EXERCISE ON FIBRINOGEN LEVEL

C. PAUL HODGKINSON, M.D.*

Using the serial plasma fibrinogen profile for diagnosis, six conditioned high school athletes were tested to determine if the competitive mile race was of sufficient catabolic influence to cause intravascular conversion of fibrinogen to fibrin. In experimental animals, the intravenous administration of thromboplastin-containing solutions can be used to completely deplete the circulating blood of its fibrinogen concentration by stimulating its conversion to fibrin. If administered rapidly, shock and sudden death occur. When given slowly, the animal may survive shock but its blood will be rendered uncoagulable because of depletion of fibrinogen. It may die of hemorrhage.

In clinical obstetrics, the syndrome of massive intravascular conversion of fibrinogen to fibrin occurs in premature separation of the placenta, long intrauterine retention of a dead fetus, and in amniotic fluid embolism. Depending upon the speed and degree with which the pathogenic process develops, symptoms of shock, combined shock and hemorrhage, or hemorrhage alone may dominate the symptomatology. In amniotic fluid embolism the process is massive and acute in onset; the result is severe shock and sudden death. In premature separation of the placenta the process is gradual; and both shock and hemorrhage are frequently observed. Gradual conversion of fibrinogen to fibrin occurs in the “dead fetus syndrome” and hemorrhage of uncoagulable blood results. A delayed form of the fibrinogen-fibrin conversion syndrome has been recognized where the terminal precapillary arterioles and the capillaries become occluded in organs whose parenchyma is supplied by arterioles of the “end-artery” type. Resulting necrosis of the cortex of the kidney, the pituitary gland and the adrenal glands have been reported.

In the syndrome of fibrinogen-fibrin conversion, theory holds thromboplastin to be the alleged etiological agent and hyperthromboplastinemia the physiologic mechanism. Shock is assumed to be caused by occlusion of the terminal arterioles with insoluble fibrin gel; and hemorrhage from critical depletion of fibrinogen.

Foster and Whipple (1922) declared fibrinogen to have the following properties:

1. it is a highly dynamic blood protein which is influenced by many stimuli;
2. its sole source of manufacture is the liver;
3. acute catabolic influences and liver destruction cause reduction of its concentration
4. pregnancy, high protein diet and chronic inflammatory states cause its increased concentration;
5. if liver function is normal, complete reconstitution of plasma fibrinogen can occur in 24 hours;

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6. it is essential for normal and abnormal cellular repair; and,
7. utilization of fibrinogen stimulates its production.

Foster and Whipple were of the opinion that the concentration of circulating plasma fibrinogen represented the homeostatic balance between normal cellular attrition and hepatic regeneration.

Fibrinogen is a soluble hydro-sol which changes to an insoluble hydro-gel under the influence of thromboplastin. Fibrin, when first formed, is an amorphous net-like gel of sticky consistency which adheres to all endothelial surfaces. In the small precapillary arterioles and the capillaries, fibrin causes, first, slowing of the blood flow and then, vascular occlusion from thrombosis. In effect, the process smothers the cells of the parenchyma, much as carbon dioxide smothers fire.

Thromboplastin as a molecular entity has never been isolated. Its presence is recognized by its property of increasing the coagulation of blood. Extracts of tissue, particularly brain, muscle, lung, placenta and gland, are known to be rich in thromboplastin activity. In vivo, cell trauma incites its production. The theory of physiologic tissue repair assumes thromboplastin is essential to the initiation of the fibrin bridge as the first step in the healing process.

Reid, Clark and Rusk stated that the difference between normal physiologic conditions and pathogenic disease was, in many instances, only a matter of magnitude or intensity of the reaction process. In physiology the forerunner of thromboplastin is cellular catabolism. In experimental thromboplastinemia, extracts of macerated animal tissue have served as standard agents for inducing intravascular thrombosis. In pathogenic clinical conditions, cell injury prevails as the common attribute of etiology.

Pathogenic thromboplastin influence has been identified with such acute catabolic influences as abnormal and excessive muscular contraction (eclamptic convulsions and uterine tetany), tissue contusion (crush injury syndrome), cell injury (surgical trauma), and cell destruction (hemolytic transfusion reactions and fetal autolysis of the "dead fetus syndrome").

This project was undertaken to determine if willful muscular exertion of non-pathogenic etiology was a thromboplastin influence of sufficient intensity to initiate intravascular fibrinogen-fibrin conversion.

**METHOD**

Venous blood samples were collected from six high school boys on each of the two days preceding a one mile race and at the following time intervals after the race: 1 hour, 3 hours, 5 hours and 16 hours. Blood samples of 4.5 cc were obtained by a single sharp venipuncture in every instance and mixed with .5 cc anticoagulant contained in a chemically clean prothrombin tube. Rough handling and forceful syringing of the blood were carefully avoided. The samples were immediately placed in melting ice until the time when all samples would be assayed simultaneously by the same technician using the Wu-Ling colorimetric method.
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Experience had shown that blood samples must be handled in this punctilious manner if curves of diagnostic value were to be obtained. Fibrinogen profiles showing erratic values were of no diagnostic value except to stand as evidence of inept and careless handling of the blood samples.

RESULTS

Complete fibrinogen profiles were obtained in two subjects, incomplete profiles in two and prerace blood samples only, in the other two. Each fibrinogen profile was a uniform curve without a single erratic fibrinogen value. Moreover, a striking consistency of values existed between individual blood samples for any single time interval and the range of variation was less than 39 mg.

![Fibrinogen - Fibrin Conversion Syndrome in Conditioned Athlete](image)

Serial fibrinogen profile constructed from the composite fibrinogen values for 6 conditioned athletes following the mile race.

The pre-race average value for fibrinogen of 198 milligrams is considerably lower than previously determined averages for healthy, non-pregnant adults (267 milligrams) and for healthy obstetrical patients at term (320 milligrams). The cause for this lower average fibrinogen concentration is speculative but may be related to the conditioning process for athletes.

The postrace fibrinogen depression of 18%, maximum at 16 hours, is characteristic of intravascular conversion of fibrinogen to fibrin. This observation suggests that muscular activity of the mile race is a catabolic influence of substantial duration and degree.
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Pre-race values averaged 192 mg. per 100 cc of plasma for 12 blood samples. The post-race values showed a steady and uniform fibrinogen depression to a low of 155 mg. per 100 cc plasma at 16 hours (Figure No. 1). The post-race prolongation of the fibrinogen depressing effect was an unexpected phenomenon, and it is regrettable that plans were not made to procure additional blood samples. High school athletes do not make ideal subjects for needle puncturing experimentation, and by the time we were aware that fibrinogen had not reversed its downward trend, the boys were not available.

These results when compared with Figures No. 2 and No. 3 are consistent with the diagnosis of subclinical fibrinogen-fibrin conversion; and the fibrinogen profile is an indictment, based upon circumstantial evidence, that willful muscular effort serves as an exigent thromboplastin influence of moderate magnitude.

PREMATURE SEPARATION
OF THE PLACENTA

Serial fibrinogen profile of a patient with proven premature separation of the placenta. This patient demonstrated clinical evidence of shock of moderate degree. Her blood formed flimsy clots; however, excessive bleeding did not occur. Her disease was classified as acute, embolic-hemorrhagic, fibrinogen-fibrin conversion.
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Group - C
Extirpation Operations

<table>
<thead>
<tr>
<th>Preop.</th>
<th>Day of Operation</th>
<th>Days Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 d.</td>
<td>A+ 1/2 hr, 1+1 hr, 0</td>
<td>0+1 d, etc = days postoperative</td>
</tr>
<tr>
<td>1st day Preop.</td>
<td>0+3 hr, 0+5 hr, 0+7 hr</td>
<td>0+2 d, 0+3 d, 0+4 d, 0+5 d, 0+6 d, 0+7 d</td>
</tr>
</tbody>
</table>

Figure 3

This serial fibrinogen profile is made up of composite fibrinogen values from patients who were subjected to radical gynecologic surgery.

The fibrinogen depression incident to the operative procedure although mild, is protracted. This is followed by a period of hyperfibrinogenemia lasting several days, probably the result of stimulated hepatic activity incident to the post-operative inflammatory phase of the healing process.

COMMENT

The diagnosis of the fibrinogen-fibrin conversion syndrome by means of the fibrinogen profile assumes that fibrinogen depression is preceded by the conversion of soluble fibrinogen to insoluble fibrin; that the degree of fibrinogen depression reflects, in a reciprocal fashion, the degree of fibrinemia. Experience has shown that clinical symptoms are seldom discernible until fibrinogen depression approximates the critical level of 90 mg. per 100 cc plasma. Below this level, shock and hemorrhage of uncoagulable blood may occur. Above 120 mg. symptoms are seldom clinically apparent and the condition goes unrecognized unless detected by laboratory means.

The mechanism whereby fibrin thrombi are dissolved in the circulating blood is not known. Considerable emphasis for this responsibility has been placed upon the naturally occurring fibrinolysins. They have been called the “fibrin scavengers of the blood.”

It is highly doubtful if the degree of fibrinemia resulting from the muscular effort of the mile race is of sufficient magnitude to adversely affect the patulous vessels of the conditioned young athlete. This is particularly true if additional studies
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confirm the relatively low average pre-race fibrinogen values observed in these six athletes, because the total mass of precipitated fibrin would be relatively small.

On the other hand, it is difficult not to speculate possible inimical effects from the fibrinemia resulting from strenuous muscular effort in the subject with partially occluded vessels of marginal efficiency, as may occur in older subjects or those with previous vascular damage. At least two deaths have been reported in runners who were attempting to break the four minute mile record. Also, it would appear that the process might adversely affect athletes whose fatigue barrier had been reduced or eliminated through the use of stimulating drugs. For the desk executive, whose average fibrinogen concentration is probably higher than that of the conditioned athlete, and who subjects himself to occasional intermittent bouts of forceful muscular exertion, and whose age is likely to be over 45 years, the process may be disastrous.

Hess and Fultz\(^3\) reported (1956) on the damaging effects of strenuous exercise in a group of 107 healthy soldiers subjected to a daily physical fitness testing program for two weeks. Four men, all over the age of 30 years, developed physical abnormalities and three of them were unable to complete the program. Four subjects developed transient albuminuria, and 20% showed minor changes in the electrocardiogram.

CONCLUSIONS

A study was undertaken to determine if the muscular effort incident to running the competitive mile race by conditioned athletes was of sufficient catabolic influence to induce depression of the serial fibrinogen profile. The positive results indicated that this form of exertion probably did serve as an exigent thromboplastin influence of moderate intensity.

Although final conclusions are not possible from this preliminary report, the study suggests certain inimical effects which might result from the transient fibrinemia incident to this physiopathologic conversion of fibrinogen to insoluble fibrin.

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