Abstracts

The Fibrinolytic Response to a Variety of Stimuli in Man

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Using a standard moderate treadmill exercise procedure and assaying the euglobulin lysis times before and after exercise, the original observations of Biggs *et al* (1947) and Iatridis and Ferguson (1963) have been confirmed, namely, that there exists, in an apparently healthy population, a small group whose ability to mobilize plasminogen activator to an exercise stress appears to be consistently impaired. Expressed as a percentage increase in relation to the pre-exercise fibrinolytic potential, the response to exercise was reproducible in any one individual (Cash, 1966). Thus a 'poor responder' to moderate exercise was always a 'poor responder', even when studied some 18 to 24 months after the original investigation. In acute exhaustive exercise studies the original 'poor responders' remained significantly impaired. However, following a very prolonged exercise procedure, some 'poor responders' to a short moderate exercise procedure became indistinguishable from other known good responders (Cash and Woodfield, 1967). Using a standard dose of intravenous adrenaline a close correlation was observed between the fibrinolytic response to moderate exercise and intravenous adrenaline (Cash and Allan, 1967a).

It was assumed that the fibrinolytic reactivity of an individual might be genetically determined and that the poor responders represented the lower ranges of a normal distribution. Subsequent studies, however, have shown that certain environmental factors may influence the fibrinolytic reactivity to exercise and operative procedures. Thus severe chronic mental stress, while not significantly altering the resting levels of plasminogen activator, may produce a profound deterioration in the fibrinolytic response to exercise (Cash and Allan, 1967b). A similar acquired defect has also been recorded in some patients during the third trimester of a normal pregnancy (Woodfield *et al*, 1968).

In summary, the concept of the poor fibrinolytic responder has now been firmly established and it may represent a failure to show the normal reaction to stress. The fibrinolytic reactivity to stressful stimuli may be genetically determined but can be influenced by certain environmental factors. The defect in some individuals may be related to defects in the

efferent pathway and/or defects in the number or function of the target cells. The biological significance of this defect is, as yet, unknown.

Effect of Venous Occlusion on Fibrinolysis before and after Delivery

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The purpose of this study was to evaluate the contribution of the vessel walls to the production of fibrinolytic activators in pregnancy and after delivery.

Twenty women (10 healthy subjects and 10 diabetics on insulin treatment) were examined in the last months of their pregnancy. In all of them the fibrinolytic activity was estimated before and after venous occlusion. The same group was analysed again after delivery, 20 before and 10 after venous occlusion. A group of 10 non-pregnant women served as normal controls. The fibrinolytic activity was determined by the euglobulin lysis time method. It was markedly reduced in all the pregnant women even after venous occlusion and no difference was found between the diabetic and the normal groups.

Normal fibrinolytic activity was found after delivery starting from the first day.

The response to venous occlusion was practically in the normal range, and the fibrinolytic activity of various blood samples taken a few hours up to a few days after delivery did not show a significant difference.

Since fibrinolytic activity measured after venous occlusion is an expression of the local release of fibrinolytic activators, the normal fibrinolytic activity generally observed after delivery proves the capacity of the vessel walls of releasing the normal amount of activators.

A Study on the Role of the Liver in the Homeostatic Regulation of the Fibrinolytic System Using Hepatic Vein Catheterization

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Hepatic vein catheterization was performed in 15 subjects with normal liver function. Blood samples were drawn from the hepatic vein, the femoral

	Before		After 10 Minutes of Xanthinol Niacinate		After 30 Minutes of Xanthinol Niacinate	
	Euglobulin Lysis Time (min)	Antiplasmin (Unit/ml)	Euglobulin Lysis Time (min)	Antiplasmin (Unit/ml)	Euglobulin Lysis Time (min)	Antiplasmin (Unit/ml)
<i>Normals</i>						
Peripheral vein	131 ± 13	73 ± 3.5	32 ± 6	78.5 ± 4	75 ± 8	77 ± 4.6
Hepatic vein	160 ± 15.6	65 ± 2.6	55 ± 9	89 ± 2.7	171 ± 13.5	68 ± 3.04
Artery	134 ± 12	78 ± 3.7	43 ± 9	80.6 ± 3.	79 ± 7.2	75 ± 3.9
<i>Cirrhotic Patients</i>						
Peripheral vein	87 ± 4.9	77 ± 4.9	19 ± 9	80 ± 2.8	20 ± 6.7	79.6 ± 3
Hepatic vein	117 ± 9.2	80 ± 31	31 ± 7.9	68.7 ± 2.9	27 ± 7.9	80.7 ± 1.9
Artery	98 ± 11	83.2 ± 2.7	28.5 ± 8	82 ± 2.9	27 ± 8.3	84 ± 4

Table Changes of euglobulin lysis time and antiplasmin levels before and after injection of 300 mg of xanthinol niacinate in normal and cirrhotic cases

¹Mean values of 15 normal individuals and 12 cases of portal cirrhosis with standard errors.

artery, and a peripheral vein simultaneously. Blood was taken from the same vessels 10 and 30 minutes after activation of the fibrinolytic system with xanthinol niacinate (XN) or after inhibition with EACA. The plasminogen activators, circulating plasmin, total antiplasmins, immediate antiplasmins, and fibrinogen levels were determined.

It was shown that a normal liver has a homeostatic function which regulates the fibrinolytic system and that this function of the liver produces antiplasmin and breaks down activator. Antiplasmins are demonstrable in the hepatic venous blood immediately following activation of the fibrinolytic system (see Table).

It was found that following EACA administration, plasminogen activator increases in hepatic venous blood and, during this period, the liver did not respond to any further activation.

This study indicates that the liver has a regulatory role on the fibrinolytic system. It can rapidly release antiplasmin into the blood and eliminate activator following stimulation of fibrinolytic activity.

Catheterization of the hepatic vein was performed in 12 cases of portal cirrhosis and the fibrinolytic system was activated using xanthinol niacinate. The results are indicated in the Table. They suggest that there is a disturbance of the anti-fibrinolytic function of the liver in this condition.