IN VIVO DISINTEGRATION OF AN EXPERIMENTALLY INDUCED THROMBUS IN THE CORONARY VESSELS

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At the present time clinicians as well as pathologoanatomists relate the origin of a myocardial infarct in the overwhelming majority of cases (75-80%) to the thrombosis of the coronary vessels. However, the causes of intravascular thrombus formation, the thrombosis of coronary vessels in particular, have not as yet been clarified in many respects. It still remains obscure why, under equal conditions contributing to the process of thrombus formation (the nutrition factor, nervous tension, changes in the vascular wall), upon the increased content of factors of blood coagulation, in some cases the thrombus is formed and in other cases it is absent. It is logical to assume the presence of special protective mechanisms which prevent their formation [1]. Our previous observations [2,3] demonstrated that the function of these protective mechanisms becomes impaired under conditions of a marked vascular spasm and experimental lipoidosis.

TABLE 1. Fibrinolytic Activity of the Blood in Dogs with Experimental Thrombosis

No. of the Experiment	Time of killing after thrombus formation (in hrs)	Fibrinolytic Activity of the Blood	
		prior to operation	within $2\frac{1}{2}$ hr after thrombus formation
2	$2\frac{1}{2}$	$2\frac{1}{2}$ hr	1 hr
3	$2\frac{1}{2}$	3 hr	2 hr
		(as per Kaulla and Schultz)	
12	$2\frac{1}{2}$	33%	53%
		(as per Bidwell)	
1	20	$2\frac{1}{2}$ hr	1 hr
5	20	3 hr	$1\frac{1}{2}$ hr
6	20	$2\frac{1}{2}$ hr	$1\frac{1}{2}$ hr
7	20	3 hr	1 hr
		(as per Kaulla and Schultz)	
8	20	36%	53%
13	20	33%	57%
15	20	33%	50%
16	20	36%	53%
		(as per Bidwell)	

As we reported previously [2], the ECG shows changes connected with acute coronary insufficiency, upon simultaneous intravenous injection of pituitrin and thrombin to a healthy rabbit in doses which produce no coronary disturbances when introduced separately. The animals perished within a short period of time and their autopsy revealed a coronary thrombosis. In order to reduce the extent of thrombosis development and the concomitant coronary disturbances we reduced the thrombin and pituitrin doses. In these cases also we observed ECG changes which indicated marked impairments of coronary circulation undoubtedly connected with thrombus formation. However, these changes would gradually abate and disappear within 1-2 hours.

We could not connect the observed changes with a vascular spasm only, since the injected dose of pituitrin did not in itself produce the ECG changes. The increased level of fibrinolytic activity, observed in the animals, led us to assume that in this case the formation of a thrombus in the coronary vessels is accompanied simultaneously by a protective reaction of increased fibrinolytic activity which contributed to the destruction of the thrombus and restoration of normal circulation. In the available Soviet and foreign literature we found no reports on the possibility of such spontaneous disintegration of the thrombus in the coronary vessels.

The aim of the present study was to trace the development of an experimentally induced thrombus in the cardiac vessels of healthy animals.

METHOD

We developed the following method of producing a thrombus in the coronary vessels. As experimental animals, 16 dogs were used weighing between 12 and 24 kg. Under general intravenous narcosis (injection of a 10% barbamyl solution at 0.2 ml per kg weight) and a controlled artificial respiration, the thoracic cavity and pericardium were opened. By means of a syringe and a special, thin needle with a curved end we injected into the anterior left descending coronary artery a heated (up to 36 deg) thrombin solution (0.5 mm with 14-16 seconds activity), obtained from the N. F. Gamaleva Institute of Microbiology and Epidemiology. During the injection and for the next 5-7 minutes the vessels above the site of injection were kept compressed. The appearance of thrombus in the vessels was noted while

the operation was in progress. The wound was then sutured in layers and the air removed from the pleural cavity. The operation was performed without complications in any of the experimental animals.

At various periods after the thrombus formation the animals were killed and a careful histological examination of the coronary vessels was performed. An electrocardiographic examination prior and after the operation was made.

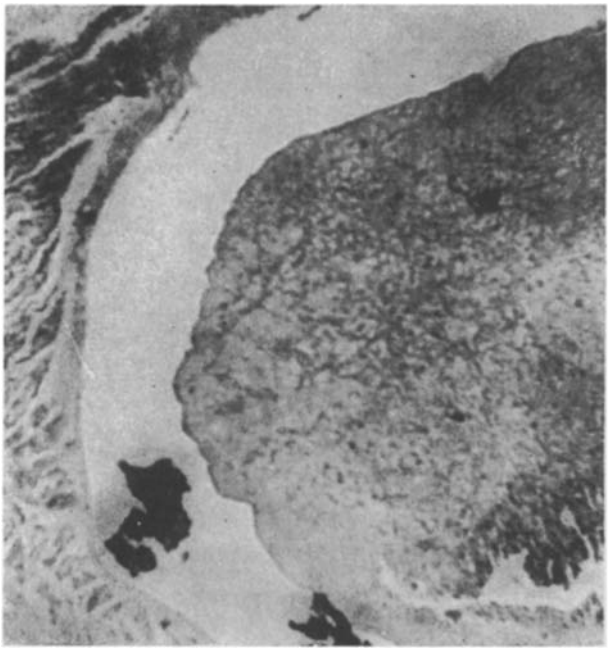

Fig. 1. Experimental thrombus within the lumen of a coronary vein of a dog within $2\frac{1}{2}$ hours after the injection of thrombin. Microphoto. Obj. 8×, oc. 10×.

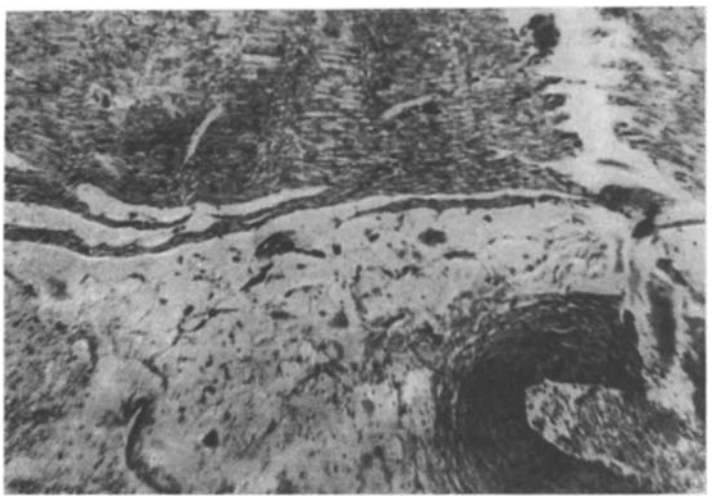

Fig. 2. Coronary vessels (an artery with the entrance opening of the needle and a vein on the left), free of thrombi, within 24 hours following thrombin administration. Obj. 8×, oc. 10×.

In the majority of animals, the fibrinolytic activity of the blood was determined. In six instances the determination was made according to Kaulla and Schultz [7] and in five--by the Bidwell method [5]. Although a number of reports [4,6] indicate that the surgical trauma per se has no noticeable effect on the level of fibrinolytic activity, nevertheless we carried out its determination for the purpose of control in four dogs whose thorax was opened but no thrombin injected.

TABLE 2. Fibrinolytic Activity of the Blood in Control Dogs.

Expt. No.	Fibrinolytic activity of the blood	
	prior to operation	within $\frac{1}{2}$ hr after the operation
1	3 hr	$2\frac{1}{2}$ hr
2	$2\frac{1}{2}$ hr	$2\frac{1}{2}$ hr
	(as per Kaulla and Schultz)	
3	33%	40%
4	33%	39%
	(as per Bidwell)	

RESULTS

Of the 16 operated dogs, four were killed during the first 30 minutes following formation of the thrombus, four — within 2-$2\frac{1}{2}$ hours, and eight — within 24 hours. The fibrinolytic activity level was determined in three dogs, killed within $2\frac{1}{2}$ hours, and in all eight dogs, killed within 24 hours. The fibrinolytic activity of the blood was determined prior to the operation and within $2\frac{1}{2}$ hours after thrombus formation (Table 1).

As control, we investigated the fibrinolytic activity of the blood in four dogs with the thorax opened, but without inducing an experimental thrombus (Table 2).

It is seen in Table 1 that the possibility of disintegration of the thrombus was higher in all cases prior to the injection of thrombin in the coronary vessels. As shown by the data of control observations, the surgical intervention was accomplished by a very slight traumatization of tissues and had a negligible effect on the fibrinolytic activity of the blood. To avoid a possible error of the method, we carried out the determination with both methods and obtained identical results.

Thus, formation of an intravascular thrombus leads to a protective reaction which is manifested, in particular, in a rise in the fibrinolytic activity of the blood, thus creating conditions for the destruction of the thrombus.

Careful histological examination of the left descending coronary artery, its branches, veins, and coronary vessels of all dogs killed within 30 minutes and $2\frac{1}{2}$ hours revealed fresh thrombi. In dogs which had survived for 24 hours after the operation the coronary vessels were free of thrombi (Fig. 1 and 2). Fig. 1 shows clearly a formed thrombus within a coronary vein. In this experiment the dog was killed within $2\frac{1}{2}$ hours after the injection of 0.5 ml of heated thrombin into the coronary artery. Fig. 2 shows clearly within the coronary artery wall the entrance aperture of the needle used for thrombin injection. The dog was killed within 24 hours and the coronary vessels were found free of thrombi.

These data indicate that the protective possibilities of healthy animals are considerable to the extent that they are capable of destroying thrombi in the coronary vessels which originated as the result of various causes. It should be noted that, although the impaired coronary circulation had been restored within 24 hours in all animals, the ECG indicated in a number of instances some myocardial changes (negative T wave and a displacement of the S-T interval). These changes are undoubtedly related to the temporary impairment of the coronary circulation.

It is quite possible that the formation of small thrombi within the lumen of coronary vessels is not as rare as has been hitherto thought. Considerable vascular spasms and sharp fluctuations in the blood coagulation system may lead to thrombus formation. However, the protective mechanisms, in particular the increase of fibrinolytic activity, contribute to their rapid disintegration and to the normalization of coronary circulation.

In reporting our initial observations of the spontaneous disintegration of experimentally induced thrombi in the coronary vessels, we hope to attract the attention of the investigators to this important problem.

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