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Level of C-Reactive Protein as a Measure of Acute Myocardial Infarction.* (21019)

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The C-reactive protein (CRP) is an abnormal constituent of human serum(1). It is in all likelihood an alpha globulin which is formed by the body in response to an inflammatory reaction(2-4). It is called C-reactive protein because it forms a precipitate with the somatic C-polysaccharide of the pneumococcus(5). Small amounts of this protein may be detected in human serum by a precipitin test using a specific antiserum from rabbits hyperimmunized with purified C-reactive protein(6,7).

Previous studies have shown that a positive test for CRP is a non-specific but sensitive indicator of inflammation of infectious or non-infectious origin(3,4). Anderson and McCarty(8), Stollerman and coworkers(9), and the authors(10) have employed the CRP test for the detection of low-grade inflammation in rheumatic fever. Since myocardial infarction in coronary artery disease is also associated with an inflammatory response, it was felt that the CRP test might be useful in determining the presence of inflammation associated with myocardial infarction.

Material and methods. The CRP precipitin test was performed according to the method of Anderson and McCarty(8). 1.5 cm each of CRP antiserum and the patient's serum were drawn up into a capillary tube (external diameter about 1 mm) and incubated for 2 hours at 37°C. The degree of precipitation (0 to 4+) was read after overnight refrigeration. Each millimeter of precipitate was considered 1+. Serial CRP tests were done on the sera of 5 of the 7 patients with coronary occlusion and myocardial infarction, and on the serum of one patient with acute coronary insufficiency and myocardial necrosis. Single specimens were tested in the other 2 patients with coronary occlusion. All these patients had a typical clinical course and showed the manifestations of necrosis, *i.e.*, fever, leucocytosis, elevated sedimentation rate, and elevated fibrinogen(11-13). These

TABLE I. CRP Tests in Patients with and without Myocardial Necrosis.

Sex	Age (yr)	Day of illness before first (+) test	Sedimentation rate (Wintrobe) mm/hr	CRP test
		Coronary occlusion; myocardial infarction		
♀	55	7	32	2+
♂	58	16	34	2+
♀	61	9	21	2+
♀	55	1½	42	1+
♀	53	3	30	3+
♂	52	2	20	3+
♂	54	2	30	2+
		Coronary insufficiency; myocardial necrosis		
♂	73	5	22	3+
		Coronary insufficiency without necrosis		
♂	59	2	8	Neg.
♂	58	7	5	"
♀	73	14	15	"
♂	50	7	30	"
♀	52	13	15	"
♂	41	7	20	"

*The CRP antiserum was kindly supplied by Schieffelin & Co. through the courtesy of Dr. E. W. Blanchard.

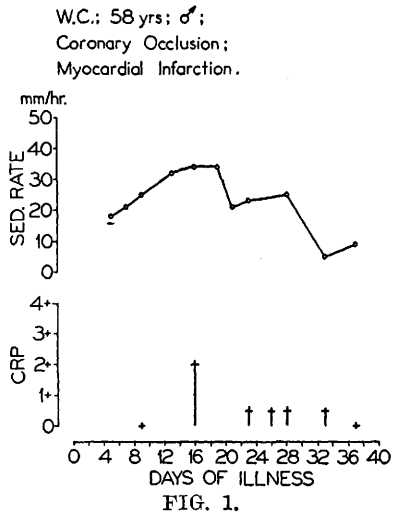

FIG. 1.

tests served as a positive control. Single CRP tests were done on the sera of 6 patients whose electrocardiograms showed RS-T and T wave changes characteristic of coronary insufficiency, but who had none of the manifestations of myocardial necrosis.

Results. Table I shows that the CRP test was positive in all 7 patients with myocardial infarction following coronary occlusion. The CRP was detected as early as 36 hours and was not detected as late as 5 to 9 days after onset of symptoms. It disappeared from the serum of one patient as early as the 15th day of illness. In 2 patients, minute amounts persisted during the 5th and 6 weeks of illness (Fig. 1). CRP was detected in the serum of one patient with severe coronary insufficiency and myocardial necrosis. His attack was precipitated by unusual effort, and the course was characterized by low-grade fever, elevated blood fibrinogen and sedimentation rate, and characteristic electrocardiographic changes.

In contradistinction, Table I shows that the CRP test was negative in 6 consecutive patients with coronary insufficiency but without signs of necrosis.

Discussion. Lofstrom(4), in his studies of pneumococcus C-polysaccharide, noted that sera of patients with myocardial infarction and fever formed a precipitate when the C-polysaccharide was added. Our data confirm this observation. The positive CRP test in all 7 patients with coronary occlusion and in the one patient with severe coronary insufficiency is unquestionably related to the presence of myocardial infarction and perinecrotic inflammation. The absence of CRP in the serum of some patients with acute myocardial infarction for as long as 5 to 9 days after the onset of illness (Fig. 1) suggests that a sufficient degree of inflammation is necessary for the elaboration of CRP. The extent of myocardial infarction is most probably the major factor contributing toward the degree of inflammation.

Coronary insufficiency(11) or coronary failure(12) may or may not be associated with myocardial infarction. RS-T and T wave changes characterize the usual subendocardial injury, but the injury may be reversible and not lead to infarction. Our data show that the CRP test was negative in patients with typical coronary insufficiency but without the criteria for myocardial infarction.

If these preliminary observations are confirmed by more extensive studies, the CRP test may prove to be a valuable aid in the differential diagnosis of coronary insufficiency, particularly as to the presence or absence of myocardial infarction. Furthermore, the pattern of the serial CRP tests in coronary occlusion with myocardial infarction (Fig. 1) suggests that the test may be useful in evaluating the subsidence of the inflammatory process in the heart.

Summary and conclusions. 1. Sera of 7 patients with coronary occlusion and myocardial infarction and of one patient with coronary insufficiency and myocardial necrosis were positive for CRP. 2. Sera of 6 patients with coronary insufficiency but without myocardial necrosis were negative for CRP. 3. These preliminary observations suggest that the CRP test may be a sensitive indicator of myocardial necrosis and inflammation.

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A Simplified Method for Determination of Lipide-C^{14} in Liver.* (21020)

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The present methods for determining lipide-C^{14} of tissues, in experiments in which slices are incubated with a C^{14}-labeled precursor, are time-consuming, and suffer from tedious manipulations, such as prolonged extraction and hydrolysis and repeated transferring of extracts from one vessel to another. These disadvantages have been completely eliminated in the simplified procedure described here. The entire analysis can be completed in less than 2 hours.

Procedure. The incubation flask is a 50-ml Erlenmeyer flask with a center well 10 mm in diameter and 20 mm high fused into the bottom. A self-sealing rubber cap is used as stopper. The general details of the incubation procedure have been described elsewhere(1). At the end of the incubation period, 0.25 ml of 30% KOH is introduced into the center well for absorption of CO_2 and, immediately thereafter, 0.25 ml of 5 N H_2SO_4 are added to the medium for inactivation of the tissue. Both alkali and acid are introduced by means of a syringe with a long hypodermic needle that is inserted through the rubber cap. Sufficient time (20-30 minutes at room temperature) is allowed for the absorption of CO_2 by the alkali, and the rubber cap is then removed. The contents of the center well are siphoned directly into a volumetric flask. The incubation medium is carefully filtered through Whatman No. 1 filter paper, so that the tissue slices are retained in the main compartment of the flask. The slices are thoroughly washed with several portions of distilled water, each of which is decanted onto the same filter paper. To avoid disintegration of the slices, the above procedure should be carried out no later than one hour after the reaction is stopped. The medium and washings are discarded unless a component of this fraction, such as glucose, ketone bodies, or the like, is to be analyzed. The filter paper is then washed with 5-10 ml of an alcohol-ether (3:1) mixture, and the washings are returned to the incubation flask. Two ml of 1 M sodium ethylate are then added to the tissue slices in the flask which is covered with a bubble

TABLE I. Test of Extraction Procedure.
To 500 mg ± 5 mg of liver slices was added one of the labeled compounds, and immediately thereafter the mixture was hydrolyzed. Extraction of the acidified hydrolysate was carried out as described in the text. Aliquots of the chloroform phase were directly mounted on aluminum discs and counted in the usual manner.

Labeled compound added to tissue slices	No. of exps.	% of added C^{14} recovered in chloroform phase (range)
*Fatty acid-C^{14}	6	99–101
Tripalmitin-1-C^{14}	3	98–100
Cholesterol-4-C^{14}	3	97–101
Alanine-1-C^{14}	3	0
Acetate-1-C^{14}	3	0
*Glycerol-C^{14}	6	0

* Biologically synthesized.

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