nitrate salts in TBPS, as compared with TBP, suggest that the organic molecules are bonded to the metal-nitrate salts in a different manner. Since the only differences in structure in the two organic molecules are the semipolar bonds, P→O and P→S, this would indicate that the interaction involves these atoms with the metal-nitrate salts to form a complex. If the metal-nitrate salt were bonded to the organic molecules through the alkyl oxygen atoms alone, one would not expect any difference in the solubilities of the salts in the two solvents. Exactly how many atoms of the organic molecules are involved in the bonding to the metal-nitrate salts is not known. It is possible that the bonding may involve the semipolar atoms in each of the organic molecules as well as the alkyl oxygen atoms.

WESLEY W. WENDLANDT
JOHN M. BRYANT
Department of Chemistry and Chemical Engineering, Texas Technological College, Lubbock

References and Notes

1. W. W. Wendlandt and J. M. Bryant, *J. Phys. Chem.* in press.
2. G. K. Estok and W. W. Wendlandt, *J. Am. Chem. Soc.* 77, 4767 (1955).
3. Kindly furnished by the Virginia-Carolina Chemical Corp., Richmond, Va.
4. A. Classen and J. Visser, *Rec. trav. chim.* 65, 211 (1946).
5. F. Hecht and H. Krafft-Ebing, *Mikrochemie* 15, 43 (1934).
6. I. Belluci and A. Chiucini, *Gazz. chim. ital.* 49, 187 (1919).
7. R. L. Moore, *U.S. Atomic Energy Commission Rept. AECD-3196* (1951).

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Serum Lactic Dehydrogenase Activity in Acute Transmural Myocardial Infarction

During experimental and clinical transmural myocardial infarction, glutamic oxaloacetic transaminase is released from cardiac muscle; this results in increased enzyme activity in the serum (*1*). This fact suggested that other enzymes in cardiac tissue might act similarly during myocardial infarction (*2*). Table 1 lists the activities of lactic dehydrogenase (LD) in dog tissue homogenates. Although the activity in the heart is less than the activity in the kidney, skeletal muscle, and liver, it is reasonable to expect LD to be released into the serum following damage to heart muscle.

The presence of LD in animal and in human-blood serum and whole-blood hemolyzates was previously demonstrated in our laboratory by spectrophotometric assay (*3*). The chemical characteristics of the enzyme in serum were studied and found to be similar to those reported for animal tissues. The normal range of activity in human serum and hemolyzates was established. The level was found to be elevated in certain disease states but notably in patients with acute and chronic leukemia, generalized carcinomatosis, and acute transmural myocardial infarction.

Table 1. Estimated lactic dehydrogenase activity of tissues of the dog.

Tissue	Activity (units/g of wet tissue)
Kidney	640,000
Skeletal muscle	600,000
Liver	390,000
Heart	240,000
Pancreas	150,000
Spleen	140,000
Brain	130,000
Lung	25,000

Serum lactic dehydrogenase was measured by adding serum to a substrate containing pyruvic acid, which oxidizes DPNH to DPN. The resulting change in optical density of the solution was measured in a Beckman DU spectrophotometer (3). The unit of serum LD is defined as the enzyme activity present in 1.0 ml of serum that causes an optical density decrease of 0.001 at a wavelength of 340 mμ in 1 minute under the conditions described. Determinations were made at 23°C. In 243 normal individuals, the range was between 200 and 680 units with a mean of 440 ± 120. The range of serum activity in the normal dog is comparable to the range of activity of human serum.

Serum lactic dehydrogenase was measured in the following: 243 normal individuals, 30 patients with cardiovascular disease that was uncomplicated by acute infarction, 35 with leukemia and malignant lymphoma, 10 with generalized carcinomatosis, 50 with localized carcinoma and other neoplastic disease, 30 with various infectious diseases, and 13 with acute transmural myocardial infarction. Venous blood was obtained for serum-LD determination regardless of the fasting state. The serum was separated from the clotted blood within a period of 2 to 24 hours after collection. It has been found that the activity is essentially unchanged if the separated serum is stored in a refrigerator from 1 to 3 days after collection. When possible, daily bleedings were made during a 5- to 10-day period.

Figure 1 summarizes the serum-LD activity on various days after infarction in 13 patients who had acute transmural infarction. Figure 2 shows the serum-LD activity during a 9-day period in a 58-year-old patient who incurred an acute, transmural, anterior-wall myocardial infarct. The LD activity was 1480 units within 48 hours and gradually fell to normal by the sixth day. The alterations in serum-LD activity in a dog, following closed-chest-wall experimental coronary-artery ligation that resulted in myocardial infarction, are comparable to the alterations seen in human infarction.

In 30 patients with heart disease, including arteriosclerotic heart disease that was associated with coronary insufficiency and/or acute and chronic congestive heart failure but that was not complicated by acute myocardial infarction, the serum-LD activity varied from 300 to 1020 units. In two of these patients, the serum-LD activity was above 680 units/ml. In one of these, chronic heart failure was present in a patient with hypertensive heart disease, auricular fibrillation, and polycystic kidney disease. The second patient had arteriosclerotic heart disease with heart failure.

All patients studied who had acute febrile and chronic infectious diseases had serum-LD activities within the normal range. Normal values were also encountered in anemia, pulmonary infarction, localized neoplastic disease, and chronic disease processes. High levels were encountered in patients with acute and chronic leukemia in relapse, generalized carcinomatosis, and, occasionally, acute hepatitis during its clinical peak, but not in patients with jaundice due to other causes. The serial LD-activity alterations that were noted following myocardial infarction have not been encountered in other clinical settings.

Our observations show that serum-LD activity rises within 24 hours in experimental and human myocardial infarction and returns to the normal range within 48 hours in dogs and within 5 to 6 days in human beings. The mechanism by which the level of enzyme activity is altered is under study but is pre-

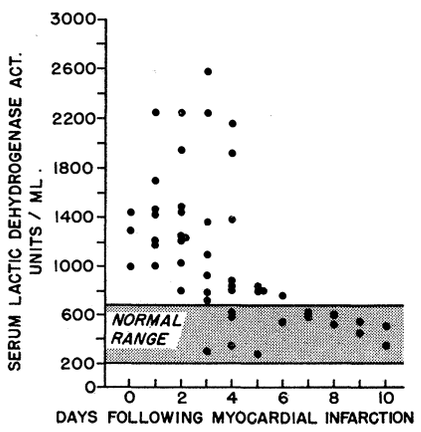

Fig. 1. Serum lactic dehydrogenase activity during the first 10 days following acute transmural myocardial infarction in 13 patients.

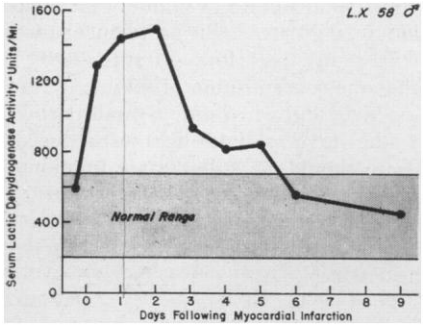

Fig. 2. Serum lactic dehydrogenase activity at the onset of chest pain and during a 10-day period following acute myocardial infarction in patient S.X.

sumed to be the result of the release of the enzyme from the infarcted heart disease. The limited number of cases presented does not permit final evaluation of these observations with regard to either their diagnostic or prognostic significance.

FELIX WRÓBLEWSKI
PAUL RUEGSEGGER
JOHN S. LADUE
Sloan-Kettering Institute and Medical Service, Memorial Center for Cancer and Allied Diseases, New York

References and Notes

1. J. S. LaDue, F. Wróblewski, A. Karmen, *Science* 120, 497 (1954); A. Karmen, F. Wróblewski, J. S. LaDue, *J. Clin. Invest.* 34, 126 (1955); C. N. Agress *et al.*, *Circulation* 11, 711 (1955); J. S. LaDue and F. Wróblewski, *Circulation* 11, 871 (1955); I. Nydick, F. Wróblewski, J. S. LaDue, *Circulation* 12, 161 (1955).
2. Supported in part by a grant from the U.S. Public Health Service.
3. F. Wróblewski and J. S. LaDue, *Proc. Soc. Exptl. Biol. Med.* 90, 210 (1955).

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Crosslinking of Latex Rubber

Most of the properties of rubber are consistent with those expected of a high-molecular-weight linear polymer of isoprene. However, there are some features of its behavior that are inexplicable on this basis. They must be the result of the presence of small amounts of structures other than the regular head-to-tail chain of isoprene units.

Bloomfield, in the first fundamental study (*1*) of the properties of rubber from freshly tapped latex, found that the tree does not continue to build indefinitely a linear polymer, but that branching reactions occur in a rested tree. These reactions eventually convert individual latex particles into substantially single molecules of enormous molecular weight. Bloomfield also observed that small amounts of oxygen are intimately associated with the hydrocarbon, even when it is isolated directly from the tree with careful exclusion of atmospheric oxygen. Craig, Juve, and Davidson (*2*) have found less certain indications of the presence of carboxyl groups, which, if they are present in the rubber in concentrations even approaching the amount indicated by their results, must be on side chains.

Watson (*3*) discovered evidence for unique links in the hydrocarbon chain at intervals of about 700,000 in molecular weight; these links dissociate at a measurable rate in solution. He has suggested that these links may be responsible for the slow "gelation" of massive rubber. Messenger (*4*) showed that this reaction is inhibited by water: samples stored in the presence of desiccants progressively increased in molecular weight (actually in solution viscosity) and finally became increasingly insoluble in the usual rubber solvents. This has recently been substantiated by further work by Wood (*5*) in connection with the "Technically Classified" rubber program (*6*).

A less well known phenomenon, although it is familiar to users of commercial latex, is the rapid development of high viscosity and relative insolubility in rubber that is obtained from preserved latex. Such rubber may become as high as 80-percent insoluble in benzene and have "Mooney" viscosities (*7*) of more than 100.

During the period 1948–50, the Plantations Division of the United States Rubber Company imported a number of samples of latex that had been preserved in a variety of ways, in the course of an intensive study of preservation methods. As a result, it was possible to obtain (*8*) data which indicate that the preservative used has a specific effect on the viscosity of the rubber (Table 1). Among other tests on the latexes, the solubility in benzene and the Mooney viscosity (ML4-212) of the rubber obtained by drying samples of the latex at room temperature were measured. Solubility was determined by the conventional procedure (developed for GR-S) in which 0.5 g of rubber supported on steel screens is left in contact with 75 ml of solvent for 24 hours in the dark, after which the concentration of an aliquot of the solution is determined.

There were not available enough high *p*H latexes containing no ammonia to eliminate entirely *p*H as a factor, but only those latexes containing free ammonia have the combination of Mooney viscosity greater than 100 and percentage gel greater than 30, indicating strongly that ammonia has a specific effect in increasing the extent of crosslinking in the latex rubber.

This is a positive effect—that is, it does not result from inhibition of degradation by oxygen during storage and handling of the latex. The rate of reaction of oxygen with latex is highest in the range of *p*H of commercial latex, and it falls sharply when the *p*H is less than 9 (*9*). The rubber from fresh latex from trees tapped regularly is usually soluble, and its Mooney viscosity is in the range of 60 to 80. Further, the viscosity increase can be induced in latexes that have been preserved without ammonia.

Small amounts of several of the low *p*H latexes listed in Table 1 were treated with ammonia (2 percent) and left standing for 6 months. The rubber in all these samples increased markedly in viscosity as compared with controls (Table 2).

It appears quite possible that the same functional groups are responsible for the crosslinking induced by ammonia and that which occurs during storage of dry rubber. During the development of the USF rubber process (*10*) C. E. Linscott observed that brief treatment with ammonia of the latex or of freshly precipi-

Table 1. Effect of preservative on gel and viscosity.

Latex No.	*p*H	Ammonia*	Other amine†	Gel (%)	ML4-212
63	11.3	–	–	0	99
47	10.4	+	–	59	118
48	10.4	+	–	38	111
66	10.4	+	–	60	>110
68	10.4	–	+	30	98
72	10.3	+	–	65	>110
73	10.3	+	–	49	103
57	10.3	+	–	52	108
35	10.3	+	–	58	111
40	10.2	–	+	16	87
74	9.8	+	–	39	>110
157	9.7	–	+	12	67
58	9.6	–	+	12	64
37	9.4	–	+	18	71
38	9.4	–	+	7	64
64	9.4	–	+	12	63
62	9.3	–	+	12	72
67	9.2	–	+	9	79
60	9.1	–	+	13	84
75	8.9	–	+	9	76
27	8.7	–	+	29	70
23	8.3	–	+	8	65
61	8.3	–	+	12	76
24	7.2	–	+	17	
39	6.9	–	+	15	77
12	6.6	–	+	15	84
1	5.8	–	–	18	75

* –, preservative absent; +, present.
† Amines other than ammonia were all low-molecular-weight aliphatic amines. Dimethylamine was the sole preservative in latex 68.

Table 2. Effect of ammonia on low *p*H latexes.

Latex	ML4-212 after 6 months	
	Control	Ammonia added
24	90	105
39	85	114
40	87	107
60	78	108
62	78	102