must, therefore, be regarded as having been naturally resistant to the action of these chemicals.

Strains of 2 of these types, 3 and 17, later became established as the etiological agents of epidemic hemolytic streptococcal respiratory infection in military establishments in which sulfadiazine was being administered prophylactically. When studied under these circumstances the degree of resistance of strains of type 3 was approximately that discovered in this study but that of strains of type 17 was much greater.[3,4]

It is probable, therefore, that both of the hypotheses previously mentioned, explaining the appearance of epidemic, sulfonamide resistant, hemolytic streptococci, are correct. Certain strains of Group A hemolytic streptococci were present in the national military population at the time that mass chemoprophylaxis was instituted that possessed two advantageous biological properties: moderate sulfonamide resistance and a high degree of communicability. These characteristics permitted these strains to spread and cause disease after their introduction into a host population undergoing sulfonamide prophylaxis. In some instances (type 17) mutation occurred and much more sulfonamide resistant variants appeared; in others (type 3) the resistance of the strain did not become greatly enhanced.

This study has not revealed a precursor for the resistant strains of type 19 that also caused epidemics. It is quite possible, however, that naturally resistant variants of this type were present in other areas.

The failure of other moderately resistant strains discovered during this study to establish epidemics may have been due to a lack of certain properties which permit a high degree of communicability or to the fact that they were never introduced into a group in which sulfonamide prophylaxis was in use.

No significantly penicillin-resistant strains of hemolytic streptococci were discovered during this study.

Summary. Strains of certain types of Group A hemolytic streptococci were discovered to be naturally resistant to moderate amounts of sulfadiazine. It is suggested that such organisms originated the epidemics of streptococcal disease among troops receiving sulfonamide prophylaxis, later becoming more resistant by mutation. No strains significantly resistant to penicillin were discovered.

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Effect of Atropine, Testosterone and Pitressin on Experimental Myocardial Infarction.*

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Recently Mokotoff and Katz[1] have made use of an experimental approach to determine the effect of drugs upon infarct size following coronary ligation. It was shown by this means that papaverine had a definite effect in reducing infarct size, while aminophyllin parenterally had a smaller, but definite effect. It was felt that other drugs might profitably be evaluated by this method. In the present report data obtained with atropine, testosterone, and pitressin are presented.

Atropine was chosen since it has been claimed recently to have a clinically beneficial effect in myocardial infarction.[2] This beneficial effect was attributed to an abolition of supposed vagus coronary constrictor tone.

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1 Mokotoff, R., and Katz, L. N., *Am. Heart J.*, 1945, **30**, 215.

2 Leroy, G. V., Fenn, G. K., and Gilbert, N. C., *Am. Heart J.*, 1942, **23**, 637.

Previous work from this department,[3] however, has shown that the vagi actually are tonic coronary dilators. Testosterone was chosen because clinical benefit had been claimed from its use.[4,5] Pitressin was used because it had been shown to be a powerful coronary vasoconstrictor[6] and might therefore be expected to act detrimentally on the course of infarct healing.

The procedure was essentially similar to that described previously.[1] In all, 47 dogs were used between controls (11), atropine-treated (13), testosterone-treated (11), and pitressin-treated (12) series. Using nembutal anesthesia (25 mg/kilo), the left anterior descending coronary artery and accompanying vein were tied completely in each dog. The animals were permitted to survive 6 weeks before being sacrificed for necropsy examination.

Atropine sulfate‡ was given subcutaneously in doses of 1.3 mg daily for 2 and 6 days per week for the remaining 4 weeks in all but 2 dogs. In these 2 dogs 0.65 mg of atropine was given twice daily for the entire 6-week period. Testosterone propionate§ was given subcutaneously in doses of 25 mg three times weekly for the 6-week period. Pitressin§ was given subcutaneously in doses of 20 pressor units daily for 2 weeks and 6 times weekly for the remaining 4 weeks.

At necropsy all hearts were opened, the ligation of the coronary artery was checked and the endocardial aspect of the infarct was traced on a glass plate. The area was determined by planimeter (*cf.* [1]). The coronary arteries were then injected and X-ray photographs were made in most instances as described previously.[1]

TABLE I.
Effect of Drugs on Infarct Size Calculated as $10^4 \times$ area of infarct (in cm²) / heart weight (in g)

	Control	Atropine	Testosterone	Pitressin
	639	447	1004	1140
	409	1118	763	619
	933	1026	683	872
	598	980	1815	1006
	922	1168	1075	762
	577	804	592	673
	1123	809	291	865
	1356	815	1099	742
	681	994	101	613
	1000	741	1555	596
	1049	612	102	506
		817		390
		690		
Arithmetic mean	844	851	826	734
Standard deviation	275	186	528	212

The data are summarized in Table I. It will be seen that no alteration in infarct size was produced by the 3 drugs used. The differences in values in each of the series and in their averages are statistically insignificant. It can therefore be concluded that within the experimental error of our method, atropine, testosterone, and pitressin in the manner administered had no demonstrable effect on the healing of experimentally produced myocardial infarcts.

The reported beneficial clinical effect of atropine and of testosterone therefore apparently operates in some way other than by coronary vasodilation. The failure of pitressin to increase infarct size outside the error of the method, suggests the possibility that its pressor effect in these dogs neutralized the coronary vasoconstriction.

It must be borne in mind that this experimental method is relatively crude and that finer differences may be concealed by inescapable variations in technic.

Summary. Atropine, testosterone, and pitressin failed to affect infarct size over a period of 6 weeks following experimental ligation of the left descending coronary artery.

We are indebted to other members of the department for their assistance and to Dr. L. N. Katz for suggesting the problem.

3 Katz, L. N., and Jochim, K., *Am. J. Physiol.*, 1939, **126**, 395.

4 Lesser, M. A., *New Engl. J. Med.*, 1942, **226**, 51.

5 Dock, W. J., *J. Exp. Med.*, 1941, **74**, 177.

6 Katz, L. N., Lindner, E., Weinstein, W., Abramson, D. I., and Jochim, K., *Arch. Int. de Pharm. et de Therap.*, 1938, **59**, 399.

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§ We are indebted to Schering and Co. for the testosterone and to Parke-Davis and Co. for the pitressin.