into tubes of Long's synthetic medium and subtilin added in concentrations ranging from 1:5000 to 1:250,000. The tubes were incubated at 37° C for 3 weeks. The highest dilution of subtilin showing no growth was 1:50,000. At the end of this period of time transfers were made to new medium. The highest dilution showing no growth in the transfer tubes was 1:10,000. These results appear to indicate that subtilin is bacteriostatic in high dilution and germicidal in greater concentration (Fig. 2).

A number of higher fungi were tested by streaking the organisms over the surface of Sabouraud's glucose agar, then placing discs of filter paper soaked in 1:1,000 dilution of subtilin in the centers of the plates. The results are recorded in Table IV.

Summary. The antibacterial product, subtilin, obtained from *Bacillus subtilis* was found to be active chiefly against Gram-positive bacteria. Two notable exceptions to the rule were *Neisseria catarrhalis* and *N. gonorrhoeae,* both Gram-negative, but also antagonized by subtilin. Acid-fast organisms, including *Mycobacterium tuberculosis,* were also found to be susceptible to the antibiotic. The agent produced a bacteriostatic action in high dilution and a germicidal effect in greater concentration. A number of pathogenic higher fungi were also found to be susceptible to subtilin.

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Action of Atropine on the Turtle Heart.

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Atropine has at least two significant modes of action on the heart, an early effect due to stimulation of the vagus center, and its well known action as an antagonist of acetylcholine. Concerning an independent direct action on heart muscle, the literature contains conflicting statements. This paper reports a study of the direct action of atropine on the turtle heart *(Pseudemys elegans).* The results indicate that the only significant direct effect of atropine on heart muscle is to depress fiber conduction when the rate of beating is abnormally high. Details of technic have been described in connection with observations on the action of digitalis.[1] The influence on rhythmicity and on contractility was observed when whole auricles or ventricular strips were suspended in a bath and the beat recorded on a smoked drum. Changes in refractory period and conductivity were followed in rhythmically stimulated ventricular strips placed on moistened filter paper; potential differences were amplified, and recorded by a piezoelectric ink writer. Two receiving electrodes were placed on the muscle strip about 15 mm apart, and each was paired with an electrode placed on the paper at a distance of about 2 cm. It has already been shown that the Q-T interval of the electrogram so recorded is an accurate measure of the refractory period, since its duration corresponds closely with measurements made by a direct method.[2] The tissue was observed for an adequate control period before the drug was added.

Effect on Rhythmicity. The effect on a natural pacemaker was studied only in the whole auricle. In the freshly removed auricle, concentrations of atropine varying from 1:200,000 to 1:50,000 caused an increase in rate of beating from 10 to 15% in 4 experiments, while in 3 no change occurred. Con-

[1] Wedd, Blair, and Dwyer, *J. Pharm. Exp. Therap.,* 1941, **72**, 394.

[2] Blair, Wedd, and Young, *Am. J. Physiol.,* 1941, **132**, 157.

TABLE I.
Effect of Atropine on the Q-T and Q-Q Intervals.

Experiment No.	Concentration × 1000	Q-T Before (sec.)	Q-T After (sec.)	Q-Q Before (sec.)	Q-Q After (sec.)
		Rate 13.4 p.m.			
1	1:100	1.86	1.88	0.2	0.2
2	1:100	1.60	1.60	X	X
	1:50	1.60	1.52	X	X
3	1:100	1.40	1.36	X	X
4	1:50	1.36	1.36	0.18	0.18
	1:25	1.36	1.12	0.18	0.18
5	1:33	1.44	1.40	X	X
6	1:20	1.48	1.42	X	X
7	1:25	1.96	1.64	0.18	0.20
8	1:25	1.44	1.48	0.42	0.58
9	1:25	1.60	1.36	.16-.20	.20-.24
10	1:25	1.64	1.60	.24-.36	.36-.40
		Rate 25 p.m.			
11	1:25	0.40	0.40	0.20	0.24
12	1:50	1.24	1.24	0.38	0.52
	1:25	1.24	1.20	0.52	0.64
13	1:25	1.16	1.16	0.28	0.40
14	1:25	X	X	0.26	0.32
15	1:25	X	X	0.36	0.50
16	1:25	1.04	1.08	0.36	0.48

centrations of 1:25,000 caused slight slowing in 3 preparations and no change in one. Observations made on auricles that had been kept cold for 24 or 48 hours gave results similar to those obtained with fresh tissues. Tonus waves when present were unaffected by the drug. Extrasystolic arrhythmias were not seen in auricular preparations and but twice in ventricular; one first appeared and the other disappeared following atropine.

Effect on Contractility. Changes in mechanical response due to atropine were studied in rhythmically driven ventricular strips which were 24 to 48 hours old. The concentrations used varied from 1:100,000 to 1:25,000. Of 8 observations, the strength of beat remained unchanged in 6; in one there was a slight increase, and in one a slight decrease. Tonus, measured by diastolic length, usually showed no change, and when a slight change did occur, the direction was not constant.

Effect on Refractory Period. This was observed by following the Q-T interval in the electrogram of rhythmically driven ventricular strips, which in most instances had been removed 24 hours before the observations were made (Table I). In the first group studied the rate of stimulation was 13.4 beats per minute. In general, concentrations of atropine varying from 1:100,000 to 1:20,000 had little effect; such action as did occur always shortened the Q-T interval; in 3 of 12 experiments the shortening amounted to 15 to 18%. In a second series for which the driving rate was 25 per minute, concentrations of 1:25,000 produced even less change; in 2 there was no change, and in 2 very slight

lengthening of questionable significance. This result was to be expected for the Q-T intervals of the second group were already shortened by the relatively high rate of beating.

Effect on Conductivity. Conduction was studied in those preparations for which excitability changes have just been described. The Q-Q interval is the conduction time for the length of muscle between the receiving electrodes. The values before and after atropine are given in Table I. In most experiments at the slow rate of beating conduction changes were slight or absent. In one in which the interval was considerably lengthened by atropine the initial conduction time was unusually prolonged. However, at the more rapid rate of beating conduction time was always increased. These results are in accord with those of Lewis and Drury[3] who stated that in the dog's auricle atropine had no effect on transmission intervals at rates of 250 per minute or less; they did not doubt that it might increase the intervals at higher rates of beating. Likewise, Megibow and Katz[4] found that in dogs in which auricular fibrillation was maintained by faradic stimulation, A-V conduction was depressed in the denervated animals by a direct action on the conducting tissues. Several experiments of the second group give striking examples of the independence of refractory period and conductivity in heart muscle; the former at high rates of beating tends to become fixed at a shortened interval, while conduction is the more easily slowed.

Summary. The direct action of atropine on cardiac muscle has been studied in the whole auricle and ventricular strips of turtle heart. In concentrations far above those that could be used therapeutically, its effect on rhythmicity, contractility, absolute refractory period, tonus, and on conductivity at low rates of beating was slight and inconstant. The only significant direct action of atropine on heart muscle appears to be a power to depress conductivity at relatively high rates of beating.

[3] Lewis and Drury, *Heart*, 1921, **8**, 83.

[4] Megibow and Katz, *J. Pharm. Exp. Therap.*, 1940, **70**, 388.

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Response to Tissue Injury of Lymphoid Tissue Previously Altered by Castration, Thyroidectomy and Thyroid Feeding.

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It has been known for some time that introduction into the body of various damaging agents causes prompt shrinkage of lymphoid tissue.[1] Lymphocytes produce, or at least contain antibodies.[2–4] These two facts have been thrown into a new light by recent work which indicates that injections of adrenal cortical extract, or secretion by the adrenal cortex induced by injections of pituitary adrenotrophic hormone, result in prompt dissolution of lymphocytes,[5,6] which thus release protein and antibodies into the lymph[7,10] with concomitant shrinkage of

[1] Selye, H., *Endocrinology*, 1937, **21**, 169.

[2] Ehrich, W. E., and Harris, T. N., *J. Exp. Med.*, 1942, **76**, 335.

[3] Dougherty, T. F., Chase, J. H., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 295.

[4] Harris, T. N., Grimm, E., Mertens, E., and Ehrich, W. E., *J. Exp. Med.*, 1945, **81**, 73.

[5] Dougherty, T. F., and White, A., *Endocrinol.*, 1944, **35**, 1.

[6] Reinhardt, W. O., and Li, C. H., *Science*, 1945, **101**, 360.

[7] White, A., and Dougherty, T. F., PROC. SOC. EXP. BIOL. AND MED., 1944, **56**, 26.