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.

15093

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

ISOLDE T. ZECKWER. (With the assistance of Giulio John Barbero.)

From the Department of Pathology, University of Pennsylvania Medical School.

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.

TABLE I.
Shrinkage of Lymphoid Tissue After Subcutaneous Injections of Formalin.

	Intact 6 pairs	Gonadectomized 4 pairs	Thyroid fed 2 pairs	Gonadectomized and thyroid fed 2 pairs	Thyroidectomized 3 pairs
Thymus, mean g					
Uninjected rats	.422	.533	.344	.415	.343
Injected "	.267	.367	.277	.303	.143
Difference	—.155	—.157	—.067	—.112	—.200
Lumbar lymph nodes, mean g					
Uninj. rats	.042	.069	.031	.035	.026
Inj. "	.021	.038	.022	.034	.012
Diff.	—.021	—.031	—.009	—.001	—.014
Mesenteric lymph nodes, mean g					
Uninj. rats	.282	.310	.218	.160	.261
Inj. "	.197	.245	.206	.134	.126
Diff.	—.085	—.065	—.012	—.026	—.135
Spleen, mean g					
Uninj. rats	.432	.461	.608	.700	.284
Inj. "	.261	.349	.526	.363	.159
Diff.	—.171	—.112	—.082	—.337	—.125
Adrenals, mean g					
Uninj. rats	.039	.042	.039	.041	.027
Inj. "	.049	.052	.039	.051	.035
Diff.	+.010	+.010	0	+.010	+.008
Body weight, mean g					
Uninj. rats	243	204	264	224	162
Inj. "	243	232	247	253	160
Diff.	0	+ 82	— 17	+ 29	— 2

lymphoid tissue.[11–14] Apparently, injection of damaging agents initiates this chain of events. Under these circumstances the adrenal cortex loses its lipoids as it discharges its secretion, evidence for which has been reviewed.[15] The adrenal cortex then enlarges in response to functional demand for its hormone, unless the damaging agents are of such magnitude as to cause adrenal exhaustion. Indications are that the adrenal factor involved is that promoting gluconeogenesis.[5,16]

As this important protective phenomenon of release of substances from lymphocytes probably depends upon secretion of the pituitary adrenocorticotrophic hormone, it seemed of interest to determine whether experimental conditions, such as castration, thyroidectomy and thyroid feeding, which are known to alter the size of lymphoid tissue[17,18] (and others) and to cause qualitative and quantitative changes in the cellular pattern of the pituitary and in its secretion of hormones, would interfere with the response of lymphoid tissue to toxic substances.

8 Dougherty, T. F., White, A., and Chase, J. H., PROC. SOC. EXP. BIOL. AND MED., 1944, **56**, 28.

9 Dougherty, T. F., Chase, J. H., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 135.

10 White, A., and Dougherty, T. F., *Endocrinol.*, 1945, **36**, 207.

11 Evans, H. M., Moon, H. D., Simpson, M. E., and Lyons, W. R., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 419.

12 Ingle, D. J., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 443.

13 Dougherty, T. F., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1943, **53**, 132.

14 Simpson, M. E., Li, C. H., Reinhardt, W. O., and Evans, H. M., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 135.

15 Sayers, G., Sayers, M. A., Fry, E. G., White, A., and Long, C. N. H., *Yale J. Biol. and Med.*, 1944, **16**, 361.

16 Venning, E. H., Hoffman, M. M., and Browne, J. S. L., *J. B. C.*, 1943, **148**, 455.

17 Chiodi, H., *Endocrinol.*, 1940, **26**, 107.

18 Reinhardt, W. O., and Wainman, P., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 257.

Groups of litter-mate rats of the same sex were used. Some were (1) castrated, (2) some thyroidectomized, (3) some fed thyroid extract and some (4) gonadectomized and fed thyroid extract. Periods of 29 to 68 days were allowed to elapse after operation so as to allow time for structural changes to result in pituitary and lymphoid tissue. Those fed thyroid extract were given daily .1 g per 100 g body weight for several weeks. Of each pair, one rat was an uninjected control. In the second rat of each pair tissue damage was produced by subcutaneous injections in the legs of .5 cc 4% formalin, twice daily for 2 days, killing the rats on the 3rd day, according to the method used by Selye[11] in intact rats.

The table gives the results. Comparisons should be made between the injected and uninjected rats, in each category, which are litter-mates. As rats of one group, such as the castrated, are not the same age as another group, such as the thyroidectomized, no conclusions have been drawn as to whether rats in one group responded with greater or less degree than those in other groups. However, since the body weights are nearly the same in the different groups, except in the dwarfed thyroidectomized rats, a rough comparison can be made. The results within each group show that the rats injected with formalin had definite shrinkage of lymphoid tissue, no matter what the previous alteration was in lymphoid tissue. In fact, 2 castrated rats which showed chronic infection at the site of operation were not excluded from the series because this additional effect on lymphoid tissue did not prevent its response after acute injury. Since observations made in each group were of the same pattern of response, with few inconsistencies, it was not thought necessary to carry out a larger series of determinations.

Conclusions. Lymphoid tissue (lymph nodes, thymus and spleen) which had been altered by various experimental conditions was capable of shrinkage in response to injury of subcutaneous tissues by formalin injections.

15094

Studies on the Absorption and Excretion of Streptomycin in Animals.

ROBERT B. STEBBINS, OTTO E. GRAESSLE, AND HARRY J. ROBINSON.
From the Merck Institute for Therapeutic Research, Rahway, N.J.

The introduction of streptomycin as a chemotherapeutic agent[1,2,3] has made apparent the need for a quantitative study of the distribution of this substance in body fluids. The present study was therefore undertaken to determine the relative concentrations of streptomycin in the blood, urine, feces, and tissues of various animal species following oral and parenteral administration.

Materials and Methods. The streptomycin* used in these studies ranged in potency from 150-400 units per mg of solid. The amount of drug administered was based on the findings in the efficacy and toxicity experiments reported by Robinson, Smith, and Graessle.[3]

The animal species used were normal monkeys, dogs, rabbits, and mice. All animals were maintained on adequate stock diet and housed under conditions of controlled temperature and humidity.

In all experiments streptomycin was admin-

1 Schatz, A., Bugie, E., and Waksman, S. A., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 66.

2 Jones, D., Metzger, H. J., Schatz, A., and Waksman, S. A., *Science*, 1944, **100**, 103.

3 Robinson, H. J., Smith, D. G., and Graessle, O. E., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 226.

* This material was prepared by Drs. Robert Denkewalter and Max Tishler from broth supplied by Dr. J. W. Foster of the Research Laboratories of Merck & Co., Inc.