

cialized epithelium which had disappeared completely was replaced by skin epithelium. A peculiarity of skin epithelium is the presence of Leydig's cells, never observed in differentiated epitheliums of enamel organs, olfactory chambers, cornea or gills. Therefore, specialized but not completely differentiated epithelium must be more sensitive to irradiation than skin epithelium.

Summary. 1) Definite suppression of growth of treated portion of the head was observed 80-110 days after irradiation with 3,000 or 6,000 r. In irradiated portions: teeth disappeared completely, growth of olfactory chambers suppressed greatly, but they never disappeared completely, anterior portion of the lower jaw had disappeared, visceral arches all shifted in rostral direction, development of the eyes was suppressed. According to sensitivity, it is possible to distribute the tissues and organs among 5 groups. (I) The teeth and lymph nodes (disappeared completely in 100% of animals). (II) Olfactory epithelium and the lens (disappeared in 28%,

damaged in 55% and normal in 17%). (III) Epithelium of the cornea (disappeared in 30%, damaged in 38% and normal in 32%) and the rods and cones layer of the retina (disappeared in 31%, damaged in 33% and normal in 36%). The gills. (IV) Other layers of retina (damaged in 16% and normal in 84%). (V) Pigment cells of choroid and other tissues of the head, which are comparatively resistant and did not show any clear signs of damage. 2) Specialized but not completely differentiated tissues can be destroyed by X-ray irradiation and after this never restored, being replaced by typical skin epithelium with Leydig's cells. This was observed in oral epithelium, olfactory epithelium and epithelium of the cornea.

1. Brunst, V. V., *J. Morphol.*, 1954, v95, 373.
2. ———, *Am. J. Roentgenol., Rad. Therapy and Nuclear Med.*, 1955, v73, 281.
3. ———, *Lab. Invest.*, 1952, v1, 432.
4. Rohrschneider, W., *Arch. f. Opth.*, 1929, v121, 537.

Received June 24, 1958. P.S.E.B.M., 1958, v99.

Myasthenia Gravis III: Lack of Inhibitory Action of Fractionated Thymus Extracts.* (24424)

SUMNER I. ZACKS (Introduced by Edgar B. Taft)

*Dept. of Pathology, Harvard Medical School and James Homer Wright Pathology Labs.,
Mass. General Hospital, Boston*

Several investigators(1-5) have studied the effects of thymus extracts on nerve muscle preparations from various animals. However, the reported neuro-muscular blocking activity of isolated frog sartorius muscle by acetone extracts of thymus glands from myasthenic patients(5), was probably due to large amounts of potassium in the extracts(6). The present study was undertaken to assay neuro-muscular blocking activity of fractionated thymus extracts free of excess potassium.

Methods. The specimen studied was a surgically resected thymoma from a 30-year-old woman with myasthenia gravis. The tumor was roughly H-shaped and weighed 48.5

g. One lobe measured 14 cm in length and contained a 5 x 7.5 x 3 cm mass covered by a firm fibrous capsule. The other lobe measured 9 x 1.5 x 1 cm. The cut surface of the tumor showed lobules of soft yellow-white tissue separated by firm fibrous trabeculae. Microscopic examination of several blocks fixed in Helly's fluid and stained with hematoxylin and eosin showed a solid tumor composed of almost equal proportions of lymphocytic and epithelial cells. Used as a control was a sample of gastrocnemius muscle obtained at autopsy from a patient who died of cardiac disease. These tissues were extracted and fractionated† by the low temperature, low

* This study was supported by research grant from Nat. Inst. of Neurological Diseases and Blindness.

† The author is indebted to Dr. Karl Schmid in whose laboratory the fractions were prepared.

salt, ethanol procedure of Schmid, Rosa and MacNair(7). When applied to human plasma, 6 fractions are obtained. Fibrinogen (I), γ globulins (II), α and β lipoproteins (IV and III), α_2 mucoproteins (IV), albumen (V), and α_1 and α_2 glycoproteins (VI) are separated. When the thymoma was fractionated according to this method, 6 fractions were obtained. The bulk of the material appeared in fractions I (175 mg), III (830 mg) and IV (990 mg). These fractions were not specifically analyzed. The skeletal muscle sample weighed 283.4 g and yielded 2 major fractions, one containing fractions I, II, and III (1269.4 mg) and the other, IV and V (6700 mg). Each fraction from the thymoma and from control skeletal muscle was tested on the isolated frog sartorius preparation in concentrations of 1 mg/ml of the lyophilized fraction in frog Ringer according to the method previously described(6). Fractions, with exception of thymoma fractions V and VI, were also dialyzed against distilled water at 4°C for 48 hours, lyophilized and tested for neuromuscular blocking activity. Several control runs with frog Ringer in place of the test extracts were also carried out to determine changes in responsiveness of isolated test muscle. Time for 50% inhibition/mg (T50) was computed for each fraction. Each fraction was tested on at least 6 frog muscle preparations. Potassium content of aliquots from each fraction was determined spectrophotometrically (Table I).

Results. Table I presents the results obtained.

Comment. The data show slight to moderate inhibition by all the thymoma and skeletal muscle fractions tested. None of the thymoma fractions showed the dramatic blocking activity that might be expected if an active principle had been isolated. Potassium content of all the extracts was in the range compatible with normal neuro-muscular

TABLE I. Activity of Thymoma and Skeletal Muscle Fractions.

Thymoma fraction	T50 min.	Td 50	(K) meq/l*
I	5.8	10.0	2.2
III	8.3	7.2	1.9, 2.6
IV	5.9	4.5	2.1
V	6.1		1.9
VI	7.0		2.5
Skeletal muscle			
I, II, III	6.5	6.9	1.7
IV, V, VI	7.8	7.5	4.9
Frog Ringer	>15		2.0

T50 = time (min.) for 50% inhibition of muscle contractions—undialysed fractions.

Td 50 = dialysed and lyophilized fractions.

* (K) of undialysed fractions.

function. Thus, by this technic no blocking activity was found.

Summary. Fractionated extracts from a thymoma surgically removed from a patient with myasthenia gravis when tested on an isolated sartorius nerve-muscle preparation failed to show significant inhibitory activity of any of the fractions when compared to similarly extracted normal skeletal muscle.

The author expresses gratitude to Dr. Benjamin Castleman for making this work possible and for encouragement and advice. Acknowledgement is due to Miss Dorothy Urbach for technical assistance.

1. McEachern, D., *Med.*, 1943, v22, 1.
2. Schweitzer, A., *J. Exp. Med. and Surg.*, 1947, v5, 264.
3. Constant, G., Porter, E. L., Andronis, A., Rider, J. A., *Texas Rep. Biol. and Med.*, 1949, v7, 350.
4. Constant, G. A., Porter, E. L., Seybold, H. M., Andronis, A., *Am. J. Physiol.*, 1949, v159, 565.
5. Wilson, A., Obrist, A. R., Wilson, H., *Lancet*, 1953, v1, 368.
6. Zacks, S. I., Cohen, R. B., *Proc. Soc. Exp. Biol. and Med.*, 1955, v90, 601.
7. Schmid, K., Rosa, E. C., MacNair, M. B., *J. Biol. Chem.*, 1956, v219, 769.

Received June 26, 1958. P.S.E.B.M., 1958, v99.