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Functional Activity of Smooth Muscle Tumors of the Uterus.*

CHARLES S. BRYAN AND SHIELDS WARREN.

From the Laboratory of Pathology, New England Deaconess Hospital.

The question of the functional activity of the cells composing various types of tumor tissue has always excited much interest. It is a remarkable fact that in some tumors cells which have all the morphological characteristics of normal cells of the parent tissue appear to have lost the characteristic functional ability of their normal relatives. In other cases the tumor cells show normal or enhanced activity. As examples may be cited the functioning and nonfunctioning adenomas of pancreas and thyroid. The ability of small metastatic nodules of chorionepithelioma to produce hormonal effects may be much greater than would be expected from their mass.

Leiomyomas of the uterus contain cells which do not differ morphologically from normal smooth-muscle cells. The following experiments were performed to determine whether or not these cells possess the ability to contract, and whether or not there are qualitative differences between their behavior and that of normal uterine smooth-muscle cells.

Method. Uteri containing leiomyomas were obtained in the operating room as soon as they were excised and were wrapped in gauze moistened with saline. Within a few minutes strips of muscle about 2.5 cm in length and 0.5 cm in diameter were excised from the tumors as well as control strips from the uterine wall and immediately immersed in warm Ringer's solution through which a constant stream of oxygen was bubbled. The vessel containing them was then immersed in a constant temperature water bath kept at 38°C and the strips attached by threads to pointers recording on a kymograph. In each experiment one strip of uterine muscle and one strip of leiomyoma were immersed in the same bath and attached to separate needles recording at different levels on the same graph. The lower ends of the muscle strips were anchored with pins to a wooden septum which could be changed easily from one container to another, thus allowing quick changes of medium with interval washing. The stimulating solutions were added directly to the Ringer's solution. The agents in the amounts added to the 250 cc of

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Ringer's solution were: (1) Pituitrin, ¼ to ½ cc; (2) histamine, 0.5 cc of a 1/1000 solution. These amounts are much larger than the minimum needed to cause contraction and were only roughly measured since the experiments were not of a quantitative nature.

At the conclusion of each experiment the muscle strips were fixed in alcohol-formalin and sectioned and stained after celloidin imbedding. In all cases the strips from leiomyoma showed the typical structure of smooth-muscle cells and connective tissue.

Results. The smooth muscle of the so-called fibroid tumor is capable of contracting in response to some of the same stimuli which cause contraction of smooth muscle of the uterine wall. To our knowledge this point has not been previously investigated. A total of 16 specimens were tested. In 4 cases there was complete absence of response in both uterine and leiomyoma strips. Usually examination of the sections of muscle which had failed to contract showed marked edema, fibrosis, degenerative changes, or predominantly cross-sectioned rather than longitudinally sectioned muscle cells with resultant mechanical disadvantage. In one case the uterine strip alone responded and in another only the tumor strip contracted. In the remaining 10 cases some degree of response was obtained from both types of tissue.

Table I shows that uterine muscle responded more constantly to pituitrin, while muscle from leiomyomas seemed much more sensitive to histamine. Uterine muscle strips often seemed refractory to histamine, sometimes contracting later to pituitrin. Although our results were not constant enough to establish this point definitely, it did appear that the reaction to histamine might represent a difference in behavior of the two types of muscle.

In one case the addition of 5 drops of extract of ergot to the bath failed to evoke contraction in a leiomyoma strip which responded immediately afterward to histamine. In another case ergot elicited no response in either uterine or leiomyoma strip, though both responded later to pituitrin.

Due to the fact that the relative number of muscle cells is smaller in the tumor than in uterine muscle, because of the large amount of connective tissue in the tumor, the extent of contraction of strips of tumor is usually less. This difference is magnified by the difficulty in obtaining strips of parallel fibres of any length from the tumor. However, in a few cases we succeeded in obtaining vigorous contractions.

In general it appeared that tissues from younger women responded to stimuli quicker and more vigorously than those from older

TABLE I.

	Uterine muscle		Leiomyoma	
	Responded	Failed to respond	Responded	Failed to respond
Pituitrin	8	4	7	5
Histamine	3	5	6	2
Ergot		1		2

The responses of the two types of tissue from each specimen are classified as positive or negative. The response was considered positive if any sample from the specimen showed activity even though other samples failed to contract. Since some specimens were tested with more than one stimulating agent, the number of responses does not correspond to the number of uteri examined.

women. This tendency was not by any means absolute, though, since little or no contraction was elicited from some tissues from women of less than 35, while often specimens from women older than 45 responded well to stimulation. No correlation could be made with the menstrual phase as determined by clinical history.

We were surprised to find that often the tissues, both uterus and tumor, retained the ability to contract for 1½ to 2 hours if the specimen was merely kept wrapped in moist gauze. In no case did an excised strip give consistent results for more than an hour. Usually after ½ to ¾ hour in the bath the uterine strips began to show irregular spontaneous contractions with gradually increasing tone and loss of sensitivity to the usual stimulating agents. The strips of leiomyoma usually did not show this increase in tone in the dying phase.

Summary and Conclusions. Tissues from 16 leiomyomas were tested for contractility using normal uterine muscle for control. The stimulating substances used were pituitrin, histamine, and ergot.

In 11 cases the tumor tissue showed definite response. Uterine muscle usually showed increasing tone in the dying phase while the tumor tissue became unresponsive without change in tone.