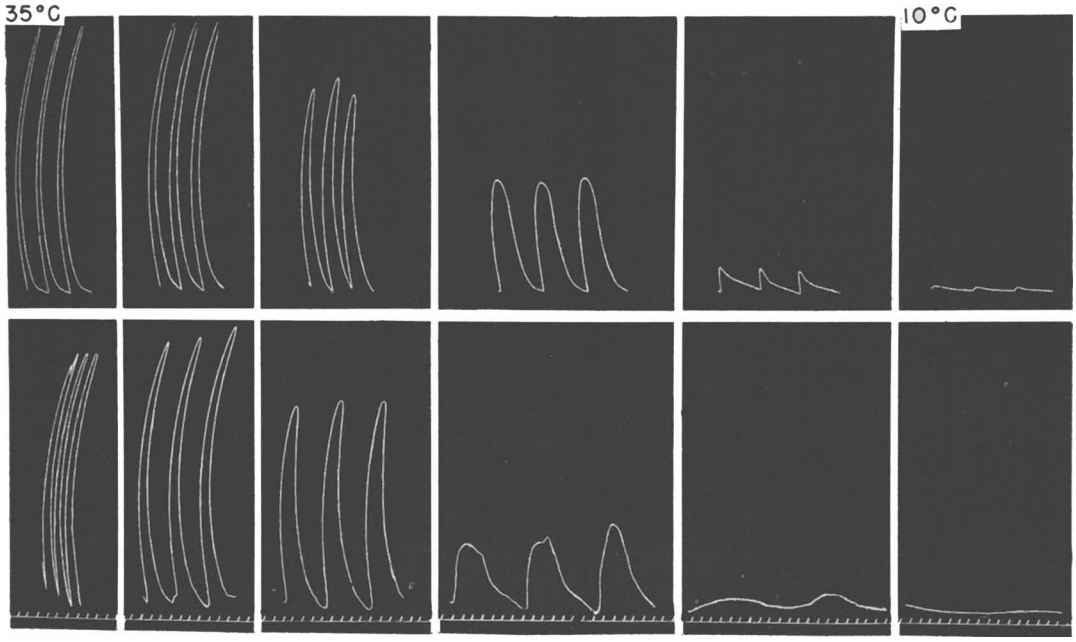

FIG. 3. Comparison of spontaneous with electrically-stimulated contractions. Rabbit 28 days pregnant. Temperature changes, by 5° steps, indicated by vertical white spaces. Time intervals, 1 min.

Summary. In agreement with the observations of others on skeletal muscle, strips of uterine muscle from rabbits in estrus undergo changes in the extent of shortening in relation to temperature. The speed of contraction and relaxation also varies with temperature. These effects occur equally whether the contractions are spontaneous or electrically simulated.

Received September 6, 1951. P.S.E.B.M., 1951, v78.

Invasiveness of Fibrosarcomata in Mice.* (19042)

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It has been shown that the characteristic of invasiveness of chemically induced fibrosarcomas (the presence of discrete nodules in the abdomen derived either by direct extension of the tumor or by the process of metastasis) is partially determined by some new principle found in the host which had been derived from its ancestry and differentially determined by litter seriation(1). These conclusions were based upon observations on 788 mice of 2 descents (Prunt and 2Prunt), which were genetically related to each other (17 generations of inbreeding in common).

In the first analysis of an association between invasiveness of fibrosarcomas and litter

* This experiment has been made possible by grants from The Anna Fuller Fund, The Jane Coffin Childs Memorial Fund for Medical Research, and The James Hudson Brown Memorial Fund of Yale University School of Medicine. The statistical analysis of the data has been done by Dr. H. Auerbach of Yale University, School of Public Health.

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TABLE I. Summary of Development of Invasive Tumors in Mice Showing Stock, Litter, Total No. of Mice Showing Invasive Tumors (I); Total No. of Fibrosarcomas (T); and % of Mice Which Developed Invasive Tumors (%). Data of 1-7, 8-15 and 1-15 Are Also Combined.

Litter	Prunt			2 prunt			Total		
	T	I	%	T	I	%	T	I	%
1	80	8	10	86	8	9.3	166	16	9.6
2	114	9	7.9	105	11	10.5	219	20	9.1
3	130	9	6.9	171	11	6.4	301	20	6.6
4	146	11	7.5	172	16	9.3	318	27	8.5
5	125	3	2.4	157	14	8.9	282	17	6
6	69	7	10.1	113	7	6.2	182	14	7.7
7	43	1	2.3	99	7	7.1	142	8	5.6
8	17	0		56	3	5.4	73	3	4.1
9	9	0		29	1	3.4	38	1	2.6
10	10	0		7	0		17	0	0
11	5	0		4	0		9	0	0
12	1	0		2	0		3	0	0
13				6	0		6	0	0
14				4	0		4	0	0
15				2	0		2	0	0
1– 7	707	48	6.79	903	74	8.19	1610	122	7.6
8–15	42	0		110	4	3.63	152	4	2.6
1–15	749	48	6.41	1013	78	7.70	1762	126	7.15

seriation (mother's age ?), the data on some of the litters were small and it became necessary to add successive litters 1 + 2, 3 + 4, 5 + 6, 7 + 8, 9 + 10 and 11 + 12, together in order to show smoother trends. There were also slight differences between the sexes and between the 2 descents, which, however, were not statistically significant.

In the present analysis dealing with the same phenomenon, 974 new data were added. The combined data on 1,762 mice are given in Table I, according to litter of origin.

The origin and genetic relationship of the Prunt and 2Prunt descents have already been described(1). All mice were injected with 1 mg of methylcholanthrene dissolved in 0.1 cc of sesame oil at 60 days of age and continued as breeders. The young, however, were discarded shortly after birth. The mice were examined weekly for tumors beginning 2 months following the injection of the carcinogen. The latent period was determined by the appearance of a solid firmly attached progressively growing nodule at the site of the injection. The mice were continued until death at which time the tumor was measured in three dimensions, a complete autopsy performed and all pathological tissues saved for histological examination. Only mice bearing fibrosarcomas are included in this analysis, which is based upon the local growing tumor at the site of the injection of the carcinogen with or without the presence of secondary nodules of similar histological appearance in the abdomen.

The percentage of mice developing fibrosarcomas which have the capacity of invading into the abdomen continue to show the same down-trend with successive litters as was found in the original series. There is no significant difference between the 2 descents. There were 6.41% invasive tumors in the Prunt descent compared to 7.70% for mice of the 2Prunt descent. The percentage of invasive tumors for mice of the sixth litter of

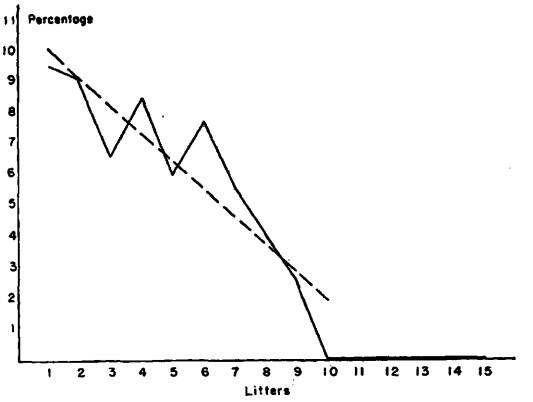

FIG. 1. % of mice showing invasive fibrosarcomas following subcutaneous injection of methylcholanthrene. Actual data are plotted on solid line; fitted straight line (dash) has a slope value of 5.5.

the Prunt descent seems to be out of trend. Nevertheless it seems permissible to combine the 2 series. The data of Table I are plotted in Fig. 1 and the slope of the combined data is also given (slope 5.5). This slope has a statistically significant difference from slope of "O".

Data for litters 1-7 were combined and compared to similar data for mice of the 8-15th litters. This comparison shows a "t" value of 2.3 which is statistically significant at the 5% level.

The new data thus permit a verification of the correlation reached in the earlier series. There appears to be a gradual loss of ability of a mouse to develop an invasive fibrosarcoma in the successive litters born to the same parents, when subjected to 1 mg of methylcholanthrene dissolved in 0.1 cc of sesame oil at 60 days of age. There is a complete loss of this ability in mice of the 8th and later litters of the Prunt descent, and in mice of the 10th and later litters of the 2Prunt stock. The present phenomenon of changes in invasiveness may also be interpreted by mice of successive litters acquiring an increased resistance to chemically induced fibrosarcomas.

Received September 10, 1951. P.S.E.B.M., 1951, v78.

Action of Coumingine on Heart Muscle.* (19043)

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It is often stated that the erythrophleum alkaloids are the only alkaloids that have a digitalis-like action. Chemically these alkaloids have the cyclopentenophenanthrene ring system common to the digitalis glycosides, but do not contain the unsaturated lactone group said to be responsible for digitalis action. However, the usually accepted criteria of digitalis action, slowing of the heart, systolic arrest and emesis following parenteral administration, cannot be considered adequate, none being specific. Straub(1) long ago emphasized that "so-called systolic standstill" was not a specific digitalis action. More recently Pisanty(2) has studied the systolic arrest and skeletal muscle shortening caused by a variety of substances and the enzyme mechanisms involved. Observations to date(3,4) have indicated that the constant, and perhaps specific, measurable action of digitalis glycosides in experimental preparations and in therapeutic usage in man is to shorten the refractory period, or systole, of heart muscle without impairment of contractility. In their study of the erythrophleum alkaloids, Maling and Krayer(5) found the outstanding action was to decrease diastolic volume. Coumingine had a positive inotropic effect in lower concentrations, but a greater tendency to cause irregularity of rhythm than the other alkaloids of the group. They concluded that as yet there was no evidence to justify the assumption that in congestive heart failure the action of erythrophleum alkaloids was truly digitalis-like.

The present paper reports observations on the effect of coumingine on the primary properties of heart muscle of the turtle *Pseudemys*

* This work was done under a grant from the Division of Research Grants and Fellowships of the National Institutes of Health (National Heart Institute), U. S. Public Health Service. Coumingine was generously supplied by Prof. P. Plattner, Eidg. Technische Hochschule, Zurich.

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