

TABLE I.
Effect of Trypsin on the Virus of Trachoma.

Exp. No.	No. of tissues pooled	Technic of digestion	Monkeys infected with tissues	
			Undigested	Digested
1	4	3 hr at 37°C	0 of 3	0 of 3
2	2	2 " " 37°C	3 " 3	0 " 3
3	4	30 min at 37° and 60 " " 25°	2 " 4	0 " 3
4	2	30 " " 37°	3 " 3	0 " 3

Table I describes the variations of the different experiments and illustrates the results obtained. It will be seen that 3 of 4 experiments recorded were successful. Two others were done but not recorded, since the original material was not infectious for monkeys. In the first experiment, complete digestion was allowed to take place, and this required 3 hours, an interval, however, which caused inactivation of the virus in the control material. In the remaining experiments, the period of incubation was gradually reduced to 30 minutes, which was not sufficient for complete digestion of the different cells. In each instance, however, *viz.*, digestion for 2 hours at 37°C, 30 minutes at 37°C, then 60 minutes at 25°C, and 30 minutes at 37°C, the virus was rendered non-infectious for monkeys. While the manner of conducting the experiments was necessarily limited because of the nature of the virus, it is nevertheless evident that measured by the inability to infect monkeys tryptic digestion causes inactivation of the virus of trachoma.

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Distribution of Metastases in the Brown-Pearce Tumor. I. In Standard Breeds of Rabbits.*

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During studies on the transplantation of the Brown-Pearce tumor into the testicle of the rabbit, certain variations were noted between standard breeds of rabbits.¹ These variations included (a) the incidence and volume of the primary tumors, (b) the incidence,

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¹ Casey, *Am. J. Cancer*, 1937, **31**, 446.

TABLE I.
Regional Distribution of Metastases Among 202 Rabbits from Standard Breeds Injected Intratesticularly with the Brown-Pearce Tumor.

	E	SA	F	AB	R	D	B	NZ	BV	HI	HA	BT	P	A	C	FS	L	G	SM	Total
	Number of Animals.																			
Injected	17	10	6	8	12	10	13	13	8	17	20	2	9	5	33	14	1	2	2	202
Negative	2	1	0	0	0	0	1	0	2	10	13	0	1	0	11	1	0	1	2	45
Primary tumor	15	9	6	8	12	8	11	13	6	7	6	2	8	5	19	12	1	1	0	149
No metastatic foci	0	0	0	0	1	2	1	0	2	3	4	0	3	0	1	3	0	0	0	20
Metastatic foci	15	9	6	8	11	8	11	13	4	4	3	2	5	5	21	10	1	1	0	137
Site	Number of Metastatic Foci.																			
Extension to tunica	10	3	2	4	5	3	3	5	1	1	0	2	3	3	5	2	1	0	0	53
Spermatic cord	11	7	4	6	8	4	8	9	2	1	1	1	3	2	15	6	1	0	0	89
Uninoculated testicle	2	0	1	1	0	0	1	2	0	0	0	0	0	0	1	0	0	0	0	8
Opposite cord and tunica	11	2	0	3	3	1	2	2	0	1	0	1	0	2	4	2	0	0	0	34
Pelvis and bladder	12	5	6	8	9	3	5	7	2	1	1	1	1	0	3	5	3	1	0	72
Para-aortic tissues	14	7	6	8	9	4	3	9	2	2	1	1	1	1	4	13	7	1	0	92
Left peri-renal area	11	5	5	7	4	2	2	3	2	1	0	0	2	2	4	3	1	0	0	54
Right " "	12	6	3	5	6	3	4	4	2	1	0	0	1	3	6	4	0	0	0	105
Left kidney	15	8	6	8	9	7	9	8	3	1	1	1	4	4	14	6	0	1	0	100
Right " "	15	7	6	7	8	7	8	9	3	2	0	1	3	3	15	6	0	0	0	47
Left suprarenal	8	2	6	3	4	1	4	6	1	0	0	0	1	2	6	3	0	0	0	60
Right " "	10	2	3	3	5	3	3	8	1	0	0	0	1	1	3	1	0	0	0	44
Parietal peritoneum	6	2	2	1	4	2	3	3	1	1	0	0	0	0	7	3	0	1	0	36
Serosa and mesentery	13	5	3	7	8	2	6	7	0	1	0	0	1	3	7	2	0	0	0	65
Omentum	12	6	4	4	7	1	6	4	1	1	0	0	2	2	9	3	0	0	0	62
Intestine	8	1	1	3	2	1	3	1	0	1	0	0	0	0	2	2	0	0	0	25
Stomach	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	3
Liver	11	4	4	5	1	3	1	6	1	0	0	2	3	2	4	1	1	0	0	49
Pancreas	1	0	2	1	2	0	0	1	0	0	0	0	0	0	2	1	0	0	0	10
Diaphragm	9	3	3	4	4	1	3	3	0	1	0	1	0	2	5	3	1	0	0	43
Spleen	3	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
Posterior mediastinum	9	2	3	5	5	0	1	1	1	0	0	2	0	1	5	3	0	0	0	37
Superior " "	13	3	3	7	5	3	1	5	2	0	0	1	1	1	11	6	1	0	0	63
Pleura, Lungs	13	6	2	7	4	5	3	6	2	1	1	1	3	2	3	7	1	0	0	67
Pericardium	4	1	3	4	0	1	1	0	3	1	0	0	0	0	1	0	0	0	0	18
Heart	4	1	2	5	0	1	1	2	1	0	0	0	0	1	0	1	0	0	0	19

Neck, anteriorly	5	2	2	2	5	2	1	2	6	1	0	0	1	0	1	0	1	3	1	0	0	0	32
Thyroid	3	2	1	1	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	9	
Parathyroids	2	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0	0	7	
Muscles of tongue	3	3	2	0	0	0	1	2	0	0	1	0	0	0	0	1	0	0	0	0	0	13	
Muscles, mastication	6	6	1	1	3	0	2	3	0	0	0	0	0	0	0	0	0	1	0	0	0	23	
Mandible	6	7	2	5	5	1	6	6	1	0	1	0	1	0	1	2	6	1	0	0	0	50	
Gums	8	6	2	5	6	1	6	8	2	1	1	1	1	0	1	0	2	5	3	0	0	57	
Eyes	5	3	4	7	3	0	2	6	1	0	0	0	0	0	0	0	0	2	0	1	0	34	
Pericranium	0	0	2	2	0	1	0	1	1	0	0	1	0	0	1	0	0	0	0	0	0	8	
Meninges	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	
Brain	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
Hypophysis	5	3	0	2	2	4	1	2	1	1	0	0	1	0	0	1	2	1	1	0	0	23	
Nose and sinuses	7	4	5	5	4	1	2	1	1	0	0	1	0	0	1	0	3	3	1	0	0	38	
Neck, posteriorly	5	4	2	3	4	2	1	4	1	0	0	0	1	0	0	1	1	0	1	0	0	28	
Interscapular space	5	4	4	2	3	1	1	5	0	0	0	0	0	1	1	1	1	1	2	0	0	30	
Muscles of scapulae	5	3	4	3	3	0	0	3	1	0	0	1	1	0	1	0	4	0	1	0	0	29	
Muscles, torso	5	5	2	4	5	0	3	4	3	0	0	1	2	0	1	0	3	2	0	0	0	39	
Hypoderma, torso	4	5	5	3	2	2	2	4	1	0	0	1	0	0	2	0	2	0	1	0	0	34	
Skin, torso	4	1	1	4	1	0	3	5	0	0	0	2	0	0	1	0	1	0	0	0	0	22	
Muscles, thigh	2	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0	0	7	
Metaphysis, femora	6	4	2	4	0	0	0	1	1	0	0	0	1	0	0	3	1	0	0	0	0	23	
Metaphysis, tibiae	8	5	3	3	3	0	1	0	0	0	1	0	1	0	0	2	1	1	1	0	0	25	
Spinal canal	3	4	2	1	2	6	0	0	0	0	0	1	1	0	1	0	4	2	0	0	0	25	
Totals	335	160	125	182	158	75	116	177	44	18	8	22	41	58	194	91	13	2	0	1819			

volume, and number of the metastases, and (c) the longevity and mortality of the animals after inoculation. All the animals were males, all received the same dosage into the testicle, all were in apparent good health, there was no significant variation in age between the breeds, and the diet and housing were uniform. The variations, moreover, were consistent and were most significant among breed samples inoculated at the same time. It was not possible, therefore, to explain the variations on the basis of sex, site of inoculation, physical condition, age, diet and housing, or season.

The results, extending from a susceptibility of about 15% to a susceptibility of about 95%, seemed to be due to the inherent constitution of the pure breed strains used. The present paper reports efforts to determine whether the differences between the breeds were influenced by a selective liability of certain organs and tissues to metastatic involvement. For this purpose the protocols on 202 animals from 19 standard breeds were employed.

In each of the animals a detailed search for tumor foci was made in each of the 50 sites listed in Table I. A site containing one or more tumor nodules was designated as a single tumor focus. Forty-five animals were devoid of neoplastic growth at necropsy, 20 had primary tumors only, and 137 had metastases in one or more of the sites listed. Among the 137 animals with metastases there were 1,819 tumor foci, which amounts to approximately 20,000 tumor nodules. That an unusual and selective regional distribution of metastases had occurred was obvious from the frequency with which the kidneys, the distant lymph nodes, the jaw, the serosal surfaces, the muscles, and the skin were affected (Table I). The involvement of the regional lymph nodes, the lungs, the liver, and the suprarenal glands is common to many neoplasms, as is the infrequent involvement of the brain, the thyroid gland, the uninoculated testicle, and the spleen.

In order to ascertain whether the varying reactions of the standard breeds could be explained on the basis of selective metastasis, a statistical analysis was undertaken; the study was limited to the more commonly involved sites and to those breeds which were represented by 10 or more animals (Table II). In the tabulation are listed not only the actual number of metastatic foci encountered, but also the number which might have been expected had the distribution been due entirely to chance. It will be noted that for each breed the actual number of foci in any given location agreed fairly well with the expected values. Apparent exceptions occurred, such as the frequency of metastatic foci in the bones and skeletal muscles of

TABLE II.
Number of Metastatic Foci in Commonly Involved Sites Among Certain Breeds of Rabbits Injected Intratesticularly with the Brown-Pearce Tumor.

	E	S	R	D	B	NZ	HI	HA	C	FS	Totals
	Actual Values.										
Regional lymph nodes	26	12	18	7	8	16	3	2	18	10	120
Extension	21	10	13	7	11	14	2	1	20	8	107
Distant lymph nodes	39	20	21	9	8	25	0	0	22	13	157
Kidneys	30	15	17	14	17	17	3	1	29	12	155
Adrenals	18	4	9	4	7	14	0	0	9	4	69
Lungs and pleura	13	6	4	5	3	6	1	1	3	7	49
Liver	11	4	1	3	1	6	0	0	4	1	31
Heart	4	1	0	1	1	2	0	0	0	1	10
Skeletal muscles	21	17	11	0	6	13	0	1	11	2	82
Bones	20	16	5	1	7	7	0	1	11	3	71
Skin	4	1	1	0	3	5	0	0	1	0	15
Totals	207	106	100	51	72	125	9	7	128	61	866
	Expected Values.										
Regional lymph nodes	28.7	14.7	13.9	7.1	10.0	17.3	1.2	1.0	17.7	8.5	120
Extension	25.6	13.1	12.4	6.3	8.9	15.4	1.1	0.9	15.8	7.5	107
Distant lymph nodes	37.5	19.2	18.1	9.2	13.1	22.7	1.6	1.3	23.2	11.0	157
Kidneys	37.0	19.0	17.9	9.1	12.9	22.4	1.6	1.3	23.9	10.9	155
Adrenals	16.5	8.4	8.0	4.1	5.9	10.0	0.7	0.6	10.2	4.9	69
Lungs and pleura	11.7	6.0	5.7	2.9	4.1	7.1	0.5	0.4	7.2	3.5	49
Liver	7.4	3.8	3.6	1.8	2.6	4.5	0.3	0.3	4.6	2.2	31
Heart	2.4	1.2	1.2	0.6	0.8	1.4	0.1	0.1	1.5	0.7	10
Skeletal muscles	19.6	10.0	9.5	4.8	6.8	11.8	0.9	0.7	12.1	5.8	82
Bones	17.0	8.7	8.2	4.2	5.9	10.2	0.7	0.6	10.5	5.0	71
Skin	3.6	1.8	1.7	0.9	1.2	2.2	0.2	0.1	2.2	1.1	15
Totals	207	106	100	51	72	125	9	7	128	61	866
Chi-square	6.2	15.8	7.3	12.8	6.0	9.0	9.7	4.3	7.7	9.6	88.28

Sable rabbits, and the scarcity with which the same sites were affected in animals of the Dutch breed.

In order to test the significance of the observed departures from the expected distribution, the chi-square test was employed.² The observed values were found to be so nearly like the expected values that departures as great as or greater than those observed could occur due to purely random sampling (Chi-square = 88.28, $n = 100$, $P = 0.6$, not significant†). The totals for each breed and each organ by this test likewise revealed no significant departures.

After transplantation into the testicle of 202 rabbits from 19 standard breeds, the Brown-Pearce tumor exhibited a selective and unusual distribution of metastases which affected each breed equally. The differences between various standard breeds of rabbits as to the incidence and number of the primary and metastatic tumor foci were apparently not influenced by a selective liability of certain organs and tissues to the growth of this neoplasm.

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Distribution of Metastases in the Brown-Pearce Tumor. II. Effect of Fifteen Years of Transplantation.*

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This analysis is concerned with the possible effect on the distribution of metastases of successive transplants of the Brown-Pearce tumor at monthly intervals for more than 15 years into a variety of rabbits. The data are derived from 2 series of rabbits. The first series of 191 young adult male rabbits of common mongrel type was reported by Pearce and Brown in 1923, shortly after discovery

² Fisher, *Statistical Methods for Research Workers*, 4th ed., Oliver & Boyd, London, 1932.

† The value of P , which is 0.6, is not to be interpreted as a statistically accurate figure, as the number of items in some of the categories is too small. While not all of the categories have the recommended number of items, the value of P indicates so clearly a difference which is not significant, that this departure from the recommended minimum probably does not vitiate the conclusions.

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