

**Distribution of Metastases in the Brown-Pearce Tumor.
V. Comparison with Certain Tumors in Man.***

BJARNE PEARSON AND ALBERT E. CASEY.

*From the Department of Pathology and Bacteriology, School of Medicine,
Louisiana State University, New Orleans.*

The relative distribution of metastases from the Brown-Pearce tumor has been shown to be constant (a) for standard breeds of rabbits,¹ (b) over many years of transplantation,² and (c) for 2 sites of inoculation.³

The distribution of metastatic foci in 4 human tumors was compared with the distribution from the Brown-Pearce tumor in rabbits. The human tumors compared were primary in the cervix, breast, prostate, and rectum. The sites of metastasis chosen for comparison were the liver, lungs, kidneys, and spleen, these being sites in which fairly accurate necropsy data are usually available.

The data for the Brown-Pearce tumor were derived from a total of 393 rabbits.² The human data were derived from a total of 1,214 cases and were compiled from various sources. The data for carcinoma of the cervix were derived from a total of 832 necropsy reports by Albers-Schonberg,⁴ McCormac,⁵ Wertheimer,⁶ and Pearson.⁷ The data for carcinoma of the breast were derived from 74 necropsy reports by Williams⁸ and Mielecke.⁹ The data for carcinoma of the prostate were derived from 138 necropsy reports by Graves and Miltzer¹⁰ and Mintz and Smith.¹¹ The data for carcinoma of the rectum were derived from 170 necropsy reports by Brown and Warren.¹²

*This work was aided by a grant from the International Cancer Research Foundation.

¹ Casey, *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 223.

² Casey, *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 223.

³ Casey and Pearson, *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 234.

⁴ Albers-Schonberg, *Jahrb. a. Hamb. Staatskrankenanst.*, 1893-4.

⁵ McCormac, *Arch. Middlesex Hosp.*, 1909, **15**, 20.

⁶ Wertheimer, *Strahlentherapie*, 1921, **12**, 90.

⁷ Pearson, *Am. J. Cancer*, 1936, **28**, 31.

⁸ Williams, quoted by Deaver and McFarland, *The Breast, Anomalies, Diseases, and Treatment*, P. Blakiston's Sons and Co., 1917.

⁹ von Mielecke, *Ztschr. f. Krebsforsch.*, 1913, **13**, 505.

¹⁰ Graves and Miltzer, *J. Urol.*, 1935, **33**, 235.

¹¹ Mintz and Smith, *New England J. Med.*, 1934, **211**, 478.

¹² Brown and Warren, *Surg. Gynec. and Obst.*, 1938, **66**, 611.

The material available was analyzed by means of the chi-square test to determine the homogeneity of cases of carcinoma of the cervix uteri (Table I), carcinoma of the breast (Table II), and carcinoma of the prostate (Table III). The test revealed no significant difference in the relative distributions of metastasis to the liver, lungs, kidneys, and spleen in any of the 3 series. The expected values in each table are enclosed in parenthesis. The third set of values represents χ^2/m or the (difference)²/expected values.

TABLE I.
Actual and Expected Instances of Metastasis to Liver, Lungs, Kidney, and Spleen from Carcinoma of the Cervix.

Author	Values	Liver	Lungs	Kidneys	Spleen	Totals
Albers-Schonberg	actual	77	23	10	7	117
	expected	(70.68)	(27.22)	(8.69)	(10.4)	(117)
	χ^2/m	0.57	0.56	0.20	1.11	2.53
McCormac	actual	14	5	3	7	29
	expected	(17.51)	(3.26)	(2.15)	(4.16)	(29)
	χ^2/m	0.70	0.93	0.33	1.93	3.89
Wertheimer	actual	20	14	1	2	37
	expected	(22.34)	(8.60)	(2.74)	(3.29)	(37)
	χ^2/m	0.24	3.39	1.10	0.50	5.23
Pearson	actual	11	5	1	2	19
	expected	(11.47)	(4.42)	(1.41)	(1.69)	(19)
	χ^2/m	0.02	0.03	0.11	0.06	.22
Totals	actual	122	47	15	18	202
	expected	(122)	(47)	(15)	(18)	(202)
	χ^2/m	1.53	5.00	1.74	3.60	11.87

($n = 12$, $P = 0.5$ not significant.) †

TABLE II.
Actual and Expected Instances of Metastasis from Carcinoma of the Breast.

Author	Values	Liver	Lungs	Kidneys	Spleen	Totals
Williams	actual	20	8	2	1	31
	expected	(17.33)	(9.98)	(2.10)	(1.57)	(31)
	χ^2/m	0.41	0.39	0.00	0.20	1.00
Mielecke	actual	13	11	2	2	28
	expected	(15.66)	(9.01)	(1.89)	(1.42)	(28)
	χ^2/m	0.45	0.44	0.00	0.24	1.13
Totals	actual	33	19	4	3	59
	expected	(33)	(19)	(4)	(3)	(59)
	χ^2/m	.86	.83	0.00	.44	2.13

($n = 3$, $P = 0.5$ not significant.) †

† While not all 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.

TABLE III.
Actual and Expected Instances of Metastasis from Carcinoma of the Prostate.

Author	Values	Liver	Lungs	Kidneys	Spleen	Totals
Mintz and Smith	actual	20	24	3	0	47
	expected	(19.20)	(25.15)	(2.64)	(0.00)	(47)
	χ^2/m	0.03	0.05	0.05	0.00	.13
Graves and Militzer	actual	9	14	1	0	24
	expected	(9.80)	(12.84)	(1.35)	(0.00)	(24)
	χ^2/m	0.06	0.10	0.09	0.00	.25
Totals	actual	29	38	4	0	71
	expected	(29)	(38)	(4)	(0.00)	(71)
	χ^2/m	.09	.15	.14	0.00	.38

($n = 2$, $P = 0.85$ not significant.)†

TABLE IV.
Actual and Expected Instances of Metastasis from Various Tumors.

Tumor	Values	Liver	Lungs	Kidneys	Spleen	Totals
Brown-Pearce	actual	79	109	168	8	364
	expected	(145.78)	(114.35)	(88.84)	(15.03)	(364)
	χ^2/m	30.59	0.25	70.53	3.29	104.66
Carcinoma cervix	actual	122	47	15	18	202
	expected	(80.90)	(63.45)	(49.29)	(8.34)	(202)
	χ^2/m	20.88	4.26	23.85	7.03	56.02
Carcinoma breast	actual	33	19	4	3	59
	expected	(23.63)	(18.53)	(13.95)	(2.44)	(59)
	χ^2/m	3.71	0.01	7.10	0.13	10.95
Carcinoma rectum	actual	57	38	4	4	103
	expected	(41.25)	(32.35)	(25.14)	(4.25)	(103)
	χ^2/m	6.01	0.99	17.87	0.01	24.88
Carcinoma prostate	actual	29	38	4	0	71
	expected	(28.43)	(22.30)	(17.35)	(2.93)	(71)
	χ^2/m	0.01	11.05	10.27	2.93	24.26
Totals	actual	320	251	195	33	799
	expected	(320)	(251)	(195)	(33)	(799)
	χ^2/m	61.20	16.56	129.62	13.39	220.77

The variation in the relative distribution of metastatic foci for the organs and tumors studied is presented in Table IV. The analysis is carried out in the manner of the preceding tables. The values for the actual and expected number of metastatic foci and for χ^2/m are presented. Chi-square for the entire series was equal to 220.77, a total which indicates more variation than should occur by chance ($n = 12$, $P = 0.00001-$). The variations were also significant for each tumor and each organ studied.

The significant variation between the 5 tumors as to the relative distribution of metastasis to the liver, lungs, kidneys and spleen con-

sisted of (a) an unusually high and significant incidence of metastasis to the kidneys in animals affected with the Brown-Pearce tumor and a relatively low incidence of metastasis to the kidneys in all 4 human tumors studied; (b) an unusually low incidence of metastasis to the liver in the Brown-Pearce tumor of the rabbit and a relatively high incidence of metastasis to the liver in carcinoma of the cervix and of the rectum; (c) an unusually high incidence of metastasis to the lung in carcinoma of the prostate and a probable significantly low incidence of metastasis to the lung in carcinoma of the cervix; (d) a relatively high incidence of metastasis to the spleen in carcinoma of the cervix. The seemingly low incidence of metastasis to the spleen from the Brown-Pearce tumor and from carcinoma of the prostate is only suggestive.

Summary. It is demonstrated by an appropriate statistical method that the relative distribution of distant metastases from the Brown-Pearce tumor in the rabbit is unique, and that the relative distributions of distant metastases from certain tumors of man are both constant and characteristic.

10368

A Pigmented Adenoma of the Intermediate Lobe in a Rat Chronically Treated with Oestrin.

C. S. McEuen,* H. SELYE AND J. B. COLLIP.

From the Department of Biochemistry, McGill University, Montreal.

Chromophobe adenomata of the anterior lobe have repeatedly been observed in rats^{1, 2} and mice^{3, 4, 5} following chronic treatment with oestrogenic preparations. In one of our cases we also noted a small adenoma of the intermediate lobe. We did not feel justified in concluding that this tumor was produced by the oestrin treatment because it occurred only in one case. Yet the fact that tumors in the anterior lobe and the mammary gland, and metaplasia of the uterine epithelium were seen in several animals of this series made

* Finney-Howell Research Foundation Fellow.

¹ McEuen, C. S., Selye, H., and Collip, J. B., *Lancet*, 1936, 775.

² Zondek, Bernhard, *Lancet*, 1936, 776.

³ Cramer, W., and Horning, E. S., *Lancet*, 1936, 247.

⁴ Cramer, W., and Horning, E. S., *Lancet*, 1936, 1056.

⁵ Lacassagne, A., and Nyka, W., *C. r. Soc. Biol.*, 1937, **126**, 1112.