

METASTASES IN CARCINOMA

Analysis of 1000 Autopsied Cases

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ONE of the most striking and disheartening qualities of cancer is the relentlessness of its spread throughout the organism. At the Montefiore Hospital for Chronic Diseases, the observation was made that widespread metastases were present in a higher percentage of the cases that reached the autopsy table than the literature would lead one to believe. Such organs as spleen, ureter, heart—usually considered rare sites of secondary carcinoma—appeared to have been involved not uncommonly. Because there have been few recent comprehensive studies of the metastases of carcinoma, it was thought that a study of the metastases of one-thousand consecutive autopsied cases of carcinoma would be of value.

METHODS

One-thousand consecutive cases of malignant neoplasms of epithelial origin were analyzed for the incidence of metastases. These cases were examined in the postmortem state at Montefiore Hospital between 1943 and 1947. Malignant neoplasms of non-epithelial origin were not included because of the controversy about the unicentric or multicentric origin of such tumors as lymphoma and because of the frequent uncertainty as to the primary site. Direct extension of carcinoma to adjacent organs was excluded as carefully as possible. Metastases to the capsules of organs, such as liver and spleen, were not considered organ metastases, but rather peritoneal metastases. The material was then collected in tabular form to indicate the percentage of involvement of organs by the entire group of neoplasms and the fre-

quency of metastatic involvement by individual neoplasms.

COMPOSITION OF THE SERIES

In Fig. 1, there is a graphic listing by site of origin of the neoplasms comprising 1 per cent or more of our series. These account for about 95 per cent of our cases. In addition, there were eight carcinomas arising from the bile ducts, seven from the tongue, six from the maxillary sinus, and five from the skin; there were three each from the buccal mucosa and the nasopharynx; two each from the laryngopharynx, fallopian tubes, external auditory canal, tonsil, palate, and adrenal; and one each arising from the vagina, gum, epiglottis, nasal mucosa, vulva, and ampulla of Vater.

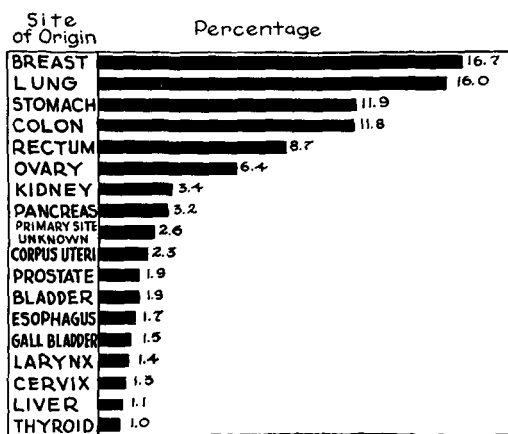


FIG. 1. Distribution by site of origin of 1000 consecutive autopsied cases of carcinoma.

These figures should not be construed as a statement of the relative frequency of occurrence of these carcinomas in the general population, since they are drawn from autopsy material. Thus, carcinoma of the skin, a common neoplasm,³² is not represented in

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our group, since it is so rarely a cause of death. It is of interest, however, that ten of the twelve most common carcinomas in this group are among the twelve most frequently found in the population.^{22, 32} These are carcinoma of the breast, stomach, colon, rectum, ovary, pancreas, uterus, lung, prostate, and bladder. Cervical carcinoma was found infrequently in our series.

INCIDENCE OF METASTATIC INVOLVEMENT

Table 1 represents the frequency of involvement of each organ in 1000 cases of carcinoma. Thus, the abdominal nodes, liver, and lungs are involved in about one half of all cases, and the mediastinal nodes in about two fifths. The pleura is involved with surprising frequency, as are the adrenals and bone. Forty-three cerebral metastases were listed, representing an incidence of about 17.6 per cent of 244 carcinomas in which the brain was examined. (There were thirty-three brain metastases involving only the brain substance; fourteen involving only the dura; and ten involving both brain substance and dura.) The pituitary was involved in eighteen cases; in fifteen, the metastases were from the breast. There were nineteen metastases to the thyroid. Ovarian involvement in 111 cases was in accord with other findings of a relatively high incidence of metastases to ovary.⁴⁹ The large number of pericardial metastases was probably related to the high incidence of breast and lung carcinoma in our series.⁴¹

Carcinoma of the Breast. The tendency for widespread metastasis from carcinoma of the breast is well known. Among 167 cases in this series, none was free of metastasis, and multiple organ involvement was common (Table 2). This was true to such an extent that five organs were involved in more than 60 per cent of the cases. In general, our figures corresponded to those of other investigators,^{16, 23, 27, 44, 48} though there were exceptions.⁴⁰ Thus, metastases to lung were found in 77 per cent of our cases, as compared to other figures of 50 per cent, 58 per cent, 67

TABLE 1
INCIDENCE OF METASTATIC INVOLVEMENT IN 1000 CONSECUTIVELY AUTOPSIED CASES OF CARCINOMA

<i>Site, metastasis</i>	<i>Freq. involv.</i>	<i>% Involv.</i>
Abdom. nodes	495	49.5
Liver	494	49.4
Lungs	465	46.5
Mediast. nodes	421	42.1
Pleura	277	27.7
Bone	272	27.2
Adrenal	270	27.0
Peritoneum	269	26.9
Gastroint. tract*	204	20.4
Diaphragm	183	18.3
Pericardium	131	13.1
Kidney	126	12.6
Pancreas	116	11.6
Ovary	111	11.1
Spleen	90	9.0
Cervical nodes	89	8.9
Axillary nodes	63	6.3
Uterus	59	5.9
Gallbladder	58	5.8
Breast	50	5.0
Skin	44	4.4
Ureter	43	4.3
Heart	38	3.8
Bladder	36	3.6
Esophagus	31	3.1
Inguinal nodes	20	2.0
Thyroid	19	1.9
Fallopian tubes	19	1.9
Pituitary	18	1.8
Common bile duct	12	1.2
Vagina	11	1.1
Prostate	7	0.7
Trachea	6	0.6
Pineal gland	4	0.4
Cervix	3	0.3
Testes	3	0.3
Epiglottis	2	0.2
Parotid gland	2	0.2
Pharynx	1	0.1
Tongue	1	0.1
Salivary glands	1	0.1
Brain † (cerebral)	43	17.6
(dural)	24	9.8
Spinal cord ‡ (dural)	4	7.7

* The majority of these were serosal.

† These figures are based on 244 examinations of the brain.

‡ These figures are based on 52 examinations of the spinal cord.

per cent, and 89 per cent (Table 3). Metastases to bone and adrenals were somewhat more common in our series. Warren and Witham⁴⁸ found bone metastases in 42.6 per cent and adrenal metastases in 30.9 per cent of 162 cases compared to our figures of 73.1 per cent and 53.9 per cent respectively. In Table 3, there is a comparison of our series

TABLE 2
METASTASES OF 167 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE BREAST

Site, metastasis	No. with metastases	%
1. Lung	129	77.2
2. Bone	122	73.1
3. Mediast. nodes	111	66.5
4. Pleura	108	64.7
5. Liver	102	61.1
6. Adrenal	90	53.9
7. Abdom. nodes	74	44.3
8. Pericardium	59	35.3
9. Axillary nodes*	55	32.9
10. Peritoneum	41	24.6
11. Diaphragm	41	24.6
12. Ovary	39	23.4
13. Breast	36	21.6
14. Skin	31	18.6
15. Spleen	28	16.8
16. Cervical nodes	25	15.0
17. Gastroint. tract†	24	14.4
18. Pancreas	23	13.8
19. Kidney	21	12.6
20. Pituitary	15	9.0
21. Heart	14	8.4
22. Uterus	14	8.4
23. Ureter	13	7.8
24. Gallbladder	11	6.6
25. Thyroid	9	5.4
26. Esophagus	7	4.2
27. Fallopian tubes	6	3.6
28. Pineal gland	4	2.4
29. Inguinal nodes	4	2.4
30. Bladder	4	2.4
31. Common bile duct	3	1.8
32. Vagina	2	1.2
33. Trachea	1	—
34. Parotid gland	1	—
35. Brain‡ (cerebral)	13	28.8
(dural)	15	33.3
36. Spinal cord§	3	—

* This is not an accurate figure, since many of the patients had had axillary-node dissections.

† The majority of these were serosal.

‡ These figures are based on forty-five examinations of the brain.

§ These figures are based on eleven examinations of the spinal cord.

with those of Gross, of Warren and Witham, and of Saphir and Parker. In Table 4, the common locations of metastases of carcinoma of the breast are compared with those of carcinoma arising from other sites.

Primary Carcinoma of the Lung. In twelve of 160 cases, no metastases were found at autopsy (Table 5). Among the remainder, the mediastinal nodes were by far the commonest site of involvement.* This corresponds to other published findings. Ochsner and DeBakey found node involvement in 75.9 per cent of 2579 cases collected from the literature; Olson, in 86 per cent; and Koletsky in 100 per cent of thirty-five small-cell carcinomas of the lung. The cervical nodes were involved in about 14 per cent of our cases. The high incidence of cerebral involvement—twenty-one of forty-nine cases autopsied—is well known in carcinoma of the lung.^{16, 29} There were metastases to the pericardium in 23.8 per cent of cases and to the heart in 7.5 per cent. In Table 6 there is a comparison of our figures with those of Koletsky, and of Ochsner and DeBakey.

Carcinoma of the Stomach. Of 119 cases of carcinoma of the stomach, nine (7.6 per cent) were free of metastases (Table 7). This striking figure is made less so by comparison with Warren's finding of no metastases in sixteen of sixty-seven cases, or 23.8 per cent.¹⁶ One wonders about the possibility of having salvaged some of these cases in which the primary lesion had not yet disseminated.

The lung was the seat of metastases in 32.8 per cent of our cases, compared to other

* These were considered metastases although the possibility of direct lymphatic extension is not excluded.

TABLE 3
INCIDENCE OF METASTASES TO COMMON SITES IN CARCINOMA OF THE BREAST

Author	No. cases	Site of metastasis in %					
		Lung	Bone	Nodes	Pleura	Liver	Adrenal
Abrams et al.	167	77.2	73.1	66.5	64.7	61.1	53.9
Gross	423	49.9	20.5	—	50.9	48.6	<5
Warren & Witham	160	58.0	42.6	71.0	34.5	54.3	30.9
Saphir & Parker	43	67.4	*	30.2	23.2	55.5	41.2

* In Saphir and Parker's cases, there were a total of thirty-six metastases to bone, but they do not state in what percentage of cases bone metastases occurred.

TABLE 4
COMMON LOCATION OF METASTASES OF CARCINOMAS ARISING FROM EIGHT
DIFFERENT PRIMARY SITES
Listed in Order of Frequency

Site, metastasis*	Primary site of carcinoma							
	Breast	Lung	Stomach†	Colon	Rectum	Ovary	Kidney‡	Pancreas
Liver	4	2	1	1	1	3	3	1
Lung	1	1	3	2	2	5	1	3
Pleura	3	5	5	6	6	6	—	—
Bone	2	4	—	—	4	—	2	5
Adrenal	5	3	6	4	5	—	4	4
Peritoneum	—	—	2	3	3	1	—	2
Pericardium	6	6	—	—	—	—	—	—
Kidney	—	—	—	—	—	—	5	—
Pancreas	—	—	4	—	—	—	—	—
Ovary	—	—	—	5	—	—	—	—
Diaphragm	—	—	—	—	—	2	—	—
Uterus	—	—	—	—	—	4	—	—

* Lymph nodes and brain have been excluded from this table.

† This order of frequency is based on our figures, plus those of Fuendeling and Hunnicutt, and Warren.⁴⁷

‡ This order of frequency is based on our figures, plus those of Harvey's collected cases and Nalle.

TABLE 5
METASTASES OF 160 CONSECUTIVE AUTOP-
SIED CASES OF CARCINOMA OF THE LUNG

Site, metastasis	No. with metastases	%
Mediast. nodes	133	83.1
Lung	75	46.9
Liver	64	40.0
Adrenal	57	35.6
Bone	52	32.5
Abdom. nodes	47	29.4
Pleura	44	27.5
Pericardium	38	23.8
Kidney	36	22.5
Diaphragm	25	15.6
Cervical nodes	22	13.7
Gastroint. tract*	17	10.6
Pancreas	16	10.0
Spleen	15	9.4
Peritoneum	15	9.4
Esophagus	14	8.7
Heart	12	7.5
Trachea	4	2.5
Thyroid	4	2.5
Gallbladder	3	1.9
Ovary	2	1.3
Inguinal nodes	2	1.3
Pituitary	2	1.3
Common bile duct	2	1.3
Prostate	2	1.3
Axillary nodes	1	—
Skin	1	—
Bladder	1	—
Ureter	1	—
Parotid gland	1	—
Brain† (cerebral)	21	42.9
(dural)	4	8.2
Spinal cord‡	1	—
No metastases	12	7.5

* The majority of these were serosal.

† These figures are based on forty-nine examinations of the brain.

‡ These figures are based on ten examinations of the spinal cord.

figures of 7.3 per cent,³⁴ 8.9 per cent,⁴⁷ 10.5 per cent,¹⁷ 18.8 per cent,²⁷ and 22 per cent.⁴⁹ In thirteen cases, metastases to bone were found, an incidence of about 11 per cent. Ovarian metastases were present in 15 per cent of our cases, as compared to Borrmann's figure of 2.3 per cent and Bland-Sutton's figure of 10 per cent. The high incidence of abdominal-node and hepatic involvement found in our series was similar to that reported in other papers. In Table 8, there is a comparison of our figures with those of Fuendeling and Hunnicutt, and Warren.⁴⁷

Carcinoma of the Colon. As in other series,⁶ more than 75 per cent of the large-bowel carcinomas in our series were in the rectum, rectosigmoid, and sigmoid (Table 9). Of 205 large-bowel carcinomas, 118 were in the colon and eighty-seven in the rectum. The lesions in the colon were distributed as follows: fifty-five in the sigmoid, twenty-six in the rectosigmoid, eight in the descending colon, eight in the transverse colon, ten in the ascending colon, and eleven in the cecum.

Seventeen cases (14.4 per cent) had no metastases. Of these, nine were in the sigmoid (about 16 per cent of fifty-five sigmoid carcinomas) and four were in the rectosigmoid (about 15 per cent of twenty-six lesions of the rectosigmoid). Our group of cases without metastases was relatively small. In Buirge's

TABLE 6
COMMON SITES OF METASTASES OF CARCINOMA OF THE LUNG
Comparison of Different Series

Author	No. Cases	Site of metastasis in %								
		Mediast. nodes	Liver	Adrenal	Bone	Kidney	Heart & pericard.	Pancreas	Brain	
Abrams et al.	160	83.1	40.0	35.6	32.5	22.5	7.5	23.8	10.0	42.9
Ochsner & DeBakey	2579	75.9	33.4	17.6	20.9	16.0	10.4	5.1	14.6	
Koletsy	100*	100	40.0	38.0	19.0	21.0	7.0	18.0	—	

* This figure applied to thirty-five small-cell carcinomas of the lung.

TABLE 7
METASTASES OF 119 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE STOMACH

Site, metastasis	No. with metastases	%
Abdom. nodes	95	79.8
Peritoneum	54	45.4
Liver	53	44.5
Lung	39	32.8
Mediast. nodes	36	30.3
Pancreas	28	23.5
Pleura	27	22.7
Adrenal	25	21.0
Gastroint. tract*	22	18.5
Diaphragm	22	18.5
Ovary	18	15.1
Gallbladder	17	14.3
Bone	13	10.9
Kidney	12	10.8
Bladder	10	8.4
Ureter	8	6.7
Spleen	7	5.8
Uterus	6	5.0
Pericardium	5	4.2
Esophagus	4	3.4
Common bile duct	4	3.4
Cervix	3	2.5
Heart	3	2.5
Inguinal nodes	2	1.7
Skin	2	1.7
Fallopian tubes	2	1.7
Vagina	2	1.7
Axillary nodes	1	—
Breast	1	—
Prostate	1	—
Brain † (cerebral)	2	8.3
No metastases	9	7.6

* The majority of these were serosal.

† These figures are based on twenty-four examinations.

281 cases, 45.2 per cent failed to show metastases. Thirty-one per cent of his cases involved the liver, 25 per cent the abdominal nodes, and 7 per cent the lung, whereas 65 per cent of our series metastasized to the liver, 59 per cent to the abdominal nodes, and 37 per cent to the lung. The adrenals were involved in 14 per cent of our cases, and the ovary in

about the same percentage. In Buirge's series, there were four adrenal metastases (1 per cent) and six ovarian metastases (2.1 per cent). Warren found regional-node involvement in 44 per cent, liver involvement in 34 per cent, and adrenal involvement in 5 per cent of sixty-four cases.⁴⁶

Carcinoma of the Rectum. Twenty-three per cent of our cases had no metastases (Table 10). In Buirge's series of 135 cases, 36.3 per cent had no metastases. Brown and Warren's group of 170 cases included 100 with no evidence of metastases (58.8 per cent). They were careful to point out, however, that "A total of 70 cases with visceral metastases among 170 seems small until it is realized that 45 deaths occurred within 1 month of resection and 33 followed colostomy within a similar time."

Surprisingly, the liver was the most common site of metastases, being involved more frequently than the regional nodes. Buirge, in 135 cases, and Bacon and Gilbert, in 318 cases (including seventeen sigmoid carcinomas), reported the same findings. This apparent higher incidence of liver metastases can probably be attributed to frequent surgical intervention and lymph-node dissection, since the incidence of node involvement at operation is greater than in autopsy series.^{12, 18}

The lung was involved in 38 per cent of our cases, as compared to other reports of 11.1 per cent,⁹ 18.3 per cent,² and 22.3 per cent.⁸ Bone lesions were found in eleven of our cases; Aufses found skeletal metastases in eight of 117 rectal carcinomas. In Table 11, there is a comparison of our figures with those of Buirge and of Brown and Warren.

TABLE 8
COMMON SITES OF METASTASES OF CARCINOMA OF THE STOMACH
Comparison of Different Series

Author	No. cases	Site of metastasis in %						
		Abdom. nodes	Peritoneum	Liver	Lung	Pancreas	Pleura	Adrenal
Abrams et al.	119	79.8	45.4	44.5	32.8	23.5	22.7	21.0
Fuendeling & Hunnicutt	200	63.0	22.0	42.5	10.5	15.0	8.0	6.5
Warren & Witham	67	61.2	20.7	34.3	8.9	10.4	4.4	2.9

TABLE 9
METASTASES OF 118 CONSECUTIVE AUTOPSIED CASES OF CARCINOMA OF THE COLON

Site of carcinoma	Sigmoid	Recto-sigmoid	Cecum	Colon			Total	% Metas.
				Ascend.	Transv.	Desc.		
No. cases	55	26	11	10	8	8	118	
.....								
Site of metastasis	Number with Metastases							
Liver	34	18	5	6	8	6	77	65.3
Abdom. nodes	33	16	4	6	8	3	70	59.3
Lung	23	11	2	0	6	2	44	37.3
Peritoneum	17	4	3	2	4	3	33	30.0
Gastroint. tract*	13	5	4	2	5	3	32	27.1
Mediast. nodes	9	5	1	1	2	0	18	15.3
Adrenal	10	4	0	1	1	1	17	14.4
Ovary	8	4	0	0	3	1	16	13.6
Pleura	9	3	1	0	2	1	16	13.6
Diaphragm	7	2	1	1	2	0	13	11.0
Bone	5	5	0	0	1	0	11	9.3
Kidney	6	2	1	0	0	0	9	7.6
Ureter	5	1	0	0	1	1	8	6.9
Spleen	1	0	0	2	2	1	6	5.1
Uterus	3	2	0	0	1	0	6	5.1
Gallbladder	2	0	1	2	1	0	6	5.1
Bladder	4	0	0	1	1	0	6	5.1
Pancreas	1	1	0	0	1	1	6	5.1
Skin	2	0	1	0	2	0	5	4.2
Fallop. tubes	3	0	0	0	1	0	4	3.4
Cerv. nodes	1	1	0	1	0	0	3	2.5
Pericardium	2	0	0	0	0	1	3	2.5
Thyroid	1	0	0	0	1	0	2	1.7
Esophagus	0	1	0	0	0	0	1	—
Heart	0	1	0	0	0	0	1	—
No metastases	9	4	1	1	0	2	17	14.4

*The majority of these were serosal.

Carcinoma of the Ovary. There are relatively few tabulations in the literature of ovarian metastases. The statement is frequently made that distant metastases from carcinoma of the ovary are rare.^{19, 35, 42, 45} Ewing gives no figures on extra-abdominal spread. Individual cases have been considered sufficiently striking to warrant case reports.^{13, 42, 45}

In our series of sixty-four cystadenocarcinomas, we found twenty-two cases—or

about one third—metastasizing to the lung. Meigs states that “carcinoma of the ovary rarely metastasizes to the lung,” and reported only one such metastasis in 131 cases. Hubeny and Mass found one fifth of thirty-nine cases with pulmonary metastases. Bernstein found five metastases to lung in 190 patients operated upon for carcinoma of the ovary. Ninety-six per cent of our cases had peritoneal spread. Geist quotes Schottländer as finding peritoneal involvement in 85 per cent of cases and

reports similar figures in his own series. Novak also speaks of peritoneal involvement in 85 per cent of cases. The liver was involved in about one half of our cases. Such sites as the thyroid, heart, bone, and breast were all involved—though infrequently—in our series.

Carcinoma of the Kidney. Willis states that the lungs are involved in about three fourths and the liver and skeleton in about one half

of fatal cases of carcinoma of the kidney. Harvey collected 217 cases from the literature, including the cases of Judd and Hand, Creevy, and Kozoll and Kirshbaum, and found the lung involved in 52 per cent, the bones in 40 per cent, and the liver in 23 per cent. About two thirds of our cases involved the lung and one fourth, liver and bone. Creevy has pointed out that a more thorough search for metastases to bone would probably reveal a higher incidence.

All of the cases in our series had metastases. The high incidence of distant metastases in renal carcinoma is thought by some to be related to its tendency to invade veins.³ In 22 per cent of 217 cases, the renal vein was involved.²⁵

In Table 14, we have compared our figures with those of Harvey and Nalle.

Carcinoma of the Pancreas. The regional nodes were involved in about four fifths, the liver in about three fifths, and the lungs in about one third of our thirty-two cases (Table 15). These figures correspond roughly with those of Grauer in his thirty-four cases. Four of our cases and three of his had no metastases. Five of ours and seven of his had bone involvement. The adrenals were involved in six instances in our series and seven in Grauer's. The high incidence of hepatic metastases is probably explained by frequent involvement of the portal circulation.

In Table 16, there is a comparison of our figures with those of Grauer.

Additional Findings. In Table 17 are listed the primary sites of metastases to organs which were involved infrequently in our series.

TABLE 10
METASTASES OF 87 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE RECTUM

Site, metastasis	No. with metastases	%
Liver	41	47
Lung	33	38
Abdom. nodes	29	33
Peritoneum	22	25
Mediastinal nodes	17	20
Gastroint. tract*	13	15
Bone	11	13
Adrenal	11	13
Pleura	10	12
Diaphragm	8	9
Spleen	5	6
Ureter	5	6
Ovary	4	5
Kidney	3	3
Uterus	3	3
Skin	3	3
Gallbladder	3	3
Bladder	2	2
Prostate	2	2
Pericardium	1	—
Inguinal nodes	1	—
Esophagus	1	—
Heart	1	—
Fallopian tubes	1	—
Vagina	1	—
Cervix	1	—
Spinal cord † (dural)	1	—
No metastases	20	23

* The majority of these were serosal.

† This figure is based on two examinations.

TABLE 11
COMMON SITES OF METASTASES OF CARCINOMA OF THE RECTUM
Comparison of Different Series

Author	No. cases	Site of metastasis in %							
		Liver	Lung	Abdom. nodes	Peritoneum	Bone	Adrenal	Spleen	Ovary
Abrams et al.	87	47.1	37.9	33.3	25.3	12.6	12.6	5.7	4.6
Brown & Warren	170	33.3	22.3	—	—	7.6	11.3	2.3	1.8
Buurge	135	36.2	11.1	22.9	12.5	1.4	2.9	2.9	2.2

TABLE 12
METASTASES OF 64 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE OVARY

<i>Site, metastasis</i>	<i>No. with metastases</i>	<i>%</i>
Peritoneum	58	96
Abdom. nodes	41	64
Diaphragm	36	56
Gastroint. tract*	35	55
Liver	33	52
Uterus	23	36
Lung	22	34
Mediast. nodes	22	34
Pleura	21	33
Spleen	17	27
Pericardium	12	19
Adrenal	11	17
Pancreas	10	16
Gallbladder	7	11
Bone	6	9
Bladder	5	8
Vagina	5	8
Fallopian tubes	4	6
Kidney	3	5
Axillary nodes	2	3
Cervical nodes	2	3
Inguinal nodes	2	3
Breast	2	3
Ureter	2	3
Skin	1	—
Thyroid	1	—
Heart	1	—
Cervix	1	—
No metastases	2	3

* The majority of these were serosal.

DISCUSSION

It should be emphasized that metastases were not found in 7.5 per cent of our cases of bronchogenic carcinoma; in 7.6 per cent of our carcinomas of the stomach, and 23.8 per cent of Warren's series;⁴⁷ in 14.4 per cent of our carcinomas of the colon and 45.2 per cent of Buirge's series; in 23 per cent of our carcinomas of the rectum, 36.3 per cent of Buirge's series, and 58.8 per cent of Brown and Warren's series. Perhaps some of these carcinomas were adventitious findings, malignant polyps as yet dormant. Some of the patients may have died of intercurrent disease, or following operation, before their tumor had reached the point of dissemination, and in others the tumor may have so invaded the organ that surgical extirpation was impossible.

Whatever the explanation, the question inevitably arises as to the possibility of having

salvaged some of these patients. This question, which must be asked in the presence of such striking autopsy figures, cannot be answered on the basis of our present information. What is required is a detailed analysis of the causes of death in a large group of cases in which no metastases have been found at autopsy. Some small measure of hindsight might thus be gained that would help the future management of such cases.

Some of our figures for metastases are higher than those reported by others. Thus, by comparison with others, we found more frequent metastases to the lung in carcinoma of the stomach, colon, rectum, and ovary; to the adrenal, in carcinoma of the breast and lung; to the liver, in carcinoma of the colon and ovary; and to the skeleton in carcinoma of the breast. In 1185 cases of carcinoma,* Hubeny and Mass found bone metastases in 12 per cent and pulmonary metastases in 28.7 per cent; we found bone metastases in 27.6 per cent, and pulmonary metastases in 46.5 per cent of our cases.

* This figure does not include the tumors of non-epithelial origin in their series.

TABLE 13
METASTASES OF 34 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE KIDNEY

<i>Site, metastasis</i>	<i>No. with metastases</i>	<i>%</i>
Lung	22	65
Mediast. nodes	16	47
Abdom. nodes	15	44
Pleura	11	32
Liver	9	27
Kidney	8	24
Adrenal	8	24
Bone	8	24
Peritoneum	3	9
Spleen	2	6
Diaphragm	2	6
Pancreas	2	6
Pericardium	1	—
Gastroint. tract*	1	—
Ureter	1	—
Thyroid	1	—
Vagina	1	—
Brain† (cerebral)	2	—
Spinal cord‡ (dural)	1	—

* The majority of these were serosal.

† These figures are based on seven examinations of the brain.

‡ These figures are based on three examinations of the spinal cord.

TABLE 14
COMMON SITES OF METASTASES OF CARCINOMA OF THE KIDNEY
Comparison of Different Series

Author	No. cases	Site of metastasis in %					
		Lungs	Lymph nodes	Liver	Kidney	Adrenal	Bone
Abrams et al.	34	65	47	27	24	24	24
Harvey et al. *	217	52	23	23	18	20	40
Nalle	58	40	16	16	2	3	19

* The cases listed under "Harvey et al." include those of Judd and Hand, Creevy, and Kozoll and Kirshbaum.

TABLE 15
METASTASES OF 32 CONSECUTIVE
AUTOPSIED CASES OF CARCINOMA
OF THE PANCREAS

Site of metastasis	No. with metastases	%
Abdom. nodes	25	78
Liver	20	63
Pleura	14	44
Peritoneum	14	44
Lung	11	34
Gastroint. tract*	11	34
Mediast. nodes	7	22
Diaphragm	7	22
Adrenal	6	19
Bone	4	13
Ovary	4	13
Gallbladder	4	13
Kidney	3	9
Cervix	3	9
Heart	3	9
Pericardium	2	6
Axillary nodes	2	6
Inguinal nodes	2	6
Bladder	2	6
Ureter	2	6
Esophagus	1	—
Thyroid	1	—
Fallopian tubes	1	—
Common bile duct	1	—
No metastases	4	13

* The majority of these were serosal.

Nine per cent of our cases had metastases to the spleen, whereas most of the figures in the literature are far lower.²⁶ Presman found only thirty-five instances of tumor metastases to the ureter reported up to 1948; we had forty-three instances in our series. Only fifty-four cases of metastasis to the uterus from extrapelvic organs had been reported prior to 1941;¹⁰ there were more than twenty such cases in our series. Glomset found 34 per cent of 821 cases of malignant neoplasms that involved the liver and 13 per cent that involved the adrenal; the incidence of hepatic

metastases in our series was 49.4 per cent and of adrenal metastases, 27 per cent.

The fact that most of the patients at the Montefiore Hospital are chronically ill must be kept in mind. This series might thus be different from one compiled in a hospital for patients with acute diseases.

It is difficult, however, reasonably to assess the importance of these differences. Too many variables are involved to allow for accurate appraisal of their statistical significance. Furthermore, it is not within the scope of this paper to explain these seeming discrepancies, but rather to report them. A few comments are in order, however, on some of the factors which made exact evaluation difficult.

Age. It would be important to know the age of the patients in the reported series. Striking age differences might be correlated with differences in incidence of metastases. It is interesting to note that the average age of our 162 cases of carcinoma of the breast—the largest group in our series—was about 52 years as compared with an average age of 57 years in the group of 160 cases* reported by Warren and Witham, with a somewhat higher incidence of metastases in our series.

Histology. The relationship of the histological appearance of tumors to the extent of metastases is still a controversial subject. Some workers have found no definite relationship between the degree of malignancy of the tumor—in terms of the histological classification—and the extent of metastases at autopsy.^{3, 44, 46} Warren and Witham, in dis-

* This figure excludes two tumors of nonepithelial origin included in their series.

TABLE 16
COMMON SITES OF METASTASES OF CARCINOMA OF THE PANCREAS

Author	No. cases	Site of metastasis in %						
		Abdom. nodes	Liver	Peritoneum	Lung	Mediast. nodes	Adrenal	Bone
Abrams et al.	32	78.1	62.5	43.8	34.4	21.9	18.7	15.6
Grauer	34	82.3	73.5	23.5	29.4	23.5	20.5	20.5

cussing carcinoma of the breast, state: "Certainly so far as distribution of metastases is concerned, there is but little evidence of correlation of histological appearance and extent of metastasis."⁴⁸ They qualify this statement with the remark that "in certain cases of markedly anaplastic tumors, duration of life has been short and distribution of metastases has been wide."

Composition of the Series. There were relatively few carcinomas of the cervix in our series, as compared to other autopsy series. This may be related to the relatively high proportion of Jewish patients at the Montefiore Hospital. Although the low incidence of cervical carcinoma in the series might affect the figures on the over-all incidence of metastases to different organs, it would obviously have no

bearing on the figures for metastases of neoplasms arising from other primary sites.

Duration of Life after Diagnosis. It is difficult to evaluate the relationship of the duration of life after the diagnosis was made to the extent of metastasis. If, uniformly, our patients had lived for many years after the discovery of their tumors, one might conjecture that their tumor had ample time to disseminate. The same finding might be interpreted, however, as evidence for a lower grade of malignancy. Conversely, a short duration of life after diagnosis might be thought to mean either rapid dissemination causing death within a short time, or insufficient time for the tumor to metastasize widely. Finally, the time at which the diagnosis of carcinoma is made gives no definite

TABLE 17
LOCATION OF PRIMARY CARCINOMAS METASTASIZING TO RARE SITES OF SECONDARY INVOLVEMENT

Site, primary carcinoma	Site of metastases											
	Heart	Esophagus	Thyroid	Fallopian tubes	Pituitary	Common bile duct	Vagina	Prostate	Trachea	Pineal	Cervix	Testes
Breast	14	7	9	6	15	3	2	—	1	4	—	—
Lung	12	14	4	—	2	2	—	2	4	—	—	—
Stomach	3	4	—	2	—	4	2	1	—	—	—	—
Colon	1	1	2	4	—	—	—	—	—	—	1	1
Rectum	1	1	—	1	—	—	1	2	—	—	1	—
Ovary	1	—	1	4	—	—	5	—	—	—	1	—
Pancreas	3	1	1	1	—	1	—	—	—	—	—	—
Primary site unknown	1	—	—	—	—	—	—	—	—	—	—	—
Corpus uteri	—	1	—	1	—	—	—	—	—	—	—	—
Prostate	—	—	—	—	1	—	—	—	—	—	—	—
Bladder	1	—	—	—	—	—	—	—	—	—	—	1
Esophagus	—	—	—	—	—	—	—	1	—	—	—	—
Gallbladder	—	—	—	—	—	1	—	—	—	—	—	—
Larynx	—	—	1	—	—	—	—	—	1	—	—	—
Liver	—	—	—	—	—	1	—	—	—	—	—	1
Thyroid	1	—	—	—	—	—	—	1	—	—	—	—
Tongue	—	1	—	—	—	—	—	—	—	—	—	—
Trachea	—	1	—	—	—	—	—	—	—	—	—	—
Kidney	—	—	1	—	—	—	1	—	—	—	—	—
TOTAL	38	31	19	19	18	12	11	7	6	4	3	3

information as to the length of time it has been present in the organism.

Treatment. Treatment might have a significant effect on metastases. The type and extent of surgery, and its chronological relationship to the onset of symptoms, in our series might differ from those in other series. Similarly, the timing, distribution, and dosage of radiation therapy would be of interest.

Many of the figures for metastases quoted in the literature were compiled before the last decade. Yet during this last decade, impressive strides have been made in supportive therapy, pre- and postoperative care, and antibiotic treatment of infections. Important advances in surgical and radiation therapy have also been made. If fewer patients are dying because of lack of resistance to infection or incapacity to withstand prolonged surgery, these might well have an appreciable effect on the incidence of metastases.

The Postmortem Examination. A last but important consideration is the thoroughness of the postmortem examination. The limitations of this examination are clear. The routine autopsy is directed at discovering the maximum amount of information about the pathological anatomy of the individual case, within the practical framework demanded by considerations of time, personnel, and available facilities. It is safe to say that the incidence of metastases discovered in autopsies will rise in direct proportion to the time spent in the gross examination, the number of organs sectioned, and the number of sections obtained from each organ. It follows that positive findings probably have greater meaning than negative findings, unless the most exhaustive and intensive search for metastases has been undertaken.

For various reasons, examinations of the

brain and spinal cord are not always included in autopsies. The failure to record the exact number of such examinations is a source of error in compiling figures on cerebral metastases. Thus, forty-three metastases to brain in our 1000 cases would appear to represent a percentage of 4.3; since only 244 brain examinations were performed, the actual percentage was 17.6. But this figure cannot be accepted as an accurate index of cerebral metastases, since clinical evidence of cerebral involvement influenced the selection of cases in which the brain was examined.

The increased use of roentgenograms and the information that they supply as to the location of bone lesions may help to explain the high incidence of bone metastases in our series.

It is difficult to estimate the extent to which the factors we have discussed explain our findings. In stressing the discrepancies between our figures and those of others, we have not intended to obscure the fundamental similarity of many of our findings to those previously reported. These findings are important in a confirmatory sense.

There remains a need for additional analyses of recent material. From these, a more accurate index of the incidence of metastases of carcinoma may be obtained.

SUMMARY

The metastases of 1000 consecutive cases of carcinoma have been described and presented in tabular form. The literature has been briefly reviewed, and comparisons made between our findings and those of other workers. It is emphasized that there was a significant number of cases in which no metastases were found at autopsy. In some instances, the incidence of metastases in our series was higher than in other reported series.

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