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STUDIES ON GENITOURINARY TUMORS WITH SPECIAL REFERENCE TO BLOOD BORNE METASTASIS

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Spreading of the malignant tumor occurs by local spread or through the lymphatics or blood vessels. Local spread and lymphatic extension to regional lymph nodes may be found and extirpated before and during the operation. However, blood-borne metastasis are not often found even during the operation. Early pre-operative diagnostics and the mechanisms of blood-borne metastasis are yet to be standardized or clarified.

Thus, the authors carried out clinical, laboratory and autopsy studies on 404 cases with genitourinary tumors at the Sapporo Medical College and Hospital during the recent 10 years in an attempt to clarify the mechanism of blood-borne metastasis.

Material

A. Clinical and autopsy cases

404 cases with genitourinary tumors have been treated at the department of Urology, Sapporo Medical College and Hospital during the recent 10 years. 362 cases were of urogenital origin and the remaining 42 were retroperitoneal tumors and secondary tumors of the urinary tract originating

from the uterus. 139 of the total 404 cases are alive to date. Postmortem examinations were done on 117 of 210 deaths. Clinical follow-up studies were carried out on 349 cases. The remaining 55 cases were not available for the follow-up study (Table 1).

Table 1 Malignant tumors of the genitourinary tract

Primary Tumor	No. of Cases	Sex		Alive	Died		Unknown
		Male	Female		Yes	No	
Renal cell carcinoma	43	24	19	12	13	11	7
Wilms' tumor	6	5	1	2	1	3	-
Carcinoma of renal pelvis & ureter	19	15	4	8	6	3	2
Bladder carcinoma	161	124	37	56	50	40	15
Bladder sarcoma	3	2	1	-	3	-	-
Prostatic carcinoma	79	79	-	39	10	24	6
Prostatic sarcoma	4	4	-	1	3	-	-
Penile carcinoma	14	14	-	4	2	2	6
Urethral carcinoma	6	-	6	-	1	2	3
Testicular tumor	26	26	-	12	7	1	6
Scrotal carcinoma	1	1	-	-	-	1	-
Retroperitoneal tumor	11	5	6	3	2	2	4
Uterine carcinoma	31	-	31	2	19	4	6
Total	404	299	105	139	117	93	55

B. Blood vessel invasion

319 of the 362 cases with primary tumor of the genitourinary tract comprises the material of this examination. In the remaining 43 cases, surgical operations of the tumor were not conducted or the specimens were not available for histological examination. Efforts to prepare as many

blocks from the specimen as possible were made and the total number of blocks for investigation came to 1,276. The average number of blocks from a single patient was 4, with 16 blocks as the highest and 1 block as the lowest.

C. Circulating cancer cells

A total of 86 patients were subjected to examination. The numbers of patients with bladder carcinoma, renal carcinoma, prostate carcinoma, testis carcinoma, penile carcinoma and others were 41, 17, 17, 5, 3 and 3, respectively.

Methods

A. Clinical and autopsy cases

a. Method of calculating survival rate: The relative survival rate was calculated by the mathematical method proposed at the international symposium on "End results of cancer therapy" (29).

b. Method of examination of lung, liver and bone metastasis: In clinical cases, lung and bone metastasis were examined by periodic check-ups of X-ray films. Liver metastasis were excluded because of the difficulty of clinical identification. In autopsy cases, lung and liver metastasis were examined histologically on all of the macroscopically doubtful points.

B. Identification of blood vessel invesion

Identification of venous invasions of the tumor cells was made by Weigert's elastic tissue staining, as conpared against hematoxylineosin staining on

the same section. Only veins with intraluminal tumor cells were accepted as evidence of tumor invasion (Fig. 1-3).

C. Examination of circulating cancer cells

Five ml. of blood were taken from the antecubital vein or veins draining the tumor, before, during and after the operation. Blood samples were also obtained from a catheter placed in the inferior vena cava through the femoral vein during the kidney tumor operation. Isolation of the atypical cells from whole blood was conducted by the fibrinogen method of Sandberg and Moore. Isolated cells were streaked on slides, immediately fixed in alcohol and stained by giemsa. A minimum of 10 slides were prepared from each samples. Identification of atypical cells was made according to a slightly modified Papanicolaou standard (15).

Results

A. Clinical and autopsy cases

a. Relative 5-year survival rate: Testicular tumor showed the most favorable prognosis (0.661) and calculations showed a gradually worsening in the descending order of prostate carconoma (0.565), cancer of renal pelvis and ureter (0.534), bladder cancer (0.405) and Wilms' tumor which showed the most unfavorable prognosis of all cases examined. (Table 2).

b. Lung and liver metastasis: Autopsy cases; lung metastasis were found in 39.3 percent of all cases (Table 3). In renal carcinoma the incidence was the highest, amounting to 84.6 percent. In bladder carcinoma the incidence was 26.0 percent. Eighteen cases with bladder carcinoma

Table 2 Relative 5-year survival rate

Primary Tumor	No. of Cases	Relative 5 Year Survival Rate	Standerd Deviation
Renal cell carcinoma	43	0.350	0.078
Wilms' tumor	6	0.237	0.177
Carcinoma of renal pelvis & ureter	19	0.534	0.137
Bladder carcinoma	161	0.405	0.044
Bladder sarcoma	3	0.000	-
Prostatic carcinoma	79	0.565	0.072
Prostatic sarcoma	4	0.000	-
Penile carcinoma	14	0.385	0.144
Urethral carcinoma	6	0.000	-
Testicular tumor	26	0.661	0.098
Retroperitoneal tumor	11	0.541	0.154
Total	372	—	—

Table 3 Incidence of distant metastasis (Autopsy cases)

Primary Tumor	No. of Cases	Organs Metastasized					Without Metastasis
		Lung	Liver	Bone	Lymph Node	Etc.	
Renal cell carcinoma	13	11	6	7	9	10	-
Wilms' tumor	1	-	-	-	-	-	1
Renal pelvic & Ureteral carcinoma	6	3	2	1	3	1	-
Bladder carcinoma	50	13	17	10	26	29	18
Bladder sarcoma	3	-	-	-	1	1	2
Prostatic carcinoma	10	5	4	7	7	9	-
Prostatic sarcoma	3	3	2	-	2	3	-
Testicular tumor	7	5	5	4	7	7	-
Penile carcinoma	2	1	-	1	2	1	-
Urethral carcinoma	1	-	-	-	1	1	-
Retroperitoneal tumor	2	1	-	1	1	2	-
Uterine carcinoma	19	4	4	2	14	19	-
Total	117	46	40	33	73	83	21

died of complications such as infections or renal insufficiency chiefly due to the urinary diversion operation after the severance of the primary tumor. In all of the 18 cases distant metastasis were not found at autopsy. The frequency of liver metastasis from bladder cancer was somewhat higher than that of lung metastasis. Bone and pulmonary metastasis were found in 7 and 5 of 10 cases with prostatic cancer, respectively. Pulmonary metastasis from the testicular tumor showed a rather high incidence, amounting to 71.4 percent.

Clinical cases: Pulmonary metastasis were found in 11.9 percent of all cases. Renal carcinoma showed the highest incidence, making a 27.9 percent (Table 4).

c. Interrelationship of occurrence between lung and liver metastasis: In autopsy cases of renal tumor, all liver metastasis cases showed lung metastasis. However, 11 out of 43 cases with bladder, prostate, testis and uterine cancer had liver metastasis without lung metastasis. (Table 5).

d. Sites of distant metastasis without lung and/or liver metastasis: Eight out of 117 autopsy cases showed distant metastasis without lung or liver metastasis. The most frequently affected organs were bones of the axis and trunk. There was one case with kidney metastasis from the opposite renal carcinoma (Table 6). Distant metastasis without lung or liver metastases were found in 39 of the 404 clinical cases. The bones of the axis and trunk were also by far the most frequently affected organ (Table 7).

e. Bone metastasis: From the observations on the sites of bone metastasis, it was noted that in all but one case the metastatic sites were

Table 4 Incidence of distant metastasis (Clinical cases)

Primary Tumor	No. of Cases	Organs Metastasized			Without Metastasis
		Lung	Bone	Etc.	
Renal cell carcinoma	43	12	5	29	20
Wilms' tumor	6	1	-	2	3
Renal pelvic and ureteral carcinoma	19	3	1	2	17
Bladder carcinoma	161	15	7	22	130
Bladder sarcoma	3	-	-	1	2
Prostatic carcinoma	79	4	17	7	58
Prostatic sarcoma	4	3	-	3	1
Testicular tumor	26	5	1	7	19
Penile carcinoma	14	1	1	7	7
Scrotal carcinoma	1	-	-	1	-
Urethral carcinoma	6	-	1	3	3
Reproperitoneal tumor	11	2	1	3	8
Uterine carcinoma	31	2	-	10	-
Total	404	48	34	97	268

Table 5 Interrelationship of occurrence between lung and liver metastasis

Site of Primary Tumor	No. of Cases Metastasized to Lung or Liver	Metastasis		
		Both to the Lung & the Liver (%)	To the Lung Separately (%)	To the Liver Separately (%)
Kidney	14	57.1	42.9	
Bladder	19	57.9	10.5	31.6
Prostate	9	55.6	33.3	11.1
Penis	1		100.0	
Testis	6	50.0	33.3	16.7
Others	1		100.0	
Uterus	7	14.3	42.9	42.9
Total	57	28 (49.1)	18 (31.6)	11 (19.3)

Table 6 Sites of distant metastasis in cases without pulmonary and/or liver metastases (Postmortem examination)

Primary Tumor	Sites of Distant Metastasis	No. of Cases
Renal cell carcinoma	Opposite kidney	1
Ureteral carcinoma	Spinal cord (Th. 7-9)	1
Prostatic carcinoma	Thoracic vertebrae	2
	Lumbar vertebrae	1
	Pubic bone	1
Penile carcinoma	Thoracic vertebrae	1
Retroperitoneal tumor	Parietal and temporal bones	1
Total	—	8

Table 7 Sites of distant metastasis in cases without pulmonary and/or liver metastases. The metastasis were found by routine clinical examination of 404 cases with genitourinary tumor.

Primary Tumor	Sites of Metastases		No. of Cases
Renal cell carcinoma	Bone	Ischium	1
		Scapula	1
	Skin	Bilateral abdomen	1
		Arm	1
	Vagina		1
Bladder carcinoma	Skin	Shoulder, arm, thigh	1
		Thigh	1
	Bone	Pubis	2
Prostatic carcinoma	Bone	Pelvis	11
		Lumbar vertebrae	7
		Thoracic vertebrae	5
		Femur	1
		Cervical vertebrae	1
		Ribs	1
	Penis		1
Penile carcinoma	Bone	Thoracic vertebrae	1
Urethral carcinoma	Bone	Pubis	1
Retroperitoneal tumor (Sympathicogonioma)	Bone	Parietal & temporal	1
Total	—		39

the axis and the trunk. This evidence seems to suggest that those tumors develope via the vertebral vein system (Table 8). The frequency of skeletal metastasis from prostatic carcinoma was 3 times higher than that of pulmonary metastasis and 4 out of 10 prostatic carcinoma with metastasis showed skeletal metastasis without lung or liver metastasis. This evidence shows that the vertebral vein system (Batson's route) may play an important role in the hematogenous dissemination of prostatic carcinoma (3-5, 8).

B. Blood vessel invasion

Vein invasion was seen in 78.9, 46.5, 47.9 and 68.2 per cent of renal, bladder, prostatic and testicular tumor, respectively (Table 9).

a. Classification by tumor cell type, grade and stage in cases with bladder carcinoma: Vein invasion was seen in 40.4, 82.4 and 75 percent of transitional cell carcinoma, squamous cell carcinoma and adenocarcinoma, carcinoma, respectively. As illustrated in Table 10, it may be roughly said that the more advanced the stage and grade, the more often the venous invasion can be seen.

b. Relation between venous invasion and istant metastasis: Vein invasion was seen in 173 of the 319 clinical cases. Distant metastasis was found in 57 (32.9%) of the 173 clinical cases with vein invasion (Table 11). It was noted that distant metastasis was found in 46 (73.0%) of the 63 autopsy cases with vein invasion (Table 12).

In other words in the present relationship, the intensity of the relationship between vein invasion and distant metastasis increased with the thoroughness of the examination.

Table 8 Site distribution of bone metastasis in patients with malignant tumors of the genitourinary tract

Site of Bone / Primary Tumor	Tibia	Femur	Pelvic Bone	Lumbar Vertebrae	Thoracic Vertebrae	Cervical Vertebrae	Skull	Sternum	Ribs	Scapula	No. of Bones Involved	No. of Cases with Bone Metastasis	Percentage of Bone Metastasis	No. of Cases Observed
Renal cell carcinoma right			1	3	2			1	1		8	9	20.9	43
Renal cell carcinoma left			1	1	1		1		1	1	6			
Carcinoma renal pelvis & ureter			1	1				1	1		4	1	5.3	19
Bladder carcinoma			6	5	2			2			15	11	6.8	161
Prostatic carcinoma	1	5	17	12	5	1			1		42	18	22.8	79
Penile carcinoma					1						1	1	7.0	14
Urethral carcinoma			1								1	1	16.7	6
Testicular tumor				3	1						4	4	15.4	26
Retroperitoneal tumor (Sympathicogonima)							1				1	1	9.1	11
Total	1	5	27	25	12	1	2	4	4	1	82	46		359

Table 9 Incidence of venous invasions in the tumor tissue of the genitourinary tumors

Primary Tumor	No. of Cases	Venous Invasion			Tumor Cell Emboli			Either Venous Invasion or Tumor Cell Emboli	
		++	+	%	++	+	%	No. of Cases	%
Renal cell carcinoma	38	23	3	68.4	15	2	44.7	30	78.9
Wilms' tumor	5	2	0	40.0	3	0	60.0	4	80.0
Carcinoma of renal pelvis & ureter	15	2	2	26.7	3	0	20.0	5	33.3
Bladder carcinoma	144	42	8	34.7	31	2	22.9	67	46.5
Bladder sarcoma	3	1	0	33.3	0	0	0.0	1	33.3
Prostatic carcinoma	73	21	4	34.2	15	1	21.9	35	47.9
Prostatic sarcoma	4	4	0	100.0	1	0	25.0	4	100.0
Penile carcinoma	11	6	1	63.6	5	0	45.4	9	81.8
Urethral carcinoma	4	2	0	50.0	2	0	50.0	3	75.0
Testicular tumor	22	8	1	40.9	10	0	45.5	15	68.2
Total	319	111	19	40.6	85	5	28.0	173	54.0

Table 10 Occurrence of venous invasion of tumor classified by cell type, grade, and stage of bladder tumors

Type of Cells	Grade	Stage A	B_1	B_2	C	D	Stage Undetermined	Total	%
Transitinal cell carcinoma	I	0/6						0/6	00.0
	II	2/24	6/11				5/22	14/58	24.1
	III	0/5	9/17	12/16	9/12	5/5	1/2	36/57	63.2
	IV				0/1	0/1		0/2	00.0
	Total	2/35	15/28	12/16	9/13	6/7	6/24	50/123	40.7
	%	5.7	53.6	75.0	69.2	85.7	25.0		
Squamous cell carcinoma			1/1	1/2	6/7	4/5	2/2	14/17	82.4
Adeno carcinoma							3/4	3/4	75.0
Sarcoma							1/3	1/3	33.3
Total								65/147	46.3

Table 11 Relationship of incidence between venous invasion in tumor tissues and distant metastasis (Clinical cases)

Venous Invasion	Metastasis +	Metastasis −	Total
+	57 (32.9%)	116	173
−	18 (12.3%)	128	146
Total	75	244	319

Table 12 Relationship of incidence between venous invasion in tumor tissue and distant metastasis (Autopsy cases)

Venous Invasion	Distant Metastasis +	Distant Metastasis −	Total
+	46 (73.0%)	17	63
−	6 (31.6%)	13	19
Total	52	30	82

C. Circulating cancer cell

a. Peripheral blood: From 86 patients with genitourinary tumor, 313 blood samples were obtained and tumor cells were found in 57 of the 313 blood samples (18.2%) and in 29 of the 86 patients (33.7%) (Table 13).

Table 13 Incidence of cancer cells in the blood

		Cancer Cells in Blood	
		+	−
No. of Patients	86	29 (33.7%)	57
No. of Blood Samples	313	57 (18.2%)	256

The incidence of tumor cells in the blood of patients with or without distant metastasis was 61.5 and 26.3 percent respectively (Table 14). (Fig. 4- 5)

b. Regional blood: Blood samples obtained from veins draining the tumor of 12 patients with renal carcinoma and 2 patients with bladder carcinoma showed tumor cells in 6 and 1 respectively (Fig. 7 - 9). Table 15 shows the occurrences of the tumor cells from caval blood before, during and after the operation or tumor massage. With special regards to Table 15 tumor cells were found in 20, 43.6 and 12.5 percent respectively.

Table 14 Incidence of cancer cells in the blood with and without metastasis

a) Patients with Metastasis:

	No. of Cases	Cancer Cells in the Blood +	-
Bladder carcinoma	6	4	2
Prostate carcinoma	7	4	3
Total	13	8 (61.5%)	5

b) Patients without Metastasis:

	No. of Cases	Cancer Cells in the Blood +	-
Bladder carcinoma	29	8	21
Prostate carcinoma	9	2	7
Total	38	10 (26.3%)	28

Table 15 Cancer cells in caval blood before, during and after the operation

Primary Tumor	Before	During(1)	During(2)	After
1. Bladder carcinoma	-	++	-	-
2. Bladder carcinoma	+	++	+	-
3. Bladder carcinoma	-	-	-	-
4. Bladder carcinoma	-	-	-	-
5. Bladder carcinoma	-	+	++	-
6. Bladder carcinoma	-	-	-	-
7. Prostatic carcinoma	-	-	-	-
8. Renal cell carcinoma			++	
9. Wilms' tumor	-	++	-	-
10. Renal pelvic carcinoma	++			
Total	2/11	4/8	4/9	1/8
Percentage	20	8/17(47.1		12.5

- Negative + Single cell ++ A clump of cells

Discussion

A. Route of dissemination of tumor cells

It is well known that distant metastasis occurs by the liberation of tumor cells into the blood stream while the local spread may be generally attributed to transportation by the lymphatic route. However, a clear cut picture of the route of distant metastasis is lacking.

a. Dissemination of tumor cells to lung and liver: Some workers reported that the occurrence of lung metastasis in the tumor of kidney, ureter and testis is about 2 fold that of liver metastasis and there are some lung metastasis without liver metastasis (1, 30, 32, 33). However, the occurrences of lung and liver metastasis in the tumor of the bladder and prostate are about the same.

As summarized in Table 16, the record of the registered autopsy cases in Japan shows the same occurrence as mentioned above (2).

Table 16 Incidence of distant metastasis of genitourinary tumors. (Autopsy cases in Japan, 1964)

Primary Tumor	No. of Cases	Organ Metastasized			
		Lung	Liver	Bone	Brain
Renal cell carcinoma	243	173 (71.2%)	85 (35.0%)	87 (35.8%)	26 (10.7%)
Wilms' tumor	17	8 (47.1%)	10 (58.8%)	3 (17.6%)	0 (0.0%)
Renal pelvic carcinoma	22	11 (50.0%)	13 (59.1%)	6 (27.3%)	0 (0.0%)
Ureteral carcinoma	17	2 (11.8%)	5 (29.4%)	5 (29.5%)	0 (0.0%)
Bladder carcinoma	256	60 (23.4%)	59 (23.0%)	22 (8.6%)	5 (1.9%)
Urachal carcinoma	3	2 (66.7%)	1 (33.3%)	1 (33.3%)	0 (0.0%)
Bladder sarcoma	6	2 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prostatic carcinoma	133	60 (45.1%)	36 (27.1%)	75 (56.4%)	8 (6.0%)
Prostatic sarcoma	4	3 (75.0%)	3 (75.0%)	0 (0.0%)	0 (0.0%)
Urethral carcinoma	-	- (-)	- (-)	- (-)	- (-)
Penile carcinoma	21	8 (38.1%)	5 (23.8%)	3 (14.3%)	0 (0.0%)
Testicular tumor	103	73 (70.9%)	64 (62.1%)	19 (18.4%)	17 (16.5%)
Retroperitoneal tumor	-	- (-)	- (-)	- (-)	- (-)
Total	825	402 (48.7%)	271 (32.8%)	221 (26.8%)	56 (6.8%)

From the results of our studies it was noted that the caval and portal vein systems may be considered as the two major routes of hematogenous dissmination of genitourinary tumors and that these two pathways are independent of each other.

b. Bone metastasis: Willis and Walther seem to be unwilling to consider the vertebra vein system as a route of metastasis to the bones. They assumed that while tumors actually were present in the lungs, they were overlooked owing to their smallness in size (30, 32, 33). According to their opinion, bone metastasis involving all cases should be regarded as "transpulmonary" metastasis.

However, Prinzmental et al. (24) have recently shown that glass beads with a diameter much larger than that of the ordinary capillaries are capable of passing readily through the pulmonary circulation system. This observation suggests the existence of arteriovenous shunts in the lungs sufficiently large to allow for the passage of almost any tumor cell. Zeidman found that suspended tumor cells injected into the systemic veins of an animal could be recovered immediately from the aortic blood and when injected into second animals actually produced tumors (34-36).

Thus, small metastatic deposits in the lungs and transpulmonary passage of tumor embli are very possible modes of tumor cell transportation which may account for bone metastasis. On the other hand, Batson suggested that cancer cells from the pelvic or retroperitoneal region could enter the vertebral veins, which is an extensive system paralelling the vertebral column and which is in rich anastomosis with the veins of the pelvis and retroperitoneum. He demonstrated that any increase in intra-abdominal pressure would facillitate the passage of emboli into the vertebral veins

by diverting the flow of blood from the caval system into the vertebral system (3-5, 7, 8, 9).

From the results of our studies it was noted that the vertebral vein system (Batson's route) is the main route of dissemination in bone metastasis from prostate cancer. To date, the role of Batson's route in tumor metastasis seems to have been underestimated. We are of the opinion that this route of metastasis should be reevaluated.

B. Blood vessel invasion

The significance of venous invasion in cancer tissue has until recently been insufficiently appreciated (12).

a. Occurrence of cancer cells in the blood of patients with genitourinary tumor: Willis, Tsuji, Igawa and others reported that careful histological examination of bladder cancer revealed a surprisingly high incidence of venous invasion of cancer cells (17, 19, 20, 22, 30, 32, 33).

Tsuji conducted a histological examination on serial sections from a bloc cut through the largest diameter of the tumor including the entire bladder wall and found tumor cell emboli at an incidence of 34 percent. Careful histological examination by use of elastic tissue staining in the presents study showed venous invasion of tumor cells in bladder carcinoma at an incidence of 47 percent. Carcinoma cells of the prostate have often been assumed to invade blood vessels readly. Franks reported that the incidenc of the venous invasion of cancer cells was 37 percent in prostate cancer (1 Careful examination of our series demonstrated that the incidence was 47.9 percent.

b. Relationship between the occurrence of venous invasion and distant metastasis: Riches reported that the occurrence of distant metastasis in

renal carcinoma with venous invasion (29 out of 38 or 76%) was twice as often as that without venous invasion (23 out of 32 or 37%) and stressed the importance of venous invasion with the presence of distant metastasis (26).

From the results of our studies it was noted that the occurrence of distant metastasis was 73 percent (46 out of 63) and 31.6 percent (6 out of 19) in genitourinary cancer with or without venous invasion, respectively.

c. Relationship between venous invasion and survival rate: McDonald and Priestley found that the 5-year survival rate of renal cancer patients with or without venous invasion was 29 and 55.4 percent, respectively (19). From the results of our studies it was noted that the relative 5 year survival in renal, bladder and testis tumor with vein invasion showed a poor prognosis as compared with those without venous invasion. However, in other types of genitourinary tumor, no significant differences of prognosis were seen between tumors with or without venous invasion.

From the results of our present studies, using elastic tissue statining and by careful examination, a remarkable high incidence of venous invasion was revealed and a definite relationship between venous invasion, metastasis and its peognosis was demonstrated.

C. Circulating cancer cells

Since the report of Engell in 1955, over 5,000 cancer patients have been studied by more than 40 investigating teams employing at least 20 different cytologic methods (6, 10, 12-16, 18, 21, 23, 27, 31). It was invariably most difficult to identify cancer cells (6, 10, 12, 15, 25). Thus, there were wide variations of the rate of incidence of cancer cells in the blood among different workers.

From the results of our studies it was noted that the highest incidence of cancer cells in the blood was seen in the blood obtained from the veins draining the tumor and the incidence of cancer cells in the peripheral blood of patients with metastasis was much higher than that without metastasis. The incidence during the manipulation of tumors was much higher than before and after the manipulation of tumors. These facts suggest that cancer cells in the blood are definitely related with blood born metastasis.

Summary and Conclusion

Studies on 404 genitourinary tumors including 117 autopsy cases were made in an attempt to clarify the pattern of distant metastasis in malignant tumors of genitourinary tract. From a viewpoint of bloodborne metastasis, three main routes, the caval, portal and vertebral vein system were considered. The caval vein system is considered to be the main route of lung metastasis from renal, ureteral and testicular tumors. The portal vein system is considered to be the main route of liver metastasis from vesical and prostatic tumor. The vertebral vein system is considered to be the main route of bone metastasis from prostatic cancer. Venous invasions of cancer cells in genitourinary tumors were found to be highly frequent and important and a close relationship between venous invasion, distant metastasis and its prognosis was demonstrated. The incidence of cancer cells in the circulatory blood of patients with genitourinary tumors was also high when examined carefully and a close relation between the incidence and distant metastasis was demonstrated.

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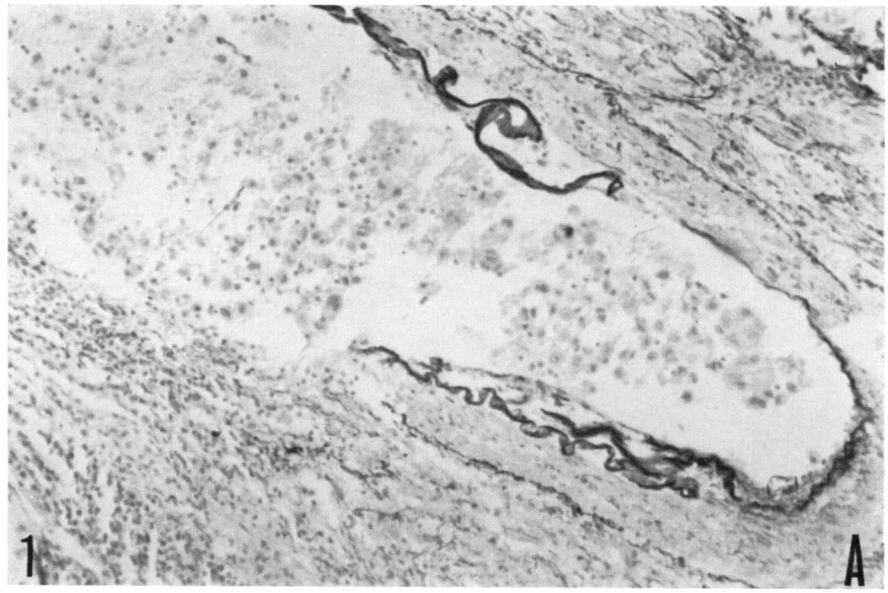
Explanation of Figures

Fig. 1 A case of renal cell carcinoma. Cross-section of a venule occupied by cancerous thrombus. Weigert's elastic tissue stain; X 100 A, X 200 B.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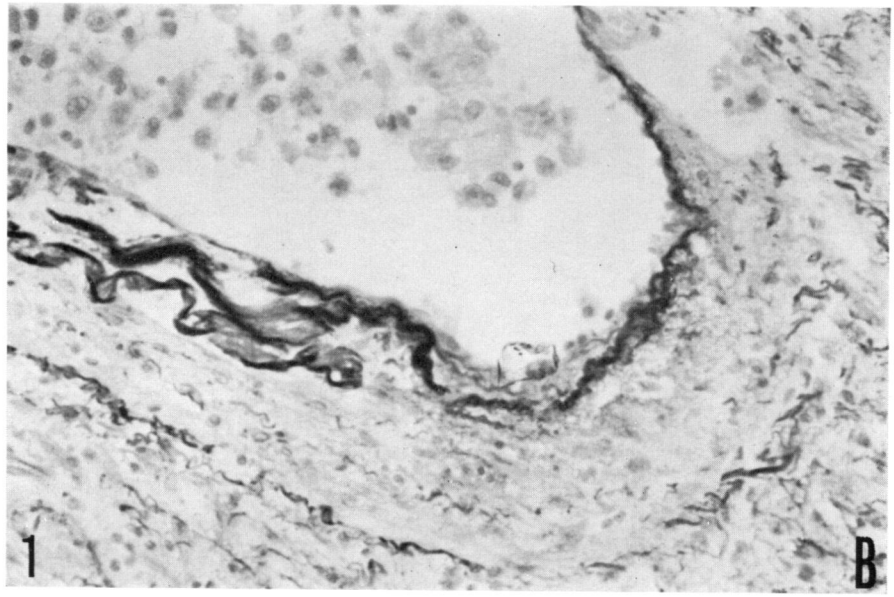
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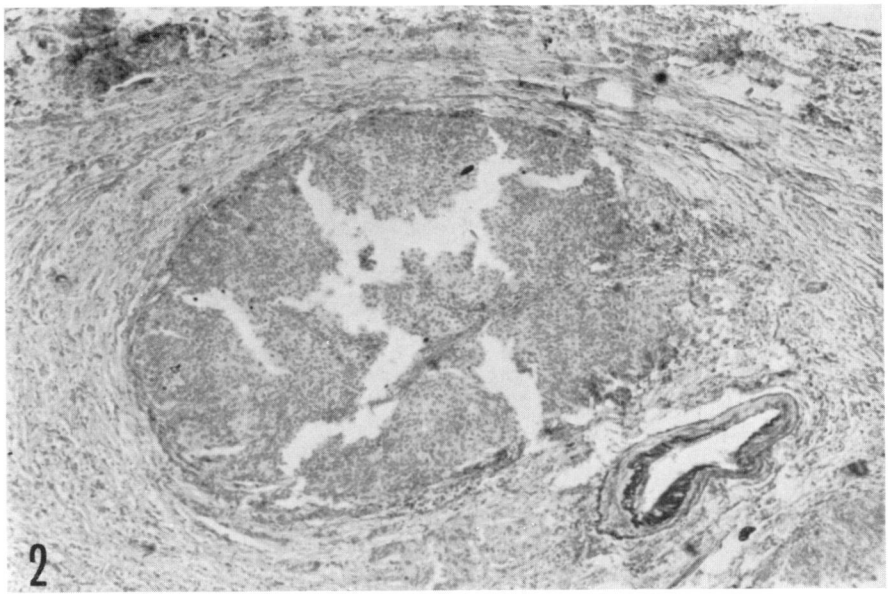
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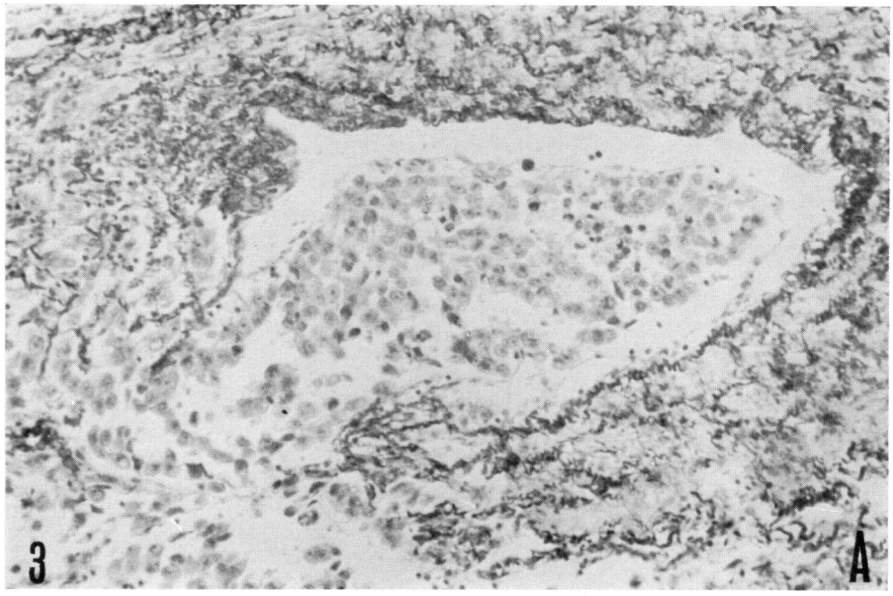
Fig. 2 A case of bladder cancer. Cross-section of a venule occupied by organized cancerous thrombus. Weigert's elastic tissue stain; X 100.

Fig. 3 A case of seminoma, showing venous invasion of tumor which subsequently produced a cell embolus in a vein of the affected testis. Weight's elastic tissue stain; X 100 A, X 200 B.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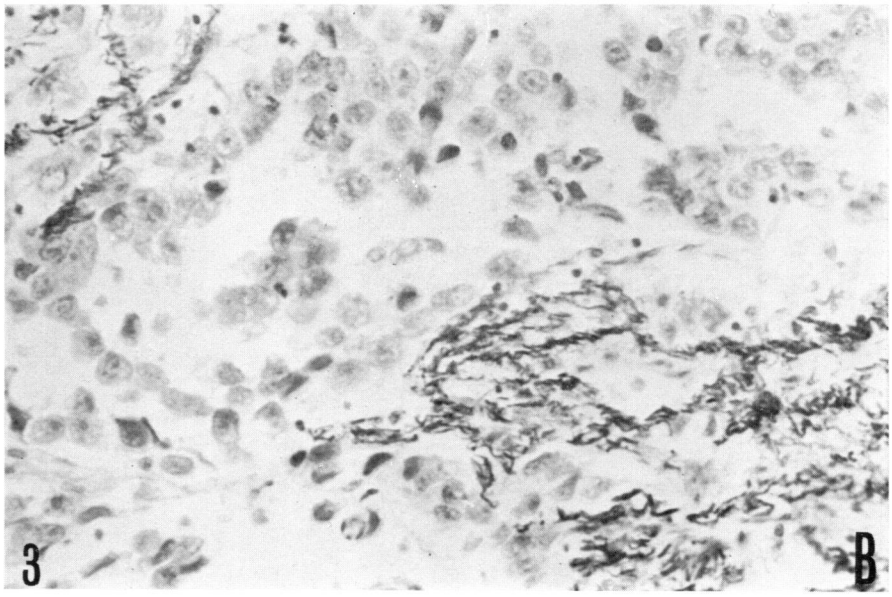
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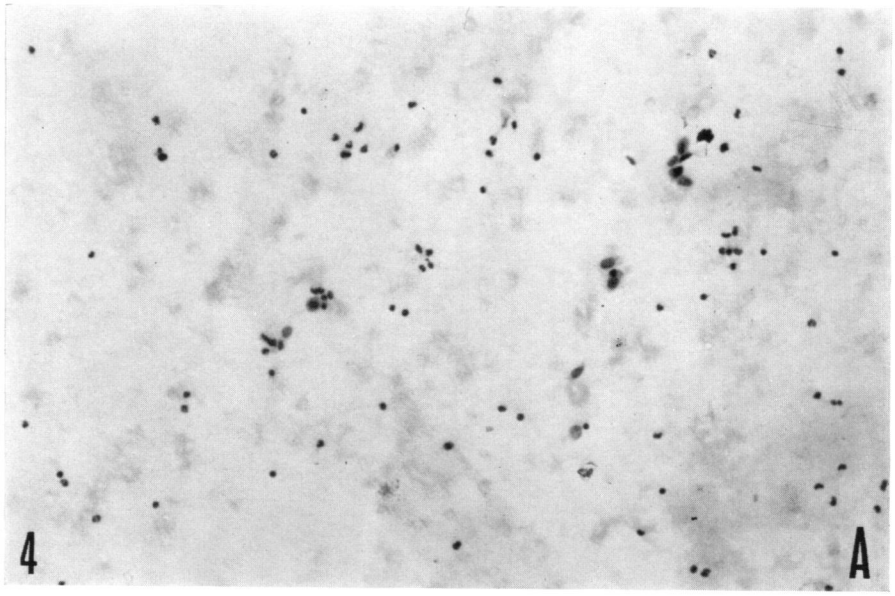
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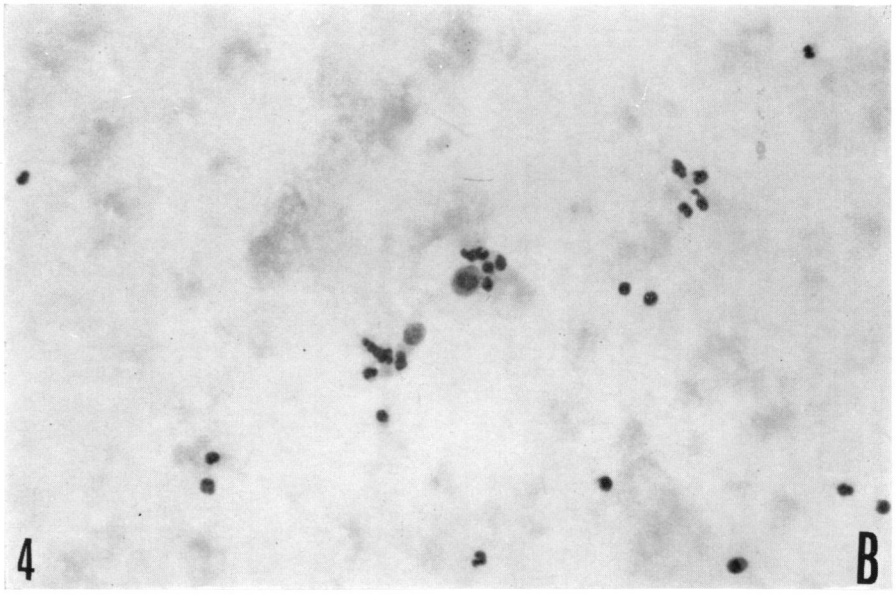
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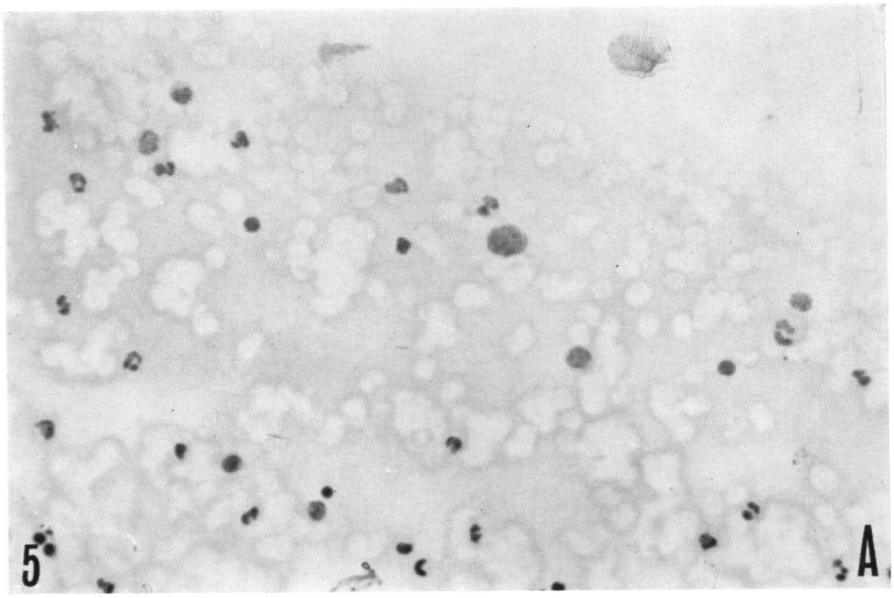
Fig. 4 Renal cell carcinoma. Malignant cells isolated from the peripheral blood (Antecubital vein) on the first postoperative day. Papanicolaou's stain; X 100 A, X 200 B.

Fig. 5 Wilms' tumor. A malignant cell isolated from the peripheral blood (Antecubital vein). Papanicolaou's stain; X 200 A, X 900 B.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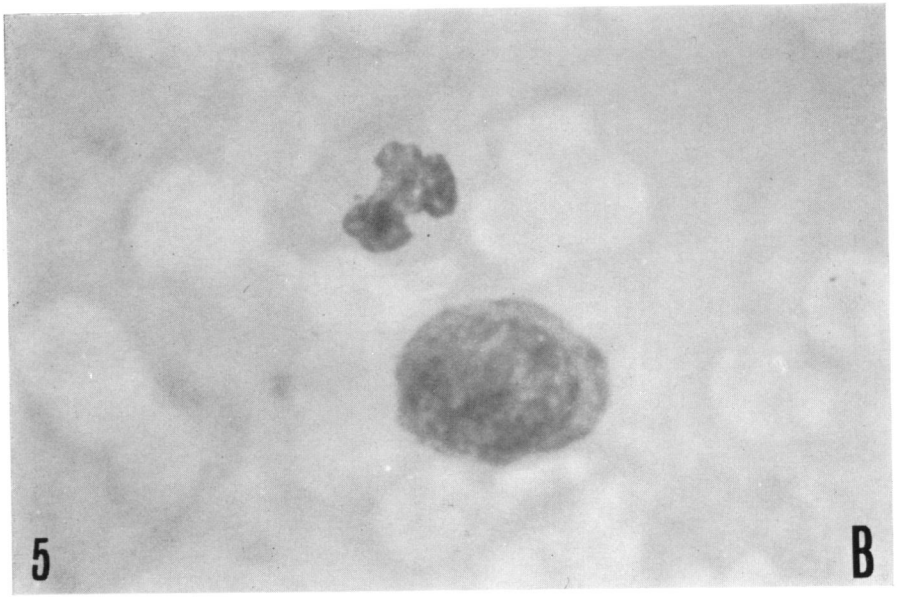
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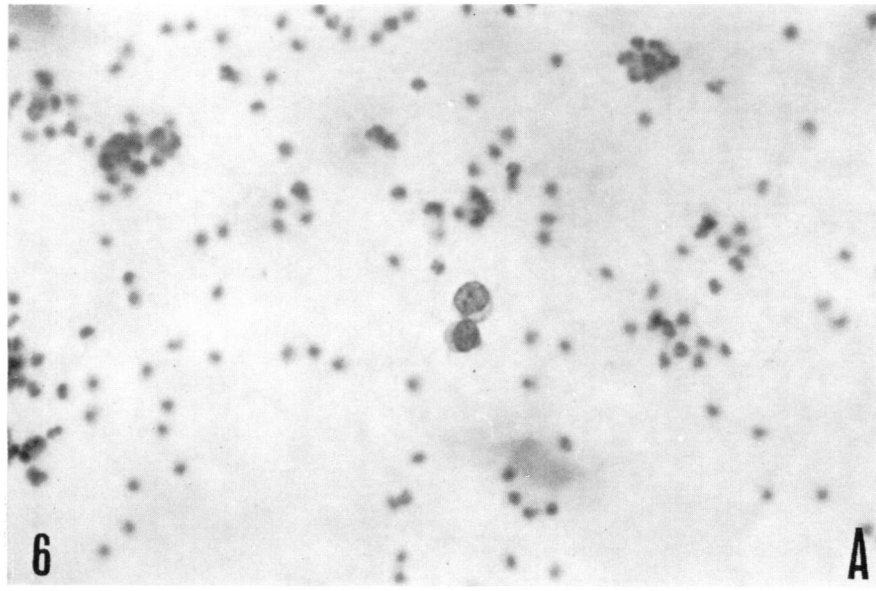
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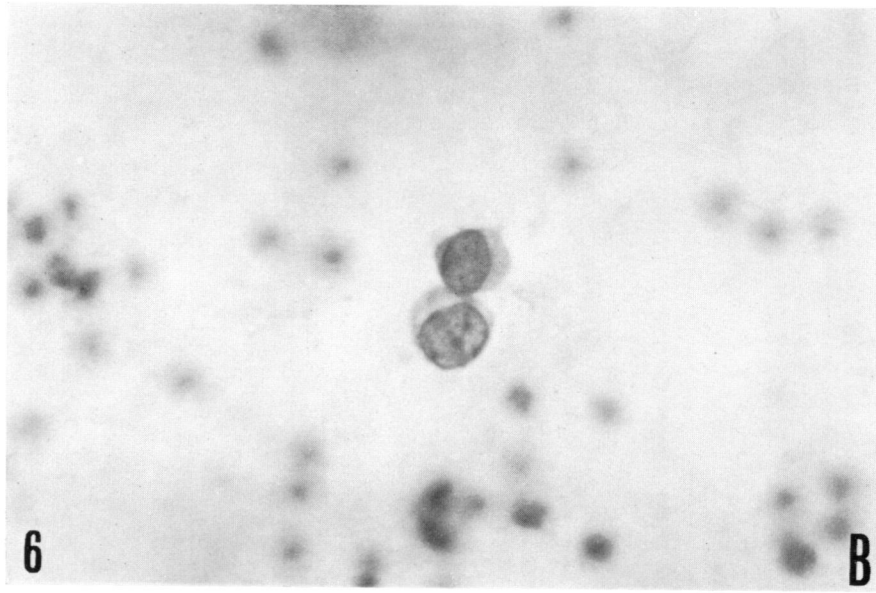
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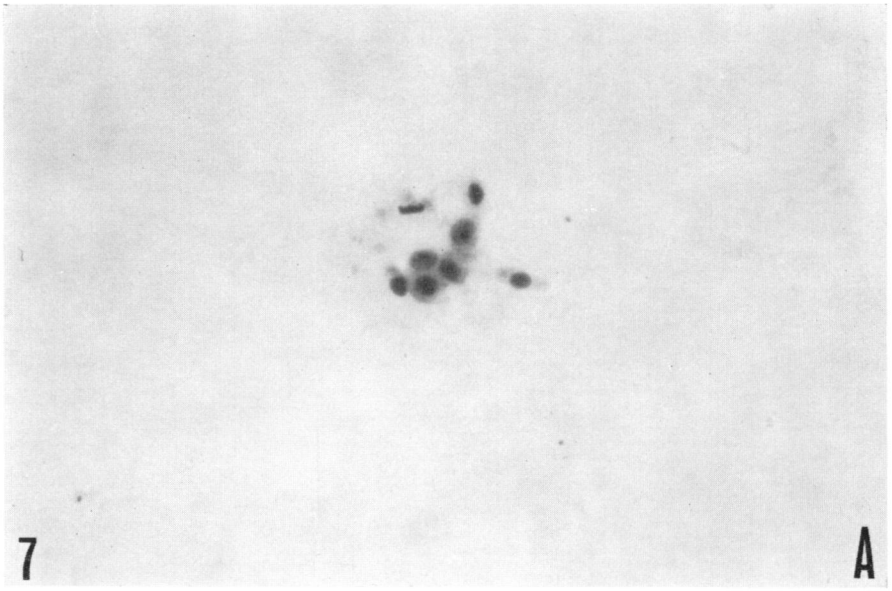
Fig. 6 Two malignant cells isolated from the peripheral blood (Antecubital vein). Papanicolaou's stain; X 200 A, X 400 B.

Fig. 7 Renal cell carcinoma. A clump of malignant cells isolated from the inferior vena cava during surgery. Papanicolaou's stain; X 200 A, X 900 B.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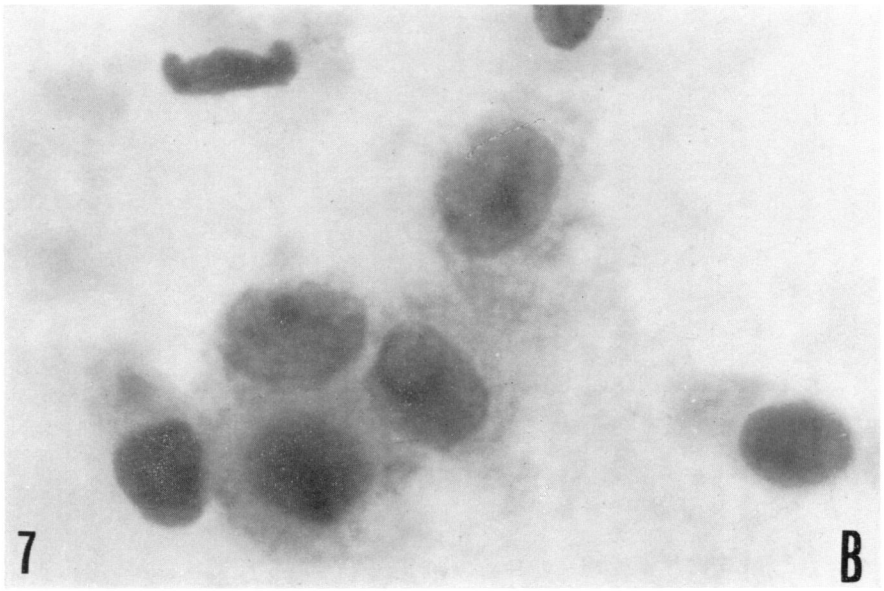
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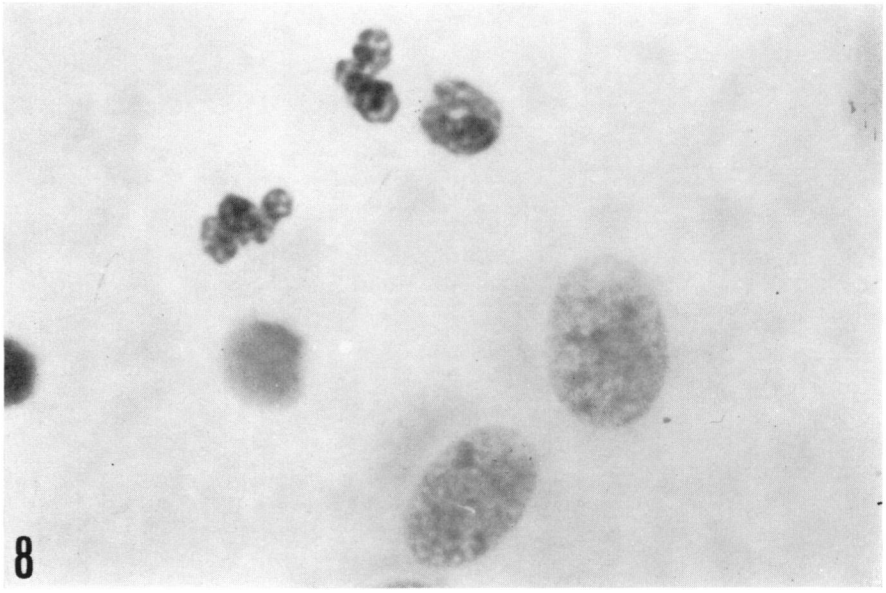
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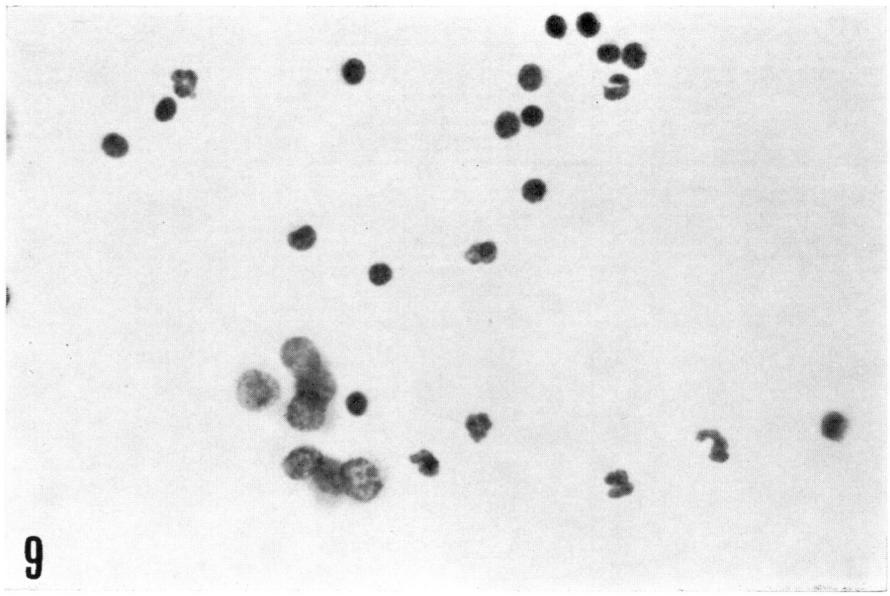
Fig. 8 Carcinoma of bladder. Two malignant cells isolated from the inferior vena cava during surgery. Papanicolaou's stain; X 900.

Fig. 9 Carcinoma of prostate. A clump of malignant cells isolated from the inferior vena cava during prostatic massage. Papanicolaou's stain; X 400.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