The Pathology of Tumors
Part IV: Behavior and Therapy of Tumors

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Functioning Tumors

Most well-differentiated tumors "function," in the sense that they are capable of synthesizing the same product as the normal parent cell: keratin can be made by an epidermoid carcinoma, mucin by adenocarcinoma, collagen by a fibrosarcoma, immunoglobulins by a plasma cell myeloma, melanin by a malignant melanoma and so on. However, the term "functioning tumors" is usually reserved for those neoplasms, generally of endocrine origin, that can synthesize hormones and release them into the circulation, with the resulting peripheral manifestations. In some cases, the amount of secretion is not large enough to induce clinical signs of endocrine dysfunction, but it can still be detected by laboratory methods. In other instances, the tumor attempts to make the hormone but because of lack of the necessary enzymes, it stops short of the active compound. The precursors and their metabolites, however, can be detected in the urine and other body fluids. To properly assess functioning tumors, it is essential for the pathologist to obtain the tissue immediately after it is excised, so that he can study it with a variety of techniques, such as electron microscopy, histochemistry, immunohistochemistry and biochemical assay.

The list of functioning endocrine tumors is large indeed, and has expanded considerably in recent years. The most important ones are listed in Table I and illustrated in Figs. 1-12. In many instances the physician may predict, from the hormone being produced, the microscopic type of tumor, its location and whether it is likely to be benign or malignant. A pheochromocytoma that secretes both epinephrine and norepinephrine will be located nearly always in the adrenal gland, because extra-adrenal pheochromocytomas lack the necessary enzymes to synthesize epinephrine. An adrenal cortical lesion producing pure aldosteronism is almost always benign, whereas feminization in an adult male is an indication of carcinoma in the large majority of cases. If a carcinoid tumor produces the typical carcinoid syndrome, the primary is probably located in the small bowel with extensive liver metastases. If, on the other hand, the carcinoid syndrome is atypical because the tumor is secreting 5-hydroxytryptophan...
instead of 5-hydroxytryptamin, the chances are that the primary tumor is in the stomach or bronchus. If a thyroid nodule is “hot,” i.e., incorporates more iodine than the surrounding gland, the chances of its being carcinoma are negligible. Most of the pancreatic tumors that secrete insulin are benign, whereas the reverse is true for those associated with the Zollinger-Ellison syndrome.

In addition to the endocrine neoplasms we have mentioned, there are a number of apparently non-endocrine tumors that manifest themselves by producing a hormone. For example, features of a hyperparathyroidism have been seen with renal cell carcinoma, lung carcinoma, malignant lymphoma and several other tumors; in some of these, the secretion of a parathormone-like substance has been documented. Polycythemia apparently due to the production of an erythropoietic factor has been seen with renal cell carcinomas, cerebellar hemangioblastomas, hepatomas and even uterine leiomyomas. Hypoglycemia secondary to mesenchymal tumors, such as mesothelioma and fibrosarcoma, has also been reported. ACTH production, with resulting Cushing's syndrome, has been recorded for a large variety of non-adrenal neoplasms. It is likely that at least some of these tumors are also endocrine tumors that masquerade under the microscope as undifferentiated carcinomas or adenocarcinomas.

Spread of Cancer

Direct Invasion

Malignant tumors can locally invade contiguous organs and invariably follow the path of least resistance. Naturally, there are barriers to invasion by certain structures such as periosteum, fibrous septa, tendon sheaths, capsules and especially cartilage. Any tumor growing within a bone may have difficulty penetrating beyond the confines of the bone and so will usually grow vigorously within the marrow cavity. An osteosarcoma that can grow through the cortical bone will encounter resistance from the periosteum; this may result in so-called Codman's triangle. The tumor will encounter even greater resistance from the cartilage in the epiphyseal line or the articular surface. Similarly, it is difficult for cancer of the endolarynx to penetrate the cartilage. Soft tissue sarcomas follow the fascial planes rather than growing through them. Cancer of the breast will grow easily in the fat of the breast but when it reaches the pectoral fascia it is at least temporarily restrained. Tumors usually grow rather freely through the capsule of a lymph node. Cancer of the body of the pancreas quickly invades the peritoneal surface, and cancer within the lung parenchyma encounters little or no resistance to its spread.

Epidermoid carcinoma of the lower esophagus often spreads to the stomach and adenocarcinoma of the cardias frequently grows upward into the esophagus. Duodenal extension is seen in one-third of carcinomas of the distal stomach.

Implantation

The surgeon must realize that cancer may be implanted during a diagnostic or therapeutic procedure. This is a risk that should be avoided or at least minimized by taking certain precautions. When a needle such as the Vim-Silverman is inserted into a lymph node, a soft tissue tumor or a parotid neoplasm, a capsule may be ruptured and tumor can grow along the needle tract through the point of rupture or can drip from the end of the needle into the surrounding tissue (Figs. 13A and 13B). If a tumor is inadequately excised or if it is incised during a surgical procedure, then it may be implanted in the operative field. If this possibility is not kept in mind during grafting, tumor can be transplanted to the graft site. There are certain general methods that can be used to avoid implantation or to minimize the risk. If needle or incisional biopsy is done, it must be planned so that when the definitive surgery is carried out, the needle tract or the area through which the previous incisional biopsy was done is adequately excised. We have demonstrated tumor implants along the needle tract at the time of excision of a salivary gland tumor. If this operation had not been planned correctly, this nidus of tumor would probably have led to local re-
crudecence of the neoplasm. In another instance, a thyroid nodule biopsied through a small incision proved to be a cancer. Later, when the entire zone was excised together with total thyroidectomy, tumor was observed growing through the area of the incisional biopsy. We practically never biopsy ulcers of the stomach at the time of operation, because if they are cancer, the danger of implantation throughout the peritoneum is too great. Under rare circumstances we do frozen sections on extremely large ulcers and on the few ulcers located high on the lesser curvature. In these two instances the risk of implantation is outweighed because the extent of surgery could be modified on the basis of frozen section diagnosis. We take the risk of implantation in debatable lesions of the periangullary zone, including the head of the pancreas, because operative mortality and morbidity are high and the chance of cure is low, particularly in cancer of the head of the pancreas. In skin grafting, instruments must be changed and contaminated areas avoided so that the tumor is not transplanted to the skin graft zone. Tumor transplantation to the skin graft zone has occurred in skin and breast cancer.

Local recurrence at suture lines is always a potential danger. Ulcerated cancers of large bowel continuously desquamate tumor cells into the lumen. Although they rarely, if ever, implant on a normal mucosa, the trauma of the bowel at the point of anastomosis provides an area where the free cancer cells can attach and cause a local recurrence. Experiments in animals have shown conclusively that cancer cells attach selectively to traumatized tissue. Because of this, a ligation of the bowel should be performed as the initial step in the operation to prevent further dissemination of malignant cells. The gross and radiographic appearance of a local recurrence of large bowel cancer is quite different from that of a primary carcinoma (Fig. 14). Suture material can frequently be identified in the region of the recurrence (Figs. 15A and 15B).

Lymphatics
Cancer invades the lymphatic vessels easily and spreads to local lymph nodes by embolization, lodging in the subcapsular sinus of one or more nodes (Fig. 16). The node acts as a barrier to future spread and may keep the cancer contained for some time. Once cancer completely fills the nodes, normal pathways are no longer followed and retrograde and extremely irregular distribution of lymph node involve-
Fig. 3. Microscopic appearance of an adrenal cortical adenoma. The cells have a large, clear cytoplasm full of lipid material.

Fig. 4. Section of bone showing the changes of osteitis fibrosa cystica disease. There is resorption of bone trabeculae by tongues of fibrous tissue and scattered osteoclasts. This patient had a parathyroid adenoma.

Fig. 5. Typical carcinoid of small bowel. Solid nests of small uniform cells infiltrate the stroma. The argentaffin reaction was positive. This patient had liver metastases, elevated urinary 5-hydroxyindolacetic acid and carcinoid syndrome.

Fig. 6. Carcinoid tumor of stomach. In contrast to small bowel tumors, those located in the foregut derivatives frequently have a glandular appearance (as in this case) and are not argentaffin.

Spread through the lymphatics is by far the most common pathway of cancer dissemination. It is much more common for carcinoma to spread in this fashion than it is for sarcoma. The spread from a primary tumor via the lymphatics takes only seconds. It is possible that manipulation may even force the tumor into the lymphatics. It is common to see small collections of tumor cells in the lymph nodes of a radical mastectomy specimen. If all...
proximal lymphatics are involved, retrograde involvement of other lymph nodes may take place. Such retrograde dissemination frequently implies a hopeless prognosis. This is certainly true for cancer of the rectum (Fig. 17). If cancer has spread to all the draining lymph nodes, then the lymphatics leading to these nodes will become completely filled with tumor: subsequent changes that occur could be termed spread by lymphatic permeation.

Careful examination of the lymph nodes submitted with surgical specimens is of great importance in determining prognosis. There may be considerable variation in the number of lymph nodes found in different patients even though the operation performed by the surgeon is the conventional one for the cancer in question. If serial sections are done on the lymph nodes, more nodes will prove to be involved than was originally thought. We find an average of 29 lymph nodes per radical mastectomy specimen; by clearing methods, it is possible to demonstrate an increased number of positive lymph nodes. If the 29 axillary lymph nodes are initially negative, any further serial sectioning of these nodes and clearing of the specimens will only infrequently add an additional positive case and will not provide information of prognostic significance. These findings regarding the breast apply equally well to the lung, stomach, large bowel and neck dissections. It should be emphasized, however, that the more careful the examination of the lymph nodes, the more accurate the pathologic report and the more accurate the prognosis.

It should be mentioned here that the growth of tumors along neural sheaths, commonly seen in cancers of prostate, pancreas and salivary glands, does not represent invasion of perineural lymphatics, as formerly thought (Fig. 18). Electron microscopy and injections with India ink have shown that these are not lymphatic channels. They simply represent spaces of minor resistance, which are easily penetrated by the malignant cells. This explains the otherwise paradoxical fact that this phenomenon is occasionally also seen in perfectly benign conditions, such as fibrocystic disease of the breast.

Correlation Between Gross Appearance of Node and Microscopic Diagnosis

A surgeon cannot palpate a lymph node at the time of operation and tell with certainty if it contains cancer. For instance, with persistent cancer of the cervix following irradiation therapy, pelvic exenteration may be contemplated. If distant nodes such as the periaortic lymph nodes are involved, operation is useless. Therefore, the periaortic lymph nodes should be routinely biopsied under these circumstances. It has not been rare to find that lymph nodes measuring only a few millimeters contain cancer. We have also seen many large, firm nodes under a variety of circumstances as large as nine cm in the inguinal area, five cm in the axillary region, eight cm in the mediastinum and seven cm in the retroperitoneal zone, all thought surely to contain cancer, but all merely hyperplastic. Palpation of the cervical area by an experienced surgeon for the presence or absence of enlarged lymph nodes is reasonably accurate. However, the axilla is extremely difficult to palpate and the inguinal area is not much better. The decision as to whether an enlarged lymph node in any of these areas contains cancer does not depend entirely upon the sensitivity of the surgeon's fingers but is related to a considerable extent to the type of neoplasm. If a patient has a melanoma of the skin of the cheek and the cervical lymph nodes are enlarged, this means in almost 100 percent of instances that the lymph nodes contain tumor. However, we know that if a patient has a verrucous carcinoma of the buccal mucosa that is infected, cervical lymph node enlargement has no significance as far as the neoplasm is concerned. In other words, the potencies of a given tumor and the presence or absence of infection must be considered in deciding whether an enlarged lymph node is likely to contain carcinoma.

Veins and Arteries

Vein invasion is a major method of cancer spread. Sarcomas were formerly thought to be the only type of cancer that spread by veins. However, it has been well documented by numerous studies that vein in-
| Tumor                                      | Hormone Produced                               | Syndrome                        |
|-------------------------------------------|-----------------------------------------------|---------------------------------|
| Pituitary gland adenoma                    | Growth hormone                                | Gigantism and acromegaly        |
|                                           | ACTH                                          | Cushing's syndrome              |
|                                           | Prolactin                                     | Forbes-Albright syndrome        |
| Thyroid adenoma                            | Thyroid hormone                               | Hyperthyroidism                 |
| Parathyroid adenoma or carcinoma           | Parathormone                                  | Hyperparathyroidism             |
| Islet cell adenoma or carcinoma            | Insulin                                       | Hypoglycemia                    |
|                                           | Gastrin                                       | Zollinger-Ellison syndrome      |
|                                           | Glucagon                                      | ?Diabetes                       |
|                                           | "Diarrheogenic hormone"                       | "Pancreatic cholera"            |
| Adrenal cortical adenoma or carcinoma      | Cortisol                                      | Cushing's syndrome              |
|                                           | Aldosterone                                   | Conn's syndrome                 |
|                                           | Estrogen or androgen                          | Adrenogenital syndrome          |
| Pheochromocytoma; paraganglioma; neuroblastoma; ganglioneuroblastoma; retinoblastoma | Dopamine, norepinephrine and epinephrine | Hypertension, paroxismal or sustained |
| Carcinoid tumor; oat-cell carcinoma; islet cell tumor; medullary carcinoma of thyroid | 5-hydroxytryptophan, serotonin, kynins | Carcinoid syndrome              |
| Granulosa-theca cell tumor of ovary; primary and metastatic ovarian tumors with "functioning stroma"; Sertoli cell tumor of testis | Estrogen | Estrinism          |
| Sertoli-Leydig cell and lipid cell tumors of ovary; Leydig cell tumor of testis | Androgen | Virilization      |
| Choriocarcinoma and other testicular tumors; carcinoma of lung; hepatoma | Gonadotropins | Gynecomastia |
| Oat-cell carcinoma of lung; bronchial carcinoid; thymic carcinoid; islet cell tumor; medullary carcinoma of thyroid | ACTH-like hormone | Cushing's syndrome |
| Renal cell carcinoma; lung carcinoma; malignant lymphoma | Parathyroid-like hormone | Hyperparathyroidism             |
| Mesothelioma; fibrosarcoma; hemangioendothelioma; hemangioendothelioma; hemangiopericytoma; hepato- toma; adrenal cortical carcinoma; other carcinomas | Insulin-like hormone | Hypoglycemia |
| Renal cell carcinoma; cerebellar hemangioblastoma; uterine leiomyoma; hepatoma | Erythropoietin | Polycythemia (usually erythrocytosis) |
| Oat-cell carcinoma of lung                  | Antidiuretic hormone                          | Schwartz-Bartter syndrome       |
Fig. 7. Medullary carcinoma of thyroid. The large amorphous acidophilic masses represent amyloid. This tumor has a very slow evolution.

Fig. 8. Granulosa-theca cell tumor of ovary. The small round holes present between the tumor cells are the so-called Call-Exner bodies. They are similar to those seen in normal follicles and are an important diagnostic feature of this tumor.

Fig. 9. Sertoli-Leydig cell tumor of ovary. The elongated cells with dark nuclei have been compared with Sertoli cells, whereas the plump cells with acidophilic cytoplasm are considered Leydig cells. This tumor is usually masculinizing, hence the alternative term arrhenoblastoma.

Fig. 10. Testicular choriocarcinoma. The tumor masses are formed by cytotrophoblast and syncytiotrophoblast, like normal chorionic villi. Chronic gonadotropins are invariably elevated.

Invasion is also common with carcinomas; in fact, vein invasion is a very important form of spread in certain carcinomas, particularly cancers of the thyroid, colon and kidney (Fig. 19). It remains an important finding in determining the prognosis in patients with renal carcinoma. Spermatic vein involvement is an ominous finding in malignant tumors of the testes. In well-delimited tumors of the thyroid it is imperative that the pathologist search carefully for vein invasion, both grossly and microscopically. The finding of vein invasion in lung carcinoma is of less prognostic significance. In a study of 226 pneumonectomy and lobectomy specimens by Spjut and Roper there were 46 five-year survivors. Twenty-two (48 percent) of these had vein invasion and 24 (52 percent) did not. However, the 22 survivors with vein invasion represented only 14.8 percent of the 149 total cases with vein inva-
sion, while the 24 survivors without vein invasion represented 31 percent of the total in this group. The same findings are extremely important in cancer of the large bowel and tumors of the adrenal, pancreas and parathyroid. Gross evidence of vein invasion is infrequent; we have seen it most commonly in lesions of the kidney and rarely in lesions of the large bowel and thyroid. Gross invasion is of course much more ominous than microscopic invasion. Microscopically, evidence of vein invasion must be based on certain criteria. The mere presence of tumor cells free within the lumen of vessel is not sufficient evidence because the cells may have been pushed there during the operation. We insist that the tumor cells be attached to the wall of the vein like a thrombus. Special stains (Verhoef-van Gieson) are useful in the identification of veins by delineating the elastic lamina.

In sarcoma, veins are the main pathway of spread. This is true of practically all soft tissue sarcomas and primary tumors of bone, such as osteosarcoma and chondrosarcoma. These tumors as a group very rarely spread by lymphatics to the regional lymph nodes. Thus dissection of regional lymph nodes is seldom indicated.

We have not mentioned spread by arteries because for practical purposes it does not occur. If a tumor is located in close proximity to large vessels such as the aorta, it may be able to destroy the vessel wall and cause it to rupture. This does occur in carcinoma of the bronchus and esophagus, but only rarely.

The Therapist and the Pathologist

In the treatment of cancer it is imperative that there be close cooperation between the surgeon, the radiotherapist, the chemotherapist and the pathologist. Biopsies must be obtained and diagnosed before therapy is introduced. The radiotherapist and chemotherapist should refuse to treat a cancer patient until a microscopic examination has proved that the patient indeed has cancer. If the case is referred from another hospital with a microscopic diagnosis already established, the slides should be obtained and reviewed by the pathologist of that institution. Most lesions that clinically resemble cancer are cancer, but in a few instances, apparently typical cancers are in reality non-neoplastic. For example, one patient had a cauliflower lesion of the cervix which many experienced clinicians believed to be advanced cancer of the cervix. They were so convinced that nine biopsies were taken in an

Fig. 11. Oat cell carcinoma of lung. This highly malignant neoplasm can be associated with a large variety of endocrine syndromes, probably due to hormonal secretion by the tumor cells.

Fig. 12. Thymoma composed of epithelial cells of plump shape admixed with lymphocytes. This is the type usually associated with myasthenia gravis.
attempt to make the diagnosis. The biopsies revealed only a benign papillomatous lesion with inflammation. It is also wise to biopsy mediastinal masses before giving a trial dose of radiotherapy. The lesion may be a radioresistant tumor or an inflammatory process.

Bone lesions that suggest Ewing's tumor should not be irradiated until biopsy has been done, for these lesions may in reality be a benign condition such as eosinophilic granuloma or subperiosteal hemorrhage (Fig. 20). Biopsy of melanoma was thought to be dangerous but the available data do not substantiate this assumption.17 There are actually reports in the literature of apparent cures of malignant melanoma by radiation therapy without biopsy, but we are certain that most of these represent either pigmented basal cell carcinoma or seborrheic keratosis with melanin pigmentation. Failure to obtain a positive biopsy before treatment may completely invalidate an otherwise carefully reported series of supposed cases of a certain type of lesion. In the field of giant cell tumors of bone, many authors have reported series of cases in which the diagnosis has not been proven pathologically and which, in many instances, do not represent true giant cell tumor. At times the extensions of a malignant process must be biopsied in order to prove to skeptics that sterilization of such metastases is possible. In cancer of the nasopharynx with metastases in which biopsy of the primary is available, needle biopsy of enlarged lymph nodes usually is not done; therefore, when these nodes disappear under radiation therapy to the primary lesion, doubters may say that the nodes were merely an inflammatory reaction to an ulcerated tumor mass.

The pathologist is frequently asked whether or not a given tumor is radio sensitive. This can only be answered in a general way. As a rule, the more undifferentiated the tumor, the more radiosensitive it is apt to be. There is also a definite relation between the tissue of origin and the degree of radiosensitivity.18 On the basis of these concepts and, most importantly, by previous evaluation of the therapeutic results achieved with
different modalities of treatment, it is possible to roughly divide tumors of various histologic types and tissues of origin according to their degree of radiosensitivity (Table 2). By using these guidelines the pathologist can make a rough estimate of the relative radiosensitivity of a tumor. A testicular seminoma can be expected to be highly sensitive in the large majority of the cases, whereas the reverse will be true for a fibrosarcoma of soft tissues. But this is as far as prediction can go.

There can be marked differences in radiosensitivity between two microscopically identical cancers. We have seen basal cell carcinomas that were extremely radioresistant. By contrast, sarcomas that have been traditionally regarded as radioresistant neoplasms occasionally show a marked response to radiation.

Suit has achieved excellent results by treating incompletely excised soft tissue sarcomas of various microscopic types with high-dose (greater than 6300 rads) radiation therapy. He has been able to achieve local control in the majority of the well-differentiated tumors regardless of the microscopic type, and a modest number of the poorly-differentiated varieties.19

The pathologist is often asked to determine if a tumor has been sterilized in a certain specimen. There are three definite rules that must be followed in this regard.

Study should be delayed until the full force of radiotherapy has taken effect. This seems obvious, but erroneous statements in the literature stem from failure to pay attention to it. If an organ is removed shortly after radiotherapy has been completed, apparently viable tumor may be present and the pathologist may report its persistence. Suit and Gallager have shown that small nodules have persisted for periods up to 110 days after radiation doses of 8100 and 9400 rads to spontaneous mammary carcinomas in mice.20 The nodules in all instances studied contained tumor cells that were morphologically intact and would be considered viable by usual criteria. However, no instance of local recurrence was observed and, on isointransplantation of the nodules, tumor growth did not take place. Thus,

![Image 1](https://example.com/image1)

![Image 2](https://example.com/image2)

Fig. 15A and B. Photomicrograph of adenocarcinoma growing within the wall of the bowel, but confined to it. Arrow in 15A (top) points to suture material. Fig. 15B (bottom) shows the suture material within the walls.

![Image 3](https://example.com/image3)

Fig. 16. Tumor cells in the subcortical lymphatic sinusoids. This is the first zone in which metastases appear.
the cancer cells were biologically non-viable, in the sense that they had lost their reproductive integrity.

In assessing tumor sterilization, the pathologist must also avoid inadequate sampling. An inadequate post-irradiation examination of a breast carcinoma (taking three or four sections) may yield the astounding information that one out of every four such tumors is sterilized by irradiation. But if 30 sections are taken, this statement might be changed to one out of every 20, or even 50.

Accurate determination of viable cancer is very important in gauging the effectiveness of radiotherapy. If the cancer shows little or no regression in cell structure, and if mitotic figures are present in a biopsy taken several months following the completion of a course of radiation therapy, then the tumor is viable. If the tumor area shows fibrosis, necrosis and only scattered remnants of cells with naked nuclei and absent cytoplasm, then the tumor has been sterilized and is no longer viable (Figs. 21 and 22). In some instances, tumors may show bizarre nuclei and some cytologic alterations and it is impossible to determine the viability of these cells. In irradiated squamous cell carcinomas of various sites, viable tumor cells are often totally absent and are replaced by large amounts of keratin surrounded by a foreign body giant cell reaction. This is interpreted as the result of accelerated keratogenesis in the irradiated malignant cells, but it is not known whether it has any prognostic significance.\(^1\)

**Summary**

Most well-differentiated tumors are capable of synthesizing the same products as the normal tissues from which they arise. However, the term “functioning tumor” usually refers to endocrine or non-endocrine tumors that produce hormones. Pathologic examination of functioning tumors requires fresh tissue that can be examined immediately after excision by electron microscopy, histochemistry, immunohistochemistry, and biochemical assay.
When tumors spread by direct invasion, they follow the path of least resistance so that certain structures will temporarily prevent local spread. Cancer may also be directly implanted by manipulation of the primary tumor. Biopsy and subsequent surgery should be planned so that possible areas of implantation (e.g., the tract of needle biopsy) will be excised with the tumor. Cancer of certain sites carries a very high risk of implantation and in these instances it might be better not to perform biopsy before surgery. The cancer surgeon must always take appropriate precautions against the possibility of tumor implantation in skin grafting and at suture lines.

The lymphatics are the most common pathway of cancer spread and careful

| TABLE 2 | TUMOR RADIOSensitivity* |
|---------|-------------------------|
| **High** | **Moderate** |
| GERM CELL | EPIDERMOID CARCINOMA |
| Ovarian dysgerminoma | Skin |
| Testicular seminoma | Upper respiratory tract |
| HEMATOPOIETIC | Upper digestive tract |
| Hodgkin's disease | Cervix & vagina |
| Non-Hodgkin's lymphoma | ADENOCARCINOMA |
| Leukemic infiltrates | Breast |
| Plasma cell myeloma | Uterus |
| EMBRYONAL | Prostate |
| Wilms' tumor | Salivary glands |
| Retinoblastoma | TRANSITIONAL CELL CARCINOMA |
| Neuroblastoma | Bladder |
| Embryonal rhabdomyosarcoma | **Poor** |
| **Mild** | BONE AND SOFT TISSUE TUMORS |
| SOME BONE AND SOFT TISSUE SARCOMAS | (other than mentioned) |
| Chondrosarcoma | Osteosarcoma |
| Liposarcoma | Malignant melanoma |
| Fibrosarcoma | Malignant gliomas |
| ADENOCARCINOMA | Malignant schwannoma |
| Stomach | Colon |
| Pancreas | Kidney |

*Courtesy of Dr. Carlos A. Perez, Washington U. School of Medicine, St. Louis, Mo.
dissection and microscopic examination of lymph nodes is very important in determining prognosis. Even the experienced cancer surgeon cannot evaluate involved nodes by palpation alone.

Vein invasion is a major mechanism of cancer spread and can be the most important single prognostic indication in certain types of cancer. Gross evidence of vein invasion is infrequent and microscopic evidence must be based on attachment of tumor to the wall of the vein rather than on the presence of tumor cells alone.

The pathologist has a definite role in cancer radiotherapy and chemotherapy. These forms of cancer treatment should not be instituted until the tumor has been examined microscopically. The pathologist is also responsible for establishing criteria of radiosensitivity of a given type of tumor and assessing the effect of irradiation. There are three rules the pathologist uses to gauge the success of radiotherapy:

1. Study should be delayed until the therapy has taken effect.
2. The pathologist must be sure that tissue samples are adequate for accurate post-irradiation examination.
3. Extreme care is necessary in determining the viability of irradiated tumor cells.
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