Early Cancer

PREVENTION · DETECTION · COURSE · TREATMENT

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Preface

THE PHYSICIAN MIGHT BOAST about the smallest cancer he diagnoses just as the fisherman boasts about the biggest fish he catches. Such angling, we can say with Isaak Walton, "has a world of other blessings attending upon it."

This book is intended to further increase the physician's skill in detecting early cancer as well as to further his knowledge of its treatment.

I am aware that the term "early cancer" is not easily defined. Its use in this book includes the beginning cancer and the localized cancer, even though the latter may have been present for a considerable time. To complete the clinical picture of early cancer, it has been necessary to mention the important characteristics and the clinical course of the more advanced lesions. In those sites where it is impossible to detect early cancer, the stage at which tumors cause the first noticeable symptom is described. A discussion of benign tumors has been included where these tumors may be confused with malignant ones.

I wish to stress two important advances in cancer control which have come into general use:

1. The widespread use of the "Pap" test for the diagnosis of early cancer.
2. The use of cobalt^{60} teletherapy in place of high voltage roentgen therapy for the treatment of cancer.

Most of the material presented is based on my personal experience and beliefs with which, I am sure, others may differ. In any case, the rewards of an awareness of the prevention and early detection of cancer are indisputable.

I wish to thank my loyal friends Mrs. Fanny Fink, the late Mary Cohen, and the Queens Borough New York Lodge of B.P.O. Elks, who have encouraged me through the years.

LEONARD B. GOLDMAN

Cancer Control Commandments

1. Circumcise at birth to prevent cancer of the penis, and to reduce the incidence of cancer of the cervix and prostate.
2. Eliminate smoking to reduce the incidence of cancer of the respiratory tract.
3. Biopsy every persistent ulcerated lesion.
4. Do not cut into a non-ulcerated tumor for a biopsy specimen unless the entire tumor is subsequently to be removed.
5. Regard every lump in the breast as malignant until proved benign.
6. Suspect an altering nevus.
7. Think of cancer first if blood appears in the sputum or urine, or comes from the rectum.
8. Exclude malignancy before treating hoarseness, cough, indigestion and constipation.
9. Treat endocervicitis to prevent cancer of the cervix.
10. Prepare to treat for cancer if vaginal bleeding appears after menopause.
11. Include a "Pap" smear of the vaginal secretions when doing physical examinations of women.
12. Complete the physical with digital, rectal and proctoscopic examination.

Contents

1. General Considerations

DIAGNOSIS OF CANCER

CANCER IS A GENERAL TERM which includes a group of diseases that have in common a malignant growth of cells. This growth, if not eradicated, usually spreads to form secondary growths, and impairs the function of the body. The development of a cancer depends upon a variety of cancer producing agents, varying mainly with the location of the growth. A cancer may take many years to develop, depending largely on the immunological resistance of the host and local tissues, and on the intensity of the carcinogenic agent. Ordinarily, a malignant growth remains localized in the beginning—the early cancer.

The earliest recognizable stage of cancer is the carcinoma in situ. This localized growth of cancer cells is characterized by an absence of stromal invasion. The in situ cancer may remain almost stationary, may regress and disappear entirely, or may develop into an invasive tumor. Whether or not all cancers pass through an in situ stage is open to question since an experimentally induced cancer ordinarily is not preceded by an in situ stage.

The in situ cancer may be multiple and may occasionally extend superficially to involve a large area without becoming invasive.

The vast majority of carcinomas in situ are so small that they are not visible grossly. However, when larger than a few millimeters, the surface lesion usually has the appearance of a dull red, superficial ulceration.

Metastases from an in situ lesion are practically unknown so that simple complete excision or destruction is the preferred method of treatment. Radical methods of treatment are unjustified if associated invasion is not present.

In their beginning many cancers can be detected before symptoms appear. Hence, a periodic medical examination is the best method of hunting out an early cancer. When symptoms caused by a cancer do appear, they are generally the most common symptom of the organ involved: mouth—a sore; larynx—hoarseness; lung—cough; stomach—indigestion; cervix—discharge and vaginal bleeding. Ordinarily, pain and loss of weight do not appear until the cancer is advanced.

Cancers which arise on exposed surfaces have a similar appearance. The minute cancer is a small, irregular ulceration, often reddish. Growth may be outward to form the everting type, or inward, to form the infiltrating type. The outwardly growing cancer becomes raised and irregularly ulcerated; the inwardly growing cancer infiltrates the tissue, and the margin of the ulceration often becomes indurated. A cancer which arises in the depth of an organ is usually firm, nodular and non-tender, often indistinguishable from a benign enlargement. With growth of the malignant nodule a more diffuse induration and irregularity occurs.

If cancer is suspected, a "wait and see" decision is contraindicated. Rather,

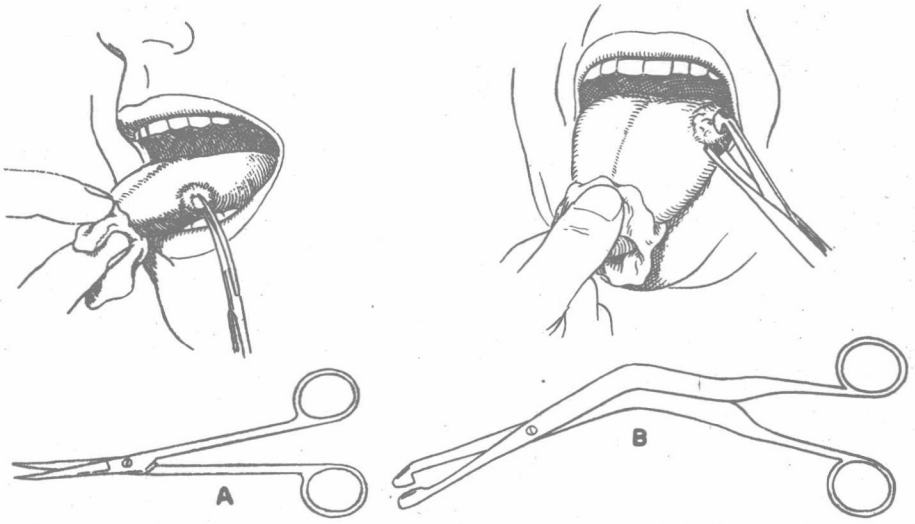

Fig. 1. Cutting method of obtaining biopsy specimen. *(a)* Using scissors. *(b)* Using punch biopsy forceps.

a biopsy specimen should be taken from every suspected growth! A report negative for malignancy and non-specific for another disease should not be accepted as final; a repeat biopsy should be done if the suspected lesion persists.

Methods of Obtaining Biopsy Specimens

1. *Cutting Method.* A small sharp scissors (fig. 1*a*) or scalpel is used to remove a biopsy specimen from ulcerated growths on the skin, lips, anterior portion of the mouth, penis, vulva and anus. The specimen should be taken from the most typical and accessible portion of the tumor, cutting towards or into the base, rather than shaving off the surface. A cutting punch forceps (fig. 1*b*) is used for an ulcerated growth presenting in a cavity: posterior mouth, pharynx, larynx, and cervix; and through an endoscope for inaccessible lesions: bronchus, esophagus, stomach, bladder, rectum and sigmoid. Slight bleeding from cutting into the tumor can generally be stopped easily with gauze pressure or packing. Rarely is a hemostatic sponge or cauterization necessary to stop the bleeding. Electrosurgery should seldom be employed to obtain a biopsy specimen, because charring may make histologic interpretation unsatisfactory.

2. *Excisional Biopsy.* An excisional biopsy specimen should include the entire lesion and a margin of normal tissue on all sides. In excising a small skin cancer, especially about the face, unually only 2 or 3 mm. of normal tissue need be included beyond the gross lesion. In a quiescent pigmented nevus only 1 mm. or so of adjacent tissue need be removed with the lesion. However, a lesion suspected of being a malignant melanoma should be removed as widely as possible.

3. *Aspiration Biopsy Method.* An aspiration biopsy is the removal of cells

and minute tissue fragments or fluid by means of syringe suction. This method may be useful in diagnosing non-ulcerated tumors, especially breast cancer, enlarged lymph nodes, cysts, soft tissue sarcomas and bone tumors. The usual technic is to insert a large bore needle through the skin and intervening tissue into the tumor. Negative pressure is then applied until tissue fragments or fluid are withdrawn. The aspirated material may be smeared on a slide and stained or prepared for conventional histological examination.

4. *Closed Punch Method.* The closed punch biopsy method (fig. 2) may also be used to obtain tissue from non-ulcerated growths. This technic has the advantage over the aspiration biopsy method in that a core of tissue is usually obtained.

The punch or aspiration method is superior to cutting into non-ulcerated tumors for a biopsy specimen as subsequent surgery or irradiation, if necessary, will not be interfered with and the possibility of spreading the tumor is lessened. However, in the group of malignant lymphomas the aspiration or punch method of obtaining a specimen is unsatisfactory since histologic diagnosis in these entities is unreliable unless made from an entire lymph node.

When using the closed punch biopsy technic, a minute nick in the skin is made before introducing the punch so that a fragment of the skin is not caught in the punch. The Silverman biopsy punch needle, as modified by Goldman, is generally used. A negative microscopic diagnosis on tissue obtained from a tumor clinically suspected of malignancy should not be accepted as final.

Whenever possible, the aspiration or the closed punch biopsy method should be employed to diagnose non-ulcerated tumors suspected of malignancy. This method avoids the need for cutting into a tumor—with its many dangers. Also, should radical surgery be necessary, the procedure can be planned. Should irradiation be necessary, skin damage is obviated and irradiation can be begun immediately.

5. *Sponge Method.* In the sponge method, a gelatin or cellulose sponge is used to obtain a biopsy specimen from ulcerated growths, especially where cutting is awkward: on the nasal septum or within a mouth closed by trismus. A 1 x 1 cm. piece of sponge is held in a forceps and pressed against the most typical part of the ulceration for about 20 seconds and then rubbed over the entire ulcerated surface. The sponge absorbs particles of tissue, tissue juice and cells. The sponge method is simple and has the advantage of gathering tumor cells from various portions of the ulceration. However, this method is not as accurate as the cutting method.

Specimens obtained by cutting, punch and sponge methods should be immediately placed in 10 per cent formalin solution so that autolysis does not occur. If special stains are to be done, the specimen should be placed in Zenker's solution.

6. *Cytologic Method.* In the cytologic method a smear is made from secretions, washings or superficial scrapings of tissue. The adequacy of a specimen should be determined not only on the basis of the number of cells present, but as to whether the cells characteristic for the site of a suspected malignant lesion are found. For example, a sputum smear may be considered inadequate if bronchial epithelial cells and "dust cells" are not seen.

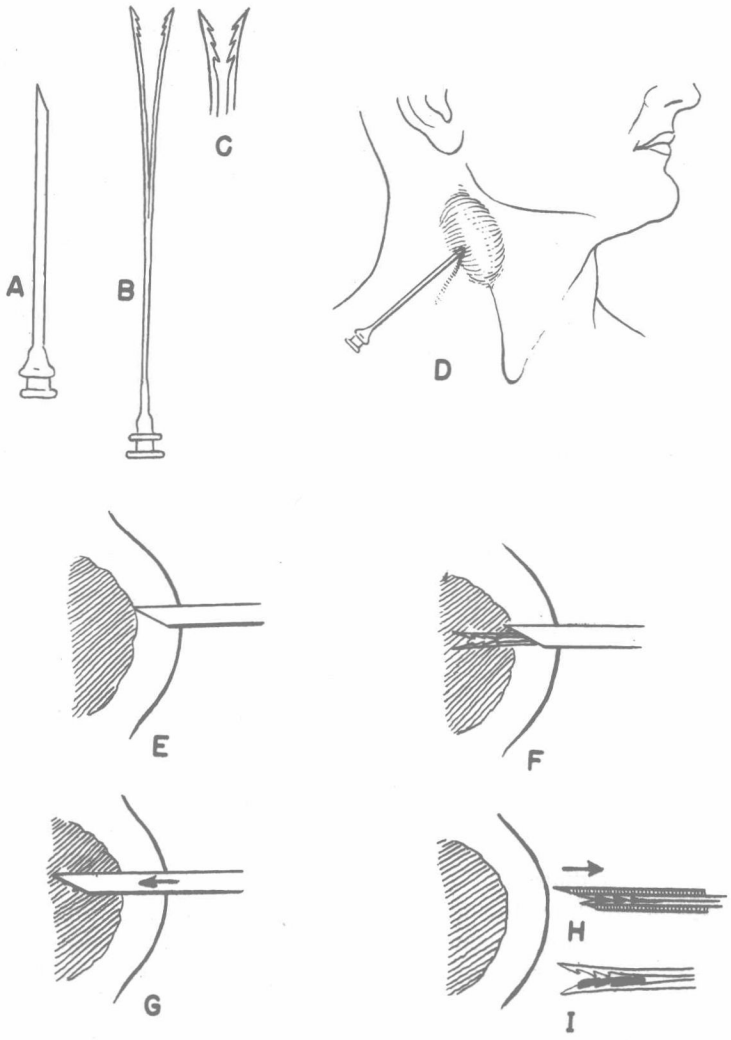

Fig. 2. Aspiration method of obtaining biopsy specimen—Silverman aspiration biopsy needle as modified by Goldman. *(a)* Outer needle, *(b)* split inner needle, 2 cm. longer than outer needle, *(c)* magnified end of split needle to show fish gills, *(d)* following a local anesthetic, a nick is made in skin with a small blade scalpel, and outer needle introduced, *(e)* outer needle advanced up to the tumor, *(f)* inner needle passed through outer needle as far as it will go, *(g)* outer needle advanced over inner needle for 2 cm., *(h)* both needles withdrawn, and *(i)* inner needle containing tissue.

The main value of the cytologic method is in screening *apparently healthy* women for early cancer of the cervix and endometrium. The cytologic method is also extremely valuable in diagnosing bronchogenic cancer by finding cancer cells in coughed-up sputum. Exfoliated cancer cells can also be found in the centrifuged sediment of fluid aspirated from cavities, so that the cause of the effusion can often be determined.

To increase the accuracy of the cytological method, care should be given to the collecting of the material, the smearing of it and the preparation of the slide. When material for a smear is taken to detect a uterine cancer, the patient should abstain from a tub bath or a douche for at least 48 hours. The smear is taken before the digital pelvic examination is done, and the speculum is wetted rather than lubricated.

The material is usually obtained by introducing a dry glass suction pipette, with pressure on the rubber bulb, into the posterior fornix of the vagina. Pressure on the bulb is then released and the suction produced aspirates vaginal fluid with its cellular content. The tip of the tube is moved from one side of the fornix to the other so that all parts are sampled.

The vaginal material is spread upon a slide and a thin smear is made. The slide is immersed immediately in alcohol-ether solution for a minimum of 15 minutes.

Material for a cervical smear may be obtained with a cotton-tipped applicator, or a wooden spatula, preferably from the region of the squamo-columnar junction, or from any area of the cervix which appears suspicious.

To obtain material for an endocervical or endometrial smear, secretions are aspirated from the endocervical canal or the endometrial cavity, by means of a cannula. Smears are then prepared from the aspirated fluid and fixed immediately in alcohol-ether.

After fixation, the cytological smear is covered with 2 or 3 drops of glycerin, and without allowing the slide to dry another clear slide is placed on the smear for protection. The two slides are then fastened together with a rubber band.

An annual cytological examination of the cervico-vaginal secretions is adequate to detect practically all uterine cancers in an early symptomless stage. However, the potential rate of error is 10 per cent. The chief causes of error are: inadequate material obtained, smears taken after the use of lubricating jelly, chronic infection, post-radiation changes, post-cauterization changes, and drying and improper staining of the smear.

The result of an exfoliative cytologic test may be reported in four categories:

1. **The material submitted is inadequate.**
2. **No evidence of cancer is seen.**
3. **Cells suspected of being cancer are seen.**
4. **Cancer cells are seen.**

Many cytologists use the original Papanicolaou classification:

Class	*Interpretation*
I	**No evidence of a malignant neoplasm; no atypical cells.**
II	**Atypical cells present but no evidence of malignant neoplasm.**
III	**Cells present causing suspicion of malignant neoplasm.**
IV	**Fairly conclusive evidence of malignant neoplasm.**
V	**Conclusive evidence of malignant neoplasm.**

The cytologic method supplements but does not replace the cutting method so that, if an ulceration is seen, a biopsy specimen should also be taken. As chronic inflammation or previous irradiation may cause cytological changes which may be indistinguishable from cancer, a diagnosis of cancer made by the cytologic method should be confirmed whenever possible by tissue diagnosis.

Occasionally, a diagnosis of cancer is made by presumption. For instance, if a primary cancer is controlled and an enlarged, hard, non-tender lymph node appears in the regional lymphatic area, the node is presumed to contain cancer and is removed with the regional lymph nodes in a block.

If a node is removed for biopsy, its capsule should be intact so that seeding is prevented; also, the node should be removed uncrushed so that its architectural pattern is not disturbed for histologic study.

Sometimes, a biopsy cannot be obtained before operation, and at operation the diagnosis is not certain from the gross appearance of the tumor. A frozen section should then be done and a diagnosis of malignancy made before radical surgery is begun. However, frozen section interpretation is unreliable in diagnosing certain tumors, such as low grade thyroid cancer, well-differentiated prostatic cancer, malignant melanoma and the lymphoblastomas. Radical surgery for these tumors may have to await a paraffin section diagnosis.

If the clinical and histologic diagnoses of cancer do not agree, the histologic diagnosis should not be considered final. An occasional mishap may occur to the specimen: the histology may be misinterpreted, the tissue block may be cut tangentially distorting the tumor pattern, the tumor may not be included in the section or the specimen may even be interchanged with another.

Histologic examination of a cancer may include its grading—the degree of differentiation of the tumor. However, the histologic grading of a cancer is of limited value, chiefly because parts of the tumor may vary in grading and because of the great unpredictability of malignant tumors. Generally, however, the more undifferentiated or the higher the grade of tumor, the more rapid is its growth and the greater the chance of local, regional and distant spread. While an undifferentiated cancer may spread rapidly, the tumor usually responds to irradiation better than a low grade cancer. For this reason, histologic grading has prognostic limitations. The main value of grading is in the choice of the type of therapy. As a rule, if there is a choice of treatment, a differentiated tumor is best treated by surgery, while an undifferentiated one is best irradiated.

A research laboratory method of identifying tumors, especially certain specific types, is the use of tissue culture. Tissue cells when cultivated in vitro may grow more distinctively than in the body, so that tissue culture may aid in the diagnosis of many tumors, especially liposarcomas, rhabdomyosarcomas, mesotheliomas and other ambiguous growths of the somatic soft parts.

The diagnosis of cancer should be made from an interpretation of all the facts: clinical, laboratory, radiologic and histologic.

TREATMENT OF CANCER

Equally as important as the early diagnosis of cancer is its adequate treatment. The basis of adequate treatment is the training and experience built

chiefly on a knowledge of tumor pathology, tumor surgery and the radioresponsiveness of growths.

Should surgery or irradiation be used to remove a cancer? If a cancer can be eradicated equally well by surgery or irradiation, the choice of the modality to be employed depends upon the skill of the particular surgeon or radiation therapist. The surgical treatment of cancer has the advantage that radiation changes are avoided, but the disadvantage that with failure, salvage is difficult by irradiation. The irradiation treatment of cancer has the advantage of better preservation of function, and the added benefit that if irradiation fails, surgery can ordinarily still be used effectively.

Surgery is generally indicated for differentiated epithelial tumors, for tumors which arise in somatic mesoderm, and for tumors which invade muscle, cartilage or bone. Irradiation is ordinarily used for poorly differentiated epithelial tumors and for those growths which are generalized or metastasize readily. However, if surgery is to be done for cancer that metastasizes or seeds readily, preoperative irradiation should be used first.

METHOD OF TREATMENT

Type	*Tissue Origin of Tumor*	*Histologic Differentiation*	*Tumor Bed*
Surgery	From somatic mesoderm: soft tissue sarcomas, bone sarcomas	Differentiated epithelial tumors: adeno, mucogenic, colloid and pigmented carcinomas. Scirrhous carcinomas, squamous-cell carcinomas, grades 1 and 2.	Tumors invading muscle, cartilage or bone
Irradiation	From myeloblasts or lymphoblasts: leukemias, lymphoblastomas	Poorly differentiated epithelial tumors: basal cell and anaplastic carcinomas. Squamous-cell carcinomas, grades 2, 3 and 4.	Lymphoid tissue bed: cancer of nasopharynx and base of tongue

CANCER SURGERY

Cancer surgery is different from other types of surgery. The results of faulty general surgery usually can be remedied by nature, drugs or reoperation, whereas faulty cancer surgery generally means recurrence and failure.

The surgical removal of a cancer generally is indicated only when the gross tumor can be amply removed. If a cancer is movable, surgery is generally successful; on the other hand, if a cancer or an organ containing a cancer is fixed, surgery generally is unsuccessful.

Successful cancer surgery depends principally on removing the tumor en bloc, that is, a cancer beneath the surface should not be seen during surgery —the tumor should be removed with surrounding tissue as if the tumor were in an envelope.

In addition to the possibility of leaving residual cancer, a major problem of cancer surgery is local and distant seeding. Generally, adenocarcinoma cells, especially of the papillary type, seed readily. On the other hand, squamous-

cell cancer, especially of the differentiated type, seeds poorly. Therefore, a major consideration in removing a malignant growth is the spread or implantation of cancer either from cutting into the tumor, or from the spilling or shedding of cancer cells. Cutting into the tumor can be prevented by resecting it well beyond its margin and by rarely doing an incisional biopsy. Subsequent surgery should completely encompass any biopsy wound or aspiration site.

To prevent spilling or shedding of cancer cells into the operative wound, an organ (uterus) or part of an organ (colon) removed for cancer should first be made drainage-proof so that cancer cells cannot leak out. The removal line is then mechanically and chemically cleansed of possible tumor cells so that possible implantation is prevented. As an example, before removing the uterus for cancer of the endometrium, the lips of the cervix are sutured tightly together and the vagina douched to remove any shed cancer cells. Then, at operation both Fallopian tubes are ligatured so that the tumor is mechanically contained within the removed specimen.

In most instances adequate cancer surgery should include removal of the regional lymph nodes in a block and in continuity with the primary lesion whenever possible. However, excision of the primary tumor alone is considered adequate when the cancer is superficial.

As apparently encapsulated tumors such as those of the parotid, thyroid and breast may be malignant, they should not be enucleated but should be removed completely, together with a margin of normal tissue. If the tumor is within a gland, the tumor should be removed, whenever possible, by removing the gland or by removing an anatomical portion of the gland, such as a lobe,

If surgery is indicated for a cancer of doubtful operability, irradiation should be given first. Preoperative irradiation will not only shrink the tumor and devitalize its cells but may occasionally cause its complete disappearance.

Continuous pain, a fixed mass or organ, overlying dilated veins and lymphedema are the most common indications of inoperability. Occasionally, however, a tumor causing distressing discharges or toxic absorptive products should be removed even if it has metastasized.

RADIATION THERAPY OF CANCER

The most common forms of irradiation used for treating cancer are:

1. **Cobalt^{60} teletherapy (fig. 3), or its equivalent, supervoltage roentgen therapy (fig. 4).**
2. **High voltage roentgen therapy (200–250 kv).**
3. **Low voltage roentgen therapy (100–125 kv).**
4. **Locally applied radium.**
5. **Radioisotopes.**

Each form of irradiation has a definite place in the treatment of cancer.

Cobalt^{60} teletherapy or supervoltage roentgen therapy is ordinarily the preferred method of external irradiation for subsurface malignant growths and is particularly indicated for certain deep seated cancers (brain, head and neck, esophagus, lung, and bladder).

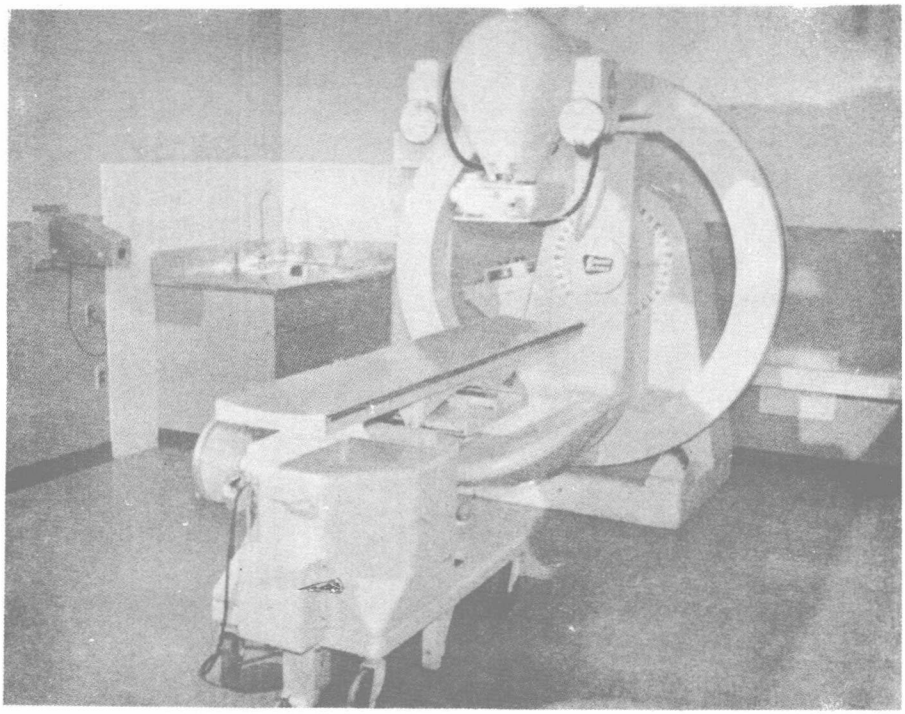

Fig. 3. Rotational Cobalt^{60} Teletherapy Unit at Queens Hospital Center The cobalt^{60} is in the center of the 22 inch lead head. Shutters in the lower part of the head allow the beam to be collimated. The moving head permits the beam to be rotated about the tumor.

The gamma rays given off by a cobalt^{60} teletherapy unit and the roentgen rays produced by a 3 million volt x-ray unit have similar physical characteristics and produce similar biological effects. Of the two, cobalt^{60} therapy is more commonly used since a cobalt^{60} unit is cheaper, and easier to house than a supervoltage unit. The gamma rays given off by cobalt^{60} are also quite similar to those given off by radium; the cost of the radium and its scarcity make its use impractical.

Cobalt^{60} teletherapy has the following advantages over conventional high voltage roentgen therapy:

1. **Increased depth dose.**
2. **Skin sparing effect (maximum ionization occurs beneath the skin instead of on the skin).**
3. **Absorption in bone is the same as in soft tissue.**
4. **Less radiation sickness (the high energy gamma rays scatter less than high voltage roentgen rays).**

ROENTGEN THERAPY

Conventional high voltage roentgen therapy has little place in the treatment of cancer if cobalt^{60} teletherapy or supervoltage roentgen therapy is available.

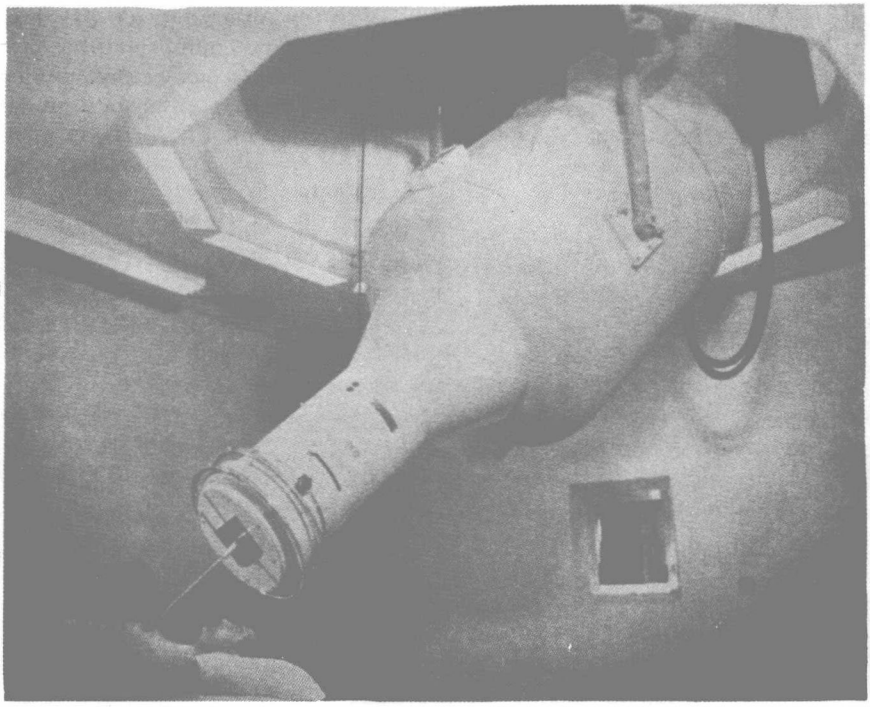

Fig. 4. G. E. two million volt x-ray unit. The unit consists principally of a low-frequency resonance transformer with a co-axially mounted scaled-off multisection x-ray tube within, both contained in a steel tank and insulated with compressed gas. The x-rays are generated at a target mounted in the end of the extension chamber projecting from one end of the tank. (Courtesy General Electric Company and Hospital for Joint Diseases, N. Y. C.)

However, low voltage roentgen therapy is still the preferred method of irradiation for most skin cancers.

Roentgen rays are produced in a vacuum tube having two electrodes: an anode—the target, and a cathode—the filament. When the filament switch is turned on, the filament heats and electrons are given off. By turning on the x-ray switch the target becomes electrically positive and the filament electrically negative. The electrons, attracted to the target (the speed depending upon the voltage), are arrested suddenly by the target, producing roentgen rays of various wave lengths. The higher the voltage, the shorter the wave length produced, and the shorter the wave length, the greater the energy or penetrating power of the rays.

Roentgen rays were measured at first by the erythema produced, but as an erythema depends upon many variables—the color and character of the skin, the age of the patient, and mainly the intensity of the radiant energy, it was impractical as a biological unit of measurement and was replaced by a physical unit of measurement, the roentgen or "r". However, the roentgen is not a true expression of radiation dosage, but is a measure of x-ray exposure and indicates the amount of irradiation in air. A truer expression of absorbed dose or