

PART II

RADIATION THERAPY

INTRODUCTION

A review of the literature for selection in this YEAR BOOK OF RADIOLOGY again emphasizes that radiation therapy is a dynamic specialty. Although this year produced no spectacular advances in the field, many good articles represent substantial scientific progress.

Progress, as reflected in the literature of each year, inches forward in a manner that is continually surprising. Some subjects of early conjecture gradually clarify and resolve themselves into every-day usage. Radioiodine in the treatment of thyroid disease has reached wide acceptance as to indications and methods. Listless reporting of some subjects flares into hot debate to bring long accepted concepts into critical review. The effect of treatment on breast cancer was challenged and defended vigorously in a round table session at the Second National Cancer Conference in Cincinnati, in March 1952. This subject was opened by Park and Lees in an article reported in this section and its publication drew sharp criticism. Other endeavor, that has struggled with seemingly monumental handicaps, gathers momentum and moves strongly toward new appreciation. The supervoltage units that were kept alive in Sunday supplements have achieved technical dependability and, despite the handicap of great cost of procurement and maintenance, are increasing in number and respect.

Impressions concerning the clinical use of so-called "supervoltage" equipment are now beginning to appear for 2,000,000 volt x-ray generators, betatrons and multicurie cobalt 60 and 50 Gm. radium teletherapy units. Information is confined largely to technics of treatment, dosage data and immediate results. The articles by Watson and Smith are of particular interest because the authors make some guarded predictions as to the usefulness and effect of the cobalt 60 units. A proper restraint is exercised by these and other authors in evaluating or predicting the effect of supervoltage radiation, so that only pallid conjecture is offered in answer to the earnest question as to the altered outlook for cancer patients. This is very understandable because of the fiendish torture that certain sections of the popular press regularly inflict upon cancer patients, their relatives and the concerned medical personnel, with their garbled accounts of each new effort in this field of therapy.

High energy radiation of the types now becoming more widely available labors under the additional handicap of the very term "supervoltage," which sometimes gives the impression that "super-effects" are to be expected. It might be well at this time to take stock of the possibilities and limitations of radiation of any energy level. The results of treatment will depend on the material selected for treatment. For most

centers, there is small likelihood that large numbers of early or potentially curable cancers will be referred for radiation therapy of this type. If the patients treated are those whose lesions are not suitable for surgery by virtue of inaccessibility, or inoperability due to invasion or metastases, as carcinoma of the lung, little effect on cure or survival rates is to be expected. Improved methods of local treatment, whether surgical or radiologic, cannot affect cure rates or survival rates when failure results from distant metastases already present at the time of treatment. Nevertheless such patients can benefit from the use of high energy radiation because the complications of treatment can be so appreciably reduced. Complications will not be reduced if this quality of radiation is considered an invitation to explore higher and higher dosages in search of the cancerocidal level.

The benefit of this type of radiation lies in this feature. Among any 100 consecutive patients with advanced cancer of a given type, there will be a small number who will benefit materially from radiotherapy, but these patients cannot be recognized and selected before treatment. If all patients could be offered adequate treatment and yet suffer no undesirable sequelae, while a few obtain positive benefit, then supervoltage radiation would play a valuable role, if not a dramatically different one. Radiation of any quality produces its effect by injury to tumor tissue, and its application is limited by the tolerance of the individual both locally and generally. An absolute change in the outlook for cancer patients as a result of higher energy radiation should not be anticipated. If the best of present results can be equaled, while eliminating to a large extent the hazards of radiation injury, the use of supervoltage will have been justified. This may seem a modest return on the scientific and economic effort that has so greatly increased the complexity of radiotherapy. No more can be expected as long as a generalized disease must be treated by only local measures, no matter how effective. Perhaps this advance may be compared with the situation about 1919, when 200 kv. therapy became generally available. It soon became recognized that so-called "deep therapy" contributed more than anything had previously. Gradual conversion to this higher voltage therapy was inevitable because of engineering and technical advances which put it within the reach of more institutions and radiologists.

Continuing interest is shown in the treatment of the common types of cancer (head and neck, cervix, breast, etc.) the radiologist encounters. Further studies were made on the wider use of radioactive materials such as the interstitial insertion of radioactive colloidal gold in the treatment of cancer of the prostate, on the relationship of ACTH and cortisone reaction and on the effects of total body irradiation. Basic research in radiobiology and in radiation physics, and a variety of new devices were developed. Results of grid and rotational technics were reported from several clinics.

An important contribution to the latest fundamental concepts of radiation effects on living systems appeared in June 1952.* It is a

*Nickson, J. J. (ed.): *Symposium on Radiobiology* (New York: John Wiley & Sons, Inc., 1952).

report of the paper and discussions presented at a symposium on radiobiology held at Oberlin College in June 1950. The meeting was sponsored by the Sub-committee on Radiobiology of the Committee on Nuclear Science of the National Research Council, assisted by the Atomic Energy Commission and the Office of Naval Research. It was an attempt to direct thought toward the solution of problems currently existing in the field of radiobiology and to point out major gaps in our present knowledge that seem susceptible of investigative attack. The essays deal with four phases of radiobiology: (1) a survey of physical interaction of ionizing radiation and matter; (2) an explanation of the chemical changes arising from the transfer of physical energy; (3) an examination of the biochemical effects; (4) a discussion of the changes occurring in living tissue.

Reported unusual late complications of heavy postoperative irradiation of testicular neoplasms proved to be instances of osteogenic sarcoma (one of which was of rare extraskeletal origin) of the lumbar spine.

Again we are grateful for the co-operation of the staff of the publishers.

—H. W. J.
—V. P. C.

HEAD AND NECK

Roentgen Therapy of Primary Neoplasms of Brain. Results of postoperative irradiation are reported by Jacob R. Fried and Leo M. Davidoff¹ (Montefiore Hosp., New York City). Treatment was principally by a single protracted course of irradiation but some patients received multiple short courses. Factors were: 200 kv., half-value layer 1.5 mm. Cu at 50 cm. target-skin distance, or 400 kv., half-value layer 4 mm. Cu, target-skin distance 70 cm. Three portals were usually used, location depending on site of tumor; size of field varied from 6×8 cm. for frontal ports to 8×10 or 8×12 cm. for vertex and occipital, and 10×10 to 10×15 cm. for lateral fields. Daily skin dose averaged 200 r; treatments were given daily when the patient's condition permitted, otherwise every other day.

In the series were 30 cases of glioblastoma multiforme. Maximal tumor dose was 11,961 r, the minimum 1,106 r. Excluding one survival of over 9 years, average survival was 11.4 months. It was concluded that survival was not influenced by the type of operation or the amount or method of postoperative irradiation. Nitrogen mustard was given to four patients without effect.

Radiotherapy was of no value in most of 15 patients with cerebral astrocytoma. Response was better in six with cerebellar astrocytoma. Average survival following operation was 29.7 months in cerebral, and 6.8 years in cerebellar tumors. In medulloblastoma (six cases) the cerebrospinal axis was also irradiated. Average survival was 28.3 months; longer survival appeared to be related to higher doses (5,500 r tumor dose). Of three patients with spongioblastoma polare, none responded to therapy; of three with meningeal sarcoma, one responded well.

Four patients had cerebellar sarcoma. This relatively new entity may be mistaken for medulloblastoma; as in medulloblastoma, seeding may occur in the spinal dura. Later in the course, however, metastases may appear outside the central nervous system, in other organs, skeletal or lymphatic systems. Roentgen therapy was of palliative value for three of the four patients. One patient with ependymoma survived 11 months after postoperative irradiation.

Value of Ventriculoencephalography in Planning Roentgen Therapy for Brain Tumors. In five cases reported by Eugene P. Pendergrass and John M. Phillips² (Univ. of Pennsylvania), simultaneous use of both procedures gave (1) accurate localization of a tumor or recurrence; (2) evidence of residual disease after operation; (3) evidence of the progress or recession of a tumor after roentgen therapy, and (4) evidence of multiple lesions, as in metastatic carcinoma.

Posterior fossa lesions can be diagnosed if x-rays made in the erect position are carefully compared with those made in the horizontal.

(1) *Radiology* 57:25-36, July, 1951.

(2) *Am. J. Roentgenol.* 66:603-612, October, 1951.

Lateral views in the erect posture are important for study of lesions in the regions of the sphenoidal chiasmatis and middle fossa.

Since a tumor can be accurately localized by this method, small portals can be planned through which radiation can be accurately directed, thus assisting in preventing overirradiation to the normal brain tissue. Factors used in treatment in these cases were: 200 kv., half-value layer 1.1 mm. Cu, 0.5 mm. Cu filter and 50 cm. distance. Portals varied in size from 25 to 80 sq. cm. and in number from three to seven.

Progressive Malignancy and Nevertheless Prolonged Course of a Cerebral Glioma is reported by H. Lill³ (Univ. of Vienna).

Woman, 42, had headache, double vision and vomiting. Neurologic study revealed sixth nerve palsy, increased left-sided reflexes, psychic changes, marked papilledema and some decrease in the left temporal field of vision. Ventriculography confirmed the clinical impression of right frontal tumor. Resection of almost all of the right frontal lobe gave symptomatic relief. The histologic picture was that of microcellular glioblastoma (astrocytoma grade 3, of Kernohan *et al.*). She was given intensive roentgen therapy and remained well for 2½ years. Because of recurrent headache she was then given another course of irradiation. Finally, 6½ years after the first admission, she was rehospitalized for headaches and vomiting and, after a few months, died. Autopsy revealed an edematous and hyperemic brain. Sections showed a tumor which spread back to the right parietal lobe and into the basal ganglions. This was found to be an astrocytoma grade 4 (glioblastoma multiforme).

The prolonged life of this patient could not be attributed to resection. Roentgen therapy was doubtless a factor, but usually such irradiation does not greatly alter the course of cerebral glioma.

Radiation Therapy of Pituitary Diseases is discussed by K. Scharer⁴ (Univ. of Zurich), who also reviews 55 pituitary tumor cases. Of 35 patients with no manifest endocrine disturbances, 14 had unsatisfactory results. Three patients given as little as 3,000 r in air were symptom-free 16-25 years later, indicating the great radiosensitivity of these tumors. Of 19 patients given 7,000-14,000 r in air (which corresponds to 3,500-7,000 r skin dose), 10 were symptom-free for 1-12 years, 2 remained unchanged 4-13 years, 4 showed no improvement because of cystic development (20% of the tumors were cystic), malignancy or long history; in 3 treatment is too recent for evaluation.

Radiation is the treatment of choice for pituitary tumors. In the 17-20% which are degenerated cystic tumors and in which response to irradiation is unsatisfactory, operation can be carried out later without increased risk. To avoid eye damage, the eyes are carefully checked during and after radiation treatment.

Of 20 patients with pituitary tumors who showed endocrine disturbances, 10 improved; response in the rest was unsatisfactory because of malignancy or other reasons. Endocrine symptoms were in no way influenced. Often, hormone therapy was poorly tolerated. Of 16 patients with acromegaly, 10 showed marked improvement after full treatment, their condition remaining unchanged as long as 10 years. Of 11 patients with Cushing's syndrome who had irradiation of the pituitary, more than 50% improved considerably and 30% improved. In seven cases of

(3) Wien. klin. Wchnschr. 63:403-405, June 1, 1952.

(4) Oncologia 4:131-166, 1952.

hypercorticism (pseudohermaphroditism and virilism), treatment gave no good results.

Radium and Surgical Treatment of Retinoblastoma. This malignant growth occurs in about 1 in 34,000 infants. It may affect either eye, and in about 25% of cases both are involved. The first indication is usually a white or yellow reflex in the pupil ("cat's eye"). At this stage, according to Robert E. Fricke, Martin Van Herik and John W. Henderson⁵ (Mayo Clinic), treatment may save vision in the other eye and the patient's life. Pain, glaucoma, congestion and diminished vision follow, with proptosis if there is extraocular extension. If the neoplasm involves one eye only, enucleation is preferred by most surgeons. If the tumor is found early (in the course of routine ophthalmoscopy), enucleation may be avoided and irradiation used. When both eyes are involved the neoplasms are usually of unequal degrees of severity. It may then be possible to remove the eye with the larger mass and irradiate the other. This type of treatment may be tried if the neoplasm is small (less than 2 disk diameters in size and not more than 3 D. in elevation), it is not near the optic nerve, the vitreous is clear and there is no white fundus reflex.

When there is nearly equal ocular involvement, the safest procedure is bilateral enucleation. If irradiation is used, the parents must realize that they share with the surgeon the responsibility for endangering the child's life by extension of the tumor along the optic nerve. Even if irradiation is successful, there is slim likelihood of retention of useful vision. When enucleation is done, as long a section of optic nerve as possible is removed to allow recognition of possible intracranial extension. The tumor should be studied by frozen section before proceeding to removal of the second eye when both are involved. If the optic nerve is invaded, the orbit should be irradiated. If only one eye is removed, the other should be examined three or four times a year for several years so that invasion of the remaining eye can be diagnosed early.

When the tumor is localized radiation therapy is directed toward eradication of the disease and preservation of vision. Radium is preferred by the authors because of ease of administration and high photon energy. It may be applied directly by an intracavitary optic radon applicator. This concave plaque containing radon tubes is sutured against the globe at the exact location of the tumor. If necessary, muscles are sectioned for placement of the applicator and resutured when it is removed. The patient is maintained under light intravenous anesthesia during the few hours of treatment to keep eye movements minimal. Depth of the tumor is estimated. A minimal tumor dose of 2,000 gamma r is given if subsequent external radium therapy is anticipated and 3,500 gamma r if external therapy is not to be used. External radium therapy is given whenever possible; three ports are used to deliver 2,300 gamma r at the center of the optic globe. Interstitial and intracavitary therapy are used postoperatively if invasion of the orbit or optic nerve has been found.

(5) S. Clin. North America. 31:1147-1155, August, 1951.

External therapy is individualized when it is used for palliation in inoperable patients. Generally a second course of external therapy is given three months after the first course to patients who have not undergone operation, even if the prescribed monthly re-examinations indicate regression of the tumor. If it continues to grow, enucleation should be performed.

In 88 cases of retinoblastoma, five year survival rate for surgically treated patients was 50%; for those treated with radium only, 45%. Of 29 patients found at operation to have involvement of the optic nerve, 17 died, 7 survived five or more years and 5 could not be traced. Prognosis for life is good if symptoms have not been present for over four months when treatment is begun; beyond this period, it becomes poorer rapidly.

[A statement of the amount of useful vision obtained by this method would have added to the value of this article. Successful results may also be obtained by precision roentgen therapy as practiced by Reese, Merriam and Martin (*Am. J. Opth.* 32:175-190, February, 1949).—Eds.]

Irradiation of Retinoblastoma: (Glioma Retinae). H. B. Stallard⁶ (London) reviews records of 29 unselected patients (16 treated with 2 mc. radon seeds and 13 with curved radium disks), 5 patients treated with radon seeds, 17 patients from the literature and 8 patients treated with radium needles in Manchester. He concludes that, when a third or less of the retina is involved in a retinoblastoma, it may be destroyed by irradiation. If half the retina is involved, results are poor. In advanced cases the eye and 10 mm. of optic nerve were excised; post-operative irradiation was unsuccessful. The dose is empiric; 2,500-3,000 r at the summit of the lesion and 6,000-8,000 r at the base is generally effective. Radium disks made to fit the scleral curvature evenly are the best form of treatment. Although deep x-ray is good in some cases with less than a third of the retina involved, it has the disadvantage of prolonged treatment, difficulty of immobilizing the child and highest incidence of complications. In comparable cases, results of treatment with radon seeds and radium disks were appreciably better than with deep x-rays.

Orbital X-ray Therapy of Progressive Exophthalmos. Arthur Jones⁷ (St. Bartholomew's Hosp., London) treated 22 patients with progressive exophthalmos (malignant in 2) and 7 with thyrotoxic ophthalmopathy. Progressive exophthalmos is usually found in middle-aged males, and males are affected in a greater proportion than in exophthalmic goiter. It may arise spontaneously or after thyroidectomy. Progressive exophthalmos may be unilateral or bilateral, and is associated with orbital and periorbital edema. External ophthalmoplegia is present due to the mechanical effects of the exophthalmos. Thyroidectomy or thiouracil was necessary in only 3 of the 22 patients. Nontoxic goiters were present in three others. There is lower thyroid uptake of I¹³¹ than in exophthalmic goiter. The pathologic changes are pronounced enlargement of extraocular muscles, with round cell infiltration, and edema of orbital fat and connective tissues, which may lead to fibrosis.

(6) *Lancet* 1:1046-1049, May 24, 1952.

(7) *Brit. J. Radiol.* 24:637-646, December, 1951.

The rationale for orbital x-ray therapy is the fact that the infiltrating cells are of the type regarded as highly radiosensitive and irradiation has been known to resolve chronic inflammatory reactions elsewhere in the body. In this series factors used were: 190-250 kv., 15 ma., half-value layer 1.3-1.85 mm. Cu, focus-skin distance 25-60 mm. Fields were mainly lateral and anterior orbital. The anterior was 8×6 cm. and the lateral 4×6 cm. In severe cases no attempt was made to protect the lens; in mild cases a lead shield was used over the cornea with the anterior field. Dose was 50-200 r daily. In bilateral cases one of four fields was treated daily; in unilateral, treatment was given twice a week. Optimal field dose appeared to be 200-400 r given in four to six weeks for mild to moderate cases and up to 900 r in frank malignant exophthalmos. The dose received by the pituitary is too small to make it likely that it is a factor in the therapy.

Malignant exophthalmos receded in the two patients. Of the 20 patients with chronic progressive exophthalmos, regression was complete or nearly so in 9 and slight in 7. The seven patients with thyrotoxic exophthalmos seemed prone to radiation conjunctivitis and only three had some decrease in exophthalmos. In only 1 of the 29 patients irradiated did cataracts develop. This occurred 18 months after therapy and may be related to senility.

[See the 1951 YEAR BOOK, pp. 262 f., for comparison of results in the different types of exophthalmos. Our results have not been good in so-called "thyrotoxic exophthalmos."—Eds.]

Results of Beta Radiation in Ophthalmology: Report of 123 Cases is presented by Manousos A. Petrohelos⁸ (Univ. of Michigan).

METHOD.—The eye was anesthetized with 0.5% pontocaine[®] and an applicator was applied in direct contact to the area to be treated. The applicator contained 10 mg. radium over an area of 1 sq. cm. and had a 0.2 mm. thick Monel metal filter. Dosage rate at the surface of the applicator is approximately 125 rep. Total dose depended on response to treatment.

The mode of action of beta radiation in keratitis is not well known. According to the literature, beta and grenz rays increase the antibody reaction in the cornea.

Therapy was given to 95 patients with various types of keratitis. Of these, 4 (4.21%) were healed; 69 (72.6%) showed improvement, 22 (23.2%) did not. In 56 patients (59%), vision improved to two or more lines; in 36 (37.9%) vision was maintained, and in 3 (3.16%) vision decreased.

Beta radiation was best for vascularized and recurrent pterygiums and episcleritis; five patients with severe and long-standing vernal conjunctivitis were relatively insensitive to irradiation. Corneal dystrophies and lupus erythematosus were not benefited. The older the lesion, the more intensive the treatment required.

Some Experiences in Management of Cancer of Middle Ear and Mastoid are reviewed by Walter L. Mattick and John W. Mattick⁹ (Roswell Park Memorial Inst., Buffalo, N. Y.). Of 10 cases of intrinsic ear carcinoma, 8 were squamous cell epitheliomas and 2 were glomus jugulare tumors, originally diagnosed angioendothelioma and xanthomatous polyp respectively. The intrinsic lesions comprised 1.5% of all

(8) Am. J. Ophth. 35:637-644. May (pt. 1), 1952.

(9) A.M.A. Arch. Otolaryng. 53:610-621. June, 1951.

cancers around the ear. Clinical evidence was hearing loss, otorrhea, pain and bleeding from ear canal.

Roentgenograms of mastoid and petrous bone showed no distinctive changes to establish an early diagnosis. In one patient there was destruction of bone; of the other nine, cloudiness and poor aeration of the affected mastoid were reported in five, sclerosis in four and poor cell outline in three. Roentgenograms were of more help in recording progress of established disease.

Treatment of choice was surgical ablation followed by intracavitary gamma irradiation until the wound was almost healed. The amount varied from 200 mc.-hr. in 0.3 mm. Au applied in the mastoid cavity to 540 mc.-hr. radium in 0.6 mm. Pt. This was followed by external x-ray therapy with either 200 or 400 kv. applied to full skin tolerance.

Of the eight patients with squamous cell carcinoma of middle ear and mastoid, two have survived five years or more and are free from disease. Of the two with glomus jugulare tumor, one patient has been free from recurrence for over five years; the other, who refused operation, is well but has had evidence of tumor for over eight years.

Treatment of Oral Cancer by Combination of Radiotherapy and Surgery. In 1929-45, Harold Wookey, Clifford Ash, W. Keith Welsh and R. A. Mustard¹ (Toronto Gen'l Hosp.) treated 1,128 patients with cancer of the lip, 342 with cancer of the tongue and 497 with lesions

FIVE YEAR SURVIVAL IN CARCINOMA OF LIP

STAGE	No.	% NET SURVIVAL	% GROSS SURVIVAL
I	690	93.9	65.1
II	290	81.4	54.1
III	116	66.2	43.9
IV	32	7.7	6.3
Total	1,128	85.1	58.4

FIVE YEAR SURVIVAL IN CARCINOMA OF TONGUE

STAGE	No.	% NET SURVIVAL	% GROSS SURVIVAL
I	55	81.0	61.8
II	114	55.4	44.7
III	121	26.9	23.1
IV	52	4.1	3.8
Total	342	40.1	33.6

FIVE YEAR SURVIVAL IN ORAL CARCINOMA (EXCLUDING LIP AND TONGUE)

STAGE	No.	% NET SURVIVAL	% GROSS SURVIVAL
I	81	74.2	56.8
II	154	50.4	39.6
III	169	29.2	25.4
IV	93	8.9	8.6
Total	497	37.6	31.8

in other sites in the oral cavity. Results are shown in the tables. The net survivals exclude patients who could not be traced and those who died of extraneous disease. In 5.4% of patients, cancer developed in some other region of the body after treatment.

In general, treatment of the primary lesion is a radiologic problem.

(1) Ann. Surg. 134:529-540, October, 1951.

Involvement of lymph nodes or bone is an indication for surgery. In only 13% of the patients with cancer of the lip were the lymph nodes involved, whereas in the rest the incidence was 60%. Therefore, in cancer of the lip, dissection of the lymph nodes is no longer done prophylactically. In the other forms of oral cancer, prophylactic dissection seems justified, particularly in the younger age group. When lymph nodes are involved, the primary lesion is irradiated and as soon as possible afterward neck dissection is done. If involvement of the lymph nodes is extensive but the patient is considered operable, dissection of the neck is done first and then the primary lesion is irradiated. When operation is impossible, roentgen therapy is given as a palliative measure.

Control of Inoperable Oral Cancer with Massive Roentgen Therapy. George White and William R. Christensen² (Pondville State Cancer Hosp., Walpole, Mass.) treated 63 patients.

TECHNIC.—One intraoral and three external ports were used. Average diameter of the intraoral port was 4 cm. Intraorally, 6,000 r (in air) was given, 400 r a day for 15 days. Two lateral ports, 6 × 8 cm. to 8 × 10 cm., and a submental port about 5 cm. in diameter were used for lesions in or about the midline. When a lesion was unilateral, the contralateral port was omitted. Treatment was given through the intraoral port and one external port daily. Factors were: intraoral port—250 kv., 15 ma., 0.5 mm. Cu plus 1.0 mm. Al filter, 40 cm. distance, 400 r a day; external ports—250 kv., 15 ma., 0.5 mm.

COMPARISON OF CONVENTIONAL AND MASSIVE ROENTGEN THERAPY

	UNDER 7,000 r	OVER 7,000 r
No. patients treated	55	63
Av. tumor dose.....	4,100 r	9,500 r
Persistent or recurrent disease — 1 yr.....	36	16
Persistent or recurrent disease — 1-3 yr.....	2	0
Dead — 1 yr., no local recurrence	11	12
Dead — 1-3 yr., no local recurrence.....	5	10
Living — 1-3 yr., no local recurrence.....	0	12
Living — over 3 yr., no local recurrence	1	13
Sequelae (radiation ulcer, osteitis or both).....	1	14

Cu plus 1.0 mm. Al filter, 50 cm. distance, 200 r at each treatment. A total of 3,000 r to each external field was set as a limit to allow for separate treatment of nodes. Tumor dose was 9,000-12,000 r in 30 days. The patient was hospitalized for therapy and released when he could eat properly.

Results in the 63 patients given massive roentgen therapy were compared with those in a previous group of 55 patients who received conventional x-ray therapy (see table). Delivery of tumor dosages in the low therapeutic range resulted in an immediate recurrence or persistence rate of well over 50%. On the contrary, the massive tumor dose effected excellent control. Recurrence rates for the high and low dosage groups were 30 and 85%. Of the 63 patients, 25 were still alive with no evidence of the primary lesion. The control group showed only six patients in whom the primary lesion had been controlled. With massive therapy, the greater assurance of control of the primary lesion allows earlier treatment of metastatic neck nodes.

[If the groups of patients treated by "conventional" and "massive" roentgen therapy are comparable, there has been a considerable improvement in survival for the

(2) New England J. Med. 245:719-723, Nov. 8, 1951.

more heavily treated patients. There is a high incidence of radiation sequelae in this group, but it is possible that this could be reduced by careful treatment planning. Multiple portal technic, particularly with intraoral cones, are apt to develop "hot spots" that are unsuspected unless dose distribution diagrams are drawn up.—Eds.]

Plasma Cell Tumors of Mouth and Upper Air Passages. Maurice R. Ewing and Frank W. Foote, Jr.,³ report on 27 patients seen at Memorial Hospital, New York City, between 1936 and 1950, who had histologically confirmed plasma cell tumors involving the mouth or upper air passages. These were divided into three groups. Group 1 consisted of nine patients with a single lesion of multiple myeloma. Group 2 consisted of seven patients with plasmacytoma confined to the soft tissues. Group 3 consisted of 11 patients with an initially solitary lesion and evidence of bone involvement.

Group 1 patients were treated for systemic disease; x-ray controlled pain in one patient. Seven died; one was alive after 5 years, and one, a practicing physician, still alive after 10 years, controls his scattered lesions with x-ray therapy.

In group 2, three patients had surgery; one had surgery and irradiation, and three had irradiation alone. Of those treated with x-rays alone, only one had a possible cure. One patient was untraced; two were disease-free 4 and 2½ years later. One patient died of other causes, and one patient died of multiple myeloma four years after diagnosis.

In group 3, three patients were treated by excision, two had surgery and irradiation and six had irradiation alone. Two patients could not be traced; four died, one from extension and one from myeloma; three were alive and well, and two were treated too recently to be assessed.

Nasopharyngeal Radium Treatment: Follow-up Study of 263 Patients. Walter E. Loch and Newton D. Fischer⁴ (Johns Hopkins Univ.) made an effort to contact all patients treated at least five years before the study; 177 returned questionnaires and 85 were actually re-examined. Earlier patients were treated with a radon applicator screened with gold 1 mm. thick; for the past 10 years, a 0.3 mm. stainless steel radium applicator was used.

No late detrimental effects attributable to radium application were found in any of the patients re-examined 3-29 years after treatment. A small amount of lymphoid tissue in the nasopharynx found in about two thirds of the patients indicates that the recommended dosage fulfils the requirement not to destroy or remove all lymphoid tissue but to relieve symptoms in selected cases. The eustachian tubes were not overgrown with lymphoid tissue in any of the patients which indicates that radium treatment effectively retards growth of adenoid tissue in this area. The best results were obtained in patients whose symptoms were due to infected lymphoid tissue and mechanical interference with function of the eustachian tubes. In 25 patients there was 100% improvement in hearing loss due to conduction difficulties; 9 patients had 75% and 2 patients had 25% improvement. In 20 patients with otosclerosis, there was no hearing change; 3 patients felt worse. The object

(3) *Cancer* 5:499-513, May, 1952.

(4) *Ann. Otol., Rhin. & Laryng.* 61:198-205, March, 1952.

of treatment in otosclerosis is to help protect residual hearing and prevent further loss. In cases of perceptive deafness, 1 patient was 100% improved, 1, 75% improved, 31 were unchanged and 1 worse. In mixed deafness, one patient was 75% improved and one patient was made worse.

Radium Treatment of Adenoid Remnants (Crowe-Burnam Method). The term "adenoid remnants" designates the entire mucosa, i.e., the epithelium with its glandular system and underlying lymphoid follicles. J. Moulinard⁵ discusses the manner in which beta rays act and the safety margin in the usual dosage.

A characteristic of the Burnam applicator is its ability to measure dosage on the basis of the time it is applied to the surface being treated. Thus one minute of application equals 370 rep. Judiciously used, beta rays have a wide margin of safety: a weak dose will cause evident reaction, but reaction to a dose 10 times as strong will still be harmless. The same principle applies to depth of dose: a few minutes of application is effective at 3 mm. depth, and with tenfold increase the reaction is limited to 3 mm. In practice, maximal effect is in the epithelium, although the highly radiosensitive underlying lymphoid tissue is also affected.

In the usual doses, the Crowe-Burnam method can be used even for the youngest patients because of its wide margin of safety. It cannot replace curettage, when a large mass of tissue is to be removed, or medication, for diffuse lesions, or radiotherapy, for lesions in the eustachian tubes; but it is indispensable for reducing pathologic processes inaccessible to other therapy. In some instances it may supplement x-ray therapy. Despite its harmless appearance, the Burnam applicator contains 50 mg. radium with only slight filtration; it is the most potent form of radium at one's disposal and should be handled most cautiously by the radiologist and his assistants, for whom it presents real danger.

[A French view of the value and use of the controversial nasopharyngeal beta-gamma applicator, with its dangers stressed.—Eds.]

Roentgen Therapy of Carcinoma of Larynx. F. Baclesse⁶ (Univ. of Paris) reports results with roentgen therapy as sole treatment in 333 patients (1919-46). Of 290 treated during 1919-44, 61 (21%) remained free from disease for five or more years. Of 201 treated during 1919-39, 34 (17%) survived at least 13 years. Of 132 treated during 1940-46, 49 (37%) were well three to nine years later. On the basis of number of patients in earlier groups with late recurrence or with secondary cancer in another organ, 4-5% reduction in survival rate can be foreseen for the last group. This gives a projected survival rate of approximately 32% for patients treated by more modern technics.

Modern technic requires use of small fields, strictly adapted to the topography of the lesion. Tumor doses above the conventional 5,000 r have proved most effective, particularly for extensive lesions and best survival rates result from fractionation of the dose over six to eight

(5) *Ann. oto-laryng.* 68:72-89, January, 1951.

(6) *J. Fac. Radiologists* 3:3-12, July, 1951.

weeks. Antibiotic therapy is important, especially for patients with extensive lesions. It is concluded that improved results are due to improved quality of x-ray treatment.

Functional Results and Permanence of Cure Following Roentgen Therapy of Intralaryngeal Carcinomas in 153 patients are reviewed by Jens Nielsen⁷ (Radium Center, Copenhagen). The following classification by stages was used: I, growths which may be considered operable by laryngofissure and extirpation of the affected vocal cords; II, those which require at least special extended technics of laryngofissure and excision; III, those judged operable by total laryngectomy or hemilaryngectomy; IV, those inoperable or borderline with invasion beyond the limits of the larynx proper, either because of direct growth or metastases to the cervical lymph nodes.

Of 18 patients with stage I carcinoma, 16 (89%) were symptom free five or more years after roentgen therapy; of 31 with stage II, 26 (84%); of 52 with stage III, 23 (44%), and of 52 with stage IV, 10 (19%). Over-all five year cure rate was almost 50%. Of 94 patients with carcinoma confined to the vocal cords, 60 (64%) survived five years.

On the basis of these cases, Nielsen decided on the following treatment policy. Patients with stage I or II lesions should be given roentgen therapy primarily, because the percentage of cures obtained seems to be of the same high order and permanence as those obtained with surgery; functional results are considerably better, and in case of recurrence the chance of doing laryngectomy without major postoperative complications is still good. For the same reasons, radiotherapy is preferred principally in stage III cases; furthermore, the cure rate is 50%. In controversial cases, radiation therapy should be tested. When a stage IV lesion originates in the vestibular area, irradiation is preferred; when it originates from the vocal cords and subglottis, laryngectomy, eventually with lymph node extirpation, followed by irradiation, is indicated.

Nielsen concluded that roentgen therapy can cure a considerable number of patients, with an excellent functional result and comparatively few lasting complications, provided the necessary time is taken for observation and treatment. If radiotherapy is unsuccessful, surgery may still be possible. In certain stages and localizations, surgery is preferred, i.e., for subglottic cancers and those with total or almost total fixation of the cords by the carcinoma.

Roentgen Therapy for Cancer of Larynx. William Harris⁸ (Mount Sinai Hosp., New York City) reports results in 128 patients treated between 1931 and 1946. Roentgen therapy was the primary method used. All patients were studied by the laryngologists first and closely observed by them during treatment and follow-up, so that recurrence or persistent disease could be detected early and surgery performed.

Grossly the tumors were classified as intrinsic or extrinsic. The former included lesions arising from the free edge of the false cord, ventricles, true cords, anterior and posterior commissures and sub-

(7) *J. Fac. Radiologists* 3:29-34, July, 1951.

(8) *Ibid.*, pp. 35-39.

glottic area. Extrinsic lesions included those in the epiglottis, aryepiglottic folds, arytenoids, false cords above the free borders, pyriform sinuses and postcricoid areas.

Among 54 of 67 patients with intrinsic tumor who were followed, relative five year cure rate was 72% and absolute rate 58%. Among 53 of 61 with extrinsic tumor who were followed, relative five year cure rate was 41% and absolute rate 36%.

Results with radiotherapy seemed to indicate that risk to the patient's life is not greater than with surgery and that many patients will survive with larynx intact and without loss of voice. Surgery following failure with roentgen therapy is safe and feasible. Early detection of failures with radiotherapy and use of radical surgery in properly selected cases should significantly increase the salvage rate.

Roentgen Therapy of Cancer of Larynx. Felix E. Leborgne⁹ (Inst. of Radiology and Cancer Center, Montevideo) treated 122 patients in 1933-44. In five, laryngectomy was necessary due to failure of x-ray therapy. When the results of roentgen therapy with or without surgery are evaluated, five year cure rate was 31.1% (38 patients); when the results of roentgen therapy alone are evaluated, 27.5% (33 patients). A variation of protracted fractionated technic was used.

TECHNIC.—The smallest possible volume of tissue was irradiated. If there was no lymphadenopathy and the growth was on the vocal cord, therapy was restricted to the larynx. If the vestibule was involved, radical roentgen therapy, including irradiation of the larynx and lymph area, was used. The laryngeal lesion was treated first; after cure, a prophylactic course of therapy was given to the lymph drainage area. If therapy failed, the patient was operated upon immediately. If there was lymphadenopathy, the nodes in some patients were treated together with the primary tumor.

Dosage was based on clinical evaluation. Limits of tolerance of the larynx are: 5,000 r in 21 days; 5,500 in 30 days; 6,000 in 43 days; 6,500 in 58 days. Two lateral fields, or fields arranged so that the central ray was normal to the thyroid ala and separated by 5 cm., were used. They were 3 × 4 cm. or 4 × 5 cm. Voltage was 180-450 kv. (quality equivalent to half-value layer of 1 mm. Cu seemed enough). Dosage rate was 4-60 r/minute. Duration of treatment was 30-60 days.

As complications of roentgen therapy, 2 patients had laryngeal obstruction and 10 necrosis.

Carcinoma of Larynx: III. X-ray Therapy. L. H. Garland¹ (San Francisco) reports on his experience in over 130 patients with cancer of the larynx treated with x-rays in 18 years.

TECHNIC.—At first treatment, estimated center of the tumor was marked on the skin on each side of the neck under fluoroscopic guidance with the patient on his side in the position to be occupied on the treatment table. Spot films with small lead markers over the central point are made when necessary. Factors were: 200-250 kv., 15-25 ma., 50-70 cm. distance, half-value layer 1-2 mm. Cu. Most series were started with two opposing 8 or 10 cm. circular beams whose size was reduced during therapy, rarely below 5 cm. diameter. A few large lesions were treated with 10 × 14 cm. fields initially. No scattering material or bolus bags were used. The initial dose was usually 100 r (air) to one lateral field. Treating alternate sides daily, this was increased to 150 r next day and 200 r on the third. Treatment was at 200 r a day to one field for a few days and in some cases 300 r. Treatments were daily, six days a

(9) J. Fac. Radiologists 3:24-28, July, 1951.

(1) Laryngoscope 62:75-89, January, 1952.

week, in many cases to 5,000 r tumor dose. In some cases the mass in the area of the tumor did not disappear until as long as three months after end of therapy.

Of 69 patients given radical radiotherapy for primary cancer of the larynx, 7 did not finish therapy, 23 died of cancer and 13 were well after five or more years. In these patients estimated midtumor dose was from 4,500 r in 30 days to 6,300 r in 52 days. In most cases the dose was about 5,300 r in 35 days (averaging 3,200) in air to each of two opposing lateral neck fields. Early edema or late chondronecrosis can be avoided by graduation of dosage in early stages and avoidance of excessive dosage in later stages.

[Among lesions for which surgery and radiotherapy are both applicable, cancer of larynx is one of the most warmly debated. If the lesion is confined to the larynx, it is surely curable by laryngectomy, but the loss of voice and a permanent tracheostomy represent a greater handicap than even amputation of a limb. Advocates of radiotherapy claim equally good results, and if this could be convincingly demonstrated, limitations might be placed on the indications for surgery. The preceding five articles deal with a total of nearly 900 cases. The five year clinical cure rates are, respectively, 61, 50, 47.7, 27.5 and 19%. Choosing from these statistics there is a figure to support any point of view. There is no reason to think that the discrepancy is due entirely to varying effectiveness of treatment techniques. The probable explanation is in the proportion of early and advanced disease and in the element of selection, apparent or hidden, which varies for each series of patients. It would be helpful if statistical reviews generally would include comment on the racial, social, economic and institutional factors that influence the patients presenting for treatment. -Eds.]

Limited Surgery after Failure of Radiotherapy in Treatment of Carcinoma of Larynx is discussed by Max L. Som² (Mount Sinai Hosp., New York City). Three patients with intrinsic laryngeal tumors and one with an epiglottic neoplasm were given 3,700-3,900 r (measured in air) to each side of the neck over 33 or 34 days. Six weeks to one year later, laryngofissure was done for local recurrence in three patients; transhyoid pharyngotomy with removal of the epiglottis was done in one. All surgery was easily performed and healing was adequate although somewhat retarded. Results showed the immediate efficacy of limited local surgery after failure of initial therapeutic procedures, but a longer follow-up period is necessary before a final evaluation can be made. Preservation of laryngeal function was encouraging.

A fifth patient had unilateral metastatic nodes. After laryngofissure and cure of the primary lesion, followed by a full course of radiotherapy to the neck, radical neck dissection was done. He was free from disease 4½ years after original thyrotomy and had an intact larynx.

[It is encouraging to know that good results can be obtained by limited surgery after radiotherapy fails. This should influence the decision to use radiotherapy as the initial method in borderline cases or when voice preservation is the important consideration. The author's experience shows the feasibility of doing radical neck dissection without disturbing a larynx which was rendered free from disease by thyrotomy or radiotherapy. -Eds.]

Roentgen Rotation Therapy in Cancer of Hypopharynx is reported by Inge Gynning³ (King Gustaf V Jubilee Clinic, Lund). At this center all carcinomas of the esophagus are treated with rotation therapy, and the method has been extended to lesions in the hypopharynx when the tumor does not extend below the seventh cervical vertebra and there is no evidence of metastasis.

(2) *Ann. Otol., Rhin. & Laryng.* 60:695-703, September, 1951.

(3) *Acta radiol.* 35:443-448, May-June, 1951.

The patient is rotated in the erect position before a stationary beam. Factors are: 165 kv., half-value layer 0.85 mm. Cu, axis of rotation-focus distance 53 cm. The lesion is localized by fluoroscopic control, and the tumor dose is measured by ionization chambers placed in series in the tumor. Of five patients treated, two had local recurrence, apparently the result of inadequate tumor dose. Two have survived seven years without recurrence, and one died of severe local radiation reaction.

A tumor dose of 5,200 r in 26 days with an average daily tumor dose not exceeding 200 r is recommended.

Radioiodine Studies in Thyroiditis. William M. McConahey and F. Raymond Keating, Jr.⁴ (Mayo Clinic) performed tracer studies on 21 patients with acute diffuse thyroiditis, 13 with struma lymphomatosa and 6 with struma fibrosa.

METHOD.—Tracer doses of 100 or 300 μc . I^{131} with 100 μg . sodium iodide as a carrier were given orally to the patients in the fasting state. Counts were made over the thyroid at 24 or 48 hours and urinary excretion of I^{131} was determined. From the curve of urinary excretion, two rates were estimated: (1) renal excretion rate, the proportional rate at which inorganic radioiodide is removed by the kidneys, and (2) extrarenal disposal rate, the proportional rate at which radioiodide is being removed by all tissues other than the kidneys.

In the patients with acute diffuse thyroiditis, uptake was less than that of normal persons. The 48 hour excretion was greater than normal. Extrarenal disposal rate was less than normal in most cases. The results suggest that acute diffuse thyroiditis interferes with iodine accumulation in the thyroid. However, liberation of thyroid hormone from the thyroid is normal or possibly increased, as was inferred from the patients' clinical condition, BMR and serum precipitable iodine level.

Most patients with struma lymphomatosa showed normal counts, including five myxedematous ones. In most, 48 hour urinary excretion of I^{131} , extrarenal disposal and renal excretion rates were normal. In patients with struma fibrosa, both iodine uptake by the thyroid and urinary excretion were normal. Extrarenal disposal rate was low.

It was concluded that in these conditions I^{131} uptake is not a measure of secretion of thyroid hormone.

Studies with Radioiodine: Treatment of Patients with Hyperthyroidism by I^{131} . Earl R. Miller, Morris E. Dailey, Mayo H. Soley, Nadine Foreman, A. V. Holmes, George L. Alexander and Glenn E. Sheline⁵ (Univ. of California) treated 100 patients. Twenty-three had mild, 48 moderate, 25 severe and 4 undecided degrees of hyperthyroidism. Dose is not directly related to severity of hyperthyroidism, and must be calculated from the relation between size and uptake of the thyroid. In this series an effort was made to give each patient an initial dose of 6,000 beta rep.

METHOD.—A test dose of 100 μc . I^{131} was given orally. Uptake was determined at one, three and six hours and daily for at least four days. Correlation of the uptake curve and gland weight determined the therapeutic dose. It was given orally and another uptake curve determined. Six weeks later a repeat uptake curve was drawn. Retreatment was given if necessary, followed by a similar procedure at 12 weeks.

(4) J. Clin. Endocrinol. 11:1116-1122, October, 1951.

(5) Radiology 57:227-233, August, 1951.

Remission was obtained in 89 patients. Except for hypothyroidism in 10, treatment had no untoward effect.

[Other workers (1951 YEAR BOOK, pp. 255-257) have had results similar to these among the first 100 consecutive cases at the University of California Hospital.—Eds.]

Responses to Radioactive Iodine Therapy in Hyperthyroidism, with Special Reference to Cardiac Problems. Farahe Maloof and Earle M. Chapman⁶ (Harvard Med. School) evaluate the response in 47 thyrocardiac patients among 330 hyperthyroid patients treated with I¹³¹. Dosage was 160 μ c. I¹³¹ (half-life eight days) per estimated gram of tissue, based on an average uptake of 70%. No patient was given more than three doses, and the largest single dose was 15 mc. The largest total dose given was 40.4 mc. No patient was made worse by treatment. Total dose was determined by graphic integration of the dose rate. There was no constant relationship among number of roentgens equivalent physical delivered, biologic half-period, and response (see table).

Radioactive iodine caused abnormal cardiac rhythm to revert to

RELATION OF ESTIMATED RADIATION TO THYROID, BIOLOGIC HALF-PERIOD AND RESPONSE OF EIGHT PATIENTS TREATED WITH I¹³¹

AGE	SEX	EST. WT. OF THYROID, GM.	RADIOACTIVE IODINE				RESPONSE
			Dose, Mc.	48 Hr. Excretion, %	Biol. Half-Period, Days	Est. Radiation to Thyroid, Rep.	
34	F	100.0	10.0	8.0	33.5	11,700	Euthyroid in 2 mo.
55	M	65.0	9.0	8.0	50.0	13,600	No response
29	M	30.0	5.0	25.0	13.0	11,000	Moderate response—still toxic and needed 2d dose
32	F	50.0	8.0	19.0	9.7	15,800	Euthyroid in 3 mo.
54	F	40.0	7.0	11.0	14.1	21,800	Euthyroid in 2 mo.
48	F	75.0	10.0	5.0	13.0	14,800	Euthyroid in 4 mo.
50	F	70.0	10.0	28.0	23.8	6,900	Good response: BMR + 12%, 21 mo. later
74	F	65.0	12.0	27.0	50.0	15,500	Euthyroid in 3 mo.

normal without use of quinidine. Continued auricular fibrillation after administration of I¹³¹ indicates either continued thyrotoxicosis or severe organic heart disease, which usually requires digitalis and other measures to control cardiac failure.

The authors conclude that I¹³¹ is useful in treatment of thyrocardiac patients. However, general medical measures for heart disease should be followed, especially during the period of response, which is usually from two to four months. Because of the possibility of malignant disease being present in nodular goiters and despite the observed good response to I¹³¹, thyroidectomy is advised for most toxic nodular goiters.

Case of Fatal Thyroid Crisis Occurring after Radioactive Iodine Therapy. Rodney B. Nelson, John B. Cavenagh and Arthur Bernstein⁷ (Cook County Hosp.) report the first such fatality.

Philippine man, 44, was hospitalized Sept. 1, 1951, after five weeks of proptosis, weight loss and ankle edema. Appetite was good. He was aware of dyspnea, hand tremor, nervousness and an irregular heart action. Pulse was 126 and irregular, blood pressure 150/70, temperature 98.4 F. and respiratory

(6) J. Clin. Endocrinol. 11:1296-1322, November, 1951.

(7) Illinois M. J. 101:265-268, May, 1952.

rate 24/minute. The eyes had a decided stare with lid lag and the thyroid was enlarged to an estimated 45 Gm. The abdomen was moderately distended and shifting dullness was demonstrated in the flanks. Pitting edema extended up to the groin. Laboratory results were essentially normal. Chest x-ray showed cardiac enlargement. He was treated with digitalis, phenobarbital and bed rest. On September 5, he was given a therapeutic dose of 5 mc. I^{131} . He insisted on going home September 7. On September 12, he reported to the clinic sweaty, tachypneic and with pitting ankle edema. Heart rate was 150 and irregular. He was given Lugol's solution, 10 drops three times a day, and 1 cc. mercurhydrin[®] and instructed to stay in bed until return to the clinic in one week. On September 14, he was brought to the clinic in a preterminal state. Temperature was 103; respiration 40/minute, pulse 140 and blood pressure 90/60. He was treated for shock and with penicillin and died two hours after hospitalization and nine days after receiving radioactive iodine. At autopsy, the thyroid weighed 50 Gm.; high columnar cells lined the acini.

The high grade of thyrotoxicosis and thyrocardiac complications in this patient may have led to thyroid crisis under any therapy. Its occurrence precisely after radioactive iodine therapy, when an increase in thyrotoxic symptoms had been witnessed, makes the association appear significant and indicates that the therapy was a factor. For severe thyrotoxic patients to be treated with radioactive iodine, the authors use compound solution of iodine alone or with propylthiouracil to control toxic symptoms in the two weeks to four months before radiation produces remission; they advise daily observation in the first two weeks. In patients with severe toxicity and limited cardiac reserve, preliminary control with propylthiouracil is advised before starting radioactive iodine.

Radioiodine Treatment of Thyroid Carcinoma. Opinions of a group of investigators who had observed about 300 cases are reported by E. E. Pochin⁸ (Univ. College Hosp., London). Cases should be selected for radioiodine treatment. Anaplastic tumors without demonstrable uptake should be rejected. In differentiated (including papillary) carcinomas thyroidectomy should be done, preferably by surgery, and radioiodine used subsequently only if uptake is then demonstrable; if not, radiotherapy may be needed.

The best criterion of uptake was biopsy when possible with counts and autoradiographs, histology being unreliable. In differentiated tumors with no initial uptake, evidence of uptake followed preliminary thyroidectomy in some cases; however, thyroidectomies done in 18 cases at Manchester were not followed by demonstrable uptake. Metastases with evidence of uptake are usually in bone, rarely in lung.

In a few early lesions thyroidectomy was followed by no demonstrable spread of secondaries. Thyroid surgery in the absence of known metastases should be total for malignant adenoma or for multiple foci in one lobe; hemithyroidectomy may be indicated if there is a single focus only.

Directional counting offers no problems in an isolated metastasis remote from the thyroid. Difficulty occurs with local metastases close to thyroid tissue, but attempts to detect uptake are worth making, using small and well shielded counters and especially scintillation count-

(8) Brit. J. Radiol. 24:461-463, August, 1951.

ers and I¹³⁰. After total thyroidectomy, functioning carcinoma may be detected by use of labeled thyroxin. Discovery of abnormally large percentages of radioiodine unaccounted for by thyroid or urinary content would imply iodine-concentrating tumor tissue.

Maximal safe dose is usually the therapeutic dose. Approximately 100 mc. is given initially with subsequent doses at 3-10 week intervals until uptake no longer occurs. Best evidence of doses being at maximal safe levels is a reduction of white blood cells, especially lymphocytes. The metabolism of a tracer dose can be used to calculate that of a subsequent dose accurately. When no uptake is found following thyroid destruction, trials should be continued for long periods, especially since such patients can be kept on thyroid until the day before the test when thyrotrophic hormone is used. There was evidence that withdrawal of thiouracil treatment will augment uptake of a tumor. Injections of exogenous thyrotrophic hormone increased uptake in metastases, but only temporarily. It was considered more practical to depend on increase of the patient's own thyroid-stimulating hormone produced by thyroidectomy. Thyroidectomy should not be done unless one is prepared to use radioiodine therapy, since thyroidectomy might be followed by rapid growth of metastases.

[This seems to be the best evaluation to date of the proper place of radioiodine in the therapy of malignant thyroid disease. Representatives of the major centers of Europe and America contributed to this symposium, which was an informal discussion of the radioiodine treatment of thyroid cancer which took place during the International Congress of Radiology at London's University College Hospital Medical School in July 1950.—Eds.]

Study and Treatment of 119 Cases of Carcinoma of Thyroid with Radioactive Iodine at Massachusetts General Hospital in six years is reported by Brown M. Dobyns and Farahe Maloof.⁹ The cases studied are classified histologically in the table.

Although follicular adenocarcinomas collect more radioactive iodine than other carcinomas of the thyroid, initial uptake of the isotope in

Follicular	27
Follicular and papillary.....	28
Papillary	22
Anaplastic and solid cellular.....	29
Anaplastic and papillary.....	5
Epidermoid	3
Lymphoma	3
Hürthle cell	2
Total	119

any of the carcinomas and their metastases was decidedly less than that of normal thyroid. However, removal of normal thyroid has resulted in increased uptake of the isotope in some cases, making radioactive iodine more useful particularly in follicular adenocarcinomas containing colloid. After administration of thiouracil (200-400 mg. every eight hours) a further increase in uptake of radioactive iodine was obtained in some instances.

Radioactive iodine therapy was beneficial in 10 of 50 patients who

(9) J. Clin. Endocrinol. 11:1323-1360, November, 1951

had had total thyroidectomy and were known to have metastatic lesions remaining. Of these 10, 6 had follicular adenocarcinoma, 3 mixed follicular and papillary adenocarcinoma and 1 papillary adenocarcinoma. In a few patients with incapacitating metastatic disease, rate of growth has been curtailed and biopsies of some lesions have shown destruction by radiation.

Uptake in rapidly growing anaplastic lesions has not been sufficient to be of therapeutic value. Some papillary lesions, however, have a follicular component and will take up appreciable amounts of radioactive iodine.

A decline in number of circulating lymphocytes of the blood is not uncommon after administration of large doses of radioactive iodine. Although a total dose of 800 mc. in divided doses and 200 mc. in single dose have been given, grave changes in other circulating cellular elements of the blood did not occur.

BREAST

Carcinoma of Breast: Results of Treatment, 1935-42, are presented by C. D. Haagensen and A. P. Stout¹ (Presbyterian Hosp., New York City). The analysis is based on 668 patients with primary disease for whom absolute five year survival rate was 47.2%. Of these, 495 were treated by radical mastectomy; relative five year survival rate was 58.2% and relative five year cure rate 48.7%. In 190 of these patients, disease was limited to the breast; they showed 71% five year clinical cures with 2.6% local recurrence rate. The remaining 305 patients had axillary metastases and showed 34.8% five year clinical cures with 19.3% local recurrence rate. With increasing duration of disease before treatment, incidence of axillary metastases increased but the cure rate did not show the expected fall. The explanation for this is unknown.

Radiation therapy was given prophylactically after radical mastectomy to 165 patients. It did not decrease the incidence of local recurrence or increase the five year clinical cure rate. However, such therapy was given more often in advanced than in early cases. Radiation therapy has been used increasingly for local recurrences and bone metastases, and there is no doubt that in these patients pain is relieved and life prolonged.

Criteria for operability derived from earlier experience were tested in selection of patients in 1935-42. Youth does not contraindicate radical mastectomy. Aged patients can stand a reasonably thorough operation. There is no real difference between the results in young and old. The authors are now inclined to operate if breast carcinoma develops during pregnancy or lactation. Carcinomas of the lower inner quadrant had the highest incidence of local recurrence and lowest cure rate, except for those in the axillary prolongation. Large size alone is not a particularly grave feature, nor is redness of the skin, edema involving less than a third of the

(1) *Ann. Surg.* 134:151-172, August, 1951.

skin of the breast, skin involvement or ulceration, when these features occur singly. Women of all ages, who are in good enough general condition to run the risk of operation, should be treated by radical mastectomy except in the presence of one of the following contraindications: (1) extensive edema of the skin of the breast; (2) satellite nodules in the skin of the breast; (3) intercostal or parasternal tumor nodules; (4) edema of the arm; (5) proved supraclavicular metastases; (6) carcinoma of the inflammatory type; (7) distant metastases; (8) two or more signs of locally advanced carcinoma. Such signs are ulceration of the skin; edema of the skin of limited extent (less than a third of the skin of the breast involved); fixation of the tumor to the chest wall; axillary lymph nodes measuring 2.5 cm. or more in transverse diameter and proved to contain metastases by biopsy, and fixation of axillary lymph nodes to the skin or the deep structures of the axilla and proved to contain metastases by biopsy.

Local recurrence rate decreased and relative and absolute cure rates improved during 1935-42. This improvement is ascribed to three factors: (1) a tendency to rely more on surgery and less on radiation therapy; (2) a tendency to adopt a more radical and more meticulous operative technique, and (3) more critical selection of patients for radical mastectomy.

[The material in this report is analyzed in 44 tables, but in no instance is the statistical significance of the results assessed. The evidence for improvement is a comparison with an earlier article by the same authors covering the period 1915-34 (Haagensen, C. D., and Stout, A. P.; Carcinoma of the breast: Results of treatment. *Ann. Surg.* 116:801, 1942.)

	1915-34	1935-42
Relative 5 yr. clinical cure rate.....	36.1%	48.7%
Absolute 5 yr. clinical cure rate.....	22.2%	38.6%
Relative 5 yr. survival rate.....	41.3%	58.2%
Absolute 5 yr. survival rate.....	25.3%	47.2%

This phenomenal improvement indicates either that revolutionary progress has been made in the treatment of breast cancer or that the two groups of patients are not comparable. To account for this improvement, the authors' analysis of results "suggests" that it has been due to a "tendency" to more radical and meticulous surgery and to less irradiation.

This seems a rather vague formula for the technical advance which would account for so great an alteration in the outlook for the patient with breast cancer. When the operative field of radical mastectomy is limited to the chest wall and axilla, as in this series, it is possible to be more meticulous but it is difficult to be more radical. It has not been shown that postoperative irradiation could cause recurrence in a patient cured by the surgical procedure. The third factor advanced for the improvement in results seems a more cogent one. Selection is necessary and justified in the application of any treatment to cancer, but the improvement in results is statistical rather than clinical. A more critical selection cures no patients in the rejected group. It is not an advance but a retreat to a more defensible position for a treatment of limited therapeutic application.

This article presents a detailed and accurate description of the natural course of breast cancer as seen at the Presbyterian Hospital, New York, in the period 1935-42. —Eds.]

Results of Surgical Treatment of Unilateral Carcinoma of Breast in Women are discussed by Stuart W. Harrington² (Mayo Clinic). The alarming increase in frequency as well as mortality from carcinoma of breast instigated a quinquennial study of factors influencing prognosis and survival. Results of radical surgery are influenced most by the ex-

(2) *J.A.M.A.* 148:1007-1011, Mar. 22, 1952.

tent of malignant involvement at the time of surgery, degree of malignancy of the primary lesion, thoroughness of surgery and the patient's general condition.

Of 7,445 patients who had radical mastectomy between 1910 and 1944, 7,325 were traced. The five year cure rate in 1910-14 was 62.6%, and in 1940-44, 85.5%. The grade of malignancy definitely influences mortality; results show a definite and uniform relationship between operative results and grade of malignancy.

Patients were divided into two groups, those with and those without metastasis to the axillary nodes. They were divided into two further groups, those who did and those who did not have postoperative irradiation; this division dates from 1915, when radiation therapy was instituted. Results for the various five year groups were not uniform or

FIVE YEAR SURVIVAL RATES AFTER RADICAL MASTECTOMY WITH AND WITHOUT POSTOPERATIVE IRRADIATION FOR DIFFERENT FIVE YEAR PERIODS

PERIOD OF OPERATION	WITH IRRADIATION			WITHOUT IRRADIATION			
	No. Traced	No.	%* WITH METASTASIS	No. Traced	No.	%*	
1915-19	361	101	28.0	231	54	23.4	
1920-24	599	141	23.5	60	15	25.0	
1925-29	668	223	33.4	94	25	26.6	
1930-34	562	202	35.9	50	14	28.0	
1935-39	616	255	41.4	46	13	28.3	
1940-44	692	274	39.6	49	18	36.7	
Total	3,498	1,196	34.2	530	139	26.2	
			WITHOUT METASTASIS				
1915-19	163	117	71.8	131	93	71.0	
1920-24	263	182	69.2	97	70	72.2	
1925-29	249	195	78.3	150	113	75.3	
1930-34	286	235	82.2	117	94	80.3	
1935-39	418	340	81.3	171	142	83.0	
1940-44	177	137	77.4	558	492	88.2	
Total	1,556	1,206	77.5	1,224	1,004	82.0	

*Based on patients traced by inquiry as of Jan. 1, 1950. Included in the three year group are only patients who had surgery three or more years before time of inquiry, i.e., 1946 or earlier; the five year group includes only those who had surgery in 1944 or earlier, etc.

consistent (see table), but there was an over-all improvement of about 8% for the group who had irradiation. Of patients without axillary nodal metastases, 82% who did not have irradiation, compared to 77.5% of those who did, were living five years after surgery. The study indicates that results of radical mastectomy in patients without axillary nodal involvement were not improved by postoperative irradiation; in fact, 4.5% more patients not so treated lived five years or longer after surgery. Current practice is to give irradiation if nodal metastasis is found at surgery, unless there are other contraindications, but to withhold it if nodal extension is not found.

[These results are given in relative survival rates, i.e., the percentage of treated patients who survive at any given time. It is regrettable that the absolute survival rate (percentage of all patients seen who survive), was not also given, in conformity with a growing practice in statistical reporting. Such procedure permits an estimation of the degree of selection exercised in the series for more valid comparison with results by other methods in other centers. It is interesting to note that in the series of Haagensen and Stout a relative five year survival rate of 58.2% was attained by more reliance on surgery and less on radiation. For the comparable period of 1935-44 on a basis of 2,727 cases, using routine postoperative radiation in the presence of nodal metastases,

Harrington attained a relative five year survival rate of 61.2%. In comparing these two treatment policies the survival rates are quoted to emphasize their similarity rather than the very slight difference.

In the introduction to his paper, Harrington states that the mortality rate for breast cancer has more than doubled in the years between 1901 and 1948. He then shows that the five year survival rate of 39.7% for the period 1910-14 improved to a value of 62.4% for the period 1940-44. This paradox of increasing mortality rate and increasingly effective treatment is not explained.—Eds.]

Carcinoma of Breast: Results of Treatment in Small General Hospital. John J. Zellinger and George C. Adie³ (New Rochelle, N. Y.) believe general surgeons should not identify their results too closely with those of larger clinics or teaching institutions where surgery is departmentalized.

During 1938-45, 153 patients were seen with breast carcinoma or sarcoma. Ten had undergone surgery elsewhere and were excluded. Most patients (74.2%) were aged 40-70. Incidence in males was 2.8%, which is three times the usual average. Multiparas were affected twice as often as nulliparas. Half the patients were seen within two months after first noticing a lump. The left breast was involved in 50.4% of the patients. The lesion was in the upper half of the breast 3.6 times more often than in the lower half and in the outer half 3.2 times more often than in the inner half.

Radical mastectomy was done on 92 patients. In five years 38 had died of breast carcinoma and 8 of intercurrent disease; 3 were lost to follow-up. Simple mastectomy and local excision were done on 39 patients. Of these, 19 died of carcinoma and 4 of intercurrent disease; 1 was lost to follow-up. X-ray therapy was given locally to 64% of the 143 patients. Four ports are used: (1) anteromedial chest wall, tangentially; (2) anterolateral chest wall, tangentially; (3) supraclavicular and infraclavicular, and (4) the axilla. Factors were: 200-250 kv., 1 mm. Cu and 4 mm. Al filtration, and 50 cm. target-skin distance. Skin dose to each port is 2,400 r, giving a tumor dose of 3,500-3,700 r. Two areas are treated at each visit with 200 r each. Treatment requires six weeks.

Five year survival rate with simple mastectomy was 38.4% and with radical mastectomy 47.8%. It is felt that postoperative x-ray therapy adds to survival results.

Absolute Curability of Cancer of Breast must be distinguished from apparent curability, with five year survival as its standard. W. Wallace Park and James C. Lees⁴ (Edinburgh) have tried to determine rate of absolute curability by (1) investigating whether curability decreases as delay in seeking treatment increases, and (2) determining how far the index of effective treatment depends on growth rate of the individual tumor. Treatment of breast cancer is based on the hypothesis that cure rate increases with early treatment. Supportive evidence is, however, poor. Many series of cases show that breast cancer is chronic in its course, with great variability of survival time. Most series studied have included lower grades of malignancy. Surgically treated tumors tend to be less extensive and to grow more slowly than cancers not so treated. The five year survival index is discredited by Park and Lees because it

(3) *Ann. Surg.* 135:173-183, February, 1952.

(4) *Surg., Gynec. & Obst.* 93:129-152, August, 1951.

does not distinguish between full curability of 5% of cases and 5% curability of all cases. Five year survivals are common in both treated and untreated breast cancers. If any relation exists between curability and delay in seeking treatment, it is at best no more than 5-10%. That is, curability rate may be no more than 10% or may be less or may not exist at all. This does not apply to radical surgery for breast cancer before metastasis. However, it does apply in deciding whether radical surgery gives a better prognosis than nonradical operation or no operation at all, if it is possible that distant metastasis (if it is going to occur) always occurs before operation is performed.

Analysis of 814 cases of breast cancer was made in relation to duration, size of tumor and metastasis. About 60% of patients with diagnosed breast cancer have microscopically detectable axillary metastases at onset of symptoms. There is an increase of up to 15% in metastases over the first three years after onset of symptoms. In only 20-30% of patients do axillary metastases fail to develop during the three years after symptom onset. Measurements indicate that average duration of breast cancer is 8-10 years (ranging from 6 months to longer than natural life expectancy). Increased incidence of axillary metastases, increased delay in treatment and increase in size of tumor are related, but correlations are not definite. Evidence from Harrington's Mayo Clinic series indicates that the proportion between axillary metastases and five year survival rates is secondary, derived from intrinsic malignancy or growth rate of the tumor. Five year survival among those operated on at symptom onset is about 40%; among those operated on three years after, 32.5%, with 7.5% as one measure of maximum apparent curability. Another measure, based on differences between five year survivals of treated and untreated cancers, amounts to 20%. Apparent curability rate can, however, be explained entirely in terms of inherent variability of growth rate of breast cancer.

Park and Lees conclude that treatment appears ineffective in reducing mortality from metastatic spread in breast cancer. Treatment has not been proved to affect five year survival rate; if it is at all effective, increase in over-all five year survival is no more than 5-10%.

[Park and Lees have painfully studied the problem and expressed the opinion that treatment appears to have little effect on the five year survival rate for patients with breast cancer. The effect of their article somewhat resembles the consternation that must have been produced by the exclamation of the child in the fable of the king's magic robe. The king had been sold a wondrous robe which only honest men could see. Understandably, all his realm admired and praised the king's costume until a little child exclaimed, "Why, the king has no clothes on!" The conclusions of this article do not challenge the accuracy of such reports as those of Haagensen and Stout, and Harrington. They do challenge the implication inherent in such compilations, that the survival rates are the result of the treatment, when in fact no effort has been made to determine how survival has been influenced by treatment.—Eds.]

Relation between Dosage Level and Incidence of Recurrence in Postoperative Irradiation for Carcinoma of Breast. P. T. Chopping⁵ (St. Thomas's Hosp., London) discusses 190 cases. There was little difference in the proportions of stage I, II and III growth (1950 Manchester staging). The patients were treated by mastectomy (usually radical), followed by x-ray therapy.

(5) Brit. J. Radiol. 24:401-402, July, 1951.

TECHNIC.—Factors were: 200-250 kv., half-value layer 1.5-1.75 mm. Cu, two opposing glancing fields for the chest wall, usually with a small dose through a third field between these at 140 kv. One anterior supraclavicular and axillary port 10 × 20 cm. was opposed by a posterior port of 10 × 15 cm. Dosage was estimated at two points, one at a depth of 5 cm. from the surface of the anterior applicator near the apex of the axilla and the other at a point of minimal dosage on a line drawn across the chest wall between the centers of the glancing fields. Treatment time was 28 days.

Eighty-four per cent of recurrences were within the first two years after operation, the commonest time being at about 10 months. Table 1 shows that there was little difference among the recurrence rates in the different dosage groups. The high dose groups did a little better, but this was not statistically significant. When grouping was done in relation to

TABLE 1.—GROUPS ACCORDING TO CHEST WALL DOSE

Chest Wall Min.	Under 3,000 r	3,000- 3,499 r	3,500- 3,999 r	4,000 r & over
Approx. skin max.	2,500- 3,000 r	3,500 r	4,000 r	4,400 r
Cases in group	23	31	58	72
Recurrences in treated area	6	7	11	14
% Recurrences	26	23	19	19

TABLE 2.—GROUPS ACCORDING TO AXILLARY APICAL DOSE

Apex Axilla Min.	Under 3,000 r	3,000- 3,499 r	3,500 r & over	Total any dose
Approx. skin max.	3,500 r or less	4,000 r	4,400 r	—
Cases in group	58	58	68	184
Recurrences in treated area	16	12	10	38
% Recurrences	28	21	15	21

the axillary dose (Table 2), results were also better in the high dose group. Nevertheless, this also was not statistically significant. The results, however, suggest that a high dose to the apex of the axilla may be more important than a high dose to the chest wall.

Radiation Therapy in Breast Cancer: Preliminary Report on Application of Technic of McWhirter's Type. Elmer A. Lodmell and Peter R. Brady⁶ (Letterman Army Hosp., San Francisco) treated 12 patients, aged 30-66 (average 49). All stages of the disease were represented. Radical mastectomy was done in four cases, simple mastectomy in six and biopsy in two. All patients were given a tumor dose to the axilla of 2,600-4,020 r and one to the chest wall of 2,600-4,480 r. An attempt was made to give a minimal tumor dose to each area of 3,750 r in 15 treatments over three weeks. Treatment was begun 12-18 days postoperatively and was given through four ports all treated daily (Fig. 330). Factors were: 220 kvp, 15 ma., 0.5 mm. Cu and 1 mm. Al filtration, focus-skin distance 50 cm., half value layer 1.4 mm. Cu.

Although McWhirter recommended a half-value layer of 3.7 mm. Cu, the tumor dose he specified (3,750 r) can be given with a much lower half-value layer and there is the advantage of no serious sequelae. The patients who had undergone radical mastectomy tolerated the dose to

(6) California Med. 75:354-358, November, 1951.

the chest wall less well and had edema of the arm. This suggests that treatment time should be extended beyond three weeks for such patients.

Since McWhirter obtained a five year survival rate of 42.9% with this relatively simple technic, and since all of the authors' patients re-

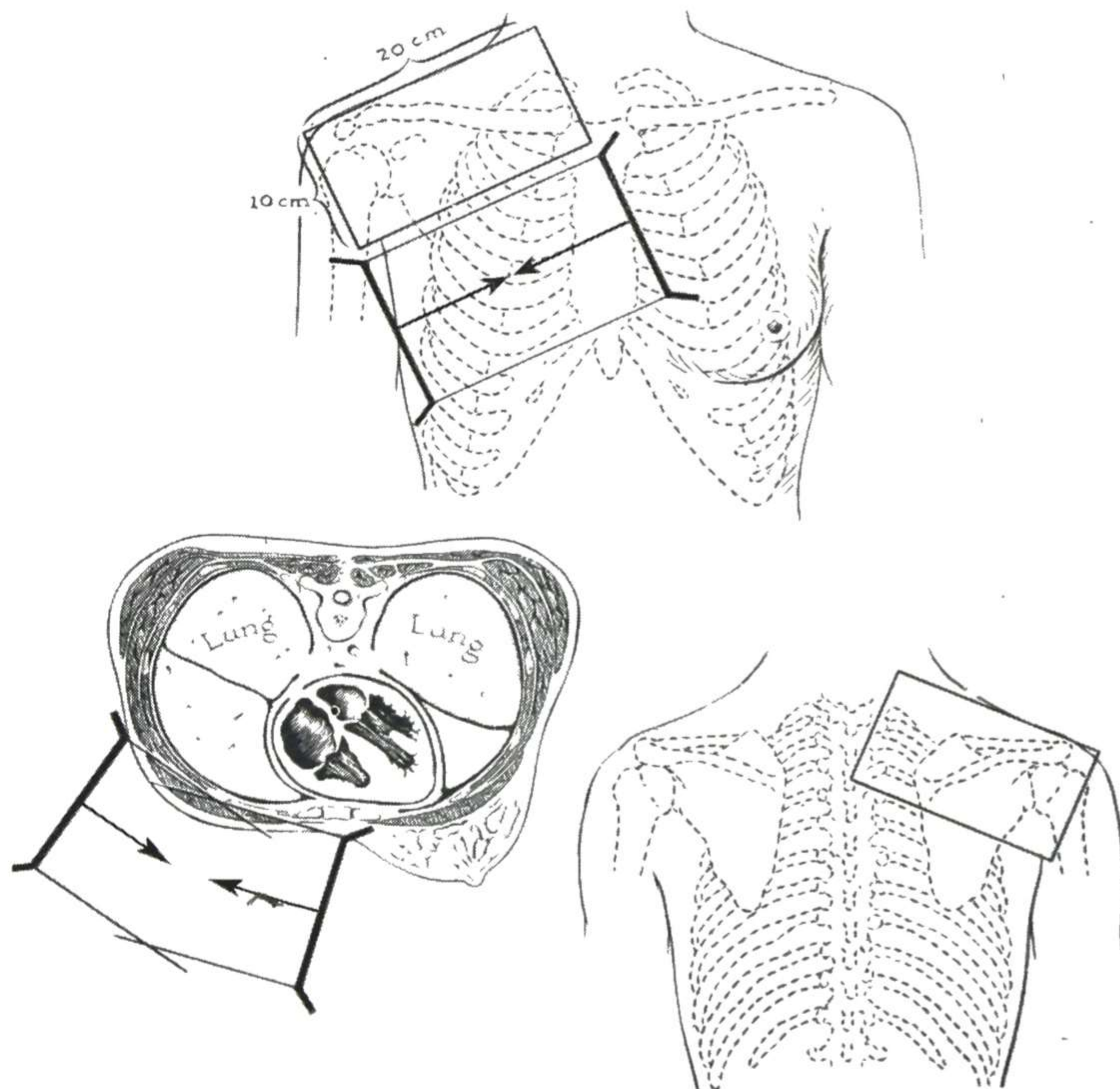


Fig. 330.—Treatment portals used. Bolus bags containing rice were used on tangential fields to chest wall. (Courtesy of Lodmell, E. A., and Brady, P. R.: *California Med.* 75:354-358, November, 1951.)

sponded well except two who died of generalized metastases a few weeks after treatment, the method should receive further trial.

[McWhirter feels strongly that heavy filtration is an essential factor in the results obtained by the technic he has developed (1951 YEAR BOOK, p. 264).—Eds.]

Metastases of Breast Cancer as Related to Various Methods of Treatment. José-Maria Fernandez-Colmeiro⁷ (Curie Found., Paris) made a comparative study of the frequency of metastases in 724 patients with breast cancer, stages I-III, on the basis of treatment. Of the series, 188 were treated by roentgen radiation alone (1936-47), 282 by surgery alone (1927-47) and 254 by combined surgery and radiation (1930-47). The Curie Foundation's classification for the extent of the lesion was adopted: stage I, tumor localized in the breast and movable, less than 5 cm. in size, without extensive adherence to the skin or involvement of axillary lymph nodes; stage II, tumor frankly adherent to the skin but free in the lower plane, measuring more than 5 but less than 7 cm., or with movable axillary lymph node involvement, less than 3 cm. in size

(7) *Bull. Assoc. franç. étude cancer* 38:317-322, 1951.

but clinically cancerous; stage III, tumor extensive or invading the whole breast, fixed in the lower plane or infiltrating the skin, with ulceration, cancerous lymphangitis, nodules, etc., and axillary involvement of more than 3 cm. or fixed. Factors other than clinical extension, such as rapidity of growth, histologic grade, physiologic condition of the mammary gland, age of patient, etc., were not considered. It should be remembered, however, that the most malignant forms of cancer—those which are acute or subacute and those occurring in young women, pregnant women and during the nursing period—are more frequent in the groups treated by roentgen radiation alone or radiation pre- or post-operatively.

Although the number of cases studied is small, it seems that in tumors of the same stage metastases occur with almost equal frequency whether surgery alone, x-rays alone or x-rays followed by surgery are used. The lowest frequency was found among patients treated with x-rays postoperatively. Late metastases are rare. Five instances were seen after 10 years in patients treated by surgery alone or surgery followed by x-ray therapy. Survival time was 16 years. In the same group of patients there were at least 77 proved local recurrences, of which 68 appeared within three years. Roentgen therapy for breast cancer, either alone or preoperatively, does not favor the appearance of distant metastases. It seems probable that they develop before treatment, especially when there is no local recurrence.

Artificial Menopause and Cancer of Breast. A. Hochman⁸ (Rothschild-Hadassah Univ.) induced the menopause in 60 patients by irradiation. Factors were: half-value layer 0.95 mm. Cu, skin-target distance 40 cm., 10 × 10 cm. fields, 350 r to each side four times. The anterior and posterior pelvic fields on one side were treated on alternate days. Patients were considered improved even if alleviation of symptoms was only subjective.

Improvement was noted in 56% of the patients. Beneficial results showed no clearcut correlation with designated stages of disease, probably due to uncertainty of classification. Bone metastases responded well, those of the lungs and pleura less favorably. Skin metastases and local recurrences were even less sensitive. Metastases in the lymph nodes showed little response, and those of the liver and brain showed no improvement. Improvement usually lasted only 1½-2 years. This may be due to the fact that artificial menopause is only temporary or incomplete.

Irradiation of the ovaries is particularly effective in typical adenocarcinoma of the breast and relatively ineffective in anaplastic carcinoma. This may be explained by the fact that adenocarcinoma has a functional resemblance to the original gland. It may be expected, therefore, that the estrogenic substance which has a stimulating action on the normal cell of the mammary gland had to some extent the same effect on the transformed cancerous cell of typical adenocarcinoma. When the hormone is withdrawn as a result of irradiation, the tumor cell is deprived of an important enhancing factor.

⁸ J. Fac. Radiologists 3:199-202, January, 1952.

Investigation of Effect of X-Radiation on Localization of Radioactive Phosphorus in Breast Tumors. F. Ellis, Cornelia Hoch-Ligeti and R. Oliver⁹ (London Hosp.) investigated the relative uptake by mammary carcinoma and by normal breast tissue of intravenously injected radio-phosphorus. Since a standard end-window Geiger-Müller tube was used for detection in vivo, only tumors attached to the skin were studied. Much greater counting rates were noted over tumor tissue and over the breast containing tumor than over corresponding sites on the normal breast. The exponential disappearance rate of the radioactivity was about the same for both breasts before treatment, so that the ratio of the activity remained moderately constant over a period. However, after several x-ray treatments the counting rate over the involved breast fell rapidly to approach that over the normal side. This result was found in all five patients studied, including one in whom both breasts were irradiated. This sudden drop in counting rate over the tumorous breast was not found after diethylstilbestrol therapy in one patient.

GYNECOLOGY

Elimination of Untoward Radiation Sequelae in Treatment of Carcinoma of Uterine Cervix. James F. Nolan and Lucille Du Sault¹ report a statistical analysis of the clinical occurrence of factitial radiation reactions in patients treated for carcinoma of the cervix uteri at the Los Angeles Tumor Institute between 1945 and 1950. The complications that depend on the amount of radiation delivered were selected and their incidence compared with the incidence of successful treatments, which has been found to depend on the stage of disease and the dose delivered in relation to treatment time. The comparison was used to answer the question as to whether these complications should be accepted as a necessary sequel to successful treatment.

The answer must be stated as "yes" and "no"—"yes" in the case of advanced lesions and "no" in the case of early lesions. The findings suggested that some complications may be decreased by improvements in treatment technics which will allow for more adequate distribution of radiation to the lateral extensions of the tumor without intensifying the dose to the paracervical regions.

Management of Carcinoma of Uterine Cervix. In 1943-50 in private practice, Ian Macdonald and Lewis W. Guiss² (Univ. of Southern California) observed 244 cases. In 1943-46, preinvasive carcinoma was rarely diagnosed. After this, four routine biopsies rather than one and use of Papanicolaou's technic in suspected cases increased the incidence from 1:100 to 1:5. Total hysterectomy was done in all cases of preinvasive carcinoma.

A total of 147 patients with invasive carcinoma were given radiation therapy. Factors were: 200 kv., half-value layer 1.50 or 1.75 mm. Cu, four 10 × 15 cm. ports (two anterior and two posterior), dose of 1,800-2,600

(9) Brit. J. Cancer 5:45-53, March, 1951.

(1) Surg., Gynec. & Obst. 94:539-542, May, 1952.

(2) California Med. 76:56-61, February, 1952.

r measured in air to each port given over 3½-4 weeks. Intracavitary application of radium followed, usually 4,000-7,500 mg.-hr. The Manchester and Fletcher technics for delivering adequate dosage at points A and B were adhered to.

Results of radiation therapy were superior to those of surgery. Of 26 patients with stage I lesions (League of Nations' classification), 84% had a five year cure; of 83 with stage II, 65%; of 24 with stage III, 12%; of 14 with stage IV, none.

There are two groups of patients in which surgery might improve on the results of irradiation. (1) Radical panhysterectomy may be beneficial when a lesion proves to be radioresistant. (2) Block dissection of pelvic nodes may be of value when residual carcinoma is metastatic to the nodes.

Study of Survival of Patients with Cervical Cancer Treated Solely by Radiotherapy. M. Stuart³ reviewed the cases of cervical cancer patients on the service of Mme. Laborde treated successfully at Institut G.-Roussy between 1921 and 1944. The post-treatment period, therefore, ranged from 6 to 29 years. To eliminate errors caused by insufficient numbers, survivals exceeding 20 years were not considered. Patients had received radium or roentgen therapy, or both successively, and were considered clinically cured five years after treatment. In selecting material and analyzing data, the author established definite criteria. (1) Patients in stage IV were eliminated. (2) Patients in stages I, II and III were grouped together with no attempt to establish separate survival figures. (3) Five classes of patients in stages I to III were eliminated: (a) those who had had previous therapy in other hospitals; (b) those treated surgically before or after radium therapy; (c) those with incomplete case histories; (d) those lost to follow-up after five years, and (e) those who were uncured although they lived beyond the fifth year. (4) Eventual cause of death, such as traffic accidents or recurrence, intercurrent disease or old age, was not considered.

Number of patients (excluding stage IV and those treated surgically) was 1,444; of these, 642 (43%) were cured at the end of the fifth year. These totals, compared with figures reported in 1937 on material selected by similar standards for the period 1921-31, show a 6.7% increase in five year cures, related chiefly to continual improvement in technic. In considering figures on patients alive during each year until 1950, allowance must be made for errors resulting from difficulty in securing precise reports; these increase with time and are most numerous in years most remote from time of treatment; also, percentages vary more because fewer patients are alive in later years. Percentages for the 17th, 18th, 19th and 20th years, therefore, can only be approximate. Patients lost to follow-up (around 10%) are considered to have met the same fate, in percentages, as the other 90%. Survival incidence, then, declines slowly from the 5th to the 14th year, decreasing only 11% (from 43% to 34%), whereas the decline (19%) is abrupt in the next six years (from 34% to 15%). Of patients alive and well after five years, 81% lived to the

(3) Bull. Assoc. franç. étude cancer 38:431-440, 1951.

12th, 76% to the 14th, 67% to the 16th and 45% to the end of the 20th year. Of patients alive 10 years after treatment, 50% were still living at the end of 20 years.

Average age of patients at time of initial treatment was 55; for the purposes of this study, however, all patients fall in three groups representing average ages of 50, 55 and 60. Comparing mortality incidence among patients five years after treatment with that of the female population in general at 55, 60 and 65 years, the study shows that patients with five year cures have almost the same life expectancy as women of like age without uterine cancer.

[These figures cannot be compared with absolute results because of the "indeterminate cases."—Eds.]

Causes of Death in Carcinoma of Cervix Influencing Modern Trends in Treatment: Analysis of 248 Deaths from Charity Hospital of Louisiana at New Orleans. Simon V. Ward, Thomas Benton Sellers and Julius T. Davis, Jr.,⁴ concur with previous reports that death is principally the result of uremia, infection or hemorrhage, rather than the tumor itself. Today ureteral obstruction takes a relatively increased toll as the immediate cause of death. The tendency to die of obstructed ureters is slightly higher among older women. Peritonitis is a relatively uncommon cause of death. Over 50% of the patients died of uremia or pyelonephritis. All showed evidence of ureteral obstruction. Distant metastases were found in 23 of the patients; in 50% they were detected clinically. In the last decade ureteral obstruction resulting from x-ray or radium therapy has been rare. No fulminating uremia after irradiation was found in this survey and autopsies revealed no inflammatory lesions or late fibrosis. Instead there was evidence of progressive obstruction after extension of the disease. Hemorrhage was the primary cause of death in 34 patients.

X-ray and radium are still the choice for cervical carcinomas except carcinoma in situ, which may require a wide hysterectomy. Relatively early surgery to correct urinary obstruction will save or prolong comfortable life in the 65% of the patients with carcinoma of the cervix who now die of urinary obstruction or hemorrhage.

Curability of Carcinoma of Cervix in the Negro. Manuel Garcia⁵ (Charity Hosp., New Orleans) analyzed 1,203 consecutive cases (789 in Negroes) seen between 1938 and 1944. In all, irradiation was the essential method of treatment. Negroes showed a greater proportion of advanced lesions than white patients, and fewer Negroes with lesions in the earlier as well as in the later stages survived five years. Impaired radiosensitivity did not appear to be a factor. There were more Negro than white women in the younger age groups, a fact which may reasonably be explained by a background of poverty and rural life, associated with early marriage. Because of their economic and educational handicaps, Negro women neglect symptoms longer, thus accounting for the large proportion with advanced lesions. They have a higher incidence of complications and intercurrent disease and consequently lower

(4) *Am. J. Obst. & Gynec.* 63:989-998, May, 1952.

(5) *South. M. J.* 45:145-152, February, 1952.

life expectancy; they refuse to complete treatment in many instances, and the number of patients lost to follow-up is greater than in the white group.

Despite these adverse factors, which Garcia believes account for the

ABSOLUTE FIVE YEAR SURVIVAL IN NEGRO WOMEN, ACCORDING TO CANCER STAGE

PERIOD	I	II	III	IV	TOTAL
1938-44					
No.	64	191	340	106	701
%	59	38	22	3	27
1945-46					
No.	18	33	126	22	199
%	88	70	31	0	39
Total No.	82	224	466	128	900
%	66	42	25	2	30

differences in results in the two races, the proportion of Negro patients surviving five years can be brought to rather satisfactory levels by improvement in radiation therapy, as shown in an additional group of 199 Negro women treated more recently (table).

Correlation of Histologic Grade, Clinical Stage and Radiation Response in Carcinoma of Uterine Cervix is made by Robert W. Kistner and Arthur T. Hertig⁶ (Harvard Univ.).

Of 354 cases reviewed, data for 100 were adequate for study. Treatment consisted of x-rays and radium. Histologic evaluation was made on cervical biopsies taken before, during and after therapy; grading consisted of the three commonly accepted degrees of differentiation, with pearl formation and keratinization decreasing as mitoses increased with increasing malignancy. Radiation response was evaluated by commonly accepted morphologic changes in tumor and stromal cells.

Radiation factors were: 200 kv., filtration 0.5 mm. Cu, 50 cm. distance, one 15 cm.² anterior and two 10 × 15 cm. posterior oblique ports, total skin dose 6,000 r in three weeks. Two doses of radium of 2,000-3,600 mg.-hr. each were given 10-21 days apart; two 50 mg. tubes were placed in the body of the uterus and four 25 mg. tubes at the surface of the cervix, all filtered by 1 mm. brass plus 1 mm. Pb.

Classified by clinical stage, 34% were in stage I, 53 in II, 9 in III and 4 in IV. Histologically, 4 were grade I, 77 grade II, 9 grade III, 9 adenocarcinoma and 1 adenosquamous carcinoma.

Over-all five year survival was 50%, with 74% of stage I, 46% of stage II, 12% of stage III and no stage IV patients surviving. Grade II occurred about equally (75%) in stages I and II, made up all of stage III and was found in 50% of stage IV cases. Salvage was about the same (50-56%) for all groups except grade III (34%). Radiation response was about the same in grade II and III lesions with a slightly lessened reaction in grade I and adenocarcinoma.

There was no direct correlation between stage and degree of response, and survival depended chiefly on clinical stage. In stages I and II, five year survival was increased when there was a marked degree of radiation response. However, treatment should depend on clinical stage

(6) Am. J. Obst. & Gynec. 61:1293-1300, June, 1951.

and to a less degree on radiation response. Survival may be improved by utilizing surgery when radioresistance is discovered.

[This is a good attempt to study radiosensitivity from the standpoint of prognosis. The clinical stage of the disease when treatment is instituted is more important than the degree of radiation response.—Eds.]

Radium Therapy for Cancer of Cervix Uteri with New Type of Colpostat. Sidney M. Silverstone, William Harris and Maurice Greenberg⁷ (Mount Sinai Hosp., New York City) elaborate on their radium system designed to deliver a cancerocidal dose to the cervix, lower uterine segment, vaginal vault, paracervical triangles and lateral parametria.

The system consists of a linear source in the uterus, the intrauterine tandem, and two unit sources in the vagina, the colpostat. The linear



Fig. 331.—X-ray showing colpostat in situ. (Courtesy of Silverstone, S. M., *et al.*: *Am. J. Roentgenol.* 67:294-299, February, 1952.)

source consists of three capsules of radium (one 10 mg. and two 15 mg. capsules) arranged as a tandem in a rubber or plastic tube. The weaker source is placed at the cervical end. The tandem is kept in place by sutures through the cervical lips and by vaginal gauze packing for 90 hours or a total dose of 3,600 mg.-hr. Filtration is 1 mm. Pt.

The colpostat consists of two ovoids which contain the radium and are attached by connecting rods to a locking pivot piece. The desired distance between the radium capsules is obtained by manipulation of two detachable handles and is measured by a calibrated arc. After the instrument is assembled and adjusted, the ovoids are loaded with radium and the entire apparatus is sterilized. The ovoids are inserted under direct vision. During the period of application of the colpostat, the patient is kept in bed. There is little discomfort. A roentgenogram of the

(7) *Am. J. Roentgenol.* 67:294-299, February, 1952.

pelvis (Fig. 331) shows the colpostat in position. Daily roentgenograms in both anteroposterior and lateral positions have shown no shift in position of the instrument.

The authors usually place a 25 mg. capsule of radium with a filtration of 1 mm. Pt in each ovoid. The time of application is 96 hours for a total of 4,800 mg.-hr. At least 4 cm. separation is usually attempted. Calculation of the dose at six representative points in the pelvis revealed that the dose to the lateral parametrium is significantly improved as the separation of the ovoids increases. With a vaginal radium separation of 6 cm., it would appear safe to increase the total radium irradiation by at least 10%, thereby improving the dose in the lateral parametrium while not exceeding the limits of tolerance. Dose in the lateral fornices is of the order of 17,000 r.

A particularly valuable feature of this colpostat is that the ovoids can be separated to the maximum permitted by the tissues of the vaginal vault, so that the maximum possible radium dose may be delivered to the lateral parametria. The authors have experimented with the colpostat for over three years in treatment of cervical cancer and also other conditions requiring radium in the lateral fornices. It has proved highly satisfactory and practical.

Intravaginal X-ray Therapy of Malignant Gynecologic Tumors is reported by R. K. Kepp⁸ (Göttingen). In the usual type of intravaginal x-radiation the focus of the tube is outside the vagina and anatomy limits

RESULTS OF X-RAY THERAPY IN CERVICAL CANCER, 1943-44

	STAGES				TOTAL
	I	II	III	IV	
No. patients	72*	76	175	6	329
Died within 5 yr.	26	28	98	6	158
Alive after 5 yr.	41	41	65	0	147
No recurrence, 5 yr.	40	37	64	0	141
Not accounted for	5	7	12	0	24
% cures (efficiency)	55.6	48.7	36.5	0	42.9

*37 patients had radical operation plus percutaneous x-ray therapy, with 18 cures; 35 patients received radiotherapy alone, with 22 cures.

the width of applicator; thus divergence of the x-ray beam is restricted. By placing the x-ray tube focus inside the vagina the x-ray beam may be given any required width and direction, with screening of all undesirable rays. The anatomy of the vagina sets an upper limit to the distance between tube focus and vaginal wall, entailing a steep dose gradient. However, the high radioresistance of the vaginal wall compensates this effect and the dose gradient facilitates protection.

In hollow anode tubes used for intravaginal therapy the electrons enter a grounded tube, the far end of which carries the anode consisting of a Cu foil, with gilt inside for increasing the x-ray yield. Applications are used to determine the beam direction and dimensions. The 60 kv. oil-immersed tube used weighs 19 lb.

Intravaginal x-radiation is always combined with radium or percutaneous x-rays. Total course is four to five weeks. Grade I or II cervical

carcinoma is best treated with radium and hollow anode tube therapy, whereas in grades III and IV addition of percutaneous x-ray therapy greatly improves chances of cure.

The usual dose is 2,400 r given at the boundary of the tumor over 12 sessions. The dose should never exceed 2,400 r at a point 5 cm. beyond the vaginal wall. Integration of all three types of therapy according to a prearranged plan is important. Radium dose is 2,600-2,800 gamma r given at a distance of 3 cm. from the capsule wall in two sittings two weeks apart. No radium is used in the vagina. In percutaneous x-ray therapy, the beam is tilted to avoid the vaginal wall: a dose of 1,200 r, spread over 12 treatments, is delivered to the pelvic wall. Results are summarized in the table.

[Most radiologists feel that the action of this radiation is altogether too superficial to influence effectively the deeper pelvic structures such as the lateral parametria.—Eds.]

Effect of Radiation on Metastatic Pelvic Lymph Node Involvement in Carcinoma of Cervix. Willis E. Brown, I. Meschan, Ernest Kerekes and J. M. Sadler⁹ (Univ. of Arkansas) carried out a project designed to deliver a controlled amount of radiation to cervical carcinoma and the lateral pelvic lymph nodes. The effect on these tissues was studied microscopically.

Forty-two patients were treated with x-rays and radium or Co⁶⁰, followed by complete hysterectomy or cervical biopsy and or pelvic lymphadenectomy. Generally, in early cases, radium was used first and followed by x-ray therapy; the reverse procedure was used for more advanced disease. Complete data were available on 24 patients. Treatment was individualized. Factors were: 220 kv., 15 ma., half-value layer 1.5 mm. Cu, focus-skin distance 50 cm. Six to eight ports were used, usually two 10 × 15 cm. anterior ports separated by a lead strip, two posterolateral 10 × 10 cm. ports and two 7 or 8 × 15 cm. posterior ports separated by a lead strip. Maximal skin dose was 3,300 r. Radium or Co⁶⁰ was filtered by 1 mm. Pt or its equivalent and given in an Ernst applicator or by means of multiple needles. X-ray treatments were given daily for 6 weeks, followed by surgery in 2-12 months.

Dosage was determined by use of Quimby's tables and standard isodose charts applied to anteroposterior and lateral teleoroentgenograms. Skin clips were used to mark the fornices and cervix. The bladder and rectum were identified by contrast mediums. Thus, it was possible to measure the distances from the various sources of rays to the points of interest (Figs. 332 and 333). Summated dosages were 9,146-24,943 r at the cervix, 3,555-7,742 r at the lateral pelvic wall, 1,000-6,016 r at the bladder and 1,470-6,109 r at the rectum. Figure 334 shows the relations of important node groups to the areas irradiated.

In 80% of the 24 patients, all known tumor tissue was destroyed. In one patient carcinoma was still present in the cervix after treatment with 20,000 r and in two others after treatment with 10,000 r. These tumors were obviously radioresistant. In all instances when the cervical lesion disappeared and the lateral pelvic wall received over 5,500 r, no

(9) Am. J. Obst. & Gynec. 62:871-889, October, 1951

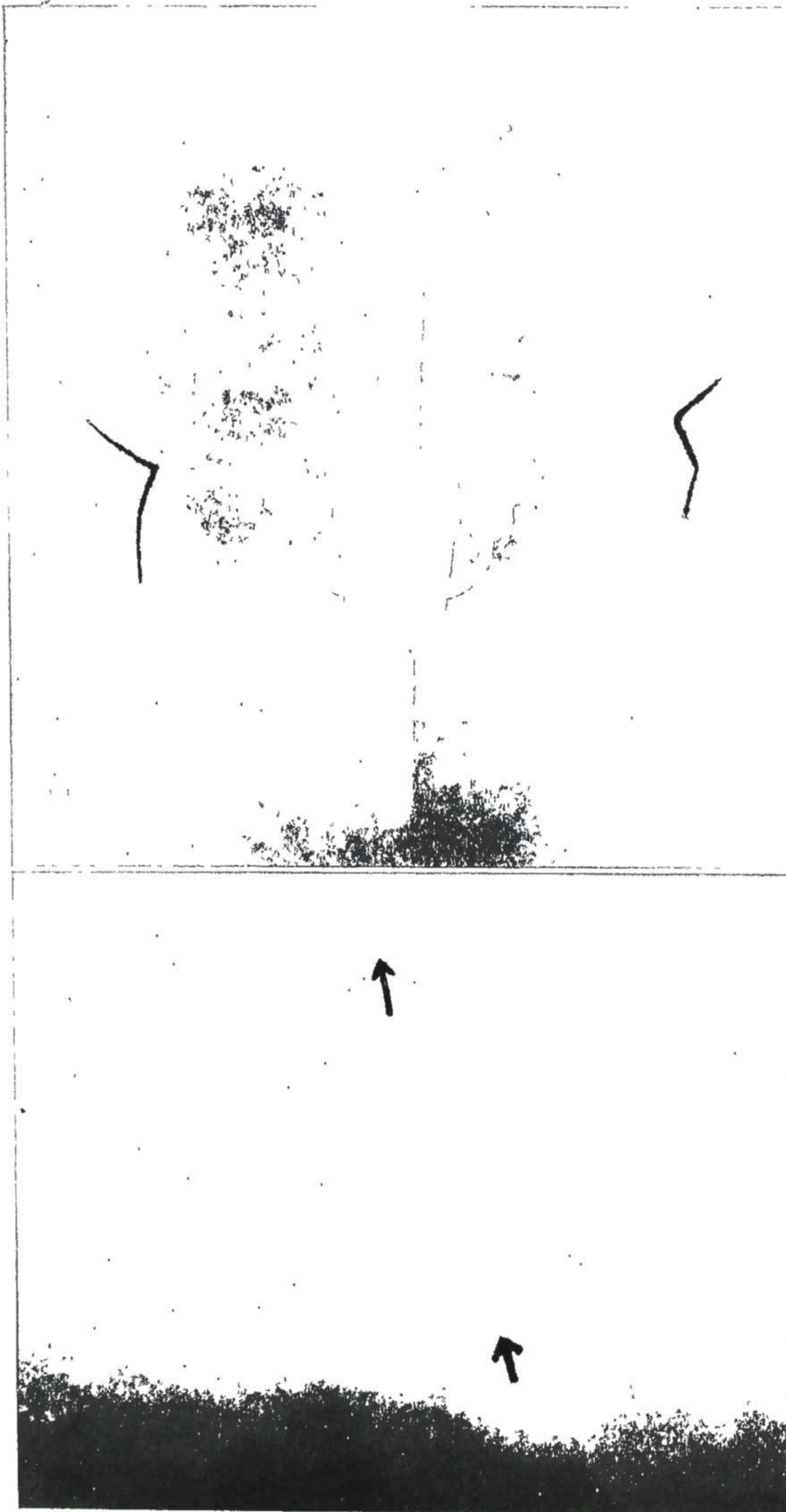


Fig. 332 (top).—Anteroposterior film of pelvis with Ernst applicator in place. Skin clips mark margin of cervix and extent of tumor in vagina. Balloon on Foley catheter filled with sodium iodide and rectum identified with barium paste. Film is taken immediately on placing of radium and permits calculation of roentgens to be delivered/hour to each point in pelvis.

Fig. 333 (bottom).—Lateral film.

(Courtesy of Brown, W. E., *et al.*: *Am. J. Obst. & Gynec.* 62:871-889, October, 1951.)

carcinoma was found. Optimal summated dosage was a minimum of 13,000 and maximum of 25,000 r to the cervix, minimum of 5,000-6,000 r to the lateral pelvic wall and maximum of 4,000 r to the rectum and bladder.

It was concluded that 5,000-6,000 "tissue r," delivered in five to six weeks, is the minimal dose that will eradicate carcinoma in the pelvic

lymph nodes if the tumor is radiosensitive. This dose can be delivered to all areas of the deep pelvis with minimal risk to normal tissue. Surgery should be done two to three months after irradiation, before collateral circulation is seriously impaired.

[Many thousands of patients with cancer of the cervix have been treated without determining the effect of radiation on the metastases in pelvic lymph nodes. This paper, despite its title, establishes, not the effect of radiation, but rather the difficulty of determining the effect of radiation on lymph node metastases. The series consists of 24 patients, of whom 18 showed no disease at the time of postradiation biopsy. It is not

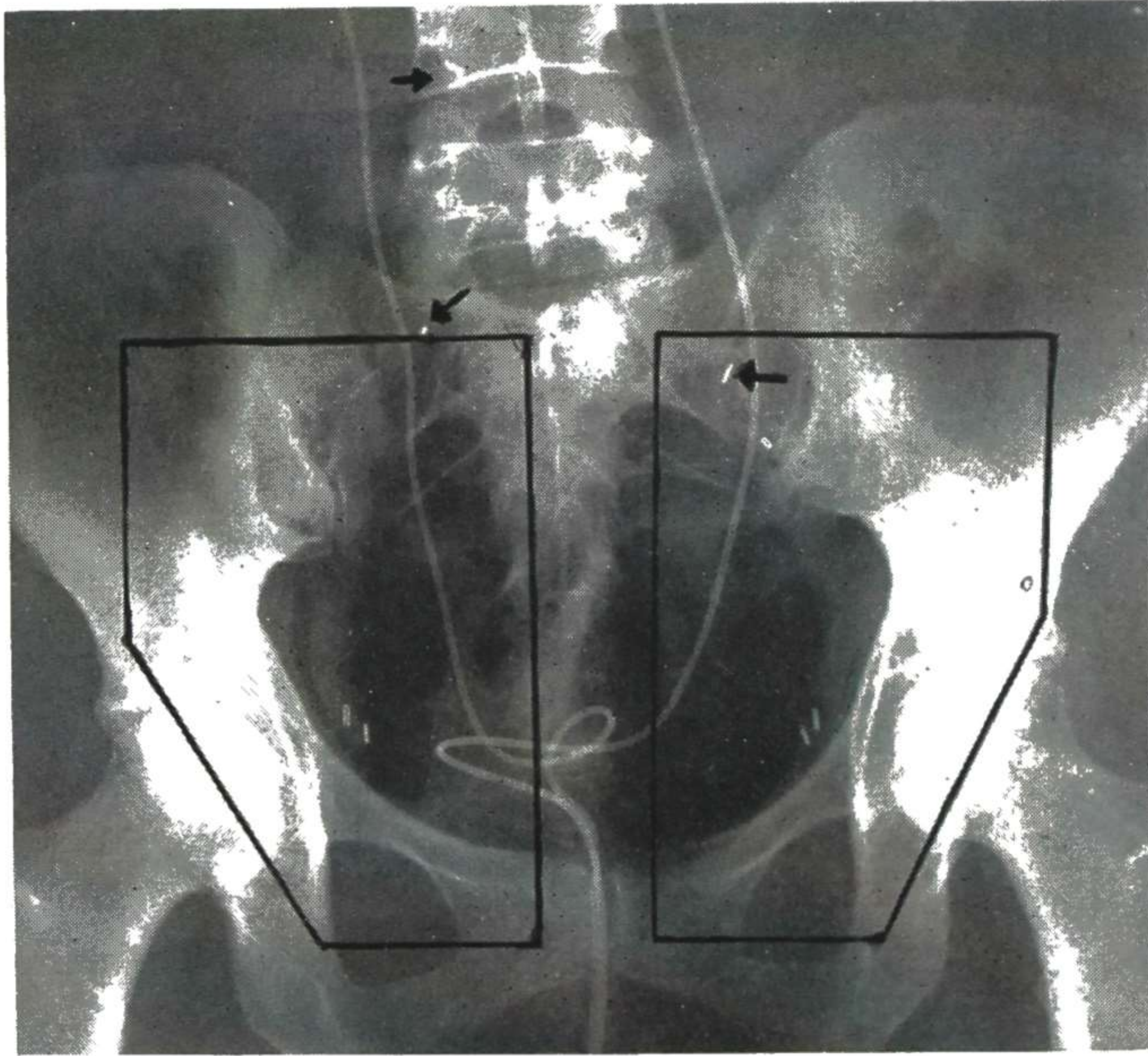


Fig. 334.—Silver clips placed on aortic, hypogastric and obturator node areas. Black lines indicate areas covered by x-ray ports. Hypogastric and iliac nodes are just within the field of effective radiation and often do not receive an adequate summated dosage. (Courtesy of Brown, W. E., *et al.*: *Am. J. Obst. & Gynec.* 62:871-889, October, 1951.)

to be assumed that all of these had lymph node metastases before treatment. The answer to the problem hinges on proving that such metastases were present or, since this is impossible, at least assessing the probability of their presence. A dose of 6,000 r can be delivered to the lateral pelvic wall, but the risk of complications is high, as the authors attest in an addendum to their article.

The evident collaboration between radiologist and gynecologist should be a model for every institution.—Eds.]

Clinical Course of 44 Cases of Cancer of Uterine Cervix during Gestation Treated by Radiotherapy at Curie Foundation between 1929-1950. Of 3,069 patients with uterine cervix cancer treated in this period, 44 (1.4%) were discovered during pregnancy or immediately after emptying the uterus. A study of these cases by Juliette Baud and Fabienne Blanchet¹ did not show a more rapid course than in those cases not associated with pregnancy. Their radiosensitivity and histologic characteristics were likewise comparable. Radiation treatment was not accompanied by serious complications.

Early diagnosis and treatment is important. Of the 25 patients treated for five years (1929-46), the diagnosis was made after a delay of one to

(1) *Bull. Assoc. franç. étude cancer* 39:48-62, 1952.

five months in 7 and 4 were cured. Of 10 patients in whom delay was one to two years, only 2 were cured; of 8 in whom diagnostic errors retarded treatment, only 1 was cured.

The great difficulty in these cases is making early diagnosis. The associated pregnancy masks the interpretation of the physical signs, retards biopsy and prevents the patient from becoming alarmed.

Effect of Radiation on Products of Conception in Case of Carcinoma of Cervix Complicating Pregnancy is reported by Joseph Rich, Alfred Angrist and Frederick Carpenter² (Flushing, N. Y.).

Woman, 28, had a thick yellow vaginal discharge for one year. For a month she had had vaginal spotting and bouts of fever and was hospitalized because of right lower abdominal pain. Examination showed an ulcerated cervix and "frozen" pelvis, and biopsy, infiltrating epidermoid carcinoma of cervix. The uterus was slightly enlarged but pregnancy was not suspected. From April 25 through April 29 she received 900 r/air to a 10 × 15 cm. anterior pelvic field and 600 r/air to a similar sized posterior field in 300 r daily alternating exposures. Beginning May 2 three corks containing 15 mg. radium filtered by 0.5 Pt were placed about the cervix for 100 hours. No intrauterine radium treatment was given. On May 14, she was admitted with vaginal bleeding and abdominal cramps, and a piece of tissue was expelled which was recognized as placenta. On May 19 and 20 she received 200 r/air to each of two pelvic portals as before. In July bilateral ureteral obstruction was diagnosed and left nephrostomy performed. She died suddenly in October. Autopsy disclosed local and generalized metastases with uremia and pulmonary congestion.

Microscopic study of the placenta disclosed changes interpreted to represent radiation effects, with edema of the decidua causing reticular fibrosis and hyalinosis on the stroma of the villi, loss of vascularization and consequent death of the fetus. Though all of these changes can be seen in the term placenta, more pronounced and selective involvement of the stroma of the villi and minimal maternal changes were noteworthy.

Application of Radioactive Colloidal Gold in Treatment of Pelvic Cancer. Alfred I. Sherman, MacDonald Bonebrake and Willard M. Allen³ (Washington Univ.) treated 13 patients. Ten had cervical carcinoma (grades 1-3, Broders' classification), 2 metastases to the inguinal lymph nodes and 1 vulvar carcinoma. Radioactive gold was chosen for several reasons. It has a half-life of 2.7 days and its emission spectrum consists of a beta ray of 0.9 Mev and a gamma ray of 0.44 Mev. In addition, the metallic form which is used is nontoxic, both chemically and physiologically. This form of gold has a purplish color which allows it to be traced visually.

METHOD.—A concentration of 1 mc. Au¹⁹⁸/cc. pectin solution was used. Under sterile conditions, a fornix was exposed. A 22 gauge needle was inserted in the paracervical area and carried through the mucosa, Mackenrodt's ligaments and continued laterally angled at 20-30 degrees from the midline, to approximate the pelvic wall. Gold was injected as the needle was withdrawn, usually into three sites on each parametrium. Dosage was 7.5-36 mc. to each parametrium. It was not intended to be cancerocidal, but only to be traceable at surgery. In three patients with cervical carcinoma, gold was injected directly into the cervix also. In patients with vulvar carcinoma or metastases to inguinal lymph nodes, injections were made directly and deeply into the sites several times. Some patients also received radium and x-ray therapy. Complete abdominal

(2) New York J. Med. 51:2166-2168, Sept. 15, 1951.

(3) Am. J. Roentgenol. 66:624-638, October, 1951.

hysterectomy and pelvic lymphadenectomy were done two weeks to three months later.

At operation, Au^{198} was found to have entered and traversed extensively the lymphatic system and to have lodged in nodes in the pelvis, at its lateral margins and as far as the promontory (Figs. 335 and 336). It was also present on the skin surface. Definite radiation effects were noted in the parametrium and corresponding lymph nodes. Observation indicated that the doses used were entirely within tolerance levels. No un-

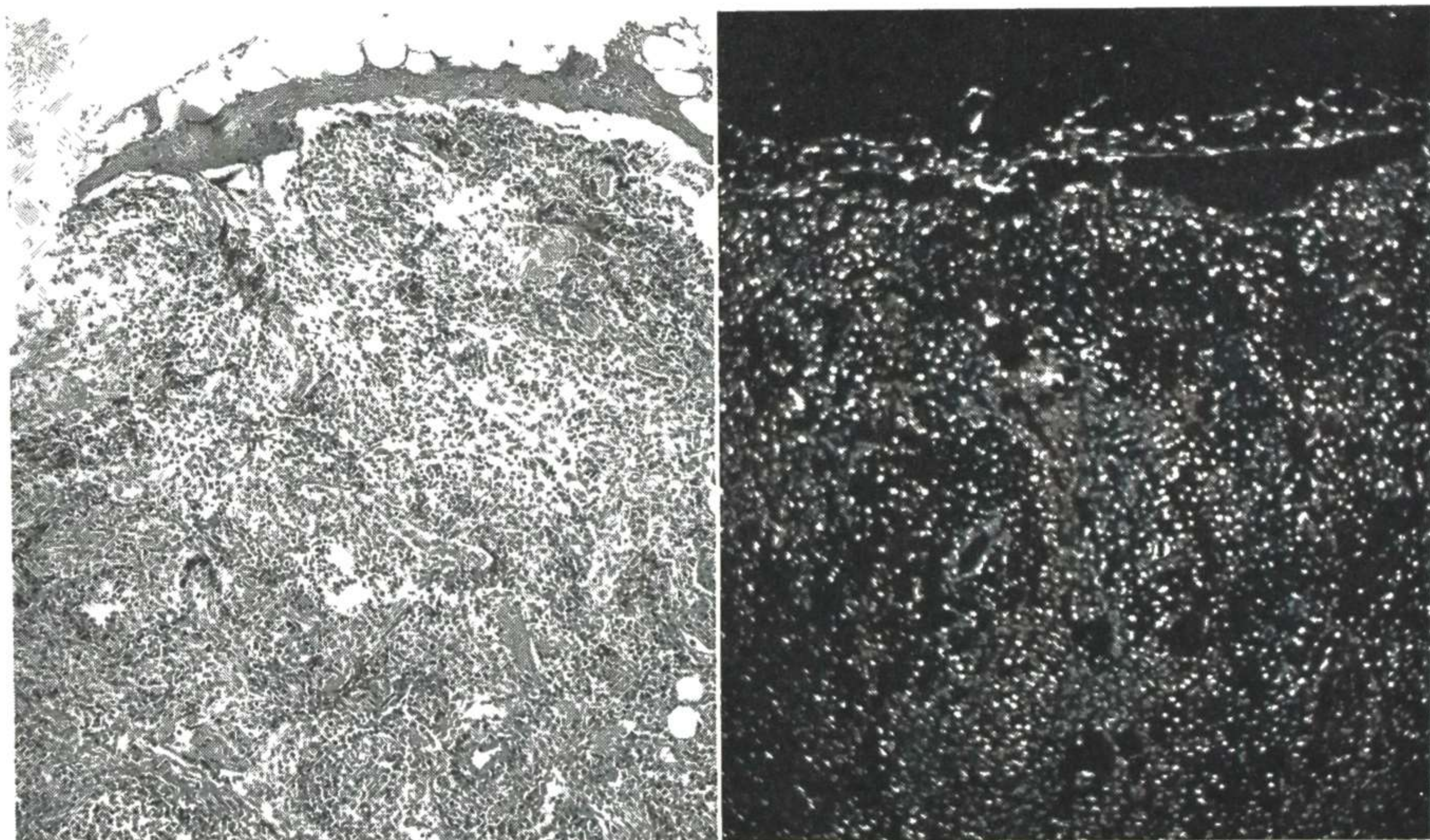


Fig. 335 (left).—Obturator lymph node after injection of radioactive colloidal gold into parametrium.

Fig. 336 (right).—Darkfield illumination of microincineration of same section. Gold particles show up as bright yellow specks.

(Courtesy of Sherman, A. I., *et al.*: *Am. J. Roentgenol.* 66:624-638, October, 1951.)

toward reactions developed except for a slight sensitivity reaction to pectin in three patients.

The results of these tracer experiments qualify the use of radioactive colloidal gold as a supplementary treatment for carcinoma of the cervix and vulva, and suggest its use as an adjunct to present methods of radiation therapy in these diseases.

[It seems premature to suggest the use of radioactive colloidal gold as supplementary treatment for carcinoma of the cervix and vulva. Dr. James F. Nolan made two important comments in discussing this paper. Adequate and safe dosage data have yet to be worked out before taking this up as a therapeutic method. We do not know that material entering the lymphatics lodges in lymph nodes containing cancer or that it could be taken up in sufficient quantity to irradiate metastatic cancer cells effectively.—Eds.]

Role of Radiation and of Surgery in Management of Uterine Carcinoma. Franklin L. Payne⁴ reviews the patients with uterine carcinoma treated at the Medical School of the University of Pennsylvania between 1931 and 1945. There were 208 with carcinoma of the corpus. Surgery was used for good operative risks when the disease was believed limited to the uterus. About one-fourth had preoperative intracavitary tandem radium. In poor surgical risks and in those with disease extended beyond

(4) *Surg., Gynec. & Obst.* 94:715-721, June, 1952.

the uterus intracavitary radium and supplementary x-ray therapy were used. Among technically operable cases, survival rate was 66%; among technically inoperable cases treated with irradiation, survival rate was 15%. The larger the uteri, the poorer the survival rates.

Between 1940 and 1945, 183 patients with carcinoma of the cervix were treated by irradiation alone. Of 46 patients with clinical stage I (League of Nations) lesions, 74% recovered; 45% of 68 patients with clinical stage II lesions recovered; 27.3% of 55 patients with clinical stage III lesions recovered, and 14.3% of 14 patients with clinical stage IV lesions survived. Over-all survival was 44.8%. Surgery should be used for radioresistant tumors, for local postirradiation recurrences or removal of regional lymph nodes. Occasionally a radical pelvic exenteration in advanced cases is justified in the hands of a highly qualified surgeon.

Corpus Carcinoma. Howard C. Stearns⁵ (Univ. of Oregon) treated 79 consecutive patients from private practice in 1940-49. In eight patients radium was applied to the cervical stump or vaginal vault after surgery; all were still alive, the longest follow-up being four years. Radium was also used for palliation in eight patients in whom the lesion was considered too far advanced for surgery; one was alive after six years. Surgery alone was used in four patients, with one alive after five years. Fifty-eight patients were treated with 3,600-5,000 mg.-hr. radium applied in tandem, followed by panhysterectomy one or two months later. Fifty-four were alive and apparently free from cancer, 29 over five years after treatment. Two patients could not be traced. One died of other causes four years after therapy and one of a presumed pulmonary embolus. Two died of the primary disease after five years.

Results showed the soundness of use of radium and surgery in most cases of corpus carcinoma. For the entire series, five year survival rate was 85.5%. Additional x-ray therapy might well be given in certain younger patients, especially those with residual cancer postoperatively. Since results of surgery alone were poor, the treatment method recommended consists of preirradiation with radium followed by surgery, radiation therapy alone being conserved as a palliative measure or as a means of treating extensions to the cervical stump and vagina.

[These excellent results show the value of combining radiation and surgery in this disease. They probably also mean that the diagnosis was made early in this group of cases.—Eds.]

Hystero graphically Visualized Radionecrosis Following Intrauterine Radiation of Cancer of Corpus of Uterus in 175 patients seen during 1946-50 is reported by Olaf Norman⁶ (Lund, Sweden). Of the 115 with changes demonstrated by follow-up hystero graphs, 35 had well defined, smooth outlined, exophytic formations bulging a few millimeters into the uterine cavity. The changes were ascribed to radionecrosis because they followed radium treatment, occurred despite previous therapy, appeared at sites in which no pathologic signs were present in hystero graphs taken before radiation and because follow-up hystero graphs showed that the

(5) West. J. Surg. 59:504-511, October, 1951.

(6) Acta radiol. 37:96-102, February, 1952.

changes gradually diminished although left untreated. In three cases the finding of radionecrosis was confirmed at operation.

Hysterograms, made 14 days after microscopic examination of curettings had confirmed the diagnosis of cancer, showed an infiltrative growth in the upper part of the uterus (Fig. 337). The next day the uterus was packed with 11 capsules, each containing 10 mg. radium element. The estimated dose was 1,800 mg.-hr. A follow-up hysterograph 21 days later showed signs of radione-

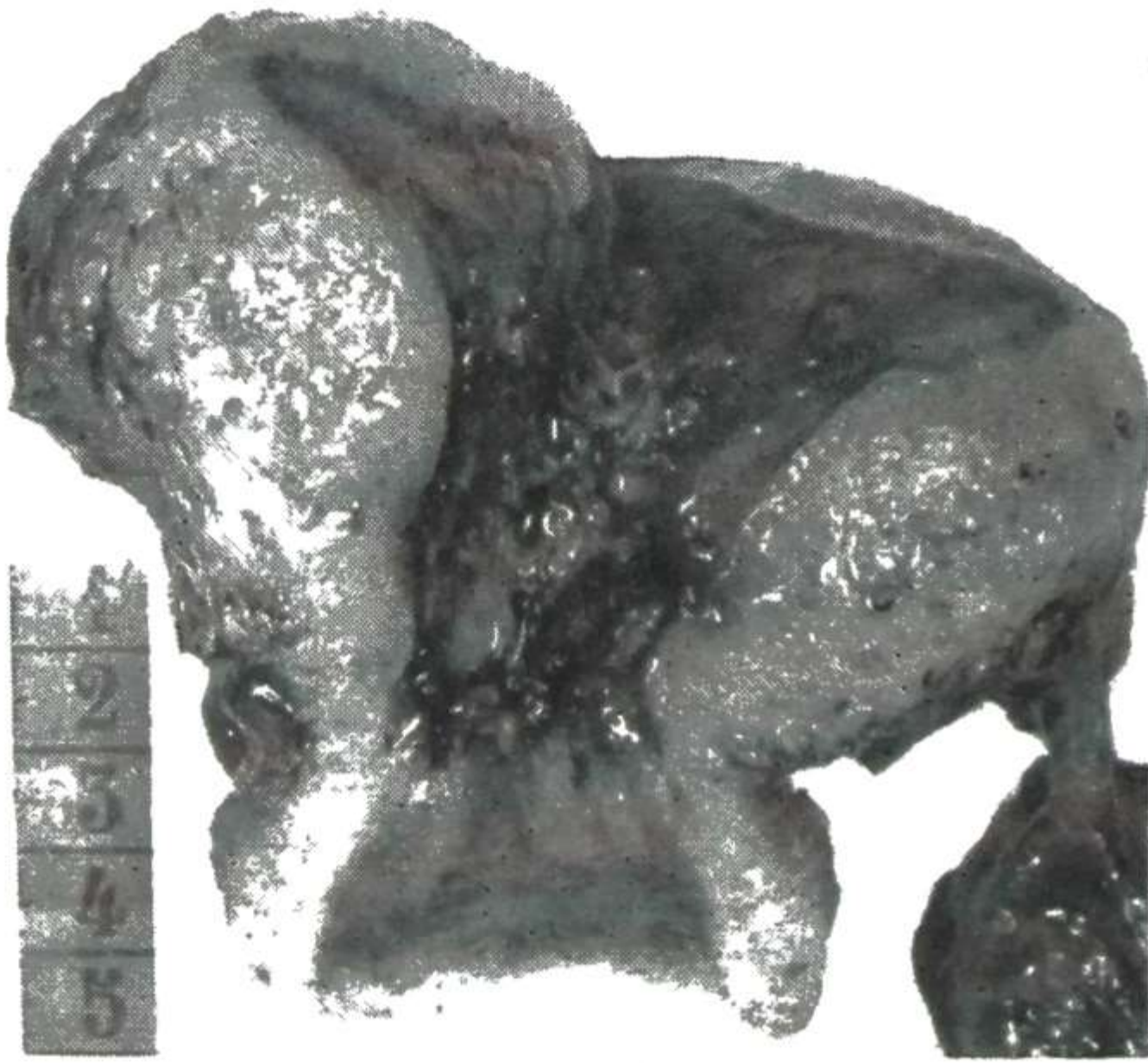
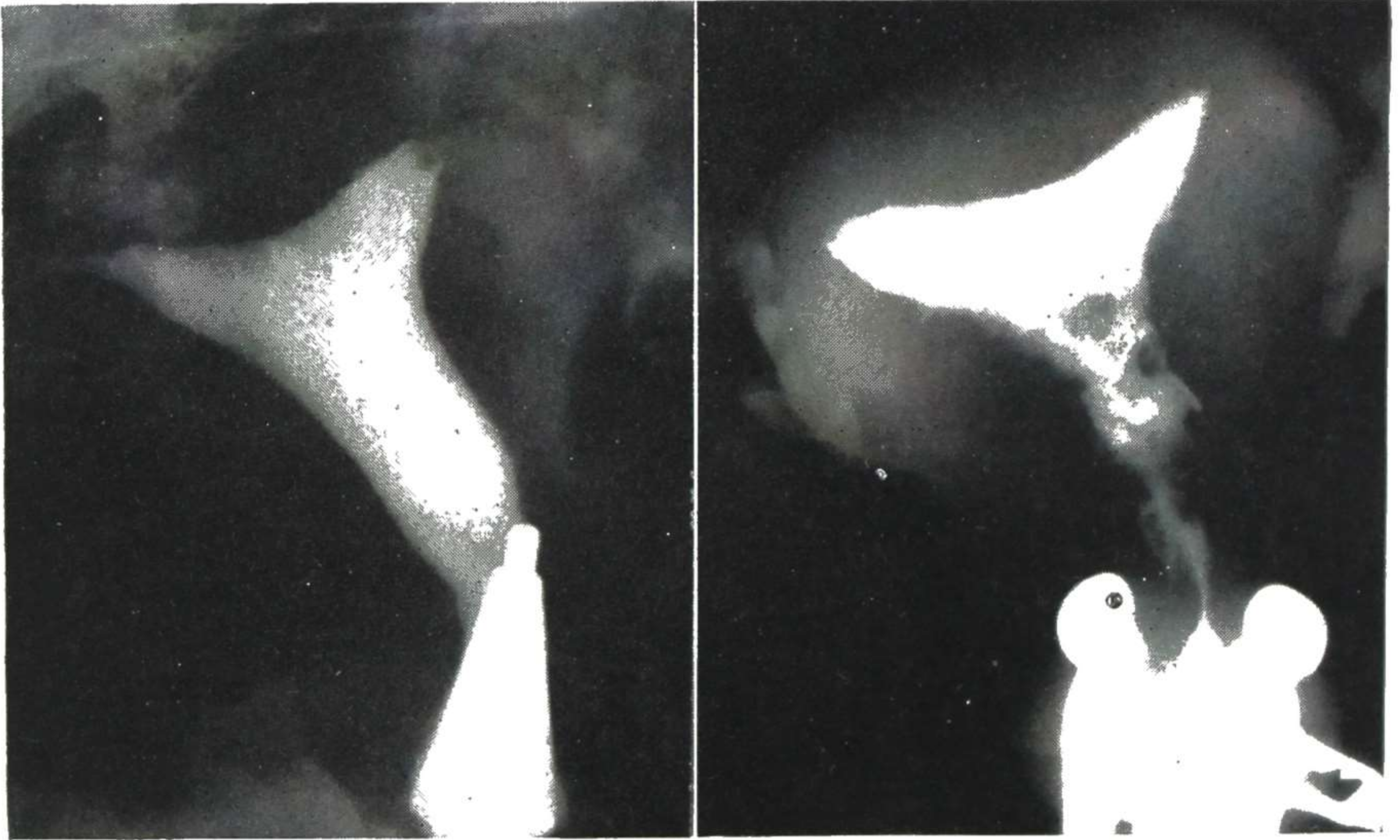


Fig. 337 (above left).—Infiltrative growth in upper part of cavity but no changes of lateral walls.

Fig. 338 (above).—Hysterogram of contrast-filled operation specimen.

Fig. 339 (left).—Operation specimen. Edematous mucosa and ulceration covered with fibrin at sites of hysterographic changes.

(Courtesy of Norman, O.: *Acta. radiol.* 37:96-102, February, 1952.)

crosis in the lower part of the corpus and in the cervix. The patient was operated on three days later. A hysterogram of the contrast-filled specimen (Fig. 338) demonstrated the radionecrosis changes clearly in comparison with the operation specimen (Fig. 339). Microscopic examination of sections from various parts of the excised uterus revealed no signs of cancer.

Radionecrosis occurred more often at the level of the internal os than in the superior part of the cavity despite equal distribution of radiation over the uterine cavity. To explain this finding, operation specimens were packed with capsules and x-rayed. They showed dilatation greatest at

the internal os level with increase in the area of the wall, resulting in a greater exposure to radiation of the distended in comparison with the undistended internal os. This may explain why radionecrosis occurs most often in this region.

Treatment of Cancer of Vulva since 1929 at Toronto General Hospital is reviewed by W. G. Cosbie.⁷ From 1929 to 1935, 20 patients were treated by radiotherapy and 20% lived five years. One patient was alive and well 16 years after treatment. One patient died seven years after treatment and two of extraneous causes. Radical vulvectomy was introduced in 1935. Prognosis is determined by extent and site of the lesion, state of the lymph nodes and the patient's age and physical condition. Five year survival rate in moderately advanced cases was 67% and in advanced cases 24%. Interstitial radium has become the method of choice in carcinoma in situ. This is used along with complete lymphadenectomy.

Autopsies on 16 patients indicated that the severely necrotic tumor is most often fatal to old and debilitated patients; that lymphatic spread is often held up in the primary group of lymph nodes and only rarely extends to nodes above the pelvis, and that widespread metastases are uncommon but when they do occur the involved organs suggest embolic spread directly from the primary lesion. Autopsies substantiate the belief that the primary tumor site must be adequately dealt with and that thorough bloc dissection of the superficial nodes as high as the cribriform fascia may be satisfactory even in the elderly patient. Complete pelvic lymphadenectomy with thorough vulvectomy should result in high cure rate.

Place of X-ray Therapy in Treatment of Malignant Ovarian Tumors. In 1940-44, Margaret C. Tod⁸ (Holt Radium Inst.) treated 125 patients. The whole peritoneal cavity, from the pouch of Douglas to the upper aortic nodes, was given the highest dose which systemic tolerance would allow.

METHOD.—A special appliance, a trunk bridge, is used to ensure homogeneous irradiation of large volumes. Four oblique fields, 30 × 20 or 40 × 20 cm., are used. Each is given 35 r the first day; dosage is increased 5 r/day until 80 r daily is reached. White cell counts are made before the start of treatment, the tenth day of treatment and twice weekly until the count starts to rise and treatment is complete. A fall to 300 monocytes is dangerous, but treatment may be continued if the total count is above 2,000 and the clinical condition good. The goal is delivery of 3,000 r to the tumor in four weeks.

The five year survival rate for all patients treated was 30% (38 of 125 patients), for all patients completely treated 37% (38 of 102 patients), and for completely treated patients with known residual disease after surgery 28% (23 of 83 patients).

Tod recognizes that even for "late" cases the five year survival rate is not negligible but from a consideration of the results of treatment by surgery alone believes that all patients with malignant ovarian tumor should receive postoperative radiation therapy.

(7) *Am. J. Obst. & Gynec.* 63:251-259, February, 1952.

(8) *J. Obst. & Gynaec. Brit. Emp.* 58:385-387, June, 1951.

Ovarian Carcinoma. Johannes Thoms⁹ (Radiation Center, Odense, Denmark) presents data on 67 patients with ovarian carcinoma treated during 1929-45. Diagnosis was confirmed microscopically in 54 cases and was based on the clinical course and results of exploration in 12. Autopsy was done in nine. Three fourths of the patients were aged 40-70. Fifty-seven were or had been married, and 37 of these and 1 single patient had been pregnant. Only six patients had a family history of cancer. Two thirds of the patients had previously been in perfect health.

The patients were grouped approximately according to Heyman's classification. There were 16 whose condition was amenable to radical surgery (group I). Four of these had bilateral involvement. Twelve patients needed radical surgery plus removal of other structures (group II). Seven had bilateral involvement. There were 15 in whom part of the tumor had to be left owing to involvement of irremovable structures (group III). Six had bilateral involvement. Twenty-four were considered inoperable (group IV), and 18 of these had bilateral involvement. Duration of symptoms was less than 1 year in 52 patients, and average duration in 66 was 6.1 months. Symptoms in order of frequency were: abdominal pain and enlargement, fatigue, seediness, weight loss, vaginal bleeding, urinary tract symptoms, vaginal discharge, defecation disturbances and dyspareunia. Ascites was present at the time of diagnosis in 27 patients, 5 of whom had right-sided and 2 of whom had bilateral effusion. All but eight patients had an increased rate. Eight had recurrences, preceded by sedimentation rate elevation.

Surgery was done on 55 patients. All but one received radiation therapy as soon as possible after operation, but this patient was not treated until 15 months after surgery. If operation was not done, irradiation was started as soon as diagnosis was made. The primary pelvic radiation in 42 cases was delivered to two abdominal and two dorsal fields, 20×24 cm. or 10×15 cm. Factors were: 165 kv., 5 ma., filtration of 0.5 mm. Cu, focus-skin distance 80 cm., daily dose of 120-240 r to each of one or two fields. Total dose to each field ranged from 960 to 2,400 r. Average total dose was about 5,500 r in air. A vaginal and/or rectal field was also used in seven cases. Repeat courses were given in 20 of the 42. Smaller doses were used in 10 cases and only palliative doses in 10.

The five year survival rate for the entire series was 26.9%. The rate for group I was 68.8%. Eleven patients were asymptomatic at the end of 5-14 years. Of the 56 who died, more than half died within the first year and about 80% within three years.

Cancer of Ovary: Results of Experiments in 79 Cases are reported by L. H. Garland and M. A. Sisson¹ (Stanford Univ.). In all cases, treatment was combined surgery and radiotherapy. Diagnosis, microscopically verified, ranged from frank malignancy to "borderline benignancy," including papillary cystadenocarcinoma, 25; pseudomucinous cystadenocarcinoma, 16; other malignant ovarian tumors, 4; un-

(9) Acta radiol. 36:411-416, November, 1951.

(1) J. Fac. Radiologists 3:66-75, July, 1951.

classified cystadenocarcinoma, 12, and carcinoma, solid or type unspecified, 22.

Staging was according to Heyman's classification: I, primary tumor and all visible metastases removed; II, primary tumor partially or totally removed, but visible metastases remain; III, recurrent malignant tumor (postoperative or postradiation); IV, inoperable tumor, or one with distant metastases.

Most of the patients were seen two to four weeks after operation, which varied from exploration and biopsy to radical removal of uterus and adnexa, which is the method of choice. The patients grouped under stage I were usually not referred for treatment. Most patients received one and some as many as four courses of irradiation. Factors were: 200 kv., 1 mm. Cu half-value layer, 70-80 cm. distance, through fields 20-35 cm. in diameter. Anterior and posterior fields were treated on alternate days and lateral fields were added when ascites rendered the patient's abdomen globular. Daily dose started with 75 r (air) to one field and was increased to 200 r as soon as possible. Total doses varied from 1,000 r tumor dose given in 10 days to 1,400 r in 20 days. Some patients received two to three times as much. Most authors recommend that irradiation be given in all but clearly localized stage I lesions. Optimal dosage and technic will vary according to the presumed extent of residual tumor, type of tumor, size of the patient and tolerance to irradiation. A tumor dose of 1,500-2,500 r in 20-30 days is desirable as an initial course in the average case. Subsequent treatment should be given as indicated by the individual circumstances. The initial course is the most important one, but as many as two or three such courses can be given over several years.

Of 60 patients receiving a tumor dose of more than 1,400 r in 20 days, 50 were followed. Relative five year arrests were 14%, the absolute arrests 11.8%. Stage of the disease and type of tumor have a definite influence on survival rate. Highly undifferentiated ovarian carcinomas have a poor prognosis, whereas partly differentiated pseudomucinous cystadenocarcinomas have a relatively good one. Truly comparable data on cases treated by surgery alone and cases treated by surgery and radiation are not available. A review of the literature disclosed "comparative" five year survivals to be: for surgery alone—256 cases, 23%; for surgery plus x-ray therapy—358 cases, 35%.

[The preceding three articles each present valuable information but, taken together, they defy comparison and baffle the reader seeking clear evidence of the effect of treatment on cancer of the ovary. Tod's article seems most helpful for its concise presentation of evidence and expression of opinion but she does not utilize Heyman's classification of four stages to facilitate comparison. Tod and Thoms report five year survival rates of 30% and 26.9%, respectively, for all patients treated, but Garland and Sisson report their results as 11.8% "arrested for five years." It would be particularly desirable to know the effect of treatment on those patients known to have residual disease at the time radiation therapy was instituted. Tod reports 28% five year survival for such patients "completely treated." Thoms reports 13.8% five year survival for patients with stage II, III or IV disease who received any treatment. Garland and Sisson are not explicit.—Eds.]

Role of Ionizing Radiations in Causation of Ovarian Tumors is examined by Harold Speert.² From the records of Presbyterian Hospital,

(2) *Cancer* 5:478-484, May, 1952.

New York City, it was concluded that among 958 patients irradiated for uterine bleeding and followed up for six years, occurrence of ovarian tumors was well within normal expectation for such a group. There were two malignant and two nonmalignant tumors. A review of 343 patients with ovarian cancer and of 247 consecutive patients with cystadenomas of the ovary, 17 (2.9%) had had previous pelvic irradiation for conditions other than carcinoma. Thus radiation castration does not appear to affect the eventual histology of tumors.

Direct experimental evidence proves that radiation can cause granulosa cell tumors in mice through a hormonal mechanism. The fact that in man there is no etiologic counterpart of the ovarian tumors that occur in mice may be attributable to quantitative differences wrought by irradiation, or it may indicate differing ovarian growth and tumor forming potentials in the two species. There is no basis for the fear that human ovarian neoplasms may result from pelvic irradiation.

Endometriosis: Its Management and End Results. Robert A. Hays and U. V. Portmann³ (Cleveland Clinic) discuss 142 patients seen in 1939-49. Dysmenorrhea, which is acquired and progressive, is the commonest symptom of endometriosis. It was present in 57% of the patients;

RESULTS OF DIFFERENT TREATMENT METHODS IN ENDOMETRIOSIS

METHOD	GOOD	FAIR	POOR	GOOD RESULT, %
Radical surgery	33	5	4	78.5
Conservative surgery	30	4	6	75.0
Irradiation	33		1	97.0
Medical	2	10	3	13.3

excessive menses in 41.5%. Headache, pelvic pain, rectal distress and dyspareunia were less frequent. Examination showed painful pelvic masses or small nodules along the uterosacral ligaments. Of the married patients, 37.1% were sterile. The ovary is the commonest site of involvement (58.5%), followed by the uterus, culdesac, uterosacral ligament and rectovaginal septum. Fibroids were associated with endometriosis in 37.7% of patients.

Treatment depends on the patient's age, extent of involvement and severity of symptoms. Ovarian function is necessary for the continued growth of the ectopic endometrium; therefore, ablation of the ovaries, either surgically or by irradiation, results in relief from symptoms and regression of the lesions. Conservative measures with preservation of some ovarian activity is desirable if possible.

In this series, 42 patients underwent radical surgery, bilateral oophorectomy with or without hysterectomy. In 40, conservative surgery was done, leaving some ovarian tissue. Fifteen received medical treatment, i.e., androgens. Thirty-four were given x-ray therapy, a skin dose of 250 r anteriorly daily to 400-600 r delivered to the ovaries. In large patients the use of the anterior field was alternated with a sacral field.

Roentgen therapy gave the best results with the least morbidity (see table). Ninety-seven per cent of the patients so treated were

(3) Am. J. Roentgenol. 66:773-782, November, 1951.

symptom free when last seen. Patients usually had one menstrual period after treatment. The only disagreeable effects of roentgen therapy were the menopausal symptoms which usually appeared about two months later. Whenever possible these disturbances should be curbed by reassurance or mild sedation. In a few patients the symptoms may be so aggravating that replacement therapy is indicated, but this should be avoided because of the possibility of inducing false menstruation or "spotting."

Postconception Pelvic Irradiation. Karl M. Neimand, Jesse Holland and Martin Shir⁴ (Jewish Hosp., Brooklyn) report a case.

Negro woman, 29, had a radical mastectomy and postoperative irradiation for carcinoma of the breast with axillary metastasis. Ovarian sterilizing x-ray treatment was given, with a dose of 1,200 r to each of four pelvic ports (depth dose to ovaries 600 r) over 14 days. Factors were 200 kv., 0.5 mm. Cu and 1 mm. Al filtration, surface-tube distance 50 cm., field 10 × 15 cm. An unknown pregnancy of about 5 weeks' duration at time of treatment was discovered by routine x-rays at 5½ months' gestation. Full term pregnancy resulted in birth of a normal boy, 3 lb. 14 oz. and 16½ in. long. Physical and mental development was normal; at age 1 weight was 22 lb.

Although underweight was the only deleterious effect in this infant, this does not presage against damage to be revealed later, since it has been conclusively shown previously that grave consequences result from irradiation of the embryo.

[This is an exceptional instance of normal development after considerable pelvic irradiation which would have been expected to produce a monstrosity. It illustrates that human biologic radiation effects do not always occur true to form. Predictions and prognoses should be tempered by knowledge of these facts.—Eds.]

Radiation Effects on Normal Endocervix and on Adenocarcinoma of Cervix are described by C. P. Cherry⁵ (Cambridge). The observations are based on study of histologic material from 56 patients with carcinoma of the cervix treated with radium, the total dose varying from 4,500 to 17,000 r over two to three weeks. In the normal endocervix radiation changes are induced sooner in the premenopausal than in the menopausal cervix. In the normal cervix glands, hypersecretion is followed by shedding of both secretion and cells, and ultimately regeneration occurs. The normal surface and duct epithelium show an eosinophilic condensation of the cytoplasm simulating parakeratosis; this change is reversible and regeneration follows.

In adenocarcinomas, after irradiation there may be a breaking up of the tumor foci, simplification of the glandular structure of the tumor, hypersecretion and eosinophilic condensation of the cytoplasm of the tumor cells. The last two changes do not indicate that the tumor cells have been rendered nonviable.

The eosinophilic cytoplasmic condensation that appears in the normal and malignant cells differs from that induced by irradiation in squamous cells.

The authors conclude that the radiation effects induced in the normal endocervix are of a similar nature to those induced in adenocarcinomas of the cervix.

(4) *New York J. Med.* 51:1641-1642, July 1, 1951.

(5) *J. Obst. & Gynaec. Brit. Emp.* 58:774-779, October, 1951.

Roentgen Castration of Ovaries and Its Effect on Blood Picture. V. Gruenberger, F. Pakesch and W. Rankl⁶ (Univ. of Vienna) investigated 69 women sterilized with x-ray, 56 because of metrorrhagia, 11 because of metrorrhagia with fibroid and 2 because of endometriosis. They received 600 r to each field in eight treatments. Peripheral blood and sternal marrow studies were made on most patients for up to 10 years. The former showed no significant changes, whereas a reduced number of megakaryocytes with nuclear hypersegmentation and predominantly basophil plasma were found in the latter during the first three years after treatment, together with increase in involutinal forms. During the next two years juvenile forms of megakaryocytes were seen. Five to seven years after treatment, increase in megakaryocytes and accelerated platelet formation were noted, but after this time the findings were by and large normal. Erythropoiesis and reticulum cells were increased during the first five years. Granulopoiesis was not affected.

These changes were not seen after surgical castration despite most patients having received intensive postoperative x-ray treatment for carcinoma. Therefore they are not due to the radiation effect on bone marrow. Changes similar to those following x-ray sterilization are found, however, up to three years after the physiologic menopause. It is presumed that small amounts of follicle hormone continue to be produced for up to seven years after x-ray sterilization, thus stimulating bone marrow. Normal platelet formation occurs only after complete cessation of ovarian activity.

GENITOURINARY SYSTEM

Treatment of Wilms' Tumor. Carl Rusche⁷ presents statistical data pertaining to Wilms' tumor in 40 patients, aged 3 months to 10 years, seen in 20 years at Children's Hospital, Los Angeles, and in private practice. Of that number, 28 (70%) are dead; 5 (12.5%) have lived

THERAPY ADMINISTERED TO 40 PATIENTS WITH WILMS' TUMOR

	DIED	ALIVE < 5 Yr.	ALIVE > 10 Yr.
Nephrectomy only	2	—	—
Nephrectomy and postoperative radiation	12	5	2
Preoperative radiation and nephrectomy	3	—	2
Preoperative radiation, nephrectomy and postoperative radiation	5	2	1
Radiation only	3	—	—
Biopsy	1	—	—
Not treated	2	—	—
Totals	28	7	5

over 10 years and may be considered cured; 7 (17.5%) have lived less than 10 years since diagnosis (see table). The five who have lived over 10 years had radiation as an adjunct to nephrectomy; three received it preoperatively. One child, reported alive 55 months after diagnosis and

(6) Wien. klin. Wchnschr. 63:525-527, July, 1951.

(7) J. Urol. 65:950-963, June, 1951.

considered a five year cure with no evidence of recurrence, received radiation therapy pre- and postoperatively.

Nephrectomy after roentgen therapy is indicated, because the main mass of the tumor contains radioresistant cells which are not completely destroyed; if unremoved, they may cause eventual recurrence. The interval between administration of first roentgen therapy and surgery allows for establishing the full effects of radiotherapy; this period among patients who died ranged from 2½ to 9½ weeks, and among those who lived, from 1 to 8 weeks. Of the three patients who have lived longest, all received approximately the same amount of irradiation in proportion to their ages.

No criteria have been found as to the most beneficial dosage, since individual structural variations of the tumors preclude uniformity of

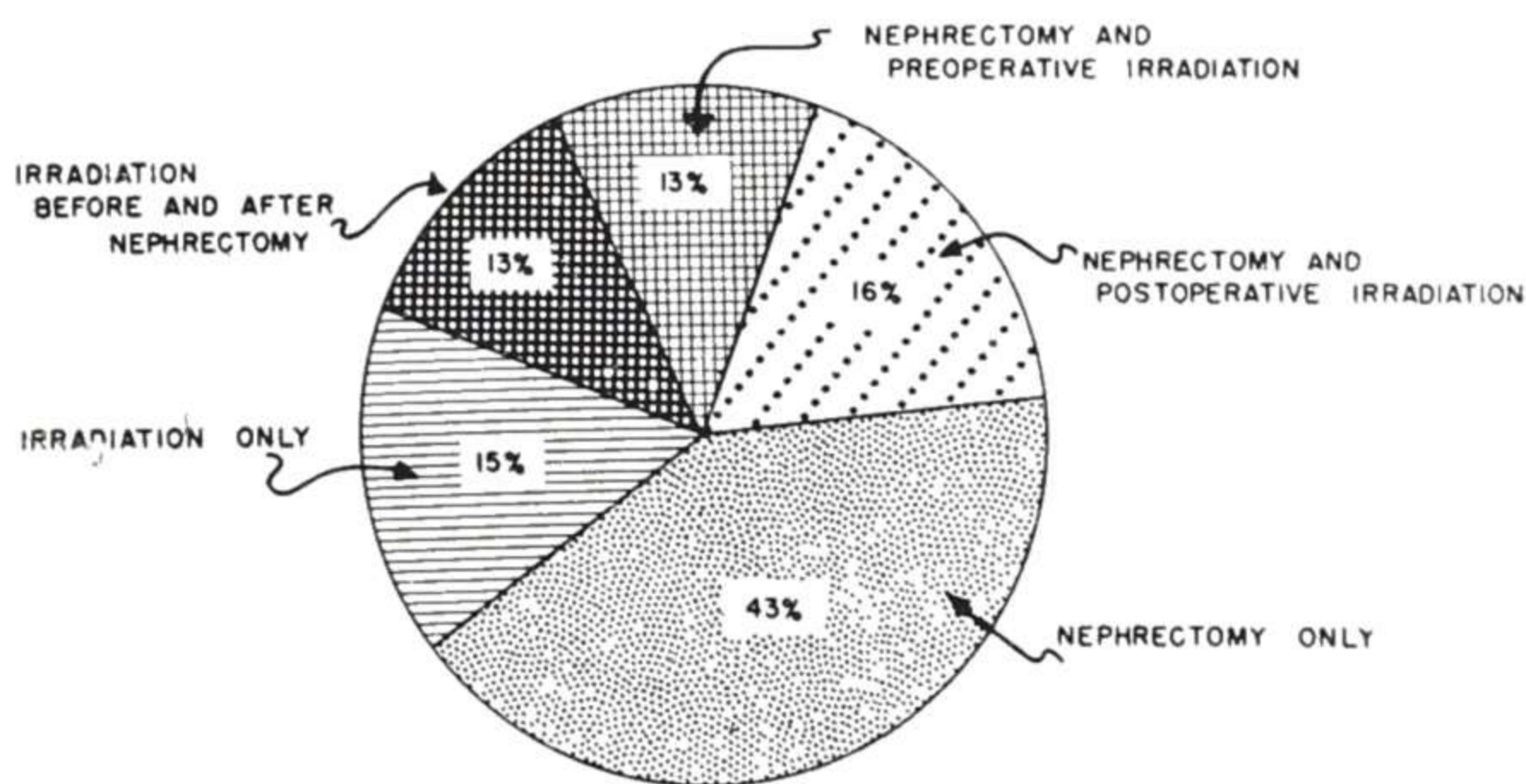


Fig. 340.—Reported five year survival of 72 patients with Wilms' tumor relative to type of therapy administered. (Courtesy of Rusche, C.: *J. Urol.* 65:950-963, June, 1951.)

response to irradiation. Opinions are divergent and recommended dosages range from 75 to 200 r/day; most of the author's patients received 150 r daily.

Of 72 patients so far reported in the literature as five year survivals, 43% had nephrectomy alone and 57% had some form of roentgen therapy. The percentage of cures relative to the type of therapy is illustrated in Figure 340.

It is concluded that radiation therapy should be instituted as soon as the diagnosis of Wilms' tumor is established and that nephrectomy should be postponed until after such treatment. Further study by a team consisting of general surgeon, radiologist and pediatrician to work out the most acceptable plan of treatment of malignant renal neoplasm in children is suggested.

Malignant Testicular Tumors: Clinical and Therapeutic Evaluation of 158 Cases is presented by Gustave Kaplan, Benjamin B. Cohen and Bernard Roswit⁸ (V. A. Hosp., Bronx, N. Y.). There were 58 of seminoma, 58 of embryonal carcinoma, 24 of teratocarcinoma, 10 of choriocarcinoma and 8 of miscellaneous and undetermined type. The commonest symptom and sign was testicular swelling. The right testis was involved in 96 patients; 2 had bilateral tumors. History of trauma was present in 26, hydrocele in 8, nondescent of the testis in 7 and

(8) *Am. J. Roentgenol.* 66:405-419, September, 1951.

history of orchitis in 3. Metastatic spread occurs almost invariably by way of the lymphatic vessels. Sixty per cent of the patients had metastases when hospitalized or at some time afterward during the disease.

Treatment consisted of surgical removal of the involved testis and immediate irradiation of the abdominal lymph node-bearing area. Deep x-ray therapy was given no matter what the type of tumor or whether there was clinical evidence of metastases. A depth dose of 150 r was given daily to the upper and lower abdominal zones alternately and 100 r daily to the inguinal region. If metastatic nodes were not demon-

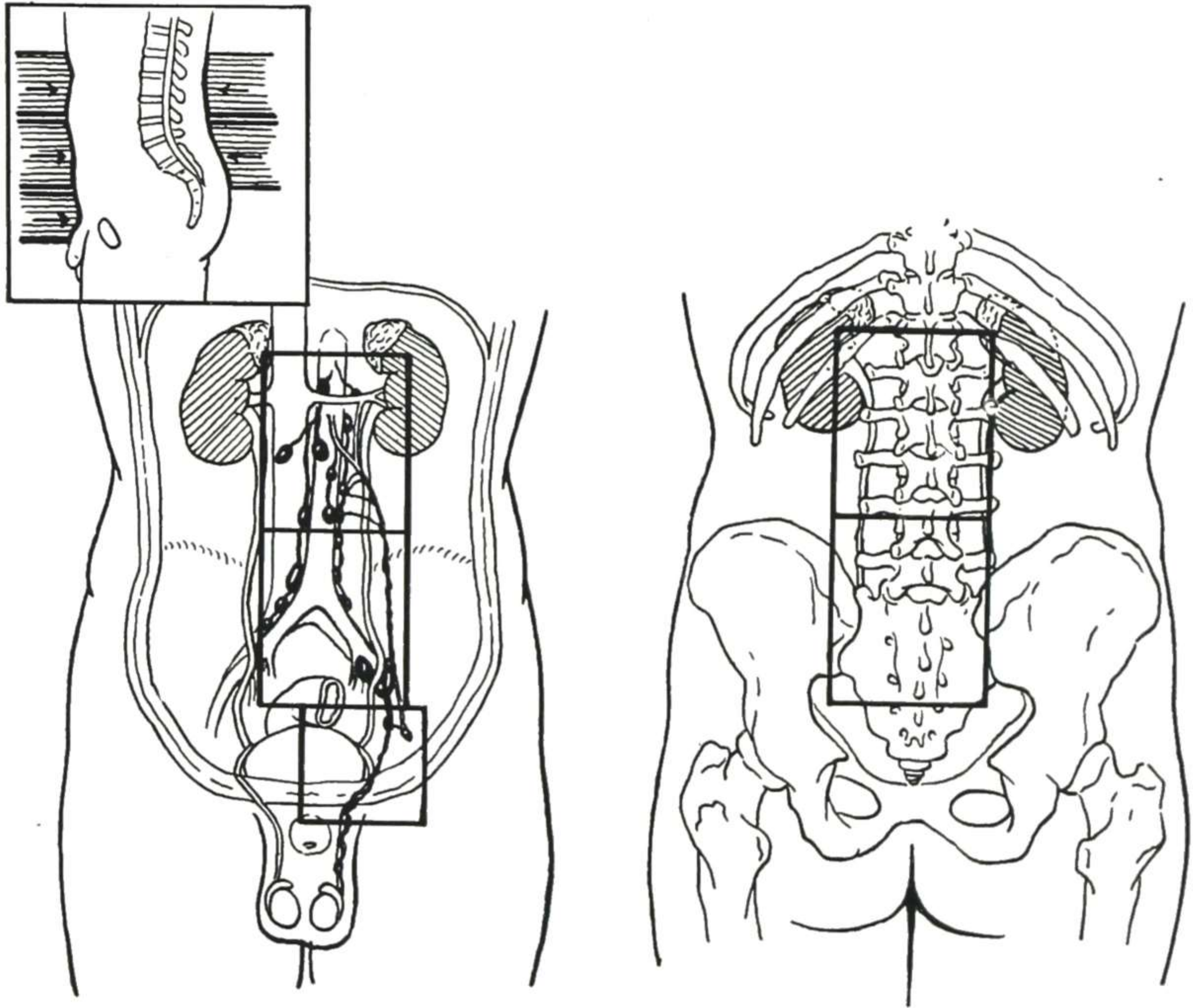


Fig. 341.—Lymphatic drainage of testis (after Rouviere) and arrangement of treatment portals for effective crossfire irradiation of upper and lower retroperitoneal zones. Note location of abdominal portals slightly to left for left-sided involvement. (Courtesy of Kaplan, G., *et al.*: *Am. J. Roentgenol.* 66:405-419, September, 1951.)

strable clinically, three anterior portals were used—epigastric, lower abdominal and inguinal—and two posterior fields—combined upper lumbar and lower dorsal, and lower lumbar (Fig. 341). Crossfire radiation was delivered to the upper and lower retroperitoneal zones and to the inguinal area for a depth dose of 2,000 r for seminomas and 3,000 r for the other groups.

Three year survival rate was highest in the seminoma group (45.5%). For embryonal carcinoma it was 32.6%; for teratocarcinoma 26.6% and for choriocarcinoma 11.1%. Over-all three year survival rate was 34%.

In each group, clinical presence of metastases was important in prognosis. Of 22 patients with seminoma and no clinical evidence of metastases, 13 survived three years. Of 27 patients in the other groups

who had no metastases when first seen, 18 survived three years. If a patient survives three years, prognosis is excellent.

Results of Surgery in Tumor of Testis, Especially Radical Removal. George F. Cahill⁹ (Columbia-Presbyterian Med. Center) reviewed 93 cases of malignant tumor of the testicle to analyze results of therapy.

X-ray therapy alone was used in five patients who had presumptive evidence of metastases. Two died in one year and one in two years. One is alive after 10 years and another after 13; in both these patients cancer had never been proved pathologically. In nine patients the testis was removed through an inguinal incision. Of five with malignant tumors, one died in one year and four survived over three years. The other four tumors were considered benign, and the patients are alive after 4, 4, 7 and 20 years.

Removal of the testis through an inguinal incision was followed by x-ray therapy in 43 patients. Eighteen died within one year, 4 in two years and 1 in four years. There were no other deaths during a follow-up of 2-18 years for 17 patients, but a number were subsequently lost to follow-up.

Radical removal alone was used in three patients. One has been followed 20 years, one 8 years and one 7; all are free from apparent disease.

Radical removal followed by x-ray therapy was used in 26 patients. Four who had metastases at the time of surgery died in one year. One died of metastases in 2 years and one in 14 years. The rest have been followed 1-20 years without evidence of spread of tumor.

Radical surgery combined with postoperative radiation therapy is the treatment of choice in malignant tumors of the testis.

Tumors of Testicle: Irradiation Therapy. These malignant tumors may be classified as follows, so far as treatment is concerned: radiosensitive—seminoma, radioresistant—embryonal carcinoma, teratoma, teratocarcinoma and chorioepithelioma, and miscellaneous. J. C. Kimbrough¹ (Walter Reed Gen'l Hosp.) points out that although seminomas are more radiosensitive than the other types, radiation therapy alone cannot be depended on to control tumor spread, because seminomas may metastasize as radioresistant types. The treatment of choice is radical surgical excision of the retroperitoneal lymphatics, testis and spermatic cord, followed by irradiation.

Treatment is started 7-10 days after operation. The treatment fields covering the lymphatic drainage channels extend from the external ring to the diaphragm anteriorly and posteriorly. Patients in whom retroperitoneal metastases are found at operation are irradiated from the diaphragm upward through the mediastinum and left supraclavicular areas. The 1,000 kv. unit is used. One field is treated daily with a 400 roentgen skin dose. Total tumor dose to the lymphatics is 2,000 r in 15 days for seminoma and 4,000 r in 25 days for all other types.

Palliative irradiation is used to relieve pain, delay the spread and prolong life in patients with hopeless metastases of various structures.

(9) J. Urol. 66:280-284, August, 1951.

(1) Surg., Gynec. & Obst. 94:535-538, May, 1952.

The dosage is established by observing the tumor reaction and the patient's general condition.

Malignant Disease of Testis: Special Reference to Radiotherapy. T. M. Prosser² (Westminster Hosp., London) discusses 147 cases (1930-50). The tumors were classified in three groups: seminoma, teratoma and chorionepithelioma. This classification is justified on clinical grounds, age incidence and prognosis. Seminoma is a carcinoma of the epithelium of the adult seminal tubules. Grossly, the seminoma is of homogeneous consistency; microscopically, it is composed of large- or medium-sized spheroidal cells with sharp outlines, clear pale cytoplasm and round hyperchromatic nuclei, disposed in sheets or bands with fine fibrillary substrate. Teratoma and chorionepithelioma are derived from totipotent germinal cells in the germinal epithelium. The teratoma contains structures derived from all three germinal layers. Microscopically, the teratoma may be mature or embryonic; grossly, it may vary considerably in consistency and contour. The chorionepithelioma is usually small, soft and subject to necrosis and hemorrhage; microscopically, it is composed of continuous syncytial masses of irregular, multinucleated, undifferentiated epithelium with a substrate of large, clearly defined polygonal cells with single nuclei. e

Clinically, teratoma had a peak incidence in the 21-25 year age group and seminoma in the 31-35 year group. The latter rarely occurs in children. In patients with these types of tumor, bilateral involvement is rare. There is an increased incidence in the presence of undescended testes. A negative reaction to a biologic test should never be allowed to influence the diagnosis when there are clinical grounds for suspecting neoplasm. A positive reaction indicates a grave prognosis. Incidence of metastases was 50% in this series, being highest in the teratoma group (54%) and lower in the seminoma group (35%). In order of frequency, spread was to the iliac and para-aortic nodes, lungs, supraclavicular nodes, and scrotal and inguinal nodes. Secondary deposits in the lungs were nearly twice as common from teratomas as from seminomas.

Treatment consisted of orchiectomy, followed by prophylactic irradiation of iliac and para-aortic drainage fields. Factors were: 220 kv., 20 ma., half-value layer 2.2 mm. Cu, focus-skin distance 50 cm., two opposing 20 × 20 cm. fields, 2,500-3,000 r tumor dose in 30 days. Six weeks later the upper para-aortic nodes were treated through two opposing 15 × 10 cm. fields.

Of patients with seminoma treated before there was clinical evidence of metastases, 66 per cent were alive and free from disease after five or more years; of patients with teratoma, 55 per cent. Fifteen per cent of patients with seminoma or teratoma who had metastases when first seen were free from disease five years after irradiation.

Radiotherapy and Testicular Neoplasms. Geoffrey Boden and Robert Gibb³ (Manchester, England) report results in 128 cases observed between 1936 and 1945. Seminomas accounted for 85% of all histologically

(2) Brit. J. Surg. 38:473-481, April, 1951.

(3) Lancet 2:1195-1197, Dec. 29, 1951.

verified lesions. There were 17 teratomas and 15 unclassified lesions.

On first examination it was found that metastases were already present in 52% of the patients. The incidence was approximately equal in the seminoma and teratoma groups (Table 1). Results of radiotherapy, with preliminary orchiectomy on all but one patient, showed that the prognosis is much more favorable for seminomas than for teratomas; 80% of patients with seminomas but no initial clinical evidence of

TABLE 1.—PRESENCE OF METASTASES ON FIRST EXAMINATION

TYPE	No.	GROUP A: NO METASTASES	GROUP B: ABDOMINAL METASTASES	GROUP C: DISTANT METASTASES
Seminoma	96	50 (52%)	29 (30%)	17 (18%)
Teratoma	17	10 (59%)	4 (23%)	3 (18%)
Unclassified	15	2 (13%)	6 (40%)	7 (47%)
All types	128	62 (48%)	39 (30%)	27 (22%)

TABLE 2.—FIVE YEAR SURVIVAL AFTER ORCHIECTOMY AND X-RAY THERAPY

GROUP	SEMINOMA		TERATOMA		UNCLASSIFIED	
	No.	No. Alive	No.	No. Alive	No.	No. Alive
A	50	40 (80%)	10	5	2	2
B	29	12 (41%)	4	1	6	1
C	17	2 (12%)	3	0	7	0
All groups	96	54 (57%)	17	6 (35%)	15	3 (20%)

metastases survived five years (Table 2). Simple orchiectomy alone has been successful in only 25% of a comparable group. Even seminoma patients with metastasis had a higher survival rate (41%) than patients with most other carcinomas that have metastasized locally.

The authors conclude that the favorable results obtainable are not widely known. It is not enough to perform orchiectomy for a testicular tumor and send the patient for irradiation only when frank metastases have occurred. This procedure halves the patient's chances of survival. All patients should be given x-ray therapy immediately after orchiectomy, whether there are secondary deposits present or not.

Carcinoma of Penis. John W. Bassett⁴ analyzed histories of 78 consecutive patients with carcinoma of the penis. The disease affects young and old alike, and in Negroes tends to appear earlier and more frequently. Circumcision in infancy or early childhood protects against penile cancer; adult circumcision is less protective. The site of origin of the epidermoid tumor did not seem to affect its gross behavior. Larger epidermoid tumors of the penis have the poorer prognosis, but no critical size was noted. Histologic grading of anaplasia of tumors was not a reliable criterion for treatment. Extent of invasion was related to higher grades of metastases. Distant metastases are uncommon. The tumor spreads by lymphatic embolization, and not by growth in continuity through lymphatic vessels. Clinical criteria are unreliable for diagnosing metastases to the groin. Histologic study confirmed such metastases in 33% of these patients. Of those with metastases at time of treatment, only one patient lived five years. After onset of symptoms almost all patients lived over two years and nearly one-third lived over six years. When possible, partial amputation of the penis

(4) Cancer 5:530-538, May, 1952.

is satisfactory treatment for the primary lesion and local recurrence thereafter is rare. No form of treatment of regional metastases has been satisfactory. Roentgen or telerradium irradiation is used before, after or independently of surgery, but there is no proof that it has ever destroyed tumor in groin nodes. Many therapists do not consider irradiation the best treatment for metastatic carcinoma of the penis. Of 21 patients treated with irradiation and surgery, 5 lived for five years. Dissection of nodes was the preferred therapy.

[The author's statement that "partial amputation of the penis is a very satisfactory form of treatment for the primary lesion" seems a rather aggressive and unilateral stand. The chance for cure depends on whether or not metastasis has occurred. If metastasis has occurred the evidence in this article indicates that cure is not possible. If there are no metastases, then the aim of treatment is to eradicate a localized accessible lesion. In these circumstances the cure rate by irradiation should be high.—Eds.]

Radiation Therapy in Diseases of Genitourinary Tract is reported by William E. Costolow⁵ (Los Angeles). Radiation is often the only treatment used in Peyronie's disease; 32 patients were treated with justifiable results between 1907 and 1947, with radium tubes or needles filtered by 0.5-1 mm. Pt equivalent applied at 1 cm. distance. Ten were clinically cured; 18 were improved and 4 were not.

Radium is preferred for small carcinomas of the penis (to 2 cm. diameter) without metastasis. Either external application (1 cm. or more distance) or platinum-filtered radium element needles of low intensity inserted around the lesion is used. Of eight patients treated between 1938 and 1948, three died, four were living after five years and one after three years.

In the literature are many reports of good results of treatment of testicular tumors by a combination of orchietomy and roentgen therapy, particularly in seminomas. Of 50 patients seen between 1926 and 1943, 23 had seminoma (survival rate 47%). Over-all five year survival rate was 36%; 56% of the entire group had metastases when first seen and 33% of these survived five years. Even with metastases, favorable results may be obtained in seminoma or in embryonal carcinoma with seminoma.

Radiation therapy is palliative in carcinoma of the prostate. With bone metastasis many patients become free from pain. Roentgen therapy should be combined with hormone therapy and castration in cases with limited painful bony metastasis.

Radiation therapy is also palliative in kidney malignancies. In Wilms' tumors it causes pronounced regression but ultimate results are poor even with surgery because metastasis is rapid and widespread.

Radiation therapy of carcinoma of the bladder varies. More appears to be accomplished by means of external supervoltage roentgen therapy than with seed and needle therapy; however, patients who have previously had seeds and needles in the bladder will not respond to external roentgen therapy when disease has extended beyond the bladder wall. Results bear out the conclusion that papillary carcinoma is more amenable to treatment than the infiltrating type. Between 1933 and 1946, of

(5) Urol. & Cutan. Rev. 55:324-327, June, 1951.

24 patients with papillary type, 33% survived five years. Of 33 with infiltrating carcinoma, only 6% lived five years. Over-all five year survival rate of 75 patients was 13.5%.

Fulguration combined with external roentgen therapy produced best results.

Radiotherapy in Treatment of Nonspecific Inflammatory Stricture of Ureter is reported by Gordon D. Oppenheimer, Lester Narins and Norman Simon⁶ (Mount Sinai Hosp., New York City).

Man, 57, had right pubic pain for two years and had noted intermittent gross, painless hematuria for three months. Examination revealed grossly bloody urine. Cystoscopy revealed several small submucosal hemorrhages around the right ureteral orifice. The right ureter was blocked to all catheters. Roentgenograms showed a right ureterohydronephrosis with narrowing of the lower ureter and no evidence of calculus. The right ureter was explored. Biopsy showed inflammatory tissue. The patient did well postoperatively but there was no decrease in degree of ureterohydronephrosis two weeks later. A T tube was removed and a resulting urinary fistula closed a month later. Despite administration of a variety of antibiotics and cystoscopic dilatation of the right ureter, pain and pyuria persisted. Acid fast studies gave negative results.

As a last resort a series of 12 x-ray treatments directed to the lower right ureter was started. Anterior (10 × 15 cm.) and posterior (15 × 20 cm.) portals each received 600 r (air) in six weeks. Factors were: 200 kv., 20 ma., Thoraeus filtration (half-value layer, 2 mm. Cu) and target-skin distance 50 cm. Three weeks after beginning x-ray treatment, he reported relief from pain for the first time in several years. The voided urine became microscopically negative, even though all antibiotics and chemotherapeutic drugs had been stopped. The intravenous pyelogram returned to normal. He remained symptom-free, with urine microscopically negative.

The authors conclude that healing may follow radiotherapy for nonspecific inflammatory lesions of the urinary tract.

[It is interesting that the authors found no reports in the literature describing this valuable method for lesions of this nature.—Eds.]

Osteitis Pubis and Its Treatment by Roentgen Irradiation. Osteitis pubis occurs as an aftermath of suprapubic transurethral and retropubic prostatectomy, according to T. Leucutia⁷ (Harper Hosp., Detroit), but it is not presumed to follow uncomplicated perineal prostatectomy. It is a self-limiting disease. Cases reported secondary to nonurologic surgery are nearly always instances of osteomyelitis or osteitis pubis complicated by osteomyelitis. External trauma to the pubis and pyelonephritis are occasional causes. Excruciating pain, tetanic contractions of the muscles of the affected area and sometimes complete disability are the clinical features. The x-ray features differ according to whether the disease is in the prodromal, destructive or regenerative stage. The appearance is characteristic. Formerly osteitis pubis was confused with metastatic malignancy (Figs. 342 and 343). Prognosis is invariably good, with no mortality and complete healing.

Treatment is symptomatic and supportive. Its aim is to alleviate pain and shorten the clinical course. This can be accomplished by roentgen therapy alone or with other methods. Pain is relieved in a few weeks or months, and the period of disability is reduced from an average of 10 months to an average of 6 months. It is recommended

(6) J. Urol. 67:476-478, April, 1952.

(7) Am. J. Roentgenol. 66:385-404, September, 1951.

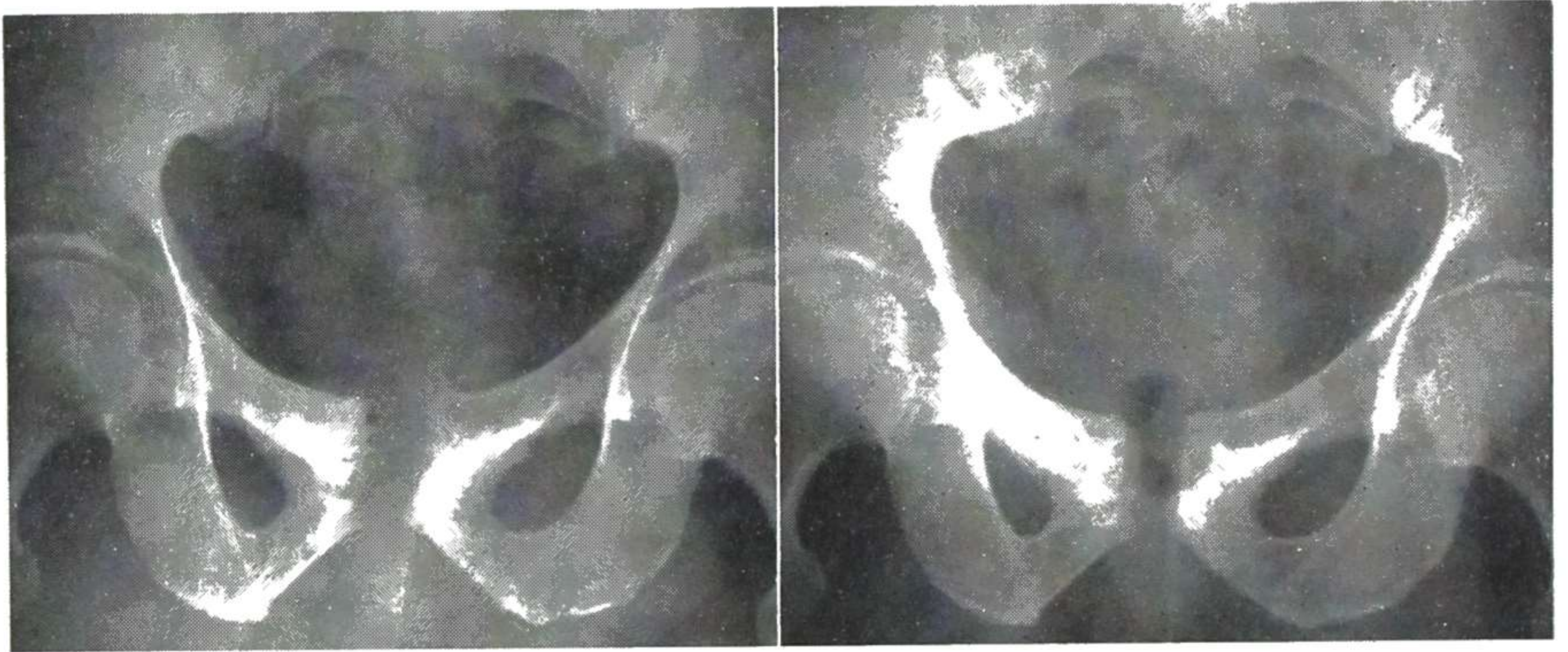


Fig. 342 (left).—Osteitis pubis erroneously diagnosed as carcinomatous extension from presumed recurrence six years following primary lesion of bladder. Before treatment.
 Fig. 343 (right).—Improvement about 1½ years after roentgen treatment.
 (Courtesy of Leucutia, T.: *Am. J. Roentgenol.* 66:385-404, September, 1951.)

that focal doses of 75-100 r be given at triweekly intervals with 200 kv., 1 mm. Cu, until acute symptoms subside and at gradually spaced intervals thereafter. Irradiation is stopped as soon as symptoms are satisfactorily alleviated. Reossification occurs in one to two years.

BLOOD DYSCRASIAS, LYMPHOMAS AND ALLIED DISEASES

Some Observations on Reticuloses and Their Treatment by X-rays.

Gwen Hilton⁸ (Univ. College Hosp., London) classifies reticuloses as Hodgkin's disease, Hodgkin's sarcoma, giant follicular lymphoma, reticulosarcoma, lymphoblastic and lymphocytic lymphomas, and mycosis fungoides. This is helpful in determining prognosis but the general treatment policy is the same for all. All patients should be treated when the diagnosis is established, regardless of whether they are asymptomatic or very ill. In no other form of malignant disease is treatment so successful in a patient who appears to be so ill.

When long-lived patients were compared with those who survived only a short time, no difference was noted in the x-ray dosage or in the general treatment plan. It cannot be determined whether treatment increases the length of life. The natural biologic course of the disease rather than the treatment method may be the most important factor in prognosis.

X-ray treatment should never be given so as to cause a severe reaction. As small a tumor dose as 600-700 r may be sufficient to cause disappearance of the enlarged glands of follicular lymphoma or lymphocytic or lymphoblastic lymphoma. Usually only a low dose is necessary if the glands are discrete and mobile, but a large mass of glands may require a tissue dose of 2,000-3,000 r.

[The term reticulosis, widely used in England, is equivalent to lymphoma or lymphoblastoma. In America reticulosis more commonly refers to the lipid storage diseases such as eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease.—Eds.]

(8) *Brit. J. Radiol.* 24:491-494, September, 1951.

Results of X-ray Treatment of Reticuloses are reported by Geoffrey Boden⁹ (London Hosp.). In 1940-44, 298 patients with reticuloses were treated at the Christie Hospital, Manchester. The table shows the results. Further analysis revealed no significant difference between sites. There was, however, a pronounced difference between generalized and localized disease. In sarcoma, crude five year survival rate was 52% for localized disease as compared to 5% for generalized disease. In Hodgkin's disease the rates were 53 and 12% respectively.

FIVE YEAR RESULTS IN 298 PATIENTS WITH RETICULOSES GIVEN X-RAY THERAPY

RETICULOSIS	No.	ALIVE	NOT TRACED	INTERCURRENT DEATH	% CRUDE SURVIVAL
Sarcoma	152	45	1	2	30
Hodgkin's disease	112	29	2	0	26
Other reticuloses	34	20	0	0	59

On the whole, the treatment method was the same for all types of reticulosis. The intent in the generalized cases was amelioration with the least discomfort to the patient. Treatment was considered palliative and the patient incurable. This does not imply inadequate therapy as elaborate technics were used. However, dosage rarely exceeded 50% of the tolerance for the appropriate volume being irradiated. Many patients, however, received radical treatment when it was reasonable to suppose that the disease might be curable despite spread outside one organ or lymph node group.

The patients with localized disease were treated according to the following principles: the zone to be treated must extend 5 cm. wide of the lesion or lymph node group in every direction; the whole anatomic lymph node group must be included in the zone to be treated, and the zone must be irradiated as one undivided volume. Local recurrence was rare, and failures were due to extension beyond the treated zone. At five years, most of the patients in the lymphoma group were apparently well and had not been retreated, whereas most of those in the Hodgkin's disease group were alive with disease and many had required additional therapy.

Since the entire reticuloendothelial system cannot be given the dosage necessary to eliminate the disease, and since cures do occur, it follows that there must be a stage of reticulosis which is not generalized. This is widely recognized in reticulosarcoma and lymphosarcoma which are true cancers.

To better evaluate reticulosis, biopsy should be repeated at long intervals on a given patient. Initially, biopsy may show nonspecific reticulosis. Only later may a more fully developed pattern be found. Since Hodgkin's disease can be cured when it is localized, earlier diagnosis is of paramount importance. Performance of more node biopsies and progressive histologic correlation may make this possible.

Treatment of Reticulosis by X-rays: II. Walter M. Levitt¹ (St. Bartholomew's Hosp., London) summarizes his treatment of primary

(9) Brit. J. Radiol. 24:494-498, September, 1951.

(1) Ibid., pp. 485-490.

lymphadenopathies, of which the classic type is Hodgkin's disease.

In stage 1, in which a single mobile node or mass is limited to a superficial area, the combination of surgery with radiotherapy is used with precautions to avoid skin or radiation damage.

In stage 2, the superficial mass is too extensive for radical surgery. Again it is important to conserve skin tolerance because the patient may require repeated treatments. The author gives 1,200-1,500 r over two weeks to the initial lesion; the larger the area treated the smaller, within these limits, the dose required. Progress is assessed every day. When dosage is reduced, no less than 50% over the dose required for eradication is given. Mediastinal irradiation (same dose) should be given in every case of cervical lymphadenoma, whether disease is demonstrable in the mediastinum or not. Pelvic nodes should be treated in the male and menopausal female when the initial lesion is in the groin.

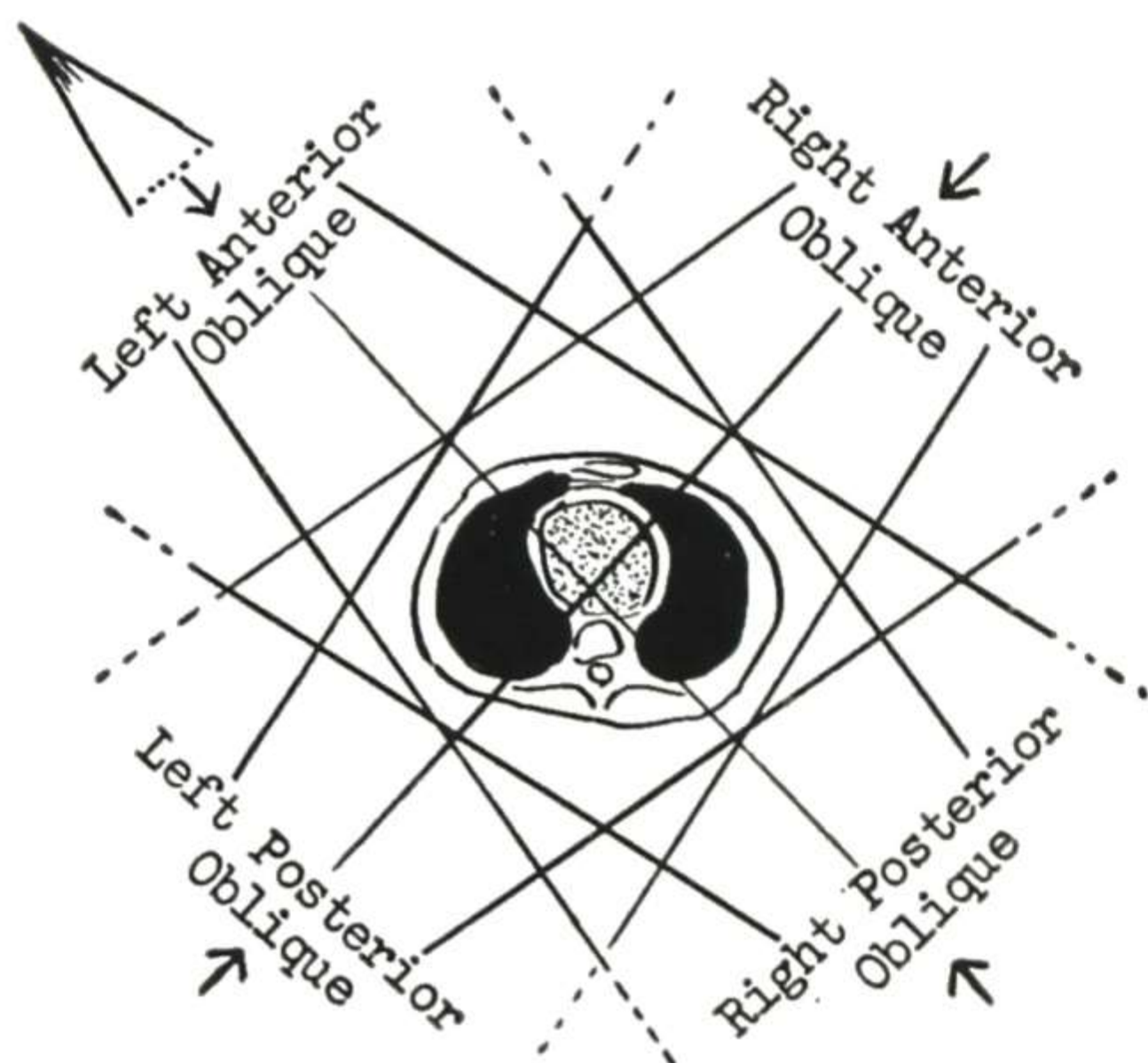


Fig. 344.—Thoracic bath technic. (Courtesy of Levitt, W. M.: *Brit. J. Radiol.* 24:485-490, September, 1951.)

In the lymphoid follicular variety of reticulosis which may rapidly become generalized, only known foci should be irradiated with dosage no higher than is required to eradicate them and with no routine irradiation of proximal deep nodes.

For a mobile remnant after irradiation of a large mass in Hodgkin's disease, surgical removal should be considered.

In stage 3, superficial nodular enlargement localized to one area occurs together with enlargement of related deep nodes. Superficial and deep nodes should be irradiated separately.

In stage 4 there are deep masses limited to a segment of the body. The patient with mediastinal, neck and axillary distribution has peribronchial extension into the lungs and should always receive bath irradiation. With a large epigastric mass there are almost certainly associated abdominal glandular masses; such patients should also receive bath irradiation. Groin and pelvis distribution should be treated more conservatively unless disease is suspected in the iliac fossae, when bath irradiation is indicated. Wherever a superficial mass is accessible, radiosensitivity should be estimated by exposing it to a small dose, say 150 r.

Early and rapid response indicates a high degree of radiosensitivity and promises almost certain relief from bath therapy.

In the thoracic bath, the whole thorax, axillae and supraclavicular regions are included in every beam (Fig. 344). The whole of the trunk can be raised to from 2,000 to 2,500 r over a period of about one month. Volume dosage is high but is remarkably well tolerated by most patients. The four field bath method provides 1,000 r to all four fields in most cases. George Innes, physicist, worked out the isodose distribution for this method (Fig. 345). Distribution is remarkably uniform and the whole section is raised about 200 r for every 100 r given to all four fields.

In the fifth stage generalization is complete. Trunk bath can be given if the long bones are shielded from radiation. Irradiation can be raised to 500 or 600 r. Trunk irradiation is not often justified in

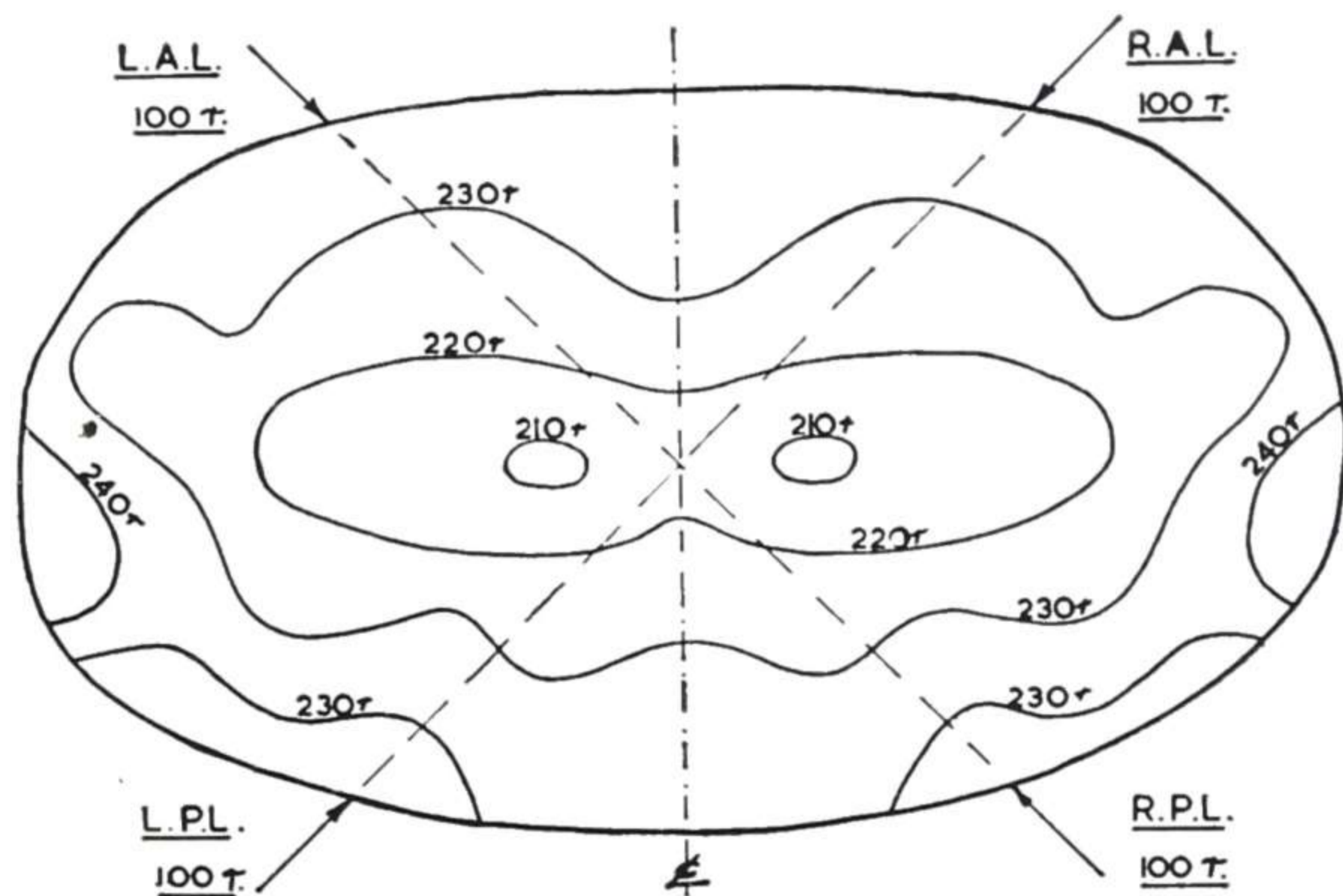


Fig. 345.—Four field bath technic. Dose distribution for 100 + to each field; 100 cm. focus-skin distance, open field, 2 mm. Cu half-value layer. (Courtesy of Levitt, W. M.: *Brit. J. Radiol.* 24:485-490, September, 1951.)

reticulosis, but is worth trying in a previously untreated case of high radiosensitivity.

Finally there is the problem patient with impalpable deep upper abdominal masses, possibly with Pel-Ebstein disease with anorexia, malaise and weight loss. Mid-bath treatment with the upper level of the field 2-3 cm. below the nipple line and the lower level 2-3 cm. above the umbilicus, will produce lysis of fever and remarkable general improvement at the end of the first week. If there is no improvement in two weeks, no harm will result from abandoning treatment.

Therapy and Prognosis of Lymphogranulomatosis. K. Hohl, Ph. Sarasin and W. Bessler² (Zurich) discuss 278 cases seen in 1922-50. Incidence did not increase in this period. The disease showed no predilection for either sex. Histologically it is differentiated by early, classic and late forms, and atypical forms. Among 113 patients who lived over five years, Peters found that 75% had early forms and 46% late forms, whereas only 25% of those with atypical forms lived five years.

(2) *Oncologia* 4:1-20, 1951.

The disease was localized in the cervical, supraclavicular or mediastinal nodes in 64% of the patients and in the axillary or inguinal nodes in 12%. In none was the spleen the primary site of the disease. Involvement of bones was always secondary. X-ray examination is of great value in establishing the diagnosis.

Sedimentation rate is 10-30 mm. in the early stage and increases to 60 mm. with extension of the disease. During successful treatment it falls to normal; a recurrent increase is a certain sign of new foci if other inflammatory processes can be excluded. Leukocytosis was present in 46% of the patients and eosinophilia of more than 3% was present in 48%. Anemia was a late symptom. Itching was noted by 38%. Fever, anorexia and weight loss were noted inconstantly.

The main form of treatment was x-ray therapy. To determine the focal dose, size of the diseased area, its distance from the surface, localization in relation to other important structures and varying sensitivity to radiation must be considered. In patients with low disease activity, 1,000-1,500 r given over 10-14 days results in freedom from symptoms for more than 10 years; when the disease is more active, 1,800-3,000 r given over two to three weeks is necessary. Mediastinal and retroperitoneal nodes require 3,000-4,000 r.

Results depend on stage and type of the disease. The former is determined by judging extension of the process: stage 1, involvement of one or more nodes in one region at the same time; stage 2, involvement of two or more adjacent regions; stage 3, involvement of several, but not adjacent, regions; stage 4, general involvement. Patients with stages 1 or 2 can be made asymptomatic for over 10 years, but this can never be accomplished in patients with stage 3 or 4.

The type or activity of the disease is determined by evaluating rapidity with which the process is spreading. Diagnosis is seldom made

RELATION BETWEEN AGE AND COURSE OF LYMPHOGRANULOMATOSIS

AGE	NO. OF PATIENTS	STAGE 1	STAGE 2	STAGE 3	STAGE 4	NO. LIVING OVER 5 YR.
1-10	4	4	0	0	0	2 (50%)
11-20	21	7	7	7	0	8 (38%)
21-30	35	11	14	7	3	12 (34%)
31-40	25	6	14	4	1	47 (28%)
41-50	22	4	11	6	1	5 (23%)
51-60	14	3	6	5	0	6 (43%)
61-70	4	2	0	1	1	0 (0%)
71-80	1	1	0	0	0	0 (0%)

in patients with very active disease in stage 1 or 2. Even when the condition is suspected, the diagnosis cannot be made with certainty because of the difficulty in determining whether the disease has spread to other regions. This explains the relatively low percentage of cures of acute and subacute cases in stages 1 and 2.

Disease activity was investigated in relation to sex, age and constitution. In comparable groups, 18% of the males and 42% of the females lived over five years. The table shows the relation between age and course of the disease, but no definite conclusions can be drawn from it. Constitutional factors could not be properly evaluated, but the

relation between accompanying symptoms and disease activity was of interest. All patients without such symptoms lived over 5 years and 64% over 10 years. Of those with symptoms from onset of the disease, 8% lived over five years.

Local x-ray treatment is preferred in stages 1 and 2, but is usually given too late (i.e., when disease activity is great). In stages 3 and 4, drugs should also be given; this is a palliative measure. In the early stages, drug therapy is a mistake, except when site of the disease cannot be located or in radioresistant cases. A combination of arsenic, nitrogen mustard, urethane and choline should be given in small doses. A summation effect is obtained and toxic effects are lessened. Three cases remained stationary for over a year with this therapy. Sex hormones were ineffective. Use of cortisone decreased temperature and pain and elicited a feeling of well-being, but no effect on the disease was noted.

Prognosis depends on stage and type of the disease. Of 124 patients in stages 1 or 2, 18% became symptom free and 3% lived 10-20 years after treatment. This did not take place with any of 41 patients in stage 3 or 4. Of patients in stage 1 or 2, 24% lived 5-10 years; 46%, 2-5 years, and 9%, 0-2 years; whereas for patients in stage 3 or 4, corresponding survival rates were 7, 52 and 41%.

[This is a careful study of a sizable group with Hodgkin's disease and it represents the present state of therapy and prognosis based on the total material of the Zurich Radiotherapy Center.—Eds.]

Quantitative Evaluation of Contribution of Nitrogen Mustard to Therapeutic Management of Hodgkin's Disease. Alfred Gellhorn and Vincent P. Collins³ (New Columbia Univ.) compared the course of the disease in two groups of patients: 67 who received radiotherapy and nitrogen mustard in alternating courses, and 65 radiotherapy alone. Nitrogen mustard was most effective in dosage of 0.2 mg./kg. body weight on two successive days. Heavy preinjection medication with barbiturates reduced nausea and vomiting. Radiotherapy was carried out with 180, 200 or 250 kv. (half-value layer 0.9-1.5 mc.). Earlier patients were treated to regression of evident disease or symptomatic improvement with a dose in air of 500-2,500 r. More recent policy has been to deliver about 70% of the tolerance dose radiation to the involved site when the disease was localized, or 50% tolerance dose when the disease was generalized.

No significant difference in four year survival rate was found in the two groups. However, amount of radiation required was less, asymptomatic period longer and economic burden lighter for patients receiving radiation and nitrogen mustard than for patients receiving radiotherapy alone.

The authors conclude that nitrogen mustard is a useful adjunct to radiotherapy in the management of Hodgkin's disease. It reduces requirements for radiation, but does not prolong life.

Simultaneous Treatment with Nitrogen Mustard and ACTH in Neoplastic Disease of Lymphatic System is reported by K. Fellingner, H. Braunsteiner, F. Pakesch and E. E. Reimer⁴ (Univ. of Vienna).

(3) *Ann. Int. Med.* 35:1250-1259, December, 1951.

(4) *Wien. klin. Wchnschr.* 63:572-573, Aug. 10, 1951.

Patient with lymphatic leukemia did not respond to irradiation of the spleen, and granulocytopenia and purpura developed. Nitrogen mustard was given in doses of 2.5 mg. for a total of 30 mg. Four equal intravenous injections of ACTH totalling 110 mg. were given, followed by smaller doses until 1,000 mg. ACTH was given for the first series. Later 150 mg. was given after a rest. The effect of ACTH was followed by measuring excretion of oxysteroids and ketosteroids and eosinophil count. Within five days, purpura receded and total leukocyte count dropped from 20,000 to 9,000, with reappearance of previously depressed granulocytes and thrombocytes. Lymph nodes became smaller; sternal marrow showed no abnormalities. During this treatment, he felt good and had increased appetite.

In over 100 patients treated with nitrogen mustard alone, no such regression of lymphadenopathy or such increase in granulocytes and thrombocytes was seen. A second patient with lymphogranuloma also promptly improved with ACTH and cortisone given in an interval between nitrogen mustard treatments.

[Our experience with the use of ACTH and cortisone in the lymphatoid diseases has been disappointing in general because the initial improvement is usually so short-lived, often less than a month. They do give a temporary "lift," however.—Eds.]

Giant Follicle Lymphoma Followed by Pregnancies. A case is reported by W. Ronald Frazier⁵ (Portland, Ore.).

Woman, 27, with documented generalized giant follicle lymphoma received x-ray therapy to a large abdominal tumor in divided doses three times a week over 32 days, to a total of 2,772 r. Amenorrhea lasting two years was followed by irregular menstrual periods. She had a single pregnancy five years after x-ray therapy and a twin pregnancy six years after treatment.

It is estimated that the pelvic organs of this patient received 970 r in divided doses of 35 r triweekly for two months, which probably constitutes a temporary or borderline sterilizing dose. Eleven years after irradiation no evidence of tumor was found and all three children were living and well.

It is recommended that caution be used in giving advice concerning sterility following x-ray therapy because of the great variation in the dose required for sterilization.

[This case illustrates the tremendous recovery power of the human ovary and represents an excellent result following conservative roentgen therapy of lymphoma.—Eds.]

Roentgen Therapy in Chronic Leukemia. Carsten Müller and Erik Poppe⁶ (Univ. Hosp., Oslo) review results in 109 patients with lymphatic and 95 with myelogenous leukemia. The patients were treated during 1914-49 and had all died at the time of the study. Duration of life was calculated from onset of symptoms.

Local irradiation was used exclusively until 1929. Later total body irradiation was used most often, with combined local and total body irradiation in some cases. Duration of life with local therapy only was on the average five months shorter than that with total body or combined therapy. This difference may be real, but there is a 30-40% chance that it is fortuitous. Improved irradiation technic and safer dosage, with increasing use of transfusions and antibiotics, may place total body irradiation in too flattering a light. In the opposite direction,

(5) West. J. Surg. 59:405-410, July, 1951.

(6) Acta radiol. 36:418-431, November, 1951.

however, lies the exclusion from this study of patients who are still alive. There is no statistically significant difference in average duration of life if patients are divided according to diagnosis, sex and method of treatment, other than that males with chronic lymphatic leukemia given combined local and total body irradiation have a higher mean survival time than those receiving other forms of therapy.

Treatment is given only in case of subjective discomfort. The red blood cell count is more important than the increase in number of leukocytes. Local irradiation should be given in lymphatic leukemia. In myelogenous leukemia, total body irradiation should be used, although excessive splenomegaly calls for local therapy. In total body irradiation the single dose should not exceed 15 r; in local irradiation, preferably not more than 100 r and never more than 125 r should be given with a field no larger than 10×15 cm.

Bone marrow aplasia occurred in 15 patients, of whom 10 died. Aplasia is no more frequent with total body than with local irradiation.

Evaluation of Radiophosphorus Therapy in Primary Polycythemia.

Charles F. Stroebel, Byron E. Hall and Gertrude L. Pease⁷ analyze data from the 199 patients with primary polycythemia treated with radiophosphorus at Mayo Clinic from 1942 to 1949. For comparison, they consider 32 patients treated by means other than radiophosphorus who died of known causes.

The patient is prepared for treatment by repeated venesections until the hematocrit reading has reached 55%. The initial dose of radiophosphorus is 5-7 mc. given intravenously as dibasic phosphate in isotonic saline solution. For oral administration the dose is increased 30%. Complete blood examinations are done after six to eight weeks, and radiophosphorus is administered at these intervals until a remission is obtained.

No criteria were found in pretreatment data on these patients which could absolutely predict the response to treatment. Nevertheless, there was about 90% success of radiophosphorus therapy in the 21 patients with no changes other than the basic criteria of elevated erythrocyte count (over 6,000,000) and hematocrit reading (over 55%). The other 10% represented lack of clinical remission. When splenomegaly, hypervolemia, leukemoid reaction, hyperuricemia or a history of vascular accidents was present in addition to the basic criteria, incidence of failure and complications was increased. Of the 148 radiophosphorus-treated patients of all categories who had adequate post-treatment study, 75.7% were treated successfully without complications. There were many fewer vascular accidents in the phosphorus-treated group than in the others, in whom vascular accidents tended to occur within the first decade of the disease. It is too early to evaluate the effect of radiophosphorus on the incidence of leukemia, for it occurred late in the course of the polycythemia in the 32 non-phosphorus-treated patients and radiophosphorus has been in use for only about 10 years.

(7) J.A.M.A. 146:1301-1307, Aug. 4, 1951.

MISCELLANEOUS CONDITIONS

X-ray Therapy in Carcinoma of Esophagus. T. A. Watson and E. M. Brown⁸ (Saskatoon Cancer Clinic) report four cases in which autopsy showed no evidence of residual tumor in the esophagus.

CASE 1.—Man, 66, had difficulty in swallowing solids for two years. He was hospitalized in August. Weight loss was not evident. X-ray examination showed an irregularity in the lower esophagus but no obstruction; esophagoscopy, a lesion 2 in. below the aortic arch. Biopsy revealed grade II epidermoid carcinoma. He was given beam-directed x-ray therapy. Factors were: 400 kv., 5 ma., half-value layer 4.4 mm. Cu, focus-skin distance 80 cm., six fields 15 × 6 cm., total tumor dose 6,000 r in five weeks (25 treatments, each field daily). In December, barium swallow showed a smooth esophagus with no obstruction. He died 38 months after treatment. Autopsy showed metastases to the liver, stomach, vertebrae, pancreas and abdominal lymph nodes.

CASE 2.—Man, 60, had difficulty in swallowing for a month. He had lost 10 lb. X-ray examination revealed a lesion in the midesophagus. This was confirmed by esophagoscopy. A chest x-ray showed an inactive tuberculous focus in the left apex. He was given beam-directed x-ray therapy. Factors were: 400 kv., 5 ma., half-value layer 4.40 mm. Cu, focus-skin distance 80 cm., six fields 15 × 6 cm., total tumor dose 5,500 r in three weeks (15 treatments, each field daily). He died of tuberculosis four months later.

CASE 3.—Man, 63, had pain in the retrosternal area and difficulty in swallowing for four months. There was no weight loss. An x-ray examination showed a lesion in the lower third of the esophagus. This was confirmed by esophagoscopy. Biopsy revealed grade III epidermoid carcinoma. He was given beam-directed x-ray therapy. Factors were: 400 kv., 5 ma., half-value layer 4.40 mm. Cu, focus-skin distance 80 cm., six fields 15 × 6 cm., total tumor dose 5,500 r in three weeks (15 treatments, each field daily). He died of coronary thrombosis 15 months after treatment.

CASE 4.—Man, 52, had difficulty in swallowing for eight months. X-ray examination showed the lesion causing obstruction to be at the level of the aortic arch; esophagoscopy, at the junction of the upper and middle third. Biopsy revealed squamous cell carcinoma. He was given beam-directed x-ray therapy with the betatron. Factors were: 22 Mev, focus-skin distance 105 cm., three fields 15 × 6 cm., tumor dose 6,000 equivalent roentgens in three weeks. He died three months later. Autopsy showed ulceration of the posterior wall of the esophagus and a retroesophageal abscess.

[This again illustrates that squamous cell cancer of the esophagus can be destroyed in its primary site by irradiation but that distant metastases and complications often nullify the results.—Eds.]

Treatment of Cancer of Esophagus with Roentgen Therapy. Jean Papillon and M. Goyon⁹ (Lyon) report results of roentgen therapy in 69 inoperable cases, many of them so far advanced that the serious general and local condition might have been considered a contraindication to irradiation. All patients referred to the authors, except those beyond help and those whose life expectancy was less than a month, were treated; of 69 given roentgen therapy, 50 were in bad condition.

TECHNIC.—Minimal tumor dose was 5,000 r, calculated according to the isodose curves of Mayneord; physical factors were: 200 kv., 1 mm. Cu filter, 60 cm. focal distance. Fields were generally 5 cm. wide, length varying according to dimensions of the tumor. Eight fields were used in treating the thoracic esophagus: three anterior, three posterior and two axillary; for the cervical

(8) J. Thoracic Surg. 22:216-218, August, 1951.

(9) Bull. Assoc. franç. étude cancer 38:212-224, 1951.

esophagus, six fields were used. Centering was verified by fluoroscopy and radiography.

Improvement was prompt in many cases; dysphagia, regurgitation and pain regressed markedly after a few treatments. Some patients regained weight and strength and had renewed activity; others, despite greater ease in eating, remained in precarious condition from radiation effects. Despite extensive and systematic use of penicillin, intensive irradiation of chronically infected tumor of the posterior mediastinum may lead to such complications as hemorrhage, perforation, mediastinitis and radiation pneumonitis. Infectious complications vary in severity and duration; antibiotics, especially aureomycin, are of value in controlling

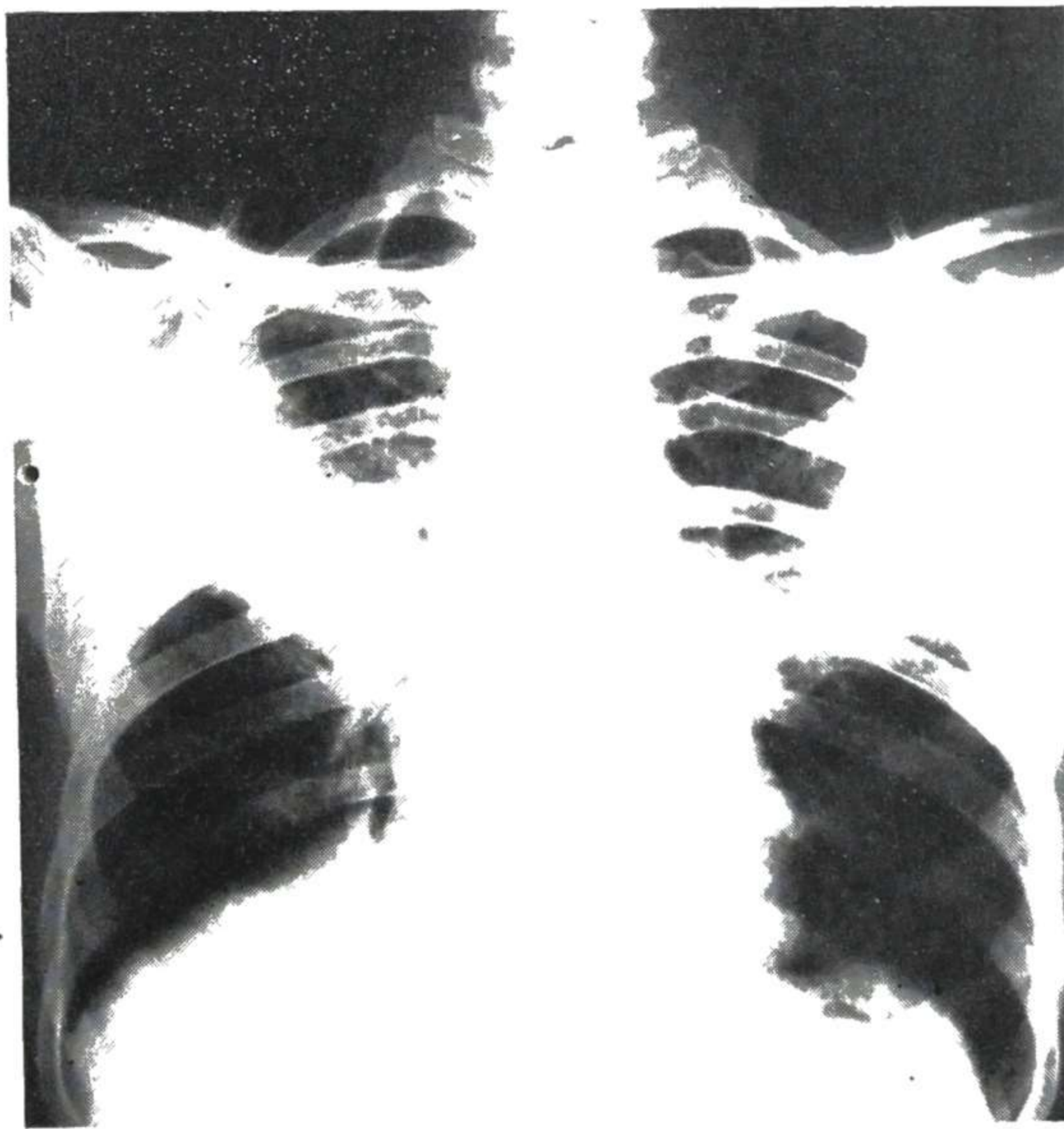


Fig. 346.—Lungs after radiotherapy; autopsy showed interstitial pneumonia and esophagus free from neoplastic cells. (Courtesy of Papillon, J., and Goyon, M.: *Bull. Assoc. franç. étude cancer* 38:212-224, 1951.)

them. Alterations in the lung parenchyma resulting from radiation appeared in three cases, accompanied by signs of bronchial irritation, with respiratory difficulty, slight dyspnea and frequent coughing. The changes did not appear until the sixth month and their effect on the general condition was slight. Radiologically they appeared as bilateral opacities, either paramediastinal or fan-shaped, suspended symmetrically in each hemithorax from hilus to axillary region, corresponding exactly to section irradiated (Fig. 346).

Of the 69 patients treated, 52 died (average survival over 6 months); 17 were living (average survival over 9 months with maximum 22 months). Prospects of survival are best when the lesion is less than 5 cm. in extent. Cures are exceptional, even though the tumor itself can be locally sterilized. Indications for radiotherapy are based on local conditions, particularly size of the tumor and the patient's general resistance

(the 50 patients in poor condition had average survival of only 5 months as against 11.7 months for those in better condition). These indications should be broad, but should include risks inherent to the treatment; sarcomas, because of high risk of perforation, should be among the contraindications.

The chief advantage of radiotherapy is in the functional field. Relief of dysphagia has psychologic as well as physical value and, even when it cannot increase life expectancy, radiotherapy is a useful and comparatively comfortable palliative procedure.

Preliminary Results of Roentgen Therapy Alone in Treatment of Epitheliomas of Esophagus. F. Baclesse, J. Reverdy, J. Desclaux and H. Jammet¹ treated 28 patients at the Curie Foundation between October 1948 and December 1949. Treatment was given through narrow, greatly elongated fields in a cross-fire pattern, after fluoroscopic centering at each session. Of the 28 patients, 3 were alive on Jan. 1, 1951, after 2 years 2 months, 2 years 1 month and 1 year 3 months. Twenty-five died of relapse; 13 had metastases via the blood (lungs, bones, liver, etc.), with local recurrence in some. Lesions in those who survived were in the middle third of the esophagus; lesions in the upper and lower thirds resulted in death.

Study of these cases led to certain major conclusions. (1) Roentgen therapy should be reserved for cancers in the upper and middle third whereas surgery is the treatment for cancers in the lower third, especially in the juxtacardiac segment. (2) Among contraindications, even for palliative treatment are: stenosing lesion, causing suprastrictural dilatation, with rapidly increasing dysphagia and weight loss; stubborn stabbing chest pains, unrelieved by irradiation (indicative of poor prognosis); supraclavicular adenopathy; paralysis of the recurrent nerve, and distant metastases (blood-borne). Only patients without these contraindications survived more than 1½ years. (3) Lymphatic dissemination may involve the full length of the mediastinum; this makes it necessary to use fields enclosing practically the total length of the esophagus. Furthermore, invasion via the lymphatics may penetrate the floor of the mediastinum and reach the subdiaphragmatic nodes, presenting a problem which can only be met by surgery. (4) Metastases carried by the blood were found in 13 patients; if the same high ratio is found in larger series, it will indicate poor prognosis for those who survive after roentgen treatment. Metastases of this kind cannot be attributed to therapy; rather, the survival period permits them to become evident. (5) When the lesion is secondary or represents a third localization of neoplastic disease, the outlook is grave; patients may apparently be cured of cancer elsewhere, only to die of cancer of the esophagus.

Rotation Therapy in Cancer of Esophagus: Some Statistical Results. L. Mallet and R. Decker² report on 157 patients, 55 in such bad condition that they either refused treatment or were unable to undergo it. The other 102 received 3,500 r or more; 40% survived for six months

(1) Bull. Assoc. franç. étude cancer 38:225-227, 1951.

(2) Ibid., pp. 308-316.

to one year and 9% for more than a year. Cancer of the esophagus is rare before age 45; only 12 patients were under 45.

In many cases surgery had been carried out either as a palliative or an exploratory procedure. Analysis of results shows that the chances of survival are slight for patients subjected to gastrostomy either before or during rotation therapy and that if a tumor is found to be inoperable on exploration, it is better to use cyclotherapy without associated surgery. Although less risky than surgery, rotation therapy requires careful attention to the patient's general condition. The authors use 190 kv., 18 ma. and focal distance 60 cm. (from anode to the skin of the sternal region). The field at the skin is 8×23 cm. The patient is seated upright on a turning platform. The daily dose to the tumor is 150 r. Most patients in this series had a total prescribed dose of 4,500 r. As a result of experience, treatment is given in series of 1,500 r (10 daily applications of 150 r), each separated by a week of rest.

Most patients have inflammation of the esophagus during treatment and as a result of it; mediastinal and bronchopulmonary reactions also occur. These difficulties are lessened when the series of treatments are separated by a week's rest. In almost all cases in which treatment can be completed, there is definite improvement, both functionally and radiologically. Diminution of dysphagia, in the absence of definite cure, enables the patient to recover his weight and morale. Death is finally caused by metastases or recurrences in situ in about equal proportions. Results could be improved with earlier treatment; 75% of the patients appeared for treatment at least three months after the condition became clinically evident. Cyclotherapy might well precede any form of palliative surgery, as in cervical cancer; by reducing inflammatory phenomena due to infection and limiting spread of the tumor, it would enable the surgeon to operate under more favorable conditions.

Roentgen Rotation Therapy in Cancer of Esophagus as practiced in the Jubilee Clinic, Lund, Sweden, is reported by Inge Gynning.³

TECHNIC.—The patient is placed in a revolving chair with the arms upstretched and the hands resting on a trapeze (Fig. 347). He is fixed by means of a band around the upper part of the thorax and another around the legs below the knees. The roentgen tube and fluorescent screen are movable in a vertical direction. Distance between the focus and rotation center is 53 cm.; between focus and fluorescent screen, 106 cm. Factors are: 170 kv., 15 ma., 0.5 mm. Cu plus 1 mm. Al filter, half-value layer 0.85 mm. Cu. Continuous fluoroscopic control is carried out from adjacent observation booth, from which the diaphragm is also manipulated. Tumor dose is measured directly, using Sievert's ionization chambers contained in rubber bougies passed into the esophagus. When there is near agreement, four to five measurements are considered sufficient. Daily dose is 200-225 r, being as high as possible without causing too great a general or local reaction. Total dose approaches 6,500 r/35 days or 6,800 r/40 days. Influence of the time factor is evaluated according to Strandqvist's fractionation diagram for treatment of carcinoma of the skin (Fig. 348).

In support of the dosage suggested, results obtained in 88 patients treated in 1943-47 are reported. Minimal time of observation was three years. The x-ray diagnosis was verified in all but three. Distinct im-

(3) Acta radiol. 35:428-442, May-June, 1951.



Fig. 347.—Position for roentgen rotation therapy of esophageal cancer. (Courtesy of Gynning, I.: *Acta radiol.* 35:428-442, May-June, 1951.)

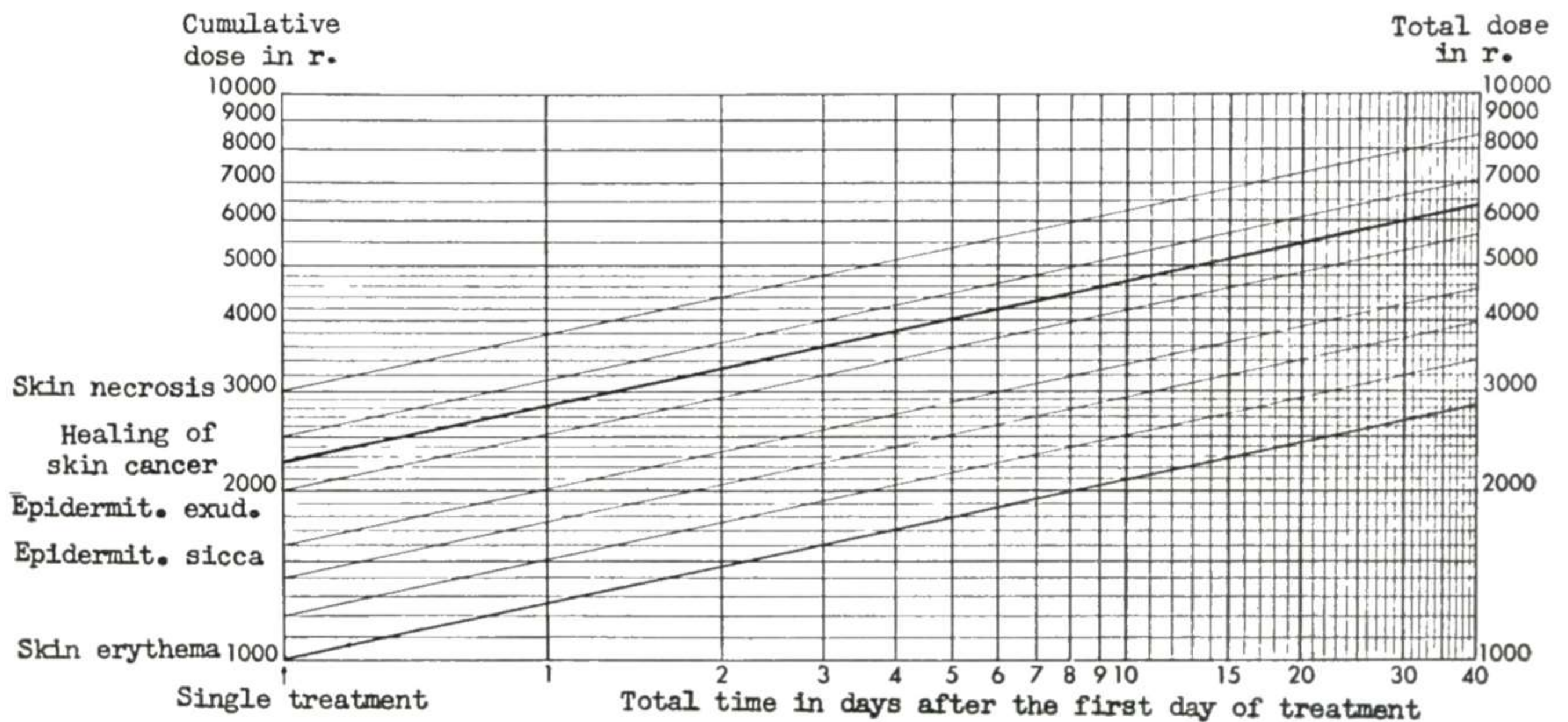


Fig. 348.—Strandqvist's fractionation diagram. (Courtesy of Gynning, I.: *Acta radiol.* 35:428-442, May-June, 1951.)

provement was noted in 70. Signs of overdosage were seen in 12, mostly ulceration in the esophagus in the tumor area. Two of these healed after gastrostomy (later closed). In four cases of overdosage, autopsy revealed no signs of a growth in the irradiated area.

Of the 88 patients, 8 were free from signs for at least three years (1 for six years; 4 for five years). They tolerated the treatment well despite old age and comparatively poor general condition. The method is of special value in inoperable carcinoma of the esophagus regardless of location.

Hodgkin's Disease of Esophagus with disappearance of lesion with x-ray therapy is reported by Jørgen Bichel⁴ (Univ. of Aarhus).

Man, 21, had severe generalized itching for a year, with fatigue and swelling of a right axillary node. Biopsy showed Hodgkin's granuloma, and the node was irradiated. He remained asymptomatic for about a year, when itching recurred together with dysphagia. X-rays of the lungs were normal, but one of the esophagus showed irregularities and narrowing of the lumen at the level of the fourth dorsal vertebra. Esophagoscopy showed a bulky, irregular tumor extending 6-8 cm. on the anterior esophageal wall about 28 cm. from the teeth. Biopsy revealed Hodgkin's granuloma. X-ray rotation therapy was given, with a tumor dose of about 3,000 r. Four months later an x-ray showed a normal esophagus. Dysphagia had disappeared. Though he died two years later of generalized Hodgkin's disease, autopsy showed the esophagus to be free from disease.

Even though Hodgkin's disease of the esophagus is rare, it should be considered in patients with Hodgkin's disease who have dysphagia. X-ray therapy in these cases may often give dramatic results.

Primary Lymphosarcoma of Stomach. George Crile, Jr., John B. Hazard and Kenneth L. Allen⁵ (Cleveland Clinic) discuss 19 histologically proved cases. Average age of the patients was 54. The commonest symptom was epigastric pain, and average duration of symptoms was 26 months. The patients were in relatively good condition. Only one had anemia. Free acid values were almost normal. X-ray examination showed a smooth, rounded filling defect which involved a large portion of the stomach, with thick gastric folds and multiple ulceration. Since the clinical picture of lymphosarcoma was so similar to that of carcinoma of the stomach, the correct diagnosis was made preoperatively in only one case. Thirteen of the 15 patients who survived total or subtotal gastrectomy also received roentgen therapy.

Thirteen patients (68%) were alive and well an average of five years after operation. Two lived 4 and 10 years, and died of other causes without recurrence. Thus, there were no known recurrences.

Since lymphosarcoma can rarely be diagnosed before operation and prognosis is good, biopsy should be done in every case of tumor of the stomach. The recommended treatment for lymphosarcoma is gastric resection followed by irradiation, or irradiation only if the lesion is not resectable.

Irradiation of Bronchial Carcinoma in 262 patients observed since 1921 is reported by K. Schärer⁶ (Univ. of Zürich). The results contradict the concept of well recognized surgeons such as Frey and Nissen who maintain that radiation therapy results only in severe damage to the patient. Early diagnosis and treatment are essential. Diagnostic methods of value include x-ray, laminagraphy, bronchography, bronchoscopy and examination of the sputum and of bronchial secretions.

Operative removal at an early stage offers the best prospect of cure and is therefore the treatment of choice. Inoperable patients are submitted to an intensive course of radiotherapy as early as possible, since in some cases cure is still possible. Treatment is usually given to three

(4) Acta radiol. 35:371-374, May-June, 1951.

(5) Ann. Surg. 135:39-43, January, 1952.

(6) Oncologia 4:5-93, 1951.

fields with the average total dosage between 2,600 and 4,300 r in air to each. In the late stages, there is no prospect of cure, but in many cases a satisfactory palliative result is still obtainable.

Roentgen Therapy of Bronchial Cancer (Statistical Study of 110 Cases) is reported by J. Papillon, R. Violland and M. Goyon.⁷ Of the 96 patients treated by irradiation alone, 53 received palliative therapy, consisting of a tumor dose up to 3,000 r given by two or four fields over an extended interval. In curative therapy, given to 43, a tumor dose of about 5,000 r was administered. Previous pneumonectomies were performed in 14 cases. A beneficial effect was observed in 75% of the patients treated.

The authors do not attempt to compare the results of surgery and of radiotherapy, since each technic applies to different patients. A gross survey of surgical statistics reveals that more than 20% of patients submitting to surgery have survived more than three years, not including operative mortality which is 15-20%.

The combination of radiotherapy and surgery may appear theoretically satisfactory but is difficult to realize. Preoperative irradiation does not render inoperable lesions operable and tolerance to postoperative irradiation is mediocre.

The radiotherapeutic technics practically eliminate the immediate mortality but cannot produce more than a small number of three year survivals. It is believed, however, that better selection of cases for irradiation could improve this percentage.

Roentgen Treatment of Bronchial Asthma in 53 patients is discussed by B. Refslund Poulsen⁸ (Esbjerg, Denmark).

METHOD.—All patients received treatment to four 16 × 10 cm. fields directed to the right and left anterior and posterior hilar areas. Dosage was 100 r × 4 to each field, treating two fields at one time. Most patients received the full course; some stopped at 300 r. Factors were 160 kv., filtration 0.5 mm. Cu and 1.0 mm. Al, at a distance of 30 cm.

Practically all of the 53 patients had had severe chronic bronchial asthma for three months to three years or more. Of 48 whose results were known, condition in 8 was unchanged, in 22 improved and in 18 considerably improved. In most cases improvement occurred not later than a week after the end of treatment. Usually the benefit was only transitory. Repeat treatment in eight patients gave improvement but failed in two.

The effect of x-rays is thought to be directly on the bronchi. The most reasonable explanation might be that x-rays produce a desensitization of the sensory nerves, giving a slight analgesic effect. Radiation should not be used in children and should be used only after all other measures have failed. It should be used primarily in middle-aged patients with long-standing chronic asthma.

Management of Bone Tumors: Some Debatable Problems are discussed by Norman L. Higinbotham⁹ (Cornell Univ.). Adequate diagnosis is of prime importance. It is a grave error to institute treatment of any bone tumor without microscopic confirmation of the diagnosis.

(7) *J. radiol. et électrol.* 33:12-21, 1952.

(8) *Acta radiol.* 37:364-368, Mar.-Apr., 1952.

(9) *S. Clin. North America* 31:317-328, April, 1951.

If the tentative diagnosis is benign tumor, the aim should be complete removal; if a tumor is suspected to be malignant, biopsy of a representative area should be performed. Aspiration biopsy with an 18 gauge needle proved satisfactory in 80% of the author's cases. For central medullary lesions, a Turkel needle can be used.

The clinician should make the final diagnosis on the basis of clinical, roentgenographic and microscopic observations. If the pathologist is experienced, the microscopic findings are the most reliable. A rare exception may be in the case of a large, bulky cartilaginous tumor which the roentgenologist reports as malignant but which appears to be a benign chondroma microscopically. It is safer to regard these as malignant and to treat them accordingly.

In general, a combination of irradiation and surgery is indicated in management of bone tumors. In primary reticulum cell sarcoma a tissue dose of 3,000-4,000 r should be given to the entire tumor area. Ewing's sarcoma should be treated by irradiation and Coley's toxin. Amputation may be used in selected cases if response to irradiation is poor.

Osteogenic sarcoma, including fibro- and chondrosarcoma, is a surgical problem. When the lower end of the femur is involved, high thigh or subtrochanteric amputation may be performed. This is justified by the lesser degree of shock, decreased morbidity and improved stump. Contraindications are central medullary fibrosarcoma or any osteoblastic sarcoma extending above the metaphyseal zone. In osteogenic sarcoma irradiation may be used for palliation or in patients who hesitate to undergo amputation. Preoperative use of irradiation appears to have no beneficial effect and serves only to delay the surgical procedure.

Metastatic lesions are almost always an irradiation problem. However, if a swollen useless extremity is a burden to a patient whose general condition is good, amputation may be indicated.

Benign bone tumors should be removed surgically. The lesions of Hand-Schüller-Christian disease and solitary eosinophilic granuloma may be irradiated. Since eosinophilic granuloma may be resistant in the second, third and fourth decades, surgical curettage is preferred. Surgical treatment of benign lesions includes curettage and local excision, segmental resection being reserved for unusual cases.

Excellent results are obtained in giant cell tumor with either irradiation or surgery. The chosen treatment method should be persisted in to its ultimate conclusion. Irradiation is of value in treating lesions in inaccessible regions. Radiation therapy should not be given postoperatively.

In evaluation of trauma, the following postulates are a useful guide: authenticity of trauma; importance or severity of trauma; evidence of integrity of the part before injury; correspondence of the tumor to the site of injury; reasonable time relationship between trauma and appearance of tumor, and a well established diagnosis. Each case, however, must be evaluated individually.

Osteosarcoma of Iliac Bone Treated by Radiotherapy. R. Valegeas¹ reports an apparent cure about five years after surgical removal of a breast tumor which followed osteosarcoma.

(1) *J. radiol. et électrol.* 32:541-542, 1951.

Girl, 18, was referred for radiography of the left hip. She had fallen on the left side 10 months previously, and 4 months later sharp pain developed in the bone and continued without relief. An x-ray showed disappearance of the trabeculae, considerable rarefaction of the cortex and, at several points, its complete disappearance (Fig. 349). Diagnosis was osteolytic osteosarcoma.

Radiotherapy was given, using three fields, anterior, lateral and posterior. Factors were: 200 kv., 2 mm. Cu plus 2 mm. Al filter, 45 cm. distance, 250 r daily, alternating the fields, to total dose 5,250 r. The general and local condition improved. Five months later 6,000 r was given.

The patient resumed her studies and passed examinations at normal school. Successive radiographic examinations showed constant improvement. Two years later, in view of the excellent results, the referring physician suggested that the tumor was not an osteosarcoma but a giant cell tumor. Since there are

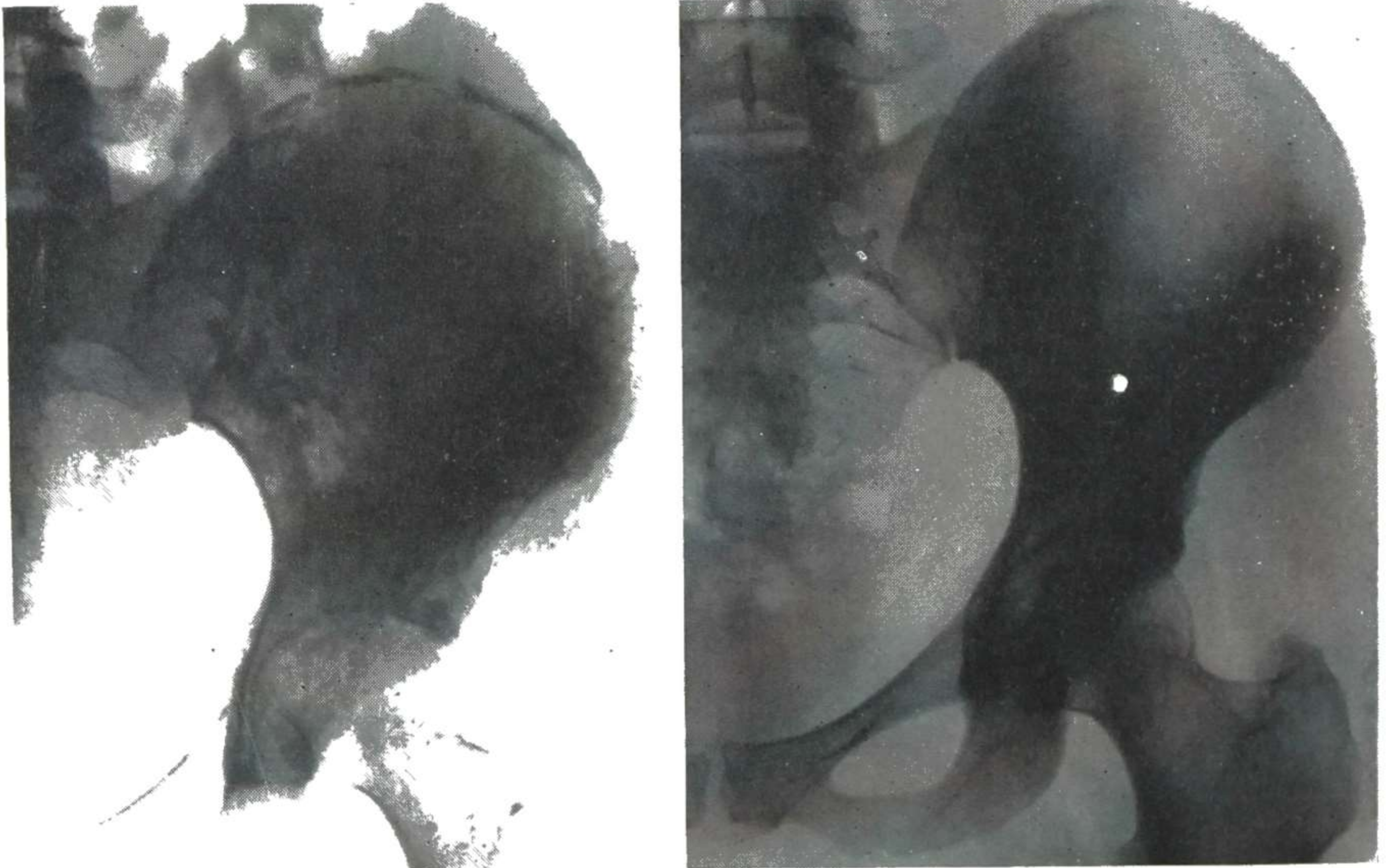


Fig. 349 (left).—Film made on admission.
Fig. 350 (right).—Film made about seven years later.
(Courtesy of Valegeas, R.: *J. radiol. et électrol.* 32:541-542, 1951.)

osteolytic giant cell tumors which cause partial destruction of the cortex, the diagnosis might be open to question. However, 2½ years after admission the patient presented herself with a breast tumor which had developed rapidly without affecting her general condition. It was removed, and laboratory examination showed it to be indisputably malignant, probably lymphoreticulosarcoma. Radiosensitivity was considered likely. The patient was given 3,000 r at the level of the axilla. Radiography of the hip two months later showed no change. No recurrence has taken place (Fig. 350), and the patient is in perfect health.

If the original diagnosis of osteosarcoma was erroneous, it must be admitted that a giant cell tumor can give rise to metastases, in this case a lymphoreticulosarcoma, or that the breast tumor was not metastatic but primary.

[While this is an interesting case report, the uncertain pathology and incomplete dosage details detract from its value.—Eds.]

Carcinoma of Thymus of Granulomatous Type, recently distinguished from Hodgkin's disease, is a cancer of young adults which starts as a superior anterior mediastinal mass and invades from that site. A clinical and pathologic study of nine cases is reported by Elizabeth Lowenhaupt

and Reynold Brown² (Univ. of California). Material for this study was obtained by excision (three cases), by biopsy of superior anterior mediastinal mass (one case) or by biopsy of an extension to skin or lymph nodes (five cases). Autopsy was performed in five instances; in two, diagnosis of Hodgkin's disease was made before death.

The tumor extends anteriorly through the chest wall, superiorly to supraclavicular areas and, later, to cervical tissues and, by retrograde lymphatic permeation, to form large retroperitoneal masses. Remote metastatic involvement is not part of the picture and is minor when compared to the extent of local process. The histologic picture indicates the epithelial nature of the tumor.

Complete surgical resection may be effective early in the disease. No effect of nitrogen mustard or melamine was noted. After surgical resection and possible cure, it does not seem reasonable to give radiation therapy to prevent development of something not present at the time of treatment.

Radiation therapy may be effective in the treated area. The amount required will need further study, but it would appear that more is needed than that ordinarily used for Hodgkin's disease. Determination of the amount of radiation to be delivered requires individual consideration. The authors plan on 5,000-6,000 r in 40-45 days if permanent arrest is being considered. After partial resection, size and distribution of the tumor must be considered in planning therapy. Presence of metastases may indicate that only as much radiation should be given as is compatible with the patient's general well-being, as no attempt at permanent arrest is being made.

Depth dose considerations indicate that 200 kv. or more with a half-value layer of more than 1 mm. Cu should be used. Target-surface distance should be 50 cm. or more. Multiple fields, laid out by means of isodose curves, may provide uniform irradiation and spare much of the lung.

The authors conclude that early diagnosis may open the possibility of permanent arrest of tumors still confined to the mediastinum.

[It would appear advisable to differentiate this epithelial type of neoplasm from Hodgkin's disease because it requires a larger amount of treatment for arrest or control.—Eds.]

Neuroblastoma in an infant with a six year cure by roentgen therapy is reported by Stanley M. Beck, Jr., and Philip J. Howard³ (Henry Ford Hosp., Detroit).

Boy, born on Nov. 4, 1944, in apparent excellent condition, was examined at age 3 weeks for occasional vomiting and a solitary mass was felt 2 cm. below left costal margin. X-rays showed a questionable mass in the left upper quadrant and the liver seemed enlarged. Blood cell count, blood studies and tuberculin test gave normal results. At 9 weeks the mass in the left upper quadrant was more definite. He was hospitalized with abdominal distention, the liver extending 8 cm. below the costal margin and left upper quadrant mass extending 7 cm. below the costal margin. Comedones and acne were present on the cheeks.

X-ray of the chest showed moderate elevation of the left diaphragm. Flat x-rays of the abdomen revealed only slight increase in density in the upper part of the abdomen, with downward displacement of intestines. Intravenous pyelo-

(2) *Cancer* 4:1193-1209, November, 1951.

(3) *Am. J. Dis. Child.* 82:325-334, September, 1951.

grams showed no excretion of dye into the right kidney. The left kidney was visualized and appeared normal. Skull and long bones showed no abnormalities. Biopsy disclosed a tumor of the left adrenal gland diagnosed as malignant neurocytoma.

Roentgen therapy was begun immediately, and he was given 20 treatments in 38 days, delivering 1,400 r to tumor site in the upper part of the abdomen. A second course, consisting of 16 treatments in 20 days delivering 1,250 r to the abdomen, was given two months after the first. Factors were: 200 kv., 25 ma., 50 cm. distance, half-value layer 1.0 mm. Cu; field size ranged from 8×10 cm. to 15×15 cm. After the second course, the skin remained in good condition and he improved generally. By July 28, 1945, one month after roentgen therapy was completed, the liver had receded to the costal margin, but a small, firm mass could still be felt in the left upper quadrant of the abdomen. At 11 months he seemed well. At 14 months, the left upper quadrant mass could no longer be felt and the liver was of normal size. At 18 months complete roentgen study was made of all long bones and skull for possible metastases but only "a suggestion of several calcified glands in the upper abdomen" was found. At 2 years he was a happy, normal boy, eating a regular diet and showing no evidence of recurrence.

In August, 1948, at $3\frac{1}{2}$ years, a small indistinct mass was palpable in the upper abdomen below the xiphoid. Retrograde pyelography showed the left kidney was lower than the right. A third course of therapy was given and consisted of 13 treatments in 16 days delivering 1,400 r to the tumor. He was in good health in July 1951, when development was normal with no mass palpable and with liver normal in size.

[The case illustrates the point that one should never give up with this disease no matter how bad the prognosis appears to be.—Eds.]

Treatment of Angiomas: Summary of 20 Years' Experience at Columbia Presbyterian Medical Center with 677 cases is reported by George C. Andrews, Anthony N. Domonkos and Charles F. Post,⁴ together with data on 562 cases from their private practices. The 1,239 cases included 321 of nevus flammeus and nevus araneus, 892 of hemangioma simplex or cavernosum and 26 of lymphangioma.

Although it is common for hemangiomas to disappear spontaneously, it is also common for them to grow larger, become ulcerated and cause soft tissue destruction with scars. In 90% of the present series the lesion was present at birth or appeared within a few weeks after birth and grew larger while the parents were waiting for it to disappear. Many of the large ulcerated angiomas actually developed as a result of the poor advice given the parents by the local doctor. Angiomas should be treated when they are first seen.

Radium treatment with gamma ray applicators is now simple and safe and gives the best cosmetic results (Figs. 351 and 352). The great majority of hemangiomas respond to simple treatment with plaques. Full strength radium plaques (5 mg./sq. cm.) are filtered through 2 mm. of brass and kept on the skin for $3\frac{1}{2}$ hours. At least three months must elapse before treatment is repeated. No more than four treatments should be given an angioma. Often, two or three suffice, and sometimes one gives a complete cure. Rarely some remnant may persist after four treatments, but this will disappear in time.

Experience has shown that some and probably many cases of ulceration and scarring, previously ascribed to radium, are due to trauma and

(4) Am. J. Roentgenol. 67:273-285, February, 1952.



Fig. 351 (left).—Angioma of right upper extremity before treatment.
 Fig. 352 (right).—Angioma after radium treatment. Skin and bone growth normal seven years later.
 (Courtesy of Andrews, G. C., *et al.*: *Am. J. Roentgenol.* 67:273-285, February, 1952.)

infection. These complications occur on angiomas not treated with radium and usually heal in a week or two with parenteral and local penicillin therapy.

[The age of patient, size, depth and location of the hemangioma influence the choice of the method of treatment. Success does not depend so much on the method as on the familiarity with a particular technic and the attention to details in using it.—Eds.]

Vertebral Angioma. J. Haguenu and C. Fauré,⁵ (Paris) state that this lesion is the commonest benign tumor of the spine. Some are asymptomatic and are incidental findings on roentgen examination. The pathologic process seldom affects the entire vertebra, in general being localized to the body, but it may involve only the posterior arch. Tomography may be helpful in diagnosis. The lesion may cause pain, deformity of spine, pulsating tumor or spastic paraplegia. The signs may be those of syringomyelia or the Brown-Séquard syndrome. In differential x-ray diagnosis one must consider tuberculosis, osteomyelitis, metastatic cancer, myeloma, Hodgkin's disease, leukemia, Paget's disease, actinomycosis and echinococcus cyst. Appearance of another angioma in skin, viscera, bone or epidural sites may help. Angiomas are more common in women than in men and often manifest themselves during pregnancy.

(5) *Presse méd.* 58:675-677, June 14, 1950.

Roentgenologically the typical appearance of the vertebra has been described as resembling a sponge, pumice stone and "striped vertebra," underlining the diagnostic importance of the vertebral stripes (Fig. 353).

The two therapeutic approaches are surgery and radiotherapy. When surgery is chosen, laminectomy is performed. This represents a major operation for angiomas and mortality is 9% but results are excellent. The technics described in radiotherapy are not unique but reported results are all alike. The authors describe the technic of Forster and Heublein, who suggested using 200 or 220 kv. and one posterior and two anterior fields. Initial daily dose is 50 r, increasing to 200 r to a total dose of 2,500-3,000 r. It seems certain that radiotherapy is effective

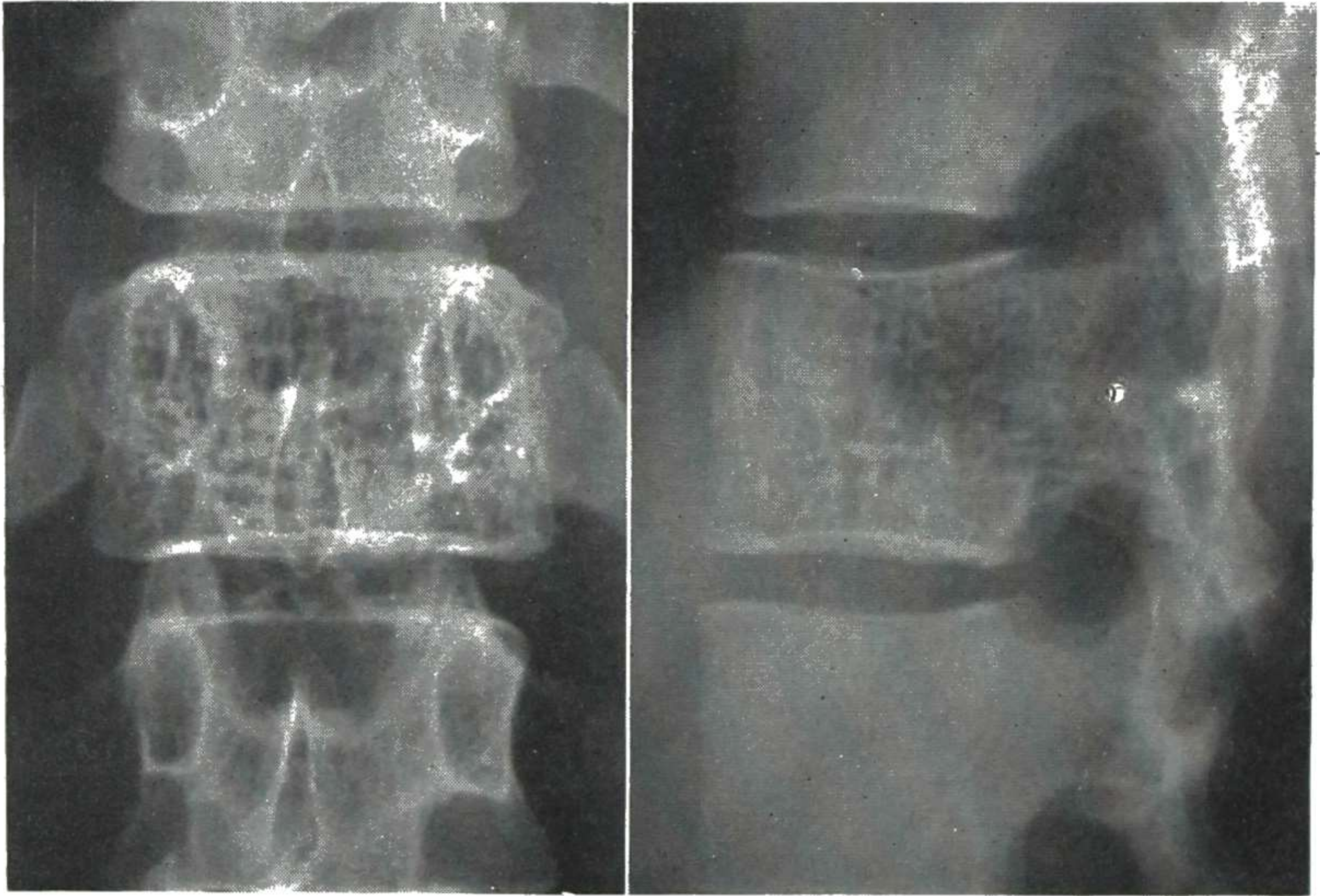


Fig. 353.—Typical appearance of vertebral angioma. (Courtesy of Haguenu, J., and Fauré, C.: *Presse méd.* 58:675-677, June 14, 1950.)

against motor disturbances. The authors suggest that surgery should be reserved for rapidly developing forms or advanced cases in which there is danger that clinical symptoms may become irreversible. All other angiomas should be treated by radiotherapy. Immobilization in a plaster of Paris jacket is suggested for painful lesions.

[In our experience the roentgen diagnosis of hemangioma of vertebral body is made more often than it is confirmed.—Eds.]

Radiotherapy of Hemorrhagic Familial Angiomatosis (Rendu-Osler Disease). Jean Pierquin, Georges Richard and Bernard Pierquin⁶ (Paris) report on 10 patients. The disease is characterized by telangiectasias which appear between ages 20 and 30 on the face, mucous membranes of nose, tongue and cheek, forearm and fingers, rarely on lower extremities, chest or abdomen. The appearance varies from starlike to papular or nodular forms. The lesions are small and vary in number. The course is characterized by hemorrhages, especially from the nose, which may endanger life. Microscopically the lesions are in the papillary and sub-

(6) *Presse med.* 59:733-734, May 23, 1951.

papillary layer of the corium, where they manifest themselves as lakes filled with blood, lined by endothelium without complete vascular structure. This accounts for the fragility of the angiomas and the permanent risk of hemorrhage. Treatment with vitamin C, cautery and electrocoagulation and carbon-dioxide snow gives only temporary relief.

The authors obtained favorable results with radiation in 10 patients with lesions confined to the face and nasal mucous membrane. For lesions of nasal mucous membranes, radium tubes were inserted in the nose. At first, two tubes of 11 mg. each, filter 1.0 mm. Pt, were inserted for 24 hours, but this was modified to three tubes of 5.5 mg. with the same filtration and time. Bleeding stopped after four to six weeks and there was no recurrence after one year. Lesions of the face were treated with 120 kv. x-rays, no filter, at 25 cm. distance. Usually two fields, right and left, were used, and 500 r was delivered at each treatment to a total of 1,500 r in six weeks.

[For a comparison of treatment technics, see the report by Glennie in the 1951 YEAR BOOK, p. 311.]

It would seem that a single exposure of 500 r of unfiltered radiation to a large area for the treatment of a benign condition is a procedure of doubtful necessity. Total doses of more than 1,000 r of such therapy are likely to produce permanent changes in about a quarter of patients so treated.—Eds.]

Pathology⁷ and Classification of Tumors of Soft Tissues. Arthur Purdy Stout⁷ defines soft tissue as most of the tissue covering the body and internally those tissues which fill in the body crevices, notably the retroperitoneum, mediastinum and orbit. The primary malignant tumors of soft parts seen at Columbia University, 1906-49, were tabulated as to type of tissue and eventual result. Fibrosarcoma was found in 222 patients. There were recurrences in 51.7% and metastases in 6.9%; 17.2% died. Of 115 patients with liposarcoma, 66% had recurrence and 34% metastases; 37% died. Leiomyosarcoma was seen in 25 patients: 90% had recurrence and 30% metastases; 80% died. Rhabdomyosarcoma was seen in 38 patients: 85% had recurrence and 40% metastases; 65% died. Angiosarcoma was found in 81 patients. Recurrences occurred in 60% and metastases in 36%; 36% died. Synovial sarcoma was found in 13 patients and lymphosarcoma in 23. Twenty-four patients had reticulum cell sarcoma, 1 plasmacytoma and 1 melanosarcoma. Myxoma was found in 50 patients, with a recurrence rate of 56%; 6 died. Mixed mesodermal tumors were seen in 19 patients. These recurred in 40% and metastasized in 60%; 60% of the patients died. Schwannoma was seen in 20 patients and neuroepithelioma in 7. Kaposi's disease, reticulum cell sarcoma, lymphosarcoma, a small liposarcoma and plasmacytoma are considered somewhat radiosensitive.

[The percentage figures, recurrences, metastases and deaths, represent only follow-up information at the time of writing. They do not imply, for instance, that the fatality rate is actually 17.2% for fibrosarcoma but only that 17.2% of the patients were dead when the material was reviewed.—Eds.]

Neurogenic Sarcoma Treated by Surgery and Radiotherapy is reported by Edward S. Murphy, William R. Lipscomb and John S. Bouslog⁸ (St. Luke's Hosp., Denver).

Woman, 48, seen June 5, 1946, had had increasingly severe pain in left leg

(7) Am. J. Roentgenol. 66:903-909, December, 1951.

(8) J. Neurosurg. 9:214-218, March, 1952.

for eight months. The pain traveled down the leg from its origin in the popliteal space and was accompanied by twitching. Examination showed enlarged heart and edema of hands and feet. The leg was flexed at knee and hip and the posterior thigh muscles were contracted. Tenderness and swelling were noted in the popliteal space. The lateral and dorsal aspects of the foot were analgesic and no reflexes could be obtained in the left leg. X-ray study showed a soft tissue mass in the popliteal space. The bone was uninvolved. A malignant tumor of the nerve trunk consistent with either cellular anaplastic neurosarcoma or sympatheticoblastoma was removed at surgery. She then received x-ray therapy with the following factors: 400 kv., 70 cm. distance, 2.25 mm. Cu filtration. Between July 25 and August 7, 1,482 r (in air) was given through two ports to the left knee. From July 30 to August 6, 741 r was given through an anterior port to the left groin. Between September 23 and 27, with the same physical factors, 988 r was given through two ports to the left knee and between September 24 and 27, 494 r was given to the anterior left groin port.

On June 25, 1948, she was seen because of cough, hemoptysis and pain in the right chest. Chest x-rays showed a round mass in the right hilus with smaller masses throughout both lung fields, interpreted as secondary neoplasm. She was treated with antibiotics and given x-ray therapy with the following factors: 200 kv., 50 cm. distance and 2.25 mm. Al filtration. From Feb. 1 to 11, 1949, she received 1,984 r to three ports over the anterior and lateral right chest. Later she received 744 r through two ports to the anterior and posterior right chest and 744 r to two ports, over the left knee using the same factors. In August, when seen with chest complaints, x-ray study showed clearing of many of the lung metastases and one large lesion in the upper part of the right lung. At a right upper lobectomy a neurogenic sarcoma was removed. On Apr. 3, 1950, a recurrent neurogenic sarcoma was removed from the left leg. She was symptom-free when she became unconscious on June 17, 1951, and died five days later. Autopsy showed cerebral thrombosis. A small neoplastic nodule in the left lung did not contribute to death. The combination of roentgen therapy with surgery extended life until her death was brought about by other causes.

Reticuloendotheliosis of Children: Treatment with Roentgen Rays.

Donald S. Childs, Jr., and Roger L. J. Kennedy⁹ (Mayo Clinic) discuss 12 patients who received x-ray therapy. All were age 4 or younger and had defects in the skull. All but one had other bone lesions. Six showed lymphadenopathy, hepatomegaly or splenomegaly. Two had pulmonary involvement. Two patients had the triad of diabetes insipidus, exophthalmos and bone defects.

In lesions of the soft tissues, skull, and mandible and long bones, a single port over the affected region was used. For liver, lungs, spleen and pelvic bones, more ports were used, usually an anterior and a posterior. In most cases a single dose of 150-200 r (in air) was given to each port; one to four ports were used daily. Factors were: 130 kv., half-value layer 0.3 mm. Cu, distance 40 cm. Estimated tumor dose/lesion/course was 200 r. In most cases, at least three courses of treatment (total of 600 r) were needed for any specific lesion.

The disease was considered arrested in nine patients. The other three died. In most, the response to x-ray therapy was prompt. Lymph node and soft tissue enlargement began to recede within 10 days. Healing of bone lesions was seen on x-ray examination 30 days after the end of treatment.

[The dosage used seems most conservative, but it is well documented that some lesions which receive no direct radiation heal as well as those treated.—Eds.]

(9) Radiology 57:653-660, November, 1951.

Acute Parotitis is usually a postoperative complication, but it can occur in the absence of surgery. Jack R. Gustafson¹ (Univ. of Michigan) reports 86 cases, 29 of which were not associated with surgery. In 25 of the 51 cases which followed surgery, opening of the peritoneum was involved.

Pain in the temporomandibular joint is usually the first clinical manifestation of acute parotitis, followed in six to eight hours by a swollen, hot, tender, indurated parotid gland. The opposite side may become involved in 6-24 hours. White cell count and temperature are elevated. The patient appears seriously ill, far out of proportion to what would be expected with a purely local infection.

Gustafson considers acute parotitis a radiotherapeutic emergency. The response is rapid and at times dramatic. The most striking initial response is rapid alleviation of toxicity and pronounced subjective improvement. Tenderness and pain disappear early; after 72 hours, induration and swelling are reduced. Often, all evidence of parotitis is gone in three to six days.

Seventy-eight of the 80 patients received x-ray therapy. When therapy was instituted in the first 16 hours, treatment was more effective. Factors were: focus-skin distance 50 cm., half-value layer 2.5 mm. Cu (150 kvp) or 0.9 mm. Cu (200 kvp). Initially a single dose of 200-450 r (in air) was used. This was changed to 250-750 r given in two to five days. Ten patients died of other causes before completion of therapy. Of the remaining 68 patients, 52 (76%) had prompt resolution without abscess formation. Even when there was suppuration, resolution was more rapid and less painful with considerably less morbidity. Surgical drainage, which was necessary in 16 of the 80 patients, is indicated for suppuration which follows x-ray therapy and in those patients who do not respond to irradiation in three or four days. One patient had a recurrence after receiving 250 r in divided doses; it resolved promptly after additional therapy had been given.

Penicillin and sulfonamides, when used prophylactically, have not been effective. In this series they were given with x-ray therapy. Results of x-ray and sulfonamide therapy were no better than those of x-ray therapy alone. All seven patients given x-ray and penicillin therapy responded satisfactorily.

Of the 80 patients, 38 died. Only one death was attributable to parotitis. Although acute parotitis is seldom fatal, this is certainly evidence of a poor prognosis.

Prophylaxis includes correction of oral and pharyngeal disease, proper general and oral hydration, correction of vitamin or nutritional deficiencies, stimulation of salivation and avoidance of drugs which depress salivation.

[This is a valuable series and the results are exceptionally good. Our experience is similar in that we see fewer cases today than formerly.—Eds.]

Roentgen Treatment of Cervical Spondylosis: Follow-up Examination of 625 Patients is reported by Johan Lundar² (Oslo, Norway). Spondylotic changes are present in the cervical spine of almost all

(1) *Surgery* 29:786-801, May, 1951.

(2) *Am. J. Roentgenol.* 66:947-955, December, 1951.

adults. The lesions include disk damage with associated bone reaction, exostotic formations and deforming arthrosis of the small intervertebral joints. Symptoms are produced in a comparatively small percentage of patients.

The 625 patients were symptomatic. They were followed one to three years. Most were aged 40-60. Seventy-six per cent were women, 73% of whom were housewives. Symptoms were stiffness and/or pain in the neck; pain in the occiput, shoulders, or arms, and paresthesias of the fingers. In 50%, symptoms had been present over two years. Certain work, particularly carrying packages, knitting, etc., was an exciting cause, although it bore no relation to severity of the spondylotic changes.

Roentgen treatment consisted of six applications of 125 r through a posterocervical field over four weeks (1st, 4th, 7th, 21st and 28th days). Six weeks later a second course was given, and in some cases a third after six additional weeks. Fifty per cent of the patients received one course.

Roentgen treatment did not visibly affect the spondylotic changes, but it alleviated pain in 90% of the patients. Results were better and more permanent when treatment was instituted early. There was usually improvement two weeks after initiation of therapy. More permanent results seemed to be obtained when three courses of treatment were given at intervals of six weeks. If three courses are unsuccessful, roentgen therapy is useless. About 50% of the patients had recurrence, but it was usually moderate and could generally be controlled by repetition of x-ray treatment.

Roentgen Therapy in Acne. G. Marshall Crawford, Ralph H. Luikart, Jr., and Robert F. Tilley³ (Massachusetts Gen'l Hosp.) report observations on 58 patients who had received roentgen therapy for acne 5-20 years earlier. Voltage varied from 75 to 100 kv. The face was treated with two exposures; each side received 60-75 r. Some patients were given an additional central face dose of 15 r. Unfiltered radiation was used in most cases and 0.5 mm. Al filtration in a few. Weekly treatments were given. Total roentgens given were 500-800 for 30 patients, 800-1,000 for 20, 1,000-1,200 for 7 and 1,450 for 1. Excellent results were obtained in 35 patients. Nineteen had an occasional lesion for varying periods of years. The other four had unsatisfactory results, but only one showed no improvement. All poor responses occurred among patients who received less than 800 r. Despite this, 56.6% of this group had a good outcome. The acne cleared in 60% of those who received 800-1,000 r. Cure was obtained in 75% who had received over 1,000 r.

Telangiectatic vessels were found in nine patients; all were probably due to causes other than x-ray treatment. No other late sequelae of roentgen therapy were found.

The authors concluded that properly administered roentgen treatment in acne, given with accepted technic, may be expected to cure 60-75% of stubborn cases. No late radiation sequelae need to be expected

(3) New England J. Med. 245:726-728, Nov. 8, 1951.

because of the limited fractional and total roentgens administered. Results suggest that patients who received 1,000-1,200 r in an uninterrupted series of treatments had the best outcome and the fewest recurrences.

Contact X-ray Therapy of Common Wart. John G. Thomsen and John E. Rauschkolb⁴ (Cleveland) describe a method for office treatment.

TECHNIC.—A Philips Metalix contact therapy apparatus is used. Factors are: 47.5 kv. (constant potential), current 2 μ v., filtration 0.2 mm. Al, half-value layer 0.3 mm. Al. Output in the past three years at 18 mm. target-skin distance has been from 150 to 160 r/second. The low voltage and short target-skin distance results in absorption of a large part of the radiation in the uppermost part of the skin, with a rapid dropping off in deeper tissue.

The lesions are first pared with a scalpel to a flat plane to insure even distribution of radiation to the area. In subungual lesions, nails are carefully trimmed to expose the entire wart. Each lesion is then outlined with ink, a margin of 1 mm. of normal skin being allowed on all sides. The hand is placed against the fixed tube. Treatment time averages 15-20 seconds. It is imperative that no area be exposed twice. Accurate charts and diagrams of lesions are mandatory.

Nail changes have sometimes been noted. Defluvium of the nail occurred once; secondary infection, twice. The site became red and tender 10-14 days after treatment. The reaction generally subsides in three weeks.

The treatment was used for 117 patients with a total of 540 lesions. Cures were effected in 276 of 321 hand lesions, 108 of 141 foot lesions and 25 of 27 other lesions. Generally, a single exposure of 2,100-2,500 r was given; some larger lesions were given smaller doses and a few smaller lesions, up to 2,750 r.

Study of Visibility of X-rays to Naked Eye. Although the fact that x-rays can be detected by the human eye without the aid of a fluorescent screen was reported by Röntgen and various other authors, it has been largely forgotten, so that today most authorities consider them to be invisible. J. Jalet and A. Olivier⁵ decided to study the problem and to see what practical use could be made of x-ray detection by the human eye. Using black paper to eliminate any light produced by the cathode filament and fixing the eyes, previously adapted to the dark, on the path followed by the x-rays, at about 10 cm. from the opening through which they are emitted, the authors perceived a luminous sensation, hard to define at first but easily recognizable thereafter. Some observers have described this sensation as a white light; to others it has seemed greenish blue. Its maximal intensity is localized around the periphery of the visual field; it ceases when emission of the x-rays stops and is not followed by any after effect; it is exactly the same whether the eyes are open or closed; it varies with intensity of the exciting current and to a lesser extent with changes in tension; it becomes weaker as distance from the source increases, but even at a great distance it is still strong. Most of the experiments were conducted under conditions suitable for fluoroscopy, i.e., 65 kv. and 2 or 3 ma.; when roentgenographic conditions were tried, with 120 kv. and 60 ma., the effect was dazzling.

When letters or numbers in lead of the type used for marking films were interposed in the path of the rays during emission, close to the

(4) A.M.A. Arch. Dermat. & Syph. 65:553-556, May, 1952.

(5) J. radiol. et électrol. 32:494-496, 1951.

eye, a clear image in black of the letters or numbers could be seen, reversed and slightly enlarged, whether the eyelids were raised or lowered. In this way, whole words or numbers could be read. Similarly, by placing the tip of the little finger before the eye, a well adapted person could see the bones through the soft parts; this amounted to direct fluoroscopy without a screen.

From these experiments, and after reviewing various theoretical considerations, the authors concluded that x-rays are visible to the naked eye because the retina can directly detect electromagnetic radiations of the order of $5/10$ A. To find a practical application of this fact, two patients with cataracts and one with iridocyclitis were tested. All had greatly impaired vision. In each case letters and numbers that could not be read by ordinary light became readable in "x" light, which proved that the retina behind the opaque crystalline was sound. Ocular symptomatology will undoubtedly profit from these studies, and theories of retinal physiology should be revised in the light of them.

Sterilization of Frozen Arterial Grafts by High Voltage Cathode Ray Irradiation. The apparatus utilized by Irving A. Meeker, Jr., and Robert E. Gross⁶ (Harvard Univ.) was the cathode ray machine at Massachusetts Institute of Technology. The accelerating force comes from an electric potential of 3 Mev which produces an electron beam about 4 cm. wide. It is possible to deliver up to several million rep in a fraction of a minute.

From a series of tests in which frozen, contaminated aortic segments of dogs were exposed to the beam by means of an endless conveyor belt, it was concluded that the range between 2 and 2.5 million rep gives the best sterilization results. When a specimen is frozen before irradiation, sterilization is nearly always obtained with little or no tissue damage; irradiation at room temperature causes serious alteration in organic composition and enzyme systems.

The method has been used to sterilize human postmortem specimens. In two patients with coarctation of the aorta, in whom wide bridging was required, vascular grafts sterilized and stored by this method were used. Two and six months after operation, respectively, results are satisfactory.

Use of K^{42} -Tagged Erythrocytes in Blood Volume Determinations. Rosalyn S. Yalow and Solomon A. Berson⁷ (Veterans' Admin. Hosp., Bronx, N. Y.) prepared tagged red blood cells by incubating 10 ml. heparinized blood with 100-200 μ c. K^{42} in 50 mg. stable potassium carrier. From 2 to 6% of the K^{42} was absorbed by the cells. The cells were then washed with saline, and a weighed volume of the saline-suspended cells was injected. Radioactivity of blood samples taken at 5 and 15 minutes was compared with that of the injected material to obtain a blood volume. Simultaneous blood volume determinations using P^{32} -tagged cells gave values which agreed within experimental error. The short half-life of K^{42} allows frequent blood volume determinations to be performed on the same patient, while its energetic beta and gamma emissions enable the radioactivity of a sample to be readily determined.

(6) *Surgery* 30:19-28, July, 1951.

(7) *Science* 114:14-15, July 6, 1951.

HAZARDS AND INJURIES

Acute Radiation Injuries in Man. Louis H. Hempelmann⁸ (Univ. of Rochester) discusses the mechanism of acute radiation injuries in man. The various forms of ionizing radiation, such as x-rays, gamma rays, beta and alpha particles, and neutrons, produce similar damage in tissues. The intracellular damage involves vital enzyme systems and genetic material. Inactivation of enzyme systems causes immediate cytolysis, in contrast with the delayed death which occurs when genetically damaged cells attempt to divide. The slower growing tissues such as bone and muscle are more radioresistant than the rapidly growing hemopoietic, germinal and intestinal epithelial tissues.

The clinical picture in radiation injury is governed by the type and dose of and duration of exposure to radiation, as well as the type and



Fig. 354.—Right hand nine days after exposure. Epidermis has been cut away. There was no blanching of dermis of palm on pressure. Fingers felt quite cold to touch. No radial pulsation could be felt. (Courtesy of Hempelmann, L. H.: *Surg., Gynec. & Obst.* 93:385-403, October, 1951.)

amount of tissue exposed. Neutrons and beta particles damage only superficial tissue, whereas gamma rays penetrate all tissues. Four cases of acute radiation injury are reported.

CASE 1.—Man, 26, handled substances emitting beta and gamma rays. The left hand received 5,000-10,000 rep in beta rays and the right much less; the body received 4.5 r in gamma rays. Initial edema of the left hand subsided but erythema became more intense on the 3d, and 4th days. By the 15th day there were large vesicles; by the 28th, they were confluent. The peak was reached on the 32d day, after which the epithelium began to dry and desquamate. Treatment was repeated surgical débridement, with skin grafting after seven months. The end result was pronounced limitation of interphalangeal motion of the second digit. There were no systemic reactions.

CASE 2.—Man, 26, in contact with a nuclear reactor, received 20,000-40,000 r to the right and 5,000-15,000 r to the left hand, with a total body dose equivalent to 480 r of 80 kv. x-rays and 110 r of gamma rays. Radiation consisted of neutrons and gamma rays mixed with a large amount of beta and some soft x-rays. Immediately after exposure there was a slight local reaction on the hands, which became more severe (Fig. 354). In the first 24 hours there was severe gastric distress; it abated in the next few days but

(8) *Surg., Gynec. & Obst.* 93:385-403, October, 1951.

was followed by progressive weakness, fever, weight loss, epilation, epidermolysis and death on the 24th day. Lymphopenia developed promptly and was sustained. Granulocytosis occurred early, then progressed to agranulocytosis terminally.

CASE 3.—Man, 34, received a total body dose equivalent to 390 r of 80 kv. x-rays and 26.4 r of gamma rays. Several hours later there were nausea and vomiting, but they disappeared after 12 hours. Except for weakness and temporary fever, recovery was rapid (in 10 days). Epilation occurred at 18 days but regrowth was complete 1 month later.

CASE 4.—Man, 54, received a total body dose of 186 r in soft x-rays and 10.7 in gamma rays. He had no symptoms; only sustained lymphopenia was present.

Treatment of local injuries is that of thermal burns, with skin grafting when the damage stabilizes after several months. General injuries necessitate use of antibiotics, blood transfusions, fluid and electrolyte replacement and bed rest with good nursing care. Late reactions are cataracts and general epithelial atrophy.

[This subject is more exhaustively presented by Louis H. Hempelmann, Hermann Lisco and Joseph C. Hoffman, "The acute radiation syndrome: A study of nine cases and a review of the problem," in *Annals of Internal Medicine* 36:279-510, February, pt. 1, 1952.—Eds.]

Pneumonectomy for Severe Irradiation Damage of Lung. Exposure of human and animal lungs to ionizing radiation produces a reaction whose pathologic appearance has been studied extensively. In man, the structural alterations resulting from exposure to relatively large quantities of radiation cause symptoms of cough, dyspnea, chest pain

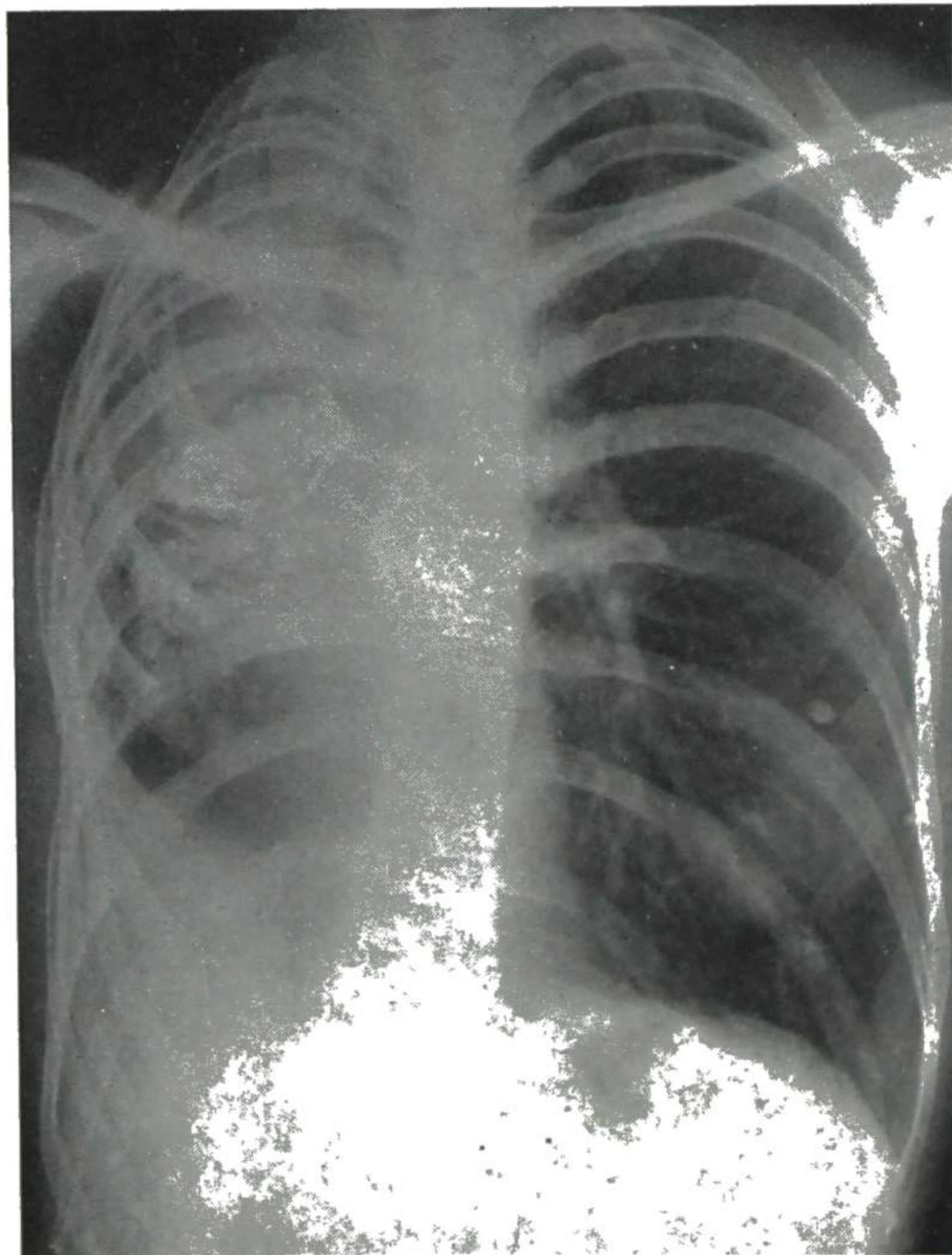


Fig. 355.—Atelectatic right lung, with residual lipiodol.® Mediastinum shifted to right and compensatory emphysema of left lung. (Courtesy of Bergmann, M., and Graham, E. A.: *Thoracic Surg.* 22:549-567, December, 1951.)

and hemoptysis. Pulmonary function is greatly compromised by the process. Martin Bergmann and Everts A. Graham⁹ (St. Louis) report two cases in which pneumonectomy was done with palliation of symptoms.

CASE 1.—Woman, 42, hospitalized because of cough and dyspnea, had undergone right radical mastectomy for breast carcinoma 22 months before admission. During the next 4 months she received two courses of roentgen therapy to the right chest and axilla and about 1½ years later a third course. Thereafter, cough and dyspnea developed. About 10 months before admission a pleural effusion developed which was tapped repeatedly.

A chest x-ray examination on admission showed displacement of the mediastinal structures into the right side (Fig. 355). The left lung was emphysematous. The right hemithorax was obscured by a homogeneous density except

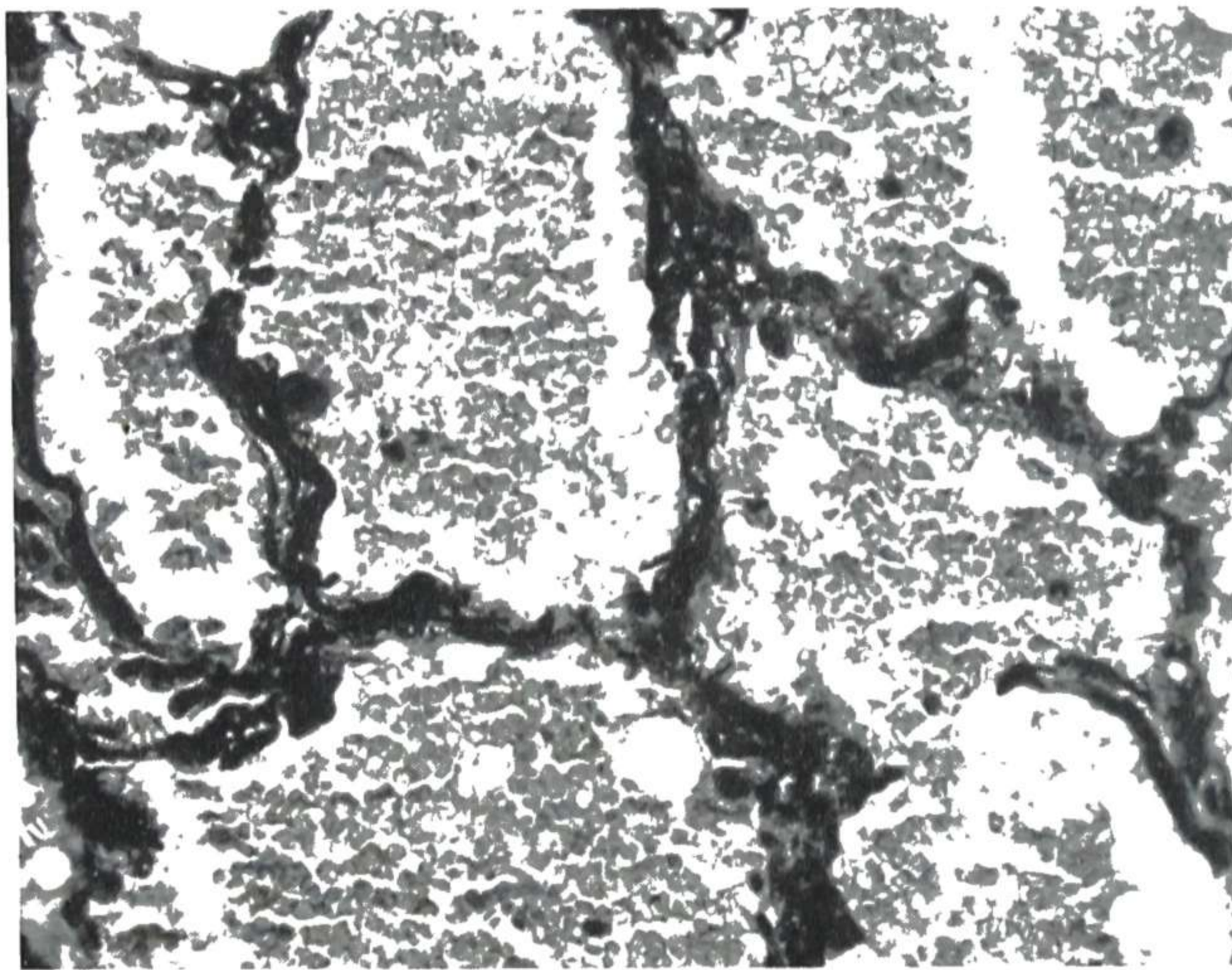


Fig. 356.—Pulmonary alveoli, showing marked increase in number and size of elastic fibers. Verhoeff-van Gieson stain; reduced from $\times 400$. (Courtesy of Bergmann, M., and Graham, E. A.: *J. Thoracic Surg.* 22:549-567, December, 1951.)

for a small amount of aerated lung. All laboratory data were within normal limits, and the patient was discharged eight days after admission.

She was readmitted 5½ months later with persistent cough and dyspnea, requiring demerol[®] nightly for three months for relief. Right pneumonectomy was carried out, with an uneventful postoperative course, and she was discharged about a month later with the cough much improved. She was improving when seen about 1¾ years later. Subsequently an empyema developed on the right side which responded to thoracostomy drainage and thoracoplasty, and she was discharged with only a small granulating cavity remaining.

The surgical specimen consisted of a small atelectatic lung with considerable fibrosis and pleural thickening. Microscopically the alveoli were preserved in only scattered areas. Where individual alveoli remained, their walls were thickened and contained increased numbers of elastic tissue (Fig. 356).

CASE 2.—Woman, 45, was hospitalized because of cough for one year. Over a year before she underwent radical mastectomy followed by postoperative x-ray treatments. A skin reaction developed, requiring daily dressings. Cough developed two months after the last x-ray treatment and became productive and paroxysmal. Examination revealed no evidence of recurrence of carcinoma, and results of laboratory studies were normal. Right pneumonectomy was

(9) *J. Thoracic Surg.* 22:549-567, December, 1951.

done with much improvement of the cough. The specimen was of firm consistency and the pleura thickened anteriorly. Microscopically the affected areas showed fibrosis and elastic fiber deposition.

Study of the surgically removed lungs showed that one of the criteria for histologic diagnosis of radiation damage in autopsy material, the finding of hyaline membranes, is probably an artefact not seen in surgically removed lungs. An increased number of thick elastic fibers scattered diffusely throughout the irradiated lung appears to be an important criterion for histologic diagnosis.

The authors urge a more general awareness of pulmonary damage after chest irradiation to avoid administration of further x-ray therapy in the belief that the changes represent pulmonary metastatic carcinoma. A relatively innocuous and largely transient reaction may thus be converted into an incapacitating and often fatal disease.

Although there is no known nonoperative treatment of radiation damage of the lung, pneumonectomy in a unilateral case appears to be an effective therapeutic measure.

[These two patients represent extreme examples of pulmonary radiation fibrosis. There are all gradations due to varying susceptibilities, but it is well to know that severe cases can be relieved by surgery. Nonoperative measures which may be effective in less severe damage include the use of cortisone (this YEAR BOOK, p. 353). In prevention, dicumarol® therapy has been tried; and repetitive series and severe skin reactions should be avoided.—Eds.]

Intrathoracic Disturbance Caused by Roentgen Therapy. J. J. Hogewind-De Nijs and H. Hogewind¹ report a case.

Woman, 45, complained of fatigue and cough. Three years previously she had been operated on for carcinoma of the right breast with axillary lymph node involvement, but chest x-rays at that time had been negative. Her general condition was good, and there was no anemia, cyanosis, dyspnea or palpable nodes. Sedimentation rate was 31 mm./hour. The right hemithorax was flattened and moved little on respiration; the right supraclavicular fossa was larger than the left, and the trachea was markedly displaced to the right.

On x-rays, the right upper lobe contained shadows, and the interlobar fissure was displaced upward and the trachea to the right. The Pirquet reaction was negative. After operation, 3,375 r had been given by the usual technic through three portals (axillary, supraclavicular and dorsal); a second series was given six months later and a third series a year thereafter. After the third series, chest films showed the same changes in a minimal degree. As a high dose had been given to the right upper lung field, diagnosis was radiation reaction.

Four months later the patient had lost 6 kg. and cough had increased and was productive. Physical examination again showed dullness of the right upper chest and, in addition, bronchophony, moist râles and bronchial breathing in the same area. Temperature, pulse rate and respirations were normal, but the sedimentation rate had increased to 90 mm./hour. A chest x-ray examination showed the same abnormalities. A lipiodol® bronchogram surprisingly showed widespread bronchiectasis in the right upper lobe, although the rest of the lung was normal. On bronchoscopy the mucosa of the lower trachea and right main bronchus was smooth and atrophic and that of the right upper bronchus was red and somewhat thickened and constantly produced mucopurulent secretions. The other bronchi showed no abnormalities. The patient was given penicillin, 200,000 units daily. Cough diminished, sedimentation rate decreased to 26 mm./hour in two weeks and weight increased. Two months later she felt much better and was doing light housework; the râles in the chest had disappeared.

[One of us (H. W. J.) has seen severe bronchiectasis follow extensive radiation

(1) Nederl. tijdschr. geneesk. 95:3160-3166, Oct. 27, 1951.

fibrosis after postoperative breast treatment. The patient did not die of this complication, but it was moderately incapacitating. Repetitive series are more likely to produce this, as in this case.—Eds.]

Use of ACTH and Cortisone in Treatment of Postirradiation Pulmonary Reaction is reported by Stuart W. Cosgriff and Morton M. Kligerman² (Columbia Univ.)

Woman, 68, had a solitary metastatic nodule in the right middle lobe. She had undergone intestinal resection for carcinoma of the sigmoid colon and left lower lobectomy for a metastatic nodule. Radiation therapy was given. Factors were: 200 kv., 25 ma., focus-skin distance 50 cm., half-value layer 0.9 mm. Cu, eight anterior and eight posterior ports 8 cm. in diameter, with cross firing to by-pass the volume of tumor-bearing tissue. A tissue dose of 4,500 r was given in 52 days. Three days after radiation therapy was completed, she showed severe inflammatory changes in the lungs. Diagnosis of radiation fibrosis seemed definite, although dicumarol[®] had been given prophylactically before and after radiation therapy. A dose of 25 mg. ACTH was given every six hours. There was dramatic improvement in 48 hours. A maintenance dose of 12.5 mg. every 6 hours was given for 30 days, but symptoms recurred within 24 hours of withdrawal. Administration of 100 mg. cortisone daily slowly brought the symptoms under control. There was no significant symptomatic relapse immediately after its withdrawal. Two months later she had no acute symptoms, but fibrosis and atelectasis had developed.

[Dr. Kligerman has submitted the following additional information.

"The patient began having increasing dyspnea approximately six months after cortisone was stopped. She was hospitalized and placed on ACTH with beneficial results. On the fifth day of treatment, she had sharp epigastric and substernal pain radiating through to the back. ACTH was stopped. Dyspnea returned and cortisone orally was started. Pain recurred substernally and cortisone was stopped. From that time until death six months later, no more hormonal treatment was given. At autopsy, extreme postirradiation changes were seen in the metastatic carcinoma. The lung was markedly shrunken so that no aeration was possible. Metastases were generalized, involving the lungs bilaterally, hilar lymph nodes, liver, pancreas, right ovary and peritoneum. There was a right hydrothorax. There was evidence of an old myocardial infarction."—Eds.]

Renal Damage from Radiation during Treatment of Seminoma Testis. Ralston Paterson³ (Manchester) investigated how much radiation the kidneys can safely tolerate. A review of technics shows that it is not safe to irradiate the whole of both kidneys in excess of 2,000 r in three to four weeks and that renal tissue is really a relatively sensitive tissue in terms of secondary vascular change which takes place a year or so after irradiation. Of 50 treated patients, 22 had known renal damage. This complication is of vital importance and poses the question whether seminoma which has spread is ever cured. In chest metastases the figures are low. Of 54 treated patients, 51 died in the first year, 1 in the second year; 2 were alive after five years, both of whom received 1,600 r. Of 19 patients with abdominal metastases only, 7 died in the first year, 1 in the second year, 8 were alive over three years, 1 over four years and 2 after eight years. In this group, cure rate is in the 50% levels. Seminoma is, therefore, a disease well worth treating despite the complication of renal damage and well worth serious study to determine the optimal dose.

Limit of Renal Tolerance to X-rays: Investigation into Renal Damage Occurring Following Treatment of Tumors of Testis by Abdominal Baths. In the prophylactic treatment of the regional lymphatic region in cases of testicular tumor x-ray baths have commonly been used

(2) *Radiology* 57:536-540, October, 1951.

(3) *J. Fac. Radiologists* 3:270-274, April, 1952.

to a dose of 2,000-3,000 r in three to six weeks, without apparent injury to health. Renal damage becomes a limiting factor when the irradiated volume is extended to include the whole of both kidneys. It may be overlooked unless specifically looked for, since the first symptoms occur several months after treatment.

P. B. Kunkler, R. F. Farr and R. W. Luxton⁴ (Manchester) report the clinical picture of postradiation renal damage in over 30 cases. The latent period averaged eight months from the beginning of therapy. The first complaints were dyspnea on exertion, headache, edema, lassitude and pallor. Some patients died within a few months due to chronic uremia or left ventricular failure, but a considerable degree of recovery was observed, even in patients with severe damage, after judicious blood transfusions and prolonged rest. Those who survived were left with signs of chronic nephritis. Improvement was usually sufficient to allow them to return to work about 18 months after the beginning of radiotherapy.

In another group of patients renal damage was not productive of symptoms but was indicated by albuminuria, hypertension and impaired renal function.

Survival rates in 93 cases and incidence of renal failure are correlated with distribution of dose through the kidneys, using various technics. In cases of renal failure the whole of both kidneys had received a dose of 2,300 r or over in five weeks. A decrease in dose to the upper poles of both kidneys characterized the "safer" technics and, at the dose levels used, is considered of greater significance than either the maximal dose or the integral dose received by the kidneys.

A homogeneous dose of 2,300 r delivered to the whole of both kidneys may cause hypertension and renal failure. This risk may best be minimized by insuring that about a third of the volume of the kidneys is outside the fields or is at least irradiated to as low a dose as practicable.

The authors conclude that renal function and location of kidneys should be determined before x-ray treatment of the abdomen is undertaken. Unsuspected ectopic and solitary functioning kidneys may be discovered, which may demand modification of a standard technic.

[Attention was drawn to this hazard by Zuelzer, Palmer and Newton (1951 ^{YEAR} BOOK, p. 320). The present article gives the dosage data necessary to minimize the risk once the hazard is recognized.—Eds.]

Late Complications Following Irradiation of Pelvic Viscera. William Crawford White and Frederick Wall Finn⁵ (Woman's and Roosevelt Hosp., New York City) emphasize that it is important to think of complications due to irradiation since these may simulate recurrence of carcinoma. The overwhelming incidence of complications is due to treatment of carcinoma of the cervix, not of the corpus.

The commonest bone injury is fracture of the neck of the femur, although fracture of the pubis has also been observed. Fracture is usually preceded by pain and ordinarily occurs more than 1 year after x-ray therapy. Fractures without displacement often heal with con-

(4) Brit. J. Radiol. 25:190-201, April, 1952.

(5) Am. J. Obst. & Gynec. 62:65-74, July, 1951.

servative therapy. Fractures with displacement are treated according to the usual orthopedic procedure.

Urinary tract injuries may result in immediate or late complications. There are indolent ulcers of the bladder, vesicovaginal fistula and intramural stricture of ureter with secondary hydroureteronephrosis. Onset of symptoms may be sudden or more insidious with bladder symptoms and sometimes pain in the flank. These symptoms should not be considered a sign of recurrence until adequate urologic studies have been made. Urologic studies should be made before irradiation and at regular intervals thereafter in order to begin treatment before severe irreparable damage is done.

Fifty-five cases of intestinal damage have been observed. Proctitis may develop during therapy. Proctoscopy shows edema and vascular congestion of the mucous membrane, especially at the level of the cervix. This may clear up or result in permanent damage to rectum, sigmoid colon and ileum. The pathologic process consists of thrombosis of the vessels, necrosis of the mucous membrane with fibrosis of the wall of the intestines and secondary contracture of the lumen. Ulcerations may erode into large vessels, resulting in massive hemorrhage, or progress to perforation, with peritonitis. Contracture may produce partial or complete obstruction. Treatment may be conservative, but supervision must be strict, because the condition is progressive. Elective rather than emergency surgery may be preferable, since this would cause less morbidity and less mortality.

Partial or Complete Pelvic Exenteration for Extensive Irradiation Necrosis of Pelvic Viscera in the Female. Partial pelvic exenteration consists of excision of the bladder, vagina, uterus and adnexa, with implantation of the ureters into the colon; complete pelvic exenteration consists of removal of all pelvic viscera. The ureters are implanted into the sigmoid colon above the colostomy, and hence there is a wet colostomy which is managed satisfactorily with a Pierce bag.

Alexander Brunschwig⁶ (Memorial Cancer Center, New York City) reports that results in a limited series of patients who have survived operation have been satisfactory in that pain has been abolished and the patients have returned to their usual general activities. Among 10 patients, the hospital mortality was 40%. That all patients accepted the procedure after it was fully explained to them is evidence of the degree of discomfort they were experiencing. If they had not been operated on they would have died of complications of the extensive pelvic necroses.

Woman, 30, with an epidermoid carcinoma of the cervix, as shown by biopsy, from February to April 1946 received pelvic cycles of x-ray therapy, 2,000 r to each of four portals, followed by vaginal cone therapy to three small ports, to a total of 3,750 r per port. In May she received 3,000 mg.-hr. radium to the cervix. In September another positive biopsy specimen was obtained, and in October she received more radium therapy (4,800 mg.-hr.).³ She was thought to have extensive pelvic recurrences and was sent home for terminal care. After eight months she was readmitted in a cachectic state

(6) Surg., Gynec. & Obst. 93:431-438, October, 1951.

(weight 94 lb.) with urinary incontinence of four months' duration and a frozen pelvis. Severe pelvic pain required liberal doses of morphine. A neurologic consultant suggested that chordotomy be considered if the tumor proved inoperable and pain continued. Complete pelvic exenteration was done in October 1947. Extensive radiation slough was noted with no evidence of viable tumor cells. The patient was discharged 30 days after operation. She returned to full normal activity and gained 55 lb. She was well three years six months after operation.

[Even more important than the treatment of such injuries should be information gained on how to avoid their repetition. In recounting some numerical details of roentgens and milligram-hours, the author evidently intends to convey some information on dose. These data are quite inadequate to permit correlation with injury. If dose delivered at the time of treatment is unknown, it is difficult to reproduce a good result or avoid an injury in the future.—Eds.]

Radiation Injuries of Hand make up a sizable percentage of any reported series of patients with radiation injuries. These injuries are not only plaguing and intractable to any treatment other than removal of the focus but, if persistent, are almost certain to become malignant. The condition is treacherous in that it may not develop for months or even years after exposure and then may not be recognized until even further irradiation has been given.

Michael L. Mason⁷ (Northwestern Univ.) reports that incidence of malignancy in radiation dermatitis of the hands is higher than that of radiation dermatitis in general, particularly among professionals. Thus,

RADIATION DERMATITIS OF THE HAND

	TOTAL	BENIGN	MALIG.	% MALIG.
Technicians	2	0	2	100
Physicians	19	9	10	52+
Dentists	12	5	7	58
Roentgen and radium therapists	7	4	3	43
Patients	28	21	7	24
Totals	68	39	29	43

the table shows 40 professional patients, in 22 (55%) of whom malignancy developed in radiation lesions.

Reactions to skin irradiation may take one of two forms: acute reaction soon after exposure to a large dose of x-rays, radium or atomic radiation, or chronic reaction which may be a sequel to acute reaction or a delayed response to repeated minimal exposures.

Acute radiation dermatitis of the hands most often follows fluoroscopic search for a radiopaque foreign body and may affect the patient, the surgeon or both. Transient erythema may appear 24 hours after exposure; but often, not for 7-10 or even 20 days does the acute erythema develop with vesicle formation, edema, exudate and desquamation. This resembles an acute burn in many ways. If the reaction is not so severe as to produce ulcers in the initial phase, acute symptoms subside and the process passes into the chronic phase.

Chronic dermatitis may follow the acute phase or may develop from 5 to even 20 years after initial exposure in patients subjected to repeated insults. The skin becomes thin, dry and atrophic and appears mottled. In severe cases painful ulcers may require heavy sedation.

Radiation dermatitis of the hand is treated by removal of the in-

(7) Quart. Bull. Northwestern Univ. M. School 25:51-59, Spring, 1951.

involved skin. This should be done before ulceration and carcinomatous breakdown occur. Split thickness skin graft usually meets the requirements of coverage on the hand, even in the palm.

If the lesions prove malignant, wide local excision is usually satisfactory. When deep ulceration and bone and joint invasion are found, amputation of the involved digit is indicated.

[Although prevention is more important than cure, it is well to know that plastic surgery can correct severe damage if it should occur.—Eds.]

Radiation Cancer of Pharynx in four patients following treatment of the neck is reported by A. W. G. Goolden⁸ (Southampton Hosp.).

CASE 1.—Woman, 69, with hoarse voice for three months, was seen in March 1949. Radiation dermatitis of the neck had troubled her intermittently for 20 years. In 1923 she had received x-ray therapy for thyrotoxicosis. Laryngoscopy revealed tumor of the pyriform fossa; biopsy showed squamous cell carcinoma.

CASE 2.—Woman, 50, with progressive dysphagia for one year was seen in February 1950. In 1920 she received x-ray treatment for thyrotoxicosis. In 1937 a skin growth developed over the thyroid gland and was repaired by skin graft. Laryngoscopy revealed a postericoid tumor; biopsy showed fibrosarcoma.

CASE 3.—Woman, 76, with progressive dysphagia for 18 months, was seen in April 1950. She received x-ray treatment for thyrotoxicosis in 1922. In 1936 she had anterior neck skin graft. Esophagoscopy revealed postericoid stricture; biopsy showed squamous cell carcinoma.

CASE 4.—Woman, 49, with pain in right ear following sore throat for seven months before, associated with dysphagia, was seen in August 1950. In 1919 tuberculous nodes had been removed from the right side of the neck after which she received prolonged x-ray treatment to the neck. Laryngoscopy revealed posterior pharyngeal wall tumor; biopsy showed squamous cell carcinoma.

In these cases, neoplastic change occurred after a long latent interval of 26-30 years. The patients were treated originally for benign conditions. Frequent repeated doses of x-rays were known to have been given for six months or more in three cases.

It is concluded that if treatment of thyrotoxicosis by intense or prolonged irradiation was common practice 25-30 years ago, more radiation cancer of the laryngopharynx may occur or perhaps has already occurred.

[Late complications such as these rightly cause radiologists to be cautious in the treatment of all benign conditions. Frequently repeated small exposures or series seem most likely to produce this late sequela.—Eds.]

Extraskkeletal Osteogenic Sarcoma Arising in Irradiated Tissue in a case of testicular tumor is reported by Oscar Auerbach, Milton Friedman, Leo Weiss and Harold I. Amory.⁹ The patient was 1 of 250 with testicular tumors who, after removal of primary tumor, received intensive x-ray therapy aimed at the periaortic and pericaval lymph nodes.

Man, 23, noted pain and a lump in the right testis in March 1943. It slowly enlarged to $7.8 \times 5.6 \times 5$ cm. in two months. A test x-ray tumor dose of 1,340 r was given in seven days from May 21 to 27. In four days the tumor had shrunk 35% in volume. Radical right orchiectomy and dissection of the right iliac and pericaval lymph nodes revealed no metastasis. The appearance of the cells and marked radiosensitivity of primary tumor were consistent with a diagnosis of seminoma.

Postoperative x-ray therapy was given from June 29 to September 6.

(8) Brit. M. J. 2:1110-1112, Nov. 10, 1951.

(9) Cancer 4:1095-1106, September, 1951.

Factors were: 200 kv., 0.5 mm. Cu and 1 mm. Al. filter, 1 mm. Cu half-value layer, 50 cm. target-surface distance. Irradiation was delivered through five fields: right suprapubic (10 × 10 cm.), umbilical (10 × 15 cm.), anterior epigastrium (10 × 10 cm.), lumbar (10 × 15 cm.) and lower dorsal spine (10 × 15 cm.). The daily dose was 400 r (measured with scattering). Although each field received the same calculated total skin dose of 4,000 r delivered over 70 days, skin reaction pigmentation was greatest over the lower dorsal spine field.

The patient remained well until June 1947, when he noted aching over the lower dorsal spine. This grew worse and five months later, on November 25, a stony-hard mass was felt in the center of the lower dorsal spine portal. Lateral x-ray views and laminagraphy showed calcific mass in the soft tissues not connected with the bone or skin. The mass grew slowly. A radiotherapist believed the skin lesions represented postradiation carcinoma, but biopsy revealed osteogenic sarcoma. The lesion grew rapidly over two months despite removal of part of it for study on Feb. 11, 1949. Wide excision was done April 18. A radiogallium (Ga^{72}) tracer study revealed inadequate concentration to warrant such therapy. Feb. 18, 1950, paraplegia developed and he died April 30, three years after onset of osteogenic sarcoma and seven years after orchiectomy for seminoma.

Autopsy showed postradiation effects and a huge osteogenic sarcoma of the right lumbar muscles with invasion of adjacent vertebrae and ribs and metastases to the lung and lymphatics.

Consistent with experience both in experimentally produced bone neoplasms and in human bone tumors occurring after exposure to irradiation, a considerable latent period (four years) intervened between the period of irradiation and the clinical onset of malignant disease.

[Evidently the lower dorsal region sustained a greater biologic effect than it could stand and malignant degeneration followed after four years. Many radiologists feel that such heavy dosage is not required in treating radiosensitive seminomas, especially as a so-called "prophylactic" measure.—Eds.]

Osteogenic Sarcoma Following Prophylactic Roentgen Ray Therapy: Report of Case of seminoma testis treated by orchiectomy is presented by Sophie Spitz and Normal L. Higinbotham¹ (Memorial Hosp., New York City).

Man, 46, with seven months of severe pain in the back radiating down the leg was temporarily relieved by chordotomy one month before hospitalization Jan. 8, 1950. Spinal x-rays showed bone destruction of laminae of the 3d to 5th lumbar vertebrae. Calcific flecks were present in adjacent soft tissues and distinct bulging of the right psoas shadow was noted. Chest x-ray showed nodular densities indicating cancer metastases.

Routine examination four years earlier (May 4, 1945) had shown that the right testicle was larger than the left. Right orchiectomy within two weeks revealed complete replacement by seminoma testis. Prophylactic million volt x-ray therapy had been given from May 28 to Aug. 29, 1945, with a three week interruption on July 5 for surgery for acute gangrenous appendicitis. A dose of 4,900 r had been delivered to each of five skin ports, with cross fire into the retroperitoneal node-bearing areas, so that "tumor dose" had been calculated at 4,405 r at the 11th dorsal, 5,289 r at the 4th lumbar and 3,281 r at the suprapubic level. He remained in good health four years after x-ray therapy had been completed.

Palliative x-ray therapy to the chest and lumbar region and nitrogen mustard administered intravenously brought a severe reaction with headaches, nausea, vomiting and leukopenia. The symptoms then subsided and he was relatively comfortable for three weeks, after which intractable nausea and vomiting, fever and jaundice developed. Deterioration was steady in the next

(1) Cancer 4:1107-1112, September, 1951.

month with evidence of liver damage and increasing oliguria. He died 55 months after completion of prophylactic supervoltage therapy and nine months after onset of lumbar pain.

Autopsy revealed osteogenic sarcoma involving the 3d to 5th lumbar segments and soft tissues of the back, with metastases to the lungs. Viral hepatitis with cholemic nephrosis (uremia), hydrothorax and ascites were terminal features noted.

Since seminoma is radiosensitive and since late radiation complications including osteogenic sarcoma arise mainly in heavily irradiated tissues, the authors suggest that prophylactic x-ray therapy, if used at all, be limited in such cases to safe dosage levels (2,000-2,400 r in seven to nine weeks).

[The reporting of this unusual late complication is of value from the standpoint of possibly avoiding its repetition. The tissue doses which the spine received were exceptionally high in view of the fact that retroperitoneal metastases had not been proved. At one point, this patient was thought to have radiation osteonecrosis of the lumbar spine. However, a high sedimentation rate and neurologic evidence of involvement of the femoral nerve made recurrent neoplasm a more likely diagnosis. It was at autopsy that a second primary neoplasm was established.—Eds.]

Sarcoma of Skin after Exposure to X-rays. F. von Moos² (St. Gallen) describes a case.

Woman, 65, had received x-ray treatment in 1917 for hypertrichosis of the face. Erythroderma of cheeks and chin persisted for some time; two weeping



Fig. 357.—Roentgen sarcoma of skin showing purulent disintegration, January 1949. (Courtesy of von Moos, F.: *Schweiz. med. Wchnschr.* 82:179-181, February, 1952.)

ulcers developed on the chin, then healed after two months. Brownish pigmentation of the affected areas remained.

After 15 years, abscesses appeared in the area treated. They healed spontaneously in two weeks. Histologic examination revealed no malignancy. In July 1946, two small nodules appeared on the chin; one broke down, whereas the other grew and infiltrated the under part of the chin. Histologic examination after six months revealed spindle cell sarcoma. She was hospitalized in October

(2) *Schweiz. med. Wchnschr.* 82:179-181, February, 1952.

1947, when a swelling beneath the chin and along the lower left side of the mandible was noted together with a small ulcerating and weeping defect left of the median line of the chin. There was a brown pigmentation of the skin of the lower half of the face and upper part of the neck. Operation could not be performed because of the extensive x-ray burn and she was sent home after the ulcer had healed.

In December 1947, she was readmitted because of a mushroom-shaped, reddish-brown tumor, the size of a peach, beneath the right mandible. The tumor was firm and not movable in relation to the bone. It was removed but a smaller growth appeared in the same place within a month. This was also removed. There was a third recurrence in January 1948. Contact radiation was ineffective, and four months later both the tumor and the ulcer had increased considerably. Therapy consisted in excision of the growths and salve bandages. In January 1949 the tumor started to break down and bleed (Fig. 357), she experienced radiating pains and in July died of cachexia. Autopsy showed spindle cell sarcoma of right lower jaw, infiltrating the larynx, thyroid, right side of the floor of the mouth and anterior muscles of the neck, and small nodular metastases in the lungs.

Simmonds' Disease Following Irradiation of Pituitary for Acromegaly is reported by Lyman O. Warren³ (Bangor, Me.).

Man, 37, with anorexia and weakness for three weeks and vomiting and black-out spells for three days, was seen July 29, 1948. Four months earlier acromegaly was treated with deep x-ray, 2,750 r, which relieved severe headaches. He was in good health for a few weeks and then his symptoms began. Blood pressure was 80/55, with postural hypotension. Red and white cell counts were normal. Hemoglobin content was 10.5 Gm. Urine was normal. BMR was -31%. Fasting blood sugar was 65 mg., serum chlorides 560 mg. and cholesterol 182 mg./100 cc. Oral glucose tolerance test with 100 Gm. dextrose showed: fasting, 68 mg.; one-half hour, 120 mg.; one hour 125 mg., and two hours, 97 mg./100 cc. Insulin tolerance test with 0.05 units regular insulin per 10 kg. body weight intravenously showed: fasting, 65 mg.; one-half hour, 55 mg.; one hour, 55 mg., and two hours, 50 mg./100 cc. The Kepler water test gave positive results. Skull x-rays showed slight enlargement of the sella with secondary changes in the bony fossa. Adrenal insufficiency was the outstanding feature. He improved on desoxycorticosterone acetate, testosterone, thyroid extract, sodium chloride tablets and a schedule of six meals a day. Implantation of testosterone and desoxycorticosterone acetate pellets was unsuccessful. Methyltestosterone was substituted for testosterone injections. The injections of desoxycorticosterone acetate were eliminated in July 1950. In July 1951 all medication except salt was stopped. Despite positive results of the water test, he remained clinically well.

Irradiation of Normal Human Hypophysis in Malignancy: Report of Three Cases Receiving 8,100-10,000 r Tissue Dose to Pituitary Gland. Keith H. Kelly, Eggert T. Feldsted, Reynold F. Brown, Paul Ortega, Howard R. Bierman, Bertram V. A. LowBeer and Michael B. Shimkin⁴ (Univ. of California) irradiated the normal pituitary fossae of three patients with advanced neoplastic disease, using the following factors: 200 kv., half-value layer 1.2 mm. Cu, target-pituitary distance 63-70 cm., diameter field size 2.5 cm., defined field size at pituitary 2.7 cm. diameter. Daily doses of 400 r (air) were delivered to one, two or three fields. The following studies were performed before, during and after treatment: visual fields, audiographs, BMR, serum iodine, blood levels of albumin and globulin, sodium and potassium by flame photometer, chloride, calcium, alkaline phosphatase, free and

(3) J. Maine M. A. 42:355-356, December, 1951.

(4) J. Nat. Cancer Inst. 11:967-983, April, 1951.

total cholesterol, blood bilirubin and nonprotein nitrogen levels, glucose tolerance, urinary 17-ketosteroids and pituitary gonadotrophins. There was no clinical evidence of reduced pituitary function or laboratory evidence of hypopituitary function. Growth of the neoplasms was not affected. Gross and microscopic examination of pituitaries of two of the patients at autopsy showed no definite abnormalities. It is concluded that the normal adult human pituitary is resistant to x-radiation in doses up to 10,000 r.

[This article shows the difference in radiosensitivity of the normal and the abnormal pituitary malfunctioning as a result of neoplasm.—Eds.]

TREATMENT TECHNICS

Value of Cross-Section Diagrams in Delivering Accurate X-ray Therapy into Female Pelvis. Jesshill Love, G. N. Combs, W. A. Askew and M. Harcourt⁵ (St. Joseph Infirm., Louisville, Ky.) describe a method which may be applied to any deep-seated tumor. The usual time required is 1½ man hours.

METHOD.—The cross sections are made by taking both anteroposterior and lateral body measurements and marking them on a sheet of paper. Heavy lead wire is used to mold a templet at the proper body level. The templet is placed on the paper to fit in the confines of the previous measurements at the same level. The finished tracing approximates the actual body contour at that level. By examination and x-rays the tumor is localized and the tumor area is then drawn on the diagram. Related organs and bones are also added.

Because of the contour of the sacral-gluteal outline, an additional silhouette diagram is made with the patient prone. Vertical lines are drawn at intervals corresponding to the distances from the fifth lumbar vertebra to the coccyx, and then to the gluteal folds. A templet is lifted from the midline of this area and made to fit the limits of the vertical lines and the tracing is drawn in. The two diagrams are used for depth dose planning and beam direction.

To prove the accuracy of the method for depth distribution a wax model of a female pelvis was cast in the correct anatomic position and then sectioned sagittally. Various points were marked with small metal washers and photographic films were placed between halves of the model and exposed through simulated ports. X-rays showed surprising compositing of all beams. Densitometer readings taken at selected points corresponded well with those on the isodose curves. This method simplifies treatment planning.

[This method seems simple and practical and should be used more often for accurate planning of the tumor dose.—Eds.]

Clinical Possibilities of Cobalt 60 Beam Unit. The rays produced by the 1,100 curie Co⁶⁰ beam unit are roughly equivalent to those generated by a 3-4 peak supervoltage x-ray machine, the therapeutic value of which is well established. T. A. Watson⁶ (Univ. of Saskatchewan) reports that, compared with a 2 Mev machine, the Co⁶⁰ unit costs less initially and for upkeep, is more compact and maneuverable and has a much more homogeneous beam. No filtration is necessary, a higher depth dose is obtained and the output is constant. Disadvantages of the unit

(5) *Radiology* 57:169-176, August, 1951.

(6) *J. Canad. A. Radiologists* 3:7-10, March, 1952.

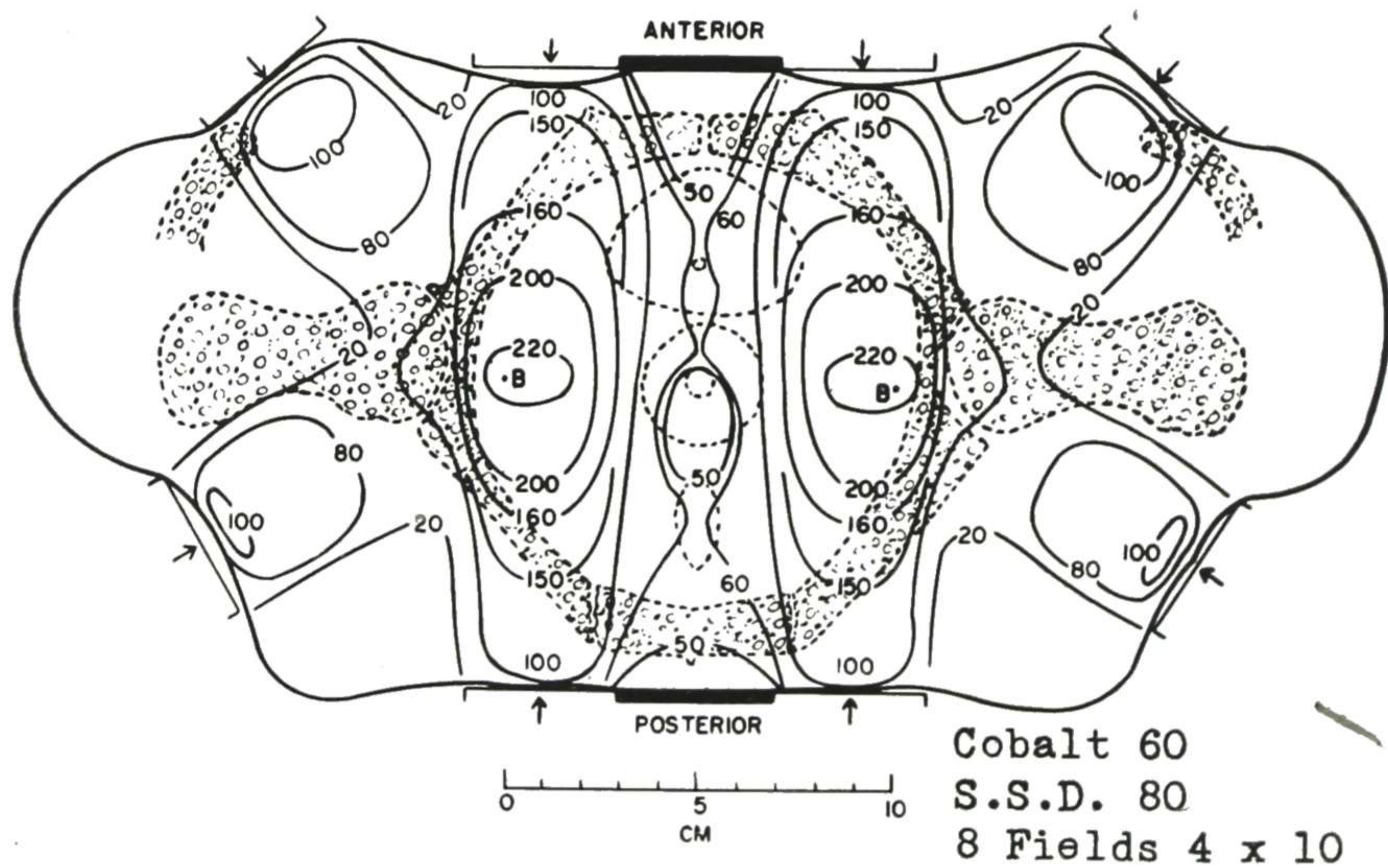
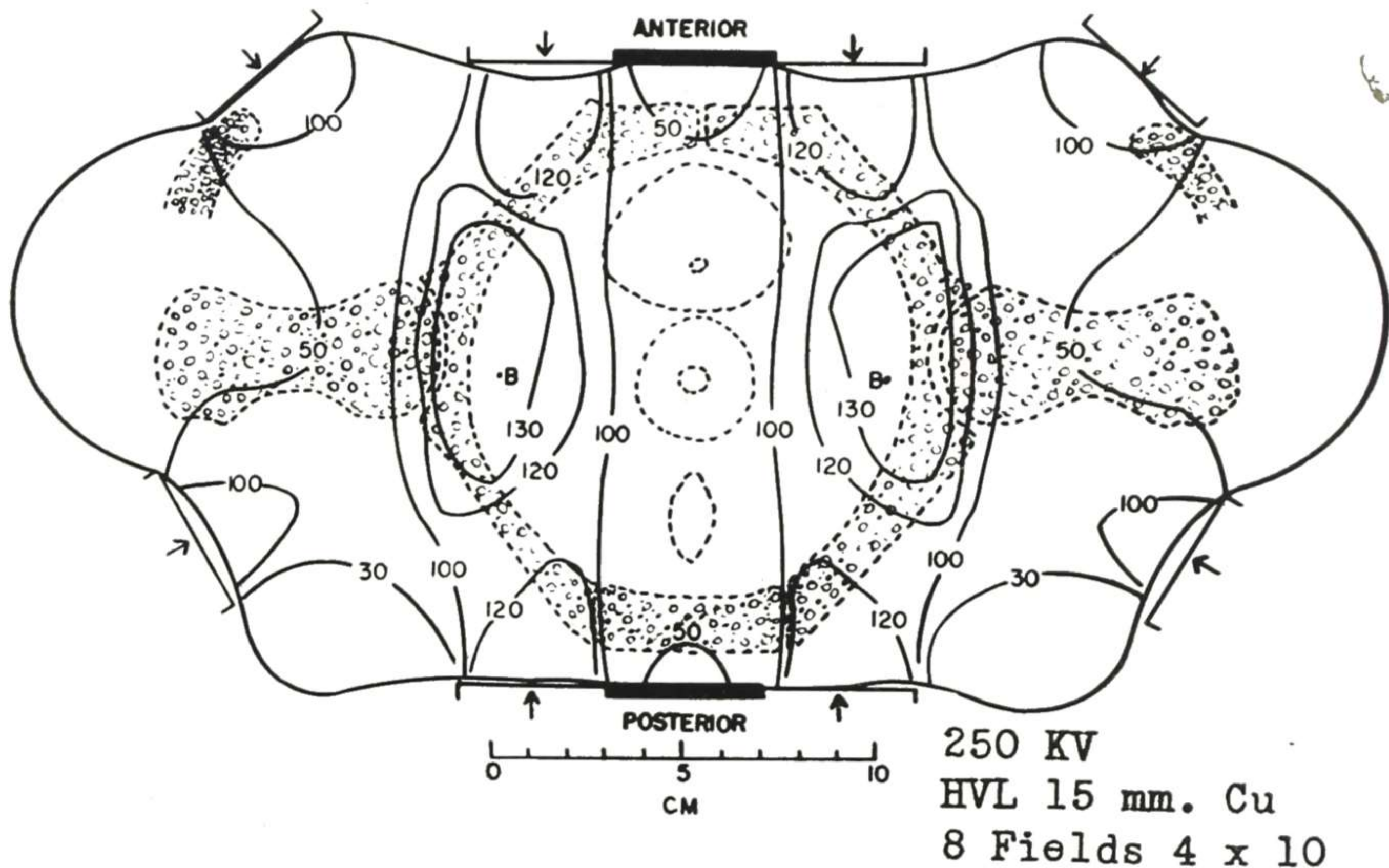


Fig. 358 (top).—Distribution of dosage in pelvis in postradium treatment of cervical cancer, using 250 kv,

Fig. 359 (bottom).—Distribution of dosage in pelvis in postradium treatment of cervical cancer, using Co^{60} unit.

(Courtesy of Watson, T. A.: J. Canad. A. Radiologists 3:7-10, March, 1952.)

are that output is considerably less than that of a 2 Mev machine and that the cobalt will probably have to be replaced in about three years. Another disadvantage is the production of a marked penumbra effect at the edge of the field with the 2.5 cm. focal spot.

The unit has been used to treat deep lesions suitable for small or medium-sized fields such as cancer of the esophagus, larynx, pharynx, throat and possibly lung. It has also been used to irradiate parametrial tissue after radium therapy for cervical carcinoma and for postoperative irradiation of the axilla and supraclavicular regions in breast carcinoma. Figures 358 and 359 demonstrate the different distributions of dosage obtained in the postradium therapy of the pelvis for cervical cancer, using a 250 kv. machine in one instance and the cobalt unit in the other. The dose received at point *B* with the former is 130% compared with a maximum to the skin of about 125%, a ratio of about 1:1, whereas with the cobalt unit this ratio is increased to 2.2:1. Wherever suitable, beam direction, using plaster cast and wax, and back pointer are employed. Ceiling suspension allows unrestricted movement on the floor. Rotational therapy, either horizontal or vertical, is to be used in selected cases. Conventional cones with open ends are employed. After determination of the best angle of incidence, size of the fields and radius of the point of entry from the point marked on the chest wall, direct measurements are made in a water container. Accurate determinations of the desired tumor dose can then be made and the daily surface dose determined. By centering the ceiling spotlight on the mark on the chest and using the pin and arc for localization, the central ray of the beam can be made to traverse the center of the tumor however much the patient is rotated.

Cobalt 60 Beam Therapy: Some Influences and Advantages. Initial impressions of this new radiotherapeutic weapon are reported by Ivan H. Smith⁷ (Ontario Cancer Found.). It is believed that Co⁶⁰ beam therapy will expand the effectiveness of therapeutic radiology. This form of treatment or its equivalent will be a "must" for any department handling 500 new therapy cases yearly; however, it will not replace conventional equipment. It will permit fullest utilization of rotational therapy. Increased costs of skilled professional and technical manpower, as well as housing and maintenance, place this type of therapy beyond the means of the average individual or hospital and point the way toward centralization and government subsidy.

Tumors of the nasal cavity, rectum and bronchus were selected to illustrate the cardinal points of therapy. In each, beam direction isodose studies were carried out for 250 kv. constant potential x-radiation with half-value layer 3.7 mm. Cu and focus-skin distance 50 cm. and compared with the radiation from the 1,300 curie-equivalent Co⁶⁰ beam therapy unit with half-value layer 14.9 mm. Cu and focus-skin distance 100 cm. Depth dose readings at 10 cm. for the 250 kv. unit were 32% as compared with 56% for Co⁶⁰ using 6 × 8 fields. Comparative output was 62 r/minute at 250 kv. versus 20 r/minute from the Co⁶⁰ plant.

(7) J. Canad. A. Radiologists 3:16-19, March, 1952.

Dosage studies of an early bronchogenic carcinoma, technically inoperable because of its carinal position, were made to deliver a 5,000 tumor dose over a 5 cm. area (Figs. 360 and 361). Considering skin dose, this was possible over three weeks with Co^{60} , but five weeks would be required for a similar plan with 250 kv. therapy. A much lower skin

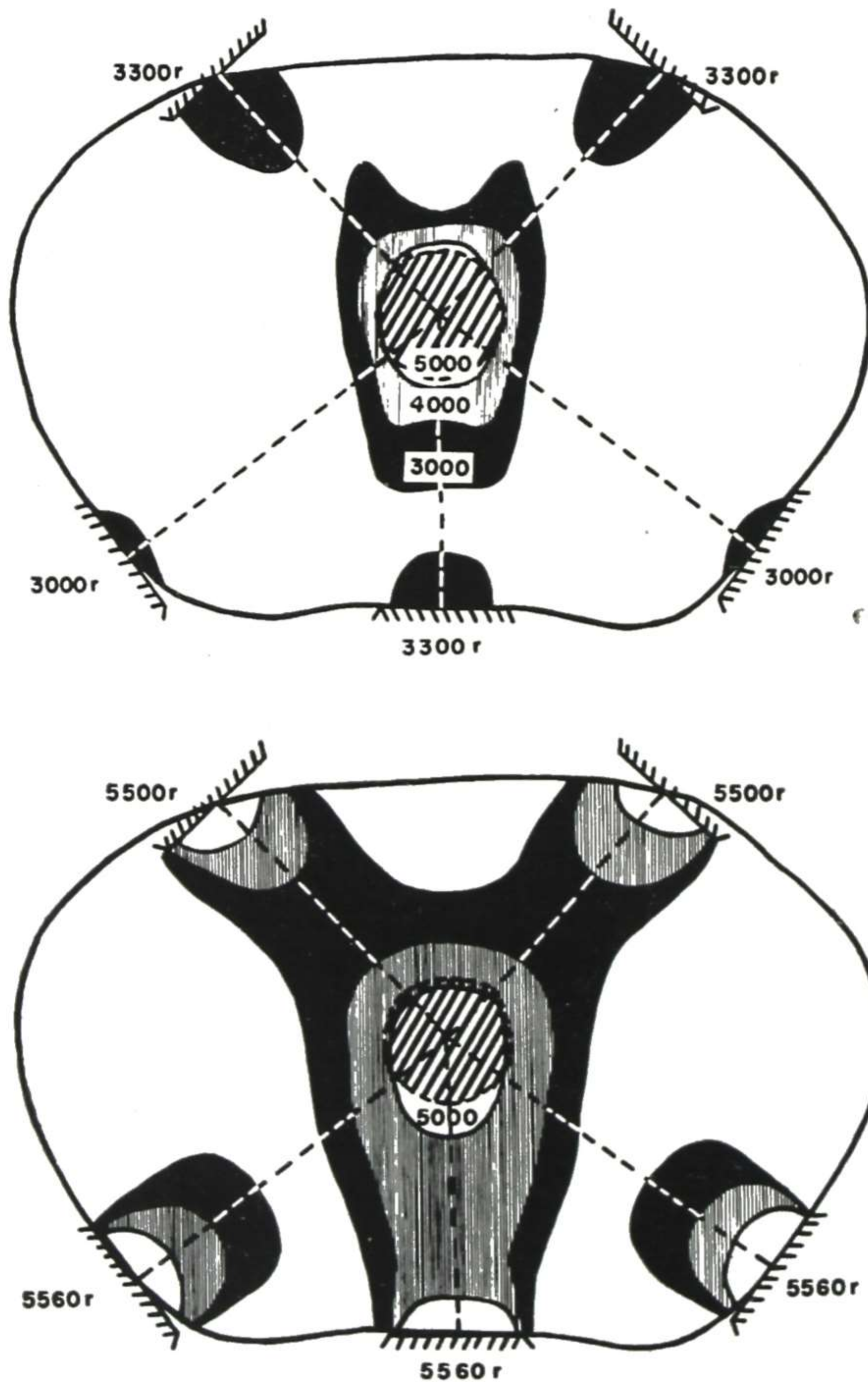


Fig. 360 (top).—Cancer of bronchus. Treatment with Co^{60} beam unit, using 6 x 8 cm. fields.
 Fig. 361 (bottom).—Cancer of bronchus. Treatment with 250 kv. x-rays, using 6 x 8 cm. fields.
 (Courtesy of Smith, I. H.: J. Canad. A. Radiologists 3:16-19, March, 1952.)

dose is required with Co^{60} , and there is a lower coefficient of bone absorption. In three cases of bronchogenic carcinoma the low volume dose did not produce any constitutional side effects, and the patients were hematologically unaffected.

[The articles by Watson and Smith are part of a symposium in the March issue of the *Journal of the Canadian Association of Radiologists*. In addition to these early clinical evaluations of the Co^{60} teletherapy units, there is information on the physical characteristics of the radiation of Co^{60} and the problems of protection, design and loading. There is an additional article "The Betatron in Cancer Therapy" by Watson

and Burkell. Watson has had the opportunity to pioneer in the clinical use of both the Metatron and the Co⁶⁰ teletherapy unit.

Concerning the evaluations of the Co⁶⁰ units, one additional disadvantage should be mentioned. They are not available. Many patients will be deprived of the benefit of high radiation if efforts to obtain such facilities are deferred until Co⁶⁰ becomes generally available.—Eds.]

Two Million Volt Roentgen Therapy Using Rotation. John G. Trump, Kenneth A. Wright, W. W. Evans, Hugh F. Hare and Samuel W. Lippincott, Jr.⁸ (Massachusetts Inst. of Technology) treated 60 patients by means of a 2,000,000 volt constant potential electrostatic accelerator of the Van de Graaf type. Microamperage is 250. Output is 75 r/minute at 100 cm. in air, with an equivalent of 6.8 mm. Pb filtration and half-value

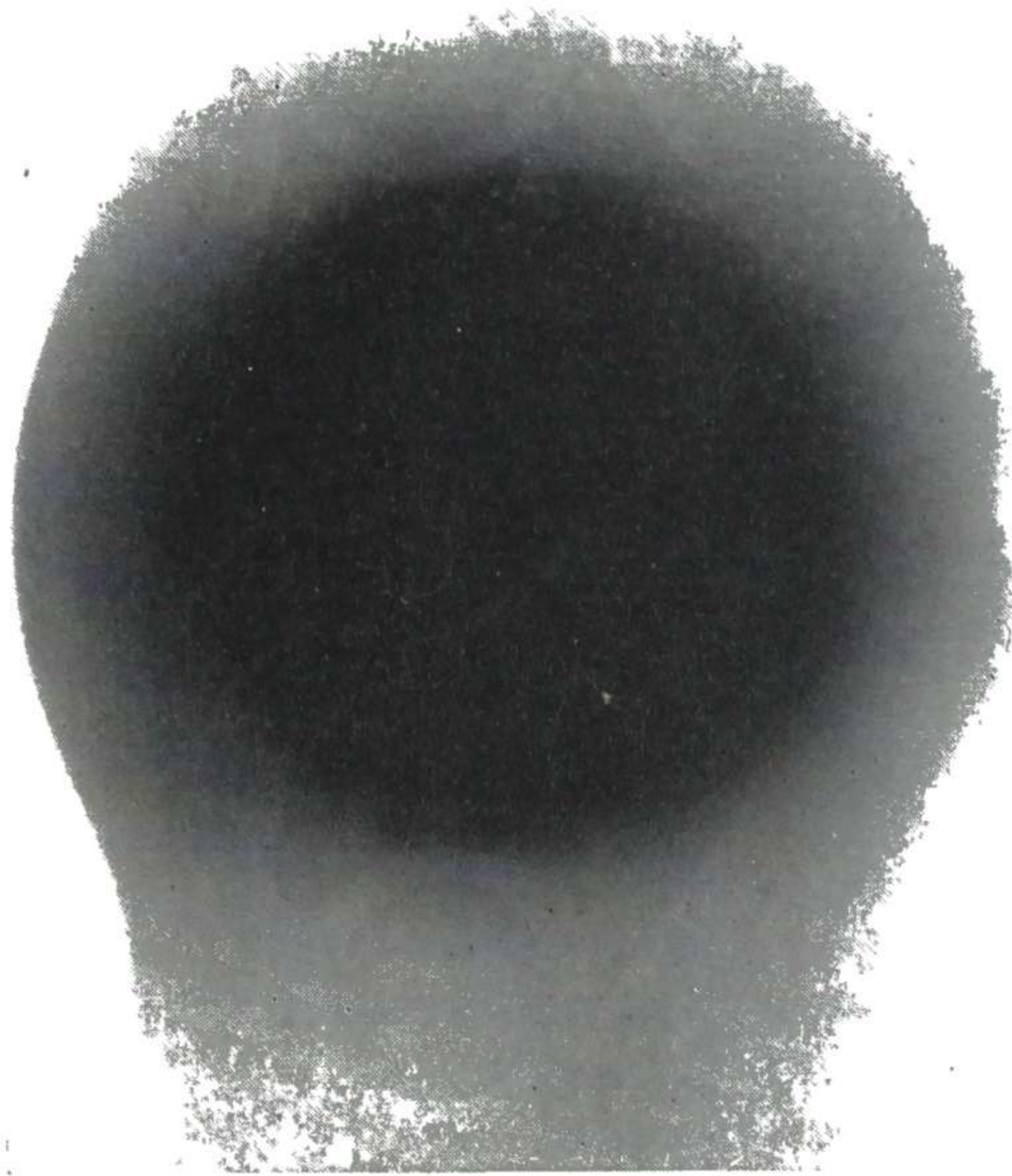


Fig. 362.—Photographic film sandwiched in pelvic section of phantom and irradiated by 15 cm. circular beam of 2 Mev roentgen rays during rotation. (Courtesy of Trump, J. G., *et al.*: Am. J. Roentgenol. 66:613-623, October, 1951.)

layer of 12.5 mm. Cu. Portals are easily varied up to 30 sq. cm.

Radiation through a 5×5 cm. field yields approximately a 50% depth dose at 10 cm. There are a sharply demarcated beam and low ionization density in the first few millimeters of tissue, with resultant increased skin tolerance. The integral dose is about 50% that of 200 kv. radiation and the spectral distribution of energy equivalent to that emitted by radium whose attractive therapeutic properties have been proved.

Photometric determination of isodose curves in phantoms, with rotation about a tumor axis, produced the favorable results shown in Figures 362 and 363. These worked out well in patients.

(8) Am. J. Roentgenol. 66:613-623, October, 1951.

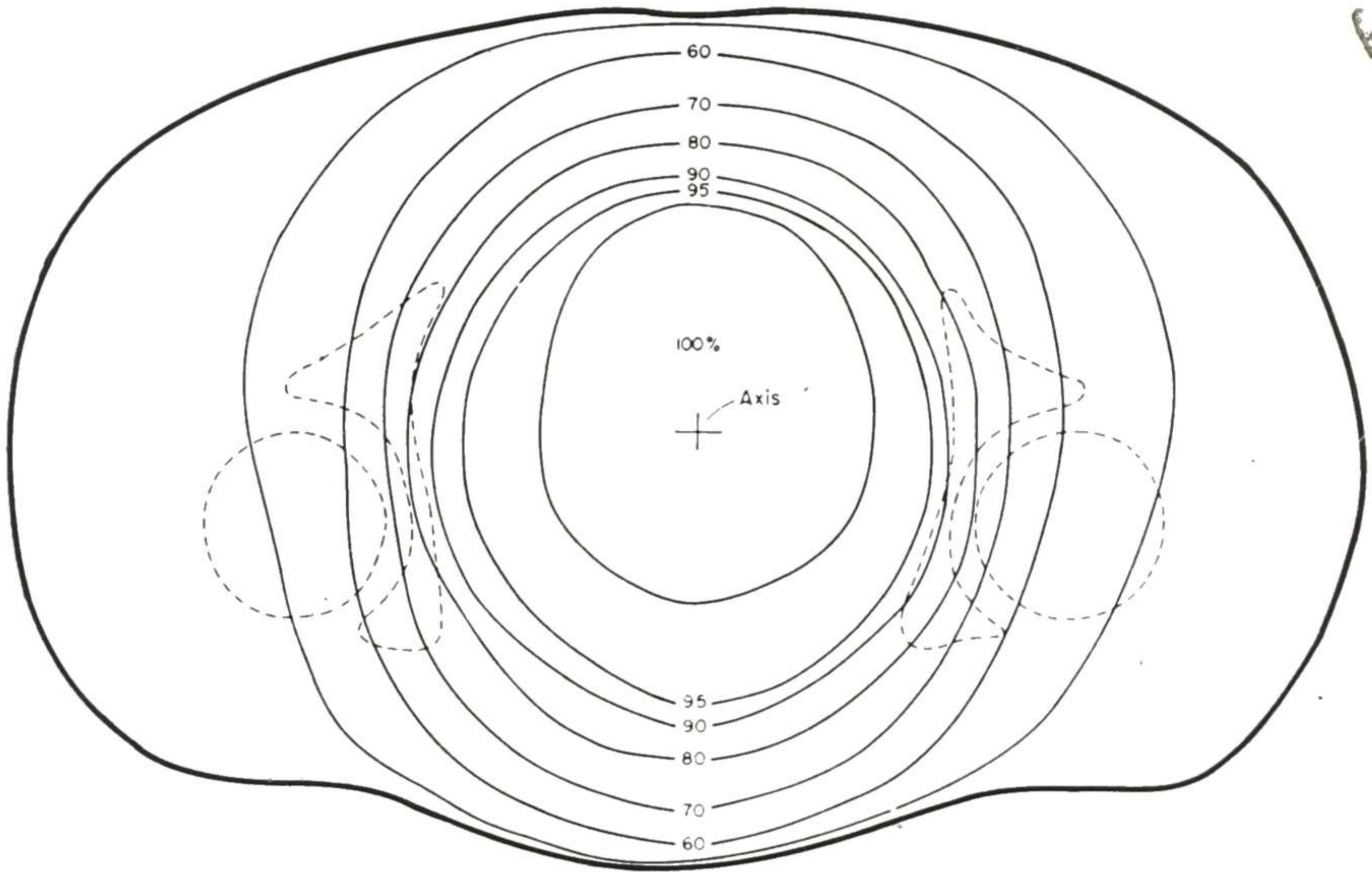


Fig. 363.—Isodose chart of rotational treatment of pelvic cavity. Factors are: 2 Mev., field 15 cm. in diameter, target-to-axis distance 108 cm. Major axis of phantom, 36 cm.; minor, 23 cm. (Courtesy of Trump, J. G., *et al.*: *Am. J. Roentgenol.* 66:613-623, October, 1951.)

A tumor dose of 6,000 r given in 35 treatment days was used for epidermoid carcinoma and carcinoma of the breast and ovary. Lymphoid tumors, when local or regional, received 2,400-3,000 r in 15 treatment days with large enough portals to include all surrounding lymphatics. Gliomas, fibrillary astrocytomas, oligodendrogliomas, glioblastoma multiforme and meningeal sarcomas received 7,500 r in 44 treatment days. Damage to skin and normal tissue was less, wet reactions were avoided and incidence of nausea was greatly diminished.

The 31 Mev Betatron at Radiotherapy Clinic, Canton Hospital, Zurich, and results of treatment with its ultrahard roentgen rays are described by H. R. Schinz and R. Wideröe.⁹ The betatron rays have a wavelength of 0.4×10^{-3} A. and in doses of 4,000-12,000 r cause little skin reaction. They are therefore especially suited for treatment of deep-seated cancers.

In seven months, 60 patients were treated. For treatment, patients are placed on tables on either side of the betatron (Fig. 364). Radiation sickness is less severe than with roentgen rays. Cancerous tissue reacts in about the same way but, with the same number of ions, the effect of betatron rays is about 65-70% of ordinary rays.

Seven patients with cancer of the pharynx and larynx treated with 6,000-9,000 r all became symptom-free, as did three of seven patients with cancer of the esophagus treated with 10,000-13,000 r. Three patients improved; one failed to respond. Of 11 women with genital cancer given 4,000-9,000 r doses, 7 became symptom-free, 3 improved and 1 failed to respond. Metastases of various kinds have been treated with

(9) *Acta radiol.* 37:374-387, Mar.-Apr., 1952.



Fig. 364.—Position of patient during treatment of esophageal carcinoma. (Courtesy of Schinz, H. R., and Wideröe, R.: *Acta radiol.* 37:374-387, Mar.-Apr., 1952.)

3,000-8,000 r doses; of eight patients, six became symptom-free and two showed improvement. These are all early results.

Possible Use of Neutron-Capturing Isotopes Such as Boron¹⁰ in Treatment of Neoplasms is discussed by William H. Sweet and Manucher Javid¹ (Massachusetts Gen'l Hosp.). Isotopes such as B¹⁰ especially tend to capture slow (thermal) neutrons, whereas normal atoms in living tissue do not. As B¹⁰ at capture yields an alpha particle of high energy which travels only about 14 μ in tissue, the site of the B¹⁰ atom determines the site of destruction of tissue after the capture reaction. Chemical analyses in 58 patients after intravenous injection of 15 Gm. borax 70 kg. body weight shows that it concentrates over three times as much in many rapidly growing brain tumors as it does in normal brain tissue. The differential is ordinarily maintained only for the first 20-30 minutes after injection. The total amount of boron that may be introduced without toxic effects yields approximate concentrations of 50 μ g./Gm. in tumor and of 15 μ g./Gm. in brain tissue. The energy yield in tumor tissue is triple that in normal tissue. The neutron beam can be used in patients with total or subtotal removal of brain tumor. Some time after recovery from immediate effects of initial surgery the cerebrospinal fluid is withdrawn from the head and replaced by air. The air should permit almost direct access to the remaining tumor by the neutrons, and injection of B¹⁰ shortly before exposure to the neutron beam may cause differential destruction of residual tumor.

New Method for Treatment of Cancer of Lungs by Means of Artificial Radioactivity (Zn⁶³ and Au¹⁹⁸) is reported by J. H. Muller and P. H. Rossier² (Univ. of Zurich). Experiments on rabbits as well as tests in patients have shown almost complete fixation of injected radiozinc-pectin suspension within the lungs, obviously through diffuse microembolism into the lung capillaries. Au¹⁹⁸ as a precipitate, with 30-50 μ

(1) *J. Neurosurg.* 9:200-209, March, 1952.

(2) *Acta radiol.* 35:449-468, May-June, 1951.

particles, in a pectin-containing solution, was used subsequently because of its longer half-life period. The new procedure was tested in two patients with Zn^{63} and in four with Au^{198} (one with pulmonary metastases of a hypernephroma, one with pulmonary lymphogranuloma and four with inoperable bronchial carcinoma).

Despite somewhat low dosage of radiogold injected in the first patient with lymphogranuloma (Hodgkin's disease), the patient improved substantially with "drying out" of pleural exudate and reduction of dyspnea. He was then well enough to tolerate extensive roentgen therapy, including infiltrations of lung remnants and numerous foci, after which he could resume his work as a hotel porter.

Topographic selectivity was later improved by means of cardiac

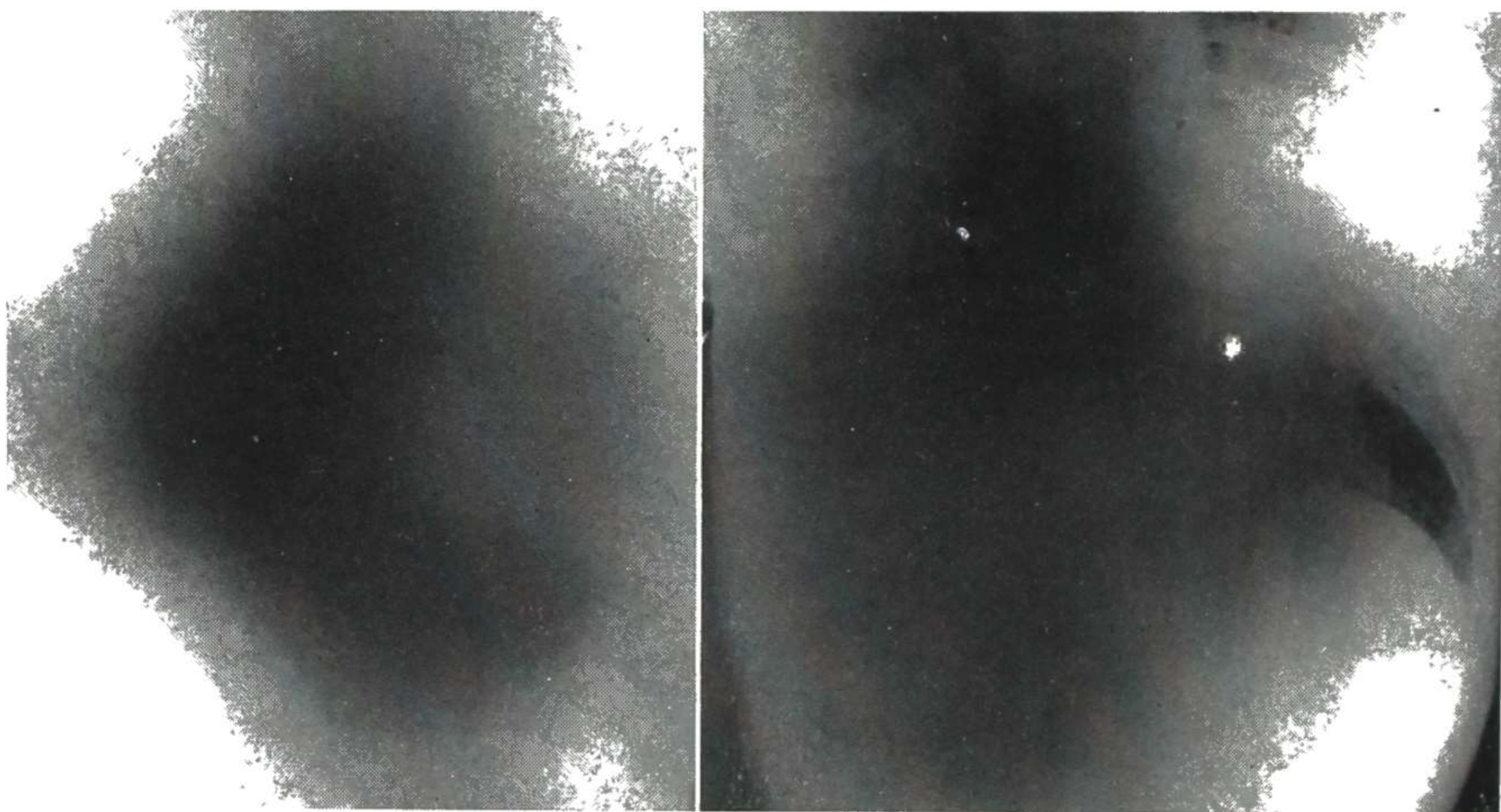


Fig. 365 (left).—Thoracic autoradiograph after intrapulmonary application of 150 mc. Au^{198} precipitate. Dosage in right lung is triple that in left lung. Pleural exudate deviates and partly compresses right lung.

Fig. 366 (right).—Same case after intrapleural injection of 100 mc. colloidal Au^{198} mixing with exudate in right pleural cavity and emitting strong radiation.

(Courtesy of Muller, J. H., and Rossier, P. H.: *Acta radiol.* 35:449-468, May-June, 1951.)

catheterization extending into the pulmonary artery segments involved.

In a man, 55, squamous cell carcinoma of the right median lobe bronchus was confirmed by bronchoscopy, cytohistology and tomography. Electrocardiogram showed Tawara rhythm indicating possible penetration of cancer into the pericardium and heart auricles. The right pleural cavity also showed a large exudate. The condition was considered inoperable.

On Nov. 21, 1950, 150 mc. Au^{198} precipitate was deposited in the lungs by cardiac catheter. Half the infusion was directed into the right ventricle, the other half into the main right pulmonary artery. Thoracic autoradiograph (Fig. 365) showed expected distribution of radiation. Two and three weeks later 100 mc. colloidal radiogold was injected into the right pleural cavity (Fig. 366). The total of 200 mc., evenly mixed with the exudate, insured strong irradiation of the diseased pleura and also convenient cross-fire irradiation of the right lung, which hung partly collapsed in the radioactive pleural bath. At first the patient showed real improvement, with total atelectasis of the right lung dissipated through reduction of invasive tumor masses obliterating the main bronchus. However, severe cardiac failure caused death on December 16.

Autopsy revealed a large squamous cell carcinoma in the right median lobe bronchus, with extensive invasion of the superior lobe, pericardium and both auricles. Carcinomatous infiltration of heart muscle was the immediate cause of death. Intensive irradiation effect was found with cytologic changes and tumor necrosis.

It is concluded that intravenous applications of Au¹⁹⁸ precipitate are clinically indicated for all such diffuse radiosensitive lung malignancies as lymphogranuloma, as well as some types of primary or metastatic carcinoma or sarcoma of the lungs. The method may be combined with intrapleural or intratumoral injections of colloidal Au¹⁹⁸ and with classic radiotherapy or surgical operations.

[Cardiovascular catheterization is an ingenious and rather heroic method of therapeutic use of a radioisotope made necessary because colloidal radiogold cannot be administered intravenously to obtain selective fixation within the lungs. This is because the very small gold particles (40-80 $\mu\mu$) pass through lung capillaries and finally are deposited in the reticuloendothelial system, especially of the liver and spleen.—Eds.]

Uses of Radioactive Gold Colloid in Therapy and Palliation of Neoplastic Disease are reviewed by William N. Harsha³ (Univ. of Kansas)

A standardized sterilized preparation of radioactive gold (Au¹⁹⁸) which can be shipped by air express to any authorized user is prepared by Abbott Laboratories. The isotope has a half-life of 27 days, decaying by emission of beta and gamma rays. When injected intravenously the colloid localizes consistently in the reticuloendothelial system in liver, spleen and bone marrow. When the colloid is infiltrated directly into the tumor, varying amounts are retained, depending on vascularity and necrosis of the tumor, the more solid tumors retaining as much as 95-99%. When therapeutic doses of 20-100 mc. Au¹⁹⁸ are instilled into the pleural or peritoneal cavities of human beings, less than 5% is lost in urine and stools. Most of the material remains in the cavities, and some is transmitted to the regional lymph nodes. Colloidal gold used in this way is often a satisfactory therapeutic agent for pleural effusion and ascites due to metastatic implants, usually reducing or stopping fluid formation. Patients receiving large doses of Au¹⁹⁸ in this manner may have local pain for some hours, nausea, vomiting, fever and bone marrow depression. These symptoms are transient if excessive doses are not used.

Harsha reports three cases in which he administered gold to reduce fluid formation, of which the following is typical.

Woman, 33, had radical mastectomy for scirrhous adenocarcinoma seven years previously. Right hydrothorax for six weeks before had necessitated thoracentesis every 10 days. After removal of 700 cc. bloody fluid to leave the thorax as free from fluid as possible, the patient received 30 mc. Au¹⁹⁸ into the right chest; 30-50 mc. was given each week for six treatments. The fluid changed character from bloody to serous, protein content dropped from 9 to 3 Gm./100 cc., and specific gravity changed from 1.029 to 1.011. After the seventh week fluid formation was undetectable. Much pleural thickening was present at this time. During treatment the white blood cell count fell from 7,100 to 1,300 and hemoglobin from 11.2 to 8.6 Gm. These values returned to normal after treatment was discontinued.

Endovesical Irradiation of Urinary Bladder Tumors with Radioactive Cobalt. W. Bessler and Th. Meister⁴ (Univ. of Zurich), on the basis

(3) West. J. Surg. 59:358-362, July, 1951.

(4) Schweiz. med. Wchnschr. 81:1214-1218, Dec. 5, 1951.

of results in 16 cases, list the following indications for this therapy: diffuse benign papillomatosis, relapsing localized papillomatosis, malignant papillomas and superficial bladder carcinomas and for follow-up treatment after incomplete tumor extirpation. It is the method of choice for tumors in the floor of the bladder which are not easily accessible for operation or those in the region of the ostia. This treatment should not be used for bladder carcinoma with extensive infiltration of the layers of the bladder wall and pelvic connective tissue.

The isotope Co^{60} is put into watery solution as the chloride. Since its half-life is 5.3 years, the solution may be used repeatedly. The value of this isotope lies in the fact that there is little beta radiation and this is stopped by the wall of the rubber balloon in which the solution is placed, so that pure gamma radiation results. Usually, 18-25 mc. of radioactive CoCl_3 in 60 cc. aqueous solution is used. This produces some 800-1,300 r daily at the surface of the balloon.

METHOD.—The empty rubber balloon is tied to one outlet of a multichannel catheter and inserted into the bladder through the urethra. One channel allows evacuation of urine during treatment. The balloon is then filled with the radioactive solution by means of a pipet held in a metal stand. A stopcock arrangement is used which allows ultimate removal of the radioactive solution with relatively less danger than with the usual glass syringe. If the floor of the bladder is to be particularly irradiated, the balloon can be pulled against this area by pulling on the catheter. After treatment, the solution is evacuated and the catheter withdrawn. The distribution of the gamma rays can be easily traced by an autoradiograph, made with the patient lying for two hours with a film affixed to the lower abdomen. It is important not to spill or lose any of the solution except onto disposable materials. Rubber gloves and other protective devices should be used to prevent contact with the radioactive solution. Contaminated objects are buried deep in the earth. The rubber balloon is tested before use by filling with fluorescein and immersion in water for 24 hours to detect leaks. For safety, other beds should be at least 250 cm. from the patient's bed. Nurses and visitors may remain no more than an hour a day at the patient's bedside.

The dose used varied from 4,160 r in four days to 11,709 r in nine days. Three patients had a papilloma (with suspicion of malignancy), seven papillary carcinoma, three poorly differentiated bladder cancer and one unspecific bladder granulomatosis. Two patients did not have tumor biopsy but cystoscopic examination indicated infiltrative bladder carcinoma. Twelve patients had had operations for the tumor; two underwent total removal and were given prophylactic radiation. Four had no operation other than biopsy.

All patients had some reaction to therapy. Mild to painful tenesmus occurred during treatment, only to disappear when catheter and balloon were removed. Spasmolytics helped control this difficulty. Most patients had cystitis which was regularly increased by treatment. Pyuria was most intense a few days after removal of the isotope; there was frequent relapse, and the organisms were resistant to antibiotics. Hemorrhagic cystitis occurred in a few cases. Bladder capacity was usually unaltered, but in three patients with chronic cystitis shrinkage was appreciable. One patient had two courses of cobalt therapy, with eventual

reduction of bladder capacity to 40 cc. Proctitis developed in one patient. A woman, 38, had no menses during the four months of follow-up. A man had recurrence of preirradiation periurethritis, leading to stricture.

Thirteen patients were alive up to 10 months after treatment. Eight were symptom-free; three had a mild to moderate cystitis and two severe cystitis. Two of the three who died had tumor recurrence (or residue); autopsy on the third showed pyelonephritis and cystitis but no residue of tumor.

Intravesical Radium Bomb: Therapeutic Failure in Bladder Tumor.

Treatment of bladder cancer remains a great problem in urologic practice. No one has achieved promising five year survival rates. In contrast to the generally pessimistic outlook, Friedman and Lewis reported encouraging results with the intracystic application of radium by means of a "radium bomb" after cystostomy. John Duff and Richard M. Hyman⁵ (Morrisania Hosp., New York City) report results in nine patients.

TECHNIC.—A 25-50 mg. source of radium in a capsule with an active length of 2 cm. and with 0.5 mg. Pt filtration was placed in the center of the lumen of a Foley catheter without obstructing the lumen. Exposure was about 4,800 mg.-hr. In addition, external irradiation was added to provide a uniform dose throughout the bladder via three ports, one anteriorly and one to the right and the other to left posterior gluteal folds. A total dosage of 12,000 r was delivered to the mucosa, or 6,000 r at 1 cm. depth. The x-radiation was given for three to four weeks before use of the bomb. It seemed better tolerated if the bladder was closed.

Every patient had received some other form of therapy before radium bomb insertion. In most cases electrosurgery by open or closed methods preceded irradiation, and in three a segmental resection had been done. In five, both x-radiation and radium therapy were combined, and in four the bomb was the sole agent of radiotherapy.

The postradiation symptoms of all patients were characterized by intense burning and excruciating perineal and suprapubic pain requiring sedation. Of the nine patients, only three were alive and free from discernible tumor 12 months after treatment. Those who died survived 3-14 months with terminal evidence of recurrent cancer and metastases.

The pain and discomfort following irradiation were not commensurate with the results obtained. However, some tumors were probably too far advanced. The authors do not want to leave the impression that radiation will never play an important role in treatment of bladder cancer.

Recent Clinical Experience with Grid in X-ray Treatment of Advanced Cancer. William Harris⁶ (Mount Sinai Hosp., New York City) reports experience with grid radiotherapy in 149 patients who were hopeless from the point of view of conventional radiotherapy or surgery. The primary aim was palliation and prolongation of useful life. A course of 6,000 r (weighed average) to the primary lesion or metastases was completed by 127 patients, including 12 with brain tumors who had had craniotomies. Results are too recent for assessment. Of six patients with

(5) *Urol. & Cutan. Rev.* 55:683-688, November, 1951.

(6) *Radiology* 58:343-350, March, 1952.

oral cancer, one had palliation for one year. A second with tongue cancer and extensive nodes showed control of the primary lesion but persistence of nodes in the neck for over one year. A patient with cancer of the floor of the mouth was free of disease for 15 months. Autopsy on the fourth, with tongue cancer, showed microscopic evidence of disease in the tongue. Of the other two patients, one was alive with disease one year after treatment and another was treated too recently to evaluate. Two patients with pharyngeal cancer died a few months after treatment with distant metastases. Of six patients with cancer of the esophagus, three had moderate palliation.

Thirty-five patients with cancer of the lung were treated. In one patient the tumor disappeared on x-ray for 12 months and the patient became asymptomatic. Two patients had thoracotomy after treatment;

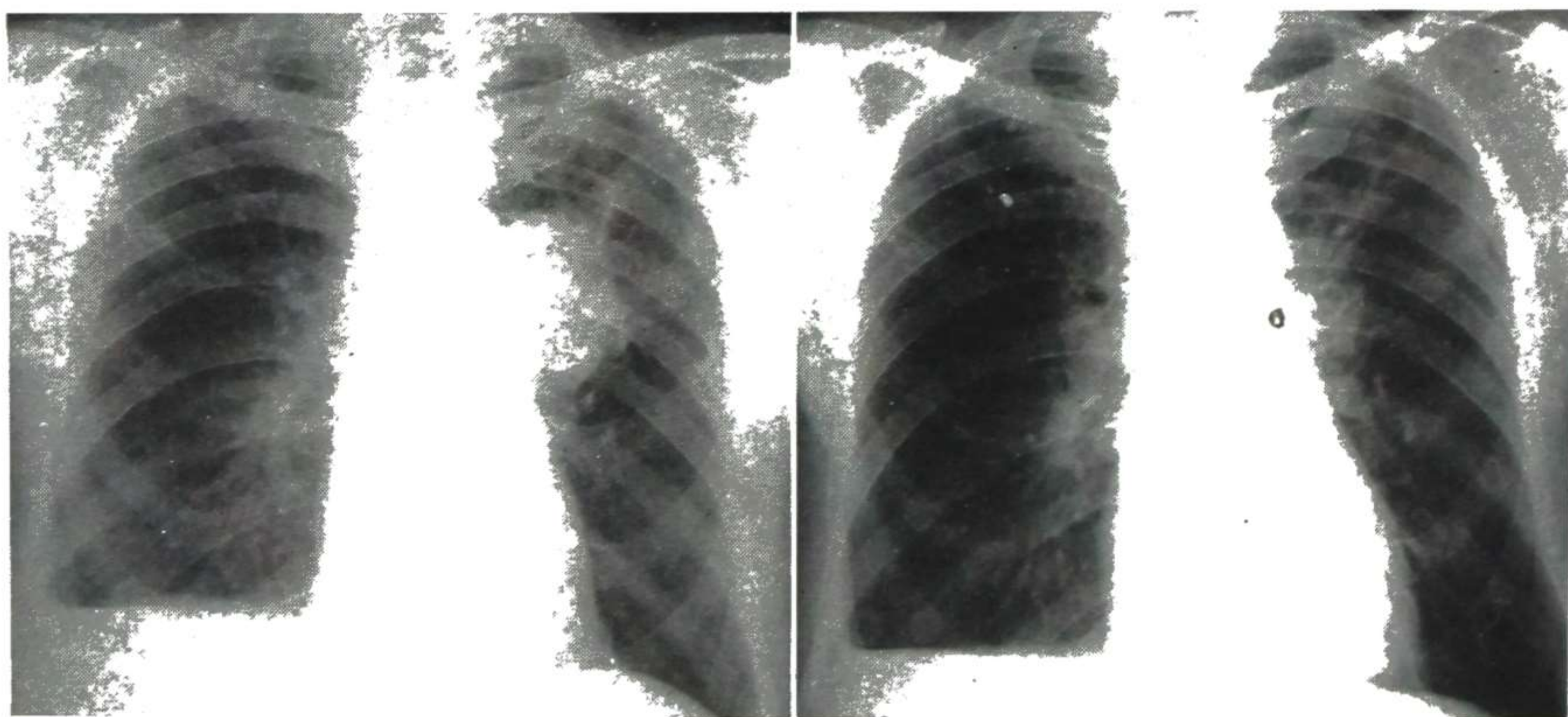


Fig. 367.—Small cell cancer of left upper lobe in patient, 66, proved by bronchoscopy. Left pneumonectomy three months after grid therapy revealed no evidence of tumor. Patient died two months postoperatively of cardiac insufficiency. Autopsy showed a tumor-free chest and a single liver metastasis. (Courtesy of Harris, W.: *Radiology* 58:343-350, March, 1952.)

residual disease was found in pulmonary tissue beneath the bronchus in both. Another patient (Fig. 367) with positive bronchus biopsy had a pneumonectomy after grid therapy. There was no histologic evidence of disease in the specimen. The patient died of cardiac insufficiency several months after surgery. A single liver metastasis was found at autopsy. Cancer in the kidney was treated in three patients after nephrectomy; two died of metastases and one was well 12 months after treatment. Cancer of the bladder was treated in 23 patients, 15 of whom were alive after brief intervals; 7 died of generalized metastases and 1 of uremia. Of eight patients with uterine cancer, one had good palliation. One patient with primary inoperable rectal cancer remained symptom-free of local disease for one year and died at the end of that time of skeletal metastases. Of 11 patients with metastatic lymph nodes, 10 showed good response for a short time.

Factors used with grid are: 200 kv., focus-skin distance 50 cm., half-value layer 0.9 mm. Cu, with a port size of 50-400 cm.², or 400 kv., focus-skin distance 70 cm., half-value layer 4.1 mm. Cu, with a port size of 50-225 cm.² The open area of the grid equals 40% of portal area, and

grid openings are 1-1.5 cm. in diameter. Total dose is 12,000-24,000 r (air)/portal.

[Attention should be called to the excellent editorial on irradiation through grids by Dr. Failla (*Radiology* 58:424, March, 1952) which emphasizes the importance of properly regulated dosage to avoid irreversible changes.—Eds.]

Flexible Indicator for Use in Connection with Radiation Therapy is described by Ove Mattsson⁷ (Karolinska Hosp., Stockholm). The scale can be applied on irregular surfaces and has proved especially useful in indicating locations of tumors of the hypopharynx.

APPARATUS.—A leather ruler 3 mm. thick and measuring 4 × 15 cm. was found most suitable. Holes large enough to hold a lead shot 2 mm. in diameter

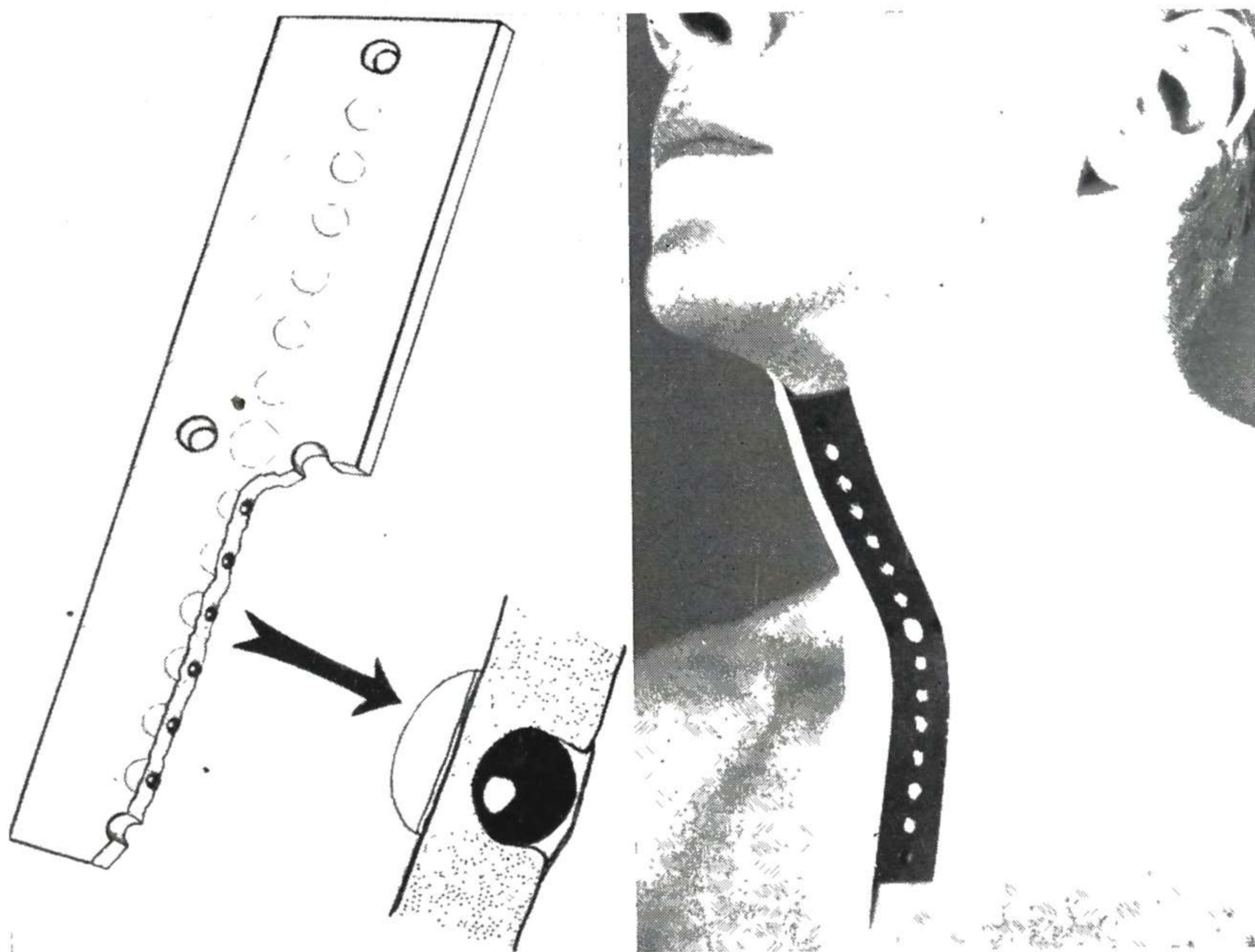


Fig. 368 (left).—Construction of indicator, partially in cross section. Note lead balls in hollows.
Fig. 369 (right).—Indicator fixed in position.
(Courtesy of Mattsson, O.: *Acta radiol.* 35:313-318, April, 1951.)

were bored in the middle of the strap and 1 cm. apart (Fig. 368). The holes were not bored completely through the leather, but enough to contain the shot which was held in place by rubber glue. The center was marked by a slightly larger ball. To make interpreting of films easier, and distinguishing of dorsal from ventral simpler, an indicator was made with a lead cube and another with a lead pyramid in the center.

Indicators are fixed to the skin by bands of adhesive tape (Fig. 369). To facilitate marking of the position of the balls on the skin, four holes were made in the leather, two showing the longitudinal direction of the row of balls and two the position of the center ball, cube or pyramid. The skin is marked through these holes and, after the indicator is removed, these points are used as guides to mark the ball positions on the skin with a celluloid stencil that corresponds to the indicator.

(7) *Acta radiol.* 35:313-318, April, 1951.

PHYSICS AND DOSIMETRY

Radiotherapeutic Physics.⁸—*Physical aspects of treatment of cancer by 22 Mev x-rays* are discussed by H. E. Johns, E. K. Darby and R. O. Kornelsen (Univ. of Saskatchewan). With a high energy x-ray beam the dose rises to a maximum some distance below the surface where equilibrium is established between the primary and secondary radiation, the skin dose being 21% of the maximum. Collimation of the beam is attained by a master collimator, a stainless steel nonmagnetic rectangular-shaped case welded to a steel plate; any of several lead plugs may be inserted into it. Because of pronounced forward scatter, a copper compensating filter is necessary to yield flat isodose curves. It does not appreciably change the spectral distribution of the radiation. To calibrate the betatron and for dosimetry, a Victoreen 25 r chamber is placed at the center of a 10 cm. Lucite cube located at the end of the treatment cone, the reading of which is compared to the number of counts from the integrator circuit. The integral dose is determined by evaluating the volume between successive isodose curves to any depths. For the same technics and tumor dose, the integral dose with 22 Mev radiation is a half to a third of that obtained with 400 kv. radiation. In betatron therapy, use of bolus material is generally contraindicated because the region of highest dose is brought to the skin surface. With sloping fields, the isodose surfaces tend to be parallel to the skin surface.

Dosage in irradiated soft tissue and bone is discussed by F. W. Spiers (Univ. of Leeds). Depending on the wavelength of the radiation, the soft tissue element in bone receives up to six times as much ionization as soft tissue remote from bone. The permissible dose to bone is about half of that tolerated by soft tissues for 200 kv. x-rays, and may be no more than a third for medium voltage and superficial x-rays. It is evident that use of radiant energy greater than 1 Mev is desirable if damage to the living elements in bone is to be minimized.

Survey of hospital physics activities at Institute of Radiophysics, Stockholm is presented by Sven Benner. A simple electronic dosage-rate meter being used consists of a small ionization chamber which is attached by a stiff metal tube to a handle containing an electrometer tube. The tube is connected by a cable to a box containing the requisite batteries, etc. Another development is a "flash roentgen" tube with a very large conical anode. In this apparatus a large high voltage condenser bank (maximal voltage 1 Mev) is charged by a six stage Cockcroft-Walton type cascade generator.

Some developments of physical aspects of teleradium therapy are reported by C. W. Wilson (Westminster Hosp., London). The type of unit which incorporates pneumatic introduction and removal of radium from the treatment head is used, with uranium for shielding and collimation. By means of an extension piece of uranium, the radium-skin distances can be varied. A 4 Gm. and a 2 Gm. unit are used, with treatment distances of

(8) Brit. J. Radiol. 24:355-391, July, 1951.

8 and 3.3 cm. respectively. The hospital physicist decides the number, position and direction of beams necessary and the radiologist attempts to realize this arrangement in practice. Plaster cases of the patient are used; they serve as the jigs, having wax seatings to locate and direct the beams.

Dosage control in interstitial gamma ray therapy is discussed by W. J. Meredy (Manchester). Three methods can be used: direct ionization measurements on the patient; ionization measurements or calculations on reconstructions of the implant, or calculations on x-rays of the implant. The best method is measurement by means of a needle-like probe containing tiny condenser chambers which is inserted into the tissue being irradiated. However, the device must be still smaller to be more generally practical. Here, x-rays taken at right angles, with additional views occasionally allow the irradiated volume to be calculated, and by the aid of Paterson-Parker dosage tables the dosage rate can be calculated.

Some aspects of problem of dosage estimation in x-ray treatment are discussed by L. F. Lamerton (Royal Cancer Hosp., London). If the variation of central axis depth dose with radius of field is known, it is easy to work out what increments of radius of field are necessary to give equal increments of dose of scattered radiation at a point at a given depth on the central axis. Diagrams of these relations for different depths can be constructed and are easily used in routine determinations of therapy.

Instrument for dosage estimation with fields of any size and shape is described by B. M. Wheatley (Royal Cancer Hosp., London). It optically integrates the relations of scattered radiation on points of the central axis of a field with the field diameter so that the dose may be determined at any point in a field of any shape. The instrument is a further step in accurately and rapidly obtaining depth dose data. The margin of error is less than 5%.

Comparison of Dose Distributions in Patients Treated with X-ray Beams of Widely Different Energies. Hugh Garrison, John Anderson, John S. Laughlin and Roger A. Harvey⁹ (Univ. of Illinois) compared the dose distributions for five patients treated with the betatron with

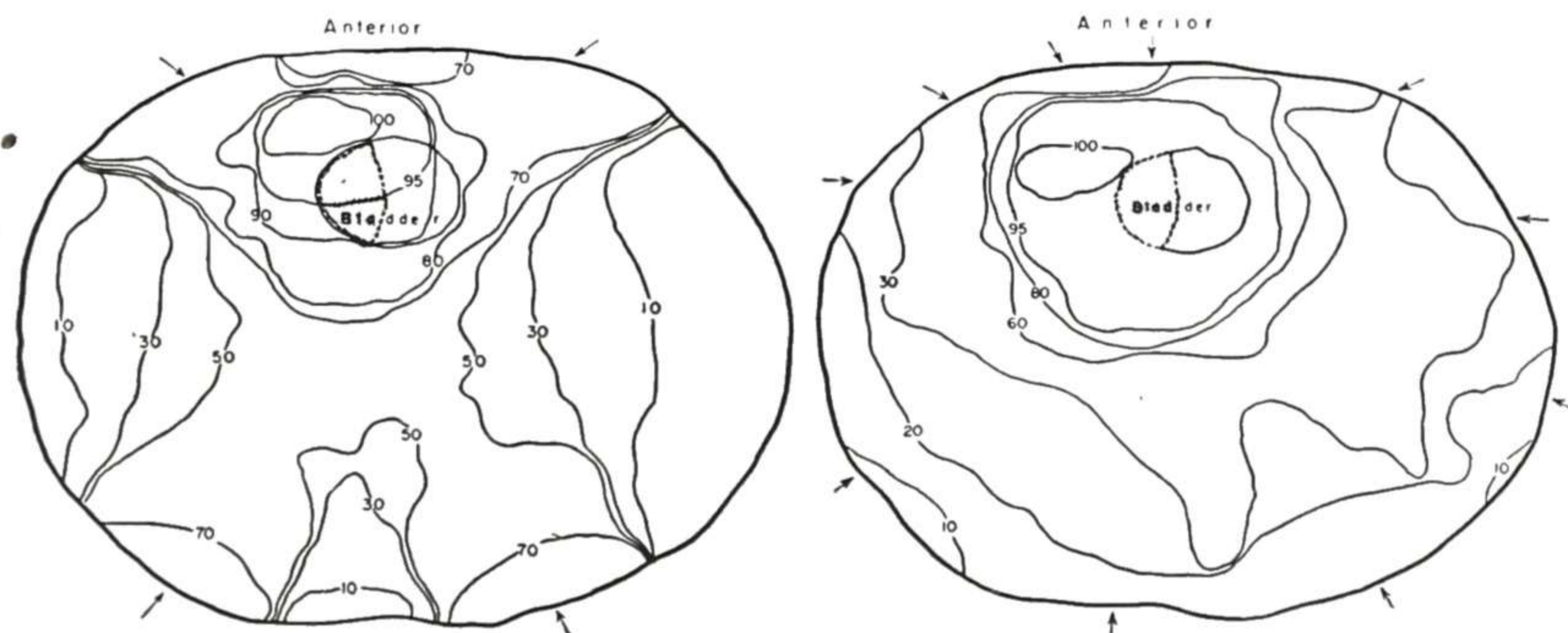


Fig. 370 (left).—Dose distribution in treatment of bladder tumor with 400 kv. Tumor zone is not ideally covered and normal tissues receive large dose. (Perineal port was also used.)
 Fig. 371 (right).—Dose distribution in treatment of bladder tumor with 23 Mev betatron x-rays. Tumor area is uniformly covered and normal tissues show steep gradient.
 (Courtesy of Garrison, H., *et al.*: *Radiology* 58:361-368, March, 1952.)

those which might have resulted with use of a 400 kv. machine. Isodose charts for a pituitary tumor, placed side by side, showed a sharp decline in gradient with the betatron; the maximal skin dose was about 20% with the betatron and 80% with the lower voltage apparatus. Isodose charts for a bladder tumor (Figs. 370 and 371) showed the tumor in the 95% zone with the betatron, with a sharp decline outside the tumor area and only a small portion of the skin receiving 60% of the maximal dose. Integral dose was calculated along with the tumor and irradiated healthy tissue doses. The integral dose to the tumor was higher with the betatron than with the 400 kv. machine and the dose received by the healthy tissue was less. The 23 Mev betatron gives a more uniform tumor dose in most neoplasms, a lower integral dose per tumor dose and a lower average dose in healthy tissue unavoidably irradiated than does the 400 kv. machine.

Comparative Study of X-ray Transmission in Thorax and Abdomen in Living Subjects. Joseph R. Nahon and Carrol P. Naidorf¹ (V. A. Hosp., Brooklyn) studied 100 patients.

METHOD.—An 8 × 10 cm. port with long axis vertical was marked on the skin of the anterior chest on the right. The diaphragm was marked under fluoroscopy so that the port would clear it and the liver. The inner boundary of

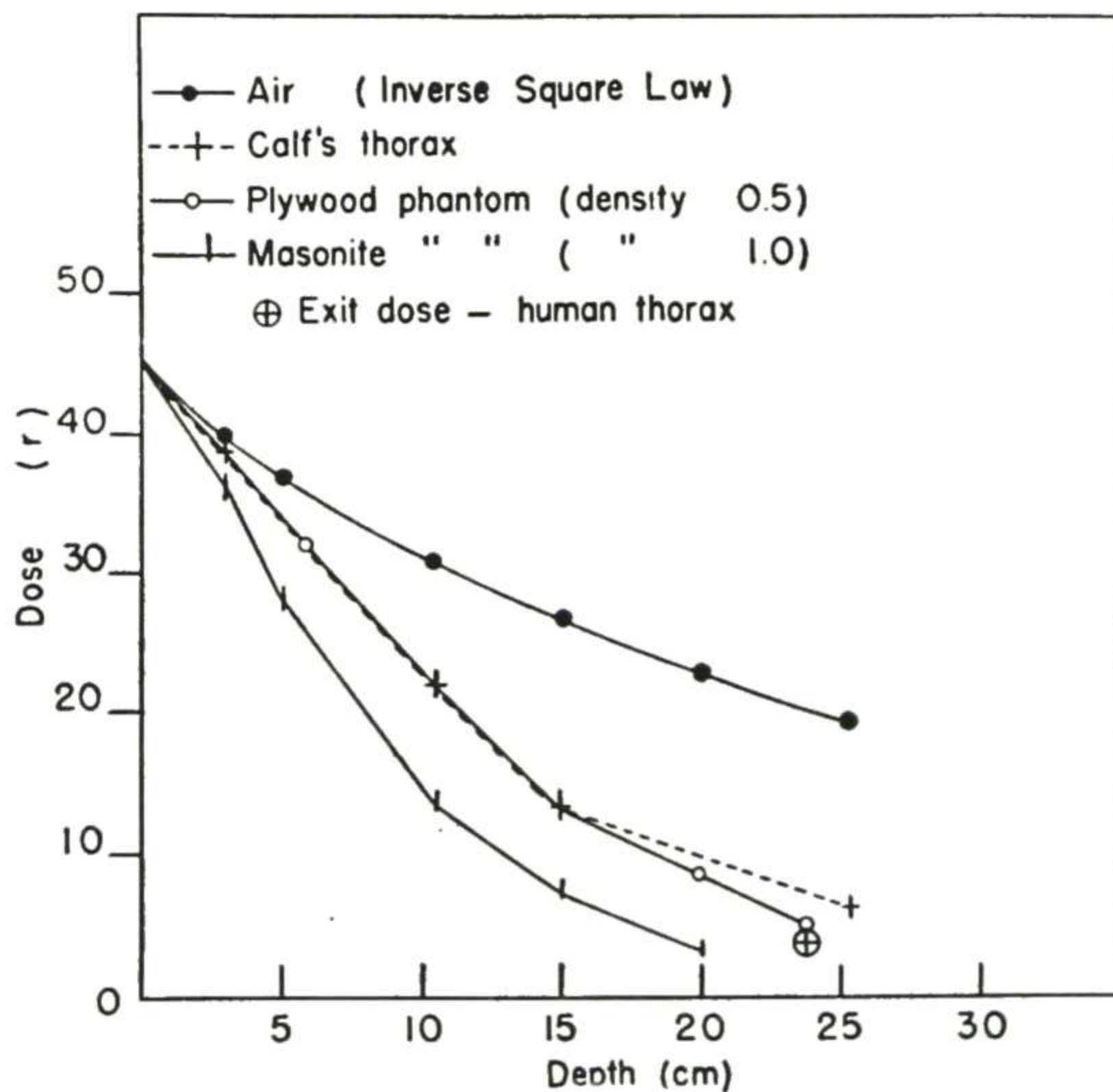


Fig. 372.—Comparison of depth dose curves in air, calf's thorax, and plywood and masonite phantoms. (Courtesy of Nahon, J. R., and Naidorf, C. P.: *Radiology* 58:241-245, February, 1952.)

the port just cleared the mediastinum. The anteroposterior diameter was measured through the center of the port. A Victoreen thimble chamber was placed under the part so that the tip lay in the central axis of the beam. A two minute exposure was given to the field and the exit dose recorded. The abdomen was studied similarly, the port lying on the left side and just clearing the spine. Factors were: 250 kv., 15 ma., 50 cm. target-skin distance, 1 mm. Cu plus 1 mm. Al filtration, 1.5 mm. Cu half-value layer, 40.6 r/minute calibration.

The two minute skin doses to the chest gave exit doses of 1.9-26 r.

(1) *Radiology* 58:241-245, February, 1952.

Average exit doses through the thorax were $2\frac{1}{2}$ -3 times greater than those through an abdomen of similar thickness. There was wide variation in exit dose for the same thickness of similar parts in different persons, up to 100% in the abdomen and up to 250% in the thorax.

When relative depth dose curves were compared in air, calf's thorax, plywood phantom (density 0.5) and masonite phantom (density 1.0), considerable variance was noted (Fig. 372). Results tended to confirm the experimental data on the thorax and abdomen. It appears that each patient should be evaluated for probable tissue capacity for transmission of x-rays and calculations based on standard tables should be modified accordingly.

Design of Wedge Filters for X-ray Therapy. A. C. Groom² (St. Mary's Hosp.) gives general formulas for construction of wedge filters to be used in the range of 180-250 kv. The most useful filters are those producing 45 degree inclined isodose curves for use with beams at right angles. Copper plateau wedges, whose width of sloped portion is 0.6 of the total wedge width, are used. Average isodose slope at any point on the central axis depends on field width and height of the plateau. The condition for 45 degree slope at the point d_{50} , using any field size, is that

$$\text{plateau height (in. of Cu)} = \frac{\text{field width (in cm.)}}{60}$$

provided the wedge filters are placed at the upper diaphragm of the applicator, the same wedge can be used for different fields. Most dose distribution requirements can be met with 45 degree slope fields combined at various angles and in conjunction with normal fields when necessary.

[Except in some of the supervoltage installations, wedge filters have been more popular in England, but perhaps they deserve more use than at present.—Eds.]

Depth Dose Investigation for Perforated Grid Therapy at 200 Kv. Lillian E. Jacobson and Ansel Lipman³ (Montefiore Hosp., New York City) investigated the dose received through a grid at the surface, at the tumor and at other depths.

METHOD.—Measurements were made in a masonite Presdwood phantom 30 cm. thick, density 1.05 Gm./cc. Each board surface was 30×30 cm.² and 0.373 cm. thick. In all measurements at least 15 cm. of material was under the ion chamber. The Victoreen 25 r and 250 r chambers were used. Groups of six boards were drilled so that the chamber fitted them at the center, one group for the 250 r and one for the 25 r chamber. Each group was divided into two parts or sets. The chamber rested in one set and the other set covered the chamber. Surface measurements were made with the chamber half "submerged" in the same manner as surface measurements are made for water. Factors were: 200 kv., half-value layer 0.94 Cu. Boards which gave a depth of 5 cm. and 10 cm. were pegged together. A piece of millimeter graph paper was pasted on the upper board in each pegged group and on each set of lower boards. Lines were drawn parallel and perpendicular to the long axis of the ionization chamber, crossing each other at a point which corresponded to the center of the air volume of the chamber. The movable table which held the phantom had two lucite plates so arranged as to form two sides of a box. The boards were pushed into the open sides of the box so that they fitted against the Lucite plates. When the boards were properly aligned the center line on the side of the phantom coincided

(2) Brit. J. Radiol. 24:676-681, December, 1951.

(3) Am. J. Roentgenol. 67:458-469, March, 1952.

with the center line of the Lucite plate. These precautions are needed to insure that an opening in the grid is aligned with the air volume of the chamber. A lead rubber grid with 1 cm. holes and a ratio of 40% open to 60% closed was used. The lead rubber was 4 mm. thick and transmitted less than 1% of the incident beam.

Comparison of number of roentgens delivered with and without the

COMPARISON OF NUMBER OF R DELIVERED WITH AND WITHOUT GRID
WHEN SKIN TOLERANCE DOSE IS DELIVERED IN EACH CASE*

DEPTH, CM.	WITH GRID			WITHOUT GRID
	Open	Closed	Av.	
Surface	27,000	4,450	13,400	5,000
5	13,200	5,300	8,400	3,250
10	5,580	3,000	4,100	1,650
15	2,450	1,440	1,850	850

*10 × 10 cm. field, 50 cm. target-skin distance, 1 mm. Cu half-value layer, dosage protracted over one month. Tolerance dose with grid, 24,000 r in air; without grid, 3,750 r in air.

grid when skin tolerance dose is given in each case was made (table). Field size was 10 × 10 cm. The surface of the open area received 27,000 r and the closed area 4,450 r. Without grid, 5,000 r was tolerance. At 5 cm. the open area received 13,200 r and the closed area 5,300 r. Without grid, 3,250 r was tolerance. At 15 cm. the dose under the open area was 2,450 r and under the closed area 1,440 r. Without grid, 850 r was tolerance. The tissue receives a greater dose even under the covered part than in ordinary therapy. Yet the "healing" effect on the skin is greater when the grid is used than when it is not.

Wavelength of X-radiation at Depth in Water Irradiated by Beams of X-rays. J. R. Greening and C. W. Wilson⁴ (Westminster Hosp., London) investigated the factors most likely to affect the wavelength of radiation in a scattering medium. X-ray quality was measured as follows.

METHOD.—An effective wavelength was used as the indication of quality. This was derived from the measured ratio of the ionization currents in two thimble chambers exposed to the radiation. The chambers were molded from an "air-equivalent" mixture of Bakelite, graphite and vanadium pentoxide. One chamber was lined; its central electrode was covered with thin aluminum foil (8 mg./sq. cm.) which was attached to the chamber by liquid glue containing powdered graphite (to make it conducting). Only small voltages were applied to minimize any leakage through the materials during irradiation. The chambers were corked and waxed into a thin celluloid tube to fix the chambers relative to each other and to keep them dry on immersion in water. The currents were compared with an apparatus similar to Kemp's except that the electrometer valve was replaced by a Lindemann electrometer. At balance the ratio Q_1/Q_2 of the charges collected by the two ionization chambers is given by

$$\frac{Q_1}{Q_2} = \frac{C' + C_1}{C'' + C_2} \times \frac{C_2}{C_1}$$

where C' and C'' are the cable capacities and C_1 and C_2 the capacities of the condensers in the potential divider. In practice, $C' = C''$. Suppose C_1 is a fixed condenser and $C'/C_1 = R$. Then

$$\frac{Q_1}{Q_2} = \frac{R + 1}{R + C_2/C_1} \times \frac{C_2}{C_1}$$

R was determined by a number of charge-sharing processes. The chamber pair was exposed to 24 different x-ray beams of known half-value layer.

(4) Brit. J. Radiol. 24:605-612, November, 1951.

In the wavelength range investigated, ionization ratio was a single-valued function of the wavelength. Measurements in air showed no significant wavelength change as distance from the central axis of the beam increased. Measurements were made with chambers half immersed in a $30 \times 30 \times 30$ cm. Perspex tank, the surface of the water being 50 cm. from the x-ray tube target. Using a 17.5×17.5 cm. field, wavelength of total radiation on the surface decreased by 2 or 3 X. units as the edge of the beam was approached and then increased suddenly as the edge was crossed and the area of scattered radiation only was entered. Measurements were made of the effective wavelength of the total radiation down to 15 cm. in water and of the primary radiation by putting water in a 2×2 cm. Perspex tube and placing the chambers about 20 cm. below the tube. The decrease in effective wavelength of primary radiation observed was due, of course, to filtration of the beam by water.

Use of Small Protection Films for Estimation of Doses Received on Fingers and Hands during Radium Manipulations is described by T. M. Robb and R. E. Ellis⁵ (Lambeth Hosp., London).

METHOD.—Standard x-ray film was cut 1×1 cm. and wrapped in a sheet of black paper. Waterproof strapping was placed over this so the whole was com-

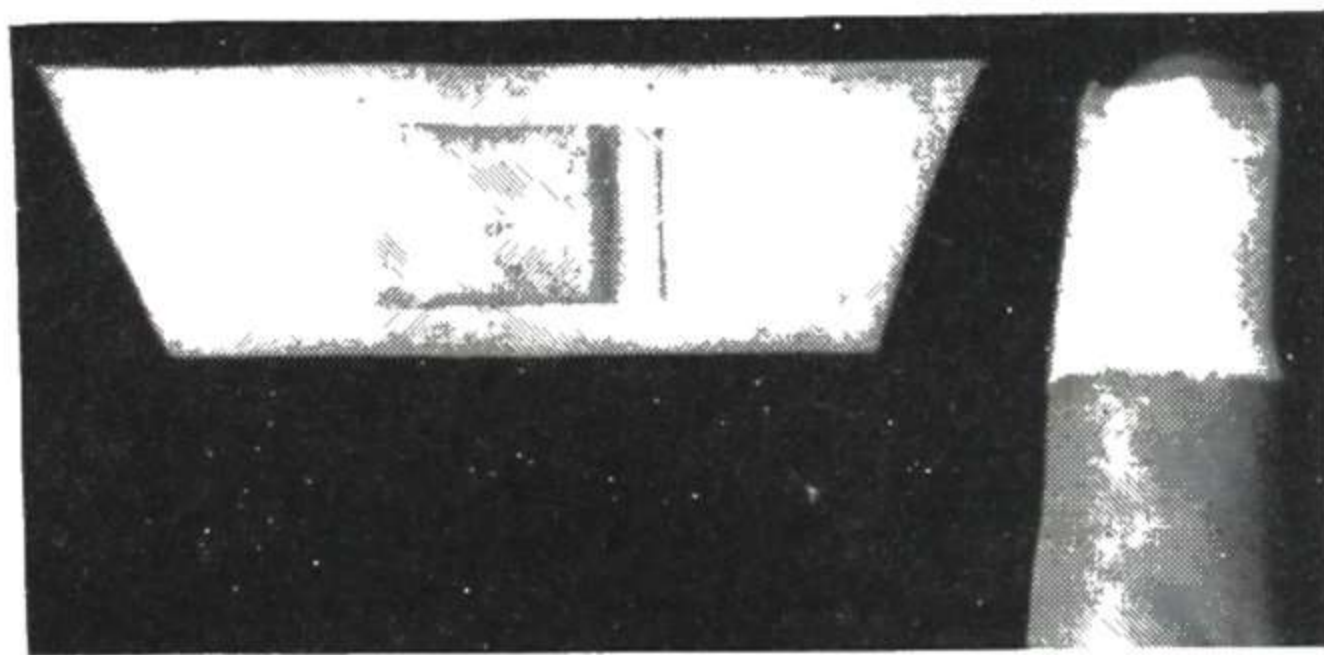


Fig. 373.—Film pack, ready for wear, placed on pulp side of finger-tip. (Courtesy of Robb, T. M., and Ellis, R. E.: *Brit. J. Radiol.* 25:100-102, February, 1952.)

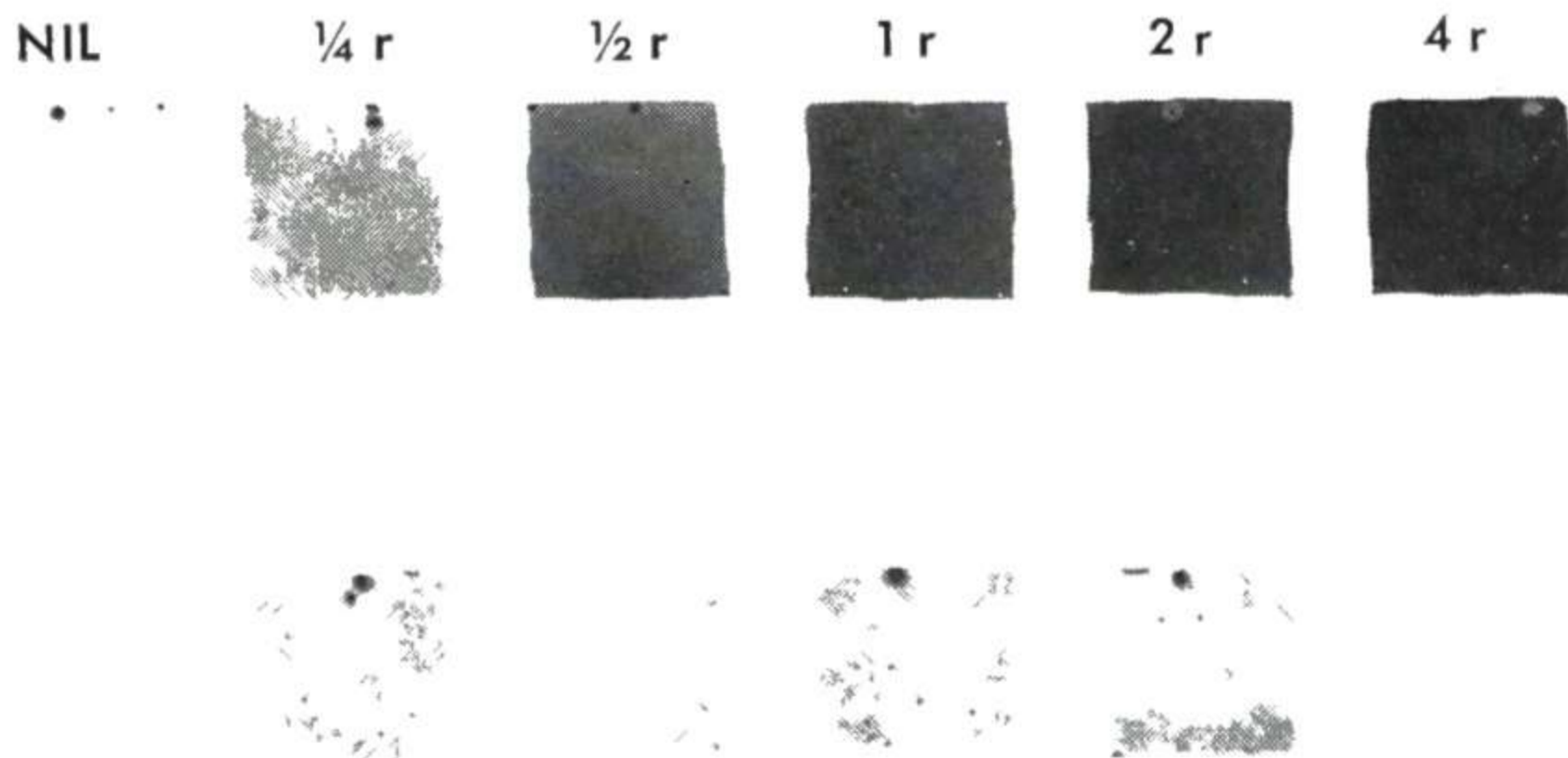


Fig. 374.—Set of standardized films and (below) a typical set of four films obtained in a gynecologic operation. (Courtesy of Robb, T. M., and Ellis, R. E.: *Brit. J. Radiol.* 25:100-102, February, 1952).

pletely waterproof. The pack was then centered on a strip of similar waterproof tape, making the pack ready to wear on finger-tips (Fig. 373), hands or wrists. Packs were numbered with India ink or ball-point pen. To estimate radiation received by the films, they were compared with similarly packed films exposed to known doses of gamma radiation. Both worn and standardized films were developed together in ID 19 at 65 F. for five minutes. The films were clipped to dental hangers and agitated. To assess the worn films, six similar packs with

(5) *Brit. J. Radiol.* 25:100-102, February, 1952.

identical number of layers of tape were given measured doses of radiation from a plaque containing 40 mg. radium spread over 2 cm.² Films were placed 5 cm. from and parallel to the plane of the plaque. Worn films were assessed by comparing density with the standards either visually (Fig. 374) or by a Hilger photoelectric microphotometer.

For comparing results, active exposure in milligram-minutes is defined as one-half the product of the total radium load (in mg.) multiplied by the over-all time in minutes. Measurements were taken during insertion of permanently loaded Perspex ovoids of radium load 20 and 40 mg. and uterine tubes of 40 and 42 mg.; using the Manchester technic. Results are recorded in the table and give the following average doses in

GYNECOLOGIC CASES—AVERAGE "ACTIVE" EXPOSURE/OPERATION, 261 MG.-MIN.*

	DOSE RATE, R \times 10 ⁻⁴ /MG.-MIN. "ACTIVE" EXPOS.	AV. DOSE, R/OPERATION
Right hand		
Thumb	5.7	0.15
Index finger	3.6	0.09
2d finger	5.1	0.13
Left hand		
Thumb	7.4	0.19
Index finger	3.6	0.16
2nd finger	9.3	0.24

*Mean finger dose/operation (133 observations), 0.164.

roentgens/operation: right hand—thumb 0.15 r; index 0.09 r, second finger 0.13 r; left hand—thumb 0.19 r; index 0.16 r and second finger 0.24 r.

Physical Measurements on Various Beta Ray Applicators. Jack S. Krohmer⁶ (Western Reserve Univ.) measured dosages delivered at depths of 0-5 mm. in tissue phantom by applicators containing radon,

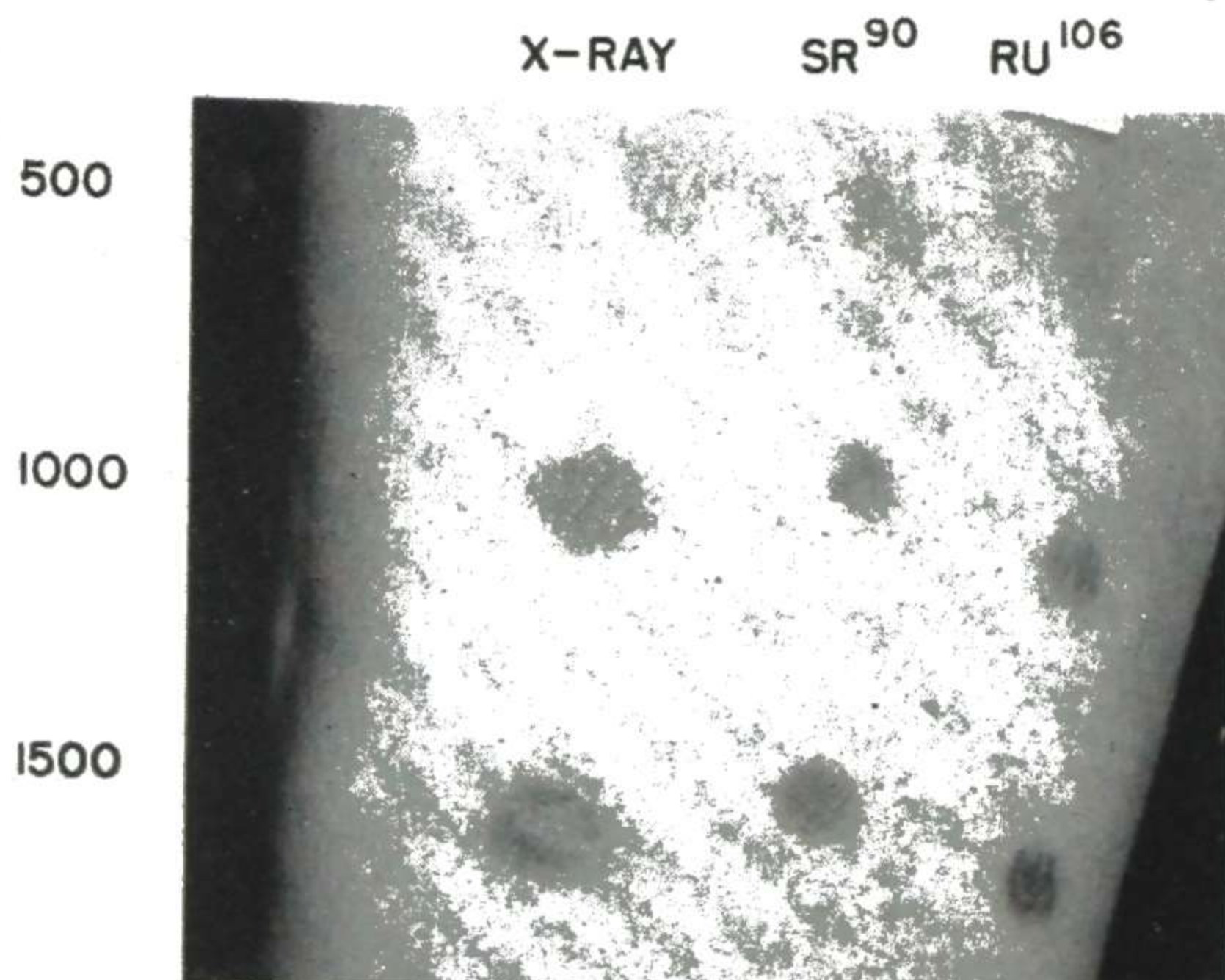


Fig. 375.—Skin erythema produced by Philips 44 kv. roentgen ray unit, Sr⁹⁰ and Ru¹⁰⁶ applicators. Dosages on left. (Courtesy of Krohmer, J. S.: Am. J. Roentgenol. 66:791-796, November, 1951.)

radium element, radium D + E, strontium and ruthenium. An extrapolation ionization chamber was used, with Lucite as the tissue phantom.

With regard to half-life, all the applicators tested were adequate. However, the value of 1.0 year for Ru¹⁰⁶ necessitates re-evaluation of

(6) Am. J. Roentgenol. 66:791-796, November, 1951.

output of roentgens equivalent physical each month or possibly more often. The Sr^{90} and Ra D + E applicators are free from significant amounts of gamma radiation, whereas the Ru^{106} and radium element applicators emit objectionable quantities which require precautionary measures.

Character of the depth dose curves for the various applicators varied considerably. In order of increasing penetration they were: Ra D + E, for which the dose after 2 mm. was less than 1% of the surface dose; radium element and Sr^{90} , which had essentially the same distribution as radon; and Ru^{106} , for which the dosage was still above 5% at 5 mm.

Results indicated that each applicator has a particular advantage which may be useful therapeutically. For most clinical uses the strontium applicator, with its long half-life and absence of gamma radiation, appears to have a slight advantage over the others.

In addition to dosage measurements, a skin erythema test was made. Applications of 500, 1,000 and 1,500 r or rep were given by three different means: superficial roentgen rays (44 kv., half-value layer 0.24 mm. Al); Sr^{90} applicator and Ru^{106} applicator. This test was run to check accuracy of the measurements and to observe the relative effects of the three means of irradiation. The reactions obtained were indistinguishable at the different dosage levels (Fig. 375).

Biologic Action of Beta Radiation from Radium (Curtis F. Burnam Applicator) is reported by Jean Moulinard⁷ (Blois). The Burnam tube contains 50 mg. radium element, filtered by 0.3 mm. monel metal. The radiations which are insufficient for the time comprise a group of isoenergetic primary beta rays and a "continuous background" of secondary rays. Depth dose studies reveal that 1 mm. tissue absorbs more

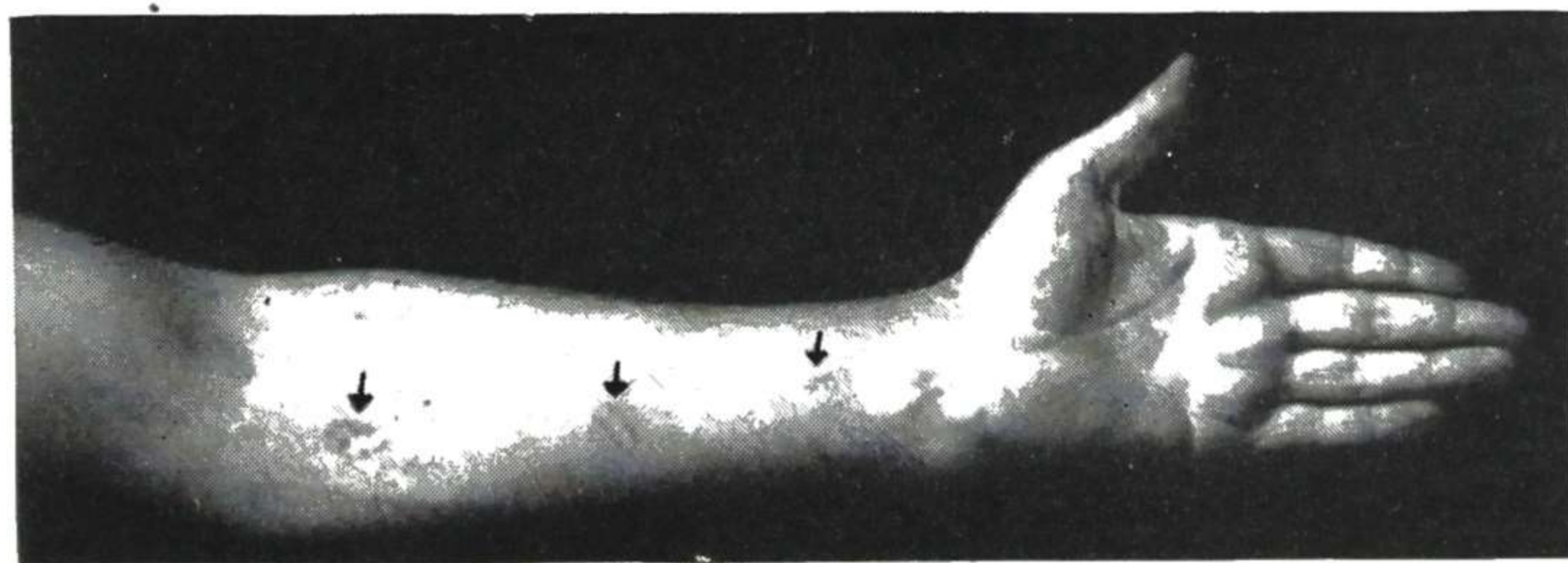


Fig. 376.—Cutaneous tests one year after application of Burnam cell in patient, 30. Arrows mark irradiated areas; left, scar following single dose of 7,400 rep; middle, scar corresponding to dose of 3,700 r; right, irradiation site for dose of 1,850 r. Note that in this patient all cutaneous lesions appear as cheloïds. This tendency is indicated by five year operative scar visible on radial aspect of forearm below elbow. In a normal patient, irradiation effects are hardly visible (Courtesy of Moulinard, J.: *J. radiol. et électrol.* 33:156-161, 1952.)

than half the rays and at 5 mm. depth only 1/20 of the surface dose remains. Beta rays may be considered in the group of feeble penetrating radiation between the rays of Chaoul and those of Bucky. Dosage is expressed more rationally in terms of the rep than in millicuries.

Experimental studies on the erythema dose in 15 subjects revealed that 1,800 r (five minutes' application) produced a second degree reaction, but a dose of 18,000 r (50 minutes' application) was followed

(7) *J. radiol. et électrol.* 33:156-161, 1952.

by an exudative radiodermatitis with satisfactory healing in three weeks. After a year there usually remains little evidence of the irradiation (Fig. 376).

The study of the action of the beta rays on the ovary of the rabbit and the adenoid tissue of man shows that besides a caustic action they have a selective action on the radiosensitive tissues.

Burnam constructed the monel applicator to irradiate the adenoid remnants, the cause of multiple middle ear affections. Actually, beta ray therapy is used for cancers of natural cavities inaccessible to the Chaoul tube. Results are good in benign and malignant skin conditions. It is the treatment of choice in certain ophthalmic conditions. The author believes that betatherapy should remain in the province of the radiotherapist.

RADIOBIOLOGY

Successful Subcutaneous Growth and Transplantation of Human Tumors in X-irradiated Laboratory Animals are reported by Helene Wallace Toolan⁸ (Sloan-Kettering Inst. for Cancer Research).

METHOD.—Young adult female rats received three doses of 200 r total body x-radiation on alternate days; similar mice, four doses of 150 r on successive days. Minced or sieved portions from 100 human neoplasms were implanted subcutaneously in the animals within eight hours after removal from the host and within one to three days after the last radiation treatment, while the animals were still in a state of lymphopenia. The cells were suspended in sterile Ringer's solution which contained glucose and penicillin. Replantation was done after eight days because tumor-stromal cell relationships were then best.

Epidermoid carcinomas grew most successfully. Thirty-three implants failed to grow initially, 34 grew for one generation (eight days) but could not be transferred to a second, and 33 were transplanted for two or more generations with evidence of active growth and vascularization. Failure of the original implant to grow was directly related to presence of infection in the implant or delay of over an hour in transfer from the human host. Figures 377-379 show the histology of the implants.

[This interesting demonstration might become clinically significant if the growth of the transplant could be correlated with the response of the patient's lesion to treatment. It is hoped that the author will offer substantiation of this work.—Eds.]

Response of Human Tissues to Radiation with Special Reference to Differentiation. A. Glücksmann⁹ (Cambridge), in studying normal tissue, found that after irradiation there is a relative increase in the extent of differentiation of cervical epithelium and a transient change in the type of differentiation (i.e., squamous metaplasia) of ducts and acini of mucin-producing glands of the oral cavity. In oral cancer this irradiation-induced metaplasia of the salivary glands causes the dryness of which the patient complains during and after treatment and which lasts about nine months.

Tumors differ from normal tissues from which they are derived by

(8) *Proc. Soc. Exper. Biol. & Med.* 77:572-578, July, 1951.

(9) *Brit. J. Radiol.* 25:38-43, January, 1952.

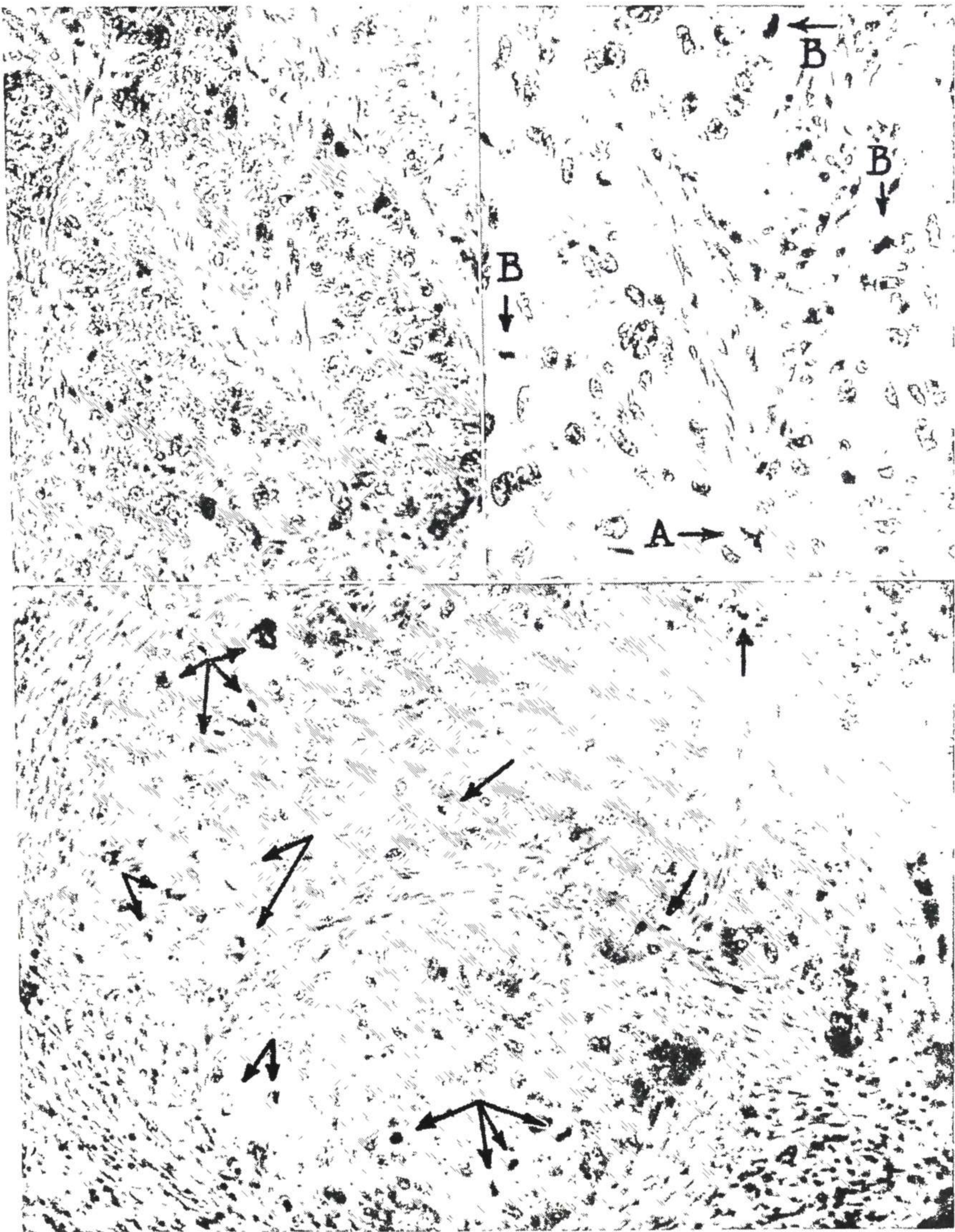


Fig. 377 (top left).—Epidermoid carcinoma of larynx; reduced from $\times 220$. Original tumor.

Fig. 378 (top right).—Tumor after three generations (25 days) in irradiated mice; reduced from $\times 350$. Arrow *A*, tripolar mitosis; arrows *B*, other mitotic figures. Original implant a sieved suspension of cells.

Fig. 379 (bottom).—Tumor after three generations in irradiated rats; reduced from $\times 200$. Arrows indicate the many mitotic figures. Original implant a sieved suspension of cells.

(Courtesy of Toolan, H. W.: Proc. Soc. Exper. Biol. & Med. 77:572-578, July, 1951.)

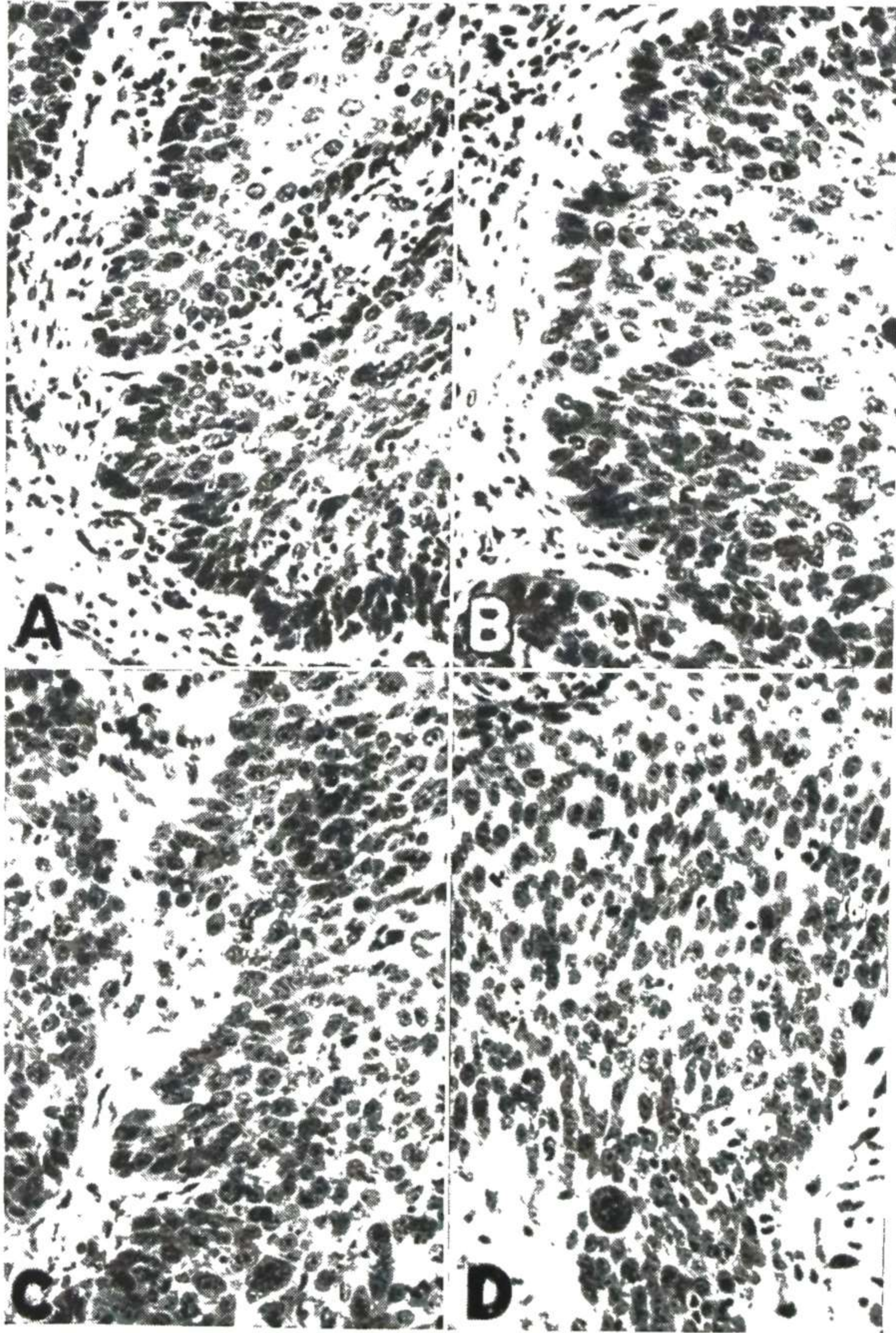


Fig. 380.—Biopsy and autopsy specimens (enlarged from $\times 200$) of carcinoma of uterine cervix, clinical stage 2, before, during and after full course of intracavitary radium treatment of Stockholm type supplemented with course of x-ray therapy to pelvis. *A* shows section taken before treatment. *B*, taken after two thirds of radiation dose had been given (12 days), and *C*, taken after total dose (35 days), illustrate unchanged persistence of viable tumor foci. Tumor appeared to regress but recurred after five months and patient died of local recurrence (*D*) seven months after treatment. (Courtesy of Glücksmann, A.: Brit. J. Radiol. 25:38-43, January, 1952.)

their lower degree and extent of differentiation. In suitable tumors striking relative and absolute increases in extent and degree of differentiation follow irradiation. Many tumors are radioincurable and show no differentiation in response to irradiation. A typical example of the histologic picture of a locally radioincurable cancer is shown in Figure 380. For such cancers an unfavorable local histologic prognosis is given and has been found correct in 95% of cases.

By using young tumor foci and comparing the local histologic prognosis with the local clinical findings subsequent to the first planned treatment, Glücksmann has obtained remarkably accurate assessments of radiation effects. Correlation of such data on 638 epitheliomas of the skin, oral cavity and uterine cervix, followed for 1-12 years, is shown in the table. The over-all agreement between histologic prognosis and local five year result of the first planned treatment is 83% for skin

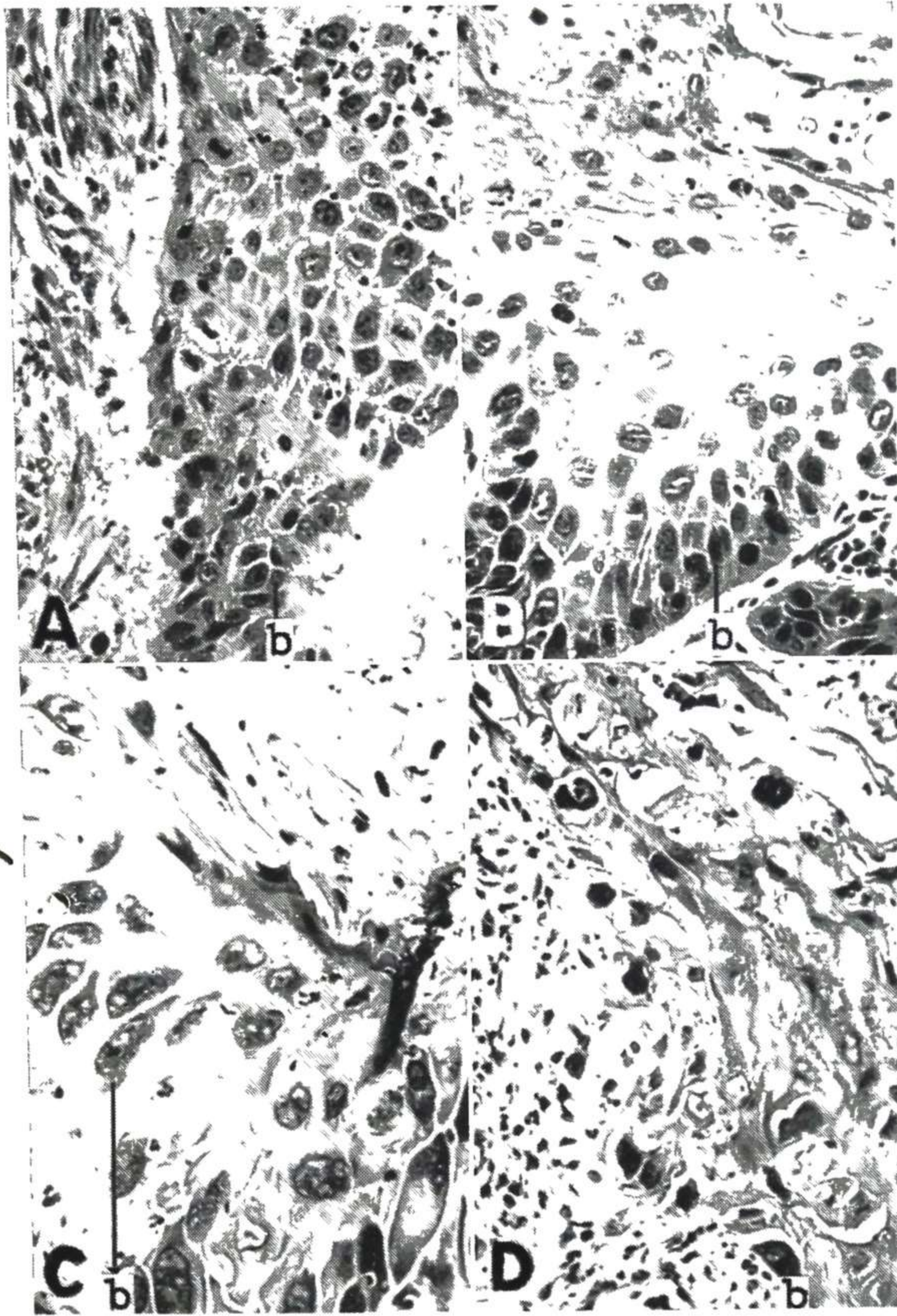


Fig. 381.—Sections ($\times 200$) of biopsy specimens taken from carcinoma of uterine cervix, clinical stage 2, before and during intracavitary radium treatment of Stockholm type. Note rapid changes induced by irradiation: disappearance of mitosis, increase in cell size and in extent of parakeratosis and also better stratification of foci. Basal cells (*b*) persist but undergo parakeratosis. *A* was taken before treatment; *B*, 48 hours, and *C*, 5 days after first radium insertion, and *D*, on 12th day of treatment, after two radium applications. Tumor regressed slowly and patient has survived symptom free for 12 years. (Courtesy of Glücksmann, A.: Brit. J. Radiol. 25:38-43, January, 1952.)

cancers, 94% for lip and oral cavity cancers and 97% for cancers of the uterine cervix.

Serial biopsies from epitheliomas at various stages during treatment

CORRELATION OF LOCAL HISTOLOGIC PROGNOSIS WITH LOCAL CLINICAL RESULT OF RADIOTHERAPY 1-12 YEARS AFTER FIRST PLANNED FULL TREATMENT

CLINICAL RESULT	LOCAL HISTOLOGIC PROGNOSIS		Total
	Favorable	Unfavorable	
Symptom free locally	112	62	174
Cancer present locally	8	456	464
Total	120	518	638
Prognosis correct, %	93	88	89

reveal that most of the resting (basal) cells are not killed outright by irradiation but undergo keratinization by postmitotic differentiation and thus sterilize themselves by differentiation (Fig. 381).

Glücksman stresses that only postmitotic differentiation such as keratinization can be a factor in successful irradiation of tumors, that increases in postmitotic differentiation occur in radiocurable but not in radioincurable epitheliomas and that cure of rodent ulcers, uterine adenocarcinomas and a variety of breast cancers by irradiation cannot be attributed to differentiation since these tissues are not capable of postmitotic differentiation.

Radiation Genetics: I. Genetic Aspects of Radiation Risks. Extensive work on radiation-induced mutations in animals has indicated that irradiation results merely in speeding-up of the spontaneous mutation rate, not in production of anything qualitatively different.

Alma Howard¹ (London) agrees in principle with Muller that any increase in the mutation rate is probably undesirable. Any addition to the natural background of radiation will presumably cause such an increase, and therefore one must be at particular pains to protect the gonads of those exposed to radiation for whatever reason. As long as the addition is very small in terms of the average of the whole population, the effect even after many exposed generations may be negligible. It is a fallacy to suppose that if the children of irradiated persons are normal no genetic damage has been done. Only the relatively rare dominants will be observed in the first generation. They will provide excellent material for the study of the induced dominant mutation rate but no information regarding total genetic damage.

More information on every question relevant to human genetics, population behavior and reproduction biology is needed to formulate a policy estimate based on more than pure guesswork.

Mutation cannot yet be controlled or directed in any way. The damage may not appear for a long time, but this does not reduce the responsibility to prevent it. To be on the safe side, as far as possible any increase in mutation rate must be avoided.

Radiation Genetics: II. Indirect Effects of X-rays on Chromosomes. According to the generally accepted target theory, mutations induced by irradiation are the direct effect of ionizations in the gene molecules. The most commonly established criterion supporting this theory is the linear dependence of mutation frequency on dosage, measured in roentgens.

G. Bonnier² (Univ. of Stockholm), in a study of *Drosophila*, found an excellent fit to the straight line. However, when extrapolating the straight line to the zero dose, the frequency was higher than that observed to occur spontaneously. The first component follows the prerequisites of the target theory (direct irradiation effect). The second component would then presumably be due to some force acting indirectly. Indirect effects of x-rays occur in *Drosophila* in the production of gynandromorphs (part female and part male). By different kinds of treatments, the rate of gynandromorphs can be increased.

The question of obtaining gene mutations from x-rays in the same indirect way via the cytoplasm of the egg was tested, and work on the

(1) Brit. J. Radiol. 25:177-179, April, 1952.

(2) Ibid., pp. 180-182.

possible induction of indirect x-ray mutations is still in progress. Recent studies indicate that radiation sensitivity may be altered by irradiating through different gases. Oxygen increases and nitrogen decreases sensitivity. These results, which show that the target theory must be modified somewhat, seem to provide a tool for increasing the indirect mutation rate.

Radiation Sickness: Clinical Investigation. Frank Ellis and Basil A. Stoll³ (London) present a statistical evaluation of treatment results.

METHOD.—To avoid selection of cases, a drug was picked as the "sickness drug" for a week. The patient was questioned one week after symptom onset. If symptoms were relieved, the same drug was continued until end of treatment; if they were unrelieved, the "sickness drug" for the second week was given, and so on. Drugs used were 50 mg. capsule benadryl[®] three times a day or 1/2 hour before treatment; 5 mg. tablet benzedrine[®] twice daily; 10 mg. tablet pyridoxine hydrochloride four times daily; 20 minims HCl diluted in a 7% water solution three times a day before meals; 10 mg. tablet pyridoxine four times a day, and 20 minims HCl three times a day with 5 gr. inert tablets (lactose) three times a day.

Whatever the drug used, vomiting is the easiest symptom to relieve and nausea only a little more difficult. Most difficult to relieve are anorexia and listlessness. The less active drugs are benzedrine,[®] benadryl[®] and inert tablets. The more active ones are pyridoxine, HCl and a combination of the two. HCl and pyridoxine together excel either one separately for anorexia and listlessness. Inert tablets gave 19-29% relief compared with 46-60% for the best drug combination. The less active drugs are useful for nausea and vomiting. No significant difference in effect of any individual drug is apparent when radiation sickness originates from treatment above or below the diaphragm. Pyridoxine combined with HCl was most efficacious in doses used in this investigation.

Relationship between Adrenal Cortex and Radiation Sickness: Review of Literature and Presentation of New Data, based on the study of 36 patients, is given by Edward C. Porter⁴ (Massachusetts Gen'l Hosp.).

Level of circulating eosinophils was used as a reliable and practical index for observing adrenal cortical response. Counts were performed by the same person daily, or before, during and after therapy. Hunter's technic for white cell count was used. In five patients 17-ketosteroid urinary levels were obtained by Albright's method. Depression of eosinophil count by at least 50% was the criterion of abnormality. Factors of therapy used varied by patients.

All patients with significantly depressed eosinophil count during treatment had radiation sickness—either severe nausea or nausea and vomiting. In 9 patients sickness preceded decrease in count by several hours and in 1 by 10 days; no significant fall was evident in 26. Four of these began therapy with abnormally low counts. In three, sickness began after the first treatment; in two it was severe. Of 22 patients with no fall in count during therapy, none had vomiting; 4 were nauseated.

(3) *J. Fac. Radiologists* 3:207-222, January, 1952.

(4) *Radiology* 58:246-258, February, 1952.

The author hypothesizes that ionizing radiation, by virtue of a still somewhat obscure action on cells, fragments the protein molecules, some of them perhaps histamine-like in make-up, which in sufficient quantities may produce a state of chemical shock called "radiation sickness." The adrenal cortex is believed the decisive factor in eradicating this shock state by counteracting the existing physiologic imbalance. This suggests possible use of cortisone as a protective agent against radiation sickness.

Estimation of Biologic Dosage Factors in Clinical Radiotherapy. L. Cohen⁵ (Univ. of Witwatersrand) previously proposed a biologic dosage unit, the roentgen equivalent clinical (rec), based on an empiric formula $D = EaT^nL^q$, relating the dose in roentgens (D) to the biologic dose in rec (E), account being taken of the relative biologic efficiency of

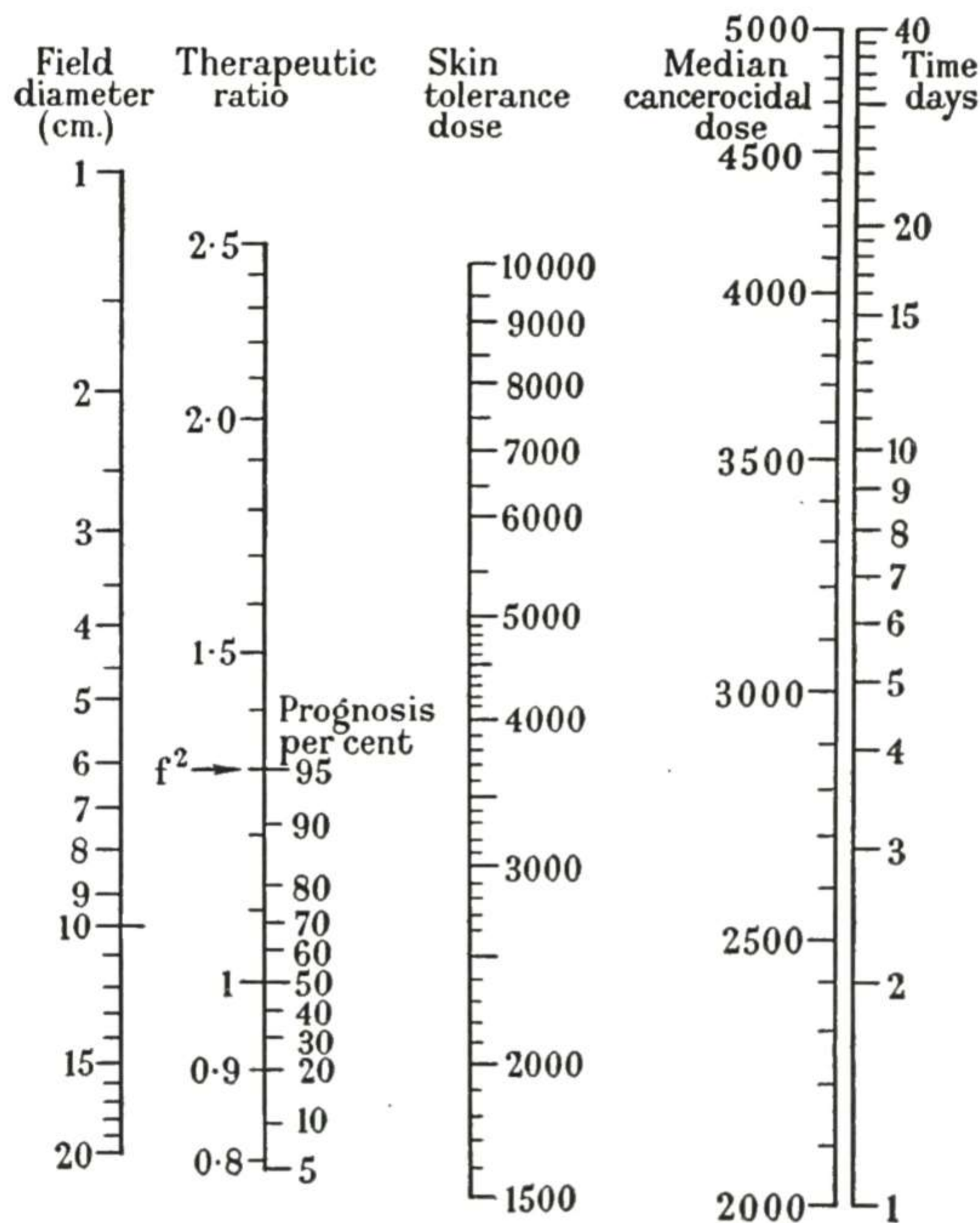


Fig. 382.—Nomogram relating skin tolerance and epidermoid cancer lethal doses with time and volume factors. Single line across diagram gives all relevant factors simultaneously. (Courtesy of Cohen, L.: Brit. J. Cancer 5:180-194, June, 1951.)

radiation of various qualities (a), over-all time in days (T) and field size in decimeters (L). The unit was then defined as the biologic effect of 1 r of gamma rays delivered through a field 1 dm. in diameter in one day. This formula assumes that the exponents n and q are independent of the quality of radiation and makes no allowance for variation among patients. An attempt was made to determine the validity of this method of estimating the biologic dosage factors in clinical radiotherapy and to determine the optimal dose for epidermoid carcinoma.

A statistical analysis was made of 150 patients. They were treated

(5) Brit. J. Cancer 5:180-194, June, 1951.

with six radiation qualities, radium gamma rays with 0.5 mm. Pt filtration and x-rays generated at 220-60 kv. with half-value layers ranging from 1.5 mm. to 0.16 mm. Cu. This revealed dependence of the skin reaction on time, field size and biologic efficacy of the radiation used, confirming the validity of the "isoeffect" formula, $D = Ea(T/L)^n$. By means of the method of least squares, estimates of a and n for the six radiation qualities were obtained and shown to agree well with data established previously.

A similar analysis was made of 100 patients with epidermoid carcinoma to determine the dependence of curability on biologic dose. The median lethal dose was found to be 3,000 rec, with a risk of necrosis of under 2%. With optimal conditions of time and area, 95% of tumors could be cured with a dose exceeding the median lethal dose by 30%. Prognosis was also proved to be a mathematical function of the therapeutic ratio. Figure 382 shows a nomogram which relates these various factors for 200 kv. therapy of epidermoid carcinoma.

[This is a report of further clinical observations along the lines proposed in an article in the 1950 YEAR BOOK (p. 344). The author points out that the scheme is based on assumptions and simplifications, the validity of which is by no means obvious. Nevertheless, only a few patients had reactions which differed remarkably from expectation.—Eds.]

Roentgen Changes after Irradiation with 31 Mev Betatron Rays and 180 Kv. Roentgen Rays. Larvae of *Drosophila melanogaster* were used by Hedi Fritz-Niggli⁶ (Univ. of Zurich) to compare the biologic effects of 180 kv. roentgen rays and 31 Mev rays from a betatron. Doses varied from 2,000 to 2,500 r for the roentgen and from 2,500 to 4,000 r for the betatron rays. Groups of 50 larvae (5 hours old) were used for the varying doses. The effects included: spreading of the wings, disturbed bristle counts and abnormal abdomens. For a given r dose, betatron rays appeared much less effective in causing biologic changes than roentgen rays. Using spread wings as a criterion, almost twice the r dose of betatron rays was needed to cause the same percentage change as was produced by roentgen rays. The difference in effect is not easily explained. Perhaps it is related to the short duration of exposure needed with the betatron. The changes in enzyme activity which are believed to cause the abnormalities might not be as readily accomplished with too brief exposures.

Effect of Single Massive Doses of Roentgen Radiation on the Liver: An Experimental Study of large doses of radiation used to produce definite morphologic changes in 96 rabbits is reported by Irving M. Ariel⁷ (New York City). Single massive doses of roentgen rays (300-100,000 r at 90 kv.) affect all of the component parts of the liver. Edema, hyperemia and leukocytic infiltration probably are manifestations of damage to the vascular system. Why edema appears to be most pronounced in the central part of the lobule and polymorphonuclear leukocytic infiltration in the portal areas is not evident.

Liver cells are damaged or destroyed in proportion to dosage, high dosages causing complete necrosis, and lower dosages producing only

(6) Schweiz. med. Wchnschr. 81:1218-1219, Dec. 5, 1951.
 (7) Radiology 57:561-575, October, 1951.

slight evidence of damage, such as swelling. In the lower dosage range, focal destruction of liver cells results, indicating apparent variable sensitivity to radiation. Repair is rapid when possible; otherwise death occurs, depending on dosage and extent of damage.

Effects of X-ray Radiation on Pancreatic Function in Dogs. Robert F. Rauch and Wilhelm Stenstrom⁸ (Univ. of Minnesota) attempted to find a means of temporarily inhibiting pancreatic function, when post-operative fistula or recurrent acute pancreatitis occur. They made a qualitative and quantitative study of the effects of irradiation on pancreatic function in dogs.

METHOD.—Pancreatic fistulas were made in five adult male dogs by modified Pavlov technic. A 30 minute fasting specimen of pancreatic juice was collected; then the pancreas was stimulated by introducing 100 cc. N/10 HCl into the stomach. Specimens were collected at 15 and 30 minute intervals. In three dogs, volume and pH were measured. Amylase activity was evaluated in four dogs and lipase and trypsin in two of these. Histologic studies were done on 10 healthy mature dogs. In two animals biopsies of the tail of the pancreas were taken 14 days before irradiation with 600 r over the pancreas. Two animals were killed 24 and 48 hours after irradiation. Four dogs got 200 r in air on alternate days to a total of 800 r; two of them were killed 36 hours after final exposure; the other two, two months later. The five fistula dogs got 400 or 600 r over the pancreas. Hydrochloric acid stimulation was done 12 or 24 hours after irradiation. These were continued up to 11 days after exposure. On the fifth day, two dogs had another 600 and 400 r and further tests were done. Factors were: 220 kv., 15 ma., 1 mm. Cu plus 1 mm. Al filter, half-value layer 1.7 mm. Cu, focus-skin distance 70 cm., 10 × 15 cm. field with pancreas at an estimated 5 cm. depth.

In five dogs with pancreatic fistulas, volume of pancreatic secretion decreased temporarily after irradiation. In a few instances there was a secondary rise above normal. No definite alteration of pH was noted after 400-1,000 r. Roentgen therapy with 400 or 600 r depressed amylase, lipase and trypsin output of the pancreas; this occurred after a 12-36 hour delay and depression was limited to a few days. Changes in amylase, lipase and trypsin output were similar and parallel except for a more persistent depression of trypsin after a second irradiation. No organic changes were found histologically in any abdominal organ after a single exposure of 600 r or after repeated doses of 200 r on alternate days for totals of 800 and 1,600 r.

Hemorrhagic Phase of Acute Radiation Syndrome Due to Exposure of Whole Body to Penetrating Ionizing Radiation in the lethal range has long been known as a prominent cause of death. In view of conflicting reports on the pathogenesis of the hemorrhagic state, E. P. Cronkite, G. J. Jacobs, George Brecher and George Dillard⁹ analyzed the current knowledge and present new data on various phases of the known hemostatic mechanisms in the dog.

At present defects in hemostasis in the irradiated animal can apparently be explained by thrombopenia and its sequelae. Ulceronecrotic lesions and infections play a prominent role in initiating hemorrhage. Once it is initiated, the thrombopenic animal has difficulty in stopping the outflow of blood from the eroded vessels. The development of

(8) *Gastroenterology* 20:595-603, April, 1952.

(9) *Am. J. Roentgenol.* 67:796-804, May, 1952.

purpura is still not entirely explained. All thrombopenic animals do not become purpuric. The precipitation of diffuse purpura is often correlated with sepsis.

The blood coagulation defect and failure to utilize prothrombin are correlated with platelet deficiency, which is corrected by the *in vitro* and *in vivo* addition of separated platelets.

There is no good evidence for deficiency of any of the plasma factors essential for blood coagulation except those connected with the platelet. On the contrary, all evidence points toward there being adequate amounts of prothrombin, plasma accelerator factors, serum prothrombin converting accelerator, antihemophilic factor and fibrinogen.

The complicated nature of hemostasis in general and the diffuse nature of radiation injury make it essential that one keep an open mind because hemostatic factors as yet poorly defined may be defective. Indirect indications of inhibitors and inexplicable disturbances of coagulation are occasionally noted in the laboratory. For example, it is necessary to increase the platelet level of the thrombopenic dog to a much higher level than anticipated to obtain results equivalent to *in vitro* studies. The presence of strong second phase anticoagulants of the heparin type has not been shown.

Observations on Lymphopenia of X-ray Irradiation: Part II. C. H. G. Price¹ (Univ. of Bristol) fractionally irradiated rats under conditions modeled on the ovarian technic used in human beings.

METHOD.—Three groups of 18 adult albino rats each were used. In group 1, factors were: 75 kv., 4 ma., focus-skin distance 10 cm., no filtration, half-value layer 1 mm. Al, 57 r/min., daily fraction 7,800 Gm.-r, skin dose 300

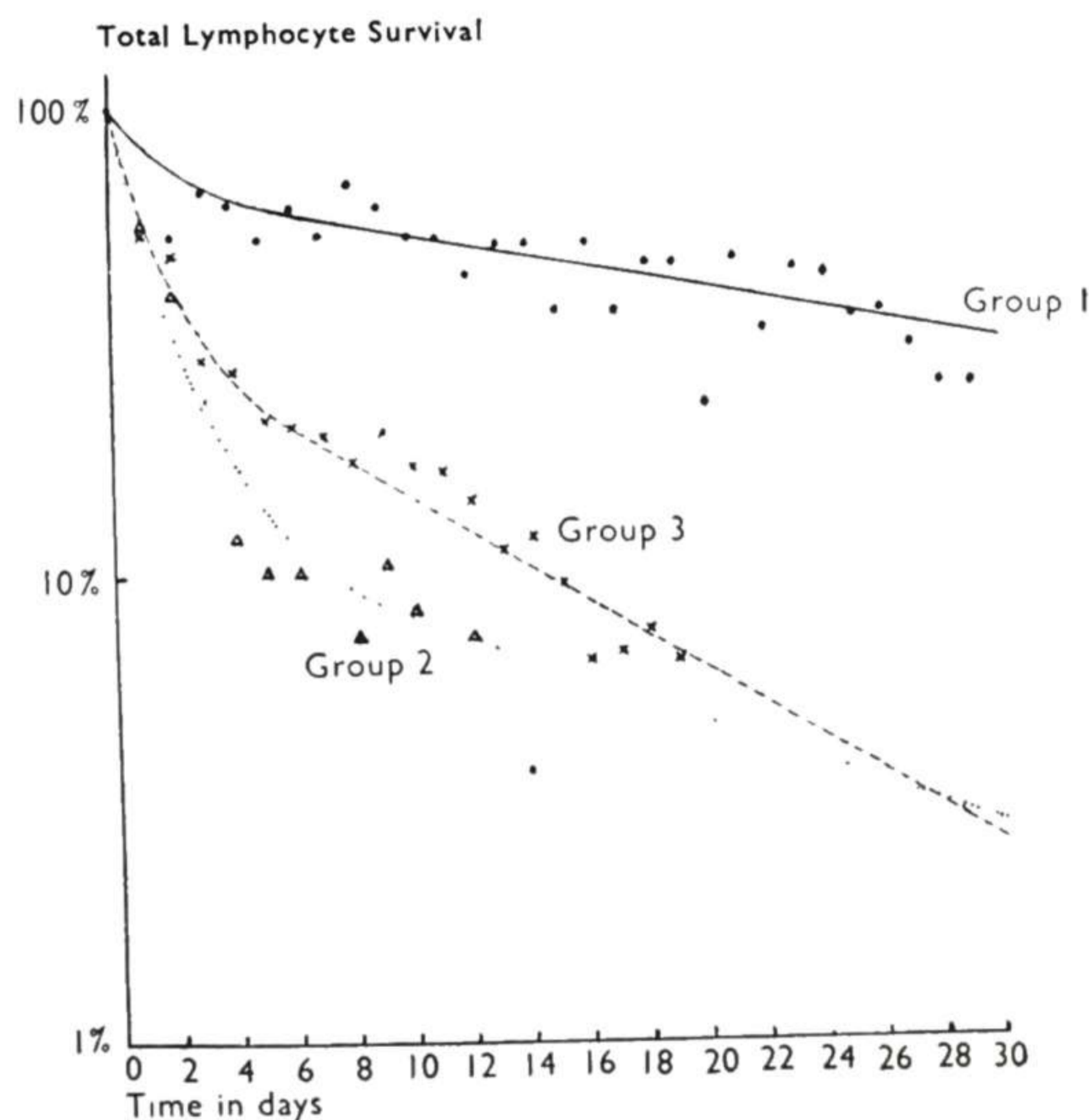


Fig. 383.—Mean curves showing per cent survival of lymphocytes. (Courtesy of Price, C. H. G.: *Brit. J. Radiol.* 24:556-567, October, 1951.)

(1) *Brit. J. Radiol.* 24:556-567, October, 1951.

r, single anterior 4×4 cm. port. In group 2: 95 kv., 4 ma., half-value layer 3.2 mm. Al, filtration 0.9 mm. Al, focus-skin distance 9 cm., 272 r/min., daily fraction 32,000 Gm.-r, skin doses 1,000 r, three 4×4 cm. fields (anterior, right and left posterior oblique). In group 3, factors were identical to those used for group 2 except dose rate was 220 r/min., filtration 1.2 mm. Al, daily fraction 10,500 Gm.-r and skin dose 377 r.

Figure 383 shows total surviving lymphocytes for the three groups plotted against treatment time. It reveals the difference in response of groups 1 and 3, which received a similar dose fraction daily but in which the number of fields irradiated varied. Rate of change of the total count was also less in group 1. Difference in dose rate did not greatly change cellular response, as exemplified by groups 2 and 3. A much higher total dose was necessary in group 1 to reduce surviving lymphocytes to a specific level, which shows the importance of volume of tissue irradiated. When total lymphocyte survival dose curves were analyzed into two separate components, the major effect could best be explained as the direct result of ionizing radiation. This effect may be regarded as a single hit target phenomenon.

Neoplasia Induced in Rat Embryos by Roentgen Irradiation. James G. Wilson, Robert L. Brent and H. Charles Jordan² (Univ. of Rochester)



Fig. 384.—Embryo, removed on 15th day of gestation, was exposed to 100 r on the 9th day and allowed to live for 6 days thereafter. Opaque spots are visible beneath the ectoderm of the head, as indicated by arrows; reduced from $\times 9$. (Courtesy of Wilson, J. G., *et al.*: *Cancer Res.* 12:222-228, March, 1952.)

describe the method of production, incidence and growth characteristics of independent tumors in embryonic and newborn rats.

METHOD.—Female rats of the Wistar albino strain were considered to have started gestation at 9 a.m. of the morning on which sperm was found in the

(2) *Cancer Res.* 12:222-228, March, 1952.

vaginal smear. The embryos were regarded as one day old 24 hours later. Nine days after start of gestation, the pregnant animals were anesthetized with nembutol® and the ventral abdomen incised. A uterine horn was brought to the surface of the incision and shielded with lead plates so that only three to five implantation sites were unshielded. The mother was completely shielded and the embryos were exposed to x-rays. The uterine horn was replaced in the abdomen and then the other one was brought to the surface but not irradiated. Before closing the abdomen all embryo sites were charted for later identification. Doses were single exposures of 25, 50, 100 or 200 r in air. Factors were: 85 kv., 10 ma., 1.0 mm. Al added filtration, half-value layer 2.0 mm. Al, target-object distance 10-20 cm. After irradiation the mothers were killed at intervals of 1-12 days and the embryos were fixed.

The nine day embryos exhibited opaque spots over the head region (Fig. 384). Incidence of such tumors was directly related to x-ray dosage. They first appeared on the second day after irradiation. Some grew for one or two days and then disappeared. Others grew rapidly to the fifth or sixth day, then underwent atrophy. Few remained in the newborn; these were small and did not show proliferative activity. Although the tumor-bearing animals had a somewhat higher mortality than the controls, neither pre- nor postnatal death could be attributed to the tumors.

Induction of Thyroid Cancer in the Rat by Radioactive Iodine.

R. C. Goldberg and I. L. Chaikoff³ (Univ. of California) studied the late effects of single injections of I^{131} in rats.

METHOD.—In the I^{131} experiment, at age 3 months, 25 rats received one intraperitoneal injection of 400 μ c. I^{131} and were killed 1½-2 years later. A block of cervical tissue ventral to the prevertebral fascia and caudal to the upper margin of the larynx was sectioned at 10 μ . Sections of other organs were also studied. After Formalin fixation, Masson's trichrome and hematoxylin-eosin stains were used. In selected animals, 10 μ c. carrier-free I^{131} was injected intraperitoneally 24 hours before the rats were killed. Radioautographs were prepared by floating a 4 μ section on an Eastman medium lantern slide and exposing it for two to four days. These sections were stained with iron hematoxylin and metalin yellow.

In the propylthiouracil experiment, rats, aged 6 weeks, were given a standard diet plus 0.2% propylthiouracil; they were killed at intervals from 3 to 32 months later. The thyroids and other organs were studied histologically.

Alveolar adenocarcinoma was found in three rats given I^{131} , papillary adenocarcinoma in one, small cell carcinoma in three and two major types of adenomas, fetal and follicular, in five rats. In no rat on propylthiouracil was a tumor observed. Metastases were found in five of seven rats with thyroid carcinoma. It is concluded that ionizing radiations emitted by I^{131} are carcinogenic in the rat.

Sensitivity of Serum Enzyme Inhibitors to a Variety of Cancer Chemotherapeutic Agents. To find a test of therapeutic response, Frank W. Ellis and Philip M. West⁴ made serial determinations of chymotrypsin and rennin enzyme inhibitors in cancer patients during three years when over 30,000 tests were made. When chemotherapy was effective regardless of drug used or type of malignancy, inhibition of tumor growth was reflected by similar changes in concentration of serum enzyme inhibitors.

(3) A.M.A. Arch. Path. 53:22-28, January, 1952.

(4) J. Clin. Invest. 30:547-557, June, 1951.

Man, 59, with right cervical Hodgkin's disease, treated by surgical resection and x-ray three years earlier, had anorexia, constipation and weight loss. X-rays of the chest and gastrointestinal tract were normal. Oral doses of 10 mg. triethylene melamine (Fig. 385) gave prompt relief, reducing serum chymotrypsin inhibitor levels, although 5 mg. doses were ineffective. Rennin inhibitor did not appreciably increase and only intensive therapy restored the balance between the factors. Periods of maximal enzyme response were associated with disappearance of fever. Enzyme values were actually the only objective basis for planning adequate treatment schedule.

The chymotrypsin inhibitor might be considered an index of "neoplastic activity" and the rennin inhibitor a reflection of "host resistance." Ineffective chemotherapy does not alter enzyme inhibitor pattern, whereas tumor-stimulating agents produce enzymatic changes

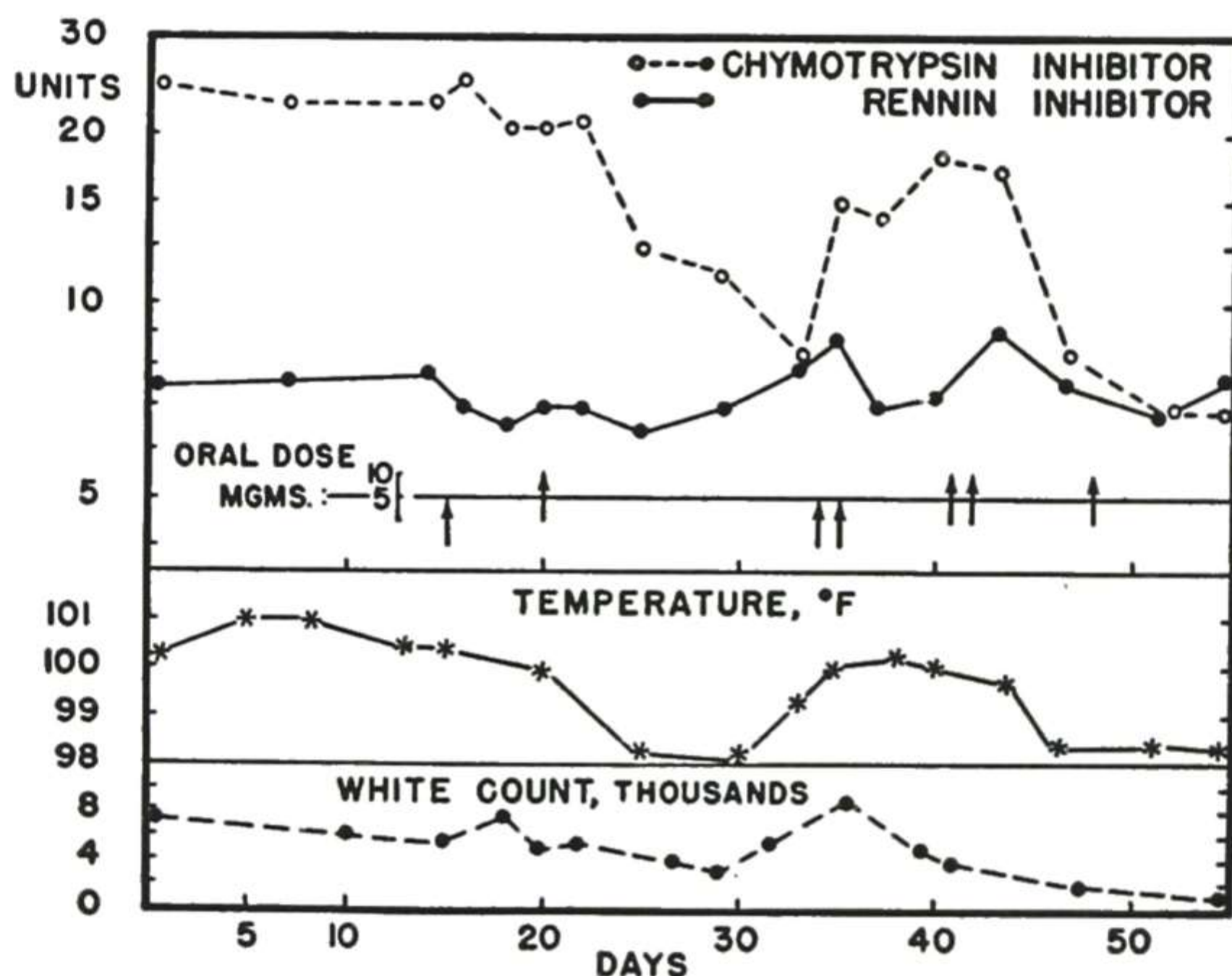


Fig. 385.—Changes in enzyme inhibitor balance paralleling clinical response of Hodgkin's disease to triethylene melamine therapy. (Courtesy of Ellis, F. W., and West, P. M.: *J. Clin. Invest.* 30:547-557, June, 1951.)

associated with increased neoplastic activity. Sensitivity, consistency and close correlation of the two factors with clinical status of the cancer patient suggest that the method has practical as well as research value in charting the course of neoplastic disease.

[This approach seems to give some promise in detecting therapeutic effects in clinical cancer research. It has been applied to patients receiving radiation therapy, and the results were reported to the Sixth International Congress of Radiology in London in July 1950 (see also 1951 YEAR BOOK, p. 370).—Eds.]

Radiation Effect on Unborn Embryo Immediately after Conception is reported by Maxwell Roland (Forest Hills, N. Y.) and Arthur Weinberg⁵ (Far Rockaway, N. Y.).

Woman, 24, a nullipara, was first seen on June 20, 1948, with a history of infertility for two years. Menses were irregular. General physical examination was negative. The cervix was long and narrow; uterus was small, smooth and faced anteriorly. Adnexae were normal. Hysterosalpingography showed the tubes to be patent. Endometrial biopsy on the 27th day of the cycle showed persistent follicular phase. Cyclic therapy for three months resulted in a normalized uterus and regular menses. The cycles were still anovulatory. Pregnant mare's serum, 500 units daily for nine days, followed by chorionic gonadotrophin, 500 units every day for nine days, produced no change. She was then given 20 mg. progesterone daily from the 20th day of the cycle for five days, without

(5) *Am. J. Obst. & Gynec.* 62:1167-1169, November, 1951.

effect. From June 8 to July 5, 1949 she was given 600 r to both the right and left sides of the pituitary, with no change in the endometrium. On Jan. 18, 1950, she was given 100 r to both right and left pelvic regions anteriorly. On January 25, she was given 100 r to both right and left pelvic regions posteriorly, through 10×12 cm. portals, with 200 kv. She was advised not to conceive during this period. On her third visit, she was several days late and therapy was discontinued. The Aschheim-Zondek test gave a positive result. She had a normal pregnancy and delivered a normal child, whose growth and development at age 6 months were normal.

The patient had received 200 r to each ovarian area. Depth dose was 30% or 60 r to each ovary. The 10×12 cm. ports allowed a 3 cm. area in the midline to be protected so that the embryo was shielded from direct radiation. It is estimated that the embryo received 18 r from back scatter.

[This happy result of a "clinical experiment" might not have been expected, since the irradiation was done so early in gestation. It emphasizes that there is much to be learned about human biologic radiation effects.—Eds.]

Effects of Ionizing Radiations on Developing Dental System.

S. Gorvy⁶ (Johannesburg) exposed the incisors of a black kitten, aged 4 days, to 1,500 r for five minutes, with the beam passing from right to left. Two controls were not irradiated. X-rays and photographs were taken periodically after irradiation. Epilation of the skin, with regrowth of coarse white hair, was noted. Development of the nasal bones was retarded and eruption of the deciduous canines and incisors depressed. Retardation on the side nearer the x-ray tube was more pronounced. The affected teeth were shed at least two months early. Their only permanent successors were a deformed, unerupted maxillary right canine, a stunted maxillary left canine and an abnormal mandibular left third incisor with a bifid crown on the side of the face away from the tube. The cat apparently developed normally after age 1. Irradiation of the oral structures alone did not primarily affect its generative system, since it gave birth to an initial litter of three normal kittens. Its second pregnancy ended in a miscarriage. The color of its coat began to change after the ninth month, attributed to interference with the harmonious interaction of genes.

Role of Infection in Radiation Injury was investigated by C. Phillip Miller, Carolyn W. Hammond and Marianne Tompkins⁷ (Univ. of Chicago). Male white mice averaging 20 Gm. in weight were given 450 or 600 r total body x-radiation in a single exposure. Factors were 250 kv., 15 ma., 27 in. distance, 0.5 mm. Cu and 3 mm. Bakelite filters, rate of about 20 r/min.

In the 450 r series, 595 mice were killed (35/day) and blood and spleen cultures were made. Positive cultures were shown by 152 mice. Sixty-six per cent occurred during the second week after irradiation, the period of greatest mortality. In the 600 r series, 288 mice were killed (20/day). Of these, 113 showed positive cultures. Eighty per cent were seen in the second week after irradiation. Cultures of unirradiated mice were all sterile.

In most animals the bacteremia was severe enough to be regarded

(6) South African J. Clin. Sc. 2:248-254, September, 1951.

(7) J. Lab. & Clin. Med. 38:331-343, September, 1951.

as an overwhelming sepsis, and caused by micro-organisms normally present in the lower bowel. It was concluded that such septicemia is largely responsible for the death of mice irradiated with these doses of x-rays.

Changes in Composition of Blood Plasma of the Rat during Acute Radiation Syndrome, and Their Partial Mitigation by Dibenamine® and Cortin are reported by Henry I. Kohn⁸ (Oak Ridge Nat'l Lab.). Adult rats received a total body exposure to 250 kvp x-rays in one dose of varying magnitude (100-900 r). Changes in the plasma were followed for about 30 days.

Magnitude of the changes varied with magnitude of the dose given. There was an initial rise in the titers of sugar, nonprotein nitrogen, cholesterol, phosphorus and chloride, but phospholipid values remained unchanged. With higher doses albumin-globulin ratio showed a rise which in some cases lasted 30 days. Total protein levels showed an initial fall. All values except albumin-globulin ratio returned to normal within 14 days. The changes in plasma chloride and cholesterol levels were prevented by use of cortin. Dibenamine® prevented the changes in cholesterol alone, and injection of sheep erythrocytes one week before irradiation blocked the rise in albumin-globulin ratio.

Radiation effects can be classified as primary, when initiated by the radiation directly within the cells in which they show, and secondary, when they occur in other cells by means of neural, humoral or other physiologic connections. The nature of the effects reported and their modifications by DCA and dibenamine® suggest secondary reactions associated with hormonal and autonomic mechanisms.

Cysteine as Local Protective to Human Skin against X-rays. A. H. Slepian (Highland Park, Ill.) and Theodore Cornbleet⁹ (Univ. of Illinois) performed tests on four subjects.

TECHNIC.—Using a freshly prepared solution of cysteine hydrochloride in a buffer solution (sodium phosphate, 0.125 M, pH 7.2), 1.5 Gm./100 cc., enough solution was injected into the left scapular area to make a wheal 2 cm. in diameter. Control areas consisted of a wheal of buffer solution alone at the midline of the back and the bare skin of the right scapula. A lead sheet with a 2 × 1.5 cm. aperture was used for a shield. Each site received 450 r (in air), factors being 70 kv., 5 ma., 25 cm. distance and half-value layer 0.6 mm. Al.

Cysteine offered no protection, as evidenced by its failure to prevent erythema in the four subjects.

Hematologic Changes in Rats Protected by Cysteine against Total Body X-irradiation are reported by Robert L. Rosenthal, Leontine Goldschmidt and Bryant I. Pickering¹ (Naval Radiological Defense Laboratory, San Francisco). After 800 r total body x-radiation, rats protected by injection of cysteine showed significantly higher neutrophil values in the blood and more numerous myeloid cells of all stages in the bone marrow than did unprotected animals given injections of saline solution. Mortality in unprotected animals was 69% compared to no deaths in the protected animals. Weight loss was also significantly lower in the protected animals.

(8) Am. J. Physiol. 165:27-42, April, 1951.

(9) A.M.A. Arch. Dermat. & Syph. 64:425-427, October, 1951.

(1) Am. J. Physiol. 166:15-19, July, 1951.

The results provide further evidence that preservation of the myeloid cells may be important in the survival of irradiated animals. This in turn again emphasizes the significant role of infection in postirradiation mortality, since infection, particularly that of endogenous origin, is controlled to an important extent by action of the myeloid cells.

Effect of X-irradiation on Rats with and without *Bartonella Muris* was investigated by Paul E. Rekers² (Cedars of Lebanon Hosp., Los Angeles). This is a common laboratory infection.

METHOD.—Six groups of rats were given single dose total body x-radiation: (1) infection-free rats; (2) rats infected during breeding and gestation periods (infected no. 1); (3) rats infected 10 days before irradiation (infected no. 2); (4) infection-free rats given 20 mg. aureomycin daily beginning 1 day before irradiation; (5) same as the previous group except that 100 mg. rutin was also given daily beginning 10 days before irradiation; (6) infected rats (a

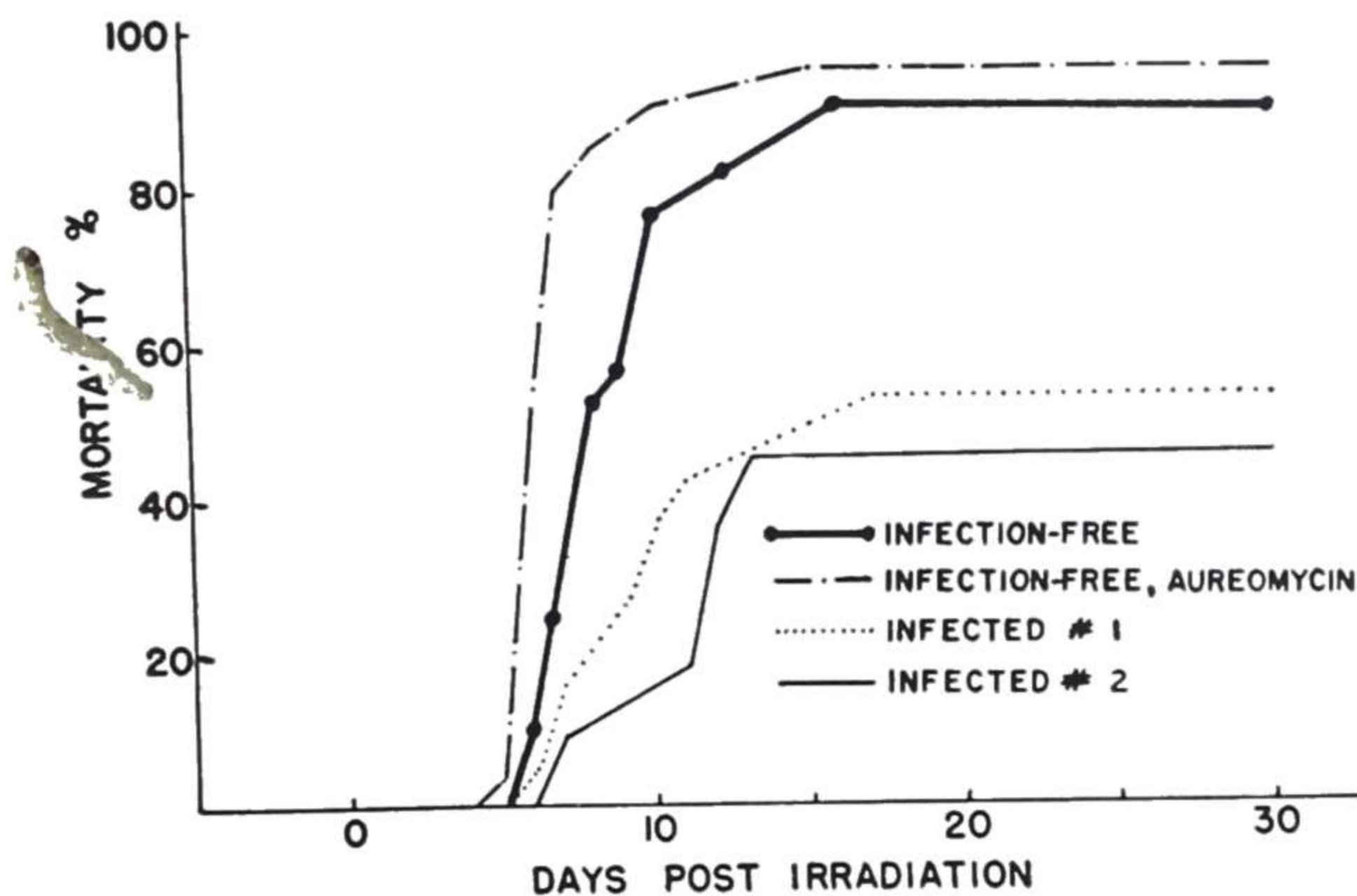


Fig. 386.—Mortality of infected and infection-free rats after irradiation with 700 r. (Courtesy of Rekers, P. E.: *J. Infect. Dis.* 88:224-229, May-June, 1951.)

different strain). Factors were: 220 kvp, 15 ma., target-skin distance 45 in., half-value layer 1 mm. Cu, output of 6 r/min. Rats weighing 150 Gm. received 700 r; those weighing 200 Gm., 750 r.

Results are shown in Figure 386. Mortality curves were similar for rats of different weights or strains and for the infection-free rats given aureomycin with or without rutin. Infection-free rats showed a mortality rate of 90%. When rats were infected with *B. muris* for 10 or more days before irradiation, survival period was not only prolonged but mortality rate was reduced to 50%. This suggests that the infection sets up a defense mechanism within the host that provides not only resistance to the infection but increased tolerance to the stress of irradiation also. The mechanism of this effect was not elucidated by these studies.

Protection of Mice against Lethal Dose of X-rays by Cyanide, Azide and Malononitrile was investigated by Z. M. Bacq and A. Herve³ (Univ. of Liège). It has been shown that repeated stimulation of an isolated frog muscle after a radiation dose of 4,000 r leads to contracture with inability to respond to further stimulation, such as is also observed

(2) *J. Infect. Dis.* 88:224-229, May-June, 1951.

(3) *Brit. J. Radiol.* 24:617-621, November, 1951.

after oxygen poisoning. Therefore, the effect of poisons which are well known for their inhibitory action on the oxidation systems of the body was studied in irradiated animals.

METHOD.—Pure breed mice, weighing about 30 Gm., were used. One group of animals was given 0.1 mg. sodium or potassium cyanide just before or immediately after irradiation. Another group was similarly given the same dosage of sodium azide. The third group received injections of 0.1-0.2 mg. malonitrile before irradiation. All mice were exposed to single dose total body radiation of 700 r. Factors were: 250 kv., 18 ma., filtration 0.25 mm. Cu, focus-skin distance 50 cm., half-value layer 0.75 mm. Cu, 10×10 cm. field, 100 r/min. A control group was irradiated only.

All control mice died 4-10 days after exposure. The animals which received cyanide before irradiation showed a 50-80% survival, whereas injection of the same dose after irradiation only delayed death. The cyanide anion, and not thiocyanate or cyanate, was shown to be the protective agent. Sodium azide permanently protected 40% of mice

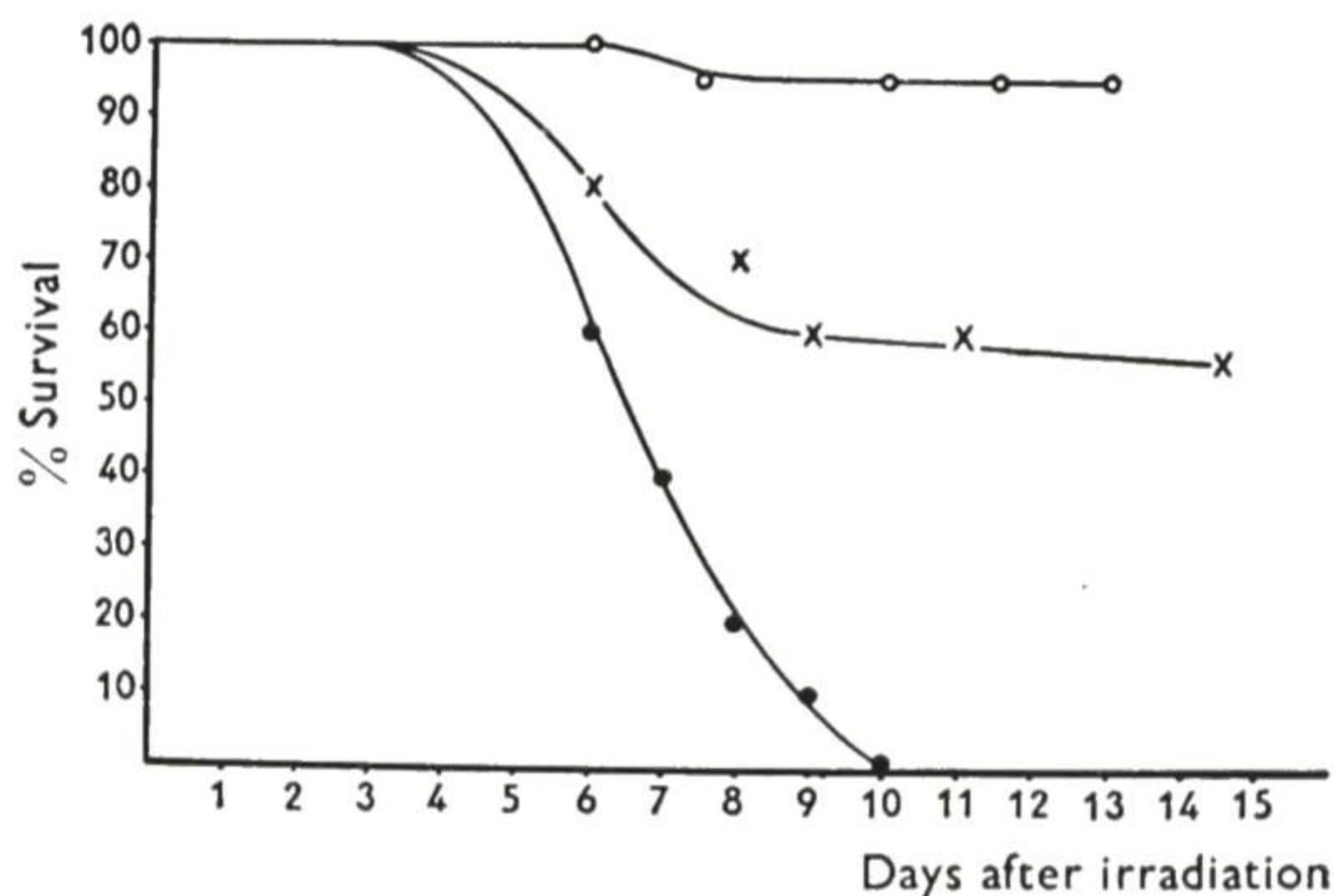


Fig. 387.—Percentage survival of irradiated control mice (solid circle), animals given an injection of 2 mg. glutathione before irradiation (cross) and animals given 2 mg. glutathione and 0.1 mg. cyanide before irradiation (open circle). (Courtesy of Bacq, Z. M., and Herve A.: *Brit. J. Radiol.* 24:617-621, November, 1951.)

given injections immediately before irradiation. Injection of malonitrile before irradiation decreased the lethal effect of 700 r to 10-20%.

Further experiments were carried out to determine if administration of glutathione and sodium cyanide before irradiation (700 r) was followed by a higher percentage survival. Results are shown in Figure 387. Various other substances were without effect. They were sodium fluoride, sodium sulfite (reducing agent), mapharsen,[®] BAL and alpha-tocopherol.

Malonitrile is more effective than cyanide because the cyanide anion is liberated over a long period. Sodium azide is known to inhibit the same enzymes as cyanide, although its chemical properties are different. The fact that they give significant protection against x-radiation seems to indicate that the temporary, reversible enzymatic inhibition induced by them is the cause of the observed protection.

Recovery from Radiation Injury of young adult mice unprotected and with various organs lead-shielded is discussed by L. O. Jacobson, E. L. Simmons, E. K. Marks and J. H. Eldredge⁴ (Univ. of Chicago).

As shown in the table, protection of any significant bulk of the

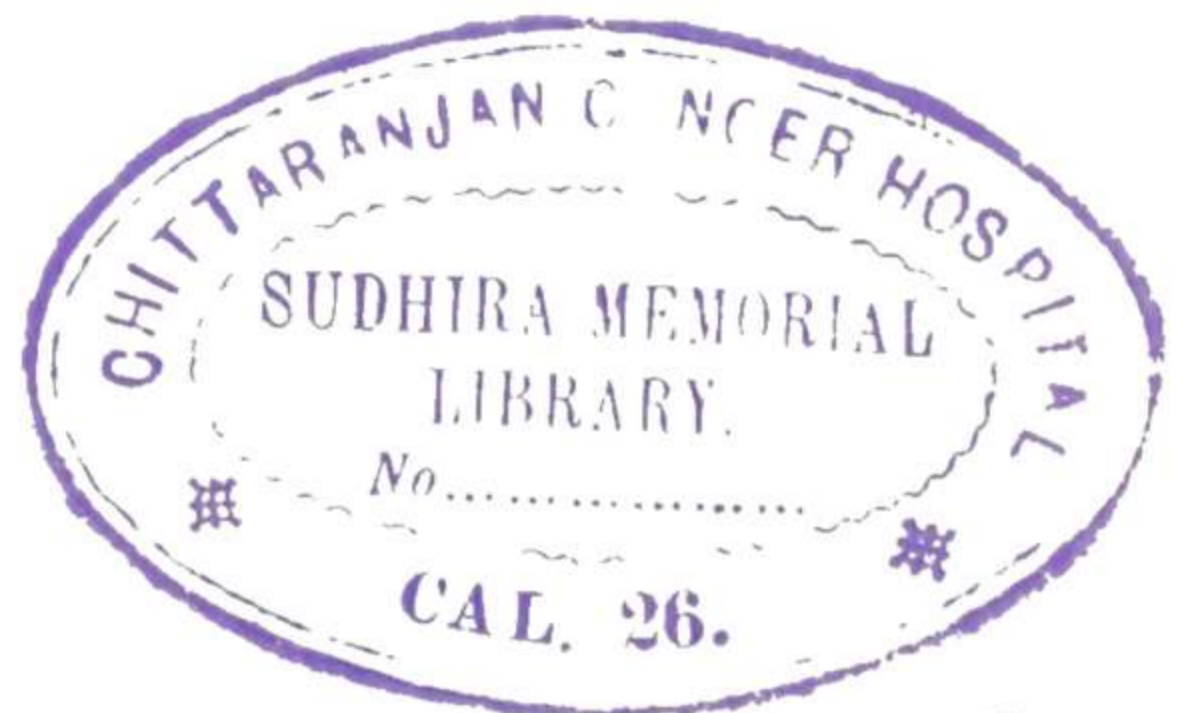
(4) *Science* 113:510-511, May 4, 1951.

body increases survival rate following exposure to 1,025 r over that for unprotected animals. However, shielding of the spleen gave the greatest survival rate, even though the weight of protected tissue was less than in any of the other groups. Surgical removal of the protected spleen six hours or more after irradiation did not reduce the beneficial

SURVIVAL OF MICE EXPOSED TO 1,025 R X-RADIATION WITH LEAD PROTECTION OF VARIOUS TISSUES

No. ANIMALS	TISSUE LEAD-SHIELDED	SURVIVAL, %	HEMOPOIETIC RECOVERY, 8 DAYS
135	Exteriorized spleen, 0.1 Gm.	77.7	Complete (++++)
93	None	0	0
15	Exteriorized lobe of liver, 0.8 Gm.	33	Nearly complete (++++)
15	None	0	0
15	Exteriorized intestine, 2.5 Gm.	26.6	Nearly complete (++++)
15	None	0	0
18	Head, 3.0 Gm.	27.7	Only partial (+)
12	None	0	0
15	Right hind limb, including thigh, 1.5 Gm.	13	Not studied
28	Exteriorized right kidney, 0.19 Gm.	0	0
8	None	0	0

effect. Transplantation of spleens from nonirradiated animals into the peritoneal cavities of those irradiated increased survival of the latter, the effectiveness being reduced if transplantation was delayed for two days after irradiation. The animals maintaining or acquiring normal splenic tissue regenerate gastrointestinal and hemopoietic tissue more rapidly and completely than the others. It is significant that the factor involved in this protection is effective even if administered following irradiation.



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