Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Roentgen Therapy

Volume IX | Friday, April 1, 1938 | Number 22

STAFF MEETING BULLETIN
HOSPITALS OF THE
UNIVERSITY OF MINNESOTA

Volume IX | Friday, April 1, 1938 | Number 22

INDEX

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Financed by the Citizens Aid Society

William A. O'Brien

I. LAST WEEK

Date: March 19, 1938

Place: Recreation Room
Nurses' Hall

Time: 12:15 to

Program: Movie: "Hawaiian Holiday"

Bile Acids
Felix Hughes Crago

Discussion: F. H. Crago
Cecil J. Watson
Frank Bryant
Maurice G. Visscher
Ancel Keys

Present: 105

Gertrude Gunn,
Record Librarian

II. MOVIE

Title: "The Milk Parade"

Released by: Milk Industry Foundation.

III. AUTHORS

1. KARL WILHELM STENSTROM
was born in Gothenburg, Sweden. He attended the University of Lund between 1910 and 1919, where he received his Ph.D. In 1919 and 1920 he was a Fellow at Harvard under the Swedish-American Union as an associate of Biophysicist William Duane. In 1920 he went to the New York State Institute for the Study of Malignant Disease, where he remained until 1926. In that year he was appointed Biophysicist for the Cancer Institute of the University of Minnesota Hospitals. Originally Associate Professor of Biophysics, he was made a full Professor in 1935. Dr. Stenstrom is widely known for his work in biophysics. He is a member of the standardization committees of the three radiological societies.

2. CURTIS BLAINE NESSA
was born in Osseo, Wisconsin, where he attended high school. He received a B.S. degree from the University of Wisconsin in 1934; M.B. from the University of Minnesota in 1936; and M.D. in 1937. An intern at the Ancker Hospital, St. Paul, 1936-37, he was appointed to the Radiological Department as a Fellow July 1st, 1937.

3. HERMAN HANS JENSEN
was born in Audubon, Iowa. He attended the University of Nebraska between 1915 and 1920, with the exception of 18 months of military service. Degrees B.A. and B.Phm., graduate study at the University of Minnesota in Pharmacology. M.S. 1921 and Ph.D. 1924. M.B. and M.D. in 1925. Served an internship at the University of Minnesota Hospitals for one year, after which he went into practice at Atwater, Minn. Returned as Radiological Fellow January 1st, 1937.

4. ARDEN L. ABRAHAM
left yesterday morning for Duluth, Minnesota, where he will enter the practice of Radiology. His report will be read by Dr. Stenstrom.

IV. BIRTHS

BOY, to Wallace and Alice Ritchie, March 23, 1938, to be named James Timothy.

GIRL, to John and Kathryn Bond, March 25, 1938, to be named later.

Congratulations and Best Wishes!

V. ROENTGEN THERAPY

W. K. Stenstrom,
A. L. Abraham,
C. B. Nessa, and
Herman H. Jensen

1. Introduction

The Citizens' Aid Society has recently donated money for the addition of a new 220 kv X-ray therapy machine. This apparatus should be installed within the next two months. As a consequence we expect to catch up with the requests for treatments next summer so that new patients can be treated immediately and will not have to wait several weeks as is the present case. It should be clearly understood that the intention is mainly to improve the methods of treatments and not to increase appreciably the number of patients accepted for treatments. The importance of giving the treatments without any delay is evident and does not need any explanation. The method of giving an extended series of daily treatments is now so well established that it must be considered the method of choice for certain types of cancer. It has not been possible for us to utilize this method to the full extent on account of the lack of facilities. It is our intention to employ this method as far as it seems advisable. We thereby hope to improve the results and to decrease the X-ray sickness and thus the discomfort of the patients.

The field of roentgen therapy is continuously undergoing changes. Treatment of certain conditions is being eliminated either because other more satisfactory methods have been developed or because it has been found after a fair trial that the results are too insignificant. On the other hand now and then a disease is being added to the list which is benefited by roentgen therapy and it is at least advisable to test this method of treatment in them. It is particularly important to carry out experiments of this type at a university hospital where cooperation of staff members in the respective departments can be obtained. Finally a new technique may make it advisable to again test the value of radiation for some diseases which did not respond so well when the older methods were employed.

Last year attention was called to the application of X-ray therapy in the treatment of bronchiectasis. The results obtained so far indicate that carefully selected patients in this group are benefited by the treatments and that the study should be continued. The treatment of peritendonitis and bursitis with X-rays has become a common practice. There is no doubt that the pain connected with these ailments is as a rule promptly relieved. Calcification is gradually absorbed and motion of involved extremities improved following the therapy. We have received more requests for treatments of peritendonitis during the last year than before. It is well to limit the treatments to rather severe cases as it must be considered a rather drastic method.

It is well to remember that there are some diseases which under certain conditions may be attacked with X-rays. Carbuncles and furuncles are treated with X-rays at many places and good results have been reported by reliable investigators. It seems that this method might be utilized here to a greater extent than has been done. Good results are obtained in hyperplastic types of tonsillitis in patients who could not be operated due to other complications. Chronic sinusitis may also respond according to some reports in the literature. As a rule when hyperplastic lymphatic tissue causes trouble it can easily be reduced by means of X-ray therapy. It is for example in this manner diphtheria carriers often may be freed from the remaining obnoxious bacteria.

A fair number of patients with tuberculous adenitis have been treated and as a rule the results have been satisfactory. It is perhaps less well known that tuberculous peritonitis often responds well to X-ray therapy though our own experience in this field is extremely limited. An experimental use of roentgen irradiation for carefully selected cases of pneumonia seems indicated. In this as in several other fields we would like to cooperate in a

study to determine the value of such method of treatment but we are reluctant to start the treatments unless we are assured of a careful follow-up of the results.

These remarks have been made to call attention to the potential possibilities of roentgen treatments and as a reminder of a therapeutic agent which should be considered in special instances for a wide range of diseases.

The results of X-ray treatments which have been particularly considered recently in our department are summarized herewith. They are: 1. Final statistical studies of carcinoma of the lip by Dr. Arden L. Abraham. 2. Results of X-ray therapy of brain tumors by Dr. C. B. Nessa. 3. A few case reports of successfully treated patients with types of tumors usually considered resistant (particularly sarcomas) by Dr. Herman H. Jensen.

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2. Revised Statistics on Carcinoma of the Lower Lip

About a year ago statistics were reported on a group of 333 cases of carcinoma of the lower lip treated at the University of Minnesota Hospitals during the years 1926 to 1935 inclusive. The reason for bringing the subject to your attention again is that after a great deal of effort we have been able to account for approximately 95% of the patients. One more case which belongs in the group has been discovered making the total number 334, of which all but 17 have been located and the results of the treatment given here ascertained. Those patients treated in 1926 have been followed ten years, those in 1935 only one year.

The total number of 334 cases has been divided into 4 groups. The first of these consists of patients who had had no previous therapy before treatment at this clinic. There are 151 such cases. All these were proven to have carcinoma of the lip by biopsy. In the second group is included all those patients who had had previous therapy of one type or other and presented themselves with persistance, recurrence or metastasis. There are 121 such cases. The other 2 groups are smaller ones consisting of 45 cases which were considered carcinoma clinically and treated as such but these patients were not proven to have carcinoma either because no biopsy was done or the material obtained was insufficient in amount or unsatisfactory for some other reason. The other group is made up of 17 patients referred here for post-operative radiation. Fifteen of these are proven cases.

Considering the last 2 groups first it would have been possible to follow 14 of them 5 years or longer. Of these, 12 have been followed 5 years or more. Two died from other causes than carcinoma of the lip. Thus the known 5 year survival is 86%. Excluding the two who died before the fifth year the 5 year survival is 100%. There have been no deaths from carcinoma in these 62 cases.

Survival curves have been made of the whole group and also separately of the 151 previously untreated cases and the recurrent group of 121 cases. These curves will be presented as lantern slides. The results are approximately 10% better than previously reported.

Of the whole group of 334 cases the "probable" 5 year survival after treatment is 62.3% (considering the unfollowed cases as behaving like those followed). If those patients who died of other causes than carcinoma of the lower lip before the fifth year are excluded the "probable" five year survival is 73.5%.

Considering all the patients (334) 92 are known to be dead; 46 of them died of carcinoma of the lower lip.

In the primary group of 151 cases the "probable" 5 year survival is 69.1%. Excluding the patients dying of other causes before the fifth year raises the 5 year survival to 88.5%. In this group 34 are known to be dead and of these only 8 died of carcinoma of the lower lip.

In the recurrent group of 121 cases

the "probable" 5 year survival is 50%. If those dying of other causes than carcinoma are again excluded the 5 year survival for this group is 56%. Fifty of the patients in this group are known to be dead, 38 of whom died of carcinoma of the lower lip.

It is interesting to note that there were no deaths from carcinoma of the lower lip after the fourth year and a lantern slide will be shown to illustrate this point.

Further statistics concerning these cases will be published at a later date.

3. Effect of Treatments of Brain Tumors with Roentgen Rays

Review of University Hospital Cases*

Introduction

A considerable amount of work has been done within the last 10 years in an attempt to correlate the responses which have been observed in the irradiation of brain tumors. At present a variation of opinion is prevalent concerning the value of X-ray therapy in these conditions. Apparently good results following X-ray therapy have been questioned because of the known variation in the survival periods of the various types of brain tumors, because of known remissions and exacerbations in untreated cases-- particularly the astrocytomas -- and because it is difficult to say how much of the improvement was due to preceding surgery and how much to irradiation. The early papers on this subject attempted to interpret the value of irradiation therapy in the light of the clinical improvement observed, but because of the above mentioned difficulties and the personal element involved, the investigations of the last 10 years have been concerned chiefly with changes in the histopathological picture of the various tumor types following X-ray therapy. This method of approach has been utilized by Davis and Weil (1), Deery (2), Alpers, Frazier, Pendergrass and Chamberlain (3), O'Connell and Brunschwig (4), Alpers and Pancoast (5), Bailey, Sosman, and Van Dessel (6), and others.

The above mentioned studies employed biopsy material obtained previous to X-ray therapy and that obtained at a later operation or at autopsy for a purpose of comparison. The main histopathological changes have been a reduction in cellularity of the neoplastic mass, an increase in the amount of fibrous tissue and eventually fibrous replacement, a reduction in the total number of mitotic figures, and occasionally the appearance or increase in the number of giant cell forms; there is also a variable amount of vessel thickening which is considered by some as an essential feature and by others as a secondary change following irradiation.

Studied by this method Davis and Weil (1) found that medulloblastomas showed very little change whereas Alpers, Frazier, Pendergrass and Chamberlain (3) have shown a marked change. Clinically this type usually shows marked improvement. These histologic variations may possible be explained by the fact that the time intervals between irradiation and biopsy varied considerably. If the time were long enough a new growth arising from tumor remnants might conceivably mask a previous regression.

Glioblastoma multiforme usually exhibit rather marked clinical improvement for a time. Sachs, Rubinstein and Arneson (7) state that the average survival period for this group is 10 to 14 months, if surgery alone is employed, and present 3 cases which were given irradiation and survived for an average of 24 months. In the histopathological studies it is very difficult to evaluate effects due to irradiation in spongioblastoma multiforme as the structure of the neoplasm varies so markedly in different portions of the growth and because the tumor during development may undergo changes similar to those which might be attributed to irradiation. Of six astrocytomas reported by Alpers, Frazier, Pendergrass and Chamberlain (3) there was a very

*Read before a meeting of the Minnesota Branch of the American Society of Cancer Research, Thursday, December 23, 1937.

definite change noted in 3; of the 3 remaining cases which showed no change only 1 had adequate treatment which these authors believe to be a tumor case of over 2000 r given at the rate of 200 r daily.

Reports have quite uniformly shown that ependymomas exhibit a marked histopathological change together with good clinical improvement; oligodendrogliomas show little or no histopathological change and there has been no recorded clinical improvement in this type except for one case reported by Sachs, Rubinstein and Arneson (7).

Many workers have stated that there is no correlation between the amount of X-ray therapy given and the histological response observed. This is no doubt due to the fact that there has been such a great variation in the methods of treatment. As Alpers, Frazier, Pendergrass and Chamberlain (3) pointed out, the correlation has been found to be high when the last series before biopsy or necropsy was considered instead of the total dose. While it is perhaps true that future advances in the treatment of cerebral neoplasms will probably come from histopathological studies, the factors used in the different clinics have varied so widely up to the present that attempts to correlate separate reports would be futile. To make future studies of value all steps in treatment must be carefully standardized. As Deery (8) suggests there must be:

(1) Exact description of the location and size of the tumor.

(2) Exact statements as to the operative procedure.

(3) Standardization of pathologists' evaluation of malignancy.

(4) General acceptance of adequate dosage and technique.

Discussion

In a group of cases which have been reviewed at the University of Minnesota Hospitals there has been no attempt to study the microscopic response since there were too few which had biopsies before and after irradiation and in these the intervals differed considerably between the time of biopsy and the time of irradiation; also a considerable number of the biopsies were done elsewhere so that the tissue was not available for study here. We have tried to determine whether a favorable response was obtained clinically in certain patients which could be attributed wholly or chiefly to irradiation. We have not attempted to draw any conclusions from the series but merely present it to show the general response which has been observed in this clinic.

Treatment factors were as follows: 200 KV peak voltage; 30 Ma current; filter 1 mm Cu plus 1 mm. Al; 60 cm. TSD; 10x10 cm fields; $\frac{1}{2}$ value layer 1.3 mm Cu; output 27.2 r/min measured in air. We have been giving 350 r every other day to one portal. Irradiation is given through 2 to 4 portals, depending on the location of the lesion, until a total dose of 2400 r has been given. This occasionally has been repeated up to 5 times at 2 to 3 months' intervals. Of the 44 cases below described 25 received but one course and 12, two courses. Recently we have begun to give daily treatments of 160 r using the above factors and giving a total dose of 5000 r over 27 days. This change has been instituted too recently to draw any conclusions from the results of this technique.

In the past 10 years 74 patients have been treated in this therapy department, but only 68 could be checked as to their subsequent course. Of this number the diagnosis was proved by biopsy or necropsy in 44. The median age for this group was 33 and the ratio of males to females was 2 to 1.

TUMORS OF CEREBRUM, CEREBELLUM AND MENINGES: VERIFIED BY BIOPSY OR AUTOPSY

(Arranged according to the classification by Cushing) (9)

		No.	Improved	Dead	Autopsy
I.	Gliomas				
	Astrocytomas	13			
	Fibular	2	0	2	1
	Cellular	3-1	2	3	1
	Cystic	1	1	0	0
	Undifferentiated	7-2	5	6	1
	Spongioblastoma Multiforme	6	6	6	1
	Medulloblastomas	1	1	1	0
	Indeterminate Type	5	3	3	2
	Oligodendroglioma	1	1	0	0
	Ganglio-neuroma	1	0	0	0
II.	Pituitary Adenomas	Not included in this series			
III.	Meningiomas	5-1	3	4	3
IV.	Acoustic Tumors	1	0	1	0
V.	Congenital Tumors				
	Teratoma	1	0	1	1
VI.	Metastatic and Invasive Tumors				
	Melanoma	1	0	1	1
	Sarcoma	1-1	0	1	1
	Neurocytoma	1	0	1	1
	Metastatic Malignancy or hemangioendothelioma	1	1	1	0
VII.	Granulomatous Tumors				
	Tuberculoma	1	0	1	1
VIII.	Blood Vessel Tumors				
	Endothelioma	1	1	1	0
	Angioblastoma	1	1	0	0
IX.	Primary Sarcoma	0	0	1	1
X.	Papilloma	1-1	0	1	1
XI.	Miscellaneous Localized Encephalitis	2	1	1	0
		44-6	25	36	16

Of the 44 patients arranged in the above chart 6, represented by the minus signs, died during or soon after treatment; since there was no time interval here in which improvement might have been observed, these were excluded from the discussion. It might seem that death was caused or hastened by irradiation in these cases. This was, for the reasons stated below, apparently not true. O'Connell and Brunschwig (4) state that there are 2 types of death which have been attributed to X-ray therapy. The first is due to increased pressure where no preceding surgery has been done and in which the symptoms appear (according to Beclere) in one-half hour following treatment. The second type is preceded by no sign of increased pressure; the decompression remains soft and even flat or sunken. Such patients become listless, anorexic and anemic. They gradually fail and finally die in a cachectic state. In the above 6 cases, however, there was a preceding decompression performed in all but 1; this latter patient was in a moribund state when treated and was only treated at the insistence of the surgical staff; only part of the treatment was given and there were no following changes which might be attributed to a sudden increase of pressure caused by irradiation. Of

the remaining 5 patients, 3 died shortly from meningitis following surgery. Regarding the second type of death without signs of increased pressure, there is no reason to believe that this might not also have occurred without roentgen treatment; one patient not treated by X-ray therapy went to just such a death 6 weeks after a preceding surgical excision which had been followed by temporary recovery; this patient received no X-ray therapy. Further, it has been shown by Davis and Weil (1) that very little change has been noted in normal brain tissue following therapy for adjacent malignancies; Davis and Cutler (10) found that necrosis around radium needles implanted in canine cerebrums was limited to the areas immediately next to the needles and that this was not appreciably greater than the necrosis found around needles not containing radium element; Demel (11) produced deficient growth of the entire body, ataxia and small hydrocephalic brains in four-day old puppies with irradiation of the brain, but Scholz (12) concludes that the brains of adult animals will withstand very high doses of X-rays; Elsber, Davidoff and Dyke (13) gave varying single doses to the brains and spinal cords of Macacus rhesus monkeys and concluded that any dose below 3000 r was safe; in treatment of the human brain Sachs, Moore and Furlow (14) have given as high as 6000 r of unfiltered radiation directly to the brain through a craniotomy wound without noting untoward subsequent effects. Because of these reasons, X-ray therapy probably should not be blamed for the 6 above mentioned fatalities in the series under discussion.

In the 38 remaining cases there was improvement of varying degree and for varying periods of time in 25. It is evident, of course, that of the 25 histologically proved cases showing improvement it could not be determined whether the clinical gain should be credited definitely to surgery, irradiation or to both. For that reason certain cases have been grouped according to the surgery which was done to show those in which the improvement was apparently due chiefly or entirely to roentgen therapy. The degree of improvement is self-explanatory; (1) refers to fair improvement, (2) to moderate improvement, and (3) to marked improvement with nearly complete regression of symptoms. The following cases are presented merely to illustrate the interpretation of such improvement.

Case 1 - Degree 1

This patient was a white female, age 37, with complaints dating from August 1931 at which time she noted a definite decrease in her visual acuity. This progressed to complete loss of vision in June 1932. During this time she had occasional attacks of vertigo and moderate frontal headaches.

She was admitted to this hospital on July 28, 1932. The pertinent physical findings at that time were bilateral optic atrophy with complete loss of vision, bilateral exophthalmos which was more pronounced on the left and dilated pupils of equal degree. Blood and urine examinations were normal. The spinal fluid was under pressure of 350 mm water but was negative to examination. X-ray films of the skull showed destruction of the posterior clinoids which was interpreted as being due to an extra sellar neoplasm. Because of the complete loss of vision surgery was deferred and X-ray therapy given. This consisted of 940 r given to each of 2 fields in 4 treatments over a period of 7 days. The patient was discharged August 25, 1932.

Following treatment there was a temporary increase in the severity of the headaches and vertigo. This soon disappeared, however, and for the next 4 years these symptoms were entirely absent. Her blindness was permanent, of course, but she stated that she generally felt much better following irradiation therapy. She worked daily and gained 40 pounds in weight during the year following discharge.

In July 1936 she experienced a sudden attack of convulsions and loss of consciousness. She recovered from this within a few minutes but in September developed pain in the eyeballs and severe frontal headaches. On the

17th of September she became comatose and was admitted to the hospital in this condition. Surgery was refused by the patient's family and X-ray therapy was begun as a last resort. She failed to rally and died before the series was completed. An autopsy was obtained and revealed an extensive meningioma beneath both frontal lobes.

Case 2 - Degree 2

This patient was a white male, age 43, who was admitted to this hospital on February 24, 1932. He gave a history of irritability and headaches for 3 months, emesis for 1½ months, constipation for 1½ months, diplopia for 3 weeks and a weight loss of 15 pounds in 3 months. Physical examination showed a somnolent individual who was mentally dull and who could not understand simple questions; there was a marked loss of memory, especially for recent events. The right pupil was larger than the left and the left was sluggish to light; the discs showed bilateral choking and there were numerous punctate hemorrhages in both fundi. Definite paresis was exhibited in the right upper extremity and a loss of stereognostic sense was noted in both hands. The patient had an unsteady gait and the tendon reflexes were more prompt on the right side of the body.

A ventriculogram was done March 4th but was unsatisfactory. Following this procedure he was continuously comatose up to the time of operation on March 9th. At that time a large tumor was found in the left frontal lobe which was resected as completely as possible; microscopic section showed it to be a spongioblastoma multiforme. He was treated with X-ray on recovery from the surgical procedure and was given 650 r to each of two fields in four treatments. At the time of discharge on March 30th the findings were about the same as on admission.

An additional 550 r was given to each of two fields in April. On May 27, 1932 he was seen in the out-patient clinic. At that time he was feeling in excellent general health. His mentality was clear, and his memory was perfectly normal. The eye grounds showed only one-half diopter choke on the right and one diopter on the left. There was only questionable slight paresis of the muscles innervated by the right fifth, eleventh and twelfth cranial nerves. The patient could write without difficulty and the grip was equal in both hands. He was free from headaches and walked in a normal manner.

About the 1st of July he developed a partial aphobia and the right arm and leg became definitely weaker. 900 r were given to each of 3 fields with only slight improvement and the patient became progressively worse and died one month later.

Case 3 - Degree 3

This patient is a white male, age 40, who was first seen here in the dispensary in July 1932 with a gastro intestinal complaint which was diagnosed and treated as duodenal ulcer; at that time he stated that he had been having headaches in the supra orbital region off and on for 18 months.

In the fall of 1932 he began to complain of impaired vision and photophobia and increasingly severe headaches; his wife noted that his memory was becoming very bad. On October 6th he suddenly became comatose and was taken to the Mayo Clinic. At that time general and neurological examinations revealed no positive findings except bilateral choked discs of two diopters and a partial third nerve palsy on the left side. The impression obtained clinically and from the ventriculogram was that he was suffering from a rapidly growing deep-seated tumor. He was given a course of X-ray therapy and discharged from the Mayo Clinic much improved. He returned for examination in January 1933 and was in excellent condition except for a bi-temporal hemianopsia and only occasional slight headache.

He was admitted to this hospital on May 10, 1933 complaining of recurring headache, impaired vision, and paresthesias of his right arm. Neuro-

logical examination showed a bi-temporal hemianopsia and constriction of the nasal fields. The visual acuity was 3/10 in the right eye and 6/10 in the left eye. There was a secondary bilateral optic atrophy and moderate external strabismus and limitation of conjugate movements upward. There was a moderate degree of deafness bilaterally, air conduction being greater than bone conduction. X-ray examination of the skull showed the trephine openings made during the previous ventriculography procedure; the floor of the sella turcica was markedly depressed, and the posterior clinoid processes were almost completely eroded. X-ray examination of the gastro-intestinal tract was negative. Diagnosis rested between an intrasellar or an extrasellar tumor. The patient was told that if his eyesight became worse operation might be attempted. He was readmitted July 5th complaining of very severe headaches and requested operation. Exploratory craniotomy was performed on July 15th at which time a soft diffuse tumor mass was found arising from the right optic nerve. Biopsy alone was done and closure was effected. Subsequent microscopic examination showed the tumor tissue to be from an astrocytoma. He recovered satisfactorily from the operation and was given 850 r to each of 3 fields. He returned and was given a similar series beginning October 30, 1933; at that time he was very much improved; his eyesight was better, there were no headaches, and he was able to be up and around most of the time.

On January 18, 1934 he was seen in clinic. He was then feeling much better, was able to read the newspaper, and was working daily. In September examination showed only slight constriction of the visual fields. There were only occasional slight headaches, and the memory was much improved. His next visit to the out-patient department was in September 1935. At that time there was again noted marked improvement; his memory seemed normal, and he was working daily on his farm. He was again seen in March 1936 at which time he was entirely symptom free; visual acuity was 20/30 in the right eye and 20/30 plus 3 in the left; the fundi were normal except for slight haziness at the nasal margins.

He continued to be neurologically negative for the next year and a half. He was admitted to the hospital on September 16, 1937 with an abdominal complaint which examination showed to be due to a ureteral stone on the right side. Ophthalmoscopic and neurological examinations revealed nothing abnormal. A ureterolithotomy was done September 21, 1937 and the patient was discharged on October 5, 1937.

In November 1937 he was again seen in clinic and complained of bloating and some vomiting. Gall bladder x-ray was negative, and the patient was put on an ulcer regime similar to that which had been employed in 1932.

CEREBRAL TUMORS PROVED BY AUTOPSY OR BIOPSY

Type	Improvement No. Mos.	Improvement Degree	No. Months to Death or Months Living after Treatment
I. NO SURGERY			
Meningioma	38	1	D 51
II. TREPHINE ONLY FOR VENTRICULOGRAPHY			
Astrocytoma	24	2	L 27
III. X-RAY BEFORE SURGERY			
Hemangioendothelioma or metastatic malignancy	6	2	D 7
IV. DECOMPRESSION AND BIOPSY ONLY			
Spong. Multiforme	5	2	D 9*
Spong. Multiforme	3	3	D 4
Spong. Multiforme	2	1	D 3
Glioma; Indet. Type	28	3	L 28
Astrocytoma	61	3	L 61*
Astrocytoma	8	1	D 26
Astrocytoma	25	2	D 32
Local Encephalitis	10	1	L 46

The above chart is self-explanatory except for the 3 following cases which merit additional explanation. In the first case no surgery was done; the history and clinical course are described in the case representing first degree improvement. It seems unusual that meningioma should respond to irradiation and such reports are few. However, Dyke (15) states that cases of fibroblastic meningiomas may respond and de Luca (16) and Nordentoft (17) each report a case of a meningioma with multiple involvement which responded well for a 5 year period following X-ray therapy. There is also a case in our series in which a basal meningioma is suspected clinically and which showed a very good response following therapy. When first seen her chief symptom was frontal headache and disturbance of vision due to a marked unilateral exophthalmos. X-ray of the skull showed hyperostosis of the lesser wing of the sphenoid which was interpreted as due to an adjacent meningioma. The patient refused surgery and she is still living and in good condition 40 months after irradiation therapy. The one patient in the third group, where X-ray therapy was given before surgery showed marked improvement. In the fourth group, where decompression and biopsy alone was done because of apparent inoperability of the lesions, the first starred case represents a patient who received a course of irradiation treatment before surgery was performed. There was about a second degree improvement for a period of 2 months. At the end of this time a recurrence developed and surgery was done. The decompression procedure and another series of X-ray treatments were followed by similar improvement for an additional 3 months. The second starred case represents the patient described in the example for a third degree improvement. In this patient there was marked regression of symptoms following irradiation before any surgery had been performed.

Twenty-one patients were treated in this clinic in which the diagnosis of cerebral neoplasm was entirely clinical. These are also arranged in groups in the following chart to show possible clinical benefit from irradiation.

CLINICAL CEREBRAL TUMORS

I. Cases Positive Clinically, by Skull Plate and by Ventriculography; No Surgery Performed

Position	Improvement No. Mos.	Improvement Degree	No. Months to Death or Months Living After R/
Rt. Ant. Corpus Callosum	71	3	L 71
Rt. Frontal	2	1	L 18

II. Cases Positive Clinically, Skull Plate Non-Localizing; No Surgery: No Ventriculography

Rt. Frontal	72	3	L 72*
Basal Lesion	44	2	D 44
Mesencephalon	6	1	D 9
Left Third Ventricle	7	2	L 10

III. Surgery Consisting of Decompression and Exploration; Ventriculography Positive in 1, 3 and 4

Left Third Ventricle	4	2	D 37
Rt. Frontal	1	1	D 5
Rt. Temporal	1	1	D 3
Rt. Parietal	2	1	D 6
Left Frontal	1	1	D 2
Pontine	18	3	L 18*

The preceding chart is self-explanatory. The second patient in the second group was improved up to the time of death which was caused by pneumonia. There have been only 6 cases of proved cerebellar and 4 clinical cerebellar tumor cases treated here.

CEREBELLAR TUMORS

I. Those Proved by Biopsy

A. Decompression Plus Exploration

Type	Improvement No. Mos.	Improvement Degree	No. Months to Death or Months Living After Treatment
Glioma; Type Indet.	95	2-3	D 95

B. Decompression Plus Resection

Glioma; Type Indet.		3	Not Followed
Medulloblastoma with Spinal Metastases	12-20	3	D 20-24

II. Clinical Cerebellar Tumors

A. Decompression Plus Exploration

Case 1	7	2-3	D 10
Case 2	45	2	D 45
Case 3	56	3	L 56

Of the 6 cases of proved cerebellar tumors, 2 died during or immediately after treatment, and 1 died one month after therapy without improvement. As in the cerebral tumors, there was no reason to believe that irradiation was a contributing cause of death. The patient in division A of the first group was improved up to death, this being caused by carcinoma of the rectum. Of the 4 clinical cerebellar tumors, 1 was a very questionable diagnosis, had no surgery performed and died 2 months after X-ray therapy without improvement. The third patient in the second group is now 10 years old, is apparently completely well and is attending school.

It is better to present the 2 cases starred in the clinical brain tumor group separately since they may not be true cerebral neoplasms. They seem to belong to the type of cases which Dandy (18) has recently described as "Intracranial Pressure without Brain Tumor."

Position	Age	Clin.	Plain Film	Vent.	Mos. Improved	Surgery
Rt. Frontal	47	Pos.	Incr. Pr.	None	72	0
Pontine	24	Pos.	Incr. Pr.	Normal	18	D - E

It will be noted that in both the above cases the diagnosis was positive clinically. The plain film of the skull showed signs of increased pressure without localization. A ventriculogram was not done in one and in the other was entirely normal. Both showed marked improvement and are living at present, 72 and 18 months after treatment. No surgery was done in the first and a decompression only was done in the second. Dandy has reported 22 cases in which a clinical diagnosis of brain tumor was made which was not substantiated by ventriculography. All of these patients had symptoms indicating an increase of intracranial pressure. In each case this pressure had been demonstrated and measured by ventricular or lumbar puncture. All plain films of the skull in his cases showed signs of increased intracranial pressure without localizing signs of tumor and ventriculography in all revealed a normal ventricular system. Four cases in which the symptoms were minor were merely observed and no treatment instituted; these 4 gradually improved without treatment and may correspond to the first of the 2 cases listed above. This report of Dandy's is particularly interesting since it is evident that a certain number of brain tumors which have been diagnosed clinically but never verified by biopsy or autopsy may fall in this group where the symptoms and signs are an expression of pathological conditions and not of brain tumors. It is therefore possible that X-ray therapy was not a factor in the improvement in these cases.

Summary

Fifteen of the 24 brain tumors diagnosed clinically showed improvement for periods varying from one to 72 months. It is quite possible that all 15 were aided by irradiation. Unfortunately this cannot be verified. However, it is quite certain that improvement in 9 of the 15 was due chiefly to X-ray therapy. If the 2 cases discussed under the title, "Intracranial Pressure without Brain Tumor" are excluded the above number is reduced to 7; 5 of the 7 showed either second or third degree improvement.

Twenty-five of the 38 brain tumors proved by biopsy or autopsy showed clinical improvement. As in the group diagnosed clinically it is likely that irradiation played a role in all 25 although this cannot be ascertained. There seems to be fairly definite evidence, however, that the improvement in 9 of the 25 should be attributed chiefly or entirely to X-ray therapy. Of these 9, 6 showed either second or third degree improvement and 4 of this number are still living.

It is evident then that regardless of the controversies regarding the value of X-ray therapy in the treatment of brain tumors, there are certain cases in which remarkable responses are obtained following its application, and presumably due to its effect. At present it is the opinion in this de-

partment that the dosage used in cases of brain tumor should be materially increased. Recently we have begun giving fractionated daily doses over a period of a month resulting in a total dose of 5000 r. Until the results from more intensive irradiation have been tabulated it will be difficult to predict the results.

This group of cases has been accumulated over a 10 year period and were not treated by the author. The records were perused by myself at the suggestion of Dr. Wilhelm Stenstrom who, together with Dr. Wm. Peyton, kindly tendered much useful advice. The biopsies which were taken here were examined by either Drs. E. T. Bell, Wm. A. O'Brien, or R. W. Koucky and the surgery performed by Dr. Wm. Peyton.

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4. Consideration of Certain Radioresistant Tumors (Sarcoma and Carcinoma) with Case Reports

Cases, presenting an atypical clinical history, unexpected response to therapeutic measures, rare pathological entities, a clinical course with unusual findings and observations, are always worthy of record in some detail. In such a group we may well include the sarcomata, and especially the malignant forms of fibrosarcoma and the osteogenic type. As late as 1915 the percentage of 5 year recoveries in osteogenic sarcoma following amputation alone was very small, perhaps not over 2-4%. It was not until 1920 that an improvement was noted, probably largely due to early roentgenographic recognition of this condition, permitting amputation before metastases occurred.

Surgical references and literature do not present too optimistic a picture in the end results from surgical management of this condition. The summaries of the statistics of 5 year cures from the larger centers indicate a 5 year recovery from amputation alone varying from 10-15%. Meyerding (1) of the Mayo Clinic in a series of 100 cases of osteogenic bone sarcoma -- exclusive of giant cell tumor -- reports 15 cases with 5 year recoveries.

It is extremely difficult to evaluate any method of therapy where the end results are not more promising than in srcomata, especially osteogenic. So far there has been incomplete correlation of the cases, incomplete and often a last resort type of treatment with irradiation; combinations of surgery and radiation therapy in widely varying methods of application, dosage and sequence. Coley (2) even as recent as 1933 doubts if either the surgeon who refers patient for irradiation, or the radiologist, has any clear idea of the end results obtained in a large series of sarcomas treated by irradiation.

The establishment of the Bone Sarcoma Department at the Memorial Hospital in 1916 permitted careful study of the various problems relative to irradiation and the end results obtained in 200 cases of sarcoma of long bones treated by irradiation (x-ray and radium) up to 1928. In spite of the all but ideal results from amputation, they were forced to conclude in 1933 (3) that osteogenic sarcoma is too highly resistant to irradiation to justify its use exclusively in these cases. This same opinion was concurred in by Janeway, Prick of London, and Ewing expressed the same opinion at the International Cancer Congress in London in 1928, and Forssell (4) questioned the value of irradiation prior to or after amputation. They continued their studies in primary irradiation following 1928 in patients who refused operation, but at the time of above report they had not had occasion to change their viewpoint. They advocated the best treatment of osteogenic sarcoma of long bones to be immediate amputation following diagnosis (without preoperative irradiation), followed by a prolonged course of Coley's toxins. Under no conditions does Coley feel they are justified in waiting 4 weeks to amputate the limb on account of preoperative irradiation.

In 1931, Magnusson (5) reported the results from radiologic treatment in

cases of bone sarcoma at Radiumhemmet from 1910-1928, including 39 cases, all of which were inoperable either due to local extension or distant spread, and including 7 cases of Ewing's sarcoma. The ages of the osteogenic group varied from a month to 70 years, it was 2 times more common in males than females, and roentgen examination was done in 36 cases and microscopy in 26 cases. Of the 39 cases, 32 died as follows: died within 1 year to 3 years -- 25 cases of osteogenic sarcoma and 7 of Ewing's sarcoma, and of the 7 cases alive after 5 years -- 5 were definitely of the former type and have been symptom free 2-3-7 and 8 years. The average time interval from onset of symptoms to roentgen therapy was 7.2 months and to death was 12.0 months. All of the patients alive were operated upon, either for recurrence before radiation, following primary preirradiation, or followed by post-irradiation. It is impossible to determine the value of irradiation in these recoveries and to compare the cases to those of exclusive surgical treatment. In general, the 20 cases in which the effect of radiation on the tumor itself was observed, only one showed complete healing and there was a reduction in the size of tumor in 5 more, but the effects manifested themselves in increased calcareous content, sharper delineation of tumor margins (1 remained reduced and stationary for 2½ years then began to grow again rapidly). Though patients were far advanced -- even to point where irradiation had to be interrupted and often discontinued when only small doses had been given -- pain was well controlled, and patients felt better. In general the reduction in size of tumor and well being of patient was greatest where doses were largest -- up to 3½ SED on skin. No definite conclusions could be drawn as to choice of technique, massive or divided doses, single or multiple series and interval between series.

In 1920 the present Bone Sarcoma Registry of the American College of Surgeons was established and an exhaustive study and report of the data made by Kolodny (6) in 1927, and a more recent brief report by Bartlett (7). Kolodny summed up his findings by stating: "The wide-spread idea of the sanctity and invulnerability of the pathologic diagnosis was undeserved and the importance of the radiologic and clinical findings stressed to better results. The benignity of giant-cell sarcoma was established and its responsiveness to irradiation; the same also for Ewing's sarcoma which resembles histologically at times round cell sarcoma. The practical therapeutic handling of osteogenic sarcoma is about at the same stage as 50 years ago, malignant bone tumors are fatal and no therapeutic method of prevention is as yet known."

Bartlett, finding large amounts of chondromatous tissue in the material in all the 31 five year cures, questioned their truly typical osteogenic sarcomatous character. Hence he states the above does not indicate the real situation and we must continue to regard osteogenic sarcoma as incurable.

Coley (2) takes exception to Bartlett's view that the chondromatous character speaks for benignancy and maintains he has permitted the refinements of histopathology to run wild as all these cases had been studied by a large group of the Registry Committee. Coley feels as a large number of other investigators -- Holfelder (8) and Borak (9) -- that there is a great variation in the degree of malignancy, but our ability to gauge these variations depends far more on the clinical evidence than upon the histopathologic picture. Recently this has been emphasized anew by Coutard (10), also by Miller (11) and Stewart (12), who state that histopathology is not sufficient to determine radiosensitivity, but the anatomic location and the degree of sclerosing and differentiation play vital roles.

Phemister (13) in 1931 reported 5 cases of sarcoma that were treated with combined radiation and surgery from 1919-1925. All patients are living after 10-8-7-6 and 4 years respectively. Biopsy had been performed in 4 of these and pathologic fracture, following previous incomplete removal, resulted in one. They were composed of round and polyhedral cells with a small amount of loose connective tissue stroma. Their

location and histologic character would suggest that these sarcoma probably should be classified as belonging to the group of fibrosarcoma of the periosteal type. These may arise from the periosteum or surrounding soft tissues, involving the bone secondarily and in varying degrees. These also have varying degrees of malignancy, being less than the true osteogenic sarcoma, and including the relatively slowly growing fibrosarcoma to the rapidly proliferating and metastasizing round-cell, spindle-cell, and mixed sarcomas. At times the undifferentiated forms may be highly radiosensitive, but the permanence of the cure from irradiation cannot be accurately gauged at this time.

Ward (14) in 1928 published his results from radiation therapy in inoperable sarcoma at the Radium Institute of London. The report includes 30 cases of the various types of sarcoma, including a case of the very radiosensitive lymphosarcoma to the more malignant osteogenic sarcoma, distributed in practically every anatomical location of importance. He concludes radiation very valuable in relief of pain and symptoms and in prolongation of life with 11 cases living and well beyond 3 years (1 as long as 15 years) and 6 additional living and well beyond 2 years, and 4 beyond 1 year of which 2 have evidence of progression. Fibrosarcoma of the hypopharynx develop in the pre-vertebral tissues or vertebral periosteum, and are generally radio-sensitive. New (15) reporting 2 different cases concludes that irradiation, external and interstitial, is the method of choice as the surgical removal, if accomplished, is accompanied by extreme hazard of hemorrhage.

Prominent proponents of irradiation of sarcoma, including osteogenic sarcoma, are Pfahler (16), Holfelder (17) and Bloodgood (18)(19). Pfahler reports 58 cases in which 41 were confirmed by microscopic examination and the other 17 by their far advanced patho-anatomical condition. Sixteen cases of the 58 were treated with deep roentgen and radium radiation and in the 9 cases who died, death followed irradiation in 2 months to 7½ years. Of the 39 cases with histologic report 14 cases (35.8%) were symptom free for 1-10 years, while in the 17 cases far advanced, only 3 cases (17%) were recovered. He concludes that only irradiation itself is a criterion of radiosensitivity of sarcoma. Holfelder (17) in 1925 reported 5 year cures in 7 cases out of 25. Of the 25 cases, 16 lived more than 3 years, and the 9 more than 2 years. He feels the histologic study is chiefly for statistical purposes and concurs in Pfahler's viewpoint. In 1931 Bloodgood (18)(19) stated that he saw no objection to a course of preoperative irradiation 3-4 weeks prior to biopsy or amputation. A year later he emphasized this by stating that with our present knowledge it is better to begin every bone lesion which in the roentgenograph is suspicious of malignancy with a thorough and complete course of irradiation -- this in spite of his observation of occasional late unfavorable radiation effect on the bone and soft parts of the member.

Summation of Present Status

If high percentages of cures are considered, the large group of sarcomas does not make interesting reading, but we may recall that they include tumors of a very high grade malignancy which varies markedly for the same type of tumor upon its anatomical location. In general regardless of the origin (muscle, fascia, bone, they metastasize early and local recurrence is the rule so that 5 year cures from the different clinics are given as varying between 5-15%. The present therapeutic procedure advocated by most seems to be a combination of irradiation and surgery, but complete agreement is not reached as to the best method of procedure. Some surgeons continue to question the value of preoperative irradiation, and to a less extent the postoperative radiation. The current opinion seems to be toward a course of preoperative irradiation, followed by excision, amputation or disarticulation in 4-6 weeks and extensive post-operative irradiation 4-6 months later as shown by Pohle (20), Holfelder (17), Pfahler (16), Phemister (13), New (15), Ward (14), Magnusson (5), Bloodgood (19) and others. In the special group of osteo-

genic sarcoma the question of tumor devitalization and arrested growth by irradiation, permitting delay of 1-2 years or longer in the amputation or disarticulation of the diseased member, has been given considerable study. Some patients have survived 2 to 3 years after radiation therapy and amputation following prolonged preoperative radiation. Though the statistical data for 5 year cures are not better at the present, it should not discourage further study in this group as the most systematic radiation studies have been confined to hopeless and inoperable cases. There is ample support for the observations that the size of the tumor may be decreased considerably at times, even to render inoperable lesions operable -- at times this may be preceded by a temporary increase in size. Pain is much relieved, the patient's general health is improved, the tumor area more sharply defined, increased calcification in tumors is seen - at times decalcification early in irradiation.

No specific technique of irradiation has been definitely established for this group. Certain observations have been made which seem to serve as a guiding principle to the majority of radiologists in the irradiation of these tumors. The dose must be rather large, not less than 1-1½ SED delivered to center of tumor preoperatively, highly filtered rays, and use of numerous portals of projections. Surgery, if contemplated in the case, should be performed in 4-6 weeks later, followed by postoperative irradiation in 4-6 months. The first preoperative series of radiation should be large and the subsequent series gradually reduced. Ultimately a radiosensitive tumor will become resistant and metastases generally respond less favorably than the primary lesion, histopathology is of little value in determining radiosensitivity, only irradiation itself. In no group of malignancy is close cooperation between surgeon and radiologist more essential than in that of sarcoma and progress in the problem appears to depend upon this association.

There are appended 5 case histories of various types of sarcomas in patients treated at this hospital, showing unusual features and response. These serve to illustrate some of the principles set forth in the discussion of the very malignant sarcomas, not including the relatively benign, fibrosarcoma, lymphosarcoma, and the generally accepted radiosensitive giant-cell sarcoma, Ewing's sarcoma, myeloma and hemangioendothelioma of bone. The cases have all had microscopic examination of biopsy or surgical specimens, radiographic studies, and some special investigations. Based on the final hospital diagnoses these are: (1) 2 cases of osteogenic sarcoma -- one of left maxilla and the other right ilium and sacrum; (2) 1 case unclassified -- (fibromyxosarcoma) tumor of thoracic vertebrae (11-12th), not neurogenic, low grade malignancy radioresistant; (3) 1 case of neuro-sarcoma ("recheck-spindle cell sarcoma") of skull, neck posteriorly, cervical vertebra; (4) 1 case spindle cell sarcoma of pharynx.

Following the cases of sarcomata 2 case histories of patients with carcinoma are recorded to illustrate almost a utopia in therapeutic response in the hopeless and extensively involved lesions: 1 case -- adenocarcinoma of rectum, grade III, inoperable; the other case massive metastatic carcinoma involvement of the right cervical region, grade II, squamous cell-primary unknown.

Sarcomata Cases

Case History I

, age 15. Admitted 7-13-34; Discharged 7-15-34.

Final diagnosis osteogenic sarcoma, left maxilla (spindle-cell). Treatment: curettage, radium and deep X-ray.

P.I. 7-19-34. About one year ago had upper molar pulled which had given trouble for 1½ years. Cautery after extraction - healed very slowly. Three months later a cyst in area of cavity found. This was treated by local dentist until recently when she came to College of Dentistry where a diagnosis of osteogenic sarcoma was made.

Exam.

Swelling involving left cheek roundish about 6 cm. in diameter. Skin was brawny, hard. Involvement chiefly of maxilla but extending to some soft tissues. Only slightly tender; no mobility. Second left upper molar missing. Swelling in roof of mouth.

Therapy

Surgery - curettage of mass in jaw. Insertion of 15.4 mc. in 14 implants 0.3 mm. gold into and about mass - 2032 mc. hrs. Radium capsule - 50 mgm in cavity for 20 hrs. = 1000 mgm h.
Radiation: Radium - 2032 mc.hrs. seeds, plus 1000 mgm hrs. 2-25 mgm. tubes in pack in cavity. - See under surgery.
Deep X-ray:

1st series:-Left lateral cheek, 3 treatments July 24, 26, 28, 1934 - 120% S.E.D., 935 r,

2nd series:-Left lateral (maxilla) cheek 3 treatments January 26, 29, 31, 1935, 130% S.E.D. Factors: 200 Kv., H.V. - 0.83, S.T.D. - 60 cm. 1300 r

Follow-up Notes

1-10-35. Lesion much reduced in size. Pathologist reviewed slides and again called it osteogenic sarcoma.

X-ray report: Considerable improvement over film taken in July 1934. Cyst has disappeared. Considerable new bone present. More therapy indicated.

1-22-35. Patient states lesion is still getting smaller. Advise more radiation.

3-7-35. Slight enlargement - less than on 1-22-35. Patient in excellent condition. Has noticed improvements since last series of X-rays.

12-9-36. Patient in good condition, no swelling, no signs of recurrence.

12-20-37. Patient in good condition and working.

Case History II

____ age 23. Admitted 12-18-34; Discharged 1-2-35.

Final Diagnosis

Osteogenic sarcoma of right ilium and sacrum (spindle cell type) with some giant cells?

Treatment

Deep X-ray therapy.

P.I. 12-18-34. Onset of present illness is not clear-cut, seems to be about 2 years when she began to have dull irritating, variable pains in the region of right hip and ilium. Pain progressed and later a mass was discovered growing in region of right ilium. Patient consulted an osteopath who treated her for sacro-iliac strain without relief. Patient consulted local physician for condition.
Surgery - only biopsy - tumor extensive - much bleeding. 11-28-34 wound packed for hemorrhage.

Pathology report:

Osteogenic sarcoma - spindle cell type, ilium and sacro-iliac right, some giant cells - some soft tissue involvement.

Radiation Therapy

Came here for deep X-ray. 1st series 9 treatments - 12-18-34 to 1-2-35 to anterior-posterior and right lateral pelvis, 120% S.E.D. to anterior-posterior and 50% S.E.D. to right lateral - 2075 r. 2nd series: 6 treatments - 4-5-35 to 4-17-35 to anterior and posterior pelvic fields; 130% S.E.D. to each field - 1850 r. Factors: 200 Kv. - H.V. 1.3 - S.T.D. - 70-60 cm.
X-ray reports -

9-24-34. Slight involvement of both sacro-iliac joints, especially the right which shows slight destruction of the joint. Congenital defect laminae 1st sacral. No other evidence of pathology.

Conclusions: sacro-iliac arthritis bilateral chronic, congenital defect.

Follow-up Notes

Improved - less pain at time of discharge.

5-27-36. Mother informed us that patient is in good condition - still a little nervous - not quite so strong as usual. Recent films show no sign of sarcoma and the bone has been healing considerably. Patient permitted to exercise.

10-7-36. Patient in good condition, slight amount of pain. At lake this summer, swimming and taking other kinds of exercise.

5-14-37. Patient still in good condition. No pain - films show bone filling in. Patient has menopausal symptoms.

9-24-37. Patient in good condition - still nervous.

11-27-37. Patient in good condition, mental attitude improved.

(Note: swelling over right joint area tender - local heat).

11-17-34. Extensive eroding process involving right wing of sacrum extending toward midline - much bone destruction also in region of right sacro-iliac joint near crest of ilium and sacrum. Re-examination of films 9-24-34 (see above) shows same process there at earlier stage. Whole appearance suggests strongly tumor arising in soft tissues and secondary erosion of sacrum, rather than bony tumor due to absence of bone reaction and character of erosion. Possibility of osteomyelitis with abscess; erosion of base cannot be excluded entirely.

Conclusion: Probable soft tissue tumor eroding sacrum on right side.
11-13-34. Much the same discussion. But rather thinks of bone tumor primary - as medullary type of sarcoma of sacrum.

12-27-34. Same as above but thinks only biopsy can determine type of tumor. Not possible roentgenologically. Also biopsy to determine radiosensitivity.

3-23-35. Marked regression of malignant tumor of sacrum. Chest negative to pathology.

7-23-35. Progress satisfactory. Bone filling in. Tumor appears definitely radiosensitive.

Case History III

, Age 55. Admitted 8-9-32;
Discharged 9-29-32.

Second admission 2-23-33;
Discharged 3-9-33.

Final diagnosis

Tumor unclassified - spinal cord - 12th thoracic vertebra. Laminectomy. Deep x-ray therapy.

P.I., 8-31-32. Resume.

About 1½ years ago patient noted stiffness and pain in her back and legs, knees, calves and ankles. This was accompanied by marked weakness so that a cane or chair was needed to assist in walking. About 1 year ago patient became very weak and severe pain in sacro-iliac region when sitting up. Had to take to bed care. These findings were progressive until admission to hospital.

Examination - Physical

Negative except for extremities:- touch sensation - absent below Poupart's ligament - 4th lumbar vertebra. Pain sensation on deep pressure of Achilles tendon or calf muscles. Superficial pain sensation absent to both dull and sharp stimuli (below 4th lumbar vertebra. Babinski + bilaterally. Position sense absent (big toe position testing) Knee jerks - marked hyperactive. Clonus + present - ankles. Patellar tendons. Deep sensibility. Paralysis almost complete in lower extremities (slight ability to move legs).

Vaginal examination - firm rounded mass to right of corpus uteri - this seems to arise from ovarian region and probably calcified ovary. Does not suggest malignancy.

Laboratory studies

Urinalysis negative. Blood - hemoglobin 86%, red blood cells 4,300,000, white blood cells 7,400, polymorpho-

nuclear 73%, lymphocytes 23%; Wassermann (blood - spinal fluid) negative. Spinal fluid negative. Nonne +; Noguchi +, clear, colorless.

X-ray Report - 8-10-32

12th thoracic vertebra distinct evidence of destruction and partial compression, destruction more marked in anterior portion of body but some compression of spinal canal may be present. Appearance suggests primary tumor of vertebral body with secondary involvement of canal rather than primary cord tumor because posterior margin is not particularly encroached upon. This might be metastatic but no other evidence of metastasis is present. Marked hypertrophic changes throughout the whole spine. Chest film - no definite evidence of pathology. Conclusion: Probable primary tumor - 12th thoracic vertebra.

8-15-32. No metastases to bones of pelvis and spine - lumbar, much arthritic hypertrophy of 4th and 5th vertebra. Osteoporosis of bones of pelvis. Calcified area in right side of pelvis over the sacrum. Negative skull - possible calcified ovary. Cervical spine - negative.

Surgery

8-31-32. Incision from 5-6th thoracic down to 2nd lumbar laminae of 9-12th thoracic vertebrae removed exposing tumor infiltrating the cord and out into soft tissues of region. Tumor extended from 10-12th thoracic vertebrae.

Biopsy: Frozen section - undifferentiated connective tissue tumor - fibromyxosarcoma. Tumor involved dura, cord only minimally - extensive compression of cord. Probably radioresistant from appearance in frozen section.

Radium - 50 mgm. in form of needles was implanted along the cord - 6 needles on left side, 3 needles on right side. About 1-1½ cm. apart. Radium to be left for 55 h. = dose of 1750 mgm hrs. Acacia solution 6% 500 cc. given on table. Blood pressure drop to 85 after transfusion up to 120.

Pathological report

Extreme variability in tissues removed. Same areas of dense fibrous tissue. Others polymorphonuclear infiltration, others with plasma cells, and other chronic inflammatory tissue reaction. Areas of loose reticular tissue, and others of tumor tissue. Tumor cells noncharacteristic of any tumor; type of low malignancy with moderately sized cells of light chromatin network.

Conclusion: Unclassified tumor - spinal cord - not neurogenic; low grade malignancy - suggesting poor response to radiation.
Deep radiation during convalescence. Slight staphylococcic infection of wound.

Radiation therapy

Radium (see surgery)

50 mgm in needles (6 needles 5 mgm on left side of cord in wound) about 1-1½ cm. apart
(3 needles 5 mgm on right side of cord in would (about 1-1½ cm. apart

Deep x-ray series:

1st series - 4 treatments anterior and posterior thoracic and upper lumbar spine 9-21, 22, 26 and 28-32. 110% S.E.D. to each portal - 1700 r.

2nd series - 4 treatments anterior and posterior thoracic and upper lumbar spine 2-24, 27 and 3-1, 3-33. 100% S.E.D. to each portal - 1300 r. Factors: 200 K.v. - 70-60 cm. H.V.l.3

Follow-up Notes

9-29-32 - Date of discharge - shows some improvement though slight - able to lift right leg off bed 8 inches and right 2 inches. Flexes thighs easily. Same sensory improvement. In general slight improvement.

1-13-33. Report Dr. Sarff.
No discomfort for 2 months-function gradually improved at present - no impairment in movement, able to stand for some time - now trying to

walk - delayed by weakness - but rapidly improving. Impaired sensation now limited to slight tingling and numbness, differentiates pain, thermal and light touch. General health excellent.

3-7-33. In for recheck - unable to elicit any objective or subjective sensory disturbances. Biceps - + bilateral; abdomen reflexes absent; knee - ankle jerks increased. Babinskis improved - able to walk little with some help - only complaint, low grade pain in hip. Advised another series of deep therapy.

X-ray 2-24-33 - spine thoracic - improved since previous x-ray due to radiation - less destructive.

1-13-37 - Letter from physician - not seen for 2-3 months - but then doing very nicely - no complaints since to my knowledge.

Case History IV

, Age 63. Admitted: 8-10-36; Discharged: 8-24-36.

Final Diagnosis: Neurosarcoma (neck posteriorly, skull, cervical vertebra).

P.I., 30 years ago patient was knocked down while sawing wood, receiving a blow from a log on the back and on right side of neck below skull. A tumor mass formed, remained freely movable at first, later fixed somewhat, progressively enlarged. 1st removed 9 years after onset - weight 3½ lbs. - incompletely; removed again 15 years after onset incompletely. After this operation shoulder dropped - not good functional use.
3rd: removed again 20 years after onset - incompletely.
4th: removed again 2 years ago (1934). About 1 year ago the tumor again removed, growing somewhat more rapidly and is painful at times, neck somewhat fixed and limited in rotation. Associated with this gait disturbances began 5-6 years ago. 2 years ago apparent difficulty in understanding what is said. Hearing decreased on right side. Normal on left side. Staggering gait if he tries to walk rapidly. No headaches. No visual disturbances. Slight weight loss - 10 lbs. 2 years.

Laboratory

Wassermann negative - Sputum - negative for tubercle bacilli; Mantoux test 3-18-37 2+. Family history: Father died of cancer. Mother died of cardiac condition. 1 brother pulmonary tuberculosis.

Physical Examination

Slight tilting of head to right side. On right side a large tumorous mass - nodular, firm, extending behind ear - backward up over occiput and down cervical region and anteriorly to beyond sterno-cleido mastoid muscle, fixed. Covered by old scar. Neck not palpable. Mass 10-12 cm. x 9 cm.

X-ray reports

Skull - destruction inferior portion right occiput and posterior margin right mastoid process + arch of 1st cervical vertebra. Suggestive of invasion from external soft tissue mass.

Conclusion: Malignancy ; soft tissues, involving occiput and arch of 1st cervical vertebra.

10-26-36 - Skull (3 weeks after last deep x-ray treatment) Slight regeneration base defect in occiput. Cervical vertebra indefinite. Large defect still remains.

2-8-37 - Skull - cervical spine and chest (4 mo. past last deep x-ray treatment). No particular improvement in defects in occiput and cervical vertebra. Chest: extensive fibrosis right upper lobe with thickening of interlobar pleura + shrinkage of lobe. Area of infiltration in middle of right lung with cavity within it. This does not suggest metastases, but long standing inflammatory process may be an atypical tuberculosis with recent lesion left upper lobe apex. Advise reexamination 1 month.

3-2-37 - Chest: right side findings have cleared considerably, suggesting this is an acute lung abscess. Right side almost complete consolidation of upper lobe with some retraction of lobe. Conclusion: Atypical pneumonia -

does not suggest metastases.

4-29-37 - Chest: Considerable resolution in right lung - restored to condition present 2-8-37. Right side cleared completely.

Conclusion: An atypical inflammatory process, varying from time to time. L.R.

6-17-37 - Chest: Same as on 4-29-37.
12-16-37 - Improvement - right upper lobe.

Surgery
8-18-36 - Highly vascular tumor - large veins leading to it. Biopsy taken. Biopsy: HO-36-2638, extremely cellular type with large number of mitotic figures - with areas suggesting rudimentary nerve tissues, lesion appears extremely invasive and proliferative.

Diagnosis: Neurosarcoma.

Review of section - due to x-ray therapy response: sarcomatous nature because of rapid growth - origin undetermined. Neurosarcoma diagnosis only an assumption, at present only change in diagnosis - call it spindle cell sarcoma, grade IV.

Augmented X-ray Therapy

9-1-36 - 10-3-36 - 28 daily treatments: 20 treatments alternately to anterior and posterior cervical region - 25% each treatment = 200% S.E.D. to each field - 3000 r.

8 treatments alternately to left and right lateral face and cervical region 25% each treatment = 100% S.E.D. to each field - 1500 r. Factors: 200 K.v. - H.V. - 0.83 - S.T.D. - 60 cm.

Progress

Improved rapidly for 1 mo. after radon treatment and slowly for 1 year.

10-26-36 - marked regression of tumor mass.
12-7-36 - good response to x-ray therapy - regression complete.

2-8-37 - no evidence of recurrence - skull defect palpable. Patient feels improved - has gained weight. Think tumor area still receding.

4-1-37 - Continues improvement.

6-17-37 - Complete regression of lesion. Very little fixation of overlying skin. Patient in excellent general health. No complaints. No pain. Pain severe during treatment - began to regress 3 weeks after last treatment. Continued for 1 year.

12-16-37 - Remarkable response for spindle cell sarcoma. History of 29 years duration.

Case History V

_____, Age 34. Admitted: 3-15-37; Discharged 3-18-37.

Final Diagnosis: Spindle cell sarcoma of pharynx.

Treatment: Pharyngoscopy and radon implantation.

P.I., About 2 months previously patient had a bad coughing spell when a small piece of tissue and some blood was raised. Patient had slight pain in the region of right side of throat near tonsillar area and base of tongue. There had been no other symptoms as dysphagia - voice or throat changes, etc. Physician had removed small tumor from pedicle incompletely, which was said to be reported as sarcoma. In hospital here 3-17-37. Thinking sarcoma resistant, a complete excision was attempted and apparently done; base of tumor was found at lower pole of tonsil near posterior pillar. All edges cauterized with coagulating endotherm point. (Flat button-like reddish flattened tumor mass).

Pathological report
HO -37-706 - No evidence of tumor present. Patient sent home 2 days later.

Pathological report
Slide 37-4130 - 3-4-37 (Mass sent in by local physician) to E.T.Bell. Spindle cell sarcoma (Recurrence certain though attached by pedicle. Or-

dinarily not radiosensitive).

12-3-37 (Recurrence - small amount of time).

Biopsy: HO-37-3630. Too small for positive diagnosis but it conforms mostly to that group of tumors, including lymphosarcoma, Hodgkin's, leukemia.

12-4-37 (General anesthesia - laryngoscope - tumor larger and more extensive and infiltrating than apparent on inspection. (Surgery apparently only hope).

X-rays: Cervical spine - negative.

Surgery: 3-17-37 - cautery and endotherm removal of local tumor tissue. No evidence of recurrence until after July, 1937.

12-8-37 - Attempted removal of recurrence - too extensive.
Radon implants: 13 seeds of 0.7 or 0.8 mc. about tumor tissue.
Radiation: 12-8-38 - Radon seeds - see surgery above: 10.1 mc. in 13 implants = 1340 mc hrs.

Follow-up Notes

Nov., 1937 - Recurrence now small. Not seen 7-26-37 when in Out-patient.

1-6-38 - Very much improved since therapy with radon.

2-4-38 - Seen in Tumor Clinic. Looks good. Only scar from radon seeds remains.

Carcinomata Cases

Case History VI

____ Age 36. Admitted: 5-28-33; Discharged 6-27-33.

Final Diagnosis
Inoperable carcinoma (adenocarcinoma Grade III) rectum.
Biopsy: Proctoscopic.
Exploratory laparotomy - permanent colostomy.
Deep x-ray - radium implants.

P.I., Pain in lower abdomen with menses since onset of menses in 1910. Pain is in the back, on defecation during menstruation, pressure sensation in epigastrium for 1 year., emesis during menstruation for 1 year. Mild constipation for several years but severe for past year, but during menstruation always diarrhea for 4-5 days. Appendectomy 12 years. In 1932 - on 5th left oophorectomy and salpingectomy were done with no relief. No blood or mucus. Pain has required morphine sulfate for relief. Menses - onset age 14 years - regular every 30 days. Loss of 10 pounds weight last year. Appetite fair. No pregnancies.

Examination
Well-developed - somewhat emaciated - general examination essentially negative. Rectal exam - about 6-8 cm. from anal orifice is a fixed, firm mass on anterior rectal wall with suggestive fixation to right pelvic wall and anteriorly to pelvic viscera.
Bimanual exam - Uncertain diagnosis - advise exploratory laparotomy with removal of uterus. Possible myoma of uterus - infiltrating on right into broad ligament.

Laboratory examination
Hemoglobin 86%, white blood count 8,300, with normal differential. Blood chemistry normal. Wassermann - blood and spinal fluid negative. Urinalysis negative.

X-ray
Intravenous - Pyelogram - negative except displacement of bladder. Colon probably negative.
Chest: bilateral pulmonary tuberculosis; fibrotic - inactive - no metastases. Thorotrast negative for metastases.

Surgery
Preoperative diagnosis: Carcinoma of rectum.
Left McBurney incision - explored - at junction of rectum and sigmoid a hard mass was palpated - adherent to uterus - left pelvic wall - on right side -hard mass - lymph node indicating extension of tumor beyond rectal wall - resection not indicated. 9 radon seeds implanted about lesion through abdomen wound. Pelvic colon brought out through incision - left just below skin - future

colostomy if more obstruction. In lithotomy position, additional 9 radon seeds implanted into tumor through rectum. Total radon - 18 seeds 0.3 gold implants of 1.6 mc. each. Total dose 3800 mc hrs.

Rectal biopsy - Adenocarcinoma, grade II.

Radiation

X-rays - 1st series 6 treatments - anterior and posterior abdomen - 6-29 + 7-1, 5, 7, 10-33 - 85% SED to each field (100% + in) - 1225 r.

2nd series - 6 treatments - anterior and posterior abdomen and pelvis - 9-8, 11, 13, 15, 18, 20-33 - 120% SED to each field - 1700 r. Factors: 200 K.v.; 70-60 S.T.D.; H.V.l.3

Radium: June 14 (9 radon seeds of 1.6 mc. each through abdominal wound)
(9 radon seeds of 1.6 mc. each through rectum)

Total - 3800 mc hrs.

(34.5 mc. in 21 - 0.3 m gold implants)

Follow-up

8-24-33 - Very good result following radiation. No symptoms except when certain foods give rise to disturbance patient calls "gas pains." Bowel function normal. Only small mass palpable behind cervix and fixed to it. No ulceration. Probably persistence of carcinoma. Not fixed to pelvic wall. Gained 7 lbs. in weight.

10-17-33 - Small mass in right side of pelvis - main lesion seems well fared for.

11-7-33 - Patient's general condition good - gaining weight - no complaints - some fixation anteriorly though tumor is movable - marked regression.

5-9-34 - Letter from patient - feeling fine - gaining every day, eats everything - no pain for long time - weight 124 lbs. (Only 83 when admitted).

12-4-34 - Letter from patient - feeling just fine, weight 127 lbs.

8-26-35 - Feel just fine - eat everything - weight 131 lbs.

3-13-37 - No complaints - symptoms all gone since above note in 1934. And examination now about same as above.

3-23-38 - Letter from patient - "I enjoy good health, take long walks, eat anything, weigh 143 lbs. University Hospital did wonders for me. I am well and have been for 4 years."

Case History VII

____ Age 50. Admitted: 9-8-37, and Discharged.

Final Diagnosis

Neck tumor - metastatic carcinoma. Primary? Squamous grade III. Excision - Coutard x-ray series treatment - radon implants.

P.I., Patient first noticed swelling on right side of neck - below posterior border of angle of mandible. About July, 1937. Its size in area, i.e., circumference, has not changed but it has grown outward from surface ½ of present size in first 7-10 days, and since then a steady, slow growth, especially in the last week to 10 days before admittance to hospital. No tenderness - very firm - but only pain is usually around ear and when he lies on left side and on ear.

Mass - physical findings - lesion: large firm and hard mass lying below and extending back of and below right ear and upward to mastoid tip. It is not attached to bone or overlying skin, seems to spring from deeper structures. About 9 x 6 cm. borders are well delineated and mass seems to extend below sternocleidomastoid muscle.
Clinical impression: probable neurosarcoma.

Laboratory

Wassermann negative, white blood cells 6,000, differential: polymorphonuclears 74%, lymphocytes 26%; X-rays: Skull - chest - G.I. study - colon — all negative to pathology.

Surgery: September 13, 1937:

Intertracheal ethylene reinforced with ether. Incision along anterior border of sternocleidomastoid muscle; tumor attached to muscle, to internal jugular vein - digastric muscle, thyroglossus and hypoglossus muscles. Several nerves course through tumor - mass itself extended deep into pterygoid fossa. Incomplete removal - (surgically - not possible - vital structure) - blood points tied with silk - skin with clips. One Penrose drain.

Pathological report

Metastatic squamous carcinoma, grade III, slide HO-37-2786 (most of tumor produces keratin and graded II - but portions undifferentiated).

Radiation treatment

1st series: 120% S.E.D. to each of 3 fields (anteroposterior and right lateral) in 18 treatments from 9-24-37 to 10-16-37 - 2700 r - daily treatments 20% S.E.D. each treatment. Radium - 1-10-38 (396) in 3 small gold 0.3 mm. implants about small gland at lower angle of incision.
1-17-38 (2030) in 15.4 mc. in 14 implants - 0.3 mm. gold - about mass in right parotid region and lower lobe of ear. Factors: K.v. 200; 60 cm S.T.D.; H.v. 0.83.

Follow-up Notes

9-30-37 - After reaching boarding house, fell unconscious to floor - remained so for 5 minutes (slight jerking at this time). Brought to hospital. Clinical impression - apoplexy - or bleeding into malignancy metastasis.

10-7-37 - Findings of right side involvement of 5, 7, 9, 11 and 12 cranial nerves on right side. Left knee jerks +, greater than right. Points to lesion right mid-pons extending to lower part of medulla. No choked disc (blood pressure normal). Patient may expire suddenly due to bulbar palsy. Notify family. May mean metastasis to brain.

12-23-37 - Paralysis of right vocal cord.

1-24-38 - well regressed lesion - except some pain in right side of neck (considerable fibrosis).

2-3-38 - Wound dressed, practically healed - very little drainage. Less pain.

2-17-38 - Wound healed well - very slight drainage.

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