

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

Roentgen Therapy

I. LAST WEEK

Date: May 13, 1937

Place: Recreation Room
Nurses' Hall

Time: 12:23 to 1:45 P.M.

Program: Movie: Sky Harbor

Abstract: The Present Day
Status of the
Vitamins

Present: 128

Discussion: Marguerite Booth
A. E. Hansen
L. S. Palmer

II. MOVIE

Title: Barrac's Night Out

Released by: M-G-M

III. DEPARTMENTAL REPORT

ROENTGEN THERAPY

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1. Introduction

Last year a report from this department was made at a Staff Meeting on April 30th (Vol.VII: 26: 296-312, (Apr. 30) 1936). The equipment available here was then enumerated. It has not been changed appreciably since. Fairly complete statistics concerning patients treated with roentgen rays and radium were given and, therefore, just a few tables will be presented at

this time. The modern developments in radiation therapy were also discussed last year. It was emphasized that proper time distribution of the dose is of special importance in many instances. The dose can be given in a single treatment, in repeated treatments, or in fractional treatments. The fractional treatments can again be divided into four groups. They can be given in short time (about a week) with high intensity, in short time with low intensity (protracted 2 to 5 r per minute), over a relatively long time (3 to 6 weeks) with high intensity and over a long time with low intensity. The fractional treatments distributed over a long time seem to give better results in some of the more resistant types of malignancy. We have therefore been using this method to an increasing extent. As the high voltage machine has been used to full capacity for several years it is evident that the number of new patients per year had to be somewhat reduced. It is, however, very difficult to refuse to treat a patient after a request for roentgen therapy has been received. The unfortunate situation has resulted in treatment delays and patients often have to be scheduled 2 to 3 weeks after the request arrives. The low voltage therapy is given immediately.

The following tables give a comparison of the number of patients treated and the number of treatments administered during the last 5 years. The first full year (1927) of high voltage therapy is also included for comparison.

TABLE I

Patients Treated with 200 kv. Roentgen Therapy

Comparison of Number of Cases and Number of Treatments per Year.

<u>Year</u>	<u>New Patients</u>	<u>Total Series</u>	<u>Total Treatments</u>	<u>Average Treatment per Series</u>
1927	266	417	1686	4.0
1932	563	868	4206	4.8
1933	604	945	4543	4.7
1934	645	925	4930	5.3
1935	694	1008	5511	5.4
1936	602	878	6441	7.3 (Note Change)

TABLE II

Patients Treated with 100 kv. Roentgen Therapy

<u>Year</u>	<u>New Patients</u>	<u>Total Treatments</u>
1932	543	1516
1933	615	1715
1934	572	1643
1935	611	1812
1936	593	1818

The major diseases which have been treated with 200 kv. therapy are listed in Table III, and the number of patients in each group is given for July 1, 1926 to December 31, 1936 as well as for the single year 1936. Table IV is a similar table for 100 kv. therapy.

TABLE III

Patients Treated with 200 kv. Roentgen Therapy
Between July 1, 1926 and December 31, 1936

Comparison of Number of Cases by Disease

<u>Disease</u>	<u>Total</u> <u>Number</u>	<u>1936</u>	<u>Disease</u>	<u>Total</u> <u>Number</u>	<u>1936</u>
Carcinoma	2800	57%	342	58%	
Breast	296	47	Hodgkins and		
Cervix uteri	511	66	Lymphosarcoma	237	17
Lip	332	36	Sarcomas	163	17
Prostate	216	44	Leukemias	133	16
Skin	158	8	Brain tumors	85	13
Rectum	143	3	Mixed tumors	67	4
Cheek, alveolus	124	13	Ocular tumors	55	12
Corpus uteri	109	18	Miscellaneous tumors	269	67
Ovary	93	17			
Bladder	89	14	Gynecological bleeding	359	67
Tongue	77	12	Thyrototoxicosis	299	46
Kidney	72	9	Tuberculous glands	95	8
Lung	48	8	Infections	59	8
Antrum, sinuses	36	3	Thymic enlargement	30	3

Table IV gives the number of patients treated per year for each of six groups of carcinoma. Some reduction (during the last 3 years) had to be made in the number of patients accepted for treatment. Prophylactic post-operative treatment of carcinoma of breast and lip has been limited to cases with metastatic nodes. This is one reason why the figures have fallen off. Carcinoma of

the rectum is now being treated as far as possible by surgery only. A reduction in numbers of certain types of carcinoma does not necessarily mean that roentgen therapy is considered inadvisable. The main reason is that the present equipment is inadequate for our needs and it has been necessary to exclude those patients who could be reasonably treated without roentgen therapy.

TABLE IV

Comparison of Number of Cases by Year for Six Types of Carcinoma

Carcinoma	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936
Breast	17	34	23	42	55	66	76	90	75	71	47
Cervix uteri	6	27	28	30	51	51	51	66	70	65	66
Lip	7	6	18	24	20	29	36	46	52	58	36
Prostate	0	10	3	15	16	21	25	25	23	34	44
Skin	6	11	18	14	14	14	10	31	18	14	8
Rectum	8	4	7	9	15	13	31	22	13	9	3

Last year a brief statement was made concerning the indication for treatment and the result to be expected for the major diseases listed. Since that time a more complete study has been made of carcinoma of the lip by Dr. Abraham, of carcinoma of the prostate by Dr. Friedell and a brief summary of these investigations will be reported here.

An attempt is now being made to treat bronchiectasis and a short statement concerning these treatments is therefore made. An example of the use of fractional treatment is also given. The particular value of roentgen therapy for Hodgkins disease and for lympho-epithelioma is brought out by some case reports. These reports have been prepared by Dr. Jensen.

2. Irradiation Therapy of Carcinoma of the Prostate.

It has become apparent in the past several years that carcinoma of the prostate is becoming more and more a radiologic problem. Prostatic cancer presents a difficult problem and many urologists believe that the control of this disease is quite impossible. Nevertheless, certain investigators have

become convinced that a considerable measure of regression of the tumor and alleviation of symptoms may be provided by means of properly instituted therapy. Barringer (Memorial Hosp. N.Y.) in a report before the Congress of the American College of Surgeons in Nov. 1935, stated that irradiation offered the only means for control of these difficult cases. He stressed particularly the combination of X-ray and interstitial irradiation. The treatment outlined by Barringer consisted of interstitial and external irradiation administered simultaneously. The roentgen therapy was given over a period of 30 days. Five portals were used about the pelvis and about 1,500 to 1,900 r delivered to each of these areas. Interprostatic irradiation was carried out by means of radium. Removable, gold screened radium needles were inserted through the perineum (if posterior lobe alone was involved) and 1,500-1,800 mc.-hrs. were given every 2 months until the prostate appeared under control. When the lateral and median lobes were involved, suprapubic insertion of radon seeds was the treatment of choice. The seeds having a strength of 1.5 mc. were inserted regularly about the lobes throughout each cubic centimeter of prostatic tissue. Homogeneous distribution of the interstitial irradiation

is a very important factor for optimum effect on the tumor. With this object in view, Ferguson described a seeding instrument which is introduced after cystotomy and the radon implanted from above. The instrument engages in the prostatic urethra and permits regular definite spacing through cylinders which guide the loading device.

Selection of Therapy

Young was able to select but 35 out of 500 cases of carcinoma of the prostate for radical resection, and of these 35, only 8 survived 3 years or more. In Young's series, only 7% were suitable for surgery and 93% were left for some other form of amelioration? Irradiation therapy promised some control in these cases, but it was shortly recognized that cancer of the prostate, highly radio-resistant for the most part, would require a heavy dose for definite regression.

Barringer found that about 80% of prostatic cancers required 10-12 threshold erythemas, delivered throughout the tumor, to produce complete destruction; whereas 20% could be controlled with smaller doses, (7-10 erythemas). It is impossible to introduce a dose of this magnitude externally and some form of interstitial irradiation must be used. External irradiation, in most instances, provides considerable regression in size, retardation in growth, and marked clinical improvement, but complete arrest cannot be expected.

At the present time, in the roentgen therapy department at the University of Minnesota Hospitals, a technique is used which is designed to introduce about 4 threshold erythemas into the prostatic area by external irradiation alone, over a period of 4 weeks. Four to six portals are used, depending upon the size of the patient. About 1,100-1,400 r are given through each portal over the 4-week period. Ferguson, in a study made in 1932, divided his cases into 2 groups for irradiation therapy.

Group 1 - Palliation only objective

- a) Prostate 5 cm. in diameter

or more

- b) Presumptive or positive evidence of metastases present

Group 2 - Suitable for radical irradiation therapy

- a) Prostate less than 5 cm. in diameter

- b) No demonstrable metastases

For the first group, palliation may be provided by external irradiation alone, supplemented with any surgical procedure necessary to relieve obstruction. In those cases in which the disease shows slow progress and the patient is in good condition, interstitial irradiation may be added.

Effects of Irradiation Therapy

In an attempt to correlate dosage with histologic change, Ferguson found that .8 SED (threshold) was necessary if any change was to be noted. Less than this had no demonstrable effect. Dosage in excess of this, but less than 1-5 SED produces changes in some instances, but not in all. Changes consisted of endarteritis, areas of fibrosis, and areas of hyalinization. Permanent modification of the tumor cell was not observed. Dosage in excess of 1.5 SED (threshold), but less than the lethal dose as described above, showed fairly marked fibrosis in every case, although all the tumor cells did not exhibit permanent lethal changes. There was marked karyorrhexis and karyolysis in a considerable number of the cells.

Clinical Classification

In order to evaluate results of therapy in cancer therapy in cancer of the prostate, it is essential that an attempt be made to classify the type of case treated. Ferguson has attempted to provide a clinical index to apply to cases of prostatic cancer in his series.

Index Factor	Group A (Least Malignant)	Group B	Group C (Most Malignant)
1. Age	Over 65	55-65	Under 55
2. Residual urine	200 cc	100-200 cc	Under 100 cc
3. Duration of symptoms	Over 20 mo.	10-20 Mo.	Under 10 Mo.
4. Extent of disease	No pain or metas.	Pain, no metas.	Pain and metas.

Life Duration of untreated cases:

Group A - 30 months to many years
 Group B - 18 months (average)
 Group C - 6 months (average)

Histologic correlation with this clinical index was attempted, and for the most part was significant. Ewing has stressed the fact that the clinical course is closely dependent upon the structural type.

Group A: A typical adult celled carcinoma with definite alveolar arrangement was noted often on previous benign prostatic hypertrophy.

Group B: Carcinoma was frequently superimposed on a chronic interstitial prostatitis. The tumor was highly invasive, lost its glandular arrangement early, and tended toward anaplasia. Direct extension occurred early.

Group C: On histological examination, the tumor appeared to be small celled, highly cellular, anaplastic and fairly diffuse. As a rule, no previous hypertrophic changes were noted. The perineural lymphatics were involved early in over 50% and frequent cellular thrombi were noted in the veins.

It is noted that a preponderance of any of these groups in a series of cases will provide a considerable diversity of survival statistics in various series. For this reason, until more definite criteria are established and larger series

studied, the clinical progress may be more significant than the survival rate. Wolff observed that 39% of his autopsied cases showed less than one year survival, while 24% lived 3 years or more after the onset of the symptoms. In Dossot's series most of the patients survived 6-18 months; but some lived 3 years or more. Widman presented a series of 152 cases which were admitted to the Philadelphia General Hospital. Of these, 82 received irradiation, the remaining 70 were untreated. The table outlines the pertinent factors.

	Number of Cases	Average Duration of Life after Therapy	Average Total Du- ration of Life
Irradiated	82	5½ Mo.	31 Mo.
No Therapy	70	2 Mo.	25 Mo.

In the above series 84% of the patients presented themselves for hospitalization with symptoms of less than 2 years duration. It should therefore be considered as a series with a large proportion of high grade malignancies.

At the University of Minnesota Hospitals an attempt was made to tabulate the result in a series of patients treated by irradiation. A number of these patients also received certain operative procedures (cystostomy and partial prostatectomy, transurethral and supra-pubic). Ninety-eight consecutive cases were chosen which received irradiation therapy from February 1927 to June 1933.

73 of these patients are known to be

dead and 25 have been followed for varying lengths of time; a considerable portion of the latter have been followed through the year 1935. X-ray therapy in all these cases was given with a 200 kv 30 ma mechanically rectified machine. 1 mm Cu and 4 mm Al were used as filter. The skin target distance was 70 cm. when the anterior and posterior fields were treated and 60 cm. when the lateral fields were treated.

The early cases in this series were usually given a series of 4 treatments (2 to each anterior and posterior pelvic field). About 120% of an erythema was given to each field in a period of about 8 days. The later cases in the series received X-ray treatment through four portals about the pelvis. About 150% of an erythema was given over a period of 4 weeks through each portal. At the present time, for those cases in which no definite pelvic metastases are apparent, the technique has been modified still further. A perineal field is used which permits a higher dose to the prostate than was possible by the previous methods.

Of the total number of cases treated, 65 patients received only one course of treatment; 21 received 2 courses of therapy; 8 received 3 courses of therapy. Four cases were treated for metastases only with no treatment given to the prostate gland.

Fifty-three of these cases received interstitial irradiation in the form of radon implants (.3 mm. gold filter) which were inserted into the prostate through the perineum. In most instances, the radon was inserted just before X-ray therapy was begun. 42 patients received only one treatment ranging from about 1000 mc - hrs. to 4400 mc - hrs. 8 patients received radon implantation on 2 separate occasions. 2 cases were implanted 3 times and 1 case had 4 implantations of radon.

55 of the 98 patients were surgically treated. Most of the surgical procedures were done for immediate relief of obstinate and prolonged retention which was present on admission or which persisted after roentgen therapy. In these

55 cases, 10 cystotomies, 28 suprapubic prostatectomies and 17 transurethral punches were done. Most of the suprapubic prostatectomies were done because of a clinical diagnosis of benign hypertrophy, but carcinoma was found on section.

<u>Type of Treatment</u>	<u>Number of Patients</u>
1. X-ray therapy	98
2. Interstitial Radon	53
3. Operative Procedure	
Cystostomy	10
Suprapubic prostatectomy	28
Transurethral Resection	17

Age Incidence

The age incidence in this series corresponded quite well with the incidence of the disease as represented by others. 69 patients, or 70% of the entire group were 65 years of age and over; 24 were between 55 and 65 years of age; and 5 were below 55 years of age.

The duration of symptoms before therapy varied from 1 month to 7 years. 39 patients or 40% of the entire group had symptoms less than 6 months; 23 patients or 23% of the entire group had symptoms from 6 to 18 months; 36 patients or 37% of the cases had symptoms over 18 months; 63% of the cases therefore presented themselves for therapy within 18 months after the first symptoms. The appearance of the first symptoms does not of course coincide with the beginning of the malignancy. The time which elapses before the patient seeks medical assistance is an important factor since it represents for the most part, the rapid progression of severity of symptoms. As it will be shown later, 44% of those patients with definite demonstrable metastases had symptoms less than 6 months in duration. This would tend to show that the cases considered here are of a high degree of malignancy, possibly because of some undetermined process of selection.

Metastases

45 patients in this group of 98 (46%) had definite demonstrable metastases. These patients with presumptive evidence of metastases were not included. About 40 patients showed metastases of bone. All of these had osteoblastic metastases but some had both osteoblastic and osteoclastic forms. Most of these were confined to the pelvis and lumbar spine. The remainder were found in the upper femora, ribs, dorsal spine and scapulae. One patient had large inguinal nodes due to metastases; one had abdominal masses; two showed pulmonary metastases on X-ray examination.

A common symptom was pain in the prostatic area, often not associated with urinary symptoms and may well have represented metastases to perineural lymphatics as shown by Warren, Harris and Grove.

The metastases in this group appeared early. 20 of the 45 cases with metastases were in the group whose symptoms were less than 6 months in duration; 10 cases with metastases had symptoms from 6-18 months; in the remaining 15 cases the symptoms were over 18 months in duration. It is to be noted that 67% of those cases with definite metastases had symptoms of less than 18 months durations.

Histologic Structure

Most of the diagnoses were made on clinical symptoms and physical findings. However, in about 28% of the cases histologic confirmation of the diagnosis was made. In 25 of the 98 cases histologic studies of portions of the prostate were made on material collected by punch operation, and by prostatectomy. In 2 cases, autopsy material was obtained.

Improvement Following Therapy

Clinical improvement was determined for varying periods of time after therapy. In order to evaluate the results of varying types of treatment the following divisions were made; Those treated with (1) X-ray alone; (2) X-ray and radon;

(3) X-ray and operation; (4) X-ray, radon, and operation. Improvement was noted in 64 of 79 cases. 15 cases showed no improvement (10 of these 15 patients were in the terminal stage of the disease and lived from a few days to 2 months after therapy was instituted). 9 of these 10 cases received X-ray alone because the moribund condition of the patient was manifest.

Clinical improvement was apparent in the reduction of the severity of pain and improvement of urinary symptoms. Gain in weight was noted in a number of patients and a considerable number showed reduction in size of the prostate.

<u>Type of Therapy</u>	Total No.	No Improvement	Improvement 6mo.	Improvement 6mo. to 1yr.	Improvement Over 1 yr.
X-ray only	27	8	14	3	2
X-ray and Radon	37	4	8	10	15
X-ray and Operation	7	3	3	1	0
X-ray and Radon and Operation	10	0	1	5	4

From the above chart it is seen that 2 (7%) of the cases treated with X-ray alone were improved symptomatically for more than one year. Of the patients treated with X-ray and radon, 15 cases (40%) were improved for more than one year. In the seven cases which had some operative procedure combined with X-ray alone, none showed improvement for more than one year. Of those having interstitial and external irradiation combined with some form of surgery, 4 (40%) were improved for more than one year. From this it would appear that interstitial radon combined with X-ray and with the punch operation (most frequent operation performed in this series) offers distinctly greater benefit; nevertheless, it must be remembered that most of the patients that received the more vigorous and extensive treatment were, in most instances, selected for this type of

treatment because they appeared to be the least advanced and offered the best hope for the prolongation of life. However, since 1932 surgery has been used for resection with little regard for general condition unless very poor. It is noted that transurethral resection provided more rapid relief of urinary symptoms than irradiation but relief seemed definitely prolonged if irradiation (interstitial or external) was added.

Survival

In view of the fact that 25 patients in this series of 98 have not been followed adequately, it would be impossible to represent the true survival rate of this entire series. Four of these patients were known to have lived at least 30 months following therapy and one is known to have lived 75 months following therapy.

In the 73 cases known to be dead, the average survival was 12 months after therapy was instituted. If the 10 cases which were in a terminal state are not included, the average duration following therapy was 14 months.

If the survival is tabulated according to type of therapy, the following results are obtained:

<u>Type of Therapy</u>	<u>Survival after Therapy</u>
X-ray only	9 mo. Average
X-ray plus Radon	15 mo. "
X-ray plus Surgery	11.5 mo. "
X-ray plus Radon plus Surgery	14.4 mo. "

As noted above, there is an increase in survival after therapy in those patients treated with interstitial radon. However, since the increase is small, no great significance can be attached to this.

An attempt was made also to tabulate the survival periods measured from beginning of symptoms to expiration. The

average duration of the disease was 28 months. The time varied from 4 to 79 months.

If the patients are classified according to group, using clinical indices similar to those outlined by Ferguson we obtained the following:

	<u>Group A</u>	<u>Group B</u>	<u>Group C</u>
Total	4- 45 mo.	8- 60 mo.	14-79 mo.
Duration of Disease	Average- 15 mo.	Average- 28 mo.	Average- 44 mo.

The duration of life noted in our series compares favorably with statistics given by others and suggests that some prolongation of life has occurred in our cases of prostatic cancer and that some appreciable control has been exercised over the progress of the disease.

An attempt is being made to follow cases which have been treated since Jan. 1, 1936, when X-ray Therapy with a modified technique using perineal field was instituted. Most of the material obtained is too meagre to present at this time; but the definite impression has been gained that the extent of clinical improvement surpasses that which has been given here.

Summary

We have presented here a summary of our results with X-ray Therapy in 98 of our earliest cases. The results outlined here do not represent the best results obtainable from X-ray Therapy, since the group of inadequately followed cases (25) could not be tabulated for survival statistics and could not be considered adequately as to length of clinical improvement. It is very probable that certain patients in this group of 25 had periods of improvement longer than the period of available follow-up; also, a certain number may well be alive at the present time.

3. Bronchiectasis

A. Case Report

The recent addition of roentgen therapy in the treatment of bronchiectasis appears to offer considerable improvement in the symptom complex. In February of this year Berck and Harris of Mt. Sinai Hospital, N.Y. published their observations during the past two years. This brief resume of their report presents the important features of the disease and the therapeutic application of radiation therapy.

(1) The rationale: The use of roentgen therapy in chronic inflammatory processes is somewhat empirical. It is known that the rays act initially and mainly on the leukocytic infiltrations causing their destruction and stimulating connective tissue proliferation as the sequelae. A direct action of the rays upon the bronchial mucous glands, analogous to that observed in the salivary glands, has been demonstrated experimentally in animals but its production in the human bronchial tree seems rather doubtful at this time. It seems more logical to assume that the effect of the rays is directly upon the tissues in the chronic inflammatory processes. It is this principle that restricts radiation therapy to the chronic type of bronchiectasis. The therapeutic consideration in roentgen therapy is directed to change a "wet" bronchiectasis to "dry", so that the control, if not actual arrest, of expectoration may result. An extensive dry bronchiectasis may be present for years without disturbing the patient sufficiently to seek medical aid.

(2) Pathology of Bronchiectasis:

Examination reveals a chronic and subchronic bronchial and peribronchial inflammation. The mucosa of the dilated bronchi is either hypertrophied or atrophic. The epithelium may be intact, or undergo mucoid degeneration or desquamation, or be replaced by a low cuboid, non-ciliated or villous mucosa. The areas of hypertrophied mucosa may show thickened, polypoid, infiltrated velvety, granular, or villous masses. The cellular infiltration of submucosa

and the deeper structures is very dense and extends into the immediate peribronchial areas. It is predominately lymphocytic and may explain the beneficial effects of radiation. The walls may become fibrous, showing a thin fibrous chronic inflammatory membrane with atrophic and hypertrophic changes throughout.

(3) Classification (Berck's and Harris's patients)

Generally patients who are ambulatory and afebrile, with a chronic lesion and a rather constant level of expectoration without marked remissions, were considered suitable for roentgen therapy:

1. First group (14)

Bronchiectasis secondary to chronic putrid lung abscess; symptomatic after drainage of abscess; discharging bronchocutaneous fistulae and expectoration of three to six ounces of muco-purulent material; rather extensive involvement from one to many lobes.

2. Second Group (3)

Bronchiectasis involving one to two lobes, expectoration of one to five ounces daily, not ill, ambulatory, very infrequent acute episodes.

3. Third Group (13)

These patients appeared chronically ill of multilobar extensive bronchiectasis, severe cough, profuse foul expectoration, marked clubbing of fingers, frequent hemoptysis and attacks of pneumonitis.

(4) Method of Treatment

Factors: 180-200KV; F.S.D, 50cm; 4-millapmeres; filters-0.5mm. copper and 1mm of aluminum; field 10x15 cm.

Roentgen therapy in large doses was given to each patient over a period of approximately 3 months, each area

"cross-fired" from anterior, posterior and lateral portals, using from 3 to 7 different areas as indicated by the extent of the disease. Total dose averaged 1200r through each portal (field), and each treatment consisted of 75r, measured in air, to 2 or 3 fields at each sitting. Patients were treated 2 or 3 times weekly with a rest period of four months before the course was repeated.

(5) Results

1. Marked reduction in amount of expectoration, as from 16 ounces to 1 daily.
2. Disappearance of foul odor of expectoration.
3. Very slight persistence to complete absence of cough.
4. Disappearance of clubbing of fingers.
5. Bronchography revealed narrowing of dilated bronchi in some; not observed in other patients even though these were clinically improved.
6. No evidence of pleural thickening, pulmonary fibrosis, or mediastinal retraction.

(6) Conclusions

"1. Roentgen therapy in moderately large dosage as the sole method of treatment for chronic secreting bronchiectasis is feasible and successful, resulting in great symptomatic improvement in a considerable proportion of cases.

2. The clinical improvement in chronic bronchiectasis treated with a moderately high dosage of roentgen therapy may be so great in many cases as to approach a practically complete cessation of the symptoms of expectoration and cough.

3. Follow-up examination over a period of two years in those cases in which there has been improvement has shown no recurrence of symptoms with infections

of the upper respiratory tract."

The following case report from this hospital illustrates the use of irradiation therapy in bronchiectasis:

P.B. - single, female, 21, - 1st admission to hospital Dec. 17, 1935.

History

Well until 10 when she contracted pneumonia and pleurisy (Nov. 1924). Extremely ill. Complicated by a "leaky-heart." Drains later inserted into left chest and left in place a month. Convalescence very prolonged and patient was in bed over 3 years. At that time family physician told her to get up, go outdoors and forget her illness. Did this and lead a very active outdoor life, engaging in athletics during the next 2 years. After this she developed a persistent cough with 3 to 6 ounces of foul-smelling, greenish-yellow sputum (daily), lost weight, became weak and tired, and was forced to bed in 1930. Had occasional attacks of hemoptysis of 1-2 ounces of blood, night sweats, and high fever up to 103-4 degrees. X-rays were interpreted as tuberculosis and strict bed rest instituted, though no tubercle bacilli could be demonstrated in the sputum. In 1935 she was admitted to the State Sanatorium, Ah-Gwah-Ching, as illness of her mother prevented further care at home.

History and Findings at Sanatorium

Emaciated and poorly nourished female. Chest findings: flat note over entire left chest, absence of all breath sounds, except near sternum and clavicle. Right side shows normal resonance and breath sounds. Chest films, before and after lipiodol: Complete loss of detail in left chest, after lipiodol filling saccular dilations of bronchi from 2nd rib to base, atelectasis and bronchiectasis at base, mediastinum retracted to left. Right side negative except for peribronchial infiltration throughout with pleurisy at base.

Laboratory

1. Sputum--negative for tubercle bacilli with smears, flotation and

guinea pig inoculation; culture showed pure culture of pyocyanus organisms.

2. Mantoux Test--negative to 1:100 dilution.
3. Widal and Wasserman reactions negative.
4. Urine--Negative.
5. Blood:--hgb. 77%; RBC 4,300,000; WBC 14,500; Diff. PMN's young-5%, trans. 16%, old 44%; Lympho-large 4% and small 31%.
6. Stools- Negative for tubercle bacilli.

Conclusion

Bronchiectasis-- advised transfer to University of Minnesota Hospitals for possible surgery.

1st Admission - 12-17-35 - 1-16-36.

Condition essentially as at sanatorium. Temperature ranged from normal to 101, sputum from 45 to 100cc. daily, laboratory as above, with Hgb. 69%; RBC 3,600,000; WBC 8-13,500, diff. PMN 50%, Lymp. 49%, monocyte 1%. Stereo films of Chest: 12-18-35. "Very marked lung fibrosis is shown on the left side with marked retraction of the mediastinum and pulling up of the diaphragm. Within this there are numerous areas of cavitation suggesting a secondary bronchiectasis or possibly multiple lung abscesses. There is some thickening of the pleura at the right base with some localized emphysema just above this, diaphragmatic adhesions being present. There is an area of density at the right base just above the diaphragm medially which may also be a residual of the same process. The absence of tuberculosis in the right lung is strong evidence against the lesion in the left being tuberculous, although the latter cannot be excluded.

Conclusions:

Chronic lung fibrosis with bronchiectasis, left side.
Localized emphysema, right.

Possible local area of bronchiectasis, right base.

Thickened pleura right base.

L.R."

Lipiodol chest: 12-20-35. "A fairly good filling of the left bronchus was made out with iodized oil. There was no obstruction of the bronchus, but an extensive saccular bronchiectasis of extreme grade is shown. The appearance would, therefore, suggest that this is a chronic lung fibrosis with secondary bronchiectasis.

Conclusions: Chronic lung fibrosis with secondary bronchiectasis, left. L.R."

Treatment:

Postural drainage, with general supportive measures.

Surgery not advised until extent of condition in right side could be determined.

2nd Admission to Hospital

May 23, 1936 -- June 11, 1936.

Feeling slightly improved though cough and expectoration continued unchanged.

Surgery: Not advised due to extensive involvement and extreme risk, Surgeon's note, "Better pursue a conservative course and accept defeat rather than to make a futile gesture."

Interdepartmental consultation resulted in deep x-ray therapy being advised.

Deep X-ray Therapy and follow-up notes:

Factors; 200KV; 30 milliamp.; F.S.D.-70 cm.; filters 1mm copper plus 2.5mm. aluminum; fields average 12-13x18-22, treatments projected from anterior and posterior portals of chest, with 200r. given at each treatment on alternate days and either anterior or posterior projection. A total of 6 treatments were given, i.e. three anterior and three posterior, a total dosage of 1200r. from 5-26 to 6-8-36 inclusive. Some increase in symptoms was observed after the second treatment.

3rd Admission for follow-up and further therapy.
7-20-36 to 8-5-36.

Factors essentially the same. Dosage as before and given in same manner, 200r per treatment projected alternately from anterior and posterior and given every other day from 7-21-36 to 7-31-36.

Staff Note: 8-5-36 date of discharge: "After fourth treatment patient began to have irregular temperature up to 101.6 with increased expectoration and cough."

4th Admission for follow-up and examination: 9-16 to 9-17-36

Condition unchanged; same amount of sputum (100-150 cc. per day).
Sent home for further care.

Follow-up Apr. 13, 1937

Letter from referring family physician under whose care she has been constantly since her return home.

"There has been considerable improvement in the condition of her lung. She has practically no temperature for several months, has about an ounce of material every other day that she coughs up and aside from an occasional disturbance, such as a gastro-intestinal upset apparently an epidemic of three weeks ago and a slight upper respiratory infection of two months ago, has been in pretty good health.

Her long confinement in bed has made her an invalid, which she enjoys. Hope to have the opportunity of taking a chest film in the near future.

It is my opinion that the x-ray treatments have produced beneficial sclerosis and that the process, clinically, seems to be quiescent."

4. Case Reports

A. Lympho-epithelioma (Cure?)

Male - 60. Referred for roentgen therapy 3-18-32.

Complaints

Sore throat since February 14, 1931.

History

Saw a physician and was given a mouth wash. February 29, 1932 saw another physician who suspected an abscess at base of tongue and tried to drain it but found it to be a solid mass. March 8th a piece was removed for biopsy.

Diagnosis

Microscopic section from lingual tonsil first reported suggestive of lympho-sarcoma. Later studied carefully by another pathologist who diagnosed lympho-epithelioma.

Examination

At the left side of base of tongue and involving left tonsil in its lower part was a soft papillary mass projecting one or two cm. above surface of tongue and measuring about 3 cm. in diameter. Some diffuse enlargement was found in the left submaxillary region. Nothing else of importance was found on the physical examination and on the chest by radiographic study.

Treatments

A series of 2 roentgen treatments to each of two lateral fields given in 8 days. A total of 900 roentgens given to a 12x17 cm. field over left cheek and cervical region and 825 roentgens to a corresponding field on the right side.

Follow-up

At the time of the last treatment the lesion seemed to have disappeared completely. It could not be seen or felt. 4-9-32. During the two weeks following the treatments patient had a rather severe reaction and had to stay in bed for about one week. At this time he is much better and there is no visible sign of recurrence or reaction.

4-17-37

Patient has been seen a number of times, first at shorter intervals and lately at intervals of from 6 months to 1 year. He has been in good health and working. No signs of recurrence have been noticed. He was in good condition at this last visit, five years after the treatments.

B. Hodgkin's Disease
(with Bone Metastases)
(Long palliation?)

Male - 29. Mechanic.

Admitted - November 1931 to University of Minnesota Out-Patient Department.

Complaints

1. Large mass in left axilla - 1 year.
2. Weakness and loss of weight.
3. Dryness and itching of skin - 2 yrs.
4. Redness, swelling and discharge from left eye.

History

Chancre 1924 - positive Wassermann August 1931. Received course of intramuscular injections for syphilis. At this time also had a skin lesion diagnosed as molluscum contagiosum for which he received treatment. Pruritis both legs for 5 yrs.

Examination

1. Dry scaly skin.
2. Palpable lymph nodes and large mass in left axilla, palpable nodes in cervical and inguinal regions.
3. Palpable spleen.
4. Biopsy - Hodgkin's disease.
5. Dec. 3, 1931: Chest film - enlargement right mediastinum consistent with Hodgkin's disease.

Diagnosis

1. Hodgkin's disease.
2. Blepharitis left eyelid.

Treatment

X-ray therapy to both axillae, spleen and mediastinum.

Follow-up

1-20-32: Chest film - marked regression of mediastinal involvement.

2-17-32: Axillary glands treated with X-ray therapy.

3-11-32: Severe pain in lower back.

X-ray films- osteoclastic and osteoblastic metastases consistent with Hodgkin's disease. X-ray therapy to lower lumbar spine and pelvis.

3-28-32: Pain and swelling of right ankle - X-ray examination negative. Also palpable adenopathy in both axillae at this time. Given X-ray therapy to right ankle and both axillae.

4-1-32 to 7-18-32: Remained well for 3 months - had no complaints.

7-18-32: Nodes in both axillae. Film of chest showed an increase in the broncho-vascular markings suggesting a Hodgkin's infiltration into the lung parenchyma. X-ray therapy to axilla and chest and patient remained well until Jan. 1933 - well 6 months.

1-17-33: Complained of cough and tight feeling in chest. X-ray film - probable Hodgkin's infiltration of lung parenchyma at left base. X-ray therapy to left chest.

3-30-33: Admitted to hospital with cellulitis of the right hand and arm. Recovered and was discharged 5-12-33. Temperature up to 105° for short intervals. At this time patient again complained of pain in his hips and spine. 5-25-33: Given another course of X-ray therapy to the lower lumbar spine and pelvis. Remained well until 3-11-36.

3-11-36: Admitted to hospital with a contact dermatitis of the exposed parts. No complaints referable to Hodgkin's disease but some enlargement of lymphatic glands. Hgb. 92%, WBC 5,900. Temperature normal.

The radiographic record follows:

12-3-31 - Chest, Abdomen

Flat plate of the chest shows a definite mass in the mediastinum bulging to the right. This is quite characteristic of an enlarged gland such as occurs with Hodgkin's disease, lymphosarcoma or leukemia. There is some infiltration at the base of the right lung with obliteration of the right costophrenic sinus which suggests that there might be some fluid here. Right lateral plate however fails to substantiate this and the whole process most likely is on the basis of an infiltration from Hodgkin's disease or lymphosarcoma. Flat plate of the abdomen shows a mass on the left side which extends well down below the 12th rib posteriorly and within about two inches of the spine. This mass is quite characteristic of an enlarged spleen. The kidney shadows are well visualized and are normal in size, shape and position.

Conclusions: Hodgkin's disease with mediastinal mass.
Infiltration in right lower lobe with possibility of a minimal amount of fluid.
Enlarged spleen. LE

1-20-32 - Chest

The mass in the right superior mediastinum has almost completely disappeared. The infiltration however at the base of the right lung is still present. It has decreased somewhat since the last examination.

Conclusions: Hodgkin's of mediastinum disappearing under therapy.
Probable Hodgkin's infiltration of lungs. LR

2-19-32 - Lower Lumbar Spine, Sacroiliac Region

Multiple areas of density are present in the pelvis about the sacroiliac joints and extending into the ilium. Some increased density of the lumbar spine alternating with areas of rarefaction is also present. There is a marked area of rarefaction in the right acetabulum. The appearance suggests an osteoblastic and osteoclastic type of metastasis such as might easily occur from carcinoma of the prostate, but also does occur occasionally

with Hodgkin's disease.

Conclusions: Osteoblastic and osteoclastic metastases to pelvis and lumbar spine from Hodgkin's disease. LR

3-18-32 - Rt. Ankle

Considerable swelling of the ankle joint is shown but no evidence of bony or cartilaginous pathology.

Conclusions: Soft tissue swelling. LR

5-27-32 - Chest

Considerable obliteration of both costophrenic angles is present, which suggests a marked pleurisy with adhesions. The right diaphragm is pulled up and partially fixed. There is no other evidence of pathology.

Conclusions: Bilateral pleurisy.
No evidence of mediastinal gland enlargement. LR

7-18-32 - Chest, Lt. Ankle

No evidence of mediastinal gland enlargement could be made out. There is some increase in the bronchovascular markings suggesting the possibility of an infiltration in the lung parenchyma itself. There is marked bilateral diaphragmatic pleurisy with adhesions obliterating the costophrenic angles. No evidence of bone or cartilaginous pathology in the left ankle could be made out.

Conclusions: Negative left ankle.
Bilateral diaphragmatic pleurisy.
Possible Hodgkin's infiltration of lungs. LR

1-17-33 - Chest

The diaphragmatic pleurisy is again shown. In addition to this there has been some increase in density at the left base, suggestive of some progression in the parenchymal infiltration previously described. No evidence of mediastinal mass can be made out.

Conclusions: Probable Hodgkin's infiltration of lung, left base.
Bilateral diaphragmatic pleurisy. LE

4-20-33 - Chest

There is some evidence of a pleurisy at the right base with pulling up of the diaphragm and some infiltration. There is no other evidence of pathology on that side. Some thickening of the pleura on the left side is also present.

5-6-33 - Lt. Shoulder

Negative.

JS

1-17-36 - Chest

There is a marked improvement in the appearance of the chest since the last examination. The mass in the mediastinum has entirely disappeared. The right diaphragm is lower than on the last picture. There is, however, some thickening of the pleura in both bases with pleural adhesions in the right base. The bronchovascular markings are also increased in both bases.

Conclusions: Thickened pleura, both bases.
Increased bronchovascular markings, both bases. HE

C. Carcinoma of Tongue - Metastasis to Cervical Glands

Fractional Method of Irradiation Therapy over Long Period

To detail procedure in fractionated method of irradiation therapy over long time in cancer of the base of the tongue, tonsillar area, and nasopharynx, with metastasis to cervical glands.

, 50 years
Colored male.
Admitted to University of Minnesota Hospitals 6-11-36.

Complaints:

Sore tongue; pain on swallowing and talking; about 6 months.

History

Early in February 1936, patient noticed

a tender and painful mass on the left posterolateral area of the base of the tongue. Swallowing and talking were painful, and pain progressed so that lately it has been constant and radiates into head and down into cervical region and throat. Saw a physician early who prescribed a salt gargle but did not palpate the tongue. Gargling seemed to ease pain some at first. Has lues for which he has received only a short course of therapy.

Examination

On the left posterolateral border of tongue there is an ulcerated lesion, 1 cm. in diameter, with raised edges. Moderately large lymph nodes are palpated in the submaxillary and submental groups, and smaller nodes also palpable in posterior cervical group.

Diagnosis

Biopsy from tongue on 6-12-36; pathologic report - squamous carcinoma. Wassermann, blood - negative.

Treatment advised

Irradiation therapy for palliation.

Deep X-ray Therapy

Patient treated daily except Sunday to cervical and lower part of face, alternating right and left sides. Fractional type of series given with total dose of 240% S.E.D. (i.e. 2550 r) to each side in 22 treatments from 6-22-36 to 7-18-36, both inclusive.

<u>Date</u>	<u>Field</u>	<u>Size</u>		<u>Filter</u>			<u>Ma.</u>	<u>Min.</u>	<u>"r" air</u>	<u>Skin Dose</u>	<u>$\frac{1}{2}$ value Layer</u>
		<u>Cms.</u>	<u>Angle</u>	<u>F.S.D.</u>	<u>Cu.</u>	<u>Al.</u>					
6-22-36	Right lateral face and cervical region	13x17	90	60	$\frac{1}{8}$	1	200	30	4.4	203	20%
6-23-36	Left lateral face and cervical region	11x12	90	60	$\frac{1}{8}$	1	200	30	4.6	213	20%
6-24-36	Right lateral face and cervical region	10x12	90	60	$\frac{1}{8}$	1	200	30	4.6	213	20%
6-25-36	Left lateral face and cervical region	11x11	90	60	$\frac{1}{8}$	1	200	30	4.6	213	20%

etc. until course was completed

0.75
mm. cu.

Weight: 110. Radon implants: 2030 mc. hrs.

Follow-up Notes

8-19-36 -

Has had a great increase in pain in tongue during past week. No glands palpable in neck at this time. Lesion on tongue is smaller. Excellent response to deep x-ray therapy. Lesion on tongue now measures 3x3 cm., but is not ulcerated. Lymph nodes are much smaller. To have radon implants into tongue.

8-25-36

15.4 mc. in 11 --- 0.3 mm. gold implants about lesion in tongue under intravenous evipal anesthesia.

12-3-36

Lesion in tongue and nodes regressing satisfactorily.

1-28-37

"A very excellent (more than expected) result following irradiation. No demonstrable carcinoma now. No complaints except some pain under sternum on coughing. To have x-ray of chest."

2-11-37

No local recurrence. Some thicken-

ing in floor of mouth. Node palpated, 1 cm. in diameter, movable, at angle of jaw on left side. Should be carefully observed.

3-25-37

Node at jaw soft, freely movable, and probably not involved. Observe. Investigate pain in chest for aneurysm, metastases, and refer to tumor clinic.

4-15-37

Small submental node, several mm. in diameter, palpated only by outside palpating finger. Node at angle of jaw unchanged. To be observed.

5-6-37

Continue observation; no change. Fluoroscopy of chest: "showed some diffuse dilation of the aorta, but no evidence of aneurysm."

5. Carcinoma of the Lip

Review of 333 cases at University of Minnesota.

From January 1st, 1926 to December 31st, 1935, 372 cases of carcinoma of the lip were seen at the University of Minnesota Hospitals. In 12 patients the lesion was situated on the upper lip. Eight of these patients were males and 4 were females. Eight had a microscopic diagnosis of squamous cell, two were called basal-squamous and two were not biopsied. Ten patients received irradiation therapy alone and two were treated by excision of the local lesion and radiation. No serious effort has been made to follow these patients but according to the hospital records six are living, four are dead, three of whom died of carcinoma, and two were not followed.

Of the remaining 360 cases, 27 cases (26 males and 1 female) were excluded from this analysis because 19 of them received no therapy either because the patient refused treatment or they were considered hopeless. The other 8 are not included because the records are incomplete.

Of the remaining 333 cases about 80% have been followed. The cases were divided into 4 groups. Group 1 is made up of 149 cases who had had no treatment before coming to the Out-patient Clinic and in whom the diagnosis was verified by biopsy. The second group consists of 122 patients all of whom had had previous therapy in one form or another, and came in with persistence or recurrence of the disease either in the local lesion or the lymph glands of the neck. Group 3 is made up of 46 patients who had had no previous therapy but were not proven cases either because a biopsy was not taken or it was unsatisfactory for one reason or another. These patients were clinically considered to have carcinoma and were treated as such. The fourth group is composed of patients sent to the Clinic for irradiation therapy following surgery elsewhere. There were 16 such post-operative cases.

Incidence

Carcinoma of the lower lip is encountered in about 0.4% of the total admissions to the hospital, and in approximately 5.5% of the admissions to the tumor service.

Age

The youngest individual in the whole series was twenty-seven years of age, while the oldest was eighty-five years old. There were 18 patients below the age of forty. The majority, or 73.6% of the patients were between the age of fifty and seventy-five.

Sex

Of the 333 cases there were 329 males and 4 females.

Etiology

There was a history of the use of tobacco in only 90 or 27.2% of the cases as given in the records. Obviously the histories are incomplete on this point. A history of trauma was given in 24 cases. Such factors as irritation from a jagged tooth, freezing, or injury from nails held in the mouths of carpenters were noted.

The majority of the patients were farmers. The occupation of these patients showed the same frequency distribution found in male patients admitted to this hospital.

Location

The location of the lesion on the lip was given in 242 cases. In 3 instances there was more than one lesion, and practically the whole lip was involved in 8 cases. The lesion was situated on the right side of the lip 91 times, and this group had a death rate from carcinoma of 14.3% while the left side was involved in 94 instances with a death rate from carcinoma of 11.7%. The lesion appeared at or near the midline in 40 cases with a death rate of 4.6%. There appears to be a significant difference in outlook when

the lesion is located at or near the mid-line. The cause of this difference in mortality is not clear but the course of the lymphatics or the mobility of the various portions of the lip might be suggested as possible factors.

Character of the Lesion

In 56 cases the process was described as being infiltrative, with a mortality rate of 8.9%. The lesion was depicted as being papillary or proliferative in 82 cases with a death rate of 10.9%. It is quite generally stated that the infiltrative lesions have the poorest prognosis; however, this does not appear to be true in this group of 138 patients.

Size of Lesion

The size was stated in 227 instances and as might be expected, the mortality from carcinoma increases with the size of the lesion. There were no deaths from carcinoma where the lesion was less than one centimeter, while in those above five centimeters the mortality rate is 20%.

Biopsies

There is a record of a biopsy in 245 cases of the whole group. Slightly more of the infiltrative type of lesions were graded three and four. The prognosis appears to be poorer in the cases with lesions graded three and four. The mortality from carcinoma was only 3% in cases with lesions in group I, and 6.1% of these cases had recurrence in the glands of the neck while the mortality rate in patients with lesions in group IV was 25% and about one fourth of these patients had recurrence in the glands of the neck.

Duration of Lesion Prior to Treatment

In the primary cases the lesion was present on the average of $2\frac{1}{2}$ years before the patient sought treatment. In this series the mortality rate increased with the duration of the disease up to about five years after which it decreased again.

In the recurrent group the patient presented himself for treatment within

3 years following previous therapy elsewhere in 57.4% of the 122 cases, and more than one-half of them came in with involvement of the glands of the neck.

Survival curves were made first

of the whole group of 333 cases used in this study, secondly of the 149 proven previously untreated cases, and thirdly of the 122 cases of recurrent lesions. The method used in constructing these survival curves is based on the principles advocated by Jacobs, of our staff, about a year ago. The curves express in percentage the number of patients living in relation to the number followed. When all of the patients in a given group are not followed, or are followed for varying lengths of time, it is possible to plot three curves depending on the way those cases not followed are included in the composition of the curve. If all of the lost cases are assumed to be dead, this assumption gives the worst possible result. If the cases not followed are considered as living, we arrive at the best possible curve. On the other hand, if the assumption is made that the lost cases behave in the same manner as the cases followed, then this curve represents the probable result. Only the probable and worst possible curves were plotted for each of the three above mentioned groups.

It should be noted that in the age distribution of these patients a large percentage normally die of causes other than carcinoma of the lip, and in the survival curve for the primary group it is seen that a greater percentage die of other causes, while only a small number, or about 20% of those dying, die of carcinoma of the lip. On the other hand, in the recurrent group the largest number, or over 90% of those dying, die of carcinoma of the lip, and the percentage dying of other causes is much less due to the fact that these patients did not live long enough to die of other causes. It should also be pointed out that the greatest drop in the curves takes place in the first two years of the ten year period. In other words, most of the patients who die of carcinoma of the lip do so in the first two years after treatment.

From the curves showing the probable results it will be seen that the percentage surviving 5 years after treatment in the whole group is approximately 50%, in the primary group about 58%, while in the recurrent group the percentage drops down to about 40%.

Treatment

No attempt was made to compare the results obtained from the various types of treatment used in these cases. However, the advisability of doing a neck dissection in the majority of the patients with carcinoma of the lip as a more or less routine procedure and the results obtained in resection of the mandible in those cases having mandibular involvement have been considered, and the results as obtained in the cases under consideration will be referred to later.

It hardly seems worth while to compare the results obtained with surgery and radiation therapy in a group such as this, since the factor of selection plays an important part in the outcome, particularly in the older cases, and also because of the continuous change in the personnel of the staff of physicians caring for these patients. In this series of cases patients have been treated by both methods and many different combinations of surgery and radiation. If the group is divided into subdivisions according to the type of treatment received, the groups become so small that a statistical analysis is more or less impossible. However, during the past few years, or since about 1932, the majority of the previously untreated patients have been treated by the following method.

First a biopsy is taken and the diagnosis established, after which the local lesion is irradiated with radium and X-rays. The radium is held in place by a dental mold. The area treated with radium usually extends about 1 to 1.5 cm. beyond the margins of the lesion. The radium dosage varies from about 100 mg. hrs. per sq. cm. of radiating surface in the smaller lesions to 60 mg. hrs. per sq. cm. in the larger lesions. At or about the same time the lower lip and local lesion are irradiated with X-rays. 1000 r (measured in air) are given to the

whole area. At the present time 100 K.V., 8 Ma, and 1 mm. Al. filter is used, and 1000 r (as measured in air) are given to the lower lip and 500 r are added to the local lesion. Unless there is some contraindication, a dissection of the submental and submaxillary lymph nodes is carried out about 6 weeks after the radiation therapy, at which time the primary lesion should be completely healed. Some of the patients refused surgery, and were given X-ray therapy to both sides of the neck. Other patients were not subjected to a neck dissection because the lesion was considered clinically and pathologically relatively benign. Some were considered poor surgical risks, and were not operated upon.

When the present procedure was started the majority of these patients also received irradiation therapy to the neck following the neck dissection, but this has been discontinued, except when the nodes have been found to be involved at operation, because it is not known at present whether or not this procedure is a necessary adjunct, and also, because the facilities for continuing this form of therapy are inadequate.

Patients coming in with metastasis to the glands are treated by neck dissection or surgical removal of the involved glands; and the area may be implanted with radon seeds or X-ray therapy given to neck, or a combination of the two may be used. Where the extent of the metastatic lesion precludes surgery, irradiation alone is the method of choice.

The very early lesions are usually treated with superficial X-rays only to the local lesion.

Persistence, Recurrence and Metastasis

Consideration was also given to some of the factors involved in the occurrence of persistence of the lesion, and recurrence of the local lesion with or without metastasis in the glands of the neck or in the mandible.

In the recurrent group, as previously

stated, the patients came in with recurrence of the local lesion or recurrence in the lymph nodes, or both, within three years following previous therapy, in 57.4% of the cases and in 5.8% after 15 years. However, it is difficult to say in many instances whether or not one is dealing with a recurrence or a new lesion in these late recurrences. An attempt was made to determine whether or not there is any relationship between the occurrence of persistence, recurrence and/or metastasis. It should be remembered that the information in regard to previous therapy was given by the patient

in some cases, and for this reason, it may not be entirely reliable. Also, the various types of treatment used do not always mean the same thing in every locality, since surgical procedure varies from clinic to clinic, and this is also true in regard to radiation therapy. Some of these cases undoubtedly had inadequate therapy. The following table shows the condition of the patients when they first appeared for further treatment and the type of previous therapy.

STATE OF LESION IN RECURRENT GROUP ON ADMISSION

<u>Previous Therapy</u>	<u>No. Cases</u>	<u>Met. to Glds. or Mand.</u>	<u>%</u>	<u>Loc. Rec. & Met.</u>	<u>%</u>	<u>Loc. Rec. %</u>	<u>Per-sist. %</u>	<u>Pers. Met. %</u>
Exc. local lesion	34	15	44.1	5	14.7	14	41.1	- - - -
Exc. & Neck Dis.	8	3	37.4	2	25.0	3	37.4	- - - -
Radiation	18	6	33.3	-	-	7	38.8	3 16.6 2 11.1
Rad. & Surgery	17	7*	41.2	5	29.4	4x	23.5	1 5.8 - -
Miscel.	45	9	20.0	5	11.1	5	11.1	19 42.2 7 15.5

* 2 had neck dis.
x 1 had neck dis.

The percentage coming in with metastasis was about 50% following the various types of therapy. Many more patients had a persistence of the lesion in the miscellaneous group than in those receiving other types of treatment.

Persistence, Recurrence in the Glands of the Neck or Mandible, and Local Recurrence after Therapy in this Clinic

Primary group: 149 cases

Persistence of disease	*6 cases or 4.0%
Recurrence in glands	x*9 " " 6.0
Recurrence in mandible	2 " " 3.4
Recurrence in local lesion	x 4 " " 2.7
Deaths due to carcinoma	7 " " 5.4

*One case included in both groups
xOne case included in both groups

Recurrent group: 122 cases

Persistence of disease	38 cases or 31.0%
Recurrence in glands	* 8 " " 6.5
Recurrence of local lesion	* 1 " " 0.8
Death due to carcinoma	39 " " 31.9

*One case included in both groups

Unproven group: 46 cases

Recurrence in glands	1 case or 2.1%
Recurrence of local lesion	2 " " 4.3
Deaths due to carcinoma	0

Postoperative group:

No persistence or recurrence of the disease and no deaths from carcinoma.

Roentgen Ulcers

Of the 146 cases which had irradiation therapy in any form to the lip, 23 developed a roentgen ulcer in from 5 months up to 4 years (1 case) after treatment. The average time after radiation therapy for the ulcer to appear was about 14 months.

8 of these cases healed spontaneously.
1 also has necrosis of mandible following heavy irradiation.
7 are living and well.

7 were excised; 5 living and well, 1 was followed 3 mos., and 1 died of carcinoma of the prostate.

6 healing. 1 excision advised after 6 months of watching, and 1 of these cases also has necrosis of the mandible.

1 not followed.

1 developed a slough of the soft tissues of the lip 1 year after a large dose of radiation. The lip is now healed, and the patient is going to have plastic procedure done.

The incidence of roentgen ulcers in the series was about 15.8. This is probably not much lower than could be expected when one considers the dosage of the irradiation therapy which the

majority of these patients received. Recently the radium dosage has been decreased somewhat. Most roentgen ulcers heal spontaneously. A few must be excised, especially where there is any question about local recurrence.

Radiation necrosis or osteomyelitis of the Mandible

Of the 269 cases which had radiation therapy to the lip or neck, or both, there were 5 cases of radiation necrosis or osteomyelitis of the mandible--an incidence of 1.8%.

1 began after a tooth extraction 3 years after X-ray therapy and radon implantation of the neck, and is living and has been followed 1 year 2 months since the onset of the osteomyelitis.

1 had one course of X-ray therapy to the neck, and 4 years and 2 months later developed osteomyelitis following a tooth extraction. This patient is living and has been followed 2 years 1 month since onset.

1 developed necrosis of mandible 1 year 7 months after heavy radiation to lip and neck, and has been followed 2 months.

Radiation Necrosis

1. Developed radiation necrosis
2 yrs. 2 mos. after radiation -
precipitated by extraction of
tooth. Living 10 mos. after be-
ginning of osteomyelitis.
2. Necrosis of mandible 6 yrs. 4 mos.
after radiation - followed 1 month.

Irradiation with radium or X-rays produces a certain amount of damage to the tissues receiving the radiation, and especially is this true where the type of lesion requires a heavy dose. The tissue undoubtedly becomes more susceptible to trauma and infections, and therefore, if possible, it would be better to do any traumatizing procedures, such as extraction of teeth, etc., before radiation therapy is given. It is usually a matter of months before the fragments of necrotic bone slough out, and the process begins to regress. These patients suffer considerable pain. The late necrosis can usually be traced to trauma and might have been avoided if the patient had been more careful in protecting the irradiated region.

Involvement of the lymph glands of the neck.

It is difficult to evaluate the clinician's accuracy in determining whether or not the lymph nodes in the neck are involved because when a note is found in the record stating that the glands of the neck are palpable, very frequently no statement is made as to whether the examiner feels that the nodes are involved in the malignant process or not. When palpable glands were present before operation, they were found to be malignantly involved in 23.5% of 34 cases in the primary group, while 57.1% of the 42 cases with palpable glands in the recurrent group were involved.

In the whole group there were 81 patients who had palpable nodes and also had a neck dissection. 39.5% of these were found to be involved microscopically. When glands were not palpable, they were found to be free from malignant disease in 96.5% of the cases out of 111.

Neck Dissection

In the whole group there were 192 patients upon whom a dissection of the submental and submaxillary glands was carried out. There were 3 surgical deaths, or an operative mortality of 1.5%. The advisability of doing a neck dissection as a routine procedure especially in the early cases without clinical involvement of the glands as a prophylactic measure is a much discussed problem and as yet is not definitely settled. An attempt was made to analyze the cases in this series by comparing the results obtained in those patients having a neck dissection with those who did not. The following table shows the results obtained.

<u>Primary Group - 149 cases</u>	<u>No.</u>		<u>%</u>		<u>Recurrent</u>	<u>Living</u>	<u>Followed</u>	<u>%</u>
	<u>D</u>	<u>cu</u>	<u>D</u>	<u>cu</u>	<u>in glands</u>	<u>5 yrs.</u>		
105 had neck dissection	7		6.6		8	28	44	63.5
*44 did not have neck dissection	-		--		-	6 ^x	9	66.6

*10 early cases
x 2 early cases

Recurrent Group - 122 cases

65 had neck dissection	14		21.6		6	19	31	61.3
57 did not have neck dissection	25		44.0		2	3	20	15.0

Unproven Group - 46 cases

19 had neck dissection	-		--		1	--		
*27 did not have neck dissection	-		--		-	2 ^x	2	100.0

*3 early cases
x1 early case

Postoperative Group - 16 cases

2 patients had neck dissection; there were no deaths or recurrences in this group.

There were 11 cases in the recurrent group who had had a neck dissection before coming to the clinic and 6 or 54.5% came in with recurrence in the glands. In the remaining 111 out of the 122 cases who did not have a previous neck dissection, there were 9 or 36% who presented themselves with involvement of the glands of the neck.

In summarizing the above findings, it must be borne in mind that the number of cases in the various groups is relatively small, and one should be guarded in drawing definite conclusions. However, it seems probable that we must expect a certain percentage of recurrences in the lymph nodes following the routine dissection of the submaxillary and sublingual lymph nodes. Some of these patients particularly in the earlier years had a more extensive neck dissection, including the deeper cervical glands. Recurrence may occur in the posterior cervical and auricular, or in the deep cervical groups of lymph nodes. Occasionally distant metastasis is seen, and there are 2 cases in this group which might possibly be placed under this

heading. Both were included in the series as dying of carcinoma of the lower lip. One died of carcinomatous metastasis to the brain 2 months after therapy here, and 1 died of metastasis to the lung 4 months after therapy for carcinoma of the lip.

There are other patients who seem prone to develop local recurrences without involvement of the lymph nodes. Several in this group had more than one recurrence of the local lesion without metastasis. One patient came in with a local recurrence, and the local lesion was treated but the surgeon advised against a neck dissection because he felt that this patient was apt to develop a recurrence again. This proved to be true at a later date.

Attention should be called to the fact that only 8 out of 34 cases in the primary group with palpable glands were proved to have glandular involvement at operation and only 3 of 71 in those without palpable nodes. While in the recurrent group, 26 of 43 with palpable glands were found to be in-

volved and only 2 of 21 without palpable glands.

One gets the impression from studying the individual cases that surgical removal of the glands when they are involved is of definite value and highly successful in the control of the disease. If all of the patients could be systematically followed and kept under observation long enough, it might be possible to dispense with the routine procedure of a neck dissection, at least in the earlier more benign cases, and defer the dissection of the glands until there is evidence of glandular involvement.

Metastasis to Mandible

There were 25 patients in whom the mandible was thought to be the seat of carcinomatous involvement, and in 18 cases the clinical impression was substantiated at operation.

Of the 18 proved cases, 3 had a neck dissection and x-ray therapy to the neck; one patient is living and well 5 years, 5 months after therapy; one was followed 3 years, 5 months and was well when last seen; the remaining patients died of carcinoma. One patient was treated with radiation therapy alone and has been followed for 10 months and now has necrosis of the mandible. Two of the patients were treated by excision of the tumor; one of these is living and well 8 months, the other died of the disease. Thus, in this group of 6 cases, 2 or 33.3% died of carcinoma.

The other 12 patients in the group of 18 proved cases were treated by resection of the mandible. Six of these patients also had a neck dissection and 8 of them had radiation therapy to the neck. One patient is living and well 2 yrs. 3 mos. after therapy. Three were followed 5 yrs. 3 mos., 2 yrs. 9 mos., and 7 mos., respectively, and were well when last seen. One patient was not followed. There was one surgical and one cardiac death. Five or 41.6% died of carcinoma and there was an operative mortality of 8.3%.

There were 7 of the 25 cases not

proved to have involvement of the mandible. Two of these are living 5 yrs. 8 mos., and 3 yrs. 7 mos. Both were treated by neck dissection and radiation. Five patients were treated by radiation alone to the neck, and all of these patients are dead.

The incidence of carcinomatous involvement of the mandible for the whole group was 7.5%.

Conclusions

1. An analysis of 333 cases of carcinoma of the lower lip treated during the ten year period from January 1st, 1926 to December 31st, 1935, is presented.
2. The lesions occurring at or near the mid-line appear to have a more favorable prognosis, and a possible explanation for this is offered.
3. In this study the mortality from the infiltrative and papillary types of lesions was about the same.
4. There was a higher percentage of deaths and recurrences in patients with lesions graded III and IV (microscopic).
5. Survival curves of the whole group, the primary group and the recurrent group were constructed, and an explanation of the method used is given. The probable 5 year survival for the whole group is 50%, for the primary group about 58% and for the recurrent group 40%.
6. The methods of treatment of the various types of cases are outlined.
7. There was an incidence of recurrence in glands of the neck in about 10% of those cases having a neck dissection in both the primary and recurrent groups, and in those not having a neck dissection, only about 4% developed a recurrence in the lymph nodes.
8. Roentgen ulcer was encountered in about 15.5% of the cases receiving irradiation therapy to the lip. The

average length of time between treatment and the appearance of the lesion was 14 months. The majority heal spontaneously.

9. There was an incidence of radiation necrosis of the mandible in about 1.8% of the cases treated with irradiation therapy. Protection of the patient from trauma after treatment is suggested as a factor in the prevention of osteomyelitis of the mandible.

10. The operative mortality was 1.5% in those patients having a neck dissection.

11. There were 17 cases proven to have carcinomatous involvement of the mandible ---an incidence of 5%. Twelve of these had resections of the mandible with an operative mortality of 8.3%. The death rate from carcinoma in this group of 12 cases is 41.6%, as compared with 33.3% in 6 proven cases, 3 of whom had a neck dissection irradiation therapy to the neck and 2 had excision of the tumor only, and 1 had irradiation only.

pig inoculations are requested.

This is being done for the reason that the guinea pig method is very expensive and it is necessary for us to cut expenses. Secondly, we have been using the cultural method for the past five years and have found as many cultures showing tubercle bacilli as we have guinea pigs. Other investigators have reported this, too. In fact, in some instances, cultures have shown tubercle bacilli where guinea pigs have been negative and vice versa, of course. In other words two methods may be superior to one, but the culture method stands up very well in contrast to the guinea pig method. We have found only one instance in which organisms isolated in cultures were non-virulent for guinea pigs. The third reason why we feel that we can do only cultures on sputums and voided urine specimens is that as a rule it is not difficult to obtain second specimens. The primary reason, however, is that it is absolutely necessary that our expenses be cut because of lack of sufficient funds and our animal work is the most expensive laboratory procedure that we have.

IV. LETTER FROM MINNESOTA DEPARTMENT OF HEALTH

Guinea Pig Inoculations

The following letter was received from O. McDaniel, Director, Division of Preventable Diseases, Minnesota Department of Health:

"On May 4, we received a specimen of 24 hour urine from - - - - - . We wish to report that no acid-fast bacilli were found microscopically.

We note that you requested that guinea pigs be inoculated with this specimen. We wish to inform you that we just now discontinued the inoculation of guinea pigs with voided urine and sputum specimens. Instead, the cultural method will be used on all specimens of sputum and voided urine on which guinea

When animal inoculation with a voided urine specimen is desired, a catheterized specimen should be sent. Under certain circumstances, we should imagine that one might wish to send 24 hour voided urine specimen rather than a catheterized one. If cultures in these cases show tubercle bacilli, we will request specimens from the right and left kidney. In all body fluids, such as pleural fluid, fluid from the right and left kidney and joint fluid, which are sent in for guinea pig inoculation for evidence of tuberculosis, the animal test will be done."