# PROGNOSIS AND TREATMENT OF MALIGNANT GOITER

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In a discussion of the prognosis and treatment of malignant goiter it is not pertinent to offer any historical account of the literature pertaining to this subject. In order, however, that the problem may be clearly understood, it is necessary to review the classifications of malignant tumors of the thyroid gland. Although I am fully cognizant of the widely diverging opinions regarding a satisfactory classification of these tumors, I shall present briefly Graham's classification,[1] since it is the one with which I am most familiar and my ideas about treatment and prognosis have been based on such a grouping of the cases.

Graham's classification is as follows:

| | | |
|---|---|---|
| I. Sarcoma | 1. Lymphosarcoma | |
| | 2. Spindle-cell sarcoma | |
| II. Mixed | 3. Carcinoma-sarcoma | |
| III. Carcinoma | 4. Scirrhous carcinoma | not in adenomata |
| | 5. Adenocarcinoma | not in adenomata |
| | 6. Papillary carcinoma | in adenomata |
| | 7. Malignant adenoma | in adenomata |

These various groups may be briefly described as follows:

*Lymphosarcoma* probably originates in the lymphoid tissue of the thyroid gland. It is a hard, rapidly growing tumor, terminating fatally, usually within a period of months, and in our experience has resisted every type of therapy.

*Spindle-cell sarcoma* is of infrequent occurrence, and here again in our experience the prognosis is universally fatal. I cannot enter here into any discussion as to whether a true sarcoma may occur within the thyroid gland, but certainly tumors of this type cannot be distinguished from the spindle-cell sarcomata and fibrosarcomata which arise elsewhere in the body. Thyroid tumors of this type are usually recognized clinically as malignant.

It is astonishing to note the rapidity with which sarcomata of the thyroid disappear under x-ray therapy, only to reappear after a few months with the same startling rapidity, when they are unaffected by x-ray.

In a small group of cases we have been forced to classify the tumor as a carcinoma-sarcoma, because both mesoblastic and epithelial elements were present. When tumors of this type are pre-

sented to pathologists, they may be called either carcinoma or sarcoma, and they always excite a discussion. In our experience, the prognosis has been fatal in 100 per cent of the cases.

*Scirrhous carcinoma* conforms morphologically to scirrhous carcinoma seen elsewhere in the body. Tumors of this type are non-encapsulated and invasive. The prognosis is fatal in 100 per cent of the cases.

Fortunately, tumors of the three types just described are present in only a comparatively small number — approximately 12 per cent — of the cases of malignancy of the thyroid gland.

*Adenocarcinoma*, not originating in adenoma, represents a group of cases cited here at the Post-Graduate Assembly in 1927, by Graham. These tumors are small, solid, non-encapsulated tumors which appear to have their origin in the non-tumorous portions of an adenomatous goiter. They are always discovered by the pathologist. In gross appearance they resemble adenocarcinoma of the breast. In a series of sixteen cases all patients are living. This is, of course, the most favorable group of the malignancies of the thyroid.

*Papillary carcinoma* originates in an adenoma. Tumors of this type are encapsulated, are usually cystic and do not metastasize as long as they remain within their own capsules. If they do break through, they may metastasize through the lymph channels, but not through the blood stream — at least metastasis through the latter route has not been noted. These tumors may reach a very large size, as will be noted in one of the cases cited below.

*Malignant adenoma* is the most important and most frequently encountered type of tumor originating in the thyroid gland. Tumors of this type have given rise to much controversy among the pathologists. Graham has pointed out, as the outstanding characteristics of these tumors, that they invade the blood vessels and metastasize through the blood stream; as in all cases thus classified, this phenomenon has been noted. He also has pointed out that in every case in which recurrence and metastasis followed the removal of an adenoma, invasion of the blood vessels could be demonstrated.

The following cases illustrate the variations in the characteristics and the prognoses and indicate the treatment which may be applied in the presence of different types of malignant goiter.

## Case Reports

*Case I.* The patient was a woman, 64 years of age, who stated that two years before she came to the Clinic her physician had called her attention to the presence of a small nodular enlargement of the thyroid gland in the midline of the neck. At that time the patient had not noticed any symptoms referable to this enlargement, but

a year later she noticed that it had increased in size and at that time she began to have paroxysms of coughing and choking which were relieved by lying down. Two months before her first examination at the Clinic, the gland began to grow very rapidly and caused marked dyspnoea, and pain under the left arm.

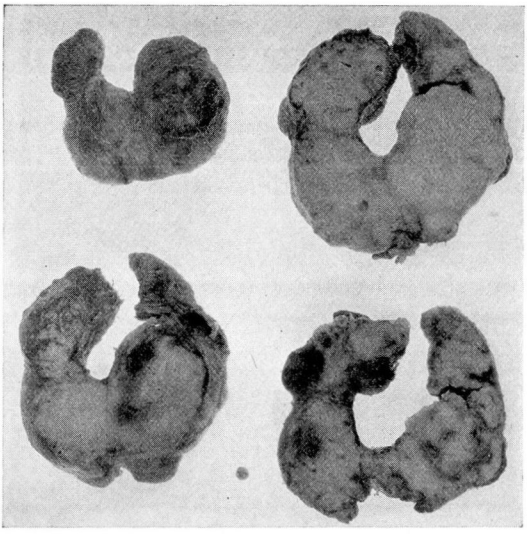

Fig. 1. Specimen: Case I

On examination, there was found to be a very large generalized enlargement of both lobes of the thyroid gland, with considerable thickening of the isthmus. The gland was quite firm throughout, with several large round nodules in the left side, extending from the mastoid to the angle of the jaw, downward toward the clavicle and posteriorly to the trapezious muscle. These nodules, which were freely movable, were thought to be lymph nodes involved in the neoplasm. On the right side of the neck another lymph node was involved, just above the clavicle. The trachea was displaced to the right and the lower border of the gland extended beneath the manubrium and left clavicle. The superficial veins over the upper chest were distended. The impression was that this was a carcinoma of the thyroid gland with metastases to the cervical glands.

On x-ray examination the chest was found to be normal, except for a substernal mass in the upper mediastinum. Laryngeal examination gave no significant findings. The basal metabolic rate was plus 21 per cent.

At operation, which was performed March 29, 1930, there was found to be a moderately hard diffuse enlargement of the whole

gland, which had a yellow-white appearance beneath the capsule. The isthmus was large and fused and completely encircled the trachea. No attempt was made to remove the cervical glands. Histological examination showed this growth to be a lymphosarcoma. Following the operation, the patient was given a course of x-ray therapy.

The patient is now under the care of Dr. Francis Carter Wood, in New York, and a recent communication from him states that she is still alive.

The unusual feature of this case is that although the tumor was a lymphosarcoma, the patient has lived for more than a year since its removal. In our experience this is an unusual sequel in a case of this type of tumor.

*Case II.* This patient, a woman 67 years of age, stated that she had had a goiter for 43 years. It remained stationary in size until

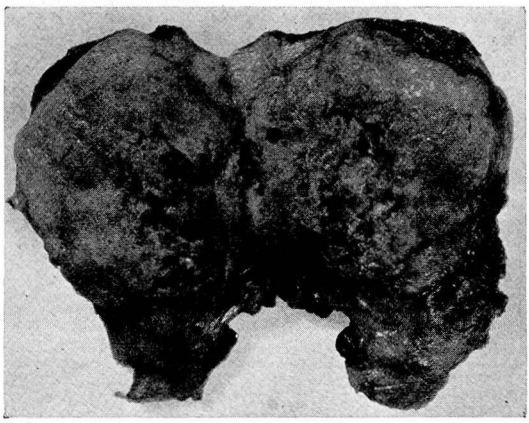

Fig. 2. Specimen: Case II

one year before she came to the Clinic, when it began to grow rapidly and became firm in texture. At the time of her examination at the Clinic the patient suffered some shortness of breath and difficulty in swallowing and from local pain which was referred to the head, the right arm and both shoulders. There had been no loss of weight and no cardiac symptoms or symptoms of hyperthyroidism. The only positive physical findings were a blood pressure of 174/100 and a very hard nodular mass in the right side of the neck, which involved the isthmus. The clinical impression was that the enlargement of the thyroid was due to a carcinoma. X-ray examination of the chest revealed a substernal goiter. At operation, a very

hard nodular gland was found and a mass about the size of a golf ball was removed. The impression at the time of the operation was that the growth was malignant and that its complete removal was impossible, although the right lobe was completely removed along with the isthmus, and a portion of the left lobe.

This patient was given x-ray therapy, but only lived for about six months.

The pathological report was fibrosarcoma.

*Case III.* The patient was a woman, 71 years of age, who five years before she came to the Clinic first noticed a small firm nodule

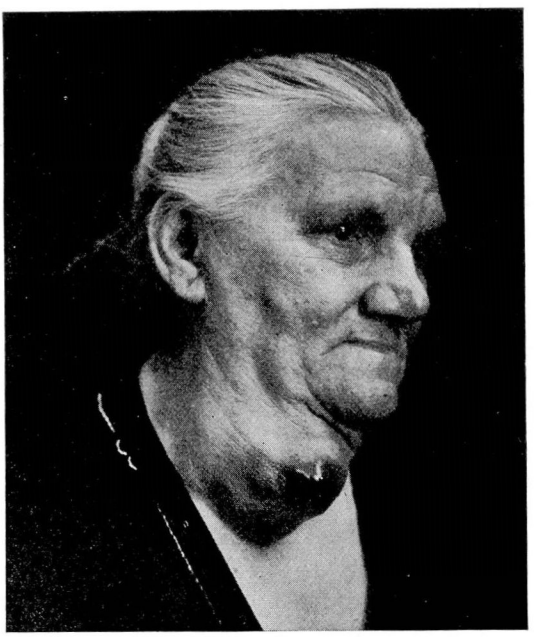

Fig. 3. Case III

in the right side of the neck. This had increased in size steadily, the greatest increase occurring during the preceding year. Four weeks before, the mass had become dark in color and soft in consistency and broken down, and a small amount of fluid had drained from it. There had been no pain or tenderness and the symptoms had always been referred to the local growth.

The only positive findings in the physical examination were a blood pressure of 224/116, and a very large irregular nodular enlargement on the right side of the neck, extending from the clavicle

to about two centimeters from the mandible. There were several soft areas on the anterior surface of the tumor. The gland was removed and the tumor found to be a papillary adenocarcinoma. The patient was given postoperative x-ray therapy and has now lived for more than two years, but at the present time there is a recurrence in the area of the operative wound.

*Case IV.* The patient was a woman, 42 years of age, who was first seen at the Clinic on January 13, 1928. Her chief complaint was goiter, with swelling of the face and shortness of breath. The patient stated that she had had a goiter for several years, but that it had recently begun to increase in size. During the preceding two weeks, shortness of breath, puffiness of the face and some duskiness of the skin had developed. She had also noted a bluish discoloration of the chest and some pain.

On physical examination the patient was found to have a dusky, puffy face, large veins over the anterior chest and a very large, hard, diffuse enlargement of the thyroid which extended well down below the sternum. The clinical diagnosis was colloid goiter with obstruction. X-ray examination revealed a large intrathoracic goiter, extending down into the mediastinum, one-half of the way into the chest.

At operation, on January 17, 1928, a large, hard, firm, fixed gland was found which extended well down into the mediastinum. The gland gave the appearance of a malignancy. I decided that it would be futile to attempt to remove the entire growth, the indications being for decompression of the trachea and later x-ray treatment.

I removed a considerable portion of the left lobe and noted at the time that on the surface of the growth there was a large, dilated, thin-walled vein, through the walls of which could be seen masses of tissue which were probably malignant, and which had broken through the wall of the vein and were being carried into the general circulation. We felt that in all probability this patient had distant metastases. The ribbon muscles were clamped on both sides and cut transversely and not reapproximated. The pathological diagnosis was malignant adenoma and study of the tumor showed many vessels with blood vessel invasion.

The patient was given x-ray therapy and at the end of the eight weeks' period practically all of the symptoms of obstruction had disappeared and her condition was highly satisfactory. However, she died approximately six months after her first admission.

*Case V.* The patient was a woman, 44 years of age, who first came to the Clinic in January, 1927. She stated that she had always

had a full neck, but was quite insistent that the tumor then present had appeared with the preceding three months.

On physical examination, the patient was found to have a movable tumor which felt cystic, and gave the impression that there had been a hemorrhage into an adenomatous cyst.

At the time of operation, however, the tumor was found to be completely filled with neoplastic tissue and the pathological diagnosis was malignant adenoma.

A course of x-ray therapy was given, but the patient returned in

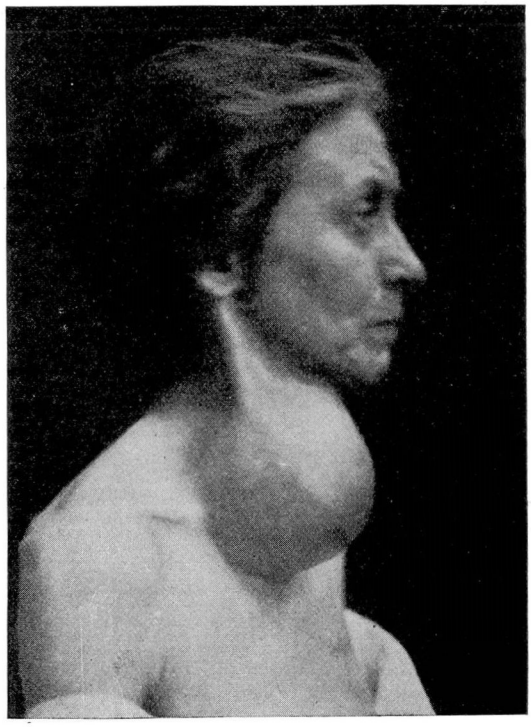

Fig. 4. Case V

three months with a recurrence in the incision line, which was removed. This was found to have cells of the same type as those noted in the previous operation. Another course of x-ray therapy was given.

The patient returned from time to time and was found to be rapidly losing weight. X-rays were taken for the purpose of discovering whether or not there were any metastatic lesions, but with the possible exception of a lesion in the left humerus, none were found.

The patient became very much emaciated and I felt that she certainly had generalized metastases which we were unable to locate. She died about eighteen months after the primary operation. Before death, a large hard tumor appeared on the side of the face. This apparently was in the parotid gland.

*Case VI.* The patient was a woman, 53 years of age, who was first seen on February 13, 1928. She complained of a goiter, which,

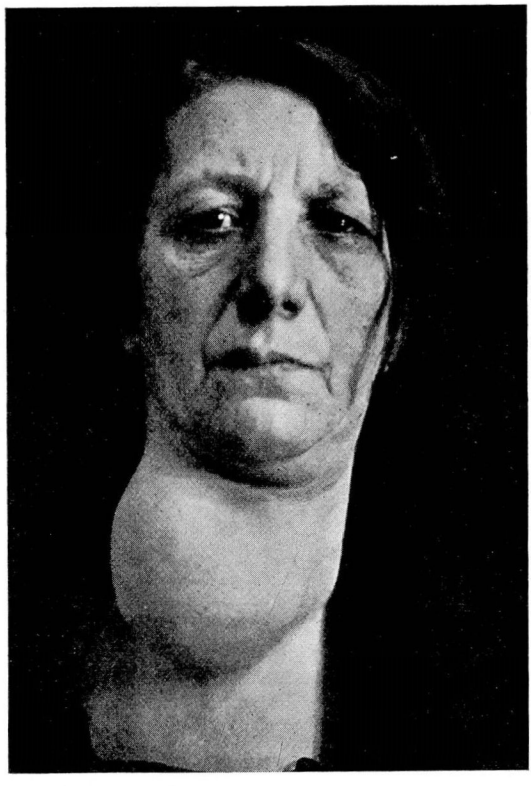

Fig. 5. Case VI

though she had had it for more than thirty years, during the preceding year had been growing rapidly and had doubled in size. The patient was nervous and irritable, had a marked tremor and had lost twenty pounds in weight. Her heart was rapid and she was dyspnoeic. There was also a history of pain in the epigastrium and of other symptoms suggesting the presence of a duodenal ulcer.

On physical examination a large adenoma on the right side of the neck was seen. This was freely movable and smooth. Our clinical

impression was that the patient had an adenoma with hyperthyroidism and duodenal ulcer, and it was considered probable that the adenoma was malignant.

The x-ray examination revealed the fact that the trachea was displaced well to the left and was compressed. When the tumor was removed, it was found to be a malignant adenoma and many veins were found to be filled with the tumor tissue.

The patient was given x-ray therapy. At the last report, two years after her operation, she was living and well.

In this case, a goiter of long duration, which showed rapid recent growth, was accompanied by the well-defined symptoms of hyperthyroidism which are seen in a high percentage of cases — 37 per cent, according to Coller.

*Case VII.* The patient was a man, 67 years of age, who came to the Clinic because of a swelling of the neck which had been first noticed ten years previously on the right side. This had gradually increased in size, especially during the preceding year and was apparently pressing on the trachea. The only other subjective symptoms were nervousness and a fluttering of the heart.

On physical examination, a large nodular, hard, irregular tumor on the right side of the neck was found. There was moderate arteriosclerosis and some irregularity of the heart, with an occasional dropped beat.

Laryngeal examination and x-ray studies of the chest revealed nothing of significance.

A clinical diagnosis of malignant goiter was made. It was thought that the tumor could probably be removed *in toto*, together with a block dissection of the glands of the neck. At operation, however, a very large tumor, with multiple masses, was dissected out, but it was impossible to remove the whole mass, as a very large, hard extension descended under the clavicle on the right side.

At this time the condition was considered to be almost hopeless, but the patient was given x-ray therapy, with the result that within a very short time the mass in the neck practically disappeared. The large glands which were present in the neck, which have become round, hard nodules, have remained stationary in size up to the present time — that is, for eight years.

This case is presented because in spite of its apparent hopelessness, being a malignant adenoma with marked extension and multiple masses, there has been a most satisfactory clinical result.

*Case VIII.* The patient was a man, 46 years of age, who came to the Clinic with a large tumor on the right side of the neck which had extended to the left of the third rib on the right side. In January,

1916, the tumor was removed, some difficulty being encountered in dissecting it from the thorax. The space left by the tumor became entirely obliterated by the pleura and the marked engorgement of the veins of the neck disappeared. The pathological report of the time of this operation was malignant adenoma.

Seven years later (June, 1923) the patient returned with a tumor in the right lower pole, about the size of a small hen's egg. This was removed and found to be a tumor of exactly the same type as that

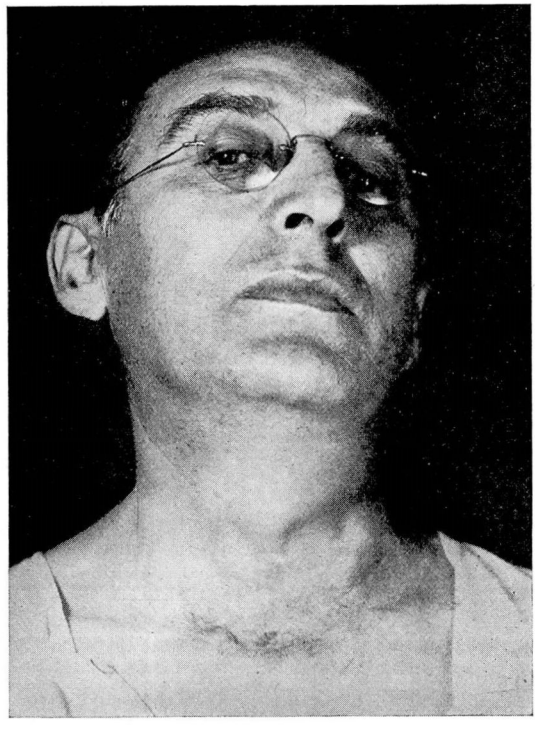

Fig. 6. Case VIII

removed at the primary operation. The patient was observed from time to time, but returned again in September, 1923, with another recurrence. At this time a mass occupied a position higher up in the neck adjacent to and including the sternocleidomastoid muscle. This mass was removed, together with a large portion of the muscle. The diagnosis at this time was again malignant adenoma.

In April, 1925, the patient again returned with a mass about the size of a large marble on the left side, lying just posterior to the sternocleidomastoid muscle, extending deeply into the neck and

firmly attached to the surrounding tissues. This mass was carefully dissected from the carotid sheath.

In September, 1928, a small nodule was removed from the level of the left sternoclavicular joint. The same type of neoplastic tissue was again found within the capsule.

In October, 1928, two small nodules were removed from the skin above the scar on the left side.

In March, 1930, he returned with a small recurrence on the right

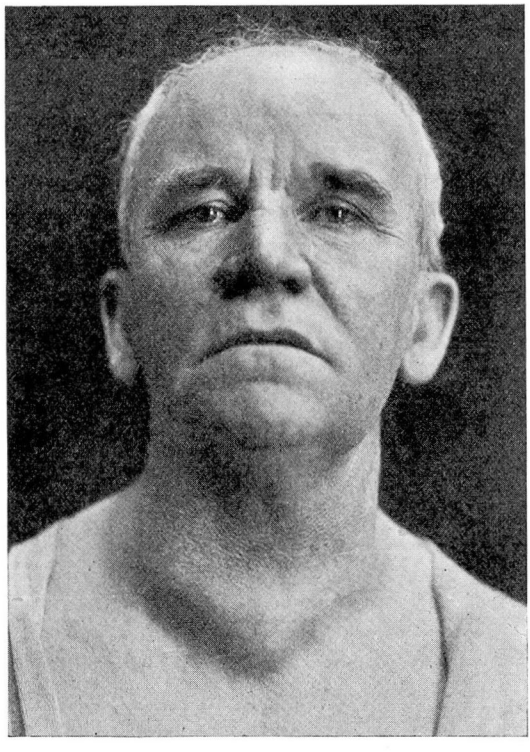

Fig. 7. Case IX

side of the neck anteriorly, near the midline. This tissue was also removed and the same pathological picture noted.

After each operation, the patient was given a course of x-ray therapy. This case is peculiarly interesting, because it presents a patient who has now lived for more than fifteen years, has had seven operations and seven courses of x-ray therapy, and throughout this period has been an active, practically well individual.

*Case IX.* The patient was a man, 63 years of age, who came to the Clinic on March 26, 1927, complaining of a hard tumor in the

neck, dyspnoea and the coughing up of blood. He stated that seven years previously he had first noted a small hard tumor in the neck just below the cricoid cartilage. This had remained stationary for three or four years and then began to grow larger, extending laterally to the right side of the neck. During the preceding six months, its growth had been quite rapid. Three months before the patient began to cough up bright blood, very little during the day, more at night. He had lost no weight, his appetite was good, but he felt that he had become somewhat more nervous.

On physical examination a very hard tumor was found in the isthmus of the thyroid, extending into the right lobe. It was stony hard but movable. The breath sounds over the chest were distant, but otherwise the physical examination disclosed nothing of significance.

It was our impression that this was a malignant tumor of the thyroid gland. Examination of the larynx showed some thickening of the cords and reddening, but both cords were movable. X-ray examination of the chest showed advanced metastases in the lungs. The patient was given x-ray therapy, however, and on May 2, 1927, there was apparent improvement, although the findings remained the same. He returned again on June 6, 1927, when it was found that the tumor had become markedly smaller in size, that the lesions in the chest were less marked, and that the general condition of the patient had improved. The x-ray films also showed some improvement in the lungs.

On August 25, 1927, there was considerably more improvement, but when the patient returned in December, 1927, metastases were noted in the ribs, although the general condition was fairly good. Surprisingly enough, this patient survived for twenty-six months after the initial diagnosis was made. This case suggests the question as to whether or not a patient with a malignant tumor in the thyroid gland and obvious metastases in the chest should be treated. We feel that they should, for certainly the marked physical improvement noted in this case and the comfort of the patient during the time he lived justify the procedure.

*Case X.* The patient, a woman 64 years of age, had had a thyroidectomy performed in 1920 by Dr. Crile and she came to the Clinic five years later with a large ulcerating mass in the neck. She stated that the incision following the thyroidectomy had never healed and that constant drainage had been present.

Upon physical examination, the patient was found to have a large, fixed mass in the neck, over the anterior surface of which was a large fungating ulcer. For the most part this tumor had been pain-

less and the patient had had few other symptoms than those presented by the local lesion.

The patient died shortly after her examination here. I think the interesting point about this case is the fact that a malignancy of the thyroid had persisted for more than five years, presenting few symptoms other than those from the local lesion.

*Case XI.* The patient, a woman 72 years of age, stated that she had had a goiter for many years; fourteen years before it had begun

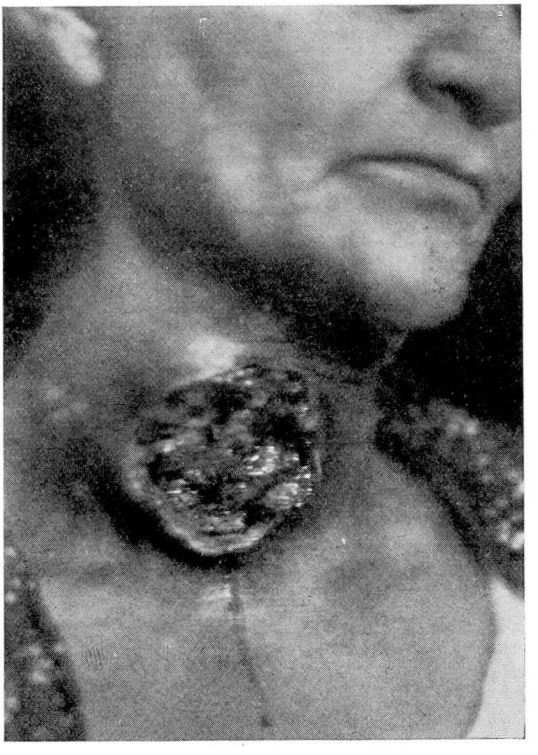

Fig. 8. Case X

to enlarge and had grown steadily since that time. Two years before an abscess developed which was opened, and the patient experienced a great deal of relief. This abscess had continued to drain and the patient had also had difficulty in swallowing.

Several x-ray treatments had been given prior to the patient's examination at the Clinic.

There were no significant findings in the physical examination, save for the tumor in the mid-line of the neck, which was very hard

and fixed. It was red in color and there was a sinus in the central portion, from which there was a slight drainage.

Laryngeal examination revealed that the entire left pharyngeal wall, including the tonsil, had been pushed to the right side by an extrinsic growth, the left pharyngeal wall coming in contact with the opposite side. The epiglottis was also pushed forward on the base of the tongue. It was absolutely impossible to see any of the laryn-

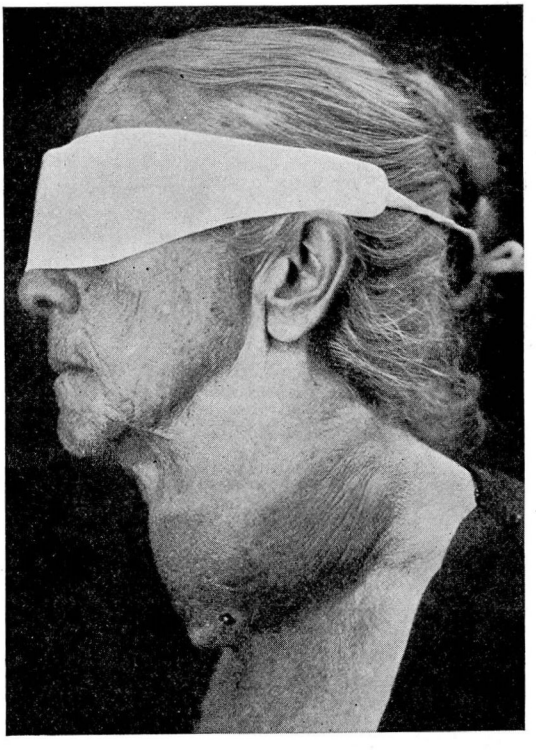

Fig. 9. Case XI

geal structures. The mucous membranes over the tumor were intact and there was no ulceration. The breathing space was small.

Due to the hopelessness of the patient's condition, and the fact that she had had recent x-ray treatment, she was not given any x-ray treatment at the Clinic.

The patient died about two months after this examination.

*Case XII.* The patient, a woman 71 years of age, stated that she had had a goiter on the right side of her neck since the age of five or six years, and that from year to year this had increased slight-

ly in size, but that during the preceding summer it had grown very rapidly on the left side. The patient complained of some dyspnoea, some nervousness and loss of weight.

Examination revealed a markedly enlarged, very firm thyroid in the left side of the neck. It was not movable, but was fixed and presented hard nodules, apparently arising for the most part from the left lobe. There was also a mass about the size of a pigeon's

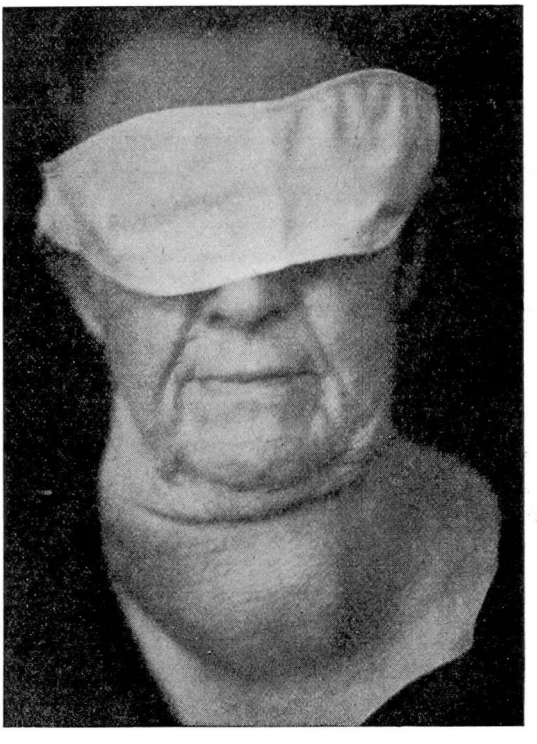

Fig. 10. Case XII

egg in the inframandibular region in the midline. The case was considered inoperable and the patient was given x-ray therapy.

She returned in two months much more comfortable and the mass was found to be smaller in size, but the patient died less than a month later.

*Case XIII.* The patient, a woman 64 years of age, stated that she had always had a goiter and that nine months before she came to the Clinic a new lump had appeared within the tumor, which had been removed, but the whole mass had grown very rapidly in size during the past few months. This very hard, firm, fixed mass presented areas which were apparently broken down and were fluctuant.

In this case, of course, the condition was absolutely hopeless. It is typical of the group of cases in which the patient allows the tumor to reach an enormous size before seeking advice.

## General Considerations

From the cases described above, it would appear that we must reconsider our former impression that in all cases of malignancy of the thyroid gland the prognosis is bad. While it is true that in the first four groups cited there is a mortality of approximately 100 per cent, we must remember that these groups comprise only about 12

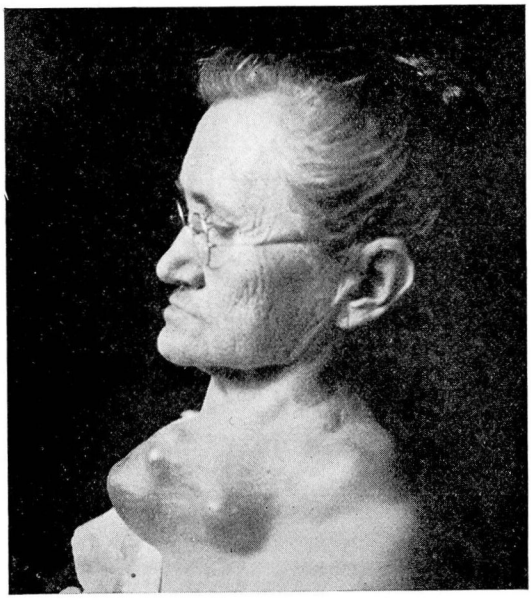

Fig. 11. Case XIII

per cent of the total number of cases of malignant goiter. I fully agree with Coller[3] and Pemberton[5] in their statements that the prognosis is better than is generally supposed, for we have many patients who have lived for a long period of time.

In his textbook, Waring[2] reports a case of carcinoma of the thyroid with cervical gland involvement which had remained well for twenty-one years and cited a case of Breitner's in which three operations, each including a tracheotomy, had been performed. The patient lived for more than a ten-year period, and at the time of this report was 66 years of age.

Obviously, there is a group, illustrated by the last cases cited, in which no hope of aid can be extended to the patient, in which cases the growth has extended into the larynx or in which massive metastasis has taken place. On the other hand, we are seeing cases which at the time of operation or of x-ray therapy have been considered hopeless, in which the patients have now lived many years.

It is also important to remember that when there is a recurrence the case should not always be considered to be hopeless, but that the tumor should again be extirpated and x-ray therapy again applied. Metastasis in the chest also should be treated with x-ray therapy, as this measure may add comfort and length of life to the patient.

In certain cases it is quite evident that any operative procedure is unjustified. It is true also that a diagnosis can be made with a reasonable degree of certainty in less than 50 per cent of the cases.

The ideal procedure, of course, is to remove the entire tumor. In these cases, the utmost care must be exercised, for I have seen instances in which a wide dissemination of the neoplastic tissue by embolism has occurred immediately following the manipulation incident to the operation.

But the question arises as to whether or not any plan of management can apply to the whole group. One important point is to ascertain whether or not the tumor is confined within the neck, that is, whether or not metastasis has taken place in any place other than in the cervical glands. For this reason, an x-ray examination of the chest should be a routine procedure, together with a careful examination of the long bones. Laryngeal examination is also important, as it is necessary to know whether extension has taken place in the larynx and whether or not the vocal cords are paralyzed. The paralysis of either or both vocal cords is important from the diagnostic standpoint, as it has been our experience that vocal cord paralysis very rarely occurs in cases of non-malignant goiter, other than thyroiditis.

Additional information can sometimes be obtained from an x-ray examination of the neck, which may disclose a cyst with a calcified wall or a calcified adenoma. It has been my personal experience that cysts with calcified walls have been the most frequent source of error in the differential diagnosis of tumors suspected of being malignant tumors.

In cases of obstruction it may be necessary to perform a so-called decompression operation, and in the absence of vocal cord paralysis this procedure often affords great relief. This operation includes a wide transverse incision, through all the preglandular muscles,

ligation of the vessels in the cut ends of the muscles and closure of the subcutaneous tissues and skin over the tumor. In like manner the removal of a portion of the tumor often results in great relief from pressure on the trachea.

In other cases, an immediate tracheotomy is required. In certain cases this operation may be technically difficult. When the tumor is large and completely covers the trachea from the substernal notch to the cricoid, it may be astonishingly difficult to find the trachea and, having found it, to recognize it, as it may be a small cord-like structure.

We have had little experience with the use of radium in these cases but rely upon x-ray therapy. We are constantly using x-ray therapy in all types of malignant tumors, but it has been of little aid in the cases of sarcoma, carcinoma-sarcoma and scirrhous carcinoma. The sarcomas, to be sure, do respond with rapidity to x-ray, but recur rapidly. In cases of small adenocarcinoma, not originating in adenomata, we do not feel that x-ray therapy is indicated and we do not advise its use, unless these tumors are on the surface of the gland and have become adherent to the trachea or the preglandular muscles. In the largest group of malignant tumors of the thyroid gland — malignant adenomata and papillary carcinomata — we certainly feel that the results are now more encouraging than we had supposed possible before the advent of the improved technic in x-ray therapy.

I feel, as Clute[4] does, that a biopsy should be done whenever possible. As he points out, by this means a diagnosis can be established and the type of malignancy revealed, this in turn making it possible to determine the probable duration of life and response to x-ray therapy.

## Conclusions

From the series of cases here presented, the following conclusions may be drawn:

1. The prognosis in cases of malignant goiter depends first upon the type of tumor, and, second, upon its extent.

2. In cases of sarcoma (20 cases) the results have indicated that the duration of life is short, as every patient, with two exceptions, has died within a short time.

3. A like prognosis must be made in cases of sarcoma-carcinoma (5 cases) and of scirrhous carcinoma, which are always fatal.

4. In cases of adenocarcinoma which do not arise from tumorous tissue, the prognosis is favorable. We know of no case in which death was due to this cause.

5. The foregoing four groups fortunately represent only 12 per cent of the malignant tumors of the thyroid gland. The remaining 88 per cent offer a prognosis which is much more encouraging than is generally supposed.

6. Papillary carcinomata treated by combined surgery and x-ray give a 50 per cent three-year cure, and malignant adenomas a 25.8 per cent three-year cure.

## References

1 Graham, Allen: Malignant Thyroid. Proc. Inter-State Post Grad. M. Assemb. North America (1927), 3: 264-269, 1928.

2 Waring, Sir Holburt J.: The Surgical Treatment of Malignant Disease. Oxford Press, New York, 1928, Chapter 25.

3 Coller, F. A.: Adenoma and Cancer of the Thyroid; A Study of Their Relation in Ninety Epithelial Neoplasms of the Thyroid. J.A.M.A. 92: 457-462, 1929.

4 Clute, H. M. and Smith, L. W.: Cancer of the Thyroid Gland. Arch. Surg., 18: 1-20, 1929.

5 Pemberton, John De J.: Malignant Disease of the Thyroid Gland: A Clinical Consideration. Ann. Surg., 87: 369-377, 1928.