RIEDEL'S STRUMA AND STRUMA LYMPHOMATOSA (HASHIMOTO)

A COMPARATIVE STUDY

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THE present rather generally accepted opinion that struma lymphomatosa (Hashimoto[1]) and Riedel's[2] struma are different manifestations of the same disease process, seems to have originated from a statement made by Ewing,[3] in 1922. As a result of the acceptance of this concept there have been very few investigators who have carefully analyzed these two conditions in an attempt to differentiate them. It is found, therefore, in reading published reports, that many cases in which the clinical and pathologic findings are quite characteristic of struma lymphomatosa are reported as Riedel's struma. From our studies we are convinced that the two conditions are separate diseases and the evidence here presented will, we hope, stimulate a more critical study of them to the end that their etiology and clinical course may be more thoroughly understood.

The clinical differences between Riedel's struma and struma lymphomatosa were emphasized by Graham,[4] in 1931, when he revived Hashimoto's original contention that the two diseases were separate entities. Lee,[5] in his review of the literature, agrees with this concept of Graham's to the extent that he separates the fibrous type from the lymphoid type of pathologic change. Lee, however, in his review, covered the same records that Graham did but in addition included the cases reported after 1931. To prevent confusing duplication in the recording of cases, we have reviewed the literature since 1930 and here record only those cases not included by Graham. Thus, we feel we have available in Graham's report and in this contribution, an account of nearly every case reported as Riedel's struma, chronic thyroiditis, ligneous thyroiditis and struma lymphomatosa. It is surprising that only 60 cases fulfill the clinical and pathologic requirements of Riedel's struma; and only 50 present the findings characteristic of struma lymphomatosa (Hashimoto). In the group we have designated as atrophy and fibrosis (Group III) are 22 cases, in 19 of which there were found foreign body giant cells. It is unfortunate that 80 cases are not available for study and accurate classification, because of insufficient data (Table I).

The literature from 1930 to date contains many incomplete reports. There were found at least 12 original articles reporting a total of 69 cases in all of which inadequate clinical and pathologic information was given.

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The statement made by Ewing, namely, that "the two lesions are different manifestations of the same disease process" has been taken too much for granted and has led many workers to report cases with inadequate clinical

TABLE I

CASES REPORTED SINCE 1931

Author	Reported As	Author's Classification Group I	Group II	Group III	Group IV
Vogel[23]	Riedel's struma	2			
Bothe[24]	Early Riedel's struma		1		
Crane[25]	Chronic thyroiditis				28
Bruce[26]	Riedel's tumor	1			
Kreuzbauer[27]	Chronic thyroiditis				1
Kreuzbauer[28]	Chronic thyroiditis	2		2	1
Prati[29]	Riedel's struma	2			
Traum[30]	Riedel's struma				1
Diez[31]	Riedel's struma	2			
Nestmann[32]	Chronic thyroiditis			1	
Oehler[33]	Eisenharte struma			1	
White[34]	Riedel's thyroiditis		1		
Angerer[35]	Eisenharte struma			Acute thyroiditis	
Melina[36]	Riedel's struma	1			
Nordland and Larson[37]	Thyroiditis				1
Eisen[38]	Riedel's struma				7
Howard[39]	Struma lymphomatosa		2		
Lester[40]	Riedel's struma		1		
Polowe[41]	Struma lymphomatosa				1
Seed[42]	Riedel's struma				5
Benson[43]	Riedel's struma			1	
Emerson[44]	Struma lymphomatosa		1		
Gilchrist[45]	Chronic thyroiditis	1			
Mallory[46]	Struma lymphomatosa		1		
Boyden, *et al.*[6]	Riedel's struma	2	1		6
Roulet[21]	Riedel's struma	2		1	
Poer, *et al.*[19]	Struma lymphomatosa		1		
Tearnan[8]	Riedel's struma		1	1	
Lee[5]	Chronic thyroiditis		3	8	
Clute, *et al.*[14]	Struma lymphomatosa		9		
Clute and Lahey[10]	Thyroiditis				17
Graham[4]	Collected	41	24	3	11
McClintock and Wright		4	4	4	
Totals		60	50	22	79

Group I represents Riedel's struma; Group II struma lymphomatosa (Hashimoto); Group III atrophy and fibrosis with foreign body giant cells; and Group IV cases with insufficient information to permit classification.

and pathologic data and without a careful analysis of all available facts. Likewise the statement of Boyden, Coller and Bugher,[6]—who not only agree with the unitarian concept of Ewing but go even farther and say,

"We do not believe that the process is a distinct entity"—cannot help but imperil a critical study of cases of these diseases. In spite of the many writers who have accepted without question the belief of Ewing, there is a growing number who feel the clinical and pathologic changes observed in each of the two types are such as to make the two diseases separate. It is the sincere hope of the authors that future contributors to this discussion will include complete records of each case in order that students of the subject will not be deprived of any opportunity to study these rare lesions.

TABLE II

SUMMARY OF CASES OF RIEDEL'S TYPE

		Literature	Graham	Author	Average
Sex	Male	14.2%	41.5%	.....	18.2%
	Female	86.8%	58.5%	100%	81.8%
Age	Youngest	24 yrs.	23 yrs.	31 yrs.	
	Oldest	78 yrs.	64 yrs.	53 yrs.	
	Average	43.1 yrs.	36.2 yrs.	41.6 yrs.	40.3 yrs.
Duration of symptoms	Shortest	2 mos.	15 days	14 days	
	Longest	2 yrs.	2 yrs.	2 yrs.	
	Average	9.2 mos.	7.3 mos.	6 mos.	7.5 mos.
Duration of goiter	Shortest	5 mos.	30 days	14 . days	
	Longest	23 yrs.	3 yrs.	8 yrs.	
	Average	7.8 yrs.	1 yr.	1.5 yrs.	3.5 yrs.
Thyroid involvement	Unilateral		48.6%	12.5%	
	Bilateral		51.4%	87.5%	69.5%
Hypothyroid	Postoperative.		19%	35%	27%
Number of cases		15	41	4	60

TABLE III

SUMMARY OF CASES OF STRUMA LYMPHOMATOSA (HASHIMOTO TYPE)

		Literature	Graham	Author	Average
Sex	Male	.....	4.2%	.....	1.4%
	Female	100%	96.8%	100%	98.6%
Age	Youngest	26 yrs.	40 yrs.	35 yrs.	
	Oldest	62 yrs.	75 yrs.	53 yrs.	
	Average	50.8 yrs.	52.4 yrs.	44.4 yrs.	49.2 yrs.
Duration of symptoms	Shortest	2 mos.	30 days	1 yr.	
	Longest	36 yrs.	6 yrs.	3 yrs.	
	Average	11.5 mos.	1.2 yrs.	2 yrs.	1.3 yrs.
Duration of goiter	Shortest	2 mos.	3 days	4 yrs.	
	Longest	15 yrs.	6 yrs.	16 yrs.	
	Average	3.8 yrs.	1.3 yrs.	7.5 yrs.	4.2 yrs.
Thyroid involvement	Unilateral				
	Bilateral	100%	100%	100%	100%
Hypothyroid postoperative		77.7%	58%	100%	78.8%
Number of cases		19	24	4	47

As a result of the studies of Graham and the observations made by ourselves, certain clinical differences are apparent. These may be summarized briefly here, and are presented in tabular form in Tables II and III.

Sex.—Sex plays little or no rôle in Riedel's struma; the ratio of female to male is nearly that found in all other types of goiter. In struma lymphomatosa (Hashimoto), however, more than 95 per cent of the patients were women.

Age.—Differences in age are present but are not always of significance in individual cases. In general, however, the average age of patients with Riedel's struma is younger than the average age of those who suffer from struma lymphomatosa. In a series of 60 cases of Riedel's struma the average age of patients was 40, while in 50 cases of struma lymphomatosa the average age was 49.

Duration of Symptoms.—In Riedel's struma the average duration of symptoms was approximately seven months while goiter had been present for an average period of 3.5 years. In struma lymphomatosa the symptoms have usually been present for a somewhat longer period, an average of 16 months with the average duration of goiter slightly over four years.

Thyroid Involvement.—In the case of Riedel's struma the lesion is not always bilateral, approximately 30 per cent of the cases exhibiting involvement of one lobe only. Of the 50 reported cases of struma lymphomatosa, however, all have been said to show involvement of both lobes of the gland.

Hypothyroidism.—Approximately 26 per cent of the patients with Riedel's struma develop hypothyroidism postoperatively while more than three-fourths of those suffering from struma lymphomatosa have definitely diminished thyroid activity after removal of the gland.

In the group which we have designated as atrophy and fibrosis are four cases in which the clinical and pathologic findings are somewhat different from the others. These cases (Nos. 1, 2, 3 and 4) are characterized by inflammatory fibrosis of the gland with the presence of many foreign body giant cells. At least 15 of the cases reported from the literature show similar findings. Clinically, the symptoms referable to thyroid involvement come on fairly rapidly and usually follow acute upper respiratory infections. There may be associated fever as well as pain and tenderness localized over the gland. Although included in this series with cases of Riedel's struma, this group seems to be of a slightly different character and, as pointed out to us by Graham,[7] it is not at all unlikely that further study of the lesion will show it to be a separate form of chronic thyroiditis.

In origin Riedel's struma and struma lymphomatosa show a marked etiologic difference. The former is conceded to be essentially a lesion of inflammatory nature. In most of our cases, as well as in some of those previously reported,[8, 9] a history of acute upper respiratory or dental infection is given as occurring just before the onset of the symptoms of thyroid disease. Clute and Lahey[10] also report a group of 21 cases of Riedel's

struma, in a number of which an acute inflammatory condition of the throat, tonsil, or teeth preceded the onset of the disease.

The mechanism of producing an inflammatory lesion in the thyroid gland, normally so resistant to infection, remains obscure. There is a well marked agreement among students of the subject that the cause is not syphilis or tuberculosis. Smith and Clute[11] report negative bacterial cultures and animal inoculation experiments with tissue from Riedel's struma, yet they still favor a chronic inflammatory process of unknown origin as the cause of the thyroid change. The microscopic picture of extensive fibrosis is in keeping with such a theory of origin. Bohan[12] has reported the isolation from dental infections of organisms which, when injected into a rabbit, produced lesions in the thyroid and thymus glands. Searls and Bartlett[13] isolated identical organisms from the thyroid gland and throat of a patient with acute thyroiditis. Such reports as these, however, are too few and too uncertain to be conclusive and for the present it seems best simply to accept the hypothesis that the lesion is inflammatory in type but of unknown etiology.

The causative factors in Hashimoto's lesion are even more obscure than are those of Riedel's struma. Recently Clute, Eckerson and Warren[14] have indicated that they are of the opinion that struma lymphomatosa is a degenerative change without evidence of an acute inflammatory process. Clute and Warren[15] further imply a difference between Riedel's struma and struma lymphomatosa when they accord separate places to these lesions in the differential diagnosis of thyroid cancer. No explanation has yet been advanced to account for an inflammatory reaction causing in one case marked sclerosis, and in the other hyperplasia of the lymphoid elements. The lymphadenoid type of thyroid has been described by Williamson and Pearse[16] as being a physiologically subnormal gland undergoing a compensatory lymphoid hyperplasia with the lymphocyte reaction proportional to the failure of the usual epithelial hyperplastic effort. Such a process would necessarily be a diffuse one, and indeed struma lymphomatosa of Hashimoto is generally of this character. Exhaustion atrophy is a recognized pathologic change in Hashimoto's lesion and this degenerative process might well be associated with some form of compensatory hyperplasia, as Williamson and Pearse suggest.

McCarrison,[17] by the use of a deficient diet, has produced experimentally a thyroid lesion which is remarkably like that of struma lymphomatosa. Dietary deficiency should also, if a part of the etiology of this lesion, produce changes in other organs. The report by Shaw and Smith[18] of a case of struma lymphomatosa in which there were adrenal lesions similar to those in the thyroid gland, as well as enlargement of the thymus, seems to indicate a causative factor of generalized character. Graham first enunciated the theory of the systemic nature of Hashimoto's lesion and although there is yet only meager proof of its truth, the concept that the changes in the

thyroid gland are only a local manifestation of a generalized disease seems to be compatible with the clinical course of struma lymphomatosa.

The history and the direct examination of the patient are of greatest importance in making a differential diagnosis between Riedel's struma and struma lymphomatosa. On palpation, tenderness and the presence of a very hard, fixed, resistant gland are strongly indicative of Riedel's struma. So hard does the gland feel on palpation that it is commonly mistaken for malignant disease. The smooth, diffuse hardness should suggest benign struma when contrasted with the irregular nodularity of neoplasm. This hardness of the gland in Riedel's struma is usually much more marked than the resilient firmness of struma lymphomatosa. Each of the lesions may cause dyspnea and dysphagia with a feeling of constriction or tightness around the neck. Weakness and fatigability may likewise be common to both, although the last two symptoms are more frequent with struma lymphomatosa.

Patients with struma lymphomatosa require a long time to return to normal, if they do at all. Their usual course is progressive hypothyroidism associated with such symptoms as fatigability, generalized weakness, and sometimes gastro-intestinal disturbances. On the other hand, those patients with Riedel's struma, following surgical treatment, tend to improve quite rapidly and frequently return to normal.

A clinical diagnosis of either of the two conditions is seldom made. There are no pathognomonic signs or symptoms in these cases and it is only by putting together all possible findings, past and present, objective and subjective, that a clinical hint may be obtained as to what is the true nature of the lesion. The age of the patient, antecedent history of upper respiratory or dental infection, degree of hardness and fixity, and the amount of gland involved, must all be carefully considered. Riedel's struma gives rise to the greatest difficulty in the clinical identification. The number of cases in which a diagnosis of carcinoma is made in cases of this disease is very high, while malignant disease is usually not suspected in the Hashimoto type of change. If the diagnosis is not made when the patient is examined clinically or by direct observation and palpation at the time of operation, rapid frozen section examination of the tissue may often be more confusing than helpful. We are, therefore, opposed to the making of such inadequate rapid studies of thyroid tissue. The most dependable findings are, we think, an accurate history, properly evaluated, and careful clinical examination of the gland.

Heretofore attention has been drawn to the clinical differences between these two lesions. However, from the standpoint of the morphology of the gland itself, there are also significant differential features which should be mentioned. Grossly the gland in Riedel's struma is very firm, usually stony hard, with extreme diffuse fibrosis. There is loss of lobulations and the incised surfaces of the gland show little evidence of the typical colloid-containing acini which characterize the normal structure.

In the case of struma lymphomatosa, on the other hand, the tissues are

firm but not hard, smoothly lobulated, and are not markedly fibrosed. The normal lobular character of the gland is still present although on section there is found definite diminution or almost complete absence of colloid material. Often the appearance of the gland resembles that of an enlarged, firm lymph node.

Histologically, too, the glands of the two diseases differ from each other. Riedel's struma is characterized by marked diffuse sclerosis of the affected portions of the gland, with varying numbers of persisting acini. Where the acini do persist, they are grouped together in small nests or clusters and appear compressed by the surrounding dense fibrous stroma. Such groups of acini apparently indicate where a lobule at one time existed. The cells of these persistent glands are not remarkable. In general they resemble those which form the normal acini. Accumulations of lymphocytes, and occasionally of other leukocytes, are often found, but these accumulations are focal in distribution and appear to be definitely of inflammatory nature. Lymph nodules are not often found.

In contrast, struma lymphomatosa, while it shows some evidence of fibrosis, is characterized chiefly by marked, often extreme, lymphoid infiltration of the gland. This infiltration is most marked in the interacinar tissues and is often associated with a peculiar, but quite typical atrophy of the neighboring acini, which tend, sometimes, to be packed closely together, sometimes to be separated from each other by lymphocytes. The cells which form many of these atrophic acini are large, parenchymatous, acidophilic, with more cytoplasm than normal and small hyperchromatic nuclei. They appear degenerated rather than normal. Colloid is diminished in amount and is often absent. Large hyperplastic lymph nodules are commonly present. These are sometimes so large that they may be recognized by the unaided eye. The lymphoid infiltration is not associated with other inflammatory cells and does not resemble that which occurs in the gland of toxic goiter after iodine treatment. The glandular stroma is not inflamed in the ordinary sense, but often appears to be actually converted into typical lymphoid tissue, which lends support to the view that the change is not primarily inflammatory, but is rather, as Williamson and Pearse have suggested, the result of hypoactivity on the part of the epithelial elements.

Even though conclusive evidence is lacking, we feel that the clinical and pathologic differences herein described warrant placing the two lesions into distinct groups. Future studies in the differentiation of the diseases, with careful recording of characteristic points observed in each lesion, will lead to better understanding of these conditions and eventually to accurate classification.

CASE REPORTS

Case 1.—Mrs. E. H., age 32, experienced pain in the neck, anteriorly, then on both sides, two and one-half months before her admission to the Albany Hospital May 27, 1930.

There had been slight fever, some dysphagia but no dyspnea. Her appetite was poor and she had lost 12 pounds in weight. Moderate increase in nervousness and fatigability had been noted.

The thyroid gland was bilaterally enlarged, being almost twice normal size. It was slightly tender and very hard. The remainder of the examination was without bearing on the thyroid problem. The blood pressure was 120/80. The clinical diagnosis was thyroiditis.

At operation the right and left lobes were found to be extremely hard and fibrous in character, particularly on the outer sides. The inner aspects of the lobes were more nearly normal in appearance. Portions of tissue were removed from each lobe.

The excised tissue was firm, hemorrhagic and glandular. On section it appeared tough and slightly edematous. Microscopically, sections from this gland showed large foci of diffuse fibrosis which involved chiefly the interlobular stroma. So abundant was the fibrous tissue that it separated and compressed the acini, causing them to appear as small atrophic gland-like spaces embedded in a dense collagenous matrix. The stroma contained moderate numbers of small arterioles and venules which were not congested. Most of the atrophic gland spaces contained colloid. Around many of them colloid had been liberated and was being phagocytized by foreign body giant cells. Here and there, small focal accumulations of lymphocytes were present in the stroma, but there was no general, diffuse lymphocytic infiltration. In a few places suggestive lymph nodule formation was noted.

The epithelial cells of the atrophied acini were small, low cuboidal or flat, pale staining, finely granular and contained large oval nuclei. Cytoplasmic granules were much less abundant in these epithelial cells than in those of the struma lymphomatosa type. Different sections from the same gland showed a varying amount of fibrosis from only a slight increase in the fibrous stroma around the lobules to the more extensive changes described above. Acini seen in the less dense stroma showed little deviation from normal. The changes in this gland were those of chronic thyroiditis with diffuse interacinar fibrosis, possibly an early stage of Riedel's stroma.

The patient was observed at intervals until February, 1932, at which time she was well, had no complaints, but was compelled to take thyroid extract, one-half grain twice daily.

Case 2.—Mrs. G. C., age 47, was admitted to the Albany Hospital January 28, 1930. Four weeks before her entrance she had had sore throat and a cold which were followed in one week by soreness in the neck and increase in the size of the thyroid gland. There had been pain of moderate severity in the enlarged gland, slight fever, anorexia and a general feeling of tiredness. Ten pounds were lost during the present illness. Occasionally in the past she had had sore throats and during childhood, scarlet fever.

Examination of the patient showed little except for the bilaterally enlarged thyroid gland that was stony hard and fixed to the trachea and surrounding structures. The blood pressure was 130/68. A clinical diagnosis of Riedel's struma was made.

Operation revealed adherence of the periglandular muscles to the capsule of the thyroid gland. The gland was stony hard, smooth and enlarged three times normal size. Wedges of tissue removed from each lobe and the isthmus were fibrous in appearance and seemed to contain very little thyroid tissue.

Sections from the gland revealed diffuse sclerosis with almost complete loss of the acini. The scar tissue was dense, hyaline and focally infiltrated with lymphocytes. Here and there, small numbers of atrophic acini which contained little or no colloid were found. The epithelial cells lining these acini were cuboidal with finely granular cytoplasm and large hyperchromatic nuclei. In some situations there were larger, more readily recognizable acini, the lining epithelium of which was almost identical with that of the normal thyroid acinus. Colloid within these latter acini

was fairly abundant. Often the colloid was infiltrated with phagocytic endothelial leukocytes and scattered diffusely throughout the dense fibrous tissue were varying numbers of foreign body giant cells about masses of colloid. Histologically the findings were those of marked thyroiditis with diffuse fibrosis, not unlike Riedel's struma.

This patient was followed clinically for 11 months. She remained perfectly well and required no medication.

Case 3.—Mrs. E. D., age 31, entered the Albany Hospital July 21, 1930, because of soreness and tenderness in her neck. This illness began six weeks before her admission and had been treated by hot applications. Four weeks before entrance a lump was noted in the middle of the neck which slowly increased in size. Slight fever, dyspnea, anorexia and a loss of 15 pounds in weight were associated symptoms. For

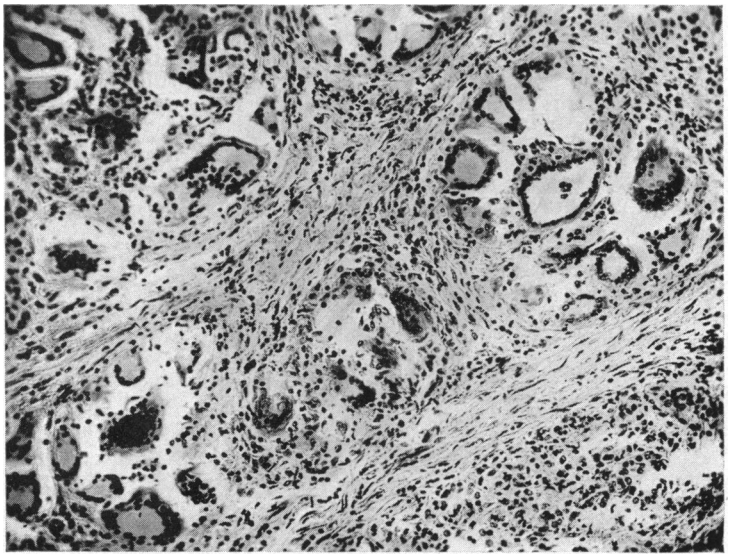

FIG. 1.—(Case 3.) Chronic thyroiditis with foreign body giant cells (×200).

about two months the patient had noticed that she became more easily fatigued than normal. For years the patient had suffered from tonsillitis and head colds.

The thyroid gland was hard, tender, diffusely enlarged to almost three times normal size, but the overlying skin and tissues showed no evidence of any inflammatory process. The blood pressure was 108/60. The clinical diagnosis was thyroiditis.

At operation the preglandular muscles were found to be adherent to the capsule of a very hard thyroid gland. Small pieces of tissue were removed from each lobe. Grossly these fragments consisted of dense, rubbery, yellowish-white, unrecognizable tissue with white fibrous bands running through it. Acini were not visible.

Sections from this gland showed it to be densely and diffusely sclerosed, the sclerosis being both interacinar and interlobular, but the lobules were still distinctly visible and appeared as scarred areas in which small to moderate numbers of atrophic acini were present. In some of the lobules no acini were recognizable, in others minute, contracted, compressed, gland-like spaces were embedded in dense stroma. These spaces were lined by small pale-staining, cuboidal cells with slightly granular cytoplasm and large hyperchromatic nuclei. In still other situations readily recognizable but irregularly sclerosed thyroid tissue was visible. The acini in these situations were lined by flat epithelial cells not unlike those of the normal thyroid gland. Separating all of the lobules, whether they contained glands or not, were dense, broad, almost acellular bands

of hyaline collagenous tissue in which small numbers of blood vessels were present. In practically all of the lobules, from one to many foreign body giant cells, which appeared to be phagocytizing colloid were found (Fig. 1).

The histologic changes were those of marked chronic fibrosing thyroiditis of the type described by Riedel and with an associated foreign body giant cell reaction.

The patient was last seen in August, 1936, at which time she was well and required no medication.

Case 4.—Mrs. F., age 48, was admitted to the Albany Hospital, October 8, 1935. Two months before admission there had been a traumatic hyperextension of the neck followed in a few days by an upper respiratory infection and coincident pain in the region of the thyroid gland. Chills and fever were present at the onset, but the acute symptoms rapidly subsided, leaving only soreness. There had been a weight loss of nine pounds. One month before admission a small swelling was noted in the region of the thyroid gland.

The general examination was not remarkable but locally there was found a bilaterally enlarged thyroid gland that was extremely hard to palpation. The right lobe was the size of a lemon and the left was slightly smaller. The gland was firmly fixed to the deeper structures of the neck. The blood pressure was 150/90. The clinical diagnosis was possible malignancy.

At operation the overlying muscles and the deeper structures, including the trachea, were found to be adherent to the capsule of the gland. At the left inferior pole were two small adenomata, one of which was cystic, but the rest of the lobe showed the same changes as were found throughout the other portions of the gland. Subtotal thyroidectomy was performed with noticeably little bleeding. The cut surfaces of the gland were grayish-white in color, tough and firm in consistency, and fibrous in appearance.

The sections showed diffusely and markedly sclerosed thyroid tissue. In some areas normal sized or slightly enlarged, colloid-containing acini were found while in other situations the recognizable acini were sclerosed and atrophied. Throughout the sections dense fibrous tissue was found, often containing giant cells grouped about colloid material in pseudotubercle formation. Large foci of lymphocytic infiltration were seen but active germinal centers were not present. There was no histologic evidence of malignancy in any of the sections. The changes were characteristic of Riedel's struma, with a foreign body giant cell reaction.

This patient is still being followed and when last seen in June, 1936, was well and required no medication.

Case 5.—Mrs. G. C., age 53, had noted a swelling in the anterior part of her neck, only two weeks before admission to the Albany Hospital, September 23, 1929. Mild dyspnea, general weakness, and a weight loss of five pounds characterized the present illness.

This patient had had typhoid fever in 1914, an hysterectomy in the same year, and a left mastectomy in 1919 for a benign tumor. Chronic nasal infection had been present for six months prior to admission.

The thyroid gland was enlarged and contained firm nodular masses in the right lobe and isthmus. The cervical lymph nodes were just palpable but were not tender. The remainder of the examination was not remarkable. The blood pressure was 118/70. The clinical diagnosis was chronic thyroiditis.

The gross specimen consisted of dense, hemorrhagic fibrous tissue which did not resemble thyroid gland. Microscopically there was marked diffuse interacinar and interlobular fibrosis of the entire gland with reduction in size of the lobules and atrophy and disappearance of great numbers of the acini. The acini which remained were contracted and atrophic, and were lined by flat or low cuboidal epithelial cells. These were pale-staining and contained finely granular cytoplasm and oval nuclei in which

were small amounts of chromatin. Many of the acini contained small amounts of colloid. In other parts no acini at all were present and the lobule remained as a small sclerosed focus, infiltrated with focal collections of lymphocytes and plasma cells, the former predominating. No typical lymph nodules were present. The interlobular stroma was abundant, very dense and almost acellular and contained moderate numbers of rather thick-walled, contracted blood vessels. The histologic changes were those of early Riedel's struma.

The postoperative course was uneventful. She was seen at intervals until July, 1931, at which time she was entirely well and required no medication. In August, 1936, she was requested to report for a check-up examination, and was found to be free from symptoms.

Case 6.—Mrs. N. B., age 45, was admitted to the Albany Hospital, October 16, 1931, complaining of swelling and tenderness of the neck. Six months previously she began to experience a sensation of tightness and pain in the neck which gradually became associated with dyspnea and dysphagia. Increased emotional instability and nervousness were described by the patient as a "nervous breakdown." In a two-month period the patient lost 21 pounds, after which her symptoms abated and there was marked improvement until two weeks before coming to the hospital, when a tender swelling was discovered in the neck. The blood pressure was 130/80.

A hard, somewhat tender thyroid gland, twice normal size, was found. No other abnormality appeared and a clinical diagnosis of chronic thyroiditis was made. At operation several indurated areas were found in both lobes, more especially the left. The gland was adherent to the surrounding structures. The isthmus and a wedge of tissue from the left lobe were removed.

Sections from this gland showed marked diffuse fibrosis with atrophy and diminution in the number of the acini. There still remained traces of the usual lobular arrangement. Within the lobules the stroma was thick, dense, and infiltrated with lymphocytes, plasma cells, and occasional endothelial leukocytes and eosinophils. The stroma about the lobules was markedly increased in amount and in places appeared almost hyaline, but showed less evidence of inflammatory infiltration. In many of the lobules there still remained small numbers of irregular acini that contained no colloid. The epithelial cells lining these acini were small with large oval nuclei and very little cytoplasm. Histologically the picture was that of marked chronic thyroiditis with diffuse fibrosis, an early stage of Riedel's struma.

The patient was compelled to take one-half grain of thyroid extract three times daily for six months, until July, 1932, since which time she has remained well.

Case 7.—Mrs. A. S., age 42, entered the Albany Hospital, April 4, 1925, complaining of a goiter that had been present for eight years. During the year prior to admission there had been a gradual increase in the size of the goiter associated with anorexia, dyspnea and dysphagia, all more marked during the last month. Weight loss during the past year was 11 pounds. She had suffered occasional acute upper respiratory infections. Her mother had suffered from a goiter.

The thyroid was diffusely enlarged, lobulated, firm to stony hard in consistency. The left lobe and isthmus were attached to the trachea and surrounding parts but the right lobe seemed freely movable. No other noteworthy changes were observed in the general examination. The blood pressure was 160/120. The clinical impression was malignant disease of the thyroid gland.

At operation wedges of tissue were removed from each lobe together with the entire isthmus. A portion of the remaining gland tissue was destroyed by cauterization.

Sections from this gland showed large foci of dense hyaline fibrosis in which the collagen was abundant and strongly resembled that found in a keloid. Scattered diffusely throughout the scar tissue were moderate numbers of plasma cells and occasional focal collections of lymphocytes and polymorphonuclear and endothelial leukocytes.

Occasional large accumulations of lymphocytes were found but there were no true lymph nodules. Blood vessels were not abundant. Here and there, atrophied acini were found. These occurred singly or in small groups embedded in the dense stroma (Fig. 2).

In other areas there was little or no evidence of sclerosis of the thyroid tissue. In these regions acini which were lined by flat, often normal appearing epithelium were found. The acini contained varying amounts of colloid which stained poorly, appeared shrunken, and was often vacuolated. Occasionally dilated acini were present. There was no evidence of malignant diseases. The histologic picture was that of ligneous thyroiditis or typical Riedel's struma.

This patient was followed from time to time until August, 1930. She remained

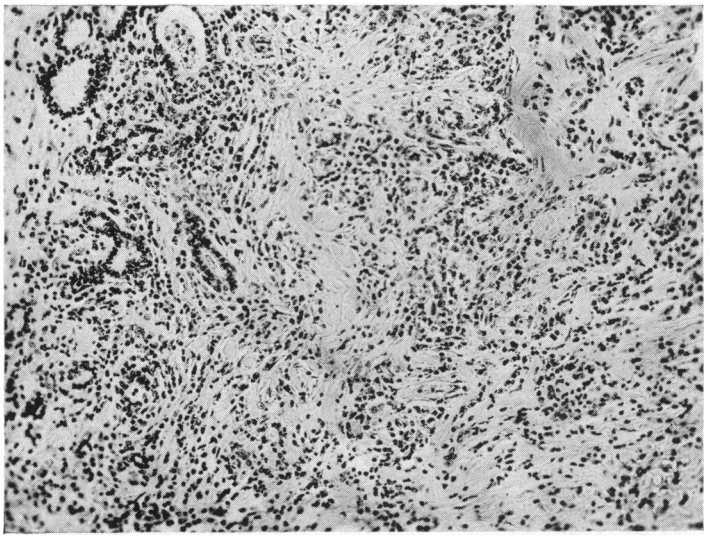

FIG. 2.—(Case 7.) Typical Riedel's struma, showing marked and extensive fibrosis, with compression of the remaining acini (×125).

well, required no medication from the point of view of the thyroid, although the blood pressure remained the same. An answer to our questionnaire in August, 1936, revealed that she was well and free from symptoms.

Case 8.—Sister M. D., age 35, entered St. Peter's Hospital on January 28, 1935, complaining of goiter of three years' duration associated with dyspnea and dysphagia for the past two years. These symptoms had become progressively more severe and were accompanied by choking sensations in the neck and occasional indefinite pains in the throat. Hardness of the goiter was noted when symptoms first began. At the onset tachycardia, tremor and nervousness were noted but had been absent for six months prior to admission.

Cholecystostomy and appendicectomy were performed in 1929; cholecystectomy in 1931, and tonsillectomy in 1932. The patient suffered from frequent sore throats before the removal of the tonsils.

The thyroid gland was bilaterally enlarged and slightly lobulated with rather a sharp margin on the left side. The gland was firmly fixed and stony hard in consistency. There was no cervical lymphadenopathy. Laboratory studies were negative. Roentgenologic examination of the chest showed no evidence of tumor metastases. A clinical diagnosis of Riedel's struma was made. The blood pressure was 124/80.

Careful dissection at operation was necessary in order to free the muscles which were adherent to the gland. The right lobe and isthmus were entirely involved in

the change but the left lobe appeared normal in its posterior two-thirds. The isthmus was excised and wedges of tissue were removed from each lobe with destruction of a part of the remaining tissue with the cautery. There was remarkably little bleeding from the gland substance. The tissue excised was whitish in color, hard, and fibrous, with only here and there a suggestion of cellularity.

Sections from this gland showed it to be composed almost entirely of dense fibrous tissue which was diffusely but only moderately infiltrated with lymphocytes and plasma cells. Only rare evidence of lobulation persisted and the dense, finely fibrillar collagenous tissue resembled that of a keloid. Between the dense strands was a more delicate fibrous meshwork throughout which inflammatory cells, chiefly lymphocytes, were diffusely scattered. In places these cells were collected in large foci but nowhere were typical lymph nodules found.

The acini were almost entirely missing, only a few round or oval glands being found in one portion of one section. In general, these remaining acini were small, compressed, and lined by cuboidal epithelial cells which were often heaped up into a double layer due to crowding. The cytoplasm of these cells was pale-staining and contained small pinkish granules. The nuclei were oval and stained rather diffusely but were not hyperchromatic. In most of the acini colloid was absent, but in some there was a small accumulation of pink-staining, often abnormal appearing colloid.

The arterioles of the gland appeared to be actually reduced in number since sclerosed and obliterated vessels were occasionally observed. Those arterioles that persisted were thick walled and markedly contracted and were not infrequently surrounded by small numbers of lymphocytes.

Very careful examination was made for evidence of malignancy but no atypical cells or gland-like structures could be found in any part of the sections. Histologically, therefore, the condition was that of Riedel's struma.

A diagnosis of scirrhous carcinoma was made at the time of operation from a study of frozen sections of the gland. An even more pertinent fact was that subsequent study of sections of this gland by five pathologists resulted in two diagnosis of carcinoma, two of Riedel's struma and one of a benign lesion probably Riedel's struma, but with malignancy not positively ruled out. The patient, however, remained well, and over a year after operation there was no evidence of local or distant recurrence, although the undestroyed portion of the gland could still be palpated.

Case 9.—Mrs. L. G., age 38 years, entered the Albany Hospital, May 18, 1933. A mass had been present in her neck for seven years. It had appeared first following the birth of her first child. The size of the mass varied but seemed to decrease somewhat until the second pregnancy three years later when it again grew larger. At that time the patient noticed that she became fatigued easily. The basal metabolic rate was minus two. A spontaneous recovery followed. After the third pregnancy two years before admission the gland again became enlarged and continued to increase slowly in size. Again unusual fatigability was an early symptom and this became more severe during the four months preceding her admission to the hospital. During the last two months of her illness there had also been dyspnea and a sense of substernal pressure. There was no loss in weight. At the age of 22 this patient had had scarlet fever and during 1918 suffered from influenza. Several relatives on her father's side of the family had had goiters.

The thyroid gland was bilaterally enlarged. The right lobe was of nearly normal consistency but the left was irregular and very firm to the examining fingers. The blood pressure was 100/60. The remainder of the examination was within normal limits. The clinical diagnosis was nontoxic diffuse goiter.

At operation, the right and left lobes were of about equal size, measuring 7.5 by 5 by 5 cm. A pyramidal lobe was present. A subtotal thyroidectomy was performed.

The most noteworthy histologic changes were the extremely marked lymphoid infiltration of the stroma and the great reduction in size of the thyroid acini. The

latter structures were small, contracted, irregular in shape. They contained little or no colloid. Their epithelial lining was composed of medium sized to large, parenchymatous, cuboidal cells, with much cytoplasm and distinct, often hyperchromatic, nuclei. Often small groups of acini were embedded, like small islands, in the dense lymphoid stroma. In many places actual lymph nodule formation was observed. Some of the nodules were minute while others were very large and contained active germinal centers. The gland was divided into indefinite lobules by thin but dense strands of hyaline connective tissue (Figs. 3 and 4). These changes were present in practically all of the lobules. The only noticeable exception was a moderately hyperplastic papillary cystadenoma which was present in one section. This apparently benign tumor was completely surrounded by lymphocyte-invaded stroma. Blood vessels of the gland were not abundant and showed only slight evidence of hyperemia. The histologic changes were those of marked struma lymphomatosa (Hashimoto). Dr. Allen Graham, pathologist to the Cleveland Clinic, concurred in this diagnosis.

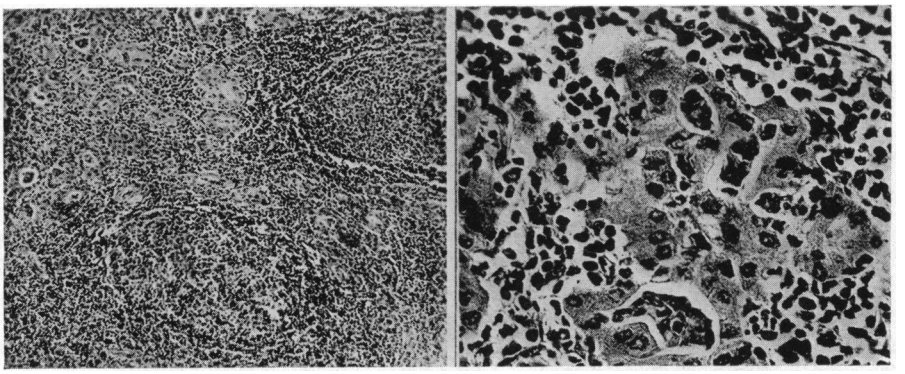

FIG. 3.—(Case 9.) Typical struma lymphomatosa showing lymph nodules, diffuse lymphoid infiltration, and the large parenchymatous acinar cells (×130).
FIG. 4.—(Case 9.) High power of Fig. 3 showing more clearly the typical acinar cells surrounded by diffuse lymphoid infiltration (×400).

After operation the basal metabolic rate was minus 18, but the patient remained symptom free until November, 1933, when the first evidence of clinical hypothyroidism appeared. The basal metabolic rate at this time was minus 30 and thyroid extract was given, one grain twice daily. This medication has been continued and increased from time to time until now, July, 1936, the patient is taking four grains daily.

Case 10.—Mrs. M. T., age 53, was first admitted to the Albany Hospital, March 31, 1929, for a goiter which had been present for 16 years but that had been producing symptoms only during the preceding three years. The principal symptoms were occasional periods of tachycardia associated with a feeling that the heart sometimes skipped beats. For three years the patient had become fatigued unusually easily. Dyspnea on exertion and periods of mental depression had been troublesome during the six months immediately preceding her admission. Throughout the present illness a sense of tightness in the neck, as if a rope were tied about it, had been experienced.

The patient had had three previous operations, hysterectomy, appendicectomy and herniorrhaphy. During childhood she had suffered from diphtheria and scarlet fever.

The right lobe of the thyroid gland was enlarged to the size of a lemon and was hard to palpation. The left lobe was also enlarged, but was nodular and of softer consistency than the right. The remainder of the examination was without note. The blood pressure was 145/90. The preoperative diagnosis was probable carcinoma.

The right lobe at operation was hard, nodular, vascular, and was subtotally resected. The blood supply to the left lobe was ligated without removal of tissue. Grossly

the excised tissue was grayish-red and nodular on its external surface. The cut surface was irregularly lobulated and yellowish-gray in color, fibrous in appearance and showed little colloid. The process was diffuse throughout the gland.

Sections from this gland showed marked diffuse infiltration of the stroma with lymphocytes. These cells varied in number in different places, in some situations occurring in great numbers and being packed between and around atrophic acini; in others being less abundant and appearing as loose accumulations in the interstitial tissue. Here and there, typical lymph nodules were present. The acini were greatly reduced in size but for the most part were composed of large, pale-staining, acidophilic cells in the centers of which were large oval nuclei with varying amounts of chromatin. The majority of the atrophied acini contained small amounts of colloid which were not infrequently infiltrated with phagocytic cells. The epithelial cells showed no evidence of multiplication and were not neoplastic in type. The blood vessels were not unduly

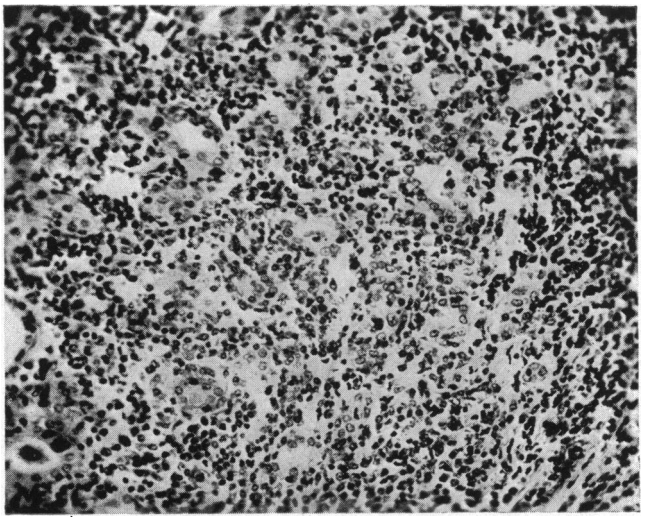

FIG. 5.—(Case 10.) Histologic changes seen at the time of the first examination. The changes are characteristic of struma lymphomatosa (×180).

abundant (Fig. 5). Foci of sclerosis were only rarely seen. The changes were those of struma lymphomatosa (Hashimoto).

This same patient was readmitted on April 7, 1931. She had regained her strength, was able to do some of her work, but her neck had never felt normal following the previous operation. Two months before the present admission she had had an acute pharyngitis and laryngitis after which she experienced dyspnea and dysphagia amounting to a sense of strangulation when lying down. Anorexia and recurrence of the weakness were noted. The general examination was no different from that of the first admission. The blood pressure was 130/70. Under the scar of the previous operation the left lobe was palpably enlarged and quite firm.

The left lobe was subtotally resected at operation and exploration of the right lobe revealed thyroid tissue, equal in volume to that of the left, which extended into the substernal region. Each lobe was subtotally resected at this operation. The outer surface of the tissue removed was bluish-gray in color; its consistency, firm to hard. Lobulation was distinctly visible on the cut surfaces which were smooth, glistening, and of reddish-bown color. Very little colloid was present.

Microscopic examination showed changes which strongly resembled those observed two years previously. Foci in which closely packed acini containing very little stroma and rare lymphocyte accumulations alternated with foci in which the stroma

was more abundant, the glands smaller, and lymphocytic infiltration more marked and diffuse. In some situations fibrous tissue was fairly abundant. In foci of the first type, which were less prominent, the acini were normal in size, were lined by flat epithelial cells, and contained colloid. Foci of the second type were more numerous. Their acini were atrophic, were lined by relatively large pale, pink-staining cells with granular cytoplasm and irregular nuclei, and contained small amounts of colloid. While lymphocytic infiltration was diffuse it was still patchy, in some areas surrounding groups of acini while in other situations the infiltration surrounded each acinus. Small numbers of lymph nodules were present. The fibrous tissue was diffusely infiltrated with lymphocytes (Fig. 6). The histologic changes were those of struma lymphomatosa with which there was also a moderate degree of sclerosis.

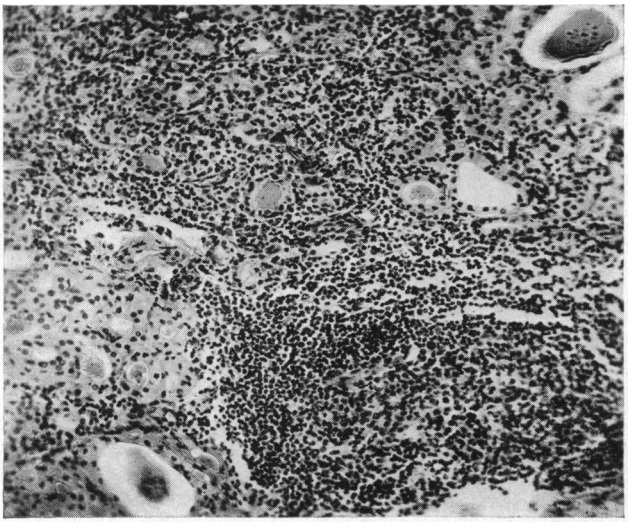

FIG. 6.—(Case 10.) Histologic changes observed at the time of the second examination, two years later. Again, the lymphoid infiltration and changes in the acinar epithelium are characteristic of struma lymphomatosa (×130).

This patient was seen in July, 1936. She stated she had been perfectly well until the Fall of 1935. Since this time she had noted rare choking sensations in the neck. Following an acute upper respiratory infection in December, 1935, she had noted she became tired more easily than before. Both thyroid stumps were palpable, and woody hard, but were apparently not fixed to the overlying structures. The patient was not greatly inconvenienced by these symptoms and was able to do her own work. She had not taken thyroid extract since May, 1934, although her skin was slightly dry and she frequently felt sleepy during the daytime.

Case 11.—Mrs. W., age 51, was admitted to the Albany Hospital, April 17, 1936, complaining of a goiter which had been present four years. During the year preceding admission she had noted pulling sensations in the neck, increased fatigability, and occasional attacks of tachycardia before entrance. There was no history of tremor or of hyperhydrosis. She had had occasional occipital headaches for about two years.

The general physical examination was not remarkable except for a blood pressure of 190/120. There were no eye signs suggestive of hyperthyroidism. The thyroid gland was diffusely enlarged, lobulated, and firm. The preoperative diagnosis was nontoxic nodular goiter.

Operation showed the entire thyroid gland to be enlarged. The glandular tissue was grayish-white in color and had the gross appearance of struma lymphomatosa. The right, left, median and pyramidal lobes were subtotally resected.

The specimen consisted of two masses of thyroid tissue, one 6 by 5 by 2 cm. in size, the other 5 by 3.5 by 2 cm. Each mass was partly covered by a thin, nodular capsule (Fig. 7). On section the tissue was rubbery in consistency, lobulated, and yellowish in color.

Microscopically the sections showed irregular, marked diffuse lymphoid infiltration between many of the acini. In some lobules this infiltration was not pronounced. Moderate numbers of typical lymph nodules with germinal centers were observed. The majority of acini were small and were composed of large cuboidal cells with eosinophilic cytoplasm and centrally placed nuclei. In a few situations the lymphocytic infiltration was so marked that acini were barely visible. There was no evidence of glandular hyperplasia. Colloid, although present, was reduced in amount. The changes were those of struma lymphomatosa.

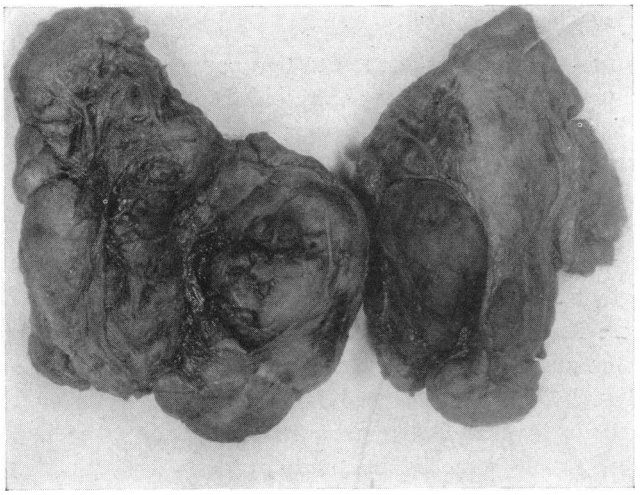

FIG. 7.—Thyroid gland removed from Case 11. Struma lymphomatosa (Hashimoto).

After operation a basal metabolic rate was plus five. The patient remained well and continued to improve until June 15, 1936, when symptoms of hypothyroidism appeared and thyroid extract, one-half grain a day, was prescribed.

Case 12.—Mrs. M. J., age 55, was admitted to the Albany Hospital, September 22, 1934, for relief of a feeling of pressure which had been present in the neck for two years. During this time the patient had had occasional choking sensations. She had a feeling that a string was tied about her neck. Dyspnea began gradually and was associated with tachycardia on exertion. The patient complained of tiring more easily during her illness than before its onset. The symptoms had been progressively increasing in severity. Blurring of vision had been present on occasions. There was no weight loss. The general physical examination showed little of note except for diffuse enlargement, slight tenderness, and moderate firmness of the thyroid gland. There were no eye signs suggestive of hyperthyroidism. Blood pressure was 170/100. The first impression was nontoxic diffuse goiter.

At operation the right lobe was found to be moderately enlarged, measuring 6 by 3 by 3 cm. in size, while the left lobe was slightly smaller. Both lobes appeared to be the seat of mild colloid goiter. Subtotal thyroidectomy was performed.

Grossly the material consisted of two partially encapsulated lobes of the thyroid gland. On section these were found to be moderately firm with small foci of colloid distention which were separated by areas in which glandular tissue could not be recognized.

Histologically the most significant changes were focal accumulations of lymphocytes in the stroma of the gland, with many large, hyperplastic lymph nodules scattered within the affected foci. Where the lymphocytic infiltration was most marked, the acini were small and shrunken and their epithelial cells were large, moderately acidophilic, and often resembled liver cells. Little or no colloid was present in these acini. Here and there moderate fibrosis was noted. Between these foci of lymphoid hyperplasia and fibrosis, somewhat enlarged acini containing from small to moderate amounts of colloid were present. In these situations lymphocytic infiltration was not present. The histologic changes were those of early struma lymphomatosa (Hashimoto).

This patient was last seen in July, 1936. Since her hospital stay she has steadily improved. Mild cramp-like pain in the muscles of her extremities had caused some discomfort but the blood calcium level has been normal. Up to the present time she has required no thyroid medication.

DISCUSSION.—In the introduction to this paper we called attention to the fact that the majority of students of thyroid disease, accepting the view held by Ewing, have considered that struma lymphomatosa (Hashimoto) and ligneous thyroiditis of Riedel were different stages or manifestations of the same disease. In recent years, however, there has been a tendency away from this unitarian concept since Graham first emphasized certain differential features in the two conditions. Lee and Clute, Eckerson, and Warren, and others now believe that the diseases are separate and distinct. Poer, Davison and Bishop[19] quote Foot as saying, "Hashimoto's struma has no connection with Riedel's struma and they represent two distinct processes—the one an overgrowth of lymphoid tissue followed later by fibrous invasion that may be more a metabolic than an inflammatory process; the other a fibrous overgrowth in response to some inflammatory stimulus."

We agree with those authors who consider struma lymphomatosa (Hashimoto) and Riedel's struma to be separate diseases, and have reviewed 12 personally observed cases. Four of these showed the clinical and pathologic changes characteristic of Riedel's struma; four exhibited a peculiar type of chronic thyroiditis characterized by diffuse fibrosis with foreign body giant cells, a lesion which may at some future time be proven to be a separate entity; and four that presented the changes characteristic of struma lymphomatosa. Although this series of cases is too small a group from which to draw valid conclusions, it is significant, we believe, that our findings in general agree, often strikingly, with those of other investigators who have attempted to separate the two diseases. That definite, though sometimes inconstant, clinical differences exist, is now quite well established.

It is evident, for example, that struma lymphomatosa occurs in an older group of patients, thereby making it difficult to accept the theory that this lesion is the precursor of Riedel's type of change. Symptoms are present over a longer period of time in Hashimoto's lesion than they are in Riedel's

struma, suggesting an etiologic difference. This latter suggestion is emphasized by the slow return to normal in patients with struma lymphomatosa and by the greater number of these cases, as compared with Riedel's struma, that require postoperative medication with thyroid preparations. Struma lymphomatosa, in all reported cases, has been bilateral while Riedel's struma has not been; the former lesion seems to develop in preexisting goiters while the latter is more often the primary change in the gland. The similarity of all these findings in the three series of cases supports the thesis that the two lesions are clinically quite separate and distinct.

Pathologically, too, there are differential features which are apparent to the practiced eye not only in the fresh specimen, but even more markedly, perhaps, in the histologic preparations. In Riedel's struma the changes are inflammatory in character with moderate to extreme fibrosis, excessive hardness of the gland, disappearance of many of the acini and shrinkage of others, and diffuse or focal infiltration with lymphocytes and occasionally other leukocytes. The persistent acini do not vary markedly from normal.

Struma lymphomatosa, on the other hand, is characterized by moderate firmness and irregular lobulation of the gland, extreme lymphoid hyperplasia with lymph nodule formation, and peculiar changes, which appear degenerative, in the epithelial cells of many of the acini. These cellular changes we believe to be significant.

The opportunity of studying one case of struma lymphomatosa at two different periods, the second time after an interval of two years, has been especially enlightening. Heretofore the majority of the reported cases which have been studied more than once have dealt with Riedel's struma. Perman and Wahlgren,[20] for example, report a case studied a second time after an interval of 18 months. In this case they felt that Riedel's struma was not preceded by changes suggestive of struma lymphomatosa. Roulet[21] has recently reported a case in which the findings were typical of Riedel's struma. This patient was operated upon twice with an interval of two and one-half years and the histologic changes in the gland were the same at each examination. Heyd,[22] however, had a patient in whom, in his opinion, struma lymphomatosa preceded typical Riedel's struma, but examination of his evidence makes us feel that, pathologically at least, the lesion was characteristic of Riedel's struma on both occasions. As far as we know, there has not been a case of struma lymphomatosa reported in which the histologic changes have been described twice, the second time several months or years after the first examination. Clute, Eckerson, and Warren[14] had one patient who was operated upon twice, the second time after an interval of two years, but in their paper they make no mention of the histologic findings on each occasion. Since the case is classed as struma lymphomatosa it may be inferred that the pathologic changes were the same at each examination.

In Case 10 the clinical symptoms and signs as well as the histologic changes at the second admission were practically identical with those found at the

time of the original examination. These findings thus shed new light on the controversial question of the possible relationship of Riedel's struma and struma lymphomatosa. They distinctly favor the contention that the two types of change are separate, distinct, and in no way related. The presence of slightly more sclerosis of the gland at the time of the second examination may be in some measure the result of the previous operation. The fundamental clinical symptoms of weakness, easy fatigability, tightness in the neck, dyspnea, and dysphagia, and the histologic changes, consisting of lymphoid infiltration with lymph nodule formation and the characteristic appearance of the acini, were still the same at the second examination as they were at the first. If struma lymphomatosa were the precursor of Riedel's struma, sufficient time had certainly elapsed in this case for the changes to have become evident, because clinically Riedel's struma has been shown to be generally of shorter duration than struma lymphomatosa, and its course is much more rapid.

Clinically and pathologically, therefore, we believe Riedel's struma and struma lymphomatosa (Hashimoto) to be separate diseases of different etiology and producing different clinical symptoms. There is no valid reason for considering the latter to be an earlier stage of the former. The two lesions, while not uncommon, occur with sufficient rarity to warrant very careful clinical and pathologic study of every possible case. We hope that further investigations will establish definitely the etiology of the lesions and thus settle once and for all the moot question of a possible relationship of the diseases to each other.

SUMMARY

(1) Twelve cases of benign struma are presented, four of the type described by Riedel and four of the type described by Hashimoto, with four associated with foreign body giant cells. Attention is directed to the possibility that future study may show that cases which are classified as Riedel's struma are in reality a group of different types of chronic thyroiditis.

(2) There is a growing tendency to regard Riedel's struma and struma lymphomatosa as separate and distinct entities. With this concept we are in agreement.

(3) Clinical differences between the two types are presented together with the pathologic changes seen in each type.

(4) Corresponding histologic findings in a case of struma lymphomatosa studied twice, the second time after an interval of two years, strongly supports the thesis that this type of change is distinct and separate from the type described by Riedel.

The authors are indebted to Dr. George E. Beilby, Albany, N. Y., for his helpful advice and for permission to present these cases from his private practice. To Dr. Allen Graham, Cleveland, Ohio, they also express their appreciation for his review of the material used in this study and for his suggestions.

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