ANGINAL PAIN IN MYXŒDEMA

BY

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It has long been recognized that myxœdematous patients beyond middle life may suffer from arteriosclerosis, hypertension, or coronary disease in addition. Until recent years it seems to have been accepted that anginal pain in a myxœdematous patient was evidence of some such complication. Inasmuch as non-myxœdematous angina pectoris is sometimes greatly relieved by the development of spontaneous or post-operative myxœdema, it has been generally concluded that treatment of a myxœdema with thyroid is likely to aggravate any co-existing anginal pain. Since 1924, however, isolated reports have appeared describing myxœdematous patients whose anginal pain improved on treatment with thyroid. Fournier (1942) found six cases recorded, and he appears to have overlooked three—one by Campbell and Suzman (1934) and two by Zondek (1941). The time would therefore seem to be ripe for a review of the whole subject of anginal pain in myxœdema.

Zondek (1918), in his original description of the “myxœdema heart” mentions slight precordialgia as one of the less frequent symptoms. Laubry *et al.* (1924) record a patient, aged 47, who had “for three years suffered from anginal crises daily or several times a day, brought on by the slightest effort”; there was typical myxœdema but no evidence of independent heart disease. Treatment with thyroid caused rapid disappearance of the anginal crises *pari passu* with reduction in the size of the heart. The patient was observed for ten years (Fournier, 1942) during which he suffered from anginal pain only when treatment with thyroid was discontinued.

A slightly different syndrome is illustrated by one of Campbell and Suzman's (1934) cases. They discuss the cardiovascular findings in eight cases of myxœdema, of whom two (Cases 7 and 8) had precordial pain; both had anomalous cardiograms, and both were thought to have independent heart disease. Case 7 had typical angina of effort which seems to have been aggravated when thyroid was given. Case 8 complained of “continuous precordial aching made worse by exertion”; this pain disappeared completely as the heart became reduced in size under the influence of thyroid. The drug was later withdrawn without the patient's knowledge; the pain returned after an interval, and its reappearance coincided with the recurrence of cardiac enlargement.

Beach (1935) describes a woman with myxœdema, who suffered, first from a feeling of oppression in the chest, and later from attacks of severe pain; they were induced by exposure to cold and relieved by amyl nitrite; she had T I inversion in her cardiogram and was thought to have independent heart disease. The attacks occurred with increasing frequency until she was having as many as eight daily, and she refused to allow her arms or chest to be uncovered for examination. Within a week of commencing thyroid therapy the attacks ceased. She was under treatment for several years during which attacks occurred only when her basal metabolic rate fell below —20 per cent.

The cases of Beaumont and Robertson (1939) and of Zondek (1941) illustrate yet another syndrome, which has been designated by Zondek “the abortive myxœdema heart.” These patients had no obvious clinical signs of myxœdema, but they had a low basal metabolic rate and a raised blood cholesterol. They complained of continuous precordial or sternal tightness

and distress; in addition, they had more or less frequent attacks of collapse with pallor, cold sweating, and a feeling of oppression in the chest. The cardiovascular findings were consistent with a myxœdema heart—enlargement of varying degree, a tendency to bradycardia and low blood pressure, and a small pulse. The cardiogram was normal in some cases, typical of myxœdema in others; T I was occasionally inverted. Nevertheless independent heart disease was thought to be absent in all. Thyroid in doses between 0.5 and 0.7 gram weekly relieved all the symptoms, while no other form of treatment seemed to be of much avail. Additional cases of anginal pain relieved by thyroid are recorded by Ziskin (1930) and Benestad (1937), but it has not been possible to obtain access to their publications.

Fournier (1942) divides cases of myxœdema with angina into two groups. When independent heart disease is present, he states that thyroid will aggravate pre-existing pain, or may induce pain in patients previously free from it; but several of the cases quoted above show that this statement is not true of all cases. In the absence of independent heart disease, he considers the anginal pain is amenable to thyroid therapy. He goes on to discuss the ætiology of the pain in this group; as five of the six cases reviewed were over 40, early coronary disease was difficult to exclude, and he believes that the angina was a response to a mixed pathogenesis. He suggests that these patients had minor coronary lesions, insufficient to produce angina in themselves but capable of doing so in the presence of superadded "myxœdematous lesions." These might take the form of mucinous infiltration of the nervous or vascular elements of the heart, of vagotonia, of hypoglycæmia, or of anæmia. Thyroid therapy, by abolishing the myxœdematous lesions, restores the "status quo" and relieves the anginal pain. In support of this theory he states that some adults with myxœdema show inversion of T I, or of T I and T II; while this may often be corrected by thyroid therapy, it invariably recurs after an interval despite continued treatment. The initial inversion is attributed to a combination of minimal coronary lesions with myxœdematous lesions, the temporary improvement to removal of the myxœdematous lesions, and the ultimate recurrence to progress of the coronary lesions.

There is much that is attractive in Fournier's ideas, and a close analogy exists in the case of patients with early coronary disease complicated by anæmia, in whom cure of the anæmia (whether by liver or by iron) may abolish anginal pain for a time. It is clear that, if this view is justified, any fundamental pathological difference between his two groups of cases disappears; the distinction becomes a matter of degree. The possibility is immediately opened that patients with somewhat more advanced coronary disease might also on occasion derive benefit from treatment with thyroid, as seems to have occurred in the cases of Campbell and Suzman, and of Beach. The problem as to why one patient should be relieved by thyroid while the next is made worse remains unsolved. One explanation seems to have been overlooked. Thyroid, by increasing the circulation rate throws a greater load on the heart, and this will tend to aggravate anginal pain; on the other hand an increase in the general circulation rate will lead to an increased coronary circulation rate unless the vessels are completely occluded, an effect which will tend to relieve anginal pain. The effect in any given patient will thus depend on which of the foregoing factors predominates; and it may well be that each patient has an "optimum" basal metabolic rate and circulation rate at which his anginal pain is minimal.

It may be noted that at least two distinct varieties of pain are represented among the cases quoted. The first is a typical angina of effort, the second a constant pain or ache made worse by effort; the latter type may or may not be accompanied by attacks of collapse. It is important to determine whether any other clinical variety of pain is encountered in myxœdematous patients, and if so, how these patients react to thyroid. In assessing the effect of thyroid, various possibilities must be taken into account. Thus development of pain during thyroid therapy might be due to the action of the drug on the circulation or to a purely coincidental coronary occlusion; disappearance of pain might be due to spontaneous

improvement after a coronary occlusion. The blood picture requires consideration inasmuch as cure of an anæmia can *ipso facto* cause disappearance of effort angina in cases of early coronary disease. Finally the possibility of psychogenic pain cannot be ignored.

The case histories of some sixty myxœdematous patients have been studied. Some of them have been hospital out-patients, some have been seen in private practice, and some have been hospital in-patients under the care of Dr. Angus Scott. I am much indebted to him for permission to make use of the records.

ANGINA OF EFFORT IN MYXŒDEMA

Twelve myxœdematous patients experienced typical angina of effort at some period. Of the twelve, ten had some form of independent heart disease—hypertensive in five, coronary in four, and an intermittent partial block of uncertain ætiology in one. In two cases the findings were consistent with an uncomplicated myxœdema heart. An additional patient who presented a curious mixture of thyrotoxic and myxœdematous symptoms also had an effort angina.

Five patients had *hypertensive heart disease* complicating myxœdema. One of them had diabetes as well; as she required insulin, thyroid was thought to be contra-indicated. One patient failed to report back and cannot be traced. The remaining three (Cases 1, 2, and 3) first complained of anginal pain while on treatment with thyroid. Case 1 had an uncomplicated myxœdema heart when she was first put on thyroid, but two years later she developed a mild hypertension with a slight anæmia; she still had no effort angina. She developed effort angina five weeks after her dose of thyroid was increased from 2 to 3 grains daily; the pain became much less severe and less frequent immediately the dose was reduced again to 2 grains daily. In Cases 2 and 3, angina of effort developed independently of any change in the dose of thyroid; Case 2 had been on treatment for three years, Case 3 for three months. In both the pain improved (in Case 3 it disappeared) although treatment with thyroid was continued; and in both there was some other feature to suggest a coronary occlusion—a diphasic T IV in the cardiogram of Case 2, and a temporary fall in blood pressure while effort angina was present in Case 3.

Four patients were considered to have *coronary disease* complicating myxœdema; all had inversion or partial inversion of T I in the cardiogram. In one I was afraid to order thyroid; another has not been traced. Case 4 had mild hypertension with slight hypertrophy of the left ventricle and calcification of the aorta, as well as T I inversion. She has been on treatment since February 1939; her effort angina is for all practical purposes abolished when she is on a dosage of 3 grains of thyroid daily, but it returns soon after she attempts to discontinue treatment. There has been no demonstrable change in her heart radiologically or cardiographically, and her hæmoglobin percentage is unaltered at 84 per cent; her blood pressure now is 155/105 as compared with 190/90 in February 1939. Unless the disappearance of the effort angina is attributed to psychological factors, which seems unlikely, it is reasonable to conclude that it is due to an improvement in the coronary circulation accompanying an increase in the general circulation rate. With her present dosage of thyroid (3 grains daily), her basal metabolic rate is still -32 per cent; despite this, she is mentally bright and able for much of her housework. Case 5 had suffered from effort angina before thyroid therapy was commenced, and she had inversion of T I and T II in the cardiogram. After a preliminary spell of rest and iron therapy, treatment with elityran was commenced while she was still confined to bed; the drug had to be discontinued after three days owing to complaint of "severe bursting pains in the arms." During the following fortnight changes developed in the cardiogram suggesting that the attack of pain was due to a coronary occlusion. Subsequent resumption of treatment with thyroid had no apparent effect on her angina of effort despite a rise in blood pressure from 145/95 to 170/100; in this respect she resembles Cases 2 and 3.

One patient had myxœdema with an *intermittent partial block* of uncertain ætiology (Case 6). Apart from the intermittent block, the cardiovascular findings were consistent with a myxœdema heart. Block appeared on two occasions, first a week after thyroid treatment was commenced, the second time when she was having no thyroid two years later. For a period of two years she attended irregularly, for three or four weeks at a time at intervals of four to six months; during each spell of attendance she received 2 grains of thyroid daily and her anginal pain improved. She ceased attending in 1937, subsequently visiting many doctors and receiving various forms of treatment other than thyroid; she continued to suffer from effort angina until 1940 when there seems to have been spontaneous improvement in her myxœdema. She has had no anginal pain since, there are no obvious clinical signs of myxœdema now, and her basal metabolic rate is +5 per cent.

Two patients had uncomplicated *myxœdema heart* with angina of effort. The first, a man of 56 whose chief complaint was angina of effort, only returned once, ten days after starting treatment; he said he was "much improved." Case 7 originally had the features of Zondek's "abortive myxœdema heart"; thyroid treatment was advised, but she escaped it by changing her doctor. She has so far had no thyroid, and in the 3 years that have elapsed the character of her pain has altered; it is now a typical angina of effort. There has been an insignificant rise in blood pressure (from 142/85 to 150/95); and she has a mild hypochromic anæmia (hæmoglobin 78 per cent, erythrocytes 5.4 million). It is questionable whether the inverted U waves which have developed should be regarded as indicating coronary disease, thus explaining the change in the character of her pain; alternatively the anæmia may provide the explanation.

One patient with a *mild myxœdema developed a spontaneous thyrotoxicosis* at the menopause (Case 8) and she now has a curious mixture of thyrotoxic and myxœdematous symptoms. The onset of the thyrotoxicosis was accompanied by development of an effort angina which was still present when she was examined a year later.

DISCUSSION

To sum up, angina of effort appeared in one myxœdematous patient who developed a spontaneous complicating thyrotoxicosis, and in four who had independent heart disease during treatment with thyroid. In one of these, the angina developed shortly after an increase in the dosage of thyroid and it improved immediately the dose was reduced to its former level though pain did not completely disappear. In the remaining three the angina seems to have been brought on by a coronary occlusion which was almost certainly coincidental in two cases, though it may have been due to some unexplained action of the drug in one. In none of these three cases was there any aggravation of the anginal pain on subsequent resumption of thyroid therapy; on the contrary, the pain ultimately disappeared in one patient, in a second it improved, while in the third it was unaltered. Angina of effort was abolished by suitable dosage of thyroid in a patient with myxœdema, hypertension, aortic calcification, and coronary disease; the findings in this case suggested improvement in the coronary circulation secondary to an increase in the general circulation rate as the most likely explanation of the disappearance of the pain. A patient with a myxœdema heart complicated by an intermittent partial block showed improvement during each of several short spells of thyroid therapy, and her anginal pain ultimately disappeared when she made an apparently spontaneous recovery from her myxœdema. The effect of thyroid in the two patients with uncomplicated myxœdema heart cannot be gauged as one avoided treatment while the other was under observation for too short a period.

Consideration of the foregoing facts suggests that, even when coronary disease is present, a suitable dose of thyroid may lead to improvement in the coronary circulation and to disappearance of anginal pain. An increase in dosage may cause a disproportionate increase in the general circulation rate and so aggravate the pain. The presence of hypertensive

disease or coronary disease with angina of effort does not contra-indicate the use of thyroid in a myxœdematous patient; but the drug should be given with caution, beginning with a small dose, and an attempt should be made to find the "optimum dosage" for that particular patient. I would make an exception to this rule only in cases of recent coronary occlusion, where it seems reasonable to withhold thyroid until the stage of convalescence has been reached; resumption of thyroid therapy at that stage has not aggravated the pain in any of the cases in this series.

Since writing the foregoing, my attention has been drawn to an article by Phillips and Milliken (1939). Discussing thyroidectomy for angina pectoris, they say: "It is not advisable to recommend thyroidectomy if the basal metabolic rate is less than -15 per cent. The anginal syndrome may be improved by elevating the metabolic rate in some cases with a low basal metabolic rate and low blood pressure. The mechanism is an improvement in the coronary circulation."

ZONDEK'S ABORTIVE MYXŒDEMA HEART

Two examples of this syndrome have been encountered. As it is somewhat rare, a more detailed description of the cases is given in the Table. Reference has already been made to Case 7 who escaped thyroid treatment; 3 years later her pain has altered in character, and she now has a typical effort angina. In Case 9, the clinical features of myxœdema were wanting when she was first seen, and the atypical behaviour of the pain led to a diagnosis of neurosis. Five years later she returned with obvious clinical signs of myxœdema and with the same pain. Her pain improved with a dosage of 2 or 3 grains of thyroid daily, and at times she was quite free from it on this dose; but she was unable to tolerate doses of 4 grains daily. In this respect she shows an analogy with the cases described in the previous section despite the fact that no independent heart disease can be demonstrated; she is aged 58. Her attacks of collapse have also been abolished since treatment was instituted five months ago, except for one occasion when an attack followed painting of the abdomen with strong iodine in preparation for an operation. It is clear that she is sensitive to iodine as well as to thyroid, as she had a well-marked iodine rash on the following day. It is possible that this attack was allergic or anaphylactic in nature; but its close resemblance to her earlier attacks suggests an alternative explanation, namely that absorption of iodine from the skin disturbed her somewhat delicate thyroid balance.

ATTACKS OF SPASMODIC ANGINA IN MYXŒDEMA

Two myxœdematous patients described attacks which suggested simple spasmodic angina. Case 10 had osteoarthritis of the spine, and had suffered from a more or less constant pain in the left side of her back radiating through to the front for many years before she developed any myxœdematous symptoms. This pain was unaffected by thyroid treatment. She had developed symptoms of myxœdema some nine months before she first attended, and during that period she had five attacks of severe sternal pain; each wakened her during the night and lasted about 45 minutes. She had a blood pressure of 130/100; the cardiogram showed left axial deviation with flat T in all leads, and a diphasic T in some beats of lead I but not in all. The remaining findings were consistent with a myxœdema heart. Because she had a flat sugar tolerance curve, and because the attacks occurred exclusively through the night, the possibility of hypoglycæmia was considered. Glucose at bedtime was ordered as well as thyroid; unfortunately both were started simultaneously so that it is not possible to say which led to disappearance of the attacks. It is now five years since treatment was instituted; she has had no further attacks, nor has she developed effort angina. Her basal metabolic rate, originally -25 per cent, is now $+13$ per cent on a dosage of 3 grains daily; she has well-defined upright T waves in leads I and II (amplitude 4 mv. in lead I with a shallow

inverted T III; her blood pressure is 170/95; X-ray shows widening of the root of the aorta and slight enlargement of the left ventricle.

Case 11 had a post-operative myxœdema (basal metabolic rate, —33 per cent) with achlorhydria and anæmia (hæmoglobin 75 per cent, erythrocytes 3·8 million). She had soft heart sounds, left axial deviation with low P and T waves in the cardiogram, and a blood pressure of 155/90. She complained of attacks of precordial pain which she said were usually induced by a sudden noise such as a cough in the ward or the dropping of a plate. The attacks ceased when, in response to treatment with iron, her hæmoglobin rose to 92 per cent. She was then treated with thyroid, and there was no recurrence of pain with doses up to 3 grains daily.

In neither of these cases is there any good evidence of independent heart disease, although in both the blood pressure reading with left axial deviation in the cardiogram raises the question of a possible incipient hypertension; both had “myxœdema T waves” in their original cardiogram. In neither case was there any aggravation of the spasmodic angina when thyroid was given, nor was an effort angina induced by it. In one, the improvement can be attributed to improvement in the blood picture in response to iron. In the other, improvement may have been due either to glucose or to thyroid.

Psychoneurotic Pain.—Although the pain in Case 9 was originally diagnosed as psychoneurotic, it is clear in retrospect that it was really a symptom of Zondek’s “abortive myxœdema heart” syndrome. The spasmodic attacks in Case 11 may have been psychoneurotic in view of the conditions by which they were induced, but the rapid response to iron treatment of her anæmia suggested that they were related to the latter. I am not satisfied that I have encountered an example of psychoneurotic pain complicating myxœdema, although it is a possibility which cannot be excluded.

SUMMARY

Several types of anginal pain may occur in myxœdema.

Angina of effort occurs frequently when there is independent heart disease and occasionally with an uncomplicated myxœdema heart. In the presence of independent heart disease, angina is sometimes aggravated, sometimes alleviated, and sometimes unaffected by thyroid therapy. For many patients there is an optimum dose, up to which improvement results but beyond which the pain is aggravated; the optimum dose is often sufficient to procure great improvement in the patient’s general condition and to permit of a fair amount of activity; in favourable cases the angina is abolished on the optimum dosage. When a patient with myxœdema and independent heart disease suddenly develops effort angina during thyroid treatment and apart from an increase in dosage, the cause is frequently a small coronary occlusion; caution suggests that the dose should be temporarily reduced or discontinued; but once the stage of convalescence has been reached resumption of therapy does not aggravate the pain, and there seems to be no reason for withholding the benefits of the drug.

A constant ache or pain, aggravated during effort, and tending to be associated with attacks of collapse, occurs in some cases of mild or sub-clinical myxœdema; it is referred to as the *abortive myxœdema heart of Zondek*. It improves with thyroid therapy, but in these cases too there may be an optimum dose. If unrecognized and untreated, the patients may develop a typical clinical myxœdema or a typical angina of effort.

Spasmodic angina occurred in two cases. Both may have had very early hypertension, but neither had any obvious or advanced complicating heart disease. In one, the possibility of hypoglycæmia was considered; the attacks ceased on treatment with thyroid and a dose of glucose at bedtime. In the other, there was a complicating anæmia; the attacks ceased when this was treated and before any thyroid was given. In neither case did thyroid aggravate the spasmodic angina nor did it produce an effort angina.

The occurrence of anginal pain in a myxœdematous patient does not contra-indicate the

cautious use of thyroid; only when pain develops in response to an increased dosage is there justification for blaming the drug, and even then it may be tolerated at a later date.

I wish to express my indebtedness to Dr. Angus Scott for access to his records of numerous cases of myxœdema, from among which cases 1, 5, and 11 are recorded; also for much helpful discussion. I have also to thank Dr. Eaton for the metabolic investigations, Dr. Wilson and Dr. McWhirter for the radiology, and those practitioners who have sent information regarding patients unable to attend for re-examination. Finally, Mrs. A. Mather has given invaluable help in tracing a number of the patients.

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TABLE AND APPENDIX OF CASE NOTES

Case No., Age, and Sex	Clinical Features	Cardiovascular Findings	Cardiogram
1. F. 62	1939, Myxœdema.	Myxœdema heart. P.B. 136/80 B.P. 150/100	Normal axis, low P and T. Slight L. axial deviation.
2. F. 68	Myxœdema with hypertension.	Enlarged heart. B.P. 190/106. Apical systolic murmur.	Left axial deviation; low P and T. T I invisible. T IV diphasic.
3. F. 54	Myxœdema with hypertension.	Enlarged heart. B.P. 220/110	Left axial deviation; low T; inverted T III.
4. F. 56	Myxœdema with coronary disease, etc. Hb. 86 per cent.	Slight enlargement left ventricle and calcified plaque in aorta.	Slight left axial deviation. Prominent Q III, no Q II. Low T. Inverted T I.
5. F. 57	Myxœdema with coronary disease. Hb. 48 per cent raised to 60 per cent before thyroid started.	Heart not enlarged, heart sounds soft. B.P. 146/94.	Left axial deviation. Inverted T I and T II, slightly elevated R-T III.
6. F. 56	Mild myxœdema	Left ventricular enlargement. B.P. 130/76.	Left axial deviation; low P and T; inverted P III and T III. Partial block twice.
7. F. 50	Mild myxœdema. Hb. 92 per cent.	Heart enlarged, sounds distant. B.P. 142/86.	Left axial deviation; low P and T; shallow inverted T III. P-R 0.24 sec.
8. F. 54	Mild myxœdema and later menopausal thyrotoxicosis.	Heart enlarged. B.P. 172/92. Apical systolic murmur. Pulse rate 100.	Left axial deviation; low T waves (max. 1.5 mm.).
9. F. 54	1938, no clinical myxœdema, diagnosed "neurosis".	Heart not enlarged. B.P. 150/86.	Left axial deviation; T of good amplitude.
	May 1942, typical myxœdema. B.M.R. -16 per cent. Hb. 120 per cent.	Slight general enlargement of heart. B.P. 166/90.	T waves now lower, otherwise unchanged.
	Oct. 1942. No clinical signs of myxœdema on 1½ gr. thyroid daily. B.M.R. -16 per cent.	Heart not enlarged. B.P. 132/76.	Unchanged.
10. F. 50	Myxœdema. B.M.R. -25 per cent.	Heart enlarged. B.P. 130/100	Left axial deviation; low T. Diphasic T in some beats of lead I.
11. F. 51	Myxœdema with anæmia. Hb. 75 per cent.	Heart not enlarged; soft sounds. B.P. 155/88.	Low voltage; slight left axial dev. Flat P and T.

Nature of the Pain and its Relation to Thyroid Treatment.

Case 1. Effort angina appeared after 3 years' treatment, 5 weeks after dose raised from 2 to 3 gr. daily. Pain lessened, not abolished, on return to 2 gr. daily.

Case 2. Sudden onset of effort angina after 3 years on 2 gr. daily. Dose temporarily halved, later restored. Ten months later, pain limited to the gums and felt only if walking against a cold wind. Diphasic T IV three months after onset of pain.

Case 3. Onset of effort angina after 3 months on 4 gr. daily, but not reported and treatment continued; B.P. gradually fell to 180/98; cardiogram unchanged. After 9 months, pain improved, ultimately disappeared, and B.P. rose to 220/110. Observed 4 years; no recurrence of pain even when dose later raised to 6 gr.

Case 4. Effort angina present prior to thyroid therapy. Pain abolished on 3 gr. daily, but returned soon if treatment stopped. X-ray and cardiogram unchanged 3 years later; B.P. 155/105; Hb. 84 per cent; B.M.R. —32 per cent, yet active.

Case 5. Effort angina present prior to thyroid therapy. Three days later while patient confined to bed, severe bursting pains in arms; treatment stopped. Sixteen days later, cardiogram showed right branch bundle block. Treatment resumed after discharge from hospital with 2 gr. thyroid daily. Effort angina unaffected by thyroid.

Case 6. Effort angina present before treatment started. Attended irregularly from 1934 to 1937 for 3 to 4 weeks every 4 to 6 months. Complaint of effort angina on each occasion, and improved while on 2 gr. thyroid daily. 1937–40: various treatments but no thyroid; effort angina persisted. 1940: reduced her activities and myxœdema seems to have improved spontaneously; no pain since; no clinical evidence of myxœdema now, and B.M.R. +5 per cent.

Case 7. Found unconscious when 47; symptoms date from this. Pain starts in l. axilla, radiates to cardiac apex and to sternum; worse when excited or after exertion. Thyroid advised but not given. Three years later, typical effort angina. Cardiogram unchanged, P–R, 0.16 sec.; Hb. 78 per cent; B.M.R. —17 per cent.

Case 8. When 48, loss of hair treated by thyroid, but was intolerant. Menopause when 49 with transient exophthalmos and later palpitation, tachycardia, and loss of weight. Effort angina since then. A thin woman with scanty hair and eyebrows, impalpable thyroid, v. Graefe's sign, tremor, and glycosuria.

Case 9. 1938. First had pain in 1935 while nursing sister who died from heart disease. Pain in bouts lasting a few days; constantly present during attack, but worse after a day's work; felt across præcordium, in left shoulder, and inner side of left arm.

May 1942. Pain constantly present at apex, worse on walking, with tightness in chest; two attacks of collapse. Improves and sometimes free from pain with thyroid in doses up to 3 gr. daily but cannot tolerate 4 gr. daily.

October 1942. Prior to operation, thyroid reduced in error to 1½ gr. daily. Attack of pain and collapse occurred an hour after abdomen was painted with strong iodine; pallor, pulse slow and weak, B.P. 140/90, heart sounds good. Attack lasted 4 hours and next day abdomen showed an intense iodine rash with pustulation.

Case 10. Five attacks of spasmodic nocturnal angina over a period of 9 months prior to therapy. No attacks in 5 years since treatment started with 3 gr. thyroid daily and glucose at night. T waves now good. B.M.R. +13 per cent.

Case 11. Attacks of precordial pain induced by sudden noise, etc.; ceased when Hb. rose to 92 per cent with iron, before thyroid started. No recurrence on thyroid, gr. 3 daily.