EMERGENCIES IN GENERAL PRACTICE**CRISES IN MYXOEDEMA**

BY

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Myxoedema is a chronic rather than an acute disease, and therefore rarely presents with a crisis. It only does so when the disease has progressed to a very advanced stage, or if an acute complication develops.

I shall start by describing how to recognize the disease, for whatever the crisis the clinical picture of myxoedema is the same. The most important thing is to keep the possibility of the diagnosis in mind, for once the diagnosis has been thought of it is usually not difficult to establish it with the appropriate questions and observations.

Signs

I put signs first because appearance, voice, or demeanour often initiate the idea of the diagnosis before the history does.

Face.—The most helpful sign is the appearance of the face. This is hard to describe but easy to recognize once a case of myxoedema has been encountered, because affected people resemble each other as closely as if they were near relations. The patient is usually a woman, but the condition can occur in men. In advanced cases the features look bloated and the normal contours of the face are smoothed away just as the wrinkles of a balloon disappear when it is blown up. Oedema collects in the lips, broadening them, and around the eyes, narrowing the palpebral fissures and forming little bags of flesh beneath them. The colour is yellowish and waxy with a contrasting burgundy-coloured flush over the cheeks; in addition, the hair is dry and scanty, with a receding hair margin that leaves a wide forehead and, in some cases, partial baldness. The eyebrows are sparse and sometimes the lashes too. The classical loss of hair over the outer third of the eyebrows is an unreliable sign because so many normal people show this deficiency.

Neck.—Feeling for the absence of thyroid tissue is not clinically rewarding—besides, myxoedema can occur with a goitre; but the presence of a thyroidectomy scar is a helpful confirmatory sign when present.

Speech.—The essential characteristics of the speech are that it is low, it is slow, it shows nasal obstruction, and has a thick indistinct quality. In a gross case the words are punctuated by peculiar grunting, snorting sounds, and sound like a bad gramophone record (running down) of a drowsy, slightly intoxicated person with a bad cold and a quinsy. In less severe cases a husky thickness is all that is observed.

Oedema.—The myxomatous infiltration gives the body tissues a spongy, swollen feel somewhat resembling ordinary fluid oedema, but not pitting on pressure. This can be best felt on the front of the upper chest, where the sensation on pressure reminds one of rubber sponge. The textbook supraclavicular pads are not at all constantly present. In the legs the myxomatous oedema may be blended with true oedema due to heart failure.

Heart.—Though bradycardia is the textbook finding, it is unusual to get a pulse rate below 70. The heart is usually somewhat enlarged, but the frequent presence of pericardial effusion makes it seem larger. It is unlikely that the size of the heart or the presence of pericardial fluid will be detected clinically, because of the thickened integument of the chest wall.

Skin.—This looks coarse and feels cold, dry, and scaly; in a gross case the observer feels as if he were touching a lizard.

Mentality.—The patient with myxoedema thinks, speaks, and moves slowly. She may sleep much of the day and night, dropping off unintentionally whenever she sits in a chair. Her memory is faulty and she is too drowsy to pay much attention to anything. Psychotic symptoms may occur (see below) even when the myxoedema is not gross.

Symptoms

The history may give little help in making the diagnosis, though it greatly helps in confirming it once suspected. The symptoms are admitted to rather than complained of, and are discovered only when the right questions are asked. Often relatives notice the changes more than the patient because the illness itself smothers self-criticism. The following symptoms are common: general tiredness and sleepiness, gain in weight, vague pains in the limbs, poor memory, constipation, deafness, falling out of hair, dryness of the skin, and a feeling of perpetual cold. The myxomatous blocking of the air passages makes the patient complain of a chronic cold, and during sleep snoring may be unusually loud. The puffiness of the face and the change in the quality of the voice may be noticed by relatives. The drowsiness may be so great that the patient drops off to sleep at all hours of the day. The feeling of coldness may be so striking that a patient with myxoedema may use an inordinate number of blankets and hot-water bottles even in summer; the position in bed is often characteristic for the same reason—the bedclothes pulled up high, with only the top of the head visible, in an effort to get warm (Fig. 1).

FIG. 1.—The "snug" sign. A case of gross myxoedema showing the typical position in bed.

Diagnosis

Essentially myxoedema is a diagnosis made by clinical observation rather than by investigations; it is unlikely in a crisis that the practitioner would need more than the blood cholesterol level (and perhaps the basal metabolic rate and a photograph if easily available). For the sake of completeness here is a fuller list of investigations that may be helpful in supporting the diagnosis in doubtful cases.

Photographic Test.—Take a photograph of the face before and after six weeks' thyroid treatment. The change in appearance is usually sufficient to leave no doubt of the diagnosis (see Figs. 2 and 3). One patient, for instance, was not recognized by her grocer, with whom she had dealt for years, because her appearance had so greatly changed with treatment.

Blood Cholesterol.—The normal value is usually between 100 and 200 mg. per 100 ml. In nearly all cases of myxoedema there is a rise in this value to between 300 and 400 mg., or even higher. However, a normal value does not exclude the diagnosis.

Basal Metabolic Rate.—Classically the basal metabolic rate is lower than minus 30 to 40% by the time symptoms appear. The basal metabolic rate is a difficult thing to estimate accurately both because myxoedematous patients are often uncooperative and because the test demands special conditions, faultless apparatus, and repeated estimations by a very experienced observer. For these reasons a misleading figure is sometimes obtained, but this should not exclude a diagnosis made on clinical grounds.

Electrocardiogram.—The dry skin makes good records hard to get. The record sometimes shows bradycardia and usually reveals a low voltage of the QRS complex with flattening or inversion of the T wave. After treatment the electrocardiogram becomes normal.

Chest Radiography.—This reveals an apparently enlarged heart, but aspiration will show that much of the enlargement is due to pericardial effusion. With thyroid treatment the enlarged cardiac shadow returns to normal.

Iodine Excretion.—The urinary excretion of radioactive iodine is followed for 48 hours after a dose of 10 mc. of I^{131} with

"I feel different, I speak different, and I am like what I used to be." A barmaid said to me, "I usen't to know how many light ales the boss had ordered and my customers used to say, 'What's come over you, Lyd? You're like an old frog,' but now they say, 'You're back to your usual self, Lyd.'" This same barmaid told how before treatment she found she had lost her power of repartee which she found so necessary in dealing with jovial regulars, and it was the return of this gift which pleased her more than anything.

Crises

1. Advanced Myxoedema

Any patient with advanced myxoedema is liable to die suddenly in the first few weeks of treatment before normal metabolism has been restored. The exact cause of death is not usually clear. The diagnosis of advanced myxoedema is easy if the patient is seen for the first time, but when a patient has been known for years the advanced condition may develop so slowly that a practitioner long acquainted with the patient can fail to notice it; the clinical newcomer has an advantage.

Before describing treatment, it must be underlined that in this (and the other crises of myxoedema) the ideal treatment is to prevent the condition ever reaching so gross a stage by diagnosing and treating myxoedema earlier.

The patient should be kept warm with plenty of bedclothes and hot-water bottles, because she is liable to develop hypothermia and go into an irreversible coma. Because of the liability to sudden collapse the patient should be moved as little as possible. People with gross myxoedema lie huddled in a torpid hibernating condition, and they should be allowed to stay thus without bothering them with much washing, visiting, or investigations. Thyroid should be started with a dose of $\frac{1}{2}$ gr. (32 mg.) twice daily for ten days and then be increased to $\frac{1}{2}$ gr. three times daily for the next week. After that the dose can be increased slowly to that level which maintains clinical improvement without overdose. This dose usually lies between 2 and 3 gr. (0.13

and 0.2 g.) a day. The clinical improvement and the blood cholesterol level help to assess the dose. Palpitations, anginal pain, diarrhoea, and undue loss of weight are indications that the dose is too large. Thyroxine has recently come on the market and can be used instead of thyroid. It has the theoretical advantages of a pure substance—certainty in action and constancy of dosage, 0.1 mg. corresponding roughly to 1 gr. (65 mg.) of ordinary thyroid; however, thyroid tablets in practice seem so efficient and certain that their general use continues.

The complications of myxoedema which can lead to crises are: myxoedema coma, acute psychosis, heart failure, intestinal obstruction, anaemia, gall-stones, and relapse.

2. Coma

This condition occurs only in fairly gross myxoedema and is often fatal. V. K. Summers reported five cases, all of them fatal. The coma may develop within a few hours, or deepen gradually for two days. The cause of the coma is uncertain, most cases have a very low temperature and the condition occurs more often in winter, so hypothermia may play a part.

It is hard to be dogmatic about treatment, because the coma is so often irreversible and treatment ineffective. Of the two cases I have seen that recovered, one came round from her coma in a few hours before thyroid had been given and thereafter progressed on $\frac{1}{2}$ gr. (16 mg.) of thyroid

FIG. 2

FIG. 3

FIG. 2.—A case of myxoedema admitted with an acute psychosis, before treatment. FIG. 3.—Same patient as in Fig. 2 after six weeks' treatment. (The loss of facial hair after treatment was only an indirect effect of the administration of thyroid. The improvement in the patient's social consciousness led to the use of a razor.)

10 mg. of potassium iodide. When hypothyroidism is present the values in the 24-48-hour period are abnormally high because the thyroid gland is less greedy for iodine than normally, but in myxoedema caused by antithyroid drugs the avidity of the thyroid for iodine is increased unless the antithyroid drug is still being given.

Temperature Chart.—There may be a low temperature, ranging between 96 and 97° F. (35.6-36.1° C.). A chart of this kind may help in suggesting the diagnosis, but the inconstancy of low temperature in myxoedema makes it of little value as a diagnostic test.

Blood Count.—Anaemia is usually found. In the blood count alone there is nothing diagnostic, for any of three types of anaemia may be shown: (1) a true macrocytic pernicious anaemia responding to liver in the usual fashion; (2) true hypochromic iron-deficiency anaemia responding to iron; and (3) a normochromic anaemia which responds neither to liver nor to iron but improves very slowly with thyroid.

Other Tests.—Among other tests the urinary ketosteroid excretion may be lowered, the protein-bound blood iodine diminished, the cerebrospinal fluid protein increased, the blood carotene raised, and the response of the blood sugar to intravenous insulin delayed. These tests are not essential for diagnosis.

What the Patient Says

Usually, despite all the diagnostic tests, the most convincing confirmation of the diagnosis lies in the spontaneous remarks of the patient or her relatives after treatment. For example: "My husband says I look ten years younger";

twice a day, whereas the other case (which Dr. C. G. Barnes, of Hillingdon Hospital, kindly invited me to see) made a good recovery after being given 10 gr. (0.65 g.) of thyroid on the first day. Probably all that can be done is to treat the patient as already described for severe myxoedema, but, if she is too deeply comatose to swallow, thyroxine sodium, 0.05 mg., can be injected subcutaneously instead of giving thyroid $\frac{1}{2}$ gr. (32 mg.) by mouth.

3. Acute Psychosis

Quite commonly an acute psychosis may result in the patient being first diagnosed as a mental case and dealt with under the Lunacy Acts. A. J. Cronin gave a vivid account of this complication in his book *The Citadel*, and it was clearly described in 1888 by the Clinical Society of London. I reported 14 cases in 1949 and have encountered eight more since. Almost any type of psychosis may occur, and the diagnosis is made on the myxoedematous appearance of the patient and not on the kind of mental symptoms. The commonest variety of psychosis is general confusion and disorientation, with persecutory delusions and hallucinations.

As there is a prospect of mental recovery within one or two weeks, the patient need not be transferred to a mental hospital if she can be managed at home or in a mental observation ward. Thyroid can be started at $\frac{1}{2}$ gr. (32 mg.) twice a day, or, if the myxoedema is not very severe, at 1 gr. (65 mg.) twice a day. Amylobarbitone, 3 gr. (0.2 g.), or paraldehyde, 2 dr. (7 ml.), may be needed at night to allay restlessness. Within a week or two the psychotic symptoms may have cleared almost completely, though if the condition has been long established mental improvement may be incomplete.

4. Heart Failure

Heart disease can occur in myxoedema because the heart is enlarged by myxoedematous infiltration of the heart muscle and because there is quite often a pericardial effusion. In addition, there may be coronary atheroma because of the high blood cholesterol. The clinical picture is that of myxoedema with the addition of dyspnoea, venous distension of neck veins, and pitting oedema.

If the myxoedema is gross it is probable that the heart failure will respond to thyroid; this should be given as already described in the treatment of gross myxoedema. In addition, digitalis should be given, 3 gr. (0.2 g.) three times during the first day, 2 gr. (0.13 g.) three times during the next day, then 1 gr. (65 mg.) three times a day for a week. If there is a pericardial effusion it should not be aspirated as it will absorb with thyroid treatment. Patients with myxoedema sleep well, so no sedative may be needed. If necessary, phenobarbitone, 1 gr. (65 mg.), can be given at night; morphine should not be given, as it may produce stupor.

5. Intestinal Obstruction

Subacute intestinal obstruction can occur as a complication of myxoedema owing to the constipation which is part of the disease and also to the myxomatous infiltration of the gut wall. One of my patients (the woman shown in Fig. 1) came in as a surgical emergency with subacute intestinal obstruction, and three other such cases have been seen at the Central Middlesex Hospital. The condition clears up with thyroid treatment. Naturally it is important to see that the obstruction is not caused by some unrelated condition such as strangulated hernia or carcinoma of the colon.

Thyroid is given as described already and a saline enema of 1 pint (570 ml.). Digital evacuation of the rectum is necessary if there are very hard scybala there.

6. Anaemia

It is unlikely that anaemia will be severe enough to be labelled as a crisis, but it may by its presence add to the critical condition of the patient.

Thyroid should be given whatever the type of anaemia if myxoedema is present. Other treatments depend on the

kind of anaemia. If there is iron deficiency the blood picture is that of hypochromic microcytic anaemia, and iron should be given by mouth as ferrous sulphate tablets, 6 gr. (0.4 g.) three times a day. If the blood picture shows true pernicious anaemia with macrocytosis and megaloblasts in the peripheral blood the case should be treated with vitamin B₁₂, 200 µg. by intramuscular injection monthly. Before initiating treatment with vitamin B₁₂ it is advisable to confirm the diagnosis of pernicious anaemia by a sternal puncture and by reticulocyte counts, which should rise to a peak on the sixth day after treatment. Transfusion should not be given for the anaemia of myxoedema, because of the liability to heart failure.

7. Gall-stones

The incidence of gall-stones is increased in myxoedematous people, so the crises of gall-stones—that is, cholecystitis and gall-stone colic—may complicate the picture of myxoedema. The treatment of gall-stones is not a matter for this article, but the associated myxoedema should be treated in the usual way.

8. Relapse

It is, unfortunately, common for people with myxoedema to stop taking their thyroid and relapse into a condition of advanced myxoedema complicated by any of the crises which have just been outlined. The reason is that patients feel so well after a few months' treatment that they think there cannot still be any need to continue it. Once a patient stops taking thyroid the mental slowing prevents her noticing her own deterioration. It is important, therefore, to explain most carefully to the patient and her relatives that the illness requires treatment indefinitely, because, unlike most illnesses, it is caused not by something wrong being present, but by something right being absent.

(Fig. 1 is reproduced by permission of *Medicine Illustrated*.)

Next article on Emergencies in General Practice.—
"Fits," by Dr. Denis Williams.

THE B.P.C. AND THE NATIONAL FORMULARY

A PHARMACEUTICAL SOCIETY LECTURE

The publication of the *National Formulary*, 1955, which was the subject of a leading article in our last issue (p. 402), a few weeks after that of the *British Pharmaceutical Codex*, 1954, has been arranged so that both compilations can be accepted for National Health Service purposes on the same date. In a lecture delivered by Dr. K. R. CAPPER, Ph.D., B.Pharm., a member of the Codex Revision Committee, at the Pharmaceutical Society of Great Britain on February 14, an interesting account was given of the work which lay behind both these publications.

Dr. CAPPER reminded his audience that to a large extent the *Codex* was produced by pharmacists for pharmacists, although many doctors served on the revision committee, and many doctors consulted the *Codex* for information, especially on the newer drugs. On the other hand, the *National Formulary* was a joint production by doctors and pharmacists, and was in fact a prescribers' handbook, easy to use in the crowded surgery hours of the general practitioner and in the dispensary of a retail pharmacy.

English or Latin Titles

The *Codex*, following the lead of the *British Pharmacopoeia*, had used English for the main titles of its monographs, whereas the *National Formulary* had reverted to an arrangement based on Latin titles and abbreviations of Latin names. Dr. Capper explained that this was the result of differently constituted committees dealing with similar