abdomen to about three fingerbreadths below the costal margin. Faint bowel sounds were heard. No abnormality was found in the chest or in the cardiovascular and nervous systems.

Blood taken on admission showed haemoglobin of 12.3 g./100 ml. and a leucocyte count of 18,050/c.mm., with 27% polymorphs, 71% lymphocytes, of which a few were atypical, and 2% monocytes. Radiology showed no abnormality in the chest, no free air in the abdominal cavity, and a spleen which appeared markedly enlarged. A tentative diagnosis of infectious mononucleosis with rupture of the spleen was made, and observation under sedation was continued.

Three hours after admission the blood-pressure had fallen to 80/55 mm. Hg and the patient was complaining of thirst and continuing pain in the shoulders which moved as the posture was altered. Laparotomy was therefore undertaken, and on opening the abdomen about 2,000 ml. of free blood was found together with a grossly enlarged spleen with a large subcapsular haematoma and a deep laceration running from above the lower pole towards the hilum. Splenectomy was performed (Dr. F. M. Mitchell and Dr. O. J. Van Dyk), and owing to the friable nature of the organ it was further lacerated during this procedure. 1,500 ml. of blood was transfused during the operation. The interval between the onset of symptoms and operation was about eight hours. Both the operative and the post-operative course were uneventful except for a temperature of 102–103° F. (38.9–39.4° C.) on the second post-operative day which was not accompanied by tachycardia or other signs. It was thought that this was due to mononucleosis.

The heterophil agglutination test was positive on admission at a 1:51,200 dilution, and the leucocyte count the day after admission was 24,300/c.mm. with 36% polymorphs and 63% lymphocytes, of which 20% were atypical. Haemoglobin was 13.9 g./100 ml. and haematocrit 43%. One week after admission the heterophil agglutination test was positive at a dilution of 1:3,200 and the leucocyte count was 17,800/c.mm. with 29% polymorphs, 68% lymphocytes (60% atypical), and 3% monocytes. The patient was discharged 10 days after admission and returned to his normal academic routine.

The spleen after removal measured 16 by 11 by 6 cm. and had three deep lacerations running from the lower surface half-way through its width. Histological preparation (Dr. W. S. Hastings) showed characteristic pulp and sinusoids in some areas, while in others there was scarcely any sinus reticulum owing to the presence of large numbers of large cells with oval nuclei which very rarely were slightly lobulated but in general resembled the large mononuclear cells of the blood stream.

COMMENT

This patient presented as an "acute abdomen" without the more usual clear history of previous illness. The precipitating trauma appeared to be contracture of the abdominal musculature to pass flatus, and this lends support to the warnings regarding the potential danger of too vigorous attempts to palpate the enlarged spleen (Leibowitz, 1953). In some cases death from loss of blood rapidly follows the onset of symptoms (Kass and Robbins, 1950; Ziegler, 1944), while in others the symptoms may be protracted up to several weeks (Chedru *et al.*, 1955). In the present case it was four hours from the onset of symptoms before the clinical signs of blood loss became unequivocal. The mortality from the condition can be reduced only by rapid surgical treatment. In English practice this type of case is most likely to present to the general practitioner or the casualty officer, and it is important that there should be widespread awareness of the condition.

I wish to thank Dr. N. S. Moore, Clinical Director of Cornell Infirmary and Clinic, and Dr. R. W. Alexander, under whose care the patient was admitted, for permission to report the case.

A. R. M. FREEMAN,* M.A., B.M., B.Ch.,
Resident in Internal Medicine,
Cornell University Infirmary,
Ithaca, New York.

REFERENCES

- Bernstein, A. (1940). *Medicine (Baltimore)*, **19**, 85.
Chedru, J., Doussot, J., Jouannot, J. P., and Laumonier, R. (1955). *Sang*, **26**, 333.
Davidson, A. S. (1958). *J. Laryng.*, **72**, 332.
Erwin, W., Weber, R. W., and Manning, R. T. (1959). *Amer. J. med. Sci.*, **238**, 699.
Garfield, J., and Gentry, J. H. (1959). *U.S. Armed Forces med. J.*, **10**, 91.
Kass, E. H., and Robbins, S. L. (1950). *Arch. Path. (Chicago)*, **50**, 644.
Leibowitz, S. (1953). *Infectious Mononucleosis*, Modern Medical Monographs, 5. Grune and Stratton, New York.
Ridgley, F. H. (1960). *Bull. Amer. Coll. Surg.*, **45**, 145.
Smith, E. B., and Custer, R. P. (1946). *Blood*, **1**, 317.
Smith, J. N. (1956). *Ann. intern. Med.*, **44**, 861.
Tidy, H. L. (1934). *Lancet*, **2**, 180, 236.
Wagman, G. F. (1957). *Arch. Path. (Chicago)*, **64**, 457.
Ziegler, E. E. (1944). *Ibid.*, **37**, 196.

Thyroid-induced Myxoedema

The practice of treating obesity with thyroid extract is now considered to be of no value (Dunlop, 1958), and it has been shown that doses of desiccated thyroid which cure myxoedema when given to normal subjects have little effect upon the basal metabolic rate (Winkler *et al.*, 1943). The explanation (Keele and Neil, 1961) may be either that there is a compensatory decrease in the secretion of thyroid hormone or that the thyroid gland removes excess hormone from the blood and destroys or stores it.

Stanley and Astwood (1949) have demonstrated that the uptake of radioactive iodine (¹³¹I) by the normal thyroid gland is suppressed if desiccated thyroid extract is administered, and they noted that as little as 1½ gr. (0.1 g.) daily produced nearly complete inhibition in one subject. It has been found that a daily dose of 300–400 µg. of thyroxine or 75–100 µg. of triiodothyronine inhibited the secretion of the normal thyroid gland (Johnson *et al.*, 1959). These doses are equivalent to 3–4 gr. (0.2–0.25 g.) of desiccated thyroid extract.

The release of thyroid hormone and the iodine-retaining capacity of the gland are regulated by a thyroid-stimulating hormone (T.S.H.) secreted by the anterior lobe of the pituitary gland, and the rate of production of T.S.H. is in turn governed by the thyroid hormone level in the blood; if this is raised by giving thyroid extract by mouth the production of T.S.H. is lowered or suppressed.

This fact has been applied in the treatment of conditions where it would be beneficial to prevent stimulation of the thyroid gland. Crile (1955), for example, recommends T.S.H. suppression in the treatment of thyroid carcinoma.

The following account emphasizes that not only is thyroid treatment useless in obesity, but that myxoedema may result especially if treatment is prolonged.

*Now at the Radcliffe Infirmary, Oxford.

CASE HISTORY

A widow, now aged 67 years, consulted a doctor in 1939 on account of obesity. At that time there were no symptoms which suggested myxoedema. She was prescribed a small dose of thyroid extract, and as she failed to lose weight this was increased after a few months to 1 gr. (65 mg.) twice daily. This dose had no effect, and after a year treatment was stopped.

In 1945 she complained of rheumatic pains in her ankles, knees, and hands. Once again she was prescribed thyroid hormone in order to lose weight, the dose being 1 gr. (65 mg.) twice daily. Although there was no significant change she felt that the treatment prevented any further gain in weight. Careful inquiry of the patient and reference to her medical records revealed nothing to suggest hypothyroidism.

In 1955 the thyroid dose was increased to 1 gr. (65 mg.) three times a day. She continued with this medication until June, 1961, when she was admitted to hospital with acute bronchitis. While in hospital she received penicillin and streptomycin, the thyroid treatment being stopped.

Until this time she had been taking thyroid extract continuously for 16 years, supposedly to control her weight, and for the past five years had taken at least 3 gr. (0.2 g.) a day.

The respiratory infection rapidly responded to antibiotic treatment, and she was discharged from hospital on the ninth day after admission.

Forty days after discharge the patient attended surgery complaining of excessive lassitude, intolerance to cold, anorexia, dysuria, and an increased frequency of micturition. There was a dramatic change in her appearance; she looked dull and apathetic and her voice was slow and hoarse. Two days later, on August 2, she was readmitted.

On examination the eyelids were swollen and there was considerable thickening of the ankles but only minimal pitting oedema. The skin was dry and rough, and painful fissures had developed in the interdigital folds between the thumbs and index fingers. She was obese, weighing 14 st. 5½ lb. (92 kg.).

The oral temperature was 96.6° F. (35.9° C.) and the rectal temperature 97.6° F. (36.4° C.). The pulse rate was 76 per min. The apex beat was not palpable. The heart sounds were normal and the blood-pressure 150/100. There was no jugular venous congestion. Examination of the respiratory system revealed no abnormality.

Investigations.—A catheter specimen of urine contained protein ++ and abundant leucocytes; no casts were seen. Culture gave a profuse growth of *Proteus vulgaris* sensitive to streptomycin, chloramphenicol, and nitrofurantoin but resistant to sulphonamides. Haemoglobin 15.1 g./100 ml. (102%). Total white cell count 6,000/c.mm. with a normal differential count, E.S.R. (Westergren) 57 mm./hr. The blood urea was 32 mg./100 ml. and the serum cholesterol 530 mg./100 ml. (normal range 160–250 mg./100 ml.). No thyroglobulin antibodies were detected (latex particle technique). A chest radiograph (Dr. H. J. Johnson) showed cardiac enlargement, predominantly left ventricle. An electrocardiogram showed changes confirming the diagnosis of myxoedema. There was a sinus bradycardia, low voltage atrial and ventricular complexes with flat T waves in all twelve leads. Standard lead II is here reproduced.

Treatment and Results.—The urinary infection responded to a five-day course of nitrofurantoin (100 mg. three times a day). Desiccated thyroid extract was started on August 5, ½ gr. (50 mg.) a day. This was increased to 1½ gr. (0.1 g.) daily after ten days, and finally the dose was raised to 3 gr. (0.2 g.) daily after a further eight days. The patient's general condition improved steadily, she became mentally alert, the skin texture improved, and her temperature, which tended to be subnormal, reverted to average levels. On

September 4 the serum cholesterol had fallen to 210 mg./100 ml. A chest radiograph on September 5 showed no significant change. She was discharged on September 6 weighing 13 st. 5 lb. (85 kg.).

Electrocardiogram—lead II: (a) before treatment; (b) after treatment.

DISCUSSION

The possibility that this patient developed primary myxoedema in 1945 is unlikely for several reasons. There was nothing to suggest myxoedema from her history apart from obesity, which had been evident for many years prior to thyroid treatment. If this was a manifestation of early hypothyroidism one would have expected other confirmatory signs to develop. Patients suffering from hypothyroidism invariably show subjective and objective improvement within a few weeks of starting treatment. In this case there was no evidence of any change in her clinical condition, and she had at no time sought medical advice for anything but her obesity and rheumatic symptoms. Her appetite was excellent and she prided herself on being an active person.

The failure to demonstrate thyroid auto-antibodies is of interest. Doniach *et al.* (1960) demonstrated thyroid auto-antibodies in 83% of their cases of primary myxoedema. Owen and Smart (1959) obtained similar results and considered that immunologically, primary myxoedema is a variant of Hashimoto's thyroiditis. In this case the mechanism causing failure of the thyroid gland may be different.

Riggs *et al.* (1945) concluded that when the administration of large quantities of desiccated thyroid extract to euthyroid subjects was stopped, the serum precipitable iodine often fell to abnormally low levels accompanied by a rise in the serum cholesterol, and they thought this probably indicated temporary inhibition of the normal thyroid gland. None of their cases developed obvious clinical myxoedema. It should be noted that although many of their patients received large doses of thyroid (some up to 20 gr. (1.3 g.) a day) the total period of administration was compared with this case relatively short, and the treatment, with one exception, was intermittent. This one exception started taking thyroid in 1934 and continued with three short interruptions until 1944 with doses ranging from 3–7 gr. (0.2–0.45 g.) daily. The authors commented that there was a tendency for the basal metabolic rate (B.M.R.) to fall over the ten-year period and that each time treatment was stopped the B.M.R. fell sharply. It is difficult to form conclusions about this subject, however, because a subtotal thyroidectomy was performed for simple goitre ten years before thyroid treatment was started.

Winkler *et al.* (1943) found that certain non-myxoedematous patients tolerated up to 6 gr. (0.4 g.) of thyroid daily for long periods of time without effect on the B.M.R. The total length of treatment was shorter than the 17 years described in this case, and again was intermittent. Further, their conclusions were based on estimations of the B.M.R., and they point out that this measurement varied considerably even in the intervals when no thyroid treatment was given. They suggested that the euthyroid subject has the ability to inactivate thyroid substance, but the patient with myxoedema fails to do this.

From the case described it seems that myxoedema can appear in a previously normal subject if the administration of thyroid is prolonged, and the most likely explanation may be failure to produce T.S.H.

I wish to thank Dr. D. G. Bennett for permission to publish this account, Dr. R. Gibson and the staff of the Bath Central Laboratory for the biochemical investigations, and Dr. H. J. Johnson for the radiographs.

M. J. REE, M.B., D.C.H., D.Obst.R.C.O.G.,
General Practitioner, Keynsham, Somerset.

REFERENCES

- Crile, G. (1955). *Cleveland Clin. Quart.*, **22**, 161.
Dunlop, D. M. (1958). In *Textbook of Medical Treatment*, 7th ed., edited by D. M. Dunlop, S. Davidson, and S. Alstead, p. 330. Livingstone, Edinburgh and London.
Doniach, D., Hudson, R. V., and Roitt, I. M. (1960). *Brit. med. J.*, **1**, 365.
Johnson, D. E., Soloman, D. H., and Greer, M. A. (1959). *J. clin. Endocr.*, **19**, 317.
Keele, C. A., and Neil, E. (1961). In Samson Wright's *Applied Physiology*, 10th ed., revised by C. A. Keele and E. Neil, p. 495. Oxford University Press.
Owen, S. G., and Smart, G. A. (1958). *Lancet*, **2**, 1034.
Riggs, D. S., Man, E. B., and Winkler, A. W. (1945). *J. clin. Invest.*, **24**, 722.
Stanley, M. M., and Astwood, E. B. (1949). *Endocrinology*, **44**, 49.
Winkler, A. W., Lavietes, P. H., Robbins, C. L., and Man, E. B. (1943). *J. clin. Invest.*, **22**, 535.

Muscular Weakness After Prolonged Ingestion of Thyroid

In 1883 Warner first described muscular weakness in hyperthyroidism, and muscular weakness and increased liability to fatigue are now accepted as common accompaniments of thyroid overactivity (Wayne, 1954). Yet, so far as we can discover, muscular weakness after prolonged overdosage of thyroid tablets has not been hitherto described.

CASE REPORT

The patient, a pilot in the Royal Air Force, was aged 42 in 1959. He weighed 12½ stone (78.9 kg.), his height was 5 ft. 9½ in. (176.5 cm.), and he believed he was overweight. As this would reduce his chance of continuing flying he consulted a pharmacist, who recommended tablets of thyroid to reduce obesity.

In June, 1959, he started to take a thyroid tablet B.P. 60 mg. (1 gr.) a day. After three weeks, as he felt that this had no effect, he increased the dose during the next five weeks to 1,080 mg. (18 gr.) a day. After one week on this dose he noticed symptoms of hyperthyroidism and then, as his weight had fallen to 11 stone (69.9 kg.), he abruptly stopped his self-medication. That same night he awoke owing to warmth and sweating: he had difficulty in moving in bed. Next morning he could barely lift his legs, and his muscles ached. Two hours after rising the weakness quickly improved and during the next week all the symptoms of hyperthyroidism disappeared.

In September he restarted taking thyroid tablets, 600 mg. (10 gr.) a day. He soon noticed the same symptoms of

hyperthyroidism as previously. After eight weeks on this dosage, on November 14 he thought his weight was within normal limits and he again stopped the tablets abruptly. At 8 p.m. on the following day he noticed heaviness of both thighs. He found it difficult to sit up from a lying position; in bed, sleep was hampered by warmth and sweating. On rising at 7.30 a.m. his legs and arms felt feeble. At 9.30 a.m. he had difficulty in getting up from the sitting position, and on trying to climb a few steps his legs gave way completely. By 11 a.m. he could not stand or sit up at all. His shoulders were also very weak though he could move his fingers and toes easily. Sensation and speech were unaffected. There was no visual upset and he passed urine without extra effort. There was no breathlessness.

At mid-day on November 16 the trunk and limbs showed a widespread symmetrical weakness. The proximal muscles were most affected and movements that were possible showed no myasthenia. There was no selective wasting, fasciculation, or involuntary movement. Tone was normal and there was no clonus. The cranial nerves were intact. All reflexes were present and normal. Sphincters were unaffected. No abnormality in cerebellar function or sensation could be elicited. There was no evidence of meningeal irritation. His pulse rate was 115 a minute, blood-pressure 170/70 mm. Hg, serum potassium 4.7 mEq/litre. He was alert, co-operative, and cheerful.

At 1 a.m. on November 17 the weakness began to improve. By 7 a.m. muscular power was normal though he still felt "bruised." During that day all muscular symptoms disappeared and he has remained completely well since.

On November 26 he divulged his story of self-medication with thyroid tablets. A full clinical examination at this time failed to reveal any abnormality; in particular, muscular power, tone, and co-ordination were normal, all reflexes were present and equal, and plantar responses were flexor. There were no signs of hyperthyroidism; the thyroid gland was not palpable and there was no exophthalmos; movements were not hyperkinetic and there was no finger tremor; the palms felt moist but not hot; the sleeping pulse rate was between 80 and 85 a minute on three occasions; blood-pressure 135/80 mm. Hg.

There was no family history of any similar condition and no previous history of any serious illness.

The investigations carried out between November 26 and 30 are summarized as follows:

Abnormal: (1) Blood:—serum proteins: albumin 4.1 g./l., globulin 3.7 g./l. Electrophoresis showed an increased γ -globulin. (2) C.S.F.: protein, 50 mg./100 ml. (3) Electromyography (Wing Commander C. B. Wynn Parry):—Electromyograms of deltoids and quadriceps were substantially normal in that interference patterns were full and action potentials were of normal amplitude and duration. Motor-conduction velocities and strength-duration curves were normal. No fibrillation was detected. However, two abnormalities were noted: (a) In several areas of both muscles, quadriceps more than deltoids, there were some high-frequency short-duration "myopathic" potentials but no long-duration polyphasic or giant units. (b) Interference patterns became substantially reduced after continued effort, and thus showed a definite myasthenic element.

Normal.—Blood: Haemoglobin, P.C.V., E.S.R., white-cell count and differential, urea, fasting sugar, liver-function tests, serum electrolytes; W.R. and thyroid precipitins negative, and serum and urine creatine and creatinine. X-rays: chest, spine, and skull. Urine: No porphyrins, albumin, or sugar. C.S.F.: sugar, albumin, and cells; W.R. negative. E.C.G. E.E.G.

DISCUSSION

The diagnosis of this patient posed a problem. Myasthenia gravis was considered, but there seemed to be little in favour of it. Acute thyrotoxic paralysis was