Summary

The 55 toxoplasmin-positive patients found in a population of 698 mental defectives have been scrutinized for evidence of toxoplasmosis. Most of the patients were children. The incidence of positive cases increased with advancing age. In two cases eye lesions suggestive of toxoplasmosis were found. Radiology and lumbar puncture showed no findings suggestive of toxoplasmosis. In no cases could the mental defect be definitely attributed to toxoplasmosis. In some cases other definite causal factors were present—for example, epiloia, phenylketonuria, mongolism. It was concluded that in mental institutions or elsewhere a positive toxoplasmin reaction is acquired like a positive Schick reaction with increasing age, and is very infrequently associated with clinical toxoplasmosis; and that toxoplasmosis is not a common cause of mental defect.

Our thanks are due to Dr. I. A. B. Cathie and Dr. J. A. Dudgeon for provision of toxoplasmin and laboratory data, to Dr. O. D. Fisher for the results of skin testing, to Miss M. Ross and Mrs. L. Mundy for psychological data, to Dr. M. I. Robinson for radiological reports, to Dr. W. W. Kay for examination of the cerebrospinal fluid, and to Dr. L. Crome, the neuropathologist, and Dr. L. T. Hilliard, the physician-superintendent of the Fountain Hospital, for help and advice.

REFERENCES

Binkhorst, C. D. (1948). *Toxoplasmosis*, p. 128. Leyden.
Christiansen, M., and Siim, J. C. (1951). *Lancet*, **1**, 1201.
Fisher, O. D. (1951). Ibid., **2**, 904.
Gard, S., Magnusson, J. H., Wahlgren, F., and Gille, G. (1949). *Pediatrics*, **4**, 432.
Kirman, B. H. (1951). *J. ment. Sci.*, **97**, 783.
Sabin, A. B. (1948). In Brennemann's *Practice of Paediatrics*, **4**, 46. Hagerstown.
Wolf, A., Cowen, D., and Paige, B. H. (1939). *Amer. J. Path.*, **15**, 657.
Zingher, A. (1923). *Amer. J. Dis. Child.* **25**, 392.
—— (1924). *Amer. J. publ. Hlth.* **14**, 955.

MYXOEDEMA AS A CAUSE OF DEATH

REPORT OF TWO CASES

BY

H. S. LE MARQUAND, M.D., F.R.C.P.

W. HAUSMANN, M.R.C.P.

AND

E. H. HEMSTED, M.B., B.Chir., D.C.P.

(From Reading Combined Hospitals)

Since the introduction of treatment with thyroid extract by Murray in 1891, it has been presumed that myxoedema as a cause of death is rare. We have been able to find only three recent references, and therefore report the following two cases.

Case 1

A woman aged 61 was admitted to hospital on January 7, 1951, with the following history. Thirty-five years ago she developed a left-sided hemiplegia, from which she made a good recovery. Two years ago she had another stroke, also involving the left side. Again recovery was fairly complete. The patient had had four children without trouble and the menopause had occurred at the age of 48. She had been in fairly good health until a fortnight before admission, when a cold and a severe cough developed. Her condition gradually deteriorated until January 6, when she first called in her doctor. He found her semi-conscious, and the following morning noticed considerable puffiness of the face.

On admission her pulse rate was 62 and temperature 97° F. (36.1° C.). She was moderately obese, and had pronounced supraclavicular fat pads. She was extremely lethargic but obeyed simple commands. Her voice was low-pitched and croaking. The scalp hair was dry and scanty, the pubic hair was extremely sparse, and the axillary hair was missing. Her skin felt dry and cold; her face, especially the eyelids, was puffy. Nothing abnormal was found in the heart, lungs, or abdomen. The blood pressure was 140/100 mm. Hg. There was pitting oedema of the legs up to the knees, and the hands were swollen but did not pit on pressure. Some evidence of previous hemiplegia was found in slight spasticity of the left side with an extensor plantar response, but there was no other abnormality in the central nervous system.

Investigations.—Urine: albumin was present; film showed scanty red cells, leucocytes, and mixed bacterial flora. The haemoglobin was 90%; blood urea, 50 mg. per 100 ml.; blood sugar, 57 mg. per 100 ml.; blood cholesterol, 390 mg. per 100 ml.; serum potassium, 18.4 mg. per 100 ml.; serum sodium, 345 mg. per 100 ml.; plasma chlorides, 595 mg. per 100 ml.; serum protein, total 7.2% (albumin 3.7%, globulin 3.5%, A/G ratio 1.1). An electrocardiogram showed flat and inverted T-waves in all leads, suggestive of myxoedema.

The diagnosis was difficult. Renal failure was suspected, but there was no confirmatory evidence on investigation. It was thought that an adrenal failure might be the cause, so treatment was started with penicillin and adrenal cortical extract, 10 ml. four-hourly. Although the patient became brighter mentally, her general condition deteriorated, respiration became laboured, and she died four days later. Her temperature remained at a low level all the time, and varied between 95 and 97° F. (35 and 36.1° C.). Her pulse rate varied between 60 and 70.

Necropsy

The following were the outstanding features: a widespread consolidation of the lungs; ante-mortem haemorrhages involving the suprarenals; remnants of thyroid gland; a heart of normal size and coronary vessels normal for her age.

Histological Examination.—Sections taken from both lobes of the thyroid gland showed marked fibrosis. A few small islets of lymphoid tissue were present in each lobe, and within these the remains of thyroid acini could be identified. The latter were composed of large pale irregular cells showing variable eosinophilic staining properties. Colloid was absent except in one small area. These remaining acini were surrounded by plasma cells and an outer zone of small lymphocytes. The *lungs* showed the picture of grey hepatization, with the alveoli distended by polymorphonuclear exudate. No heart-failure cells were present. *Kidneys:* the cortex was thinner than normal and patchy interstitial fibrosis was present. A considerable number of normal-looking glomeruli were to be seen. The vessels showed some thickening of the walls, but no elastosis.

Evidence of antemortem haemorrhage was found in the *suprarenal gland.* The *pituitary gland* was larger than normal. Acidophilic staining cells were noted to be extremely scanty, otherwise the histological appearance was within normal limits.

Case 2

An unmarried woman aged 50 was admitted to hospital on January 7, 1952. The previous history was that she had been well enough to do her own housework until five months before admission. Since then she had complained of weakness and of feeling cold, and these symptoms had gradually become worse. On the day of admission she suddenly complained of loss of vision, and the doctor found her lying across the bed unconscious.

On admission her temperature was 95° F. (35° C.) and pulse 42. She was semi-conscious and repeated such sentences to herself as, "What have I done?"; but she would obey simple commands. Anasarca was present and the face and eyelids were swollen. The skin was coarse and dry. The scalp, pubic, and axillary hair was scanty; the superciliary hair was absent. Coarse rales were heard at the bases of both lungs, and there was tracheal rattle; the heart sounds were normal; the blood pressure was 250/140 mm. Hg. Nothing abnormal was found in the abdomen or in the central nervous system.

Investigations.—Urine: albumin was present; film showed many Gram-negative bacilli. The blood urea was 25 mg. per 100 ml.; blood cholesterol, 495 mg. per 100 ml.; serum sodium, 295 mg. per 100 ml.; plasma chloride, 420 mg. per 100 ml.; alkali reserve, 44 c.cm. CO_2; serum protein, total 6% (albumin 3.4%, globulin 2.6%, A/G ratio 1.3). The cerebrospinal fluid contained 1 white cell per c.mm. and 56 mg. of protein per 100 ml. An electrocardiogram showed flat T-waves in all leads; the tracings were compatible with the diagnosis of myxoedema.

Ten hours after admission the patient had a tonic fit. She was given a small amount of thiopentone intravenously, when the respiration stopped and the pulse became impalpable. Artificial respiration was started and she recovered. She was treated with continuous oxygen and penicillin, 1,000,000 units six-hourly. She improved considerably, but remained confused and slightly maniacal. Her blood pressure was about 160/100 mm. Hg. On January 10 she was given 10 mg. of thyroxine, with great improvement in the general condition. The puffiness and the subcutaneous oedema disappeared and the blood cholesterol fell to 388 mg. per 100 ml. Nine days later her temperature went up to 101° F. (38.3° C.), her breathing became laboured, and her general condition deteriorated. On the 21st day she became unconscious and her pulse impalpable, and she died.

Necropsy

A full post-portem examination revealed very little positive information. Macroscopically the heart and coronary arteries appeared normal.

Histological Examination.—The *thyroid gland* was slightly enlarged and the cut surface firm and pale. The histological appearance was that of a Hashimoto or lymphadenoid goitre. *Kidneys:* Both were of normal size and appearance. Histological examination showed slight thickening and elastosis of the vessels. An occasional glomerulus was undergoing hyalinization. Adequate numbers of normal-looking glomeruli were present, however, and there was no evidence of tubular degeneration or interstitial fibrosis. The appearance was thought to fit in with an early hypertensive kidney.

The *pituitary gland* seemed to be quite normal. The ovaries were fibrotic.

Discussion

In our opinion myxoedema was the main cause of death in both cases. In Case 1 it can be presumed that a patient with severe untreated myxoedema was exposed to the stress of pneumonia and that this produced suprarenal failure. McGavack (1951) says that there is atrophy of the zona fasciculata in myxoedema and the excretion of 17-ketosteroids and glucocorticoids is greatly diminished. It seems feasible that when such a gland is exposed to additional stress acute adrenal cortical failure may ensue. The fact that there was widespread haemorrhagic destruction of the adrenal glands is in agreement with this assumption.

Case 2 is not quite so conclusive. Hypertensive encephalopathy had to be considered in the differential diagnosis. The reasons, however, against hypertension playing a major part in the fatal outcome of this case are: (1) the normal appearance of the eye background; (2) the normal size of the heart; and (3) the electrocardiogram, which was suggestive of myxoedema rather than of hypertension. The fact that the blood pressure, except on admission, was within normal limits is also against this diagnosis.

Recent reports of death due to myxoedema are scanty. The largest series is that by McGavack and Schwimmer (1944), who described nine deaths, all due to cardiac complications of myxoedema. One case was described by Foster and Barr (1944) in which there was myxoedema of long duration with slow deterioration. A case was reported by Chiolero and Meerwein (1939), but it was doubtful whether myxoedema was responsible for death, as the case was complicated by the presence of schizophrenia and chronic ulcerative colitis. The largest series described was in a Report on Myxoedema (1888) in which 22 cases were mentioned. There it was stated that the majority of the patients died from intercurrent diseases, mainly pulmonary or renal, but in some cases death was the direct result of myxoedema. These cases showed intense anaemia and a variety of nervous symptoms, such as maniacal excitement, coma, etc.

A very interesting report has recently been published by Sheehan and Summers (1952) which stressed the important part that hypothermia played as a cause of coma in similar cases. In their patients the rectal temperature was recorded as 77 and 83° F. (25 and 28.3° C.). They point out that the clinical thermometer does not register below 95° F. (35° C.) and therefore this condition goes unrecognized. In retrospect, it is probable that our two cases fall into the same class. The temperature recorded in Case 1 was between 95 and 97° F. (35 and 36.1° C.), which most likely meant that the thermometer did not register, and the difference in the temperature depended only on how far the mercury column was pushed down by the nurse. In Case 2 the temperature was recorded on admission as 95° F. (35° C.). Only after the administration of thyroxine were temperatures above 98° F. (36.7° C.) recorded. The pulse rate in both cases was very low, which is in agreement with the observations recorded by Sheehan and Summers. Perhaps a significant fact is that both cases were admitted in the middle of winter, when the danger of hypothermia is obviously greatest.

The lesson to be learned from our cases is that under certain circumstances myxoedema may be a fatal disease. Therefore it is essential to diagnose these cases early and to treat them promptly. Unfortunately, the possibility of myxoedema may not even be considered. In our cases the diagnosis on admission was chronic nephritis, and that is probably the most common mistake. The patients may also be treated with iron and liver in the belief that the condition is due to anaemia, or cardiac disease may be suspected. It is important to stress the fact that the diagnosis may not only be missed in life but that, even when a necropsy is done, it may remain uncertain because the thyroid gland may not be examined.

In Case 2 the thyroid gland was of normal size, and only on histological section could destruction be confirmed. For these reasons we think that this condition may often remain undiagnosed.

Unfortunately, treatment of these two cases was not successful. In Case 1 adrenal cortical extract was used but did not prevent the fatal outcome. In Case 2 we had the experience of the first to suggest the possible diagnosis. The patient was given an adequate dose of thyroxine without success. Probably, irreversible change had taken place before treatment was begun. The answer is, of course, early diagnosis.

Summary

Two cases in which death was due to myxoedema are reported. It is suggested that this diagnosis is often missed, and that it is necessary to examine the thyroid gland after death as a routine procedure, particularly in elderly people.

Treatment of myxoedema in the last stages is ineffective; therefore it is essential to diagnose and treat it early.

Our thanks are due to Dr. A. J. Hardy, who performed the necropsy on Case 2 and allowed us to be present and gave facilities for histological examinations; to Dr. A. Anderson for help in the interpretation of electrocardiograms; and to the laboratory staff of the Royal Berkshire Hospital, Reading.

REFERENCES

Chiolero, J., and Meerwein, F. (1939). *Schweiz. med. Wschr.*, **20**, 623.
Foster, M., and Barr, D. P. (1944). *J. clin. Endocr.*, **4**, 417.
McGavack, Th. H. (1951). *The Thyroid*, p. 145. London.
—— and Schwimmer, D. (1944). *J. clin. Endocr.*, **4**, 417.
Report on Myxoedema (1888). *Trans. Clin. Soc. Lond.*, **21**, Suppl.
Sheehan, H. L., and Summers, V. K. (1952). *British Medical Journal*, **1**, 1214.

PELVIC EVISCERATION WITH PRIMARY BOWEL AND URETERIC ANASTOMOSES

BY

G. E. MOLONEY, M.B., F.R.C.S.Ed., M.R.C.P.
Assistant Surgeon, the Radcliffe Infirmary and Churchill Hospital, Oxford

The operation of pelvic evisceration, which was conceived and had its early years in the United States of America, has aroused general interest and has now been sporadically practised here. A modification of this operation, on a patient with a carcinoma of the rectosigmoid region invading the bladder, is presented. In one stage the affected portion of the bowel, with the bladder, prostate, and vesicles, was excised, the pelvic colon was anastomosed to the stump of the rectum, and the ureters were transplanted into the colon. This case represents a fusion of the present tendency towards widespread excision of pelvic organs for advanced carcinoma and that of preservation of the anal sphincter where indications are favourable. The satisfactory functional result has prompted an early report, but final assessment must await the years.

Case Report

A married man aged 55 eighteen months before admission to hospital had had an attack of "colitis" which lasted 10 days. Subsequently he had had two normal stools a day until the week preceding his visit, when his stools had increased to four a day. For three weeks he had had dysuria and frequency, and admitted to having passed wind and some solids in his urine.

Examination showed a large sausage-shaped tumour in the line of the descending colon and then curving above the inguinal ligament. An enema reduced this swelling to a small mass in the pelvis, easily palpable bimanually. A barium enema confirmed a blockage in the sigmoid colon. On sigmoidoscopy no rectal abnormality could be found, and no tumour could be reached with the sigmoidoscope at the maximum attainable distance of 8 in. (20 cm.). Microscopical examination of the urine showed a large number of pus cells with 520 mg. of protein per 100 ml., and cultures gave a profuse growth of *Bact. coli*. The blood urea was within normal limits. By intravenous pyelography the kidneys seemed normal, but the bladder shadow was distorted superiorly by an irregular filling defect. Cystoscopy confirmed a fistula in the postero-superior part of the bladder with marked granulation or tumour formation about the opening.

A carcinoma of the sigmoid colon with vesico-colic fistula was diagnosed, and the possibility of having to excise all the pelvic viscera was considered. The bowel was prepared for operation with phthalylsulphathiazole, 2 g. six-hourly for six days.

Operation

On March 13, 1952, a large mass was found in the pelvic colon extensively adherent to the bladder at two distinct points—one in the lower pelvic colon and the other in the sigmoid. The proximal point of adherence was the site of the fistula. The appearances were those of a carcinoma, but the diagnosis was not certain because of some thickening of the mesentery and the extensive length of bowel involved. It was decided to separate the bowel and bladder, partly to help in establishing the diagnosis and partly for access, as the pelvis was largely occupied by the loop of adherent bowel. This meant possible opening into tumour tissue. On cutting across the fistula the bladder was found to be invaded by what appeared to be a carcinoma, but this was still uncertain. It was necessary to leave a hole an inch (2.5 cm.) wide in the bladder. The bowel and bladder were next separated at the lower point of adhesion, leaving a further area at the back of the bladder, possibly the site of malignant infiltration. Most of the pelvic and sigmoid colon and the upper third of the rectum were excised with the usual block of glands. The colon was then slit up and the lesion was clearly seen to be a carcinoma.

The bladder had then to be dealt with. Experience of local excision of malignant vesico-colic fistulae had made me pessimistic of achieving a satisfactory clearance of growth, and in this instance there was so much inflammatory induration of the bladder that it seemed unsafe to try to close the defect in it. I decided on total cystectomy and proceeded to remove the bladder, prostate, vesicles, and gland fields. In addition, a further portion of rectum was removed, together with the whole of the pedicle of the superior haemorrhoidal vessels, thus giving a satisfactory clearance below the lower point of adherence of bowel to bladder. There remained a rectal stump above the levator ani about 1½ in. (3.8 cm.) in length. After mobilization of the remnant of pelvic colon and descending colon it was possible to make a loose approximation to the rectal stump, and, as there had been wide excision beyond the margin of growth and there was free bleeding at the bowel ends, I proceeded to make a junction.

Prior to anastomosis it was necessary to clear the colon above by milking of faeces still remaining in it. After the bowel ends were joined the ureters were transplanted into the pelvic colon by a submucosal tunnel technique. At the completion of the anastomosis the floor of the pelvis was dry, but gauze was packed on the levator ani. A drainage tube was placed to the bottom of the pelvis, the abdominal wound closed, the rectal sphincter dilated, and a tube stitched into the anus for about 1 in. (2.5 cm.) for possible urinary drainage. The patient was given 2 pints (1,140 ml.) of blood and a pint (570 ml.) of saline during the course of the operation, and was in good condition at the end. The anaesthetic was low spinal, thiopentone, nitrous oxide and oxygen, and enough gallamine triethiodide for the introduction of an endotracheal tube.

Histological Examination (Dr. R. A. Sladden).—"The tumour in the colon is a moderately well differentiated adenocarcinoma, Broder's grade II, invading the muscular coats and at one point penetrating to the serosa. There is no lymph-node involvement found. The bladder wall is thickened to 2 cm. posteriorly by an intense chronic inflammatory reaction. There is no microscopical evidence of spread of growth into the bladder wall in the sections examined. The paravesical lymph nodes show no evidence of metastases."

Further Progress

On March 15 a general anaesthetic was given for removal of the pack. As the patient had not yet passed any urine and was showing moderate distension, the rectal tube was removed. The opportunity was taken of inspecting the ureteric and bowel anastomoses, which were satisfactory, but the intestine, including the colon, was somewhat distended; as it seemed likely that this distension would be