The coronary vessels were relatively free of atheroma. At the lung bases there was some bronchopneumonic consolidation, but no evidence of tuberculosis or bronchiectasis was found.

The liver was grossly enlarged, weighing 74 oz. (2,100 g.). It was firm and waxy. The cut surface was pink, due to staining with Congo red. The lining of the stomach was also of a very striking pink colour throughout, and so to a lesser extent was the lining of the small intestine. The large intestine did not show any staining with Congo red. The spleen was small but firm and waxy. The kidneys appeared normal macroscopically. None of these organs gave the typical colour with iodine. Thrombosis of the superior mesenteric and left common iliac arteries was also found.

Microscopically the myocardium, liver, spleen, stomach, and small intestine were found to contain a large quantity of amyloid, which did not stain typically with methyl violet. The kidneys were only mildly affected.

Discussion

Wilks (1856) was the first to differentiate primary amyloidosis ("simple lardaceous disease") from the more common secondary variety, originally described by Rokitsky (1842). It was not until 1929 that Lubarsch described the different histological characteristics of primary amyloid.

A search through the literature has revealed 145 previously reported cases. Only 29 of these were diagnosed correctly in life. The reason for the lack of correct diagnosis in the remainder of cases is not far to seek. Probably the most important factor is the close resemblance to more common diseases which primary amyloidosis often shows. The clinical picture thus produced is, however, only rarely absolutely typical, and often several unrelated syndromes are present. Analysis of the literature suggests that primary amyloidosis should be suspected in cases of congestive heart failure of unknown cause and in patients presenting with what appears to be a collection of unrelated conditions, especially if some peripheral nerve involvement is also present. Idiopathic macroglossia often occurs in this disease, and when present is an important physical sign.

It is in the laboratory investigations that the other main difficulty is met. Primary amyloid material has very much less constant staining reactions than the secondary variety (Lubarsch, 1929; Koletsky and Stecher, 1939). It frequently fails to show the staining reactions with Congo red, iodine, and methyl violet. Thus the *in vivo* Congo-red uptake test is negative in over 50% of cases, through failure on the part of the amyloid to take it up (Eisen, 1946; Mathews, 1954), though some authors believe that the liver needs to be affected for this test to be positive (Jackson and Slavin, 1954). If a biopsy of the organs concerned can be done this will usually confirm the diagnosis, but again the absence of typical staining reactions must be borne in mind.

A high serum alkaline phosphatase level is usual in this disease, and is a useful diagnostic aid if other causes for this finding can be excluded (Gutman, 1955). The albumin/globulin ratio is stated to be reversed even in cases with purely cardiac involvement (Jackson and Slavin, 1954).

The aetiology of this disease is very obscure and theories of causation vary greatly, including unrecognized plasmocytomas (Apitz, 1940), non-bacterial hypersensitivity states (Lindsay and Knorp, 1945), and a collagen type of aetiology (Ehrich, 1952).

On the basis of the last theory corticotrophin therapy has been advocated (Jackson and Slavin, 1954). Cortisone has been tried, but without apparent effect (Williams, 1955), and there is some experimental evidence to show that corticotrophin and cortisone in fact increase the production of amyloid in animals with suppurative affections (Peräsalo and Latvalahti, 1954). Thyroid extract seems to have some inhibiting property. Success has been reported in cases of secondary amyloidosis with desiccated liver (Grayzel and Jacobi, 1938), but no attempt to treat the primary disease by this method has so far been recorded.

The congestive heart failure in these cases, if present, is very resistant to digitalis and diuretic therapy.

Summary

The remarkable similarity of the symptoms of primary amyloidosis to those of other conditions is shown by the 145 cases cited from the literature, of which only 29 were diagnosed correctly in life, the remainder being ascribed to a variety of more common diseases. The patient whose case is described above was believed to be the victim of several different conditions before the correct diagnosis was established.

The main diagnostic difficulties are attributable to the extremely variable clinical picture, the close resemblance to other more common diseases, and the frequency of non-specific staining reactions.

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EPIDEMIC OF MENINGOENCEPHALITIS AND BORNHOLM DISEASE

BY

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The occurrence of a localized epidemic of meningo-encephalitis and Bornholm disease during the latter part of the summer of 1956 has provided an exceptional opportunity for studying the conditions clinically, tracing the possible sources and spread of infection, and considering the problems of immunity. The study has been purely on clinical grounds; the bacteriological aspect is still being investigated.

The relationship between meningitis and Bornholm disease has been reported on previous occasions (Howard *et al.*, 1943; Finn *et al.*, 1949; Warin *et al.*, 1953), but, except for an outbreak in Sweden, meningeal involvement has been noted in less than 10% of patients in large epidemics. A Swedish group of investigators (Gabinus *et al.*, 1952) have described an outbreak of Bornholm disease with a high incidence of aseptic meningitis associated with Coxsackie virus group B type 3. They

advanced a hypothesis that the virus entering a highly susceptible population affects persons of all ages, with pleurodynia and myalgic symptoms as predominating features, especially amongst older children and adults; on the other hand, in a relatively immune population, where children are primarily affected, aseptic meningitis may be a prominent feature. Our own findings on clinical grounds tend to support this theory.

Present Epidemic

The epidemic occurred within a radius of about 1½ miles (2.4 km.) in the small hamlet of Stretton Grandison (population 550) and Eggleton (population 133), and was centred at the school. The early cases during August and September were of Bornholm disease. This epidemic merged at the end of September into an outbreak of meningo-encephalitis, centred largely in Stretton Grandison school. At the end of October encephalitic cases became fewer and Bornholm cases again reappeared.

An interesting feature of the epidemic was that three groups of cases were observed: (1) typical Bornholm disease, (2) typical encephalitis, and (3) a small group of intermediate cases. The Bornholm cases appeared to be related to an epidemic of this disease occurring in the neighbouring Bromyard district.

These cases showed a sudden onset with excruciating abdominal and thoracic pain (Devil's grip), accompanied by great prostration. The thoracic pain was aggravated on respiration, and the patients often feared to move. The infection lasted from two to ten days, and the adults were prone to relapse. The incubation period was two to ten days, often five.

The encephalitic cases appeared to be similar to those occurring in other parts of the country—"Nottingham meningitis." These cases often had a prodromal period of several days of lassitude and anorexia, but perhaps more frequently the onset was sudden, with severe frontal headache, pyrexia, vomiting, neck stiffness, and photophobia. The headache in some cases was paroxysmal and devastating. In a few cases a rash was observed with an erythema of wide distribution or a local macular rash. Sore throat and sore mouth were present in a few cases in the prodromal or acute phase. Coryzal symptoms were also noted in a few instances. Clinically either neck stiffness or a positive Kernig's sign was found. C.S.F. findings in the cases subjected to lumbar puncture showed an increase in lymphocytes.

The intermediate cases occurred in houses where there was already one type of case. In these cases there was headache and vomiting but no photophobia or neck stiffness.

A "Pickles chart" shows that the incidence increased until the end of September and beginning of October, when a peak was reached (Fig. 1). This peak was due to the explosive outbreak at Stretton Grandison school.

Altogether 52 subjects were affected: 27 with meningo-encephalitis and 17 with Bornholm disease; 8 were intermediate cases. Of the 52 cases 25 occurred at the school, where there were 47 children (see Table). Of these 25, 15 were meningoencephalitis, 3 intermediate, and 7 Bornholm disease.

FIG. 1—Incidence of cases (August–November, 1956).

Incidence at School

	Boys	Girls	Total	No. Affected
Juniors	8	11	19	8
Infants	18	10	28	17

The following possible sources of infection have been considered. (1) The neighbouring Bornholm epidemic (with a possible change of type, or mode of action of the virus producing the encephalitic features). (2) Introduction from the influx of "travellers" (hop- and fruit-pickers) which occurred in August. (3) From mice, fleas, lice—but they appear to have played no part. (4) From food and water at the school. The food seems to be beyond suspicion, but is handled by the wife of the latrine attendant. The water has been condemned for three years and is boiled before use. Recently two brothers, young active farm-workers in this area, contracted poliomyelitis simultaneously. From the history it seemed probable that they contracted the disease from contaminated food. Barber (1938) described an epidemic of poliomyelitis in a school where the source of the infection seemed to resemble that of food-poisoning. There does not, however, appear to be any direct evidence of food contamination in the present epidemic.

The spread of infection seems to have been by direct contact, by finger-mouth route. This is supported by the plan of the seating arrangements at the school. The school is a mixed one, with two classes only. The seating arrangement in the infants' class (where there was a larger proportion of cases) is not constant. In the junior class the children adopt a permanent seating arrangement, and all the cases occurred in one section of the room only (Fig. 2).

FIG. 2.—Relative positions of pupils in junior class. Shaded areas indicate cases.

The children have their meals at the school desks.

Where children seemed to contact a massive infection, as in the school, a large proportion contracted the disease. In the homes the attack rate seemed to depend on susceptibility. It is remarkable that some adult males seemed to be particularly susceptible and developed very severe attacks. This may explain how sporadic cases appear. In one house all five members contracted the infection, but in another of 14 members only one contracted the disease.

In the school the vast majority of cases were of encephalitis, with only a few Bornholm and intermediate cases. Several home contacts of the encephalitic cases developed Bornholm disease. In one family the father and three children had typical encephalitis, and the mother had a very typical Bornholm disease. In another family the mother and one child had Bornholm disease, another had encephalitis, and the father had an intermediate condition.

It is interesting to note that in the neighbouring schools of Yarkhill and Ashperton no cases occurred, although the Stretton Grandison children travel on the same bus as the Ashperton children.

Two children who had a benign encephalitis in 1955 developed Bornholm disease during the epidemic. No children in the school have been vaccinated against poliomyelitis, and so the relationship of this to the development of immunity could not be studied.

The Research Laboratory at Colindale have so far isolated a cytopathogenic agent (not poliomyelitis) from the cerebrospinal fluid or faeces of 10 cases.

Summary

An attack of Bornholm disease and encephalitis is described clinically and an attempt made to link the two conditions on epidemiological grounds. A similar outbreak in Sweden is mentioned for comparison.

We are indebted to the following for help received in studying this epidemic and compiling the data: Dr. J. S. Cookson, Dr. W. Hogg, Dr. A. T. Roden, of the Ministry of Health, and Dr. D. R. Christie.

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Medical Memorandum

Three Cases of Torsion of the Testis

Torsion of the testis is uncommon, and when it has a gradual onset it can easily be mistaken for acute epididymitis. Three new cases are recorded which emphasize the difficulties in early diagnosis described in full by Kennedy (1948) and Walton (1952).

CASE 1

A private soldier aged 19 woke with pain and swelling in the left testicle. Four and a half hours later he was referred for admission as a case of acute epididymitis. On examination he was afebrile and not in severe pain. The left side of the scrotum was swollen, red, oedematous, tender, and faintly ecchymosed round its neck. The skin was not adherent to the testis. Lifting the scrotum made no difference to the pain. Through a shallow hydrocele the epididymis could just be made out, lying anterior to the testis. The cord and opposite testis were normal. Examination per rectum and of the urine showed nothing abnormal.

Operation.—The testicle was delivered through a left inguinal incision. The hydrocele contained blood-stained serous fluid. The testis and epididymis were congested, with petechiae and subserous haemorrhages, and were rotated on a narrow pedicle through 180 degrees. After untwisting the testis the colour gradually returned. The surplus tunica vaginalis was resected, and after the testis was replaced the wound was closed without drainage.

Post-operative prophylactic streptomycin was given for 48 hours. Recovery was uneventful. Six weeks later the testis and epididymis were found to be normal in size, position, and consistence.

CASE 2

A lance-corporal aged 20 had intermittent sharp pain in the left loin whilst lifting heavy crates. Two days later the left testicle began to ache, and the next day it became swollen, and a diagnosis of acute epididymitis was made elsewhere. He was admitted on the following day. On admission he remembered three identical attacks in the last four years, during the first of which his appendix was removed. On examination he was afebrile. There was a red tender oedematous swelling of the left scrotum, the skin of which was not bruised or adherent to the testis. Elevation made the pain worse. The testis was indistinguishable from the epididymis; a tense hydrocele was present, and the cord was swollen and tender. Examination per rectum and of the urine showed nothing abnormal.

Operation.—Through a left inguinal incision an elongated tense purple hydrocele containing serofibrinous fluid was delivered. The testis and epididymis were attached at their upper pole by a rounded pedicle which had been twisted through almost one complete turn. The testis was pale, cyanosed, and black at its inferior pole, and the epididymis was congested and haemorrhagic. The vas deferens made a long loop in the parietal layer of the tunica vaginalis, which therefore could not be resected. When the colour was restored the testis was replaced in the scrotum and sutured to the dartos, and the skin closed without drain-

age. Prophylactic streptomycin was given for two days. Recovery was uneventful. One month later the testicle was normal in size and sensation.

CASE 3

A private soldier aged 21 was admitted complaining of lower abdominal pain and nausea for four days and swelling and pain in the right testicle for two days. Acute epididymitis had been diagnosed and sulphonamides had been given for two days before admission. On admission he was afebrile, and the only abnormal finding elsewhere was a scar, from tuberculous glands in the right side of his neck when he was 8. The left testis was normal. The right side of the scrotum was swollen, oedematous, red, and tender, and the testis and epididymis were indistinguishable in a tense hydrocele which adhered to the skin. Elevation made the pain worse. Examination per rectum and of the urine revealed nothing abnormal.

Operation.—Through a right inguinal incision a black hydrocele containing a haemorrhagic effusion was delivered. The testis had rotated anticlockwise through one and a half turns and was cyanosed and soft, while the epididymis resembled a clot of blood. Twenty minutes after untwisting the testis its colour had scarcely improved, but it was returned to the scrotum, and after dusting with penicillin-sulphathiazole powder the skin was closed without drainage.

Prophylactic streptomycin was given for five days afterwards, and recovery was uneventful. One month later, at a second operation through a small scrotal incision, the left testis was sutured to the areolar tissue of the scrotum. Eight weeks later both testicles were found to be normal in size, consistence, and sensation, and the patient was enjoying normal intercourse with his wife.

COMMENT

In adolescent boys "epididymitis" must be regarded as torsion of the testis or its appendix until proved otherwise (Dix, 1931). It is no less important to find good reason for a diagnosis of epididymitis in older patients, for many cases of torsion give a misleading history, lacking the story of trauma, abdominal pain, and vomiting of classical description (Kennedy, 1948). In early cases the local signs are ambiguous, swelling, redness, oedema, and hydrocele being common to both conditions, and unless seen very early the abnormal relations of the parts are obscured by swelling and pain. Dillon's sign (tethering of the skin in torsion) can occur in either condition, and elevation of the scrotum is of doubtful value, being painful whenever the scrotum is tender. Torsion is equally common on either side (Kennedy, 1948), and fever may occur with either condition.

The only reliable guide is the presence or absence of urinary infection, so a careful examination of the urethra, prostate, vesicles, and urine must be done in each case. If there is still any doubt then one should explore, rather than wait until gangrene of the testis makes itself plain. The different estimates of the survival time of the organ (Walton, 1952; Bailey, 1953) can only be a rough guide, because the tightness of the twist may vary from case to case. It is never safe to wait.

If operation is done in time the testis can be untwisted. A frankly gangrenous testicle is usually removed, but a doubtfully viable organ should, I feel, be restored, for it may recover against every expectation, as did Case 3.

If the underlying anomaly—abnormal mobility of the testis within the tunica vaginalis—is bilateral, the other testicle will be apt to twist. If one is already damaged, or absent, this risk should be explained to the patient and the remaining testicle made secure at a later operation, if he wishes.

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