non-smokers. It cannot be concluded from these figures that penicillin reduces the risk of post-operative chest infections when given immediately before operation.

TABLE III

	Penicillin	No Penicillin
Severe post-operative chest complications	27	30
Mild post-operative chest	15	23
No change post-operatively	161	159
Post-operative improvement	16	9
Total	219	221

Summary

An attempt has been made to assess the value of penicillin given to prevent post-operative chest infection. Comparing two similar groups, one given penicillin before operation and one not, no evidence has been obtained that penicillin is useful for this purpose.

I am indebted to Dr. R. A. Shooter for advice during this investigation and the preparation of this paper, also to Mr. M. P. Curwen for statistical assistance. I also thank many of the resident surgical staff at the Bridgend General Hospital for their willing co-operation.

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PRIMARY AMYLOIDOSIS PRESENTING WITH A CONFUSING CLINICAL PICTURE

BY

IAN N. LEE, M.B., B.S.

Late House-physician, the Middlesex Hospital

It is well known that primary amyloidosis closely resembles other diseases. It can affect most organs, giving rise to a clinical picture which is often indistinguishable from that produced by a more common disease. When several unrelated organs are affected multiple diagnoses are often made.

The heart by itself or in company with other organs is most commonly involved, such cases usually presenting with congestive heart failure (Eisen, 1946; Lindsay, 1946). The picture may simulate that of failure due to cardiac ischaemia or constrictive pericarditis (Mathews, 1954), but often no obvious cause of failure is found.

Liver disease, often suggestive of cirrhosis, is a frequent mode of presentation. Nephrosis is another common presenting syndrome (Mathews, 1954). The alimentary tract is also a frequent site of infiltration, and a diagnosis of carcinoma may be made in these cases (Koletsky and Stecher, 1939). A sprue-like picture also occurs sometimes (Steinhaus, 1902; Golden, 1945; Adlersberg and Schein, 1947; Schein, 1947; Finley and Adams, 1948). Carcinoma of the lung (Koletsky and Stecher, 1939; Dirkse, 1946) and even of the bladder have been simulated by this disease on occasion. Arthritis and osseous disease have also been reported (Mathews, 1954). Peripheral neuritis is frequently present (De Navasquez and Treble, 1938; Götz and Krücke, 1941; Finley and Adams, 1948), but is often mild and apt to be missed.

The present case is of interest, because it prompted three different diagnoses, besides peripheral neuritis, before the true nature of the disease was established.

Case Report

The patient, a man aged 50, had had no illnesses of note until 1955, apart from a duodenal ulcer for which a gastro-enterostomy had been performed in 1942. In August, 1955, he developed a sensation of food sticking in the epigastrium after meals, with regurgitation of food and anorexia. He was admitted to a hospital, where hepatomegaly was noted. A barium-meal examination revealed a rigid stomach, suggestive of carcinoma. Gastroscopy showed a rigid mucosa and absent pyloric peristalsis. A diagnosis of carcinoma of the stomach was made, but subsequent laparotomy failed to confirm this. Liver biopsy taken at the time was thought to show a pericellular fibrosis. He was sent to a convalescent home in January, 1956, where he developed swelling of his legs with pain and numbness in his left foot and an increase in the size of his abdomen. He attended the out-patient department of the Middlesex Hospital in March, 1956.

On examination he appeared to be wasted, with early clubbing of the fingers, dilated and pulsating neck veins, gross hepatic enlargement, considerable ascites, and oedema of both legs, scrotum, and anterior abdominal wall. The heart appeared to be of normal size, gallop rhythm was not heard, and there were no significant cardiac murmurs. A tentative diagnosis of constrictive pericarditis was made, and he was admitted on March 10.

Investigations.—The venous pressure was 160 mm. of blood, the circulation time (arm-tongue) 30 seconds. The electrocardiogram showed a low-voltage curve with T wave inversion over the left ventricle, suggestive of pericardial change. X-ray examination of the chest showed a slightly enlarged heart, with no pericardial calcification, which pulsed normally on screening. The urine contained a variable quantity of protein from day to day (1–14 g. per litre), but Bence Jones proteose was not present. The haemoglobin was 103% (Haldane) and the white-cell count was normal. The total plasma proteins were 4.5 g. per 100 ml. (albumin 2.1 g., globulin 2.4 g.). The serum bilirubin was 0.6 mg. per 100 ml.; serum alkaline phosphatase 6.2 K-A units per 100 ml.; and serum acid phosphatase 7.2 K-A units per 100 ml. The flocculation tests were all within normal limits. The bromsulphthalein excretion was grossly impaired. The blood urea level was 29 mg. per 100 ml., and the serum cholesterol 260 mg. per 100 ml.

After consideration of these results the diagnosis of constrictive pericarditis was changed to one of severe parenchymal liver disease associated with congestive heart failure of unknown aetiology.

On closer inquiry into the patient's social history, it was found that he had been a wine-waiter for 20 years, and that for some years before the onset of his symptoms his alcohol intake had been excessive and his diet inadequate. This, together with some of the biochemical findings, suggested a diagnosis of portal cirrhosis. The symptoms and signs in the left foot were thought to be those of peripheral neuritis.

The previous liver biopsy was then reviewed and the possibility of amyloid disease was suggested. The section, however, showed so much autolysis that histological diagnosis was uncertain. A Congo-red uptake test was positive, the one-hour sample containing only 30% of the dye in the four-minute sample, with only a trace in the urine. A further liver biopsy by needle confirmed the diagnosis of amyloid disease.

While investigations were being carried out the patient was treated on the usual lines for congestive heart failure, with digitalis and diuretics. This was only moderately successful. Cortisone therapy was contemplated, but the patient died on April 3, before this was begun.

Post-mortem Findings

At necropsy bilateral pleural effusions, gross ascites, and a small pericardial effusion were found. The heart was slightly enlarged and the myocardium was of a waxy consistency.

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

H. G. LANGDALE-SMITH, M.B., Ch.B.

D. M. LANGDALE-SMITH, M.B., Ch.B.

AND

B. R. WILKINSON, M.B., B.S.

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