Summary

A case of rheumatoid arthritis is described in which bouts of high fever occurred over a period of three months and of low-grade fever continued for a further four months before the diagnosis was evident. On two occasions a temperature of 105.2° F. (40.7° C.) was recorded after a rigor.

The highest leucocyte count was 30,800, recorded on admission; the next highest was 26,200 eighteen weeks later.

My thanks are due to Dr. G. D. Kersley for his help and for details of the patient's treatment and progress while under his care in the Royal National Hospital for Rheumatic Diseases, Bath; to Dr. D. H. Davies, under whose care the patient was admitted to Southmead Hospital, for advice and criticism; and to Dr. P. Phillips, the medical superintendent, for permission to publish.

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FIBROCYSTIC DISEASE OF THE PANCREAS*

BY

W. J. MATHESON, M.D., M.R.C.P., D.C.H.

(*From the Paediatric Unit, St. Mary's Hospital, London*)

[WITH PHOTOGRAVURE PLATE]

Although the American literature on this subject is now fairly extensive there have been few reports from this country. Doubtless many cases have gone unreported, but there is still a widespread belief that the disease is rare, and personal experience has shown that it is often misdiagnosed. The only large series described here is that of Bodian (1946), who reported 30 cases. Henderson (1945) recorded one case and MacGregor and Rhaney (1948) two cases in siblings. Previously, under the title of congenital steatorrhoea, Miller and Perkins (1920) and Cockayne (1933) each described one probable case of fibrocystic disease, and Clarke and Hadfield (1924) a proved case, for necropsy showed the pancreatic lesions which are now associated with this disease. It is unlikely that the case described by Garrod and Hurtley (1913) under the same title was one of fibrocystic disease, since Garrod (1920) subsequently reported that this patient was of normal development and activity at the age of 14 years.

Although the association of pancreatic disease and steatorrhoea had been known for over a century it was not until 1905 that Landsteiner described the pancreatic lesions now associated with fibrocystic disease. Passini (1919) first reported a case in which the association of the digestive disturbance and the pathological lesion of the pancreas was recognized. Parmelee (1935) described the cases of two patients with congenital steatorrhoea who died of bronchopneumonia, and in both of whom necropsy revealed cystic fibrosis in the pancreas; he had found in the literature only four cases with a similar history and post-mortem findings. Blackfan and Wolbach (1933) had, however, described six similar cases among 10 reported as cases of vitamin-A deficiency in infants, and Harper (1930) one case among two reported under the title of congenital steatorrhoea.

*Based on a thesis submitted to the University of Edinburgh for the degree of M.D., September, 1948.

Harper (1938) reported eight further cases under the same title, in five of which necropsy showed typical pancreatic lesions, and Blackfan and May (1938) described 35 cases with similar pancreatic lesions which in lesser degree they had observed in a further 200 cases; but they considered that it was not possible to determine accurately dependable diagnostic features in life in these cases. Fibrocystic disease of the pancreas was, however, becoming recognized with increasing frequency at necropsy; and, finally, Andersen (1938) showed that the disease was a definite and common clinical entity with a characteristic course and clinical history. She has since written extensively about the disease in all its aspects, and recently gave in this country a summary of her work (Andersen, 1949).

Case 1

This patient, a boy aged 10 (Fig. A), was first seen at the age of 8. Since birth his stools had been bulky, loose, pale, and offensive. Despite a good appetite and an adequate diet, he had never gained weight well. An irritative cough had been present since the age of 2 years, and had become worse and been accompanied by purulent sputum in the past nine months since an illness diagnosed as pertussis and bronchopneumonia. When 2 years old he was taken to another hospital, where coeliac disease was diagnosed. Dietary treatment for two years brought no improvement, and the diagnosis was altered to tabes mesenterica when his Mantoux reaction was found to be positive and calcified glands were seen in the abdomen at laparotomy performed on account of recurrent abdominal pain. He had had bronchopneumonia at 2 weeks and rectal prolapse at 6 months. His parents were not blood relations. One sibling aged 8 months is alive and well. The patient's weight was 44 lb. (19.96 kg.) (average, 57 lb.—25.85 kg.); height 48 in. (122 cm.) (average, 51 in.—130 cm.). His abdomen was prominent and his fingers were clubbed. Chest: percussion note hyperresonant; persistent crepitations in right lower and mid zones.

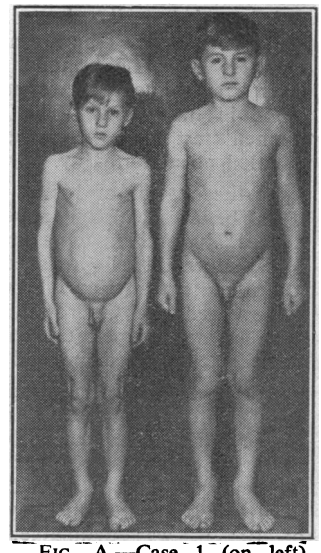

FIG. A.—Case 1 (on left) with normal boy of same age.

Investigations.—Duodenal juice contained no trypsin. Microscopical examinations of the stools revealed numerous fat globules and completely undigested muscle fibres; the fat content was 50%, of which 80% was split fat. Nitrogen excretion on a normal diet was 4.47 g. per day in faeces and 7.8 g. in urine. Blood counts showed no anaemia, but persistent polymorphonuclear leucocytosis. The predominant organism in the sputum was a penicillin-sensitive pneumococcus. Radiography of the chest showed emphysema with a generalized bronchitic appearance and parenchymal changes at the right base.

Progress and Treatment.—For 18 months he has been treated with a low-fat, high-protein, and high-carbohydrate diet and 30 g. of casein hydrolysate and 16 g. of pancreatin in the form of enteric-coated capsules and extra vitamins. He has gained only 4 lb. (1.81 kg.) in weight and 2½ in. (6.25 cm.) in height. At first his activity was greatly increased, but accesses of the pulmonary infection, although relieved by penicillin inhalations, have recently been occurring so often (about once a month) that his activity is now about the level maintained before specific therapy was started. Stools are now formed and not very offensive. On the same diet faecal nitrogen has been found to be diminished when pancreatin is given.

W. J. MATHESON: FIBROCYSTIC DISEASE OF THE PANCREAS

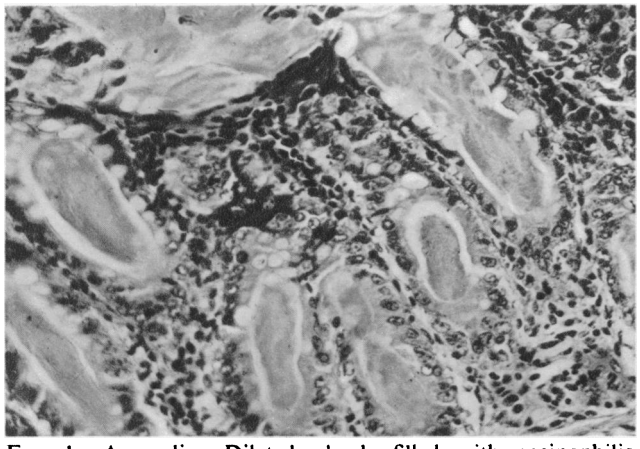

FIG. 1.—Appendix. Dilated glands filled with eosinophilic material, in places continuous with similar material filling the lumen. (× 190.)

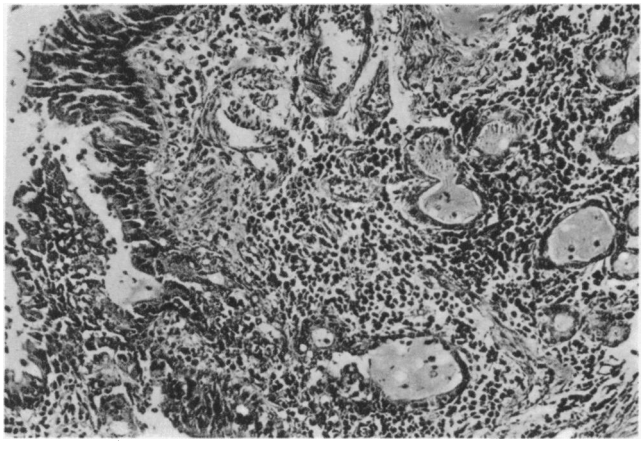

FIG. 2.—Bronchus showing dilated glands in wall. (× 105.)

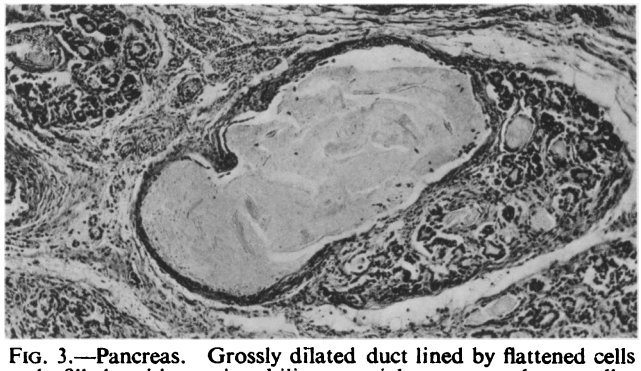

FIG. 3.—Pancreas. Grossly dilated duct lined by flattened cells and filled with eosinophilic material, as are the smaller ducts. (× 60.)

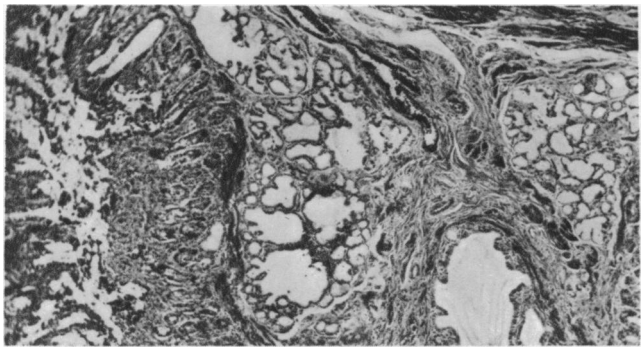

FIG. 4.—Duodenum showing dilated glands in wall. (× 90.)

S. N. DE: STREPTOMYCIN IN DEVELOPMENT OF HYDROCEPHALUS IN TUBERCULOUS MENINGITIS

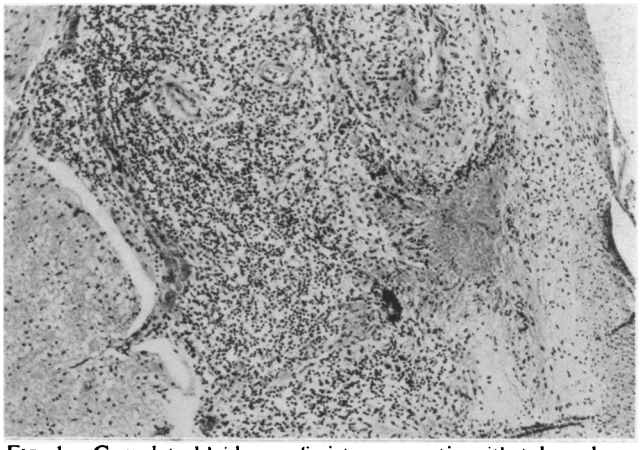

FIG. 1.—Complete blockage of cisterna pontis with tuberculous granulation tissue. Hydrocephalus followed meningitis not treated with streptomycin. H. and E. (× 65.)

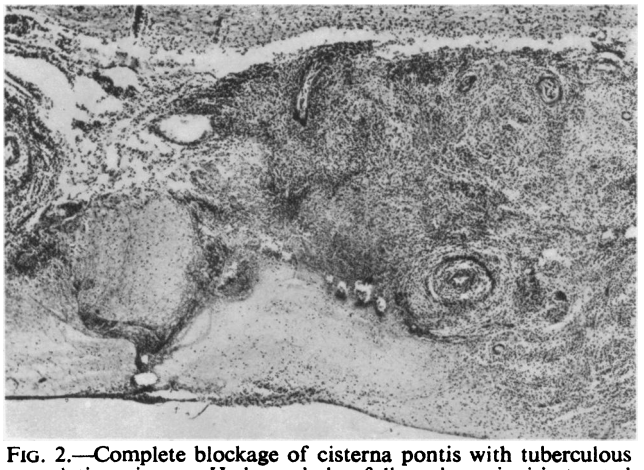

FIG. 2.—Complete blockage of cisterna pontis with tuberculous granulation tissue. Hydrocephalus followed meningitis treated with streptomycin. H. and E. (× 25.)

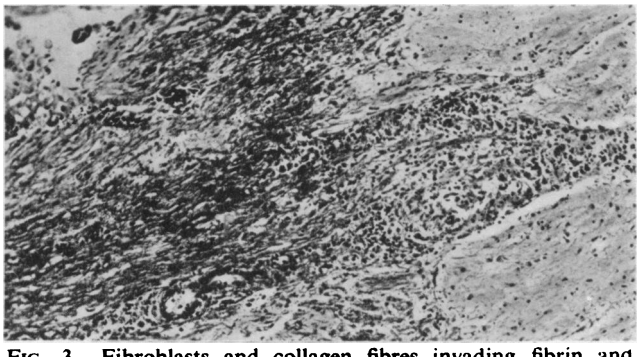

FIG. 3.—Fibroblasts and collagen fibres invading fibrin and tubercles within meningeal exudate. Hydrocephalus followed meningitis treated with streptomycin. H. and E. (× 65.)

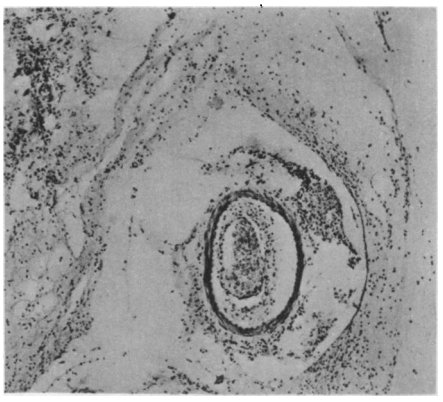

FIG. 4.—Patent subarachnoid channels within cisterna pontis. Tuberculous meningitis treated with streptomycin. No hydrocephalus. H. and E. (× 45.)

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Case 2

A boy aged 2 years was admitted to hospital on Sept. 13, 1948. Since the age of 2 months he had wheezed continually; a diagnosis of asthma was made and never altered. One month before admission he began to cough and lost weight and energy. Rectal prolapse had occurred repeatedly in the past two months. Despite a good appetite, he had never thrived, his weight at 8 months being 15½ lb. (7 kg.) and at 1 year 18½ lb. (8.4 kg.) (birth weight was 7½ lb.—3.4 kg.). From the age of 6 months or so his stools had been frequent and unformed, bulky, and very offensive. He was the third child. The eldest died of acute bronchitis at 11 weeks. The second, aged 5 years, is alive and well. A paternal aunt, who had never thrived, died at 16 days.

On examination his temperature was normal, pulse 120, and respirations 32; he was dyspnoeic, with frequent paroxysmal coughing. His weight was 21 lb. (9.5 kg.) (average, 27 lb.—12.2 kg.); height, 30 in. (76 cm.) (average, 33 in.—83.5 cm.). Chest: percussion note hyperresonant; rhonchi and crepitations in all areas. The liver was palpable two fingerbreadths below the costal margin in the nipple line.

Investigations.—Numerous fat globules and undigested muscle fibres were found in the stools; the fat content was 30%. A laryngeal swab revealed *Staphylococcus aureus* sensitive to streptomycin only. Duodenal intubation was unsuccessful. Blood counts showed a progressive fall in haemoglobin to 75% on Oct. 28; there was a persistent polymorphonuclear leucocytosis up to 40,000 per c.mm. Radiographs of the chest showed increasing spread and confluence of bronchopneumonia in all areas of the lung fields.

Progress and Treatment.—Wheezing disappeared after two weeks, but despite the use of streptomycin, given by inhalation and intramuscularly, the cough became more severe, crepitations persisted in the lungs, and a swinging temperature soon developed and persisted. Cyanosis was present in the fortnight before death on Nov. 19. His appetite had been good for six weeks, and on a low-fat diet with extra protein and 26 g. of casein hydrolysate and 8 g. of pancreatin (in the form of enteric-coated granules) daily his weight had risen to 22 lb. (9.98 kg.) but then fell progressively. His stools had continually been frequent, unformed, and very offensive. The liver had remained enlarged.

Post-mortem Report.—There was much mucopurulent material in the air passages, and in the lungs extensive bronchopneumonia with bronchiolectatic abscesses. The pancreas appeared normal macroscopically. The liver was "nutmeg," and the appendix was thickened. Microscopically, the pancreatic ducts were considerably dilated and filled with eosinophilic material, and there was much surrounding fibrosis; the lumen of the appendix was filled with eosinophilic material continuous with that in the dilated glands of the wall (Plate, Fig. 1). Similar lesions were seen in the mucous glands of the trachea and bronchi (Fig. 2), the salivary glands, the duodenal wall, and the periurethral glands.

Case 3

A girl aged 2 years was first seen in January, 1947, at the age of 21 months, with rectal prolapse, which was attributed to inadequate intake of vitamin D. Her weight was then 24 lb. (10.88 kg.). When next seen, a month later, she had developed a slight cough and had lost weight despite a good appetite. She was admitted early in May, 1947, for correction of the prolapse, but was discharged five days later as she was thought to have pertussis. At home the cough became more severe, the weight-loss was accelerated, and she was readmitted at the end of May. Even in infancy her gain in weight had never been satisfactory, although her appetite was so good that she was fed three-hourly with amounts prescribed for four-hourly feeds. Her stools had always been bulky, pale, and very offensive.

She was the fourth child of healthy unrelated parents. Her three siblings had all died of bronchopneumonia before the age of 6 months; none had thrived, and all had had very offensive stools. The maternal grandmother had lost five out of eight children in infancy from unknown causes. The paternal grandmother had lost six of 12 children in infancy—four at birth and two of pneumonia during the first year.

On May 22 her temperature was 101.6° F. (38.7° C.), respirations 64, pulse 128, weight 18¼ lb (8.28 kg.) (average, 24 lb.—10.88 kg.). She was wasted and dyspnoeic. Chest: Fine crepitations in all areas. The abdomen was protuberant. The liver was enlarged to the umbilicus. The spleen was not palpable.

Investigations.—The faecal fat amounted to 49%, 86% of it being split fat. Blood counts showed a progressive anaemia. Three attempts at duodenal intubation were unsuccessful. Mantoux, negative at 1 in 1,000. Serum proteins (June 25) were 7 g. %—albumin 2.8, globulin 4.2. Chest radiographs showed increasing bronchopneumonic changes.

Progress and Treatment.—Sulphamezathine and penicillin failed to control the respiratory infection. Cyanosis was only temporarily relieved by oxygen. The stools were frequent, unformed, and very offensive; appetite was never good, and weight fell progressively. Pancreatin given in the last three weeks had no appreciable effect. Peripheral oedema, unrelieved by blood transfusion and intravenous "casydrol," appeared four weeks before death, and petechiae terminally.

Post-mortem Report (July 22).—Much mucopus in the air passages. In the lungs marginal emphysema was present, with extensive bronchopneumonia and numerous bronchiectatic abscesses in practically all areas. The pancreas on section showed dilated ducts. The liver was large and pale. Microscopical examination showed gross dilatation of pancreatic ducts filled with eosinophilic material, much surrounding fibrosis, and almost complete disappearance of acinous tissue. There was bronchopneumonia with, in places, destruction of bronchial walls and dilated bronchial glands. The liver showed gross fatty degeneration.

Case 4

A girl aged 4 months was transferred on July 16, 1948, from another hospital, where she had been treated for six weeks for bronchopneumonia without improvement. Despite a good appetite she had never thrived, and her stools had always been frequent and offensive. At 3 months she developed pneumonia, which did not respond to treatment with sulphonamides and penicillin. She had three siblings alive and well. A maternal uncle, who had never thrived, died at 10 years of "consumption of the bowels."

On examination on July 16 the temperature was 99° F. (37.2° C.), respirations 48, weight 8 lb. 15 oz. (4 kg.) (expected weight, 12½ lb.—5.67 kg.). She was wasted; the abdomen was prominent. There was dyspnoea with frequent cough. Chest: percussion note impaired at left base; fine crepitations audible over the entire left chest.

Investigations.—Duodenal juice contained no trypsin. Faecal fat: (*a*) on skimmed milk 40%, (*b*) on half-cream milk with pancreatin 21% (96% split). A laryngeal swab contained predominantly a penicillin-sensitive *Staph. aureus.* Hb was 65%. Radiography of the chest showed left basal consolidation.

Progress and Treatment.—Penicillin was continued, but the respiratory trouble spread. Appetite was poor. Stools were always frequent, bulky, and very offensive. She died on Aug. 4.

Post-mortem Report.—The immediate cause of death was bronchopneumonia. The pancreas was smaller than normal, was nodular, and presented an increased resistance to section. Microscopically, typical changes were seen in the pancreas and salivary glands.

Case 5

A boy aged 4 months was admitted to hospital on Aug. 3, 1948. His appetite had always been good, but weight-gain had never been satisfactory (his best weight was 8 lb. (3.63 kg.) at three months). Stools had always been frequent but not noticeably offensive. A frequent dry cough had been present since birth.

On examination the temperature and respirations were normal and the weight 7 lb. 11 oz. (3.48 kg.) (expected weight,

12¼ lb.—5.55 kg.). Mediastinal shift to right with hyperresonant percussion note over left chest.

Investigations.—Three attempts at duodenal intubation failed. Faecal fat (on full-cream milk), 72% (50% split). Laryngeal swab revealed *Staph. aureus.* Blood counts showed a progressive anaemia.

Progress and Treatment.—Ten days after admission he developed a pulmonary infection which did not respond to penicillin. Appetite was very good, and on a skimmed-milk diet with pancreatin and hydrolysates weight increased slowly to 8 lb. 10 oz. (3.91 kg.). Stools were always bulky, frequent, and very offensive.

Post-mortem Report (Sept. 21).—The immediate cause of death was bronchopneumonia. The pancreas was normal externally, but dilated ducts were seen on section. Microscopically, typical changes were seen in the pancreas, salivary glands, and bronchial and intestinal walls.

Case 6

A girl aged 5 months, an only child, was admitted to hospital on Nov. 1, 1947, with right basal pneumonia. She had had a cough since birth, but weight-gain had been satisfactory, and she had reached 12¼ lb. (5.55 kg.) (expected weight, 12 lb. —5.44 kg.) when pneumonia developed two weeks before admission. Chemotherapy and antibiotics failed to control the respiratory infection, and although she ate well her weight fell. Stools were first noticed to be offensive two weeks after admission ; the fat content was 40% (on half-cream milk feeds).

Post-mortem Report (Dec. 17).—The immediate cause of death was bronchopneumonia. The pancreas was smaller and more nodular than normal. On the surface of the liver were small nodules up to 2 mm. in diameter. Microscopically the pancreas showed the typical changes in an advanced stage (Fig. 3). In the liver the nodules were seen macroscopically to consist of cirrhotic areas in which were numerous bile ducts filled with eosinophilic material. Similar lesions to those in the pancreas were found in the salivary glands and in the duodenal wall (Fig. 4).

Case 7

A girl aged 16 months was transferred on July 30, 1948, from another hospital, where she had been treated for two months for coeliac disease without improvement. Weight-gain was never satisfactory, and from the age of 4 months her stools were bulky and offensive. This abnormality became more noticeable at 1 year. She had had bronchitis at 8 months.

On July 30 her weight was 15¼ lb. (6.92 kg.) (average, 22 lb. —9.98 kg.). She had a coeliac appearance. Her chest was normal. Duodenal juice showed tryptic activity in undiluted juice but not in a dilution of 1 in 10. Faecal fat: (*a*) on a normal diet, 60% (75% split ; (*b*) on a low-fat diet with pancreatin, 15%. With specific dietary treatment she gained 3 lb. (1.36 kg.) in three weeks. Her stools were always unformed and offensive.

Discussion

The seven cases described were seen between June, 1947, and September, 1948. To ascertain the hospital incidence it is necessary to exclude Cases 4 and 5, which were transferred from other hospitals because of our known interest in fibrocystic disease ; the remaining five cases occurred among 240 medical admissions to the children's ward—an incidence of 2%. Andersen (1938) found evidence of the disease in 3% of all necropsies on infants, and Bodian (1946) in 3.4% of 500 necropsies on children. The disease therefore is by no means uncommon. The failure to appreciate this prior to 1938 is undoubtedly due to the fact that bronchopneumonia, the usual cause of death, was taken to be an adequate cause and consequently the pancreas was not sectioned.

The evidence points to the disease being inherited (Andersen, 1949). In this series no other proved case has occurred in an affected family, but there is presumptive evidence of the disease in the family history of Case 3 and suggestive evidence in Case 2. The inheritance may be explained by incomplete dominance : Fisher (quoted by Cockayne, 1947) has shown that many dominant defects are gradually becoming recessive, this being brought about by the selection of genes which prevent a dominant condition becoming manifest when in the heterozygous state ; moreover, a defect may behave in one family as a recessive and in another as a dominant.

The pancreatic lesions were formerly sometimes ascribed to dehydration, but Farber (1942) disproved this. Blackfan and Wolbach (1933) first advanced the hypothesis that they were caused by inspissation of viscid secretion in the ducts ; this was confirmed by Farber (1942), who reproduced the lesions in kittens by vagal stimulation. It remains to be seen if similar experiments will reproduce the lesions occurring in other organs also, and the cause of the abnormal secretion has yet to be determined.

Farber (1944) reported the finding of dilated glandular structures in both the respiratory and the intestinal tracts ; he concluded that the disease affected all mucus-secreting glands, the lesions being caused by inspissation of viscid secretion, and that it was the loss of normal mucus from the bronchial tree that was responsible for the susceptibility to pulmonary infections. Bodian (1946) also has stressed that this is a pluriglandular disease, as have Continental workers (Glanzmann, 1946 ; Riniker, 1946). Andersen (1949), however, while accepting Blackfan and Wolbach's explanation for the pancreatic lesions, considers that the pulmonary infection is conditioned by dietary deficiency, and that the lesions observed in the bronchial walls are secondary to infection. But this explanation does not suffice for the similar lesions found in other organs in which there is no infection ; moreover, dogs in whom the pancreatic duct had been tied did not die from pulmonary infections (Ivy, 1936). The pathological findings in this series have again confirmed the pluriglandular nature of this disease, and there seems little doubt that Farber's hypothesis is correct.

Earlier observers (Parmelee, 1935 ; Harper, 1938) considered that a high percentage of neutral fat in the stools indicated pancreatic disease. Andersen (1945a), however, has shown that faecal fat can be split in the colon and outside the body by bacterial action, and Fourman *et al.* (1948) consider that increased nitrogen excretion in the faeces is the most reliable test of pancreatic steatorrhoea. Fat analyses of three-day collections of stools, as carried out in these cases, will usually detect steatorrhoea (Fourman *et al.*, 1948), but the determination of split and unsplit fat is of no diagnostic value (May, 1947).

Andersen (1938) showed that cases fell into three main groups : (1) cases of meconium ileus which present within a few days of birth with intestinal obstruction ; (2) cases which present in the first six months of life with respiratory infections—nutritional difficulty is also present (this is the largest group) ; (3) cases which present later with nutritional difficulty as instances of the coeliac syndrome or with rectal prolapse or with chronic respiratory infection. The typical history is of a poor gain in weight despite an adequate diet and an excellent appetite, dating from early infancy. The stools are frequent, unformed, bulky, and very offensive ; these abnormalities are more often noticed by mothers who have previously borne normal children, and usually date from early infancy. Sooner or later respiratory infection supervenes and dominates the picture.

Although it is generally agreed (May, 1947 ; Andersen, 1949) that estimation of trypsin in the duodenal juice is necessary to establish the diagnosis, nevertheless it is

desirable to make a diagnosis on clinical evidence whenever possible, and experience has indicated that this can be done. In all the present cases the diagnosis was made clinically and was never disproved by subsequent examination of the duodenal juice or by necropsy. The clinical picture is highly characteristic, but it must be emphasized that an accurate history is essential, and close questioning may be required to obtain this, as noted by Miller and Perkins (1920).

The disease should be suspected in all cases of chronic nutritional difficulty and chronic respiratory infection in children, and specific questions asked about appetite, weight-gain, the character of the stools in regard to number, size, and smell, the exact date of onset of any abnormality noted, and the family history, especially of infantile deaths. In a number of cases the abnormality of the stools, while present from early infancy, becomes more obvious when solids are added to the diet or even later, and this overshadows the history. Cough may be present without signs of infection, and is then presumably due to efforts to expel viscid mucus from the bronchial tree. The clinician should himself examine the stools, for their offensive smell is characteristic. The typical history, associated with the clinical findings, enables a firm diagnosis to be made.

Sheldon (1948) considers that it is usually possible to distinguish coeliac from fibrocystic disease on clinical grounds alone. In typical cases, therefore, duodenal intubation is superfluous and should be reserved for cases in which the picture is not characteristic—e.g., Case 6. It is important to remember that in some children any chronic infection may produce steatorrhoea and that the association of bronchiectasis and steatorrhoea does not justify a diagnosis of fibrocystic disease without supporting evidence.

It is not only desirable but sometimes necessary to make a clinical diagnosis, since duodenal intubation has often been unsuccessful, and repeated attempts do not improve the condition of children already wasted. Moreover, the absence of trypsin from the duodenal juice is not pathognomonic of fibrocystic disease. Dr. G. M. Bull, to whom I am indebted for these particulars, has under his care two adults—brother and sister, aged 18 and 22 years respectively —who have suffered from steatorrhoea since early infancy. Recently duodenal intubation has shown a complete absence of trypsin in both, but there is no pulmonary infection. These patients are not suffering from fibrocystic disease as regarded generally. Their cases are, however, similar to the case reported by Garrod and Hurtley (1913). Either the underlying lesion may be a congenital stenosis of the main pancreatic duct or these cases may be analogous to that reported by Farber (1944) in which lesions typical of fibrocystic disease were found only in the lungs and liver; vice versa, there may be cases in which the pancreas is affected and not the lungs.

Treatment.—The diet used has been that recommended by Andersen (1949), but pancreatin has been more extensively employed than casein hydrolysates, since the latter are unpalatable and older children are loath to take them. It is unfortunate that hydrolysates are so unpleasant, since the evidence indicates that they are of more value than pancreatin (West *et al.*, 1946).

Results of Treatment and Prognosis.—Of the seven patients, five have died of bronchopneumonia and one of the survivors has extensive bronchiectasis. The prognosis therefore depends on the respiratory infection, and the failure of appropriate chemotherapeutic and antibiotic agents to control it has been most disappointing. Specific dietary treatment also has proved of limited value. Pancreatin does, however, seem to be of value in increasing the utilization of food, and this effect is especially noticeable in infants.

The number of cases reported here is small, but no evidence has been found to support Andersen's (1949) contention that appropriate chemotherapy, given early in the course of the respiratory infection, combined with specific dietary treatment, may result in the control of the infection. Personal experience of cases diagnosed before the onset of respiratory infections is limited, but Andersen's (1945b) evidence that most, when given specific therapy, do not contract chronic respiratory infections and develop normally is not fully convincing. In assessing the results of any therapeutic regime in this disease it is important to remember that the oldest proved case in the literature, aged 14½ years (Parmelee, 1935), was treated by a low-fat and high-protein diet only. Moreover, Cases 1 and 7 in this series showed that pulmonary infections in infancy do not invariably become chronic even without treatment. Also there are a few cases which, although they lack trypsin in their duodenal juice, do not develop pulmonary infections at all.

Since in the great majority of cases of bronchopneumonia in children a good response is obtained, the failure of chemotherapy to control the pulmonary infections in these cases suggests that unusual factors are involved. One unusual factor is the abnormality of the mucous glands of the air passages, and the treatment so far possible cannot be expected to influence this. The rational treatment would be to liquefy the mucus in the bronchial tree by some substance (e.g., hyaluronidase) aimed at restoring normal conditions in the respiratory system.

Summary

Seven cases of fibrocystic disease of the pancreas are described which occurred among 2% of routine admissions to a children's ward.

Inheritance by incomplete dominance is postulated.

The pathological findings have again confirmed that this disease affects mucus-secreting glands throughout the body.

The diagnosis can usually be made clinically provided an accurate history is obtained.

The results of treatment have been disappointing, since five of the patients have died of bronchopneumonia and one of the survivors has extensive bronchiectasis.

It is suggested that measures directed at liquefying the mucus in the bronchial tree might lead to more successful results than those generally at present obtained.

I wish to thank Dr. Reginald Lightwood for much helpful advice and criticism and for permission to publish these cases, except Case 5, for which I am indebted to Dr. Ursula James. I also wish to thank the staff of St. Mary's Hospital, Paddington, for carrying out the investigations; Mr. E. V. Willmott for the photomicrographs; and Mr. A. Evason for the clinical photograph.

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FATAL CASE OF POLIO-ENCEPHALITIS DUE TO POLIOMYELITIS VIRUS

BY

G. H. JENNINGS, M.D., F.R.C.P.
Senior Physician, Edgware General Hospital

J. L. HAMILTON-PATERSON, M.D.
Pathologist, Edgware General Hospital

AND

F. O. MacCALLUM, M.D., B.Sc.(Toronto)
Director, Virus Reference Laboratory, Central Public Health Laboratory, Colindale

[WITH PHOTOGRAVURE PLATE]

The case of fatal polio-encephalitis described in detail below is reported because of its interesting clinical picture and because of the striking proof of the diagnosis by intracerebral inoculation in a monkey. The similarity of the lesions in the cord of the human victim to those in the monkey inoculated with a filtered saline extract from the child's brain and cord can easily be seen by reference to the illustrations.

Case Report

A well-developed child of 3½ years was admitted to Edgware General Hospital on Aug. 3, 1948. He had had pertussis at 1½ years, but had otherwise been well until he began to attend a nursery school one month before his admission. He was not happy at the school, slept irregularly at night, and was sleepy in the mornings. Three weeks before admission he had an illness of influenzal type lasting one day, during which he vomited and was febrile and drowsy. On July 31 he was said to have fallen from a swing, though apparently with no untoward effect. However, the next day he became drowsy and slept through much of it, would not eat, complained of abdominal pains, and vomited twice. During the night he awoke three times and complained of headache and pains in the back of the neck and in the legs. On Aug. 2 he still complained of the pains, and some weakness of the left side of the face developed, the face being drawn to the right. Although he was febrile and eager for fluids, he appeared to swallow with difficulty. He talked normally throughout the day. By evening he was generally stiff and showed a tendency to restlessness and twitching of the limbs. The bowels were constipated from that day to the end, and he again vomited once. On the day of admission he was not easy to rouse and would not speak; the restlessness and twitchings continued.

On admission he was very drowsy, toxic, and cyanosed. His temperature was 102° F. (38.9° C.), pulse 88, respiration 56. His tongue was moist but furred. The throat was not inflamed, but the tonsillar glands were palpable. There was pronounced stiffness of the neck and spine. Kernig's sign was not present and the legs were not stiff. His pupils were equal and reacted to light, though sluggish. The disks were normal. He had slight weakness of the left side of the face. No other apparent abnormality in cranial nerves was observed and no weakness was noted in the limbs. Tendon-jerks were absent in the left lower limb but brisk on the right side. Plantar response was extensor on the left side and indefinite on the right. No abnormality was noted in other systems.

Lumbar puncture showed clear fluid under normal pressure; total protein, 80 mg. per 100 ml.; Pandy + ; white blood cells, 55 per c.mm (degenerate polymorphs 5%, lymphocytes 20%, large endothelials 75%); chlorides, 710 mg. per 100 ml.; no organisms seen; sterile on culture.

Overnight his condition had deteriorated rapidly, and when seen by one of us (G. H. J.) next morning (Aug. 4) he was almost completely unconscious. He was still toxic and cyanosed; respirations were stertorous, but the rate was only 22. His temperature was 98° F. (36.7° C.) and pulse 80. A tendency to show slight general convulsions was noted. The disks were normal, as were the pupils, apart from the persistent sluggish reaction to light. Neck stiffness was slight and Kernig's sign was negative. The face was now almost expressionless as a result of general weakness. The left side of the body, though still showing voluntary movement, appeared definitely weaker and more flaccid than the right. The tendon-jerks, though sluggish, were all elicited except the right ankle-jerk. The abdominal reflexes were all present. The left plantar response was still definitely extensor, but that on the right remained indefinite.

Lumbar puncture showed C.S.F. under very low pressure; no block; opalescent fluid; fibrin clot formed after 15 minutes; white blood cells, 195 per c.mm. (lymphocytes 86%, polymorphs 14%); red blood cells, 465 per c.mm.; normal sugar content; sterile on culture. A blood count showed: Hb, 90%; red cells, 5,090,000; white cells, 4,700 (polymorphs 68%, lymphocytes 28%, monocytes 4%.

A diagnosis of a neurotropic virus infection was made, and since the prodromal illness three weeks before admission was within the reported maximal incubation period of 35 days for the poliomyelitis virus it was considered that the case was possibly one of polio-encephalitis. The child's condition continued to deteriorate; the temperature became subnormal, the pulse rate increased to 120–136, and the respiration rate remained at 24–26. He died early on the following morning (Aug. 5) after many hours of complete unconsciousness.

Post-mortem Examination

This was performed five hours after death. The body was that of a normally developed male child.

Brain (1,350 g.).—Meninges normal. Surface of brain intensely congested. On section the cortex of the hemispheres was plum-coloured, but showed no petechiae; white matter normal except for a few tiny petechial haemorrhages in the occipital lobes. The cerebellum, mid-brain, pons, and medulla were macroscopically normal.

Spinal Cord.—Macroscopically normal.

Skull.—Normal except for a small quantity of yellow glairy fluid in the right mastoid cavity. Films of this fluid showed occasional pus cells, and on culture a few colonies of *Bacterium coli* and *Streptococcus faecalis* were grown.

Comparison of Histological Lesions of Central Nervous System in the Case described and in the Inoculated Monkey

	Human	Monkey
Motor cortex, left	Congestion only	Early perivascular cuffing
„ „ right		Nil
Sensory cortex, left	—	Nil
„ „ right	—	Nil
Olfactory bulb ..	—	Nil
Basal nuclei	—	Nil
Brain stem	Few small areas of perivascular cuffing and very early neuronal changes	Perivascular cuffing and early neuronal degeneration
Cervical cord ..	Marked perivascular cuffing. Slight cellular infiltration of anterior horns. Early neuronal degeneration	Marked perivascular cuffing. Cellular infiltration of grey matter, most marked in anterior horns. All stages of neuronal degeneration, including neuronophagia by histiocytic cells. The changes increase in severity, progressing from cervical to lumbar region
Thoracic cord ..	—	
Lumbar cord ..	Marked perivascular cuffing. Marked cellular infiltration of anterior horns, particularly on left side. Advanced neuronal degeneration	