is about T₄. It is of no value in Pancoast tumours. Leucotomy must be considered for some patients; this can save sometimes quite untellable misery. In most cases, however, pain due to chest wall invasion can be quite satisfactorily controlled by morphia.

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CLINICAL SECTION

POLYCYSTIC DISEASE OF THE KIDNEYS

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Polycystic disease of the kidneys was first described in 1700 by Litré of Paris. Its familial nature was suggested in 1843 by Adamkiewicz, and is now generally accepted. The kidneys, in polycystic disease, become converted into a mass of cysts. In some cases this may be a cause of stillbirth or death in infancy, but in others the condition remains latent until early middle age. Rarely does the disease declare itself between infancy and middle age and in some cases the renal lesions may be insufficient to impair renal function, in which case the condition may only be found at autopsy.

The incidence of the disease can be seen from the accompanying figures.

Cases admitted to hospital : 1 in 3,500.

Cases found at autopsy : 1 in 375.

The two striking points shown by these figures are the difference between the number of cases found clinically and those found at autopsy, and the two distinct age groups in which the disease occurs.

Polycystic kidney disease may be divided into two types : the infantile type and the adult type. The latter may be sub-divided according to whether the condition produces symptoms or not, into clinical and subclinical groups.

In the infantile type of polycystic kidney the child is either stillborn or dies in infancy; he rarely lives longer than a year. In some cases the kidneys may be so large as to hinder labour and occasionally delivery is only possible after evisceration of the foetus. The kidneys are grossly enlarged and on section show a honeycomb

FIG. 1.—Diagram showing the age incidence of polycystic disease of the kidneys in 239 cases (after Küster).

appearance with small cysts of fairly regular size distributed throughout the cortex and medulla, the number of nephrons being markedly reduced. Too little renal parenchymal tissue exists to permit more than a few months of life.

In the clinical adult type of polycystic kidney, the kidneys are greatly enlarged. (One pair of kidneys on record weighed over 7 kg. each.) The surface of the kidney is nodular and the cut

FIGS. 2a and 2b.—Photographs of a kidney removed at autopsy from Case III₅.

surface shows a mass of cysts of varying size distributed throughout the cortex and medulla (see fig. 2 a and b). The cysts are much larger than those of the infantile type and may measure up to 10 cm. in diameter. The cysts contain a clear yellow watery fluid. This fluid has a high concentration of urea, uric acid and creatinine and it may contain exudate, frank blood due to haemorrhage into the cyst, or pus, due to infection of the cyst. The cysts are lined with a low flattened epithelium with occasional tuft like papillary bunches which resemble glomeruli. The walls of the cyst are surrounded with pale staining connective tissue which has replaced destroyed renal parenchyma. The smaller arteries and arterioles show thickening. Schacht (1932) thinks that this arteriosclerosis may be associated with the hypertension shown by many cases of polycystic kidney disease.

In both infantile and adult cases there are sometimes other congenital abnormalities. In the infantile type, the abnormalities are much commoner, common abnormalities being horse-shoe kidney, supernumary fingers, clubfoot and spina bifida. In adults associated abnormalities usually take the form of cysts in other organs especially the liver and the pancreas. The

incidence of cystic liver has been estimated as 33 per cent. and that of cystic pancreas as 9 per cent. (Rall and Odel 1949). The common abnormalities of the infantile type are not common in the adult type—the implications of this will be discussed.

In subclinical polycystic disease the cysts are not so numerous and do not enlarge so much. In consequence there is no renal dysfunction and the condition is never discovered until autopsy. Probably about 9 cases out of 10 remain subclinical; thus there is bound to be a discrepancy between the number of cases diagnosed clinically and the number found at autopsy.

Unilateral polycystic disease is very rare. Indeed many writers question its existence at all. Braasch and Schacht (1932) categorically state 'Polycystic kidney is always bilateral in the adult.' In some cases symptoms may be produced by one kidney well in advance of the other leading to an incorrect diagnosis of unilateral polycystic kidney.

The reason that some infants survive until early middle age is obscure. It may be explained by the theory that if the condition is very severe at birth the child dies, and if not, he lives until the very slowly enlarging cysts embarrass his renal function. Oppenheimer (1934) quotes a case in which a girl who died from polycystic kidney disease at the age of 17, was known to have had a kidney tumour since she was a few months old.

FIG. 3.—Pedigree of the Paddington family.

There are several such cases in the literature and they serve as connecting links between the two age groups. It has also been suggested that the infantile and adult types are, in fact, distinct conditions. It is interesting to note that Cairns (1925) and Fergusson (1949) could not find in the literature any report of the infantile and adult types occurring in the same family. This may be explained by the fact that where stillbirth has occurred in a family suffering from the adult type, no record exists to show what caused it.

Aetiology

As regards the cause of polycystic kidney disease there are many theories. Virchow (1856) suggested that the cause of the lesion might be inflammatory and others held that the cause might be neoplastic, but it is now generally accepted that the cause is one of abnormal development.

Ribbert (1900) put forward the theory that the secretory and collecting parts of the tubule, which develop separately, fail to join up, the blind collecting part subsequently forming a cyst.

McKenna and Kampmeier (1933) found that early generations of kidney tubules develop only

to become cystic and disappear. They were able to demonstrate these early tubules in a normal foetus of about 3 months and that the tubules were not present in a foetus a few weeks older. They attribute the formation of cysts in polycystic kidney disease to the persistence of the cysts formed from these early generations of tubules.

Allen (1952) bases his theory of the formation of the cysts on a different concept of the development of the nephron. Allen postulates that the secretory and collecting parts of the tubule do not develop as two separate tubules but as two rods of tissue which join and canalize to form the nephron. Failure of the entire tube to canalize would give rise to cysts. This theory and that of McKenna and Kampmeier explain the fact that the cysts in polycystic kidneys are distributed throughout the cortex and medulla, whereas if the theory of Ribbert were correct one would expect the cysts to be limited to the cortex.

Polycystic kidneys have been produced experimentally in mice by irradiating their abdomens and breeding from them. Careful examination of the third and fourth generations of these mice has shown polycystic kidneys, renal aplasia and

horseshoe kidney. It was found that the tendency to develop renal abnormalities was inherited as a Mendelian recessive. This work has not been related to man.

Heredity

Many pedigrees have been produced to show the familial tendency of polycystic kidney disease: this being the chief reason to believe that the condition is congenital. There is the pedigree of a Paddington family shown in Fig. 3 which further illustrates this. Cairns (1925) reported a family in East London in which three generations were affected and noted that he could not find record of more than three generations being affected. Fuller (1929) produced a family in which four generations were affected, and Werner (1940) reported on 109 affected families in only three of which were four generations affected. There appears to be no record of more than four generations affected.

Fergusson in 307 individuals showed that there was no sex incidence and also that there was no sex incidence in the transmitting parent. From the evidence of those families already in the literature it is fairly generally accepted that the condition is inherited as a Mendelian dominant. The infantile type of polycystic kidney disease occurs more rarely, that is, it is unusual to find many cases in any particular family. Weitz (1936) is of the opinion that whereas the adult type is inherited as a dominant, the infantile type is inherited as a recessive.

Since cases occur from time to time in individuals of normal parents, the hereditary nature of the disease has been questioned. In such cases it is possible that one of the parents had subclinical polycystic kidneys, or that they died in such a way that in the absence of post mortem examination a renal cause was never suspected. Possibly if the family history could be traced back in these cases, evidence might be found of three or four consecutive generations of the patient's forebears who had clinical polycystic kidneys. Whether the condition skips generations or not cannot really be decided since subclinical polycystic kidneys need never be suspected.

In any case limitation of progeny in affected families seems wise. Braasch and Schacht even go so far as to advocate sterilisation among the less intelligent.

Clinical Features

In the early stage of the adult type the condition may be diagnosed by the discovery of bilateral palpable kidneys, though in many cases the kidneys do not become palpable until after the onset of the symptoms. Once symptoms declare them-

selves the patients may be divided into two groups: the surgical and the medical groups.

Patients in the surgical group present with infection or trauma of the cysts. There may be acute rupture into peri-renal tissue. There may be palpable kidneys with localized pain and tenderness with fever and leucocytosis. Haematuria or pyuria may accompany these symptoms. Renal colic may occur due to the passage of blood clots or associated calculi. In such cases nephrectomy may be necessary.

In the medical group the majority of symptoms are directly attributable to renal insufficiency, the usual cause of death being uraemia. Patients come to hospital complaining of weakness, vague abdominal pains, vomiting, abdominal distension with diarrhoea or constipation. They may complain of frequency, burning on passing water, or incontinence owing to a secondary infection of the urinary tract. Associated with these symptoms there is generally albuminuria, there may be intermittent haematuria, (sometimes producing anaemia) hypertension and rarely, oedema. Hypertension probably occurs in 75 per cent. of cases and death is sometimes caused by cerebral haemorrhage or by heart failure. In advanced stages of the disease there may be polyuria with a diminished ability to concentrate urine. Pregnancy affects the condition by increasing the work of the kidneys thus intensifying symptoms already present, or bringing out latent symptoms.

Diagnosis

If both kidneys are palpable diagnosis should present little difficulty since bilateral enlargement of the kidneys practically never occurs in anything except polycystic disease. Braasch and Schacht found bilaterally palpable kidneys in 151 of 199 patients (with symptoms), 30 had unilaterally palpable kidneys, the remaining 12 had no palpable kidney tumour. In cases where there is only one mass, or none at all, diagnosis has to rely almost entirely on radiography. Intravenous pyelography is often poor owing to the poor excretion of the dye by badly damaged kidneys. Retrograde pyelography shows a typical picture: the so-called dragon deformity. After diagnosis has been made in one member of the family, pyelography frequently reveals the disease in asymptomatic members of the same family.

Fergusson (1949) has tried to relate polycystic kidney disease to other factors known to be inherited. If it were possible to establish a linkage with a known factor it might be possible to establish a diagnosis in an asymptomatic person on the presence of this factor alone. The principle being the same as that used for sexing day old chicks. Cairns noted in his East London family

that many of the members of this family (affected with polycystic disease) showed myopia. However he could establish no relationship between the two conditions. Fergusson tried to establish a relationship with other known factors. Unfortunately these factors are few and he was unable to establish any linkage with the blood groups (including Rh, M, N and P), the ability to taste phenylthio urea, the secretion of haptenes in the saliva or with the rather more vague physical peculiarities such as eye colour. Though he was unable to establish a linkage he is hopeful that when more of these factors are known one may come to light which is linked with the polycystic kidney factor.

Fergusson also examined children of affected parents radiographically. He was never able to show a case of a negative pyelogram becoming positive. He suggests from this that it is possible that if one is ever going to have a positive pyelogram one always has it. If this is so then the need for knowledge of factors associated with polycystic kidney disease will not be necessary for diagnosis. In any case, at present, early diagnosis makes no difference to the prognosis, since there is no surgical treatment and medical treatment consists of treating the symptoms and limiting the patient's worry and exertion.

Prognosis

Braasch and Schacht found that 45 per cent. of 193 patients lived less than four years after the onset of symptoms (though one lived as long as 36 years). The average expectation of life after the onset of symptoms appears to be about ten years, though this naturally depends on the severity of the symptoms. It is interesting to note that patients suffering from uraemia resulting from polycystic kidney disease seem to be able to tolerate it for much longer and at higher levels than do those whose uraemia has been caused by other renal diseases. This may be due to the slowness with which the renal function is impaired.

The Paddington Family

The abbreviated case-notes of the known and suspected cases shown in the pedigree :

I₁ Charles B. died aged 51. Suffered from Bright's disease. He had a stroke just before he died and had haemorrhage from navel and rectum associated with haematuria. Death Certificate : Nephritis and Cardiac failure.

II₃ Michael B. died aged 48. Complained of a swelling in his right side, abdominal pain and haematuria together with dysphagia and partial aphonia. He was diagnosed as a neoplasm of the right kidney with secondaries in the larynx. At p.m. he was found to have polycystic kidneys—

death being caused by uraemia. His dysphagia is not explained in the existing notes.

II₁₀ William B. died aged 49. When first seen he complained of a cough, vomiting and asthenia. His blood pressure was 270/145 and he had bilateral, nobby, ballotable masses in his loins. He had no haematuria, frequency or dysuria. He died after dieting for 9 months. There was no p.m.

III₃ Kate E. 49. When she was 39 she had an attack of pain in the back associated with haematuria. Radiographically she was diagnosed as a right-sided Grawitz tumour. A nephrectomy was performed and a large polycystic kidney was removed. When last seen (10 years after operation) she complained of tiredness, headache and nausea especially after getting up. She refused to be examined.

III₅ William B. died aged 40. Had first attack of haematuria and frequency when he was 38. He then had bilaterally palpable kidneys, his blood pressure was 180/110 and his blood urea 125 mgm. per cent. During the next 18 months his blood urea remained raised, he had occasional attacks of haematuria and became anaemic, his frequency was worse and later he had headache, nausea and weakness. He died in uraemia in January 1953. At post mortem both kidneys were found to be polycystic.

III₂₅ Mary M. aged 25. In November 1952, she attended the antenatal clinic at Queen Charlotte's Hospital when 3 months pregnant. Her blood pressure was 174/98. An intravenous pyelogram showed the right kidney to be almost normal but the left showed the typical signs of polycystic disease.

IV₁ Rose S. In 1949 when 25 she had a normal delivery in the Borough General Hospital, Ipswich. Later in the puerperium it became necessary to do a right nephrectomy for suppuration in a polycystic kidney. Urea clearance tests and radiography showed no abnormality of the remaining kidney.

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