that failure to immobilize a sprained ankle will result in any serious long-term disability.

Summary

The diagnosis and treatment of ankle sprains is discussed.

The clinical findings in 85 simple sprains and 18 fractures around the ankle are compared. The relative incidence of injury to the principal ankle ligaments is calculated, and by including all the ankle fractures seen in the hospital during the period of investigation the relative frequency of fractures and sprains in a central London casualty department is deduced.

The sprains were treated at random with adhesive strapping or by the injection of hyaluronidase in normal saline into the injured ligament. The effectiveness of the two methods of treatment in relieving pain and restoring function is compared.

The patients were followed up two years after treatment and those with complaints referable to the treated ankle were re-examined.

It was found that simple sprains accounted for approximately three-quarters of all ankle injuries and that four out of five involved only the anterior fasciculus of the lateral ligament (anterior talo-fibular ligament).

Sprains of this ligament gave rise to a definite and constant clinical picture, enabling a positive diagnosis to be made and making radiography unnecessary in excluding more serious injury.

In the absence of a positive diagnosis of an anterior talo-fibular ligament sprain alone, x-ray examination is desirable.

Complete ruptures of the ankle ligaments occurring as isolated injuries and giving rise to instability are uncommon and routine inversion radiographs with or without anaesthesia do not seem to be justified.

Treatment by injecting hyaluronidase and normal saline into the site of injury resulted in more rapid relief of pain and quicker return to normal function than the conventional treatment with adhesive strapping.

There would appear to be no long-term disadvantages of this treatment. In particular, failure to immobilize the sprain did not result in late instability.

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FAMILIAL VISUAL DEFECTS ASSOCIATED WITH POLYCYSTIC KIDNEY AND MEDULLARY SPONGE KIDNEY

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Polycystic kidneys have long been recognized as a familial condition, but the familial occurrence of pyelonephritis, glomerulonephritis, and other types of renal disease has been noted more recently (Hawkins and Smith, 1950; Perkoff *et al.*, 1951; Hilson, 1957; Robin *et al.*, 1957; Goldsmith *et al.*, 1958; Williamson, 1961). One feature of familial renal disease has been its association with other congenital anomalies such as malformations of the ear (Hilson, 1957; deafness (Alport, 1927; Williamson, 1961), multiple structural abnormalities (Hawkins and Smith, 1950), and the other defects of Marfan's syndrome (Loughridge, 1959).

Visual defects, including congenital cataracts, have been described in association with inherited renal disease in Lowe's syndrome (Lowe *et al.*, 1952; Schoen, 1959) and in familial nephritis (Sohar, 1956; Hilson, 1957; Goldbloom *et al.*, 1957). Cairns (1925) described a family in which polycystic kidneys occurred in association with severe myopia.

The family reported below in which cystic renal disease occurred in association with cataract and other visual defects provides a further link in this somewhat irregular chain. The occurrence of cystic disease of the medullary pyramids in two members of the family and polycystic kidneys in another suggests a developmental relationship between these two disorders.

The Family

The family tree is shown in Fig. 1.

Case 1 (Propositus: III 6).—A man, aged 22 at the time of death in 1960, was admitted to the Royal Melbourne Hospital complaining of nausea and vomiting for the previous five months. He had been blind from birth, and polydipsia and nocturia with occasional episodes of frequency had been present as long as he could remember. On examination pallor, bruising, coarse nystagmus, and central cataracts were noted. The blood-pressure was 150/110. He was only able to distinguish between light and darkness. There was intermittent proteinuria (0.4 g. in 24 hours) and slight glycosuria. On microscopy the urine showed six leucocytes per high-power field in the centrifuged deposit. There was no growth on culture. Excess cystine was present on the amino-acid chromatogram. The blood urea was 349 mg./100 ml., the haemoglobin 5.1 g./100 ml. and the leucocyte 15,000/c.mm. The glucose-tolerance test showed a diabetic type of curve. The electro-

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cardiogram was normal. The renal shadows were not seen on a radiograph of the abdomen. He deteriorated steadily and died of uraemia three weeks after admission. Permission for necropsy was granted only for examination of the kidneys. These were classical polycystic kidneys (Fig. 2), both macroscopically and on microscopical examination.

FIG. 1.—Family tree. The arrow indicates the proband.

Case 2 (III 7).—A sister of the proband, aged 18 at the time of death in 1957, was somewhat underdeveloped physically and mentally, owing, it was said, to meningitis in childhood. She was known to have been blind from birth. She was admitted to Fairfield Hospital for Infectious Diseases, Melbourne, because of vomiting and fever of two days' duration. On the day of admission an epileptic fit occurred, followed by pain and numbness of the lower limbs. Examination showed widespread bruising. Central cataracts and nystagmus, neck-stiffness, hypertonic lower limbs, ankle clonus, and an extensor plantar response were noted. The blood-pressure was normal. She lapsed into coma and died three days later. Proteinuria was present but there was no abnormality on microscopy of the urine. Lumbar puncture revealed evenly blood-stained fluid which clotted. The haemoglobin was 80% and leucocyte count 18,000/c.mm. The blood urea was not done. Necropsy showed a small pituitary adenoma, thickened meninges on the base of the brain, and some gliosis. The kidneys were shrunken and granular and showed medullary cysts. In histological sections much of the medulla was replaced by cysts which were lined by a low cuboidal epithelium (Fig. 3). The cortex showed extensive scarring, cellular infiltration, and hyalinization of most glomeruli. The appearances suggested that the direct mechanical effect of the cysts, together with chronic pyelonephritis, had caused the marked cortical atrophy.

Case 3 (III 8).—Another sister of the proband, aged 18 in 1960, was asymptomatic. She had a history of pyloric stenosis in infancy, and was examined because of renal abnormalities and blindness in the family. She had severe myopia dating from early childhood. Her blood-pressure was 110/70. Other findings were normal. On investigation the urine showed slight proteinuria (30 mg./100 ml.) with 1–2 pus cells per high-power field on microscopy. Blood urea, urea clearance, and urea concentration tests were normal. A radiograph of the chest, an intravenous pyelogram, a full blood examination, and urinary amino-acids were also normal.

Case 4 (III 9).—A brother of the proband, aged 16 in 1960, with no symptoms, was examined because of known renal abnormalities in the family. His vision was normal, his blood-pressure 130/80, and physical examination revealed nothing abnormal. The urine showed slight proteinuria (30 mg./100 ml.), and all investigations mentioned above for Case 3 were again entirely normal.

Case 5 (III 10).—The youngest sister of the proband, aged 14 in 1960, was asymptomatic apart from blindness

dating from birth. There was no nocturia and no history of dysuria or frequency. On examination the blood-pressure was 120/80. There was rotatory nystagmus and she was only able to distinguish hand movements. The eye was hypermetropic and the lens showed no abnormality. There was mild but definite papilloedema in each eye and fine peripheral retinal pigmentation. The vessels showed no vascular sclerosis but were small, indicating an abiotrophic process in the retina. The urine showed intermittent proteinuria (0.5 g./day). Microscopy of centrifuged deposit was normal, as were blood urea (27 mg./100 ml.), urea clearance, and urea concentration tests. The creatinine clearance was 130 ml./min. The haemoglobin was 15 g./100 ml. and the leucocyte count 15,000. Chest radiography and electrocardiogram were normal. The intravenous pyelogram (Fig. 4) showed grape-like clusters of cysts in the region of the medullary pyramids on both sides. The appearances were typical of medul-

FIG. 2.—Polycystic kidneys discovered at necropsy in Case 1. Cut surface of left kidney and outer surface of right kidney are shown.

FIG. 3.—Histological section of kidney from Case 2. Low-power view showing the large cysts which replaced the medulla. A small area of scarred cortex is shown on the left.

lary sponge kidney or cystic disease of the medulla. The renal outlines of a length of 15.5 and 16 cm. in a girl only 5 ft. 1 in. (155 cm.) in height are abnormally large. This raises the possibility of associated polycystic disease as was found in her brother, but no other supporting evidence of this was found.

FIG. 4.—Intravenous pyelogram from Case 5. Collections of small cysts are present, grouped around several calices. These are the characteristic findings in cystic disease of the renal pyramids.

Rest of the Family.—The father and mother and two maternal aunts were examined, and these showed no eye or urinary abnormalities. Intravenous pyelograms in the mother and one maternal aunt were normal. Other members of the family were not available for examination, but there was no known renal disease and certainly no blindness in those shown in Fig. 1. There was no known consanguinity in the family. The chromosomes were examined in the only living child (III 10) in whom cystic renal disease and blindness were present. Only eight mitoses were counted, but the chromosome configuration appeared normal.

Discussion

The renal disease in the five children in this family is apparently of genetic origin. Cystic renal abnormalities were found in the three blind children, but the cause for the proteinuria in the other two is obscure. Investigation was limited because of the need to avoid arousing suspicion in the remaining children that they also had fatal renal disease.

The mode of inheritance in this family is not easily explained. Without further evidence of abnormalities in other members of the family it is not possible to define the mode of inheritance with certainty, and unfortunately most members were not available for examination. There were definitely no other instances of blindness in the members shown in Fig. 1, but it is only possible to exclude renal disease in those examined.

It is difficult to explain an abnormality occurring in all five siblings on any genetic basis. Even with a dominant mode of inheritance one would expect only about half the children to be affected, and as the parents are normal and the grandparents and other members of the family shown in Fig. 1 are probably normal a dominant type of inheritance seems unlikely. Furthermore, one would have to invoke incomplete penetrance in the parents in order to accept this explanation.

If one ignores the proteinuria in siblings III 8 and III 9 and the severe myopia in III 8 one is left with three siblings all of whom were blind and had cystic renal disease. This is more acceptable as the distribu-

tion expected with a dominant pattern of inheritance but it could also be due to a recessive gene, both parents being heterozygotes. There seems to be no means of distinguishing between these two possibilities. A dominant mutant arising in the gonadal cells of one or other parent provides another possible explanation. Hawkins and Smith (1950) described a family in which renal dysplasia occurred in association with a number of other different hereditary abnormalities and attributed these to a single rather versatile gene showing variations in the degree of penetrance. Sorsby (1953) suggests that more than one gene closely associated on the same chromosome could be responsible for Hawkins and Smith's cases. It seems that either explanation may apply to our cases but that there is no way of determining which is in fact responsible.

Cystic renal disease was present in all three blind children. Classical polycystic kidneys, which were found in Case 1, have not hitherto been linked in any way with medullary sponge kidney (cystic disease of the renal pyramids), which was present at necropsy in Case 2 and demonstrated on the intravenous pyelogram in Case 5.

The ophthalmological abnormalities present in this family were of three different types. Cases III 6 and III 7 had central cataract, a lesion which has previously been recorded in association with inherited renal disease (Lowe *et al.*, 1952; Schoen, 1959). In our cases two different types of renal lesion occurred in association with central cataracts. Case III 8, whose only renal abnormality was proteinuria, had severe myopia which may not be related to the other eye lesions but is the only eye lesion which we have found recorded in association with polycystic kidney (Cairns, 1925). The third blind child had yet another abnormality, that of a retinal dystrophy, although her renal lesion was essentially similar to that of Case III 7. Thus there was a confusing combination of renal and eye abnormalities in this family.

Cystic disease of the renal pyramids or medullary sponge kidney is not a widely recognized clinical entity, although it is probably not as rare as the paucity of clinical reports suggests. Most reported cases have been recognized on intravenous pyelograms, and in these the cysts were present in normal-sized or large kidneys (Vermooten, 1951; Mulvaney and Collins, 1956; Lindvall, 1959; Rubin *et al.*, 1959; Ekstrom *et al.*, 1959; Fenna, 1961; Levin *et al.*, 1961; Rowling, 1961). This method of detection automatically excludes cases with poor renal function and the other group of cases such as those described by Smith and Graham (1945) and Hogness and Burnell (1954) which were found at necropsy. In these the kidneys were small and the clinical course had been one of insidious uraemia and anaemia. Case 2 showed the features of medullary sponge kidney associated with renal atrophy similar to the latter group of cases. Typical cysts replaced most of the medulla, and the histology of the renal cortex suggested that the severe atrophy has resulted from a combination of pyelonephritis and the mechanical effects of the cysts compressing adjacent medullary tubules. Similar changes were present in Smith and Graham's (1945) case and in the four cases recorded by Hogness and Burnell (1954).

The family described provides the first link between shrunken kidneys with medullary cysts and the classical large medullary sponge kidney demonstrated radio-

logically which may be compatible with a normal life-span. Although cystic disease of the medullary pyramids is not common the number of reported cases has recently increased sharply, possibly because of the use of improved contrast media in pyelography. Patients may have no symptoms or they may have painless haematuria, recurrent renal infection, or colic due to passage of stones. Small calculi are almost always present within the cysts (Ekstrom *et al.*, 1959) and may give rise to apparent radiological nephrocalcinosis (Pyrab and Hodgkinson, 1960). Grape-like clusters of cysts in the medullary pyramids, as in Case 5, usually show better on intravenous pyelograms but may be filled in a retrograde manner (Ekstrom *et al.*, 1959) thus demonstrating communication with the pelvis, which may be clearly apparent in kidney specimens. The condition may be unilateral and symptoms may be relieved by nephrectomy (Mulvaney and Collins, 1956).

Mechanical pressure from enlargement of cysts, infection, and calculus formation are all potential causes of deterioration in renal function. Very few data are available about renal function in this group. A recent report indicates impairment of tubular function in one patient in whom the glomerular filtration rate was normal (Levin *et al.*, 1961). Possibly the extent to which the medulla is replaced by cysts is the most important factor determining whether the patient will die from uraemia in childhood or have a normal life-span.

The aetiology of medullary sponge kidney has not been established. Its occurrence in association with other congenital anomalies in more than one member of this family strongly suggests that it is an inherited defect. This view receives support from the occurrence of polycystic kidneys in another member of the same family. Polycystic kidneys are known to occur in association with other congenital anomalies, and Hogness and Burnell (1954) reported this association in cystic disease of the medulla.

There is little to support Vermooten's (1951) view that uric-acid infarcts in infancy cause cystic disease of the medullary pyramids.

Micro-dissection studies (Lambert, 1947) revealed that in the adult form of polycystic disease three types of cysts occur—glomerular cysts which are blind, cysts which connect with proximal tubules, and cysts of medullary excretory tubules. Because of the association noted here between polycystic disease and cystic disease of the medulla, it seems possible that the latter condition is a variant of polycystic disease in which only medullary excretory cysts occur.

Clinical episodes of infection, together with pathological evidence of chronic pyelonephritis, suggest that infection may be an important cause of deterioration in function in medullary sponge kidney. Calculi constitute a further potential hazard.

The only surviving blind child in this family has undoubted medullary cysts, and an attempt will be made to prevent recurrent infection and to reduce the risk of calculus formation by maintaining a high urine output. Her abnormally large palpable kidneys suggest that she may have cortical as well as medullary cysts. She gives no past history of symptoms suggestive of infection and has had none over a two-year period of observation since the medullary cysts were diagnosed. Her renal function has shown no evidence of deterioration over this time, and the creatinine clearance is still normal.

Summary

A family is recorded in which all five siblings have proteinuria. Two have died at an early age; one of these had polycystic kidneys and the other had atrophic kidneys with cystic disease of the renal pyramids. One of the three living children has large kidneys with cystic disease of the renal pyramids. All three in whom cystic renal lesions were present were blind from birth.

The clinical and pathological features of cystic disease of the renal pyramids are discussed. One type presents with uraemia and atrophic kidneys, the common type has large or normal-sized kidneys and frequently a normal life-span.

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Proposals have been issued for new regulations on mineral oil in food that the Minister of Agriculture, Fisheries and Food intends to make jointly with the Minister of Health. Similar proposals are being issued by the Secretary of State for Scotland. The proposed regulations would implement the recommendations of the Food Standards Committee's report on mineral oil in food. They would lay down specifications for mineral oil permitted in food, and allow its use on the rind of whole pressed cheeses, and for the sealing of eggs. The remaining provisions of the Mineral Oil in Food Order, 1949, as amended, would remain in force. Copies of the proposals can be obtained from Food Standards Division, Ministry of Agriculture, Fisheries and Food, Great Westminster House, London S.W.1. (Telephone: VICTORIA 8511, Ext. 371). Comments should be forwarded to the Division by May 31.