children of similar age and intelligence. The mild group was easily defined, and from cases attending the clinic, grouped according to the age-groups used for medical inspections, the mild cases were selected. Table III shows these figures.

The percentage of mild cases in each of the three age-groups does not differ greatly as between the sexes, but on the whole it is the girls rather than the boys who seem to have the higher proportion of mild cases. There is nothing here to suggest that severity has a marked bearing on the trend shown and that boys tend to recover because they have milder asthma than girls.

The influence of environment might affect the course of the disease and account for the sex difference. In this country, however, we treat boys and girls very much the same up to the age of 15, and it is difficult to accept that a difference in environment could account for it. It is strange that the sex difference should be slowly abolished as puberty occurs and adult life approaches. If it were due to a hormonal difference the opposite would be expected. It is too difficult and uncertain to attempt to estimate hormonal activity in large numbers of children with the techniques at present available. There must, however, be some explanation for this clearly defined sex difference, which is in keeping with the experience of physicians such as Bray (1937) in this country and Dees (1957) in the United States, who reported that two to three boys attended their clinics for every girl. The phenomenon may provide a clue to some unknown factor in the aetiology of asthma even if we do not know where it leads at present.

Summary

An investigation of the prevalence of asthma among schoolchildren in Birmingham revealed an overall prevalence of 1.76%, which is in keeping with Scandinavian reports. There was a striking sex difference in that asthma was much more prevalent in boys than in girls. This was greatest in the youngest age-group and least in the oldest age-group owing to a falling prevalence in boys while that in girls remained almost stationary. There is evidence that the fall in prevalence in boys continues, so that in early adult life the sex difference is abolished. Although the explanation of the sex difference in the natural history of asthma cannot at present be explained it is thought to provide a possible clue to some important factor in the aetiology which has yet to be discovered.

This survey could not have been undertaken without the help of Dr. H. M. Cohen, the Principal Medical Officer for Schools in Birmingham, and his staff. I am indebted to Miss C. Butt, the school health visitor attached to the asthma clinic, for her help; to Mrs. D. Bailey for secretarial assistance; and to Dr. D. A. Williams, of Cardiff, and Dr. V. H. Springett, of Birmingham, for their encouragement and criticism.

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NEW DATA ON THE PATHOLOGY OF "TRUE SCLERODERMA KIDNEY"

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[WITH SPECIAL PLATE]

Scleroderma, or progressive systemic sclerosis, is known to produce in certain rare cases characteristic morphological changes in the kidneys, accompanied by symptoms of rapidly developing and mostly fatal renal insufficiency.

The morphological pattern—in the proximal part of the interlobular arteries, mucoid intimal thickening with gross reduction in lumen; in the distal part, fibrinoid necrosis involving also the arterioles and a more or less pronounced ischaemic necrosis in the renal cortex—is diagnostically characteristic of scleroderma and constitutes what has been called "true scleroderma kidney" (Calvert and Owen, 1956).

Material and Methods

The discrepancy between the marked morphological changes and the virtual absence of clinical symptoms in the early stages led us to investigate with more sensitive methods the renal function of 25 patients suffering from scleroderma of varying severity. On routine clinical examination these patients showed no sign of renal disorder. We have, however, proved that in 80% of the cases the *para*-aminohippurate (P.A.H.) clearance (indicating effective renal plasma flow—R.P.F.) was reduced, while endogenous creatinine clearance (C_{Cr} , a measure of glomerular filtration) remained normal and the filtration fraction (F.F.) increased. On the basis of the above we assumed that reduced R.P.F. indicates sclerodermal renal involvement much earlier than do ordinary clinical tests (Urai *et al.*, 1958). Rodnan *et al.* (1957) assume renal vascular spasms in the pathogenesis of sclerodermal renal involvement and believe them to be similar to Raynaud's phenomenon.

There can thus be no doubt that the vascular structure of the affected sclerodermal kidney undergoes considerable changes. The histological picture, however, offers information only as to the character of these vascular changes. Morphological examination of the cases reported in the literature and of those in our own experience reveals a more or less severe lesion of all medium and small arteries, while a considerable part of the glomeruli seems morphologically intact.

As histological study does not provide adequate information on the vascular structure of the whole kidney, we sought another method of investigating this problem. This was supplied by Munkácsi's new corrosion preparation method (Munkácsi, 1957), in which a polyvinyl chloride solution is used. This method was utilized by Gömöri and co-workers (1960) to study the circulation of the hypoxic kidney. In their report they give a critical discussion of the technique and application of the method.

Below we describe a case of scleroderma showing no signs of renal involvement at the time of the patient's admission to hospital or in his past history. Acute renal insufficiency developed while he was in hospital, and progressed rapidly, leading to oliguria and death within three weeks.

Case Report

A 56-year-old man, formerly a worker in a sand-blasting shop, was under observation by us from April 14 to his death on June 12, 1959. In 1953 he was found to be suffering from silicosis which developed as an occupational disease. From 1956 onwards he complained of "pains in the joints," and from February, 1959, gradually progressive manifest sclerodermal changes of the skin developed. The histological pattern of a skin biopsy indicated a chronic sclerodermal process (Special Plate, Fig. 1). The patient suffered from dyspnoea on exertion and dysphagia.

Examination on admission (April 14) showed diffuse sclerodermal changes of the skin, silicotic changes in the lungs, signs of moderate cardiac decompensation, and a painful stiffness in the joints of the hands. Blood-pressure, 150/80 mm. Hg. Urine: specific gravity 1026; trace of protein; sediment contained one or two white blood cells; creatinine clearance 76 ml.; non-protein nitrogen 24 mg. per 100 ml. The daily diuresis varied between 800 and 1,600 ml. On April 29 urine analysis showed: specific gravity 1019; trace of protein; one or two white blood cells in the sediment. On May 12 creatinine clearance was 46 ml. and blood-pressure 160/100 mm. Hg. Daily diuresis varied between 900 and 1,100 ml. On May 22 urine analysis showed a specific gravity of 1010; protein 1+; sediment containing two or three white and red blood cells and one or two granular casts. Blood-pressure 220/110 mm. Hg. On May 28 the patient's condition deteriorated suddenly, and he vomited several times a day. Blood-pressure rose to 230/140 mm. Hg and non-protein nitrogen was 45 mg. per 100 ml. He was given a daily infusion of 1,000–1,500 ml. of Ringer's solution, and his daily diuresis was between 900 and 1,600 ml. On June 3 urine analysis showed: specific gravity 1010; protein 2+; sediment two or three white and red blood cells and one or two granular casts. Creatinine clearance 10 ml.; non-protein nitrogen 60 mg. per 100 ml.; blood-pressure 260/160 mm. Hg. The patient became stuporous. On June 5 the non-protein nitrogen was 96 mg. per 100 ml. With infusion of the same quantity of Ringer's solution the daily diuresis was only about 600 ml. The patient had fascicular twitches. On June 9 the total daily diuresis was not more than 360 ml. On June 10 the patient was again stuporous and had Kussmaul respiration. Creatinine clearance 4 ml.; non-protein nitrogen 147 mg. per 100 ml.; daily diuresis 170 ml. On June 11 the daily diuresis fell to 120 ml., and urine findings were: specific gravity 1010; protein 3+; non-protein nitrogen 174 mg. per 100 ml. The blood-pressure also fell suddenly, and the patient became comatose. He died on June 12, having excreted only 80 ml. urine during the day.

Post-mortem Findings

Post-mortem examination confirmed that death was due to sclerodermal renal involvement. The histological picture is in complete agreement with the morphological criteria of "true scleroderma kidney."

In the kidney all subdivisions of the arteries, starting from the origin of the interlobular arteries—occasionally even the arcuate arteries—showed pathological lesions, indicating a combination of productive endarteritis and necrotic panarteritis, endarteritis predominating in the larger vessels. Concentric proliferation of the intima consisted of mucoid connective tissue which stained metachromatically with toluidine blue. In the smaller distal arteries fibrinoid necrosis predominated and extended to a section or the whole of the vascular wall (Special Plate, Fig. 2). Cellular inflammatory reaction, even in and around the most

damaged vessels, was conspicuously slight. The lumen of a number of vessels was almost completely occluded as a result of combined arteritis and thrombosis. In some of the afferent arterioles fibrinoid necrosis could be demonstrated. The glomeruli were generally intact, though in some fibrinoid necrosis of the afferent arterioles had spread to part of the glomerular loops (Special Plate, Fig. 3). Because of vascular obstruction, numerous microinfarcts had developed in the subcapsular region of the renal cortex. Here and there small necroses appeared even in the medullary substance. The epithelium of the tubules showed regressive changes of varying severity and type, probably connected with anoxia: isolated necroses, hydropic hyaline droplets, or fatty degeneration, and epithelial atrophy with severe dilatation of the lumen. Some amorphous bodies were found in the distal channels. There was no noticeable change in the interstices, except a minor inflammatory reaction at the cortico-medullary demarcation.

Corrosion Preparation

A corrosion preparation was made of one kidney by filling it through the renal artery with a 5% polyvinyl chloride solution in a mixture of equal parts of cyclohexanone and acetone, and precipitating the polymer in the vascular system with 20% alcohol. The renal parenchyma was removed by corrosion in concentrated hydrochloric acid.

Owing to its viscosity the 5% polyvinyl chloride solution penetrated no further than the vasa efferens. Hence by this method the interlobular arteries, the arterioles, and the glomeruli—that is, the entire renal vascular system up to the vasa efferens, including the eventually present arteriovenous shunts—are filled, while the post-glomerular capillaries, the thinner vessels of the cortex corticis, and the capillaries of the medullary substance are not. Owing to the lack of transcapillary saturation, normal venous saturation does not occur.

Specimens of various segments of the arterial vascular system obtained in this way were prepared, mounted with Canada balsam on microscope slides, and examined stereomicroscopically. This method enables any lesions in the arterial system and the glomeruli to be determined. For comparison a similar corrosion preparation of a healthy kidney was made in the same way. This allowed the following conclusions on the renal vascular system of the scleroderma kidney to be drawn. All ventral and dorsal branches of the lobes of the renal artery had been well filled. The number of interlobular arteries was less than in the normal kidney, about one-third of them being missing (Special Plate, Figs. 4 and 5). The almost complete absence of glomeruli in the scleroderma kidney—about 98% were missing—was most characteristic. Those that were still visible were mainly at the cortico-medullary zone (Special Plate, Figs. 6 and 7). Though it is not certain that these were in fact juxtamedullary glomeruli, as their efferent arterioles had not been filled, their position nevertheless justified such an assumption. The crowded appearance of the aglomerular arterioles of the interlobular and interlobar arteries (arteriae rectae verae) was also characteristic. It is probable that, as a consequence of the obstructed glomeruli, this represented a dilated system of the vasa recta. In the region of the interlobular arteries in particular, we found a large number of such vascular structures (Special Plate, Fig. 8). A reduction of the lumen in many interlobar and interlobular arteries corresponding to the negative cast of the intimal proliferation on the histological slide (Special Plate, Fig. 9) was also observed.

Discussion

Examination of the corrosion preparation of this scleroderma kidney showed that circulation through the glomeruli ceased not only in the subcapsular region of the kidney—corresponding to the microinfarcts which had developed in this region—but also in practically the entire cortex except for the juxtamedullary layer. This

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FIG. 1.—Skin biopsy showing chronic sclerodermal process.

FIG. 2.—(a) Artery with much-reduced lumen due to productive endarteritis. (b) Artery of same size as (a) with fibrinoid necrosis in its walls, its lumen filled by thrombus.

FIG. 3.—(a) Necrotic afferent arterioles. (b) Fibrinoid necrosis spreading from afferent arterioles to glomerular loops.

FIG. 4.—Photographs (slightly reduced) of corrosion preparations of (A) a healthy kidney and (B) a scleroderma kidney. The poorer vascular system of the scleroderma kidney is evident.

FIG. 5.—Detail of Fig. 4 much enlarged. In the healthy kidney (A) the completely filled glomerular system is clearly visible. In the scleroderma kidney (B) the larger arteries can be seen in the background with a paucity of interlobular arteries and an almost complete absence of filled glomeruli.

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FIG. 6.—Lateral view of interlobular arteries of a normal kidney. Note the complete, well-filled system of glomeruli.

FIG. 7.—Scleroderma kidney, same position and enlargement as Fig. 6. The vascular region contains very few glomeruli and a reduced number of interlobular arteries.

FIG. 8.—Lateral view of a segment of the vascular system of the scleroderma kidney. The arrow indicates the agglomerular vessels.

FIG. 9.—Lateral view of a segment of the vascular system of the scleroderma kidney. The arrows indicate the reductions in lumen of the corrosion preparation corresponding to the intimal proliferations of the interlobular arteries as seen histologically.

is due to the fact that, starting from the interlobular arteries, sclerodermal vascular changes had become so serious in some sections of most vessels as to cause total obstruction of the lumen. One-third of the interlobular arteries were missing, while in the remainder the lumen was so narrowed that the polymer used could no longer fill the majority of the arterioles originating from them. This explains why, with the exception of those at the cortico-medullary zone, only a small percentage of the glomeruli were filled.

In the histological preparations necrosis could be seen wherever the interlobular arteries or their proximal vascular segments had been obstructed. The question now arises: Why did massive tubular necrosis not develop in other regions, though the afferent arterioles and glomeruli were almost completely missing? It is generally accepted that the tubules in the region of the cortex are fed by the post-glomerular capillary system, but in our opinion this discrepancy can be explained by the fact that the post-glomerular plexus receives anastomoses for the maintenance of the circulation from the aglomerular arteries. Apart from the widespread absence of glomeruli, the outstanding feature of the corrosion preparation was just such a marked dilatation of the aglomerular arteries and a relative increase in their number. Although we were unable to demonstrate in the corrosion preparation the presence of an arterio-venous connexion, it might nevertheless be assumed that—because of the obstructed glomeruli—this dilated vasa recta system fulfils in the living organism the role of the secondary opened “functional” shunts. This might partly explain the fact that, as we have shown in previous investigations, the morphological and functional integrity of the tubules is maintained for a relatively long time in spite of the marked reduction in the flow of blood through the kidney (Urai *et al.*, 1958).

While about 98% of the glomeruli are missing in the corrosion preparation, in the histological preparations about 60% are morphologically intact. This discrepancy is probably due to the fact that in many places the obstruction of the afferent vessels is not complete, but they are so narrowed that the polymer used for the corrosion preparation is unable to penetrate them. Such narrowing of the lumen, however, makes it probable that the much reduced transglomerular circulation is no longer sufficient to maintain filtration pressure in the glomeruli. Luminal reduction of the arterial system is obviously extremely rapid, for only this can account for the fact that the quantity of urine excreted decreased within 10 days from 1,000 ml. a day to almost nothing, simultaneously with the reduction of creatinine clearance to 4 ml. and the development of uraemia. The practically complete loss of glomeruli which followed these vascular changes might also explain the patient's rapid deterioration and death.

Death due to characteristic sclerodermal renal involvement is relatively rare, and we have been able to use Munkácsi's method of examining these renal changes in only one case. It was, however, a typical one from both the clinical and histological viewpoints.

Summary

One of the kidneys of a patient suffering from scleroderma, who died from renal failure within three weeks, was examined by Munkácsi's corrosion preparation method. The histological picture corresponded to the morphological criteria of a “true scleroderma kidney.”

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The majority of the interlobular arteries and arterioles were almost completely obstructed, corresponding to the obstructions seen histologically. This resulted in a sharp decrease in glomerular filling. A considerable increase in the number of aglomerular arteries was demonstrated.

On the basis of these findings the connexion between the morphological pattern and the clinical data is discussed.

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A CASE OF RUPTURED UTERUS AND CARDIAC ARREST, WITH RECOVERY

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Rupture of the uterus occurs approximately once in every 1,500 deliveries (Morrison and Douglass, 1945), and usually a definite predisposing factor can be incriminated. This is a potentially lethal condition as shown by the Ministry of Health (1960) report, in which it is stated that 33 patients died in England and Wales as a sequel to ruptured uterus. We feel that the following case is both interesting and unusual because of the uncertain nature of its origin and the rather alarming sequel to its treatment.

Case History

The patient, a married woman aged 27, was expecting her second baby on August 30, 1958. The first child, weighing 6 lb. 6 oz. (2.992 g.), was delivered normally in 1954 after a labour lasting six hours and ten minutes. There had been no complications in the puerperium. In February, 1956, a diagnostic curettage was performed at St. James' Hospital, Balham, for menorrhagia, and the histopathological examination showed “fragments of endometrium displaying chronic inflammatory changes.” There had been no post-operative complications and nothing to suggest that the uterus was perforated at that time. Her menorrhagia had ceased after this procedure. She miscarried, spontaneously, at eight weeks in 1957, and was treated at home. There was no other relevant past history.

Her antenatal care was undertaken by her own doctor (M. K. T.), who first saw her at 22 weeks. He recorded the following: blood-pressure 130/80 mm. Hg, no oedema, urine clear, weight 11 st. 8 lb. (73.5 kg.), height 5 ft. 3 in. (160 cm.), blood group A, rhesus-positive, and haemoglobin 13.5 g./100 ml.

External cephalic version was attempted, unsuccessfully, at the thirty-second week, but a week later spontaneous version had occurred. Two days before term her blood-pressure, which previously had not exceeded the original reading, was 130/90 mm. Hg, and there was slight pretibial