THE HEALING OF RENAL RICKETS

BY

WILFRID SHELDON, M.D., F.R.C.P.

Physician to the Children's Department, King's College Hospital ; Physician to Out-Patients,
The Hospital for Sick Children, Great Ormond Street, London.

Little has been added to the knowledge of the treatment of renal rickets since the paper by Graham and Oakley (1938), and the reader is referred to their work for a summary of the previous literature of this condition. Whether or not in fact rickets is the principal bony lesion has been questioned by Langmead and Orr (1933). From a morbid anatomical study, they concluded that osteitis fibrosa was the outstanding pathological change in the bones, and attributed this to osteoclastic activity caused by excessive parathyroid function. They were able to demonstrate the presence of hypertrophy of the parathyroid glands. Their view has received support in America from such authorities as Park and Eliot (1942), and Hamilton (1940) who considers the hyperparathyroidism to be secondary, and called into being in order to rectify the low blood calcium level so often present in chronic nephritis. It is not the purpose of this communication to discuss the underlying pathological process in the bones, although it may be pointed out that so-called renal rickets may occur with a normal blood calcium, as in the cases reported by Karelitz and Kolomoyzeff (1932), but to place on record the history of a boy with chronic nephritis whose bone changes, characteristic of renal rickets, underwent such complete healing during the eight months prior to his death that histological examination of a radius showed neither rickets nor osteitis fibrosa, ossification appearing to be proceeding in an orderly manner.

Case history

The patient, a boy aged 4½ years, was seen in consultation on April 2, 1942. He was the fifth and youngest child, the parents and older children being healthy. From birth (the newborn period having been apparently uneventful), at intervals of six months, the patient had been subject to attacks of feverishness, vomiting, and drowsiness lasting up to a week, and between attacks he was noticeably listless, suffered from thirst which would cause him to wake twice each night for a drink, and passed large quantities of urine which was at times offensive. He had learned to walk, but during the previous four months bowing of the legs had rapidly progressed, and for the last fortnight he had been too weak to stand.

Examination showed him to be of short stature, and weighing only 31 lb. Although cooperative, he was very apathetic. His mouth and skin were dry, and he appeared severely anaemic. The heart was not enlarged, and the systolic blood pressure was 70 mm. Hg. Apart from the scar of an operation for inguinal hernia, the abdomen was normal, and the kidneys could not be felt. The tonsils appeared healthy. There were no retinal changes. An obvious feature was the coarse tremor of the trunk and limbs during voluntary movements. The boy gave a positive Chvostek sign of latent tetany, but no evidence of active tetany. Signs of rickets abounded; the epiphyses at the wrists and ankles were swollen, the costochondral junctions were beaded, Harrison's sulcus was present, and the left leg was bowed inwards to form a pronounced genu valgum while the right showed an equally severe genu varum. The urine was cloudy, specific gravity 1008, and contained a thin cloud of albumin and a few pus cells; culture gave a growth of *B. coli*.

On the above evidence, a diagnosis was made of renal fibrosis with renal rickets and chronic uraemia. Because of the presence of urinary infection, it was considered that the fibrosis of the kidneys might be associated with some congenital abnormality of the urinary tract, but an attempt to obtain a pyelogram following the intravenous injection of 12 c.c. of perabrodil failed because the kidneys were unable to excrete the drug sufficiently rapidly to give a high enough concentration.

Treatment. The patient was admitted to hospital on April 6, 1942. On admission the serum calcium was 4.6 mgm. per 100 c.c., and the absence of active tetany in spite of so low a calcium level was considered to be due to the acidosis accompanying the chronic nephritis. The alkali reserve was considerably reduced. It was decided to attempt the relief of the uraemia by giving alkalis, but in case this should precipitate active tetany, calcium gluconate (30 grains thrice daily) was given, and this dose was maintained until within a week or so of death. Alkali was given in the form of sodium bicarbonate and sodium citrate, 10 grains of each every four hours. There was some difficulty in getting the child to tolerate this amount, and at first it caused vomiting, but by starting with smaller doses and gradually increasing them, the full dose of 100 grains daily was attained, and persisted with for four months. The dose was then lowered to 60 grains daily for another two months, when, in the face of progressive uraemia and early nephritic

oedema, the alkaline treatment was abandoned. It had incidentally served the purpose of keeping the urinary infection at bay.

In the hope of forcing up the blood calcium, and thus possibly leading to an improvement in the rickets, large amounts of vitamin D were given: 10,000 I.U. of calciferol were given twice a day from the middle of April until the end of October. The effect on the blood calcium was disappointing, the child remaining hypocalcaemic throughout (see table 1), but during this period the bones steadily healed until eventually the x-ray picture became virtually normal. The risk that such big doses of vitamin D, together with calcium orally, might lead to calcification in the soft tissues, was appreciated, and a watch was kept on the kidneys and medium-sized arteries by repeated x-ray examinations, but metastatic calcification did not appear.

Throughout the child's stay in hospital, anaemia was persistent and severe. Monthly blood counts showed the red cell count varying between 2 million and 2½ million per c.mm., the haemoglobin hovering between 40 and 45 per cent. The leucocytes ranged between 7000 and 9000 per c.mm., the polymorphs gradually dropping from 74 per cent. in May to 44 per cent. in August. Treatment of the anaemia by a proprietary iron preparation, to which was later added 1/200 grain copper sulphate, made no impression on the blood count. The kidney function was so defective that blood transfusion was held to be contra-indicated.

The blood calcium, blood phosphorus, phosphatase, and blood urea were repeatedly estimated, and are presented in the following table:—

TABLE 1

Date	Blood calcium: mgm. per 100 c.c. serum	Blood phosphorus: mgm. per 100 c.c. serum	Phosphatase: units	Blood urea: mgm. per 100 c.c. serum
9.4.42	4.6	8.9	62.8	410.0
7.5.42	7.7	—	53.0	150.0
18.6.42	6.8	10.3	62.3	190.0
23.7.42	6.8	13.8	54.3	294.0
23.8.42	6.8	—	—	249.0
15.9.42	5.4	—	—	236.0

Course. A week after admission to hospital, and coincident with the beginning of alkaline therapy, the boy went into an attack of acute uraemia, but recovered under treatment by gastric and colonic lavage. His general condition then improved slightly, and as serial x-ray examinations showed improvement in the degree of rickets, splints were applied to try to correct the deformity of the knees, and special boots were on order in the hope that he might be able to walk. However, he never attained this degree of improvement, remaining in bed throughout his stay in hospital. A month before he died, puffiness of the face appeared, and from then oedema became progressively more severe and widespread, and was accompanied by ascites. Eventually, after eight months in hospital, he died in uraemia.

Post-mortem examination. At post-mortem

examination, both kidneys were much contracted, and their surface granular. The left renal pelvis was thickened and dilated into a small hydro-nephrosis; the right renal pelvis was normal. The parathyroid glands were not examined. The lower end of one radius was examined; the shaft of the bone appeared well calcified, the calcification extending right down to the epiphyseal line, which was straight and even.

Histological examination of the kidney and radius was kindly carried out by Dr. F. M. Creed, and his report was as follows:—'The kidney is badly disorganized. A large proportion of the glomeruli are completely hyalinized, others show various stages in the process. All the glomeruli are comparatively bloodless. In a few there is a dilated glomerular space, but for the most part the tuft fills the capsule and is partially or wholly adherent to it. In many places there has been complete atrophy and disappearance of tubules, elsewhere dilated tubules persist. Interstitial tissue is enormously increased and there is much infiltration with lymphocytes and plasma cells. The vessels show great intimal thickening, often nearly or quite occluding the lumen, and there is medial hypertrophy. The bone shows no evidence of osteitis fibrosa, nor of rickets, and ossification appears to be proceeding in an orderly manner.'

X-ray appearances. In addition to repeated x-ray examinations of the soft tissues in order to detect metastatic calcification, which, as has been stated, did not arise, the wrists and ankles were x-rayed once a month. The first x-ray examination in April, 1942, showed the typical appearance of severe renal rickets; successive films revealed steady healing, until by October, 1942, healing seemed to be complete. The accompanying illustration (fig. 1 and 2) show these stages.

Discussion

Discussion turns on the mechanism which led to healing of the bones in the face of a deteriorating renal lesion. Parsons (1927) has stated that in renal rickets the bones are in a state of flux between alternate healing and relapse, and that this is dependent upon the falling and rising of the blood phosphorus, coincident with the renal function being in a phase of improvement or retrogression; and that in this way healing of the bones may occur in the absence of any particular therapeutic measure. In the case here recorded, during the first three months of treatment, the blood phosphorus estimations showed a steady rise, and in spite of that, the x-ray examination showed progressive improvement in the bony condition, from which it would seem that the healing of the bones in this particular case cannot be explained by the view expressed by Parsons.

Graham and Oakley (1938) treated their two cases with sufficient alkali to maintain a normal alkali reserve, giving the equivalent of 20 gm. and 12 gm. of sodium bicarbonate daily to their respective cases, and they offer an explanation of how this treatment could lead to healing of the bones; but as their patients also had 6000 I.U. vitamin D daily, they were unable to decide whether the

FIG. 1 and 2.—X-ray pictures of wrist (fig. 1) and ankle (fig. 2) showing stages in the recovery of renal rickets.

alkali or the vitamin had been responsible for the recovery. The same dilemma arises in the case here described, although the amount of alkali (100 grains daily for four months and 60 grains daily for a further two months) was much less than that given by Graham and Oakley, while the amount of vitamin D was more than three times as great. To give calcium by mouth would, of itself, be unlikely to improve the state of the bones, although it may possibly have tended to prevent the calcification of the bone ends taking place at the expense of the calcium in the shafts. In spite of the high dose of vitamin D, calcification of the soft tissues did not occur, presumably because a state of hypercalcaemia was never attained.

The two noteworthy features of the case here recorded are the degree to which the bones recovered, and that this occurred in the face of a high and rising blood phosphorus value and a persistent hypocalcaemia.

Summary

The case of a boy aged 4 years with chronic nephritis and renal rickets is recorded, in whom the bones underwent complete healing under treatment with alkalis, calcium and large amounts of vitamin D. The recovery in the bones is regarded as not fortuitous, but it is not possible to decide whether this result came about because of one therapeutic measure alone, or because of the combined therapy.

REFERENCES

- Eliot, M. M., and Park, E. A. (1942). *Brennemann's Practice of pediatrics*, Hagerstown, 1, Chapter 36, p. 1.
- Graham, G., and Oakley, W. G. (1938). *Arch. Dis. Childh.*, 13, 1.
- Hamilton, Bengt. (1940). *Holt's Diseases of infancy and childhood*, New York, 11th edition, p. 705.
- Karelitz, S., and Kolomozyeff, H. (1932). *Amer. J. Child. Dis.*, 44, 542.
- Langmead, F. S., and Orr, J. W. (1933). *Arch. Dis. Childh.*, 8, 265.
- Parsons, L. G. (1927). *Ibid.*, 2, 1.