CHRONIC DIFFUSE NEPHRITIS IN CHILDHOOD

REPORT OF A CASE WITH A REVIEW OF THE LITERATURE *

CARL H. GREENE

ROCHESTER, MINN.

Chronic diffuse nephritis during childhood is a rare condition though of no less interest because of its infrequent character. The possibility of its occurrence was first suggested in 1872 when Gull and Sutton¹ described a case of "contracted kidneys" in a 9 year old girl. Its actual occurrence was confirmed two years later by Barlow² who gave the first complete case report of this condition. Since the time of Barlow, a gradually increasing number of cases have been reported, particularly in England where the name of "renal infantilism" has tended to emphasize the associated general bodily changes, as well as the original kidney lesion. In Germany, likewise, there has been a series of similar case reports. Under these conditions it would seem desirable that the whole field be surveyed, all available cases reviewed, and the findings correlated. This has been attempted in the present paper. The clinical and pathologic findings in an additional case are presented.

REPORT OF CASE

B. M., Harriet Lane Dispensary, No. 24,377; age 4 years, of American parentage. Complaint: "Nervousness, convulsions and vomiting."

Family History.—Unimportant. There was no history of nephritis in either parent. The mother had four miscarriages.

Past History.—Full term child, spontaneous labor. Feeding was difficult during the first year and the gain in weight was slow. She had frequent attacks of bronchitis but no measles, scarlet fever, or other infectious diseases.

Present Illness.—March 7, 1920, an eruption was noticed on the chest. This was called measles by the family physician. By March 14 the eruption had disappeared, but the child was drowsy and vomited solid food. She was thought to have had fever from March 7 to March 14. No change in her condition occurred until March 27, when her eyes became crossed. She was admitted to the Harriet Lane Home, March 28.

* Received for publication, Nov. 26, 1921.

* From the Harriet Lane Home, the Johns Hopkins Hospital.

1. Gull, Sir W. W. and Sutton, H. G.: On the Pathology of the Morbid State Commonly Called Chronic Bright's Disease with Contracted Kidney, *Med. Chir. Tr.* **55**:273, 1872.

2. Barlow, W. H.: Notes and Remarks on a Case of Granular Contracted Kidney (Cirrhosis of the Kidney in a Child of Five Years and Eleven Months), *Lancet* **2**:151, 1874.

Physical Examination.—A very ill child. Temperature 100.8 F.; pulse, 120; respirations, 32. Very drowsy. She had a left sided convulsion shortly after admission. No rash was present but there was a fine scaly desquamation over the back. No general glandular enlargement was present.

Head: Anterior fontanel admitted one finger tip. The frontal bosses were prominent. Eyes negative, no strabismus or nystagmus. Pharynx slightly injected and tonsils hypertrophied.

Chest: Chest showed moderate costochondral beading.

Lungs: The lungs were clear on percussion and auscultation.

Heart: Systolic heave. The point of maximum impulse was in the fifth interspace outside of the mamillary line. A systolic murmur was present at the apex and over the precordium.

Abdomen: Muscle tone was fair. The liver and spleen were not felt. The bladder was distended.

Extremities: Muscular development was poor. Following the convulsion the limbs were flaccid. Slight twitching of the right hand and arm occurred during the examination.

Reflexes: The knee jerks were absent on admission. Later both superficial and deep reflexes were present and bilateral ankle clonus was obtained.

Ophthalmoscopic Examination: There was slight haziness of the nasal portion of both discs with moderate engorgement of vessels.

Lumbar puncture: Clear fluid under an increased pressure was obtained. Tests for globulin were negative; two cells per cubic millimeter.

Laboratory Examination.—Urine: A catheterized specimen was clear, straw colored and acid; specific gravity, 1.018; albumin, positive; sugar, negative; acetone, faint trace; guaiac, negative. Microscopic examination showed frequent leukocytes but no casts.

Leukocytes: 18,200.

Wassermann, negative.

Course in Hospital.—The patient was admitted with a temperature of 100.8 F. Shortly after admission she had a convulsion lasting three minutes and involving the left side of the body. During the convulsion there was twitching of the left eyelid and face, and clonic spasm of the left arm and leg. Chloroform was used to control the convulsion, followed by morphin. Later the child developed hyperpnea and the breath had a sweetish odor. The bicarbonate capacity of the blood serum was 14 volumes per cent. Sodium bicarbonate was given by gavage in 60 grain doses at 8:30 p.m., 11 p. m., and 12 m., and 5 per cent. glucose was administered by Murphy drip. The child remained comatose March 29 with a temperature at noon of 98.8 F. and at 3 p. m. of 105.4 F. Died at 4 p. m.

Report of Necropsy.—Necropsy No. 6,195.* Body was that of a well developed, well nourished, female white child. The serous surfaces of the abdominal cavity were smooth and glistening, there was no excess of fluid. The thoracic organs were normally situated. The pleural cavities showed a smooth and glistening surface and contained no excess of fluid. There was a moderate sized thymus weighing 5 gm.

Heart: The pericardial lining was smooth and glistening. The pericardial fluid was of a clear straw color and not excessive in amount. The heart appeared to be somewhat enlarged. The epicardium was smooth and glistening. The myocardium was of normal consistency and the usual color. The cut surface showed nothing unusual. The wall of the left ventricle was somewhat hypertrophied. The cardiac chambers however were not dilated. The endocardium was smooth and glistening. The valves were normally formed. Those on

3. Necropsy by Dr. J. R. Cash of the Department of Pathology. I am indebted to Dr. Cash for permission to report the pathologic findings in this case.

the right side of the heart were delicate and translucent. The mitral valve was also quite delicate but contained two small patches of atherosclerosis in its center. The edges were slightly thickened but apparently this did not interfere with the function of the valve. The aortic valves were appreciably thickened. Their size had not been reduced, however, and there was apparently no change in their function. In the sinuses of Valsalva there was a definite atherosclerosis which extended a short distance up the ascending arch of the aorta. The coronary arteries were unobstructed and their intima was undamaged. Weight, 100 gm.

Lungs: The right lung weighed 105 gm.; the left, 140 gm. Both lungs were of similar appearance. The pleural surface was smooth and glistening. The upper lobes were quite crepitant throughout. The lower lobes were somewhat less so and contained numerous red elevated circumscribed areas of consolidation. The bronchi showed slightly injected walls and contained a slight amount of mucus.

Spleen: Weighed 20 gm. and measured 9x3x2 cm. It was normal in shape, size and position. The capsule was smooth and glistening and not thickened. On section the cut surface was of a dark mahogany color, quite firm, and did not readily scrape away with the knife. The malpighian bodies were very distinct. The interstitial connective tissue was not increased in amount.

Pancreas: Weighed 25 gm., length 12 cm. It was normal in shape, size, position and consistency.

Liver: Weighed 560 gm. and measured 19x13x4 cm. It was normal in shape, size and position. There were no external signs of scarring or other degenerative changes. On section the liver cut normally. There was no scarring, hemorrhage, necrosis, or fatty change to be made out.

Suprarenals: Weight, together, 7 gm. They were normal in shape, size, position and consistency. On section no unusual changes were seen.

Kidneys: The right kidney weighed 17 gm., the left kidney, 19 gm. The kidneys were quite small and extremely pale. Their surface was marked by many large and small scars giving a rough granular appearance. There were numerous small cysts over the kidney surface. The capsule was stripped with great difficulty leaving a rough torn surface but with no hemorrhages to be seen over it.

On section both kidneys had a similar appearance. The cut surface was extremely pale and of a yellowish-white color. The kidney architecture was not distinct. The cortex was very much thinned, in some places measuring only 2 mm. in thickness. The glomeruli could not be seen. The cortical striations could only be seen in a few areas and here they were quite indistinct and irregular. The pyramids were fairly well developed but the tubules were irregularly arranged. There were no areas of hemorrhage to be seen in either kidney. The pelves were of normal size and their interior surfaces were smooth and glistening. The ureters were normal in all respects.

Pelvic organs: The bladder walls were of normal thickness. The mucous membrane was smooth and glistening, delicate, and everywhere intact.

Brain: The meninges were delicate but presented no adhesions. Externally the brain showed nothing unusual. No exudate was seen at any point on the brain surface.

MICROSCOPIC NOTES

Kidneys: The surface was irregular and numerous old scars could be seen beneath it. The glomeruli showed marked changes. There were many adhesions between the capillaries and Bowman's capsule. Many glomeruli were obliterated or partly obliterated by scar tissue and showed hyalin degeneration. Throughout the kidney substance and especially in the cortex there was a dense infiltration of round cells. Many of these appeared to be lymphocytes but many wandering cells could be seen among them. The tubules were distorted by diffuse scarring and many of them contained blood and polymorphonuclear

leukocytes. Many tubules were compressed or obliterated by the scarring and cellular infiltration. Most of the others were dilated. The pelvis appeared normal though just beneath the pelvic epithelium a slight infiltration of wandering cells was noticed.

Lungs: The alveoli were filled with coagulated fluid. A few red blood cells polymorphonuclear leukocytes and epithelial cells could be seen within the alveoli and small bronchi. The lymph follicles surrounding the bronchi showed some hyalin change in their central portions.

Fig. 1.—Cortex of the kidney showing the well marked interstitial nephritis. The atrophy of the glomeruli, the dilatation of the tubules and the round cell infiltration with scarring are characteristic.

Spleen: The malpighian bodies were very distinct and somewhat enlarged. The sinuses were engorged with blood.

The heart, pancreas, thymus, suprarenals, lymph glands and liver were normal.

Previous reports of chronic nephritis in childhood have varied greatly in value. Many have been simply case histories, without pathologic study of the kidneys. In any case of primary nephritis in childhood the clinical history is of great importance in judging the

nature of the renal lesion. The earlier collections by Sawyer⁴ or Nettleship,⁵ of cases of chronic nephritis in children, were made with but little discrimination. They included practically all cases to be found in the literature at the time. In many of these cases the history clearly indicated the presence of a definite secondary nephritis. In other cases the history was so defective that the possibility of a secondary nephritis could not be excluded.

Fig. 2.—Glomerulus showing the atrophic condition of the tuft. The partially dilated tubules and the round cell infiltration are also shown.

All cases with a history of scarlatina must be excluded rigidly in any critical study of primary nephritis in childhood, though there is no similarity between the clinical picture of a chronic diffuse

4. Sawyer, J. E.: The Etiology of the Granular Kidney of Childhood, *St. Thomas Hosp. Rep.* **35**:459, 1906.

5. Nettleship, E.: On Renal Retinitis in Young Subjects and on the Relative Frequency of Juvenile Interstitial Nephritis in the Two Sexes, *Roy. Lond. Ophth. Hosp. Rep.* **16**:1, 1904.

nephritis and a postscarlatinal nephritis. Syphilis likewise must be excluded as chronic renal change is occasionally found in the congenital syphilitic.

In the present report these criticisms have been kept in mind and an effort has been made to present only those cases in which the histories show a more or less uniform clinical picture. In most instances the symptomatology can be traced from the first year of life if not actually from birth. An effort has also been made to rule out preceding infections that might play a rôle in the development of the nephritis. With the exceptions noted in the abstracts, all cases with histories of scarlatina or syphilis have been carefully excluded. In addition a complete pathologic report with a description of the renal changes has been felt desirable, owing to the confused state of the nomenclature in renal pathology. Furthermore, with increasing age the history becomes of progressively less value in excluding conditions which may be the determinants of the later nephritis. This study, therefore, was arbitrarily limited to children under 10 years of age.

A search of the literature has revealed the reports of nineteen cases meeting the requirements mentioned. Reference should also be made to eight other cases of apparently the same condition, but in which the reports lack completeness.

REVIEW OF LITERATURE

1. *Cases of chronic diffuse nephritis with reports of the complete clinical and pathologic findings.*

WEIGERT, 1879.⁶—A 6 weeks old infant. The clinical pathological findings in this case included cyanosis, congenital fusion of the pulmonary valve leaflets, hypertrophy of the right ventricle and an open ventricular septum.

Further evidences of congenital disturbance were found in the kidneys which measured 1.7 x 1.0 x 0.5 cm. and 2.0 x 1.1 x 0.4 cm., respectively. The kidney substance was pale with the cortex greatly decreased on both sides and with many small cysts on the surface of one kidney. Microscopically the kidneys showed numerous shrunken patches with increased interstitial tissue adjoining well preserved kidney substance. The epithelium of the malpighian corpuscles was large-celled and showed fatty changes.

DEMOCH, 1902.⁷—Boy, aged 2 months. Apparently well for the first month and then was brought to the hospital for cough and laryngospasm. Physical examination showed distinct edema, especially at the ankles, an enlarged heart and palpable spleen. The urine contained albumin together with fatty and hyalin casts. Postmortem examination showed generalized anasarca, cardiac hypertrophy with dilatation, pulmonary edema with lobular pneumonia and visceral congestion.

Kidneys of equal size, 5.0 x 3.0 x 2.5 cm. The consistency was increased and the capsule stripped with difficulty leaving a rough granular surface. Two

6. Weigert, C.: Die Brightsche Nierenerkrankung vom pathologisch-anatomischen Standpunkte. Sammlung Klinischer Vorträge (Volkmann). **162**: 163:1460, 1879.

7. Democh, I.: Genuine Schrumpfniere im Säuglingsalter. Arch. f. Kinderh. **33**:283, 1902.

pinhead sized cysts were present on the surface of the left kidney. On section the cortex was from 3 to 4 mm. in thickness and yellowish brown in color. Microscopically the tunica albuginea of the left kidney was thickened and closely attached to the cortex. The glomeruli were of varying size but were not contracted and the capsule was not thickened. In the convoluted tubules the epithelium was swollen but the nuclei were distinct. The interstitial tissue in the cortex of this kidney showed no increase. The medullary rays were distinguishable to the periphery of the cortex and showed an increased nuclear content though there was no increase in connective tissue. In most of the tubules the epithelium was swollen, filling the lumen, though there were some dilated tubules filled with hyalin material. The vessels showed an indefinite slight thickening of the media and adventitia. A few small hemorrhages were present between the cortical convoluted tubules.

Compared to the left kidney the right showed an increase in interstitial tissue. Many of the glomeruli were contracted and the cortex contained many small cysts arising from degenerated or destroyed glomeruli. The convoluted tubules were dilated and their epithelium was degenerated. The medullary substance was mottled with the heaping up of fresh connective tissue rich in blood vessels and showed occasional hemorrhages. The process had more of a parenchymatous character than that in the left kidney.⁸

HELLENDALL, 1897.¹⁰—Girl, aged 6 months. This child, the younger of two similarly affected sisters, was weak and sickly from birth. She died at the age of 6 months from infantile atrophy following measles. Necropsy showed bronchopneumonia and enteritis.

The kidneys were very small but of similar size, $3.3 \times 2.0 \times 0.6$ cm., and weighed 4.0 gm. each. The surface was hyperemic and distinctly granular. The cortex was pale yellowish, the medulla cyanotic. A pea-sized cyst was present on the surface of the right kidney. The intracapsular space in the glomeruli was wide and the tufts small and shrunken. The glomeruli varied greatly in size, those lying near the surface showing marked changes with thickened capsules and degenerated loops. The nearer the glomeruli to the medulla the larger and less changed they were. There was cystic dilatation of the convoluted tubules with flattening of the epithelium. The larger arteries also showed thickening of the adventitia. In addition to the interstitial changes, Heliendall describes five chondromata in the renal cortex.

FRÖLICH, 1904.¹¹—Girl, aged 15 months. The parents of this child were well but a maternal uncle died of chronic nephritis, and an older sister born two years previously was similarly affected. Symptoms were first noted at

8. In her discussion of this case Democh pointed out the difficulty in differential diagnosis between a primary and secondary nephritis. She thought the nephritis was of congenital origin though there was a possibility of its being secondary to the preceding gastro-enteritis. Borrmann⁹ in a later discussion of this case dismisses the possibility of gastro-enteritis as a cause of the nephritis and because of the unilateral character of the nephritis considers it secondary to an ascending pyelocystitis. There was no evidence at necropsy of such a condition. In view of the fact that the child was apparently well up to the onset of the gastro-enteritis at the age of one month and died 4 weeks later, the author agrees with Democh in considering the nephritis as of probable congenital origin.

9. Borrmann, R.: Harnapparat. In *Handb. d. allg. Pat. u. path. Anat. d. Kind.* (Brüning-Schwalbe) Wiesbaden. 2:227, 1913.

10. Heliendall, H.: Hereditäre Schrumpfnieren im frühen Kindesalter. *Arch. f. Kinderh.* 22:61, 1897. (Case 2.)

11. Frölich, T.: To tilfælde af hereditær, familiaer, kongenital (?) nefrit. *Norsk. Mag. f. Laegevidensk.* 5:905, 1904; abstracted in *Jahrb. f. Kinderh.* 64:244, 1906. (Case 2.)

two weeks. The infant did not gain in weight and albumin and casts were found in the urine. Later the child developed periodic attacks of vomiting. At necropsy hypertrophy of the left ventricle and pneumonia were found.

The kidneys were small, weighing right 18 gm. and left 17 gm. The surface of the right kidney showed fetal lobulation but was smooth. The left was slightly granular with shrunken contracted areas on the surface. The left kidney showed slight dilatation of the pelvis and the first portion of the ureter. Sections of the most normal kidney showed an extensive degeneration of the tubular epithelium. Some of the tubules were filled with hyalin casts. The glomeruli in the deeper layers of the cortex showed beginning contracture with slight changes in the surrounding stroma. The stroma was normal throughout the rest of the parenchyma. Single dilated tubules were present in the superficial layers of the medulla. Sections from the more contracted kidney showed a striking increase in the stroma with clumps of round cell infiltration. In these areas the glomeruli were atrophic and contracted and occasionally showed hyalin degeneration. The tubular epithelium was degenerated and single tubules were dilated and filled with a granular coagulum. There was a general thickening of the stroma with areas of round cell infiltration and connective tissue increase.

PATERSON, 1920.¹²—Boy, aged 1 year and 9 months. This boy was apparently well at 11 months, though undersized. He refused solid food. Rachitis-like deformity appeared at this time and progressed to an extreme degree. For six months previous to admission he had irregular attacks of vomiting associated with loss of weight, so that he only weighed 10½ pounds when first seen. Uremia and death followed a change to a solid diet with meat.

The left kidney was extremely small and cirrhotic. The right kidney was slightly larger but was also abnormal. Its condition suggested an old inflammation. The weight of the kidneys was 27 gm. each. Microscopically they showed a marked degree of fibrosis, the kidney substance in some areas being entirely replaced by fibrous tissue. Many of the glomeruli were obliterated and in some places the tubules showed enlargement as though in an early stage of cyst formation. The arteries were greatly thickened.

HELLENDALL, 1897.¹³—Girl, aged 2 years. An older sister of the other child reported above.¹⁰ She likewise was weak and sickly from birth. Backwardness in development was marked and at the age of two she could neither walk nor talk. Marked rachitic deformity was present. Besides the defective development it was noticed that she drank a great deal, especially at night. In addition she had occasional attacks of vomiting and of swelling of the feet. No cardiac hypertrophy was observed at necropsy following death from bronchopneumonia.

The kidneys were very small, of about the same size, 4.0 x 2.5 x 0.7 cm. and weighed 6 gm. each. The surface was granular with yellow flecks. Pinhead sized cysts were seen on the surface of the left kidney. The glomeruli were irregular in size, some normal, some enlarged with a cellular increase, and still others shrunken, poor in cells and surrounded by a fibrous ring. The convoluted tubules are in part slightly, in part markedly dilated. Fatty metamorphosis was present in the convoluted tubules. Around the glomeruli the interstitial tissue was arranged in broad fibrous bands while in other parts it was less well developed, more wavy and richer in nuclei. In the medulla there was a marked increase in connective tissue between the tubuli recti which were crowded together, but they did not show as marked a change as in the cortex. The increase in connective tissue was a diffuse and not a localized process. The blood vessels showed nothing unusual.

12. Paterson, D. H.: Three Cases of Renal Dwarfism Associated with Curious Bony Changes, *Proc. Roy. Soc. Med.* **13**: Sect. Dis. Child., 107, 1920 (Case 2).

13. Hellendall, H.: *Arch. f. Kinderh.* **22**:61, 1897 (Case 1).

HEUBNER, 1913.¹⁴—A 3 year old child. Heubner reports that in all of his experience he only saw one case of "Schrumpfniere" in the strictest sense of the word. His original report could not be obtained but in this later abstract he reports a case of idiotic child of a father suffering from lead poisoning. There was no edema. The pulse was irregular. The urine showed marked albumin and many granular casts. Section showed an enormous contraction of both kidneys with diminished amount of parenchymatous tissue and dilated tubules.

MILLER AND PARSONS, 1912.¹⁵—Girl, aged 3 years and 6 months. She was pale, cyanotic and wasted, being markedly underdeveloped and weighing but 16 pounds. Clinically, polyuria and polydipsia had been noticed as well as the occasional presence of a variable degree of edema. The urine had a specific gravity of from 1.001 to 1.004 with a trace of albumin, but no casts. At necropsy there was slight hypertrophy of the left ventricle.

The kidneys each weighed approximately 30 gm. The changes in the kidneys were described as being the same as those in the 6 year old girl described by the same authors.

OFFENHEIM, 1891.¹⁶—Boy, aged 4 years. Polyuria was the first symptom noticed and was observed early in life. Later headache and nausea were present. In the hospital the child was feverish, vomited a great deal, and complained of headache. His appetite was poor and feeding was difficult, with the result that his weight fell from 11.9 to 9.6 kilos. At the same time he developed diarrhea and great thirst. No edema was noticed. Dimness of vision was complained of shortly before death but no ophthalmoscopic examination was made. He died in uremic convulsions. Necropsy showed congestion and massive edema of the lungs. The heart was not enlarged.

The left kidney measured 7.5 x 3.0 x 2.5 cm. Weight, 43.7 gm. The right measured 7.0 x 3.5 x 2.5 cm. Weight, 48.6 gm. Fetal lobulation was present in both. The capsule was more firmly adherent than normal, the surface granular, and the cortex decreased in thickness. The microscopic picture was that of beginning contraction. Wedge shaped contracted areas were present, apparently rich in glomeruli because of atrophy of the interlying parenchyma. In part, the glomeruli were shrunken, with thickened capsules and cellular proliferation, or complete degeneration of the tuft. The tubules were compressed by the proliferation of the interstitial tissue. In places the tubules showed varying degrees of atrophy and there were many dilated tubules containing hyalin masses. The interstitial tissue was luxuriant, in some places more so than in others. The process was evidently only beginning, for nowhere was there heavy, fibrous scar tissue. The vessels showed distinct thickening, especially of the adventitia.

BARLOW, 1874.²—Girl, aged 5 years, 11 months. This child was always weak and delicate. She developed enuresis when about 4 years old and was later observed to have polyuria, passing from 3 to 4 pints of very pale urine daily. The specific gravity varied between 1.010 and 1.015 but albumin was only found shortly before death. No casts were found. The child died in uremic convulsions. Cardiac hypertrophy was present.

The kidneys measured 5.0 x 3.7 x 1.2 and 5.6 x 3.5 x 1.5 cm. and weighed 13.7 and 23.0 gm., respectively. A few small cysts were present in the right kidney. The microscopic examination was necessarily incomplete owing to

14. Heubner, O.: Ueber chronische Nephrose im Kindesalter. *Jahrb. f. Kinderh.* **77**:1, 1913; abstracted from *Festschr. f. von Leuthold (Berlin)* **1**:351, 1906.

15. Miller, R., and Parsons, L.: Renal Infantilism, *Brit. J. Child. Dis.* **9**:289, 1912 (Case 5).

16. Oppenheim, A.: Ueber Schrumpfniere im Kindesalter. *Inaug. Dissert.*, Halle. 1891.

the rudimentary development of histological technic at the time, but sections showed a general fibrous tissue overgrowth and vascular sclerosis.

MILLER AND PARSONS, 1912.¹⁷—Girl, aged 6 years. She weighed 2 pounds at birth and was always small, backward and underdeveloped. Though six years old she was only 36 inches tall. She had suffered from polyuria, nocturia, and thirst for the greater part of her life and was admitted to the hospital in uremic convulsions. There was very slight hypertrophy of the left ventricle found at necropsy.

Both kidneys were small, weighing together 32 gm. and measuring 4.3 and 4.75 cm. in length and 3.0 cm. in breadth. The capsule was slightly thickened but stripped easily leaving coarsely granular surface. The cortex was greatly diminished, from 4 to 6 mm. in thickness. Histologically, the glomeruli varied greatly in shape and size. A few were completely sclerosed. Others showed fibrotic changes with capsular adhesions. The condition in the tubules was apparently secondary to the interstitial change. The tubules were irregularly dilated and some appeared to be cystic. The epithelium was healthy, however, except for flattening from pressure. There seemed to be no active parenchymatous changes. The interstitial tissue was much increased. The new formed connective tissue was cellular and many accumulations of small round cells were present. The vessels were moderately thickened.

PARSONS, 1911.¹⁸—Girl, aged 6 years and 6 months. Was brought in complaining of "drinking diabetes." She was a very much underdeveloped child with moderate edema of her legs and face. The urine was large in amount, pale, specific gravity 1.010 and with a trace of albumin but no casts. Death was from bronchopneumonia. Necropsy showed definite hypertrophy of the heart.

The kidneys were extremely small and together weighed less than 30 gm. Their capsules stripped readily leaving granular surfaces. The cortex was diminished. Microscopic examination showed extensive general fibrosis of cortex and medulla. The glomeruli varied in size, some being larger and others smaller than normal, and many exhibited some degree of fibrosis. Some showed hyalin changes. The epithelium of the tubules was normal in some areas, but in others was granular and desquamating. Some of the tubules also showed dilated or cystic lumina. The degree of fibrosis varied, being more dense in some areas than others, and was extremely cellular in places. The vessels showed thickening of the middle and outer coats and in some the lumina were nearly occluded. "The whole condition exhibited a degree of fibrosis as marked as, or more marked than ever obtained in the most advanced cases in adults."

JACOBS, 1913.¹⁹—Girl, aged 7 years. This patient had had scarlatina four weeks before her admission to the hospital. Nine days before admission she developed edema of the eyelids and a marked albuminuria. Death was from bronchopneumonia. Postmortem examination revealed a generalized anasarca, pulmonary edema, bronchopneumonia and cardiac hypertrophy.

The kidneys were small and firm with somewhat adherent capsule. The surface was irregular with coarse greyish granulations. They measured 5.5 x 4.4 x 2.2 and 5.1 x 3.2 x 2.2 cm. and weighed 29 and 27 gm., respectively. On section the cortex was narrow, the markings indistinct and the glomeruli visible. Microscopically, the glomeruli were enlarged, arranged in clumps, and surrounded by a cellular infiltration. There was no hyalin change. The interstitial tissue was everywhere increased. Atrophic tubules were present in the

17. Miller, R., and Parsons, L.: *Brit. J. Child. Dis.* 9:289, 1912 (Case 2).

18. Parsons, L.: *Infantilism Associated with Chronic Interstitial Nephritis*, *Brit. M. J.* 2:481, 1911.

19. Jacobs, C.: *Ueber Granularatrophie der Nieren im Kindesalter*. *Berl. klin. Wchnschr.* 50:2418, 1913 (Case 1).

subcapsular layers while in the deeper layer there were groups of normal or dilated tubules without an increase in the intervening stroma. Small focal masses of lymphocytes were strewn through the whole tissue, especially in the neighborhood of the glomeruli. The epithelium in the dilated tubules was large, swollen, and granular with desquamated cells or masses of coagulum in the lumen of the tubules. The walls of the smaller vessels were normal but the smaller arteries showed a thickened media.²⁰

MILLIGAN, 1902.²²—Boy, aged 7 years. This patient was an underdeveloped anemic child who had been weakly since birth. He suffered from polyuria and nocturia. Headaches and dimness of vision developed later. The specific gravity of the urine was 1.006 with a large amount of albumin present. Hyalin and granular casts were found in the terminal samples. His condition rapidly became worse with polyuria up to four pints a day and with increasing quantities of albumin. The headaches became more marked and ophthalmoscopic examination showed typical albuminuric retinitis. Edema developed as a sequel to cardiac dilatation and collapse. Necropsy showed moderate cardiac hypertrophy. In this case there was dilatation of the right pelvis and ureter without apparent cause.

The kidneys were granular. The right kidney was smaller than the left. A section from the left kidney showed the condition to be an advanced interstitial nephritis. The renal tubules were in places completely obliterated by fibrous tissue. Some of the tubules were devoid of their epithelial lining though the epithelium was present in others. The blood vessels showed great thickening of their walls.

GUTHRIE, 1900.²³—Girl, aged 7 years. Was weakly as an infant but except for diarrhea and measles had never been sick previous to coming under Guthrie's observation. Two months previous to entering the hospital she began to complain of frontal headaches and to suffer from attacks of vomiting. She was a thin, undersized girl. No edema was present. The heart was enlarged and the brachial arteries were palpable. The urine had a specific gravity of 1.010 and contained albumin. Granular casts were occasionally present. The patient developed a hemiparesis with convulsions and died in coma. Necropsy revealed a left ventricular hypertrophy, arteriosclerosis and two cerebral hemorrhages. The left kidney weighed 40 gm., the right 112 gm.

Both kidneys were distorted, puckered and shapeless. The capsules were partly adherent and the distortion was marked in these areas. The kidneys were coarse and tough on section. Little apparent distinction was present between the cortex and medulla, but where it could be identified the cortex was atrophied. Microscopically the capsules of the glomeruli in many places were thickened and surrounded by a recent inflammatory infiltration. Some of the glomeruli were only represented by patches of opaque hyalin material. In some places the epithelium seemed healthy but for the most part it was granular. There was a general diffuse increase of interstitial tissue. In parts

20. The case reported by Croke²¹ would suggest that a chronic nephritis may develop very rapidly (two months) following scarlatina. In this case, however, only one half of that period had elapsed and the pathological picture was very suggestive of an advanced process. The changes in the arteries, and the cardiac hypertrophy would further suggest that in this case the kidney condition antedated the attack of scarlet fever. Such a view, however, would not interfere with the hypothesis that the scarlatina precipitated an acute nephritis that was responsible for the fatal outcome of the case.

21. Croke, G.: Discussion, *Lancet* 1:1179, 1890.

22. Milligan, W. A.: A Case of Chronic Interstitial Nephritis in a Boy Aged Seven Years, *Rep. Soc. Study Dis. Child.* 2:99, 1902.

23. Guthrie, L.: A Case of Chronic Interstitial Nephritis in a Girl Aged Seven Years, *Rep. Soc. Study Dis. Child.* 1:69, 1900.

of the supporting stroma there were disseminated patches of cellular infiltration supervening on a fibrosis of old standing. The arterioles were patent yet all their coats showed considerable hypertrophy and in some the lumen was almost occluded. The pelvis of the left kidney was dilated, but not the ureter, and there was no obstruction of the latter. Guthrie considered the condition of the kidneys to be a diffuse interstitial nephritis, both of long standing and of apparently recent date.

PATERSON, 1920.²⁴—Girl, aged 7½ years. She was a premature infant and had never thrived. Paterson reported this case with especial reference to the bony changes which were extreme. The wrists were bent from birth. The legs were contracted so that walking was impossible. Though over 7 years of age the height was but 34 inches. The urine contained a trace of albumin but no casts. The phenolsulphonaphthalein output was low. Following operation the patient became comatose, developed suppression of the urine and died. The kidneys weighed 45 gm. each. The kidneys were cirrhotic, their capsules stripped with great difficulty and on section several small cystic spaces could be seen. Microscopically, there was a marked increase in fibrous tissues throughout the kidney with a tendency to cyst formation. The tubules were greatly enlarged and filled with colloidal material. The glomeruli were fibrosed in places.

ARRAGA, 1904.²⁵—Boy, aged 9 years. The history of this case was quite typical in that the mother noticed great thirst almost from birth. When about 4 years old the boy began to have attacks of weakness and palpitation on exertion. Headaches became frequent and later almost constant. The polydipsia and polyuria also increased though no volumes were recorded. The patient also suffered from a generalized neuralgia from the time he first walked at the age of 18 months. It was this neuralgia, called rheumatism, that led to his coming under Arraga's care. Slight edema of the ankles developed shortly before admission and the patient died following a 48-hour suppression of urine. No urinalysis was obtained. The necropsy findings other than in the kidneys were not reported.

The kidneys were greatly decreased in volume, weighing 25 gm. The right showed fetal lobulation. The capsule was detached with difficulty leaving a granular surface. The cortex was very much diminished in thickness and the cut surface showed small pinhead cystlike cavities. Histologically, the capsule was thickened with small masses of round celled infiltration among its fibers. The capsules of the glomeruli were thickened, and in some glomeruli the intracapsular space was obliterated. In many glomeruli there was proliferation of the cells of the tuft and in others it was completely converted into a fibrous block with some round cell infiltration. The convoluted tubules showed swelling of the epithelium. Many tubules contained hyalin casts. The loops of Henle had undergone changes similar to those in the convoluted tubules. The arterioles were unchanged for the most part but some showed an obliterative endarteritis.

This case is of interest because of the fact that the mother suffered from malaria during pregnancy and took large doses of quinin during that time. Arraga reports the case as one of congenital malaria but gives no details other than a statement of this parental infection. This circumstance would undoubtedly have to be kept in mind in considering the possible congenital origin of the nephritis.

NAISH, 1912.²⁶—Boy, aged 9½ years. Infantilism was marked, for while this boy was 9½ years old his apparent age was but four. Polydipsia had been

24. Paterson, D. H.: *Proc. Roy. Soc. Med.* **13**:107, 1920 (Case 3).

25. Arraga, A.: *Néphrite interstitielle chez un enfant. Manifestée dès la naissance, mort à neuf ans*, *Arch. de méd. d. Enf.* **7**:285, 1904.

26. Naish, A. E.: *Infantilism with Chronic Interstitial Nephritis*, *Brit. J. Child. Dis.* **9**:337, 1912 (Case 1).

noticed since weaning. The urine was pale and albumin and casts were irregularly found. The boy died in a semi-comatose condition with a partial suppression of urine. Necropsy showed moderate enlargement of the heart.

The kidneys were small, together weighing 31 gm. The surface was irregular but not granular. The capsule was partially adherent. One or two small cysts were present. The cortex was diminished. The glomeruli showed considerable change with thickening of Bowman's capsule and occasional fibrous contracture of the tuft. The convoluted tubules were dilated, especially toward the surface. Some of them formed cysts. The collecting tubules showed little change. The interstitial tissue was greatly increased, and near the surface it was markedly cellular. The arteries were slightly thickened.

GLASER, 1918.²⁷—Girl, aged 10 years. This girl was idiotic, as was also an aunt. The mother died in childbirth of chronic nephritis. A sister died at the age of 2½ years from renal disease. The exact time relationship of these two occurrences to the patient's history was not given. In the reported case polyuria and polydipsia were noted at the age of 15 months. At this time albumin was found in the urine and a diagnosis made of nephritis. The development was greatly retarded both mentally and physically. The mental age when admitted into the clinic was about 3 years and the physical development was not much further advanced. The urine was pale, daily volume, 2,000 c.c.; specific gravity, 1.005, and it contained albumin, 0.25 gm. per liter. Hyalin and granular casts were present. The blood pressure was 100 mm. The arteries were palpable and the heart enlarged. Ophthalmoscopic examination showed albuminuric retinitis. The patient was admitted with diphtheria and died from cardiac failure though there were evidences of impending uremia at the time of death. At necropsy the wall of the left ventricle was thickened and the mitral valve leaflets contained two white plaques. Pulmonary edema, hyperplastic splenitis and enteritis were also found.

Both kidneys were greatly shrunken and the surface was wholly granular. Microscopic examination showed the kidney cortex infiltrated with fibrous scar tissue that was relatively poor in nuclei, hyalin, sclerotic, and of a nodular character. In this scar tissue were atrophic tubules, at times showing evidences of repair. The tubules, in part, were widely dilated and the lumen filled with albuminous material. Well recognized glomeruli were only found in a few areas. Some were completely transformed by scar tissue. Some of the glomeruli were completely destroyed, some showed proliferation of the epithelium. Both in the cortex and in the boundary between cortex and medulla there were many small round cell changes. In the medullary rays the interstitial tissue was diffusely increased, the tubules dilated and the lumina filled with masses of casts. In the larger arteries there was a distinct thickening of the walls while the smaller arteries showed greatly thickened walls with narrowed lumen.

2. *Cases of probable chronic diffuse nephritis in which the complete clinical and pathological findings were not reported.*

FRÖLICH, 1904.²⁸—Girl, aged 11 months. A sister of the other case reported by Frölich.¹¹ The parents of these children were well but a maternal uncle died of chronic nephritis. This child was apparently well at birth but failed to gain and later developed irregular attacks of vomiting. At the age of 4½ months albumin and casts were found in the urine. The child died from pneumonia at 11 months. (There was no examination of the kidneys but the younger sister showed typical changes.)

27. Glaser, F.: Ueber juvenile primäre Schrumpfnieren, *Jahrb. f. Kinderh.* 87:95, 1918.

28. Frölich, T.: *Norsk. Mag. f. Laegevidensk.* 5:905, 1904 (Case 1).

CHRONIC DIFFUSE NEPHRITIS IN CHILDHOOD. TABULATION—

Case	Sex	Age	Family History	General Development	Rachitis	Urinary Findings			
						Polyuria	Specific Gravity	Albumin	Casts
1. Weigert ⁶	..	6 wks.							
2. Democh ⁷	♂	2 mos.	Negative.....	Normal during first month				+	Fatty and hyalin casts
3. Hellendall ¹⁰	♀	6 mos.	Mother and sister had nephritis	Always weak; died of atrophy		Not observed			
4. Frölich ²⁸	♀	11 mos.	Uncle and sister had nephritis	Did not gain in weight well				0.6 gm. per L. found at 4½ mos.	Found at 4½ mos.
5. Frölich ¹¹	♀	15 mos.	Uncle and sister had nephritis	Did not gain in weight or do well after first two weeks				Found at 2 wks.	Negative
6. Paterson ¹²	♂	17 mos.		Never took solid food; small and weak; underdeveloped; weight, 10½ lbs.	Extreme rachitis				
7. Hellendall ¹³	♀	2 yrs.	Mother and sister had nephritis	Weakly from birth; never walked or talked	Rachitis marked	Drank much especially at night			
8. Sawyer ²⁰	♂	2 yrs. 5 mos.	Negative.....			Polyuria and polydypsia 33 oz.	1.002	+	Negative
9. Heubner ¹⁴	..	3 yrs.	Father had lead poisoning	Was idiotic.....				+	Granular casts
10. Sequeira ³⁰	♂	3 yrs.	Negative.....	Undersized and anemic, weight 16¾ lbs.	Rachitic	Noticed at 8 mos., 20-40 oz.	1.010	Trace	Negative
11. Miller and Parsons ¹⁵	♀	3½ yrs.	Negative.....	Markedly underdeveloped, weight 16 lbs., anemic		Polyuria and polydypsia	1.001-04	Trace	Negative
12. Author's case.....	♀	4 yrs.		Did not gain well during the first year	Slightly rachitic		1.018	+	Negative
13. Oppenheim ¹⁶	♂	4 yrs.		Weighed 26 lbs.	Rachitic	Polyuria noticed in early life			
14. Morel-Lavelle ⁶³¹	♂	5½ yrs.	Negative.....	Was not well after 18 mos., lost weight	Rachitic			+	
15. Barlow ²	♀	5 yrs. 11 mos.		Always weakly and delicate		Noted at 4 years, 3-4 pints	1.010-15	Found only just before death	Negative
16. Miller and Parsons ¹⁷	♀	6 yrs.		Small, backward and underdeveloped, length 36 in.		Polyuria and polydypsia			
17. Goodhart ²²	♂	6 yrs.	Cousin similarly affected	Underdeveloped, weighed 31½ lbs.		Polydypsia noted since weaning	1.005	Trace	Negative
18. Parsons ¹⁸	♀	6½ yrs.		Very much underdeveloped		Complaint was "drinking diabetes"	1.010	Trace	Negative
19. Jacobs ¹⁰	♀	7 yrs.						+	
20. Milligan ²²	♂	7 yrs.		Weakly from birth, underdeveloped and anemic		Polyuria and micturia 4 pints	1.006	++	Found in terminal stage
21. Guthrie ²³	♀	7 yrs.	Mother had six miscarriages	Was weakly as an infant			1.010	Large amounts in late stage	Occasionally present
22. Paterson ²⁴	♀	7½ yrs.	Negative.....	Premature, bone deformities present from birth, length, 34 in.	Marked rachitis			Trace	Negative
23. Arraga ²⁵	♂	9 yrs.	Mother had malaria during pregnancy			Polyuria noted			
24. Naish ²⁶	♂	9½ yrs.		Small and infantile from birth, apparent age 4 years	Late rachitis	Polydypsia noted on weaning		Irregularly present	Irregularly present
25. Förster ²⁴	♂	9½ yrs.	Sister similarly affected, father luetic	Small and underdeveloped, weight 39 lbs.		Polyuria noted at 4½, 24 liters	1.004-10	Present in later stages of disease	
26. Glaser ²⁷	♀	10 yrs.	Mother had nephritis, sister similarly affected	Very backward idiotic child, mental age 3 yrs.		Polyuria and polydypsia at 15 mos.	1.005	Trace	Present in late stage of disease
27. Goodhart ²⁸	♀	10 yrs.		Was never strong	Marked rachitis	Polyuria and polydypsia from 7 yrs.			

—OF THE CLINICAL AND PATHOLOGIC FINDINGS

Weight of Kidneys			Measurement of Kidneys		Manifestations of Uremia	Clinical and Pathologic Evidences of Arteriosclerosis and Hypertension		Cause of Death
Right, Gm.	Left, Gm.	Normal ¹⁴⁸ Gm.	Right, Cm.	Left, Cm.		Blood Vessels	Heart	
....		18.0	1.7×1.0×0.5	2.0×1.1×0.4			Right ventricle hypertrophied, congenital defect	Congenital defect in the heart
....		15.0	5.0×3.0×2.5	5.0×3.0×2.5		Slight microscopic thickening of renal arterioles	Enlarged clinically, hypertrophied and dilated	Pulmonary edema, bronchopneumonia
4.0	4.0	20.0	3.3×2.0×0.6	3.3×2.0×0.6			Negative.....	Bronchopneumonia and atrophy
....		30.0			Had irregular attacks of vomiting			Pneumonia
18.0	17.0	30.0			Had periodic attacks of vomiting	Atheromatous changes in aorta	Hypertrophy of left ventricle	Pneumonia
27.0	27.0	36.4			Died in uremia.....	Thickening of renal arterioles	Negative.....	Uremia
6.0	6.0	38.4	4.0×2.5×0.7	4.0×2.5×0.7	Had periodic attacks of vomiting		Negative.....	Atrophy, bronchopneumonia
24.0	24.0	50.0			Had "fits" and vomiting spells, died in uremia		Negative.....	Uremia
....		50.0						
....		50.0			Apparently died in uremia		Slight hypertrophy of left ventricle	Uremia
30.0	30.0	50.0					Slight hypertrophy of left ventricle	
17.0	19.0	56.0	4.0×2.5×1.0	4.0×2.5×1.0	Died in convulsions	Slight atheromatous changes in aorta	Enlarged clinically, left ventricle hypertrophied	Uremia
43.7	48.6	56.0	7.0×3.5×2.5	7.5×3.0×2.5	Had periodic attacks of vomiting, died in uremia	Had headaches and dimness of vision, renal arterioles slightly thickened	Negative.....	Uremia
....		59.0						Atrophic cirrhosis of liver
13.7	23.0	59.0	5.0×3.7×1.2	5.6×3.5×1.5	Died in convulsions	Showed sclerosis of renal arterioles	Heart hypertrophied	Died in convulsions
Comb. Wt. 32.0		124.9	4.3×3.0× —	4.75×3.0× —	Died in uremia.....	Renal arterioles slightly thickened	Slightly hypertrophied	Uremia
....		59.0			Had recurrent attacks of "tetany" and vomiting	Renal vessels thickened	Hypertrophied and dilated	Died in convulsions
Comb. Wt. 30.0		133.6				Renal vessels thickened	Enlarged clinically, heart hypertrophied	Bronchopneumonia
29.0	27.0	67.0	5.5×4.4×2.2	5.1×3.2×2.2		Smaller arterioles thickened	Heart hypertrophied	Bronchopneumonia
....		65.0				Headaches and albuminuric retinitis present, renal vessels thickened	Enlarged clinically, hypertrophied with dilatation	Cardiac failure
112.0	40.0	65.0			Died in coma.....	Arteries palpable, two cerebral hemorrhages	Enlarged clinically, left ventricle hypertrophied	Died in coma
45.0	45.0	65.0			Died in uremia following operation			Uremia
25.0	25.0	78.0			Suppression of urine preceded death	Had attacks of dyspnea and palpitation, obliterative endarteritis		
Comb. Wt. 31.0		156.0			Died in coma with suppression of urine		Hypertrophy of heart	Died in coma
....		78.0				Cerebral vessels sclerosed	Heart hypertrophied	
....		81.0				Albuminuric retinitis, arteries thickened	Enlarged clinically, left ventricle hypertrophied	Diphtheria, cardiac failure
....		86.0	2.9×3.0× —	2.9×3.0× —	Died in uremia.....		Left ventricle slightly hypertrophied	Uremia

SAWYER, 1903.²⁹—Boy, aged 2 years and 5 months. This baby developed "fits" at the age of 7 weeks though no history of any specific fever was obtainable. He habitually suffered from polyuria and was thirsty in addition. He vomited occasionally. He was rachitic and undersized (weight, 15½ pounds). The urine had a specific gravity of 1.002 and contained a trace of albumin but no casts. The average daily volume was 33 ounces. He finally developed uremia and died in coma. No hypertrophy of the heart was present.

The kidneys were small, weighing 24 gm. each. The surface was irregular and the renal tissue was greatly decreased. The left renal pelvis was slightly dilated. Microscopically, there was considerable fibroid overgrowth with marked absorption of the pyramids and destruction of the epithelium. Bowman's capsule was thickened in most instances. (The pathologic description in this case is not complete.)

SEQUEIRA, 1900.³⁰—Boy, aged 3 years. Polyuria was first noted at 8 months, following whooping cough. The child was underdeveloped, rachitic and markedly anemic. The weight on admission to the hospital was 16¾ pounds. The retinae showed no signs of albuminuric involvement. The urinary volume was large, from 20 to 40 ounces daily. The specific gravity was 1.010 and a trace of albumin but no casts were found. The child gradually became comatose, and apparently died in uremia. There was some hypertrophy of the left ventricle. The kidneys were large and granular showing cirrhotic changes on microscopical section. (The pathologic discussion of the kidneys in this case is inadequate for accurate diagnosis of the lesion present.)

MOREL-LAVALLEÉ, 1885.³¹—Boy, aged 5½ years. He had complained of swelling of the abdomen from the age of 18 months. Examination showed a rachitic infant with marked ascites. Paracentesis was performed three times before death. Albumin was present in the urine the last few days of life. Necropsy disclosed a bronchopneumonia, atrophic cirrhosis of the liver, an enlarged fibrous spleen and cirrhotic kidneys.

The kidneys had an essentially normal gross appearance. Microscopically there was sclerosis around the glomeruli with capsular involvement. The tubules were healthy in some areas but in others they were dilated, the epithelium desquamated, and the lumen of the tubule filled with granular detritus or casts. The principle lesion was the increase in the interstitial tissue.

(The determining factor in the clinical picture of this case was the cirrhosis of the liver. The same is probably true of the pathological picture and the changes in the kidney can hardly be called primary. While this case has been included by Oppenheim¹⁶ and others in their tabulations, it seems better to follow the example of Glaser²⁷ and eliminate it from the series of accepted cases.)

GOODHART, 1890.³²—Boy, aged 6 years. This infant was bottle fed and intense thirst was noted at the time of weaning from the bottle. When 3 years old he had an attack of fever and vomiting of unknown etiology. After that he had periodic attacks of tetany and of vomiting. The urine was regularly of low specific gravity with traces of albumin irregularly present.

29. Sawyer, J. E.: Chronic Interstitial Nephritis in Children, Birmingham M. Rev. **54**:511, 1903 (Case 4).

30. Sequeira, J. H.: A Case of Polyuria in a Child Aged Three Years, Rep. Soc. Study Dis. Child, **1**:17, 1900.

31. Morel-Lavallée, M.: Cirrhose atrophique du foie, de la rate et des reins chez un enfant de cinq ans-autopsie. Rev. mens. de malad. d. l'enf. **3**:166, 1885; abstr. in Jahrb. f. Kinderh. **23**:459, 1885.

32. Goodhart, J. F.: Acute and Chronic Bright's Disease, Cyclopaedia of the Diseases of Children (Keating), Phila. **3**:541, 1890.

He was greatly underdeveloped and when seen at the age of 6 weighed but 31½ pounds. Urine had a specific gravity of 1.005 and contained a trace of albumin but no casts. There was no edema. Died in one of the recurrent attacks of tetany. The heart was large but flabby and dilated.

Both kidneys were small and shriveled, the capsules adherent, the surface pale, the cortex diminished and the pelvis a little dilated. There was a large excess of fibrous tissue in the cortex and many of the glomeruli were shrunk and hyalin. The vessels were thick. (This case is reported by Goodhart as a parenchymatous nephritis with the added note that it was a very perplexing case. The reported data are entirely compatible with the presence of a chronic diffuse nephritis, but the discussion of the pathological changes in the kidney is too brief to permit of a definite and final determination of the renal lesion. Goodhart also reports a cousin of this boy who presented essentially the same clinical picture but who did not come to necropsy.)

GULL AND SUTTON, 1872.³³—Girl, aged 9 years. Among their case reports Gull and Sutton include a description of the kidneys of a nine year old girl in whom there was left ventricular hypertrophy and dilatation. "The kidneys were very much smaller than natural especially the left; one weighed 2 ounces, the other 1½ ounces. The kidneys in consequence of being greatly contracted were much out of shape; their surfaces were irregular and puckered, not finely granular." "The arterioles of the kidneys were much thickened by fibroid change." (This case is of interest because it apparently is the first description of the kidneys from a case of chronic nephritis in childhood. The clinical history was not given.)

FÖRSTER, 1887.³⁴—Boy, aged 9½ years. This boy was thirsty from early life and at the age of 4½ polyuria became prominent with the excretion of two to four liters of urine daily. The specific gravity varied from 1.004 to 1.010. Albumin was found only during the latter part of his illness. He was markedly underdeveloped and at the age of 9 weighed but 39 pounds. He died after a week of increasing lassitude, and tiredness, etc.

Necropsy showed the presence of sclerotic changes in the brain, cardiac hypertrophy and contracted kidneys. A sister died at 8¼ after a similar clinical course, but no postmortem examination was made. In this case the father was syphilitic. (The kidney pathology was not studied or reported microscopically.)

GOODHART, 1890.³⁵—Girl, aged 10 years. A small girl with marked rachitic deformity. She had never been strong and her legs had been crooked since she first began to walk. Polyuria and polydipsia had been noted for two years prior to admission, and more recently headaches, dyspnea and coma. She was admitted to the hospital in coma and died in a convulsion twenty-four hours later. The left ventricle was somewhat thickened.

The kidneys were very small, 2.8 x 3.0 cm. They were firm and pale, the capsule adherent and the surface granular. Hardly any of the cortex remained. The section showed copious nuclear growth and not mere fibrosis with atrophy. Thick irregular bands of highly nucleated material spread from the cortex downward to the medulla and within them were thickened and shriveled capsules and wasted tubes. They had a basis of fibroid material and showed well marked puckering or cicatrization. Outside them were tracts of comparatively healthy tubes. (The pathologic picture lacks definitiveness.)

3. Cases of chronic diffuse nephritis in children over 10 years of age.

33. Gull, Sir W. W., and Sutton, H. G.: *Med. Chir. Tr.* **55**:301, 1872 (Case 8).

34. Förster, R.: *Ueber Schrumpfnieren im Kindesalter*, *Jahrb. f. Kinderh.* **26**:38, 1887.

35. Goodhart, J. F.: *Cyclopedia of the Diseases of Children* (Keating) **3**:556, 1872.

FILATOFF AND RACHMANINOFF, 1883.³⁶—Girl, aged 12 years. This girl was weakly from birth and during childhood suffered from urinary frequency and later cardiac palpitation. At the age of eleven she had a left sided hemiplegia. She complained of headache and dimness of vision. Albuminuric retinitis was found on ophthalmoscopic examination. She was apathetic and showed marked anemia. No edema was present. Postmortem examination showed "granular atrophy of the kidney" with a left sided cardiac hypertrophy, chronic endarteritis, and old cerebral hemorrhage. (This case is available in the German abstract only, so the full details of the renal pathology cannot be discussed.)

BRILL AND LIBMAN, 1899.³⁷—Girl, aged 14 years. The family history is quite complicated in this case. There were twelve children. Six of these died in early life, causes unknown. Of the remaining six, four presented the clinical picture of chronic interstitial nephritis. The patient was always weak and undersized. Edema developed a year previous to admission and was present for a short time. Following a severe fright she developed a left-sided hemiplegia. At that time the urine had a specific gravity of 1.010 with 1.4 gm. of albumin per liter. Both hyalin and granular casts were present. Ophthalmoscopic examination showed albuminuric retinitis. Death followed pneumonia and pulmonary edema. In addition there was cardiac hypertrophy, general chronic arteritis, cerebral hemorrhage and hemorrhages in the lungs, spleen and mesentery found at necropsy.

The kidneys were small, measuring 2.0 x 4 x 3.0 and 6.25 x 3.5 x 2.5 cm., respectively, and weighing 59 and 34.5 gm., respectively. The capsules were adherent and the surface granular. The cortex was greatly narrowed. The pelves of both kidneys were greatly enlarged. Microscopically, the right kidney showed a marked chronic interstitial nephritis with complete replacement of the renal parenchyma with fibrous tissue in some areas. Many of the glomeruli were converted into fibrous balls. Some of the tubules were dilated, others atrophied with marked degeneration of the epithelium. The arteries showed obliterative endarteritis and many were completely closed. The left kidney showed essentially the same changes as the right. Both kidneys presented the signs of chronic congestion and scattered through them were many small areas of calcification similar to like areas occurring in the liver.

DISCUSSION OF THE CLINICAL FINDINGS

The reported cases show a remarkable similarity in their clinical manifestations, though these latter show variations dependent on the age of the patient and the severity of the symptoms as well as on the individual viewpoints of the different authors. These lesser diversities serve to emphasize rather than to detract from the essential similarity. In all cases the outstanding causal factor seems to be a severe and progressive diminution in the functional activity of the kidney.

Evidences of nutritional disturbances in early infancy, often very severe, were almost universally noted. As a rule, they did not make their appearance until weaning, or the latter part of the first year in life, though in the cases of Miller and Parsons,¹⁵ Milligan,²² and

36. Filatoff, N. and Rachmaninoff, J.: Ein Fall von primärer Nierenschrumpfung und atheromat. Degeneration der Arterien bei einem 12 jährigen Knaben. *Jahrb. f. Kinderh.* 20:209, 1883.

37. Brill, N. E., and Libman, E.: A Contribution to the Subjects of Chronic Interstitial Nephritis and Arteritis in the Young and Family Nephritis; with a Note on Calcification in the Liver, *J. Exper. M.* 4:541, 1899.

Naish,²⁶ the symptoms dated from birth itself. In my case the history indicated that the feeding was difficult and that the child did not do well during the first year of life. The feeding becomes progressively more difficult with weaning and change to a solid diet. The boy of Paterson¹² refused solid food up to the time of death at 21 months. Oppenheim¹⁶ also reported a case in which the refusal to eat and consequent loss in weight undoubtedly were factors in the final development of uremic acidosis and death. The explanation of this self limitation in diet is not clear but the presence of a severe type of nutritional disturbance in these patients is unquestionable.

These children apart from refusal to eat showed marked backwardness in their physical development. Many were markedly undersize and underweight and nearly all were described as "weakly" or "delicate." Mental as well as physical retardation was present though the mental retardation was the less marked. The children described by Heubner¹⁴ and Glaser²⁷ were idiotic, but for both an etiology of the idiocy other than renal was present.

In addition to being undersized and backward in physical development many of these children had pronounced bony deformities. The children reported by Oppenheim¹⁶ and Paterson²⁴ in particular showed extensive skeletal deformities developing during the first year of life. This backwardness in development and the associated deformities have been especially emphasized by the English writers under the name of "renal infantilism" or "renal dwarfism." This literature has recently been summarized by Paterson.¹² He pays especial attention to the extensive bony changes found and thinks them nutritional in origin but he does not consider the changes to be completely identical with those in true rachitis. Rachitis is usually recognized as being nutritional in origin. The recent work of McCollum, Simmonds, Shipley and Park³⁸ has indicated that it may be caused by a disturbance in the balance of inorganic salts in the diet when combined with an insufficiency of an organic factor. The blood of rachitic children has also been shown to contain a normal or slightly lowered amount of calcium while the inorganic phosphates are markedly reduced in quantity.³⁹

Barber,⁴⁰ in particular, has reported several cases and emphasized the occurrence in older children of a variety of late rachitis that is associated with a chronic interstitial nephritis. It is this type of case in particular that he classifies under the name of "renal dwarfism."

38. McCollum, E. V., Simmonds, N., Shipley, P. G. and Park, E. A.: Studies in Experimental Rickets. VIII. The Production of Rickets by Diets Low in Phosphorus and Fat-Soluble A, *J. Biol. Chem.* **47**:507, 1921.

39. Howland, J. and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rachitis, *Am. J. Dis. Child.* **22**:105, 1921.

40. Barber, H.: Renal Dwarfism, *Quart. J. Med.* **14**:205, 1921.

Barber's cases were striking because they all were in older children. These children were often backward in development during childhood but it was not until the age of from 10 to 15, apparently at about the onset of puberty, that rachitic changes appeared. Genu valgum was the preponderant lesion in all. The etiology of this condition is obscure and its complete identity with the condition seen in younger children has still to be proved.

Pallor and anemia is a well recognized accompaniment of chronic nephritis in childhood but accurate blood studies are lacking in these cases. Anemia is present in practically all cases of rachitis and is also a characteristic feature of chronic diffuse nephritis in adults. Apparently the renal insufficiency in these cases is responsible for a general nutritional disturbance which leads to the development of a severe secondary anemia, but further study is desirable in order to establish the exact etiology of this anemia.

Miller and Parsons¹⁵ pointed out the similarity between the clinical pictures in "renal infantilism" and in some cases of diabetes insipidus. They think that the condition of the child with chronic nephritis may, in part, be due to the general disturbance in nutrition but this last in turn is dependent on the drain put upon the system by the long continued polyuria and albuminuria.

It is true that the polyuria does not reach the extreme degree seen in cases of diabetes insipidus but undoubtedly it is one of the earliest and best marked symptoms of chronic infantile nephritis. The immediate symptom may be any one of the different after effects of an increased water metabolism. Great thirst and consequent drinking of large quantities of water is common and may be recognized as soon as weaning occurs, as in the case of Arraga²⁵ or Naish.²⁶ It is possible that the increased intake of fluids fails to attract the attention and the increased output is first observed as either nocturia, enuresis or polyuria. In the case of Parsons¹⁸ the complaint was "drinking diabetes."

The examination of the urine reveals essentially the same characteristics as those found in chronic diffuse nephritis in adults, and indicates a relative severe degree of kidney damage. As has been mentioned above, the volume of the urine is large, it is pale, acid, and the specific gravity is low. The specific gravity varies between 1.001 and 1.018, though this last represents a terminal value in my case.

In all these cases albumin was present in variable though always in relatively small amounts. In general, the quantity of albumin is very low while the child is fairly well and it occasionally may even be absent. The amount is increased during uremic attacks or in the terminal stage of the condition. The quantity of the albumin, however, does not furnish a reliable guide to the prognosis. Casts were of relatively infrequent occurrence though they occasionally were present.

They were certainly more common in the terminal stages of the nephritis. At this time both hyalin and granular casts may be found though they were absent in the author's case.

In the case of Paterson²⁴ the phenolsulphonephthalein excretion was found to be markedly lowered. The newer methods of studying renal function have only recently been applied to children. This case of Paterson's was the only one in the present series in which functional studies were made. The clinical evidence indicates the presence of an extreme degree of renal insufficiency but this should be confirmed by exact chemical methods. Such studies are of particular value in the differential diagnosis between this condition and the clinically similar diabetes insipidus.

Edema was of relatively infrequent occurrence and was only observed in six instances. In the majority of these cases the edema was terminal and was associated with cardiac failure rather than with the renal disturbance.

Chronic diffuse nephritis in adults presents a definite picture of cardiovascular as well as of renal change. In this hypertensive type of adult nephritis the urinary findings correspond very closely to those seen in children with chronic diffuse nephritis.

The cardiovascular system of these children then is worthy of especial note because of possible light that it may throw on the more complicated problems of adult medicine. Of thirteen children under 5 years of age only five showed evidences at necropsy of cardiac hypertrophy. This hypertrophy in most cases was slight and involved only the left ventricle. In one of these five cases (my own) there were slight arteriosclerotic patches on the mitral valve together with slight thickening of the aortic cusps. In the other seven cases the heart and blood vessels were apparently normal, both on macroscopic and histologic examination. Microscopic examination of the kidneys in nearly all these cases revealed the presence of some change in the walls of the renal arterioles, but this change was usually limited to a slight adventitial thickening.

A slightly different picture is presented in the cases reported of children between 5 and 10 years of age. Out of eleven such cases there are only four in which there was no cardiac hypertrophy. The other cases all showed more or less hypertrophy either of the left ventricle or else of the heart as a whole. The other seven children presented more extensive changes. In the child reported by Glaser²⁷ definite atheromatous patches were present on the mitral valves, and the brachial arteries were thickened and palpable, as in the girl described by Guthrie.²³

Both these children complained of dimness of vision and in both an ophthalmoscopic examination revealed the presence of a typical

albuminuric retinitis. Dimness of vision was also complained of by the boy reported on by Oppenheim¹⁶ but the eye grounds were not examined. The girl seen by Guthrie²³ had a left sided hemiplegia, and two old cerebral hemorrhages were discovered at necropsy, as in the final stage in adult hypertension. The cases of Filatoff and Rachmaninoff³⁶ and of Brill and Libman³⁷ also might be included in this series of cases by extending the age limit a few years. Both these children, aged 12 and 14 years, respectively, had cardiac hypertrophy, generalized arteriosclerosis and hemiplegia.

Other less well defined symptoms of hypertension, such as headache, vertigo, nausea and vomiting, dyspnea on exertion, palpitation and angina, are mentioned in the different reports but do not appear with any degree of regularity. In the greater number of these cases there was no record of blood pressure estimation, so that there is no direct evidence available as to the degree of hypertension pressure. From a comparative point of view it may be said that the chronic nephritis of congenital origin in childhood presents essentially the same clinical picture as that of primary chronic diffuse nephritis in the adult, with the difference that the nutritional disturbance is more marked in the infant and cardiovascular or hypertensive phenomena are less striking than in the adult. In fact, these children very definitely seem to show a direct correlation between age and the extent of the cardiovascular change. The same correlation between the age and the severity of the renal lesion is not observed. Quite as extensive a fibrosis of the kidney was found in the younger children without cardiac hypertrophy as in the older children with marked arteriosclerosis. This observation unquestionably leads to the conclusion that the renal lesion is primary while the cardiac hypertrophy and the arteriosclerotic changes are secondary.

Uremia was present in nearly all the cases studied. In six cases there was a history of periodic attacks of vomiting or convulsions that were evidently uremic in origin. In the majority of instances the uremia was a terminal condition. Oppenheim¹⁶ and Paterson¹² both reported cases in which starvation acidosis undoubtedly was a factor in the development of the uremia. Barber⁴⁰ and Paterson²⁴ have also pointed out the danger of uremia as a postoperative complication in these cases. The importance of the newer chemical methods for the study of renal function should be emphasized, both from the standpoint of diagnosis and of recognition of impending uremia. My patient was admitted to the hospital in convulsions with a diagnosis of lethargic encephalitis. The child was in extremis at the time and it was the urinary findings alone that made possible clinical recognition of the condition.

In the majority of these cases death was due to uremia. The weakness and debility of these patients are important, however, for next to uremia, bronchopneumonia is the most frequent cause of death.

DISCUSSION OF THE PATHOLOGICAL PICTURE

The pathologic picture in these different cases was remarkably uniform. The kidneys were small, pale and atrophic and about equally affected. In some instances one kidney showed slightly more marked changes than the other but the difference was always one of degree rather than kind and never extreme. The capsule was slightly adherent though it stripped fairly readily, leaving a roughened granular surface. In the more advanced cases there was definite scarring of the kidney surface as well.

On section the cut surface was pale, yellowish red and showed marked atrophy of the cortex which was only from 2 to 4 mm. in thickness. Small pinhead sized cysts were present in some cases but they were isolated and indicated no relation to the changes found in congenital cystic kidney.

Microscopically, the glomeruli showed extensive change, depending on the degree of kidney damage. In the less affected kidneys, or in the less affected areas of a single kidney, they were enlarged and hypertrophied. Others showed a connective tissue infiltration around the glomeruli that led first to fusion of the different loops comprising the tuft, or to adhesions between the tuft and the capsule. This led to a final condition of atrophy of the glomeruli with subsequent hyalin change.

The tubules showed swelling and degenerative changes in their epithelium. In many cases the epithelium was desquamated and the lumen of the tubule filled with cellular detritus. Granular and hyalin casts were also present in varying amounts. The condition of the tubules varied greatly in the different cases reported. In the majority of instances both atrophy and dilatation were present in different parts of the section. In other cases either atrophy or dilatation of the tubules was the predominating condition. In the new case reported here the tubules for the most part were distorted or obliterated by scarring and cellular infiltration, but dilated tubules could be found throughout the section.

I have pointed out the importance in renal pathology of the study of the tubule as a whole.⁴¹ Sections permit careful investigation of the component parts of the tubule but fail to give the relationship between these parts. In the present instance the tubules were dissected free

41. Greene, C. H.: Bilateral, Hypoplastic, Cystic Kidneys, to be published.

after maceration of the kidney in concentrated hydrochloric acid. The contracted condition of the glomeruli was striking but there was no change in the architecture of the tubule as a whole. The difference is marked in this respect between this condition and the clinically similar hypoplastic cystic kidney.⁴¹

Increase in the interstitial connective tissue was uniformly present in all cases, though very variable in amount. It was usually present as a diffuse infiltration of fibrous tissue but clumps of round cells were present in many of the cases. Thickening was likewise present in the walls of the smaller arterioles and in the older children the vascular change suggested an obliterative endarteritis.

ETIOLOGY OF THE KIDNEY LESIONS

The etiology of this condition is not clear. Scarlatina is the prime cause of acute nephritis in childhood and this may later become chronic. In the series of cases discussed, however, there was no history of scarlet fever and in most instances a specific statement as to its absence. The case of Jacobs¹⁹ was an exception, but it seems probable that the chronic nephritis in this case antedated the attack of scarlatina. Measles was the only acute illness noted with any frequency, but measles was by no means uniformly present and is known to be a very infrequent cause of nephritis.⁴²

The most striking feature in many of these case histories was the report that the child was delicate from birth. In nearly every instance the child was weak and sickly, and more or less backward in development. Even with the marked frequency of malnutrition in children, the universal presence in all these children of a severe grade of nutritional disturbance would seem to indicate an underlying cause other than simple malfeeding. A chronic nephritis, of greater or less severity, existing at birth could well be the cause of such a nutritional upset. Three of the children were less than 1 year old, and the patient of Wiegert⁶ died at the age of 6 weeks. An acute nephritis may exist at birth, for Karsner⁴⁴ has reported one case and collected three more from the literature. These cases were all rapidly fatal. That any such infection should occur and then develop into a chronic nephritis similar to those cases here discussed is not likely, and that it should do so without observable symptoms is even less probable. It would seem,

42. Aronade⁴³ has presented a case of acute nephritis following measles in a girl aged 5 and this later developed into a chronic kidney lesion but the clinical course and behavior of the patient was entirely distinct from the present series.

43. Aronade, O.: Ueber chronische Nephritis im Kindesalter, *Jahrb. f. Kinderh.* **69**:652, 1909.

44. Karsner, H. T.: Congenital Nephritis, *New York M. J.* **88**:1076, 1908.

therefore, that the kidney lesion in these cases was not only primary in nature but congenital in origin as well.

While the congenital nature of this type of lesion is recognized, the underlying cause is by no means clear. The first thought is of a hereditary or familial defect in the kidney. In a number of instances families have been reported in which the adult members of two or more generations suffered from chronic nephritis.⁴⁵ Inasmuch as the late development of the nephritis in these latter cases raises doubts as to its congenital origin, they will not be discussed here. In the majority of the cases studied the family history was either noncommittal or else entirely negative as to familial nephritis but this was not true in all. The two children reported by Förster³⁴ were brother and sister. The parents of the two children studied by Frölich¹¹ were apparently healthy, but a maternal uncle had died of chronic nephritis. The children discussed by Barber⁴⁶ were likewise brother and sister. They were the result of the seventh and eighth pregnancies and it was noted that the mother was not well during either pregnancy. It is a peculiar coincidence that the two sisters reported by Hellendall¹⁰ were also the result of the seventh and eighth pregnancies. About the fourth month of the seventh pregnancy the mother, who had previously been well, noticed swelling of the feet and was said to have later developed symptoms of chronic nephritis. During the eighth pregnancy these same symptoms recurred in a more severe form. In the report of Glaser²⁷ it was stated that the mother of the patient died during childbirth of chronic renal disease, and that a sister died at the age of 2½ years from a malady similar to that of the patient. In this group of cases there is evidence to indicate a familial origin of the disease.

In some of the remaining cases the presence of congenital or developmental defects indicated that the kidney lesion possibly was part of a larger process. The child reported on by Weigert⁶ had a congenital malformation of the heart. The girl reported on by Glaser²⁷ was idiotic, as was the child discussed by Heubner.¹⁴ The father of this latter infant was a sufferer from lead poisoning. This has been known to affect the parental germ plasm with the production of developmental defects in the offspring.⁴⁷ The chondromas present in the kidney of the younger of the two infants described by Hellendall¹⁰ may also be looked on as evidences of congenital defects of development.

45. Kidd, J.: The Inheritance of Bright's Disease of the Kidney, *Practitioner* **29**:104, 1882.

46. Barber, H.: Chronic Interstitial Nephritis in Children, *Brit. M. J.* **2**:1204, 1913.

47. Ballantyne, J. W.: *Manual of Antenatal Pathology and Hygiene, The Foetus*, Edinburgh, 1902, p. 258.

Recently ⁴¹ I reported a case of bilateral hypoplastic cystic kidneys. This child presented the characteristic clinical picture of chronic diffuse nephritis. Urine examination showed the presence of a marked renal insufficiency of the type found in chronic diffuse nephritis. This would indicate that it was the functional rather than the morphologic changes in the kidneys that determined the symptomatology of the disease. The microscopic appearance of the sections in this case of congenital defect in the development of the kidney corresponds very closely with the appearance of the illustrations of the kidney published by Paterson.²⁴ It is possible that the case of Paterson and perhaps others from this series were cases of defective development of the kidney rather than of diffuse nephritis.

The boy reported on by Arraga²⁵ was born of a mother suffering from malaria and taking quinin throughout pregnancy. Furthermore, it should be noted in the reports cited above, especially those of Hellendall¹⁰ and Barber⁴⁶ that the affected children were born of mothers who suffered from renal disorders during pregnancy. It is possible, then, that these cases while congenital were not familial in origin but rather represented the results of maternal intoxications.

Sawyer⁴ and Guthrie²³ in particular have advanced the idea that this condition was syphilitic in origin. It is true that the mother of the child reported by Guthrie had six miscarriages and that the father of the children described by Förster³⁴ died of syphilis. With these exceptions syphilis either was not mentioned in the clinical reports or else there was a specific statement as to its absence. In view of our present day knowledge of congenital syphilis, this condition can be ruled out as an etiologic agent in this series of cases.

Glaser²⁷ suggested the possibility of a primary renal vascular hypoplasia as underlying the pathologic changes. In this connection it should again be pointed out that in the younger children the vascular changes were relatively slight. The renal vessels were reported as being only slightly thickened if at all, and there was no evidence of general arteriosclerosis or cardiac hypertrophy. In my case there was a slightly hypertrophied left ventricle and the mitral valve contained two thickened plaques. The renal vessels showed only slight changes on microscopic examination. In the children over 5 the cardiovascular changes became progressively more prominent. Cerebral hemorrhage occurred in the case discussed by Guthrie²³ and in the somewhat older children reported by Filatoff and Rachmaninoff³⁶ and Brill and Libman.³⁷ A lesser degree of vascular change and cardiac hypertrophy was present in others of the older children. If cerebral hemorrhages may be taken as an indication of the presence of a severe degree of cardiovascular sclerosis with hypertension, then it is noteworthy that these changes were present only in older children

in which there had been time for the vascular changes to appear. Though not entirely conclusive it would seem as if the primary lesion in the kidney was renal and not vascular in origin.

In the other cases reported no clue as to the origin of the lesion was found. Until more is known of the pathology of fetal development any assignment of a cause for this condition would seem to be largely a matter of individual opinion and choice.

SUMMARY

A careful study of the reported cases of chronic nephritis in childhood indicates that chronic diffuse nephritis is a distinct clinicopathologic entity of probable congenital origin though no definite etiology may be ascribed.

It is characterized by evidences of functional insufficiency of the kidneys dating from early infancy. Children so affected show great developmental disturbance with associated stunting and backwardness in growth, difficulty in feeding, anemia and rachitis. The renal insufficiency is more directly evidenced by the excretion of large volumes of dilute urine with a low specific gravity. This urine contains a slight amount of albumin and casts are present in small numbers. In those cases in which it has been determined the phenolsulphonephthalein excretion is low. Death usually results from uremia. The pathologic picture in these cases is similar to, if not identical, with the chronic diffuse nephritis of adults.

48. Vierordt, H.: Anatomische, physiologische, und physikalische Daten und Tabellen, Jena, 36, 1906.