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.

By N. E. BRILL, A. M., M. D., Visiting Physician, and E. LIBMAN, M. D., Assistant Pathologist.

(*Mount Sinai Hospital, New York City.*)

Plate XXV.

Chronic nephritis in children and adolescents is a condition which has been much overlooked. Especially is this true of the chronic interstitial type (contracted kidney). Dickinson was of the opinion that the latter condition was not infrequent in children. Heubner (1), who has lately written a monograph upon this subject, from which many of these introductory remarks are cited, states that of 251 cases of chronic nephritis which he observed in Leipsic, 214 occurred in adults and 37 in children. Later, in Berlin, he saw 28 cases in children, mostly after scarlet fever. Of these 65 cases, there were 3 of parenchymatous nephritis, 4 of contracted kidney and 5 of chronic hæmorrhagic nephritis (Wagner). Of 33 cases of chronic interstitial nephritis observed by Bartels (2), one occurred at the age of 18, one at 19, and two at 20. Of Dickinson's (3) 308 cases, one occurred between 11 and 20 years, and 24 between 21 and 30 years.

From these figures it is seen that under the age of 20, chronic interstitial nephritis is uncommon, but not so rare as the omission of reference to it in many text-books on children's diseases would indicate. The condition is even more frequent than these figures would lead us to infer, as many of the cases are overlooked and treated for anæmia for a long time. This is especially true of the subacute cases of productive nephritis described by Delafield (4).

Of the interstitial cases, which alone interest us here, Heubner states that there are but thirty on record in which post-mortem examinations were made. Besides these, there are numerous other instances reported in which the patients were not observed until the fatal termination, or where no autopsy was performed. To these cases, Heubner adds four from his

own experience; three in males, aged respectively 14, 9 and 24, and one in a female aged 11. Of these four cases, however, one was probably of amyloid disease. In none of these cases is there any post-mortem examination recorded. In all the cases which Heubner cites the disease was very insidious, but was easily discovered upon properly examining the patients. As a rule the disease lasted for many years. It can, however, be rapid in its course, as in Crooke's (5) case, where, at the autopsy on a boy nine years old, who died on the 68th day after the onset of scarlet fever with diphtheria, the kidneys were found to be distinctly granular. Delafield (4) has drawn especial attention to these rapid cases (acute productive nephritis).

According to Heubner, there are seven cases in the literature in which there is no history of a previous acute attack, so that they can be looked upon as instances of primarily contracted kidneys. These are the cases of Barlow (6), Bull (7), Filatoff (8), Morell-Lavalée (9), Oppenheim (10), and Förster (two cases) (11). The case reported by Morell-Lavalée is of a special type, as the condition was complicated by a cirrhotic liver. In the other cases, which died at the ages of 5, 6, 10, 13, and 14 years respectively, it is noted that the children were always weak, of capricious appetite, pale, and had weak resisting powers.

Accidentally, or at the occurrence of a slight œdema, the albumin in the urine was discovered. It is, of course, possible, as Heubner states, that these children had had an attack of acute nephritis in earliest infancy or childhood, so that the question of the occurrence of a primarily contracted kidney in children must remain an open one. Of the four cases which Heubner has seen, one is probably a case of amyloid kidney as stated above, and two are probably secondary cases. Only one is possibly a primary case. This is that of a boy aged 9 years, who presented typical symptoms of chronic interstitial nephritis, but of whose history only a part is known.

It may be of interest to give details of some of the reported cases:

Barlow's case was that of a girl aged 6 years. She suffered from headache, pallor and vomiting, and died with uræmic symptoms. At the autopsy there was found a very marked chronic interstitial nephritis. The right kidney weighed 13 grammes and measured 5x4x0.5 cm. The left weighed 21 grammes and measured $6x3\frac{3}{4}x1\frac{1}{4}$ cm. The arteries were thickened.

Bull's case was that of a girl thirteen years old. The left kidney weighed 20 grammes, was 5 cm. long and 3 cm. wide. The right measured $7\frac{1}{2}x4\frac{1}{2}$ cm.

Filatoff's case was of a girl aged 12, who was always weak and passed

very much urine. In her 11th year, she had an apoplectic attack with left-sided hemiplegia. Later she had headache and vomiting and began to lose her eyesight. An albuminuric retinitis was found. Before her death she became slightly œdematous and had a severe nasal hæmorrhage. The urine was clear, 1500 cc. daily, and slightly albuminous. The arteries were tense and hard, the apex beat was exaggerated and situated below and to the left of the normal position. The autopsy showed granular kidneys, hypertrophy of the left ventricle, endarteritis of the aorta and the vessels at the base of the brain, and an old hæmorrhagic extravasation in the right corpus striatum.

In Lavalée's case, a child 5½ years old suffered from ascites with fever At the post-mortem examination there was found cirrhosis of the liver, spleen and kidneys.

We have not been able to consult Oppenheim's article.

Förster's two cases occurred in the same family. The boy died at the age of 9½ years, after an illness of 5 years' duration. The autopsy showed typical contracted kidneys. The girl died at 8¼ years, having been ill 3½ years. Several weeks before her death she developed a hæmorrhagic diathesis, having several severe hæmorrhages from the mucous membrane of the mouth. An autopsy was not performed. Both cases during life resembled cases of diabetes insipidus.

To these seven cases gathered by Heubner, making eight with his own case, we may add a few others which we have found. Westphal (12) reports the case of a man aged 24 years in which there was found an atrophic kidney on one side and a contracted kidney on the other. There was no history of any previous illness and the patient succumbed after having been sick a very short time. It is of interest to note that Curschmann had diagnosed the existence of a contracted kidney with the probability of one kidney not functioning. Baginsky (13), in his textbook, mentions a case in a girl aged 4, which stimulated diabetes insipidus. There is no autopsy reported. Ashby and Wright (16), mention two cases which seem to belong in this group. They both occurred in girls, one 11½ and the other 10½ years. v. Buhl reported a case in a child of one and one-half years (cited by Eichhorst (28)).

It is a remarkable fact that even congenital cases have been described. Baginsky (13) mentions two such occurrences in his experience but gives no details. Weigert (14) describes briefly the following case: At the autopsy performed on a child six weeks old, who had suffered from marked cyanosis, there was found an atresia of the pulmonary artery, an open septum and hypertrophy of the right ventricle. The kidneys measured 1.7x1x0.5 cm. and 2x1.1x0.4 cm. The cortex was narrow and

the substance pale and firm. There were small cysts on the surface. Microscopically, there were found fairly normal parts with fatty degeneration of the epithelium and areas of marked chronic interstitial inflammation. The epithelium of the Malpighian tufts still consisted of large cells, and, like the cortical cells, showed fatty degeneration. Hellendall (14*a*) has reported two instances of contracted kidney, probably of congenital origin, in infants, the one six months and the other two years old.

The following case, which was observed at the Mount Sinai Hospital, adds another to this list of cases, and it is so interesting from many other points of view that it is considered worthy of publication.

Ida W., school-girl, aged 14 years. Admitted January 13, 1898. *Family history* is of special interest and will be given in detail subsequently (p. 554).

Previous history: The girl has always been weak and under-sized. She generally stayed at home because running around on the street made her short of breath. She has never menstruated. One year ago, her face and feet were swollen during the whole winter. She always felt better during the summer. For some time past she has had a cough with expectoration. When six months old she suffered from an attack of gastro-enteritis of a few days duration. She has had no other known acute illness.

Present history: One week ago, she became very much frightened at a fire in the neighborhood at 2 P. M. She was apparently well until 11 P. M., at which time she went to sleep. The next morning it was noticed that the left side of the body was paralyzed. She complained then and still does of headache. She had fever for the first time three days ago, and two days ago she coughed up a small quantity of blood. Urination and defecation are stated to be normal. Her intelligence and memory have not been impaired. The paralysis has improved somewhat; she has twitchings of the entire left side of the body.

Physical examination: Under-sized girl, poorly nourished, with a dirty, anæmic color. The tongue is moist and coated. There are no defects in the teeth and there is no lead-line present. There are no signs of any corneal inflammation, and no changes in the ears. She has a left-sided hemiplegia with some rigidity. Sensation is unimpaired in the upper but diminished in the lower extremities. *Lungs,* negative. *Heart,* dulness extends from 1 cm. to the right of the sternum to 5 cm. to the left of the mammillary line. The upper border is at the third

rib. The apex beat is in the fifth space in the axillary line. It is forcible and fairly localized. The heart's action is tumultuous and forcible. There is a systolic murmur over the mitral area, transmitted a short distance to the left. Over the aortic orifice there is heard a systolic murmur transmitted up and down the sternum and to the vessels of the neck. The second aortic sound is accentuated and reduplicated. The radial *pulse* is tense, the artery is very much thickened and slightly tortuous. The *liver* dulness extends from the fourth space to the free border of the ribs. *Spleen,* negative. *Abdomen,* negative. The right pupil is slightly larger than the left.

Subsequent history: January 12, 1898. Pulse 120. Respiration 32, temperature 101.8° F.

January 13. Urine neutral, 1010, clear, and contains albumin—1.4 grammes to the litre (Esbach); urea 6½ grains to the ounce; hyaline and granular casts and a few pus cells are present. The quantity of urine could not be measured because the urination was involuntary. She has some cough and complains of pain in her stomach.

January 14. Temperature normal; labial herpes; patient somewhat soporose.

January 15. Urine contains albumin, red and white corpuscles, but no casts.

January 17. The movements from the bowels contain some blood.

January 19. Urine again shows hyaline and granular casts.

January 20. Mental condition has improved. Paralysis unchanged. Pain in abdomen less marked.

January 30. Marked restlessness.

February 3. Temperature elevated to 103°. She complains of pain in the left hypochondriac region. By percussion the spleen is found to be enlarged. It can be felt and is tender.

February 5. Temperature 104.6°. Has severe coughing spells. Over the first four interspaces on the right side anteriorly and posteriorly are numerous crepitant râles, increased voice and breathing and a dull percussion note.

February 6. Temperature 102°.

February 7. Over right lower lobe behind there is bronchial voice and breathing. Severe abdominal pain. Temperature 100°.

February 8 to 10. Patient's condition worse. She lies in a semi-comatose condition and complains of severe abdominal pain. The hemiplegia has remained unchanged. The physical signs on the right side have partially cleared up. Electrical examination shows an almost com-

plete loss of reaction to the faradic current in both the left upper and lower extremities.

February 15. Ulcers found on the upper and lower gums with necrotic, easily bleeding bases.

February 18. Over the upper lobe of the left lung is an area of dulness, increased voice and breathing, crepitant râles. Hæmoptysis.

February 23. Necrotic areas in the mouth have increased in size and number. Ophthalmoscopic examination shows retinal hæmorrhages.

February 25. Continued hæmoptysis with signs of consolidation of a large area in the left lower lobe posteriorly.

February 26. Temperature suddenly drops to 96.4°. The patient had very severe pain in the abdomen and passed a large amount of blood with the stool. Pulmonary œdema.

February 27. Temperature still remains subnormal. Marked tympanites. Subcrepitant and crepitant râles heard in front and behind below the second rib down to the base on the right side. Râles heard yesterday have almost entirely disappeared. Urine contains albumin, 16 grammes to the litre. Urea 4 grains to the ounce. Temperature subnormal.

March 3. Very marked pericardial friction sounds heard even at a distance from the patient.

March 5. Crepitant râles over the upper part of the left chest with bronchial voice and breathing. Temperature 94° to 96°.

March 6. Return of the pulmonary œdema. Exitus.

Clinical diagnosis: Chronic interstitial nephritis. General arteritis. Atheroma of aorta and aortic valve. Cardiac hypertrophy. Cerebral hæmorrhage. Hæmorrhages into the lung and spleen. Hæmorrhages in the area of distribution of the superior mesenteric artery. Fibrinous pericarditis.

Post-mortem examination: Five hours after death. Body very much emaciated. Slight general œdema, more marked on the left side of the body, with marked œdema of the feet.

Lungs: Slightly adherent at the apices. Moderate pulmonary œdema. Both lungs are very firm. In the right upper lobe there is a very dense non-crepitating area which is infiltrated with blood. In the right lower lobe there is a similar smaller triangular area. In the left upper lobe, are several patches of consolidation and one large hæmorrhagic area. In the left lower lobe, there is a large recent hæmorrhage. There is marked subpleural emphysema of both lungs.

Heart: On the anterior aspect there is very much fresh fibrin; the left ventricle shows marked hypertrophy, the thickest part of the wall

measuring 3½ cm. and the thinnest 2 cm. The aortic valves show moderate atheroma. The flaps of the mitral valve are slightly thickened. The wall of the right ventricle is somewhat hypertrophied. The aorta shows patches of atheroma especially around the openings of the coronary arteries. The coronary arteries are markedly atheromatous. On the endocardium between the aortic and mitral valves, and on one cusp of the mitral, are patches of marked atheroma. The cardiac muscle is pale but firm.

Spleen weighs 80 grammes; measures 5x8½ cm. Malpighian bodies are very distinct. Almost the entire spleen is taken up by a large hæmorrhage.

Kidneys, small, red. The right weighs 59 grammes and measures 9x4x3 cm. The left weighs 34½ grammes and measures 6¼x3½x2½ cm. The capsules are very adherent; the surface irregularly granular. The kidney substance is firm; the cortex is very narrow. The pelves of both kidneys are markedly enlarged, and surrounded by fat. The markings are very indistinct. On the surface of the kidney are enlarged veins, and some of the glomeruli can be indistinctly seen as white dots. The left kidney is more markedly affected than the right, the parenchyma being only 0.5 cm. wide.

Stomach: Catarrhal inflammation. A few hæmorrhagic erosions near pylorus.

Intestines: There is a large hæmorrhage in the mesentery. No emboli nor thrombi can be found in the mesenteric arteries or veins or their branches. The superior mesenteric artery is markedly atheromatous. The small intestine shows catarrhal inflammation; the contents are mucoid and bloody. The large intestine shows catarrhal inflammation with marked injection of the walls.

Pancreas is indurated.

Liver somewhat enlarged, is fairly firm, shows chronic congestion and some increase in the connective tissue. In the right lobe on the anterior and inferior surfaces are triangular areas reaching to the surface in which there is a firm deposit in and along the vessels looking as if the vessels were firmly thrombosed.

The brain could not be examined.

Microscopical examination: Lungs show the changes characteristic of brown induration with a fair amount of increase in the interstitial connective tissue. The lower lobe shows areas where the air-vesicles are filled with epithelial and pus-cells and numerous red blood-corpuscles. The right upper lobe shows the same condition with a larger and more recent hæmorrhage. The left upper lobe contains a large area of

croupous pneumonia. The left lower lobe shows marked recent infiltration with red blood-corpuscles.

Liver: The capsule is thickened. The capillaries are dilated and there is a little increase in the interstitial connective tissue. The liver cells show marked degeneration and pigmentation. There are small hæmorrhages under the capsule. The walls of the hepatic veins are thickened and the veins themselves are dilated. The arteries show marked obliterating endarteritis. Scattered throughout the parts of the liver which showed such a peculiar condition macroscopically, are irregular areas (Plate XXV, Fig. 1) which stain very darkly with Delafield's hæmatoxylin and look necrotic. These areas seem to follow the branches of the hepatic artery, surrounding and sometimes obliterating the lobules. On the addition of dilute hydrochloric acid to the unstained specimen, these areas become much paler without the evolution of gas bubbles, and when thoroughly washed out and then stained with the same solution, they appear more homogeneous and stain with about the same intensity as the surrounding parts of the liver. They are, therefore, areas which have become impregnated with lime salts. The absence of any evolution of gas bubbles on the addition of the acid shows that they consist of calcium phosphate.

Spleen shows the changes of acute inflammation. The capsule is thickened and there is an increase in the interstitial connective tissue. The pulp is infiltrated with red blood-corpuscles. The arteries are the seat of a marked obliterating endarteritis.

Kidneys (Plate XXV, Figs. 2 and 4): The right kidney shows a marked chronic interstitial nephritis. In some areas the renal parenchyma is entirely replaced by fibrous tissue. Many of the glomeruli are converted into fibrous balls. Some of the tubules are dilated, others are atrophied; some contain casts, others granular material or blood. The epithelium shows marked degeneration. There are small scattered hæmorrhages present and signs of chronic congestion. The arteries show marked obliterating endarteritis (Plate XXV, Figs. 2 and 3), many of them being entirely closed. Scattered throughout the kidney are very small areas similar to those which have been described as occurring in the liver. The left kidney shows the same changes as the right, and in even more marked degree.

Pancreas contains areas of infiltration with round cells between the lobules, and in some places in the centre of the lobules.

Coronary arteries: There is extreme thickening of the intima, fibrous metamorphosis of the media and extensive calcific deposits and necroses in the intima (Plate XXV, Fig. 5). One of the smaller peripheral

arteries shows, microscopically, a thickening of all the walls; the intima contains calcified and necrotic areas, and there are broken-down thrombi attached to it. The media is almost entirely replaced by connective tissue. There are small hæmorrhages in the adventitia. *The superior mesenteric artery* likewise shows irregular thickening of the intima and of the media with small calcific areas in the intima.

Anatomical diagnosis: Pulmonary œdema; brown induration of lungs; hæmorrhages into lungs, spleen and mesentery; lobular pneumonia; cardiac hypertrophy; general chronic arteritis; chronic congestion of the liver, with calcific deposits; acute splenic tumor; catarrhal inflammation of the gastro-intestinal tract; chronic interstitial nephritis (small red kidney).

Remarks on the results of the post-mortem examination.—The kidneys from this case are among the smallest that have been recorded in the chronic nephritis of early life. In a few of the other recorded cases, the size of the kidneys has been as follows: Handford (15), 12-year-old girl, right kidney, 60 grammes; $8\frac{1}{2}$x$4\frac{1}{2}$x$2\frac{3}{4}$ cm. Left kidney, 15 grammes; 5x4x2 cm. In Ashby and Wright's (16) cases, from the one case of a girl $11\frac{1}{2}$ years old the right kidney weighed 75 grammes, the left kidney, 22 grammes. The kidneys from the other case weighed together 45 grammes and each measured 5 cm. in length. In one of Kidd's cases (17) one kidney weighed 60 grammes and the other 30 grammes.

The change in the liver, which is reproduced in Plate XXV, Fig. 1, is certainly very striking. In places it made the impression that the process began in the walls of the arteries and that then the parts supplied became degenerated and infiltrated with lime salt. The occurrence of such calcification in the arteries, beginning in the intima, was demonstrated in the kidneys and is illustrated in Plate XXV, Figs. 2 and 3.

The presence of calcified areas in the liver is extremely rare. Babes mentions an instance in an article on the technique of staining with safranin.* The liver described by him was obtained from a patient who suffered from tuberculosis of the femur and the hip-joint.

* Virchow's *Archiv*, 1886, cv, p. 511.

None of the other organs showed similar changes. The liver was large, grayish-brown in color, and presented grayish-yellow patches corresponding to the central veins, so that it looked like a nutmeg liver of a peculiar character. It felt sandy, and cutting it caused a grating sound. The deposit proved to be composed of lime salts in and around the central veins and their branches and in the surrounding cells. Around these areas the cells had lost their nuclei and their contours were obliterated. Babes considered the condition to be due to lime resorption from the bone disease and its later deposition in the liver. Virchow thought likewise, but the exact manner of its occurrence could not be determined.

Similar, but smaller and fewer areas of calcareous impregnation, were found in the kidneys and in the walls of many of the vessels. Figure 5 (Plate XXV) shows the deposits in the walls of the coronary artery. It also shows the other changes noted in the report of the microscopical examination. In Fig. 4 (Plate XXV) are shown the changes in the kidney, the part represented, however, not being that most markedly affected. The large number of vessels almost or entirely closed is very striking. As stated above, an examination of the brain was not permitted, but it is probable that the hemiplegia which marked the onset of the symptoms was due to a right-sided hæmorrhage.

For the sake of completeness we may note here that a blood culture was made 14 hours before death. A pure culture of Staphylococcus albus was obtained, and after death the same organism was cultivated from the heart's blood. We lay no stress upon this observation, as the agony was very prolonged and the bacteræmia may have been due to an agonal invasion.

General Remarks.—(1) As to the diagnosis of the main conditions, only a few words are necessary. At first sight the case might have been considered as primarily cardiac in nature with secondary renal changes of the chronic interstitial type. The marked hypertrophy of the heart, however, with the distinctly accentuated second sound caused us to suspect a primary affection of the kidneys. The finding of the diseased radial vessels supported this view. It must be remem-

bered, however, that a similar clinical picture can be produced by disease of the vessels without involvement of the kidneys. This fact, which has not received proper recognition, is strikingly illustrated by a case recorded by Hawkins.* As this case resembles ours to a great extent, we present it in detail:

A girl, aged 11 years, in the summer of 1891, had a week's illness, probably attributable to infarctions of the lung. In January, 1892, similar symptoms again appeared, the pain being first on the left side and later on the right. The cough, with blood-stained sputum, persisted up to the end of the illness. February 7, the legs became œdematous and later the face. The urine showed a trace of albumin, no casts, and was diminished in quantity. February 25, the urine was bloody and contained a little albumin, and the patient vomited. The child died after three weeks from what seemed to be uræmic poisoning, the case being considered one of acute nephritis. There was no syphilitic history. At the autopsy all the arteries of both the aortic and pulmonary systems were found to be diseased. There was consolidation with infarctions of portions of both lungs. Both renal arteries were occluded by thrombi. There were small clots in each of the lateral lobes of the cerebellum. The left ventricle was dilated and hypertrophied. For a distance of three inches above the bifurcation the aorta was so narrow as scarcely to admit a bullet-probe. The arterial wall measured only one-half inch in breadth when opened. The kidneys microscopically showed no signs of nephritis. The arteries, macroscopically, showed gray translucent spots and patches, smooth or corrugated. Microscopically, these were composed of indistinct fibrocellular tissue in the intima. In the media and adventitia were collections of leucocytes, especially around the vessels. The new tissue was not the seat of fatty or degenerative change, with the exception of some deeply-stained patches of amorphous material (lime?) on the surface.

(2) The hæmorrhages in our case caused prominent symptoms during life. Those in the lungs were easily made out. The intrasplenic hæmorrhage was diagnosed from the acute enlargement and tenderness of the spleen and the rise in temperature. The extravasation in the mesentery was indicated by excessive abdominal pain, bloody stools, and tympanites; and the sudden occurrence of sub-

* *Transactions of the London Pathological Society*, 1892, p. 46, cited in part by Delafield (4).

normal temperature indicated a large hæmorrhage. The question whether the hæmorrhages were due to thromboses, embolisms or ruptures of smaller or larger vessels had to be left open as any one of these conditions was possible. The marked bleeding from the gums, however, indicated that it was not necessary to assume the existence of embolism or thrombosis and that the hæmorrhages might be explained by the existence of a hæmorrhagic diathesis. Such a diathesis in similar cases has been noted by Filatoff (8) and Förster (11).

(3) The arterial changes present were very advanced. The question naturally arises whether these or the renal changes were primary. This is frequently a very difficult problem. From the examination of two other members of the same family, we are inclined to believe that the lesion in the kidney was primary, as these two persons have long-standing chronic nephritis with but little evident arterial change. Of course, it is possible that their peripheral arteries may not show arteritis, while this may exist elsewhere, and, therefore, a positive opinion is not warranted.

Throughout the records, there are occasional references to cases of chronic arteritis in children, and it has been noted that there exists in certain families a tendency to the development of arterial changes early in life. The most common occurrences have been aneurisms of the cardiac valves and dilatation of the aorta (Baginsky). Jacobi, (18), in reporting a case of aneurism of the abdominal aorta in a child, refers to twenty-eight other recorded cases of aneurism in early life. Since then at least two more cases have been described. These cases need classification, however, as some of them were not due to primary arterial changes but were mycotic in origin (Eppinger). Among the striking instances of advanced arterial disease reported in childhood, are the following:

Fenomenoff has recently reported a congenital aneurism of the abdominal aorta which obstructed delivery (Eichhorst). Oppe (19) describes an aneurism of the basilar artery in a boy seven years old. Sanné (20) reports the case of a child of two years with narrowing of the aorta due to chronic aortitis. Pendin (21) describes in a girl of 12 an aneurism of traumatic origin. Andral (22) saw calcific plates in the aorta of

a girl 5 years old. Moutard-Martin (23) saw atheroma of the arch in a boy aged two years. Hodgson (24) records calcification of the temporal artery in a girl of five, and Hoffnung (25) describes an aneurism of the pulmonary artery in a girl of ten months. Generalized arterial disease in connection with chronic interstitial nephritis without any syphilitic history has been described by Filatoff (8) and Barlow (6).

The changes found in our case were as advanced as in well-marked arteriosclerosis of adult life. While the character of the lesions suggested syphilis, a very thorough examination of the whole family failed to elicit anything corroborative of such a view.

(4) The absence of any usual etiological factor drew our attention to the possibility of the case being an instance of so-called "family nephritis." Senator's recent volume on the diseases of the kidneys, in Nothnagel's Handbuch, cites several instances of nephritis occurring in several members of the same family.

Dickinson (26) reports a family in which in the first generation two sisters had albuminuria for many years and died at the ages of 48 and 49. Of the four children of a brother, one son had albuminuria for 14 years and died at the age of 26, and one daughter died at 34, after having been sick sixteen years. Two other daughters had no albuminuria and lived to the ages of 38 and 40. Of six children in the third generation, five had albuminuria, one daughter having it, from the age of nine months, for twenty years, and one son of 20 for an unknown length of time. Another son of 15 had it for two years and one daughter of five years was albuminuric since the age of six months.

Tyson (27) mentions the instance of a man of 30 with contracted kidneys whose father and mother died of the disease, and one brother at the age of 37. Two children of the brother had chronic nephritis at the ages of four and seven respectively. One brother died at 29 from convulsions. Two older brothers and one sister, aged 23, 32 and 36 respectively, had the disease for five or six years. One cousin on the mother's side and numerous relatives in earlier generations died of chronic nephritis.

Eichhorst (28) gives the history of an artist's family who were sufferers from the disease. The grandmother (who had no gout) died of uræmia. The mother and a daughter 24 years old suffered from chronic interstitial nephritis, the former for fifteen years. Two sons died of

uræmia. A daughter, aged 22, showed signs of the disease at the time of the report.

Kidd (17) reports the case of a woman of 60 who died of nephritis of long standing, as did also her brothers. Of 12 children, 7 died with the same disease, and two had it at the time of his report. In two of the fatal cases a post-mortem examination was made and contracted kidneys were found. Possibly Förster's cases belong in this category.

Samelsohn (29) observed chronic nephritis in two brothers, and noted its probable existence in two sisters and a son in the same family.

Pel (30), in a recent article, mentions several families in which he has noted the tendency to the development of chronic nephritis, and reports one instance of family nephritis not less striking than that of Dickinson. The disease affected 18 members (9 males and 9 females) of the family in three generations. Of 60 children of the fourth generation, none at the time of Pel's report was affected, but as, in contrast with the observations cited above, the disease in this series appeared later in life, their subsequent fate must remain for the present in doubt. Pel notes that in this family the tendency was for the sons to inherit from the father and the daughters from the mother—an exception to the Darwinian rule of heredity.

An examination into the family history of our case and a personal investigation of the members of the family, which was possible only after repeated efforts, revealed the following interesting facts:

The father died at the age of 42 of lobar pneumonia. His previous history was negative so far as can be determined. The mother is 45 years old and in good health, presenting no signs of renal or arterial disease. Of the 12 children, six died very young of causes which are unknown. The living children are as follows:

1. A girl of eight, who seems to be in good health and whose urine and heart show no changes.

2. A boy, aged 13, who is also in good health and in whom the physical and urinary examinations reveal nothing abnormal.

3. A girl of fourteen, who complains of severe headache. She is very well developed and her heart and arteries show no deviation from the normal. The urine has a specific gravity of 1016 and contains no albumin nor casts.

4. A girl, aged 19, who has been ailing for at least six years (probably over 10 years). She has no history of any acute disease. Menstruation be-

gan at 12 and has always been irregular and profuse. She complains of very great thirst and has to arise several times at night to drink water. She passes very much urine. The appetite is poor. She has no headache and no vomiting. She has occasional cough and palpitation, but complains only of her excessive thirst. An examination on November 5, 1898, showed the following: There is marked anæmia. The pulse is of high tension and the walls of the radials are somewhat thickened. The sphygmographic tracing shows marked elastic vibrations and only a slight dicrotic notch. The apex beat is in the fifth space just to the left of the mammillary line and is very forcible. The urine is very light in color and has a specific gravity of 1001½. There is albumin present, 0.14 per cent (Esbach), no sugar. The microscopical examination shows only epithelium and a few leucocytes. When seen two weeks later, there was marked œdema of the eyelids and some headache, which disappeared after a few days. At the date of writing, March 1, 1899, she is in good health, except for her inordinate thirst. She is evidently suffering from a very advanced chronic interstitial nephritis, which is running a slow and quite latent course.

5. The oldest son, aged 24, gives no history of any acute disease in childhood. He has always been anæmic. Six years ago, he suffered all winter from a severe cough and had general œdema which began in the face. He has felt perfectly well since then and, therefore, for a long time opposed any personal examination. On February 19, 1899, the following facts were made out. There is a moderate anæmia. The apex beat is in the sixth space, one-half inch to the left of the mamillary line, and is very forcible. There is a booming first sound and an accentuated second sound at the apex. At the aortic orifice, there is a slight systolic murmur and an accentuated second. The pulse is 86, the radial artery is slightly thickened, the pulse shows moderate tension. The urine is clear, 1012; contains no albumin and no casts; urea 9 grains to the ounce. Although he has no symptoms at present, and the urine shows nothing abnormal, there can be little doubt from his history and physical examination, that he has a chronic interstitial nephritis and belongs to that unusual class of cases in which for a time at least the urine shows no abnormalities. We have been permitted thus far to examine only one specimen of the urine, and it is quite possible that when we next examine it we may find albumin.

It is evident that we have to deal with a family in which there is a tendency to the development of chronic interstitial nephritis, this having occurred in the three eldest children.

The main points of interest in the case herewith presented are as follows:

1. The occurrence of a very advanced primary chronic interstitial nephritis at the age of fourteen years.

2. Its presence in other members of the same family.

3. The extensive and marked arterial changes present.

4. The hæmorrhagic diathesis and especially the occurrence of a large hæmorrhage in the mesentery.

5. The occurrence of calcific deposits in the liver.

6. The case draws our attention again to the latency of some of these cases of chronic nephritis in children. There is no doubt that some of them have been regarded as instances of diabetes insipidus. The necessity of a careful and continued observation of the heart and vessels in such cases is apparent. Others are treated for a long time for anæmia without its cause being discovered. Still others do not present themselves for treatment until the fatal termination is close at hand, the patients having had no marked symptoms. The fact that chronic nephritis may run so latent a course and may occur at any age should lead us to pay as much attention to the examination of the urine of children as of adults.

We are indebted to Dr. F. S. Mandlebaum, the pathologist of Mount Sinai Hospital, for much valuable assistance in connection with the histological part of this investigation.

DESCRIPTION OF PLATE XXV.

Fig. 1.—Section of liver showing areas of calcification. Low magnification.

Fig. 2.—Section of kidney showing obliterating endarteritis, calcified vessel, and chronic interstitial nephritis. Low power.

Fig. 3. Section of calcified artery seen in Fig. 2, with higher magnification.

Fig. 4.—Section of kidney showing the lesions of advanced chronic interstitial nephritis.

Fig. 5.—Section of wall of calcified coronary artery of the heart.

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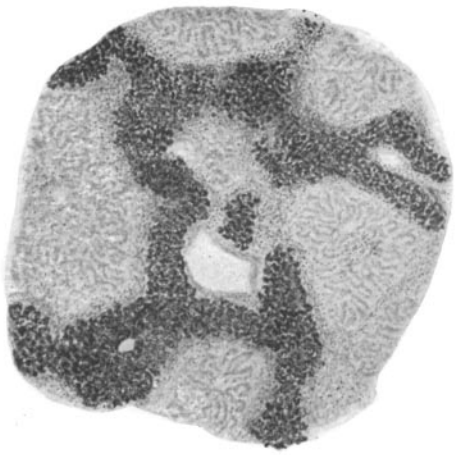

FIG. 1.

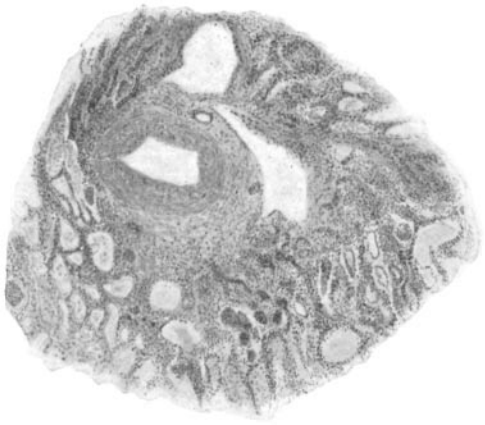

FIG. 2.

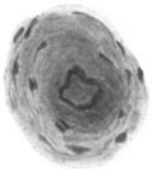

FIG. 3.

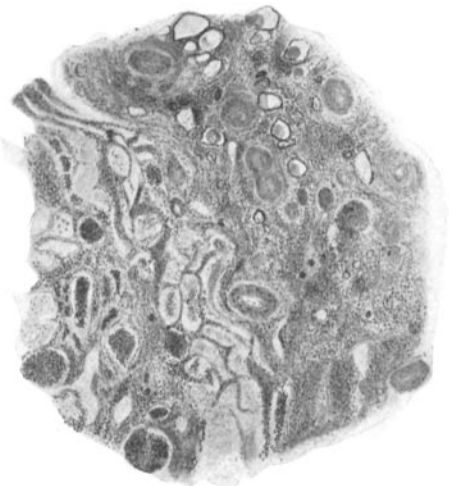

FIG. 4.

FIG. 5.