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CHRONIC INTERSTITIAL NEPHRITIS IN CHILDHOOD.

A Paper read before the Harveian Society of London on Nov. 19th, 1896.

BY

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Reprinted from THE LANCET, February 27 and March 13, 1897

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CHRONIC INTERSTITIAL NEPHRITIS IN CHILDHOOD.[1]

WHEN an adult aged upwards of forty years complains of headache and vomiting, drowsiness, languor and wasting, and on examination we find him sallow, cachectic-looking, and emaciated, the pulse hard, the heart hypertrophied, the urine of low specific gravity and increased in quantity, with or without a trace of albumin, we do not usually hesitate to diagnose granular kidney, although there may never be a sign of dropsy. Then if he dies comatose after a series of convulsions or gets a large cerebral hæmorrhage, the course of the case is not unusual. It is too common to be worth recording. But it is otherwise when young children suffer from similar symptoms. It is true that granular kidney is no longer regarded as essentially a disease of old age, but all agree that it is excessively rare under twenty.

I have collected seven cases of children aged between five and fourteen years who succumbed to chronic interstitial nephritis. In all of these the diagnosis was confirmed by post-mortem examination. Two of these, a girl and boy aged twelve and fourteen years, are recorded by Dr. Dickinson.[2] Dr. Goodhart quotes two from Dr. Ashby of Manchester, both girls, aged ten years and eleven and three-quarter years respectively. He also mentions a boy aged six years who died from the complaint.[3] Dr. W. H. Barlow[4] has related very fully and completely the history of a girl aged five years in whom typically granular kidneys were found after death.

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[1] A paper read before the Harveian Society of London on Nov. 19th, 1896.

[2] Albuminuria, second edition, p. 194.

[3] Keating's Encyclopædia of Children's Diseases, p. 541.

[4] THE LANCET, Aug 1st, 1874, p. 151.

Finally I have myself met with a little girl, aged seven years, who suffered from characteristic symptoms of granular kidney during life and in whom the lesions of interstitial nephritis were disclosed by post-mortem examination. A more extended research into the literature of the subject would doubtless reveal additional numbers, but those collected are sufficient to show the general nature of the symptoms and physical signs which may be expected in the course of the disease. I shall supplement them by impressions drawn from other cases which, being imperfect, I shall not mention in detail.

In this paper the so-called granular kidney is regarded as the product of interstitial nephritis in its last stage. In some of the cases in childhood to which reference is made, the kidneys in all respects answered to the classical description of small, red, granular or contracted kidney. In others, as in my own, they were only on their way to become granular or contracted. The process is, I believe, the same in all. It consists in small round cell infiltration of the renal stroma, apparently beginning in the cortex, and spreading in the form of bands towards the centre of the organ. It chiefly involves the glomeruli and blood-vessels at first. In time these bands of cellular infiltration become converted into fibroid tissue which contracts and thus causes peculiar distortion and shapelessness of the kidneys. The capsules gradually become adherent, and sometimes the inflammation spreads into the perinephritic cellular tissue, and may involve the suprarenal capsules, perhaps thus causing definite symptoms resembling those of Addison's disease. The entire process is extremely gradual, and affects successive portions of the kidney until the whole is involved, and the organ becomes generally contracted, or granular. Patches of recent cellular infiltration may be seen side by side with contracting areas of fibrosis. The effects on the secreting structures of the kidney are secondary to infiltration, and subsequent contraction of their stroma. The tubules become narrowed or strangulated and may form small cysts. Their epithelium undergoes fatty or granular degeneration. The Malpighian tufts shrink, and are converted into hyaline or amorphous masses, whilst their capsules are thickened. Parenchymatous changes are always less apparent than interstitial. The walls of the blood-vessels share in the general enlargement which affects those of the arterioles

throughout the body. I shall refer to this more fully in dealing with cardio-vascular hypertrophy. Finally, the entire process is extremely insidious and generally slow. The duration of the symptoms affords no clue to that of the disease. There are reasons for believing that interstitial nephritis may commence in early childhood, or even infancy, and not prove fatal for many years. The time at which it causes death will depend on the speed and the degree with which successive portions of the kidney become affected; and also, I believe, on the extent to which cardio-vascular compensation occurs and is maintained.[5]

Physical Signs and Symptoms.

The most striking physical signs which attend the disease are :—1. Wasting. 2. Dryness, absence of perspiration, coarseness, inelasticity, and pigmentation of the skin, together with anæmia. 3. High arterial tension and cardio-vascular hypertrophy.

The chief symptoms are :—1. Cerebral, including headache, vertigo, vomiting, and convulsions. Tetany and visual disturbances, such as amaurosis or diplopia, have been noted and also cerebral hæmorrhage in two cases.[6] 2. Gastro-intestinal, consisting of easily excited attacks of vomiting and diarrhœa, not necessarily uræmic. Sometimes there may be obstinate constipation or constipation alternating with diarrhœa, epigastric or abdominal pain. 3. Urinary symptoms including polyuria, often associated with thirst, and sometimes with enuresis. Low specific gravity of urine, albuminuria, and hæmaturia. 4. Pulmonary symptoms such as dyspnœa, bronchial catarrh, and those of pulmonary œdema have been noted. Asthma as in adults may possibly occur. 5. Cardiac symptoms, such as præcordial pain or distress with dyspnœa may arise. They do not appear to be so marked as in adults. 6. Dropsy is rarely met with in cases of interstitial nephritis.

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[5] The pathology as given above is not in accordance with the more modern views that granular kidney is the product of parenchymatous atrophy rather than of interstitial inflammation. A discussion as to the correctness of either theory would be out of place in a paper which deals with diagnosis and treatment rather than morbid anatomy.

[6] Filatoff records a third in a child aged eleven years. Emmet Holt, Diseases of Infancy, 1897, p. 621.

Yet sometimes slight general anasarca may occur, seldom lasting more than a day or two. It usually is noticed in connexion with an attack of headache or vomiting, and is associated with scanty, smoky, and albuminous urine containing blood casts. Such attacks might be considered to mark the onset of the mischief, but the general appearance and condition of the patient show that the disease is of long standing, although the dropsy and hæmaturia have been the first indication of illness.

Wasting.—The patients are generally stunted, undersized, and wizened. The wasting is usually of long standing and often dates from some illness in infancy or early childhood associated with vomiting, diarrhœa, and great prostration. Wasting, when of long standing, is apt to be regarded as constitutional, or as the patients' normal condition. Advice is not sought because they are thin, but because they easily take cold, or bronchitis, and suspicions of phthisis have been aroused, or on account of headaches with or without attacks of diarrhœa or vomiting. More rarely we see them because they are always thirsty, pass large quantities of urine, and are supposed to be diabetics. (Diabetes, by the way, like "consumptive bowels," is more readily suspected by the public than by medical men.) With polyuria and thirst there may be incontinence of urine, and this is the first symptom which has attracted attention. Wasting is from the first associated with a peculiar dryness and deficient perspiration of the skin, which later on becomes inelastic, and when pinched up, tends to remain in folds and wrinkles. This inelasticity is a most unfavourable sign. Dr. Eustace Smith has drawn attention to the condition which he rightly regards as significant of renal mischief in infants and young children. It is also met with in adults who are suffering from interstitial nephritis. Commonly the gums and conjunctivæ are singularly pale, but there is general capillary congestion which produces a dusky flush in the face and masks the anæmia.

Pigmentation.—With dryness, coarseness, absence of perspiration, and eventually inelasticity of the skin there is often pigmentation or discolouration, varying from mere sallowness to marked bronzing usually general in distribution, sometimes intensified in patches. Pigmentation is a physical sign which, although alluded to in text-books, has not, I think, received the attention it deserves. Bartels

says: "In this disease [granular nephritis] the skin not infrequently assumes a dirty faded colour." Dickinson mentions that one of his patients exhibited an appearance which he describes as "pallor luteus." Barlow was struck by the "brownish yellow" discolouration of the skin, contrasting with the steely whiteness of the conjunctivæ which his patient presented. My first patient, who died, looked dirty, though not actually so. Her general appearance was that of an anæmic person who had been much browned by the sun. Here and there the skin assumed a purplish hue due to capillary engorgement. Other cases seen since have led me to regard this pigmented appearance as a great aid in the diagnosis of interstitial nephritis. On several occasions I have been led by this alone to test the urine of children and usually it has been found in such cases to be slightly albuminous and of low specific gravity. Further examination has also brought to light other symptoms and signs of the disease. The pigmentation in many respects strongly resembles that of Addison's disease, but it has not been found to affect the mucous membrane, neither have the "sepia spots" and melanosis of old scars, characteristic of Addison's disease, been observed. It is usually more marked about the abdomen and flanks than elsewhere, but sometimes is seen to excess in the folds of the axillæ and groins. Within the last four years I have met with three girls, aged nine, ten, and eleven years respectively, who all showed marked pigmentation of the body generally. In two of them a diagnosis of Addison's disease had been actually given. But in all three it seems more likely that interstitial nephritis was the primary condition, for two of them had fairly well-marked signs of cardio-vascular hypertrophy and slight albuminuria, whilst the urine of the third is habitually of low specific gravity and its amount is considerably above normal. The duration of the pigmentation—eight, ten, and four years—the absence of perspiration and presence of a dry, coarse skin are also against the diagnosis of Addison's disease in all three cases. Two of these are at present under observation; the history of the third cannot, unfortunately, be traced. Such pigmentation occurs in adults also and may lead to confusion.

I have post-mortem notes on two women, both aged thirty-six years, who died in the North-West London Hospital. They were both under the care of my colleague, Dr. Harry

Campbell. My notes state that both showed marked general umber-brown discolouration of the skin, not more excessive about the neck, axillæ, and inguinal folds than elsewhere. Both bodies were much emaciated, but not dropsical. The kidneys in both instances showed most advanced granular degeneration. The suprarenal capsules appeared normal in one case, but in the other the right adrenal was firmly adherent to the under surface of the liver. In the latter case the heart showed no signs of hypertrophy, neither were the arteries thickened, but in the former cardio-vascular hypertrophy was very considerable. Dr. Campbell tells me in a letter concerning them: "The first case I was actually inclined to diagnose as Addison's disease on account of the pigmentation, anæmia, prostration, and vomiting (which latter was, as it turned out, uræmic). I did not suspect granular kidney in the second case until the albumin was discovered, for the cardio-vascular changes were not obtrusive. I can recall two other cases of granular kidney recently seen in which the pigmentation was well marked. These patients were well past the middle age, and there could be no mistake about the diagnosis."

I would draw attention to the fact that children often suffer from severe enteritis at the commencement of their troubles. I shall presently mention cases which seem to show that acute interstitial nephritis may occur in infancy with mainly gastro-intestinal symptoms, and shall suggest that this may end in the more chronic varieties of granular kidney.

The cause of pigmentation in interstitial nephritis is sometimes, probably, interference with the functions of the suprarenal bodies by the morbid processes affecting the adjoining kidneys. It is true that with the exception of Dr. Campbell's case to which I have alluded no mention is made of the suprarenal capsules in the fatal cases which I have collected, and the presumption is that they appeared healthy. But in my own fatal case there was considerable inflammatory matting noticed about the peri-nephritic cellular tissue. It is possible that although the adrenals themselves looked healthy yet their vessels and lymphatics may have been involved in the inflamed tissues around, and thus the organs may have been rendered functionless. Dr. Rolleston [7] suggests a similar explanation

[7] Goulstonian Lectures (1895), THE LANCET, March 23rd and 30th, 1895.

of cases of Addison's disease, in which the adrenals have been healthy, whilst the sympathetic or semilunar ganglia have been involved in adhesions or a new growth, such cases having been held to support the sympathetic origin of Addison's disease. Dr. Rolleston's explanation may account for pigmentation in some cases of interstitial nephritis; or it may be that general deterioration of the blood in interstitial nephritis tells on the adrenals as on other organs, and interferes with their functions. In cases of long-standing exophthalmic goitre the skin often becomes deeply pigmented as in Addison's disease. In the museum of St. Bartholomew's Hospital there is a coloured picture of a female, labelled "Addison's and Graves's disease." One of the most marked degrees of pigmentation that I have ever seen was in a woman, aged about sixty years, whom I visited in consultation with Dr. Rountree of Camden Town. She was dying from heart failure consequent on Graves's disease of many years' duration. She died shortly afterwards, but unfortunately a post-mortem examination was not allowed. The causation of pigmentation in Graves's disease is as obscure as in interstitial nephritis, pregnancy, and, one may add, in Addison's disease itself. Morbid conditions of the abdominal sympathetic will not alone account for it because they are not constant. Perhaps when we have said that toxæmia is the result of disease affecting the thyroid gland, the suprarenals, and the kidneys, and that such toxæmia in some manner interferes with the disposal of pigment by the 'carrier" cells, we have admitted as much as our present knowledge of the subject allows.

The causes of pigmentation cannot be fully discussed here; the point on which stress is laid is that pigmentation practically indistinguishable from that of Addison's disease is a most important diagnostic sign of interstitial nephritis in both old and young, although not existing invariably.

Cardio-vascular conditions.—In all the fatal cases but one marked hypertrophy of the heart was noted; in the remaining one the heart is said to have been found widely dilated after death. Probably the dilatation here was secondary to hypertrophy. In an unfinished case of Dr. Goodhart's it is stated that the heart and vessels were normal, and also in one of Dr. Campbell's cases to which I have alluded. Thickening of the vessels in the kidneys and elsewhere was observed in

several of the fatal cases. Though it is not mentioned in all yet it is almost certain that the condition would have been found if looked for. Cardio-vascular hypertrophy is, therefore, in children as in adults, a most useful indication of interstitial nephritis. Increase of pulse-tension during life is not recorded except in my own cases, where it attracted attention from the first. Yet there can be little doubt that when the heart is found hypertrophied and the vessels thick after death there must have been high pulse-tension at one time or another during life. Possibly it escaped observation, as in most of the fatal cases the diagnosis of interstitial nephritis was not completed during life. One's estimation of the hardness of a pulse is apt to depend to some extent on the knowledge that albuminuria is present. If albumin is found the nicety of one's perception appears to be increased, and a pulse is recognised as hard which was previously not accounted so. I do not mean to imply by this that the high tension is imaginary, but that it may be unrecognised unless one is prepared to find it. In young children the pulse-tension may in some cases be difficult to gauge owing to the smallness of the vessel, but, as a rule there is no such difficulty. As regards the physical signs of cardiac hypertrophy; by the time children come under observation, increase in size of the left ventricle is usually obvious; but in earlier stages the hypertrophy is only manifest after repeated examination. It should be remembered that in young children the apex beat is normally nearer the nipple than in adults. Even when increase in cardiac dulness cannot be made out, the heaving, forcible impulse, the dull, heavy first sound, and the accentuation or re-duplication of the second sound point to incipient hypertrophy. In later stages temporary bruits are often heard over various parts of the heart. Sometimes they are merely hæmic, but at others they suggest temporary incompetence of the various valves and indicate failure of cardiac compensation.

For practical purposes signs of cardio-vascular hypertrophy may be regarded as constant in children suffering from this disease. But there may be apparent exceptions to this rule. For instance, a heart which is naturally smaller than the average may become very considerably hypertrophied and yet remain well within the limits of normal weight and thickness. I have notes of a necropsy on an adult female whose heart

weighed only three ounces. Except that the great vessels looked disproportionately large the organ seemed in every way healthy. Such a heart might have increased its bulk fourfold and yet would not have been regarded as hypertrophied. A similar explanation may apply to cases in which the walls of the vessels do not appear to be unduly thickened.

Absence of dropsy, its causation and connexion with cardio-vascular hypertrophy and high arterial tension.—In all the fatal cases of interstitial nephritis which I have mentioned, with one exception, dropsy was said to be entirely absent; in the exceptional case it only occurred shortly before death and was apparently limited in extent. In an adult one is quite prepared to suspect the existence of nephritis, although there may not be the slightest sign of anasarca. But in a child all will agree that the outward and visible sign of nephritis is dropsy, and if this sign is absent one does not readily think of nephritis, although the symptoms may be precisely similar to those of the adult. Dropsy was absent in all but one of these cases, and it is within the scope of this paper to inquire why. As to the causation of dropsy, it is sufficient to say that the recent researches of Dr. Starling [8] have done much to confirm the view that dropsy depends on (1) difference between intra-capillary and extra-capillary blood pressure; and (2) on increased permeability of the capillary walls. In cardiac dropsy it is probable that increase of intra-capillary blood pressure, due to cardiac incompetence and subsequent venous engorgement, is the prominent factor. In renal dropsy it seems likely that increased permeability of the capillary walls due to lowering of their vitality and nutrition by the circulation of impure blood is the primary cause; whilst if such permeability is increased it is obvious that any excess of intra-capillary pressure will favour transudation or dropsy, and that it will be further favoured by stagnation of blood within the capillaries. To counteract the effects of increased permeability of the capillary walls, intra-capillary pressure must be kept low. Intra-capillary blood pressure may be lowered by general constriction of arterioles, the result of which will be to deliver less blood in a given time

[8] The Arris and Gale Lectures (1896), THE LANCET, May 9th, 16th, and 23rd, 1896.

to the capillary area, than usual. But such constriction will produce an enormous increase of labour for the heart. If the heart fails to meet it and becomes incompetent or dilated, backward pressure must occur in the veins; this will spread to the capillaries, and, given the fact that the permeability of their walls is increased, one may expect increased transudation or dropsy. Therefore, constriction of the arterioles alone is not sufficient to lower intra-capillary pressure by reducing the blood supply unless the heart remains competent. But, supposing the heart by becoming hypertrophied is able to meet the increased labour thrown upon it by constriction of the arterioles in front, the result will be that the blood supply from the arterioles to the capillaries will be reduced in volume. Its velocity will also be increased, for Bayliss and Starling[9] have shown that the result of general constriction of arterioles is the equivalent of plethora, whilst Cohnheim has demonstrated that in plethora the velocity of the blood is largely increased. It seems reasonable to suppose that transudation through damaged capillary walls will be lessened by the delivery of smaller volumes of blood at a higher rate of speed than normal into the capillary area, and also that stagnation in the capillaries, which must naturally favour the occurrence of dropsy, will thereby be prevented. In interstitial nephritis, constriction of arterioles, and increased force of cardiac action undoubtedly exist, and it may be that the absence of dropsy in this disease is due to the increase in velocity and diminution in volume of blood delivered to the capillary area thus produced.

In other words, cardio-vascular hypertrophy and high arterial tension are the direct antagonists of dropsy.[10] The clinical evidence of this is (1) that the initial dropsy of renal disease tends to decrease *pari passu* with increase of pulse-tension and hypertrophy of the left ventricle;[11] (2) that if the arterial tension remains low, dropsy increases (Sansom); and (3) if, whilst pulse tension remains high, the heart does not become hypertrophied, but dilated, with incompetent valves, dropsy is again the result.

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[9] Journal of Physiology, April 17th, 1894.

[10] Cf. W. H. Dickinson, Baillie Lectures, THE LANCET, July 20th, 1895, p. 139.

[11] Cf. Proceedings of the Royal Medical and Chirurgical Society, 1892, p. 113, et seq.

But what are the causes of cardio-vascular hypertrophy itself? The left ventricle enlarges because it has increased work to do owing to obstruction in front. The obstruction must to some extent occur in the capillaries if it be true that their walls are damaged by the circulation of impure blood. This is Dickinson's view. But the late Sir George Johnson always held that the obstruction was due to spasmodic contraction of the muscular walls of the arterioles and not to capillary resistance. It is obvious that such spasmodic contraction would produce high arterial tension and throw increased work on the heart, which accordingly would become hypertrophied. But what is the evidence that the arterioles are in a state of spasmodic contraction in nephritis? It is (1) that high arterial tension can be lowered in early cases where it exists, by nitrite of amyl (Sir W. Broadbent); and (2) also that the muscular walls of the arterioles are found hypertrophied after death. This hypermyotrophy can only depend on the constant exercise of the muscular function of arterioles, which is to contract. Discrepancy as to the existence of hypermyotrophy of the arterioles may be explained by the fact that the muscular coats of vessels require prolonged staining before showing their characteristic structure. (For this observation I am indebted to Dr. T. Savill.) Increase of the fibrous tissues of vessels, which is also present but less marked than that of the muscular coats, may perhaps depend on congestion of the vasa vasorum. Few at the present day accept the view of Gull and Sutton that granular kidney is merely a part of a general arterio-capillary fibrosis affecting viscera and vessels alike. On the other hand, it is not disputed that such general arterio-capillary fibrosis may occur as part of senile degeneration. There is, therefore, evidence which warrants the belief that high arterial tension is due largely to muscular contraction of the arterioles, and that this leads both to hypertrophy of the left ventricle, and hypertrophy of the muscular arterioles themselves; whilst it has been maintained that muscular contraction of the arterioles combined with increased force of cardiac action, will have the effect of delivering small quantities of blood at a high rate of speed to the capillary area, and thus transudation through unduly permeable capillary walls, or dropsy, will be lessened and intra-capillary pressure reduced. Thus cardio-vascular hypertrophy is nature's method of relieving and preventing

dropsy. When it fails to occur or to be maintained dropsy is the result.

Why is dropsy early and extreme in parenchymatous nephritis, whilst it is late and usually insignificant or absent in interstitial nephritis? I take it that these differences depend chiefly on the natures of the two morbid processes. In parenchymatous nephritis the secreting portions rather than the stroma of the organ are affected, and the whole at once rather than successive portions. This must lead to enormous accumulation of poisons in the blood with corresponding damage to, and increase of permeability of, the capillary walls. But this is not all. High arterial tension prevails as much in parenchymatous as in interstitial nephritis. But in the former the resulting strain on the heart occurs before it has time to acquire sufficient force to meet it. As Sir W. Broadbent has pointed out, the cardiac phenomena of acute parenchymatous nephritis are those of acute dilatation.[12] Hence the resultant dropsy in early parenchymatous nephritis is partly cardiac, as is the case in its later stages. In interstitial nephritis, on the other hand, the secreting structure is only involved slowly, secondarily, and by degrees. Elimination is carried on for a lengthened period whilst polyuria prevails. Yet the blood must be impure and the arterioles resist its passage by becoming constricted. But the resistance is gradual and insidious as is the rest of the morbid process. The heart has time to acquire sufficient strength and becomes by degrees hypertrophied in order to meet the increasing labour thrown upon it. Finally, as in parenchymatous nephritis, the heart gives way, for compensation cannot go on for ever, and dropsy of the true cardiac type is the result.

Summary.—1. Toxæmia is present in all forms of nephritis. 2. The poison irritates and lowers the nutrition, thereby increasing the permeability of the capillary walls. 3. It also causes spasmodic constriction of the arterioles either by direct irritation or through the vaso-motor centres. 4. The result of spasmodic constriction of the arterioles is: (*a*) to reduce the capillary blood supply; and (*b*) to produce hypermyotrophy of the arterioles and usually in time of

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[12] Transactions of the Royal Medical and Chirurgical Society, 1892, p. 123

the heart. 5. If the heart is able to meet the labour thrown upon it, the velocity of the blood stream into the capillaries is increased, whilst its volume is lessened by constriction of the arterioles. These conditions of the circulation will tend to lessen transudation through the capillary walls, lower intra-capillary blood pressure, and therefore control dropsy. 6. If the heart fails to meet the demand, whether in early or later stages of renal disease, dropsy is maintained in the one case and produced in the other.

Mental characteristics.—Children suffering from this complaint seem to be shrewd, precocious, and intelligent beyond their years. This was noted particularly in Dr. Barlow's fatal case. In my own fatal case there was a peculiar mental perversity. The patient apparently soon discovered that she was an object of interest, and did all she could to attract attention. She would scream incessantly and feign unconsciousness during the friends' visiting hour at hospital, but afterwards would confess that she knew all that was going on. She would beg that poison might be given her and disturb the whole building by her shrieks at night, but would be quiet directly she had succeeded in having the house physician called up to see her. It was difficult to ascertain whether she were actually in pain or only counterfeiting it.

I have observed in other cases that intelligence appears to be above the average. It is possible that the active cerebral circulation in such cases due to cardio-vascular hypertrophy may conduce to premature mental development. There may be more truth than W. S. Gilbert supposed in his ballad concerning the precocious child, who died "an enfeebled old dotard at five."

Cerebral symptoms.—Headache and vomiting were prominent features in four of these fatal cases. In two headaches were frequent, but there is no mention of vomiting. In one vomiting was frequent, but not headache. Vertigo and amaurosis accompanied headache and vomiting in my own fatal case. The localisation of headaches is of no value; it is usually frontal, but may be occipital, coronal, or lateral. They resemble those of migraine in their periodicity, severity, and association with visual disturbance or vertigo, and in being often relieved by vomiting. Also, at first they

commonly occur on waking in the morning, as in migraine, though later they may happen at any time of the day. I shall mention presently points by which they may be distinguished from other headaches. As to the cause of headaches in interstitial nephritis, in many cases they are doubtless uræmic, especially when occurring late in the course of the disease. But they may also be produced by alterations in the cerebral circulation, dependent on the increase of arterial tension which prevails. Their occurrence in the early morning may depend on sudden increase of tension in arterioles which have been previously relaxed during sleep. The later or more strictly uræmic headaches may also occur chiefly on first rising, owing to the effect of the accumulation of toxins in the blood during the night.

Vomiting may occur either with or without headaches; it may be independent of food or otherwise. It may be strictly cerebral and, like headache, produced by vascular conditions of the brain. Sometimes it seems to be purely gastric and due to congestion, catarrh, and irritability of the stomach. These are probably the causes in early stages of the disease, whilst late vomiting is, like late headache, dependent on uræmia. There can be no doubt that uræmia occurs far later and is far graver in interstitial nephritis than in parenchymatous.

Albuminuric retinitis might be expected to occur in children as in adults suffering from chronic interstitial nephritis. But it is not mentioned in any of the cases collected, and in my own patients I have never discovered it. Convulsions were prominent in two of the cases; in two they only occurred just before death; in one they were absent, death being due to gradual exhaustion; in one there were attacks of tetany and opisthotonos, after one of which the boy died comatose; and in one, recorded by Dr. Goodhart,[13] there were also attacks of tetany and cramp in the legs, but the subsequent history is unknown to me. Convulsions are, therefore, fairly common in this disease; but they are far more common, they occur earlier, and are more usually recovered from, in cases of parenchymatous than in interstitial nephritis. In adults it is not uncommon to find granular

[13] Keating's Encyclopædia of Children's Diseases.

kidneys in a patient who has remained in apparent health until attacked by a series of convulsions during or directly after which he has died.

A point of interest about my own fatal case is that the convulsions were almost entirely unilateral. I do not doubt that they were uræmic, although the right side was chiefly affected. Large hæmorrhages in the right cerebral hemisphere were found after death, which probably, although not directly involving the motor tract, lowered its power of conducting impulses from the cortex downwards. A few days before death there was some transitory left hemi-paresis. Had the convulsions been due to the hæmorrhage, of course they would have affected the left and not the right side. Cerebral hæmorrhage occurred in one of Dr. Dickinson's fatal cases as well as in my own. I have not met with any other cases of hæmorrhage into the substance of the brain due to nephritis in children.[14] Cerebral apoplexy in children from any cause is, indeed, rare. It occurs in cases of purpura, commonly of scorbutic origin, but is usually then meningeal, forming the condition known as pachymeningitis hæmorrhagica. It is rarely intra-cerebral. Sometimes hæmorrhage, either intra- or extra-cerebral, is caused by rupture of miliary aneurysms of the arteries. The aneurysms themselves may be produced by syphilitic endarteritis or by weakening of the vessel wall consequent on embolism or thrombosis. During paroxysms of whooping-cough hæmorrhages into the brain or meninges or elsewhere may take place. In my own case no source of the larger hæmorrhages could be discovered, but one at least of the smaller extravasations was in the neighbourhood of a small thickened arteriole which had apparently burst. The larger hæmorrhages may have been similarly caused. The character of the symptoms rendered it unlikely that they were due to sudden rupture of large vessels.

Some cases of infantile hemiplegia or monoplegia are doubtless caused by hæmorrhage. But they are seldom fatal at the time, and when death occurs many years later all traces of hæmorrhage have disappeared, or else cysts may be found which may or may not have been hæmorrhagic in origin.

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[14] A third case has been reported by Filatoff in a child aged eleven years. (Emmett Holt: Diseases of Children, 1897, p. 621.)

The intestinal symptoms are not peculiarly distinctive of interstitial nephritis. Sometimes the appetite is capricious or enormous, and, as already stated, there may be extreme thirst. Diarrhœa, like gastric vomiting, may be dependent on catarrh or irritability of the bowels. It is provoked by the slightest indiscretion in diet. The motions are slimy, mucous, or frothy, and at times contain blood. There may be epigastric or abdominal pain. The attacks are soon over as a rule, but when obstinate and of long standing one must suspect the occurrence of albuminuric ulceration of the bowels. Sometimes constipation alternates with diarrhœa. One of Dr. Dickinson's patients suffered before death from purulent peritonitis. I have only seen one instance of this complication. But this was in a child, aged four years, who died from general dropsy and uræmic convulsions. Parenchymatous and not interstitial nephritis was found after death, and the kidneys contained abundance of uric acid crystals. Probably peritonitis in children, as in adults suffering from chronic nephritis, occurs in a proportion of about 10 per cent. It was found in 46 out of 406 cases collected by Sir William Roberts.

Urinary symptoms.—Polyuria was noted in four of the fatal cases, as much as three, four, or even five pints of urine being passed per diem. It is probably an early symptom in all cases, but is not likely to attract attention unless, as in Dr. Barlow's patient, it is associated with enuresis. Even in adults suffering from granular nephritis the symptom is rarely made the subject of complaint – in fact, it is usually regarded as a favourable sign that urine is passed freely; diminution in quantity, on the other hand, both in the child and adult, at once excites alarm. The amount, however, shows considerable variations, and when at its lowest, eclampsia is wont to occur. In my own fatal case the average amount of urine passed per diem was forty-eight ounces, but on the two days on which fits occurred, the amount fell to twenty-five ounces and eighteen ounces. On the days immediately succeeding the fits, the amounts were fourteen ounces and eighteen ounces, whilst on the second days following the fits, the quantities rose to eighty-four ounces and 106 ounces respectively. A similar reduction in quantity of urine in association with eclampsia is noted in two other cases. Generally speaking, there

is something to be said for the popular view that polyuria is a favourable sign, indicating as it does the completion of cardio-vascular compensation. Naturally, the greater the quantity of urine the greater the elimination of toxins. It is, none the less, an important symptom of a grave disease. Polyuria was associated with thirst in three of the fatal cases.

The specific gravity is generally low. In my own fatal case it was almost invariably 1010, occasionally 1008, and once only reached 1015. In two other cases, where it is mentioned, the specific gravities were 1004 and 1005 respectively, whilst in a third it varied between 1010 and 1020. It does not appear to be influenced by the amount of urine passed to any great extent. In my own fatal case it was 1010 when 106 ounces were passed in twenty-four hours, but only 1015 when the amount was fourteen ounces. Whilst Dr. Barlow's patient was passing from four to five pints of urine a day, the specific gravity was 1015, and it only rose to 1020 when the amount had declined to three-quarters of a pint.

The albumin varies greatly in quantity. It may be entirely absent at first. Generally speaking, the amount is not large—or not so large as in cases of parenchymatous nephritis. In one only the urine is said to have become at times almost solid on boiling. This occurred during attacks of vomiting and tetany, when, instead of the usual polyuria, there was marked scantiness of the urine.

Casts in the urine are rare. They are usually of the hyaline variety, but sometimes are granular. Blood casts may occur in association with the acute exacerbations already mentioned in the course of the disease. Ordinarily there is seldom abundance of any deposit. The urine generally is clear, pale, and acid.

No statement is made as to the percentage of urea in any of these cases. In all probability it would have been found reduced below normal. To avoid fallacy it is worth remembering that children normally pass a larger relative quantity of solid matter than adults. (According to Dr. Eustace Smith the average amount passed by a child is five grains for each pound of body weight. In the adult Dr. Parkes estimates the amount as 3½ grains per pound weight.)

Pulmonary symptoms.—Children suffering from interstitial nephritis are often subject to recurrent attacks of bronchial

catarrh as well as of gastro-intestinal catarrh, and may first be seen on this account. They are often somewhat breathless after exertion, but the dyspnœa is not usually extreme except in the last stages of the disease, when pulmonary œdema is common. In adults the recent occurrence of attacks of spasmodic asthma in a patient who is not a typical asthmatic, and who does not suffer from chronic bronchitis or heart disease, suggests uræmia. Such attacks when uræmic are of extemely fatal augury. Asthmatic attacks, however, are not necessarily uræmic; the speedy relief afforded by nitrite of amyl suggests that they may be due to constriction of the pulmonary arterioles in some cases. I have not met with them in children suffering from interstitial nephritis. But my experience is limited; and as the symptoms in children in other respects precisely resemble those of adults, it is probable that children also might suffer from asthma. In adults suffering from granular kidney, pleurisy, pleuro-pneumonia, and pericarditis commonly end the scene. I have not met with such instances in children, nevertheless they may doubtless occur.

Cardiac symptoms are not obtrusive. There may be slight præcordial pain or distress on exertion. In two of my cases these were amongst the first symptoms which arose. Probably slow cardiac hypertrophy is unattended by symptoms unless it is on the point of failing.

Etiology of Chronic Interstitial Nephritis.

Once it was thought that all granular kidneys were simply large white kidneys in their final or contracted stage. But this cannot be so in all cases, because a large white kidney sufficiently diseased to end in contraction, must have been attended by definite symptoms of severe illness, including dropsy. Yet the majority of those who die with granular contracted kidneys have not been severely ill until shortly before death, and are said never to have had dropsy, and dropsy is not a condition which can be readily overlooked.

Possible scarlatinal origin.—One naturally thinks of scarlet fever in these cases. This is undoubtedly the origin in some, but in the majority there is no history of scarlet fever. Mild scarlet fever may easily escape recognition, it is true, and so may subsequent desquamation and also slight attacks of

nephritis. But attacks of scarlet fever so mild as to escape recognition at the time are hardly likely to be followed by lasting progressive and finally fatal renal mischief. Even in the worst cases of undoubted scarlatinal nephritis the prognosis is generally good. Children very rarely die from it. And if the prognosis is good in the worst cases it must be better in the mildest. Otherwise, the milder the initial fever the more hopeless would be the prospect. Scarlet fever cannot be regarded as the cause of all cases of interstitial nephritis, though doubtless it is so in some.

The character of the nephritis.—Is the nephritis of an ascending character due to previous bladder trouble or obstruction of the ureters or exit of the bladder? In my own fatal case and also in the two recorded by Dr. Dickinson the kidneys were very unequal in size and the pelvis or upper part of the ureter connected with the smaller kidney were found somewhat dilated. In one of Dr. Dickinson's patients a vesical calculus had been removed many years before death, and he suggests that in both cases there may have been some bygone obstruction to the exit of urine, although no actual obstruction was found after death. Dr. Goodhart[15] was struck by the cases he had himself seen and by those recorded by others, in which a shrunken kidney was found with a dilated pelvis. He regarded the latter condition not necessarily as a proof of obstruction, but possibly merely an indication of atony of the ureter. At the same time he held that impaction of small calculi in the ureters was not uncommon in children. This is indisputable, but it is difficult to see how impaction of a calculus in one ureter should produce interstitial nephritis in both kidneys. For the affection of the two kidneys only differed in degree, and not in kind. Yet I am inclined to think that the dilatation of the ureter on the side of the kidney most contracted (though not the nephritis) may be dependent on obstruction brought about as follows: Polyuria is a marked symptom of granular nephritis: the result of this would be more or less constant fulness of the bladder with a certain amount of backward pressure in the ureters. Now if granular kidneys secrete more water than normal it follows that the more granular the kidney the more

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[15] Keating's Encyclopædia of Children's Diseases.

water it will secrete. Hence if any obstruction to the entrance of water into the bladder is occasioned by distension of the latter it follows that the obstruction will be most felt by the kidney which secretes most water. We may therefore get dilatation of the ureter on the side of the most contracted kidney. However, such obstruction would be secondary to nephritis, and not its primary cause.

Cystitis.—As regards their dependence on cystitis, no mention of the bladder is made in any of the cases which I have quoted, and I can only assume that it was healthy in all, as it undoubtedly was in my own.[16] Hence I must regard all the cases as being interstitial nephritis of primary nature. Dr. Dickinson gives as the causes of granular kidney, gout, lead, alcohol, cardiac changes leading to renal congestion, pregnancy, obstructional anuria, mental conditions, worry, &c., perhaps intermittent fever, and "a general fibrotic tendency affecting many organs and tissues, notably the arteries and kidneys." The last I have already referred to in the section on cardiac vascular changes. Lead and alcohol may be excluded in all the children to whom reference has been made. Of the other causes we may dismiss without discussion all but the first—namely, "gout," or rather uric-acidity, which may be regarded as the equivalent of gout, in childhood.

Uric acid nephritis.—Children who have what is termed the uric acid diathesis often suffer from attacks of pain referred to the loins or especially the sites of the ureters or bladder. These attacks are commonly associated with headache or gastro-intestinal disturbance. The urine is usually highly acid and of high specific gravity, irritating, and small in quantity. It contains abundant crystals of uric acid or oxalates. Often there are intermittent attacks of hæmaturia, hæmoglobinuria, or albuminuria. It is believed that the urinary symptoms are due to the passage of sharp and lacerating crystals of uric acid or oxalates through the urinary tracts, and it is certainly conceivable

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[16] In the Transactions of the Pathological Society, 1896, I have reported the case of an infant, aged ten weeks, in whom suppurative interstitial nephritis with dilatation of the ureters were caused by congenital malformation of the bladder and consequent cystitis.

that a long continuance of such irritation might lead to diffuse nephritis. Dr. Eustace Smith[17] says: "In a case where a child habitually passes large quantities of uric acid I should be disposed to fear the occurrence of Bright's disease; and the occasional presence of a trace of albumin would add strength to my apprehensions." My own experience of such cases, which are common enough, is that the patients speedily get well so far as the urinary symptoms are concerned under very simple treatment. They are, however, prone to run the whole gamut of rheumatic affections, such as tonsillitis, pericarditis and endocarditis, chorea, arthritis, and peliosis. I am inclined to think that the occasional presence of blood, free or in casts, and of albumin, are purely accidental in uric acid cases, and are due, as I have said, to slight renal laceration, and are not to be taken as evidence of nephritis.[18] In none of the fatal cases of interstitial nephritis which I have collected was the passage of uric acid a feature, and in none of them is there mention of the occurrence of rheumatic symptoms. I would therefore regard cases of so-called uric acid nephritis as in a totally different category to that of true interstitial nephritis.

Primary cause of granular kidney.—Dr. Emmet Holt[19] has collected twenty-three cases of primary nephritis in infants aged between two and a half months and two years, and of these eleven were fatal. Post-mortem examinations were made in ten. In five the kidneys showed ordinary parenchymatous nephritis, but in the remaining five the conditions found were regarded as those of acute interstitial nephritis characterised by infiltration of the renal stroma by small cells in scattered areas, with sometimes formation of new connective tissue. These cases, verified by post-mortem examination, prove that young infants may suffer from an acute form of interstitial nephritis. The characteristic lesions were found in one case after an illness of only three days' duration, in some after the

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[17] Diseases of Children, p. 757.

[18] It must be admitted that most forms of nephritis may be associated with the passage of uric acid in the urine, and after death in many cases uric acid may be found in the kidneys. Whether the uric acid is the cause of the nephritis, or only a product of disordered metabolism, dependent on the nephritis, must be left an open question. Many people pass large quantities of uric acid for a considerable portion of their lives, and appear, like birds and reptiles, none the worse for doing so.

[19] Archives of Pediatrics, 1897 vol. iv., p 1.

disease had lasted several weeks. The symptoms are mainly gastro-intestinal, such as vomiting, diarrhœa, or looseness of the bowels. In many there are marked cerebral symptoms, restlessness, screaming, convulsions, drowsiness or coma, as in meningitis. High fever is common, and hyperpyrexia may occur. The symptoms are not characteristic of nephritis. Dropsy was absent in all the fatal cases in which interstitial nephritis was found. The condition of the urine may or may not afford a clue to the nature of the disease. The urine may often be suppressed or scanty and of low specific gravity. Albumin was found in eight of Dr. Holt's cases, in one of them only three days before death, the illness having lasted more than two weeks. In one it was only found in the bladder after death. Casts (blood and hyaline) were present in four cases. Blood and pus were present in two.

As to the causation of acute interstitial nephritis.—Scarlet fever may be fairly excluded. Dr. Holt regards its existence as non-proven in all his cases. There is no evidence that any of these were cases of secondary or ascending nephritis or that the inflammation was syphilitic or tuberculous. Primary parenchymatous nephritis, when not scarlet fever, is usually held to be due to exposure to cold. Dr. Eustace Smith draws attention to the custom of short-coating babies at an early age and thus leaving them practically naked below the armpits and exposed to chills. He regards this practice as the possible cause of infantile parenchymatous nephritis, and, if so, it may also account for the interstitial form of the disease.

It might be thought that the deep situation of the kidneys in the body would afford them protection against the effects of chill to the surface of the skin. But mere depth of covering cannot render them immune any more than other organs. Otherwise, the obese would lead a charmed life. There can be no doubt that exposure to cold will produce nephritis in one person just as in others, it may be the exciting cause of tonsillitis, acute rheumatism, pneumonia, pleurisy, or hepatitis. Probably in all cases chill to the surface vitiates the functions of the blood, thus causing either actual generation of toxins or hindrance to their elimination, or perhaps imperfect phagocytosis. The organs which are weakest in the individual will be those to suffer.

We cannot predict whether it will be his tonsils, his lungs, his liver, or his kidneys, or explain why one organ should be attacked rather than another. If all are sound he may escape all ill effects. The nature of the poisons, generation or non-elimination of which, cause inflammation of the kidneys, as well as that of the poisons which are retained in the system in consequence of nephritis, remain unknown at present.

Granting the existence of a primary interstitial nephritis caused by chill, we can well believe that in such cases as recover from the immediate effects new connective intertubular tissue may gradually become contracted and produce in time the characteristic appearance of granular kidney. This may account for cases of renal cirrhosis of long standing even in adults in whom evidence of the other causes enumerated is wanted.

Summary.

Diagnosis.—In some cases the diagnosis presents no difficulty. We must suspect the existence of interstitial nephritis in a child who is emaciated, whose skin is coarse, dry, inelastic, and pigmented; who suffers from uncontrollable periodic attacks of vomiting, vertigo, and maddening headaches. Then if we find the heart's apex displaced outwards, the left ventricle hypertrophied, the second sound accentuated, the pulse hard, the urine of low specific gravity, increased in quantity, and albuminous, the diagnosis of interstitial nephritis is complete. Yet in such a case the disease is already far advanced and the end is not far off. It is characteristic of the complaint, both in adults and children, that the symptoms do not attract attention until there can be but little hope of recovery. Hence it is of the greatest importance to discover the disease in its earliest stages. Probably, wasting, gradual and progressive, is the first symptom to occur. Polyuria and thirst are also early symptoms. The first indication of polyuria may be enuresis. Pigmentation is also an early sign, though it may amount only to mere sallowness at first. A patient suffering from interstitial nephritis never looks well, although he may not complain of any symptoms. Headache, vomiting, and diarrhœa may not occur until the disease is well advanced. In all cases when suspicion of

nephritis is aroused, one examines the skin for dryness, coarseness, inelasticity, and pigmentation, the heart for incipient hypertrophy, the pulse for hardness, the urine for low specific gravity and albumin. When one or more of these conditions are absent others may take their place. Pigmentation may be wanting or slight in degree, but anæmia, with rough, dry skin, will be found. On the other hand, pigmentation, when the skin remains moist, smooth, and supple, is rather suggestive of true Addison's disease than of adrenal disease secondary to Bright's. But in true Addison's disease the heart is not hypertrophied and the pulse remains feeble and soft throughout, whereas in interstitial nephritis cardio-vascular hypertrophy and high arterial tension are almost universal. Yet cases of interstitial nephritis may run their course without apparent thickening of the heart or vessels. When this is so there may still be albuminuria to guide us. With cardio-vascular hypertrophy are usually associated headaches, increasing quantity and low specific gravity of the urine, but there may be no albumin. In adults, when compensating cardiac hypertrophy fails and gives way to dilatation, the urine usually is reduced in quantity, becomes albuminous, and dropsy appears. But in children suffering from interstitial nephritis dropsy is very rare, yet it may occur and may be the first symptom, together with scanty, smoky, and albuminous urine which draws attention to the disease. The condition of the skin and vascular system will serve to distinguish such attacks from those of ordinary acute nephritis. The differential diagnosis in these cases is most important. The absence of albumin, even after frequent and systematic testing, does not exclude the possible existence of the disease. Albumin may only occur occasionally or not till late. Hence the importance of frequent and systematic testing for its presence.

History of infantile nephritis.—Some help towards the diagnosis may be gained from a past history of a tedious gastro-intestinal complaint in a child who has remained emaciated, cachectic-looking, and with easily disturbed digestion ever since. The significance of violent periodic headaches, especially if associated with vomiting or vertigo, and occurring in the early morning, is very great. Like convulsions, they may not appear until the last stage of the

disease is at hand, but whenever they do occur, urinary symptoms or cardio-vascular changes will almost certainly be present to aid the diagnosis. The somewhat similar attacks due to cerebral tumour may be distinguished from them by being less periodic than chronic, with exacerbations, and by the presence of optic neuritis. Probably there will also be other nervous symptoms and conditions, such as paralysis or focal epilepsies, which will make the diagnosis of tumour certain. Wasting is in cases of cerebral tumour rare, except in the latest stages, unless the tumour is part of general tuberculosis; whilst in interstitial nephritis it is, I believe, universal. Headaches due to local conditions of the eyes, nose, throat, ears, and teeth are easily identified. Headaches due to simple anæmia, constipation, and general debility require no comment. Migraine headaches may at times be difficult to distinguish from those of interstitial nephritis, but they are unaccompanied by permanent cardio-vascular and urinary changes. Uric acid headaches may resemble those of interstitial nephritis, and the diagnosis may be further obscured by the occurrence of temporary attacks of hæmaturia and albuminuria and also by the cardiac enlargement often present in those of the so-called uric acid diathesis. But the presence of uric acid or oxalate crystals in the urine sufficiently accounts for the hæmaturia and albuminuria and does not *per se* indicate interstitial nephritis. The enlargement of the heart dependent upon valvular disease or pericarditis, met with in uric acid or rheumatic cases may be distinguished from that which forms part of the cardio-vascular changes of interstitial nephritis by the presence or history of other rheumatic signs and symptoms, such as tonsillitis, arthritis, appendicitis, peliosis, and chorea.[20] The distinction is important, especially in the case of pericarditis, as this complication is, I believe, speedily fatal in adults suffering from granular kidney, and would probably be so in children, whereas the immediate prognosis of ordinary rheumatic pericarditis in children is fair. Pulmonary symptoms in the interstitial nephritis of children are probably the same as in adults. Slight dyspnœa and attacks of bronchial catarrh may first lead the patient

[20] The permanence and fixed locality of the bruits in ordinary valvular disease will distinguish them from the temporary and shifting murmurs met with in commencing failure of the hypertrophied heart in interstitial nephritis.

to seek advice. Pulmonary œdema in late stages of the disease may mark the onset of uræmic convulsions. In either case the patient's appearance, heart, pulse, and urine will serve to distinguish such attacks from those of the ordinary pulmonary affections of childhood. Finally, it may be said that the symptoms of interstitial nephritis are as insidious and gradual as the morbid process itself. In many cases we can only suspect the existence of the disease. It may be months or even years before such suspicions prove to be well founded or are set at rest.

Prognosis.—Interstitial nephritis may go on for many years without causing the patient or his friends to think there is much amiss. The typical granular kidney must require a very long time to arrive at its condition. It is even possible that in an adult it may date from an attack of acute interstitial nephritis occurring in infancy. Yet the duration of the symptoms of which complaint is made rarely exceeds a few years, and may be only a matter of months or even weeks. In one of the fatal cases collected, symptoms had lasted three weeks. In two the duration was three months, and in three, symptoms had been observed for two, three, and five years respectively. As I have endeavoured to show, the effects of cardio-vascular hypertrophy are to avert, or at all events to compensate, for those of renal disease. Dropsy is reduced or is prevented by the circulatory changes, and uræmia by the polyuria which occur. Cardio-vascular compensation attains its height in interstitial nephritis, and the onset of symptoms depends to a great extent (1) on the failure of such compensation, and (2) on its being carried to excess. In adults failure and dilatation of the heart and degeneration of the bloodvessels are often the chief causes of the fatal symptoms. But in children and also in adults they may be actually due to excess of cardio-vascular compensation. Thus may be produced the violent headaches for which advice is often first sought. Extremely high general tension due to constriction of arterioles, combined with a powerfully acting heart, may cause hæmorrhage or cerebral apoplexy. Constriction of pulmonary arterioles may give rise to dyspnœa, asthma, or pulmonary apoplexy, or in the extremities it may cause Raynaud's disease or gangrene, whilst constriction of renal arterioles when carried to excess may, instead of increasing the amount of urine, actually

reduce it, and so bring about uræmia as well as further damage to the kidneys. So the prognosis will largely depend on the degree at which cardio-vascular hypertrophy is maintained and on our ability to aid or thwart its progress as required. Bad signs will be, commencing heart failure, headaches, vomiting, dyspnœa, with diminution of urine, increasing albuminuria, progressive wasting, and pigmentation. It is needless to point out that the prognosis will be more grave when symptoms of Addison's disease are superadded to those of interstitial nephritis. The surroundings of the patient and his liability therefrom to chills and consequent inflammations, so often fatal in this disease, must be considered in the prognosis. Finally, although the conditions of heart, pulse, skin, and urine make the existence of the disease evident, life may not be endangered unless signs of failing or of excessive cardio-vascular compensation arise. In the first case the child is no better off than the adult—both are doomed; but in the second case treatment may ward off danger for the time.

Treatment.—The treatment is symptomatic rather than curative; yet it is rational and follows the lines of pathology laid down. In parenchymatous nephritis, when dropsy threatens, or is present, and cardio-vascular hypertrophy is slow to occur and at first insufficient, we give digitalis, squill, and citrate of caffein, which are not only powerful heart tonics, but also have a constricting effect on the arterioles and thus promote diuresis. The utility of ergot and cantharides may be similarly explained. Citrate and acetate of potash become converted into alkaline carbonates in the "primæ viæ," and Brunton, Cash, and Gaskell [21] have shown that the effect of alkalies is to contract bloodvessels, whilst that of acids is the reverse. Bi-tartrate of potash is also a remote antacid. If it be true, as I have contended, that dropsy is averted or cured by constriction of arterioles and increased cardiac force, we can understand that the use of such drugs is rational. In interstitial nephritis, on the other hand, cardio-vascular compensatory hypertrophy is carried out to perfection, and this, together with consequent polyuria, prevents dropsy and also uræmia from occurring. Hence these drugs—cardio-vascular tonics—are not called

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[21] Brunton: Disorders of Digestion, 1886 edition, p. 343.

for in interstitial nephritis, unless cardio-vascular compensation fails. But it must be admitted that nature's endeavours to cure are at best imperfect. Cardio-vascular hypertrophy may be carried to excess in interstitial nephritis. Thus may be produced headaches or even apoplexy by rupture of vessels owing to excessive tension; dyspnœa and possibly asthma by constriction of the pulmonary arterioles, Raynaud's disease and gangrene by constriction of the arterioles in the extremities, and, above all, uræmia by suppression of urine due to constriction of the renal arterioles. The treatment commonly followed in such cases is rational. We lower arterial tension and relieve the heart by giving vascular depressants such as nitro-glycerine, nitrite of amyl, nitrites and nitrates generally; we promote elimination from the skin by warm or vapour baths, liquor ammoniæ acetatis and other diaphoretics, and from the bowels by hydragogue cathartics. Similar treatment is followed in cases of parenchymatous nephritis, where pulse tension is high and the heart threatens to give way owing to the obstruction in front. This is the "cardio-vascular depressant" as opposed to the "cardio-vascular excitant" mode of treatment. It is logically combined with catharsis and diaphoresis. So the treatment of interstitial nephritis in some cases consists in counteracting the effects of excessive cardio-vascular hypertrophy, and at the same time promoting the action of the skin and bowels in order to compensate for deficient elimination through the kidneys. In the later stages of interstitial nephritis, however, the whole system of cardio-vascular compensation tends to fall through, and then we must have recourse to the cardio-vascular excitants which are so useful in the early stages of parenchymatous nephritis. Possibly when supra-renal inadequacy is indicated by the presence of pigmentation, treatment by supra-renal extract may be of use, and this extract has also an extreme power of constricting vessels, which therefore may be beneficial in another way. The general conduct of the case aims at prevention of complications arising from chill by supplying suitable clothing and, if possible, climate. As to other complications: iron is always necessary to combat progressive anæmia; dyspepsia due to gastric congestion and irritability is best treated by bismuth, arsenic, and prussic acid; eclampsia may be checked by inhalation of chloroform or by rectal injection of chloral and bromides. Head-

aches may also be relieved by the latter taken internally, but free purgation is the most rational mode of treatment. Venesection is, I believe, both useless and dangerous in the late eclampsia of interstitial nephritis in children. Catharsis and diaphoresis are the best methods of depletion. Dry-cupping, however, may be useful in pulmonary œdema, pleurisy, and pericarditis. Finally, no drug can cure a damaged kidney. Sooner or later the morbid process going on must end in death. Treatment at best can only be palliative, yet by it we may hope to stave off the evil day, and I am convinced that the guiding principle should be—"Watch the heart and pulse."

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