

PROGRESS IN PEDIATRICS

RECENT CONTRIBUTIONS TO OUR KNOWLEDGE OF NEPHRITIS *

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PRODUCTION OF NEPHRITIS

Dickson¹ has succeeded in producing a chronic diffuse nephritis in rabbits, guinea-pigs and dogs by the repeated administration of uranium nitrate. The histologic picture closely resembled that found in man except for the absence of demonstrable arterial lesions. In guinea-pigs death was usually due to an attack of acute nephritis, frequently accompanied by more or less anasarca. In the more severe cases there was usually found also some hypertrophy of the left ventricle of the heart.

O'Hare² has also produced a chronic nephritis by injecting living cultures of colon bacilli intravenously into animals under the influence of uranium nitrate. In all, he experimented on 40 rabbits, but excludes from further consideration 22 which died shortly after the first injection. The kidneys of 12 of the remaining 18 showed sufficient chronic change to justify the term chronic experimental nephritis. "The lesions so produced are closely similar to those involving the renal tissues in chronic interstitial nephritis in man." The kidneys of the remaining six rabbits showed no more change than is frequently found in the normal animal.

Christian and O'Hare³ report on the glomerular lesions produced by acute uranium nephritis in the rabbit, and describe the following five forms: "There is a type of degenerative lesion evidenced mainly by the appearance of hyaline droplets in the capillary walls. Another type of lesion consists in the formation of fibrin thrombi in the capillaries. A third type is hemorrhagic in nature and appears usually as a rounded mass of fibrin enmeshing blood-corpuscles. A fourth type is a dilatation of the glomerular space with granular material. A fifth type is a proliferative lesion affecting chiefly the capillary endothelium, and to a much less extent the capsular epithelium."

* Submitted for publication March 1, 1914.

1. Dickson, E. C.: *Arch. Int. Med.*, 1912, ix, 557.

2. O'Hare, J. P.: *Arch. Int. Med.*, 1913, xii, 49.

3. Christian, H. A., and O'Hare, J. P.: *Jour. Med. Research*, 1913, xxiii, 227.

O'Hare⁴ has compared the lesions produced by uranium nitrate on dogs and on rabbits, and concludes that the dog is much more resistant to the poison, as a dose of uranium nitrate three and a half times as large per kilo of body weight as the one commonly employed in the rabbit produced no more extensive lesions. "The glomerular lesion with the formation of hyaline droplets is produced with great difficulty in the dog."

Baehr⁵ injected uranium nitrate in 0.35 to 0.8 mg. doses directly into the renal arteries of rabbits and found far more severe changes in the glomeruli than he did in the tubules. From 40 per cent. to 50 per cent. of the glomeruli were affected. Subcutaneous injections produced a similar but less marked result. Injections of 1 c.c. of a 2 per cent. solution of potassium chromate caused a high grade necrosis of the tubules, especially of the first and second parts of the tubuli contorti. One drop of croton oil diluted with fifty drops of olive oil, emulsified in 1 c.c. of distilled water and injected into the renal artery, led to severe glomerular changes with the formation of hemorrhagic cysts. A 0.02 to 0.05 per cent. aqueous solution of iodine produced a contracted kidney with secondary vascular sclerosis, without affecting the glomeruli.

MacNider⁶ made a careful anatomical study of the effect of the various kidney poisons on dogs, and decided that cantharidin, potassium dichromate, uranium nitrate and sodium arsenate all produce an acute nephritis by affecting first the vascular elements of the kidney and then the tubular. Uranium nitrate and potassium dichromate usually caused tubular changes much earlier than did cantharidin or sodium arsenate. In the early stages of the nephritis when the kidney under the microscope showed only vascular changes, the output of urine was increased. Then as the tubules became involved the amount of urine diminished. All the animals which had anuria showed also varying degrees of obstruction of the lumina of the tubules by desquamating epithelium. None of this was found in the animals who were killed during the stage of polyuria. Pearce⁷ considers that cantharidin and arsenic cause a vascular nephritis characterized by marked changes in the power of the kidney to respond to such stimuli as adrenalin or diuretin; and that potassium chromate, uranium nitrate and corrosive sublimate belong to another type with striking histological changes, namely, a tubular nephritis. Nevertheless, neither type can be obtained pure; for instance, in cantharidin nephritis, after the third day, many mitotic figures can be found in the tubular epithelium. Hence "great caution must be observed in ascribing

4. O'Hare, J. P.: *Arch. Int. Med.*, 1913, xii, 61.

5. Baehr, G.: *Beitr. z. path. Anat. u. z. allg. Path.*, 1913, lvi, 544.

6. MacNider, W. deB.: *Jour. Med. Research*, 1912, xxi, 79.

7. Pearce, R. M.: *Jour. Exper. Med.*, 1913, xvii, 542.

the physiological disturbances of kidney function caused by cantharidin as due to a vascular injury and in regarding cantharidin nephritis as a pure type of vascular nephritis."

The action of tartrates on the kidney has also been studied by Pearce.⁸ He has given the salt to dogs by mouth, intraperitoneally and subcutaneously, and finds that it produces necrosis of the convoluted tubules with fatty changes in the loops of Henle, and sometimes also in the collecting tubules. Exudative glomerular lesions occurred in about half of the severe cases. The mode of administration was without influence on the result. The urine is much diminished, is clear, of low gravity; and contains albumin and casts. Underhill, Wells and Goldschmidt⁹ found that sodium tartrate injected subcutaneously into rabbits failed to appear in the urine and concluded that the disintegrative effect of the salt on the convoluted tubules was sufficient to prevent its elimination. Evidently the glomeruli were unable to take over this function of the tubules. The same authors¹⁰ have also found that the administration of an alkali by mouth (sodium carbonate or citrate) during tartrate nephritis slightly favors the elimination of the urinary constituents and also has a slightly beneficial effect on the pathological changes in the kidneys.

Pearce¹¹ has found that crotalus venom caused an acute exudative glomerular nephritis in rabbits characterized by a persistent albuminuria and cylindruria, emaciation and death in five or six weeks. He was unable to produce any subacute or chronic glomerular lesions by this means.

Hirsch and Maschke¹² in the course of experiments on dogs, the details of which are not given, found that intraperitoneal injections of egg-white did not cause severe kidney degeneration. They state that by staining histological preparations of the kidneys they were able to trace the excretion of the egg white and that it was excreted through the glomeruli and not through the tubules.

Longcope¹³ has studied the action of foreign proteins on the kidney. He worked with horse serum and egg white on a large series of dogs, cats and rabbits, giving first a small sensitizing injection, and later repeated small doses insufficient to cause symptoms of anaphylactic shock. He found that changes were especially marked after peritoneal injections in the peritoneum and after intravenous injections in the liver of rabbits

8. Pearce, R. M., and Ringler, A. I.: *Jour. Med. Research*, 1913, xxiv, 57.

9. Underhill, F. P., Wells, H. G., and Goldschmidt, S.: *Jour. Exper. Med.*, 1913, xviii, 317.

10. Underhill, F. P., Wells, H. G., and Goldschmidt, S.: *Jour. Exper. Med.*, 1913, xviii, 322.

11. Pearce, R. M.: *Jour. Exper. Med.*, 1913, xviii, 149.

12. Hirsch, C., and Maschke, W.: *Berlin. klin. Wehnschr.*, 1912, xlix, 145.

13. Longcope, W. T.: *Jour. Exper. Med.*, 1913, xviii, 678.

and cats, and in the myocardium and kidneys of all groups of animals. In dogs and rabbits there developed a well-marked nephritis characterized by degeneration and necrosis of the epithelium of the loops of Henle, of the collecting tubules, and less frequently of the convoluted tubules. There were also acute and chronic alterations in the glomeruli of all groups of animals. He decides that "though it is impossible at the present time to say definitely that the development of nephritis depends exclusively on the previous sensitization of the animal to these substances (the foreign proteins), it seems probable that at least any primary toxicity of the protein for the kidney cells was heightened by this procedure, and that the lesions in the kidney as well as those in the liver, myocardium and peritoneum are to be interpreted as a generalized reaction analogous to the local 'Arthus phenomenon' in the skin of the rabbit." He makes no mention of the production of fever as a result of the repeated protein injections.

PROTEIN AND THE KIDNEY

The retention of foreign proteins by the kidney has been studied at length by Pearce.¹⁴ He injected a series of rabbits with egg white or horse serum, killed them at varying intervals after the injection and made extracts of their kidneys. He concludes that "extracts of the kidneys of normal rabbits prepared one, two, three and four days after the intravenous injection of egg-white and horse serum have the power to sensitize guinea-pigs to a second injection of these proteins. The sensitization by first- and second-day extracts was constant and intense, that by the third-day extracts was less marked and sometimes was not evident, and that by the fourth-day extracts was only occasional, and when present was always weak. Comparative studies of the power of the blood, liver and kidney to sensitize indicate that this sensitization depends on the content of the foreign protein in the circulating blood and not on its accumulation or fixation in the tissues of an organ. This opinion is supported by other experiments in which the sensitizing power of the blood and of the extracts of unmarked kidneys was compared with the sensitizing power of marked kidneys. The weak sensitizing power of washed kidney extracts is taken as evidence that foreign proteins of the kind used are not held in the tissues of the kidney, and, if these results may be applied to nephrotoxic proteins, it follows that nephritis is not due to selection and persisting fixation of a protein by the renal cells, but is due to the action of such proteins merely during the process of elimination. In experimental acute nephritis of the type due to uranium nitrate, the power of sensitization to egg albumin is prolonged for

14. Pearce, R. M.: *Jour. Exper. Med.*, 1912, xvi, 349.

twenty-four hours, and in the chromate type for forty-eight hours, thus indicating that in nephritis of the acute type at least the elimination of a foreign protein is delayed." His attempts to obtain sensitization in this way with vegetable or bacterial proteins failed.

Vaughan¹⁵ comments on this as follows: "In our opinion the possibility of harm coming to the kidney or any other organ from the deposition of a foreign protein in it is not due to any directly poisonous effect of the foreign protein, but to the liberation of the poisonous group when the body cells become sensitized and split up the foreign protein."

Folin¹⁶ has applied his new methods for nitrogen determination in the blood to cats suffering from various forms of acute experimental nephritis. In the tubular type, as illustrated by chromate nephritis, there was only moderate nitrogen retention; whereas in uranium and cantharidin nephritis, in which both tubules and glomeruli are involved, the additional lesions in the glomeruli led to a marked retention of nitrogenous waste products.

CHLORID IN NEPHRITIS

Borchardt¹⁷ concludes from a review of the literature that sodium chlorid is excreted through the glomeruli by filtration and then concentrated by the reabsorption of the water during its passage through the tubules. When the tubular epithelium is injured the salt also is reabsorbed, so that the urine cannot be concentrated. In the acute stage of glomerular disease there is chlorid retention because of the lessened area of filtration. On the other hand, in a mild acute glomerulonephritis, or during the chronic stage, the chlorid excretion is normal. In general, "a normal sodium chlorid excretion speaks strongly against a severe disease of the kidney epithelium."

Ambard and Weill¹⁸ consider that the concentrations of urea and chlorid in the urine, and the total amounts of each excreted, bear a certain definite relation to each other, both in health and in disease. If this is true, and if it is granted that some nephritis is primarily tubular and some primarily glomerular, then the prevailing view, that chlorids are excreted by the glomeruli and urea by the tubules, must necessarily be false. Their argument is based on clinical studies of nephritis in man.

Widal, Amberg and Weill¹⁹ have studied the influence of a salt-free diet on the threshold for the excretion of chlorids by the kidney. They

15. Vaughn, V. C.: *Protein Split Products*, Lea & Febiger, Philadelphia, 1913, p. 363.

16. Folin, O., Karsner, H. T., and Denis, W.: *Jour. Exper. Med.*, 1912, xvi, 789.

17. Borchardt: *Deutsche Med. Wehnschr.*, 1912, xxxviii, 1723.

18. Ambard, L., and Weill, A.: *Semaine méd.*, 1912, xxxii, 217.

19. Widal, F., Amberg, L., and Weill, A., *Semaine Med.*, 1912, xxxii, 361.

found that in cases of nephritis with edema the threshold was considerably raised and that there was a more or less marked retention of chlorids. By giving or withholding salt in the diet they were able in most cases to raise or lower the threshold at will and simultaneously to cause the appearance or disappearance of the edema. In cases of nephritis without edema they found no retention of the chlorids.

DIURETICS IN NEPHRITIS

Boycott and Ryffel²⁰ have compared the effects of the so-called "secretory" and "mechanical" diuretics in acute experimental nephritis in rabbits. The former are supposed to act on the tubules and the latter on the glomeruli. As representative of the first class the authors used caffein and of the second class Ringers solution and 5 per cent. sodium chlorid solution. They produced a tubular nephritis by the subcutaneous injection of uranium nitrate. Theoretically, caffein should then "fail to excite the secretion of urine while Ringer's fluid or 5 per cent. salt solution should still be effective diuretics." Contrary to their expectation, the authors found that "in any case where a 'secretory' diuretic has failed, 'mechanical' diuretics have also failed, and where the one sort has been effective the other sort has acted equally. The response of the normal kidney to caffein is slower than to the other diuretics used. The response of the nephritic kidney to all three diuretics is slower than that of the normal kidney, and the response to caffein remains slower than to Ringer's or salt solution. The urine produced by the kidney in the early stages of uranium nephritis is smaller in amount and contains less chlorid than normal. Caffein urine in normal animals contains less chlorid than that produced by the injection of Ringer's or salt solution; in nephritic animals all three urines contain less chlorid than normal, and caffein urine still contains less than the other two. In the course of the response to any one diuretic the concentration of chlorid in the normal urine increases as the rate of secretion decreases; in the nephritic urine there may be a very slight increase in concentration, or the concentration may fall as the rate of secretion becomes less. Uranium causes glycosuria; the method of experiment also causes glycosuria in normal rabbits. This has to be taken into account in considering the variations in the concentration of chlorid."

These experiments were performed on rabbits. Previous to this, MacNider²¹ had done somewhat similar work with dogs. He found that early in a uranium nephritis they developed polyuria and glycosuria.

20. Boycott, A. E., and Ryffel, J. H.: *Jour. Path. and Bact.*, Cambridge, 1913, xvii, 458.

21. MacNider, W. deB.: *Jour. Pharm. and Exper. Therap.*, 1912, iii, 423.

The administration of an anesthetic at this stage rendered them partly or completely anuric. "Such animals, under the effect of caffeine, theobromin, digitalin and 0.9 per cent. salt solution, show a normal response in the blood-pressure rise and in the vascular response of the kidney (measured by oncometer)." Some of the animals responded to the diuretics used, while others, under exactly similar conditions, remained anuric. There was no difference in the vascular response of the kidneys of the two groups. Histologically, however, the tubules of the animals which remained anuric were found to show much more severe epithelial lesions and to be practically blocked. MacNider considers that "this investigation indicates that epithelial changes are more responsible for the production of anuria than are the vascular changes."

Christian²² reviews the work done at his laboratory on the action of diuretic drugs in acute experimental nephritis. He and O'Hare²³ produced a severe uranium nephritis in eighty-two rabbits, half of which were then given theobromin, while the rest were kept as controls. "The nephritis . . . was fatal in all except twelve rabbits, nine of which had received theobromin sodium salicylate. Of those receiving theobromin sodium salicylate by stomach tube and dying, the average duration of life was 6 days; of controls 6.94 days. Of those receiving theobromin sodium salicylate intravenously the average duration of life was 4.56 days; of controls 6.23 days. Thus under the conditions of our experiment theobromin sodium salicylate materially shortened the life of animals with severe acute fatal nephritis." Walker and Dawson²⁴ under Christian's direction, performed similar experiments on rabbits with other drugs. "The average duration of life was as follows: caffeine, 5 days; theocin, 4 4/7 days; potassium acetate, 4 4/7 days; spartein sulphate, 6 days, with one surviving animal, while control rabbits lived 8 1/5 days. These results are essentially similar to those obtained with theobromin sodium salicylate." Water alone, given intravenously, "produced but little change in the average duration of life." Christian²² also reports on the phenolsulphonephthalein excretion of rabbits with acute uranium nephritis. "The excretion of phenolsulphonephthalein was measured before and after giving the uranium. There was a prompt decrease in the ability of the kidney to excrete this coloring matter after uranium had been given. This decrease in phenolsulphonephthalein excretion in rabbits having a very severe nephritis appeared to be uninfluenced by theobromin sodium salicylate." In a somewhat milder nephritis "the phthalein output was less markedly decreased in the animals receiving theobromin sodium salicylate than in those not receiving the drug."

22. Christian, H. A.: Jour. Am. Med. Assn., 1913, lxi, 267.

23. Christian, H. A., and O'Hare, J. P.: Arch. Int. Med., 1913, xi, 517.

24. Walker, C., and Dawson, R. P.: Arch. Int. Med., 1913, xii, 171.

Sellei²⁵ has reported on the action of theocin in human beings. He used the sodium acetate in 0.3 gm. doses. With normal kidneys there was a diuresis lasting three to four hours. The specific gravity and chlorids of the urine were unchanged and the phosphates were slightly diminished. In pyelitis the result was the same as in the normal kidney. In nephritis there was usually diuresis, the specific gravity was lowered, the chlorids were diminished but the phosphates were usually increased.

Picot²⁶ describes three cases of oliguria in which he produced diuresis by giving 25 gm. of urea in a glass of milk.

Widal, Amberg and Weill,¹⁹ in connection with their work on the threshold for the excretion of chlorids, report that theobromin has the same effect as a salt-free diet and produces a marked reduction of the threshold. Its action is directly antagonistic to that of sodium chlorid.

KIDNEY FUNCTION

There have been many attempts to correlate the various tests of renal function with the different forms of nephritis, both clinical and experimental, but so far none have been very successful. The difficulty lies partly in producing experimentally a purely tubular or purely glomerular nephritis, and partly in the fact that the great majority of cases of nephritis in man are of a mixed type. Fitz and Rowntree²⁷ state that they "have considered the excretion of lactose as an index of vascular functional capacity; that of phthalein as an index of total renal function (though predominantly tubular); and the excretion of a salt and iodid as an index of tubular functional capacity." They produced kidney lesions in rabbits by clamping off the renal circulation for varying periods of time and found that "except in the most extreme cases, there is no definite relation possible by the functional tests used between the pathological and the functional disturbances produced.

Baright²⁸ makes use of the accompanying table and attempts to fit his patients into one of the three groups, but is forced to admit that most of them are mixed types. He states that nephritis with delayed lactose excretion is common, comprising 40 to 50 per cent. of the cases. Cases of urea retention and of delayed iodid and chlorid excretion are rare in pure form. "Acute beginning nephritis is usually a mixture of the three types, with lactose retention, strong potassium iodid and urea retention, some increase in blood-pressure and perhaps hematuria — glomerular irritation; oliguria and edema — tubular injury, and uremic troubles due to accumulation of nitrogenous wastes in the blood — not necessarily

25. Sellei, J.: *Ztschr. f. Urol.*, 1912, vi, 264.

26. Picot, G.: *Jour. d'urol. méd. et chir.*, 1912, ii, 203.

27. Fitz, R., and Rowntree, L. G.: *Arch. Int. Med.*, 1913, xii, 24.

28. Baright, H. E.: *Med. Rec.*, New York, 1913, lxxxiii, 699.

urea. It may heal or may resolve into chronic vascular, chronic tubular or chronic uremic type."

TABLE OF DIFFERENT FORMS OF NEPHRITIS AS DETERMINED BY FUNCTIONAL TESTS

Experimental Type Clinical Type	Cantharides Vascular	Corrosive Tubular	None Uremic
Function Tests			
Excretion Time	Normal		
2.0 gm. lactose	4°	5-12°	4°
0.5 gm. potass. iodid	40°	40°	80-100°
10.0 gm. sod. chlorid,	24°	24°	72°
10.0 gm. urea	24°	24°	24°
			Retained

Conzen²⁹ has tried the lactose and potassium iodid tests on 37 patients who later came to autopsy. He states that the tests were a great aid in diagnosis. "The intake of 10 gm. salt increases the albuminuria and leads to water retention and general malaise only in true nephritis and in severe congestion of the kidney."

Normenbruch,³⁰ from a study of clinical cases, concludes that the congested kidney functionally resembles a pure nephritis, approaching the tubular variety in chlorid excretion and the severe vascular variety in water excretion. Nitrogen excretion is fairly good, thus differing from the cases of true vascular nephritis. Nevertheless there is some nitrogen retention whenever the oliguria becomes marked.

Wolfheim³¹ considers that it is possible to differentiate the different forms of nephritis by means of functional examinations, basing his opinion on the study of 28 cases on a strict milk or milk and rice diet, with or without the addition of given amounts of salt or of water. He found normal nitrogen elimination in acute nephritis. There was salt retention in the oliguric stage of both vascular and tubular nephritis. Edema did not necessarily follow retention of chlorid, but all cases of edema showed some chlorid disturbance either from retention or from the flushing out of retained deposits.

Frothingham, Fitz, Folin and Denis³² have made a comparative study of the relation between the non-protein nitrogen retention and the phthalein excretion in uranium nephritis using the new methods for the determination of the nitrogen in the blood. They reached the following conclusions: "In acute uranium nephritis in rabbits the excretion of phthalein in the urine and the amount of non-protein nitrogen and urea in the blood vary from the normal during the course of the nephritis and return to normal as the nephritis heals. The degree of variation from

29. Conzen, F.: *Deutsch. Arch. f. klin. Med.*, 1912, cviii, 353.

30. Normenbruch, W.: *Deutsch. Arch. f. klin. Med.*, 1913, cx, 162.

31. Wolfheim, W.: *Ztschr. f. klin. Med.*, 1913, lxxvii, 258.

32. Frothingham, C., Fitz, R., Folin, O., and Denis, W.: *Arch. Int. Med.*, 1913, xii, 245.

the normal agrees on the whole with the amount of destruction demonstrated histologically in the kidney. The phthalein excretion in the urine drops rapidly to its lowest point and returns rapidly to normal with the recovery of the kidney. Non-protein nitrogen and urea accumulate gradually in the blood and return to normal gradually as the kidney recovers. In general, the tests parallel each other as indicators of renal function, but have this essential difference: the amount of phthalein excretion shows the renal function at the moment; the amount of non-protein nitrogen and urea in the blood is rather a measure of an accumulating difference between the amounts of waste nitrogen produced in the metabolism and the amounts eliminated by the kidneys. The time elements, the duration of the condition, is therefore an important factor in this test."

ACTION OF "OTHER THINGS" IN NEPHRITIS

MacNider³³ gave uranium nitrate to dogs in doses of 6 to 7 mg. per kilo of body weight and produced an acute nephritis in which both the vascular and the epithelial element of the kidney is involved, the latter rather more than the former. He found that the older the animal the more severe were the changes. "Following the use of an anesthetic these changes are increased in severity. The degenerative changes following the use of an anesthetic are also more pronounced in adult animals than in puppies. Of the anesthetics which have been employed in this investigation, Grehant's anesthetic, chloroform and alcohol, is more toxic than is morphin-ether."

Previous to this, Apperly³⁴ had studied the effect of chloroform on the kidney and decided that it did as much damage to the tubular epithelium as it did to the liver where its toxic action had long been known. He states that ether produces not nearly the same effect.

Underhill³⁵ has confirmed the observation of Baer and Blum that sodium tartrate given subcutaneously greatly diminishes the output of nitrogen and dextrose in the urine of phlorizinized dogs but considers that it is due to the acute tubular changes with anuria brought on by tartrate. He states that the phlorizin contributes nothing to the nephritis.

Hess and Wiesel³⁶ found lesions in the adrenals of dogs dying of uranium nephritis and hence were led to try the effect of the administration of adrenalin during the course of the nephritis. They conclude that it is possible to preserve life in uranium-poisoned dogs by simultaneous injection of epinephrin, provided that the latter is given before the

33. MacNider, W. deB.: *Jour. Med. Research*, 1913, xxiii, 403.

34. Apperly, R. E.: *Brit. Med. Jour.*, 1912, ii, 624.

35. Underhill, F. P.: *Jour. Biol. Chem.*, 1912, xii, 115.

36. Hess, L., and Wisel, J.: *Wien. klin. Wehnschr.*, 1913, xxvi, 317.

onset of anuria, even if an almost invariably fatal dose of uranium has been given. At the same time they observed a decrease of albumen and an increase in the amount of urine — signs of a functional improvement. Anatomically, however, the renal lesions resulting from uranium cannot be influenced by epinephrin.

Georgopulos³⁷ produced uranium nephritis in eighteen dogs, half of which had been thyroidectomized, and found that the thyroidectomized animals lived from one to three days longer than the controls. He believes that this was due to hyperfunctioning of the parathyroids following thyroidectomy and suggests that the parathyroid secretion counteracts the systemic intoxication in nephritis and thus an extract of these glands might prove useful in the treatment of nephritis in man.

MISCELLANEOUS

Baehr³⁸ has reported the results of histological study of the renal lesions in human cases of endocarditis due to various organisms. He reached the following conclusions: "In most cases of subacute bacterial endocarditis due to the endocarditis coccus, there exists a distinctive glomerular lesion due to bacterial emboli. There is an involvement of one or more loops of a variable number of glomeruli, absence of disease in other glomeruli, and association of all stages in one microscopic section. The lesion does not occur in cases of acute endocarditis, or in subacute cases due to other bacteria. Healed cases of subacute endocarditis show the healed stage of the distinctive glomerular lesion, although it is less extensive than in the active bacterial cases. These cases are probably those in which the endocardial vegetations have become bacteria-free early in their course and are now healing or healed. During the active stage of the disease, if the emboli are not too numerous, the only sign will be an almost constant slight hematuria. More marked cases may show a hemorrhagic nephritis. Numerous glomerular lesions with recovery may lead secondarily to a contracted kidney."

Underhill, Wells and Goldschmidt³⁹ gave a mixture of sodium chlorid and urea intravenously to rabbits during tartrate nephritis and found that the extra salt reappeared in the urine within forty-eight hours, while there was no increase in the urinary nitrogen. In view of the primarily tubular character of tartrate nephritis this result may be taken as strongly confirmatory evidence of the old theory that chlorids are excreted by the glomeruli and urea by the tubules.

37. Georgopulos, M.: *Ztschr. f. klin. Med.*, 1912, lxxvi, 261.

38. Baehr, G.: *Jour. Exper. Med.*, 1912, xv, 330.

39. Underhill, F. P., Wells, H. G., and Goldschmidt, S.: *Jour. Exper. Med.*, 1913, xviii, 347.

Kraus⁴⁰ has carried out very thorough metabolism experiments on four dogs with uranium nephritis. He found that in the normal animal any creatinin injected was excreted "in toto" and did not affect the other urinary constituents. Creatinin injected during acute uranium nephritis caused both the endogenous and the injected creatinin, and uric acid, chlorids and water, to be excreted in decreased amounts, and sometimes caused death. Inasmuch as fever increases the amount of endogenous creatinin, the onset of fever in a case of acute nephritis may well overtax the kidney and cause death.

The relation between the urea and the total nitrogen in the urine, known as the nitrogen coefficient, has been used as a diagnostic aid. Boulud⁴¹ has carried out some experiments on dogs with corrosive, chloroform and quinin nephritis, and found a nitrogen coefficient as low as 60. Normally, in both men and dogs, it is 80 to 82. Furthermore, in cases of human nephritis he found a similar decrease, and in the cases of albuminuria where the nitrogen coefficient was normal, some other cause for the albumen always could be found.

Opie⁴² tries to explain the occurrence of edema in nephritis as the result of changes in the blood-vessel walls produced by the same substance which causes the nephritis. In support of his opinion he brings forward the following experimental observations. Cantharidin in addition to causing nephritis, increases the flow of lymph and simultaneously blocks the lymph channels of the liver by injuring the lining cells and producing a fibrinous coagulum. Hence there develops well-marked edema of the liver coincident with and not as a result of the nephritis. Opie, however, makes no mention of the occurrence of edema during cantharidin poisoning elsewhere than in the liver.

The subject of the formation of renal casts has been taken up by Erdman.⁴³ As the result of microscopic and clinical studies, he believes that the hyalin casts are moulded from mucus in the tubules. The amount of mucus is increased in a concentrated acid urine and diminished in a dilute alkaline urine. Cylindroids he considers to be hyalin casts in the making. Granular casts may be formed in any one of three ways; either from the degeneration of the epithelial cells of the convoluted tubules, or from exudative material from the capsular spaces, or from the granular disintegration of coagulated blood.

The amount of permanent damage done by an attack of acute nephritis in childhood has been investigated by Ernberg.⁴⁴ He succeeded in

40. Kraus: *Arch. Int. Med.*, 1913, xi, 613.

41. Boulud, R.: *Lyon méd.*, 1912, cxix, 505.

42. Opie, E. L.: *Jour. Exper. Med.*, 1912, xvi, 831.

43. Erdman, H. B.: *Jour. Am. Med. Assn.*, 1912, lix, 1952.

44. Ernberg, H.: *Nord. med. ark.*, 1911, xlv, 109.

locating and examining 40 out of 106 adults who had had acute nephritis before the age of 15 years, mostly in connection with an acute infection, and found normal urines in all. Furthermore, he examined 16 out of 50 adults whose acute nephritis had occurred between the ages of 15 and 30 years, and found that all were normal except 4. Two of these gave evidence of nephritis of recent origin; the other 2, whose original attack had been subacute rather than acute, showed albuminuria. If these figures give us a true picture we certainly have been unduly pessimistic about the prognosis of acute nephritis in childhood.

Pollitzer⁴⁵ considers that a slight opalescence or turbidity in urine following the addition of acetic acid indicates the presence of chondroitin sulphuric acid. He has found it present in cases of tonsillitis, arthritis, chorea and endocarditis preceding the development of albuminuria and lasting after the albumin had disappeared. He has also found it constantly present in orthostatic albuminuria and believes it to be a sign of damage to the kidney.

Quinan⁴⁶ has made quantitative analyses of the lipoids of the blood-serum and reports that in chronic parenchymatous nephritis they are increased up to 2.6 per cent. from a normal of about 1 per cent.

Fischer's colloidal theory of nephritis has been generally discredited as being based on insufficient evidence. The recent literature on the subject has brought forward no new arguments.⁴⁷

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45. Pollitzer, H.: *Deutsch. med. Wehnschr.*, 1912, xxxviii, 1538.

46. Quinan, C.: *Cal. State Jour. Med.*, 1912, x, 64.

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