the distribution of which, in relation to the pelvis, is such that three-fourths of the blood supply is carried anteriorly, while one-fourth runs posteriorly. The relative size of the two systems may occasionally be $\frac{4}{5} : \frac{1}{5}$, $\frac{2}{3} : \frac{1}{3}$, but rarely $\frac{1}{2} : \frac{1}{2}$. The arteries are end arteries in the strictest sense of the word and the branches of the anterior division never cross over to the posterior side and vice versa. They do not anastomose with each

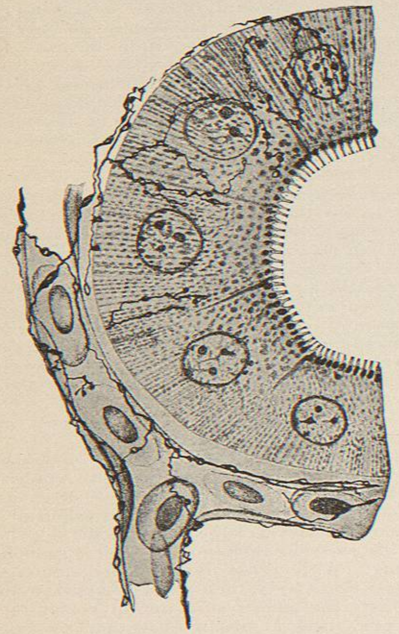

FIG. 3060.—Cross Section of a Convoluted Tubule from the Kidney of a Frog, Injected with Methylene Blue, fixed by Bethe's Method, and Counter-stained with Cochineal. In the neighborhood of the tubule are two nerve fibres, one of which passes to the wall of the tubule, while the other goes to the blood-vessel. On the epithelial cells of the tubule, varicose fibres are seen, which form free endings of different form; these epithelial nerve endings arise from nerve fibres which lie at the periphery of the tubule on the outer surface of its sheath. Around the blood capillary, varicose nerve fibres form a plexus, which forms two small endings in the walls of the capillary; one of these consists of three short fibrils and the other of two, which end in a knob. (Smirnow.)

other. To Hyrtl apparently is due the credit of having first mentioned this 'natürliche Theilbarkeit der Niere,' by which he means that in a corrosion specimen, the two arterial systems are completely separated by the pelvis. He also affirms that this arrangement of the renal arteries is found 'without exception in all mammalia from the whale to man.'"

The surgical significance of this work of Broedel's is seen in the possibility of an incision through the renal substance in the plane separating the areas supplied by these two independent systems. Concerning the veins, Broedel states: "While there is a complete arterial division in the plane connecting the posterior calices and terminating in the lateral half of the upper and lower calices, the veins follow quite a different arrangement. Around the bases of the pyramids they anastomose and form the familiar venous arches. They unite in large branches that run between the sides of the pyramids and the columns of Bertini to the necks of the calices, where they lie between the pyramid and the arterial branches. The thickness of these collecting veins accounts for the peculiar lobulated appearance of the bases and sides of the pyramids. Around the necks of the calices, both anteriorly and posteriorly, these veins form a second system of anastomoses, much shorter and thicker than that at the base of the pyramids. This appears as a number of thick loops or rings which fit like a collar around the necks of the calices. Nearly all the collected blood of the posterior region is carried anteriorly through these short thick stems, to join that of the anterior portion."

Lymph clefts have been described in the labyrinth of the kidney, especially around the convoluted tubules and around the blood-vessels, and also around the blood-vessels of the capsules and of the medullary portion of the kidney. These unite into true lymph vessels, which are divided into superficial and deep. The former arise on the surface of the organ, as their name indicates, and pass toward the hilum. The deep vessels accompany the blood-vessels toward the sinus, where four or five are usually found, one for each division of the artery. They, with the superficial lymph vessels, pass to the lumbar lymph glands which are nearest to the hilum.

Stahr has recently reported the results of some work on the lymph apparatus of the kidney. He found two systems of capillaries in the capsule: one in the fatty capsule (superficial) and one in the fibrous capsule, connected to the lymph capillaries of the cortex. He finds no lymph capillaries in the glomeruli. The capillaries of the cortex, like the blood capillaries, form a network and collect at quite regular intervals in the medullary rays and pass down vertically to the border of cortex and medulla, where they form arches. These arches are in communication with the lymph vessels, which pass straight through the medullary substance.

Nerve supply of kidney. The nerves of the kidney are derived mainly from the sympathetic through the solar and aortic plexuses, the semilunar ganglia and the splanchnics. They communicate with the spermatic plexuses, and some filaments have been traced to the pneumogastrics (Morris).

The mode of distribution and termination of the nerves in the kidney has been investigated by Retzius, Kölliker, von Ebner, Berkeley, and many others. Smirnow has quite recently reported the results of his extensive investigations on these nerves by means of the Golgi method and the Ehrlich methylene blue method. He states that the nerve trunks enter the sinus renalis, partly with the blood-vessels and partly accompanying the renal ducts. These trunks consist of non-medullated nerves and medullated nerves of different calibre. These nerves form a plexus in the sinus renalis, in the meshes of which he was able to demonstrate multipolar nerve cells. He describes motor nerve endings in the smooth muscle of the walls of the renal pelvis and of the ureters, sensory free endings in the connective tissue of these structures and also interepithelial fibres. In the fibrous capsule numerous nerve fibres were found which ended partly on the blood-vessels, in which both motor and sensory endings were observed, and partly in the connective tissue. All the blood-vessels of the kidney are provided with nerves, in many of them both motor and sensory nerve endings having been observed. From the plexus in the vasa afferentia, non-medullated nerve fibres penetrate into the glomerulus, ending partly on the capillary vessels of the glomerulus and partly in free endings on the outer surface of Bowman's capsule. In addition to the nerves supplying the blood-vessels of the kidney, there are also nerves arising from trunks which accompany the arteries, which end on the urinary tubules of both the cortex and medulla. There is a close anatomical relation between the nerves of the renal parenchyma and the vascular nerves. The urinary tubules of both cortex and medulla are provided with non-medullated nerves, which run in the sheath of the tubules, branch repeatedly, forming a plexus on the outer surface of the membrana propria of the tubules. From this plexus varicose fibres arise, which end on the surface of the membrana propria (epilamellar nerve endings). From the epilamellar plexus, fine fibres arise, which pass through the membrana propria into the tubule and form, on the surface of the epithelial cells, endings of different form (hypola-

mellar endings). These are found in the convoluted tubules, in the straight collecting tubules, and in the main excretory ducts of the kidney. The mode of ending of the nerve fibres and the relation of the vascular and secretory nerves are shown in Fig. 3060 taken from Smirnow's report.

Thus the kidney is shown to have a large number of nerves and nerve endings, from which we must conclude that the nervous system exerts a constant influence on the excretion of the urine.

Development of Kidney.—The development of the kidney is associated with the development and degeneration of certain fœtal structures, known as the pronephros and the mesonephros. The former originates in the cells of the middle plate and consists of a long tube, the pronephric duct, and transverse tubules, which open into the pronephric duct and communicate with the body cavity. These are invaginated by glomeruli. This organ functionates as an excretory organ in certain of the lower forms, but in man it either does not occur or is very primitive. The mesonephros, or primitive kidney or Wolffian body, is established on the part of the pronephric duct, immediately behind the pronephric tubules, and consists of a duct, the mesonephric duct, which grows backward from the pronephric duct and opens into the cloaca, and a number of transverse tubules originating in the nephrotomes. The transverse tubules are in communication with the body cavity and later connect with the the Wolffian duct, while the central portion becomes sacculated and then invaginated to form the primitive Malpighian corpuscles. This organ develops in man by the seventh week and retrogression begins in the eighth week, the Malpighian bodies having disappeared by the fifth month.

The permanent kidney or metanephros begins to develop as early as the fifth week of embryonic life. From the cloacal end of the mesonephric duct an evagination grows forward into the mass of mesoblastic tissue known as the blastema and forms the anlage for the ureter. From the extremity of the ureter, tubules bud out, become elongated and convoluted, and the extremity invaginated by the mesoblastic tissue, which forms the blood-vessel and connective tissue of the organ. Two distinct views are expressed in the literature regarding the development of the permanent kidney: one is that the pelvis of the kidney, collecting tubules and uriniferous tubules all develop from this evagination from the mesonephric duct. This view is upheld by Müller, Remak, Kölliker, Schweiger-Seidel, Toldt, Nagel, Minot, Gerhardt, Haycraft, Heisler, and others. This view is well summarized by Haycraft. He states: 1. That the connective tissue and blood-vessels of the kidney develop from the blastema, while the epithelium of the tubules proliferates from the cells originally lining the ureter and Wolffian duct.

2. The tubules which first sprout into the blastema terminate in dilatations, the primary renal vesicles.

3. Then these form branching cavities which always remain at the periphery of the cortex; from these the urinary tubules bud off, the older ones sinking down into the medulla.

4. The tubules which first sprout from the ureter soon become turned inside out to form the pelvis of the kidney.

5. Many of their prolongations into the rapidly dividing renal vesicles also become evaginated, thus increasing the number of tubules passing between the pelvis and the renal vesicles at the cortex.

6. Those that remain form the collecting tubules.

7. The Bowman's capsule is moulded into its shape upon the bent tubule long before the glomerulus is formed. It is invaginated rather by its tubule than by the glomerulus.

The second view is strongly supported by Kupffer, Gegenbaur, Wiedersheim, Hamburger, Schreiner, Chievitz, and Herring. Herring thus summarizes the views held by these authors: The kidney arises from two distinct structures which come together at an early period and remain intimately associated during further development.

1. *The Kidney Blastema.*—This consists of a mass of cells closely related to the blastema of the Wolffian body, and apparently formed from the intermediate cell mass or the peritoneal epithelium. It is therefore mesoblastic. It forms an envelope around the ends of the ureter branches, and persists as a thin cellular investment under the capsule and between the lobules, until the end of the eighth month, after which it entirely disappears.

2. *The Ureter.*—This structure is an outgrowth from the Wolffian duct. It appears at the end of the first month, and grows forward, as a solid column of cells, to reach and embed its peripheral branches in the kidney blastema. The balance of recent opinion is in favor of the ureter being epiblastic.

At the beginning of the second month, the ureter has come into apposition with the kidney blastema and the result is the beginning of the formation of the permanent kidney. The ureter branches early, and its lumen dilates anteriorly to form the future pelvis and calices. The primary branches are of a definite number, and at their extremities masses of cells appear constituting the "Nierenbecke" of the German writers. From these masses of cells in the kidney pelvis are developed the collecting tubules of each lobule. Ureter, pelvis, calices, and collecting tubules are formed from the Wolffian duct and these are the only parts formed from this structure, unless we include part of the intercalated tubule. From the kidney blastema arise the Malpighian bodies, convoluted tubules, Henle's loops, and the junctional tubules, the connective-tissue framework and the capsules. Malpighian bodies and their tubules begin to appear at the end of the second month, uniting at an early stage with the branches of the ureter. Each Malpighian body with its tubule arises as a solid mass of cells at the periphery of the lobule in close relation to the dilated extremity of a branch of the ureter. The solid mass acquires a lumen and assumes an S-shape. The lower limb of the S becomes a Malpighian body, the upper and middle limbs become convoluted tubules, while the bend between them develops into the Henle's loop; the extremity of the upper end joins the collecting tubule and forms the greater part of the junctional tubule. The cells lining the tubules are at first similar, but become differentiated as the organ functionates.

Schreiner, in the last number of the *Zeitschrift für wissensch. Zool.*, gives an extensive report on his work on the development of the kidney in which he studies thin serial sections, also reconstructing the developing kidney at different stages of development, and reaching conclusions very similar to those just quoted from Herring.

Both views are so strongly supported and the decision seems so difficult to make, that more work and by other methods than those that have been used seems to be necessary; however, the careful and decisive work of Kölliker, Minot, Golgi, and Haycraft, as well as analogy with the mode of development of other glandular structures of the body, seems to make the conclusion undeniable that all the glandular portion of the kidney is developed from the one anlage derived from the mesonephric duct. The groups of cells of the blastema, described as forming the uriniferous tubules, no doubt form the connective-tissue stroma and blood-vessels of the organ.

II. PHYSIOLOGY OF THE KIDNEY.—Two portions of the kidney have been regarded as of primary physiologic importance and have therefore received most exhaustive study—a study which has resulted, however, in views which are most widely divergent. These two portions are the glomeruli, including the capsule of Bowman, and the convoluted tubules, including the loops of Henle. As stated under the Anatomy of the Kidneys, the glomeruli consist of branching and anastomosing loops of capillaries, between which is a small amount of reticular connective tissue, the entire structure being imperfectly divided into lobules by strands of connective tissue. The glomerulus is covered by a single layer of much flattened epithelial cells, the glomerular portion of Bowman's capsule. Between this and the peripheral portion of the capsule is a space, which connects with the lumen of the uriniferous tubule and hence forms the beginning of this structure. We have therefore a structure analogous to that of the lungs. The blood is found in thin-walled capillaries, separated from the urinary space only by the thin wall of the capillary and a single layer of flattened epithelium—the typical condition for osmosis. The endothelium-like cells of Bowman's capsule have been carefully studied with the view of determining whether any changes of structure of these cells occur during the process of secretion, and Van der Stricht states that clear droplets of fluid have been seen by him in these cells between the granules of protoplasm. The cells lining the convoluted tubules and loops of Henle have been studied by various methods by Heidenhain, Henle, Krause, Nussbaum, Tornier, Van der Stricht, Zimmermann, Sauer, and many others. The rod structure, ciliated border (Bürstensaum), granular and vacuolated appearances of the cells have been described somewhat in detail under the Anatomy of the Kidney and need not be repeated here. Nicolas states that the inner portion of these cells is destroyed during secretion as in the cells of the mammary gland, the cells being then rebuilt from the peripheral portion of the cell. Most of these authors agree that the cells of the convoluted tubules and Henle's loops undergo certain important changes of structure, which they ascribe to the processes of secretion, the fluid being collected in the cell in the meshes of the protoplasmic network, and finally extruded into the lumen; Sauer, however, refuses to admit that the appearances described have anything to do with the processes of secretion, being found in all phases of secretion alike. These cells are in many respects like the cells lining the intestinal cavity, which are known to be absorptive rather than secretory in their function; the Bürstensaum is comparable to the striated cuticular border of these cells while the striated protoplasm is met in many types of cells, especially of gland ducts. The variations observed by different authors and even by the same author in different preparations may be, in part at least, due to different methods of fixation or to other differences of technique.

That certain portions of the urine are excreted by the glomeruli is admitted by all authors, but views differ widely in regard to how much, what constituents, and whether the process is purely physical, a process of filtration, or whether the glomerular epithelium is actively concerned in the process, so that it becomes a vital process of secretion. Many physiologic experiments have been undertaken to determine these points, and two diametrically opposed views have arisen, each of which is supported by a long line of investigators.

1. *The Bowman-Heidenhain Vital Theory.*—This theory was first formulated by Bowman in 1842 on a purely anatomical basis and it was later (1874) confirmed by Heidenhain on the basis of experimental data. It is briefly stated as follows:

"(*a*) In the kidney, as in all other glands, the secretion depends on the active intervention of special secretory cells.

"(*b*) The first type of these cells is represented by the simple layer of epithelium covering the glomerular loop of capillaries. The office of these cells is to secrete water and such salts of the urine as are found in all other parts of the body in watery solution (*e.g.*, sodium chloride).

"(*c*) Another system of secretory cells, forming the lining investment of the convoluted tubules and ascending limb of the loop of Henle, secrete the specific constituents of the urine (urea, uric acid, etc.).

"Under some conditions, they may also secrete a certain amount of water.

"(*d*) The activity of the two kinds of secretory cells is determined: (1) By the amount of water or urinary constituents contained in the blood; (2) by the velocity of the blood flow through the capillaries of the kidney, inasmuch as on this factor depends the supply of oxygen and of substances to be secreted to the cells.

"(*e*) The great variability in the constitution of the urine may be explained by differences in the secretory activities of these two types of cell."

Heidenhain based his conclusions largely on the fact that after the injection of indigo carmine, the cells of the convoluted tubules and of the ascending limb of Henle's loop were colored by the dye, while the other portions of the kidney were quite free from the pigment. In the kidneys of birds, crystals of uric acid were found in the same cells by Bowman and v. Wittich, while indigo carmine, carmine, Ehrlich's tricolor mixture, and other dyes have been used by other investigators with similar results.

Dreser concludes from his observations that the production of urine is attended by the doing of work on the part of the kidney and must therefore be looked upon as a process of secretion, while Adami states that the glomerular epithelium must be looked upon as possessing powers of a selective secretory nature. Thompson decides from his experiments with atropine and morphine that the production of urine is to a certain extent analogous to the manufacture of the secretion of other glands which are influenced by atropine. Magnus and Gottlieb conclude from their experiments with diuretics that, while there is usually an increase in the blood content of the kidney, shown oncometrically, as a result of the administration of diuretics, yet diuresis may occur without a corresponding increase of the blood flow through the kidney. The increased flow of blood is regarded as an auxiliary factor in the increase of the secretion, and the diuresis may be checked by causing contraction of the renal arterioles. From these data, they conclude that "the relations between the circulation and excretion in the kidney are similar to those in the salivary glands."

2. *Ludwig's Mechanical Theory.*—In 1844 Ludwig presented his well-known theory, which is briefly formulated as follows:

"(*a*) The secretion of water is a purely mechanical process, depending only on the blood pressure in the glomerular capillaries and the permeability of the filtering membrane.

"(*b*) This dilute fluid is concentrated in the tubules by giving up its water to the surrounding lymph, in consequence of differences of concentration between the glomerular fluid and the lymph.

"(*c*) All the urinary constituents are turned out of the blood with the water through the glomeruli."

This theory depends on the connection between the circulation through the kidney and the amount of urine excreted. A mechanical filtration must depend largely on differences of pressure between the blood in the capillaries and the urine in the tubules; partly also on the rapidity of the blood flow through the glomeruli.

The blood pressure is raised: (1) By a rise of the general blood pressure; (2) by dilatation of the renal arterioles, and (3) by obstruction of the renal vein. This last factor, while it raises the pressure of the blood, will also retard the blood flow and, as shown by the work of De Souza and others, causes a diminution or cessation of the urinary excretion.

The theory, so far as the absorptive function of the epithelial cells of the tubules is concerned, is confirmed by the facts mentioned by Korányi that the concentration of the urine increases with the length of the convoluted tubules and diminishes in proportion to the rapidity with which it passes through the tubules, as after diuretics, when the urine is very dilute. Dreser decides that the work of the convoluted tubules is purely absorptive, but regards this as a vital process, because of the fact that in pathologic conditions, when the cells of the tubules are diseased and incapable of doing work, the urine is more dilute. Korányi draws the conclusion that only the physical processes of metabolism are so far explained and that, while many facts still remain tending to confirm the vitalistic theory, these are becoming fewer and fewer, and the probability is that, with the further advance of our knowledge on this subject, physical processes will more and more predominate over the vital.

Cushney states that the relative amounts of chloride and sulphate in the urine vary independently of their proportions in the blood plasma and also of the degree in which each is present in excess, a fact which he explains by saying that the tubules alter the glomerular fluid by absorbing some of its constituents, the sulphates being absorbed with greater difficulty than the chlorides. His experiments on diuresis have so important a bearing on the settlement of this vexed question that a fuller reference to them will not be out of place here. He, in a number of experiments, injected into rabbits solutions of sodium chloride, sodium sulphate, sodium phosphate, and urea. The urine having been examined before the experiment, mixtures of two of the solutions were injected into the jugular vein, the urine being collected and examined at frequent intervals. In the first stage of diuresis after the injection of the mixture of chloride and sulphate, the chloride of the urine was to that of the plasma as 2 : 3, while in the last phase it was in the ratio of 1 : 5. The sulphate in the first phase was as 2 : 1, and in the last phase as 10 : 1. The only assumption necessary to explain these results is that the sulphates are absorbed by the tubules with greater difficulty than the chlorides, an assumption which is in accord with their behavior toward the epithelial cells of the intestine, red blood cells, and others. The precipitation of the carbonates in the normal urine of the rabbit is also better accounted for by the reabsorption of the solvent than by any other hypothesis. This absorption, however, he regards not as a simple diffusion, as Ludwig at first assumed, but there must be an unknown force causing a current from the lumen toward the blood as in the intestine. Which constituents of the glomerular fluid shall be subjected to this force, however, is determined by their diffusibility into the cells. The injection of urea resulted in similar phenomena; the percentage was high in the normal urine, fell during diuresis, and rose gradually as the quantity of urine returned to normal. The urea thus resembles the sulphates and phosphates, apparently passing through the capsules readily, but failing to penetrate the epithelium of the tubules so readily as the chloride. Cushney, therefore, explains his results in conformity with the mechanical theory of renal secretion modified by the acceptation of active absorption in the tubules. The diuretics cause a hydræmia, which induces an increased flow through the capsule, the fluid carrying with it salts in the same proportion in which they occur in the plasma. The rapid flow through the tubules permits of only imperfect absorption, but a certain amount of the water and chloride are returned to the blood, while the less diffusible bodies are excreted, it may be, in a form more concentrated than in the blood. Later more perfect absorption takes place and the urine becomes more concentrated, and the proportions are changed. Cushney concludes his argument with the statement that "the epithelium lining the renal tubules is often compared to that of a true secreting gland, such as the salivary, but it resembles that of the intestine as closely histologically and in its reaction to chlorides, phosphates, and sulphates, is analogous from a physiological point of view."

All the points raised by the adherents of the vitalistic theory seem therefore to have been satisfactorily answered. The structure of the renal epithelium can be explained quite as well on the assumption of an absorptive function as on the secretory basis. The precipitation of an indigo carmine and other dyes in the convoluted tubules may be due to a concentration of the solution by absorption, quite as well as to a secretion of the substance through the tubules. The presence of special nerve endings on the epithelial cells, as described by Berkeley and Smirnow, might seem to point to a secretory function of these cells, if it were not for the fact that they also describe similar endings on the cells of the collecting tubules. We may well therefore conclude that the weight of evidence is in favor of the Ludwig theory with the modification that not only the water of the excretion is absorbed by the cells of the tubules, but there is also an active absorption of other constituents of the glomerular fluid, the amounts absorbed varying with the diffusibility of the substances through the cells.

The question of renal sufficiency has recently been investigated by many workers and by various methods.

1. The functional activity of the kidney has been investigated by the use of aniline dyes, especially methylene blue; the important points observed are the time of the first appearance of the blue in the urine, the intensity of the excretion, and the duration and character of the process. All these factors vary in different pathologic conditions.

2. Ureteral catheterization was then used to determine in these experiments, which kidney is functionating normally or abnormally.

3. Kryoskopie, the method suggested by Korányi, depends for its value upon the physical principles (*a*) that the osmotic pressure of a fluid is proportional to its concentration (*i.e.*, to the number of molecules dissolved in a unit of volume).

(*b*) Solutions which are in proportion to their molecular weights, volume and temperature being equal, have the same osmotic pressure.

(*c*) The freezing point of solutions is lowered in proportion to the amount of solid dissolved (*i.e.*, the concentration).

Hence the lowering of the freezing point can be regarded as the measure of molecular concentration and the functional sufficiency of the kidney can be estimated by determining the difference between the lowering of the freezing point of blood serum and of urine.

The urine is a fluid of very complex composition, excreted by the kidney and representing many of the end products of tissue metabolism in the body. Its composition is shown in the following tables taken from Schäfer's "Text-book of Physiology":

I. Parkes' table showing normal twenty-four hours' excretion of main urinary constituents.

	Percentage composition of solids.	Absolute weight in grams.	Weight per 1,000 of body weight.
Urea, CH_4N_2O	45.75	33.18	0.5000
Creatinin, $C_4H_7N_3O$	1.25	.91	.0140
Uric acid, $C_5H_4N_4O_3$	.75	.55	.0084
Hippuric acid, $C_9H_9NO_3$	.55	.40	.0060
Pigment and other organic substances	13.79	10.00	.1510
Sulphuric acid, SO_3	2.77	2.01	.0305
Phosphoric acid, P_2O_5	4.36	3.16	.0480
Calcium	.35	.26	.0004
Magnesium	.28	.21	.0003
Potassium	3.45	2.50	.0420
Sodium	15.29	11.09	.1661
Chlorine	10.35	7.50	.1260
Ammonia	1.06	.77	.0130
	100.00	72.54	1.1057

II. A table derived from Bunge, representing the twenty-four hours' excretion of a young man, upon a diet consisting in one case entirely of beef with a little salt and spring water; in the second case of bread with a little butter and with some water.

	Meat diet.	Bread diet.
Amount of urine in twenty-four hours	1672 c.c.	1920 c.c.
Urea	67.2 gm.	20.6 gm.
Creatinin	2.163 "	.961 "
Uric acid	1.398 "	.253 "
Sulphuric acid (total)	4.674 "	1.265 "
Phosphoric acid	3.437 "	1.658 "
Lime	.328 "	.339 "
Magnesia	.294 "	.139 "
Potash	3.308 "	1.314 "
Soda	3.991 "	3.923 "
Chlorine	3.817 "	4.996 "

III. The differences between the excretion of certain constituents of the urine by males and females respectively is indicated in the following table, given by Yvon and Berlioz:

	Male.		Female.	
	Per litre.	Per diem.	Per litre.	Per diem.
Specific gravity	......	1.0225	......	1.0215
Volume	......	1360 c.c.	......	1100 c.c.
Urea	21.5 gm.	26.5 gm.	19.0 gm.	20.5 gm.
Uric acid	.5 "	.6 "	.55 "	.57 "
Phosphoric acid	2.5 "	3.4 "	2.4 "	2.6 "

A human adult usually excretes from 1,200 to 1,700 c.c. of urine in twenty-four hours and the specific gravity varies from 1.015 to 1.025, and is in general inversely proportional to the amount excreted.

Normal urine gives an acid reaction, the acidity being due to the presence of acid salts. The question has been frequently asked and investigations have been undertaken in the effort to answer it, how it is that the urine is acid, while it is derived from the alkaline blood. Dreser and others concluded as the result of their experiments that the urine, as it passed through the glomeruli was alkaline, and that the change to the acid reaction was brought about in the cells of the convoluted tubules. Diuretics often cause alkalinity. The change in reaction may be the result either of the secretion of acid salts or the absorption of alkaline salts, by the cells of these tubules.

The degree of acidity is a resultant of two opposing factors: (1) acid production in metabolism; (2) the ingestion of unsaturated or unstable basic compounds, together with the production of ammonia. To these should be added the elimination of acids or bases by other channels than the kidney. Thus the acidity increases with increased proteid metabolism, with exercise, and with the consumption of food containing but a small amount of the bases, especially flesh food. It diminishes when the food contains abundant bases. This explains the fact that the urine of herbivorous animals is alkaline, while that of man may become alkaline, at least for a time, when a vegetarian diet is maintained (Hopkins).

Urea.—By far the greater part of the nitrogen eliminated from the body is eliminated in the form of urea, a nitrogenous substance first demonstrated by Rouelle in 1773. It is derived by the metabolism of proteid substances. The proteids form ammonium carbamate, which is changed by the liver cells into urea. This was shown by the experiments of Schroeder, Schöndorff, and others. They found that by passing the blood of a dog through the vessels of the liver, there was a marked increase of the urea present; this did not occur if the blood were passed through the vessels of the kidney or other organs. If the liver was removed, as shown by the experiments of Hahn, Pawlow, Masson, and Nencki, carbamates appeared in the urine, with a corresponding decrease in the amount of urea. Some urea is, however, found in the urine, after removal of the liver, so it is probable that some other organs have the power of forming urea, though to a much less degree than the liver. While urea is neutral to litmus, it exhibits weak basic properties and forms loose compounds with acids, so that urea nitrate, urea oxalate, and urea phosphate are met. About 30 gm. of urea are excreted in the urine in twenty-four hours. Urea itself crystallizes in the form of colorless needles or rhombic prisms, while its salts crystallize in various forms.

Creatinin is a crystalline nitrogenous substance found constantly in the urine. It is derived partly from the creatin in the meat eaten and partly from the destructive metabolism of the tissues of the body. As not nearly all the creatin taken into the body is excreted as creatinin, it is probable that a portion of the creatin is changed to urea.

Uric acid is found constantly, but in relatively small quantities in the urine of mammalia, while in birds it forms the main urinary constituent, occupying the same place with them that urea occupies in the human urine. In birds it has been shown that the uric acid is formed in the liver, as the urea is in mammalia. It has been suggested that uric acid represents an end-product in the metabolism of leucocytes and the spleen has been suggested as the place of its formation. Neumeister states: "The spleen stands in close relationship to uric-acid formation, as is evident from experiments on animals and from pathologic observations. This function is simply explained by the richness of the spleen in leucocytes and therefore also in cell nucleins, from the decomposition products of which—the nuclein bases—uric acid seems to arise, at least in mammalia." The same observations were made by Hammarsten, Horbaczewski, Spitzer, and others. Mendel and Jackson, however, working on splenectomized animals concluded that the "spleen is by no means the chief organ involved in uric-acid production in the living body, if indeed it normally plays any part whatever in this process. After the exclusion of the liver and spleen, it is natural to turn to other forms of lymphoid tissue, and the lymphatic glands are at once suggested. It might be supposed that after splenectomy these glands would take up the work of the spleen. Enlargement of the lymphatic glands has been recorded after removal of the spleen in man. But the very recent investigations of Vincent, made to ascertain this fact in the dog, fail to bring to light any permanent hypertrophy of the lymphatic glands after splenectomy. It seems improbable, therefore, that the formation of uric acid in mammalia can be assigned at present to any definite organ or group of organs. While the amount of uric acid present in the urine is small, it is of considerable importance from the pathologic point of view, since it is increased in certain pathologic conditions. The xanthin bases, which are analogous to uric acid, are found in the urine in variable but small amounts.

Hippuric acid occurs in the normal urine in small amount, the quantity varying with the diet. It is not entirely eliminated even in starvation, however, so that it arises in part also from the metabolism of the tissues. A fruit diet increases the amount, and in herbivora it is present in much larger amounts.

Albumin in traces may be present in the normal urine, arising probably from the surface of the urinary tract. This is not, however, sufficient to react to the ordinary tests for albumin. After violent exercise an appreciable quantity may appear in the urine.

Normal urine has been found to contain also not only glucose, but also a sugar of the maltose type, known as isomaltose.

Oxalic acid is found in small amounts, arising, as was recently shown by Lommel, partly from the oxalic acid in the food and partly from the carbohydrates in the food. He states that there is no direct relation between oxalic-acid excretion and proteid metabolism, and that food rich in nuclein increases both the uric acid and the oxalic acid in the urine.

The inorganic constituents of the urine are derived mainly from the food, and the amount and the form in which they are excreted are therefore very variable. A portion of the sulphuric acid occurs in the form of conjugate sulphates, the acid radical being combined with an aromatic base, so that we find indoxyl and skatoxyl sulphuric acid. About nine-tenths of the sulphuric acid occurs in the form of ordinary sulphates, the relation being changed as a result of abnormal putrefactive changes in the body and also when a larger amount of the aromatic bodies are ingested.

Phosphates and chlorides are also excreted in varying amounts and combinations. The amounts vary with the food and also with the different pathologic conditions.

In closing, I would call attention to some experiments performed by Bradford to show the result of the excision of larger or smaller portions of one or both kidneys. He states that the excision of portions of one kidney is followed by an increase of the amount of urine, without an increase of the solids of the urine. The excision of about three-fourths of the total kidney weight is followed by a very great increase in the amount of urine and also an

increase of the amount of urea excreted. The increased output of urea is, however, effected by the excretion of very large amounts of water, the urine not being concentrated. After excision of large portions of the kidney substance, there is a considerable increase in the nitrogenous extractives in the blood and tissues, especially in the muscles, the quantity being too great to be accounted for by the mere retention of the products of normal metabolism. These experiments, as well as some performed by other investigators, have suggested the possibility of an internal secretion from the kidney, the cessation of whose action causes the muscles and other tissues to break down and liberate urea. Boyd recently reported the results of the excision of large portions of the medulla of the kidney, in which he states that there was no increase in the secretion of urine or of urea, and no increased metabolism of the tissues. If the conclusions of both these observers are to be relied upon, it would seem to indicate that the increased metabolism reported by Bradford is due to some change, possibly the withdrawal of an internal secretion, brought about by the loss of the cortical substance of the kidney. *Lydia M. De Witt.*

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KIDNEYS, DISEASES OF: ANOMALIES.—Under this heading are included deviations from the normal position, size, shape, and number. Several of these anomalies may be combined; for instance, the horseshoe kidney is usually dislocated. Abnormalities are both congenital and acquired. In this article attention is paid chiefly to the congenital variety. The acquired anomaly is frequently recognized during life, the congenital very seldom, since there may be an entire absence of symptoms.

Malformations.—Newman classifies the malformations of the kidney as follows: A. Displacements without mobility. (1) Congenital displacement; (2) congenital displacement with deformity; (3) acquired displacements. B. Malformations of the kidney. (1) Variations in number: (*a*) supernumerary kidney; (*b*) single kidney, congenital absence of one kidney, atrophy of one kidney, absence of both kidneys. (2) Variations in form and size: (*a*) general variations in form, lobulation, etc.; (*b*) hypertrophy of one kidney; (*c*) fusion of two kidneys, horseshoe kidney, sigmoid kidney, disc-shaped kidney. C. Variations in pelvis, ureters, and blood-vessels.

A. An otherwise normal kidney may be found in various abnormal positions. It may lie on the vertebral column, either on its own or on the opposite side. It is usually in the neighborhood of the promontory of the sacrum, seldom rising as high as the fourth lumbar vertebra; but on the other hand, in a few cases, it is situated deep in the pelvis in the concavity of the sacrum. According to Kupfer, these anomalies depend on a deficient energy in the movements of the embryonic rudiments of the kidneys, which up to a certain time are situated immediately in front of the point of bifurcation of the aorta. Congenitally dislocated kidneys are usually altered in form. They may be flattened, roundish, and sometimes three- or four-cornered. The hilus is directed forward. Fœtal lobulation of the surface is usually strongly marked. It occurs chiefly in men—and the left kidney is more often affected than the right. It is impossible to differentiate a congenital displacement from a floating kidney which had become fixed later in life. The practical importance of this abnormality is slight. A deep-seated kidney might be mistaken for a tumor in the pelvis. A complete rectal examination should help clear up the diagnosis.

B. Anomalies in Form and Size.—Secondary alterations in the form of kidneys are of course very frequent and are produced by numerous diseases of the kidney itself, such as cyst, abscess, hydronephrosis, chronic nephritis, new growths, and by tumors of neighboring organs, etc.

As examples of congenital alterations in form may be mentioned: (1) *The Lobulated Kidney.* On the surface of this organ there are shallow grooves, which mark the boundaries of the various renculi. This is a relic of the fœtal condition, which usually disappears soon after birth, but sometimes persists. From seven to twenty renculi are found in the state of permanent lobulation.

(2) *Horseshoe Kidney.* This type represents a combination of anomalous form and position. The fusion of the two kidneys occurs at three points according to which this variety of deformity is divided into three classes. (*a*) The most common anomaly is where the fusion takes place at the lower ends of the kidneys. This represents the pure type of the horseshoe kidney (Ren Unguiformis, Renes Arcuati; Ren Soliformis). The concavity looks inward and upward.

(*b*) The second form is not so common. In it the union takes place in the middle between the two hila. There may be only a thin bridge of tissue between the two kidneys.

(*c*) The third form is the rarest. The fusion takes place at the upper end.

In the highest grade of this variety, the fusion may involve almost the entire kidney, leaving only the lower end free; at times they are separated by only a shallow depression. The fusion may be such as to give the kidney a sigmoid or a disc shape.

These anomalous forms of kidneys may prove of surgical interest from the standpoint of diagnosis and operative treatment. Landwith mentions a case in which