The History of Our Knowledge regarding the Function of the Kidneys.
Synopsis

I. Knowledge of the kidney among early non-Greek peoples

II. The Greek contribution: reliance on observed facts rather than on supernatural interpretation: Hippocrates

III. Reaction to formalism in Greece: Erasistratus, Herophilus

IV. The experimental method: Galen

V. The Medieval Period: no questioning of accepted facts, however insufficient the premises: Galen, Henri de Mondeville

VI. The Renaissance: Vesalius, Harvey, Borelli, Bellini.

VII. The Advent of the Microscope: Malpighi

VIII. Chemistry makes its contribution: discovery of the constituents of the urine and their estimation, and of the synthesis of uric acid in the kidney.

IX. Anatomy and Chemistry cooperate: Bowman and Heidenhain

X. Physical ideas (sensoria) play their part: Ludwig

XI. The present position: Cushing
The History of Our Knowledge Regarding the Functions of the Kidneys

I

"Without Hero philus we should have had no Harvey and the rise of Physiology might have been delayed for centuries; had Galen's works not survived, Vesalius would never have reconstructed anatomy, and surgery too might have stayed behind with herUiHgtL sister alchemy." In these words Charles Singer in "The Legacy of Greece" expresses our indebtedness to the earliest observers. Remembering this indebtedness we shall review some early references to the kidneys and their functions before proceeding to consider the work of those physicians who have left written record of it.

In Herophilus' "History of Medicine" we are told that in ancient China the kidneys were known to be black and that they were thought to descend from the 14th vertebra. As regards renal function, however, the Chinese seemed to visualize a continual contest between heart and kidneys for the mastery of the body; for example, in an account of the attempt to diagnose disease by inspection of the tongue it is stated "If in disease of the heart, the tongue, which should normally be red is black (the colour of the kidney) it signifies that the kidneys, enemies of the heart, have acquired the mastery, whereas the prognosis indicates destruction of the heart and a fatal issue."

Jewish literature makes several references to the kidneys but without description. In the Talmud popular tradition concerning the functions of various organs is recorded: "The kidneys advise, the heart proceeds..."
The tongue, membranes, sound, etc. The kidneys seem to be regarded as the seat of emotion, even of counsel for action of the body as a whole. So the psalmist: "I will bless the Lord who hath given me counsel; my reins also instruct me in the night seasons." Psa. 16:7.

According to Garrow's "History of Medicine," the inspection of urines as part of the priest's auguries in Babylon led to the examination of urine. It seems then that the Babylonians may have guessed at some connection between the kidneys and the secretion of urine, but such a fact had been nowhere definitely stated, so far as our records go.

The early civilizations, then, seem to have known no more of the kidneys than that they existed, their shape and their approximate position. The functions of the kidneys were for them hidden in the mists of supernatural belief and conventional dogma. As Herder says: "The next step in the direction of scientific advancement would be the elimination of the supernatural."
emphasise shifted, for he insisted that to see clearly is fundamental, and that in what is seen is final and authoritative. The studied natural processes in disease, disregarding theories of supernatural favour or grudge. He observed that any definite illness tends to follow a certain defined course, which could be predicted from careful observation of its earliest signs and symptoms. Thus it came about, that with regard to the kidneys, and their functions, it is to appreciate that we owe our first exact knowledge. In his writings he gives no exact description of the kidneys, beyond that they are "heart shaped", but by detailed observation of the results of their derangements, he not only shows the functions he attributes to them, but also establishes a method of study which is a sure foundation of further advance. For example in "Epidemic Diseases" Book I § 13, page 4 he states that he notices "white clouds in the urine" in the case of those, "wise of penalties. And here are some quotations from "Hygienia": "When bubbles settle upon the urine, they indicate disease of the kidney and a prolonged illness" (VII, 34).

If blood or pus is passed in the urine it indicates ulceration of the kidney or bladder" (W. 45).

If a little piece of flesh, like hair, are passed in thick urine, they are secreted from the kidneys (W. 46).

"Kidney troubles and affections of the bladder are equal with difficulty when the patient is aged" (VI. -)

In our age such statements, even true in the extreme, only by comparing them with the beliefs of other ancient peoples, and even with those of Greek physicians who followed him, can we appreciate the advance he made by his simple observation of cause and effect, unaided by any assumption of supernatural intervention.

In the Syriac, "Book of Maladies" translated into Syriac from the Greek early in the Christian era, and made
available for the English reader by Wallace Badge, like a critical tribute to Hippocrates. Describing kidney disease, the writer refers to the "very fine tubes" that are occasionally observed in the urine, which Hippocrates himself wrote of in his book. These tubes were very long, and "wondered," given the writer, that the kidneys were large enough for anything of the kind to subside in them. Therefore it seems to me that the place where they were produced most certainly be in the veins. It seems then, that Hippocrates was the first to observe in the urine as evidence of altered functions of the kidney, what may have been casts of the tubules.

III.

Other Greek physicians were not able to feel their thinking so definitely to factual observation. Again the Syriac account of "physic" enlightened us to their beliefs: "The kidneys perform two functions in the bodies of the children of men: first they draw the urine from the liver and transmit it to the bladder and secondly they all up the organ of the seed. They may draw the seed to the bladder, and after describing the position of the kidneys, "they are got along with the veins that bring the deal and with these that bring the urine. They are nourished by a great vein that is called "kotlia" (i.e. "the cavern") which brings the blood from the liver and their nature is flushy and purulent like that of the heart."

So after the time of Hippocrates (5th Century B.C.), no noteworthy addition to our knowledge of renal failure was made for almost six centuries. In fact Aristotle (4th Century B.C.), when he ran the line of the middle age regard to their oracle, taught that the bladder was the chief
seem. Of urine formation and that the kidneys were attached to it "not of actual necessity, but as a matter of greater finish and perfection. This is unquestionably a progressor. In the 3rd century B.C. Erasistratus stumbled upon the idea of the capillaries as a logical necessity in his conception of the circulation of the blood, though their existence could not be verified until the invention of the microscope, and he did not realize their significance in relation to the renal function. In relation to the kidneys, his name is chiefly noteworthy by reason of the omen which Galen quoted when he was omitting to state the manner in which secretion occurs. But he certainly knew that it occurred in the kidney. Aeschylides, who introduced Greek medicine to Rome in the 1st century B.C., suffered a similar notoriety from the son of Galen, who called the "renoduct of the Aeschylean" because he conceived of the valvular and subsequent condensation of the fluid drunk to account for the presence of urine in the bladder. Below, a first century Roman writes, following Aeschylides, with the Greek word almost skeptically as if receiving his own judgment: "Again, from the two kidney veins, white in colour, lead to the bladder; the Greeks call these veins because they believe that through them the urine descending drops into the bladder." Erasistratus and Aeschylides Galen writes: "Evanilus (Erasistratus) kept silent. I am not going to do so. For I know that if one fuses over the Hippocratic view and makes one's pronouncement about the function of the kidneys one cannot fail to make oneself ridiculous. It was for this reason that Erasistratus kept silence and Aeschylides lied. It is somewhat ironic that this same Galen had to postulate a theory of "attraction" attributed to the kidney, by his own
suggestion as to the method of secretion, a theory as
uncontrollable as that of Fallopio. Yet it is to
Galen himself that the next advance in our known
is due.

IV

Galen founded his thinking on what he
believed to be the teaching of Hippocrates, “that there
exists in any part of the animal a faculty for attracting
its own special quality”, that the kidney was
organ for percolating out the urine and that they
sold this by their own faculty for attracting urine.
He gives a naive analogy of what he means by this
faculty. — “Here let us forget the absurdity of
steeping, and, in company with those who are
persuaded that the urine does flow through the
kidney, let us consider what is the character of
this function. For, most assuredly, if by its own motion to the kidneys,
considering this its primary course (active with the urine
off to market!) or, if this be impossible, the same
other reason for its conveyance must be found.
What then, is this? If we are not going to grant
the kidney a faculty for attracting this particular
quality, as Hippocrates held, we shall disagree
on this reason. For, surely everyone sees that either the
kidney must attract the urine, or the veins must hold
it — if, that is, it does not move of itself. But if
the veins did exist a fortuitous action when
they contract, they would squeeze out into the
kidney not merely the urine, but along with the
whole of the blood which they contain. And if this is
impossible, we shall still show, the remaining explanation
is that the kidneys do exert a reaction.” Galen On the Natural Faculties
It will be realized that Galen's contribution to our knowledge of renal function was not the story. What he did contribute was his confidence in experiment. Just as to Hippocrates, we owe to Galen not chiefly the theories he deduced but the method he employed. He was the first actually to demonstrate that the kidneys of usually secreted urine. He describes his experiment thus: "The fact is that those who are enslaved to their sects are not merely deficient of all sound knowledge, but that they will not even stop to learn. Instead of listening, as they ought, to the reason why liquid can enter the bladder through the ureter, but is unable to go back again the same way, instead of admiring Nature's artistic skill, they refuse to learn; they even go so far as to scoff, and maintain that the kidneys, as well as many other things, have been made by Nature for no purpose."

"Now the method of demonstration is as follows. One leg is divided into the forepart and in front of the ureter, the other is secured with ligature, and next, having bandaged up the animal, set things (for it will not continue to urinate.) After this one loosen the external bandage, and show the bladder empty, and the ureter quit full and distended — in fact almost on the point of rupturing. One removes the ligature from them, one by slight necessity, the bladder becoming filled with urine. When this has been made quite clear, then before the animal urinates, she has to tie a ligature round his legs and then to squeeze the bladder all over; still nothing goes back through the ureter to the kidneys. And then, it becomes obvious that not only in a dead animal, but in one which is still living, the ureter are prevented from receiving back the urine from the bladder.
Observations having been made, one now loosen the ligature from the animal's penis, and allows him to urinate, then one again ligature one of the ureters and leaves the other to discharge into the bladder allowing then some time to elapse, one now demonstrates that the ureter which was ligatured is obviously full and distended on the side next to the kidney, while the other one—that from which the ligature has been taken—is itself fluid, but the filled the bladder will now. Then again one must divide it still more and demonstrate how the urine exerts out of it like blood in the operation of vesicotomy, and after the one cut through the other also, and both being thus divided, one bandages up the animal externally, if water enough time seems to have elapsed, one take off the bandages, the bladder will now be found empty, and the whole region between the intestines and the peritoneum full of urine, as if the animal were suffering from dropsy.

Galen "On the Natural Faculties", Book I, XIII. 

Galen's experimental approach to the problem was not only unique, it was isolated. After the medical science, in common with all the other arts in which the Greeks had excelled, deteriorated into a formal, mechanical scheme, as Diderot puts it in "History of Medicine": "With the death of Galen in 201 A.D., the active prosecution of anatomical and physiological inquiry ceased absolutely. The curtain descended once and for the subject we are discussing... the dark ages have begun. Rational medicine in the pagan world descends into darkness as surely and even more abruptly than Philosophy."
"When Europe came back to life, more than fifteen hundred years after the death of medicine and physiology was just as it left it. (Macfie: "The Romance of Medicine"). The fall of Rome before the Goths and the overwhelming of Northern Europe before successive waves of invasion from east and north led, culture and knowledge in all its forms. Scholars took refuge in Constantinople with their various precious books, separated from Western Europe by a great wedge of barbaric tribes. Gradually ordered life was re-established, the Holy Roman Empire rising on the ruins of the old Roman Empire. The and Emperor certainly did a great deal for medicine by good medical legislation and by the encouragement of institutions of healing and learning, but mental life in the middle age was stagnated by the demand for conformity. All must accept the ideas saved from the shambles of the old learning, lest the centrifugal force of society overcome the centripetal. There was no room in such an age for individual experiment or for the testing of accepted ideas. Since Galen's works had survived, they became, with all their mixture of crude empiricism, the accepted body of medical truth until the Renaissance.

But even in such an age isolated voices dared to contest the dominance of Galen. "God did not exhaust all the creative power in making Galen," wrote Peter de Alverdaville (1260-1320). And the Peter de Alverdaville and his preceptor William de Soligte (1210-1280) added something to our knowledge of renal function by the indirect route of observing the association between dropy, albuminuria, and contracted kidney. Soligete's book was the first work on surgery ever to be..."
It is unnecessary to give a precise account of the channels through which the re-vitalizing current of the New Learning became available for medicine. After the work of Vélasquez (1514-1564) did not throw much light on the functions of the kidney, he must be mentioned because he freed anatomical study from the chains that bound it to Galen and Aristotle. His allegiance was to the "vision et receptum," that, actually seen and discovered, and thus, one of the apostles of the New Learning, he proved the long for the anatomical and histological study of the kidney.

William Harvey's (1578-1657) demonstration of the circulation of the blood made it necessary that previous views about all the organs should be reconsidered. The old idea about the kidney was that its substance
Strained off from the blood, not only of the veins but also of the arteries, some but not all of the "praeosity" and that the, gathered in the pelvis of the kidney as urine, was conducted by the ureters to the bladder. The problem was to know exactly how the contact substance of the kidney could actually do the straining. When it was shown that blood had come to each organ by the arteries alone, and left it through the veins, the problem was more than ever insistent.

To Giovanni A. Borelli (1608-1679) belongs the honour of beginning to solve the problem. As a mathematician, he believed that there was a mechanical explanation of the phenomena of secretion, depending only upon the size and shape of the particles to the secreted and of the channels through which they flow. Here is his own conclusion about the secretion of the urine from his "De motu animalium" (Sinclaire J.'s translation): "Who then would wish to think that the particles of the blood are picked out, separated from the watery particles (of the urine) and placed in separate receptacles by some magnetic virtue or by some ferment, acting like a servant possessing eyes? Certainly, unless we wish to lay hold of folies and wonders we are bound to confess that (in the kidney) there exist two kinds of orifices, after the manner of two sieves, namely, one a venous one, which by reason of its adjusted configuration receives the particles of blood only, not those of the watery urine, and another, the proper orifice of the kidney, the shape of which is fitted for absorbing the particle of urine but not the particle of the blood."

Lorenzo Bellini (1643-1703) was a pupil of Borelli who carefully examined the kidney of a deer under his direction. In "De structure Renaudin", he describes what
he saw. No one before him had observed, with understanding of their nature, the minute tubules (urinary canaliculi), radiating from the pelvis of the kidney toward its surface, though bastardini had seen something of them describing them as "fuscosus sulci." Bellini himself did not distinguish between the twisted and the straight tubules, which have since been named after him, but he saw enough to formulate a theory of secretion. "The middle arteries," he says, "discharge their content into spaces in the parenchyma of the kidney, whence the aqueous secretion of the blood passes into the beginnings of the urinary canaliculi, while the rest of the blood finds its way out by the veins. The selection of the one path and the other is determined by the size and configuration of the particles; fluids of the aqueous secretion fit into the channels of the canaliculi, while the rest of the blood does not." (Dr. Michael Foster, translation of "De Structura Renum").

VII

Such study of the kidney must provide rely on the naked eye alone until the invention of the microscope offered up new worlds of knowledge to the investigator. The great Swiss microscopist and the first to use the instrument on kidney structure (was Marcello Malpighi, 1628-1694). In his preface to "De Renibus," he writes: "I am ananlyzing that you should not be concerned about whether these descriptions are new or old, but that you should enquire whether they conform to the facts of nature. One thing I tell you and that is that I have not studied this kidney structure
effectively from books but by means of long and patient use of the microscope in various stages. (London edition 1689 of De Viscom) - p. 174). This statement plainly shows that Galvani has the spirit of the Renaissance. He admits that his predecessors were hampered: "It seems to me that leeches, because of lethargy, or because of the primitive nature of the instruments used, certain structures recently demonstrated by observation have not been hitherto discovered. These twisted channels (arteria et sinus) pierce through the whole substance of the kidney. A black liquid injected through the network of vessels (emulgentia vaca) will show them up." (Opus cit. p. 179) In his "Treatise on the History of Physiology" - Scipio Foschi writes, "Of all physiologists, Galvani is in his tract on the kidneys went far beyond Bellini. He showed that in man at least the kidney really consisted of several kidneys, and that the several constituent kidneys might be distinguished as masses of Bellini's tubules, arranged in the form of pyramids, like pyramids since known as the pyramids of Bellini. He showed how in each pyramid, Bellini's tubules, ended in orifices at the summit of the pyramid, from which formed the apex of the pyramid, and further down in the cortex of the kidney, the tubules were not straight as Bellini had described them but curiously and irregularly twisted. Lastly he pointed out how many at least, of these tubules began as initial swellings or capsules, round like the eggs of fishes, and how these capsules contained a "root of blood vessels. "And when the same kidney is cut lengthwise, you will see," says Galvani, "between the bundles of urinary vessels and the spaces produced, at the same little glands in almost
countless numbers which are lying like apples upon the floor vessels swollen with black liquid are extended into the form of a sort of tree. (Deduced from Dr. H. W. D. Somers' translation.) Calafishchi states his conviction that these calices must play an important part in the secretion of urine.

After he had demonstrated so clearly to the world the structure of the kidneys and made a suggestion as to how they function, it seems a strange irony of fate that renal disease should be a contributory cause of Calafishchi's own death. He had, however, placed the correlation around which subsequent workers could build their assurance theories of renal function and a sound treatment of renal disease.

VIII

Thus, after Calafishchi had arrived at a clear conception of the structure of the kidney and the work had long to wait for any further large addition to our knowledge of this organ. It is true that we owe a minuter knowledge of the distribution of the renal vessels to the skilful injections of Rugeck 1638-1748, who was called to the chair of anatomy in Lucca while Calafishchi was at Ellwangen, but he, unfortunately, assigned a wrong function to the blood vessels regarding them as the very nerve of secretion. It is also true that Antoine Ferrier, Professor at Montpellier and Paris made some addition to our knowledge in 1749 by his description of the rays of straight tubule shooting up into the cortex, since known as the pyramids of Ferrier. Apart from the descriptive work, however, "we may almost say that our knowledge of the kidney remained where Calafishchi left it until..."
took up the subject again in the 19th century (Sir W. Foster, "History of Physiology...").

Just as physiology work would have been impossible but for the invention of the microscope, so Bowmar and more recent investigators were dependent on advances in chemical knowledge and on the improvement of the techniques and apparatus of organic chemistry made in the late 18th and in the 19th centuries. One application of this development was that the normal and pathological constituents of the urine were investigated. Soon it began to be realised that it is part of the function of the kidneys to excrete the waste products of nitrogenous metabolism, in particular urea and uric acid, as well as the inorganic constituents not required by the body. The names of Gabriel Andre Wilhelm von Bürck, Florian Keller (the inventor of the spectroscope), Bright, Liebig, Wöhler, von Helmholtz, Blackett, Wolfe, von Hörden, H. Gaffé, Emil Fischer, Sir Frederick Polyne, and Otto Hahn are memorable for the indirect contribution they have made to our knowledge of renal function by their investigations into the nature of urine in health and disease.

One aspect of this work has special bearing on our subject, namely the discovery of another function of the kidneys—a synthetic function which places them in line with other glandular organs. This is that hippuric acid is built up and secreted. Justus von Liebig (1803-1873), one of the principal founders of physiological chemistry, discovered hippuric acid in 1829. Friedrich Wöhler (1800-1882), who in 1828 synthesized urea—the first organic synthesis in 1828, and in 1842 confirmed a discovery which became the starting point of the modern chemistry of metabolism, namely that the benzoic acid taken with the food appears as hippuric acid in the urine.
A year before Alexander the of Edinburgh had found out that benzoic acid is changed to hippuric acid in the body (Provincial Med. Surg. Journal, London, 1881), Max von Pettenkofer (1818-1901), a pupil of Lister, had observed in a child with St. Vitus' dance who partook of an inordinate amount of apple jam that the urine contained large quantities of hippuric acid. Oswald Schmiedeberg, the German pharmacologist, investigated the synthesis of this acid. In 1881 he established a ferment, histoxyme, which will deintegrate or synthesize hippuric acid and proved conclusively that in dogs the urine of benzoic acid and glycine take up not in the kidneys themselves. Later it was discovered that the same synthesis may be effected by ground up kidney tissue, mixed with blood and kept under oxygen at 60° C. (Bachet, and Turner, "Zeitschrift f. Physiol. Chemie," 35, 324, 1902).

It was believed by Charles Edward Brown-Séquard (1817-1894), who will Claude Bernard was the founder of the doctrine of the internal secretions, that the kidney had another function, namely that it elaborated a hormone (which he called "Cortex Pyroglandin," normal weight: Paris, 1872, 5. p. 478-486). In view of this, it is of interest to note that in one of the most recent books, which were consulted (Genito-urinary surgery, Thompson-Waller 2nd Edn., 1st Edn., 1935) reference is made to the possibility of the internal secretion of the kidneys which regulates nitrogen excretion.

TX.

With knowledge of the nature of the kidney secretion, Sir William Bowman (1818-1892) was now in a position to consider how it actually takes place. To take up the anatomical work of Schwann and develop it further in the light of the facts about urine
revealed by the chemist. In a paper read before the Royal Society, "On the Structure and uses of the Alhaffigian Bodies of the Kidney" (Phil. Tr., London, 1842, p. 217), he described the renal tubes as consisting of a basement membrane—a term used for the first time by the author—lined by epithelium. All the blood of the renal artery, with the exception of a small quantity distributed to the capsule and fat, enters the capillary tufts of the Alhaffigian bodies; thence it passes into the capillary vessels surrounding the tuft of the tubes, leaving the kidney by the renal vein. The Alhaffigian bodies and the origin of the renal tubes from around them are clearly described. There are two perfectly distinct systems of capillary vessels, that of the Alhaffigian Bodies, which may be termed the portal system of the kidney, and that of the capillary vessels surrounding the tubes. This view is confirmed by examining the kidney of the hog. (Sir Wm. Hale White, "Great Doctors of the 19th Century").

Bowman's conclusions, in his own words—"It would be difficult to conceive a disposition of parts more calculated to favour the escape of water from the blood than that of the Alhaffigian body... Tissue is so wonderful an apparatus placed at the extremity of each sinuous tube if not to furnish water, to aid in the separation and solution of the various products from the epithelium of the tube." To sum up, he regarded the watery secretion as mainly a means of flushing out the tubules in which the cortex etc. were sacked in solid form.

Bowman's theory remained without experimental evidence until 1844, when it was extended and supported by Rudolph Heiderlein (1832–1894), professor of physiology at Breslau, who is intimately associated with the interpretation of all secretory phenomena, as
intracellular, rather than as mechanical processes. The most complete statement of the Bowman-Hisler view is given by Hisler in Hermann’s “Handbuch der Physiologie” (1881, V) in which he holds that both the glomeruli and the tubules possess a secretory function. The glomeruli secrete water and salt, while the epithelium of the convoluted tubules and of the wide part of Henle's loop eliminates most of the solute of the urine including urea, uric acid, hydrochloric acid and pigments—these secretions being performed by a selective and vital process (Henle's loop is named after the great German histologist Jacob Henle 1809-1885 who was the first to describe this part of the renal mechanism—“Handbuch der Physiostudien” 1862, II. 300-305). Fastly, the solute secreted by the tubules are accompanied by a minimal amount of water under normal conditions, but in the diuretics caused by urea and salts, the increased water comes from the tubular epithelium and not from the glomerulus. In short, Hisler holds that the glomerular capsule is normally secreting a dilute fluid, apparently not suspended from a deproteinized lymph in conjunction with fluid as it passes down the tubules, carrying with it the product secreted by their walls, such as urea, uric acid, and salts, and urine in its collecting tubules as the normal urine.” (P.R. Cusack: “The Secretion of the Urine”)

Cusack describes Hisler's staining of the kidney cells by the injection of indigo carmine into the blood, which gave an impresion argument in favour of secretion by the tubules. His spinal cord was divided in a series of rabbits in order to reduce the blood pressure and the secretion in the kidney, and a saturated solution (about 17%) of indigo carmine was injected intravenously. If the animal was killed in about ten minutes, the cells of the
tubules were found stained blue, while if it was allowed to survive an hour, the cells were colourless and the pigment lay in masses in the convoluted tubules. And the white part of Henle’s loop. It usually was found in effete cast and the capsule remained colourless. Beiderlein therefore believed that the pigment is taken up from the blood and lymph by the epithelial cells of the tubules, which secrete it into the lumen, and that the secretion occurs in the absence of glomerular activity and without the secretion of urine. In fact, if the capsule is active, as in rabbits with undisturbed cord, its appearance of the kidney is quite different, as the pigment is swept away from the convoluted tubules and appears in the collecting tubules and eventually in the ureter and bladder. (A. R. Bastard, “The Secretion of the Urine”)

It is now to physical science that we turn for further knowledge about the kidney. Carl Ludwig (1816-1875) elaborated his mechanical theory of the secretion of the urine by osmosis in “Beiträge zur Lehre vom Mechanismus der Harnsekretion.” Abding 1823 and Wagner’s Handwörterbuch d. Physiologie.” 1844, it, 631. His theory starts with the idea that the secretion of the urine depends upon the beating of the heart, the blood pressure causing the urinary constituents to pass from the blood through the capillary walls and accumulate liquid. The capsule is a simple filter, which allows all the constituents of the plasma to pass through it except the proteins, and that in its tubule this filtration is elaborated into the urine by the return of much of the fluid into the blood through a process of diffusion of water to the more
concentrated lymph outside.

In 1867-1870, Ludwig, in collaboration with his pupil, Rokitansky, performed an experiment which forced him to modify his views somewhat. Gannen quotes from "Ab. a. d. Physiol. Acta. Z. 1876, v. 9, p. 217." "This consisted in dividing the medulla in the neck of a dog, causing the blood pressure to fall, and stopping the urinary secretion. Subsequent injection of urin into the veins caused a revival of the urinary secretion and forced Ludwig to conclude that the effect of pressure was dependent upon the chemical constituents of the blood; in other words, upon osmosis through a selective semi-permeable membrane.

Although Ludwig's work was of importance in the discussion between the vitalists and the mechanists, it possesses only historical interest, no one at the present time supposing that the secretion of the urine can be explained by purely physical forces. It will be seen from Rokitansky's experiment, however, that the admission of the effect of urinary content leaves the way open for future discussion.

XV

The theories of Bowman and Ludwig together formed the basis of a new theory put forward by Arthur D. Gushin (1865-1926) in his early years as a pupil of Schmidtberg (vide p. 16 supra) and at the time of his death Professor of materia medica and pharmacology in Edinburgh. In his book "On Hisit" C. C. Pfiffert gives a summary of Gushin's theory which may be quoted here: "The glomerular transudate is filtered out from the blood and transformed into urine by processes of absorption
occurring in the tubules. He contended that there was no need to assume the possession of secretory functions by the kidney tubules, and considered that there is no absorption of urea but that the whole of the diuresis and the greater part of the sodium and potassium chloride are absorbed. According to this view, the constituent of the glomerular filtrate may be divided into two classes: (1) threshold substances, secreted when they reach a certain threshold value. Such substances are creatine, chloride, bicarbonate and protein. (2) Non-threshold substances, secreted in proportion to their absolute amount in the plasma. The most important of these are the nitrogenous waste products, ura, urea, acid, creatinin and amino acids. The non-threshold substances are absorbed by the cells of the tubules, whereas the threshold bodies are absorbed in different proportions determined by their normal values in the plasma. Foulon further stated that the tubule, out of the glomerular filtrate returned to the blood the fluid best adapted for the tissues and allow the rest to escape.

Authorities still differ in their opinion as to whether Foulon's theory covers all the known facts, in particular whether it takes sufficient account of the differentiation of tubule. Hence, therefore, we must leave the question of the exact method of kidney secretion for future investigators to elucidate.

As evidence of the wide interest aroused by the discussion, it may be mentioned, that there are no fewer than fifty-three papers included in volume 18 of The Quarterly Cumulative Index, dealing with the physiology of the kidneys. With regard to the state of the literature, the late Professor J. D. Haldane pertinently remarks,
"...there are long and very inconclusive discussions of the possible mechanisms of secretion, but hardly any attention is given to the absolutely dominant fact that, in whatever way the kidneys accomplish it, they are constantly engaged in regulating the composition of the blood with a finesse which is almost incredible until one attempts to measure it quantitatively in the same way as the finesse of the regulation of the breathing or circulation is measured." (Paper read before the Edinburgh Pathological Club, January 1918, reprinted in "The New Physiology.")

Since the Great War attention has been directed, for practical reasons, to the testing of the efficiency of renal function in individuals. Forty-eight cases on this aspect alone are mentioned in volume 18 of the Quarterly Cumulative Index Medicus, July-December 1935. This work, however, is beyond the scope of our present subject."
Books Consulted

1. Alfort; A.C. : On Nephritis 1929
2. Aristotle : History of Animals Translated Crasswell 1862
3. Bashford; H.H. : The Harley Street Calendar 1929
5. Braasch ; W. F. : Psychophysics 1915
6. Brock ; A. J. : Greek Medicine
7. Campbell; D. : Arabia : Medicine and Its Influence on the Middle Ages. 2 vols. 1926
10. Cleveling; L. : Behind the Doctor 1933
12. Cushing; H. : Life of Sir Wm. Osler
14. Evans : Recent Advances in Physiology 4th Edn. 1930
15. Finlayson; J. : Ancient Egyptian Medicine 1893
16. Finlayson; J. : Herophilus and Erasistratus 1893
14 Fulton; Selected Readings in History of Physiology 1930
18 Foster; Sir Michael. Lectures on the History of Physiology during the 16th, 17th and 18th Centuries 1901
19 Galen; On the Natural Faculties. (Loeb Classical Library)
             Translated A.J. Bock
20 Garrison; F.H. An Introduction to the History of Medicine 1915
21 Haldane; J.S. The New Physiology and Diet. Addresses 1919
22 Hale-White; S.W. Great Doctors of the Nineteenth Century 1933
23 Hippocrates 2 volumes (Loeb Classical Library)
             Translated Jones & Wellington
24 Howell; W. H. Textbook of Physiology 12th Ed. 1933
25 Libby; W. History of Medicine 1922
26 Macfie; R.C. The Romance of Medicine 1909
27 McLean; H. Modern Methods in Diagnosis and Treatment of Renal Disease 2nd Ed. 1924
28 MacMichael The Gold-Headed Cane 1824
29 Major; R.H. Classic Descriptions of Disease 1932
30 Malfigli; M. De Viscerum Structure Exercitato Anatomica. London 1669
31 Newburger; M. History of Medicine Vol I
              Translated E. Playfair 1910


34. Rolleston, Sir Humphry D. *Life of Sir Clifford Allbutt* 1929

35. Scafier, Sir Edward A. *Physiology Vol I* 1898

36. Short, *The New Physiology in Surgical and General Practice* 5th Ed. 1922

37. Sigerist, H. R. *Great Doctors. English Edn.* 1933

38. Singer, C. *The Legacy of Greece*

39. Singer, C. *A Short History of Medicine* 1928

40. Starling, E.H. *Principles of Human Physiology* 6th Ed. 1933

41. Stirling, W. *Some Aspects of Physiology* 1902

42. Stables & Bligh *60 Centuries of Health & Physick* 1931

43. Syrian Anatomy, Pathology & Therapeutics or "The Book of Medicines" translated by E. A. Wallis Budge. Pub. 1913

44. Thompson Walker *Examination of Pelvic Function in Urinary Surgery* 1908

45. Thompson Walker *Genito Urinary Surgery* 1935

46. Wittington *Medical History from its Earliest Times* 1891

47a. Biographic Universelle Ancienne et Moderne 1854

47b. Dictionary of National Biography
The titles of papers used in the essay but not included in this list have been obtained from standard books of reference.