Історія медицини

History of medicine

ISSN: 2411-6181(on-line); ISSN: 2311-9896 (print)
Current issues of social studies and history of medicine. Joint Ukrainian -Romanian scientific journal, 2020, №:2(26), P. 107-110
***UDK** 612.1/.8*
***DOI** 10.24061/2411-6181.2.2020.188*

РОЗВИТОК УЯВЛЕНЬ ПРО ФІЗІОЛОГІЮ СЕЧОУТВОРЕННЯ (XVII–XX СТ.)

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DEVELOPMENT OF IDEAS ABOUT THE PHYSIOLOGY OF URIN FORMATION (XVII-XX CENTURIES)

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Тимофийчук Инга, Семененко Светлана, Борейко Лиля, Юрнюк Святослава. На сегодняшний день научные представления о механизмах формирования мочи детально изучены и освоение данного материала не вызывает трудностей не только у студентов медико-биологических вузов, но и школьников старших классов. Накопленный опыт и знания, полученные путем экспериментальных и клинических исследований, подарили научному миру вполне понятную и доступную теорию мочеобразования, которая включает три последовательных этапа: фильтрацию, реабсорбцию и секрецию. Необходимость обобщения и дополнения исследований о процессе становления и развития почечной физиологии в историко-научном аспекте обуславливает актуальность данной статьи. **Целью** данного исследовательского обзора является анализ основных достижений в области физиологии почек и водно-солевого обмена, начиная с открытия в XVII веке беллиниевых протоков и мальпигиевых телец и заканчивая исследованиями середины XX столетия. **Основная часть.** Процесс становления и развития предпосылок формирования почечной физиологии можно условно поделить на два этапа: 1) *анатомо-физиологический* (Л. Беллини XVII век), который связан с описанием почечных канальцев и продлился до возникновения первой секреторной теории мочеобразования (У. Боумен середина XIX века), что стало началом 2) *собственно физиологического* периода. «Последние точки над і расставила» современная теория А. Кэшни (начало XX века), которая положила конец почти вековой борьбе виталистов-антивиталистов, и послужила мощным стимулом для изучения роли почек в обеспечении постоянства внутренней среды, что нашло отображение в работах акад. Л.А. Орбели (середина XX века) и его учеников. **Выводы.** Таким образом, ко второй половине XX века было сформировано целостное представление о механизме мочеобразования. Последующее развитие данного направления связано с изучением механизмов регуляции гомеостатических функций почек и их онтогенетических особенностей.

Ключевые слова: *история физиологии, физиология почек и водно-солевого обмена, мальпигиевы тельца, капсула Шумлянского-Боумена, теория мочеобразования, клиренс, осморецепция.*

Introduction. According to Yu.V. Natochin, clinical nephrology and renal physiology were always in close cooperation, and physiological research was always dictated by the clinic's requests[1]. "The collaboration between the clinic and physiological science in medicine lasted until the end of the 19th century. During the time of S.P. Botkin and I.M. Sechenov, doctors trained at the physiological laboratories of K. Ludwig and K. Bernard, and the congresses of doctors were called the congresses of naturalists and doctors, physiological laboratories were structural units of the clinics. Logy was still at the stage of development, the idea of renal processes and functions in its infancy, were competing in a relationship and common urine formation theory did not exist. The idea of medicine existed kidney gland as having secretory function products of nitrogen metabolism[2].

Historiographical context of the study. The development of physiology largely determines the progress of clinical medicine. Successes in understanding the nature of the process of urine formation associated with the works of K. Ludwig, R. Geidengain K. Ustimovich, N. Vvedensky. The construction of an adequate scheme of urination required a new step - penetration into the nature of the regulation of renal function in the body. Every step in science has an author's name. The works of famous physiologists and clinicians were studied, including in the historical aspect, which was reflected in the works of Giebisch G., Jamison, R., Kutia S., Razumovskaya E., Natochin Yu., Samoilov V.

The main body of the article. Beginning the study of processes of urine formation was laid Bartolomeo Eustachio, who in 1564 g in the treatise "Opuscula anatomica" in the section "De renum structura, officio et administratione" described education look like grooves on the surface of the cross-section of the kidney. Eustachio believed that the kidneys are a solid body that is cut like wax held in the style of the furrow, by which the urine goes out, seeping out. A century later, in 1662 Lorenzo Bellini, at the age of 20

[1] Natochin, Yu. V. 100 let izuchenia fiziologii pochki v Rossii [100 Years of the Kidney Physiology Research in Russia]. *Spetsialnyi vypusk zhurnala Vestnik* [RFFI], 2017, №1, P. 39–51. Ortiz-Hidalgo, C. The professor and the seamstress: an episode in the life of Jacob Henle", *Gaceta Medica de Mexico*, 2017, N 151, P. 762–769.

[2] Natochin Yu.V., Chernigovskaya T.V. Evolutionary Physiology: History, Principles. *Comp Biochem Physiol,* 1997; N 118 A, P. 63–79.

years, opened tubules in the dermal papilla of the kidney, now known as the "ducts of Bellini" or "tubules of Bellini". In the treatise "Exercitatio anatomica de structura et usu renum" Bellini showed that buds formed thousands of glands and many tubules and vessels that have fibrous flesh tubular, hollow inside[3]. Probably, at the time, Eustachio saw a cluster of tubules of Bellini, but was not aware of the existence of tubes, mentioned by Bellini, which, if desired, can be seen for liquid injection and are genuine and true by the current of urine. This treatise marked the beginning of wide renown Bellini as anatomist and his glory, of the researcher, which with age grew stronger and stronger. In 1666, another Italian scientist, Marcello Malpighi, was opened in the kidneys of animals of the spherical formation associated with blood vessels, known today as "malpighii calf". Being one of the pioneers of microscopic anatomy, Malpighi detected in renal cortex multiple "tiny gland is attached to the arteries"...like apples <...> in the shape of a beautiful tree", later described them in "De Renibus"[4]. This contradicted the then prevailing view of the fact that the renal cortex is composed of fibers. Malpighi argued that the veins arise from the same areas in which the end terminal artery. Although he could not see intermediate links, he suggested that "gland" must also contain capillaries and the separation of blood and urine starts there. Although Malpighi did not see the connection between the glands and tubules with holes on the surface of the renal papillae open Bellini, he expressed the truth that urine is separated from blood in the glands and somehow finds its way to these excretory[5]. Following the discovery made in 1782 A. M. Shumlyansky allowed to communicate malpighii bodies with renal tubules. A. M. Shumlyansky was the first researcher of the structure and function of the kidney. Thesis for the degree of doctor of medicine: "De structura renum, tractatus physiologico-anatomicus edente" described by the original study.

A. M. Shumlyansky established vascular nature malpighia calf, and called it the glomerulus — a ball. He has shown that each renal tubule leaves the cavity in which hangs a ball of blood capillaries and tubule without interruption, not reported from neighboring and opens into the collecting tube. A. M. Shumlyansky described a knee-shaped bend in the course of renal tubules. Thanks to the work of F. Henle (1862), the notion of a structural unit of the kidney-the nephron. In his thesis A. M. Shumlyansky attempted to describe the function of kidneys in norm and at a pathology. It was a real breakthrough in the study of renal function and the writings of A. M. Shumlyansky did not go unnoticed. In the period from 1783 to 1803 was published eight essays and reviews of the work of A. M. Shumlyansky, and in 1788 dissertation was published the second edition in Würzburg[6].

New knowledge and ideas about the capsule that every student remembers as Shumlyansky-Bowman, 60 years later, in 1842, was completed by William Bowman. In the work of the "On the Structure and Use of the malpighian bodies of the Kidney, with Observations on the Circulation through that Gland" William Bowman described thin capsule that encloses the capillary glomerulus and the walls of the cavity in which it hangs. In their studies W. Bowman getting close to understanding the processes of reabsorption and secretion, describing two completely different systems of capillary vessels, through which blood. W. Bowman formulated secretory theory of formation of urine, according to which only water flows through the glomerular tuft, whose main purpose is to provide for the dissolution of the urea, uric acid, salts and other small-sized substances secreted tube. However, experimental evidence of this theory is not enough, and in explaining physiological processes in reasoning by William Bowman appeared inherent in the doctrine of vitalism "vitality"[7].

In 1844 K. Ludwig was experimentally proved the role of liquid filtration in the glomeruli of the kidney, occurring under the influence of physical factors – blood pressure – as the first stage of urine formation with subsequent reabsorption of part of the ultrafiltrate in the tubules. Carl Ludwig (1816-1895) defended his doctoral dissertation, which was rejected participation "vitality" in urine formation. Being one of the leaders antidialectical group, who believed that physiological phenomena can be explained exclusively by the laws of inorganic chemistry and physics, K. Ludwig described the process of urine formation as entirely reducible to physical processes: blood filtration in renal corpuscles and the reverse absorption of the filtrate in the tubules[8]. He suggested that the glomerular capillaries, like other capillaries, is permeable to all components of blood except the formed elements, lipids and proteins. Liquid containing all of the remaining solute passes through the capillary under the action of hydrostatic pressure. The separation of the blood is a process of filtration and tubular secretion. However, this does not explain the discovery of large quantities of certain substances in the urine in the absence of secretion. K. Ludwig suggested that the filtrate volume should be much greater than the volume of urine to contain these substances, and came to the conclusion that most of the filtrate must be re-absorbed by the tubules. Laboratory studies K. Ludwig and his colleagues have confirmed this hypothesis. Theory K. Ludwig explained many observations: the effect of dehydration and excessive water consumption to the level of urination, and the presence of glucose and uric acid in the urine when their concentration in the blood is high[9].

In 1862, a pathologist F. Henle opened U-shaped division of the nephron, called in the next loop of Henle connects the proximal and distal convoluted tubules. In the manuscript called "Zur Anatomie der Niere" he showed that in the medulla of the kidneys there are two types of tubules: some were already known as the tubules of Bellini, and the other was a tube of smaller diameter, which was lined with squamous epithelium, parallel collecting tubes and returned, forming "lasso" or "loop" is in the direction of the medulla. F. Henle failed to show the relationship of these tubules with the rest of the collecting system of the kidney.

In 1863 G. F. Zavarykin, who worked jointly with

[3] Kutia, S. A., Razumovskaya, E. A., Grigoryants, A. V., Sataieva, T. P., & Shaymardanova, L. R. Lorentso Bellini (1643–1704) i ego otkrytie pochechnykh kanaltsev [Lorenzo Bellini (1643–1704) and his discovery of the renal tubules], *Urologiia* [Urology], 2018, N *5*, P. 182–185.

[4] Natochin Yu.V. Istoriya issledovanij funkcii pochek v Sankt-Peterburge– Leningrade [The history of investigations of kidney functions in st. Petersburg – Leningrad], *Nefrologiya* [Nefrology], 2007. V. 11, N 1. P. 123–28.

[5] Jamison, R. L. Resolving an 80-yr-old controversy: the beginning of the modern era of renal physiology. *Advances in Physiology Education*, 2014, N *38*, P. 286–295.

[6] V.V. Razumov Azotemicheskoe raspyatie mediciny I dezorganizaciya pochechnyh funkcij kak funkcionalnaya rekapitulyaciya [Asothemic cracism of medicine AND disorganization of kidney functions as functional recapitulation], Novokuzneck, 2016, 36 p.

[7] Giebisch, G. Transport of Electrolytes Across Renal Tubules, *Renal Physiology. People and Idea,* 1987, N 1, P. 165–216.

[8] Samoilov, V. O. Illiustrirovannyi ocherk istorii fiziologii [Illustrated essay on the history of physiology] 2005, N ,P. 134.

[9] Aizman, R. I., & Subotyalov, M. A. Etapy stanovleniia i razvitiia pochechnoi fiziologii v Novosibirske [Stages of formation and development of renal physiology in Novosibirsk]. *Biulleten' Natsional'nogo nauchno-issledovatel'skogo instituta obshchestvennogo zdorov'ia imeni N.A. Semashko,* 2015, N *3*, P. 12–14.

K. Ludwig, told about the peculiarities of the structure of the cortex and medulla of the kidney and lymph circulation, promote the filtration and reabsorption.

K. Hufner conducted a study on the comparative anatomy of the renal tubules of fish, frogs, turtles, birds and mammals and concluded that the same 4 segments are present in the tubules of all vertebrates, but that their length and diameter are highly variable".

K. Ustinovich, head of the Department of veterinary physiology Department of St. Petersburg medical-surgical Academy, worked in the laboratory of K. Ludwig, in the thesis "Experimental studies of the theory of urine formation" in 1873, spoke in favor of the influence of chemical properties of substances contained in the blood, in particular urea, in the process of urine formation that complements the physico-mechanical theory of urine formation K. Ludwig include chemical (resp. osmotic in the modern sense) composition of blood: "...to the hypothesis of pressure you need to attach a new condition, namely, that the validity of the pressure on the formation of urine is dependent on quantity contained in the blood-forming substances urine; ... and the richer their blood, the more urine is formed at the same pressure the blood".

In 1873 Bunge G. established the existence of reciprocal interactions in the excretion of sodium and potassium in essentialization ratios of these ions in the diet ("the phenomenon Bunge" by D. gamble).

In 1874 histologist R. Heidenhain suggested a secretory method of urine formation. He completely exclude the possibility of the process of reabsorption in the tubules. The subsequent work of other researchers confirmed the existence of a secretory process in the kidney, although obligate, and bearing for its activities in nature, but playing in the process of urine formation role.

In the last quarter of the nineteenth zoologist A. O. Kovalevskiy made concerning histophysiologic study of the excretory organs of invertebrates and draw conclusions about the existence of functional equivalents in morphologically different secretory organs of animals[10].

Lviv pharmacologist W. Sobieransky advanced (1893-1903), was the theory of active tubular reabsorption by the tubular epithelium, which most researchers have attributed a secretory function. His ideas not only reformed the theory of Ludwig, but also tweaked the performance of R. Heidenhain, seen in the tubules secretion where in fact there was a reabsorption.

In 1887 Tigerstedt and Bergman at the XII International Congress of therapeutic in Moscow reported the detection in aqueous extract of kidneys of rabbits substances that increase blood pressure, and called it renin[11].

Peters K. (1909) according to comparative anatomical studies the structure and development of the kidney in vertebrates came to the conclusion that the longer the thin part of loop of Henle in mammals, the more concentric the urine they can produce under conditions of dehydration[12].

In 1913, Bernard K. the experiments were repeated Jungmann and Meijer, stated at the impact on the brain development along with polyuria significant increase in the concentration and quantity of chlorine in the urine. "Saline injections" have caused the loss of about 1/5 of the total chlorine content in the body.

In the early 20's, the presser and antidiuretic actions have been identified as chemically identical to a substance of the hormone of the posterior lobe of the pituitary gland called oxytocin-vasopressin[13].

Filtration-reabsorbtion no theory of urine formation, which is considered modern and today was presented the English pharmacologist A. R. Cushny, 1917. The theory was based on the principles of K. Ludwig, but is supplemented by recognition of the activity of the process is tubular reabsorption, and later obligative of tubules secretion[14].

But by the early twentieth century, or the physico-chemical and laboratory tests or organic - and pathophysiology, neither the experiment nor the classical representation of causal relationships in pathology was not satisfied medicine; did not indicate further ways of its development. As noted by Einstein, first, "... physics has influenced the development of medicine that made people believe in scientific methods... However, it has introduced biologists to the temptation to interpret the processes of life too primitive"[15].

"... Two big coup last exchange, which made pathological anatomy and biological interpretation of disease, led us, in spite of brilliant conquest and success, to a standstill," wrote in 1925, a German surgeon F. Sauerbruch, one of the founders of thoracic surgery[16]. At this crossroads of medicine, S. P. Fedorov wrote in 1926 that "... in front of shining biological problems, it is felt that we should go there, that this path will lead us, probably in a big way. But how to go this route? On the right we paths and correctly goes on our work?".

D. D. Pletnev future of medicine seen in synthetic alloy of its social aspects with biological content of pathological processes, in turning it into a biosocial factor in the development of society, but without specifying paths this transformation of medicine.

Thus, the concern of scientific medicine ways to further her development, dissatisfaction with the interpretation of pathological phenomena from the standpoint of mechanistic materialism emerged in the first decades of the last century.

By the early 20's, last century the data of A. V. Palladin 1916 on excretion of creatinine with urine as an indicator of status of protein metabolism in muscles has allowed R. V. Rehberg, 1926 to develop creatininemia method of determining glomerular filtration and tubular reabsorption. At the same time, the beginning of use in the clinic, serum creatinine values as an indicator nitrogen excretion of kidney function, the instructions for which can be found in the monograph by E. M. Tareeva "Anemia britikov"[17].

[10] Koshtoyanc H.S. Osnovy sravnitelnoj fiziologii. [Basics of comparative physiology], Moskva -Leningrad: Izd-vo AN SSSR, 1950, V.1, 524 p.

[11] Bradley, S. E. Clearance Concept in Renal Physiology, *Renal Physiology. People and Idea* New York: Springer, 1987, P. 63–100.

[12] Kravchinskij B.D. Sovremennye osnovy fiziologii pochek [Modern basics of kidney physiology], L.: Medgiz, 1958, 364 p.

[13] Costello-Boerrigter L.C., Smith W.B., Boerrigter G., Ouyang J., Zimmer C.A., Orlandi C., Burnett J.C. Vasopressin-2-receptor antagonism augments water excretion without changes in renal hemodynamics or sodium and potassium excretion in human heart failure, *J. Physiol. Renal. Physiol*, 2006, V. 290. P. 273–278.

[14] Medici D., Shore E.M., Lounev V.Y., Olsen B.R. Conversion of vascular endothelial cells into multipotent stem-like cells. *Nat. Med,* 2010, N 16, P. 1400–1406.

[15] Zelig K. Albert Ejnshtejn [Albert Einstein], Moskva: Atomizdat, 1964, 206 p.

[16] Thurau, K., Davis, J. M., Haberle, D. A. Renal Blood Flow and Dynamics of Glomerular Filtration: Evolution of a Concept from Carl Ludwig to the Present Day, *Renal Physiology. People and Idea* New York: Springer, 1987, P. 31–61.

[17] Ibidem.

After the works A. N. Richards, 1922-1924, 1935-1938, showed the method microfunction studies of amphibians identity of composition of the ultrafiltrate in the cavity of the capsule of the glomerulus and blood plasma, and at the same time and the dependence of urine formation from the blood pressure in a single nephron, and similar studies microfunction A. C. Walker c et al. (1937-1941) in rats and Guinea pigs filtration-reabsorbtion theory A. Keshni has become a generally accepted theory of the formation of urine that incorporate the real of the kidney activity of the kidneys, which were each competing to her the various theories of urine formation. Since that time the way of clinical physiology of the kidney and renal physiology began to disperse, which was not accidental, but was prepared by the previous course of development, physiology General biology.

It should be noted that before implementation of cleaning research methods the focus of the study of the kidneys were dictated by far not only one of the queries practice. The vector of scientific research in the physiology and morphology of the kidneys was determined by the laws of the natural development of biological Sciences and natural Sciences[18].

Conclusions. The chronological overview shows that in biology, regardless of the medicine was a natural accumulation of data on the narrative, environmental, experimental, comparative and ontogenetic morphology and physiology of the kidney of humans and animals. The inclusion in these studies of man as a mammal provided the contact physiological and medical research, contributed to the mutual penetration of ideas and methods between medicine and biology.

More or less close unity clinic and renal physiology to first third of the twentieth century was in the period of formation of representations about kidney processes and renal functions on the basis of natural scientific study of the manifestations of its activity with the materialist position – the laws of physics, chemistry, mechanics, osmosis, diffusion, perceived initially, summative, descriptive style. It was a time of mostly quantitative study and quantitative assessment of the physiological mechanisms of the renal activity. The opposing notions in the physiology of the kidney about the way it works and the survivability of the notions of it as a secreting gland completely coexisted with the clinical notions of the excretory function of the kidney as the basis for it, with the notion of the kidney as an organ of excretion in which the (semantic) is completely corresponded to the etymological, and the visible and contemplated - the allocation, excretion – the essential. The experiments of A. Richards and D. Wyrn finally settled the dispute 80 years ago. By the middle of the 20th century, a holistic understanding of the mechanism of urination was formed.

Тимофійчук Інга, Семененко Світлана, Борейко Ліля, Юрнюк Святослава. Розвиток уявлень про фізіологію сечоутворення. (XVII–XX ст.). На сьогоднішній день наукові уявлення про механізми формування сечі детально вивчені і освоєння даного матеріалу не викликає труднощів. Теорія сечоутворення включає три послідовних етапи: фільтрацію, реабсорбцію і секрецію. Необхідність узагальнення і доповнення досліджень щодо становлення і розвитку ниркової фізіології в історико-науковому аспекті обумовлює актуальність даної статті. **Метою** даного дослідницького огляду є аналіз основних досягнень в області фізіології нирок і водно-сольового обміну, починаючи з відкриття в XVII столітті беллиниевых проток і мальпигиевых тілець і закінчуючи дослідженнями середини XX століття. **Основна частина.** Процес становлення та розвитку передумов формування ниркової фізіології можна умовно поділити на два етапи: 1) анатомо-фізіологічний (Л. Белліні XVII століття), який пов'язаний з описом ниркових канальців і тривав до виникнення першої секреторної теорії сечоутворення (У. Боумен середина XIX століття), що стало початком 2) власне фізіологічного періоду. «Останні крапки над і розставила» сучасна теорія А. Кешні (початок XX століття), яка поклала кінець майже віковій боротьбі віталістів-антивіталістів, і послужила потужним стимулом для вивчення ролі нирок у забезпеченні сталості внутрішнього середовища, що знайшло відображення в роботах акад. Л. А. Орбелі (середина XX століття) і його учнів. **Висновки.** Таким чином, до другої половини XX століття було сформовано цілісне уявлення про механізм сечоутворення. Подальший розвиток цього напряму пов'язаний з вивченням механізмів регуляції гомеостатичних функцій нирок та їх онтогенетичних особливостей.

Ключові слова: історія фізіології, фізіологія нирок і водно-сольового обміну, мальпігієві тільця, капсула Шумлянського-Боумена, теорія сечоутворення, кліренс, осморецепція.

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Received: *27. 04. 2020*
Advance Acces Publischer: *June2020*

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