The kidney revisited

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Abstract

The author reviews the historical process leading to the modern knowledge of renal physiology and comments upon the Internists enchantment on this matter in the beginning of the 60ths.

After emphasizing the relevant contribution of dialysis in the management and prognosis of renal failure, he writes about the future treatment of glomerulopathies and about the mysteries of renal physiology and pathology that persist in our days.

Key words: renal physiology, renal failure, dialysis, glomerulopathies.

Secure in our knowledge of the biochemical operations carried out by the kidneys in order to produce just over than one liter of urine a day (operations that we prosaically call renal function), it is hard for us to imagine the ignorance of our ancestors on facts that nowadays seem to be so obvious. Perhaps for this reason, it is worth taking some time to remember.

We shall start, then, in Classical Antiquity. Aristotle considered the kidneys as totally superfluous adornments, whose function was limited to enabling the bladder to carry out its function better. Hippocrates, a pragmatic clinician of rare intuition, wanted to avoid venturing into fictional theories, and so restricted himself to initiating a simple practice that continues to be extremely useful more than 2000 years later: observing the urine. Galeno, founder of the experimental method in Medicine (a fact that has not always been recognized), did what was necessary to challenge a series of nonsense claims by Asclepiads, who believed that liquids passed into the bladder in the form of steam, before condensating. Galen blocked the ureters and observed that while they became distended with urine above the blockage, below the blockage the bladder remained empty. Through this elegant demonstration, he proved that the urine was actually produced by the kidneys, but the taboos and limited technical means available at that time prevented him from going any further.

The Renaissance gave Medicine two famous personalities. Vesalius, the founder of Anatomy, who did not understand the kidneys very well, and whose description of them was pure fantasy; hollow organs with two compartments separated by a membrane similar to a sieve. Paracelsus (who rejected the Galenism and replaced it, to no great advantage, with Hermetism) had the idea of conducting a chemical analysis of the urine, but was limited by the knowledge available at the time, and hampered by the contradictions of his own theories, which meant that he was unable to obtain satisfactory results: from his work came a process of intentions, out of which others would later develop.

With the advent of van Leeuwenhoek's microscope, new perspectives of knowledge on the kidneys were opened up. It was then that Malpighi described the famous glomeruli, which he called "glands", later named after him. Little suspecting that these were actually capillary tufts, it was he who started the era of microscopic anatomy of the kidney.

But another century was to pass before Bowman finally described the capsule, also named after him, and the close anatomical relations between this structure and the glomerulus and renal tube. Unveiling the architecture of the kidney was a huge step forward. However, attempting to use this knowledge to explain the formation of urine, Bowman merely speculated on a possible tubular secretion which was not based on any demonstration. In fact, it was only later, after some fundamental aspects of the kidney structure had been clarified that the conditions were created that would enable the renal physiology to be unveiled.

Here, it is worth remembering that a short while before, another great figure of Medicine had made a decisive contribution by establishing, for the first

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time, a clear relationship between albuminuria and anasarca, and the renal lesions found in autopsy. He was Richard Bright, and together with Addison and Hodgkin, they formed a kind of “wonderful trio” of Guy’s Hospital from 1820 onwards. His influence was so strong that until the middle of the century, the expression “Bright Syndrome” was still used to express chronic renal insufficiency of the sclerotic and atrophic kidney, the final result of a wide range of diseases.

The beginning of the 20th century was marked by a personality who ushered in modern renal physiology: Arthur Cushny. In his book, The Secretion of the Urine, published in 1917, he made the first clear distinction between two different processes that influence the formation of urine: filtration, which occurs in the glomerulus and is a physical process, and reabsorption, which occurs in the tubes and depends on what was called “vital activity” of the epithelium. From there, the field was ripe for the Works of brilliant physiologists such as Alfred Richards, Robert Chambers and Homer Smith, who would unveil the secrets of renal function as we know it today.

I recall that in 1957, when I began my internship, it was mandatory to read Fishberg’s book Hypertension and Nephritis, but it was also considered good taste (or rather, the height of snobbery) to cite Homer Smith. Knowledge of the kidney physiology, at that time, had a fascinating intellectual power over those who were just starting their careers in Internal Medicine, while at the same time, it was a source of reflection, perplexity and also frustration.

Firstly, it was finally realized that the kidney is far too complex for the essential task that was attributed to it, namely, maintaining the composition of the liquid that bathes the cells of the organism and which Claude Bernard called the “milieu intérieur”. The fact that in order to achieve this, it was necessary to filter something like 170 liters of water and one kilogram of sodium chloride a day, then reabsorb more than 90% of these amounts, then cause small molecules to move like crazy along the nephron, could not help but appear to be something of an exaggeration. But that is how it was, and it remained like this due to the simple fact that the kidneys were not the result of an instantaneous act of creation, but rather, of a long phylogenetic evolution. It is known today that living creatures, by abandoning the “lost paradise” – seawater - many millions of years ago, to venture into fresh water, and then onto land, had to create mechanisms, first to get rid of water first, and to conserve it. For this reason, just like a “train on which our ancestors traveled”, our kidneys transport a wide range of solutions, which include a highly efficient ultrafiltration apparatus - the Malpighi glomerulus - a zone specialized in reabsorption - the proximal tube - and a complex system of hydroelectrolytic adjustments, governed by the distal tube and Henle’s loop.

This digression was all very stimulating from an intellectual point of view, but it did little to change our capacity to influence the evolution of renal diseases, particularly when they reached the phase of terminal uremia. Since we had no effective therapies, we had to restrict ourselves to helplessly watching patients die.

That was the state of play when artificial kidneys came onto the scene. Based on a very simple concept – a semi-permeable membrane placed between the patient’s blood on one side and a dialysate bath on the other - these machines managed, through ion exchanges governed only by the laws of Physics and conditioned by osmotic and hydrostatic pressures, to maintain the normal composition of the plasma and of the interstitial fluids that bath the cells of the organism. It was then demonstrated that our “natural’ kidneys had mechanisms that were far more complex than the basic function attributed to them, and that, after all, it would be possible to obtain the same results using far simpler processes.

From that point on, and based on successive technological improvements, artificial kidneys became faster and more operational. It became possible to gradually widen the indications of dialysis to almost all cases of uremia, and instead of compassionately watching patients die, we were now able keep them alive and active; without doubt, a significant difference.

With all these developments, the fascination that the renal function had exerted among academics began to wane. Now, it was a time of efficient and well-organized assembly lines that could “wash” the uraemic blood. In them, a technically sophisticated apparatus could be easily activated by paramedics who, after appropriate training, did not need to know the wonderful secrets of physiology, or the scientific fundamentals that had enabled the conception and construction of the equipment they were handling: all they had to do was to know which buttons to press.

But all advantages come at a price. In this particular case, we refer not only to financial costs,* but in particular, to the tyranny of machines, which in order to be effective, require the patient's presence over a period of several hours, two or three days a week. The arduous physical and psychological dependence of dialysis patients on the equipment, and the potential problems (see the aluminum case), have generated phenomena of mutual solidarity which, over time, have become real lobbies of renal insufficient patients.

However, for more than twenty years now, no one in their right mind could view dialysis techniques as anything other than a temporary solution, designed to meet the need in a transition phase and win time until Science would create more comfortable, effective and cheaper methods. How will this be possible? There are two answers to this question: either by taking a step forward in the area of transplants, or by taking a step backwards to control the pathogenesis, with early diagnosis and therapy of diseases of the renal parenchyma, particularly glomerulopathies. With the emergence of cyclosporine and the logistical improvement of organ collection, the "transplant" solution reached its peak and will remain there through to the next millennium. But what comes next? Will we be able, in the future, to better understand the genesis of diseases of the renal parenchyma to the point of avoiding and treating them before they reach the terminal phase? Yes, it may be possible. But until that happens let's come back to present.

After several decades, during which new technologies enabled the survival of terminal uraemic patients – either at the expense of the (re)creation of a kidney by man, or through posthumous re(use) of someone else's kidney – it remains to be seen whether, in this area, there is still a role for the internist and the general practitioner**

It has been known for a long time that terminal chronic renal insufficiency is usually only the tip of the iceberg, with the part under water corresponding to the development of a renal disease that started a long time before. Asymptomatic and without showing any changes in the laboratory tests for decades, it emerges later, either through biochemical alterations detected in routine analysis, or in a sequence of acute episodes that lead to the decompensation of a kidney whose functional reserve is already reduced. Meanwhile, the glomerular filtration rate decreases over time, from normal values, close to 120 ml/min, to 10ml/min. Below these levels, life is only possible through the use of dialysis. But before reaching this stage, the internists and general practitioners have a fundamental role, which includes intensive therapy of some glomerulopathies, control of hypertension, low protein diets, prevention and treatment of decompensation factors, and correction of early metabolic and hydro-electrolytic alterations. It will then be possible to reduce costs, avoid unnecessary discomfort, provide patients with a better quality of life and, in some cases, delay the emergence of terminal chronic renal insufficiency.

Here is the long and complex saga of how, from a state of total ignorance about how the kidney functions, we have arrived at the vast knowledge and modern technologies available at the end of this 20th century. It has been a history full of hesitations and detours, but the marvelous results are there and cannot be disputed. But despite all this, the kidney still has its well-guarded secrets, which present a permanent challenge to our imagination and capacity. An example is its role in endocrine secretion, the knowledge of which is relatively recent, and another prime example is the fascinating immunological phenomena that take place in that tiny and mysterious space, the glomerulus. Therefore, all we can do is await for the surprises that the coming decades will inevitably reveal.

*"Although renal patients represent no more than 0.05 per cent of the Portuguese population, Portugal spends more the 30 trillion escudos a year on the treatment of chronic renal insufficiency" (Correio da Manhã, 21/05/1997)

**See p. 125 of this issue "O doente insuficiente renal do ponto de vista do internista"

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