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EDITORIAL

# Kidney function tests at the crossroads☆

## Las pruebas de función renal en una encrucijada

**Víctor M. García Nieto*, María Isabel Luis-Yanes, Patricia Tejera-Carreño, Teresa Moraleda-Mesa**

*Sección de Nefrología Pediátrica, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain*

*In memory of our teachers on renal function test and other subjects of this speciality and of life, Doctors Juan Rodriguez Soriano, Alfredo Vallo Boado and Gonzalo Castillo de la Arena.*

There have been significant changes and improvements in the tests designed to assess renal function since chemists that started to specialise in medical chemistry thought of heating up the urine of oedematous patients and demonstrated that it formed a sediment produced by the transition to the solid state of the proteins previously suspended in the urine. The following functional tests were stimulus tests. These tests explored changes in the smell of urine following ingestion of turpentine or asparagus, or in its colour following administration of methylene blue or phenol red. Joaquín Albarrán (1860–1912), a Cuban-Spanish urologist, devised a new test that he called ''experimental polyuria''. Through the insertion of a catheter in each ureter, he could observe changes in urine volume following fluid restriction or administration. The outcome was different in individuals with healthy kidneys versus diseased kidneys.

The direct precedent of the concept of clearance was the concept of the ''urea ratio''. In 1928, Möller, McIntosh and van Slyke coined the term ''maximum blood urea clearance''. Soon after, the endogenous creatinine clearance (CrCl) started to be used to calculate the glomerular filtration rate (GFR) and was defined as the millilitres of blood that were cleared of creatinine per unit of time. The formula for calculation of CrCl has the creatinine excreted in urine in the numerator and the serum creatinine in the denominator. In 1976, Schwartz et al. argued that since the level of creatinine is associated with the muscle mass and the muscle mass to the height, the numerator of the classical formula could be replaced by the height multiplied by a constant that varied based on age (0.55 for ages 2–12 years and women aged 13–21 years). This was the origin of the classic Schwartz formula.[1] With its advent, the collection of timed urine samples for calculation of the GFR became unnecessary. The possibility of obtaining a standardised measurement of creatinine with the IDMS method and the belief that the classic formula overestimated the GFR on account of the proximal tubular secretion of creatinine led to modification of the formula by a similar formula where the constant became 0.413. Constant values have not been calculated for infants aged less than 1 year or adolescents of either sex. An additional concern with this formula is that it was validated in paediatric patients aged 7.7–14.3 years with chronic kidney failure. Both formulas were used by Ubetagoyena et al. in the article published in the current issue of *Anales de Pediatría*.[2] The Pearson and intraclass correlation coefficients assessing the agreement between the CrCl and the modified Schwartz formula were higher compared to those found for the agreement between the CrCl and the original formula.

Until the mid-20th century, the rate of elimination in urine of calcium or any other solute was expressed in mg/24 h, a practice that continues today, especially in the adult population. In 1959, Christopher Nordin proposed the first ratio to be applied in clinical practice, comparing the urine concentrations of calcium and creatinine. This author noted that this ratio exhibited a good correlation with the

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* Corresponding author.
*E-mail address:* vgarcianieto@gmail.com (V.M. García Nieto).

calcium concentration obtained from analysis of 24-h urine samples.[3] In the early 1950s, the tubular reabsorption of phosphate (TRP) started to be calculated in the evaluation of hyperparathyroidism. The armamentarium of functional tests soon grew with the fractional excretion (FE) of other substances that could be measured in both blood and urine. Ratios and RE values can also be calculated from spot urine samples. The study of Ubetagoyena et al. cited above found an excellent correlation between the clearance of sodium and potassium in urine calculated based on 24-h urine samples and the respective FEs of these ions.[2]

The title of this editorial alludes to a crossroads we are currently facing in regard to renal function tests. We base this statement on the following:

1 In our experience, the collection of timed urine samples considered the gold standard for decades is no longer necessary, save in specific cases. The article published by Ubetagoyena et al confirms what our research group had already argued in an Editorial written for *Anales de Pediatría* 6 years ago.[4]
2 Those of us trained in the first courses of paediatric nephrology, offered in the 1970s, learned to perform renal stimulation tests not known to younger generations of physicians. By this we refer to, for instance, the hyposaline infusion test, to tests aimed at assessing the transport maximum and the threshold for reabsorption of bicarbonate or phosphate, or different methods to assess the acidification capacity of the kidney. The diagnosis of Bartter syndrome was made based on the results of renal stress tests performed after hyposaline loading and administration of angiotensin. At present, a genetic test is available, rendering such methods unnecessary. Something as basic as the assessment of the urine concentrating ability of the kidneys, in which we have based part of our scientific careers,[5] is now neglected by many nephrology groups. All of this may have a deleterious effect on the training of young specialists.
3 In all likelihood, the 3 approaches for estimating the GFR mentioned in the article of Ubetagoyena et al will soon be obsolete. This is due to the introduction in clinical practice of the measurement of cystatin C, a protein of low molecular weight synthesised by all nucleated cells that is a good marker of glomerular function and whose levels, unlike those of creatinine, are independent of age, sex and body mass. At present, as members of the Asociación Española de Nefrología Pediátrica (Spanish Association of Paediatric Nephrology), we have at our disposal a software application that, in addition to calculating the modified Schwartz formula, allows the calculation of the estimated GFR (eGFR) by means of 8 different formulas that use the levels of creatinine and cystatin C. The correlation coefficient for some of these formulas is as high as 0.99.
4 Some internationally renowned journals have even accepted works where the measurements of substances in urine were given as absolute values. This is obviously nonsense. Urine may be diluted or concentrated based on the demands of the body and water intake, so any substance we measure will be equally diluted or concentrated. Thus, excreted amounts must be reported in ways that bypass this problem, such as FEs or ratios. We recently addressed a letter to the editor of one such journal with the aim of rebutting this wrongful practice.

Lastly, we would like to take this opportunity to highlight a basic function test that is little known. We refer to the volume of urine relative to 100 mL of plasma filtered by the kidney (GFR). Ubetagoyena et al. have found an excellent correlation between this parameter and the volume of urine per minute corrected for a body surface area of 1.73 $m^2$. This is a simple method to determine whether a patient has polyuria without collection of a 24-h urine sample.

## References

1. Schwartz GJ, Haycock GB, Edelmann CM Jr, Spitzer A. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics. 1976;58:259–63.
2. Ubetagoyena Arrieta M, Areses Trapote R, Mendia Ubetagoyena J, Pérez Revuelta M, García Albizua I. Función renal basal en pediatría: correlación de métodos que dependen de la recogida de orina de 24 h con otros más sencillos que no requieren orina minutada. An Pediatr (Barc). 2020;92:65–70.
3. Nordin BEC. Assessment of calcium excretion from the urinary creatinine ratio. Lancet. 1959;2:368–71.
4. García Nieto V, Luis Yanes MI, Arango Sancho P. Las pruebas básicas de función renal revisadas. ¿En el ocaso de la recogida de orina de 24 horas en pediatría? An Pediatr (Barc). 2014;80:275–7.
5. García Nieto VM, Luis Yanes MI, Arango Sancho P, Sotoca Fernández JV. Usefulness of basic renal function tests in decision-making in children with loss of renal parenchyma and/or dilation of the urinary tract. Nefrología. 2016;36:222–31.