individuals, using T:R ratio of 0.75 can potentially miss a significant amount of T-wave changes from the baseline.

An understandable shortcoming of this paper was the lack of a baseline ECG in the absence of hyperkalemia which could be used for comparison. This left the authors unable to determine if the effects on the ECG were from hyperkalemia or from intrinsic heart disease. Immediate short-term reversibility of ‘tented’ T-wave or other signs of hyperkalemia (P–R interval, QRS duration, QTc interval, etc.) with intravenous infusion of calcium, in a patient with true hyperkalemia-related ECG changes, is used at our institution as a diagnostic tool to evaluate the effect of hyperkalemia on cardiac conduction. This physiological approach can be used to assess the risk of hyperkalemia for the patient in the acute clinical setting and also warrants systematic study.

Importantly, this study emphasizes how essential it is for clinicians to be competent in the interpretation of an ECG using the clinical content rather than solely relying on a computer’s interpretation. While a formal curriculum on ECG interpretation is required in internal and emergent medicine programs, proof of competency is not assessed by the majority of them. Furthermore, this paper provides a framework for further study into the management of hyperkalemia. The authors have made a significant start to systematically study the predictive tools for adverse events in hyperkalemia. Clearly, this is an area that deserves further study and innovation.

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Increased prevalence of acute interstitial nephritis: more disease or simply more detection?

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Acute interstitial nephritis (AIN) is the second leading cause of acute, intrinsic kidney disease [1]. Unlike acute tubular necrosis, the most common cause of intrinsic kidney injury, AIN is known to have a high potential for reversibility if identified early [2]. The diagnosis of AIN is often made empirically based on the clinical presentation (e.g. a case of acute kidney injury (AKI) accompanied by a history of rash and fever, peripheral eosinophilia and a urine devoid of protein), yet a true diagnosis of AIN can only be established by a renal biopsy. Indeed, because AIN most commonly occurs in the absence of supportive clinical or laboratory findings, the importance of kidney biopsy to firmly diagnose AIN as the cause of AKI cannot be understated. A biopsy not only confirms the pathologic diagnosis but can also provide information on the severity of the injury, activity versus chronicity of the lesion, and the presence of other significant glomerular or vascular abnormalities that may influence treatment decisions [3].

In this issue of ‘Nephrology Dialysis Transplantation’, Goicooceha et al. report findings from kidney biopsies in the Spanish Registry of Glomerulonephritis over a 16-year period (1994–2009) [4]. Of the total 17 680 native kidney biopsies cataloged in the registry, 468 (or 3%) met the histopathologic criteria for the diagnosis of AIN. In the subgroup of 3059 biopsies performed for the indication of AKI, 392 cases (or 13%) were diagnosed with AIN. As the authors note, these findings are not particularly novel, as the 3% prevalence of AIN has been shown in other biopsy series, as has the higher prevalence in patients presenting with AKI [5]. The intriguing features of their report, however, emerge in the analysis of
biopsies according to distinct time periods and age groups. Specifically, the biopsy incidence of AIN increased over the duration of the time period examined from 1.5% (1994–1997) to 1.8% (1998–2001) to 3.2% (2002–2005) to 4.2% (2006–2009). The most dramatic increase in AIN occurred among elderly patients, as a nearly 8-fold increase in AIN was seen in patients >65 years of age [4].

Goicoechea et al. provide two potential explanations for this rising prevalence of AIN in the elderly population. The first is a higher current overall biopsy rate in the elderly population compared with previous decades. In their registry, the number of biopsies performed each year did not increase over the time periods analyzed, yet the average age of patients diagnosed with AIN rose from 46 years in 1994–1997 to 61 years in 2006–2009 (P < 0.001) [4]. This suggests that the number of biopsies performed among elderly patients has risen compared with the other age ranges analyzed, although such specific counts are not provided. Indeed, recent reports have shown that kidney biopsies in both elderly (>65 years) and very elderly (>80 years) patients are as safe and as likely to yield treatable lesions as renal biopsies in younger counterparts [6, 7]. As AKI is the most common indication for kidney biopsy in elderly patients, accounting for 25–50% of all biopsies in this age range [5, 7, 8], it is not surprising that more cases of AIN are being identified. For example, in a series of histopathologic findings in elderly patients in the USA biopsied for AKI (n = 259 participants >60 years, mean age 71.8 years), AIN was seen in 47 (19%) biopsies [5].

The second explanation proposed for the rise in AIN in elderly patients in this Spanish registry is what the authors refer to as an ‘uncontrolled’ and ‘increased’ use of antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) over the past two decades [4]. Without detailed historical information on the patients in this registry, including no data on etiologies of AIN such as specific medication use, this suggestion can only be labeled conjecture and highlights the limitations of this type of retrospective review. While the authors are likely correct that the use of NSAIDs and antibiotics has increased, the rising prevalence of AIN also raises the question as to whether, similar to other parts of the world, there has been a significant increase in the use of proton pump inhibitors (PPIs) in the Spanish hospitals that comprise the registry. Although the rate of true, biopsy-proven AIN with PPIs remains low, PPIs currently stand as one of the leading causes of AIN due to the exponentially increasing use of these medications for softer and non-approved indications [9]. Previous studies have suggested a higher susceptibility to AIN with NSAIDs among the elderly, [10] and a similarly higher susceptibility with PPIs may also exist in this age group.

The role of steroid therapy in the treatment of AIN is not mentioned by Goicoechea et al. as an influence for the rising prevalence in their registry. Although no prospective, randomized controlled trials have emerged to support the use of steroid therapy for AIN, during the 16-year period covered in this study, reports demonstrating the benefits of steroid therapy for AIN have evolved and improved from anecdotal case reports [11] to larger cohort series [12] that demonstrate favorable outcomes in treated versus non-treated patients. Appropriate use of steroids, alongside removal of the offending agent, can potentially reverse AIN lesions, restore kidney function and minimize risk of progression to chronic kidney disease and/or end-stage renal disease. This potential, though, appears to rest primarily on how quickly the lesion is identified and how early steroid therapy is introduced. Thus, with more data suggesting a beneficial effect of early steroid therapy on biopsy-confirmed AIN, the threshold to biopsy has likely been lowered in order to facilitate timely treatment decisions. In our own hospital, this has surely been the case, and we presume that many of the 120 hospitals in the Spanish Registry have experienced a similar shift in thinking about AIN, even if this is not entirely borne out by the presenting serum creatinine and estimated glomerular filtration rate trends over time in this cohort.

Leukocyturia is often considered a hallmark finding in AIN, yet up to 25% of patients with AIN have bland urinary findings; thus, a high clinical suspicion of AIN in patients with AKI should prompt biopsy regardless of urinary abnormalities. In this cohort, the incidence of microscopic hematuria (33%) was higher than that of leukocyturia (22%); this difference was seen in individuals across all age groups, although the incidence of leukocyturia was noticeably higher in elderly patients (27%). Interestingly, gross hematuria was reported in ~5% of all patients with biopsy-proven AIN [4]. While microscopic hematuria is a common finding in AIN, gross hematuria is considered a rare clinical manifestation and raises the possibility of another, concomitant diagnosis to explain hematuria. The authors acknowledge the limitation of their registry only including data on the main histopathologic diagnosis. This missing data clouds our ability to interpret the higher prevalence of gross hematuria and heavy proteinuria (another uncommon finding in AIN) seen in this cohort.

The results presented by Goicoechea et al. provide data on a large-scale epidemiologic cohort on biopsy-proven AIN, for which there is still a dearth in the currently available literature. Over a 16-year period (1994–2009), the Spanish Registry of Glomerulonephritis demonstrated a rising prevalence of AIN that is principally explained by an increased rate of diagnosis among the elderly patients >65 years of age. Whether this rising rate of AIN is due to a truly higher incidence of disease or merely a higher rate of detection is difficult to discern from the available data in the registry, which is limited by a lack of data on biopsy counts among specific age groups, etiologies of AIN (including specific medication use) and secondary pathologic diagnoses. Still, with the growing evidence supporting the benefits of steroid therapy for selected cases of biopsy-proven AIN, the trend displayed here should be met with encouragement and, likely, even more biopsies to confirm clinically suspected AIN.

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