

theless, in our fully adjusted model, the 95% CI for the hazard ratio associated with the administration of paricalcitol versus calcitriol included the point estimate reported by Teng *et al.*<sup>3</sup> Paricalcitol appears to confer no survival advantage over doxercalciferol. The point estimates for hazard ratios for doxercalciferol versus paricalcitol ranged from 0.99 to 1.06 and each 95% CI included 1.0. However, we cannot exclude the possibility that doxercalciferol may be associated with a small benefit or disadvantage over paracalciferol.

Our retrospective study reflects clinical practice. Since different vitamin D preparations became available at different times, the treatments were not simultaneous, and switching was the major cause of censoring. The vitamin D analogs were not dosed according to KDOQI guidelines, since most of the study occurred before these were published.

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## Immunofluorescence on proteinase XXIV-digested paraffin sections

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**To the Editor:** In their comparison of immunofluorescence (IF) on frozen sections with pronase-digested paraffin sections, Nasr *et al.*<sup>1</sup> found that pronase digestion was a useful technique for IF on paraffin (IF-P) sections. However, the sensitivity of this technique was low for membranous glomerulopathy and anti-glomerular basement membrane disease (50 and 20%, respectively), which was mainly due to weak staining of IgG (immunoglobulin G).

In our laboratory, we use bacterial proteinase XXIV (Sigma, St Louis, MO, USA), as described by Bancroft and Gamble,<sup>2</sup> instead of pronase. We compared IF-P on proteinase XXIV- and pronase-digested paraffin sections. We selected five cases of lupus nephritis that showed full-house fluorescence staining on frozen sections. In all cases, staining intensity was similar or better on proteinase XXIV-digested slides, and less background was observed. Importantly, staining for IgG and C1q was more intense in sections digested with proteinase XXIV than in those digested with

pronase. In addition, we tested five cases of anti-glomerular basement membrane disease. One of these was negative after pronase, as well as after proteinase XXIV digestion, one was positive with both techniques, whereas the remaining three were positive only after proteinase XXIV digestion. Finally, in nine cases of membranous glomerulopathy, diagnostic IF-P staining for IgG was obtained in six cases after pronase digestion and in five cases after proteinase XXIV digestion.

In conclusion, we agree with Nasr *et al.* that IF-P is a valuable salvage technique for renal biopsies. To this, we would like to add that IF-P on sections digested with proteinase XXIV is generally more sensitive than IF-P on pronase-digested sections.

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## Machiavelli and urinalysis

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**To the Editor:** I read with great interest the article on the history of urinalysis in Western culture by Armstrong.<sup>1</sup> It gives a detailed outline of how uroscopy developed into a prominent medical diagnostic tool, and later was abandoned due to the poor scientific basis of such practice. In Dr Armstrong's article, however, it is not mentioned that uroscopy was so popular to be included in the most famous play by Niccolò Machiavelli, 'La Mandragola (The Mandrake)',<sup>2,3</sup> making fun of presumptuous physicians and credulous patients. In another important paper on uroscopy by Voswinckel,<sup>4</sup> the contribution of Machiavelli is not mentioned as well.

Niccolò di Bernardo dei Machiavelli (May 3, 1469 to June 21, 1527) was an Italian political philosopher. He is a central figure of the political component of the Italian Renaissance, most widely known for his treatises on realist political theory (*The Prince*). However, he also was a musician, poet, and romantic comedic playwright.

The Mandragola has been widely performed and very popular since the sixteenth century. The title comes from the popular tale that a woman who drinks a potion made from the mandrake root is certain to conceive a child, the only drawback being that the man with whom she first has sex after taking the potion will die within 8 days. The story evolves around Callimaco, a lovesick Florentine who came from Paris to conquer the heart (and the graces) of Lucrezia, the beautiful young wife of Messer Nicia Calfucci, a

**Table 1 | Transcript of the play 'La Mandragola', relevant to uroscopy, from the original Scene 6, Act II, in Italian and Latin, followed by English translation**


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CALLIMACO Avete voi el segno?  
NICIA E' l'ha Siro, sotto.  
CALLIMACO Dàllo qua. Oh! questo segno mostra debilità di rene.  
NICIA Ei mi par torbiccio; eppur l'ha fatto or ora.  
CALLIMACO Non ve ne maravigliate. *Nam mulieris urinae sunt semper maioris grossitiei et albedinis, et minoris pulchritudinis, quam virorum. Huius autem, inter caetera, causa est amplitudo canalium, mixtio eorum quae ex matrice exeunt cum urina.*  
NICIA Oh! uh! potta di san Puccio! Costui mi raffinisce in tralle mani; guarda come ragiona bene di queste cose!  
CALLIMACO Io ho paura che costei non sia, la notte, mal coperta, e per questo fa l'orina cruda.  
NICIA Ella tien pure addosso un buon coltrone; ma la sta quattro ore ginocchioni ad infilzar paternostri, innanzi che la se ne venghi al letto, ed è una bestia a patir freddo.  
CALLIMACO Infine, dottore, o voi avete fede in me, o no; o io vi ho ad insegnare un rimedio certo, o no. Io, per me, el rimedio vi darò. Se voi avrete fede in me, voi lo piglierete; e se, oggi ad uno anno, la vostra donna non ha un suo figliolo in braccio, io voglio avervi a donare duemila ducati.  
NICIA Dite pure, ché io son per farvi onore di tutto, e per credervi piú che al mio confessore.

CALLIMACO Have you got the specimen?  
NICIA Siro's got it, under his mantle.  
CALLIMACO Give it to me. Oh! This specimen shows a weakness of the kidneys.  
NICIA Indeed, it looks quite cloudy to me; and yet she just did it.  
CALLIMACO You should not be surprised. *Nam mulieris urinae sunt semper maioris grossitiei et albedinis, et minoris pulchritudinis, quam virorum. Huius autem, inter caetera, causa est amplitudo canalium, mixtio eorum quae ex matrice exeunt cum urina. (In fact, urine from females is always thicker and whiter, and less exquisite, than urine from males. Of such things, among others, the cause is the width of the channels, combined with the materials which exit from the body matrix with the urine).*  
NICIA Oh! uh! Pussy of Saint Puccio! This man gets better and better while I listen to him; see how well he speaks about these things!  
CALLIMACO I fear the patient may not be well covered at night, and perhaps this is the reason why her urine is not well matured.  
NICIA She is well covered, with a good blanket, but then she'll spend four hours on her knees threading paternosters together, before she comes to bed, and yet she is as strong as an ox when it comes to standing the cold.  
CALLIMACO Well now, sir, the question is, have you faith in me, or haven't you; and do you want me to teach you a certain remedy or don't you? For my part, I'm ready to give you the cure. If you have faith in me, you'll get it, and if your wife doesn't have a baby in her arms by this time next year, then I'll be willing to give you two thousand ducats.  
NICIA Go on then, tell me, because I am ready to give you credit and honors for everything, and ready to believe you more than my own confessor.

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foolish wealthy merchant whose only thought is having an heir. The clever Callimaco therefore disguises himself as a physician, and to gain Nicia's faith, he performs an hilarious uroscopic exam (Act II, Scene 6), reported in Table 1.

Machiavelli reports how easy could be for an educated imposter to play the part of an expert doctor, without seeing his patient. It is crucial to note the importance of Nicia's credulous attitude towards someone who could speak Latin, educated in a foreign Country, asking for an absolute faith in his previous experience. It is possible that Machiavelli took his inspiration from the first printed medical books on uroscopy, such as the *Epiphaniae Medicorum*<sup>5</sup> or the *Fasciculus Medicinae*.<sup>6</sup> In any case, he tried to denigrate the inappropriate use of uroscopy much earlier than Thomas Brian.<sup>7</sup>

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## Classification of pediatric lupus nephritis

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**To the Editor:** We read with great interest the review by Markowitz and D'Agati<sup>1</sup> on the 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) classification of lupus nephritis (LN).<sup>2</sup> We agree that the new classification has provided a standardized approach to renal biopsy interpretation which was required to compare outcome data across centers and facilitate intervention trials in LN.

The authors highlight the controversy regarding the introduction of a subclassification within diffuse LN (class IV)