

## Annotations

# Orthostatic proteinuria

Is orthostatic proteinuria in children and adolescents a cause for concern? It is well known that the incidence of orthostatic proteinuria greatly exceeds that of chronic renal disease, so a natural conclusion might be that in many cases the condition is harmless. However, this general statement offers little help in dealing with an individual child who has orthostatic proteinuria. Is there enough risk of serious disease to warrant attention? What causes it?

### What is orthostatic proteinuria?

An individual who excretes an abnormally large amount of protein in the urine while in an upright position is said to have orthostatic or postural proteinuria. It is important to stress that protein excretion in recumbency should be within normal limits because a patient with constant proteinuria secondary to known renal disease may further increase an already abnormal protein excretion rate when upright.<sup>1</sup> In an obvious case, these criteria may be satisfied by the simple determination of urinary protein concentration at rest and again after standing, but in many instances a more rigorously controlled test is necessary to avoid misinterpretation. The protein concentration of a random urine specimen is often misleading because no allowance has been made for urinary concentration or dilution; the measurement of actual protein excretion rates in timed recumbent and upright urine collections is therefore preferable. Two provocative measures, exercise and forced lordosis, appear to induce proteinuria more often than mere standing.<sup>2,3</sup> Exercise proteinuria and lordotic proteinuria should probably be distinguished from orthostatic proteinuria as more physiological phenomena, and only slow ambulation should be used in tests for orthostatic proteinuria. Often after standing, proteinuria disappears only gradually in recumbency,<sup>4</sup> and the patient should lie down for at least half an hour before starting to collect urine in the supine position.

Absence of proteinuria in an orthostatic test does not exclude the diagnosis. Fewer than half of all patients with orthostatic proteinuria show a 'fixed and reproducible' pattern—that is, upright posture inducing proteinuria consistently at all times. The remainder will have a 'transient' orthostatic pattern with positive orthostatic tests only occasionally.<sup>5</sup>

No particular degree of proteinuria is characteristic of orthostatic proteinuria in children; upright protein excretion varies from barely above normal to more than 0.5 g per hour.<sup>4</sup> The total 24-hour excretion however, rarely exceeds 1 g.<sup>4</sup>

### How common is it?

No accurate figures on the prevalence of orthostatic proteinuria exist, but only a rough estimate from indirect evidence. The prevalence for all types of proteinuria combined ranges from less than a few per cent in infants to at least ten per cent in adolescents.<sup>4,6-8</sup> As many as half of proteinuric children of school age have either transient or fixed and reproducible orthostatic proteinuria.<sup>9</sup> It is not certain whether orthostatic proteinuria occurs to an appreciable extent in infants and toddlers.

### What causes it?

It is likely that in most cases orthostatic proteinuria is a result of increased glomerular filtration of protein rather than of decreased tubular reabsorption of the filtered protein, because even if tubular reabsorption were stopped completely, it could not by itself account for the degree of proteinuria often present. The earlier notion that an increased glomerular protein filtration was somehow caused by an abnormal renal haemodynamic response to orthostasis is now refuted. Firstly, the measured response, a decrease in renal plasma flow and glomerular filtration rate and an increase in filtration fraction, is in the same direction and of the same magnitude in patients with orthostatic proteinuria as in control subjects.<sup>10</sup> Secondly, young adults with orthostatic proteinuria have been reported to excrete slightly more protein than controls even when lying down, although the rates are within normal limits.<sup>10,11</sup> And finally, the available morphological evidence, although scanty, indicates that subtle anatomical deviations can often be found in the glomeruli of both adults and children who have orthostatic proteinuria.<sup>4,5,12</sup> Thus there is at least a suspicion that mild glomerular injury contributes to orthostatic proteinuria, but it would be an oversimplification to consider that orthostatic proteinuria is an aetiological entity. Rather, as with many other renal

histopathological appearances, such a glomerular abnormality could be caused by any of a number of aetiological agents, the nature of which is currently unknown.

### Prognosis and management

The pathophysiological speculations do not answer the most important question: What is the future of a child who has orthostatic proteinuria? There are no truly long-term, prospective studies that can give a definitive answer. In adults, there is indirect evidence based on retrospective data to suggest that the long-term prognosis is good.<sup>13</sup> Likewise, a continuing prospective study on young men with fixed and reproducible orthostatic proteinuria shows no progression into overt renal disease during a 10-year observation period, but the authors are still cautious about predicting the final outcome.<sup>14</sup> Only short-term studies have been published on children and these indicate a good 1- to 6-year prognosis.<sup>8, 12</sup>

Renal biopsy cannot be conclusive regarding the prognosis. However, if there were clearly an increased risk of developing chronic renal disease, one would expect to be able to diagnose at least a few cases if a large enough number of patients with orthostatic proteinuria were examined. Remarkably, histological reports on children with *isolated* orthostatic proteinuria have failed to find any diagnostic changes, although several biopsies have shown minor alterations.<sup>4, 12</sup> In one such study the 17 children with orthostatic proteinuria who were biopsied had been chosen from 900 proteinuric children because of the degree and persistence of the proteinuria, thus rendering the absence of serious disease statistically convincing.<sup>4</sup>

Although no systematic studies on children with *non-isolated* orthostatic proteinuria have been reported, there are examples of renal biopsy disclosing an underlying disease in children with the combination of orthostatic proteinuria and microscopic haematuria.<sup>15</sup>

From the data one cannot be certain that there is absolutely no increase in chronic renal disease in patients with orthostatic proteinuria, yet it is clear that the vast number of children with this condition cannot be extensively investigated. The alternative is to look for other signs of kidney disease using simple, non-invasive methods—such as physical examination, urine analysis, and serum creatinine determination. In most, no other abnormality will be found, and the orthostatic proteinuria can be called isolated. Fortunately, the risk of present or future renal disease in such children seems slight; further investigation would not give any additional information, and to keep a child under close long-

term observation would create a chance for misinterpretation on the part of the family, leading to unnecessary anxiety, and possibly restrictions on the child over the years of follow-up. I believe that the family would be better served by being assured of a good prognosis, and at the same time, keeping the diagnosis of orthostatic proteinuria in the child's records as a reminder should any additional sign be manifest in the future.

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