# Henoch-Schönlein purpura in children

## Use of corticosteroids for prevention and treatment of renal disease

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### Abstract

**Question** A few patients have previously presented to my clinic with palpable purpura, joint inflammation, and severe abdominal pain characteristic of Henoch-Schönlein purpura (HSP). Considering that renal injury is the primary long-term complication of HSP, are corticosteroids effective in preventing or treating renal disease in children with HSP?

**Answer** Henoch-Schönlein purpura is self-limiting in 94% of children, but permanent renal injury is reported in one-fifth of children with nephritic or nephrotic features. Corticosteroids have been considered as candidates for preventing and treating renal involvement in HSP. There is a moderate level of evidence to suggest corticosteroids are not effective in preventing renal involvement in HSP. However, based on low-level evidence and similarities with primary immunoglobulin A nephropathy, experts recommend corticosteroids in treating renal involvement in HSP to prevent long-term kidney injury. Dose and duration of therapy should be carefully considered in consultation with a pediatric nephrologist.


# Le purpura Henoch-Schönlein chez l'enfant

## Recours aux corticostéroïdes pour prévenir et traiter les néphropathies


### Résumé

**Question** Quelques patients se sont présentés antérieurement à ma clinique souffrant de purpura palpable, d'inflammations articulaires et de sévères douleurs abdominales qui sont caractéristiques du purpura Henoch-Schönlein (PHS). Étant donné que les lésions rénales sont la principale complication à long terme du PHS, les corticostéroïdes sont-ils efficaces pour la prévention ou le traitement des néphropathies chez les enfants atteints du PHS?

**Réponse** Le purpura Henoch-Schönlein disparaît de lui-même chez 94 % des enfants, mais des lésions rénales permanentes sont signalées chez un cinquième des enfants ayant des caractéristiques néphrétiques ou néphrotiques. Les corticostéroïdes ont été envisagés comme candidats possibles pour prévenir et traiter les problèmes rénaux liés au PHS. Il existe un degré modéré de données probantes qui laissent entendre que les corticostéroïdes ne sont pas efficaces pour prévenir les affections rénales dues au PHS. Par ailleurs, en se fondant sur des données probantes de faible niveau et sur les ressemblances avec la néphropathie primaire à immunoglobuline A, des experts recommandent les corticostéroïdes pour traiter les problèmes rénaux liés au PHS, dans le but de prévenir des lésions rénales à long terme. Il y a lieu de choisir avec soin les doses et la durée de la thérapie en consultation avec un néphrologue pédiatrique.


Henoch-Schönlein purpura (HSP)—also known as immunoglobulin A (IgA) vasculitis—is the most common systemic vasculitis in children, with a median age of onset of 4 years,[1] a reported incidence of 3 to 27 per 100 000 children per year, and known ethnic variability.[2,3] Henoch-Schönlein purpura is characterized by IgA1-dominant immune deposits in small blood vessels and renal glomeruli,[1,2] and commonly presents with palpable purpura, gastrointestinal pain, joint pain, and glomerulonephritis.[1,4] A study of 417 patients from a single centre in Spain found that skin lesions (56%), nephropathy (24%), gastrointestinal involvement (14%), joint symptoms (9%), and fever (6%) were the most common manifestations at disease onset.[5] Although HSP has been reported to be a self-limiting condition in 94% of children,[6] permanent kidney injury—including hypertension, proteinuria, or decreased kidney function—is reported in 20% of children with nephritic or nephrotic features.[7,8] In a prospective study of 223 children younger than 16 years of age with HSP, nephritis occurred on average 14 days after HSP diagnosis, and within 1 month of diagnosis in 87% of cases.[9] Overall, nephritis occurs in 20% to 50% of children with HSP.[10] Several risk factors of HSP nephritis have been identified in 1 meta-analysis of 13 studies and 2398 children (**Table 1**).[11] Despite its high prevalence, there is currently no consensus regarding the prevention or treatment of nephritis in children with HSP.[2] Corticosteroids have been proposed owing to their anti-inflammatory and immunosuppressive properties.[2,12]

**Table 1. Factors associated with high risk of nephritis in children**

| RISK FACTOR | ODDS RATIO (95% CI) |
|---|---|
| Older age | 0.90 (0.61 to 1.19) |
| Older than 10 y | 3.13 (1.39 to 7.07) |
| Male sex | 1.36 (1.07 to 1.74) |
| Abdominal pain | 1.94 (1.24 to 3.04) |
| Gastrointestinal bleeding | 1.86 (1.30 to 2.65) |
| Severe bowel angina | 3.38 (1.17 to 9.80) |
| Persistent purpura | 4.02 (1.22 to 13.25) |
| Relapse | 4.70 (2.42 to 9.14) |
| White blood cell count > $15 \times 10^9$/L | 2.42 (1.39 to 4.22) |
| Platelet count > $500 \times 10^9$/L | 2.98 (1.22 to 7.25) |

Data from Chan et al.[11]

## Corticosteroids for prevention

As inhibitors of proinflammatory cytokines,[13] corticosteroids have been used to treat short-term and prevent long-term kidney injury in many forms of glomerulonephritis, including systemic lupus erythematosus, antineutrophil cytoplasmic antibody vasculitis, and primary IgA nephropathy; similarly, corticosteroids have been proposed as candidates for preventing nephritis in HSP.[12-14] In a prospective assessment of 168 children with new-onset HSP and no evidence of kidney injury at enrolment, 1 mg/kg per day of oral prednisone for 2 weeks in the steroid group resulted in no cases of nephropathy after 2 to 6 weeks, compared to 10 cases of nephropathy in the control group (12%); the same trend existed for renal involvement after 2 to 6 years (0% and 2.3% for the steroid group and the control group, respectively).[12] However, a retrospective study of 69 children 1 to 15 years of age seen between 1979 and 1991,[10] a randomized controlled trial (RCT) in 40 children 2 to 15 years of age seen between 1996 and 2000,[15] and an RCT in 352 children younger than 18 years of age seen between 2001 and 2005[16] found that administration of oral prednisone at presentation was not associated with lower risk of nephritis 3 weeks after initial normal urinalysis,[10] decreased kidney injury 1 year after the initial visit,[15] and decreased proteinuria 1 year after disease onset,[16] respectively.

In a Cochrane review of 5 studies in 856 children with HSP, including 3 of the aforementioned studies,[12,15,16] no significant difference in the risk of persistent kidney injury was found at 1, 3, 6, and 12 months after treatment in children given prednisone prophylactically for 14 to 28 days, compared to children given placebo or supportive treatment.[4] This suggests lack of support for the preventive use of oral corticosteroids in HSP.

## Corticosteroids for treatment

A prospective study of 171 children younger than 16 years of age with newly diagnosed HSP who presented to 14 hospitals in Finland reported that although administering 1 mg/kg per day of prednisone for 2 weeks, with weaning over the subsequent 2 weeks, did not prevent renal symptoms, it was effective in treating them.[17] In 71 children who presented with kidney involvement (urine protein level >200 mg/L, urine albumin level >30 mg/L, or urine erythrocyte level >5/vision field) or who developed it during the 1-month treatment period, 61% of those treated with prednisone recovered compared to only 34% of those given placebo ($P$=.024).[17] Prednisone appeared to be most effective in treating renal disease in children older than 6 years of age who had or developed renal symptoms during the first month after their HSP diagnosis (63% in remission in the prednisone group compared to 15% in the placebo group; $P$=.001).[17]

Based on similarities between HSP nephritis and IgA nephropathy,[18] and in the absence of robust data for treatment of HSP nephritis, the KDIGO (Kidney Disease: Improving Global Outcomes) Glomerulonephritis Work Group guidelines recommended that HSP nephritis be treated similarly to IgA nephropathy.[14,19] As angiotensin-converting enzyme inhibitors (ACEIs) were beneficial in reducing proteinuria and maintaining glomerular filtration rate among 66 IgA nephropathy patients aged 9 to 35 years,[20] the guidelines suggested that ACEIs or angiotensin receptor blockers be prescribed when the proteinuria level is between 0.5 and 1 g/day from a 24-hour urine collection.[14] In cases with proteinuria levels above this range, a glomerular filtration rate greater than 50 mL/min/1.73 $m^2$, and an unsuccessful trial of ACEIs or angiotensin receptor blockers,[14] the guidelines suggest prescribing a 6-month course of corticosteroids based on 2 studies of children with HSP nephritis and 2 RCTs of adults with IgA nephropathy.[17,19,21,22] For crescentic HSP with nephrotic syndrome or deteriorating kidney function, the guidelines recommended the same treatment be offered as for crescentic IgA nephropathy and antineutrophil cytoplasmic antibody vasculitis: steroids and cyclophosphamide.[14] Overall, owing to the lack of high-quality evidence regarding HSP nephritis, these recommendations remain controversial.[23]

Finally, based on the opinions of 16 experts in pediatric rheumatology, pediatric systemic vasculitis, and pediatric nephrology across Europe, the recent SHARE (Single Hub and Access Point for Paediatric Rheumatology in Europe) initiative recommends corticosteroids be used for treatment of HSP nephritis in children, regardless of severity, as shown in **Table 2**.[2] In the absence of reliable data regarding mild and moderate HSP nephritis treatments, these experts rely on studies of severe HSP nephritis in both adults[24] and children[19,25] to recommend 1 to 2 mg/kg per day of oral prednisolone or prednisone depending on the severity of nephritis, and 10 to 30 mg/kg (for a maximum of 1 g per day for 3 consecutive days) of pulsed intravenous methylprednisolone as an option for moderate and severe nephritis. For severe

**Table 2. Classification of HSP nephritis severity based on expert opinion from the SHARE initiative**

| SEVERITY | DEFINITION |
|---|---|
| Mild nephritis | GFR > 80 mL/min/1.73 m$^2$ and early morning UP:UC ratio of < 250 mg/mmol |
| Moderate nephritis | < 50% crescents on renal biopsy findings and GFR of < 80 mL/min/1.73 m$^2$ or early morning UP:UC ratio of > 250 mg/mmol for at least 4 wk |
| Severe nephritis | > 50% crescents on renal biopsy findings and GFR of < 80 mL/min/1.73 m$^2$ or early morning UP:UC ratio of > 250 mg/mmol for at least 4 wk |

GFR—glomerular filtration rate, HSP—Henoch-Schönlein purpura, SHARE—Single Hub and Access Point for Paediatric Rheumatology in Europe, UC—urine creatinine, UP—urine protein.
Data from Ozen et al.[2]

nephritis, the authors drew on experiences with similar forms of systemic vasculitis[26] to recommend intravenous cyclophosphamide in combination with high-dose steroid therapy to induce remission, followed by azathioprine or mycophenolate mofetil in combination with low-dose steroid therapy as maintenance treatment.[2] Dose and duration of therapy should be carefully considered in consultation with a pediatric nephrologist.[2]

## Conclusion

Routine use of corticosteroids for prevention of renal involvement in children with new-onset HSP is not universally recommended. Based on low-level evidence and accepted treatments for IgA nephropathy, experts suggest prescribing corticosteroids for treating renal involvement in HSP. Dose and duration of therapy should be determined by consulting with a pediatric nephrologist.

**Competing interests**
None declared

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