# Guidelines for the Management of Henoch Schönlein Purpura (HSP)

Children's Kidney Centre

University Hospital of Wales

Cardiff CF14 4XW

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Version 1, S. Hegde/Jan 2011

# Guidelines for the Management of Henoch Schönlein Purpura (HSP)

Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis of childhood. Approximately 75% of HSP cases occur in children aged 2-11 years (50% < 5yrs).

Renal involvement occurs in 20 -100% of children with HSP with a wide spectrum of manifestations ranging from microscopic haematuria and mild proteinuria to nephritic/nephrotic syndrome or even rapidly progressive crescentic glomerulonephritis and renal failure.

IgA plays a critical role in the immunopathogenesis of HSP, as evidenced by increased serum IgA concentrations, IgA-containing circulating immune complexes, and IgA deposition in vessel walls and renal mesangium. IgA nephropathy has developed in patients with a history of HSP. HSP and IgA nephropathy have occurred in the same families.

**A. Clinical features:** HSP affects multiple systems… (Table 1)

| Skin | Gut (50-70%) | Renal (20 -100%) | Joints (50 -80%) | Other |
|---|---|---|---|---|
| Purpuric rash<br>Urticarial rash<br>Subcutaneous oedema | Abdominal pain<br>Nausea & vomiting<br>Intestinal bleed<br>Intussusceptions<br>Pancreatitis | Haematuria (micro/gross)<br>Proteinuria<br>Hypertension<br>Renal failure | Arthralgia /arthritis<br>Periarticular oedema (ankles/knees) | Headache/fits<br>Cerebral bleed<br>Orchitis<br>Testicular torsion<br>Pulmonary bleed |

## B. Diagnosis:

Diagnosis is mainly clinical. The following criteria can be used

Table 2. Diagnostic criteria for Henoch–Scho¨nlein purpura

| Palpable purpura (mandatory) in the presence of at least one of the following four features: |
|---|
| 1. Diffuse abdominal pain<br>2. Arthritis (acute) or arthralgia<br>3. Renal involvement (any haematuria and/or proteinuria)<br>4. Any biopsy showing predominant IgA deposition |

**Differential diagnosis:** Rule out any other cause of a non-blanching rash, meningococcal sepsis, SLE, Wegeners, microscopic polyarteritis, polyarteritis nodosa and acute haemorrhagic oedema of infancy.

## C. Investigations:

**ALL** patients need- Clinical assessment, weight, blood pressure measurement and urine dipstick.

**Selected** patients (needing admission, unwell, uncertain diagnosis) –To assess extent of organ involvement and exclude other causes (Table 3).

Table 3

| Blood | Urine | Other |
|---|---|---|
| FBC, Clotting, U&E, LFT, bone profile, auto antibodies, C3, C4, ANA, dsDNA, ANCA, immunoglobulins.<br>**Unwell child**- Blood cultures, swabs, urine for microscopy and culture, Viral serology & throat swabs and ? CXR.<br>**Nephritic child**- ASOT and antiDNAse B titres | Protein: creatinine ratio (EMU sample) if proteinuric on dipstick | Renal/Abdominal US where indicated |

EMU= Early morning urine

## D. Admission:

Admit if the patient is unwell, has significant of joint pain, severe abdominal pain, G I haemorrhage, neurological symptoms, hypertension, evidence of acute glomerulonephritis, nephrotic syndrome or abnormal renal function.

## E. Clinical course:

HSP is usually self-limiting (most remit within 6 weeks) with mortality <1%. A proportion of children (up to 25-40%) may relapse. Significant morbidity is associated with disease of the gastrointestinal (GI) tract in the short term and nephritis in the long term.

## F. Management

No specific therapy. Outlines of management for involvement of different systems (Table 4)-

Table 4

| Joint symptoms | GI tract | Testes /CNS |
|---|---|---|
| Treat with paracetamol. Avoid NSAIDS if at risk of dehydration, any renal impairment, or hypertensive | Simple analgesia.<br>**Severe symptoms**- Early steroids Rx might prevent GI bleed/intussusception (prednisolone 1mg/kg daily, max 50 mg for 2 weeks & wean it over 2 weeks).<br>**Protein-losing enteropathy/severe GI bleed**- Consider methylprednisolone IV 10 mg/kg for 3 days followed by prednisolone as above.<br>**Intussusceptions** –contrast enema /surgery | Consider (for severe cases) prednisolone for 2 weeks (1 mg/kg/day, max 50 mg) & then wean it over 2 weeks.<br>Pulmonary bleed - consider steroids. |

### Renal Involvement:

Renal involvement may precede skin manifestations (1-4% of patients) but is usually evident during the acute phase of the disease (within the first 4 weeks of illness in 80% patients and within 3 months in 97–100% of cases, but rarely can present as late as a year). In most cases, the severity of nephritis is not related to the extent of other HSP manifestations but often correlates with findings on biopsy ( % age of glomeruli with crescents may be the most important prognostic indicator).

Long-term renal impairment has been reported in up to 19.5% of those with a history of nephritic or nephrotic syndrome. HSP nephritis (HSPN) accounted for up to 15% of children with end-stage renal failure according to previous reports but recent data put it at 1.8–3%.

1. **Renal outcome related to clinical presentation**:

1. Microscopic haematuria only
2. Proteinuria (without nephrotic syndrome) + mico/macroscopic haematuria
3. Acute nephritis (haematuria + ↑BP + ↑creatinine)
4. Nephrotic syndrome
5. Mixed nephritic/nephrotic syndrome

Poorer outcome ↓

**2. Monitoring for renal involvement-** See flow chart

**3. Referral to paediatric nephrologist-** See flow chart

**4. Early referral** to Paediatric Nephrologist is indicated for children with –

Table 5

| Children with HSP needing early referral to paediatric nephrology | |
|---|---|
| Acute glomerulonephritis | Persistent (>2+ on dipstick) or increasing proteinuria |
| Nephrotic syndrome | Macroscopic haematuria lasting >5days/ >1 episode |
| Persistent hypertension | Impaired renal function |

The aim is for early detection of those with severe renal involvement, for treatment with immunosuppression, prior to the development of renal scarring.

**5. Renal Biopsy-**

Consider renal biopsy if the child has –

1. Nephrotic syndrome
2. Nephrotic range proteinuria (early morning urinary protein: creatinine ratio >250 mg/mmol for >4- 6 weeks)
3. Acute nephritic syndrome
4. Acute renal failure (pre-renal cause excluded)
5. Early morning urinary protein: creatinine ratio >100 mg/mmol for >10-12 weeks

Although severe changes on early biopsy may lead to institution of successful treatment, a biopsy that is too early may be falsely reassuring and re-biopsy should be considered if the clinical condition does not improve. The ISKDC histological grading system has been widely used to classify the severity of biopsy findings in HSPN (Table 6). The renal lesion of HSPN is indistinguishable from that of IgA nephropathy.

**Table 6. ISKDC classification of kidney biopsies in Henoch-Schönlein purpura**

| ISKDC grade | Pathoanatomical findings |
|---|---|
| I | Minimal alterations |
| II | Mesangial proliferation |
| III A | Focal proliferation or sclerosis with < 50% crescents |
| III B | Diffuse proliferation or sclerosis with < 50% crescents |
| IV A | Focal proliferation or sclerosis with 50 – 75% crescents |
| IV B | Diffuse proliferation or sclerosis with 50 – 75% crescents |
| V A | Focal proliferation or sclerosis with > 75% crescents |
| V B | Diffuse proliferation or sclerosis with > 75% crescents |
| VI | Membranoproliferative glomerulonephritis |

ISKDC=International Study of Kidney Diseases in Children

## 6. Treatment of HSP nephritis

There is no specific therapy but there is a risk of long-term consequences for those with untreated significant renal disease. Treatment of HSPN remains controversial, due to lack of clear evidence of the benefits of treatment. Therapy is often based on data from number of uncontrolled case series showing some benefit of immunosuppressive therapy. The various therapeutic options (see below) can be used alone or in combination at the discretion of the on call consultant nephrologist (usually based on biopsy findings).

**A. Prevention of HSP nephritis**:

At the current time insufficient data are available to support early prednisone therapy to **prevent renal involvement** and hence not recommended**.**

### B. Treatment of established nephritis (following renal biopsy)**:**

a) **Treatment of non-crescentic HSP nephritis:**

Possible treatment options, based on anecdotal reports, include:

1. Prednisolone 2mg/kg for 4 weeks with or without initial Methylprednisolone pulses. At 4-week assessment, if there is no improvement, prednisolone may be rapidly weaned and stopped. If there is improvement, oral prednisolone can be continued at the discretion of the consultant.

2. Fish-oil (Omacor) ?

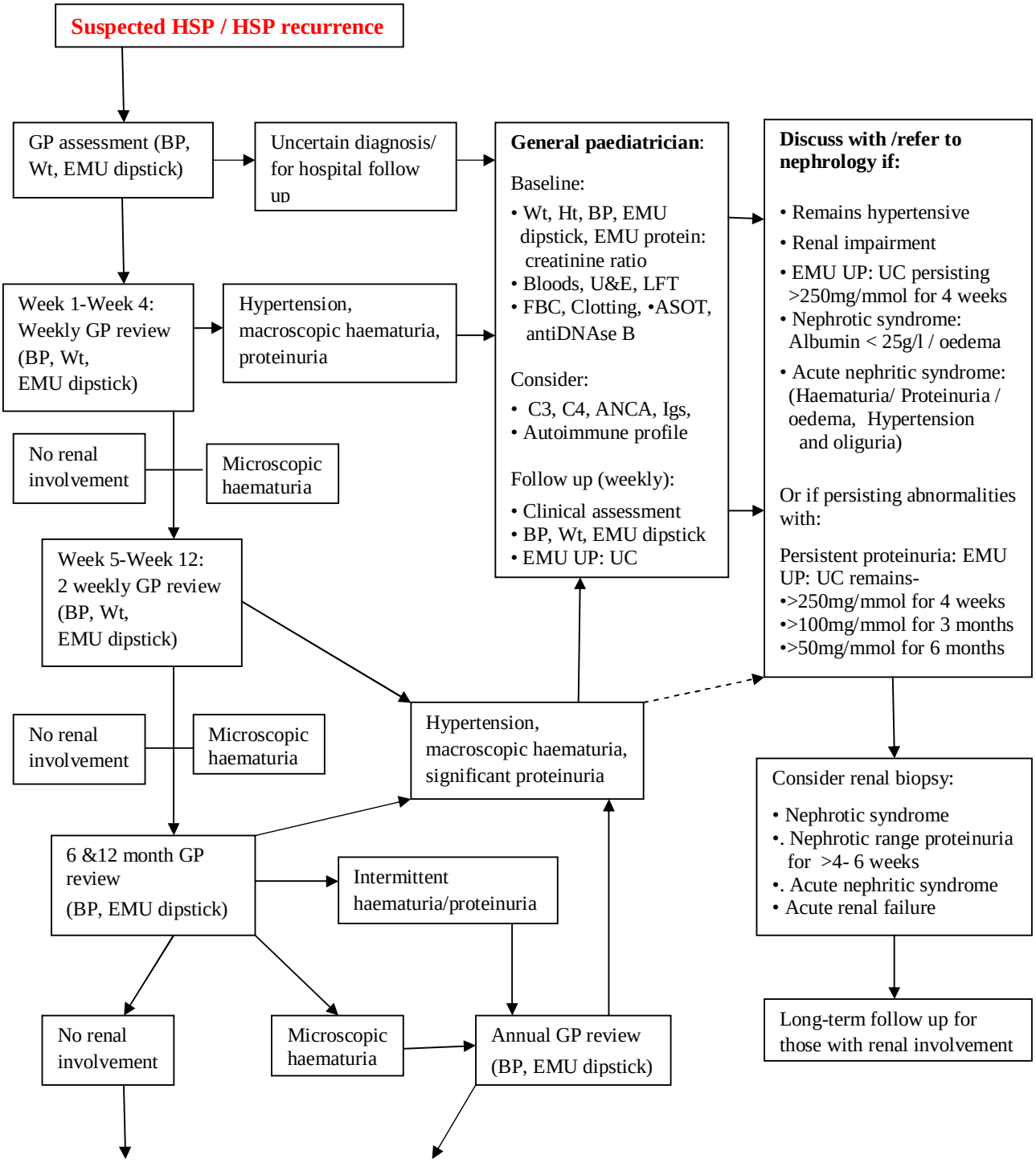
b) **Treatment of crescentic HSP nephritis:**

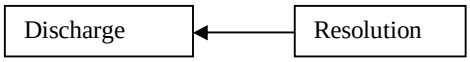
There are uncontrolled data supporting the use of the following options:

| **Biopsy/clinical status** | **Therapy** |
|---|---|
| **< 25 % crescents** | If EMU UP: UC >200 mg/mmol for >4 weeks, **Prednisolone** 60 mg/m²/day for 4 weeks, then 40 mg/m² on alternate days for 4 weeks then taper over 2-3 months |
| **25-50 % crescents** | **Methylprednisolone** 10mg/kg/day IV for 3 days then, **Prednisolone** 60 mg/m²/day for 4 weeks, then 40 mg/m² on alternate days for 4 weeks then taper over 2-3 months |
| **>50 % crescents** | **Methylprednisolone** 10mg/kg/day IV for 3 days then, **Prednisolone** 60 mg/m²/day for 4 weeks, then 40 mg/m² on alternate days for 12 weeks then taper over 2-3 months. PLUS…<br>**Cyclophosphamide** 2-3 mg/kg/day for 8 weeks AND…<br>Consider **plasma exchange** in severe cases |
| **Dialysis dependant** | Consider **plasma exchange** PLUS...<br>**Methylprednisolone** 10mg/kg/day IV for 3 days then, **Prednisolone** 60 mg/m²/day for 4 weeks, then 40 mg/m² on alternate days for 12-16 weeks then, taper over 2-3 months. PLUS…<br>**Cyclophosphamide** 2-3 mg/kg/day for 8 weeks (following plasma exchange) |

| | |
|---|---|
| | |

## Detection and Monitoring of patients with HSP /HSP nephritis






EMU= Early morning urine  UP= urinary protein  UC= urinary creatinine  Igs-Immunoglobulins

**Use of renin-angiotensin-system (RAS) blockade in HSP nephritis**.

There is accumulating evidence supporting the beneficial effect of RAS blockade in proteinuric states in general. Thus, patients with HSP nephritis and significant proteinuria (abnormal urine albumin/creatinine ratio and/or proteinuria >4 mg/$m^2$/h) should be given an ACE inhibitor and/or ARB.

## 7. Outcome /follow up:

In patients, who present with a nephritic, nephrotic, or nephritic/nephrotic syndrome, 19.5- 44% have hypertension or impaired renal function on long-term follow-up, whereas 82% who present with hematuria (with or without mild proteinuria) are normal. Children with renal manifestations in the acute phase require prolonged follow-up. Overall 1 - 5% of children with HSP progress to end-stage renal failure.

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