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SPECIALISTS' CORNER

When Not to Worry about Henoch-Schoenlein Purpura

J. Patrick Whelan, MD, PhD
Pediatric Rheumatologist

"From its origin, the exanthem spreads over the whole body with the exception of the palms and soles of the feet. Clearly wrong is the notion that only the covered and thus exposed to heat parts of the breast are effected by bumps, since also it appears as frequently on the neck and in the face. By the way, the development of the exanthem never happens all at once, but always in bouts (immer stossweise.) And that's characteristic of the bumps, because other exanthems don't do that."

-- Dr. Johann Schonlein, in 1834 lecture notes about "purpura rubra," Pathologie und Therapie (vol 2, p320.)

When parents bring children with Henoch-Schoenlein purpura (HSP) to the emergency room, they can generally be reassured that their child will recover completely more than 90% of the time, despite the dramatic presentation with a mixture of spotty rash, abdominal pain, joint symptoms, and fever. As the most common form of systemic vasculitis in childhood, and one of the more common childhood causes of renal failure, there are plenty of horror stories that feature prominently when a parent searches for "HSP" online.

The Schoenlein in HSP was one of the fathers of both microbiology and mycology. Johann Schoenlein was the first person to associate a particular infection with a known disease, having recognized the presence of mycelial threads in scrapings from crusted Tinea capitus (ringworm) lesions. He proposed that a fungus was the cause of this common scalp lesion, 40 years before Koch and Pasteur embarked on their rivalry.

Schoenlein was considered one of the great clinicians of his day, until he fled to Switzerland in the 1830s because of a crackdown on liberals of his ilk. He was later recruited to a professorship in Berlin, and became the personal physician to the kaiser. He was not the first to recognize HSP, but he became linked to the disease because some of his students decided to publish for profit his popular lecture notes dealing with the subject.

Most HSP cases (probably 90%) occur before age 10, with the majority between 3 and 7 years of age. But reading this literature can be misleading, because the adult disease is so different from the pediatric presentation and tends to have a worse prognosis. Most significantly, the risk of chronic renal disease is dramatically lower in children. Chronic kidney disease (stage 3 or worse) is seen in 10-20% of adults, but only about 2% of children under 10, with teens falling in between. A retrospective study published earlier this year involving 128 children in Indonesia found kids 11-15 years old were more than 3-times as likely to developed significant renal disease compared with those who were younger.

Significantly, the largest metanalysis of pediatric studies (Narchi H. *Arch Dis Child*. 2005;90:916-920) found that no children with normal urine analysis at presentation went on to develop chronic kidney disease later, compared to 20% of those with nephritic or nephrotic syndrome at onset.

There are other differences between children and adults with HSP. Significant pulmonary involvement (alveolar hemorrhage) occurs almost exclusively in older adolescents and adults. A retrospective study published earlier this year (Yang K *et al.,* J Korean Med Sci 2014;29:198-203) found that purpura in adults is more likely to occur in the upper extremities, whereas the legs and buttocks are the norm in children. Adults are half as likely as children to have arthritis/arthralgia. Although abdominal pain is a frequent presenting symptom, particularly under age 5, diarrhea is very uncommon in children (but occurs in lots of adults). Perhaps because renal disease is so much more common in adults (about 2-1/2 times), anemia is much more commonly a feature of the adult disease.

The pathogenesis of HSP remains something of a mystery, despite considerable study over the years. The disease is very similar to IgA nephropathy, a common cause of chronic kidney disease that occurs almost exclusively after age 10 and before age 40, and is not associated with purpura/petechia. Both HSP and IgAN involve the deposition of IgA1 in the mesangium of the kidney. At one time serum IgA levels were proposed as a screening test. But elevated IgA occurs 7 times more often in adults with HSP, and is rarely seen in children. Genetic factors like mutations in MEFV, the Familial Mediterranean Fever gene, play a role (about 1 in 15 FMF patients develop HSP at some point). Respiratory infections, like Group A strep, also likely play some part as triggering factors.

The decision tree in evaluating a sick child with purpura or petechiae begins with determining whether they are thrombocytopenic (eg. leukemia or idiopathic thrombocytopenic purpura) or have a coagulopathy that could signify something like hemolytic uremic syndrome or possibly sepsis. When purpura is palpable, it signifies that an inflammatory process has targeted the post-capillary venules in the skin. An influx of activated macrophages then lay down a fibrin fire-wall—creating the characteristic punctate induration consistent with vasculitis, and not observed in non-palpable purpura.

The differential diagnosis at that point is the spectrum of systemic vasculitis, either primary (such as HSP) or secondary (in children with an established diagnosis of juvenile lupus or juvenile idiopathic arthritis). Kids in the same age group frequently experience hypersensitivity vasculitis in response to medications or acute infection, manifest by palpable purpura, joint pain and constitutional symptoms (but without evidence of IgA deposition on biopsy). Mixed cryoglobulinemia can look similar in adults. Rare cases of acute hemorrhagic edema, with finger swelling and purpura but no visceral involvment, occur before 18 months of age.

The decision to treat children with HSP most often involves the 50% who have abdominal symptoms during the first week of the illness, across a spectrum from mild nausea to emesis, ileus, intussception (in about 1%) and even ischemia, necrosis and bowel perforation in rare cases. Although occult blood is common, major bleeding events are rare. Several studies have shown a benefit for use of glucocorticoids to abbreviate the suffering of kids with the more severe manifestations of GI involvement.

Schoenlein himself didn't recognize the GI element in this condition. But his student Eduard Henoch, a pediatrician, subsequently published a description of abdominal pain and bleeding in this condition. Around the time of Schoenlein's death, Henoch's name became attached to the established term of "Schoenlein's purpura."

Schoenlein wrestled with the question of whether HSP was an infection, or possibly even a result of exposure to airborne byproducts of local Bavarian beer brewing. He recognized the presence of renal disease in some patients, and speculated that "*since the skin is only a limited surface, only a certain amount of rash can occur. But as the amount of the surface area of the skin is exhausted, the internal organs then become affected."*

Sir William Osler was the first to propose an "allergic" mechanism of the pathogenesis for HSP. But the search continues for an underlying cause of one of the scariest reasons that young parents find their way for the first time to a rheumatologist.

Dr. Patrick Whelan completed a PhD in microbiology and immunology at Texas Children's Hospital in Houston, trained in internal medicine at Scripps in La Jolla and rheumatology at Harvard, and spent 15 years in pediatric rheumatology practice at Massachusetts General Hospital in Boston. He is originally from Los Angeles and practices now in Burbank with Lakeside Community Healthcare. *Thanks to Lorraine Smith for research assistance with this article, and to Daniel Brown MD PhD for his helpful critique.*
