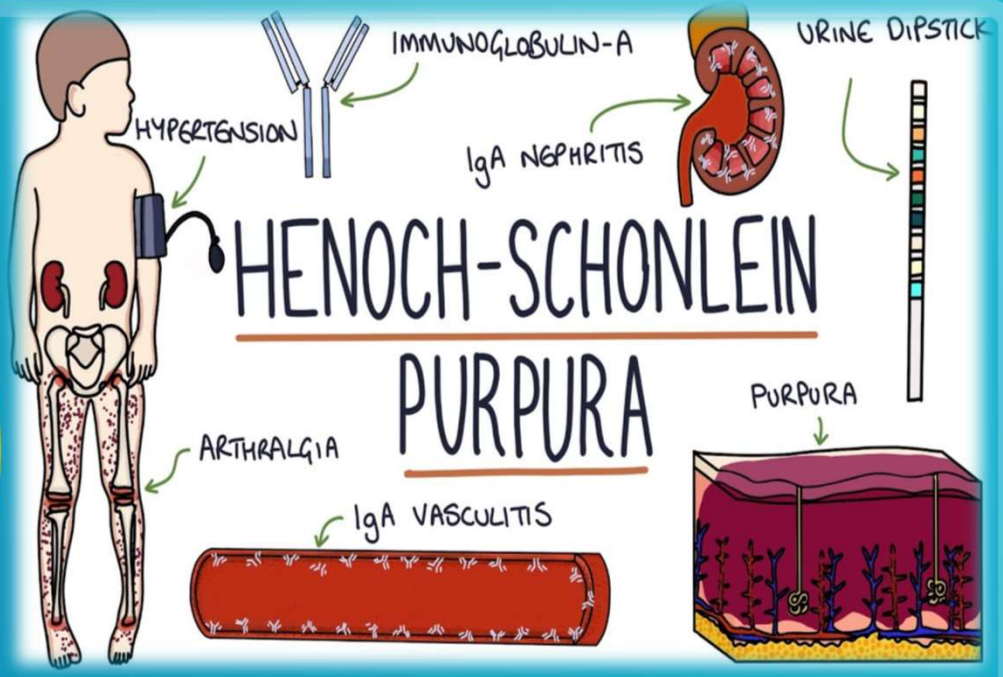
One type of Immune Complex Small-Vessel Vasculitis

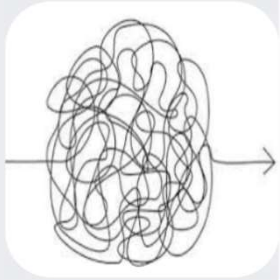


Dr.shabnam Hajiani,M.D
Assistant professor of pediatric Rheumatology diseases of sums

Definition

- ***Necrotizing vasculitis*** that affects small blood vessels (esp postcapillary venules, capillaries, arterioles) is often caused by immune complex deposition and may show ***leukocytoclastic vasculitis*** on histology.

- The term *leukocytoclasis* refers to the infiltration of PMNs into vessel walls, resulting in necrosis with scattered nuclear debris



- This is the redominant inflammatory reaction in **IgAV**, **hypersensitivity vasculitis**, **mixed cryoglobulinemia**.

- It is also observed in the **ANCA-associated** vasculitides and the vasculitis of other **CTDs, such as SLE**.

- It is sometimes observed in **drug hypersensitivity**, **infectious endocarditis**, **or hematological malignancies.**

BOX 33.1 Conditions Associated with Leukocytoclastic Vasculitis

- Immunoglobulin (Ig)A vasculitis (Henoch–Schönlein)
- Hypersensitivity vasculitis
- Hypocomplementemic urticarial vasculitis
- Mixed cryoglobulinemia
- Cutaneous polyarteritis
- Antineutrophil cytoplasmic antibody (ANCA)-associated small-vessel vasculitis*
- Goodpasture syndrome
- Rheumatic disorders
  - Systemic lupus erythematosus (SLE), juvenile dermatomyositis, mixed connective tissue disease (MCTD), scleroderma, juvenile idiopathic arthritis (JIA)
- Mucha–Habermann disease
- Relapsing polychondritis
- Köhlmeier–Degos syndrome
- Antiphospholipid antibody syndrome
- Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome
- Malignancy-associated disease
- Sweet syndrome
- Cronkhite–Canada syndrome
- Stevens–Johnson syndrome
- Erythema elevatum diutinum

*Leukocytoclastic vasculitis may occur in cutaneous lesions in some patients with ANCA-associated vasculitis and collagen vascular diseases.

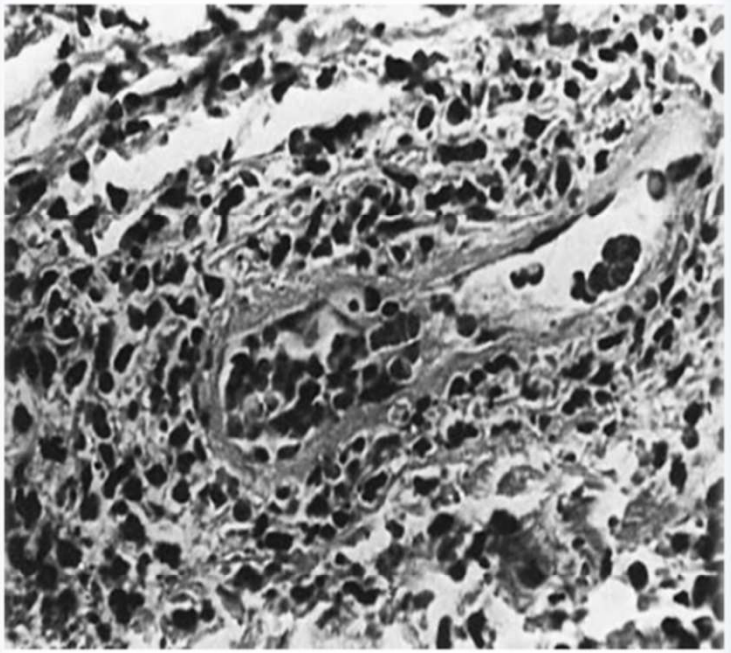


Fig. 33.1 Histopathological demonstration of leukocytoclastic vasculitis. The characteristic "nuclear dust" is seen as granular, dark-stained material in the vessel wall. Hematoxylin-eosin stain.

Definition and Classification

- IgAV is **the most common systemic vasculitis of childhood**.
- It is characterized by **non thrombocytopenic purpura**, **arthritis**, **arthralgia**, **abdo.pain**, **GI hemorrhage**, **GN**.
- The ACR criteria for the classification of HSP in 1990 were based on adult data and have been superseded by new criteria for pediatric vasculitides in 2010.
- These criteria(**The PReS/ EULAR criteria**) require **palpable purpura** with **lower limb predominance** plus at least **one** among the following four features:
  - (1) diffuse abdominal pain,
  - (2) biopsy showing typical leukocytoclastic vasculitis or proliferative GN with predominant IgA deposition,
  - (3) arthritis or arthralgia,
  - (4) renal involvement (any hematuria and/or proteinuria).

ACR criteria

- In 1990, a committee of the American College of Rheumatology (ACR) established criteria to classify seven types of vasculitides including IgAV. The ACR criteria for the diagnosis of IgAV are as follows:

✓ **• Palpable purpura**

✓ **• Age at onset ≤20 years**

✓ **• Acute abdominal pain**

✓ **• Biopsy showing granulocytes in the walls of small arterioles and/or venules**

- In 2005, pediatric consensus criteria were developed by the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PRES) and were subsequently validated in conjunction with the Pediatric Rheumatology International Trials Organization (PRINTO) .

EULAR/ PRINTO/ PRES criteria

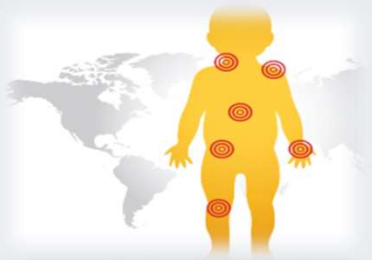
TABLE 33.1 **2010 Classification Criteria for IgA Vasculitis (Henoch–Schönlein)**

Criterion	Definition	Sensitivity	Specificity
Purpura (mandatory)	Purpura (palpable, in crops) or petechiae, with lower limb predominance,* not related to thrombocytopenia	89%	86%
And at Least 1 out of 4 of the Following:			
Abdominal pain	Diffuse, acute, colicky pain; may include intussusception and gastrointestinal bleeding	61%	64%
Histopathology	Leukocytoclastic vasculitis with predominant IgA deposits; or proliferative glomerulonephritis with predominant IgA deposits	93%	89%
Arthritis, arthralgias	Arthritis: acute joint swelling or pain with limitation of motion Arthralgia: acute joint pain without joint swelling or limitation of motion	78%	42%
Renal involvement	Proteinuria: >0.3 g/24 hr; spot urine albumin to creatinine ratio >30 mmol/mg; or ≥2+ on dipstick Hematuria: red cell casts; urine sediment showing >5 red cells per high-power field or red cell casts	33%	70%

he overall sensitivity and specificity of the classification for IgAV is 100% and 87%, respectively.
f purpura presents with atypical distribution, demonstration of IgA deposit on biopsy is required

1 EPIDEMIOLOGY

- A disease of childhood .A similar syndrome reported in adults, but more severe
- with an incidence of 3 to 26.7 cases per 100,000 children
- most frequently between the ages of 3 and 12 yrs
- rare in children younger than 2 y/o
- more common in boys than girls, M/F :0.9 to 1.8
- Mean age at onset observed ranges from 6.1 to 6.5 years at Dx.

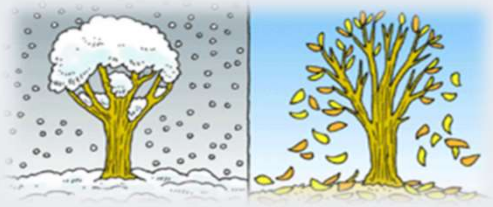


- A ubiquitous disease ,no clear geographical, racial, or ethnic variations in risk.
- Striking seasonal variations, most in winter, often (30% to 50%) preceded by an URI

2 ETIOLOGY AND PATHOGENESIS

- Although a variety of infectious and chemical triggers
- underlying cause of IgAV is unknown

- striking autumn-winter incidence peak suggest a climate-related environmental trigger, esp for infection



- It is linked to a wide array of pathogens including:
  - 1-bacteria (β-hemolytic *streptococcus, Mycoplasma pneumonia, Bartonella henselae,* and *H.pylori*)
  - 2-viral infections (VZV, HBV, HAV)
  - 3-protozoa

- but no consistent causative agent has been identified

new

- Studies in China :very high rates of ***H. pylori*** infection in children with IgAV, esp those with **GI symptom.**

- also, → ***eradication*** therapy was associated with
  - ameliorated ***clinical manifestations***
  - decrease of IgAV***recurrence***

- IgAV may develop after exposure to pharmaceutical agents,
- (antibiotics or antirheumatic therapy: MTX & TNF agents)

- All cases showed fullresolution of disease after discontinuing the medication
- several cases restarting the same anti-TNF agent led to a recurrence of IgAV.

- possible link of IgAV with vaccinations

- A possible pathogenic role of IgE in IgAV suggested for some of IgAV nephritis.

- In adults, IgAV is linked to an increased incidence of concurrent or preceding solid cancers, esp in renal disease.

- IgAV is a predominantly IgA-mediated dysregulated immune response to antigen and may operate through the alternative complement pathway

- Although the pathogenic mechanisms of nephritis are still not delineated, studies suggest high levels of Gd-IgA1 which is recognized by antiglycan IgG or IgA antibodies (perhaps triggered by infection) as a "second hit" , leading to the formation of large circulating immune complexes and their mesangial deposition, results in renal injury in IgAV

- the genes controlling IgA1 glycosylation are unknown, but it is likely that

genetic predisposition,
mucosal infection,
concomitant IL-6 production.
…..all play a role

3 Genetic Background

- **No mutations have been shown to directly cause IgAV.**
- **The disease almost always occurs sporadically.**
- **genetic predisposition, likely plays a minor role.**

❖ comparing genetic variants between healthy and IgAV :

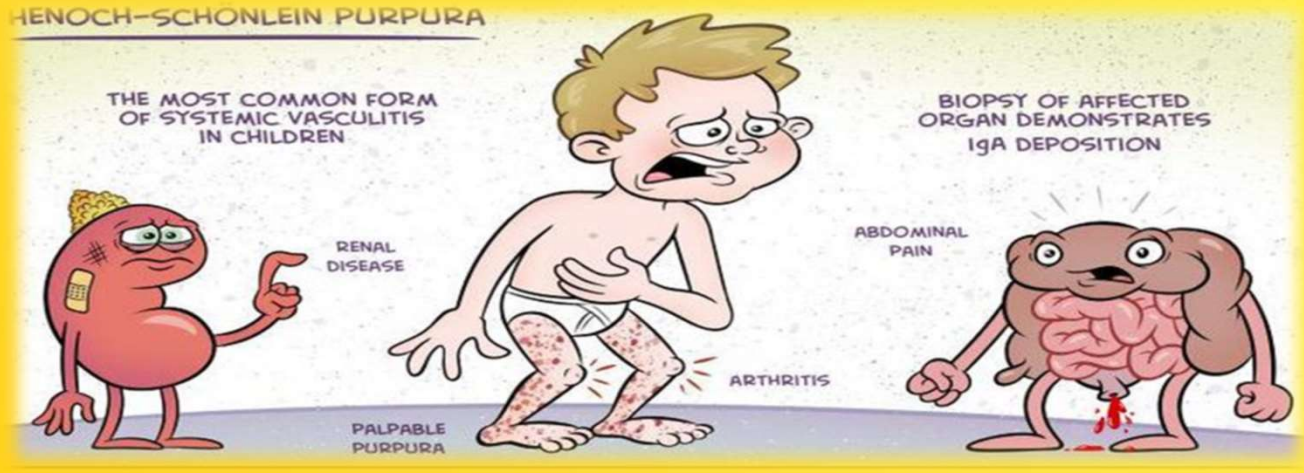
✓ the biggest difference found in *HLA* genes: Variants HLA-DRB1*01 and HLA-DRB1*11 associated with IgAV susceptibility, but HLA-DRB1*07 was negatively associated with IgAV. HLA-B*4102 found to be a susceptible.

✓ Other genes involved in: cytokine and chemokine production, the renin-angiotensin system, complement activation, and endothelium activity regulation also implicated in IgAV susceptibility

(*MEFV*) gene

In some studies, mutations in the familial Mediterranean fever (*MEFV*) gene were frequent in patients with IgAV, patients with these mutations may have more severe clinical findings with a higher inflammatory response.

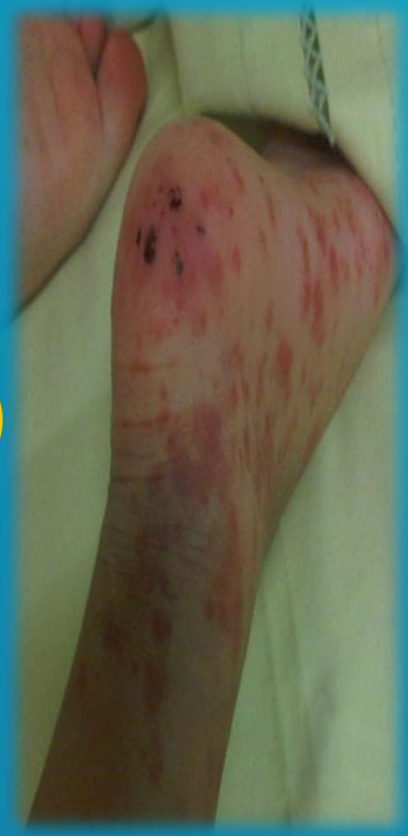
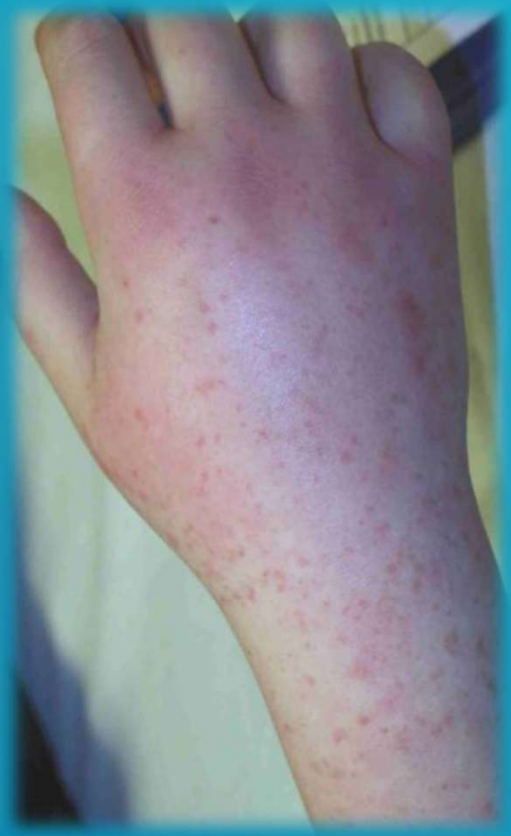
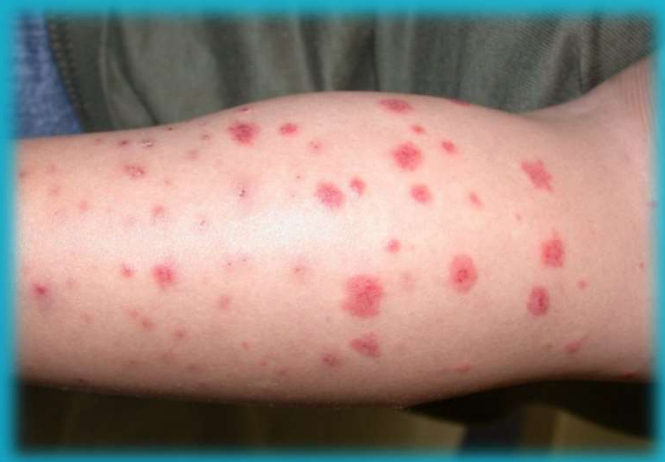
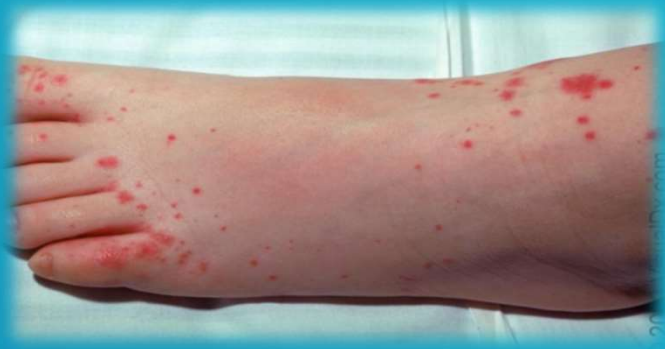
4 CLINICAL MANIFESTATIONS



- The is often acute onset,
- with the principal manifestations appearing sequentially over several days to weeks.
- Nonspecific constitutional signs, such as a low-grade fever or malaise, are often present.
- Skin manifestation is the presenting symp in approximately three-quarters of cases in one study preceding other symp by a mean of 4 days whereas joint or GI involvement preceded skin symp in 15% and 11%.

cutaneous involvement

- ***palpable purpura*** **is characteristic**
- most prominent on dependent or pressure-bearing surfaces, esp lower ext. & buttocks.
- The cutaneous lesions range from small petechiae to large ecchymoses to rare hemorrhagic bullae; tend to occur in crops progress in color from red to purple to brown.
- Ulceration may occasionally develop in large ecchymotic areas.
- The rash is often preceded by maculopapular or urticarial lesions.
- Subcutaneous edema over the dorsa of the hands and feet and around the eyes, forehead, scalp, & scrotum may occur early in the disease, esp in the very young child.

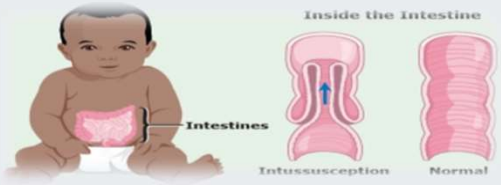





Gastrointestinal Disease

- In approx. half to two-thirds of children
- Usu. within a week after onset of the rash & almost always within 30 days;
- in 11% to 19% of cases, abdo.pain precedes other manifestations. In such cases, Dx is sig. more difficult.
- Abdo. pain was severe in 42% of children, usu. colicky and periumbilical or epigastric.
- Symptoms range from mild (n/v, abdo. pain) to more severe.
- The frequent presence of fecal **occult blood**, increased **stool alpha-1-antitrypsin**, and **hypoalbuminemia without proteinuria** suggest mucosal injury even in patients without GI symp.

Gastrointestinal Disease

- Occult blood and, less frequently, overt bleeding were observed in 18% to 52%
- The small bowel is the most frequently involved site in the GI tract because of its predilection toward ischemic injury
- Edema and submucosal & intramural hemorrhage resulting from vasculitis of bowel wall can lead to intussusception (usu confined to the small bowel), gangrene, or overt perforation.
- intussusception the most common surgical complication occurring in 0.7% to 13.6 %



- Less common involvement includes **obstruction** & **stricture** formation, **PLE, steatorrhea**, **hepatobiliary** disease, **acute pancreatitis**, **mesenteric vasculitis**, and **massive GI hemorrhage**

Arthritis

- **Arthralgia or arthritis** involving only a few joints occurs in **50% to 80**% of children with IgAV.
- It typically develops early in the disease, and if it precedes the skin symptoms (in **15%),** this is usually by a day or two only.
- Large joints such as the knees and ankles are most commonly affected, but other areas including the wrists, elbows, and small joints of the fingers may be involved.
- periarticular swelling and tenderness, usually occurring without erythema, warmth, or effusions but with considerable pain and limitation of motion.
- The joint disease is transient, although **usually not migratory**, and resolves within a few days to a week (even without treatment) without residual abnormalities

Renal Disease

- Glomerulonephritis affects up to one-third of children but is serious and potentially life-threatening in less than 10%.
- Renal disease, like abdominal pain, seldom precedes the purpura
- if serious renal disease develops, it does so within 4 to 6 weeks of the onset of the rash
- The spectrum of **features ranges** from **microscopic hematuria** and **mild proteinuria** to **nephrotic syndrome**, **acute nephritic syndrome**, **hypertensio**n, or **renal failure**

The intensity of renal symptoms at onset determines the severity of glomerular lesions.

In summary

A meta-analysis of 2398 children identified 13 risk factors associated with developing renal involvement

These included **male gender**, **older age**, **severe gastrointestinal symptoms**, **arthritis/arthralgia**, **persistent purpura**, **relapse**, **raised white blood cell** and/or **platelet count**, **elevated antistreptolysin titer** and **low complement (C3).**

The presence of microscopic dermal edema and perivascular deposition of C3 on direct immunofluorescence of skin biopsy may also be predictive of renal disease.

Renal Disease

- In a few children, however, nephritis may not occur until much later in the course of the disease, sometimes after several recurrences of the purpura.
- Renal involvement characteristically develops early, but end-stage disease may not be evident for many years.
- In a small number of children, renal abnormalities occur alone, and clinically and immune-pathogenically resemble IgA nephropathy in adults.

Renal Disease

- The ***SHARE guidelines*** *(*Single Hub and Access point for pediatric Rheumatology in Europe) recommend that all children with suspected IgAV must investigated for renal involvement, at diagnosis and throughout follow-up.
- This should be done by,

- ✓ **blood pressure measurement**,
- ✓ **early morning urinalysis** (to avoid orthostatic proteinuria),
- ✓ **renal function** with estimated glomerular filtration rate (eGFR)
- ❑ calculated from plasma creatinine and height using the Schwartz formula.

- Urinalysis should include determining the presence of hematuria and quantification of albuminuria and/or proteinuria by determining the ratio of each to creatinine in the urine, rather than 24-hour urine collections.

BOX 33.2 Indications for Renal Biopsy in IgA Vasculitis as Suggested by the SHARE Guidelines

Indications for renal biopsy in immunoglobulin (Ig)A vasculitis:

- Impaired estimated glomerular filtration rate (eGFR)
- Severe or persistent proteinuria (as defined in Table 33.3)
- Renal biopsy should be considered in cases of
  - Acute kidney injury with worsening renal function as part of rapidly progressive glomerulonephritis
  - Nephrotic syndrome (heavy proteinuria, hypoalbuminemia, and edema)
  - Nephritic syndrome (impaired eGFR, hypertension, hematuria/proteinuria)

Definitions of severity of IgAV nephritis

- **Mild IgAV nephritis** indicates normal eGFR and **mild to moderate proteinuria**. It generally corresponds to either no clear indication for renal biopsy or (if biopsied) histological evidence of **class I** (minimal changes) **or class II** (mesangial changes only), according to the International Study of Kidney Disease in Children (ISKDC) histological classification of IgAV nephritis.

- **moderate proteinuria** (urine protein:urine creatinine [UP:UC] ratio 100 to 250 mg/mmol) and/or impaired eGFR (<90 mL/min/1.73m2), a pediatric nephrologist should be consulted and a biopsy performed.
  Moderate IgAV nephritis usually equates to **class III** histology;

- **severe IgAV nephritis** usually corresponds to **class IV or V** in the ISKDC histological classification, with more than 50% crescent formation.

new

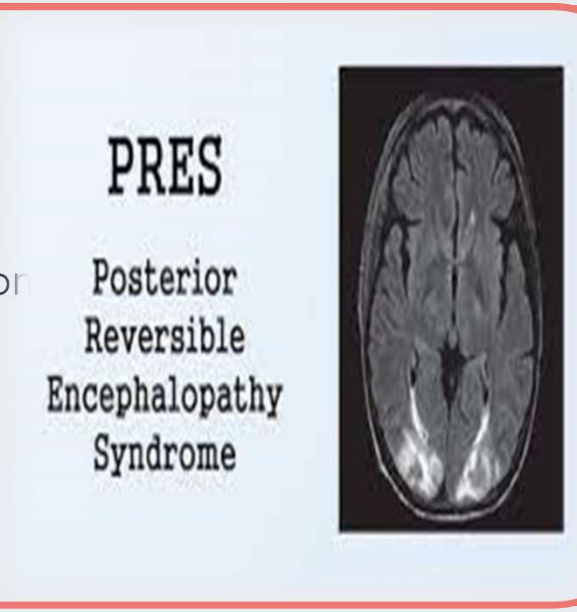
TABLE 33.3 Definitions of Severity of IgA Vasculitis (IgAV) Nephritis from SHARE Guideline

Severity of IgAV Nephritis	Definition
Mild	Normal GFR (>80 mL/min/1.73 m^2) and mild (UP:UC ratio <100 mg/mmol [in an early morning urine sample]) or moderate (UP:UC ratio 100–250 mg/mmol [in an early morning urine sample]) proteinuria
Moderate	<50% crescents on renal biopsy and impaired GFR (<80 mL/min/1.73 m) or severe persistent proteinuria (>250 mg/mmol for at least 4 weeks)[42]
Severe	>50% crescents on renal biopsy and impaired GFR (<80 mL/min/1.73$m^{2)}$ or persistent proteinuria (>250 mg/mmol for at least 4 weeks)[42]
Persistent proteinuria	UP:UC ratio (early morning urine) >250 mg/mmol for 4 weeks UP:UC ratio >100 mg/mmol for 3 months UP:UC ratio >50 mg/mmol for 6 months

Other manifestations

- **Central nervous system** involvement is rare with a reported frequency of less than **1%**

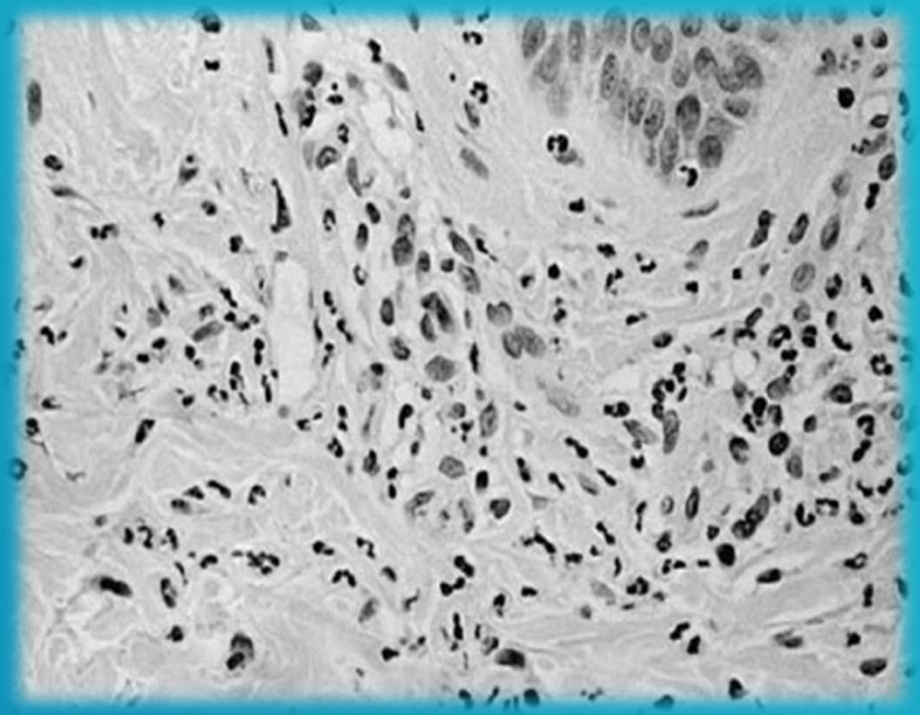
- isolated central nervoussystem vasculitis
- seizures
- coma, a hemorrhage
- Guillain–Barré syndrome
- posterior reversible encephalopathy syndro
  ataxia;
- central and peripheral neuropathy.
- Headaches without neurological signs



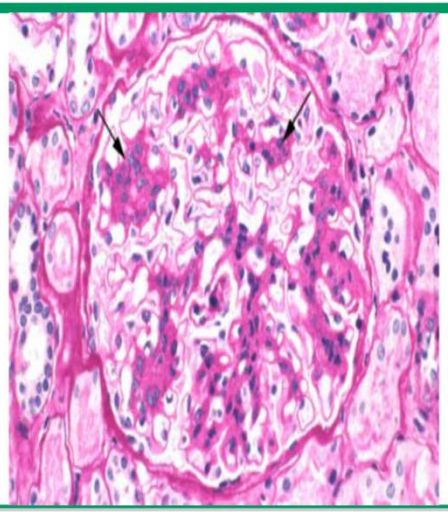
- **ocular involvement**; intramuscular, subconjunctival, pulmonary hemorrhages; interstitial pneumonitis; recurrent epistaxis
- carditis; and stenosing ureteritis.
- **Scrotal pain and swelling** are relatively frequent, occurring in **2% to 38**% of boys

Pathology

Leukocytoclastic vasculitis

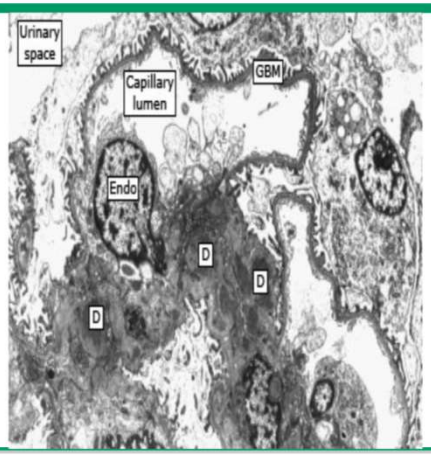


Light micrograph showing mesangial proliferative glomerulonephritis



Light micrograph of a mesangial glomerulonephritis showing segmental areas of increased mesangial matrix and cellularity (arrows). This finding alone can be seen in many diseases, including IgA nephropathy and lupus nephritis.

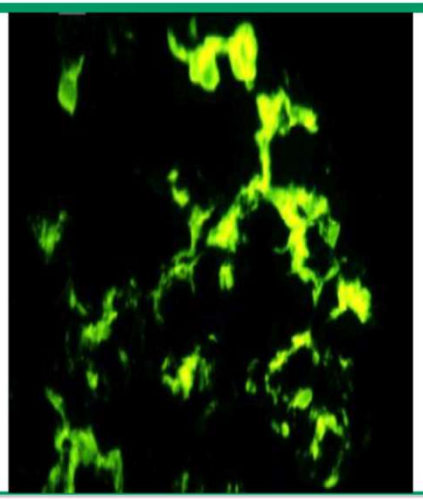
Electron micrograph showing mesangial immunoglobulin A (IgA) deposits



Low-power electron micrograph in IgA nephropathy. The primary finding is electron-dense deposits that are limited to the mesangial regions (D). The glomerular basement membrane (GBM) is normal, and there are no glomerular capillary wall deposits.

Endo: endothelial cell nucleus.

Immunofluorescence microscopy showing mesangial immunoglobulin A (IgA) deposits



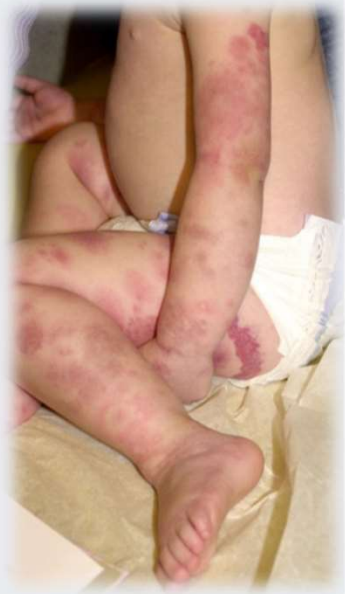
Immunofluorescence microscopy demonstrating large, globular mesangial IgA deposits that are diagnostic of IgA nephropathy or IgA vasculitis (Henoch-Schönlein purpura). Note that the capillary walls are not outlined since the deposits are primarily limited to the mesangium.

Differential diagnosis

- diagnosis relies on clinical criteria and laboratory findings
- ANCA-associated vasculitis, particularly in older children and adolescents
- immune thrombocytopenic purpura
- acute post streptococcal glomerulonephritis
- SLE
- septicemia
- disseminated intravascular coagulation
- hemolytic-uremic syndrome
- papular-purpuric gloves-and-socks syndrome associated with parvovirus B19
- acute surgical abdomen, gastrointestinal tract bleeding
- Intussusception
- acute pancreatitis
- Crohn disease

Infantile Acute Hemorrhagic Edema

- Between **4 and 24 months** of age
- acute onset of fever, purpura, ecchymoses, and inflammatory edema of the limbs, ears, and face.
- spontaneous remission in **1 to 3 weeks** and a benign course are characteristic, attacks may recur.
- Internal organ involvement (kidneys, gastrointestinal tract) is considered **rare.**
- Histopathology shows **leukocytoclastic vasculitis** with occasional demonstration of perivascular IgA deposition
- It is unclear whether this condition is truly a separate entity from IgAV



IgAV in Adults

- IgAV is less common in adults with a reported incidence of 0.8 to 1.8 per 100,000.
- Joint manifestations are **less frequent** in adults
- incidence and severity of renal disease are **higher** and carry a poorer prognosis for renal outcome.
- Several studies have reported **higher relapse** rates in adults.
- Intussusception is **rare** in adults

- Differences in laboratory data have been observed with a higher frequency in adult patients for anemia, elevated C-reactive protein, antinuclear antibody (ANA), and level of IgA, the latter especially in patients with renal involvement

Laboratory Examination

- no diagnostic laboratory abnormalities
- platelet count is normal or increased
- moderate leukocytosis
- Normochromic anemia
- fecal calprotectin biomarker for identifying gastrointestinal and renal involvement

- ~~ANA, ANCA, and rheumatoid factor (RF)~~
- Urinary findings
- C1q, C3, C4 are usually normal

- von Willebrand factor antigenare elevated
- Serum IgA concentration

Radiological Examination

- **Plain radiographs** may demonstrate decreased intestinal motility with dilated loops of bowel in children

- **Ultrasound** studies can identify **hematoma**, **bowel wall edema**, and **peritoneal fluid** and should be performed in severe abdominal pain to **exclude intestinal intussusception**.

- **Contrast enemas** are usually **not helpful** in ileo-ileal intussusception.
- Epididymal enlargement, subcutaneous scrotal swelling, hydrocele, or, rarely, testicular torsion can be confirmed, if necessary, by **scrotal ultrasonography**

- **Magnetic resonance imaging and magnetic resonance angiography** of the brain can define the extent of **cerebral vasculitis**.

5 Treatment

Treatment

- Treatment is supportive with maintenance of proper hydration, nutrition, and electrolyte balance.
- Edema of the lower limbs, genital area,and buttocks improves with rest and elevation of the affected areas.

- Pain from arthralgia and arthritis and diffuse abdominal pain can be significant and should be adequately controlled.
- Nonsteroidal antiinflammatory drugs (NSAIDs) are not contraindicated if renal function is normal.

- If necessary, control of hypertension is required
- glucocorticoids dramatically decrease the severity of joint and cutaneous disease, they are **not usually indicated** for the management of these manifestations.

- ***Glucocorticoid therapy***, however, should be considered in patients with **orchitis**, **cerebral vasculitis**, **pulmonary hemorrhage**, and **severe gastrointestinal involvement**.

- Organ- or life-threatening involvement may require additional cytotoxic **immunosuppressants** (such as **cyclophosphamide**) or **plasma exchange** as suggested by the SHARE group for rare systemic vasculitides

- There is no strong evidence on which to base recommendations for the treatment of recurrent IgAV.
- **Refractory IgAV** in children has most commonly been treated with corticosteroids
- Additional studies have reported the use of steroid-sparing medication, including **cyclosporine,mycophenolate mofetil** (MMF), **methotrexat**e, **IV immunoglobulin**, **cyclophosphamide**, and **azathioprine**(AZA)

- Several case reports describe the successful resolution of chronic, ***recurrent cutaneous lesions*** of children with IgAV with ***colchicine*** treatment (in one case in combination with aspirin)

✓ Recommended
doses of oral corticosteroids are prednisolone **1 to 2 mg/kg/day**
for 1 to 2 weeks with weaning over the subsequent fort night

✓ severe cases, pulsed intravenous methylprednisolone (IVMP)
10 to 30 mg/kg with a maximum of 1 g/day for 3 consecutive days
may be considered.

Management of IgAV Nephritis

- Avoiding permanent renal damage is critical, but high-quality evidence for the treatment of IgAV nephritis is lacking.

- Several studies demonstrated a beneficial effect of renin-angiotensin blockade in patients with proteinuria. Therefore, in children with IgAV who have renal involvement with persistent proteinuria (beyond 3 months), the SHARE guidelines recommend that an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) should be considered to prevent or limit secondary glomerular injury.

- ****There is evidence, however, that prophylactic corticosteroid treatment to prevent the development of IgAV nephritis is ineffective and is therefore not recommended**.

Treatment of mild IgAV nephritis

- For patients with **mild IgAV nephritis**,
- **oral prednisolone should be used as first-line** treatment. However, for patients with **persistent proteinuria**, the addition of **Azathioprine (AZA)** or **CellCept (MMF)** may be considered as second-line treatment or corticosteroid-sparing effect.

- Pulsed IVMP is rarely required for those with genuinely mild IgAV nephritis but was included as an option in the SHARE guidance.

- **Cyclosporin**, despite some anecdotal evidence, **is not routinely recommended** in the SHARE guidance for IgAV nephritis.

Treatment of moderate IgAV nephritis

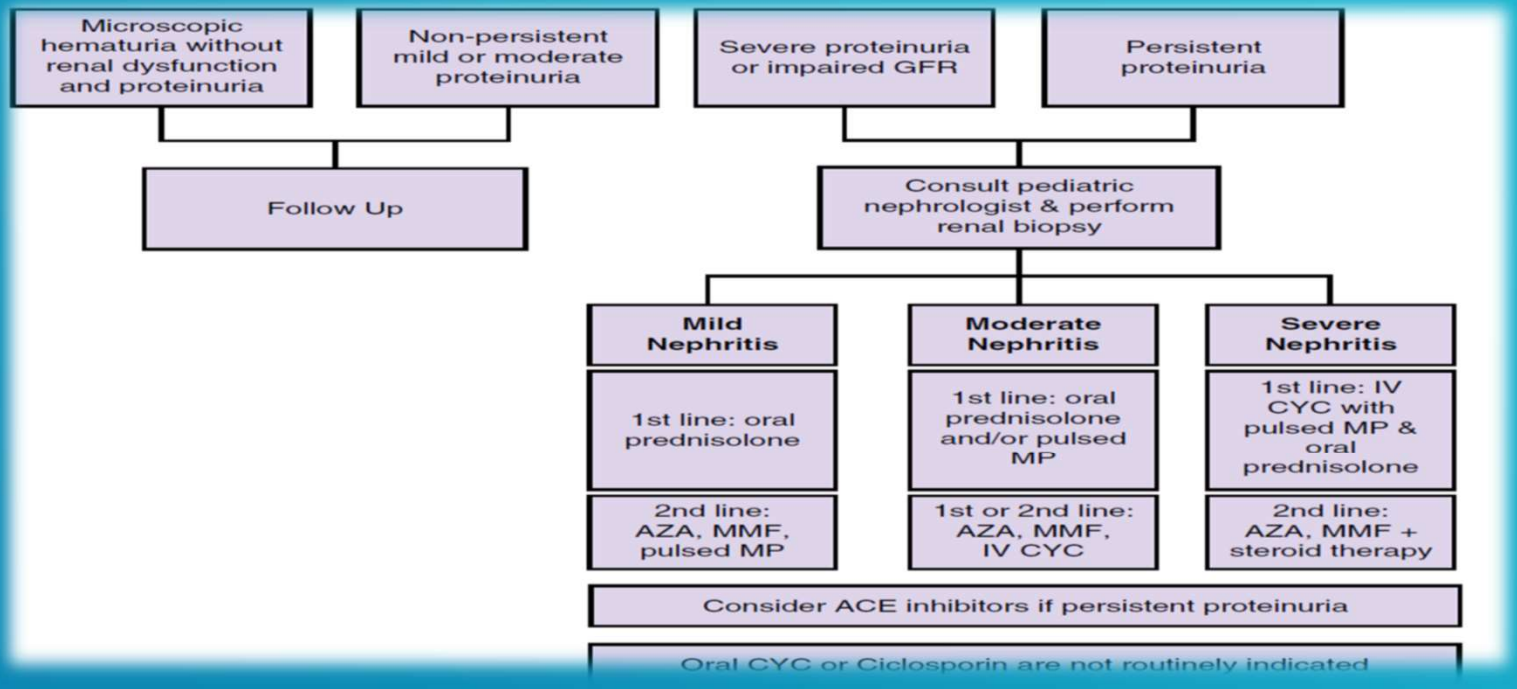
- For patients with **moderate IgAV nephritis**, **oral prednisolone or pulsed IVMP should be used as first-line treatment.**
- Additionally, **AZA, MMF**, or **IV cyclophosphamide** may also be used in the first- or second-line treatment according to the histopathological findings in the renal biopsy.
- **There **was insufficient evidence** to recommend **cyclosporine or oral cyclophosphamide routinely** in the treatment of moderate IgAV nephritis

Treatment of severe IgAV nephritis

- **Severe IgAV** nephritis is treated similarly to **systemic small-vessel vasculitis with kidney involvement** (e.g., ANCA-associated vasculitis)
- **highdose corticosteroids and IV cyclophosphamide** to **induce remission**
- **lower doses of corticosteroids** combined with **AZA or MMF** as **maintenance** treatment.
- (Shenoy et al) reported 14 children with severe IgAV nephritis treated successfully with **plasma exchange** alone.

new

Summary of SHARE recommendations for the treatment of mild, moderate and severe IgAV nephritis



Renal Transplantation for IgAV Nephritis

- Renal transplantation has been successful in some children who progressed to end-stage renal disease. However, recurrence of IgAV nephritis leading to graft loss can occur. In pooled data, there was a **35%** risk of **recurrence** 5 years after transplantation and an **11%** risk of **graft loss.**

- A retrospective cohort study of 339 adult patients with IgAV using the United Network of Organ Sharing database observed a graft survival of 80% at 5 years and 58.8% at 10 years; graft loss from recurrent disease occurred in 13.6 %.

- The overall graft survival in kidney recipients with IgAV, however, appears to be comparable with those with other renal disease

6 Course of the Disease

Course of the Disease

- In **2/3** of children, IgAV runs its entire course within **4 weeks** of onset.
- **Younger children have a shorter course and fewer recurrences than do older patients

- Up to **1/3** of the children have at least one **recurrence** that commonly consists of a rash and abdominal pain,with each episode usually similar but briefer and milder than the preceding one.
- Most exacerbations take place within the initial **6-week** period but may occur as late as 2 years after onset. They may be spontaneous with repeated respiratory tract infections.

- **A more severe course of the disease with gastrointestinal or joint involvement is associated with a higher incidence of recurrence.
- ****The severity of the cutaneous leukocytoclastic vasculitis does not correlate with visceral involvement**

Prognosis

- Prognosis is excellent for most children.
- Significant morbidity or mortality is associated with **gastrointestinal tract lesions** in the **short term** and with **nephritis** in the **long term**.
- **Poor prognosis factors**:
- The development of major indications of renal disease, particularly those with a mixed nephritic-nephrotic syndrome within the first 6 months after onset, or the occurrence of numerous exacerbations associated with nephropathy
- **Other poor prognosis factors**:
- decreased factor XIII activity; hypertension; renal failure at onset,
- Or in kidney biopsy: increased number of glomeruli with crescents; macrophage infiltration; and tubulointerstitial disease.

Disease outcome

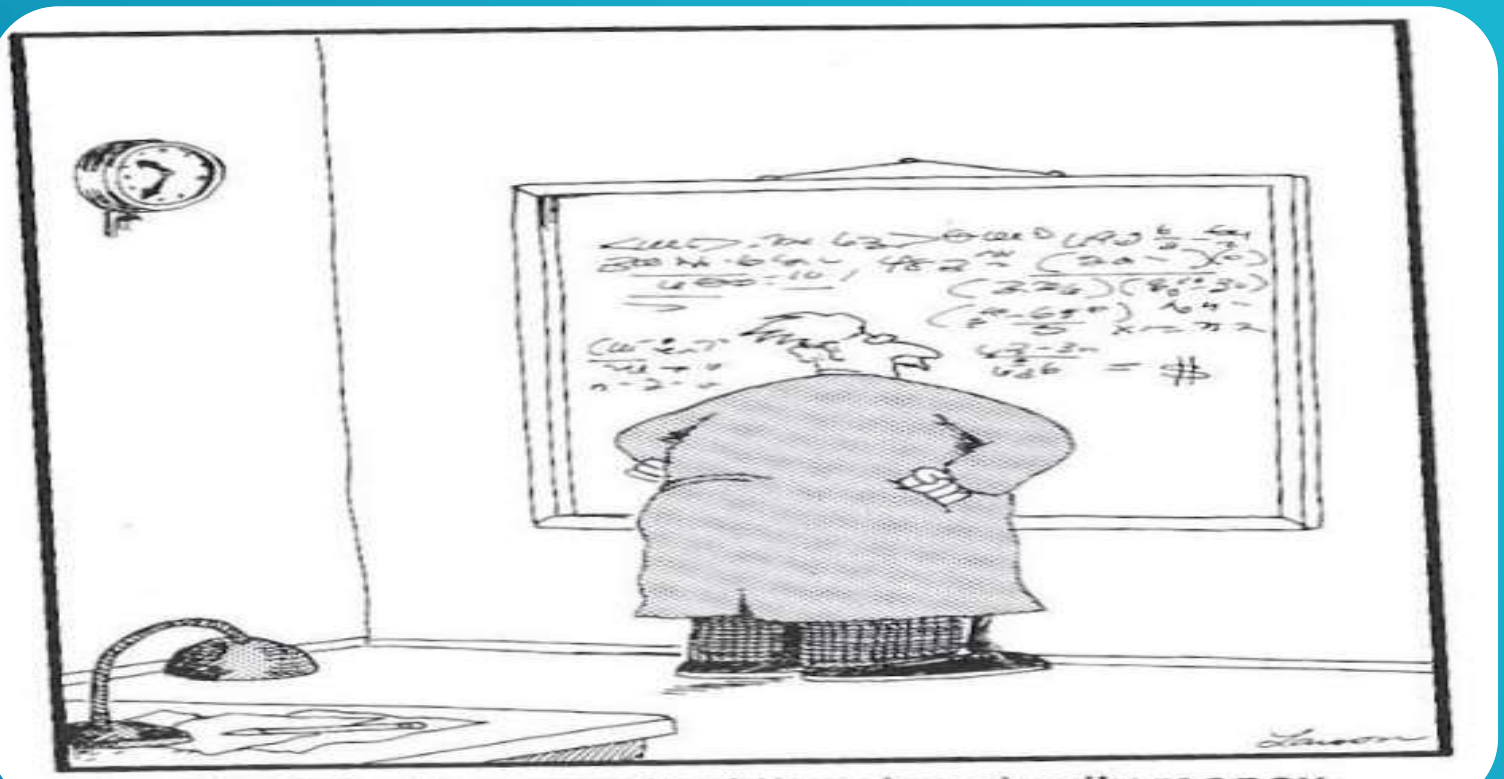
- The reported outcome of children with renal disease is highly variable.
- **With minimal lesions**, more than **75% recover** within 2 years;
- in contrast, 66% of children with crescentic glomerulonephritis in more than 80% of glomeruli progress to renal failure within the first year.
- The **worst** outcome is associated with the presence of the **nephrotic or nephritic syndrome** at onset.
- Almost **half of such children** have active renal disease or renal insufficiency at follow-up periods of 6 or more years.
- **Thus the extent of renal disease is an important determinant of long-term outcome

ESRD in children with IgAV nephritis

- Overall, less than 5% of children progress to **end-stage renal failure**.
- IgAV accounts for less than 1% of children with **renal failure** from all causes.

- In a follow-up evaluation of 64 children, the renal survival rate at 10 years was 73%, and **renal insufficiency at presentation was the best predictor of the future course of nephritis.**

- Similar results were found in a multicenter study on 443 patients with IgAV nephritis from Turkey, in which 87% of patients had a favorable outcome and 13% had an unfavorable one; 1.1% of children showed end-stage renal disease at follow-up.
- All patients who showed end-stage renal disease had nephritic-nephrotic syndrome at presentation and greater than 50% crescents on renal biopsy.



Einstein discovers that time is actually money.

THANKS FOR YOUR ATTENTION