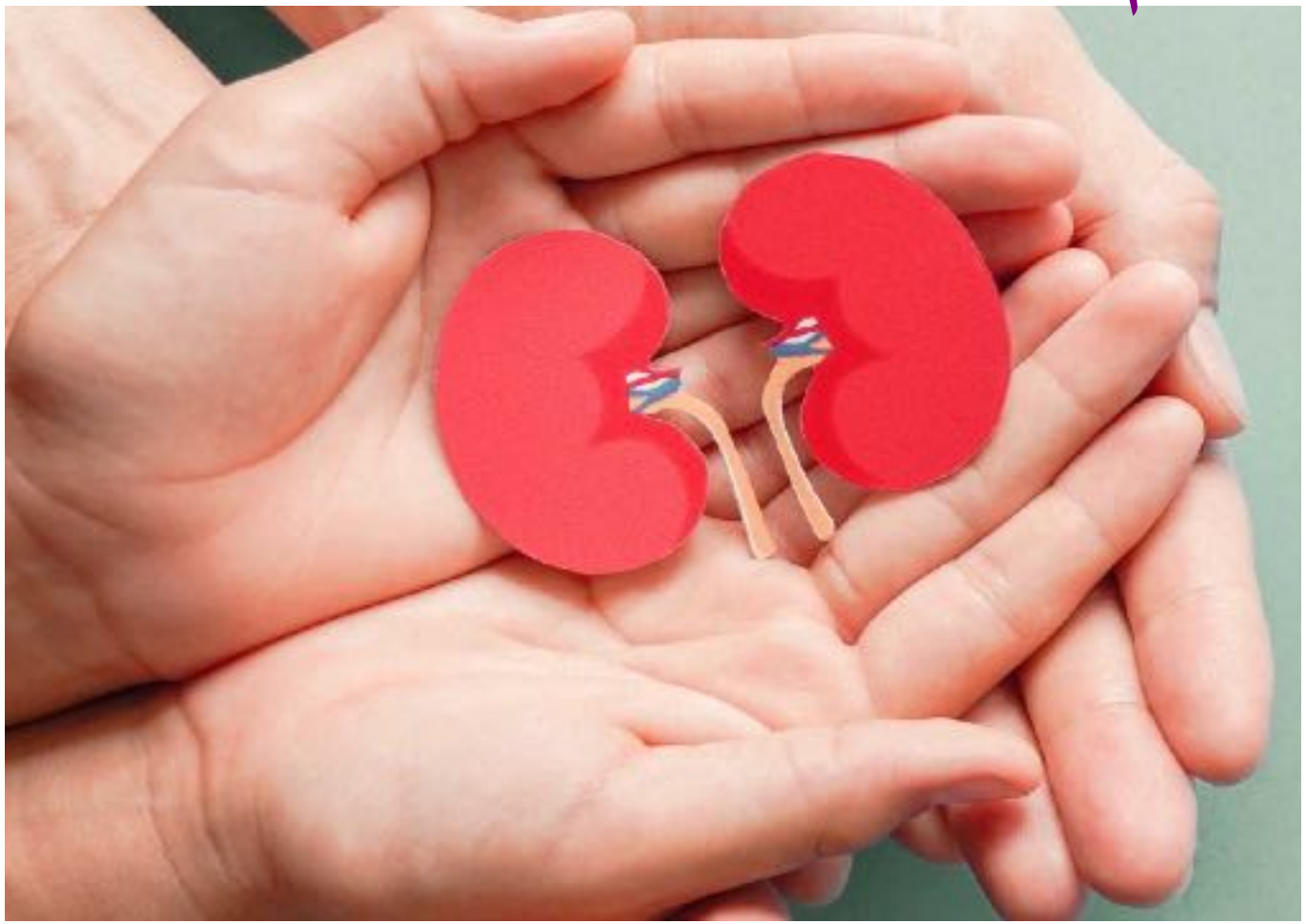
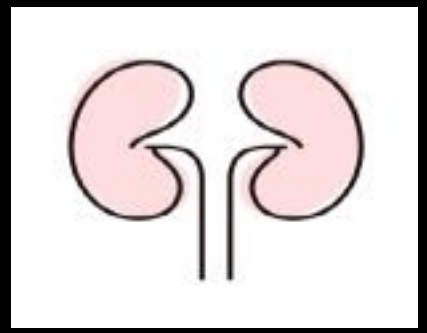

بسم الله الرحمن الرحيم

اللهم إنى أسألك علما نافعا





INFECTION INDUCED NEPHROPATHY

MOHAMED ALAA THABET

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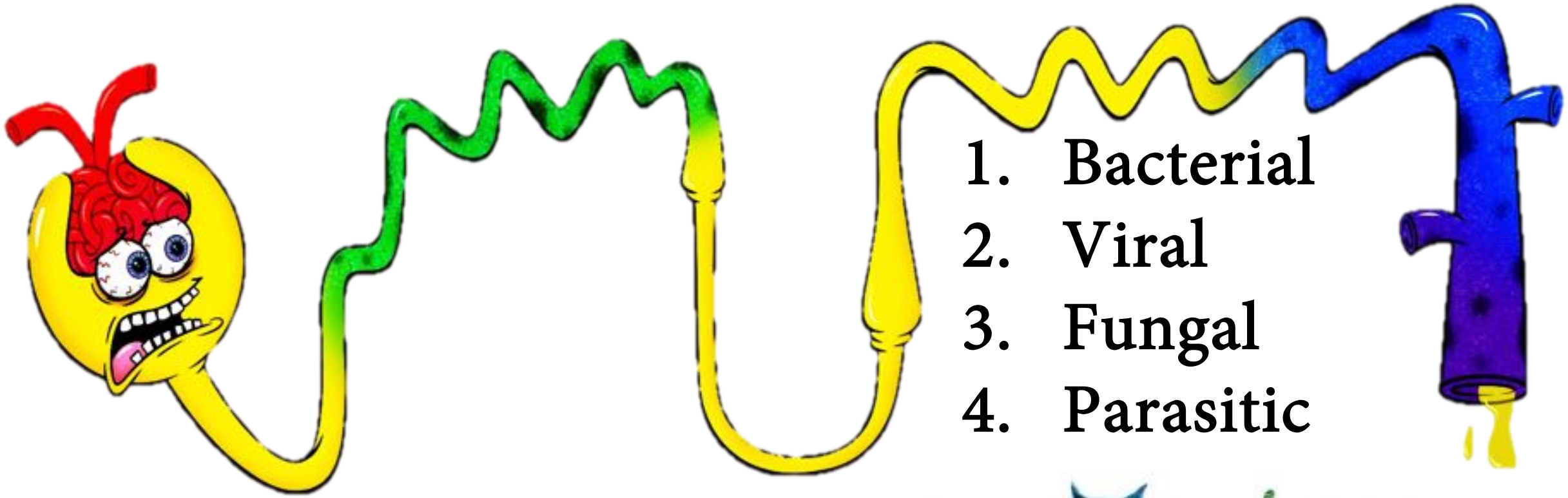
ALEXANDRIA UNIVERSITY

INFECTION INDUCED NEPHROPATHY

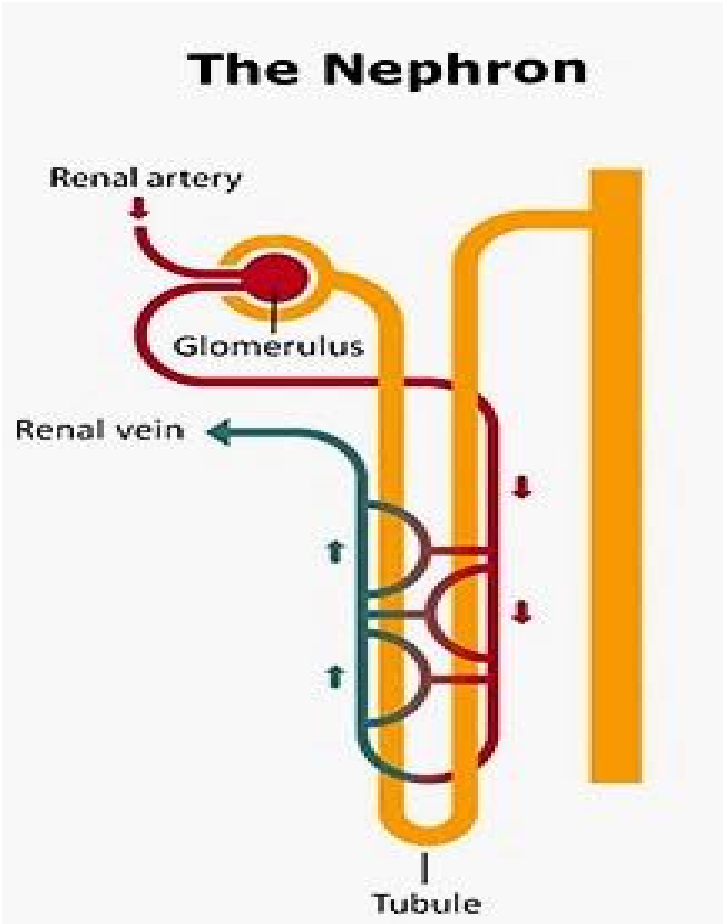


1. Bacterial
2. Viral
3. Fungal
4. Parasitic

Directly or Indirectly

INFECTION INDUCED NEPHROPATHY

1. Glomeruli
2. Tubules
3. Vessels
4. Interstitum



INFECTION INDUCED NEPHROPATHY

1. Glomerulopathy
2. Tubulopathy
3. Vasculopathy
4. Interstitalopathy

INFECTION INDUCED NEPHROPATHY

1. AGN
2. ATN
3. HUS
4. AIN

ACUTE

CHRONIC

The spectrum IS DIVERSE

INFECTION INDUCED NEPHROPATHY

During infection

Or

After infection

Glomerular Diseases

Review Article

Glomerular Dis 2021;1:82–91
DOI: 10.1159/000515461

Received: November 13, 2020
Accepted: February 24, 2021
Published online: April 28, 2021

Infection-Related Glomerulonephritis

Mazda
*Departm
Chicago

frontiers in Medicine

REVIEW
published: 28 November 2018
doi: 10.3389/fmed.2018.00327

Infection-Induced Kidney Diseases

Latency, Anti-Bacterial Resistance Pattern, and Bacterial Infection

Elenjickal Elias John
Vinoi George Davi

REVIEW

www.nature.com/clinicalpractice/neph

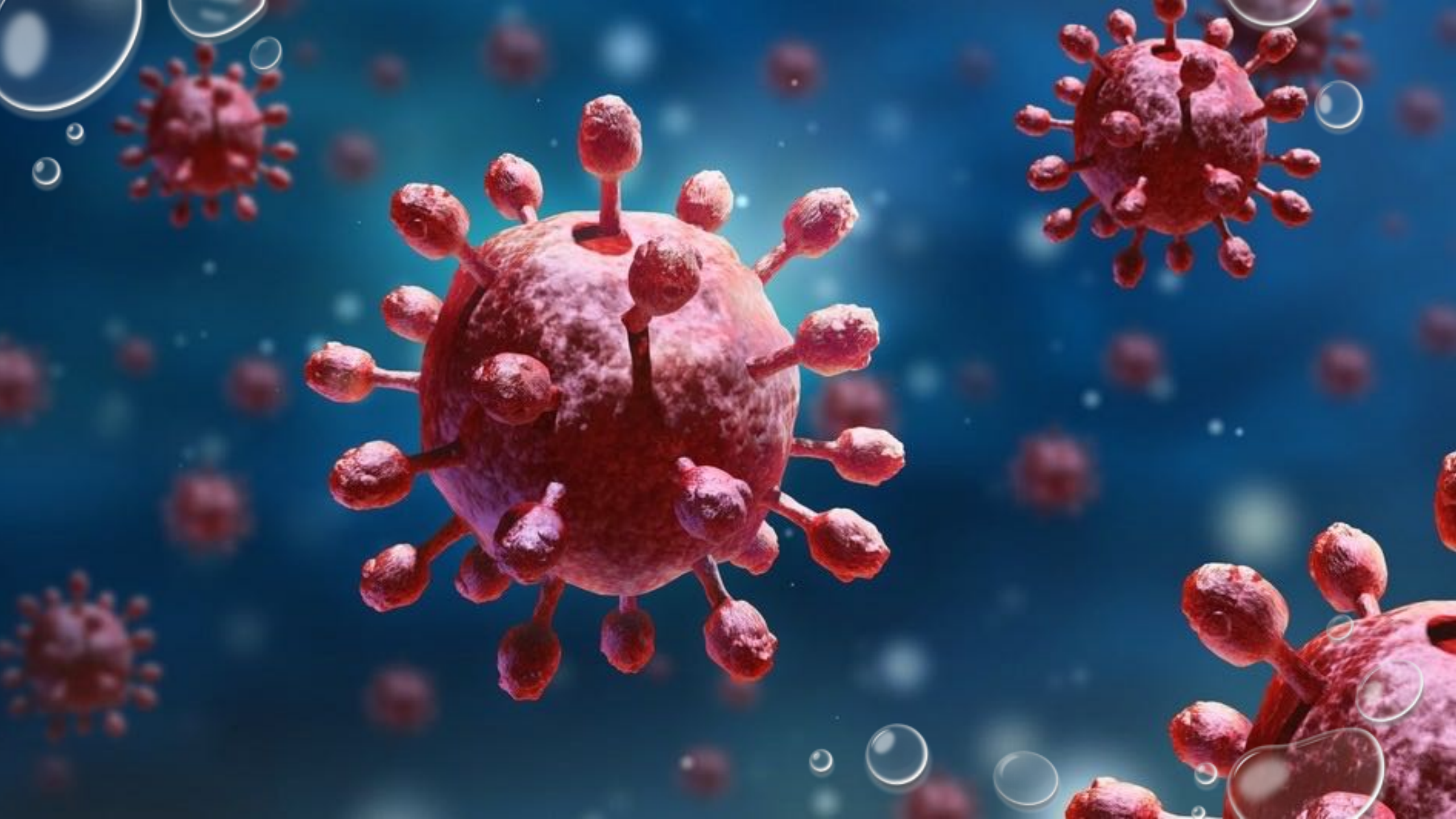
Viral nep

Andrew SH Lai ar

Epidemiology, pathogenesis, treatment and outcomes of infection-associated glomerulonephritis

Anjali A. Satoskar[1]*, Samir V. Parikh[2] and Tibor Nadasdy[1]

Bacterial
Viral



Review Article

Kidney360

COVID-19-associated acute kidney

WJMA

World Journal of Meta-Analysis

Submit a Manuscript: https://www.f6publishing.com

World J Meta-Anal 2021 June 28; 9(3): 220-233

DOI: 10.13105/wjma.v9.i3.220

ISSN 2308-3840 (online)

J Nephropharmacol. 2021; 10(1): 07.

NPJ

http://www.jnephropharmacology.com

DOI: 10.34172/npj.2021.07

Journal of Nephropharmacology

Glomerulonephritis associated with SARS-CoV-2 infection

Mohsen Akhavan Sepahi[1], Bhaskar VKS Lakkakula[2], Bijan Roshan[3], Banafsheh Yalameha[4]

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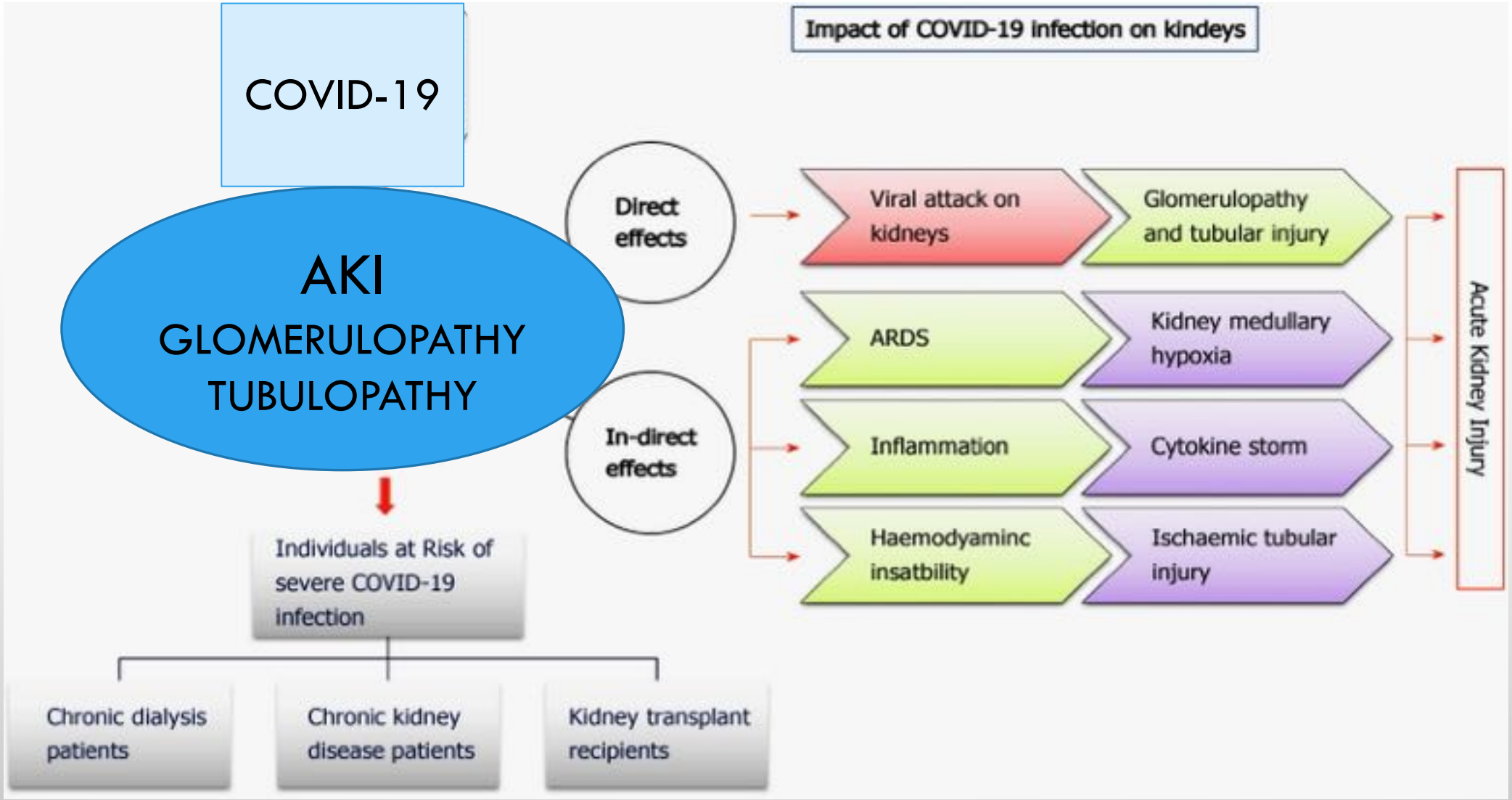
[2]Department of Zoology, Guru Ghasidas Vishwavidyalaya, Bilaspur, India
[3]Division of Nephrology, Scripps Clinic, La Jolla, California, USA
[4]Nickan Research Institute, Isfahan, Iran

COVID-



Srivastava S & Garg I. Post COVID-19 infection: Long-term effects on liver and kidneys. *World J Meta-Anal* 2021; 9(3): 220-233

THE SPECTRUM IS **DIVERSE**

ACUTE & CHRONIC GLOMERULONEPHRITIS

ACUTE OR CHRONIC TUBULOINTERSTITIAL NEPHRITIS

Prasad and Patel : Infection and Kidney
Frontiers in Medicine | www.frontiersin.org 4 November 2018 | Volume 5 | Article 327

THE SPECTRUM IS **DIVERSE**

AKI

RPGN

HUS
PAN

NEPHROTIC SYNDROME

TABLE 2 | Bacterial infections and associated nephropathies.

Bacteria*	Renal involvement
Streptococcus pyogenes	PIGN, IRGN, ATN
Staphylococcus (aureus, epidermidis)	IRGN, PIGN, DPGN, ATN, AIN, IgA-PIGN, MPGN
Salmonella (typhi, paratyphi)	ATN, HUS, AIN
Escherichia coli	HUS,
Leptospira	ATN, AIN, DPGN, MGN
Mycobacterium tuberculosis	CIN, GIN, DPGN, amyloidosis
Mycobacterium leprae	MPGN, DPGN, GIN, amyloidosis
Ligionella spp.	AIN
Yersinia enterocolitica	AIN
Brucella species	AIN, ATN, DPGN
Campylobacter jejuni	AIN, MesPGN, DPGN
Corynebacterium diphtheriae	AIN

ACUTE

BACTERIAL NEPHROPATHY

The spectrum IS DIVERSE

ATN
AIN
DPGN
RPGN
MPGN
MesPGN

HUS

TABLE 1 | Viral infections and associated nephropathies.

Virus	Renal involvement
ACUTE	
Dengue	ATN, ICGN, MesPGN
Hantavirus HFRS	ATN, MesPGN
Varicella-zoster	DPGN
Parvovirus	ICGN, PAN, TMA, HSP
HAV	ICGN, MesPGN, ATN
HBV	ATN, DPGN
CMV	cFSGS, MN, IgA, HSP, ICGN, MPGN, TMA
EBV	ICGN, MN, MsPGN
SUBACUTE	
Parvovirus	cFSGS
EBV	cFSGS, MN
HBV	PAN
HCV	PAN
CHRONIC	
HBV	MN, Type I MPGN, MPGN1, MC, PAN, IgA, FSGS
HIV	HIVAN, HIVICK, ncFSGS, TMA
HCV	MPGN1, MC,MPGN2, PAN, IgA, MN

ACUTE

CHRONIC

VIRAL NEPHROPATHY

ATN
DPGN
MPGN
MesPGN

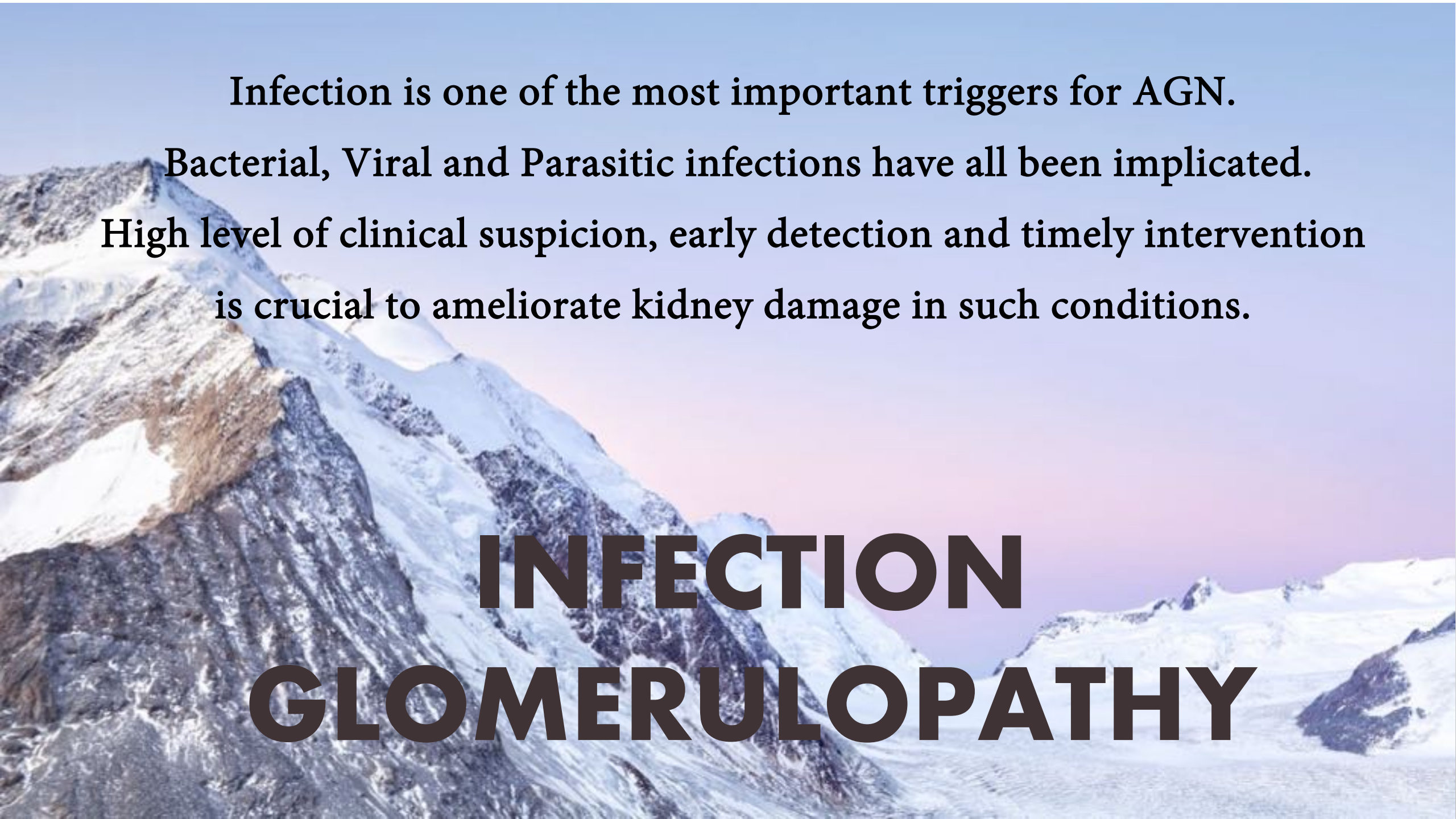
MN
IgA
PAN
HSP
cFSGS

HAV, EBV & parvovirus B19 cause AGN;

Hepatitis B, C, HIV & parvovirus B19 cause chronic GN;

coranavirus, & influenza A cause interstitial nephritis


Hisham Nasser
PHOTOGRAPHY



Infection is one of the most important triggers for AGN.

Bacterial, Viral and Parasitic infections have all been implicated.

High level of clinical suspicion, early detection and timely intervention is crucial to ameliorate kidney damage in such conditions.

INFECTION GLOMERULOPATHY

INFECTION GLOMERULOPATHY

DPGN

MEMBRANOUS NEPHRITIS

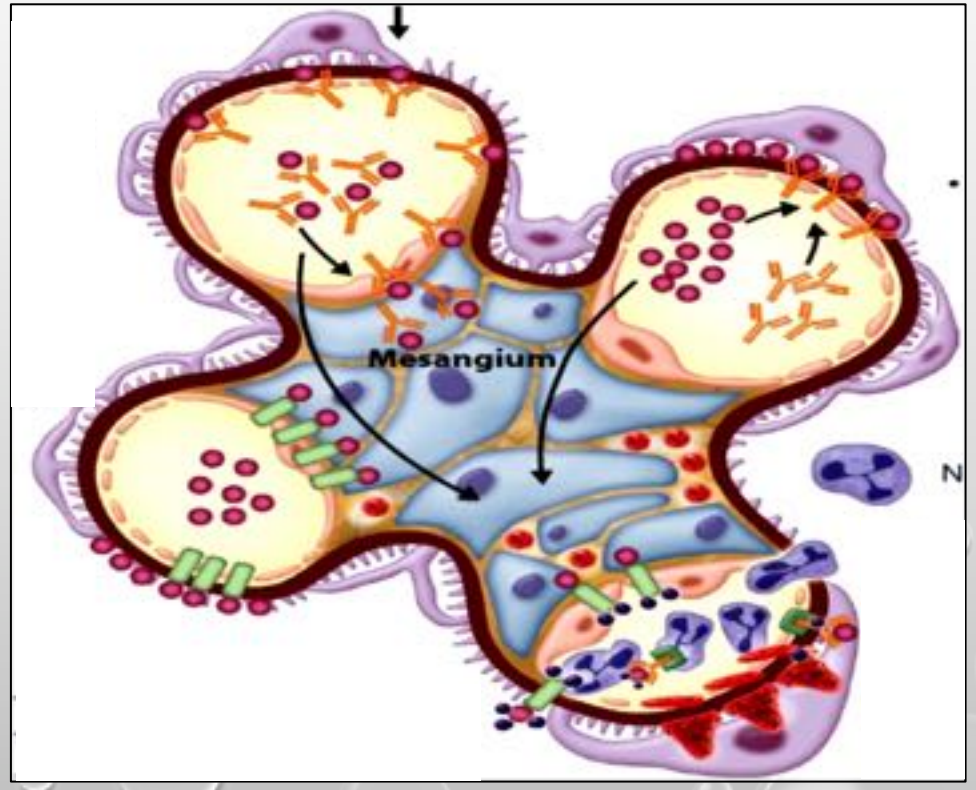
cFSGS

MesPGN

IGA NEPHRITIS

MPGN

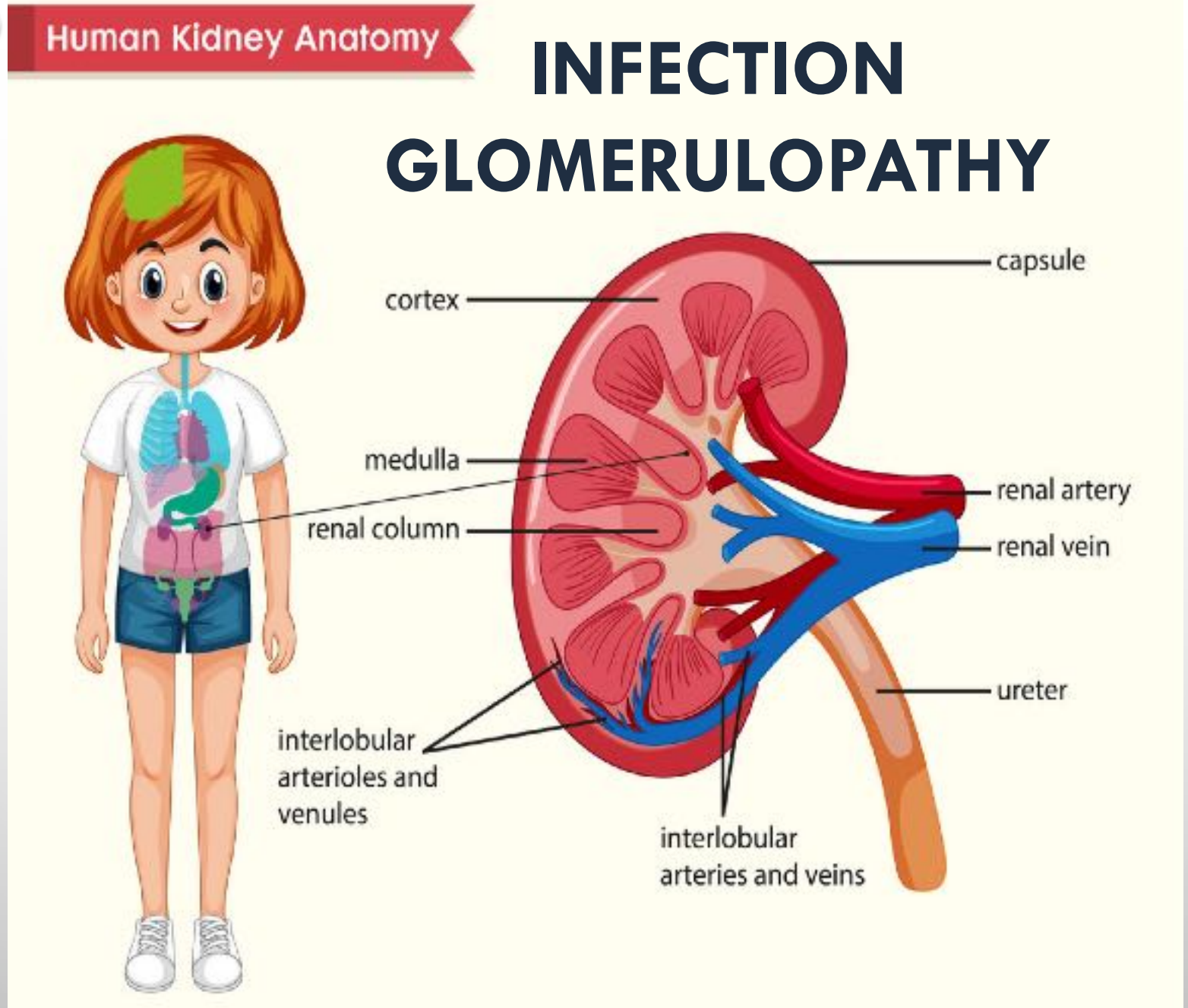
Immune complex—mediated



INFECTION GLOMERULOPATHY

PIGN

IRGN



INFECTION GLOMERULONEPHRITIS

Post-infection Glomerulonephritis (PIGN)

Broad group of acute nephritis

that follows a variety of infectious events.

Acute Post-streptococcal Glomerulonephritis (PSGN)

- Children: 2–15 years old.
- A β- haemolytic *Streptococci*

Infection-Related Glomerulonephritis (IRGN)

IN ASSOCIATION with PERSISTENT BACTERAEMIA

1. BACTERIAL ENDOCARDITIS
2. SHUNT NEPHRITIS.
3. DEEP SEATED INFECTIONS

GN with evidence of ongoing infection

at another site.

PIGN

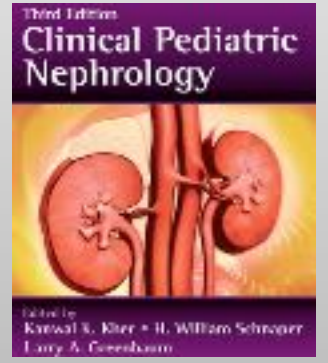
1. Bacterial
2. Viral
3. Fungal
4. Parasitic

(PIGN)

Bacterial

Bacterial infections

- Group A β-hemolytic streptococcus
- Staphylococci
- *Streptococcus pneumoniae*
- *Yersinia*
- *Mycoplasma pneumoniae*
- *Mycobacterium tuberculosis*
- Syphilis
- Brucellosis
- *Rickettsia rickettsii*
- *Granulicatella adiacens*



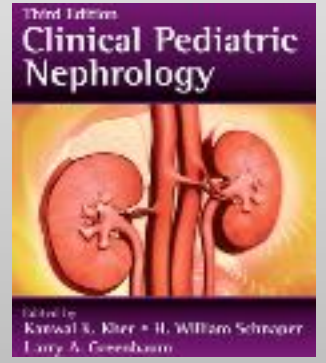
DIEGO H. AVILES & V. MATTI VEHASKARI. Acute Glomerulonephritis.
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

PIGN

Viral

Viral infections

- Hepatitis B
- Hepatitis C
- HIV-1 infection
- Cytomegalovirus (especially in immunocompromised and kidney transplant patients)
- Parvovirus B19
- Influenza virus
- Adenovirus
- Coxsackie virus
- Epstein-Barr virus
- Varicella virus
- Mumps virus



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PIGN

Fungal

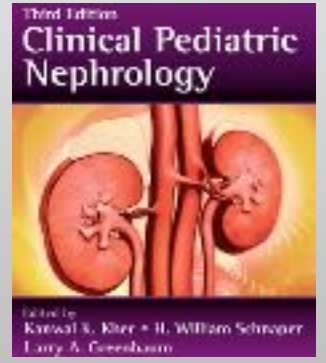
Parasitic

Parasitic infections

- Malaria
- Schistosomiasis

Fungal infections

- Histoplasmosis
- Cryptococcosis
- Coccidioidomycosis



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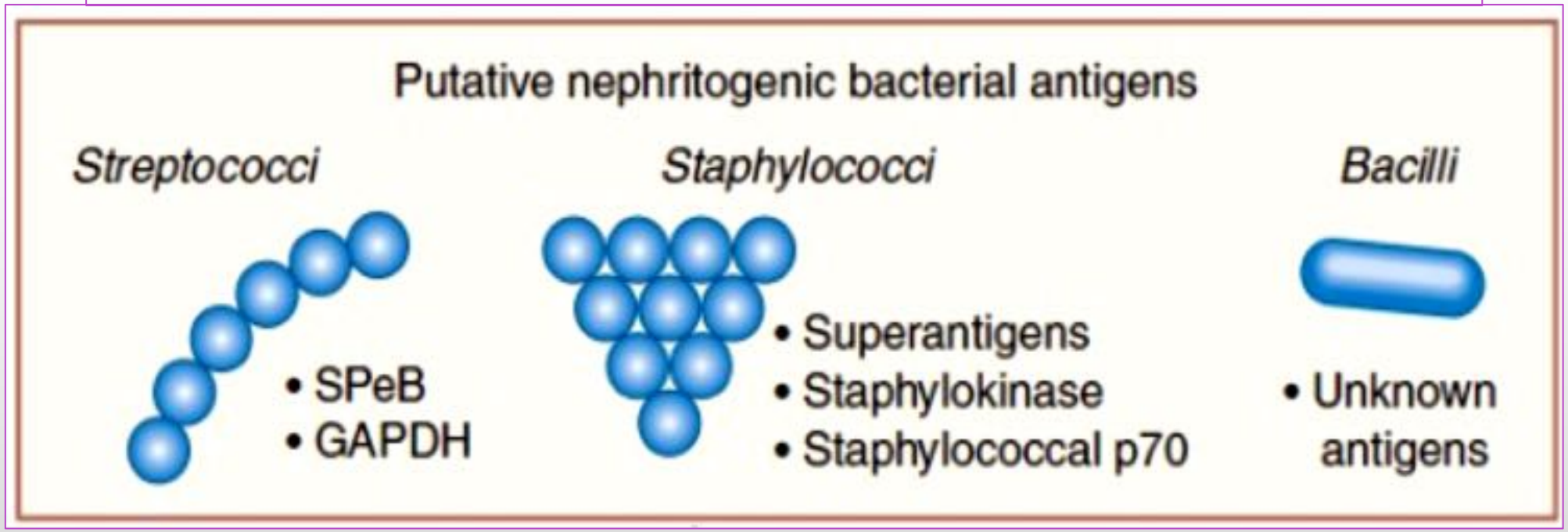
NEPHRITOGENIC ANTIGENS IMPLICATED IN THE PATHOGENESIS OF PIGN



Host factors
- Genetic susceptibility
- Abnormalities in the alternative pathway of complement

Acute Poststreptococcal Glomerulonephritis (APSGN)

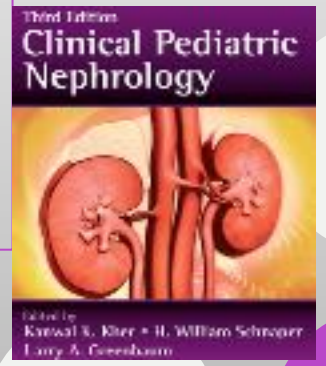
- It is an acute diffuse inflammatory disease of glomeruli mediated by immune complex deposition and presenting as acute nephritic syndrome

- After infection with group A β-hemolytic streptococci,

Nephritogenic strains:

✓ serotypes 1, 2, 3, 4, 12, 18 & 25 with pharyngitis-associated APSGN,

✓ serotypes 2, 42, 49, 55, 57& 60 with skin infection–associated APSGN.



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Acute Poststreptococcal Glomerulonephritis (APSGN)

- The attack rate is variable,
- Not every infection is followed by AGN.

Host immune responses determine whether GN will develop or not.

< 2% of children infected with nephritogenic strains of streptococci, show clinically obvious signs of acute GN.

Host factors
- Genetic susceptibility
- Abnormalities in the alternative pathway of complement

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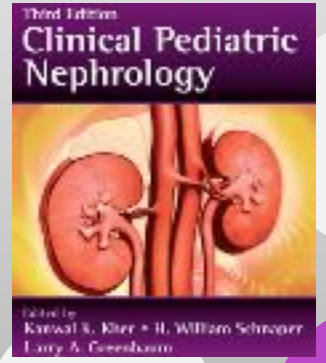
Acute Poststreptococcal Glomerulonephritis (APSGN)

- Asymptomatic cases are more common than symptomatic cases.
- Siblings of affected patients are more at risk for asymptomatic APSGN.



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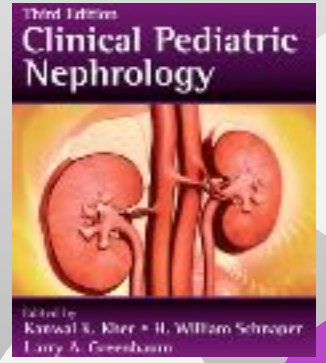
Acute Poststreptococcal Glomerulonephritis (APSGN)

APSGN may occur at any age

2 & 15 years

PARENTS also can be affected.



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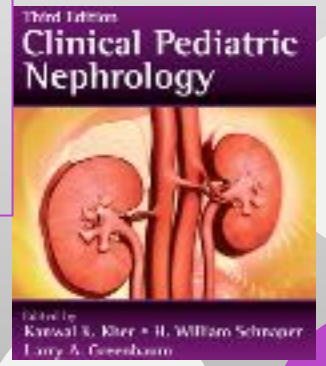
DOES APSGN OCCUR AFTER AGE OF 15?

- Can affect individuals aged over 15 years,
- Frequently reported among elderly (aged over 60 years).
- Adult APSGN has atypical clinical features & additional co-morbidities.

Acute Poststreptococcal Glomerulonephritis (APSGN)

- 1- 2 weeks after tonsillopharyngitis
- 6 weeks following impetigo.
- **Scabies** is often present in those manifesting pyoderma.
- **Scarlet fever** may be a manifesting feature of some cases.
- **The primary infection** may remain undetected in some cases.



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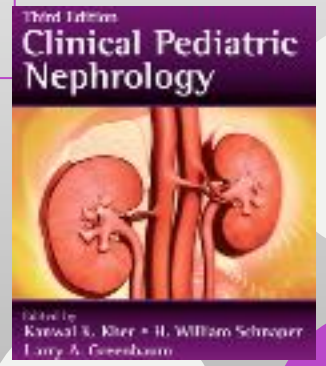
Acute Poststreptococcal Glomerulonephritis (APSGN)

- Characteristic triad: Edema, hypertension & hematuria
- Pulmonary edema in up to 50% cases on CXR



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Acute Poststreptococcal Glomerulonephritis (APSGN)

Clinical and laboratory findings
Edema
Arterial hypertension
Oliguria
Hematuria
Moderate proteinuria
Nephrotic proteinuria
Decreased C3
Increased ASO titer
Increased serum creatinine
Mild/moderate
Severe
Chest x-ray: Pulmonary edema

Hypertension,

Periorbital & LL edema,

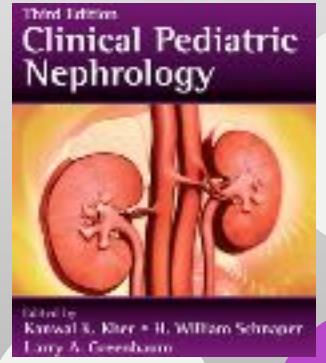
Gross hematuria, Oliguria,

Dull abdominal or flank pain

Malaise

Hepatomegaly

Frank nephrotic syndrome in 3-27%



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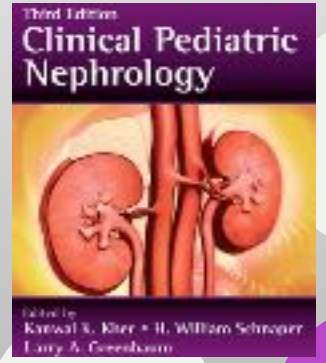
Acute Poststreptococcal Glomerulonephritis (APSGN)

Clinical and laboratory findings
Edema
Arterial hypertension
Oliguria
Hematuria
Moderate proteinuria
Nephrotic proteinuria
Decreased C3
Increased ASO titer
Increased serum creatinine
Mild/moderate
Severe
Chest x-ray: Pulmonary edema

ASOT

Very low C3.

A modest Azotemia



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Lab findings in APSGN

- Dysmorphic RBCs
- RBC casts in urine

- Decreased C3 level.

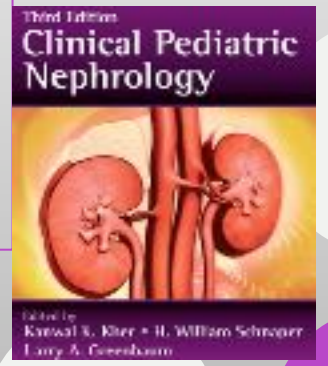
- ↑ Urea & ↑ Creatinine.

- ↑ASOT(in throat infection only).
- ↑Anti DNase B antibodies in all cases.

- Serum protein is normal or slightly decreased due to hemodilution.

Acute Poststreptococcal Glomerulonephritis (APSGN)

- A self-limited disease,
- May lead to life-threatening complications :
  1. **Severe hypertension and encephalopathy,**
  2. **Acute kidney injury (AKI), need for dialysis,**
  3. **Pulmonary edema & CHF.**



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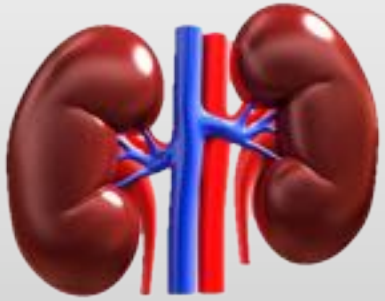
Acute Poststreptococcal Glomerulonephritis (APSGN)

Asymptomatic

Symptomatic



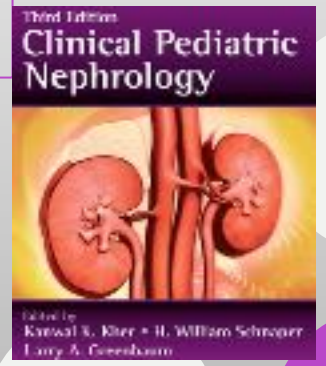
Classical

Atypical

Complications

Acute Poststreptococcal Glomerulonephritis (APSGN)

- Incidence significantly declined in Western world.
- However, it remains a public health concern in some regions



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Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis
NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

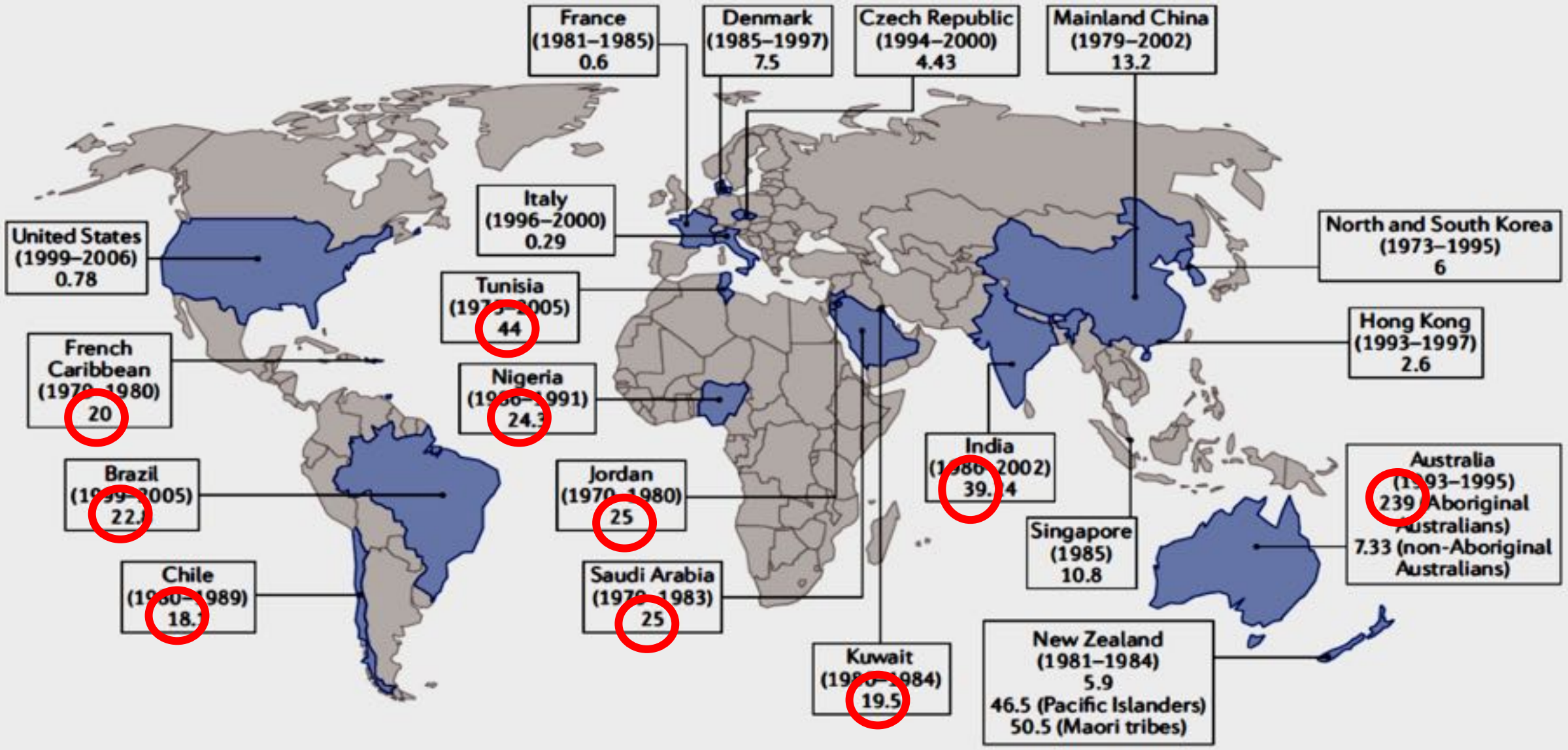
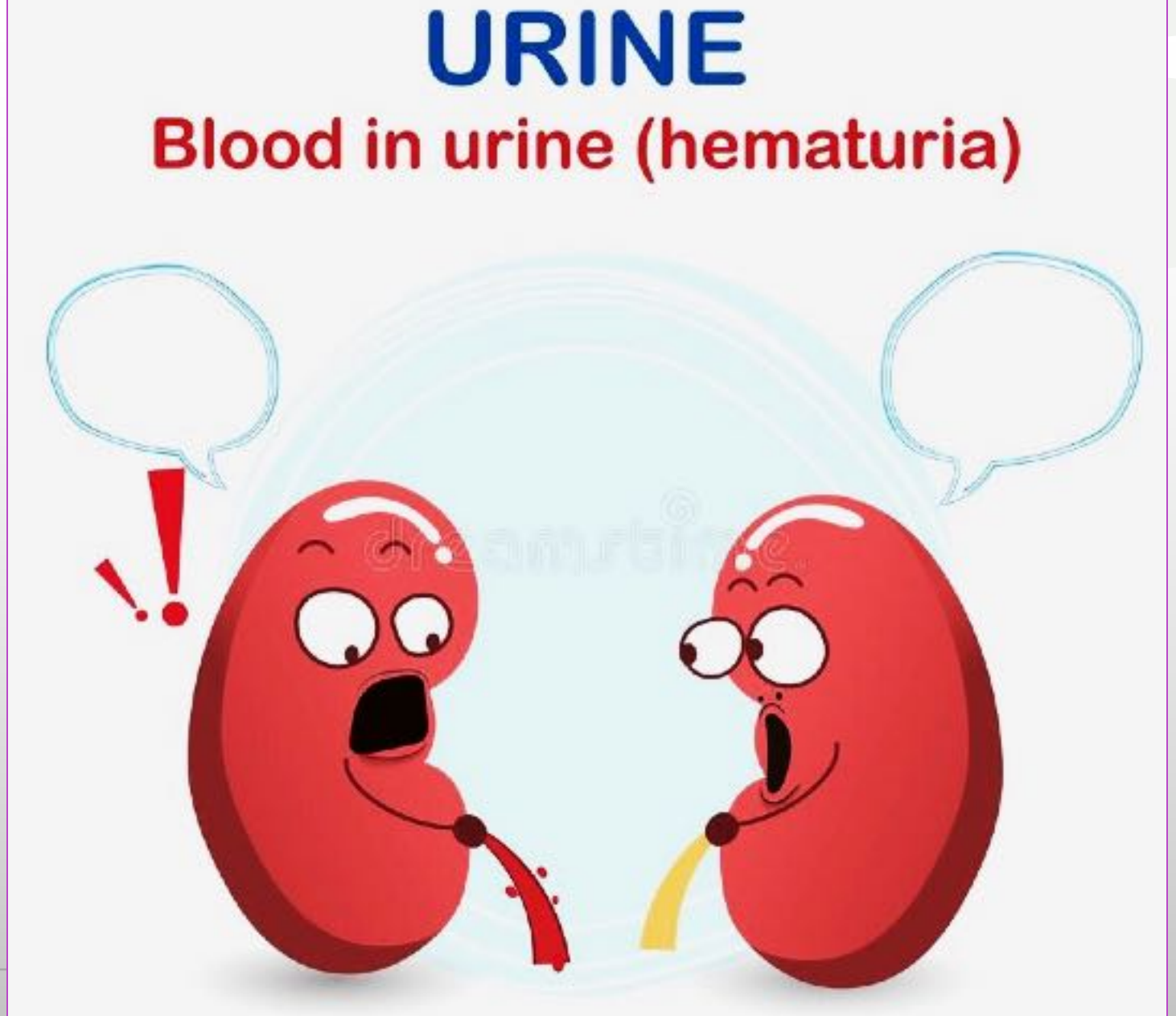


Fig. 2 | **Global APSGN incidence.** World map showing the incidence of acute post-streptococcal glomerulonephritis

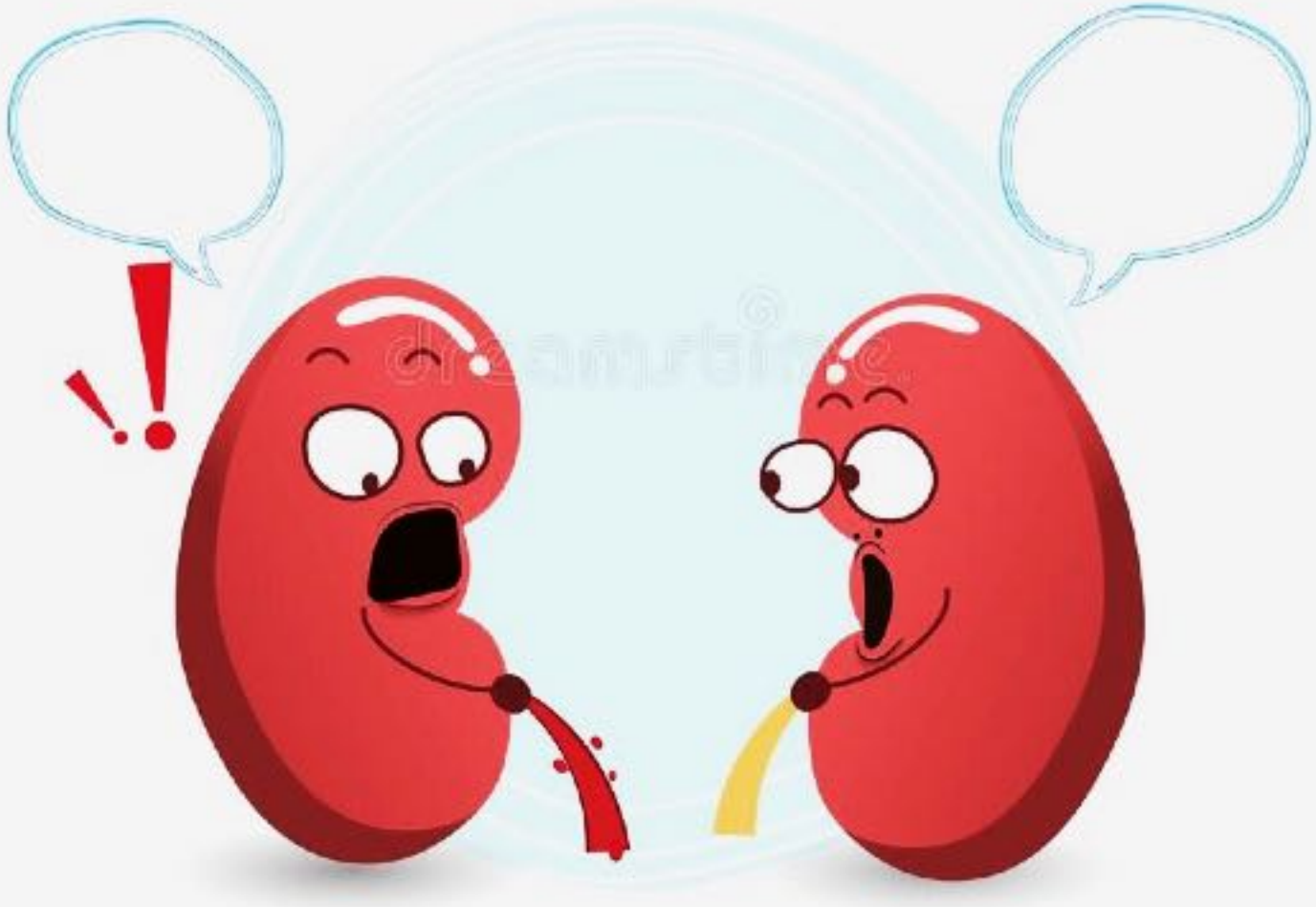
PERIORBITAL
EDEMA

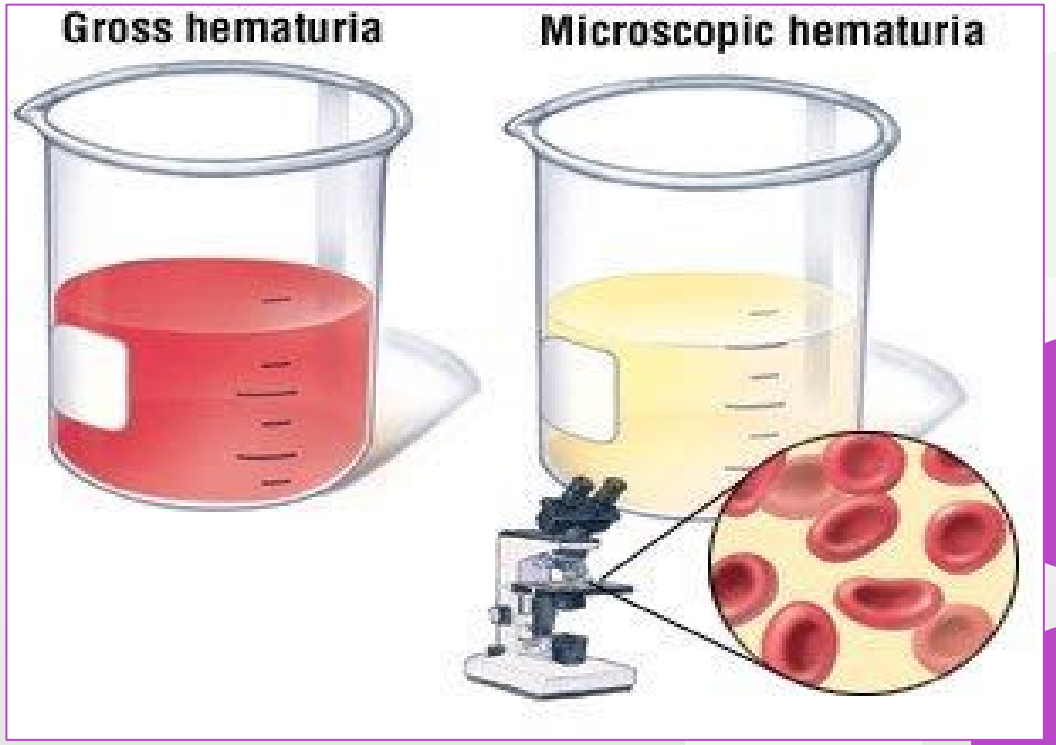


HTN

URINE

Blood in urine (hematuria)

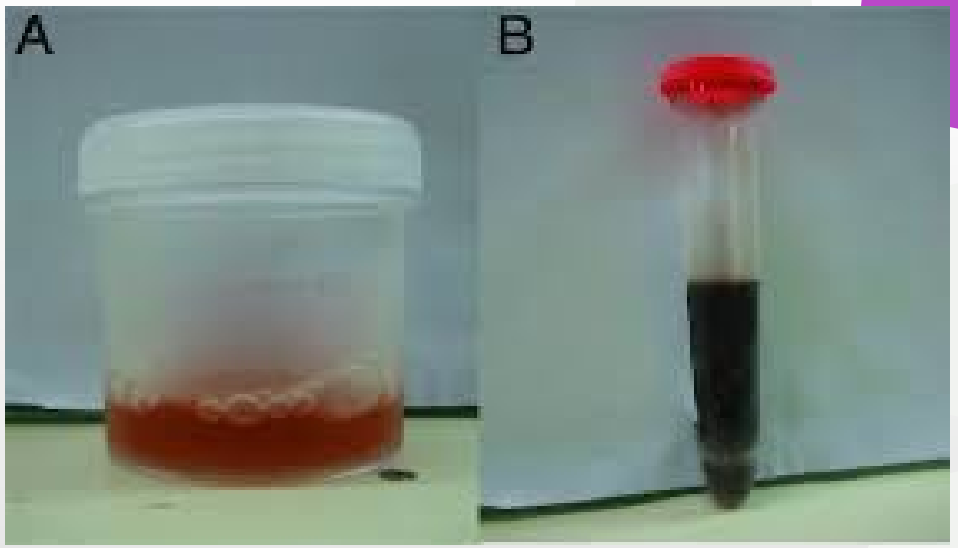




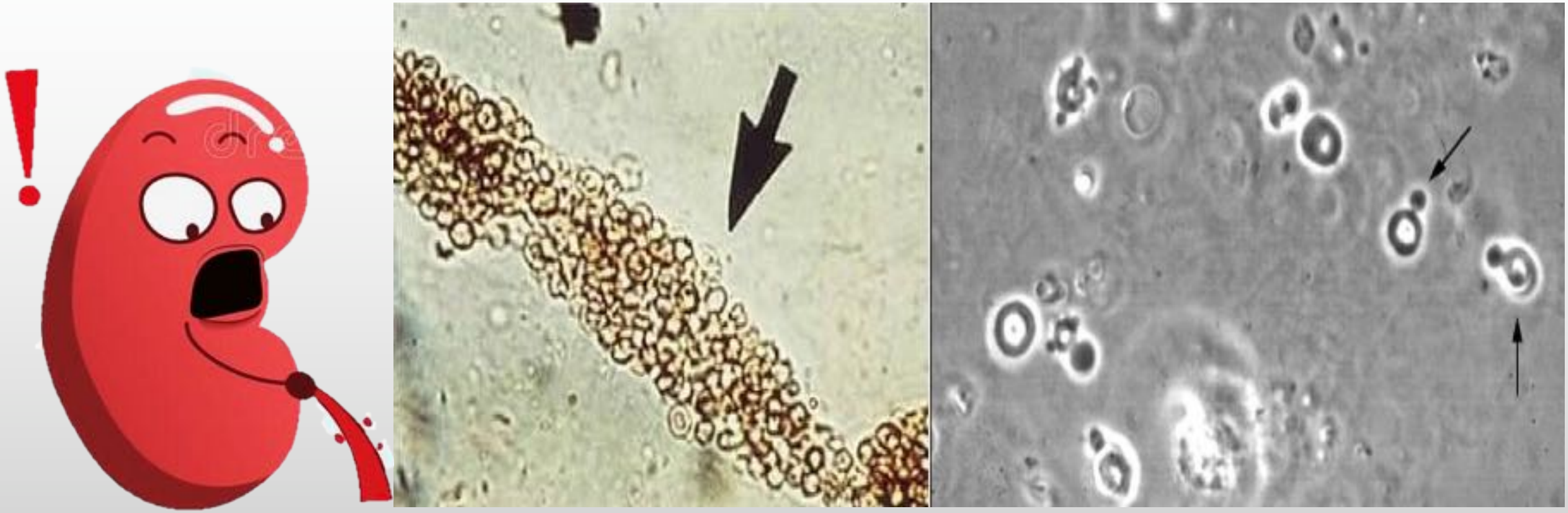
Glomerular hematuria

RBC casts

Dysmorphic RBC


A
B

Urine microscopy of hematuria from a glomerular source demonstrates red blood cell casts and dysmorphic red blood cells.



Mahmoud Kallash, and Michelle N. Rheault Kidney360 2020;1:1014-1020

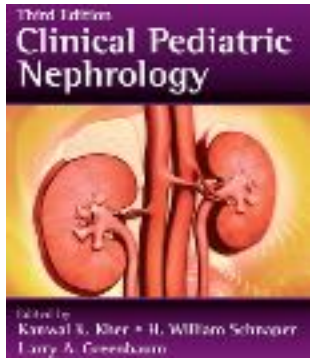
Kidney360

Urinalysis

Hematuria

Proteinuria

Leukocyturia, with a positive leukocyte esterase



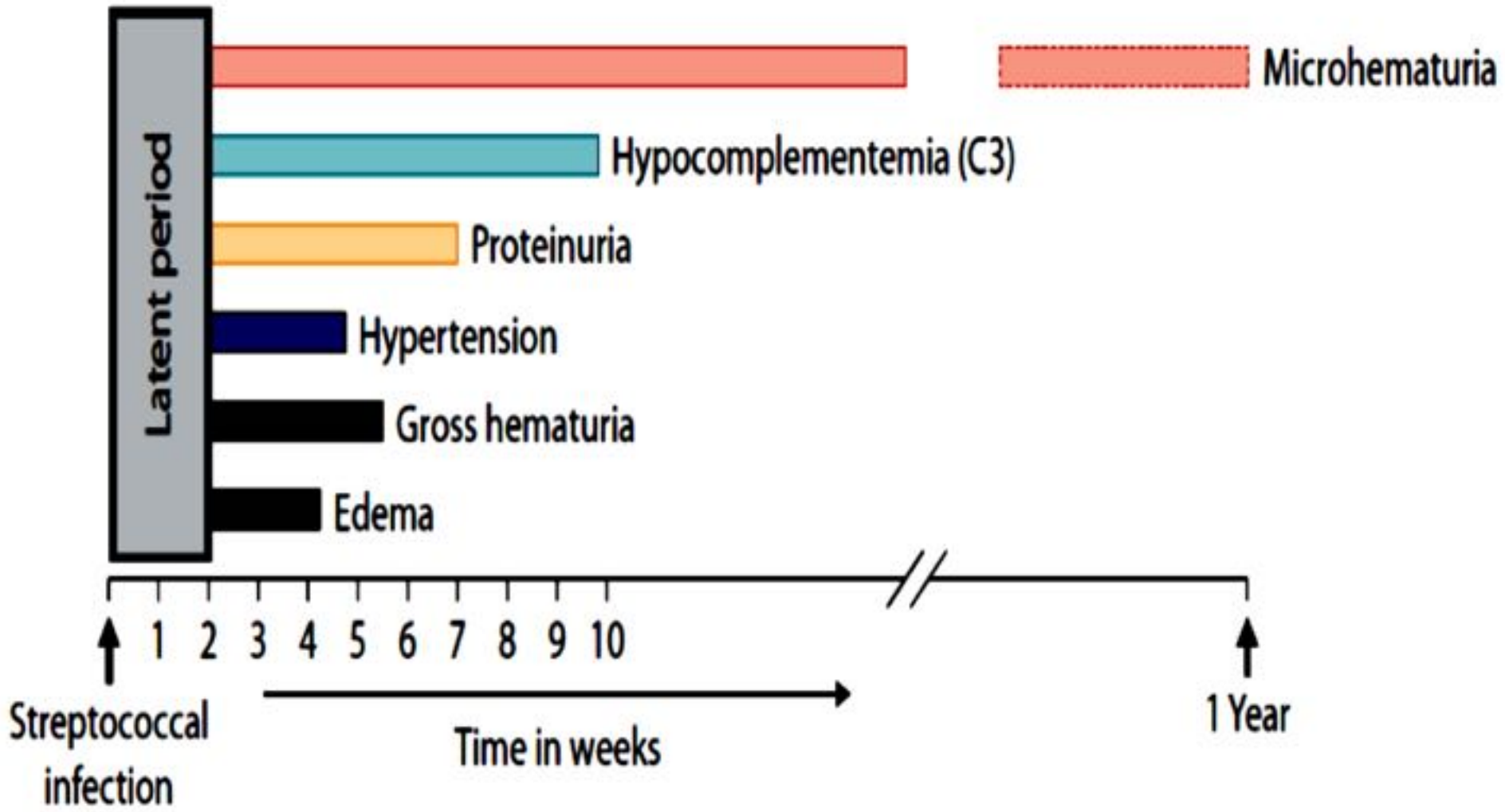


Figure 21.1 Time course of clinical manifestations of acute poststreptococcal glomerulonephritis.

DIEGO H. AVILES & V. MATTI VEHASKARI. Acute Glomerulonephritis.
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

COURSE AND PROGNOSIS of APSGN

ESKD IS RARE

EXCELLENT LONG-TERM OUTCOME

EVEN IN PATIENTS WITH ACUTE CRESCENTIC GN

MICROSCOPIC HEMATURIA AND LOW- LEVEL PROTEINURIA PERSIST IN UP TO 20% OF PATIENTS AS LONG AS 5 YEARS

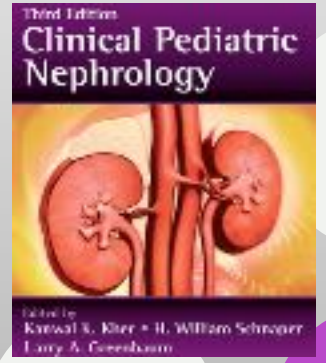
PROGNOSIS IS WORSE IN ADULTS APSGN THAN IN CHILDREN,

INDICATIONS FOR A RENAL BIOPSY in APSGN

1. Rapid deterioration of renal function, raising a suspicion of RPGN, MPGN, SLE-associated nephritis & IgA nephropathy.

2. Persistently low C3 beyond 8 weeks,

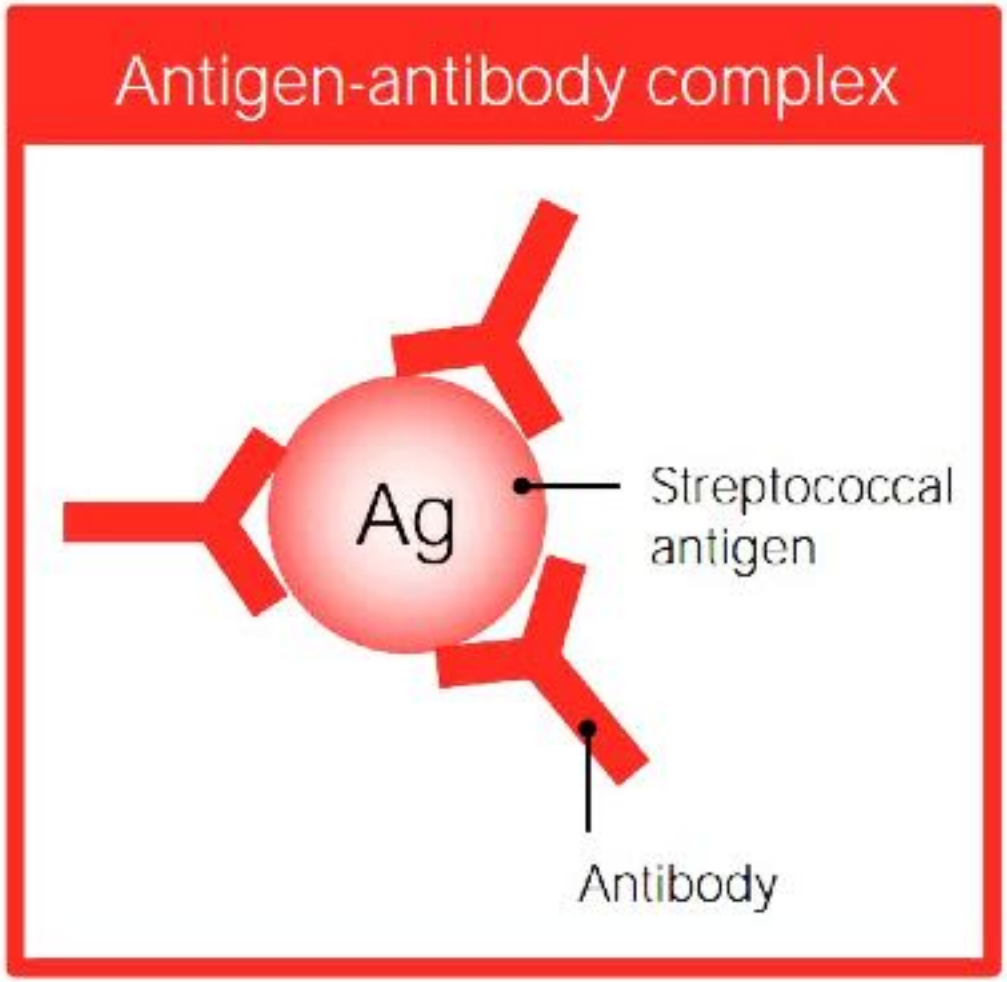
3. Prolonged proteinuria > 6 weeks to rule out chronic GN (MPGN or C3-associated nephropathy).



DIEGO H. AVILES & V. MATTI VEHASKARI. Acute Glomerulonephritis.
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

ANTIBIOTIC TREATME

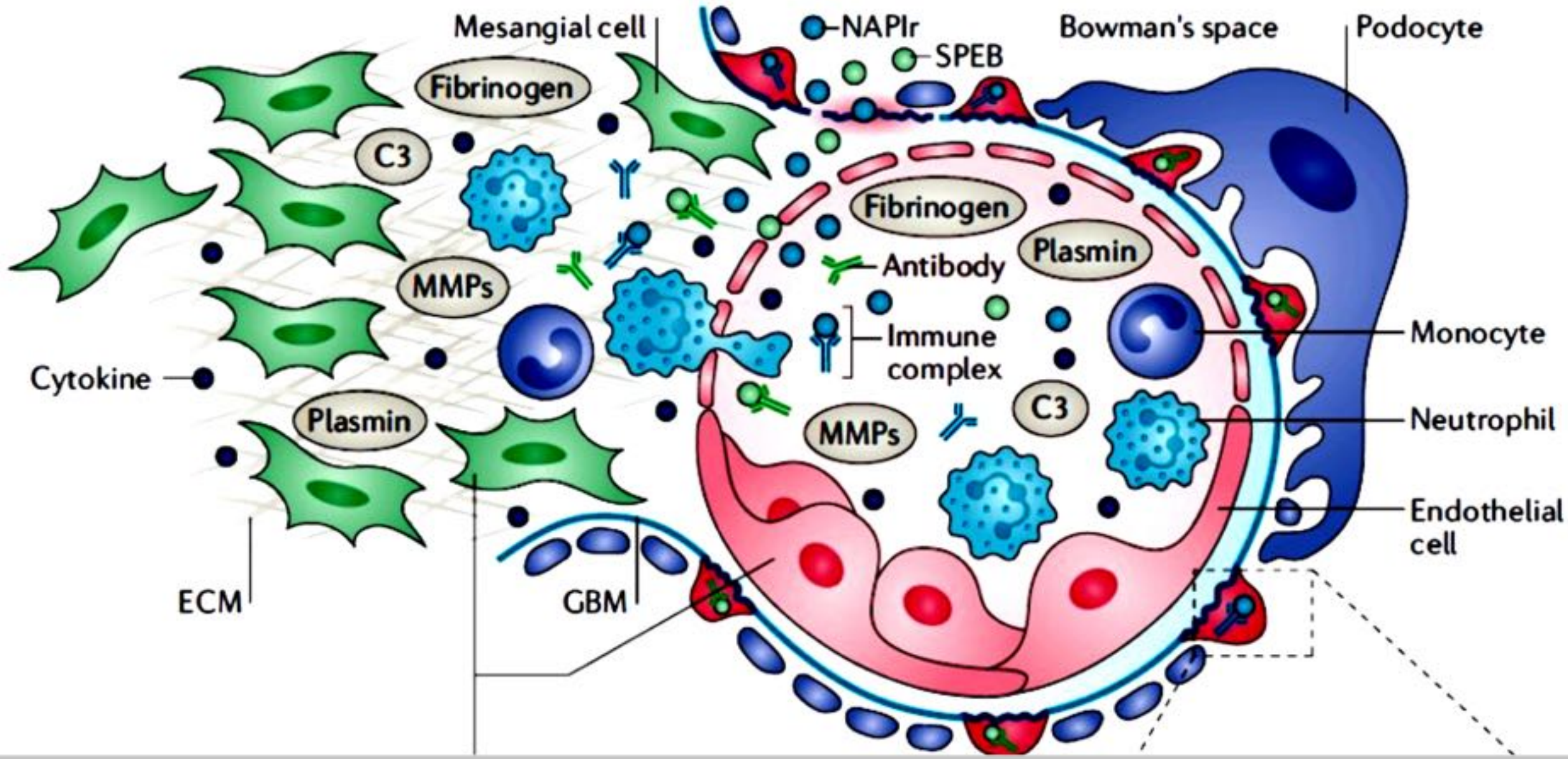
- After onset of APSGN does not alter the course of the disease.
- Prophylaxis given to family members may reduce the risk of APSGN.
- Prophylaxis outside the household contacts, is not recommended.



A complex interplay of environmental triggers, genetic predisposition & dysregulated immunity lead to formation & accumulation of immune complexes in the glomeruli. The immune complexes triggers influx of effector immune cells, cytokine release & matrix metalloproteinases (MMPs), that damage the glomerular capillary tuft.

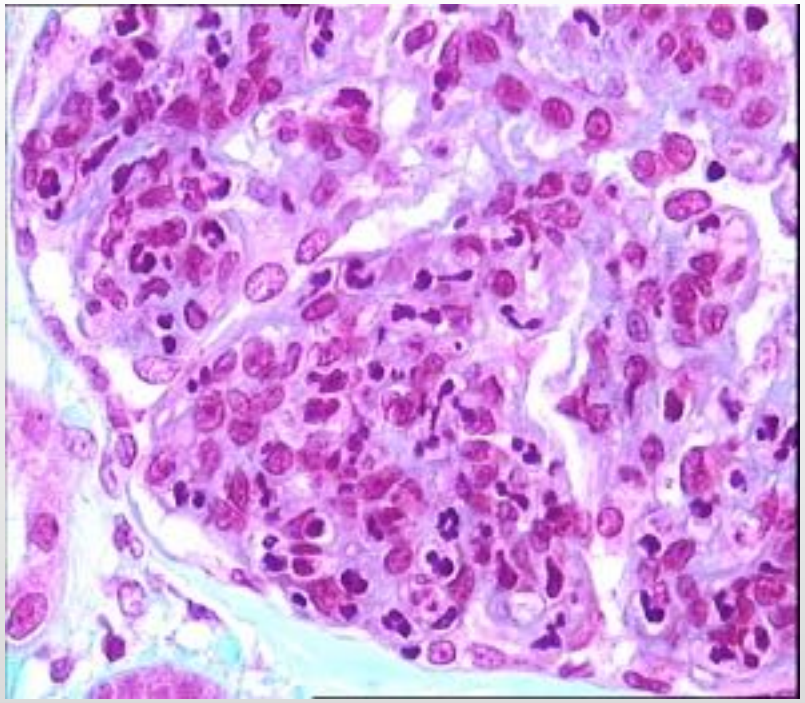
NEPHRITOGENIC ANTIGENS IMPLICATED IN THE PATHOGENESIS OF APSGN

1. nephritis- associated plasmin receptor (NAPlr)
2. streptococcal pyrogenic exotoxin B (SPEB)



Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis. NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

Light Microscopy



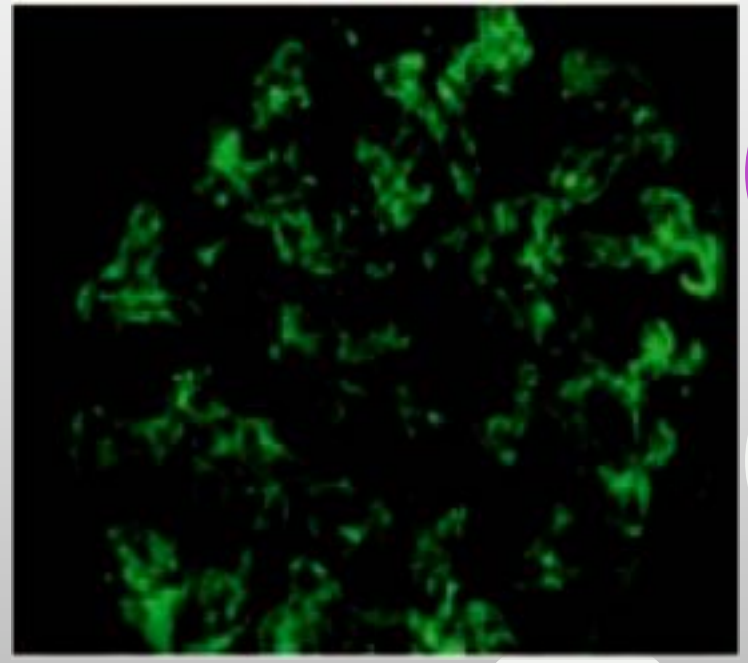
Diffuse proliferative GN (DPGN)

- Diffuse endocapillary & mesangial cell proliferation
- Narrowing of the glomerular capillary lumens
- Infltration of the glomeruli with neutrophils & monocytes

Immunofluorescence microscopy

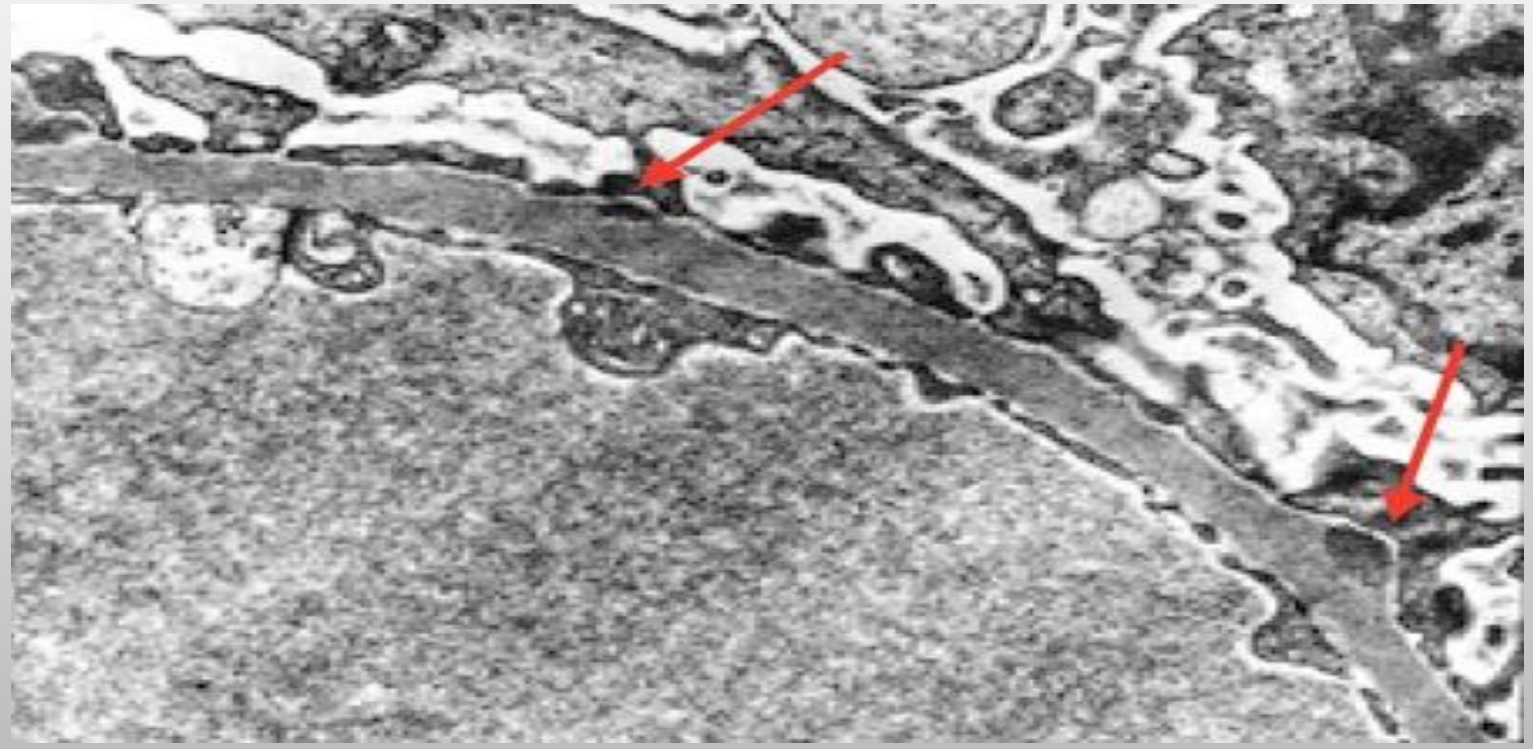
Granular staining of the capillary loops with IgG and complement C3.

1. Starry sky (generalized distribution),
2. Tree stalk (mesangial),
3. Garland (capillary wall).



Electron Microscopy

- Electron-dense deposits (humps) in the subepithelial space
- Characteristic of APSGN.



Now we need a step by step procedure to come up with the perfect solution for the problem

.....

THOROUGH
HISTORY
THOROUGH
HISTORY
THOROUGH
HISTORY
PHYSICAL

Initial evaluation

when APSGN is strongly suspected

1. Urinalysis
2. CBC (rule out HUS)
3. ASOT,C3, C4
4. CXR
5. BUN, creatinine,
6. Electrolytes, serum albumin
7. Urine protein:creatinine ratio

Further evaluation
if APSGN is unlikely

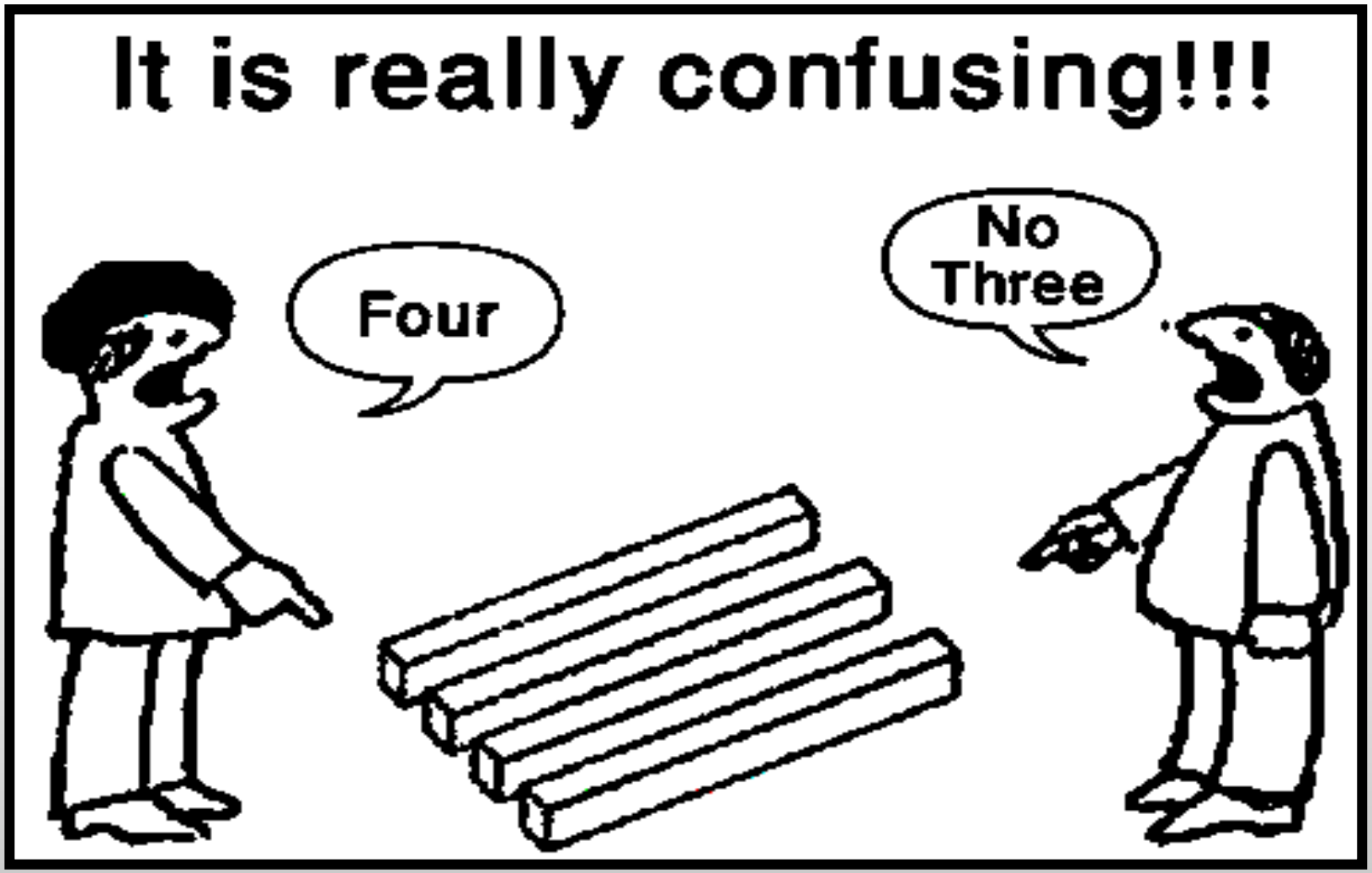
- Hepatitis B panel,
- hepatitis C titer
- HIV-1 antibody
- ANA (full lupus panel if ANA is positive)
- ANCA
- Anti-GBM antibody titer
- Renal biopsy as indicated

Further evaluation

IF CHANGING TRENDS SUSPECTED

- ECHO
- SEPSIS WORK UP,
- ABDOMINAL & PELVIC US

KEEP CALM AND MAKE A DIFFERENTIAL DIAGNOSIS


It is really confusing!!!
Four
No
Three

D.D.

1. MPGN,
2. IgA nephritis,
3. Lupus nephritis,
4. Henoch-Schönlein nephritis.

D.D. MPGN

1. Chronic with acute presentation,
2. Progressive worsening of proteinuria beyond 3 mo,
3. Nephrotic syndrome,
4. Severe hypertension,
5. Failure of C3 to return to normal,
6. Renal biopsy is eventually necessary to clinch the diagnosis

D.D. IgA nephritis

- Misdiagnosed as APSGN because of gross hematuria with respiratory infection.

- However, gross hematuria in IgA nephropathy occurs within 24 to 48 hours of onset of URTI(usually viral) and C3 is normal.

D.D. SLE

- Nephritis may be the first sign of SLE,
- Even before extrarenal manifestations appear.
- Hypocomplementemia in SLE nephritis further complicate the distinction between the two disorders.
- ANA & anti–double-stranded DNA antibody


KEEP
CALM
AND BE
OPEN
MINDED
imdancingintherain.com

Changing Trends

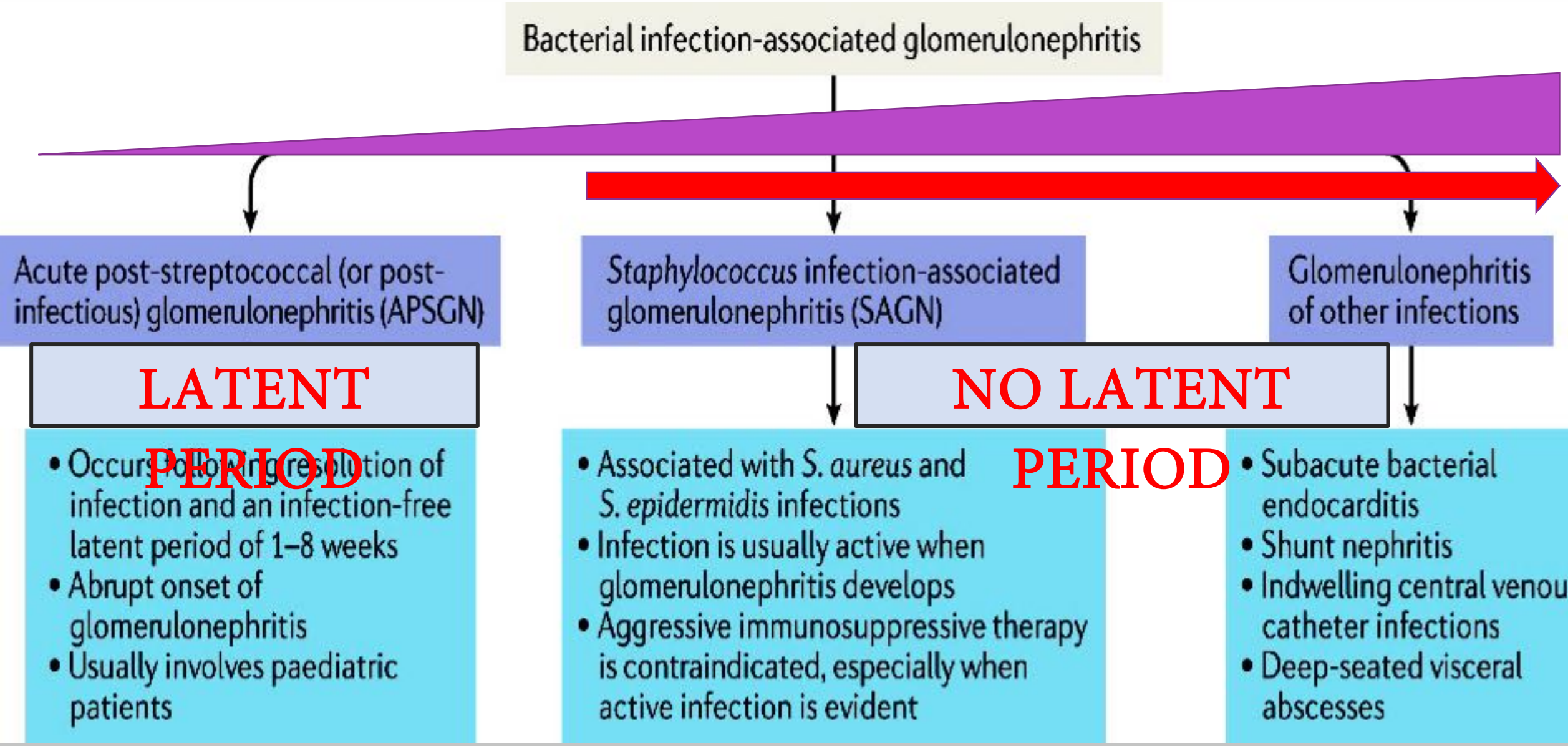
Changing Trends

Before	APSGN

- Acute poststreptococcal glomerulonephritis (APSGN)
- Pathogeneic agents mainly group A streptococcus
- Age group - pediatric
- Prognosis- complete recovery >95% of patients

Current	PIGN

- Post Infectious glomerulonephritis (PIGN)
- Pathogeneic agent : includes staph and gram negative bacteria
- Age group – older
- Prognosis- complete recovery in 50-60% of patients



Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

Current Global Epidemiology, of Infection Associated GN

- APSGN has sharply declined in the Western world,
- *Staphylococcus* associated GN (SAGN) cases increased,
- (SAGN) is now more prevalent than APSGN, at least in developed countries

Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis. NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

Current Global Epidemiology, of Infection Associated GN

- *Staphylococcus* infections range from superficial skin infections to deep- seated invasive infections such as endocarditis,

- SAGN is markedly different from APSGN

Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis. NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

Feature	APSGN	SAGN
Age group	Mainly paediatric age group (peak incidence in the first decade)	• Mainly adults, between 50 and 80 years of age • Younger patients with IVDU
Bacterial strain	Nephritogenic strains of *Streptococcus pyogenes* (GAS)	MRSA, MSSA, MRSE, MSSE
Type of infection	Streptococcal pharyngitis, tonsillitis, mastoiditis, peritonsillar abscess, otitis media, pyoderma, streptococcal superinfection of scabies	Endocarditis, skin infections (usually leg ulcers), cellulitis, skin abscesses, osteomyelitis, septic arthritis, pneumonia, bacteraemia of unclear source, post-surgical site infections
Infection-free latent period	• 1–2 weeks for streptococcal sore throat • 3–6 weeks for pyogenic streptococcal skin infections • In many patients, GN may remain a subclinical disease	• No infection-free latent period • Infections can be occult and deep-seated • Co-morbid conditions may mask signs of infection. Infection may come to attention after the patient presents with acute nephritis

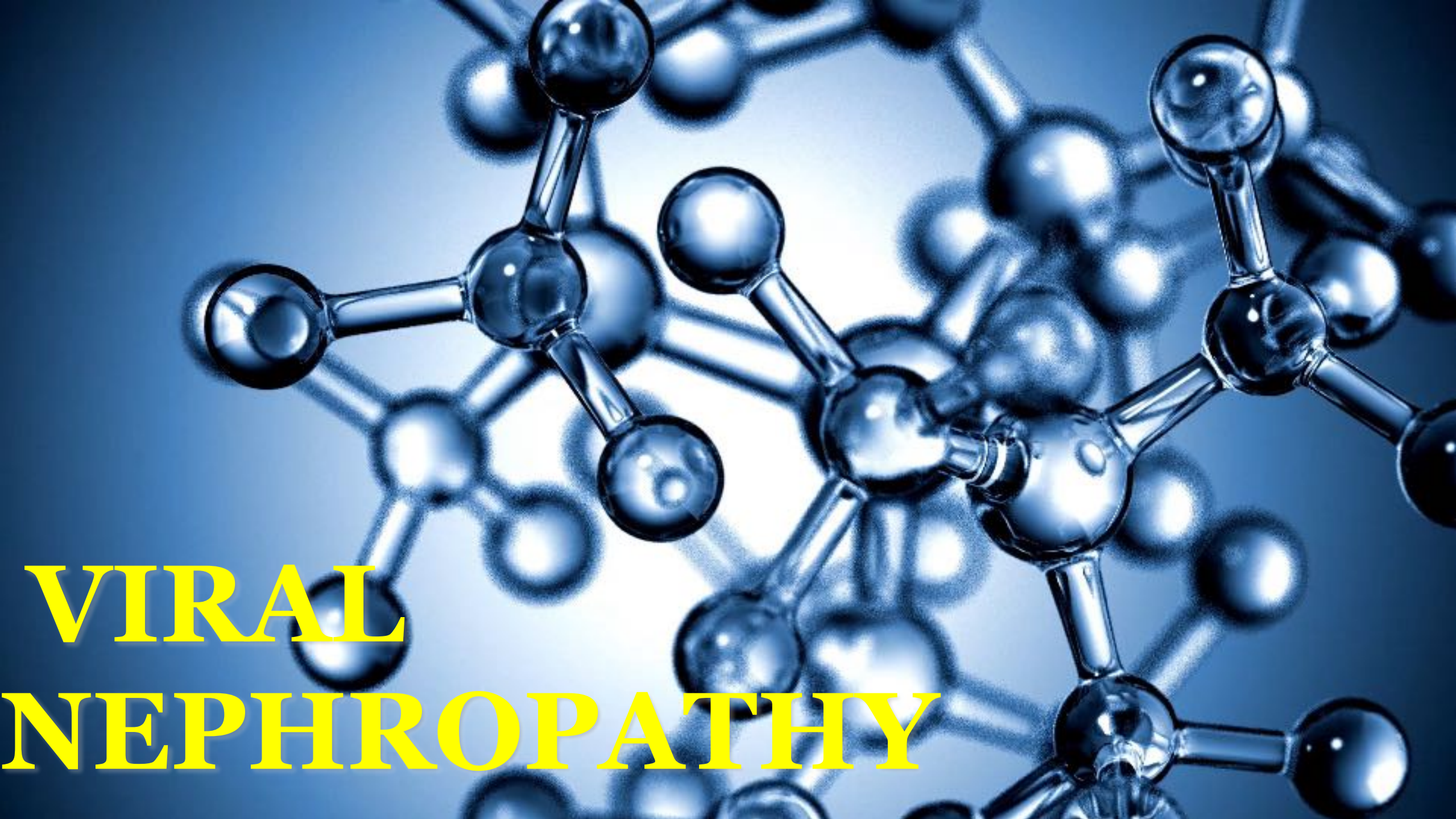
Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis. NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

Feature	APSGN	SAGN
Clinical presentation	• Renal function normal or mildly elevated serum creatinine levels. Dark-coloured urine ('cola-' or 'tea-coloured' urine). Proteinuria sub-nephrotic range • Abrupt onset oedema (prominent facial oedema) • HTN in half of the affected children	• AKI, microscopic haematuria, heavy proteinuria (nephrotic range) • Worsening of underlying co-morbid conditions such as diabetes mellitus, HTN, heart failure • Subset of patients present with LCV rash
Laboratory findings	• Low C3, normal C4 levels • Rising ASO titres	• Low C3 in 30 to 50% of patients, C4 usually normal • Positive ANCA serology in a subset of patients. Often dual positivity for myeloperoxidase and proteinase 3. Usually, titres are low positive
Outcome	• Usually complete recovery in paediatric patients • For adult patients, prognosis is less favourable. Rare cases can progress to chronic kidney disease when the kidney shows numerous crescents	• Prognosis is unpredictable • Poorly controlled diabetes, advanced age, endocarditis, ANCA positivity with crescents in the biopsy portend worse prognosis

Satoskar A, Parikh S and Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection associated glomerulonephritis. NATURE REVIEWS | NEPHROLOGY volume 16 | January 2020.

SAGN is challenging

- Purpuric skin rash similar HSP (20%),
- Positive (ANCA),
- Normal serum C3 levels in > 50%.


VIRAL
NEPHROPATHY

ARE VIRAL NEPHROPATHY BENIGN ?

Respiratory viral infections are associated with relapse of MCD

MacDonald NE,WolfishN,McLaine P, Phipps P, Rossier E. Role of respiratory viruses in exacerbations of primary nephrotic syndrome. *J Pediatr.* (1986) 108:378–82.

ARE VIRAL NEPHROPATHY BENIGN ?

Measle

Varicella

Remission of MCD

Schattner A. Consequence or coincidence?: the occurrence, pathogenesis and significance of autoimmune manifestations after viral vaccines. *Vaccine* (2005) 23:3876–86.

Hepatitis B Virus

MEMBRANOUS GLOMERULONEPHRITIS	IgA nephropathy
MPGN CRYOGLOBULINEMIC GN	POLYARTERITIS NODOSA (PAN)

MGN is more common in children whereas (MPGN) and IgA,N are common in adults.

Hepatitis C Virus

MIXED

MPGN

CRYOGLOBULINE MIA

PAN

HIV-1	• Collapsing glomerulopathy
	• Glomerulonephritis
	  • Lupus-like glomerulonephritis
	  • Membranoproliferative glomerulonephritis
	  • IgA nephropathy
	• Others
	  • Membranous nephropathy
	  • Fibrillary and immunotactoid nephropathy
	  • Thrombotic microangiopathy

HBV	• Membranous nephropathy—most common in children • Membranoproliferative glomerulonephritis • IgA nephropathy • Polyarteritis nodosa
HCV	• Membranoproliferative glomerulonephropathy (with or without cryoglobulinemia)

VIRAL NEPHROPATHY

- (HIV-1), (HBV) & (HCV),
- (CMV),
- Parvovirus B19 (PVB19),
- Epstein-Barr virus (EBV).

VIRAL NEPHROPATHY

The spectrum IS DIVERSE

The clinical manifestations range from subtle abnormalities, such as sodium wasting, microscopic hematuria, or proteinuria, to severe nephritic syndrome, nephrotic syndrome, (AKI), and (TMA).

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

Kidney lesions associated with **HIV** infection include collapsing glomerulopathy, immune complex disease, thrombotic angiopathy, and drug induced nephrotoxicity.

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

- MN, MPGN, MesPGN, IgA nephropathy, and PAN have been described in patients with chronic **HBV** infection.

- In children: Chronic HBV is most commonly associated with MN

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

MPGN is the predominant glomerular disease associated with **HCV**

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

- **PVB19** is the etiologic agent of erythema infectiosum, or fifth disease, a highly contagious childhood exanthem.

- PVB19 has been increasingly reported in association with various renal diseases

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

- AGN & TMA are the most frequently reported renal disease in **PVB19** infection
- AGN typically occurs within **2 weeks** of the viral infection.
- **Hypocomplementemia.**

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

PARVOVIRUS B19 ACUTE NEPHRITIC SYNDROME

- **Onset 2 weeks** (3-45 days) after infection
  - **Hypocomplementemia**
  - Proteinuria
- **Renal biopsy:** Mesangial proliferative glomerulopathy, TMA, FSGS, Collapsing glomerulopathy.

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

VIRAL NEPHROPATHY

- Although the most common clinical presentation with **EBV** infection is infectious mononucleosis in adolescents and adults, most EBV infections are asymptomatic or nonspecific in infants and children.

JEFFREY B. KOPP. Kidney in viral infections
Clinical Pediatric Nephrology , 3rd Edition. ED: Karrwal K. Kher, H. William Schnaper, Larry A. Greenbaum

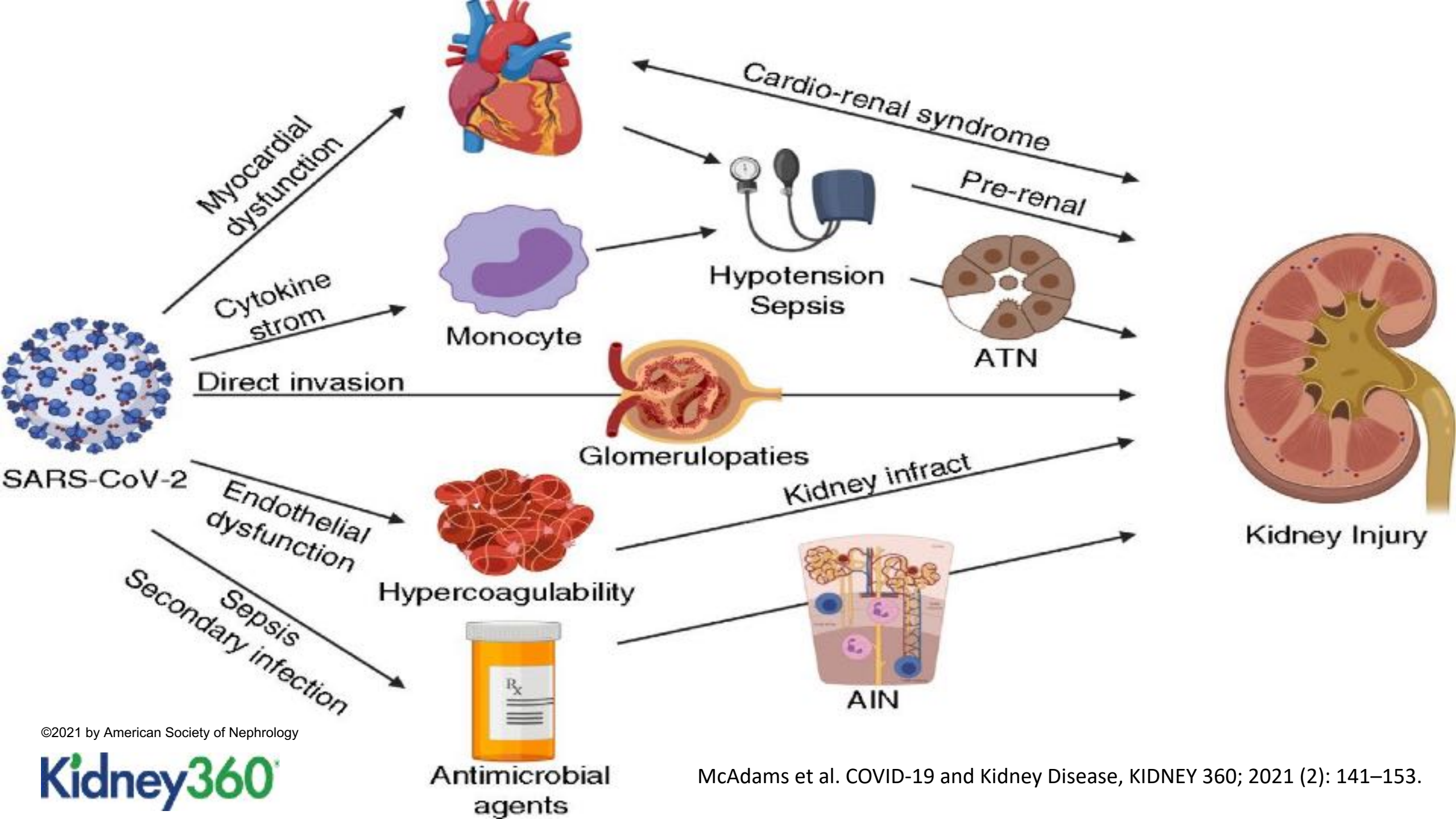
EBV Nephropathy

- 15% of **patients** with infectious mononucleosis
- **Onset 3-17 days** following clinical onset
    1. Bilateral flank pain
    2. Mild proteinuria
    3. Microscopic hematuria
    4. Acute kidney failure (1.6 -4.8%).
    5. Tubular dysfunctions: Fanconi syndrome, glucosuria, urinary frequency resulting from impaired urine concentrating ability
- **Renal biopsy:** Acute Tubulointerstitial Nephropathy

Immune complex GN, MCNS HUS are rare.

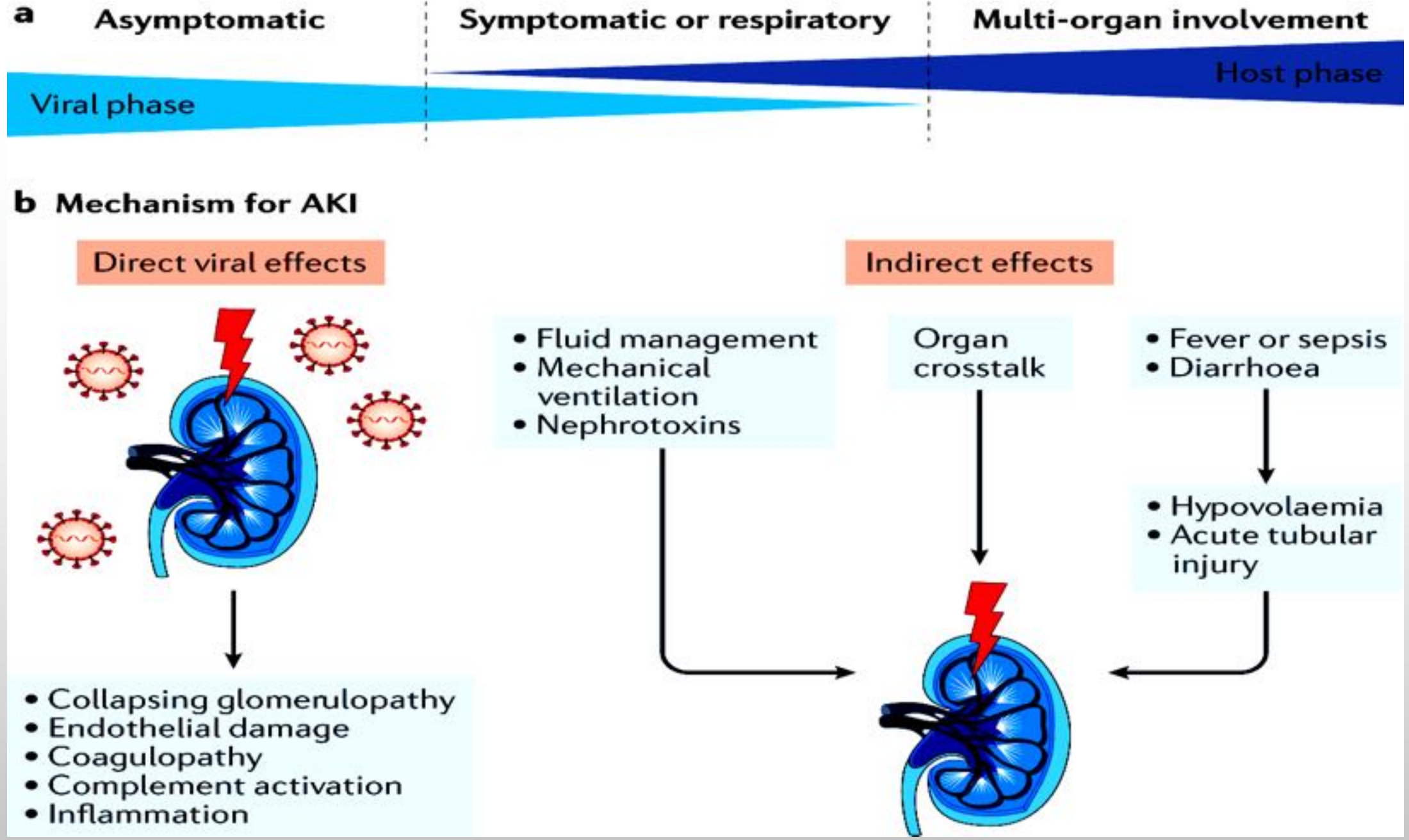
Mechanisms of viral nephropathy.

They may cause disease by infecting the cells, such as HIV, but frequently they cause disease through the formation of immune complexes, as is the case with hepatitis viruses.



Kidney360

McAdams et al. COVID-19 and Kidney Disease, KIDNEY 360; 2021 (2): 141–153.



Nadim, M.K., Forni, L.G., Mehta, R.L. *et al.* COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. *Nature Reviews Nephrology* **volume 16**, pages747–764 (2020)

DIRECT VIRAL EFFECT

- *In situ* immune-mediated mechanisms
- Expression of proinflammatory factors in tissue inducing :
  - ✓ necrosis,
  - ✓ apoptosis
  - ✓ cell dysfunction
- Release of cytokines, chemokines, adhesion molecules & growth factors.

TROPISM OF THE VIRUS IN THE KIDNEY

DIRECT CYTOPATHOGENIC EFFECTS

ABNORMAL IMMUNE COMPLEXES,

COMPLEMENT ACTIVATION

ENDOTHELIAL DYSFUNCTION

- nature reviews | **nephrology** volume 16 | December 2020 | 749

INDIRECT VIRAL EFFECT

- HEMODYNAMIC DISTURBANCE
- MULTIORGAN FAILURE
- ORGAN CROSSTALKS
- NEPHROTOXIC DRUGS

DISSEMINATED INTRAVASCULAR COAGULOPATHY

- nature reviews | **nephrology** volume 16 | December 2020 | 749

THROMBOTIC MICROANGIOPATHY (TMA)

- TMA is characterized by the triad of hemolytic anemia, thrombocytopenia, and organ dysfunction, especially renal dysfunction.

- Hemolytic anemia in TMA is microangiopathic, with peripheral smear of blood demonstrating burr cells, helmet cells or schistocytes, and teardrop cells

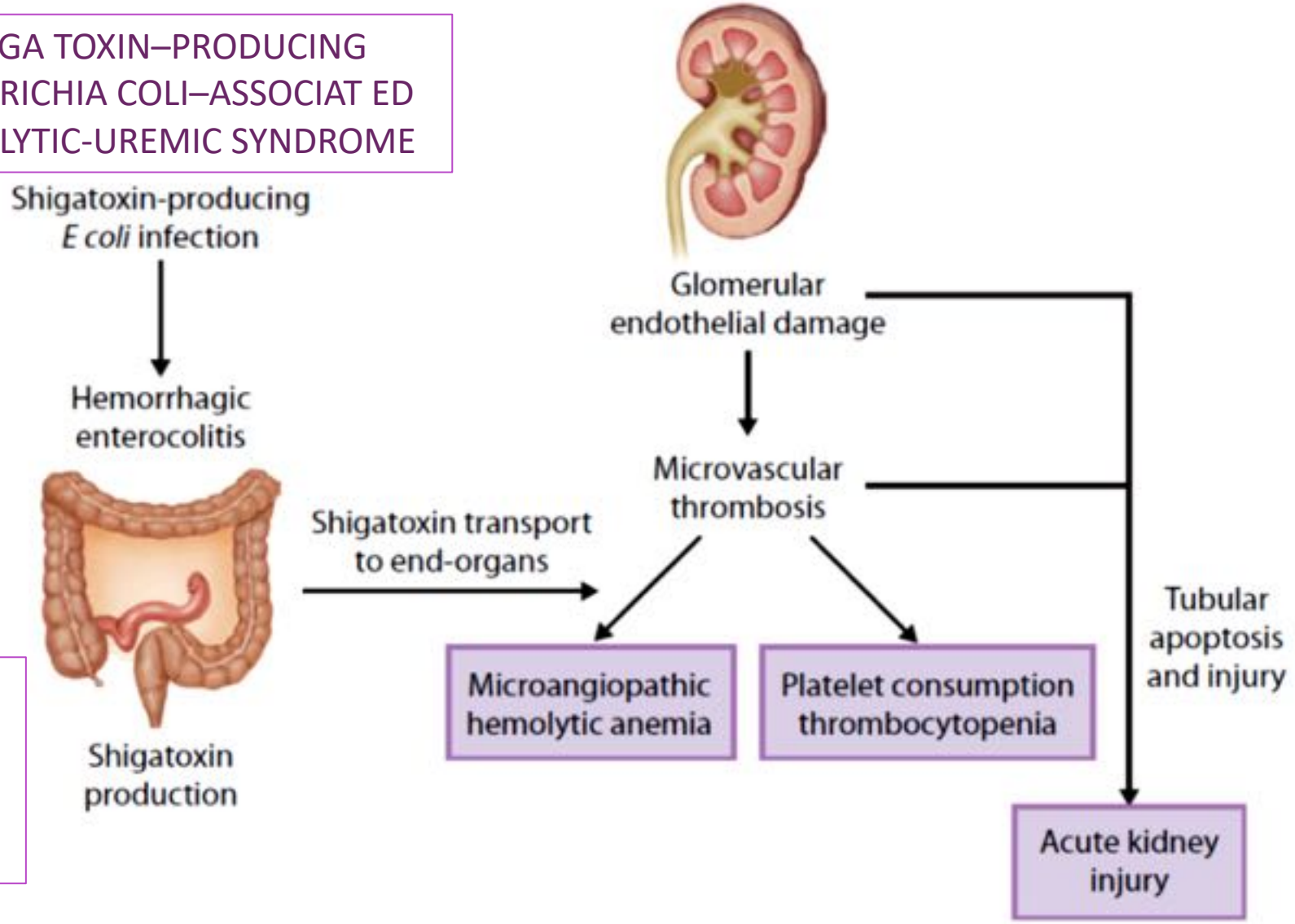
HUS

- *E. coli* (STEC)
- *Streptococcus* pneumonia
- *Mycoplasma pneumoniae*
- HIV infection
- Cocksackie virus, influenza virus
- Epstein-Barr virus
- Rubella
- Histoplasmosis

HUS secondary to *E. coli* infection is the most common form of HUS in children (90%).

E. coli serotype O157:H7 is the most common pathogen associated with STEC-HUS. Other serotypes may be involved in STEC-HUS.

SHIGA TOXIN–PRODUCING ESCHERICHIA COLI–ASSOCIAT ED HEMOLYTIC-UREMIC SYNDROME



STEC-HUS is more common in children younger than 5 years of age

Figure 24.2 Pathogenesis of Shiga toxin–producing *Escherichia coli* hemolytic-uremic syndrome–related acute kidney injury.

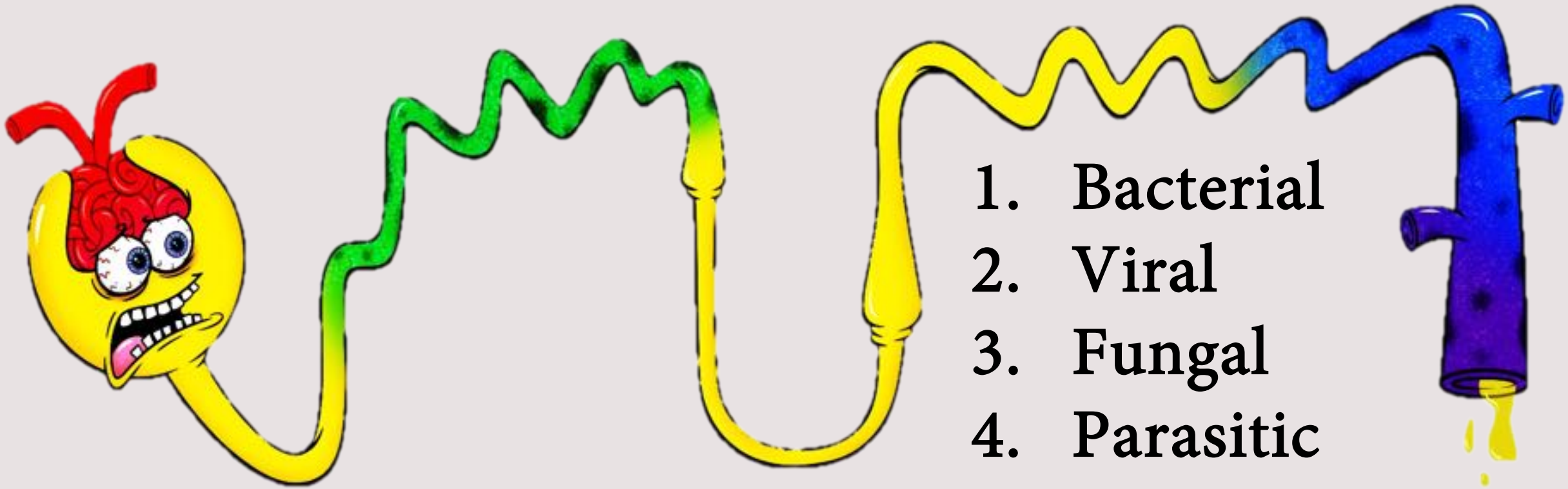
المنتزه سنة ١٩٤٢

قصر السلاملك

وقصر الحرملك

يظهر بجانب المنتزه خربيتا
التى تحولت إلى المعمورة

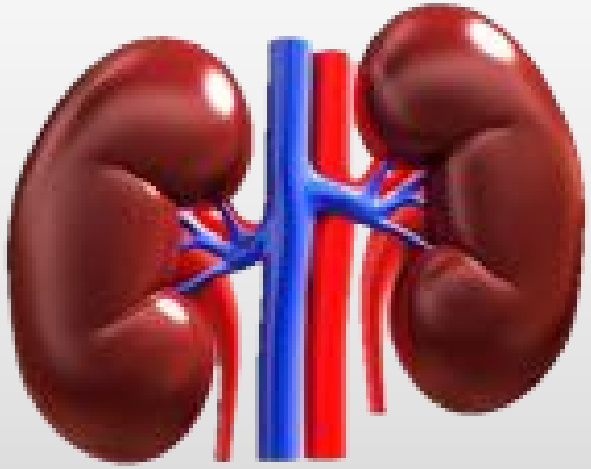
INFECTION INDUCED NEPHROPATHY



1. Bacterial
2. Viral
3. Fungal
4. Parasitic

Directly or Indirectly

Infection induced nephropathy



AKI

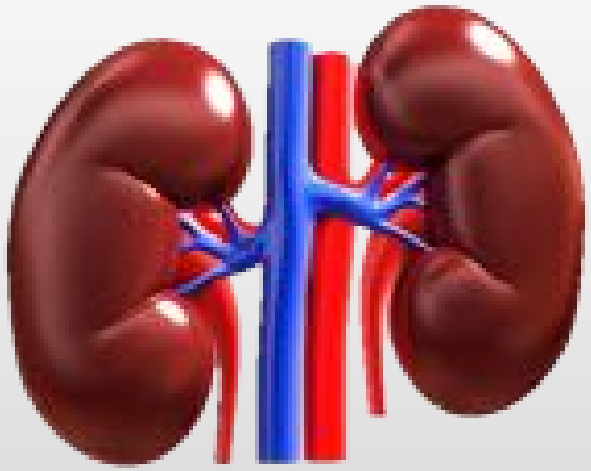
ATN, AIN

HUS, PAN

NEPHROTIC

NEPHRITIC

Infection induced nephropathy



ACUTE

SUBACUTE

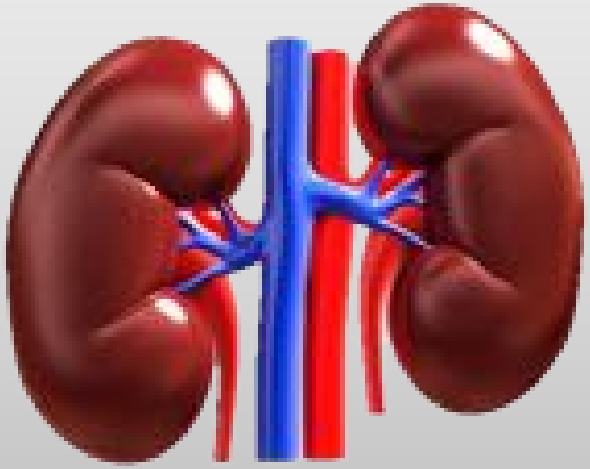
CHRONIC

Infection induced nephropathy

AFTER COMPLETE RESOLUTION OF THE INFECTION

WITH AN ONGOING INFECTION

IN BOTH CASES, INFECTION MIGHT BE ACUTE OR CHRONIC.



Infection induced nephropathy

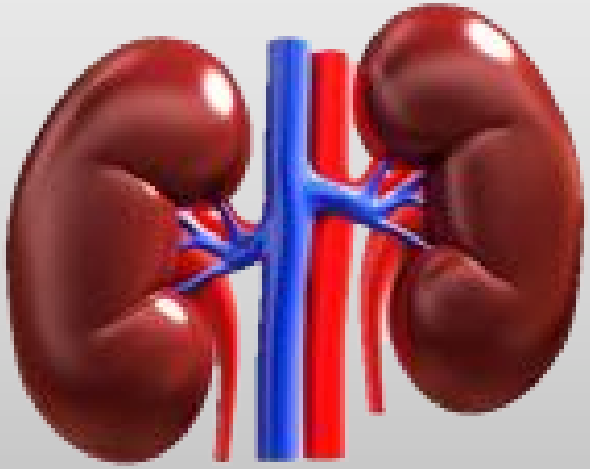
Latent period

Post infection

N

No latent period

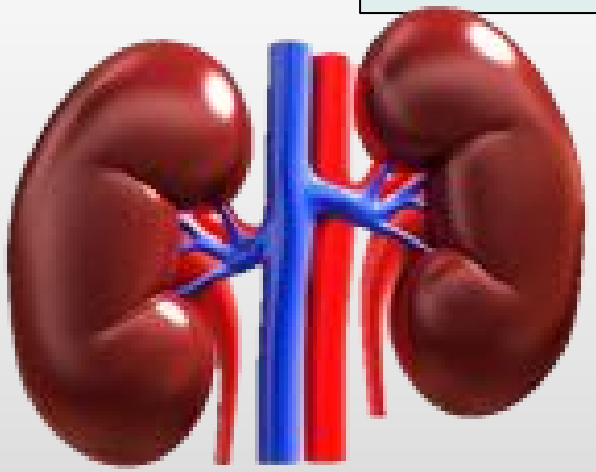
Infection related N



Infection induced nephropathy

IMMUNE COMPLEX–MEDIATED

DIRECT CYTOPATHIC EFFECT



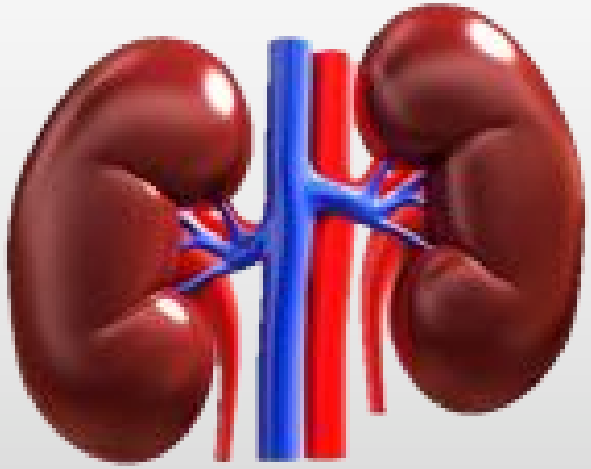
INFLAMMATORY CYTOKINES

COMPLEMENT ACTIVATION

ENDOTHELIAL DYSFUNCTION

Infection induced nephropathy

NEPHROTOXIC THERAPY



ORGAN CROSSTALK

COAGULOPATHY

HEMODYNAMIC INSTABILITY

”اللهم انفعنا بما علمتنا,
وعلمنا ماينفعنا,
وزدنا علما“


Thank you

Be a Problem Solving Ninja

MCQ 1

HIVAN MAY MANIFEST WITH WHICH OF THE FOLLOWING?

A. IMMUNE COMPLEX GLOMERULONEPHRITIS

B. COLLAPSING GLOMERULOPATHY

C. DRUG-INDUCED NEPHROTOXICITY

D. NONE OF THE ABOVE

E. ALL OF THE ABOVE

MCQ2

THE *MOST* COMMON FORM OF KIDNEY DISEASE ASSOCIATED WITH HEPATITIS B INFECTION IS:

A. MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

B. POSTINFECTIOUS GLOMERULONEPHRITIS

C. MINIMAL-CHANGE DISEASE

D. MEMBRANOUS NEPHROPATHY

E. FOCAL SEGMENTAL GLOMERULOSCLEROSIS

MCQ 3

A 9-YEAR-OLD CHILD PRESENTS WITH FEVER, RASH, ENLARGED SPLEEN, AND SWOLLEN GUMS. URINALYSIS SHOWS 2+ PROTEIN AND 3+ BLOOD. A KIDNEY BIOPSY SHOWS A PROLIFERATIVE LESION WITH EPIMEMBRANOUS IMMUNE COMPLEX DEPOSITS. THIS CHILD IS LIKELY TO HAVE INFECTION WITH WHICH OF THE FOLLOWING VIRUSES?

A. HEPATITIS C

B. HEPATITIS B

C. HUMAN IMMUNODEFICIENCY VIRUS-1

D. EPSTEIN-BARR

E. PARVOVIRUS B19