با نام و یاد خدا

Post infectious GN

clinical manifestation
and
Differential diagnosis

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Infection-related renal complications in children

- Direct invasion of renal parenchyma
- Stimulation of an immune reaction
- Injury to the capillary endothelium
- Induction of a humoral response
- Nephrotoxicity associated with the therapy

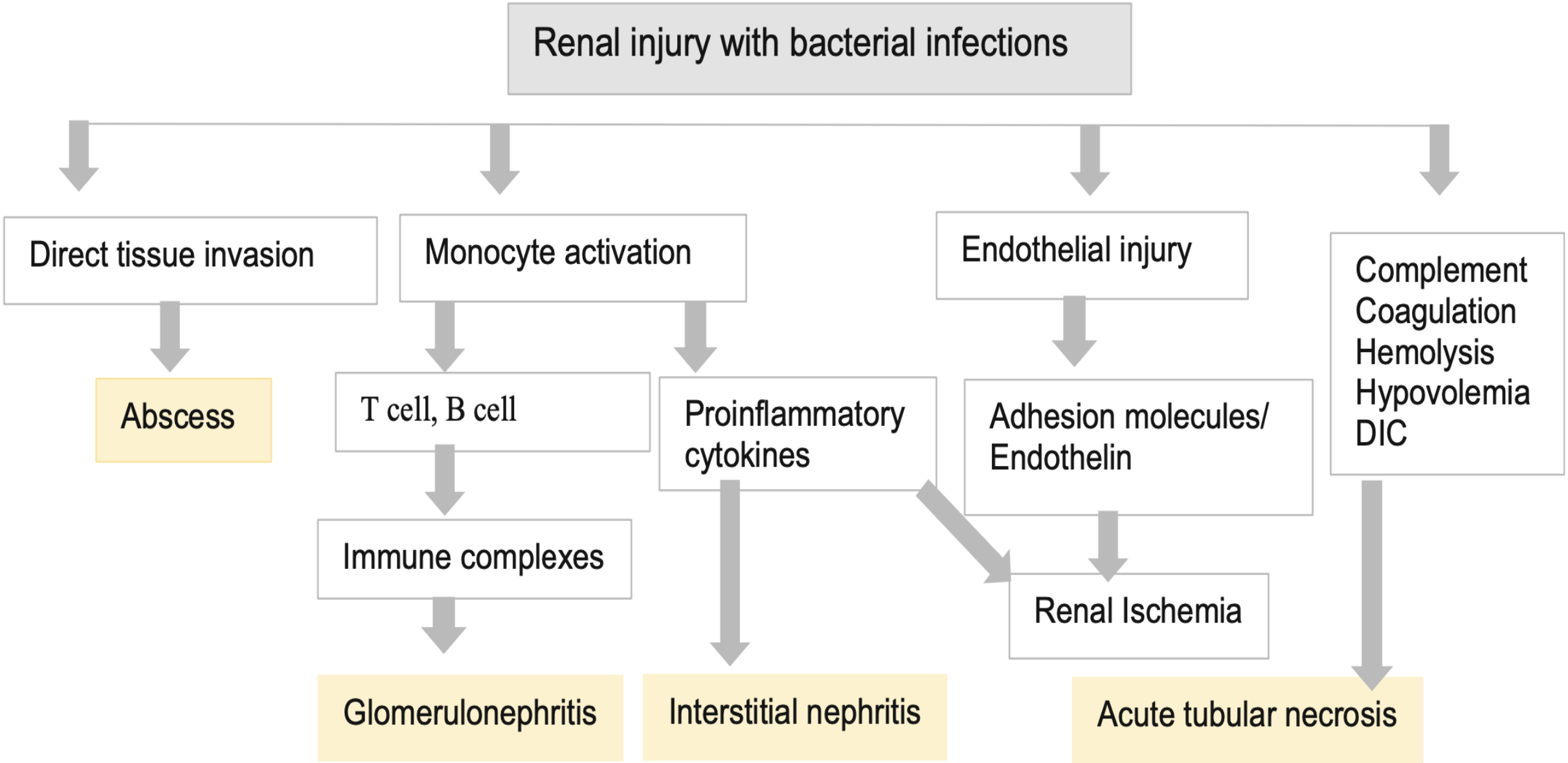

Fig. 1 Mechanisms of renal injury due to bacterial infections. (Adapted from reference [1])

Causes of glomerulonephritis in children

Primary glomerulonephritis
Membranous glomerulonephritis
Immune complex-mediated membranoproliferative glomerulonephritis
C3 glomerulopathies (Dense deposit disease, C3 glomerulonephritis)
IgA nephropathy
Anti-glomerular basement membrane disease
Idiopathic crescentic glomerulonephritis
Secondary glomerulonephritis
Post-streptococcal glomerulonephritis
Other post-infectious glomerulonephritis
Infective endocarditis
IgA vasculitis (Henoch-Schönlein purpura nephritis)
Systemic lupus erythematosus nephritis
Granulomatosis with polyangiitis (formerly called Wegener's granulomatosis)

IgA: immunoglobulin A.

Bacterial and viral agents associated with post-infectious glomerulonephritis

Bacterial infections
Skin or throat (Streptococcus group A)
Endocarditis (Staphylococcus aureus, Streptococcus viridans)
Visceral abcess (Staphylococcus aureus, E. coli, Pseudomonas, Proteus mirabilis)
Shunt nephritis (Staphylococcus aureus, Staphylococcus albus, Streptococcus viridans)
Pneumonia (Diplococcus pneumoniae, Mycoplasma)
Typhoid fever (Salmonella typhi)
Viral infections
Epstein Barr virus
Parvovirus B19
Varicella
Cytomegalovirus infection
Coxsackie
Rubella
Mumps
Hepatitis B
Parasitic infections
Schistosoma mansoni
Plasmodium falciparum
Toxoplasma gondii
Filaria

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PSGN

- PSGN is the most common cause of acute nephritis in children
- Children from 4–14 years old
- Infrequently seen below the age of 2 years or above the age of 20 years
- Boys develop APSGN with twice the frequency of girls
- APSGN usually follows a respiratory or skin streptococcal infection
- The latent period between GAS infection and PSGN is dependent upon the site of infection:
  - One and three weeks following GAS pharyngitis
  - Three and six weeks following GAS skin infection

Clinical presentation

- Asymptomatic, microscopic hematuria
- Acute nephritic syndrome, characterized by:
  - Red to brown urine
  - Proteinuria
  - Edema
  - Hypertension
  - Elevation in serum creatinine

Most common presenting signs in children

- Subclinical cases of PSGN are characterized by microscopic hematuria
- Gross hematuria − Gross hematuria is present in approximately 30 to 50 percent of patients. The urine looks smoky, and tea or cola colored.
- Edema − Generalized edema is present in approximately two-thirds of patients
- In severe cases, fluid overload leads to respiratory distress due to pulmonary edema.
- Hypertension − Hypertension is present in 50 to 90 percent of patients
- Hypertensive encephalopathy is an uncommon but serious complication
- Magnetic resonance imaging (MRI) may show posterior reversible leukoencephalopathy

Laboratory findings

- **Renal function**
  - Rise in serum creatinine. Acute renal failure requiring dialysis is uncommon
- **Urinalysis**
  - Hematuria with or without red blood cell casts
  - Varying degrees of proteinuria. Nephrotic range proteinuria is uncommon(5%)
  - Pyuria
- **Complement**
  - In approximately 90 percent of patients, C3 and CH50 are depressed
  - C4 and C2 levels may below in some patients
  - C3 and CH50 return to normal within four to eight weeks after presentation.
- **Culture**
  - Approximately 25 percent of patients will have either a positive throat or skin culture
  - In patients with impetigo, there is an increased likelihood of obtaining a positive skin culture

Laboratory findings

- **Serology**
  - Elevated titers of antibodies is evidence of a recent GAS infection
  - The streptozyme test, which measures five different streptococcal antibodies, is positive in more than 95 percent of patients due to pharyngitis and approximately 80 percent of those with skin infections. It includes the following antibodies:
    - Anti-streptolysin(ASO)
    - Anti-hyaluronidase(AHase)
    - Anti-streptokinase(ASKase)
    - Anti-nicotinamide-adeninedinucleotidase(anti-NAD)
    - Anti-DNase B antibodies

- Only the anti-DNase B and AHase titers are typically increased after a skin infection.
- The rise in ASO titer may be blunted in patients with pharyngitis who have received antimicrobial therapy.

DIAGNOSIS

- Based upon clinical findings:
  - Acute nephritis
- Demonstration of a recent group A beta-hemolytic streptococcal (GAS) infection.
  - Documentation of a recent GAS infection includes a positive throat or skin culture or serologic tests(eg,anti- streptolysin [ASO] or streptozyme test)
- Low C3 and/or CH50

DIFFERENTIAL DIAGNOSIS

- Progressive disease beyond two weeks,
- Persistent hematuria or hypertension beyond four or six weeks
- There is not adequate documentation of GAS infection
- Persistent urinary abnormalities and hypocomplementemia beyond four to six weeks
- Further elevation in serum creatinine

DIFFERENTIAL DIAGNOSIS

- C3 glomerulopathy
  - Patients with C3 glomerulopathy continue to have persistent urinary abnormalities and hypocomplementemia beyond four to six weeks and possibly a further elevation in serum creatinine.
- MPGN
- IgA nephropathy
- Secondary causes of glomerulonephritis
- Postinfectious GN due to other microbial agents
  - The clinical presentation is similar to that of PSGN except that there is no documentation of an antecedent GAS infection
- RPGN

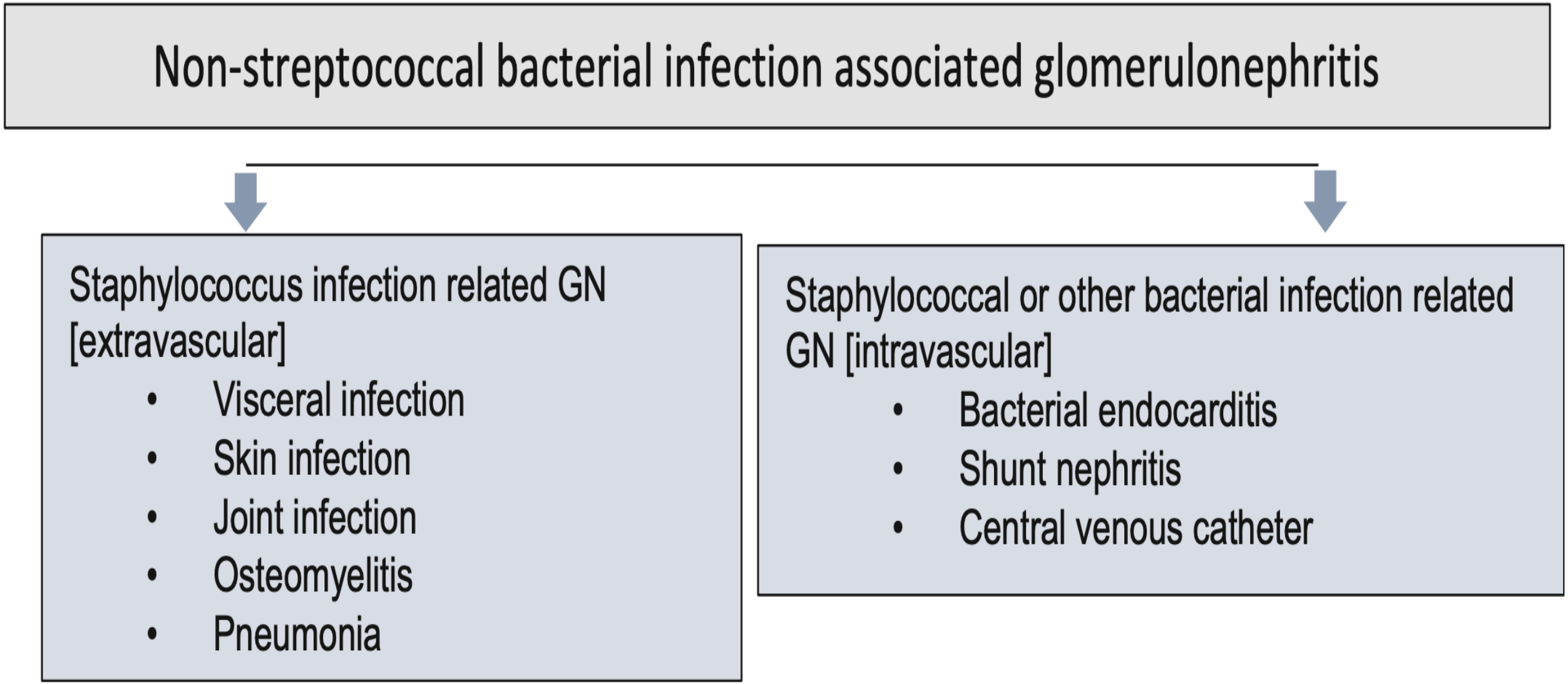

Fig. 5 The clinical entities associated with non-streptococcal glomerulonephritis. (Adapted from Refs. [81, 84])

Table 2 Differences between PSGN and SAGN. (Adapted from reference [77])

Parameters	PSGN	SAGN
Age	Mainly children	Mainly adults, occasionally children
Infection source	Pharyngitis, pyoderma, otitis media, tonsillitis, infected scabies	Endocarditis, skin abscess, leg ulcers, osteomyelitis, septic arthritis, pneumonia
Infection free latent period	Present	Not present
Clinical features	Hematuria, hypertension, oliguria, mild proteinuria, occasionally renal dysfunction	AKI, microscopic hematuria, nephrotic range proteinuria, occasionally leukocytoclastic vasculitis rash
Laboratory features	Low C3, normal C4	Low C3 in 30–50%, normal C4
Renal histopathology	LM: Diffuse exudative proliferative GN	LM: Mesangial hypercellularity, endocapillary proliferation in some, segmental necrotizing lesions common, acute tubular necrosis frequent
	IF:C3 with or without IgG along capillary loops and mesangium EM: Predominantly subepithelial deposits	IF: IgA dominant or codominant with C3 or exclusive C3, pauci-immune in a few. EM: Predominantly mesangial deposits
Outcomes	Usually complete recovery	Unpredictable