



Predisposing factors to urinary tract infections in children

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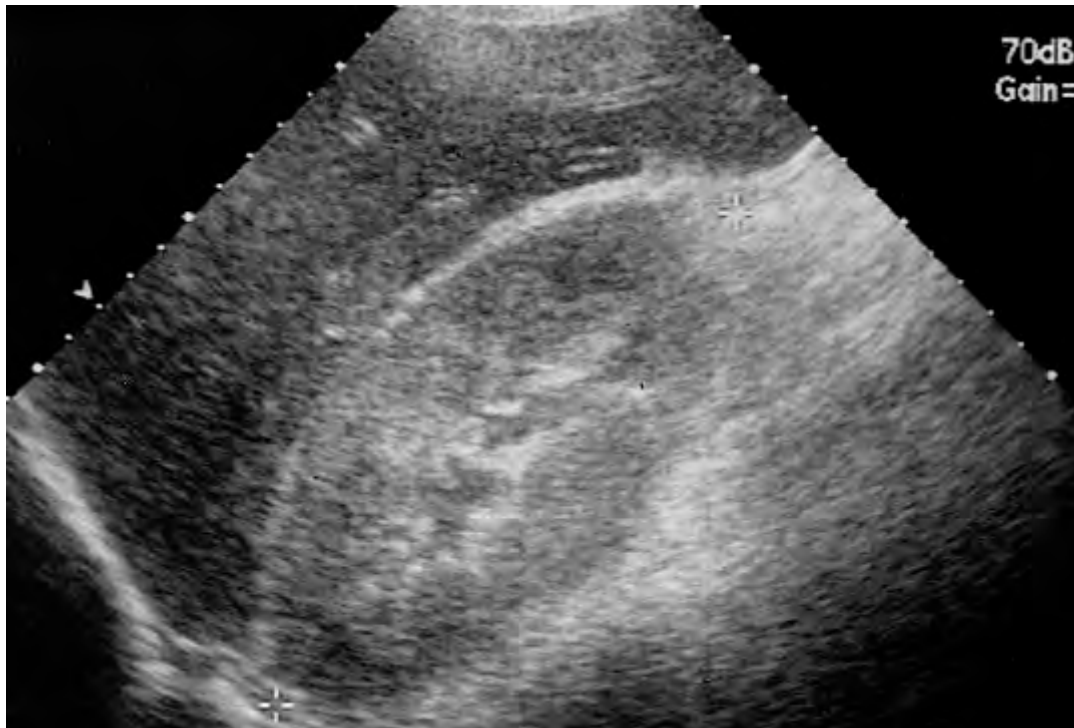
UTI: Predisposing factors

- Virulent bacteria
- Sensitive host

- For a successful treatment one should consider all (known) predisposing factors, in order to
 - Eliminate the infection
 - Prevent recurrences
 - Prevent late complications

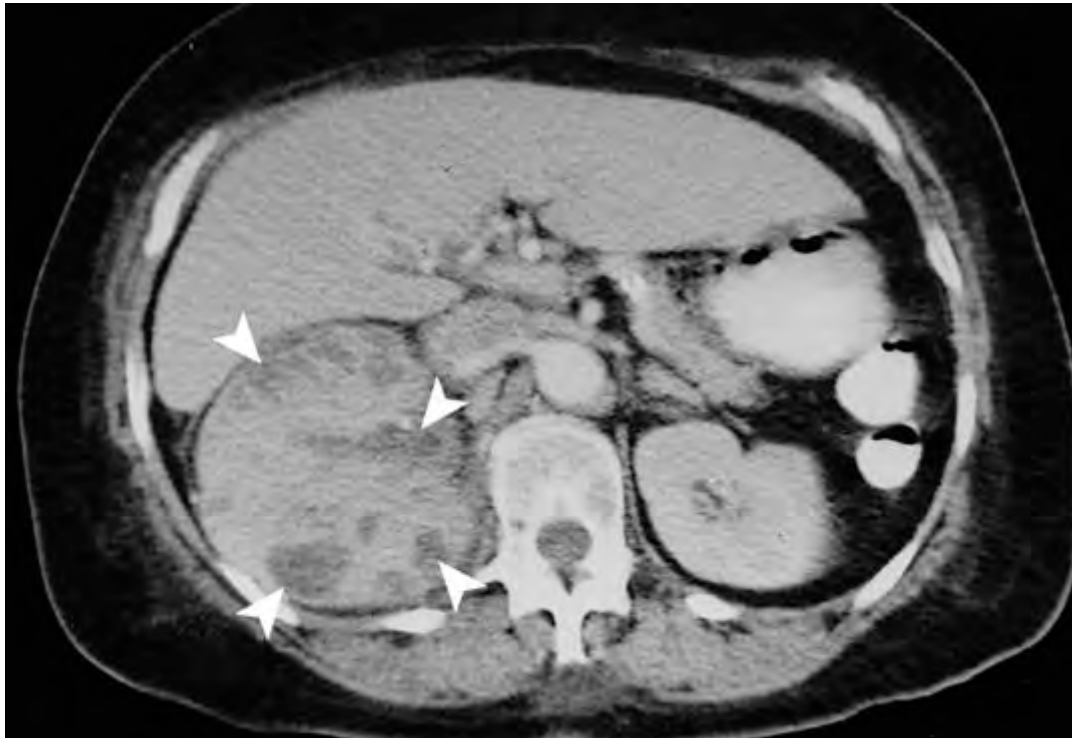
Acute pyelonephritis US (1)

Enlarged kidneys,
Blurred structure, abscess?



Acute pyelonephritis CT (2)

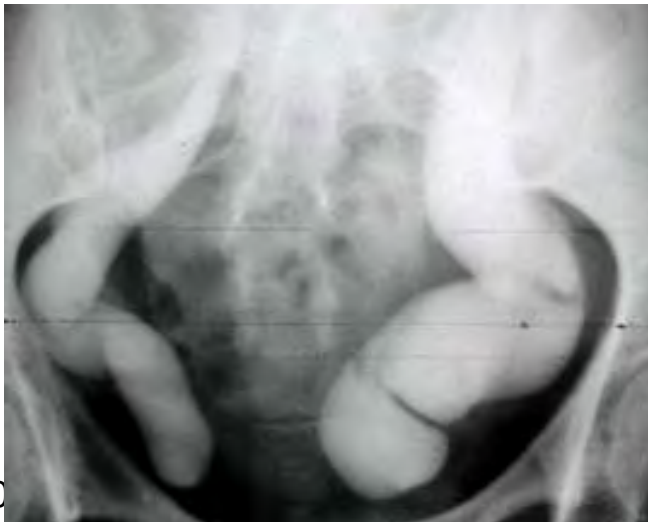
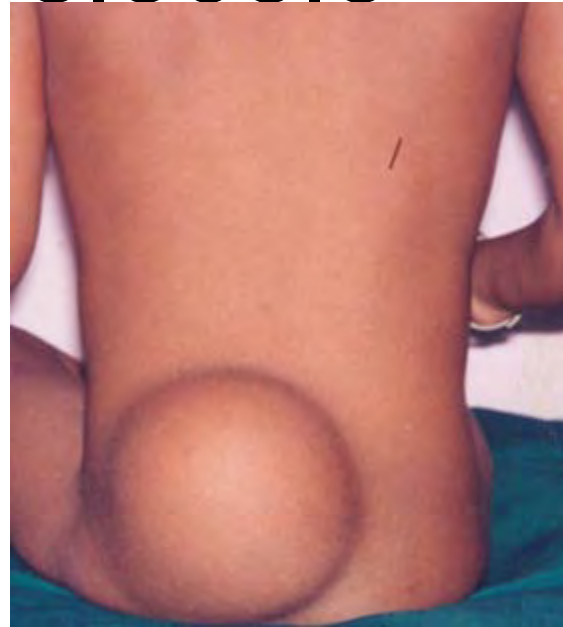
Enlarged kidney,
Multiple abscesses



Prune-belly syndrome



Meningomyelocele

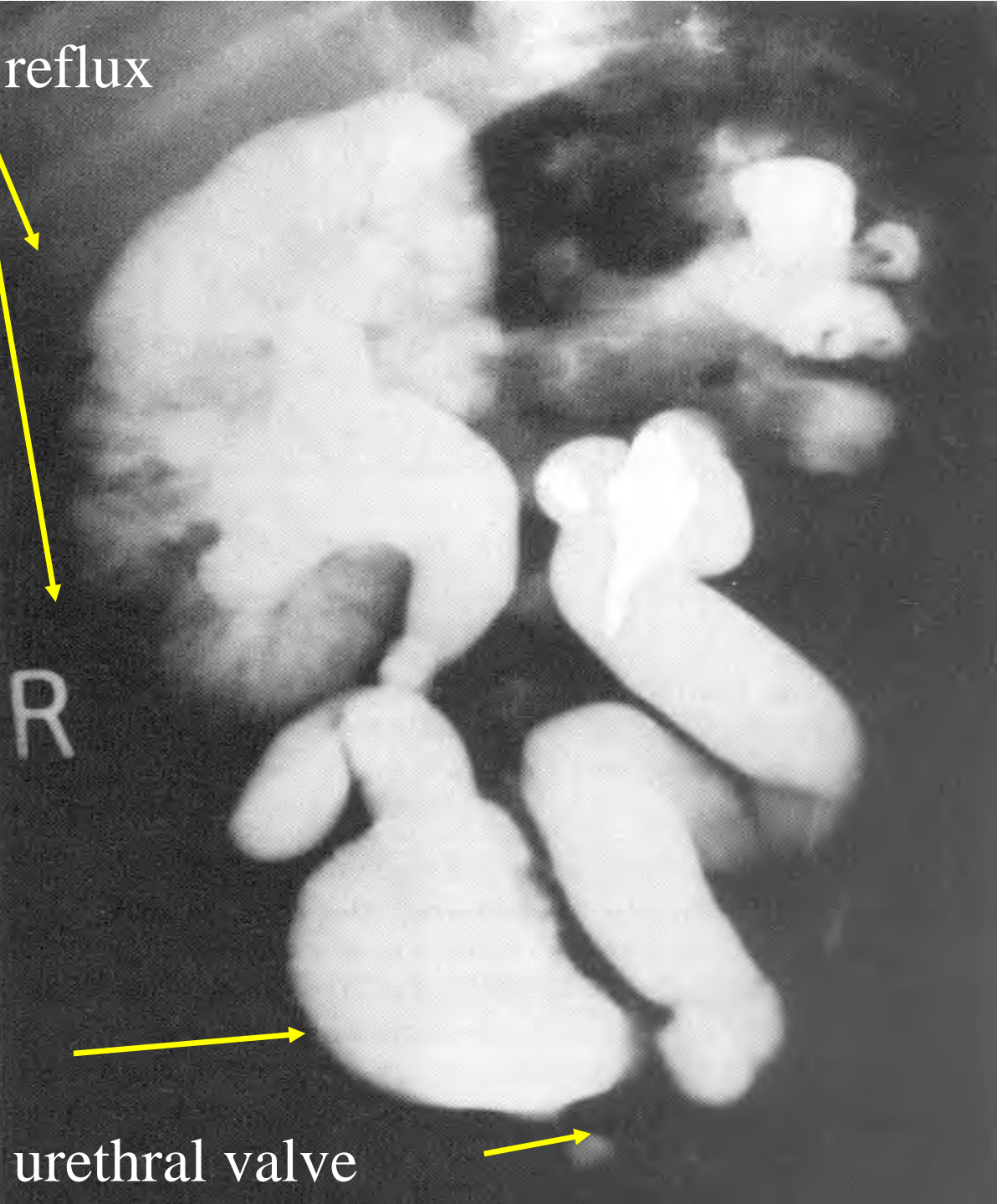


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Intrarenal reflux

R

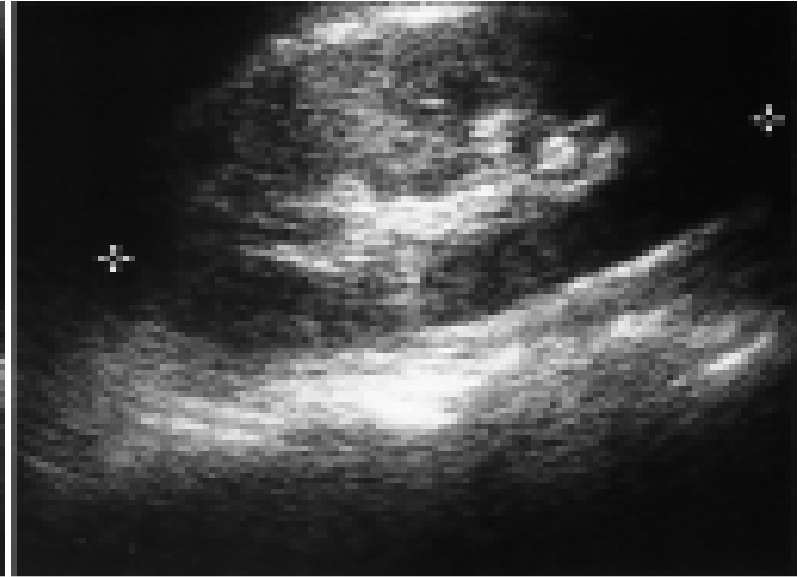
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Posterior urethral valve



Kidney fibrosis

a: small hyperechogenic kidney

b: normal kidney



b



UTI: Predisposing factors

Virulent bacteria

Sensitive host

Bacteria (1)

- Definitions
 - bacteriuria
 - significant bacteriuria
 - cystitis
 - pyelonephritis
 - unspecified
 - asymptomatic bacteriuria
- Sampling techniques
 - collecting bag
 - midstream urine
 - catheter urine
 - suprapubic puncture

Bacteria (2)

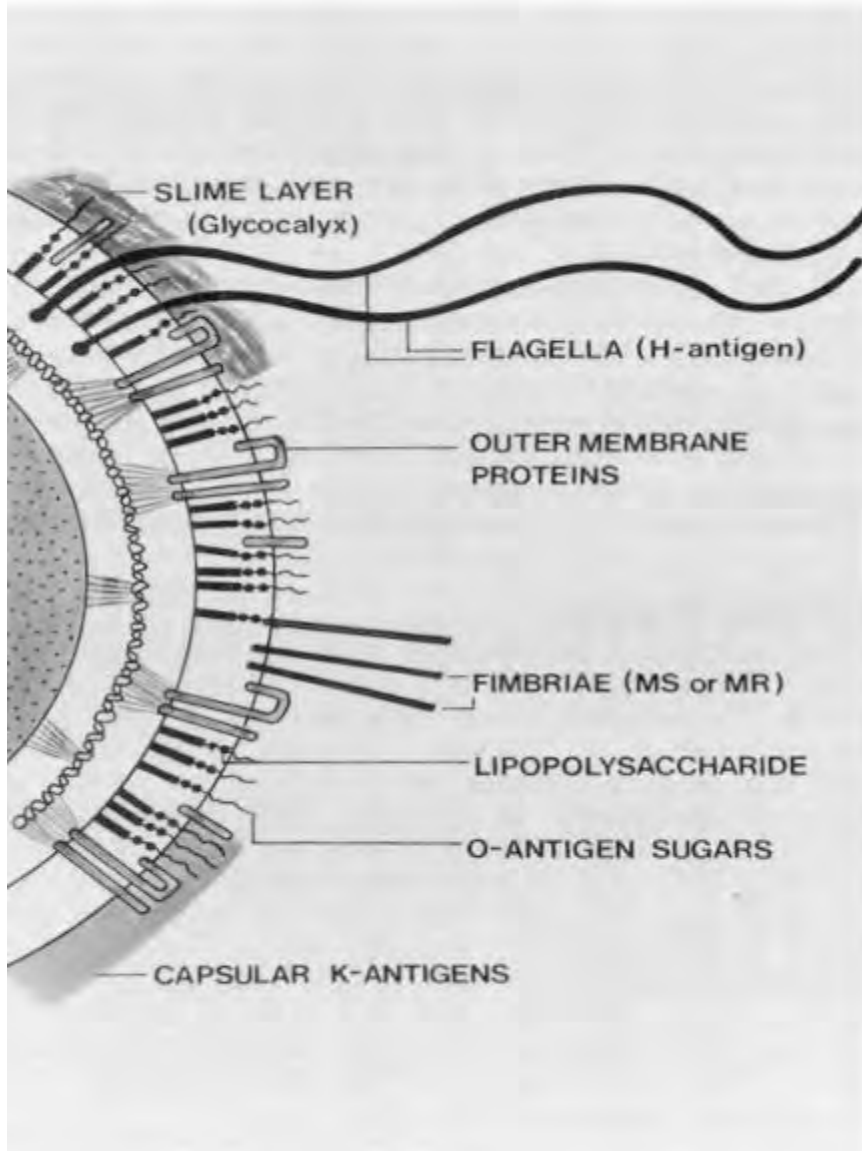
- ERRORS

- Inappropriate sampling – misleading bacteriology – misleading sediment
- Bacteriology should be considered together with urine sediment and the clinical syndrome
- Controls should not rely solely on bacteriology, use urine sediment instead routinely

Bacterial virulence

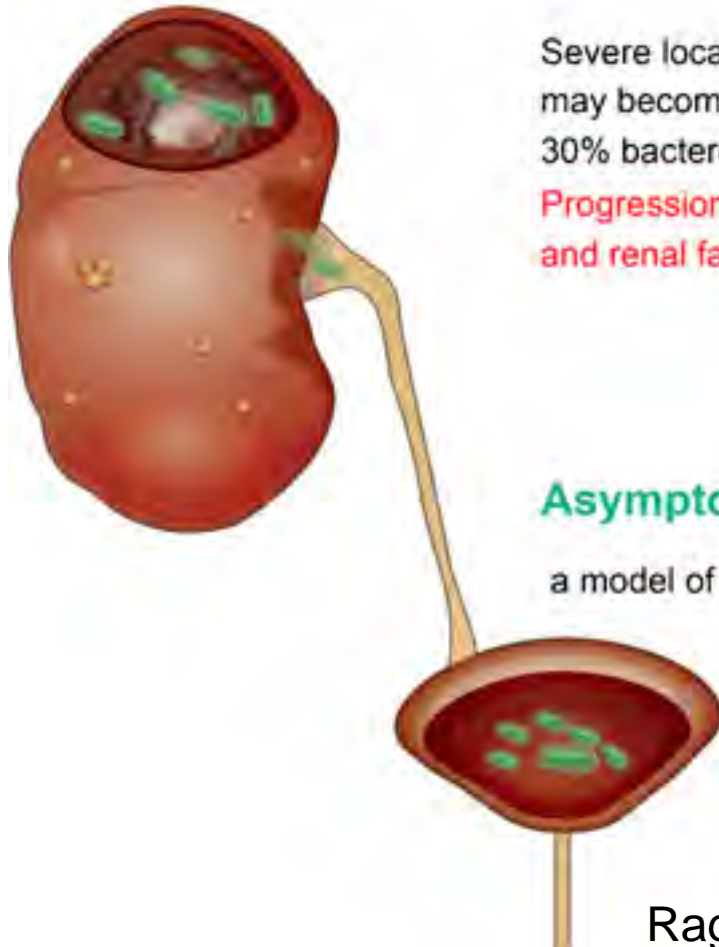
- Virulence=factors that enable bacteria to invade the urinary tract
- Surface antigens
 - O: lipopolysacharides with endotoxin properties. Induces fever, local inflammation
 - K: (capsular) antigen, prevents phagocytosis
- “P” fimbriae: bind to glycolipid receptors of the P blood group family
- A number of additional factors not routinely checked

Bacterial virulence



- Pyelonephritis: 3-4 (known) virulence factors
- Cystitis: 0-2 factors
- CAVE: OBSTRUCTION !!
MALFORMATION !!

Bacterial virulence



Acute pyelonephritis (APN)

Severe local and systemic inflammation, may become life-threatening.
30% bacteremia in adults.

Progression to chronic infection and renal failure

APN strains

Fimbriae,
Toxins
Capsules,
iron binding molecules
Inhibitors of innate immunity

Asymptomatic bacteriuria (ABU)

a model of commensalism in the bladder

ABU strains

Attenuated pathogens
Smaller genome size
virulence genes contain deletions or mutations

Bacterial virulence

Bacterial spectrum at the 1st Dept. of Pediatrics

N=7850	(%)
• E. coli	49
• Enterococcus faecalis	13
• Proteus indol neg.	10
• Klebsiella	7
• Pseudomonas spp	7
• Enterobacter spp	6
• Proteus indol pos	3
• Staphylococcus	3
• Other	2

UTI: Predisposing factors

- Virulent bacterium
- **Sensitive host**

Sensitive host

- **Age related factors**

- Anatomy (short urethra, phimosis and adhesio cellularis preputii et labia minora, diaper, obesity)
- colonization
- Immunological susceptibility
 - Mucosal barrier
 - » Inherited/acquired (innate immunity: IL8, TLR) (Karoly E et al: Pediatr Res 2006; 61:371–374)
 - Age related immunresponse
 - » Inherited/acquired

Innate rather than adaptive immunity is essential for bacterial clearance during UTIs

T, B cell or RAG mutant mice are fully resistant to UTI.

Tlr4^{-/-} mice become asymptomatic carriers with low innate immune responses.

mCxcr2^{-/-} (IL-8 receptor deficient) mice develop acute, lethal septic pyelonephritis and surviving mice develop chronic renal damage.



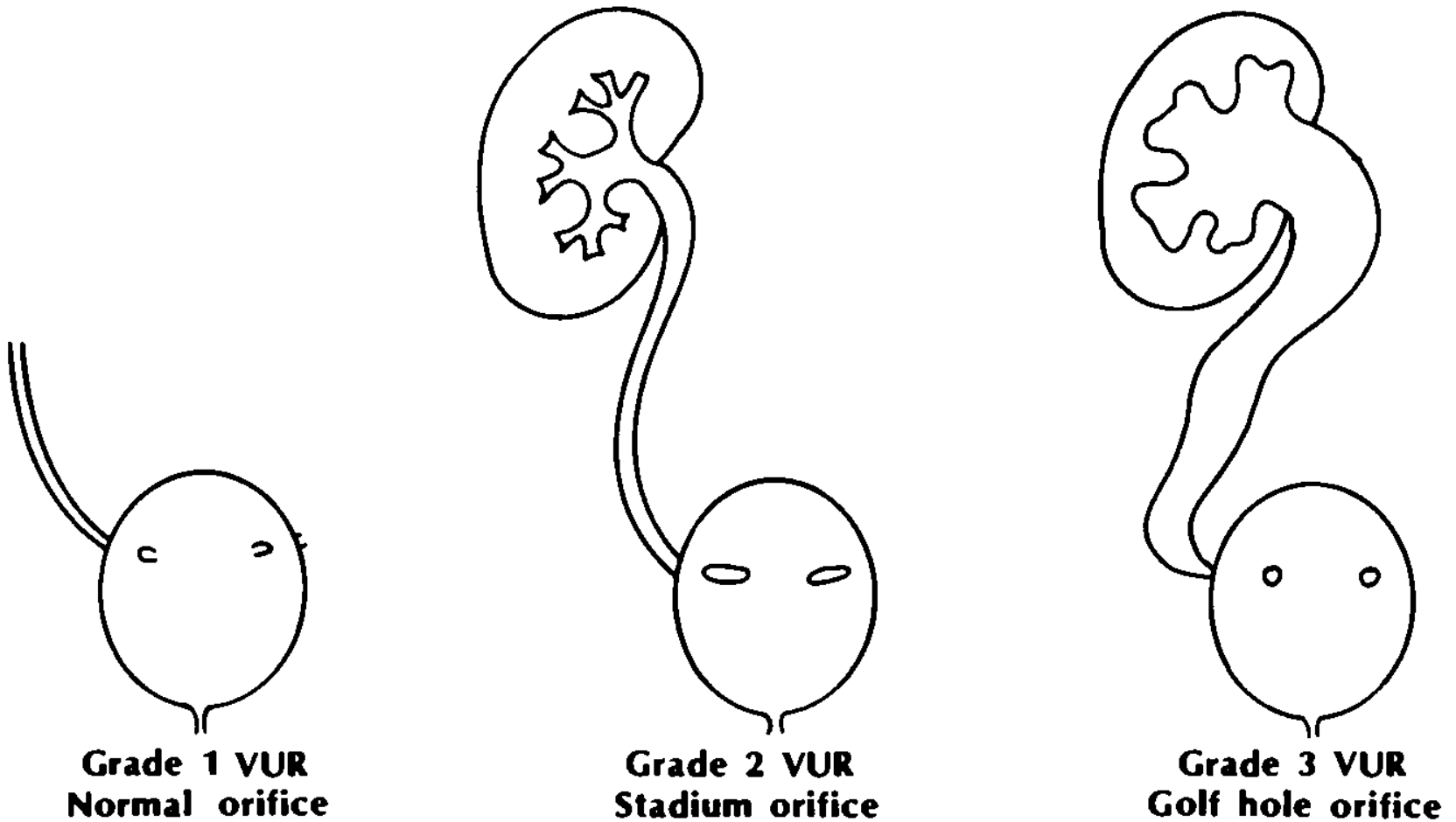
Sensitive host

- **Anatomical malformations**
 - obstruction
 - VUR
 - meningomyelocele
 - prune-belly syndrome
 - Stone disease, etc

VUR (1)

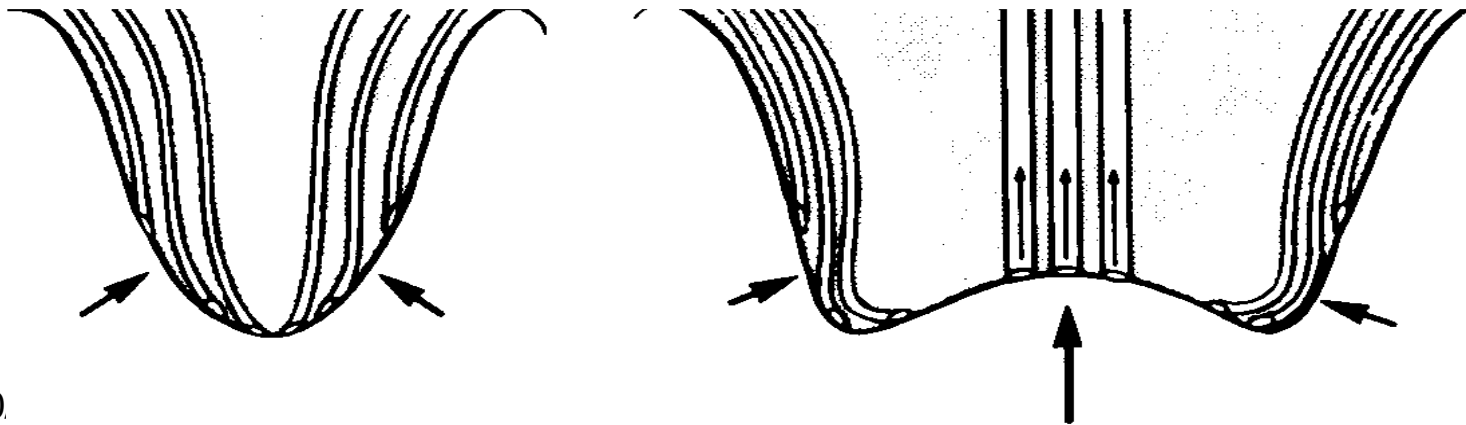
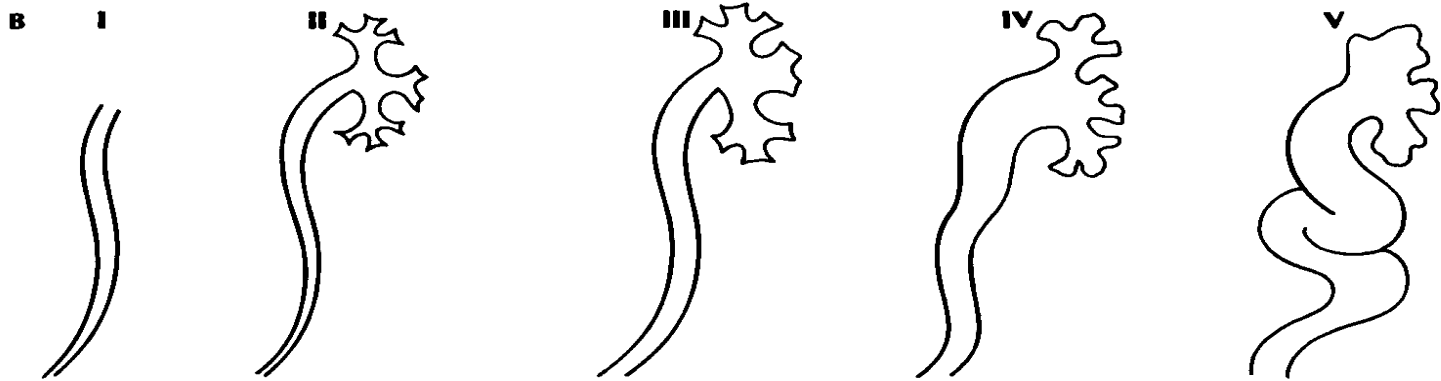
anatomy of the ureteral orifice

A

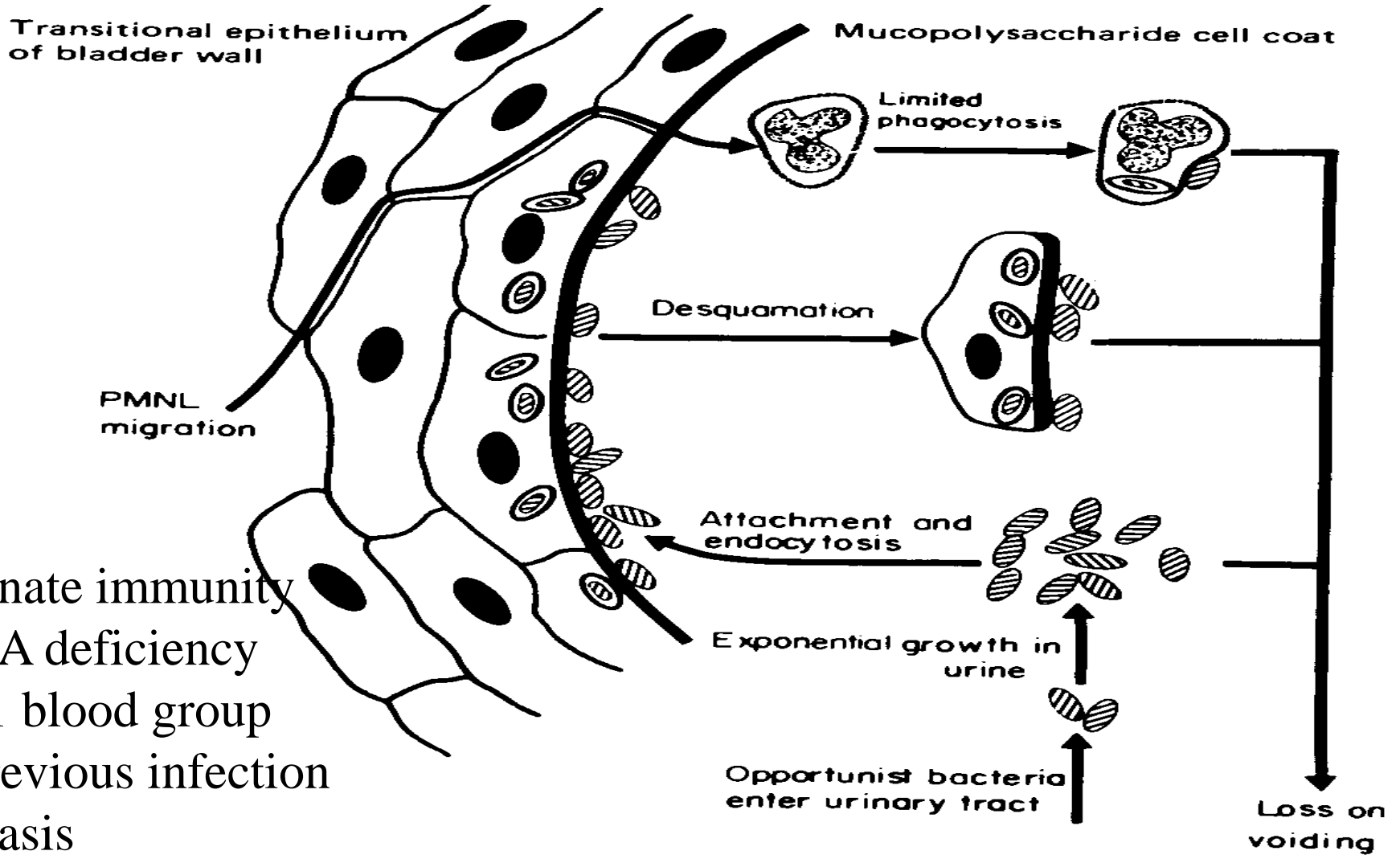


VUR (2)

grading of reflux

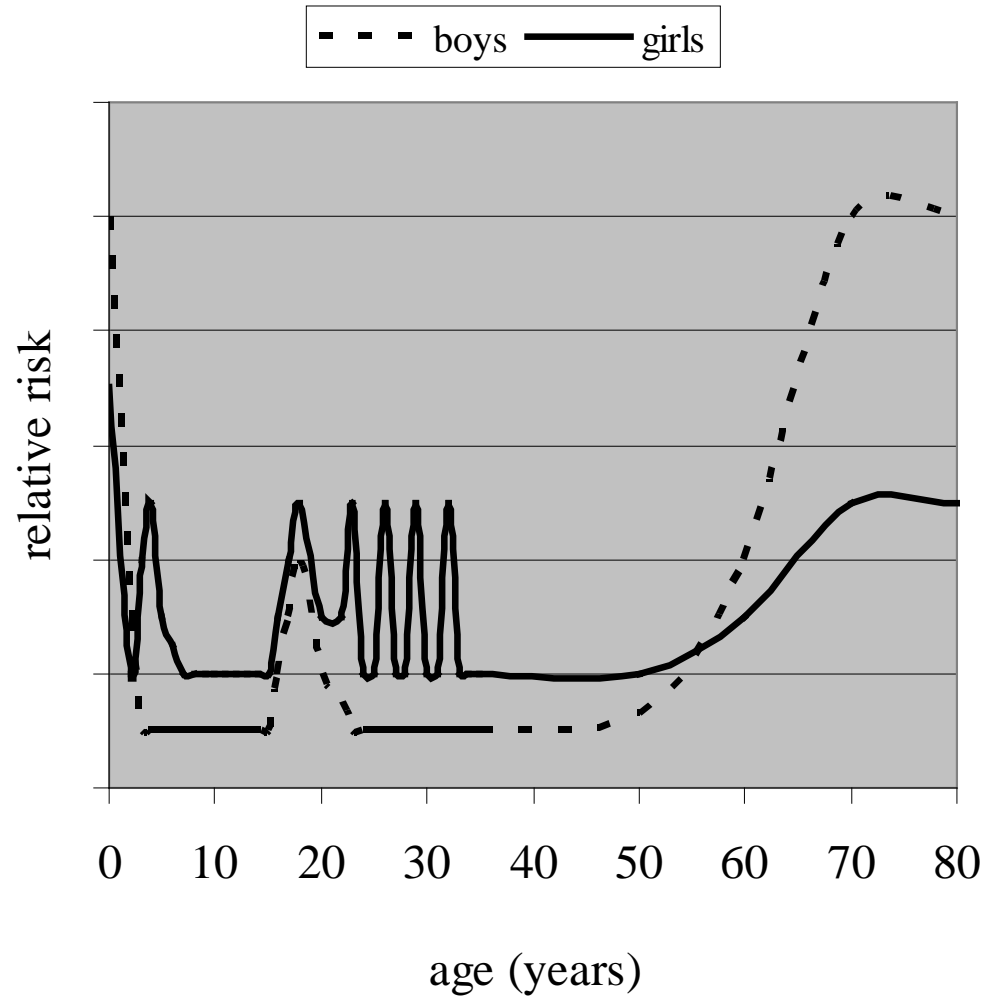


Mucosa barrier

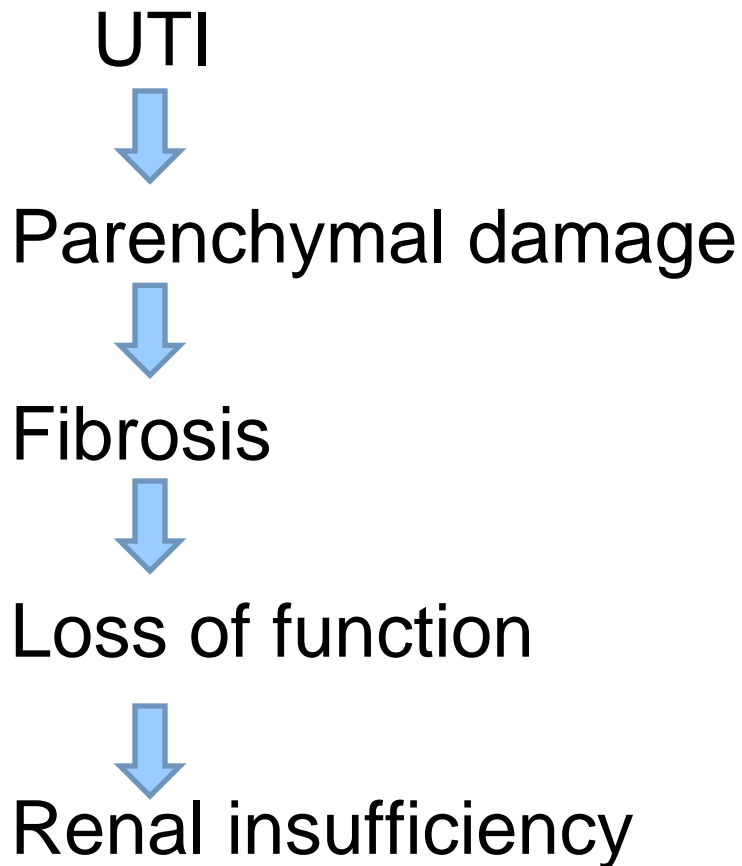


- Innate immunity
- IgA deficiency
- P1 blood group
- Previous infection
- Stasis
- Dysbacteriosis (antibiotics)

Age-related incidence of UTI

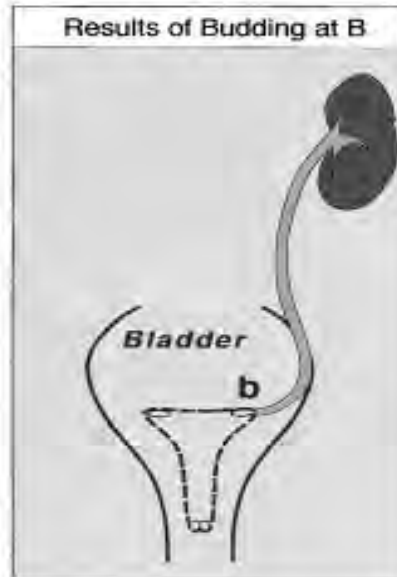
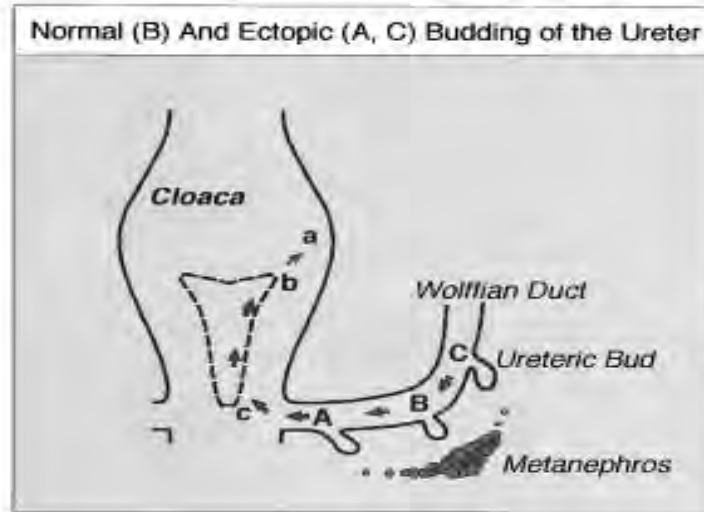


Sequence of kidney damage 1.



- Anatomic malformations
 - Subvesical Obstruction
 - VUR
 - UV - stenosis
 - PU - stenosis
 - Meningomyelocele
 - Prune-Belly-Syndrome
- Immun deficiency
- Virulent bacteria

Ichikawa I et al: Paradigm shift from classic anatomic theories to contemporary cell biological views of CAKUT. *Kidney International* (2002) 61, 889–898;

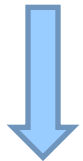


Sequence of kidney damage 2.

Primary bilateral parenchymal defect (hypoplasia/dysplasia)



Low nephron number



Secondary lesion hyperfiltration



Fibrosis



Loss of function



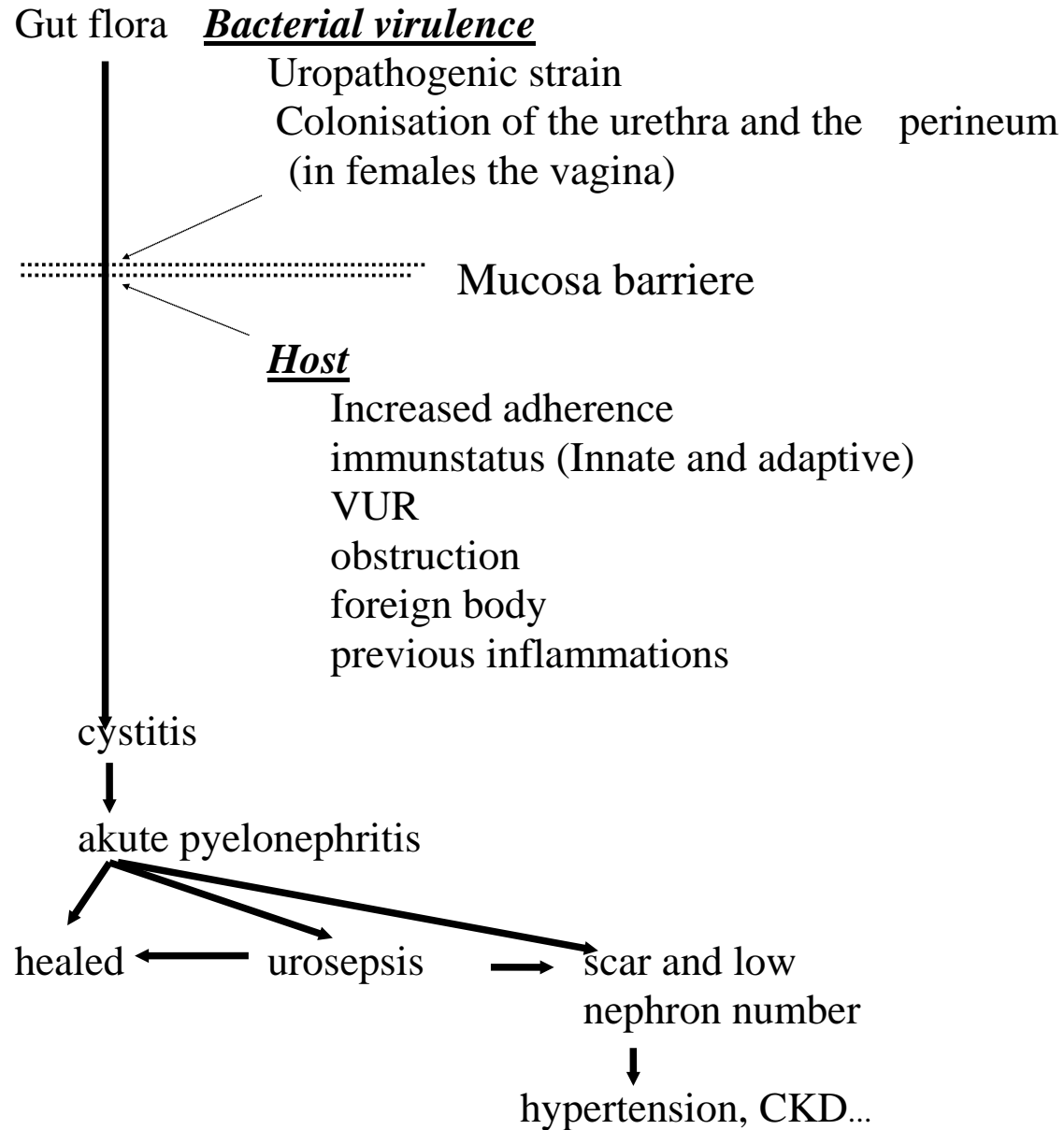
Renal insufficiency

- Hypoplastic kidneys, low nephron number

- UTI
 - Subvesical Obstruction
 - VUR
 - UV - stenosis
 - PU - stenosis
 - Meningomyelocele
 - Prune-Belly-Syndrome
 - Immun deficiency
 - Virulent bacteria

- Vicious cercle

Causes and course of UTI



Summary

- UTI is a frequent condition in children
- There are a number of predisposing factors to UTI, that are not related to pathological anatomy
- Primary renal hypoplasia with reduced nephron number accompanying the most severe anatomical malformations is a major factor leading to deterioration of kidney function

scar



Reflux
nephropathy

