Nutrient support for urinary tract health

FX Medicine

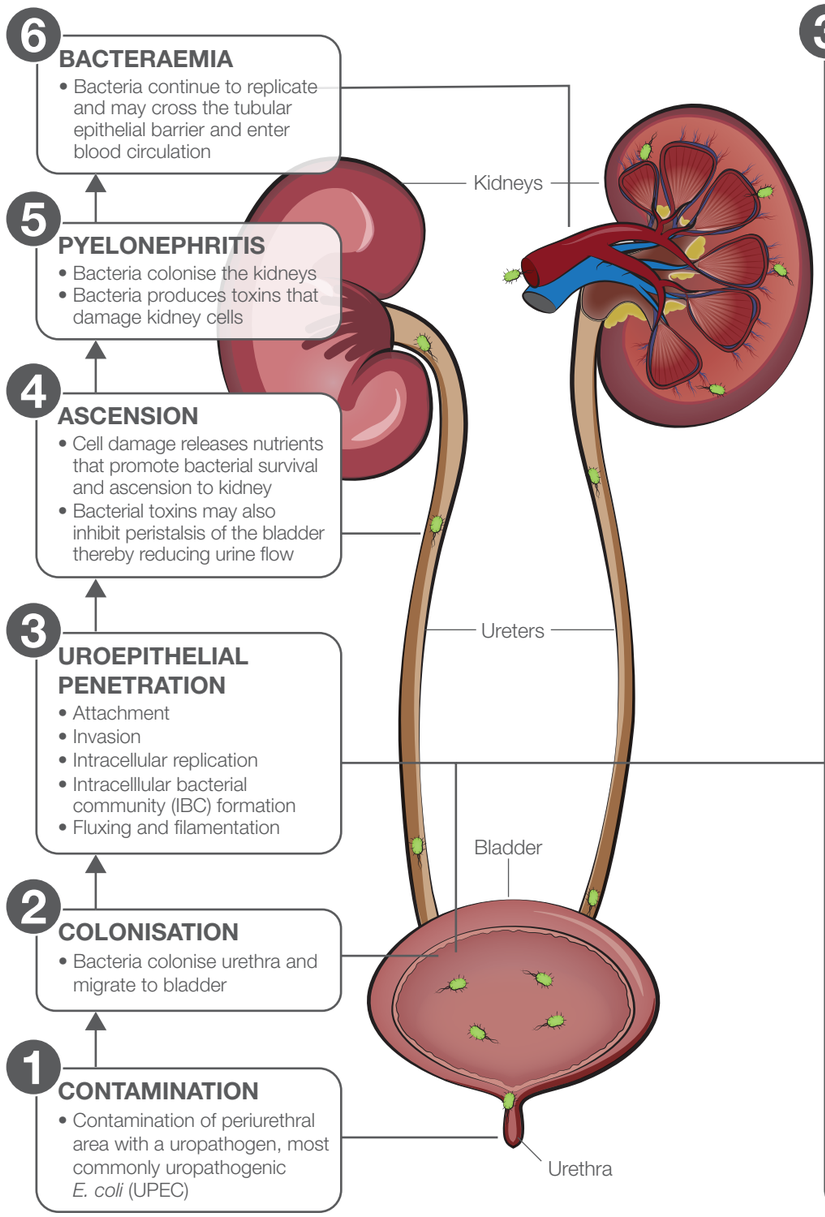
UTIs (urinary tract infections) are among the most common bacterial infections, affecting **150 MILLION PEOPLE WORLDWIDE EACH YEAR**[1]

1 in 2 WOMEN will suffer from a UTI within their lifetime[1]

UTIs don't always cause **signs and symptoms**, however symptoms may include:[2]

- A strong, persistent urge to urinate
- Passing frequent, small amounts of urine
- Strong-smelling urine
- A burning sensation when urinating
- Urine that appears cloudy
- Urine that appears red, bright pink — a sign of blood in the urine
- Pelvic pain

PATHOGENESIS OF UTIs[1-15]



6 BACTERAEMIA
- Bacteria continue to replicate and may cross the tubular epithelial barrier and enter blood circulation

5 PYELONEPHRITIS
- Bacteria colonise the kidneys
- Bacteria produces toxins that damage kidney cells

4 ASCENSION
- Cell damage releases nutrients that promote bacterial survival and ascension to kidney
- Bacterial toxins may also inhibit peristalsis of the bladder thereby reducing urine flow

3 UROEPITHELIAL PENETRATION
- Attachment
- Invasion
- Intracellular replication
- Intracelllular bacterial community (IBC) formation
- Fluxing and filamentation

2 COLONISATION
- Bacteria colonise urethra and migrate to bladder

1 CONTAMINATION
- Contamination of periurethral area with a uropathogen, most commonly uropathogenic *E. coli* (UPEC)

3 UROEPITHELIAL PENETRATION

A ATTACHMENT (immediate)

UPEC must overcome innate defences, such as mucin, antimicrobial peptides (cathelicidin) and competitive inhibition of commensal bacteria, and attach to the urothelium.

UPEC attach to D-mannose receptors on facet cells using fimbriae (hair-like, adhesive fibres).

Attachment triggers aggressive host responses including cytokine production, inflammation and exfoliation of infected urothelial cells.

B INVASION (15 min - 1 hour)

UPEC invasion of facet cells is a critical event in acute urinary tract infection.

Inside the host cell, bacteria can subvert host defence mechanisms and resist antibiotic treatment.

Lipopolysaccharide (LPS) released by UPEC is sensed by toll-like receptor 4 (TLR4), which also stimulates an immune response including an influx of neutrophils.

C INTRACELLULAR REPLICATION (1 - 12 hours)

UPEC reside within vesicles in facet cells and replicate.

LPS stimulation also triggers the expulsion of intracellular UPEC and host cell exfoliation.

While exfoliation attempts to remove infected cells it also results in loss of urothelial integrity and exposure of deeper layers of the urothelium to UPEC.

D IBC FORMATION (4 - 16 hours)

UPEC elude expulsion and escape into the nutrient-rich cytoplasm, where they rapidly replicate and form intracellular bacterial communities (IBCs).

The formation of bacterial biofilm contributes to the persistance and resistance of UPEC infection.

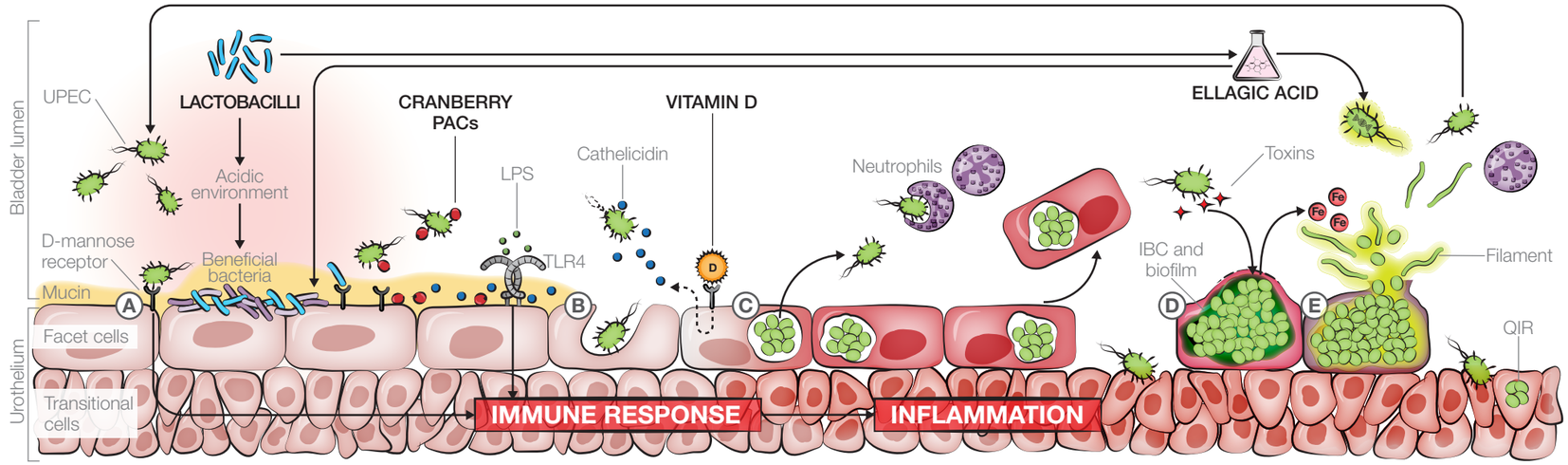
UPEC secrete toxins that cause damage to host cells. Cell damage facilitates the release of iron and nutrients from host cells to promote UPEC survival.

E FLUXING AND FILAMENTATION (16 - 24 hours)

Bacteria flux away from IBCs and emerge from dying urothelial cells, often in filmentous form which are not recognised by neutrophils.

Once inside the lumen, bacteria may go on to colonise and invade neighbouring cells.

UPEC may form quiescent intracellular reservoirs (QIRs) in underlying cells. QIRs may persist in the urothelium long after the acute infection has resolved and may go on to seed a new infection.



NUTRIENT SUPPORT

LACTOBACILLI
L. plantarum, L. rhamnosus
- Help to maintain healthy urogenital microbiota
- Produce lactic acid, which maintains an acidic environment and deters pathogenic bacteria
- Induce mucin production
- *L. plantarum* competitively inhibits UPEC from binding to D-mannose receptors
- *L. plantarum* frees ellagic acid from pomegranate

CRANBERRY
- Contains proanthocyanidins (PACs), which interfere with UPEC attachment
- Contains ellagic acid, which inhibits bacteria replication

VITAMIN D
- Stimulates production of the potent antimicrobial peptide cathelicidin from urothelium cells

ELLAGIC ACID (from pomegranate and cranberry)
- Disrupts UPEC replication by modulating bacterial DNA production in a similiar manner to quinolone antibiotics
- Disrupts biofilm formation
- Provides a substrate for fermentation by commensal bacteria