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Mechanism of UTI in healthy female anatomy

BACTERIAL FACTORS

E.coli is able to bind tightly to the urothelial surface- THIS PREVENTS WASH-OUT!

Moving urine is the greatest enemy of colonising bacteria.

This binding is mediated by the FimH adhesion located at the tip of the bacterial type 1 fimbrium.

Bacterial Reservoirs may form on the inside of the bladder, causing recurrent attacks

Colonisation of Vaginal introitus with E.Coli

Crucial first step!

stasis of urine
genetics
frequent intercourse

E.coli spreads up the urethra

Abnormal defences
Genetics
Stasis of urine

E.coli colonises bladder urothelium

INFLAMMATORY RESPONSE:

Neutrophils and macrophages flock to the site and begin to do their inflammatory thing.

DYSURIA:

The urethra is inflamed and thus the pain endings are hyper-sensitized by the inflammatory mediators; hence any urine moving through it will cause burning pain.

URGENCY AND FREQUENCY

The bladder muscle (detrusor) becomes oedematous and stiffened; hence it can no longer comply as well with distension pressure, and will want to void at a much lower volume.

THUS YOU NEED TO PEE MORE OFTEN

COMPLICATIONS

If stasis persists, the infected urine ill reflux up into the ureters and into the kidney! THIS IS PYELONEPHRITIS

- **Leucocytes**
- **Blood cells (sometimes)**
- **Protein**
- **And of course BACTERIA**

…Are now present in the urine

HOST FACTORS

Stagnant urine: reduced washout

This may result from

- **Childhood voiding dysfunction**, eg. detrusor instability
- **Vesicoureteric reflux** forma part of this, and also predisposes you to pyelonephritis as the bacteria get washed into the kidneys though the dysfunctional refluxing vesicoureteric junction

Abnormal genital flora: reduced competition

Normally, the vaginal flora consists mainly of lactobacilli and staphylococcus; both of these are so well adapted to living in the vagina that they tend to out-reproduce any invaders, and thus monopolise the nutrients and attachment space. E.coli cant get a foothold in such a competitive environment.

THUS:

- **Antibiotic use** can disrupt the normal flora and give E.coli a chance to grab some lebensraum.
- **Ageing changes the vaginal flora,** and the elderly get weirder, more exotic pathogens invading their urinary tract. This may be attributed to the fact that the normal vaginal flora mainly feeds on the secretions of the vaginal mucosa, and these wane with age, leaving the poor staph and lactobacilli stranded in a strange land without food. Thus the mucosa becomes undefended.

ABNORMAL IMMUNE DEFENCES:

- **IgA (mucosal antibody in the UT fluctuates depending on the point in the mentrual cycle** so there are times during the month when your humoural defences are down.

FREQUENT INTERCOURSE:

Actually it doesnt have to be that frequent. Most people report at least 4 episodes in the month preceding their presentation, not exactly orgiastic. There is also some role played by **SPERMICIDAL AGENTS** which seem to interfere with the normal flora, opening a path for E.coli

GENETICS:

About 50% of recurrent UTIs have a positive maternal history, but does this reflect shared environmental and behavioural factors? Either way, animal studies suggest it's a complex multigenic trait, with some recessive components.

Candidate genes are:

- **ABH Blood-group antigen secretion gene:** The gene encodes for one of the many glycosyltransferases that determine the carbohydrate composition of cell-surface glycoproteins andglycosphingolipids, some of which are also a binding site for uropathogenic *E coli*. The vaginal epithelium of nonsecretors expresses two extended-chain glycosphingolipids that bind *E coli* more avidly in the urinary tract.
- **Interleukin-8 receptor gene:** IL-8 is an inflammatory cytokine that promotes neutrophil migration across theinfected uroepithelial cells. Crappy Il-8 receptors impair this process and delay the immune response in this setting.

Toll-like Receptors (type 4): the sensory mechanisms of macrophages; toll-like receptors detect bacterial cell wall components. In this case a low-affinity erecptor means macrophages are less reactive to E.Coli lipopolysaccharide.