

Paediatric Urinary

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Epidemiology and pathophysiology

The incidence of urinary tract infections (UTIs) is highest during the first year of life, with the majority of infections occurring in males. These rates then fall off in boys, with the risk being 4 to 10 times greater in uncircumcised males, while they remain relatively high in females. A study by Hellstorm et al. (1991) reported a cumulative incidence rate of 7.8% in girls by the age of seven.¹

The importance of this condition is highlighted by various published papers, including Hoberman et al. (1993), in which it was reported that up to 5% of young children (<2 yrs) presenting with fever at paediatric casualty would have a UTI.²

Viruses, fungi and even parasites can all infect the urinary tract. However, most cases of infective pathology of the urinary system, at least in our part of the world, are caused by bacteria.

Common urinary isolates principally from hospitalized patients of all ages in St Luke's hospital include:

- *Escherichia coli* (which is by far the most commonly encountered organism)
- *Proteus mirabilis*
- *Enterococcus faecalis*
- *Pseudomonas aeruginosa*

These last three are isolated as above at more or less equal frequencies, but much less than *E. coli*.

In addition, various other gram positive and negative bacteria are isolated from time to time as being potential infective candidates from a patient's urine, but at a much reduced incidence when compared to the above four agents.

Laboratory Diagnosis

There are obvious difficulties in taking a history and examining the very young

patient. In this case, laboratory diagnosis has an especially important role.

The gold standard for confirming a UTI is still by growing bacteria from a patient's urine. What may appear as a relatively easy procedure is fraught with difficulties, with the taking of a proper specimen especially problematic in a child.

In the very young, the "mid-stream urine" (MSU) technique is not feasible to perform, while the urine bag is considered to give a high rate of false positive cultures. Suprapubic aspiration is very specific but is a somewhat invasive procedure and is said to have a low success rate unless done under ultrasound guidance.

During specimen collection, bacterial contamination is inevitable, even when a proper MSU is obtained. For this reason, a cut off point was established early on in this branch of clinical bacteriology, such that 100 000 colony forming units per ml (cfu/ml) of urine is the established infection

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Use in patients with impaired renal function: The dosing recommendations described in Use in adult apply to patients with mild to moderate renal impairment (creatinine clearance >30-50 ml/min). Since sildenafil clearance is reduced in patients with severe renal impairment (creatinine clearance <30 ml/min) a 25 mg dose should be considered. Based on efficacy and toleration, the dose may be increased to 50 mg and 100 mg. Use in patients with impaired hepatic function: Since sildenafil clearance is reduced in patients with hepatic impairment (e.g. cirrhosis) a 25 mg dose should be considered. Based on efficacy and toleration, the dose may be increased to 50 mg and 100 mg. Use in children: VIAGRA is not indicated for individuals below 18 years of age. Use in patients using other medicines: With the exception of ritonavir for which co-administration with sildenafil is not advised a starting dose of 25 mg should be considered in patients receiving concomitant treatment with CYP3A4 inhibitors. In order to minimise the potential for developing postural hypotension, patients should be stable on alpha-blocker therapy prior to initiating sildenafil treatment. In addition, initiation of sildenafil at a dose of 25 mg should be considered. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Concomitant use with nitric oxide donors (such as amyl nitrite) or nitrates in any form is therefore contraindicated. Agents for the treatment of erectile dysfunction, including sildenafil, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure). The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: severe hepatic impairment, hypotension (blood pressure <90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases). **Special warnings and special precautions for use:** A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes, before pharmacological treatment is considered. Prior to initiating any treatment for erectile dysfunction, physicians should consider the cardiovascular status of their patients, since there is a degree of cardiac risk associated with sexual activity. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Prior to prescribing sildenafil, physicians should carefully consider whether their patients with certain underlying conditions could be adversely affected by such vasodilator effects, especially in combination with sexual activity. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g. aortic stenosis, hypertrophic obstructive cardiomyopathy), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure. VIAGRA potentiates the hypotensive effect of nitrates. Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of VIAGRA. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of VIAGRA without sexual activity. It is not possible to determine whether these events are related directly to these factors or to other factors. Agents for the treatment of erectile dysfunction, including sildenafil, should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease), or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia). The safety and efficacy of combinations of sildenafil with other treatments for erectile dysfunction have not been studied. Therefore the use of such combinations is not recommended. The use of PDE5 inhibitors is not recommended in patients with a previous episode of non-arteritic anterior ischaemic optic neuropathy (NAION). Co-administration of sildenafil with ritonavir is not advised. Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing. In order to minimise the potential for developing postural hypotension, patients should be haemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25 mg should be considered. In addition, physicians should advise patients what to do in the event of postural hypotension symptoms. Studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside in vitro. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore sildenafil should be administered to these patients only after careful benefit-risk assessment. The film coating of the VIAGRA tablet contains lactose. VIAGRA should not be administered to men with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. VIAGRA is not indicated for use by women. **Side effects:** Very common headache, flushing, Common: Dizziness, altered vision/increased perception of light, blurred vision, Chromatopsia (yellow and green tinge to vision), palpitation, nasal congestion, dyspepsia, Uncommon or Rare: Immune system/hypersensitivity reactions, Eye disorders: eye pain, red eyes/tearful eyes, non-arteritic anterior ischaemic optic neuropathy (NAION), retinal vascular occlusion, visual field defect, Cardiac disorders: tachycardia, ventricular arrhythmia, myocardial infarction, unstable angina, sudden cardiac death, Vascular disorders: hypotension, hypertension, epistaxis, syncope, cerebrovascular haemorrhage, transient ischaemic attack, Gastrointestinal disorders: vomiting, skin and subcutaneous tissue disorders: skin rash, Reproductive system and breast disorders: prolonged erection, priapism.

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Tract Infections

Test done on a urine specimen	% Sensitivity	% Specificity
Gram stain	93 (80 – 98)	95 (87 – 100)
Dipstick – Nitrite	50 (16 – 72)	98 (95 – 100)
Dipstick – L. Esterase	83 (64 – 89)	84 (71 – 95)
Either Nitrite or Esterase positive	88 (71 – 100)	93 (76 – 98)

Table 1: A comparison of sensitivity and specificity values for different tests carried out on urine samples

threshold for adults. Urinary bacterial counts which are lower than this are normally considered to signify the presence of bacterial contaminants, and typically ignored.

It has been suggested that this cutoff point may be too high for young children, with a 10 000 cfu/ml of urine a better cutoff point in these cases. In fact, a study by Hoberman *et al.* (1994) showed that 65% of urine specimens taken from febrile children with a bacterial count of 10 000 – 49 000 cfu/ml showed evidence of contamination. If, in the attempt to increase sensitivity, a lower threshold is chosen (i.e. 10 rather than 10⁵ cfu/ml), then one must accept a higher incidence of false positive results.

Another significant drawback of relying on a urine culture for diagnosis is the time delay, with the result not being available for at least 24 hours. Such delays in starting treatment may not be acceptable. In this case, rapid testing, preferably by the patient's bedside, may be useful in helping to confirm a clinical impression. But which tests, and how useful are they in practice?

A meta-analysis by Gorelick *et al.* (1999) compared the predictive value of a number of rapid laboratory tests. The results are summarized in [Table 1](#).

If we are to take the gram stain as our 'gold standard' for rapid urine testing, then it is comforting to know that by using a good urine dipstick, we can get excellent sensitivity and specificity, comparable to the gram.

Treatment of UTI

Below are listed some treatment options:

- Amoxicillin – is a good first line agent, however, a significant proportion of hospital acquired *E. coli* infections are ampicillin resistant. The extent to which this occurs in the community is unclear.

- Co-amoxiclav – some hospital acquired *E. coli* infections will also show intermediate or full resistance to this. Once again, we have no data on resistance rates outside hospital.

- Third generation cephalosporins, such as cefpodixime – are usually active against most strains of *E. coli* and *Proteus mirabilis*, but not *Enterococcus faecalis*.

- Trimethoprim – sulfamethoxazole – mostly effective against *E. coli* and *Proteus mirabilis*.

- Nitrofurantoin – will usually work against *E. coli* and *Enterococcus faecalis*, but not *Proteus mirabilis*.

In practice, all listed antibiotics have strengths and weaknesses. A *Pseudomonas* UTI, especially if confirmed by repeated isolations from the same patient, would require specialized treatment.

While there has been the tendency to try and shorten the duration of antibiotic therapy in adults, in children various studies such as Keren *et al* (2002) have suggested an optimal antibiotic treatment duration of between 7 to 14 days.⁶ This is also the recommendation by the American Academy of Pediatrics (1999) for all children between the ages of 2 months to two years with urinary tract infections.³

Epilogue

Repeated infections in childhood require careful investigation to rule out abnormalities of the urinary tract. Sometimes no obvious abnormality will be detected. In this case, one would do well to check on the child's bowel habits. One paper by Newmann (1973) reported a decrease in recurrent UTI by correcting constipation.⁷

A more controversial topic is the existence of a condition sometimes referred to as dysfunctional elimination which is sometimes suggested to be a cause of repeated UTIs in children with an apparently normal urinary tract. It has been described as a disorder of the normal voiding or emptying reflexes, leading to a chronic abnormal pattern of elimination which does not allow the bladder or bowel to empty completely.[\[X\]](#)

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