URINARY TRACT INFECTION AND HAEMATURIA

URINARY TRACT INFECTIONS:

- UTI is described by location → urethritis, cystitis or pyelonephritis
- UTI is significant bacteriuria in the presence of symptoms
- FOUR AGE GROUPS AT RISK:
    - Neonates
    - Girls
    - Young women
    - Older men
- UTI in young, healthy women is associated with:
    - Sexual activity (specifically increased intercourse frequency in the previous month)
    - Spermicide/diaphragm use
    - New sex partner in thee last 12 motnhs
    - Age at first UTI <15
- In males < 50 → think STD, but if >50 → think prostatic obstruction as the cause

PATHOPHYSIOLOGY:

- URETHRITIS AND CYSTITIS:
    - Infections of the lower urinary tract
    - Given the appropriate symptosm of dysuria, frequency and urgency, the best diagnostic standard is a positive result on urine culture
    - Competent ureteric valves prevent ascent of the bacteria to kidneys in most cases
    - In otherwise healthy, nonpregnant young women → benign illness
- PYELONEPHRITIS:
    - An infection of the upper urinary tract → an infection of the renal parenchymal and pelvico-calyceal system with syndrome or FLANK PAIN, COSTOVERTEBRAL ANGLE TENDERNESS, FEVER AND OTHER SYSTEMIC SYMPTOMS
- UNCOMPLICATED UTI:
    - UTI without structural or functional abnormalities within the urinary tract or kidney parenchyma, without relevant comorbidities that place the patient at risk and are not associated with GU tract instrumentation
- COMPLICATED UTI:
    - Defined as infection involving a functional or anatomically abnormal urinary tract, or infection in the presence of comorbidities that place the patient at risk for more serious outcome
    - A VERY HETEROGENEOUS GROUP
    - More likely to be infected with resistant organisms
    - Risk factors are outlined below:

Table 94-1 Risk Factors for Complicated Urinary Tract Infection (UTI)	
Risk Factor	**Comments**
Male sex	In young males, dysuria is more commonly secondary to sexually transmitted disease; suspect underlying anatomic abnormality in men with culture-proven UTI.
Anatomic abnormality of the urinary tract or external drainage system	Indwelling urinary catheter, ureteral stent, nephrolithiasis, neurogenic bladder, polycystic renal disease, or recent urinary tract instrumentation.
Recurrent UTI	No universal definition exists. A pragmatic definition is three or more per year.
Advanced age in men	Presence of prostatic hyperplasia, recent instrumentation, recent prostatic biopsy.
Nursing home residency	With or without indwelling bladder catheter.
Neonatal state	See Chapter 126, Urinary Tract Infection in Infants and Children.
Comorbidities	Diabetes mellitus, sickle cell disease, others.
Pregnancy	See Chapter 102, Comorbid Diseases in Pregnancy.
Immunosuppression	Active chemotherapy, acquired immunodeficiency syndrome, immunosuppressive drugs.
Advanced neurologic disease	Stroke with disability, spinal cord injuries, others.
Known or suspected atypical pathogens	Non–*Escherichia coli* infections.
Known or suspected resistance to typical antimicrobial agents for UTI	Resistance to ciprofloxacin predicts multidrug resistance.

- ASYMPTOMATIC BACTERIURIA:
  - Presence of >10^5 CFU/mL of a single bacterial species on two successive urine cultures in a patient without symptoms → two cultures required to eliminate those with transient colonisation
  - Occurs in up to 30% of pregnant women and in up to 40% of female nursing home residents
  - Also common in those with IDC and those with disorders that prevent complete emptying of the bladder
  - STRONG PREDICTOR OF UTI → occurs within a week in 8x more cases than those without it
- RELAPSE AND REINFECTION:
  - RELAPSE → recurrence of symptoms within a month, caused by the same organisms → TREATMENT FAILURE
  - REINFECTION → development of symptoms 1-6 months later, after treatment
  - If a patient has had ≥3 recurrences in one year, a more complete evaluation may be warranted to look for the presence of structural abnormalities, tumour, renal calculi or associated systemic illness (DM)
- BACTERIOLOGY:
  - Most common pathogen remains Escherichia coli (see below for others)

Table 94-2 Etiologic Agents in Uncomplicated Urinary Tract Infection	
Organism	**Incidence (%)**
Escherichia coli	>80
Klebsiella species	5–20
Proteus species	
Enterobacter species	
Pseudomonas species	
Group D streptococci	<5
*Chlamydia trachomatis**	
*Staphylococcus saprophyticus**	
Mycobacterium tuberculosis (in HIV infection)	

- Anaerobic organisms do not grow well in urine
- Although complicated UTI can be caused by E coli, they are more likely to be caused by unusual pathogens → Pseudomonas or Enterococci
- MECHANISMS OF INFECTION:
    - Urine is generally a good cultures medium
    - Factors UNFAVOURABLE TO INFECTION → low pH, high concentration of urea, presence of organic acid
    - Intact bladder mucosa removes organisms from a thin residual film of urine after emptying
        - Incomplete bladder emptying renders this mechanism ineffective and is responsible for the increased frequency of infection in patients with neurogenic bladder and in women with bladder or uterine prolapse
        - Frequent and complete voiding is associated with a decreased incidence of UTI
- FACTORS ASSOCIATED WITH INCREASED RISK OF UTI:
    - Advanced age
    - Pregnancy
    - Prolonged symptoms prior to seeking care
    - ≥3 UTI in the previous year
    - Immunocompromise
    - Poor general health/comorbidities
    - Obesity
    - Institutionalisation
    - Need for self-catheterisation or long-term IDC
    - DM
- The infective process of UTI can progress into THREE PATTERNS OF RENAL INFECTION NO COMMONLY CONSIDERED PART OF THE UTI SPECTRUM:
    - ACUTE BACTERIAL NEPHRITIS
    - RENAL ABSCESS
    - EMPHYSEMATOUS PYELONEPHRITIS → a rare, gas-forming infection within the kidney, nearly always in diabetics → appear toxic and septic, nephrectomy may be required for source control
        - The above diagnoses are made on imaging

CLINICAL FEATURES:

- UTI requires the presence of BOTH bacteriuria AND clinical symptoms for definitive diagnosis
- Common symptoms → painful urination (dysuria), haematuria, increased urinary frequency, urgency, hesitancy, suprapubic discomfort, renal angle tenderness and fever
- The presence of FOUR SPECIFIC SYMPTOMS and ONE SIGN independently increase the clinical probability of UTI:
    - DYSURIA
    - FREQUENCY
    - VISIBILE HAEMATURIA
    - FEVER
    - RENAL ANGLE TENDERNESS
- Unfortunately, the correlation between symptom and the presence of infection is INEXACT:
    - Only 50-60% of women with dysuria HAVE SIGNIFICANT BACTERIURIA
    - INTERNAL DYSURIA → a burning suprapubic pain during urination accompanied by bladder tenderness, is more assoicatedw tih UTIs than EXTERNAL dysuria → a burning sensation as urine passes over inflamed perineal tissue
        - In females, external dysuria or a history of vaginal discharge or irritation is more often associated with vaginitis, cervicitis or PID than with UTI
- Flank pain, renal angle tenderness or costovertebral angle tenderness may be associated with cystitis (due to referred pain) → however, when these findings occur in association with fever, chills, N+V and prostration, the CLINICAL DIAGNOSIS IS PYELONEPHRITIS
- In males → dysuria with urethral discharge indicates urethritis → consider gonococcus/Chlamydia
- For patients at risk for complicated UTI → it should be suspected in more complex cases in patients with atypical or diverse signs and symptoms → weakness, malaise, altered mental state, fever and flank/abdominal pain

DIAGNOSIS:

- COLLECTION OF THE URINE SPECIMEN:
    - Midstream urine voiding specimen is AS ACCURATE AS URINE OBTAINED BY CATHETERISATION if the patient follows instructions
    - If properly collected → it should contain no epithelial cells
    - Bacteria in urine double each hour at room temperature, so urine should be refrigerated if not sent directly to the laboratory
    - Catheterisation is indicated if the patient cannot void spontaneously, or is too ill or immobilised or is extremely obese
        - Unnecessary catheterisation SHOULD BE AVOIDED → 1-2% of patients develop a UTI after a single catheter insertion

- URINALYSIS:
  - Visual inspection or assessment of odour IS NOT HELPFUL
  - UTI often results in positive dipstick test for protein, but this finding is not specific enough to be useful
  - The dipstick test is used to determine the PRESENCE OF LEUKOCYTE ESTERASE AND NITRITES
  - Urine for microscopy is routinely centrifuged prior to analysis → cloudiness in urine is most often due to large amounts of protein or amorphous phosphate , NOT DUE TO WBC/BACTERIA
- URINE WHITE BLOOD CELL COUNT OR PYURIA:
  - WBC>5 per high power filed is abnormal in the patient with appropriate symptoms
  - Lower degrees of pyuria with/without symptoms may be clinically significant
  - False negative pyuria → dilute urine, systemic leukopenia, partially treated UTI
    - PYURIA MAY BE INTERMITTENT OR ABSENT IF THE PATIENT HAS AN OBSTRUCTED AND INFECTED KIDNEY
- BACTERIURIA BY MICROSCOPY:
  - Bacteriuria is a sensitive tool for detection of UTI in the symptomatic patient
  - The presence of any bacteria is significant and highly correlates with culture results ➔ 95% sensitive and >60% specific
  - False positive results occur when vaginal or faecal contamination occur
- NITRITE REACTION ON DIPSTICK:
  - Urine nitrite reaction has a VERY HIGH SPECIFICITY (>90%) and a positive results is very useful in confirming the diagnosis of UTI caused by bacteria that convert nitrates to nitrite ➔ E coli → note that Pseudomonas, enterococcus and Acinobacter DO NOT CONVERT NITRATES TO NITRITE IN THE URINE AND THUS ARE NOT DETECTED BY NITRITE TESTING
  - Low sensitivity → thus a negative result does not rule out the diagnosis of UTI
- LEUKOCYTE ESTERASE BY DIPSTICK:
  - Overall sensitivity 48-86% and specificity 17-93% according 2004 meta-analysis
  - THUS → a positive urinary dipstick nitrite or leukocyte esterase test result supports the diagnosis of UTI, but a negative result does NOT EXCLUDE IT
- URINE CULTURE:
  - For the patient with typical symptoms of cystitis or an uncomplicated UTI and “positive” findings on UA, or pyuria/bacteriuria on microscopy → culture is not required
  - Culture should be performed if → complicated UTI, pregnancy, children, adult males, those with relapse or reinfection
- BLOOD CULTURE:

- A retrospective study found that blood cultures in clinical pyelonephritis are positive in 29% of cases and that organisms in blood cultures matched those on urine culture, resulting in NO CHANGE OF MANAGEMENT

- IMAGING:
  - NOT INDICATED IN OTHERWISE HEALTHY PATIENTS WITH ACUTE PYELONEPHRITIS
  - Male, elderly, diabetic or severely ill patients should be considered for imaging, especially if there is a renal stone
  - If emphysematous pyelonephritis is suspected → CT is the best imaging modality

TREATMENT OF UTI:

Nonpregnant women

Any of the following regimens can be expected to cure the majority of acute uncomplicated lower UTI in nonpregnant women. Use:

1 **trimethoprim 300 mg orally, daily for 3 days**

OR

2 **cephalexin 500 mg orally, 12-hourly for 5 days**

OR

3 **amoxycillin+clavulanate 500+125 mg orally, 12-hourly for 5 days**

OR

3 **nitrofurantoin 100 mg orally, 12-hourly for 5 days.**

Amoxycillin (without clavulanate) is only recommended if susceptibility of the organism is proven.

Single-dose therapy is not as reliable as multiple-dose therapy in preventing relapse. However, in remote Indigenous communities, treatment with nitrofurantoin 200 mg orally, as a single dose, has been found useful.

Fluoroquinolones should not be used as first-line drugs as they are the only orally active drugs available for infections due to *Pseudomonas aeruginosa* and other multiresistant bacteria.

If resistance to all the above drugs is proven *and* if susceptible, a suitable alternative is:

norfloxacin 400 mg orally, 12-hourly for 3 days.

Pregnant women

Prescribers should consider the Therapeutic Goods Administration (TGA) category of risk posed by the use of the particular antibiotic during pregnancy (see Drugs and their categories in pregnancy and breastfeeding). For empirical therapy, while awaiting culture results, use:

1 **cephalexin 500 mg orally, 12-hourly for 5 days (TGA pregnancy category A)**

OR

2 **nitrofurantoin 100 mg orally, 12-hourly for 5 days (TGA pregnancy category A)**

OR

3 **amoxycillin+clavulanate 500+125 mg orally, 12-hourly for 5 days (TGA pregnancy category B1).**

Amoxycillin (without clavulanate) (TGA pregnancy category A) is only recommended if susceptibility of the organism is proven.

Repeat urine culture at least 48 hours after completion of treatment to confirm clearance of infection.

Men

An underlying urinary tract abnormality is common in men with cystitis and there is often associated infection of the posterior urethra, prostate or epididymis. All males with a UTI should be investigated to exclude an underlying abnormality, which determines the choice and duration of antibiotic therapy and need for other therapy (see, for example, Prostatitis).

For empirical therapy, while awaiting results of investigations, use:

1 **trimethoprim 300 mg orally, daily for 14 days**

OR

2 **cephalexin 500 mg orally, 12-hourly for 14 days**

OR

3 **amoxycillin+clavulanate 500+125 mg orally, 12-hourly for 14 days.**

TREATMENT OF PYELONEPHRITIS:

Mild infection in adults

Mild cases (low-grade fever, no nausea or vomiting) may be treated by oral therapy alone. For empirical therapy, while awaiting culture results, use:

1 **amoxycillin+clavulanate 875+125 mg orally, 12-hourly for 10 days**

OR

1 **cephalexin 500 mg orally, 6-hourly for 10 days**

OR

1 **trimethoprim 300 mg orally, daily for 10 days.**

If resistance to all the above drugs is proven or the causative organism is *Pseudomonas aeruginosa*, use:

1 **norfloxacin 400 mg orally, 12-hourly for 10 days**

OR

2 **ciprofloxacin 500 mg orally, 12-hourly for 10 days.**

A follow-up urine culture at least 48 hours after the conclusion of therapy is advised.

Severe infection in adults

For patients with sepsis or vomiting, give parenteral treatment initially while awaiting culture results. Use:

gentamicin 4 to 6 mg/kg (see Table 2.24) (severe sepsis: 7 mg/kg) IV, for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Table 2.25)

PLUS

amoxy/ampicillin 2 g IV, 6-hourly.

In patients hypersensitive to penicillin (see Table 2.2), gentamicin alone will usually suffice.

If gentamicin is contraindicated (see Box 2.7), as a single drug, use:

1 **ceftriaxone 1 g IV, daily**

OR

2 **cefotaxime 1 g IV, 8-hourly.**

These regimens do not provide adequate cover for *P. aeruginosa* or enterococci.

Note that fluoroquinolones are NOT first line agents, as they are used for suspected pseudomonas and overuse has led to growing pathogen resistance

Consider fluoroquinolones or addition of anti-pseudomonal penicillin in cases of treatment failure or in the host with a structural or immunologic defect

DISPOSITION AND FOLLOW UP:

- For those with uncomplicated UTI/cystitis → discharge home with oral antibiotics and advise frequent urination
- In those with pyelonephritis → if young and otherwise healthy → oral antibiotics pending culture results with advice to return if they experience increasing pain, fever or vomiting (overall 80-90% of patients respond well to outpatient oral therapy)
- The decision to admit is based on age, host factors and response to initial ED interventions
    - Approximately 1-3% of patients with acute pyelonephritis die from the infection → younger patients experience fewest complications. UNFAVOURABLE FACTORS INCLUDE:
        - Advanced age/debilitation
        - Renal calculi or obstruction
        - Recent hospitalisation or instrumentation
        - Diabetes mellitus
        - Chronic nephropathy
        - Sickle cell anaemia
        - Underlying carcinoma
        - Immunocompromise
    - Dangerous complications of acute pyelonephritis include:
        - Acute papillary necrosis with possible ureteric obstruction
        - Septic shock
        - Perinephric abscesses
        - Emphysematous pyelnephritis
- SPECIAL POPULATIONS:
    - HIV/AIDS → resistance to bactrim has arisen due to long-term PCP prophylaxis → hence use fluoroquinolones as a first line agent. Also consider TB UTI.

HAEMATURIA:

EPIDEMIOLOGY:

- MACROSCOPIC HAEMATURIA ➔ visible to the eye, vs microscopic haematuria, which is usually detected in the course of evaluating other symptoms
    - Other pigments (e.g. myoglobin) may discolour the urine
    - Bleeding from a non-urinary source may also contaminate the urine specimen
    - Pain may accompany haematuria and haematuria is often found in UTI
    - Painless haematuria is more often due to neoplastic, hyperplastic and vascular causes
- It takes about 1mL of blood per litre to result in macroscopic haematuria → may result in false proteinuria as 1mL contains 50mg of albumin

- About 3% of the population reports at least one episode of haematuria → higher in women

PATHOPHYSIOLOGY:

- Any process that results in infection, inflammation or injury to the kidneys, ureters, bladder, prostate, male genitalia or urethra may result in haematuria

Table 94-7 Most Common Causes of Hematuria

Cause	Associated Age
Infections	Any
Nephrolithiasis	Usually >20 y
Neoplasms	Typically >40 y (except Wilms)
Benign prostatic hypertrophy	Males >40 y
Glomerulonephritis	Mostly young patients and children
Schistosomiasis	Any—most common cause worldwide

Table 94-8 Differential Diagnosis of Hematuria

Urologic (lower tract)
Any location
Iatrogenic/postprocedure
Trauma
Infection
Stones/calculi
Erosion or mechanical obstruction by tumor
Ureter(s)
Dilatation of stricture
Bladder
Transitional cell carcinoma
Vascular lesions or malformations
Chemical or radiation cystitis
Prostate
Benign prostatic hypertrophy
Prostatitis
Urethra
Stricture
Diverticulosis
Foreign body
Endometriosis (cyclic hematuria with menstrual pain)
Renal (upper tract)
Glomerular
Glomerulonephritis
Immunoglobulin A nephropathy (Berger disease)
Lupus nephritis
Hereditary nephritis (Alport syndrome)
Toxemia of pregnancy
Serum sickness
Erythema multiforme

Nonglomerular
Interstitial nephritis
Pyelonephritis
Papillary necrosis: sickle cell disease, diabetes, NSAID use
Vascular: arteriovenous malformations, emboli, aortocaval fistula
Malignancy
Polycystic kidney disease
Medullary sponge disease
Tuberculosis
Renal trauma
Hematologic
Primary coagulopathy (e.g., hemophilia)
Pharmacologic anticoagulation
Sickle cell disease
Miscellaneous
Eroding abdominal aortic aneurysm
Malignant hypertension
Loin pain–hematuria syndrome
Renal vein thrombosis
Exercise-induced hematuria
Cantharidin (Spanish fly) poisoning
Bites or stings by insects and reptiles having venom with anticoagulant properties

CLINICAL FEATURES:

- A careful history, including information regarding sexual activity, recent urologic procedures, medications, used and HIV (and other TB risk factors) should be obtained
- Examine general health, vital signs, external genitalia and prostate (males)
- With new haematuria → determine when the blood appears during micturition
    - Initial haematuria that clears → suggests urethral disease
    - Between voiding → lesions at the distal urethra/meatus

    - Total haematuria → visible throughout micturition and is associated with disease of the kidneys, ureter or bladder
    - Terminal haematuria → disease of the bladder neck or prostatic urethra
- Haemorrhagic cystitis with invasive infection of the bladder wall by bacteria resulting in shedding and bleeding is a common cause of haematuria and resolves with appropriate antibiotics
- Gross haematuria more often indicates a lower tract cause, whereas microscopic haematuria tends to occur with kidney disease → brown or smoke-coloured urine with RBC casts and proteinuria suggests a glomerular source
    - Red, clotted blood in the urine indicates a source below the kidneys
- In younger patients, microscopic haematuria is most often caused by nephrolithiasis or UTI → but consider GN, immune complex disease, Goodpastures, HSP
    - In kids → think HSP, Wilm's tumour, sickle cell anaemia, PSGN → treatment of the primary streptococcal infection DOES NOT REDUCE THE INCIDENCE OF PSGN
- In older patients → infections and nephrolithiasis remain common, but closer follow up warranted in patients >40 due to higher rates of BLADDER, RENAL AND PROSTATE CANCER
    - Do not attribute macroscopic haematuria to ANTICOAGULANTS ALONE, AS UNDERLYING DISEASE MAY BE AS HIGH AS 80%
- Associated HT and oedema imply nephrotic syndrome
- Think renal infarction in case of AF or murmur (endocarditis) → very rare

DIAGNOSIS:

- LAB EVALUATION:
    - A urine dipstick can detect as little as 150microg/L of free haemoglobin → false negative may occur if high concentration of ascorbic acid or high specific gravity. False positive for myoglobin, free haemoglobin, porphyrins
    - Many causes of FALSE HAEMATURIA ON VISUAL INSPECTION:

Table 94-9 Causes of False Hematuria on Visual Inspection
Munchausen syndrome, malingering, drug seeking
Patients may add blood to voided urine for secondary gain
Medications
NSAIDs, phenytoin, phenothiazines, quinine, rifampin, sulfasalazine, others
Foods and dyes
Beets, berries, rhubarb
Serratia marcescens infection
Amorphous urates
Hemoglobinuria, myoglobinuria, porphyrins

    - Abnormal RBC morphologic characteristics, RBC casts and proteinuria suggest a glomerular source and need for further work up

    - Presence of normal RBC without evidence of infection should prompt urological follow up to determine site of bleeding
    - A minority of patients (5-15%) with acute symptomatic urinary lithiasis have NO HAEMATURIA → thus if clinical picture fits for renal colic, still evaluate the patient
- IMAGING:
    - CT or renal US → does not need to be done emergently unless the clinical condition is urgent
        - High resolution CT clear delineates most renal tumours, obstruction or stones
        - Renal US is useful when screening for obstruction, hydronephrosis or AAA, but it rarely identifies or locates stones
    - Gross haematuria in patients with blunt or penetrating trauma to the abdomen, flank or back warrant an aggressive approach to identify the source of bleeding and to guide management

TREATMENT, DISPOSITION AND FOLLOW UP:

- Discharged patients should not have significant anaemia or acute renal insufficiency
- Patients <40 with asymptomatic bacteriuria and microscopic haematuria should be referred to a primary care physician for repeat UA. Persistent haematuria warrants urologic follow up, particularly if risk factors for significant disease exist (see below):

Table 94-10 Risk Factors for Significant Disease in Patients with Microscopic Hematuria
Smoking history
Occupational exposure to chemicals or dyes (benzenes or aromatic amines)
History of gross hematuria
Age >40 y
Previous urologic history
History of recurrent urinary tract infection
Analgesic abuse
History of pelvic irradiation
Cyclophosphamide use
Pregnancy
Known malignancy
Sickle cell disease
Proteinuria
Renal insufficiency

- Proteinuria is a sign of prognostically significant glomerular disease → requires further follow up if persistent
- IMPORTANTLY → MACROSCOPIC HAEMATURIA MAY LEAD TO INTRAVESICAL CLOT FORMATION AND BLADDER OUTLET OBSTRUCTION AND ACUTE URINARY RETENTION:

- Placement of a triple-lumen urinary drainage catheter and intermittent or continuous bladder irrigation with normal saline
- Manual irrigation using a syringe may be necessary if the catheter does not drain → once drainage is present, irrigation using gravity to wash clots out of the bladder → the rate of flow is determined by the appearance of the output → the goal is clear to only pink-tinged drainage
    - If placement of a three-way irrigation catheter is unsuccessful → urology input for cystoscopy may be required