Anatomy 2nd lecture:

1- (Ureter)	
Definition	It is a muscular tube transporting urine from kidney to urinary bladder.
Length	25 – 30 cm
Beginning	It begins as a continuation of renal pelvis (pelvis of ureter).
Coarse of ureter	
In abdomen	▪ It descends anterior to psoas major muscle (opposite the tips of lumbar transverse processes). ▪ It crosses anterior to the end (bifurcation) of common iliac artery to enter the pelvis.
In pelvis	▪ It runs downward & backward to the level of ischial spine. ▪ It runs obliquely for ¾ inch in wall of bladder before opening (valve-like part).
Termination	▪ opens at upper lateral angle of base of urinary bladder
Sites of constriction*	▪ At Uteropelvic junction ▪ At Pelvic inlet ▪ At site of entrance of bladder
Arterial supply	▪ Renal artery ▪ Gonadal artery ▪ Common iliac artery ▪ Internal iliac artery

3 - (Urethra)

Males	Females
▪ Length = 20 cm. PROSTATIC URETHRA (Length=3 cm): - Widest & most dilatable - Extends from neck of bladder inside prostate gland **[Structures openings into prostatic urethra] :** • Ejaculatory ducts: containing sperms& secretion of seminal vesicles • Ducts of prostate gland MEMBRANOUS URETHRA (Length=1 cm): - Surrounded by external urethral sphincter PENILE (SPONGY) URETHRA (Length=16 cm): - Extends inside penis & opens externally through external urethral orifice (narrowest part of whole urethra)*	Length = 4 cm. Has only urinary function. Extends from neck of urinary bladder to open externally through the external urethral orifice (anterior to the vaginal opening)

2- (Urinary bladder)

It has the shape of three-sided pyramid placed on one of its angle (NECK).

Apex

- directed **A**nteriorly and forward.
- Lies behind the upper border of symphysis pubis.
- Is connected to umbilicus by the median umbilical ligament (remnant of urachus).
- It is the same for both males and females.

Base

- directed posteriorly and backward.

Males	Females
1-Vas deferens 2- Seminal vesicle of both sides.	Is related to vagina

Superior surface

Males	Females
1-Coils of ileum. 2-Sigmoid colon	Is related to the uterus

2 Infero-lateral surfaces

- Are related to Retropubic fat separating them from pubic bones.
- Accomodates distention of bladder.
- Continuous with anterior abdominal wall.
- Rupture of bladder escape of urine to anterior abdominal wall.

Neck

- Is the lowest & most fixed part of urinary bladder.
- Is continuous with urethra.
- Is related to (lies behind) lower border of symphysis pubis

IN MALE:

- Is related to upper surface of prostate gland (inferiorly, it rests on the base of prostate).

Interior part of the urinary bladder

Trigone

- A triangular area in base of bladder bounded by : 2 ureteric orifices & internal urethral orifice
- Its mucous membrane is elastic (not folded)

Uvula vesicae

- Elevation behind internal urethral orifice, produced by median lobe of prostate gland
- Mucous membrane is folded.

Capacity of Urinary bladder

Empty

- Accommodates from 300 – 500 ml of urine

Distended

- Is circular in shape
- Bulges into abdominal cavity

Urinary bladder Supply

Arteries

Internal iliac artery

Veins

Internal iliac vein

Lymph

internal iliac lymph nodes

Nerves

1) **Parasympathetic: pelvic splanchnic nerves from:** [S2, 3, 4].
2) **Sympathetic: from** L1,2
3) **Sensory:** transmitting pain due to overdistention of bladder. (via general visceral afferent fibers from bladder to CNS).

Pharmacology 1st lecture:

Thanks for 435 Pharmacology teamwork

Renal Excretion	Glomerular filtration		Location: glomerulus. Glomerular filtration (GFR) depend on : Renal blood flow and the hydrostatic pressure that flow to the capillaries Glomerular filtration occurs to : 1- Low MW drugs 2 - Only free drugs 3- Polar or ionized or water soluble drugs 4- Drugs with low volume of distribution (Vd)
	Active tubular secretion		Location: mainly proximal convoluted tubule Secretion increases drug conc. In lumen, requires energy, carrier mediated: 1. transporters of Organic acids (e.g. penicillin), 2. transporters of organic bases (e.g. catecholamine) **-Two drugs using the same carrier compete for excretion:** -Advantages of competition: *inhibition of organic acids secretion e.g. probenecid & penicillin (increasing their conc. In plasma) -Disadvantages: *probenecid Decreases nitrofurantoin's efficacy in UTIs.
	tubular reabsorption	Passive	- location: distal convoluted tubules & collecting ducts - Unionized(lipophilic) drugs: highly reabsorbed, poor urinary excretion - Ionized(hydrophilic)drugs: poorly reabsorbed, high urinary excretion -basic drugs are ionized in an acidic environment, while acidic drugs are ionized in a basic environment. - Ion trapping: changing urine pH to enhance reabsorption or clearance of certain drugs (toxicity). -Urine favors excretion of basic drugs because its slightly acidic. -Urine acidification: By NH4Cl, enhances excretion of basic drugs (e.g., Amphetamine). -Urine alkalization: by NaHCO3, increases excretion of acidic drugs (e.g. Aspirin).
		Active	- energy dependent -Endogenous substances or nutrients that the body needs to conserve.(e.g. glucose) - probenecid acts as a uricosuric in gout (inhibits uric acid reabsorption)

Factors affecting renal excretion of drug:

molecular size	Larger molecular size = less excretion Small molecular size = more excretion
Lipophilicity	Lipid soluble = less excretion. Water soluble = more excretion.
protein binding	Highly protein bound = less excretion. Poorly protein bound = more excretion.
Plasma concentration	High plasma conc. Of drug = more excretion. Low plasma conc. Of drug = less excretion.
Volume of distribution	High volume of distribution = less excretion. Low volume of distribution = more excretion.
Degree of ionization	Polar drugs (water soluble) are easily filtered = more excretion
Renal blood flow	Increase renal perfusion = more excretion. Decrease renal perfusion = less excretion. NSAIDS e.g aspirin and ibuprofen inhibit the production of PGs and therefore reduce renal perfusion and GFR. (may lead to acute kidney injury)
Biological factors	Renal clearance is reduced in neonates and elderly, thus Dose reduction is advisable, otherwise toxicity may occur.
Disease states	Impairs the elimination of drugs, thus may increase half-life (t ½) of drugs. This may occur due to: -Reduced renal blood flow. -Decreased renal excretion.
Urine pH	-Normal urine pH = 5.3 (slightly acidic) and favors excretion of basic drugs. - Urine pH varies from 4.5 to 8 depending upon the diet e.g. meat causes more acidic urine and carbohydrates rich food may increase urinary pH. -Most of acidic drugs will be reabsorbed back into body.

Orders of elimination of drugs:

Zero-order	First-order
The half-life is **Not equal** At two places on the curve	The half-life is **equal** At two places on the curve
Constant **Amount** is lost per unit time	Constant **Percentage** is lost per unit time
rate of excretion is independent of the concentration of drugs in the plasma.	**rate of excretion is directly proportional with concentration of drug in plasma (that is, with each half-life, the concentration decreases by 50%)**
E.g. Ethanol(alcohol), phenytoin, aspirin	**E.g.** penicillin, aminoglycoside , quinolones

Creatinine clearance and drugs excretion

For male :	Female: CrClest
CrClest = (140 – age)BW / SCr × 72	0.85(140 – age)BW / SCr × 72

Renal clearance is especially important for :

- drugs with narrow therapeutic index **(warfarin, lithium ,digoxin)**
- drugs mainly excreted by the kidney. These drugs should be prescribed carefully in **Renal failure patients & Elderly patients**

this decrease in renal clearance may increase the half life of drugs and may result into drug toxicity .

In renal impairment what should we do?

1-Choose drug with biliary excretion: no **dose adjustment** is needed.

2-Drugs that are primarily excreted by the kidney **need dose adjustment:**

Minor dose adjustment if CrClest is 30-60 mL/min

Major dose adjustment if CrClest less that 15 mL/min.

Pharmacology 2nd and 3rd lecture:

UTI'S

UTI

Upper urinary tract infections *most serious*	Kidneys and ureter
Lower urinary tract infections	Bladder , urethra and prostate

Bacteria responsible of UTI.

Gm- bacteria (most common):	Gm+ bacteria :	limited to urethra, unlike E.coli may be sexually transmitted
- **E.coli** - Proteus mirabilis - Klebsiella - Pseudomonas aeruginosa	- Staphylococcus Saprophyticus	• Mycoplasma • Chlamydia trachomatis • N. gonorrhea

Treatment of UTI (Antibiotics)

					Adverse effects		
Co-trimoxazole (used in recurrent UTI)	Sulfamethoxazole (**SMX**) Trimethoprim (**TMP**) (concentrate in the prostatic fluid)	Alone, each agent is **bacteriostatic** Together they are **bactericidal**	*Inhibition of (**Dihydropteroate synthetase**) to inhibit Nucleic acid synthesis* *Inhibition of (**Dihydrofolate reductase**) to inhibit Nucleic acid synthesis*	More Binding protein (70) More lipid soluble		**Acute hemolytic anemia** (G6PD) Megaloplastic anemia	CONTRAINDICATIONS **1. Pregnancy 2. Nursing mother 3. Infants under 6 weeks 4. Renal or hepatic failure 5. Blood disorders**
Nitrofurantoin (first line in treatment only in **uncomplicated lower UTI**) **Not** use in Upper or systemic infection.	Gram – only **E.coli** and Gram +	**Bactericidal**	inhibits various enzymes and damages DNA.	-Concentrated in the urine -Urinary pH is kept <5.5(acidic) -It turns urine to a dark orange-brown		**hemolytic anemia** (G6PD)	ONTRAINDICATIONS: -G6PD deficiency -Neonates -Pregnancy
Tetracyclines (used in UTI's and chronic Prostatitis due to **Mycoplasma & Chlamydia**)	Doxycycline **(reversibly)**	**bacteriostatic**	Inhibit protein synthesis by binding **reversibly** to 30 s subunit	- **Food & di & tri-valent cations (Ca, Mg, Fe, AL) impair absorption** **-Cross placenta and excreted in milk**		**Brown discolouration of teeth in children** and **growth inhibition of bones**	ONTRAINDICATIONS -Pregnancy -Breast feeding **-Children** (below 10 yrs)
Aminoglycosides Severe infections caused by **gram -** (pseudomonas or enterobacter).	GENTAMICIN (**irreversible**)	**Bactericidal**	Inhibits protein synthesis by binding **irreversibly** to 30S ribosomal subunits	More active in alkaline medium		-Ototoxicity -Nephrotoxicity -Neuromuscular blocking effect	ONTRAINDICATIONS -pregnancy -with hearing proplem
Cephalosporins (used in Sever and complicated UTI and prostatitis)	3rd generation : Ceftriaxone & Ceftazidime		**Acts by inhibition of cell wall synthesis**	Given IV		-hypesensitivity reaction -thrombophlebitis.	against **gram-** bacteria.
Quinolones UTIs caused by multidrug resistance organisms as **pseudomonas**. And prostatitis.	Fluroquinolones (ciprofloxacin)			Inhibits DNA gyrase enzyme		**Damage of growing cartilage (arthropathy)** Because of that we can not give it to children.	

Antibiotics

Used for recurrent cases for **prophylactics**	**Recommended** during pregnancy	**Contraindicated** during pregnancy	**Recommended** In children	**Contraindicated** in children
- TRM-SMX - Nitrofurantoin	- Amoxicillin - Cephalosporins	- Aminoglycosides - Tetracycline - Nitrofurantoin - Chloramphenicol - Metronidazole	- TRM-SMX - Cephalosporins - Penicillins - Gentamicin 'with precaution'	- Tetracycline - Quinolones

Micro 1st lecture:

Thanks for Microbiology 435 teamwork and Ola Alnuhayer.

Urinary tract infection (UTI)			
introduction	• anatomically, divided into upper & lower UTI • patient presents with urinary symptoms and significant bacteriuria 10^5 (= 100,000) CFU/ml • significant bacteriuria + no symptoms → asymptomatic bacteriuria		
prevalence	↑ with age, more in females (especially during childbearing years → 17 - 45)		
classification	Lower UTIs	• Cystitis (infection of the bladder, superficial mucosal infections) • Urethritis (**sexually** transmitted pathogens) • Prostatitis and epididymitis	
	Upper UTIs	• Acute pyelonephritis or chronic pyelonephritis	
	Uncomplicated UTI	• healthy non-pregnant young sexual active female	
	Complicated UTI	• nosocomial UTIs • relapses • structural or functional abnormalities • urologic dysfunction UTI of men	
different microorganisms that can cause UTI (from the practical)			
gram +ve cocci	Enterococcus	anaerobic / colon normal flora	
	Streptococcus agalactiae (group B)	-ve catalase colon normal flora / **pregnant women** & neonates & diabetic patients	
	Staphylococcus saprophyticus	+ve catalase / -ve coagulase / novobiocin-resistant normal flora of the female genital tract & perineum **females in childbearing years** (the risk ↑ with sexual activity → honeymoon cystitis)	
	Staphylococcus aureus	+ve catalase / +ve coagulase [usually with systemic manifestation (bacteremia)]	
gram -ve bacilli	+ LF	Escherichia coli	-ve urease & -ve citrate / +v indol test **most common** / colon normal flora
	+ LF	Klebsiella	+ve urease & +ve citrate mucoid colonies in CLED agar
	- LF	Proteus	-ve oxidase / +ve urease swarming growth in blood agar / **stones formation particularly in children**
	- LF	Pseudomonas aeruginosa	+ve oxidase **nosocomial** (hospital-acquired infection) / blue-green colonies in nutrient agar
others	Candida albicans		in immunocompromised patients / catheterization
	Schistosoma haematobium		parasite / in endemic area
	Tricomonas vaginalis		causes vaginitis

cystitis

risk factors *	in women	• Genetic factors • Short wide urethra + sexual intercourse • Pregnancy (progesterone, obstruction) • Decreased estrogen production during menopause
	in men	• persistent bacterial infection of the prostate.
	in both sexes	• Presence of bladder stone • Sexual transmitted disease (gonorrhea, herpes, chlamydia) • Urethral stricture • Catheterization of the urinary tract • Diabetes mellitus

pathogenesis

1. The infection results when the bacteria ascends from the urethra to the urinary bladder,causing frequent irritations of their mucosal surfaces
2. These bacteria are either resident or transient members of the perineal flora that are derived from the large intestine flora nearby.
3. Toxins then get produced.

- Condition that create access to bladder: Sexual intercourse due to short urethral distance.

etiologic agents	infectious cystitis	non infectious cystitis
	• gram -ve: E.coli is the most common (90%). Klebsiella pneumoniae, Proteus spp, P.aeruginosa. • Gram +ve: Enterococcus faecalis, group B Streptococcus Staphylococcus saprophyticus (honeymoon cystitis) • **Candida species (rare)** • **venereal diseases** (gonorrhea, Chlamydia) may present with cystitis • **Schistosoma hematobium** in endemic area (eosinophilic cystitis)	• **traumatic cystitis** in women • **interstitial cystitis** unknown cause, may be due to autoimmune attack of the bladder • **hemorrhagic cystitis** due to radiotherapy or chemotherapy

Pathogens involved		
	Uncomplicated UTIs	**E. coli (64%) Enterobacteriaceae (16%), Enterococcus spp (20%)** S. epidermidis, S. saprophyticus, Yeasts Viruses (adeno, varicella), Chlamydia trachomatis
	Complicated UTIs	**E. coli, Enterobacteriaceae, Pseudomonas spp, Acinetobacter spp**

clinical presentation *

Symptoms usually of acute onset:

- Dysuria (painful urination or micturition)
- Frequency (frequent voiding)
- Urgency (an imperative call for toilet)
- Hematuria in 50% of cases.
- Usually no fever (localized)

Laboratory diagnosis of cystitis	Specimen collection	• Most important is clean catch urine [Midstream urine (MSU)] to bypass contamination by perineal flora and must be before starting antibiotic. • Supra-pubic aspiration or catheterization may be used in children. • Catheter urine should not be used for diagnosis of UTI.
	Microscopic examination	• About 90% of patients have > 10 WBCs /mm³ (pyuria) • Gram stain of uncentrifuged sample is sensitive and specific (rarely done) • One organism per oil-immersion field is indicative of infection. • Blood cells, parasites or crystals, casts can be seen
	Chemical screening tests (Not specific)	• Urine dipstick rapidly detects: ○ nitrites released by bacterial metabolism. ○ leukocyte esterase from inflammatory cells. • negative results doesn't mean there is no cystitis
	Urine culture	• important to: ○ identify bacterial cause ○ identify antimicrobial sensitivity. • Quantitative culture typical of UTI ($>10^5$ /mm³). • Lower count (10^4 for example) is indicative of cystitis if the patient is symptomatic. • NOTE: the specimen should be taken in the right way [MSU] (to bypass contamination). and the specimen shouldn't stay more than 2 hours without processing because during this time the microorganism will proliferate and ↑ in number → false positive result
recurrent cystitis	• 3 or more episodes of cystitis /year • Requires further investigations such as Intravenous Urogram (**IVU**) or ultrasound to detect obstruction or congenital deformity. • Cystoscopy is required in some cases	
management	treatment	• Empiric treatment commonly used depending on the knowledge common organism and sensitivity pattern. • Treatment best guided by susceptibility of the causative bacteria. • Common agents: Ampicillin, Cephradine, Ciprofloxacin, Norfloxacin, Gentamicin ,TRM-SMX or nitrofurantoin (study pharma)
	duration	• 3 days for uncomplicated cystitis • 10-14 days for (complicated & recurrent cystitis) + upper UTI
	prophylaxis	• for recurrent cases required by Nitrofurantoin or TRM-SMX
	prevention	• drinking plenty of water and prophylactic antibiotic

Dysuria + frequency are seen in cystitis (80% of cases) but they are also associated with other things:	
vaginitis (5%)	Candida spp. - Tricomonas vaginalis
Urethritis (10-15%)	Chlamydia trachomatis - Neisseria gonorrhoeae - Herpes simplex
Non infectious (<1%)	Hypoestrogenism - Functional obstruction - Mechanical obstruction - Chemicals

cystitis vs urethritis

- Cystitis:
  - more acute onset
  - more sever symptoms
  - Pain, tenderness on the supra-pubic area
  - Presence of Bacteria in urine (bacteriuria)
  - Urine cloudy, malodorous and may be bloody

Drugs used in UTI (Pharmacology + Microbiology) :

Treatment of UTI (Antibiotics)	Pregnancy	Recommended	- Amoxicillin - Ampicillin - Nitrofurantoin - Cephalosporins	
		Contraindicated	- Aminoglycosides - Tetracycline - Nitrofurantoin (after38 Weak of pregnancy) - Quinolones	
	children	Recommended	- TRM-SMX - Cephalosporins - Penicillins - cephalexin - Gentamicin 'with precaution'	
		Contraindicated	- Tetracycline - Quinolones	
	recurrent	Postcoital antibiotic	ciprofloxacin	- TRM-SMX - Cephalexin (1st generation of Cephalosporins)
		Prophylactic antibiotic	nitrofurantoin	
	Complicated	Cephalosporins 3rd generation		
	Uncomplicated	- Amoxicillin - Cephalosporins (1st and 2nd generation) - Nitrofurantoin (lower UTI) - TRM-SMX - Fluroquinolones		
	Pyeloneohritis	Uncomplicated	- Amoxicillin and clavulanate - Cephalosporins - TRM-SMX - Fluroquinolones (ciprofloxacin)	
	Urethritis in men	- Doxycycline - Azithromycin		
	Vesicoureteral reflux	- Gentamicin - Cefixime (3st generation of Cephalosporins)		

physiology 4th lecture:

Physiology of Micturition

Urinary Bladder

Anatomical

- **Body:** Wall of bladder contain smooth muscle (detrusor muscle)
- **Neck**
- **2 Sphincters :** External US (smooth muscle) Internal US (skeletal muscle).

Innervation

-**Parasympathetic** (pelvic N.) from LHCs of the Sacral 2,3,4 :contraction of bladder & relaxation of neck ."passage of urine"

-**Sympathetic** (hypogastric N.) from Lumbar 1,2,3
: Stimulate mainly the blood vessels also relaxation of bladder and contraction of neck. ."storage of urine"

-**Somatic** (pudendal N.)from AHCs of S 2.3.4
: control skeletal muscle in sphincter.

Micturition

It is the process of emptying the urinary bladder through the urethra. Consist of 3 processes: Filling of bladder -> Micturition Reflex -> Voluntary control.

Micturition reflex

- **Center:** S 2, 3 & 4.
-**Receptors:** stretch (receptor) in the wall of bladder.
- **Afferent & efferent**: pelvic N.
- **Response:** 1- Contraction of detrusor muscle .2.Relaxation of internal sphincter of urethra. 3.Relaxation of external urethral sphincter

Sensations from the U.B at different urine volumes

- from **150 –300** ml ⇒the first urge to void urine.
- From **300 –400** ml ⇒sense of fullness of the bladder.
- From **400 –600** ml ⇒sense of discomfort.
- From **600 –700** ml ⇒sense of pain.

#Micturition reflexes start to appear at the first stage. They are progressively intensified in the subsequent stages up to stage 4. Micturition reflexes can be voluntarily suppressed.

At about **700 ml** ⇒break point ⇒micturition **CAN NOT** be suppressed.

Control of micturition reflex

It is a complete autonomic spinal reflex to get urine outside the body, that is facilitated or inhibited by higher brain centers.

Voluntary control :

Higher centers control :
1-Cerebral cortex: either stimulation or inhibition.
2- Hypothalamus: There is facilitatory area.
3- Midbrain: inhibition.
4- Pons: facilitation.

mechnism

Filling of the bladder beyond 300 –400 ml causes stretching of sensory stretch receptors. These sensory signals stimulate sacral segment, which is consciously appreciated by higher centers.

Condition is Favorable	Condition is unfavorable
(+) of sacral micturition center.(-) of pudendal nerves -> relaxation of external urethral sphincter ,Contraction of anterior abdominal muscle &Contraction of Diaphragm. **(inntensifies the micturition reflex-> urination)**	Higher centers will inhibit the micturition reflex (-) of sacral micturition center (+) of pudendal nerves -> contraction of sxternal sphincter. **(Inhibit the micturition reflex -> No urination)**

Disturbances of micturition

Denervation **of both afferent and efferen**t nerve supply such as in tumor or trauma	Denervation of the **afferent** supply only such as in Tabes Dorsalis. Outcome -> There is retention with overflow**. (Dribbling of urine when the bladder becomes over filled)**	**Spinal cord transaction** (Above the sacral region) the spinal cord transaction

Micturition

- What is it?

The process by which the urinary bladder empties when it becomes filled. → This process involve two main step:

1- The bladder fills progressively until the tension in its wall rises above threshold level.
2- Nervous reflex (***Micturition reflex***)

- Physiology & Anatomy of the bladder:

- The lower part of the bladder nick called: *Posterior urethra.*
- *Detrusor muscle*: Smooth muscle of the bladder. → Contraction of it is the **major step** in emptying the bladder.
- The urethra passes through the ***urogenital diaphragm*** → contain layer of muscle called external sphincter of the bladder (Skeletal muscle = voluntary) → Can be used to prevent urination even when involuntary controls are attempting to empty the bladder.
- The stretch signals from the post. urethra are especially strong and mainly responsible for initiating the reflexes that cause bladder **emptying**.
- The skeletal motor fibers transmitted through the *pudendal nerve* (S2,3,4 AHCs) to the external bladder sphincter.

- Transport of urine from the kidney through the ureters & into the bladder:

- Urine flowing from collecting ducts into the renal calyces stretches the calyces & increase their inherent **pacemaker** activity → initiate peristaltic contraction → spread into renal pelvis → bladder.
- Peristaltic contractions in the ureter are enhanced by paraSymp. Stimulation (Pelvic nerves; S2,3,4 LHCs) & inhibited by symp. stimulation (Hypogastric nerve; mainly L2 LHCs)

- **Vesicoureter reflex**: a condition in which some of the urine in the bladder is propelled backward into the ureter.

- When ureter become blocked → intense reflex constriction occurs → sever pain → the pain impulses cause symp. reflex back to the kidney to constrict renal arteriols → Decrease urine output → This effect is called **Uretorenal reflex**.

- Cytometrogram:

- Filling of the bladder & bladder wall tone.
- Shows the approximate changes in intravesicular pressure as the bladder fills with urine.
- When there is no urine in the bladder, the intravesicular pressure is ~ 0.
- 150 – 300 ml → 1st urge to coid urine.
- 300- 400 ml → Sense of fullness of the bladder.

- 400-600 ml → Sense of discomfort.
- 600-700 ml → Sense of pain.
- ≥ 700 ml → micturition reflex can not be suppressed.
- هو العلاقة بين حجم البول الداخل للبلادر وضغط البلادر، التناسب بينهم طردي.
- إذا مرة زاد حجم البول -> بيزيد المكتوريشن رفلكس -> بيصير فيه شيئين:
  1- فيه أوامر من فوق تعطي أوامر للكونتراكشن للاكستيرنال مسل.
  2- فيه أوامر من تحت يسويها الباراسمبثتك عشان تسوي انهبشن للاكسترنال.
  اللي يتغلب منهم هو اللي بيسوي الاكشن حقه.

- Micturition reflex:

- As the bladder fills, many superimposed micturition contractions begin to appear.
- They are the result of a **stretch reflex** initiated by ***sensory stretch receptor*** in the bladder wall, especially in the posterior urethra & trigone.

- The micturition reflex is a single complete cycle of:
  1- Progressive & rapid ↑ of pressure.
  2- a period of sustained pressure.
  3- return of the pressure to the basal tone of the bladder.
- Once the micturition reflex becomes powerful enough → it causes another reflex, which pass through the *pudendal nerves* to inhibit the external sphincter. * If this inhibition is **more** potent in the brain than the voluntary constrictor signals to the external sphincter → Urination will occur.

- Facilitation or inhibition of micturition by the brain:

- The micturition reflex is a complete **autonomic** spinal cord reflex, can be inhibited or facilitated by centers in the brain.
  - These centers include:
    1- Strong facilitated & inhibitory centers in the brain stem,
    (in Pons)
    2- Cerebral cortex. (stimulation or inhibition of micturition).
    3- Midbrain. (Inhibition of micturition)
  - The micturition reflex is the basic cause of **micturition**, but the higher centers normally exert final control of micturition as follows:
    1- The higher centers keep the micturition reflex partially inhibited, except when micturition is desired.
    2- The higher centers can prevent micturition, even if the micturition reflex occur, by **tonic contraction** of the external bladder sphincter.
    3- When it is time to urinate → the cortical centers can facilitate the sacral micturition centers to help initiate a micturition reflex and **at the** same time inhibit the external urinary sphincter → urination occur.

- *Voluntary urination* is usually initiated in the following way:
  Contract abdominal muscles → ↑ the pressure in the bladder → allows extra urine to **enter** the bladder **Neck & post. urethra** → stretching their walls → stimulate stretch receptors → excites the micturition reflex and simultaneously **inhibit** the external urethral sphincter.

- Abnormalities of micturition:

Ab.	Lesion	Causes	Features
Atonic bladder	Sensory nerve (Aff)	- Crush injury to the sacral region. - ***Tabes dorsalis*** : Syphilis → constrictive fibrosis → The resulting bladder condition ***Tabetic bladder***.	- Micturition reflex can not occur → prevent transmission of stretch signals from the bladder → Lose bladder control even if Eff & neurogenic connection are intact. - The bladder fills to capacity → overflow a few drops when Volume > capacity. → (***Overflow incontinence***) - The bladder becomes distended, thin walled & hypotonic.
Automatic bladder	Spinal cord damage above sacral region *Sacral segment are intact.	Crush injury to area above sacral region.	- Typical micturition reflex **can still occur**, but are no longer controlled by the brain. - During the **1st few days** after the damage, the micturition reflexes are suppressed bc of the state "Spinal shock" caused by sudden loss. But the excitability of the reflex gradually increase until typical micturition reflex return. - Some pts control urination by stimulating the skin in the genital region. - مثل الطفل، يصير ما فيه تحكم بالسوماتك نيرف، فأول ما تتعبى البلادر يبوّل. - الخلل في التوصيل فقط!
Uninhibited neurogenic bladder	Partial damage in the spinal cord or brain stem that interrupts most of the inhibitory signals.	Lack of **inhibitory** signals from the brain	- Result in frequent & relatively uncontrolled micturition. - Small quantity of urine elicits an uncontrollable micturition reflex → promoting frequent urination
Denervation of the aff & eff	Aff & Eff	- Tumour - Injury to cauda equine -↓Degradation of acetyl choline by process of reuptake. -↓Cholinesterase in the tissue -↑ No. of cholinergic receptors.	- Reflexes are **abolished**. - **Intrinsic** responses of the smooth muscles are increased. - The bladder is hypertonic. - Associated with uncontrolled periodic micturition about 25 – 100 ml at a time. - كأنها عضلة مفصولة من الجسم -> تصير هايبرتونك -> في انقباضات دائمة -> أي تجمع يصير فيها تطلعه خارج الجسم دفعة وحدة (بدون قطرات)

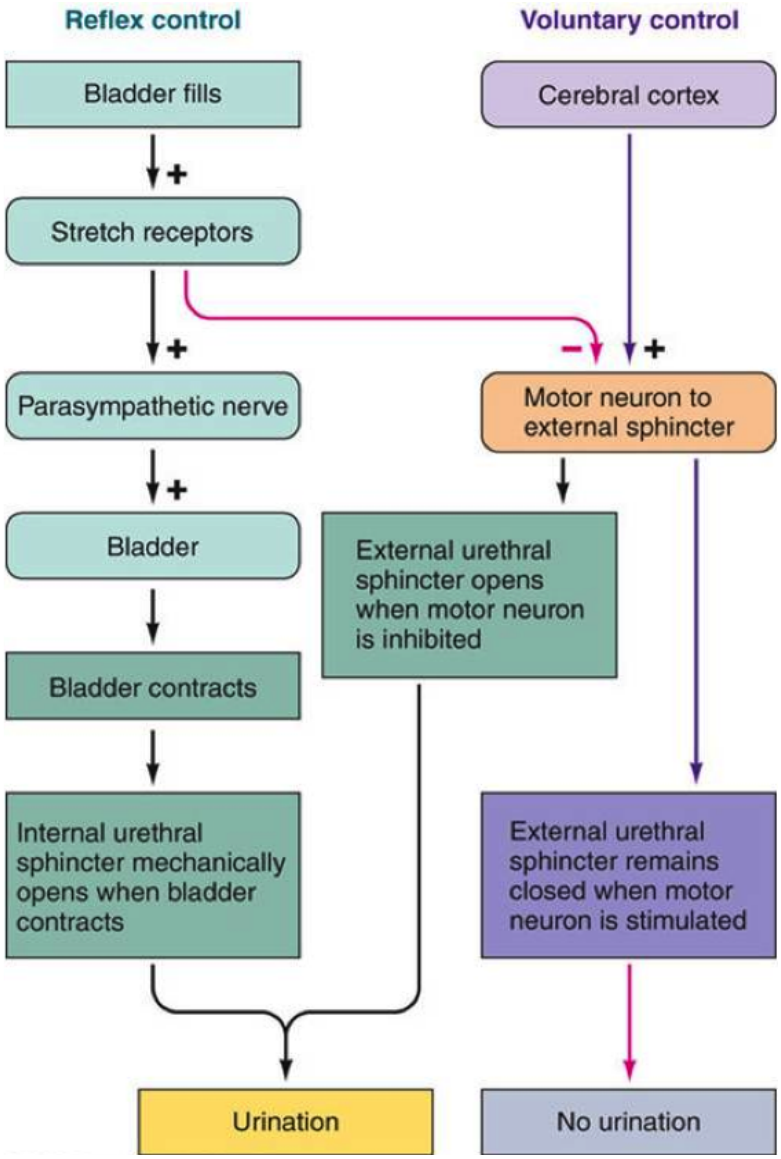
Notes

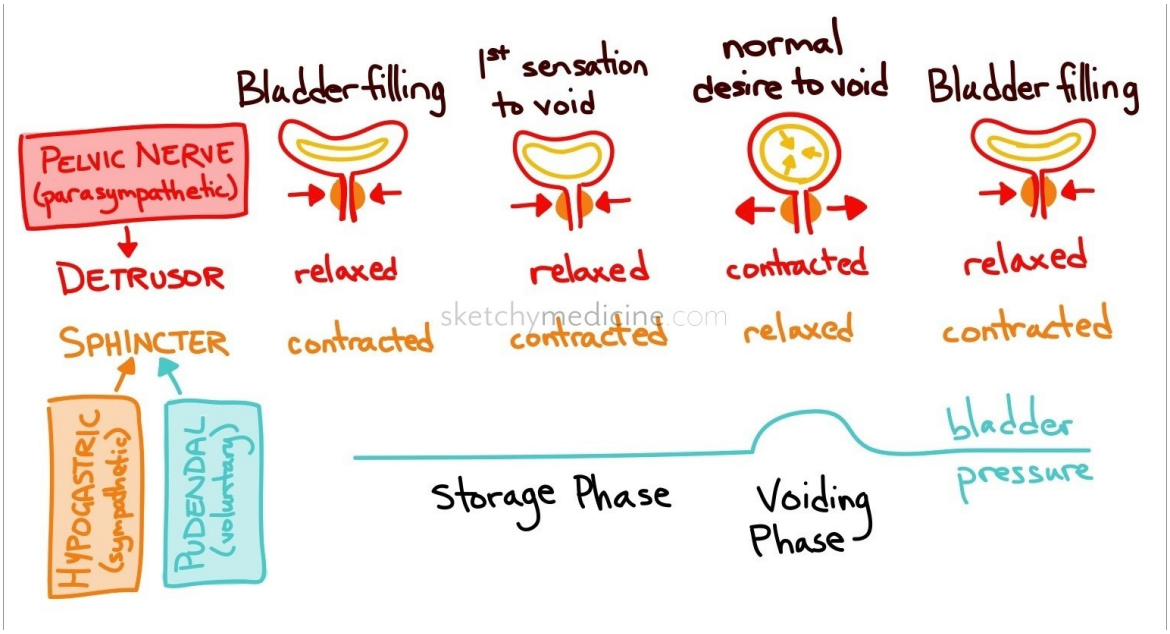
- Bladder → Store urine, controlled by symp. & parasymp.
- Innervation of bladder & bladder neck:
  - Parasympathatic: Pelvic nerve (S2,3,4 in LHCs)
  - Sympathatic: HypogaStric nerve (L1,2 in LHCs), Storage of urine.
  - Somatic nerve: Pudendal nerve (S2,3,4 in AHCs)

- Babies have a normal micturition, but they urinate spontaneously bc the innervation of external sphincter muscle still developing.
- Trigon & post. urethra → more sensitive → ↑ stretch receptors.
- In cystometrogram, there is a region of pressure constant (~ from 90 – 250 cm\H_2O) this is bc of the type of bladder epithelium (transition) → widening, and Laplas law => P=2T\r الضغط في هذي الحالة بيبقى ثابت لأن كلما زاد الشد بيزيد نصف القطر مرتين.
- About cystometrogram curve: البلادر مثل البالونة، أول ما أبدأ يصير صعب النفخ، بس بعدها تصير تنتفخ بسهولة لكن لما توصل حدها تنفقع.
- Hypothalamus → control of autonomic.
- Micturition reflex: Aff → لما يدخل الحبل الشوكي يرسل رسالة للدماغ يعلمه إن فيه كمية بول عشان يثبّط عمل الpudendal nerve وينشّط الباراسمبثتك أكثر، النتيجة حالتين:
  ١- إذا كنت في حالة you want to urinate هنا بيصير الانهبشن لل.pudendal n
  ٢- إذا كنت في محاضرة مثلا، و you don't want to urinate هنا راح يصير:
  Stimulation of pudendal nerve to continue contraction of external sphincter muscle.
- Injury to lumbar region → X sympathetic, √ parasympathetic → √ micturition reflex.
- Injury above sacral → √ parasympathetic, X control → يصير فيه تبوّل مثل الطفل.
  - أول الأسابيع بعد الحادث ما يشتغل أي شيء، فيصير يتبول بالتقطير، لكن بعد فترة يستوعب إن الباراسمبثتك يشتغل كويس فيسوي شغله.

- Resources: Guyton & Hall and Dr.mannan's 2016 lecture & notes.

Done by: Atheer Alnashwan.


Reflex control
Voluntary control
Bladder fills
Cerebral cortex
Stretch receptors
Parasympathetic nerve
Motor neuron to external sphincter
Bladder
External urethral sphincter opens when motor neuron is inhibited
Bladder contracts
Internal urethral sphincter mechanically opens when bladder contracts
External urethral sphincter remains closed when motor neuron is stimulated
Urination
No urination


Bladder filling
1st sensation to void
normal desire to void
Bladder filling
PELVIC NERVE (parasympathetic)
DETRUSOR
SPHINCTER
relaxed
contracted
relaxed
contracted
contracted
relaxed
relaxed
contracted
HYPOGASTRIC (sympathetic)
PUDENDAL (voluntary)
bladder pressure
Storage Phase
Voiding Phase
sketchymedicine.com

pathology L(2&3):

A big thank for pathology team

Summary:

AKI Could be?

- Prerenal – Hypovolemia and shock
- Post renal – obstruction
- Intrarenal:
    - Tubules
    - Tubules and interstitium
    - Blood vessels
    - Glomeruli – crescentic glomerulonephritis

What could drugs give us?

- Acute tubular necrosis.
- Acute tubulointerstitial nephritis

What can we see in a drug-induced injury?

- Eosinophils
- Plasma Cells
- Granuloma. (After few days, one week)

Clinically what do we see?

- AKI
- High creatinine and urea

Summary:

Acute pyelonephritis:

Acute onset with fevers and so on.

These patients usually have predisposing factors and most commonly an ascending infection.

And they may have complications.

Acute Pyelonephritis	Chronic Pyelonephritis
- Duration. - Neutrophils	- Lymphocytes - Fibrosis

Summary:

Chronic pyelonephritis:

Specific type of pyelo:

- Could be related to TB – caseating granuloma
- Related to intracellular bacteria or other kind of bacteria giving us staghorn
- Or extracellular bacteria giving us xanthogranulomatous = foamy histiocytes and granuloma.

Summary:

Tubulointerstitial nephritis:

- Related to drugs.
- Most cells found are eosinophils and plasma cells
- Chronic type could be insidious (not acute or noticed)

Acute pyelonephritis:

- Polymorphs in the interstitium + tubules

Chronic:

- Fibrosis + lymphocytes.
- Reflux
- Obstruction

Xanthogranulomatous pyelonephritis:

- Staghorn + mainly foamy histiocytes

Malakoplakia:

- Might occur in the kidney + all urinary tract. But most frequent in the bladder.
- Michaelis gutman body.

Lower UTI:

Bladder + Acute cystitis + Chronic obstruction in cystitis (Diverticula). + Stones.

Caseating granuloma:

- In drugs & In different places as well.
- Eosinophils

Kidney stones

Conditions favoring kidney stones formation

1- High urinary conc. of constituents of GF.

Due to:

- ↓ Urinary volume
- Restricted fluid intake.
- ↑ fluid loss over a long period of time.
- ↑ rate of excretion of metabolic products forming stones:
- ↑ plasma volume (that increases filtrate level)
- ↓ tubular reabsorption from filtrate

2- pH of urine

Acid → uric Acid stone

Alkaline → Ca^{2+}stone → Upper UTI → Mg ammonium phosphate crystals (Struvite stone)

4- Urinary stagnation

Due to obstruction of urinary outflow.

5- Lack of normal inhibitors of stone formation in urine.

- e.g.:
1- Citrates.
2- Pyrophosphate.
3- Glycoproteins

- Inhibit the growth of Ca^{2+} salts crystals.

- In type I renal tubular acidosis, hypocitraturia → renal stones.

Constituents of Kidney Stones

Condition	Types \ characteristics	Causes	Notes
Stones of Ca^{2+} salts	- Type of salt depends on: – **pH** of urine – Availability of **oxalate** 1- Ca^{2+} oxalate → Most common form of stones. → smaller, lodge in ureter. 2- Ca^{2+} phosphate → Less common. → staghorn, in renal pelvis (big)	1- Hypercalciuria: - Due to hypercalcemia (1ary hyperPTH) - SMTM there is no hypercalcemia. 2- Hyperoxaluria: "more imp" - Formation of Ca^{2+} oxalates. → Caused: - exogenous (diet) - 1ary hyperoxaluria - ↑ absorption (in **fat malabsorption**) لما يقل الأبزوربشن للفات، يزيد الأبزوربشن للoxalate ولما يزيد الأوكزاليت = بيرتبط مع الكالسيوم في الدم ويتسوى له فلتريشن، بعدها بيسبب الكالسيوم ستونز مع كثرته.	Management: - Never tell the pts to reduce Ca^{2+} intake. لأن الأوكزاليت لما ما يلقى كالسيوم يرتبط معه بيصير يمتصّه من أورقانز ثانية تحتاجه فبيسوي مشكلة أكبر. - Acidification of urine (bc Ca^{2+} stones favor alkaline urine)
Uric acid stones	- May be associated w\ **hyperurecemia**. - Favors acid urine. - Characteristics: 1- Small, friable & yellowish. 2- may form staghorn if big. 3- Radiolucent "can't be seen by plain x-ray". 3- Visualized by ultrasonography, or IV pyelogram.	**Treatment** - Treat the cause of hyperuricemia. - ↓ purine-rich diet. - Alkalinzation of urine (e.g. by potassium citrate).	

Mg^{2+} ammonium phosphate stones	- Caused by chronic UTI. → By urease enzyme → splitting organisms' uric acid to urea → NH_3 product - Favors alkaline urine (infection)	- Urine acidification. - May require complete stone removal (**percutaneous nephrolithotomy**) - treatment of future urinary tract infection
Cystine stones	- Rare. - Occurs in case of homozygous cystinuria - Soluble in alkaline urine = favors acid to form stone.	- Alkalinzation of urine. - Penicillamine. (analog the amino acid cysteine)
Investigations of patients with renal calculi	1- Stone is **available** (with urine or by surgical intervention) (يعني ملموسة، نستطيع رؤيتها وتتحسسها باليد)	Laboratory investigations for detection of stone chemical constituents: - to **know the cause.** - for decision of lines for **preventive treatment.**
	2- Stone is **not** available بمعنى إنها تعمل أثر لكن لا نستطيع رؤيتها أو تحسسها باليد	Blood analysis: Ca^{2+}, uric acid & PTH. Urine analysis: volume, Ca^{2+} & oxalate Urine pH: > 8 suggestive of UTI (Mg amm. phosph.) Screening of urine for cystine: qualitative (if +ve: 24 hs urine) Renal tract imaging: CT, ultrasonography & IV pyelogram

Notes

- ↑ PTH may cause stones. (Ca^{2+} stones).
- Bacterial infection → persistent pH change.
- Uric acid stone → not seen in x-ray, we can see it by ultrasonography.
- For all forms of stones we advise the pts to ↑ **fluid intake**, except for pts with glomerular failure.

Extra (imp. In pathology)

Radoipaque	Radiolucent
- Ca^{2+} oxalate - Ca^{2+} phosphate - Mg^{2+} amm. Phosph	Uric acid

Done by: Atheer Alnashwan

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Done by :
Afnan alMalki
Razan alSabti
Munerah alOmari
Nouf Altwaijri
Nouf Alabdulkarim.