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Lots of mitochondria in the basal parts of the cell are for active transport. The brusher border microvilli will increase the surface area. The lateral intracellular space increase the surface area. The cells are only attached by tight junctions on the apical surface. Reabsorption can occur paraceullarly or transcellularly.

Cells lining the nephron here are different. Larger and heavily nucleated cells form the macula densa. This is thought to be a sodium sensor. Cells lining the afferent arteriole at the juxta-gglomerular apparatus are modified smooth muscle. They lack the actin and myosin and instead have granules containing renin. The masonry is also here and these are contractile cells.
MAP is about 95mmHg. The hydrostatic pressure starts here. There is a sharp fall in blood pressure as we enter arterioles since these are higher resistance vessels and so blood loses energy here. Remember that arterioles are the major resistance vessels of the CVS. Hydrostatic pressure then falls through the system.

Colloid oncotnic pressure is roughly 25mmHg in the blood. This only changes when we get to the glomerular capillaries as fluid moves into the bowman’s capsule, which rises the concentration of proteins and as such raises the oncotnic pressure. This will begin to fall in the peritubular and vasa recta capillaries. The hydrostatic pressure here is lower than oncotnic and as such **reabsorption occurs**. This lowers the oncotnic pressure, as fluid will move into the capillaries and thus dilute the protein concentration. This is supported by the highly viscous, slow moving blood which gives a longer time frame to increase the reabsorption.

Thus the kidney has 1 capillary bed for flirtation and 2 for reabsorption.
We may also have post renal obstructions. In men this can be the prostate, but other causes include tumours and stones.

Kidney diseases tend to be silent until the late stages of the disease.

**Chronic kidney disease**

This is usually due to a structural or functional abnormality that persists over 90 days. It is slow progress. Usually asymptomatic until late and there are multiple causes. It is common – 8.5% of general population. This can make people ill with other things for example if you have pneumonia this can be very dangerous in these patients.

**Acute kidney injury**

Occurs over days or weeks. There are many causes (volume depletion, drugs, systemic illness). Creatinine takes 24 hours to change and so lags behind real change. Affects about 15% of all UK hospital admissions. This does tend to be reversible once cause is found and dealt with. Risks include sepsis, increased, diabetes and anti-hypertensives. 1 in 5 die if presenting with sepsis cause i.e. a high mortality.

**Nephrotic syndrome**

A triad of albuminuria, hypoalbuminaemia and oedema. So: check ankles, if swollen, check for proteinuria and hypoalbuminanemia. Low albumin = shows as high in urine – think Nephrotic and refer to specialist. Complications include DVT, PE, High lipids and infections. Usually due to glomerular disease. Often treated with steroids and cytotoxics. Complications include high risk of infection and clotting problems. Antibodies and clotting factors are lost in the urine in this condition.

In cases with a high blood pressure, small protein and small blood in urine this is most likely due to IgA nephropathy. This can fatal. Has a rule of thirds. 1/3 get better; 1/3 get chronic and 1/3 have acute injury requiring dialysis or urgent treatment.

**Glomerulonephritis**

Complete loss of renal function over days / weeks with inflamed blood vessels. Often with stetmic symptoms and signs. It is uncommon. Treatment includes steroids, cytotoxics and plasma exchange.
Systemic signs may be fever, unwell, weight loss. Rash may appear which, when you press down, doesn’t remove the red spots. Creatinine is often in 1000’s [should be about 100]. We need to rule out this serious condition first. It can be caused by antibodies against the BM, IgA nephrititis and vascular disease. Plasma exchange works by removing the IgA so that they can’t attack themselves.

**Impact on patients**

These are lifelong conditions. They may need lifestyle adjustments such as diet (low phosphate, potassium and protein diets).

**What can be done**

Need to take a good history, and check their volume status. We check the volume by checking for ankle oedema, JVP and lungs for pulmonary oedema. We should do a urine dipstick in all cases. There are only two causes of anuria: obstruction and goodpasture’s syndrome which are anti-glomerular Ig’s.

We can treat the complications:

- Anaemia – with iron etc.
- Hyperparathyroidism – replace the vitamin D.
- Fluid balance: 1L a day. Also control diet salt to control thirst and increase adherence to regime.
- Symptoms such as itch, nausea, tiredness can be helped to.

There is a slow progression of kidney disease with time. In the UK the biggest cause is diabetes. ACE inhibitors and anti-renin angiotensin drugs will slow progression of kidney disease.

**Haemodialysis.** Here we make a fistula between an artery and a vein and allow this to mature so as to put in a large needle. If not use the internal jugular or a graft into the arm. This can be hard to do with poor access. Life expectancy is about 8 years.

**Peritoneal dialysis.** This is for our younger, fitter patients. Here, fluid (about 2L) enters the peritoneum and stays there for a few hours and is then drained. This is all done by the patient at home. Peritonitis is a common side effect. Can cause capsulizing scerosing peritonitis which is when the peritoneum hardens and compresses the abdominal organs.

**Transplant.** Need to be fit and have a donor. Then need immunosuppression. 1/3 of patients will have a rejection episode in first year. Risks from cancer and infection rise, such as cytomegalovirus which can be fatal. About a 15 year life expectancy.
Hematocrit is equal to total cell volume which is: blood cells/whole blood

Thus 1-haemotcrit is plasma/whole blood

So, whole blood flow is plasma flow/ 1- hematocrit.

THUS

Assuming a haematocrit value of 45%,

\[
\text{Renal blood flow} = \frac{700}{1 - 0.45} = 1,270 \text{ ml/min} = 1.27 \text{ l/min}
\]

Baring in mind cardiac output is 5L a minute the kidneys use about 25% of blood. They take a disproportionate amount of blood for their size.

Remember PAH isn’t endogenous and needs to be infused and needs to reach stable levels in the blood before its measured.

**Hormones Secreted by the Kidney**

**Formation of active form of vitamin D**

\[
\text{Cholesterol derivatives in form of 25, hydroxycholecalciferol} \rightarrow \text{24, 25 dihydroxycholecalciferol (in absence of PTH)} \rightarrow \text{1, 25 dihydroxycholecalciferol (1,25 DHCC; active vitamin D; calcitriol)}
\]

- Increased absorption of calcium and phosphate from gut PLUS increased reabsorption of calcium and phosphate by kidney

Inactivated form is excreted in the urine in the absence of PTH.

Vitamin D deficiency leads to:
- Rickets (Deformed bones in children).
- Osteomalacia (weak bones in adults).

And there is growing evidence for cardiovascular disease. Calcitriol (active vitamin D) can be administered exogenously in vitamin D deficiency that is caused by kidney failure.
Lecture 13: Control of Body Fluid Osmolality and Volume 2

The kidneys act to regulate blood volume which in turn will regulate blood pressure in the long term. Blood volume is about 5 litres of which 60% is fluid [the rest is cells- haematocrit is about 40%]. Plasma volume may also be referred to as effective circulating volume. These are the same except for conditions in which there is stasis of blood such as shock. Here plasma volume remains the same but the effective circulating volume is decreased because of mass vasodilation.

A decrease in blood volume is hypovolaemia. This, according to Starling’s law of the heart, will decrease cardiac filling (preload) and thus reduce stroke work and cardiac output and thus reduce blood pressure.

An increase in blood volume is hypervolemia. This increases cardiac filling and so increases cardiac output and thus arterial blood pressure.

Thus, alterations to effective circulating volume require correction to maintain arterial blood pressure within normal ranges. The kidneys are central to this; they act to control Na excretion. If we retain sodium, then water will follow and also be retained.

Hypovolemic Shock

In stage 1 there is a slight decrease in venous pressure but the baroreceptors respond. There is also an inotropic response to release adrenaline. Note palor occurs because the blood is being diverted away from the skin to go to the central organs.
A rise in diastolic pressure is indicative of a rise of systemic vascular resistance [i.e. vasoconstriction].
The parasympathetic system will make us sweat.
- SPA-supra-pubic aspirate
- CCU- clean catch urine
- Bag urine
- Pad urine

Other specimen’s may include: ileal conduit, cystoscopy, urostomy and nephrostomy.

Dipstick tests include: nitrite test (most pathogens reduce nitrate to nitrite), leucocyte esterase test (this is a marker for leucocytes), protein and blood.

**Microscopy**

Now done by computers. Abnormal white cells is above 10/mm$^3$ but UTI’s commonly exceed 100. Presence of epithelial cells may suggest contamination. A UTI may be suggested if there are over $10^5$ organisms/ml. We also culture bacteria for extended spectrum b-lactamase activity (ESBL).

We may also do imaging: plain AXR, IVP, Ultrasound or CT (consider cost and radiation exposure).

**Asymptomatic Bacteriuria**

This is diagnosed by culture and microscopy of urine but does not need treatment unless:

- Patient is pregnant. Can cause pre-term delivery and low birth weight. Screen at 1$^{st}$ scan.
- In children under 5. These patients have a risk of ascending infection due to the vescicoureteric reflux.

The foetal skull may obstruct the ureter. The calyces may be more dilated in pregnancy due to progesterone.

**Urethral Syndrome**

50% of woman presenting with frequency and dysuria will have no bacteruuria. The aetiology is unclear- perhaps a chemical irritation, but it is hard to culture organisms. This tends to resolve over 2-3 days with no specific therapy. It often recurs.

**Antibiotics for Lower UTIS**

1$^{st}$ line: trimethoprim, Nitrofurantoin and Cephalexin.
Duration: 3 days for uncomplicated in women, 7 days for UTI in children or men.

Complications or lower UTIS include: recurrence (20% of young women), ascending pyelonephritis [inflammation of the kidney], sepsis and renal failure.

**Catheter Related UTI**
Risk of acquiring infection is 5% a day. Many patients on long term catheters will have infection or colonisation – usually exceeding $10^5$ bacteria per ml and over 100 WBC/mm$^3$. Often a mix of organisms and presents asymptomatically. Complications include: symptomatic infection [note may present unusually in demented and elderly], blocked catheter and sepsis. Treatment of asymptomatic infection / colonisation does not prevent symptomatic infection.

**Pyelonephritis**

Typically, with fever, chills, rigors, malaise, progressive flank pain +/- symptoms of cystitis. Atypically may have headache, pain in the abdomen or pelvis and confusion.

To investigate do blood cultures and MSU.

Treat: gentamicin or ciprofloxacin. You need to achieve a good urinary concentration of antibiotic.

Complications include sepsis, renal failure, papillary necrosis, intra-renal abscess and perinephric abscess.

**Prostatitis**

Can be caused by ascending infection, reflux, haematogenous, lymphatic or trans-rectal.

Acute prostatitis can be a complication of acute UTI. May cause febrile [fever] illness with systemic upset. Can cause obstructive and irritative symptoms. Organisms are the same as acute UTI. Treat with ciprofloxacin for 4 weeks.

For chronic there is often a range of symptoms:

- Urethral: dysuria, discharge, frequency and nocturia.
- Prostatic: anorectal dysaesthesia and inguinal pain.
- Sexual: loss of libido and erectile dysfunction.
- Others: myalgia and headache.

Diagnose with stamy localisation test. Collect first urine, then mid stream. Then massage prostate and collect secretions then collect terminal urine.

Treatment: Ciprofloxacin for 4-6 weeks.
Poor Flow and Terminal Dribbling

This is often caused by increased resistance of the outflow tract (e.g. prostate enlargement) and a significant problem is the retention of urine after voiding.

Bladder Outlet Obstruction

Most commonly occurs in men with enlarged prostates - benign prostatic hyperplasia. Although this is a normal feature of ageing, 20-30% of men will need medical or surgical treatment before they reach 80. Symptoms include: decreased flow rate, hesitancy on initiation of voiding, incomplete bladder emptying and stopping and starting of voiding. Essentially the prostate closes the urethra. We see on investigations that flow rate is poor for a large change in detrusor pressure. Note normal flow is about 25mls per second.

Management:

Stromal tissue of the prostate contains smooth muscle thus use agents that relax smooth muscle should reduce obstruction - Smooth muscle contains α1-receptors. α-adrenergic receptor blockers

- Nonselective α-blockers - phenoxybenzamine
- Selective short-acting α1 blockers - prazosin, alfuzosin, indoramin
- Selective long-acting α1 blockers - terazosin, doxazosin.
- Partial subtype (α1A)-selective agents - tamsulosin, silodosin.

Prostate growth depends on the conversion of testosterone to dihydrotestosterone by the enzyme 5-α-reductase. Thus, inhibition of 5-α-reductase should shrink the prostate. 5-Alpha reductase inhibitors

- 5-α type II blocker - finasteride (Proscar). 30% show symptom improvement
- 5-α type I and type II blocker - dutasteride (Avodart).

If there is residual urine in the bladder after voiding intravesical pressure is high during filling. The rising bladder pressures reflect into the ureter and kidney causing renal failure (post). We can surgically remove the prostate tissue to cut away the stricture. Note this surgery uses fluid that can induce hyponatremia.

Urethral stricture may be also occluding normal flow.

If there is spinal cord damage or spinal bifida the switch from the parasympathetic and somatic to contract the bladder and open the urethral sphincter may be lost. The unmyelinated system is usually silent but kicks in here. This can only switch the detrusor muscle on though – it can’t open the external sphincter so you are pushing against a closed valve and thus lose your control mechanisms. Control by the brainstem over sacral spinal cord coordination of the bladder (contraction) and outflow (relaxation) is lost. The bladder contracts against a high resistance and voiding is poor.