Physiology of ureter and renal pelvis

Transport of urine from renal pelvis to bladder *active* process requiring:

- Pacemaker cells
- Propagation of electrical impulse
- Adequate mucosal coaption
- Intraluminal pressure > bladder pressure

Electrical activity

Development of resting membrane potential dependent on K+

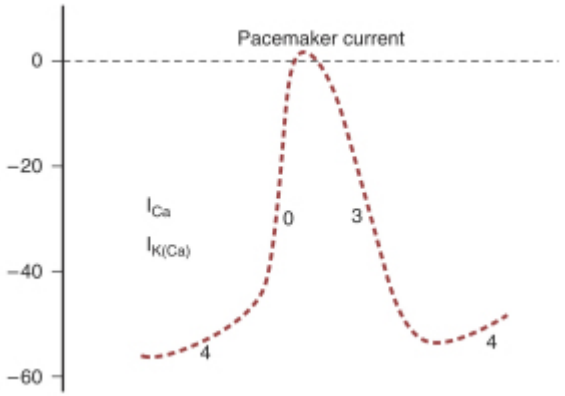
Inside K+; outside Na+: K+ leaks out of cell down concentration gradient through open potassium channels.

Electrochemical gradient thus set up with **inside negative** cf. outside, stopping further K+ efflux

Typical resting membrane potential of ureteral cell = -30mV to -70mV

Depolarisation in pacemaker cells:

- Pacemaker cells located near pelvicalyceal border
- Pacemaker cells differ from ordinary cells in that **Na+ permeability is unchanged by depolarisation**
- Opening and slow closure of Ca+ channels offset by opening and slow closure of K+ channels alone, leading to rhythmic depolarisation and repolarisation



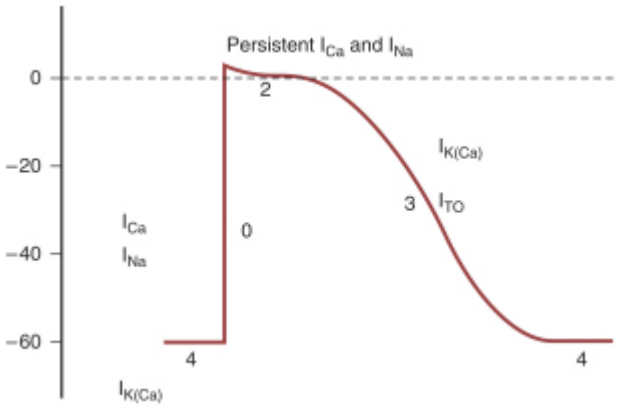
- Believed that prostaglandins and tachykinins (prostanoids) regulate/amplify pacemaker cell activity
- Propagation of depolarisation via intermediate/gap junctions; speed 2-6cm/s [NB. ureter 22-30cm long in adults]; frequency of driven action potentials 3-5/min

Depolarisation in non-pacemaker cells:

- Opening of Na+ and Ca+ channels; closure of K+ channels
- Na+ in fast, Ca+ in slow – rapid depolarisation then plateau
- Raised cytosolic Ca+ stimulates smooth muscle contraction*
- Raised intracellular Ca+ re-opens voltage-gated K+ channels
- Rapid K+ efflux repolarises cell**

* depolarisation also transmitted via tubules to endoplasmic reticulum stimulating Ca release

** restoration of electrolyte balance by Na+/K+ ATPase and cAMP (drives Ca+ back into endoplasmic reticulum)



Mediators of peristaltic activity

	Contraction	**Relaxation**
Neuromodulators	Alpha-adrenoceptor Tachykinins Histamine Angiotensin ? cholinergic stimulation ? serotoninergic PGF2a	Calcitonin gene-related peptide Beta-adrenoceptor PGE1 and PGE2*
Drugs	? opiates	Progesterone Calcium channel blockers Potassium channel openers (nicorandil)

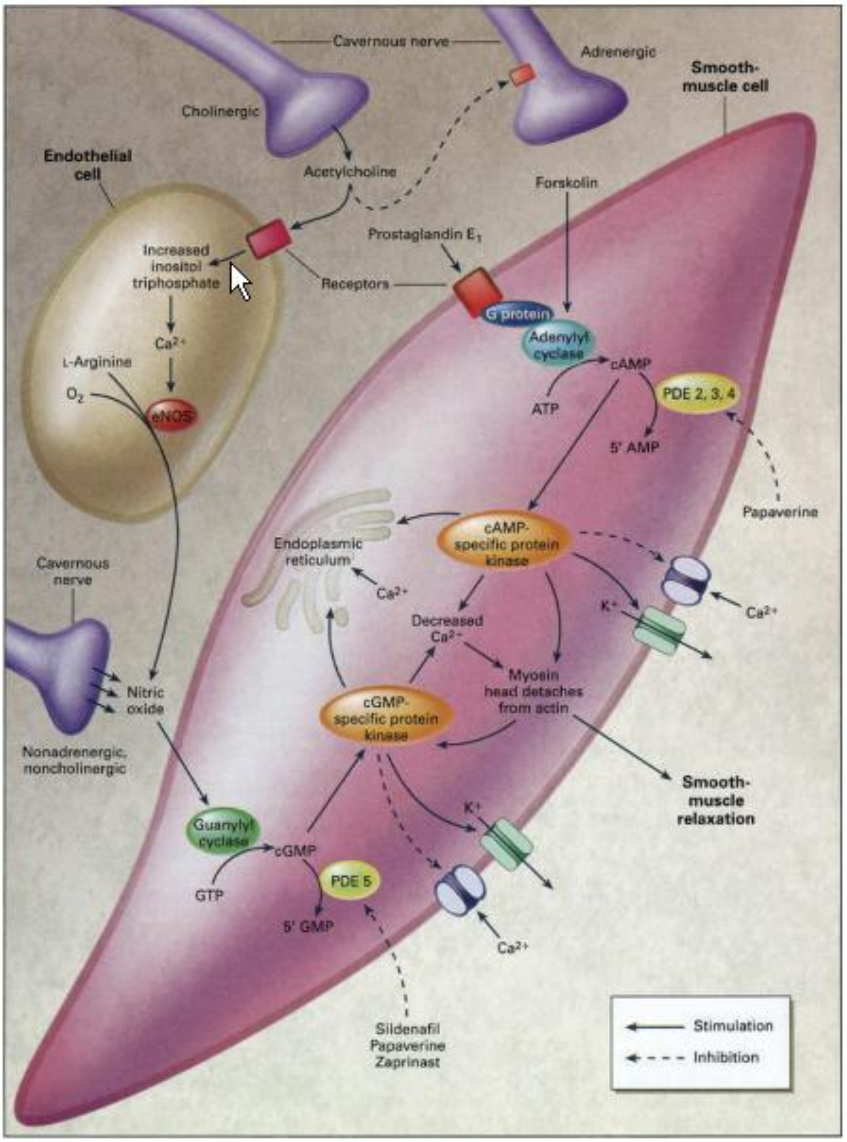
* Surprisingly NSAIDs have not been shown to affect frequency of strength of ureteric contraction. They are believed to work by inhibiting prostatglandin mediated afferent arteriolar dilatation (reducing pelvic pressure and therefore pain) and reducing ureteric inflammation

Urine transport

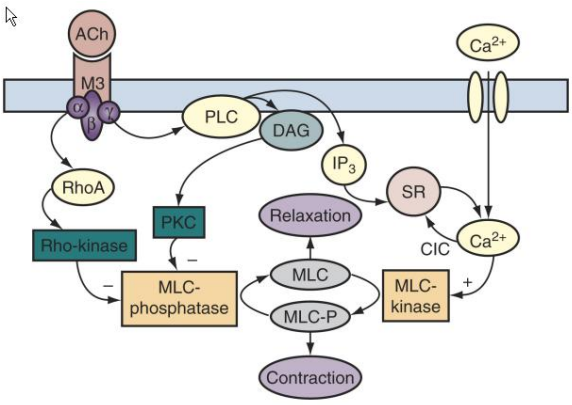
At normal urinary flow boluses of urine are formed by peristaltic waves
Resting ureteric pressure = 0 - 5 cm water
Peristatic waves = 20 – 80 cm water
Frequency = 2 – 6 times per minute
At very high flow rates, mucosal walls do not coapt and urine transported as a continuous column
Decompensation when bladder pressure > 40cm water

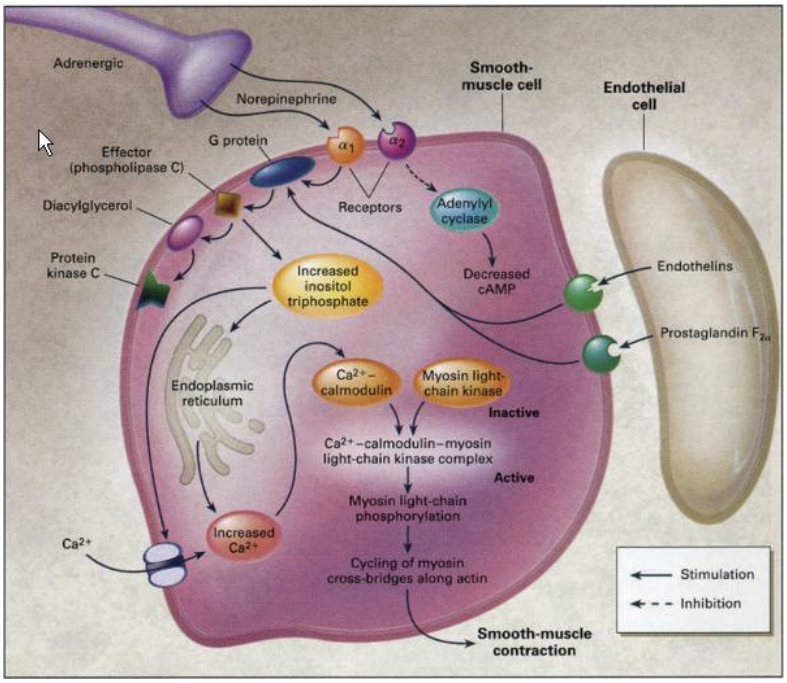
Appendix

Smooth muscle relaxation



Smooth muscle contraction




Adrenergic
Norepinephrine
Smooth-muscle cell
Endothelial cell
G protein
α_1
α_2
Effector (phospholipase C)
Receptors
Adenylyl cyclase
Diacylglycerol
Protein kinase C
Increased inositol triphosphate
Decreased cAMP
Endothelins
Prostaglandin $F_{2\alpha}$
Endoplasmic reticulum
Ca^{2+}–calmodulin
Myosin light-chain kinase
Inactive
Ca^{2+}–calmodulin–myosin light-chain kinase complex
Active
Myosin light-chain phosphorylation
Increased Ca^{2+}
Ca^{2+}
Cycling of myosin cross-bridges along actin
Stimulation
Inhibition
Smooth-muscle contraction