“The greater the ignorance the greater the dogmatism.”

Sir William Osler (1849 – 1919)

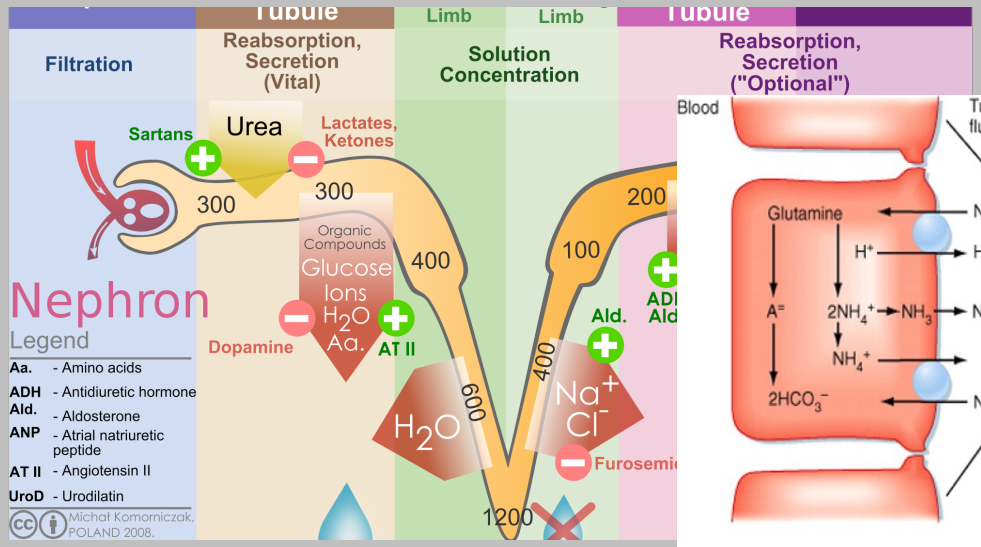
My talk with a fluids theme

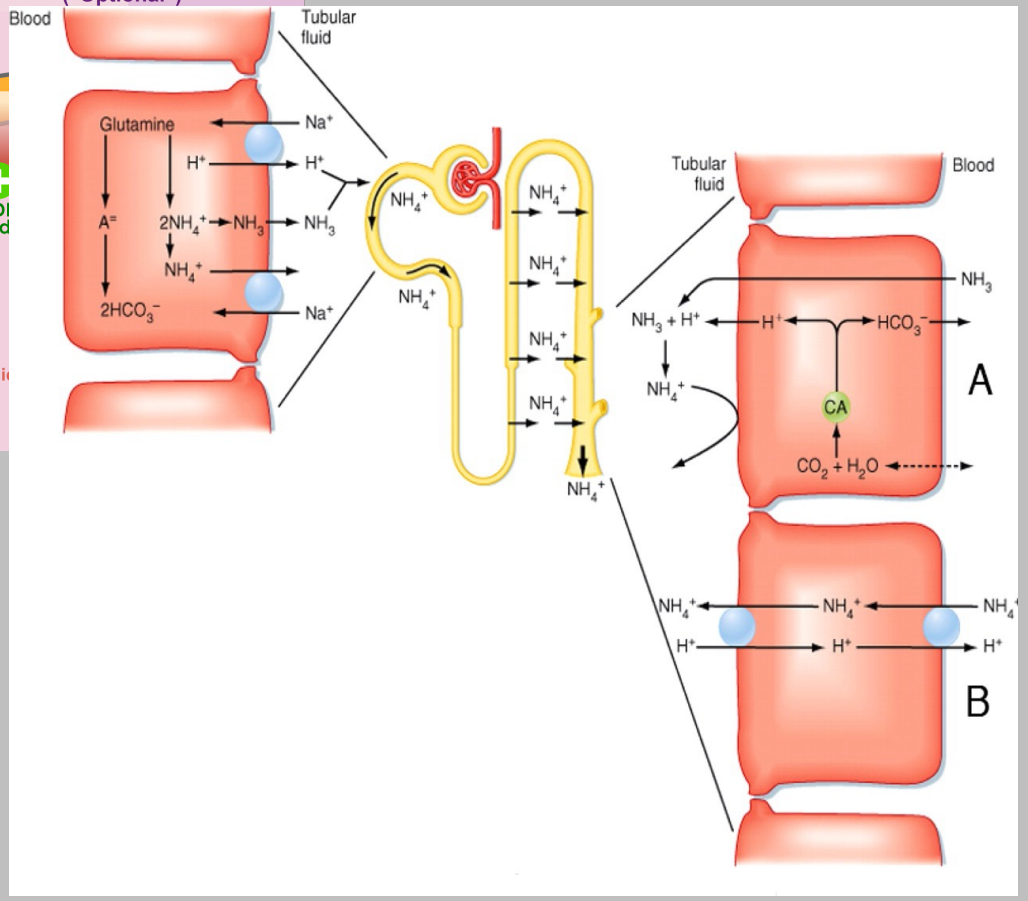
Dr Nick Grant

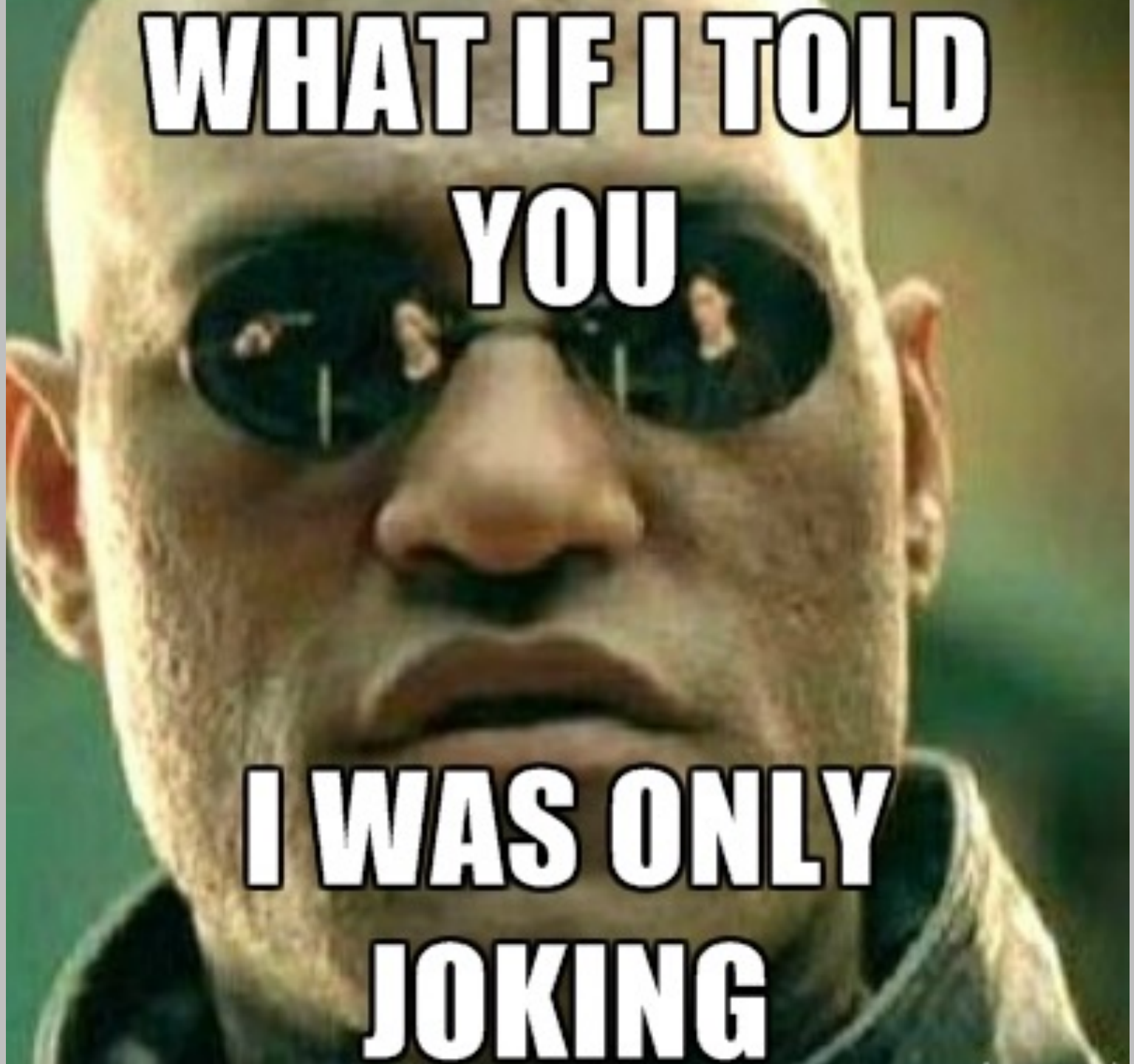
FACEM

WDHB/North Shore Hospital

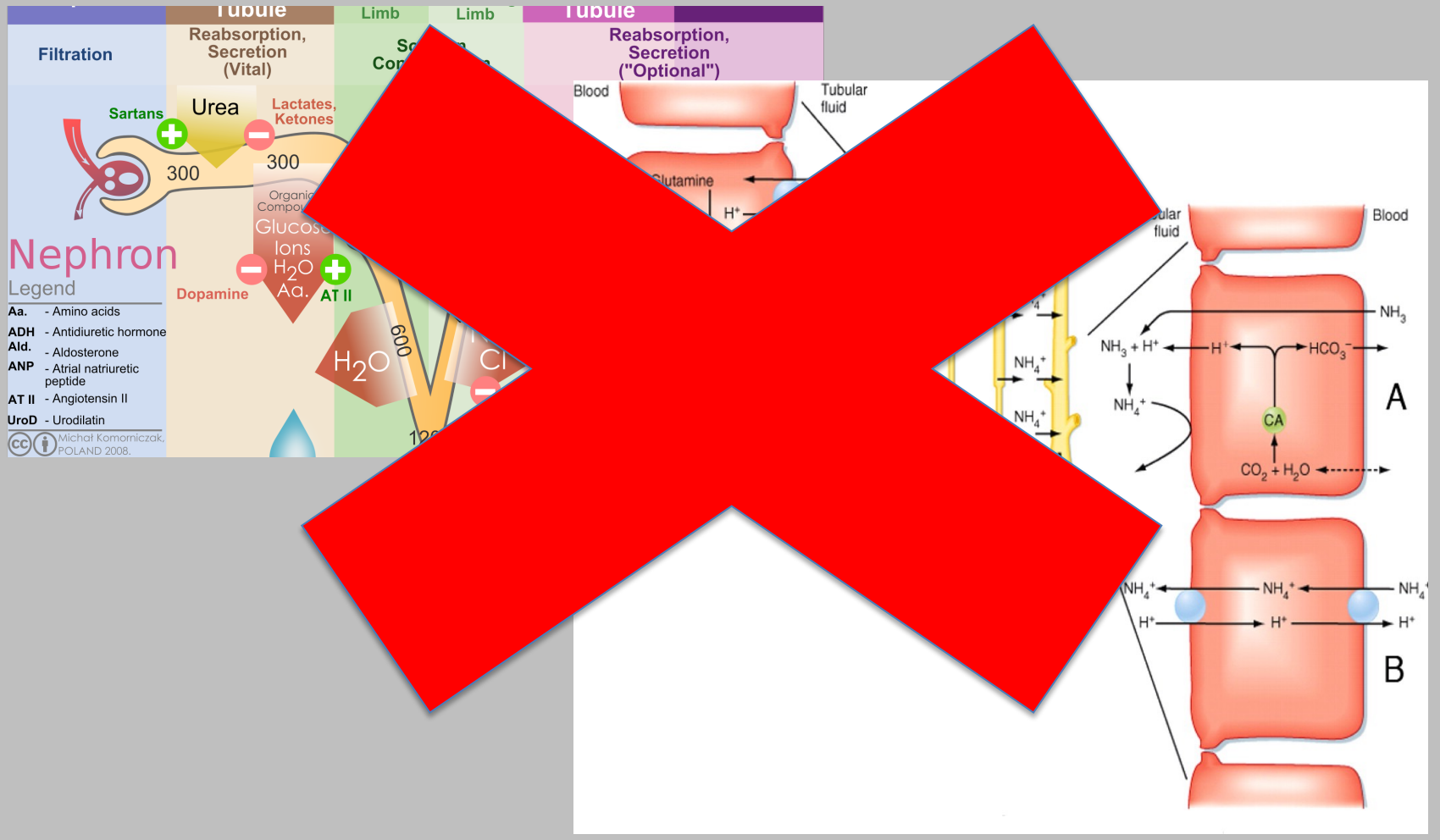
Renal Colic


Filtration
Tubule
Reabsorption, Secretion (Vital)
Limb
Solution Concentration
Limb
Tubule
Reabsorption, Secretion ("Optional")
Sartans
Urea
Lactates, Ketones
300
300
Organic Compounds
Glucose
Ions
H_2O
Aa.
Dopamine
AT II
400
600
H_2O
1200
400
100
200
Ald.
Na^+
Cl^-
Nephron
Legend
Aa. - Amino acids
ADH - Antidiuretic hormone
Ald. - Aldosterone
ANP - Atrial natriuretic peptide
AT II - Angiotensin II
UroD - Urodilatin
Michał Komorniczak, POLAND 2008.


Blood
Tubular fluid
Glutamine
H^+
Na^+
$A^=$
$2NH_4^+$
NH_3
$2HCO_3^-$
NH_4^+
Tubular fluid
Blood
NH_3
$NH_3 + H^+$
H^+
HCO_3^-
CA
$CO_2 + H_2O$
A
B


WHAT IF I TOLD YOU
I WAS ONLY JOKING

Renal Colic


Filtration
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Michał Komorniczak, POLAND 2008.
Dopamine
AT II
600
Blood
Tubular fluid
Glutamine
Blood
Tubular fluid
A
B
CA

Outline

- Use renal colic management as an example of dogmatism
  - A gap between clinical practice and evidence

- What is renal colic.
  - Why does it hurt so much?
- Some myths

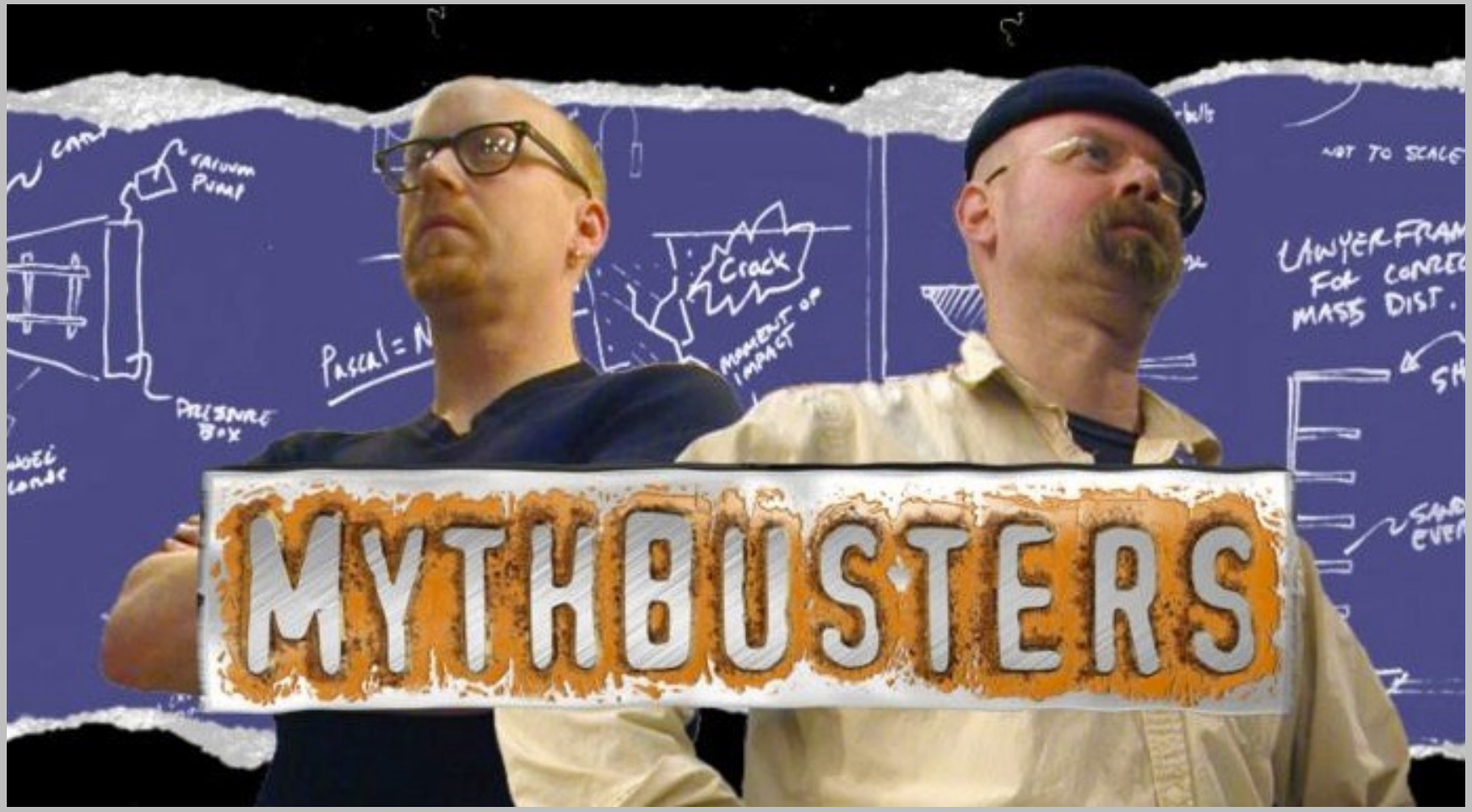
  Myth 1:IV fluids are useful

  Myth 2:Everyone needs a CT scan

  Myth 3: Alpha blockers help stone expulsion

- Please think to yourselves
  - What common practices or management strategies am I (or my dept) involved in.
    - Clinical pathways?
  - What (if any) evidence supports or refutes what we do?
  - How am I (or my dept) keeping up with current literature/evidence/ideas.

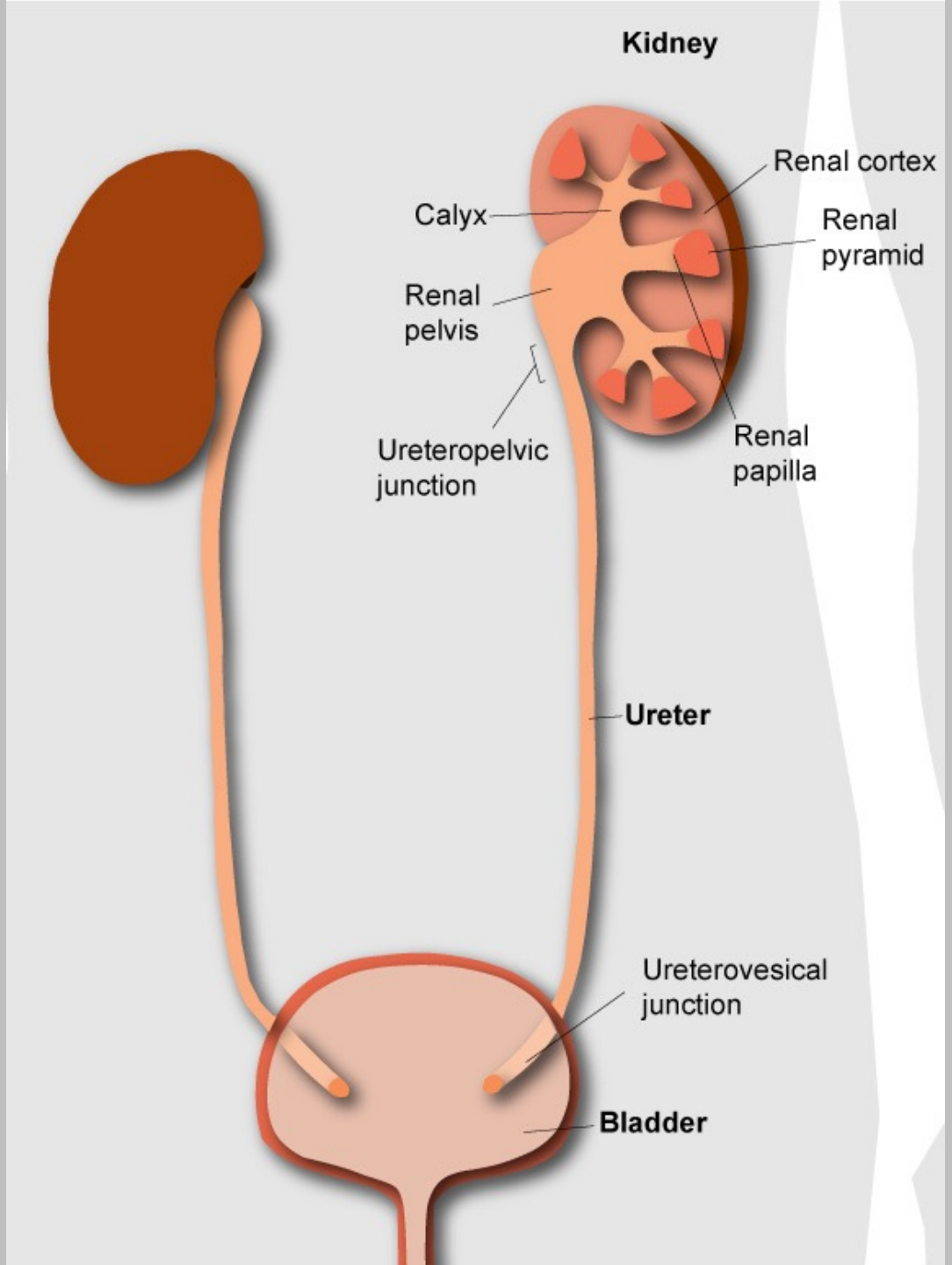
Renal Colic



Renal colic

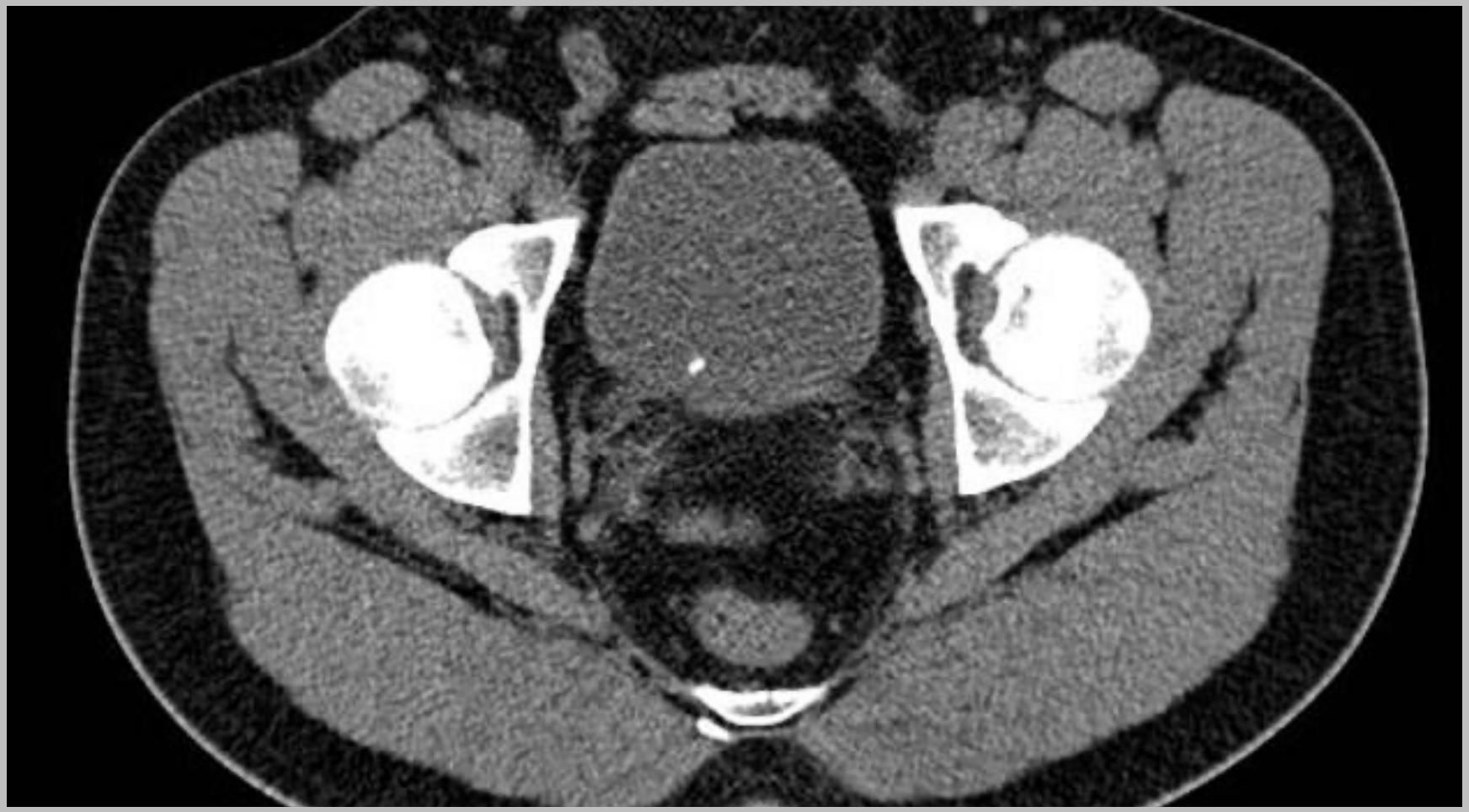
- abdominal and flank pain due to obstruction and distension of the ureter, pelvicalyceal system and renal capsule.

- Most often refers to the above caused by renal calculus (“kidney stone”)
  - Other causes: extrinsic obstruction (eg tumour), PUJ configuration, blood clots, renal papillary necrosis


Kidney
Renal cortex
Calyx
Renal pyramid
Renal pelvis
Ureteropelvic junction
Renal papilla
Ureter
Ureterovesical junction
Bladder

….an example…..

….an example…..



Why is it so painful?

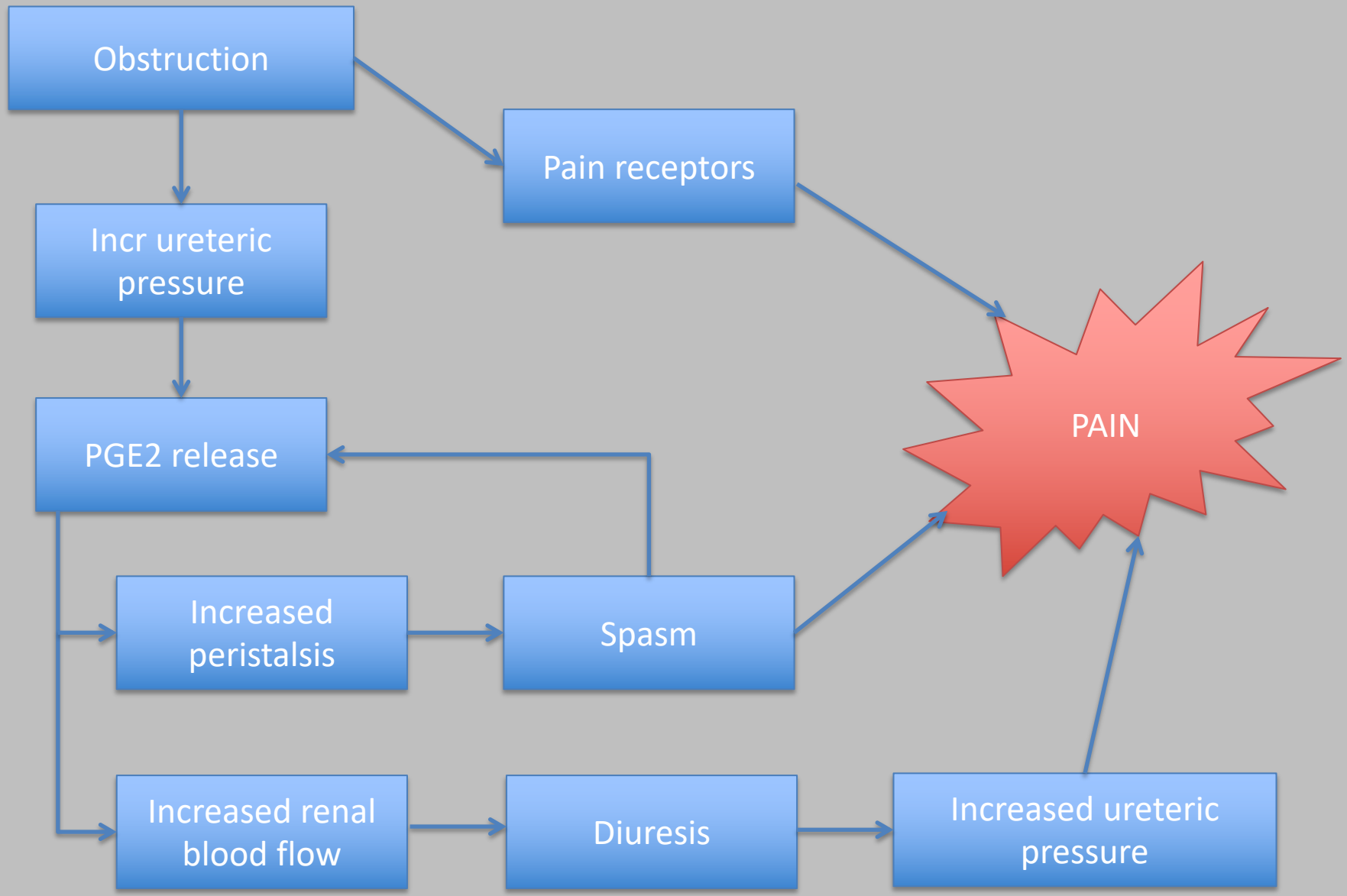
- Often described as pain similar to giving birth
- “10/10”
- Pain/vagal-induced nausea and vomiting (50%).
- Such a misery from such a small (relatively) object…..1-10mm.

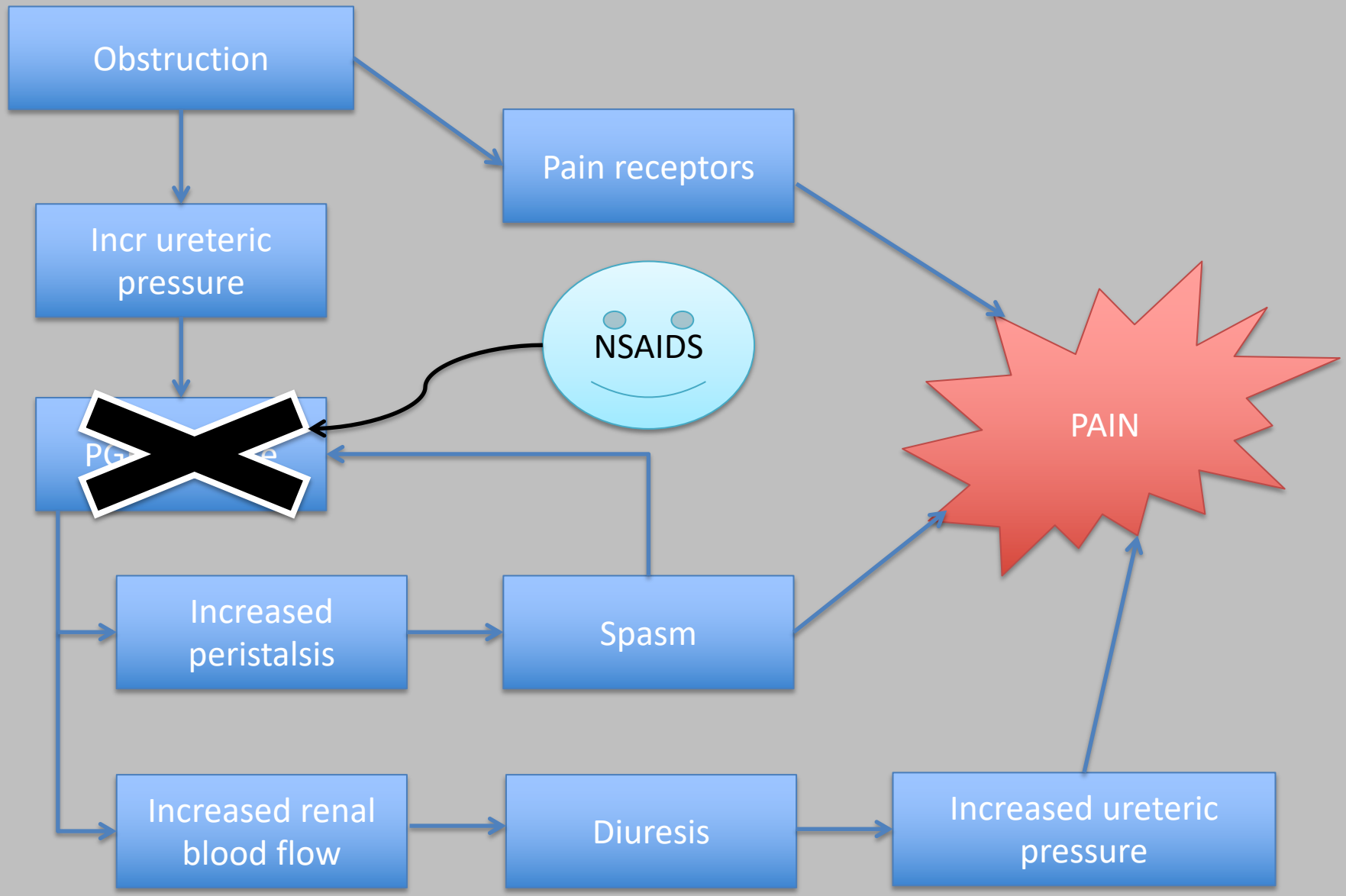
In 400BC…

“an acute pain is felt in the kidney, the loins, the flank and the testis of the affected side; the patient passes urine frequently, gradually the urine is suppressed. With the urine, sand is passed, as the sand begins to pass..it causes severe pain which is relieved when it is expelled, then the same suffering begins again”

- Hippocrates

Pathophysiology


Obstruction
Pain receptors
Incr ureteric pressure
PAIN
PGE2 release
Increased peristalsis
Spasm
Increased renal blood flow
Diuresis
Increased ureteric pressure


Obstruction
Pain receptors
Incr ureteric pressure
NSAIDS
PAIN
Increased peristalsis
Spasm
Increased renal blood flow
Diuresis
Increased ureteric pressure

Nick….what was up with that quote?

"The greater the ignorance the greater the dogmatism."

— Sir William Osler (1849 – 1919)

Ignorance + Dogmatism

- Ignorance
  - is a state of being uninformed (lack of knowledge)
- Dogma
  - is a belief or set of beliefs that is accepted by the members of a group without being questioned or doubted.

How we manage Renal Colic

- An example of dogmatism more than ignorance
  - Increasing body of literature that contradicts some common practices
- Three evidence based ways we can do things differently.

Myth #1: Giving IV fluids might flush out the stone

- Concept: there is a blockage we might be able to “flush out” by pushing IV fluids.

Do forced IV fluids provide benefit? NO

- Springhart WP, Marguet CG, Sur RL, et al. Forced versus minimal intravenous hydration in the management of acute renal colic: a randomized trial. J Endourol. 2006;20:713-716
  - RCT 58 patients
  - 2L normal saline over 4 hours vs no fluid
  - No difference in hourly pain scores, rate of spontaneous stone passage
- Edna and Hesselberg (1983)
  - RCT 66 patients
  - 3L fluids vs no fluids
  - No difference in pain scores at 6hrs, no difference in likelihood of spontaneous stone passage.

Do forced IV fluids provide benefit? NO

- 2012 Cochrane review

  ….”forced IV fluids cannot be recommended currently”

Can forced IV fluids cause harm?

Can forced IV fluids cause harm? YES

- Uretic rupture can cause:
  - Urinoma
  - Abscess
  - Urosepsis
  - irreversible renal impairment

- Can exacerbate CHF
- Can dilute someone who is already anaemic.

(Kazoulis et al 2002, Galuti et al 2013, Katumalla et al 2006.)

How common is it to give IV fluids?

- Philips et al (2009)
  - Surveyed 2603 hospital based ED Physicians in USA
  - 30%-45% gave 1-2L IV fluids
  - 2.5% gave 3L

When (if ever) should I give IV fluids for renal colic?

- Signs of dehydration are the only indication
  (in my opinion!!)

- A few vomits, I wouldn't bother.

- Elevated creatinine indicates high grade obstruction – do not give IV fluids to this person until size/position of stone and degree of hydronephrosis is established using imaging.

Myth 1: Giving IV fluids improves stone passage

Myth #2: everyone with suspected renal colic needs a CT

- Concept: We need to CT because
  - We need to know the size and location of the stone
  - We need to know about hydronephrosis
  - We might find another (bad) cause for pain on the CT that we would miss if we used ultrasound.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ultrasonography versus Computed Tomography for Suspected Nephrolithiasis

R. Smith-Bindman, C. Aubin, J. Bailitz, R.N. Bengiamin, C.A. Camargo, Jr., J. Corbo, A.J. Dean, R.B. Goldstein, R.T. Griffey, G.D. Jay, T.L. Kang, D.R. Kriesel, O. J. Ma, M. Mallin, W. Manson, J. Melnikow, D.L. Miglioretti, S.K. Miller, L.D. Mills, J.R. Miner, M. Moghadassi, V.E. Noble, G.M. Press, M.L. Stoller, V.E. Valencia, J. Wang, R.C. Wang, and S.R. Cummings

N ENGL J MED 371;12 NEJM.ORG SEPTEMBER 18, 2014

CT vs USS for nephrolithiasis

- 2759pts
- Randomized to three groups
  - Initial investigation Bedside Ultrasound (ED)
  - Initial investigation formal USS
  - Initial investigation CT
- Three primary outcomes
  - High-risk diagnoses or complications that could be related to missed or delayed diagnoses
  - Cumulative radiation exposure from imaging
  - Total costs

Results

- Incidence of high risk diagnoses with complications in the first 30 days was low (0.4%) and **did not vary** according to **imaging method**
- Mean 6-month cumulative radiation exposure was **significantly lower** in the USS group than CT group ($p<0.001$)
- No difference in adverse events, pain scores, return ED visits, hospitalisations across the groups.

Put another way

- When CT used as initial imaging: much higher radiation exposure with no reduction in adverse outcomes.
- When USS used as initial imaging: reduced radiation exposure with no increase in adverse outcomes.

Myth #2:
Takehome Points.

- We don’t have to CT everyone
- U/S is a safe initial investigation of choice
  - Bedside USS is fine if trained ED Physician does it.
  - access to formal US can be difficult, but still makes no difference to outcome!
- Consider NOT imaging someone if they have prior Hx of renal colic, normal renal anatomy, pain is controlled and good renal function.

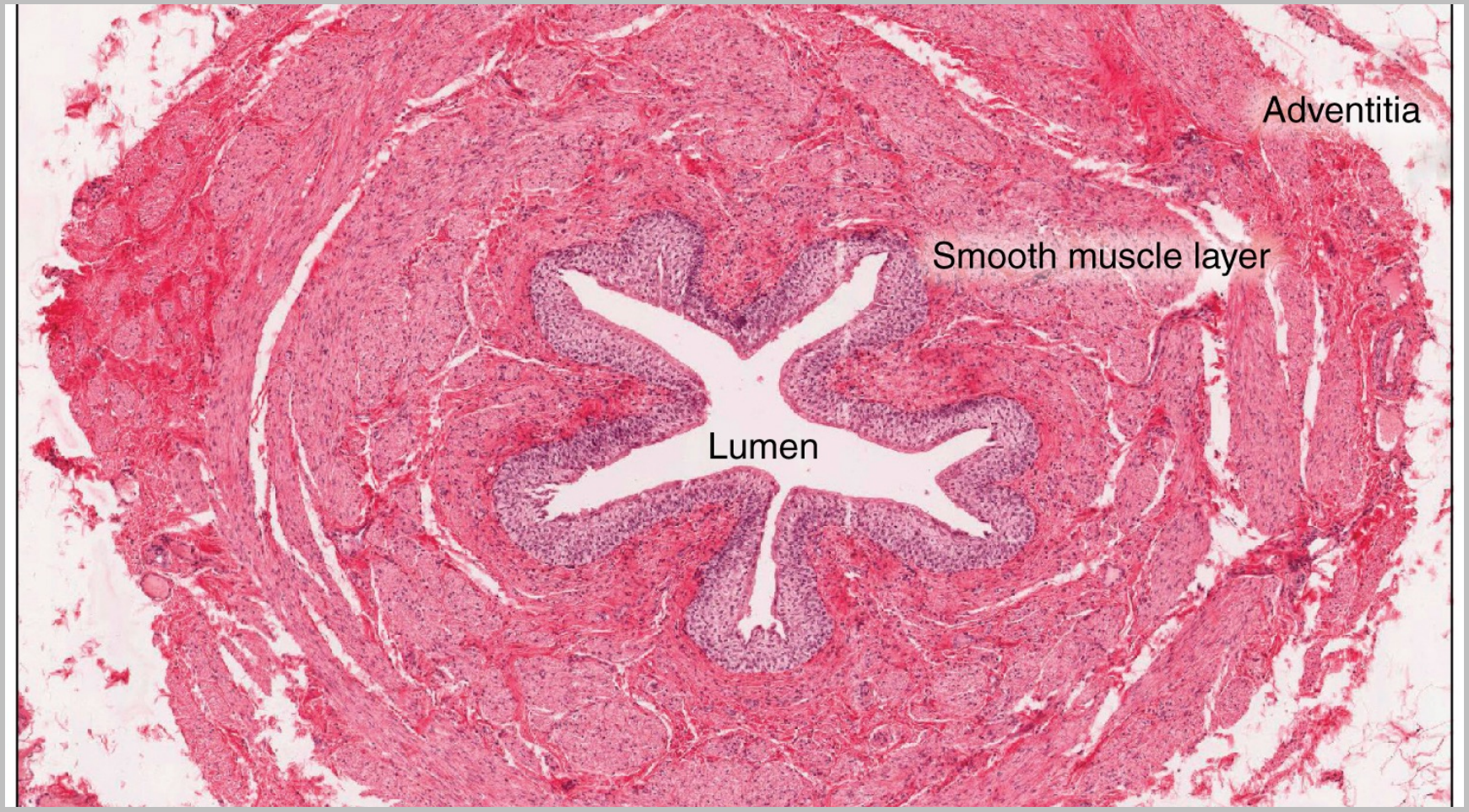
Myth 2: everyone needs a CT

Myth #3: Doxazosin (Tamsulosin) helps stone expulsion

Myth #3: Doxazosin (Tamsulosin) helps stone expulsion

- Concept
  - Ureters contain smooth muscle
  - The bladder wall is smooth muscle.
  - If we can relax both of these structures by using alpha blockers (doxazosin, tamsulosin), then stone passage will be improved

…a ureter…



What is Doxazosin (Tamsulosin)?

- α1 receptor blocker
- α1receptors are in smooth muscle
  - Blood vessels
  - Bowel wall
  - Ureters
  - Bladder

- Blocking the α1 receptor causes the smooth muscle to relax

Myth #3:
Earlier evidence is a bit mixed

1. Hollingsworth, JM, Rogers, MA, Kaufman, SR et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. Lancet. 2006; 368: 1171–1179.
   Suggested a slight benefit, but these were poor quality, heterogeneous studies.

1. Vincendeau S et al. Arch Int Med 2010. RCT. Small study, well-done, small overall stone size (3.1 mm) and showed no benefit.

3. Hermanns T et al. Eur Urology 2009. RCT. small study, okay methodology, small overall stone size (3.9 mm) and showed no benefit.

4. Ferre RM et al. Ann Emerg Med 2009. RCT. small study, non-blinded, small overall stone size (3.6 mm) and showed no benefit.

5. Al-Ansari A et al. Urology 2010. small study, RDCT that showed benefit. However, the results are suspect.
   (They calculated an 80% power to detect a 25% difference. They did not detect a 25% difference but rather a 21% difference)

Myth #3:
Newer evidence

- Pickard R et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet May 19, 2015
  - Randomized 1200 patients to tamsulosin vs nifedipine vs placebo for 4 weeks.

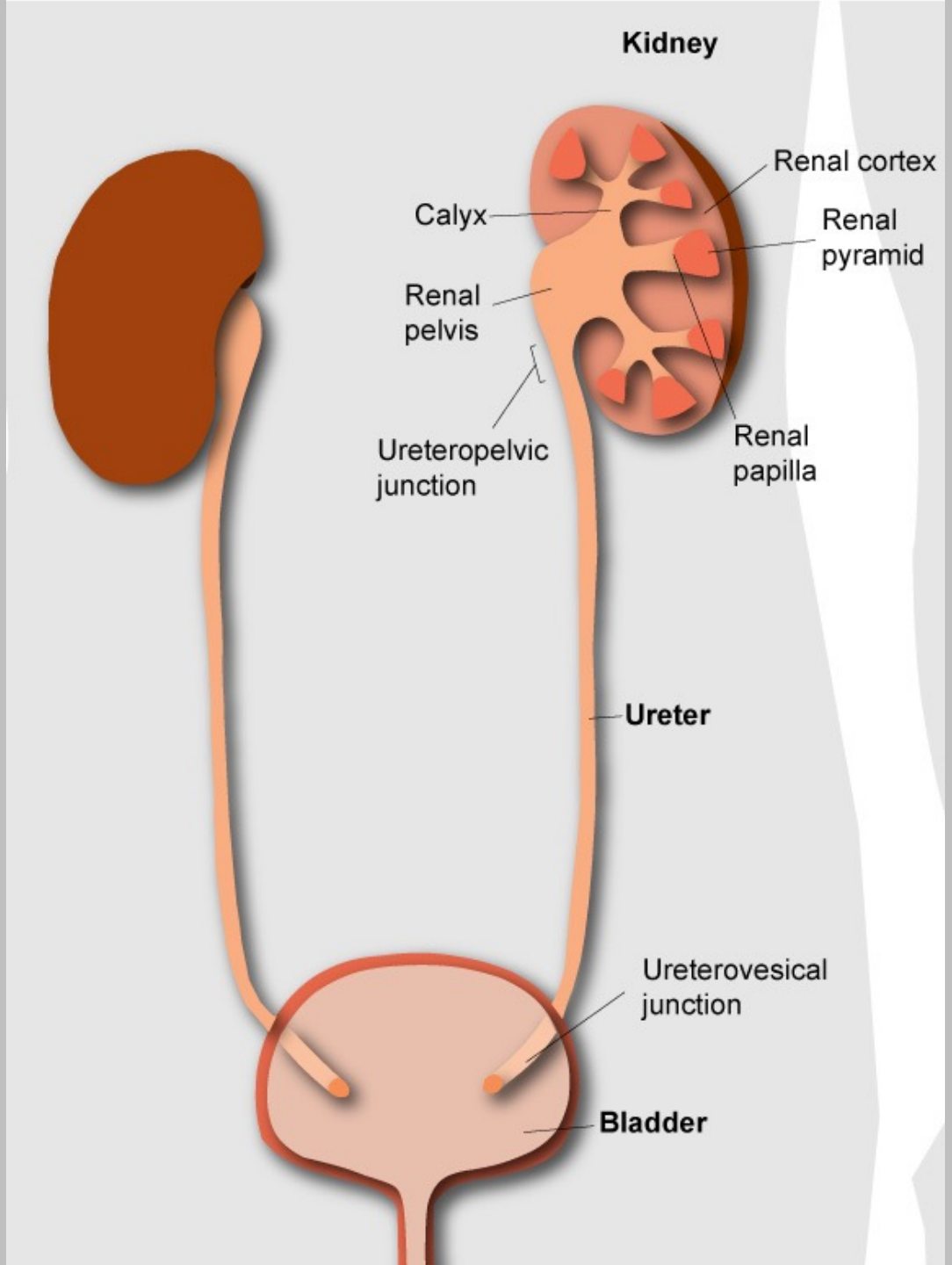
- Primary outcome:
  - spontaneous stone passage in 4 weeks, defined as the absence of need for additional interventions to assist stone passage at 4 weeks after randomization.

- Outcomes
  - No difference in outcomes
    - Stones are not more rapidly expulsed by alpha or calcium channel blockers.

More recent research

- Furyk Et al. Distal Ureteric Stones and Tamsulosin: A Double-Blind, Placebo-Controlled, Randomized, Multicenter Trial. Annals of EM Jan 2016.

  - 403 Pts with CT confirmed stones, randomized to Tamsulosin vs placebo. Repeat CT at 28 days (is the stone still there).
  - Outcomes
    - Mostly, no benefit.
    - Subgroup: Distal Stones between 5-10mm small benefit to tamsulosin.


Kidney
Renal cortex
Calyx
Renal pyramid
Renal pelvis
Ureteropelvic junction
Renal papilla
Ureter
Ureterovesical junction
Bladder

Side effects of Doxazosin

- Asthenia, Dizziness, Postural hypotension, Fatigue, Headache, Malaise, Oedema, Rhinitis, Somnolence, Vertigo, Urinary incontinence, blurred vision, cholestasis, epistaxis, haematuria, jaundice, leucopenia, pruritis, purpura, rash, thrombocytopenia, abdominal pain, diarrhoea, headache, dyspnoea, cough, anorexia, indigestion, restlessness, joint pain, myalgia, palpitations, Atrial fib, dry mouth, flatulence, anxiety, personality changes, alopecia.

Myth #3
Takehome Points

- Doxazosin given to “all-comers” doesn’t work.

- May have a small benefit in larger (>5mm) stones that are near the VUJ.

Myth 3: Doxazosin helps

(sort of)

Take home messages

- **Myth 1: IV fluid therapy** (to push out the stone) **does not work**, and it may **cause harm**.

- **Myth 2**: Consider **Ultrasound** (or even NO imaging!) **rather than CT** for confirming stone and hydronephrosis.

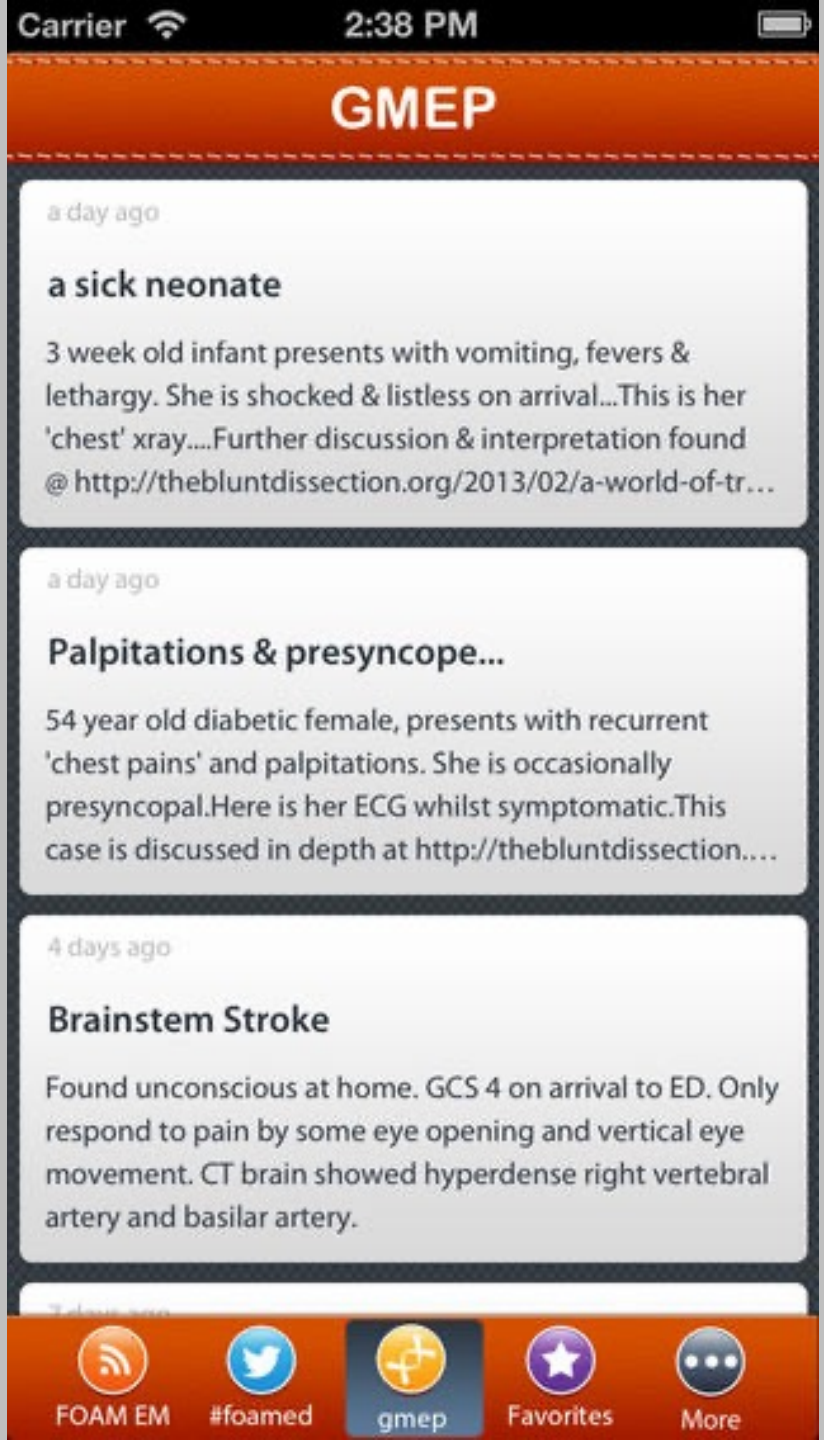
- **Myth 3: Doxazosin** is **probably beneficial in larger (>5mm) distal stones**. Should be reserved for this group only.

To reiterate

- Please think to yourselves
  - What common practices or management strategies am I (or my dept) involved in.
    - Clinical pathways?
      - When were they last updated?
  - What (if any) evidence supports or refutes what we do?
  - How am I (or my dept) keeping up with current literature/evidence/ideas.

FREE
OPEN
ACCESS
MEDUCATION

FOAM



Ref's

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- Pickard R et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomized, placebo-controlled trial. Lancet. 2015;386(9991):341-9.
- Hollingsworth, JM et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. Lancet. 2006; 368: 1171–1179.
- Vincendeau S et al. Tamulosin Hydrochloride vs placebo for the management of distal ureteral stones: a multcentric, randomized, double-blind trial. Arch Int Med. 2010;170(13):2021-7.
- Hermanns T et al. Is there a role for Tamulosin in the Treatment of Distal Ureteric stones 7mm or less? Results of a Randomized, Double blind, Placebo-controlled trial. Eur Urology.2009;407-12
- Ferre RM et al. Tamulosin for Ureteral Stones in ED: a Randomised controlled trial. Ann Emerg Med. 2009;54:432-9.
- Al-Ansari A et al. Efficacy of Tamulosin in the management of Lower Ureteral Stones: a Randomized Double-blind Placebo Study of 100 patients. Urology. 2010;75:4-8.
- Kazoulis et al. Spontaneous renal rupture due to ureteric calculi in a paraplegic man. Nephron. 2002;91(4)766-77.
- Galuti et al. A spontaneous rupture of renal pelvis. Am J Emerg Med. 2013;31(4): 762-4.
- Katumalla FS et al. Bilateral urinoma due to unilateral impacted ureteral calculus. Indian J Urology. 2006;22:374-5.
- Philips E et al. Emergency room management of ureteral calculi: Current Practices. J Endourology. 2009;23(6):1021-4.