Post-AKI

藥事照護經驗分享

臺北榮民總醫院 藥學部

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Outline

- Case Scenario
- Introduction of Acute Kidney Injury (AKI)
- Drug-induced AKI
- Management of AKI
- Take Home Message

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Case Scenario_1

Mrs. B, 95 y/o, 155 cm, 61.6 Kg

- **Chief complaint**
  - Developed disoriented speech, which progressed gradually for >10 days, simple phrases instead of a whole sentence, sometimes meaningless and used the wrong words (指窗外路燈說月亮)

Case Scenario_2

- History of present illness
  - Diarrhea, decreased appetite, poor intake and general weakness with mental status changes
  - Progressive symptoms 3 days before admission

Case Scenario_3

- **Past medical history**
  - Hypertension (HTN)
  - Ischemic heart disease (IHD)
  - Congestive heart failure (CHF) New York Heart Association (NYHA) functional class II
  - Atrial Fibrillation (AF) ($CHA_2DS_2VAS_C$=6)
  - Chronic Obstruction Pulmonary Disease (COPD)
  - Gastroesophageal reflux disease (GERD) Los Angeles (LA) Grade A
  - Senile dementia
  - Bipolar affective disorder (BAD)

Case Scenario_4

- **Personal history**
  - **Smoking (-)**
  - **Alcohol (-)**
  - **Allergy (-)**
- **Family history (-)**
- **Physical examination**
  - **BP (109/42 mmHg)**
  - **BT/PR/RR (36.2 °C/ 56 bpm/ 18 rpm)**

Case Scenario_5

- **Impression**
  - **Acute kidney injury (AKI), drug, dehydration and volume depletion related**
- **Plan to do**
  - **Hydration and closely follow up renal function and electrolyte**

SMAC

	BUN	SCR	ALT	NA	K	GLU	CRP
08/02	17	1.14	-	141	4.4	-	-
08/28	42	2.9	9	140	4.1	109	1.16
08/29	39	2.31	-	140	4.0	-	-
08/29	35	1.99	11	144	4.1	-	-
08/31	25	1.29	-	151	3.5	-	-
09/02	9	1.13	-	153	2.5	-	-
09/26	23	0.94	30	140	5.1	-	0.15
09/29	22	0.97	29	142	3.9	-	-

CBC&DC

	WBC	HGB	PLT	INR	PT	APTT	BAND	SEG
08/28	14600	12	214K	1.04	10.5	28.8	0	80.2
08/29	16300	11.4	192K	1.08	10.9	28.5	0	75.6
08/30	-	10.6	-	1.1	11.1	28.9	-	-
08/31	15400	11.3	157K	-	-	-	0	81.5
09/02	13000	11.7	98K	-	-	-	0	82.1
09/05	10800	11.3	129K	-	-	-	0	73.3
09/08	7200	9.8	161K	-	-	-	0	57.1
09/11	7000	10.7	188K	0.95	9.6	25.1	0	64.7
09/20	5600	11.5	142K	-	-	-	0	65.8
09/26	9700	11.4	150K	-	-	-	0	75.9
09/29	9410	12.1	165K	-	-	-	0	67.6

Patient Drug Profile of Outpatient

藥名/含量/劑量/頻次			日期 途徑	8 2	8	9	10	11	12	15	28
Sennosides tab 20 mg	1 tab	hs	PO	—	—	—	—	—	—	—	
Atorvastatin tab 10 mg	1 tab	qod	PO	—	—	—	—	—	—	—	
Valsartan tab 80 mg	1 tab	qd	PO	—	—	—	—	—	—	—	
Diltiazem cap 120 mg	1 cap	qd	PO	—	—	—	—	—	—	—	
Nitrostat tab 0.6 mg	X25 tab	q5mprn	SL	—	—	—	—	—	—	—	
Rivaroxaban tab 10 mg	1 tab	qdcc	PO	—	—	—	—	—	—	—	
Furosemide tab 40 mg	1 tab	qdcc	PO	—	—	—	—	—	—	—	
Quetiapine tab 25 mg	0.5/0.5/1 tab	qd/noon/qn	PO	—	—	—	—	—	—	—	
Clonazepam tab 0..5 mg	1 tab	qnprn	PO	—	—	—	—	—	—	—	
Zopiclone tab 7.5 mg	1 tab	qnprn	PO	—	—	—	—	—	—	—	
Magnesium oxide tab 250 mg	1 tab	tid	PO		—	—					
Acetaminopen tab 500 mg	0.5 tab	tid	PO		—	—					
Fexofenadine tab 60 mg	0.5 tab	tid	PO		—	—					
Ibuprofen tab 400 mg	0.5 tab	tid	PO				—	—	—	—	
Calcium carbonate 600 mg + Bismuth subnitrate 150 mg + Butinolin phosphate 2 mg tab	1 tab	tid	PO				—	—	—	—	
Chlorpheniramine 2.5 mg + Dextromethorphan 5 mg + Acetaminophen 240 mg + Salicylamide 250 mg + Caffeine 25 mg + Hesperidin 5 mg + Thiamine 5 mg cap	1 cap	tid	PO				—	—			

診所

Patient Drug Profile of Inpatient

藥名/含量/劑量/頻次			給藥途徑	8/29	30	31	9/2	5	6	7	10	12	14
Atorvastatin tab 10 mg	1 tab	qod	PO		NGT								
Diltiazem cap 120 mg	1 cap	qd	PO		NGT								
Nitrostat tab 0.6 mg	X25 tab	q5mprn	SL										
NS inj	500 ml	qd	IVD										
D5-1/2S inj	500 ml	qd	IVD										
Apixaban tab 5 mg	0.5 tab	bid	PO									NGT	
Quetiapine tab 25 mg	0.5 tab	qd/noon	PO										
Quetiapine tab 25 mg	1 tab	qn	PO							NGT			
Clonazepam tab 0..5 mg	1 tab	qnprn	PO										
Zopiclone tab 7.5 mg	1 tab	qnprn	PO										
Somatostain inj	6 mg	stat	IVD										
Esomeprazole inj	40 mg	q6hv	IVA										
Esomeprazole tab 40 mg	1 tab	qdac	NGT										
D5W 100 ml + 20 mEq KCl inj	100 ml	qd	IVD										
Dioctahedral smectite powder 3 g	1 wp	tidac	NGT								tidprn		
Furosemide tab 40 mg	0.5 tab	qd	NGT										

8/29 Upper gastrointestinal endoscopic foreign body removal

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AKI

- Previously known as acute renal failure (ARF)
- Acute decline in the GFR from baseline, with or without oliguria/anuria
- Results in retention of nitrogenous waste products, such as urea, creatinine, electrolyte and acid-base abnormalities
- Often asymptomatic and are diagnosed by observed elevations in blood urea nitrogen (BUN) and serum creatinine (SCr) levels

Common Symptoms of AKI

- Anorexia, fatigue, nausea, vomiting, pruritus and mental status changes
- Seizures can occur if BUN levels are extremely high and shortness of breath can result if volume overload is present
- Alterations in urine volume may be the only symptom that patient notice

This patient: Anorexia, mental status changes

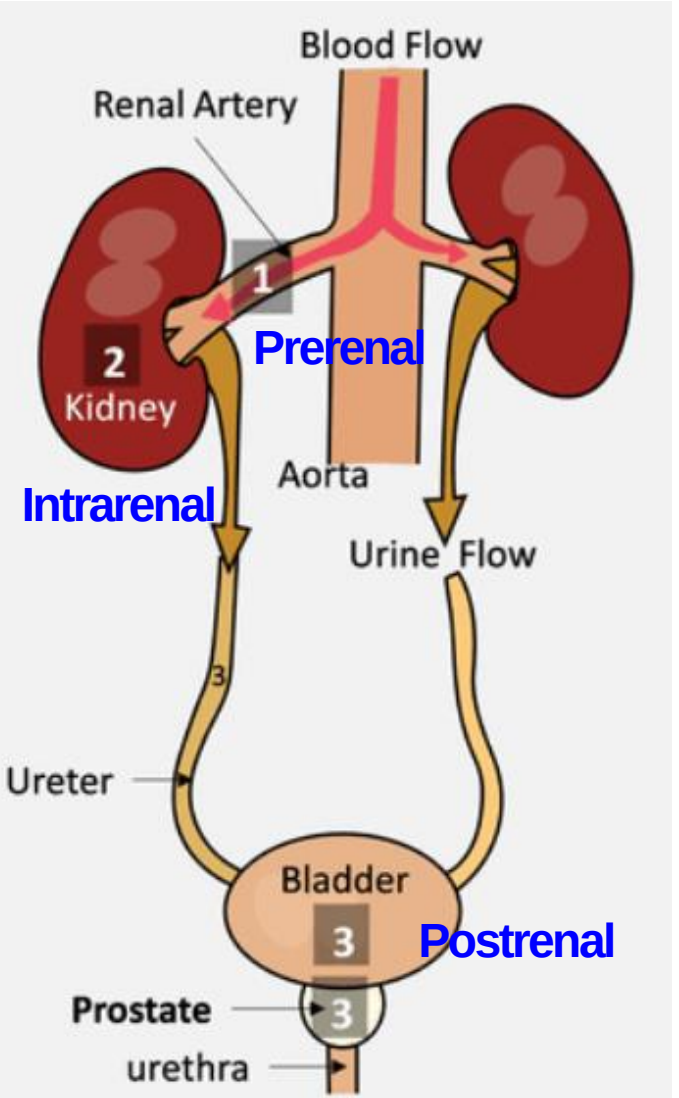
Risk Factors of AKI

Class	Risk factor
Susceptible kidney	Elderly, pre-existent renal disease, renal transplantation
Comorbid condition	Diabetes mellitus, multiple myeloma, proteinuria, systemic lupus erythematosus
Sodium-retaining states	Liver cirrhosis, heart failure
Diminished effective circulation	Sepsis, shock, dehydration and volume depletion
Electrolyte or acid-base disturbance	Acidosis, hypokalemia, hypomagnesemia, hyperuricemia, hyperuricosuria
Nephrotoxic drugs	NSAID, cyclosporine, tacrolimus, ACEI, ARB, aminoglycoside, amphotericin B, sulfonamide, diuretics, acyclovir, methotrexate

This patient: Elderly (95 y/o), heart failure, dehydration and volume depletion, nephrotoxic drugs (Ibuprofen + Valsartan + Furosemide)

Etiology of AKI

Class	Etiology
Prerenal	55% reduced renal perfusion, sudden and severe drop in blood pressure (shock) or interruption of blood flow to the kidneys from severe injury or illness
Intrarenal	35% intrinsic renal disease, direct damage to the kidneys by inflammation, toxins, drugs, infection or reduced blood supply
Postrenal	10% obstruction, sudden obstruction of urine flow due to enlarged prostate, kidney stones, bladder tumor or injury



J Clin Med 2020;9:1104-26

Staging of AKI

Stage	SCr	Urine output
1	1.5–1.9 times baseline within 1 wk or ≥0.3 mg/dl increase within 48 hrs	<0.5 ml/kg/h for 6–12 hrs
2	2–2.9 times baseline	<0.5 ml/kg/h for ≥12 hrs
3	3 times baseline or increase in SCr to ≥4 mg/dl or initiation of renal replacement therapy (RRT) or in patients <18 yrs, decrease in GFR to <35 ml/min/1.73 m^2	<0.3 ml/kg/h for ≥24 hrs or anuria for ≥12 hrs

This patient: SCr (mg/dl) 1.14 to 2.9, increase 2.54 fold, stage 2

Kidney Disease: Improving Global Outcomes (KDIGO), 2012

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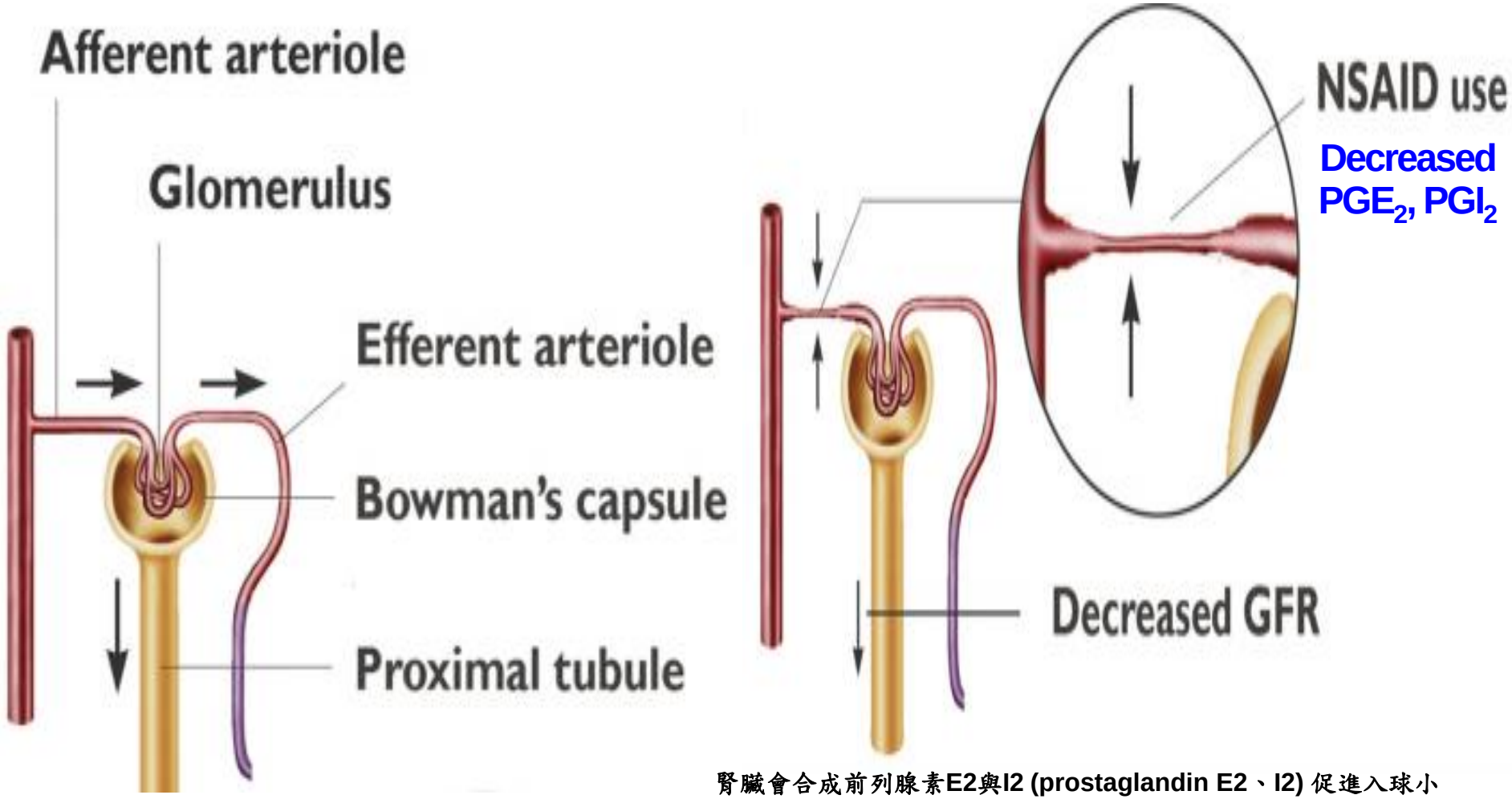
Drug-induced AKI

Class	Drug	Etiology
Prerenal	NSAID, cyclosporine, tacrolimus	Increased afferent arteriolar resistance
	ACEI, ARB	Decreased efferent arteriolar tone
	Diuretics	Result in dehydration
Intrarenal	NSAID, cyclosporine, tacrolimus, aminoglycoside, amphotericin B	Acute tubular necrosis (ATN)
	NSAID, loop/thiazide diuretics, sulfonamide	Acute interstitial nephritis (AIN)
Postrenal	Sulfonamide, acyclovir, methotrexate	Tubular precipitation

This patient: Ibuprofen + Valsartan + Furosemide

NSAID Reduced Perfusion Pressure

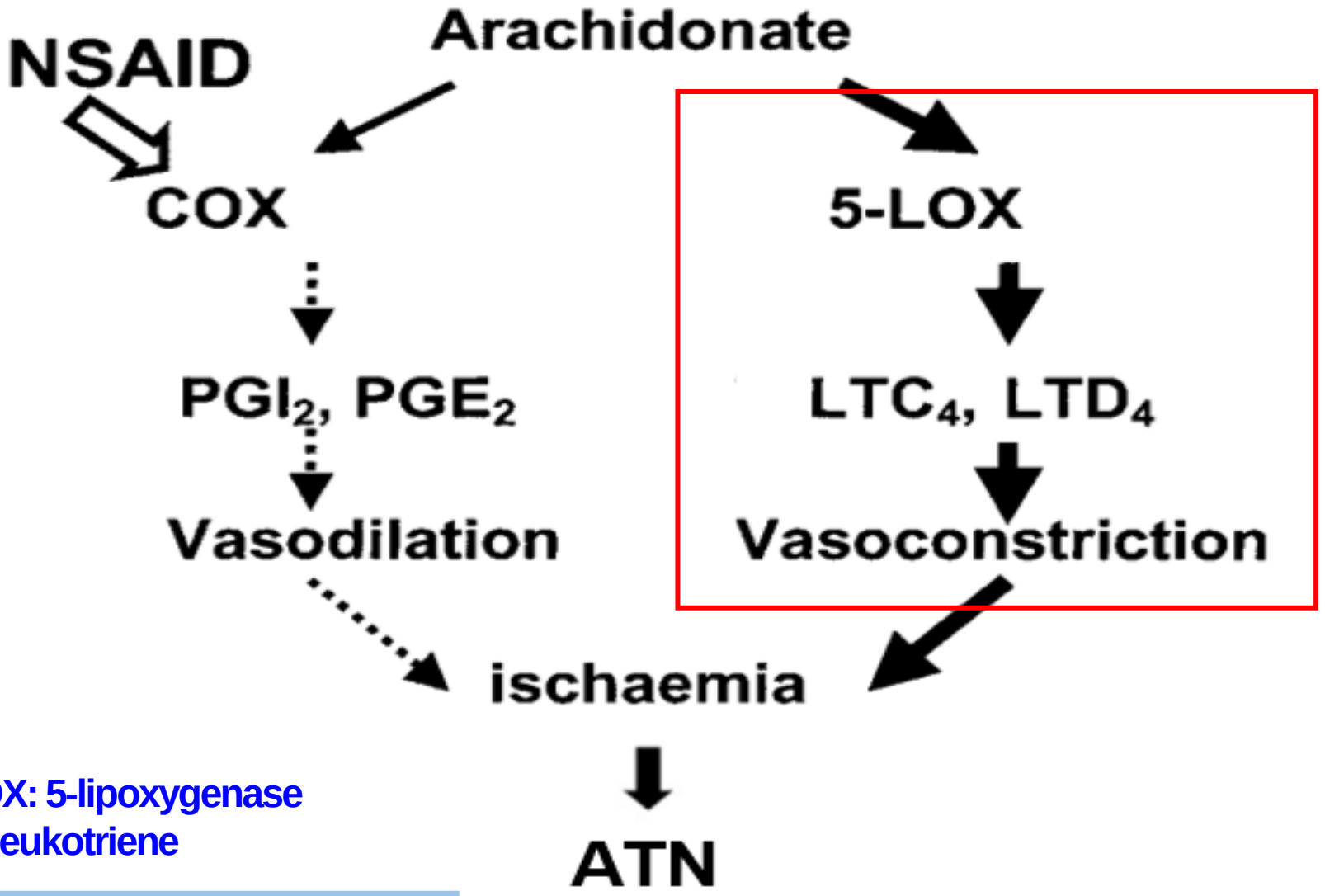


腎臟會合成前列腺素E2與I2 (prostaglandin E2、I2) 促進入球小動脈血管平滑肌擴張，以增加腎臟血流，當服用NSAIDs抑制環氧合酶 (cyclooxygenase, COX) 時，會抑制前列腺素的合成，使入球小動脈收縮進而導致腎臟血流灌注不足而引發AKI

This patient: Ibuprofen

Kidney Int Rep 2017;2:785-99

NSAID-induced ATN

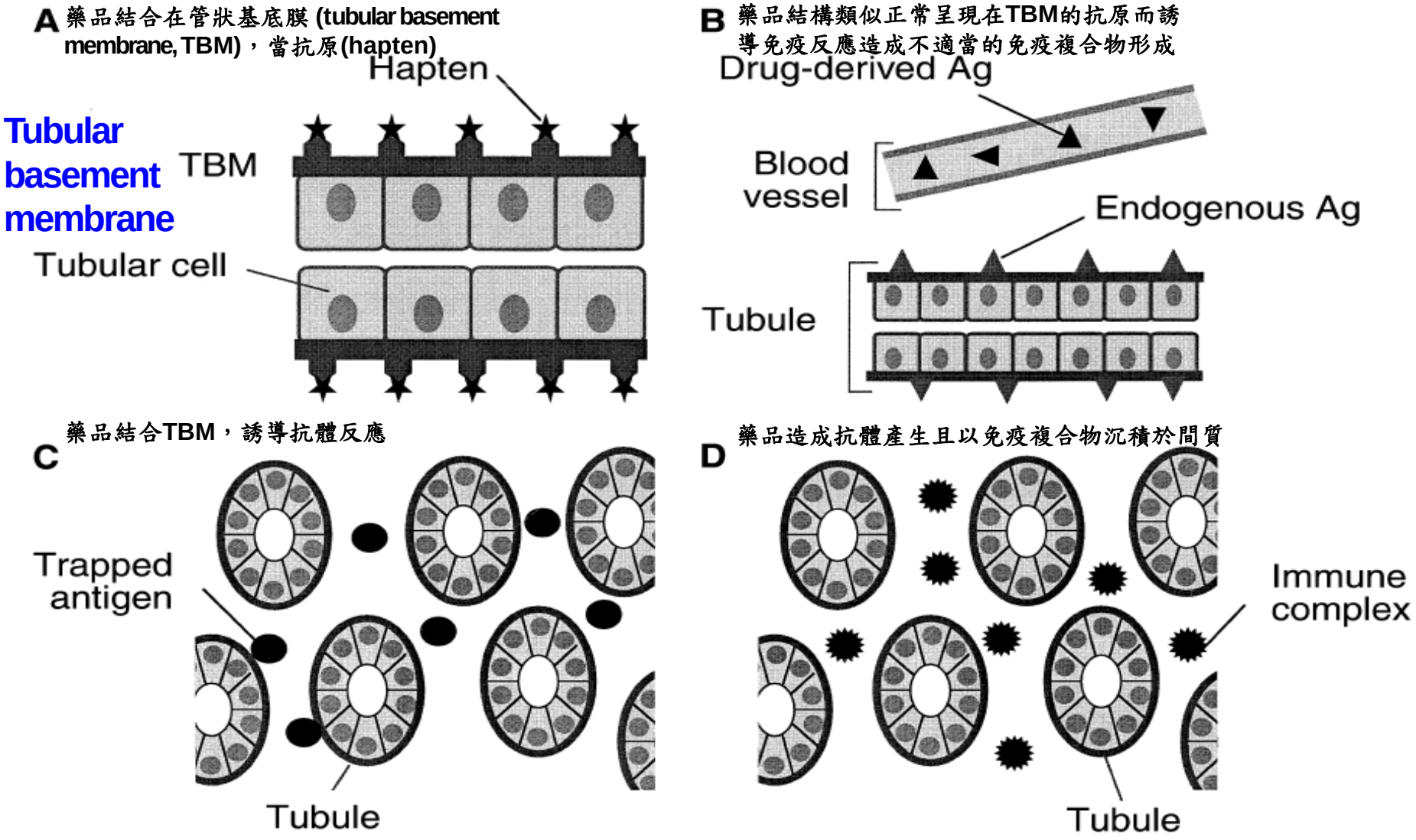


5-LOX: 5-lipoxygenase
LT: Leukotriene

This patient: Ibuprofen

Nephrol Dial Transplant 2002;17:1159-62

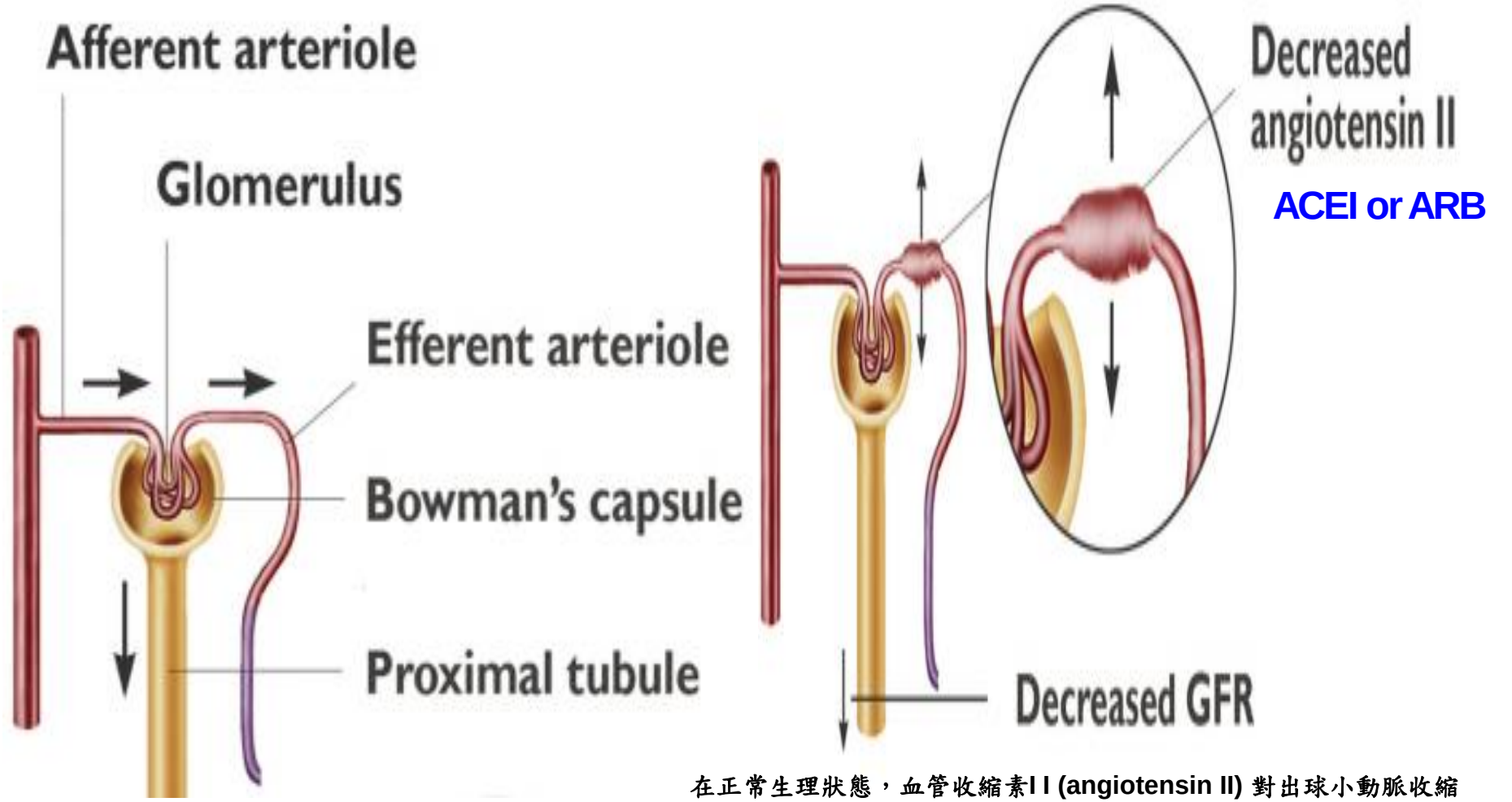
NSAID or Loop/Thiazide Diuretics-induced AIN



This patient: Ibuprofen + Furosemide

Nat Rev Nephrol 2010;6:461-70

ACEI or ARB
Reduced Perfusion Pressure



在正常生理狀態，血管收縮素I I (angiotensin II) 對出球小動脈收縮作用大於入球小動脈，維持腎絲球內壓而達到正常腎絲球過濾率，ACEI或ARB會抑制血管收縮素II生成或阻斷血管收縮素II受體作用，導致出球小動脈舒張而使腎絲球內壓下降並引發AKI

This patient: Valsartan

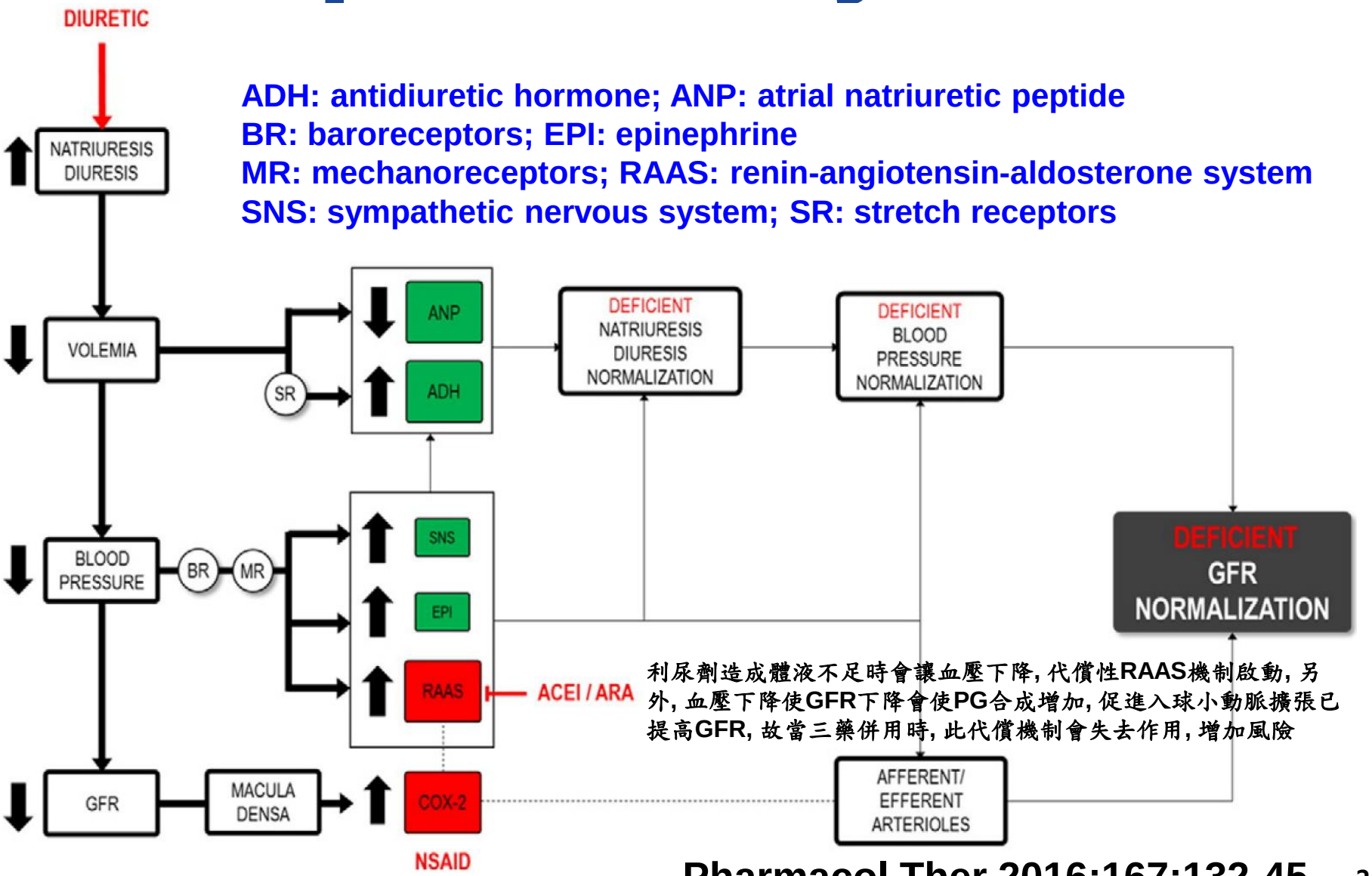
Kidney Int Rep 2017;2:785-99

Triple Whammy Effect

- **Definition**
  - Risk of AKI when concurrent use of a triple therapy combination containing ACEI or ARB, NSAID and diuretics
- **Incidence**
  - Combination was prescribed in 4.7-7.9% of patients in Australia

This patient: Ibuprofen + Valsartan + Furosemide

Mechanisms of Triple Whammy Effect



ADH: antidiuretic hormone; ANP: atrial natriuretic peptide
BR: baroreceptors; EPI: epinephrine
MR: mechanoreceptors; RAAS: renin-angiotensin-aldosterone system
SNS: sympathetic nervous system; SR: stretch receptors

利尿劑造成體液不足時會讓血壓下降, 代償性RAAS機制啟動, 另外, 血壓下降使GFR下降會使PG合成增加, 促進入球小動脈擴張已提高GFR, 故當三藥併用時, 此代償機制會失去作用, 增加風險

Pharmacol Ther 2016;167:132-45

Triple Whammy Effect Increased The Risk of AKI

Current use*	Cases (n=2215)	Controls (n=21 993)	Rate ratio (95% CI)	
			Crude	Adjusted†
Diuretics only	209 (9.4)	2632 (12.0)	Reference	Reference
Diuretics plus NSAIDs	156 (7.0)	1739 (7.9)	1.16 (0.93 to 1.44)	1.02 (0.81 to 1.28)
ACE inhibitors or angiotensin receptor blockers only	148 (6.7)	1889 (8.6)	Reference	Reference
ACE inhibitors or angiotensin receptor blockers plus NSAIDs	138 (6.2)	1907 (8.7)	0.96 (0.75 to 1.22)	0.89 (0.69 to 1.15)
Diuretics plus ACE inhibitors or angiotensin receptor blockers	414 (18.7)	2432 (11.1)	Reference	Reference
Diuretics plus ACE inhibitors or angiotensin receptor blockers plus NSAIDs	544 (24.6)	2424 (11.0)	1.34 (1.17 to 1.54)	1.31 (1.12 to 1.53)

BMJ 2013;346:e8525

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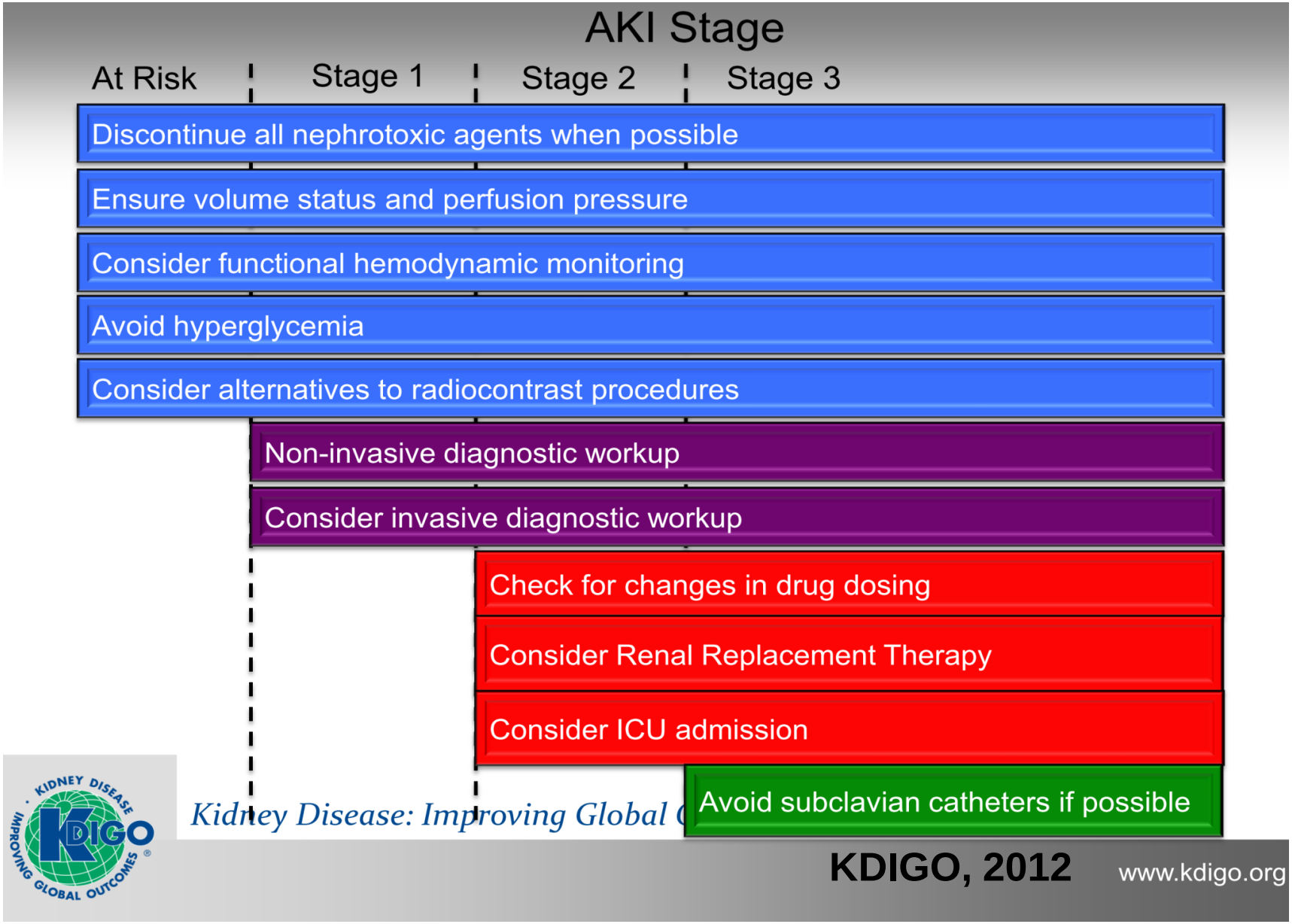
Management of AKI



General Management_1

- Etiology of renal dysfunction and the patient's volume status
- Main goal includes maintenance of adequate hemodynamic status to ensure renal perfusion and avoidance of further kidney injury
- No evidence that drug therapy hastens patient recovery in AKI, decreases length of hospitalization or improves survival

General Management_2

- Prevention of adverse drug reactions by discontinuing nephrotoxic drugs or adjustment of drug dosages based on the patient's renal function is desired
- Options are limited to supportive therapy
  - Fluid management
  - Electrolyte management
  - Nutritional support
  - RRT

This patient: Stop ibuprofen, valsartan, furosemide and hydration with NS, D5-1/2S

Hemodynamic Monitoring and Support

- Suggest isotonic crystalloids (晶體，如 normal saline) rather than colloids (膠體，如 albumin、starch or dextran) as initial management for expansion of intravascular volume in patients with AKI in the absence of hemorrhagic shock
- Fluid therapy should be prescribed based on patient's clinical setting and requirement
  - **Hypovolemia, administer 1-3 liter with assessment of clinical response, then maintenance requirement is ≥75 ml/hr**

Diuretics

- Suggest not using diuretics to treat AKI, except in the management of volume overload
- Consider loop diuretics for treatment of fluid overload or edema in AKI
  - Starting dose of IV furosemide for the treatment of AKI is 80 mg, if urine output is no definite augmentation within 2 hrs, the dosage can be increased to 160 mg (max: 200 mg)
- Monitor electrolyte status to prevent electrolyte abnormalities, such as hypokalemia

Vasodilator Therapy

- Recommend not using low-dose dopamine (1-3 μg/kg/min) to treat AKI
- Low-dose dopamine predominantly stimulates dopamine-1 receptor, leading to renal vascular vasodilation and increased renal blood flow and may expected to increase GFR
- No benefit of dopamine for therapy of AKI
- Adverse reactions that may be associated with low-dose dopamine: tachycardia, arrhythmias, myocardial ischemia, decrease intestinal blood flow (gut ischemia)

RRT

- RRT emergently when life-threatening changes in fluid, electrolyte and acid-base balance
- Initiate RRT in patients with AKI to treat volume overload who have oliguria/anuria, that is refractory to diuretics, hyperkalemia/ metabolic acidosis refractory to drug therapy, or uremia
- 5-30% patients with AKI treated with dialysis will not have recovery of their renal function and will need to remain on long-term dialysis

Nutritional Support

- Total energy intake of 20-30 kcal/kg/day with any stage of AKI
- Avoid restriction of protein intake with the aim of preventing or delaying initiation of RRT
  - AKI stage 1, 0.8-1 g/kg/d
  - AKI stage 2-3, 1.2-2 g/kg/d
  - CRRT, 1.5 (max:2.5) g/kg/d
- Carbohydrate intake should be 3-5 (max: 7) g/kg/d
- Fat intake should be 0.8-1 g/kg/d
- Suggest providing nutrition preferentially via the enteral route in AKI

2020臺灣急性腎損傷處置共識

CRRT: Continuous Renal Replacement Therapy (連續性腎臟替代療法)

Other Treatment

- **Hyperkalemia**
  - **Shift K into cells**
    - ✓**Regular insulin with glucose**
    - ✓**Sodium bicarbonate**
    - ✓**β_2 agonists**
  - **Promote K excretion**
    - ✓**Calcium polystyrene sulfonate**
    - ✓**RRT**
- **Metabolic acidosis**
  - **Sodium bicarbonate can be administered if the serum bicarbonate fall below the normal range of 22-29 mmol/l**
  - **RRT**

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Take Home Message

- Risk factors for AKI include elderly, pre-existent renal disease, dehydration and volume depletion, electrolyte or acid-base disturbance, nephrotoxic drugs
- Primary goal of therapy ameliorates any identifiable underlying causes of AKI such as hypovolemia, nephrotoxic drug administration or ureter obstruction
- Supportive therapy remains the primary approach to prevent or reduce the complications associated with AKI, include fluid, electrolyte management, nutritional support and RRT

Thanks for Your Attention