常見中毒的處理

114-05-02

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Risk Assessment

- Toxicological risk assessment:
    - To predict & guides triaging of patients & initiation of therapy → resuscitation & supportive care.
        - To Identify:
            - poison (what?),
            - exposure (how much?),
            - duration (how long?)
            - patient factors (who?)
            - timing (when?).

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Risk Assessment

- A **Toxidrome (shared clinical characteristics)**
    - e.g., serotonin toxicity, sympathomimetic, cholinergic, opioid, and anticholinergic
    - may help identify a poison **when** clinical information is lacking.
- **Investigations** essential to the toxicological risk assessment:
    - **electrocardiogram**
    - **blood gas**
    - **routine blood chemistry** including **kidney function**
    - **drug assays.**

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    - **blood gas**
    - **routine blood chemistry** including **kidney function**
    - **drug assays.**

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Risk Assessment

- Chronic poisoning (e.g., over weeks)
    - may be associated with persistent toxicity
    - due to intercurrent illness with AKI or drug-drug interactions→ accumulation of a therapeutic drug over time. e.g.:
        - neurotoxicity including confusion and seizures from lithium
        - complete heart block from digoxin
- clinical toxicity may be severe despite relatively lower plasma concentrations than acute poisoning.

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Risk Assessment

- risk assess
    - is adjusted according to
        - new information from history and/or investigations
        - clinical progression
- Advice by a clinical/medical toxicologist or Poison Control Center.
    - Is recommended in most cases

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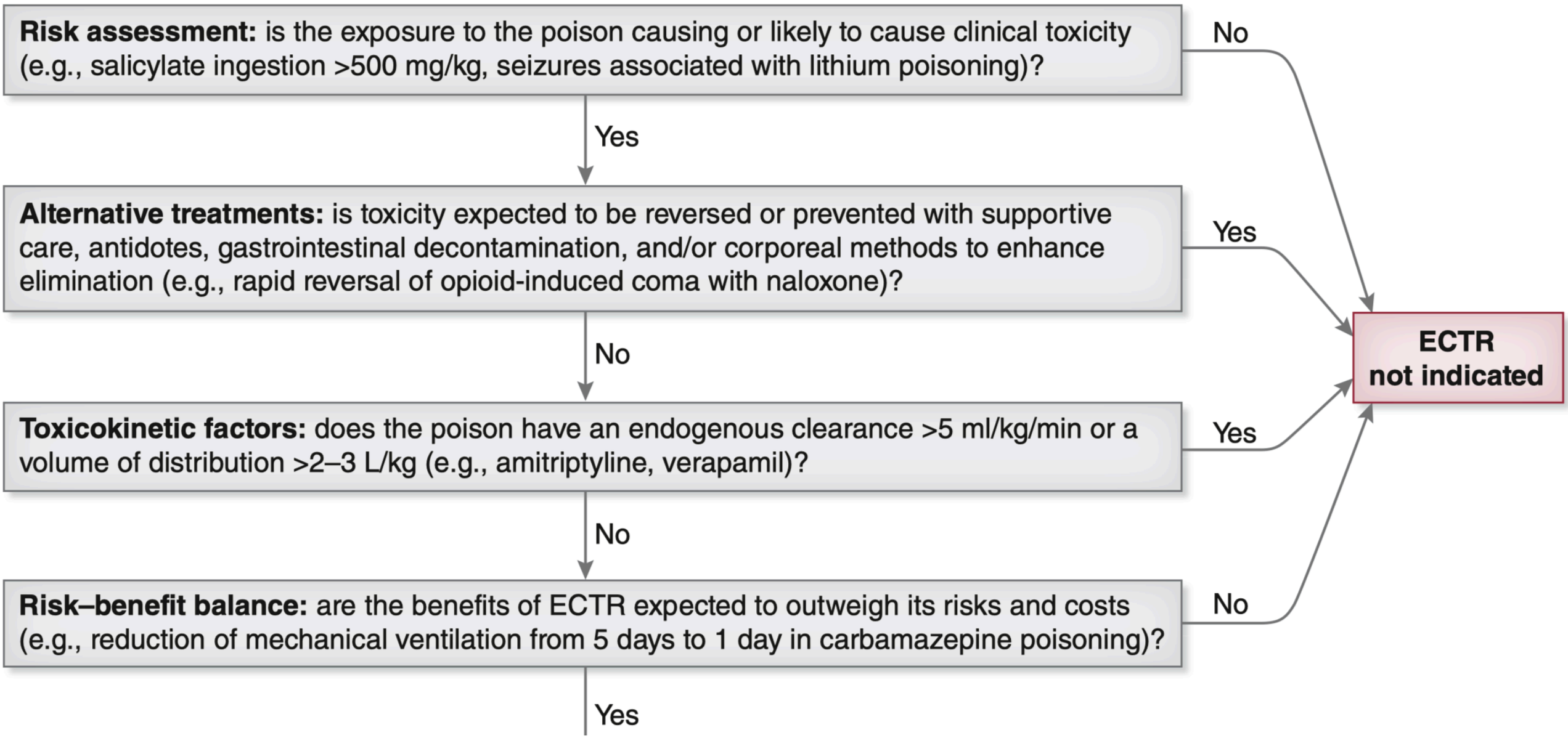
Schematic approach to extracorporeal treatment.(1)



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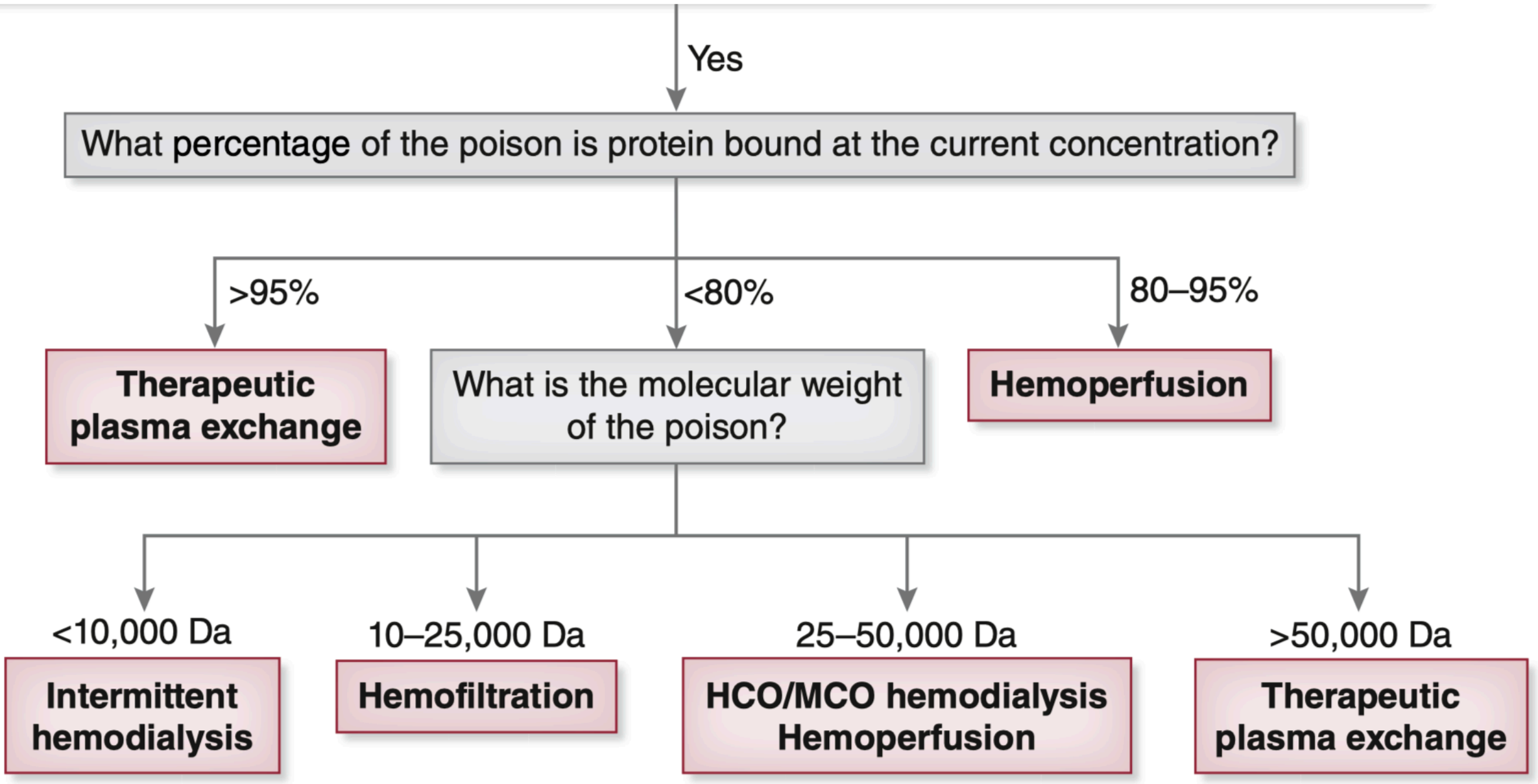

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Gastrointestinal Decontamination

Activated charcoal

- ↓ severity & duration by ↓ amount absorbed
- Activated charcoal:
    - The most commonly used (50 g in adults)
    - should within ~2 hours of ingestion
        - exceptions: extended-release medications (e.g., diltiazem, theophylline) & enteric-coated medicines (e.g., valproic acid)
        - A second dose:
            - may be 2–4 hours later in large exposures (e.g., acetaminophen, valproic acid, salicylates).
- is not effective for:
    - acids/alkali, alcohols, ions, or metals
        - e.g., ethylene glycol, methanol; lithium, iron

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Gastrointestinal Decontamination

Whole bowel irrigation

- enteral administration of a large volume (1 L/h) of an isotonic solution until the rectal effluent is clear
    - polyethylene glycol (macrogol)

- Indications:
    - nonresponsive to activated charcoal
    - extended-release formulations
    - “body packers”
    - highly toxic exposure

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Gastrointestinal Decontamination

- Patients at risk of aspiration:
    - vomiting, depressed conscious state, or seizures.
    - using a nasogastric or orogastric tube once intubated for airway protection
- Other forms: gastric lavage & forced emesis
    - almost never recommended
    - Lavage requiring intubation.
        - large bore orogastric tube

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Antidotes

- Direct or indirect agonists or antagonists to→ effect of a poison
    - Actions at a receptor (e.g., naloxone for opioids),
    - Inhibitors of metabolism (e.g., fomepizole for methanol),
    - Binding for inactivation (e.g., chelators, antivenoms).
- Dosage varies depending on the poisoning exposure
- specific considerations relevant to nephrologists:
    - up-titration (e.g., ethanol or fomepizole)←removal by extracorporeal treatments
    - down-titration (e.g., EDTA)←accumulation in advanced kidney disease
    - repeated doses of antidotes (e.g., dabigatran, digoxin10)← persistent or recurrent toxicity in advanced kidney disease

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Examples of poisons for which antidotes are recommended.

Poison	Antidote
Acetaminophen(paracetamol)	N-acetylcysteine[a]
Anticholinergic drugs	Physostigmine for significant delirium
Anticholinesterase insecticides	Atropine and possibly pralidoxime or obidoxime
Benzodiazepines	Flumazenil (rarely required)
β-adrenergic antagonists	Adrenaline, insulin-dextrose infusion
Calcium channel blockers	Calcium, insulin-dextrose infusion
Carbon monoxide	Oxygen
Cyanide	Hydroxocobalamin and/or thiosulfate
Dabigatran	Idarucizumab
Digoxin	Digoxin Fab antitoxin, atropine
Envenomation(e.g., snake, spider)	Antivenom
Ethylene glycol/methanol	Ethanol or fomepizole[a]
Iron	Deferoxamine
Isoniazid	Pyridoxine[a]
Lead	Ca,Na2 -EDTA or succimer (DMSA)
Methotrexate	Folinic acid, glucarpidase
Opioids	Naloxone
Poison-induced methemoglobinemia (e.g., dapsone, alkyl nitrite)	Methylene blue
Salicylates	Bicarbonate
Sulfonylureas	Octreotide, glucose
Tricyclic antidepressants	Bicarbonate
Valproic acid	L-carnitine[a]
Warfarin	Vitamin K

DMSA, dimercaptosuccinic acid. (2,3-二巯基丁二酸 for 鉛 汞 砷 銻)

[a]The dose of the antidote must be adjusted during extracorporeal treatment.

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Enhanced Elimination

Elimination enhancement modalities

- Modalities divided:
    - Corporeal treatments, which augment physiological process
    - Extracorporeal treatments, which require an artificial device located outside the body.

- Extracorporeal treatments and urine alkalinization are increasingly used.

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Corporeal Treatments

- **Urine Alkalinization**
    - Often for: salicylate, chlorpropamide, phenobarbital, herbicides (e.g., 2,4-dichlorophenoxyacetic acid [2,4-D], 4-chloro-2-methylphenoxyacetic acid, mecoprop), fluoride, methotrexate
    - ↑ urine pH →↑ solubility ↑ionized weak acid
    - efficacy ← relative contribution of kidney clearance to total body clearance
        - Criteria: (1) eliminated unchanged by kidney (2) smaller Vd (3) lower protein binding (4) a weak acid(pKa 3~7)
    - Target urine pH 7.5-8.5 (maintain blood pH≤ 7.55)
    - Serum K should ≥ 4 mml/L prior to
    - Complication: hypokalemia, hypocalcemia, hypernatremia, pulmonary/cerebral edema
    - Carbonic anhydrase inhibitors are contraindicated, especially in salicylate poisoning.
- Fecal Elimination Enhancement
- Forced Diuresis

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Corporeal Treatments

- Urine Alkalinization
- **Fecal Elimination Enhancement**
    - Multiple doses of activated charcoal (MDAC)
        - Typical dosage: 25 g every 2 hrs until clincical or biochemical end points.
        - Used For: carbamazepine, dapsone, phenobarbital, quinine, theophylline, colchicine, Amanita phalloides, salicylates, cardiac glycosides, or phenytoin.
    - Ion exchange resins: sodium polystyrene sulfonate↓lithium half-life
    - Prussian blue: binds radiocesium and thallium in the bowel lumen
- Forced Diuresis

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Corporeal Treatments

- Urine Alkalinization
- Fecal Elimination Enhancement
- **Forced Diuresis**
    - large volumes of isotonic fluids with or without loop diuretics → rarely used today (low efficacy, risk of complications: pulmonary edema/electrolyte abnormalities).

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Extracorporeal Treatments(1)

- **Recommendations :**
    - EXtracorporeal TReatments In Poisoning (EXTRIP) workgroup
- **Decision Making in the Absence of Recommendations**

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ACETAMINOPHEN *(PARACETAMOL)*

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General Recommendation

- ECTR is suggested in severe acetaminophen (APAP) poisoning (2D)

Indications

ECTR is recommended:

- If the [APAP] more than 1000 mg/L (6620 µmol/L) and NAC is NOT administered (1D)
- If the patient presents with altered mental status, metabolic acidosis, with an elevated lactate, and an [APAP] is more than 700 mg/L (4630 µmol/L) and NAC is NOT administered (1D)
- If the patient presents with an altered mental status, metabolic acidosis, an elevated lactate, and an [APAP] is more than 900 mg/L (5960 µmol/L) even if NAC is administered (1D)

ECTR is not recommended

- On the basis of the reported ingested dose if NAC is administered (1D)

ECTR is not suggested

- On the basis of reported ingested dose alone even if NAC is NOT administered (2D)

Extracorporeal Treatments(1)

- **Decision Making in the Absence of Recommendations**
    - risk assessment, clinical effects, time course of poisoning, other treatments available, expected risk versus benefit of extracorporeal treatments, the poison's physicochemical characteristics and pharmacokinetics, available extracorporeal treatments (**Figure**)
    - case-by-case basis. (Ex, AKI in metformin, baclofen)
- A. Clinical toxicology of the poison
- B. Expected clinical impact of extracorporeal treatments
- C. Characteristics of poisons that influence the irremoval by extracorporeal treatments
    - Molecular Weight
    - Protein Binding
    - Endogenous Clearance
    - Volume of Distribution

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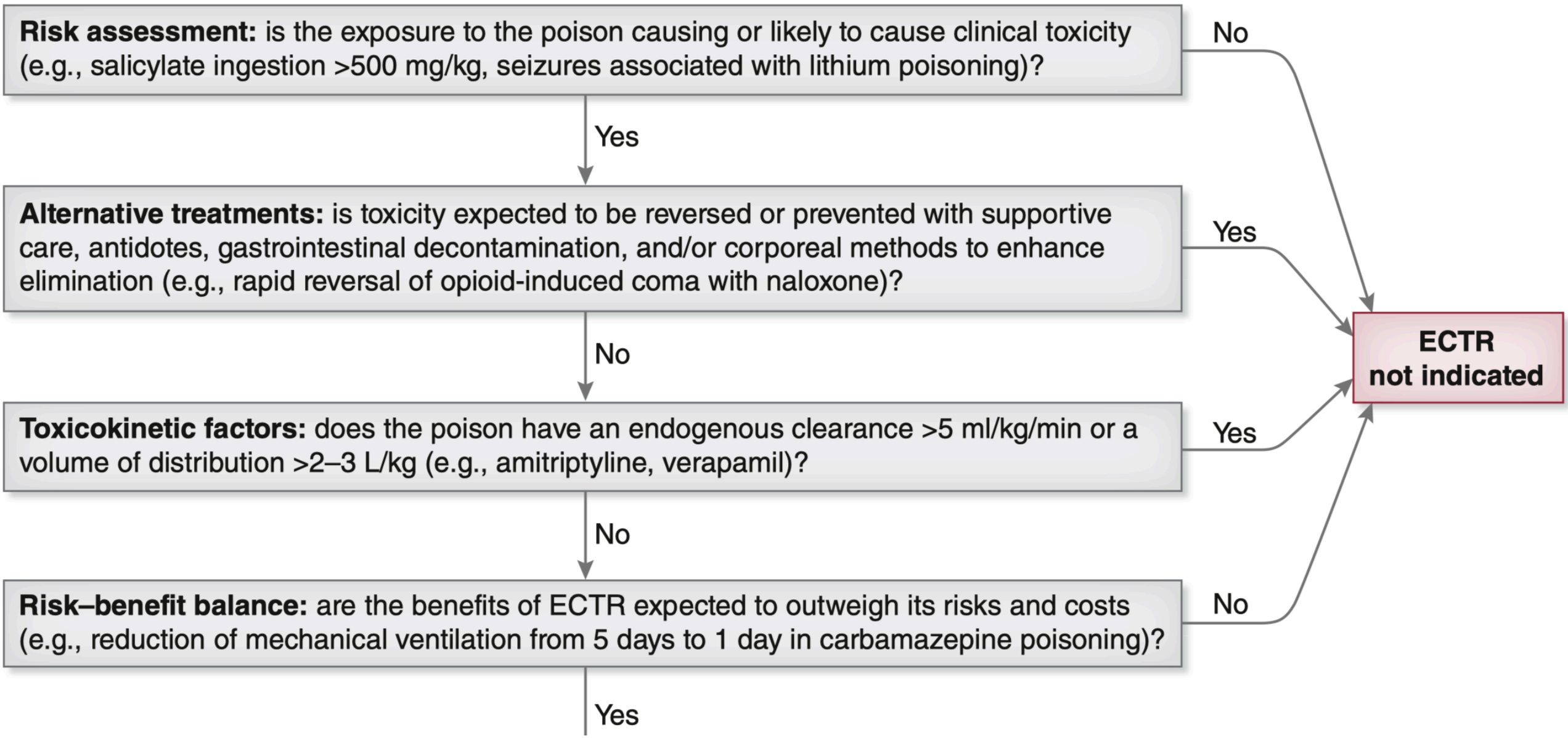

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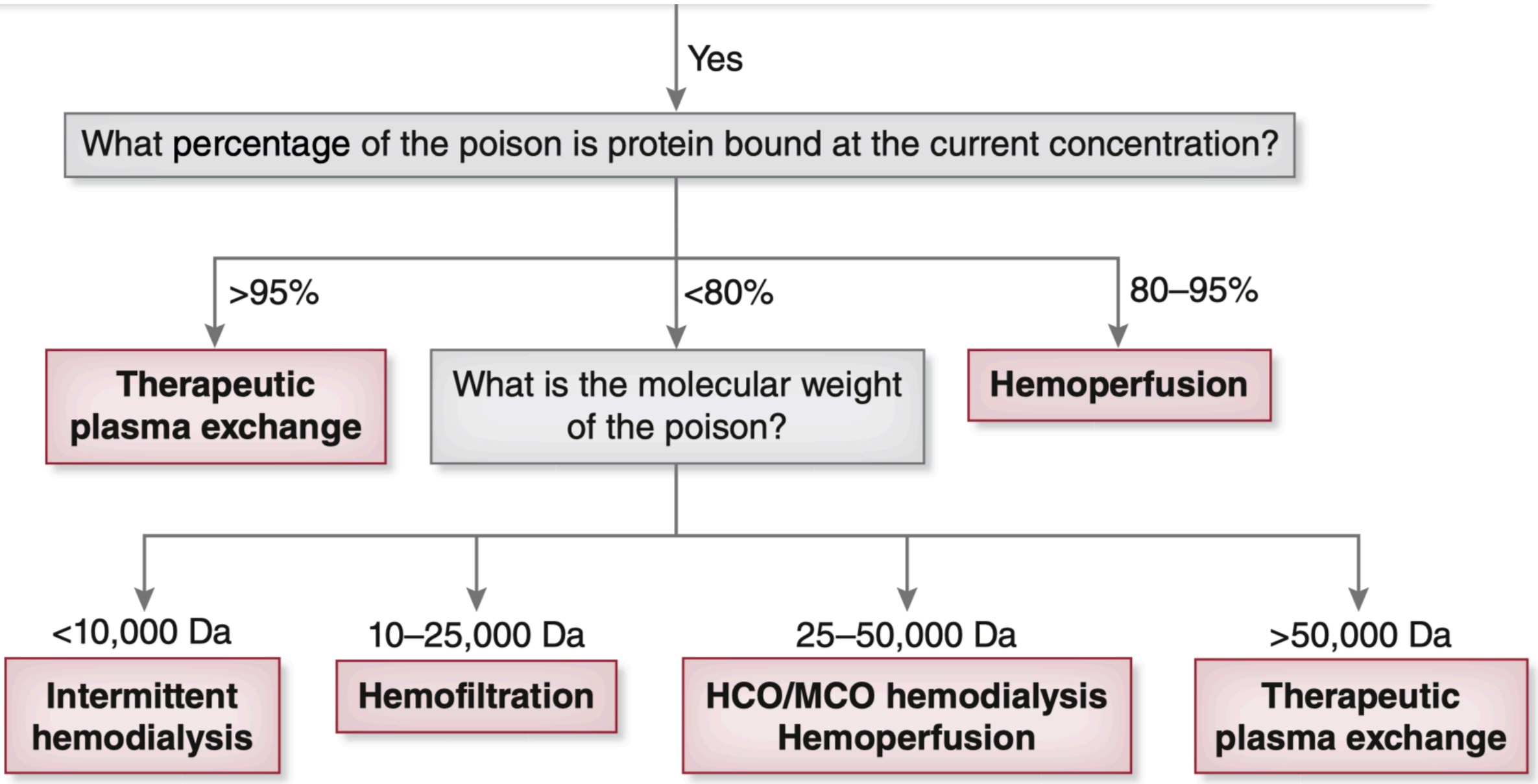

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Poisons whose elimination may be enhanced by corporeal techniques.

Table 2. Poisons whose elimination may be enhanced by corporeal techniques

Urine Alkalinization	Multiple-Dose Activated Charcoal	Sodium Polystyrene Sulfonate	Prussian Blue
Chlorophenoxy herbicides (*2,4-D, MCPA, MCPP*)	Carbamazepine	Lithium	Radiocesium
Chlorpropamide	Colchicine	Potassium	Thallium
Diflusinal	Dapsone		
Fluoride	Digoxin		
Methotrexate	Phenobarbital		
Phenobarbital	Phenytoin		
Salicylates	Quinine		
	Salicylates		
	Theophylline		
	Yellow oleander		
	Amanita phalloides		

2,4-D, 2,4-dichlorophenoxyacetic acid; MCPA, 4-chloro-2-methylphenoxyacetic acid; MCPP, methylchlorophenoxypropionic acid (Mecoprop).

Extracorporeal Treatments(2)

- D. Available extracorporeal treatments
    - Hemodialysis
    - Hemoperfusion
    - Hemofitration
    - Continuous Techniques
    - Peritoneal Dialysis
    - Therapeutic Plasma Exchange
    - Exchange Transfusion
    - Extracorporeal Liver Assist Devices

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二、常見中毒的類型與機制

(1) 藥物與毒品中毒

鴉片類 (Opioids, 如嗎啡、海洛因、芬太尼)

機制：抑制中樞神經系統，影響呼吸中樞

症狀：呼吸抑制、縮瞳、昏迷

解毒劑：納洛酮 (Naloxone)

鎮靜安眠藥 (如苯二氮䓬類、巴比妥類)

機制：GABA 受體作用，抑制中樞神經

症狀：昏迷、低血壓、呼吸抑制

治療：支持療法，對 BDZ 類可使用 氟馬西尼 (Flumazenil)

興奮劑 (如安非他命、可卡因)

機制：增加多巴胺、去甲腎上腺素釋放

症狀：高血壓、心律不整、狂躁、癲癇

治療：降溫、控制高血壓 (如苯二氮䓬類鎮靜)

二、常見中毒的類型與機制

(2) 工業與環境毒物

一氧化碳 (CO) 中毒

機制：與血紅素結合形成碳氧血紅素 (Carboxyhemoglobin)，降低氧運輸

症狀：頭痛、嘔吐、暈眩、嚴重時意識喪失

治療：高流量氧氣治療，嚴重時使用 高壓氧療法

有機磷 (Organophosphates, 殺蟲劑中毒)

機制：抑制乙醯膽鹼酯酶，導致膽鹼能危象

症狀 (DUMBBELLS)：流涎、流淚、尿失禁、肌肉抽搐、縮瞳

解毒劑：阿托品 (Atropine) + 氯解磷定 (Pralidoxime, 2-PAM)

二、常見中毒的類型與機制

(3) 食物與植物毒物

河豚毒素 (Tetrodotoxin, TTX)

機制：鈉通道阻滯，影響神經傳導

症狀：口唇麻木、肌肉無力、呼吸衰竭

治療：支持性治療，無特效解毒劑

毒蕈 (Amanita Phalloides, 毒蠅傘菌中毒)

機制：肝細胞毒性，影響 RNA 聚合酶

症狀：延遲性嘔吐、腹瀉、肝衰竭

解毒劑：N-乙醯半胱氨酸 (NAC)、Silibinin (水飛薊素)

食物中毒處理原則

定義

- 二人以上（包括二人）攝取相同食物而發生相似症狀，並且自可疑食物檢體及患者糞便、嘔吐物、血液等人體檢體，或者其他有關環境檢體〈如空氣、水、土 壤等〉中分離出相同類型的致病原為生物、毒物或有毒化學物質，則稱一件「食物 中毒」。
- 症狀以消化系統及神經系統障礙為主，由以急性腸胃炎症狀如嘔吐、腹瀉、 腹痛等最常見；
- 但如因攝取肉毒桿菌或急性化學中毒而引起死亡時，即使只有一人也是一件「食物中毒」事件。

常造成食品中毒的主要病因物質

1.細菌：常見的致病菌有腸炎弧菌、沙門氏桿菌、病原性大腸桿菌、金黃色葡萄球菌、仙人掌桿菌、霍亂弧菌、肉毒桿菌等。

2.病毒：如諾羅病毒等。

3.天然毒：包括植物性毒素、麻痺性貝毒、河豚毒、組織胺、黴菌毒素等。

4.化學物質：農藥、重金屬、非合法使用之化合物等。

更新日期：2024-09-13; Taiwan Food and Drug Administration

台灣常見的細菌性食品中毒其原因食品有哪些？

1.引起腸炎弧菌食品中毒的原因食品主要為生鮮海產及魚貝類等。

2.引起沙門氏桿菌食品中毒的原因食品主要為受污染的畜肉、禽肉、鮮蛋、乳品及豆製品等。

3.引起病原性大腸桿菌食品中毒的原因食品主要為受糞便污染的食品或水源。

4.引起金黃色葡萄球菌食品中毒的原因食品主要為肉製品、蛋製品、乳製品、盒餐及生菜沙拉等。

5.引起仙人掌桿菌食品中毒的原因食品主要為米飯等澱粉類製品、肉汁等肉類製品、沙拉及乳製品等。

6.引起肉毒桿菌食品中毒的原因食品主要為低酸性罐頭食品、香腸及火腿等肉類加工品及真空包裝豆干製品等。

更新日期：2024-09-13; Taiwan Food and Drug Administration

常見的食物中毒及症狀：

- 1. 葡萄球菌中毒：潛伏期約 1～8 小時（平均 24 小時）。 主要症狀有噁心、嘔吐、腹瀉等。 主要感染者之鼻涕、痰 、糞便、傷口或濃包所致。

- 2. 腸炎弧菌中毒：潛伏期為 2～48 小時，通常在 12 小時發病。 其病徵為腹痛、水瀉、便血、便中有粘液、發燒、頭痛等。 主要是由海鮮類及涼拌類食品未妥善處理所造成。

- 3. 沙門氏菌中毒：潛伏期為 5～72 小時，通常在 12～36 小時內發病。 其病徵為腹痛、腹瀉、發燒、嘔吐、寒戰等。 由感染的動物或人類糞便傳染，不清潔的蛋殼易引起。

- 4. 仙人掌桿菌腸胃：潛伏期為 8～16 小時 。 其病徵為噁心、腹痛、水瀉等。 主要由游不潔或過時之雞蛋、牛奶、布丁、穀類製品所引起

- 5. 病原性大腸桿菌中毒：分毒素型侵入型，潛伏期為 8～16 小時。 毒素型主要症狀為湯狀腹瀉、嘔吐、腹瀉侵入型主要是因受感染水源、糞便或帶菌動物所造成。

食品中毒

- 加熱的重要性：適當的加熱過程可以殺死活的細菌，也可以除去某些細菌產生的毒素，例如肉毒桿菌的毒素即可在100°C加熱10分鐘後失去活性。
- 但是，有許多細菌產生的毒素可以耐熱，例如金黃色葡萄球菌產生的毒素在高溫烹煮過後仍然不會被破壞。

- 危險溫度帶？溫度介於7~60°C之間。

更新日期：2024-09-13; Taiwan Food and Drug Administration

身體檢查

常見中毒症候群(1)

心血管症狀		
心搏過速與/或高血壓	**心搏過緩與/或低血壓**	**心臟傳導延遲 (寬QRS)**
安非他命	乙型阻斷劑	古柯鹼
抗膽鹼劑	鈣離子通道阻斷劑	三環抗抑鬱藥
抗組織胺	Clonidine	局部麻醉藥
古柯鹼	毛地黃素與相關配糖體	Propoxyphene
茶鹼/咖啡因	有機磷與氨基甲酸酯	抗心律不整藥物 (e.g., quinidine, flecainide)
戒斷狀態	乙型阻斷劑	古柯鹼

身體檢查

常見中毒症候群(2)

中樞系統與代謝症狀		
癲癇	**中樞神經系統與/或呼吸系統抑制**	**代謝性酸中毒**
三環抗抑鬱藥	抗憂鬱藥 (多種類型)	氰化物
Isoniazid	苯二氮平類(BZD)	乙二醇
選擇性與非選擇性去甲腎上腺素再攝取抑制劑(eg, bupropion)	一氧化碳	Metformin
戒斷狀態	乙醇	甲醇
	甲醇	水楊酸類藥物
	鴉片類藥物	
	口服降血糖藥	

一氧化碳中毒之照護

- 什麼是一氧化碳中毒？

- 一氧化碳是一種無色、無臭、無味、無刺激性的氣體，比空氣略輕，與血紅素結合的能力是氧氣的200~300倍，使體內細胞缺氧，導致組織缺氧或細胞功能受傷害。需氧量較大的器官通常影響較大，如腦部、心臟。造成一氧化碳中毒的原因，主要是含碳氫化合物燃燒不完全所致，常見曝露來源如熱水器或木炭爐等燃燒不完全之加熱系統、內燃機引擎廢氣、火災等。

一氧化碳中毒症狀

HbCO 量 (%)	症　　狀
10-15	頭痛
25-30	噁心、嘔吐、呼吸困難
30-35	皮膚吐櫻桃紅色
35-40	暈眩、視力模糊
40-45	運動失調 （ataxia）
45-50	心博加速
50-55	呼吸加速
55-60	抽筋、Cheyne-Stokes 呼吸
>60	昏迷、死亡

環境事故應變諮詢中心

一氧化碳中毒要怎麼處理？

一氧化碳中毒要怎麼治療：

- **1.** 立即改善通風及儘速將病人自中毒處移開，若出現意識不清狀況，需保持呼吸道暢通並立即送醫治療。

- 2. 立刻給予高濃度氧氣使用，並監測血液中一氧化碳血紅蛋白濃度。

- 3. 併發症預防與治療，包括腦水腫、延遲性神經病變，血液中酸鹼平衡及電解質平衡等。

- 4. 考慮使用高壓氧治療。

有機磷

General chemical structure of organophosphorus compounds. E

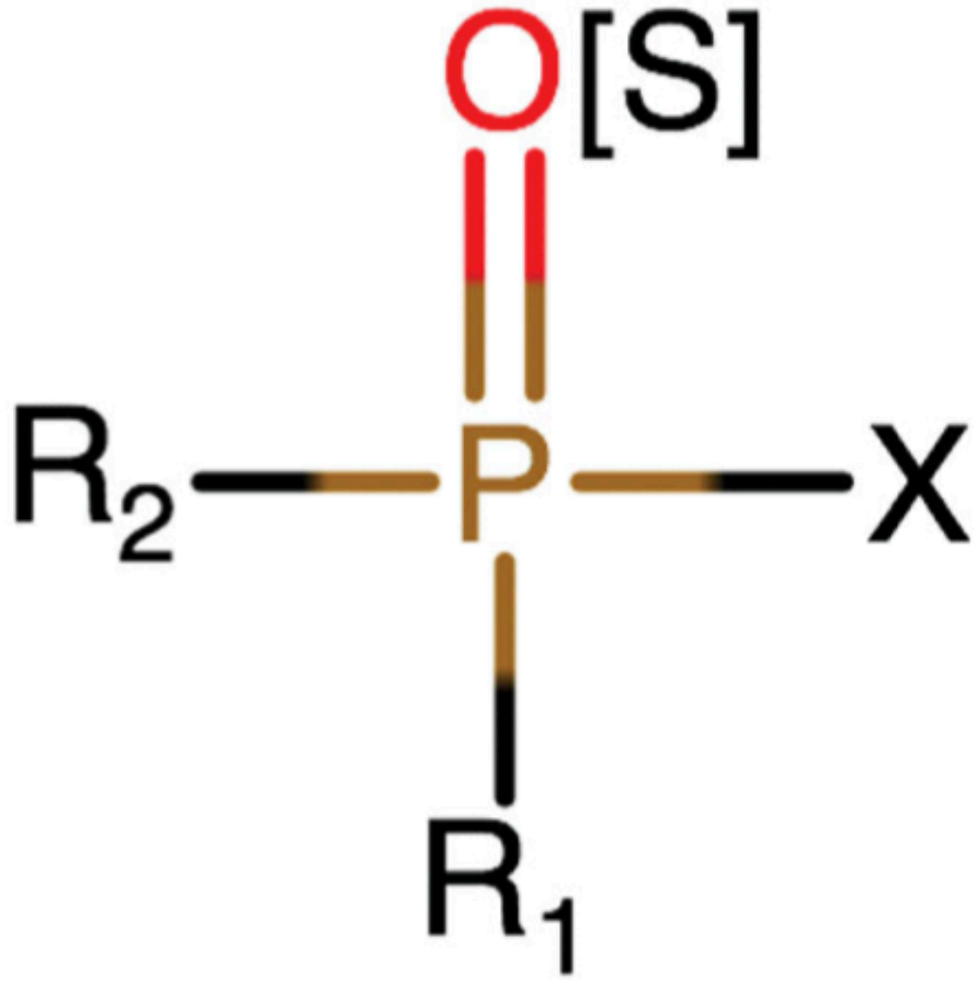
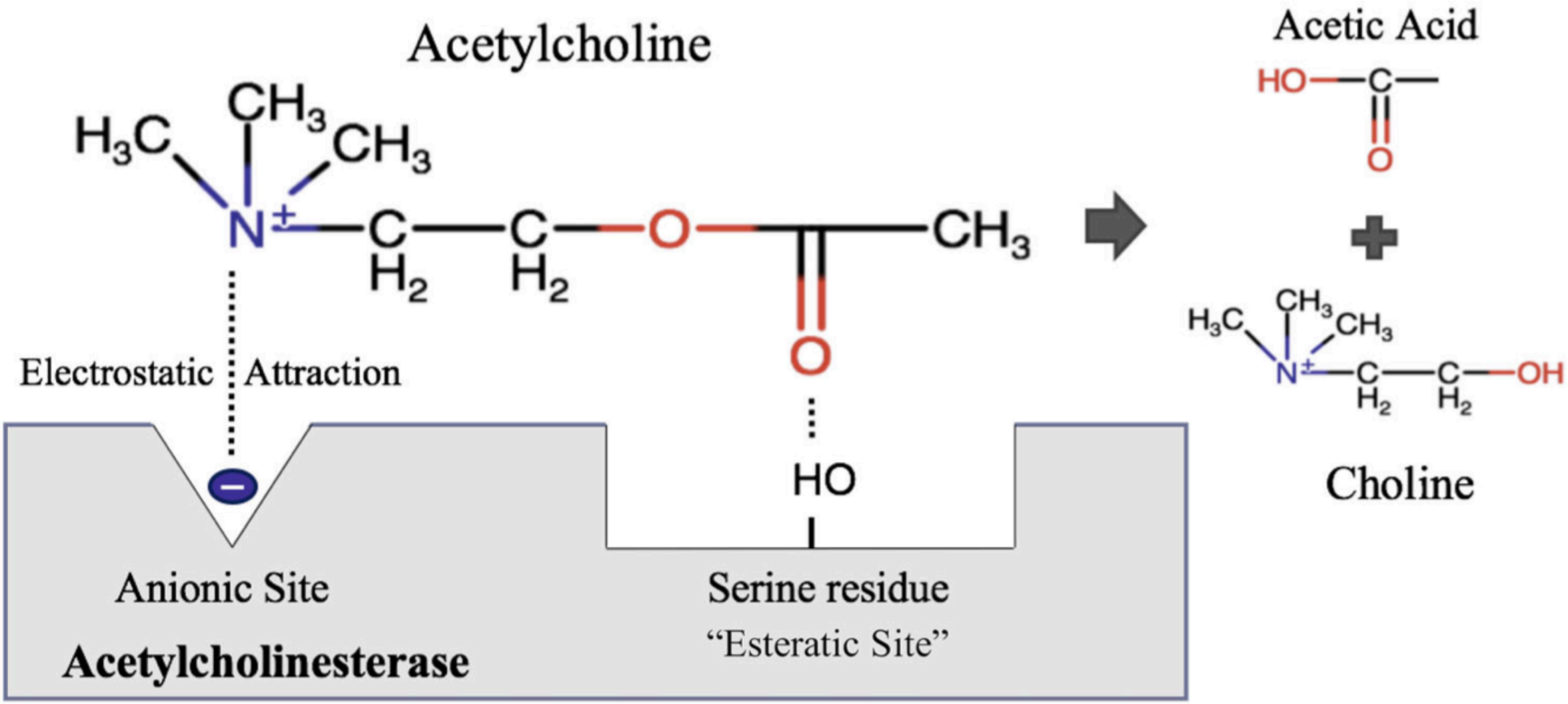


Figure 1. General chemical structure of organophosphorus compounds. Each organophosphorus agent (OP) has different alkyl substituents. The leaving group (X) is displaced upon binding of the OP to the active site of the acetylcholinesterase (AChE) enzyme.

Crit Rev Toxicol. 2020 Oct;50(9):764-779.

有機磷

Role of acetylcholinesterase (AChE) in the hydrolysis of acetylcholine (ACh).



Crit Rev Toxicol. 2020 Oct;50(9):764-779.

有機磷中毒之症狀與處理原則

Hemodialysis

- Several studies including retrospective analyses (Dong et al. 2017; Jiang et al. 2019) and a non-randomized controlled trial (Peng et al. 2004) assessing the clinical efficacy of hemoperfusion alone and hemoperfusion combined with hemodialysis have demonstrated several advantages for these procedures.
    - → associated with reduced incidence rates of poisoning complications and medication-related adverse reactions, shortened AChE reactivation time, shortened ventilation time, improved clinical outcomes, elevated overall survival rates.

Crit Rev Toxicol. 2020 Oct;50(9):764-779.

有機磷中毒之症狀與處理原則

（六）農藥中毒

1. D.D.T 中毒

（1） 症狀：眩暈、噁心、嘔吐、麻木、肌肉顫抖、昏迷、呼吸衰竭等。

（2） 急救：

a.> 禁用油性瀉劑。

b.> 維持呼吸道暢通，立即送醫。

2. 巴拉刈 （Paraquat）中毒

（1） 症狀：口腔食道潰爛、噁心、嘔吐、腹痛、肺水腫會漸進肺纖維化而死亡，肝、腎亦會被破壞。

（2） 急救：

必考題

a.> 不可給氧氣。

b.> 衣物如有污染立即清除，並清洗皮膚。

c.> 儘速送醫治療。

CCB過量/中毒

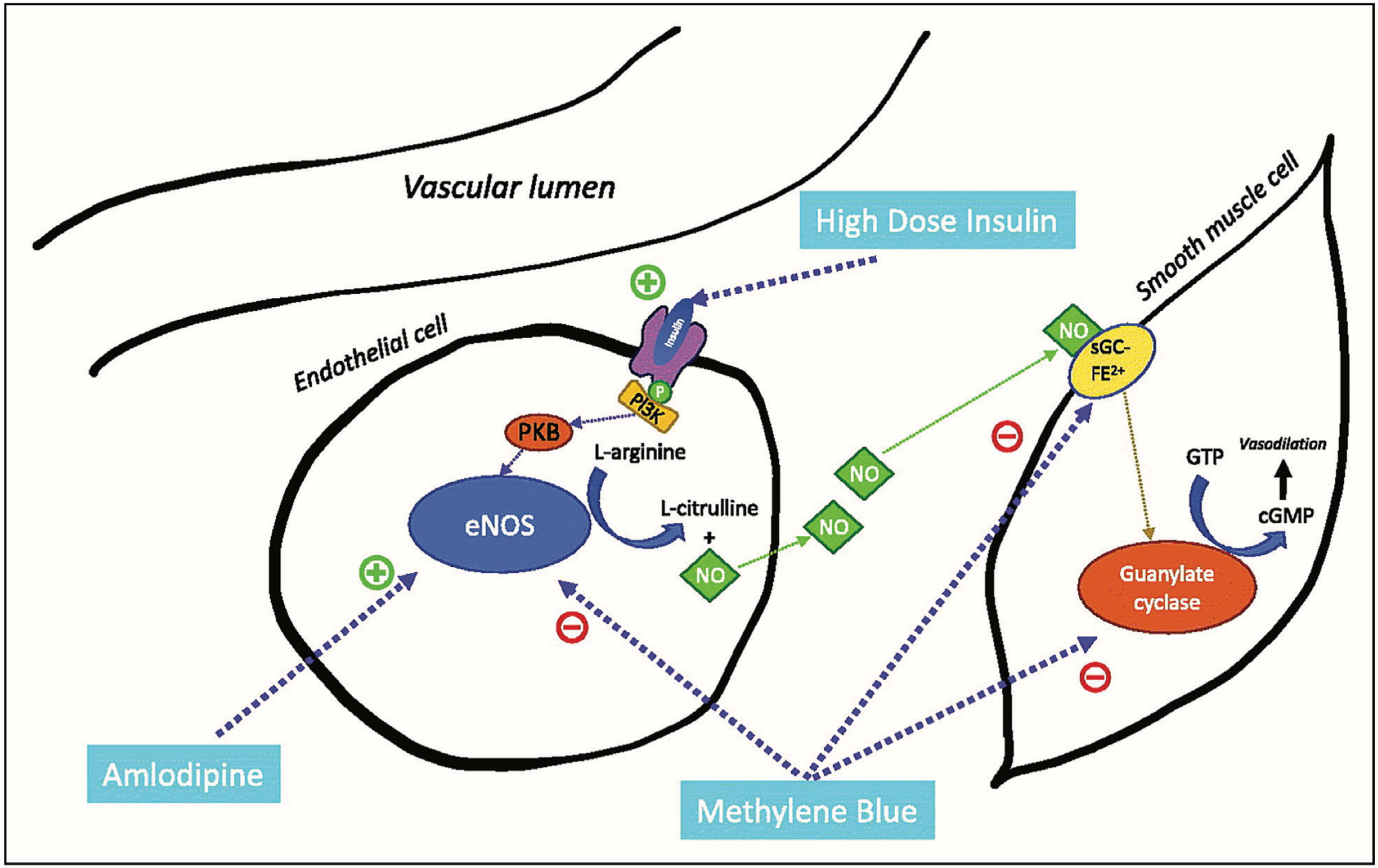
calcium channel blocker poisoning

Table 1. Characteristics of calcium channel blocker classes

Class	Dihydropyridine	Nondihydropyridine
Predominant site of toxicity	Vascular smooth muscle	Myocardium
Specific drug examples	Amlodipine, nifedipine, nicardipine	Diltiazem, verapamil
Laboratory findings	Possible hyperglycemia	Hyperglycemia
Expected hemodynamic changes	Hypotension, tachycardia	Hypotension, bradycardia
Primary cause of shock	Distributive	Cardiogenic

Curr Opin Crit Care 2024, 30:603–610

Mechanisms of potential synergistic vasodilation between amlodipine and high-dose insulin.



PI3K, phosphatidylinositol 3-kinase. PKB, protein kinase B. eNOS, endothelial nitric oxide synthase. NO, nitric oxide. sCG-Fe2, soluble guanylate cyclase. GTP, guanosine triphosphate. cGMP, cyclic monophosphate.

Curr Opin Crit Care 2024, 30:603–610

Comparison of contemporary Guidelines for calcium channel blocker poisoning management

Guideline	Experts Consensus Recommendations for the Management of Calcium Channel Blocker Poisoning in Adults	American Heart Association Focused Update on the Management of Patients With Cardiac Arrest or Life-Threatening Toxicity Due to Poisoning
Year of publication	2017	2023
Treatment	Recommendation	
Intravenous calcium	Recommended as first-line in symptomatic patients (1D)[a]	Reasonable to administer (2a, C-LD)[c]
Atropine	Suggested for symptomatic bradycardia or conduction delays (2D)[b]	Reasonable for hemodynamically significant bradycardia (2a, C-LD)
Pacing	Suggested for unstable bradydysrhythmia without myocardial depression (2D)	Might be reasonable for refractory bradycardia (2b, C-LD)[d]
Vasopressors	Recommend vasopressors in shock (1D); recommend norepinephrine in distributive shock (1D); suggest epinephrine or dobutamine in cardiogenic shock (2D)	Recommended for hypotension (B-NR)[e]
HDI	Recommended for myocardial dysfunction (1D); suggested as monotherapy for myocardial dysfunction or in conjunction with vasopressors in absence of myocardial dysfunction (2D)	Recommended for hypotension (B-NR)
ECMO	Suggested for refractory shock, periarrest, or cardiac arrest, if available (2D)	Reasonable for refractory cardiogenic shock (2a, C-LD)
ILE	Recommended for refractory shock, periarrest, or cardiac arrest (1D); suggested for shock refractory to first-line treatment	Routine use not recommended (No benefit, C-LD)[f]
Methylene blue	Not recommended as first-line treatment (1D)	Usefulness is uncertain (2b, C-LD)

[a]Strong recommendation, very low level of evidence.
[b]Weak recommendation, very low level of evidence.
[c]Moderate strength recommendation based on limited data.
[d]Weak recommendation based on limited data.
[e]Strong recommendation based on nonrandomized studies.
[f]No benefit based on limited data.

ECMO: venoarterial ECMO
HDI: High-dose insulin
ILE: Intravenous lipid emulsion

Curr Opin Crit Care 2024, 30:603–610

毒藥物諮詢中心

必要時可電話向毒藥物諮詢中心洽詢有關事宜。

北區： 台北榮民總醫院毒藥物防治諮詢中心 （24 小時服務）

02-28717121，02-28757525

中區： 台中榮民醫總院毒物諮詢中心

04-23599783，04-23592525

南區： 高雄醫學大學附設醫院毒藥物諮詢檢驗中心

07-3162631，07-3121101~7563

環境事故應變諮詢中心

TCA 抗憂鬱劑中毒

- TCA 藉由抑制 pre-synaptic nerve terminal neurotransmitter 之 receptor ， 及抑制muscarinic H 1 及 Alpha-1 adrenergic receptor 造成其藥理作用。

- 處理上由於 anti-cholinergic effect 造成 gastric emptying 減緩，洗胃是必要的。

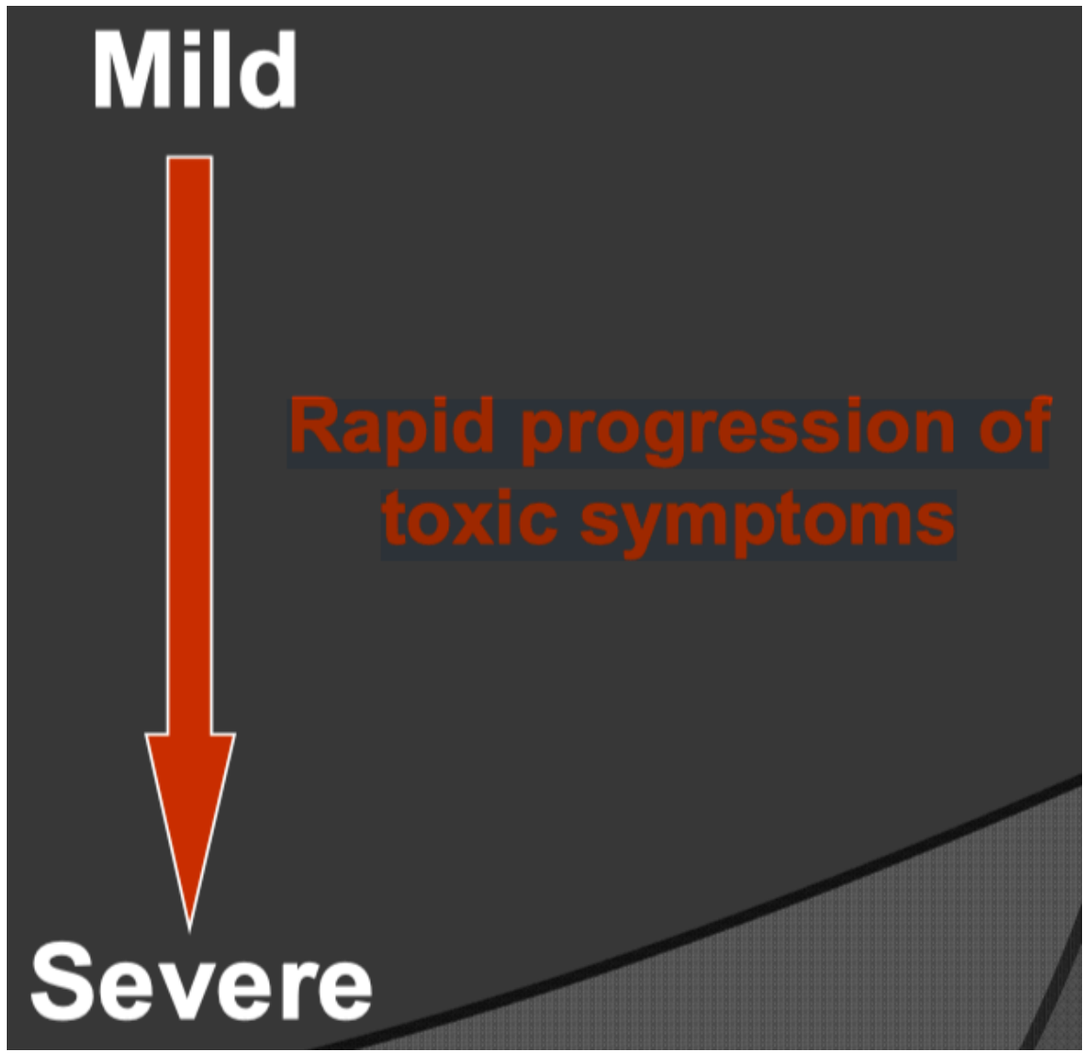
- 由於病人常很快的發生 seizure 或意識變 化，催吐不建議使用。

三環抗憂鬱劑
(TCA)
Tricyclic antidepressant

- 阻斷神經末梢對serotonin再吸收。
- Doxepin(sinequa®)、imipramine(tofranil®)
- 原用於治療憂鬱症，但目前對慢性焦慮症恐慌症、懼曠症、廣泛性焦慮症、強迫症等療效不錯
- 起效慢，但服藥過程可出現口乾舌躁、排尿困難、便秘、青光眼惡化、姿勢性低血壓等副作用，過量時有中毒致死風險。

TCA

- Mild-to-moderate toxicity
    - Drowsiness / lethargy
    - Slurred speech
    - ↓BP, ↑HR
    - Hypoventilation
- Severe toxicity
    - Coma
    - Seizures
    - Arrhythmias
    - Hypotension



TCA: Severe Toxicity

- Complications::
    - Marked conduction disorders (QRS >120 ms)
    - Marked tachycardia/bradycardia
    - Ventricular arrhythmias
    - Significant hypotension
    - Seizures or coma

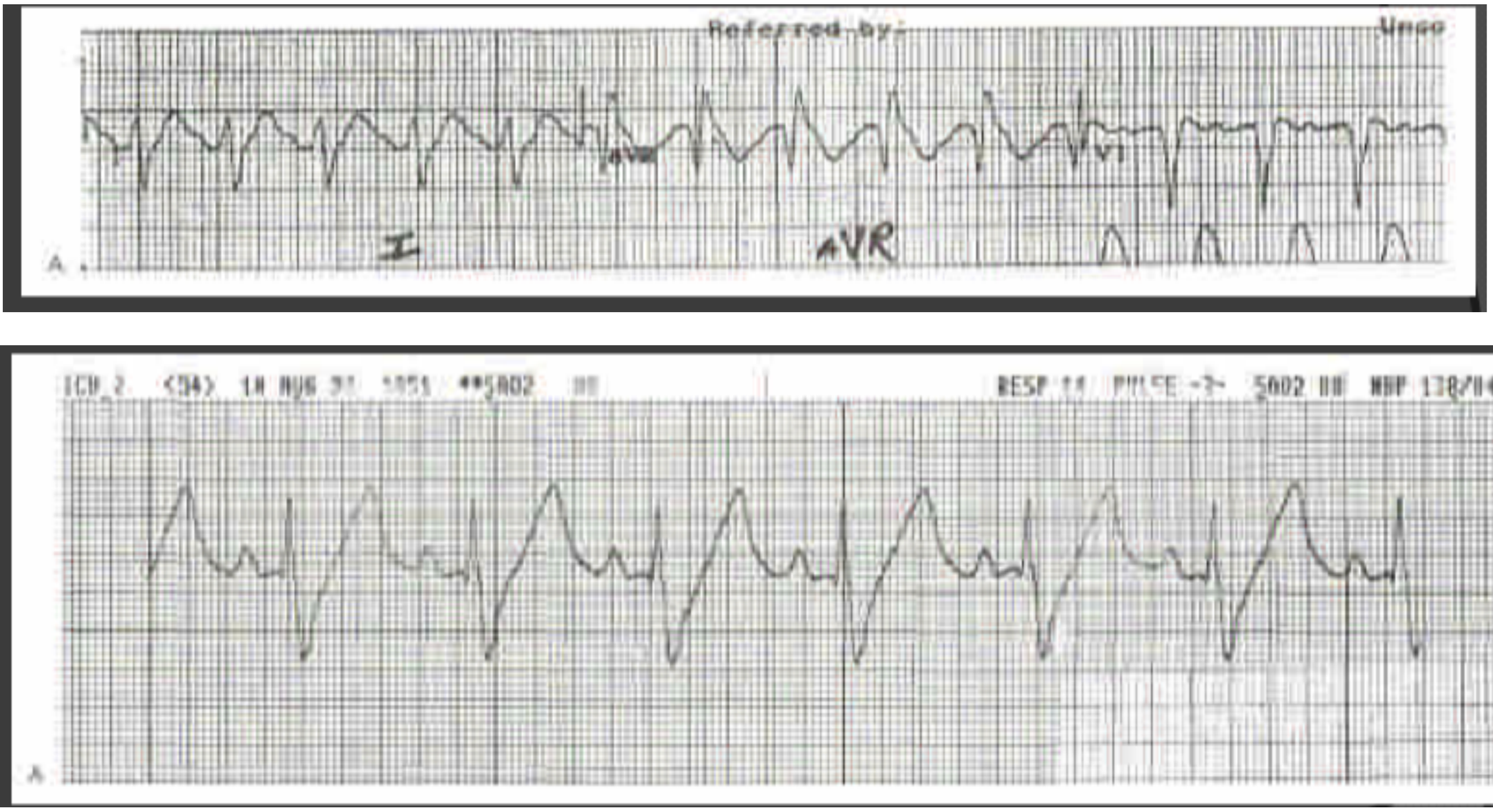
七、副作用

7.1 劑量 [2, 3]

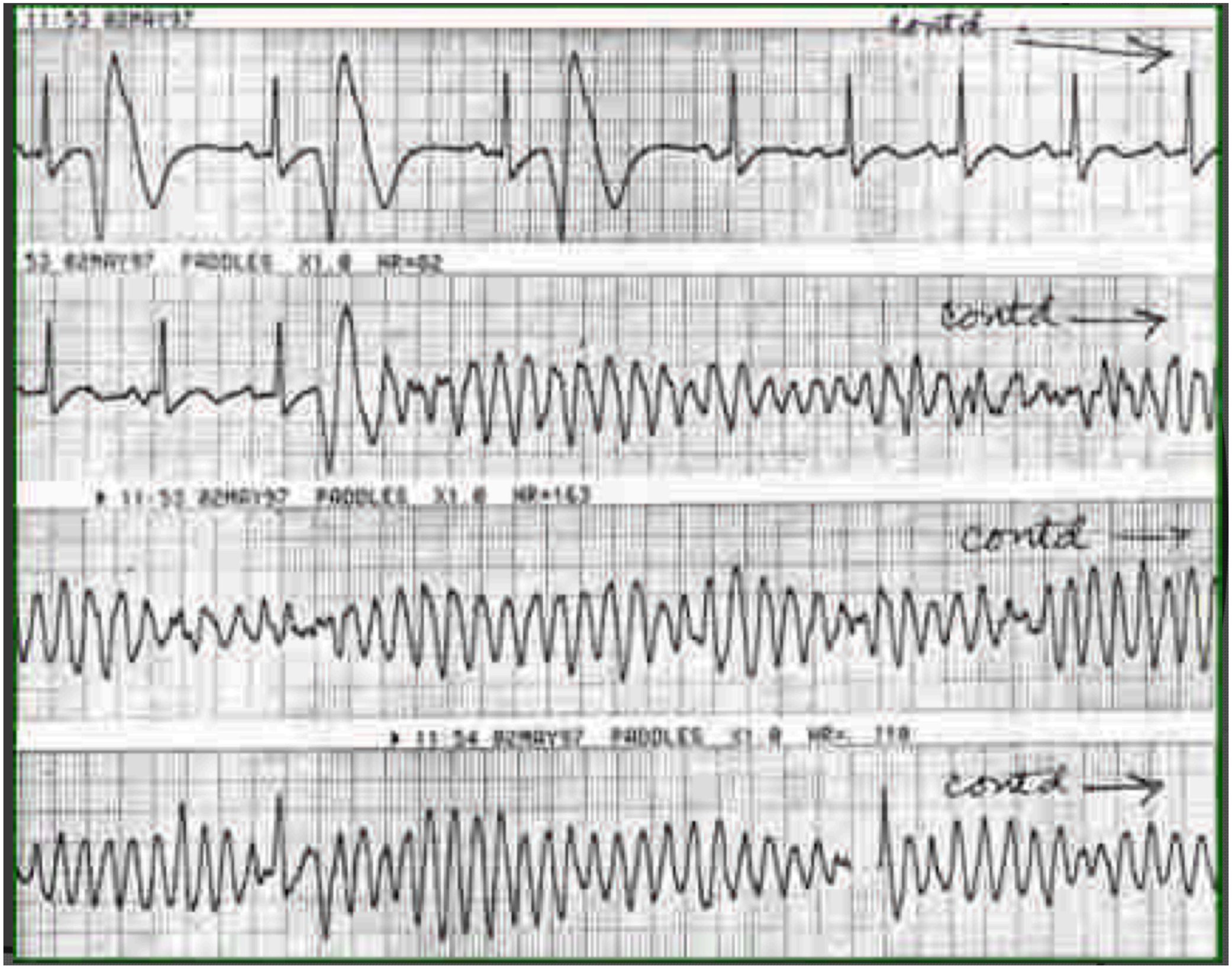
藥物	抗膽鹼作用	鎮靜	姿態性低血壓	癲癇	傳導異常
TCA					
Amitriptyline	++++	++++	+++	+++	+++
Clomipramine	++++	++++	++	++++	+++
Doxepin	+++	++++	++	++++	++
Imipramine	+++	+++	++++	+++	+++
Trazodone	0	++++	+++	++	+
SSRI					
Fluoxetine	0	0	0	++	0
Fluvoxamine	0	0	0	++	0
Paroxetine	+	+	0	++	0
Sertraline	0	0	0	++	0
SNRI					
Venlafaxine	+	+	0	++	+

- 一名29歲女子過去有憂鬱症,被家屬送來 急診,主訴2小時前疑似吃了一個星期份的藥物
- V/S: 36 80 12 100/65 mmHg
- GCS: E1V1M4
- 請問你要怎麼處理?
- 要不要洗胃? 要不要用活性碳?on endo?
- 要不要給flumazenil?

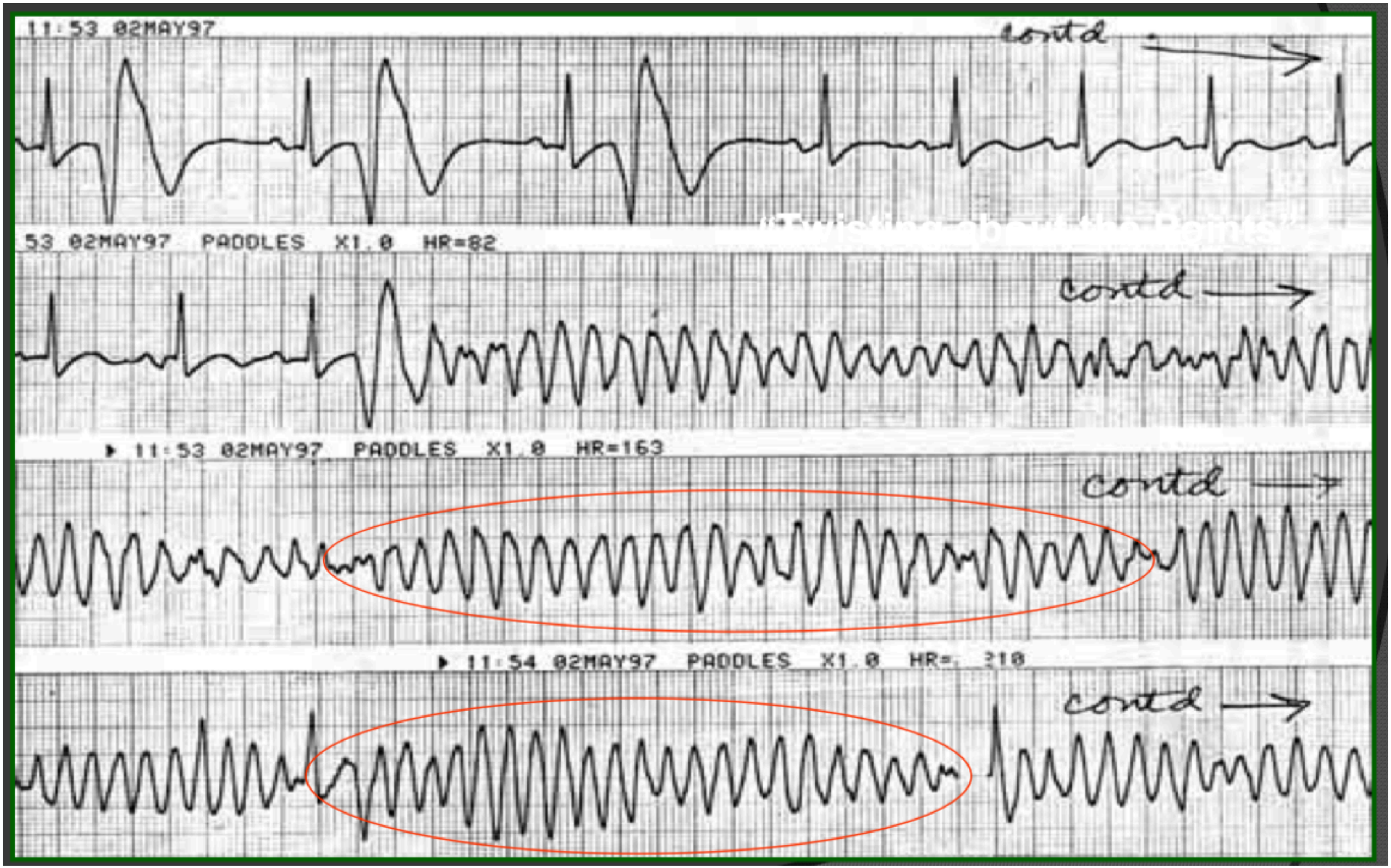
EKG


Referred by:
Verge
I
aVR
A
ICU 2 <34> 18 AUG 91 1051 **5802 II
RESP 14 PULSE -?- 5002 II NBP 138/84
A

EKG



Torsades de Pointes (Polymorphic VT)



TCA 抗憂鬱劑中毒

- Repeat dose activated charcoal 可加速排除，但 要小心。
- 病患中毒第二天以後，常死之致命性的心室性 心律不整。如有aVR的R波變高或心律不整，可 alkalinization 用 sodium bicarbonate 1 mEq/Kg 使 serum pH 7.45 ~ 7.55 。
- 而下列藥品應避免使用：Physostigmine，beta-blocker，verapamil 及 Ia 之 antiarrhythmics 。
- Forced diuresis 及 血液透析 (HD) 均無效，有少 數用血液灌洗 (HP) 成功的病例報告。

TCA 中毒之治療

- $NaHCO_3$ - best antidote!
    - Target pH: 7.45 to 7.55
- Levophed (avoid Dopamine)
- Avoid procainamide and physostigmine
- Stop TCA seizures with bicarbonate, BZDs,, phenytoin
- Circulatory-assist devices in cases refractory to maximal medical therapy
- Prolonged CPR if cardiac arrest: good neurologic outcome possible

三環抗抑鬱劑中毒

三環抗抑鬱劑中毒要注意些什麼？

1 moderate to serious exposures - 10 to 20 mg/kg PO.

2 QTc prolonged, QRS widening, 小心R on T, Torsade de pointes

3 conscious disturbance

4 測血中濃度，本院毒藥物諮詢檢驗中心可檢測

三環抗抑鬱劑中毒

2. 應如何治療？

1 $NaHCO_3$ 5Amp+N/S 500c.c.+15%KCl 5c.c. IV for one hour st

$NaHCO_3$ 2Amp+N/S 500c.c.+15%KCl 5c.c. IV q6h

保持 pH 7.45 ~ 7.55或尿液 pH 7.5 ~ 8.0

2 如 VT 則照 ACLS 上治療，不可給 antiarrhythmia Class Ia 之藥物 (例 procainamide)

3 支持性療法

八、過量/毒性處理[7]

環狀抗憂鬱藥過量之中毒反應通常服藥後 6 小時以內發生。一般中毒反應分為心臟血管及神經毒性，心臟血管毒性之症狀為傳導異常(例如：QRS 較寬及節律障礙)，神經毒性症狀為快速地心情惡劣、癲癇及昏迷。其他症狀包括有橫紋肌溶解症、腎衰竭及酸中毒。毒性處理原則採用支持性療法：(依病人症狀給藥)

1.去除藥物：使用活性炭 1 g/kg (最大量:50 g)吸附藥物或洗胃(避免使用吐根糖漿催吐)

2. ORS 變寬(節律障礙)：IV $NaHCO_3$ 1-2 mEq/g，維持血清中 pH 7.45-7.55，若 $NaHCO_3$ 對於節律障礙沒有改善，則改用 lidocaine 及 bretylium

3. 癲癇：IV diazepam 5-10 mg, or lorazepam 1-2 mg

4. 避免使用下列藥物：Flumazenil, procainamide, physostigmine, quinidine, disopyramide.

5. 監控參數：連續性的 EKG、心臟功能及中樞神經之反應

TCA Screen(Rapid test kit)

引用 (9)

2024/12/25 14:24:28

4905

檢驗項目(中文)	三環類抗抑鬱藥篩檢	**檢驗健保碼**	10801B	**檢驗計價碼**	66019123
檢驗項目(英文)	TCA Screen(Rapid test kit)	**可自費**	是	**自費價格**	312元
參加認證	否	**完成檢驗申請的說明**	由EHIS進行醫囑建立		
委託其他實驗室代檢	無	**接受代檢**	是		
檢體種類	尿液	**檢體容器**			
檢體量	10 ml	 S-Y紅蓋尖底離心尿管 (編號:47)			
檢體件數之限制	不適用				
採檢部位	中段小便				
病人準備說明	無需特別準備				
病人自行採檢說明	收集中段小便。				
最適採檢時間	無特殊要求	**檢體接收與退件條件**	請參考實驗室規範		

鋰鹽 (lithium) 中毒

1. 鋰鹽中毒要注意些什麼？

1 治療躁鬱症 (manic-depressive disorder) 者可能使用

2 活性碳或瀉劑，無治療效果

2. 鋰鹽中毒症狀？

1 嗜睡、神智混亂、記憶力變差、譫妄、抽搐、昏迷、近端肌肉無力、步態不穩、失禁、異常反射、肌肉束抽動、類似巴金氏症

2 腸胃道毒性：噁心、嘔吐、腹瀉

3 腎毒性：夜尿、尿崩症、遠端腎小管酸血症、近端腎小管異常(高劑量時)及暫時性的腎功能異常

4 心臟毒性： ST-T 波的異常、傳導阻礙、QT 間隔延長、U 波及偶發性的低血壓

鋰鹽 (lithium) 中毒

3. 鋰鹽中毒檢查

1 心電圖、生化檢查、血球計數、動脈血液氣體分析

2 測血中濃度，本院毒藥物諮詢檢驗中心可檢測

a. 治療濃度： 0.6-1.2 mEq/L

b. 輕度至中度中毒濃度： 1.5-2.5 mEq/L

c. 嚴重中毒濃度： 2.5-3 mEq/L

d. 亡死中毒濃度： 3-4 mEq/L

e. 第一次服食鋰鹽患者中毒濃度 3-6 mEq/L 可能沒有症狀

鋰鹽 (lithium) 中毒

4. 鋰鹽中毒治療

1 0.9% 的氯化鈉溶液

2 furosemide 利尿劑使用，但是 thiazides and spironolactone 之使用反而使鋰鹽升高。

3 血液透析

a. 血中濃度達 3.5-4 mEq/L

b. 慢性鋰鹽中毒：中樞神經、心血管、腎衰竭的症狀

c. 急性中毒：< 3.5-4 mEq/L，症狀 (+)

巴拉刈中毒

1. 巴拉刈中毒需和年年春區分，這兩者是除草劑中毒最多的兩種

1) 巴拉刈是藍綠色，而年年春是淡茶色

2) 巴拉刈通常 **24hr** 後才表現口喉之疼痛及潰瘍。年年春除表現嘔吐、噁心、腹瀉及脫水外，口喉之疼痛常常喝過後即發生

3) 巴拉刈可測尿中定性試驗 (sodium dithionite)，如尿液變藍色，則表示中毒

巴拉刈中毒

2. 巴拉刈中毒之治療

1) 最重要是立即用胃管清洗乾淨，再用活性碳吸附

2) 點滴大量輸液，2500～3500c.c./day，視病人年齡及心肺功能而定，如因腎功能變壞，尿液流量下降則應減量

3) 目前無有效解毒劑，給予支持性療法即可，如欲加 hydrocortisone、VitC、VitE、acetylcysteine．．亦可，但效果不佳

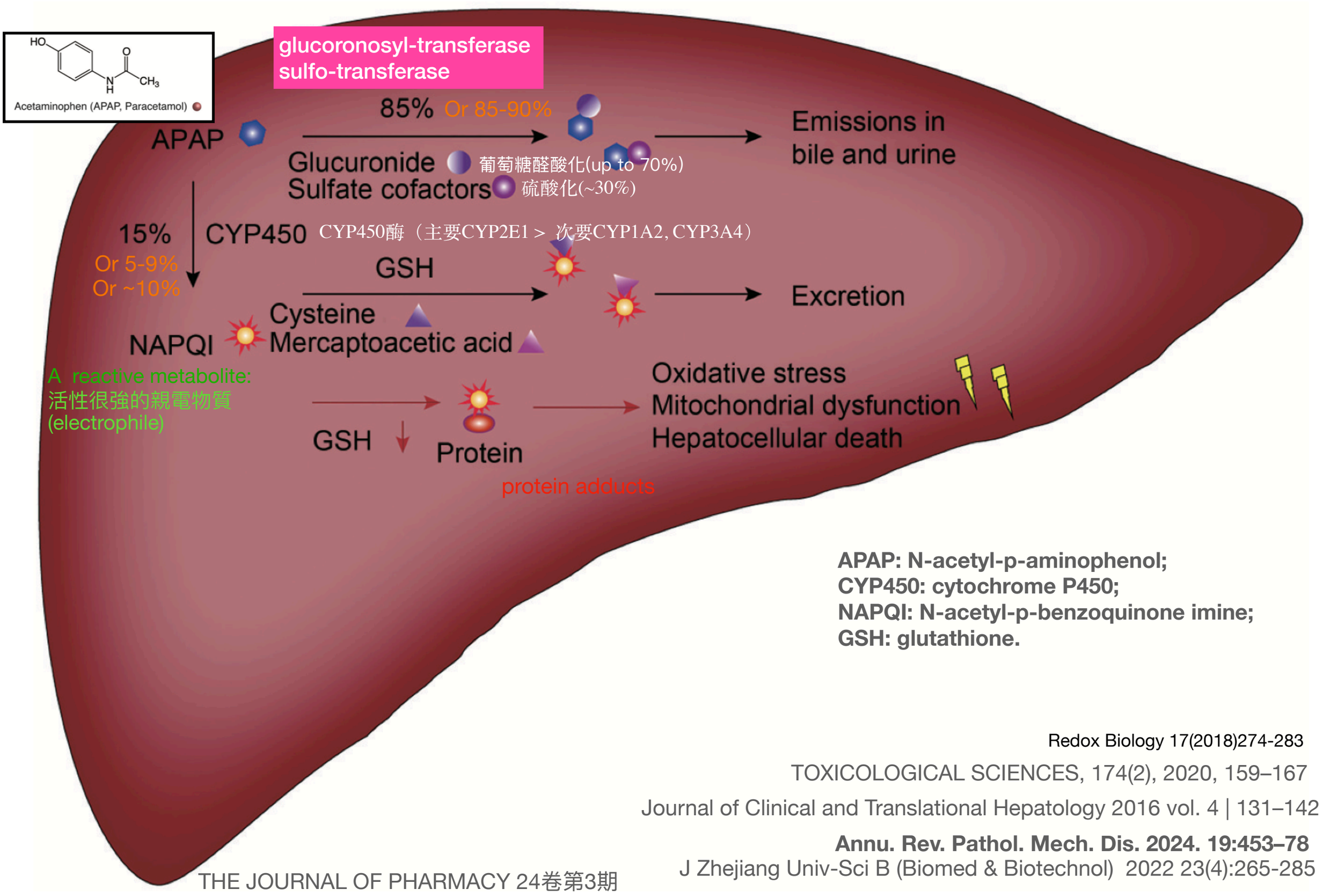
4) 病人呼吸喘時，原則是讓病人舒適，給O2 使 PaO2 維持60 mmHg 左右最適當

5) HP 對血液中之 paraquat 清除率高，但對組織中之 paraquat ，則效果不佳，除了年紀較輕，發現時間 3～4 小時內，且服用三口以內，一般不建議使用

3. 巴拉刈中毒因無解毒劑，故口服之量及洗胃之時間早晚，成了存活之重要條件，如果吃一口還有存活之希望，超過一口則存活渺茫。

Acetaminophen中毒

Schematic diagram of APAP metabolism & Liver Toxicity



APAP: N-acetyl-p-aminophenol;
CYP450: cytochrome P450;
NAPQI: N-acetyl-p-benzoquinone imine;
GSH: glutathione.

Redox Biology 17(2018)274-283

TOXICOLOGICAL SCIENCES, 174(2), 2020, 159–167

Journal of Clinical and Translational Hepatology 2016 vol. 4 | 131–142

Annu. Rev. Pathol. Mech. Dis. 2024. 19:453–78

J Zhejiang Univ-Sci B (Biomed & Biotechnol) 2022 23(4):265-285

THE JOURNAL OF PHARMACY 24卷第3期

Mechanism of hepatocellular injury by acetaminophen overdose

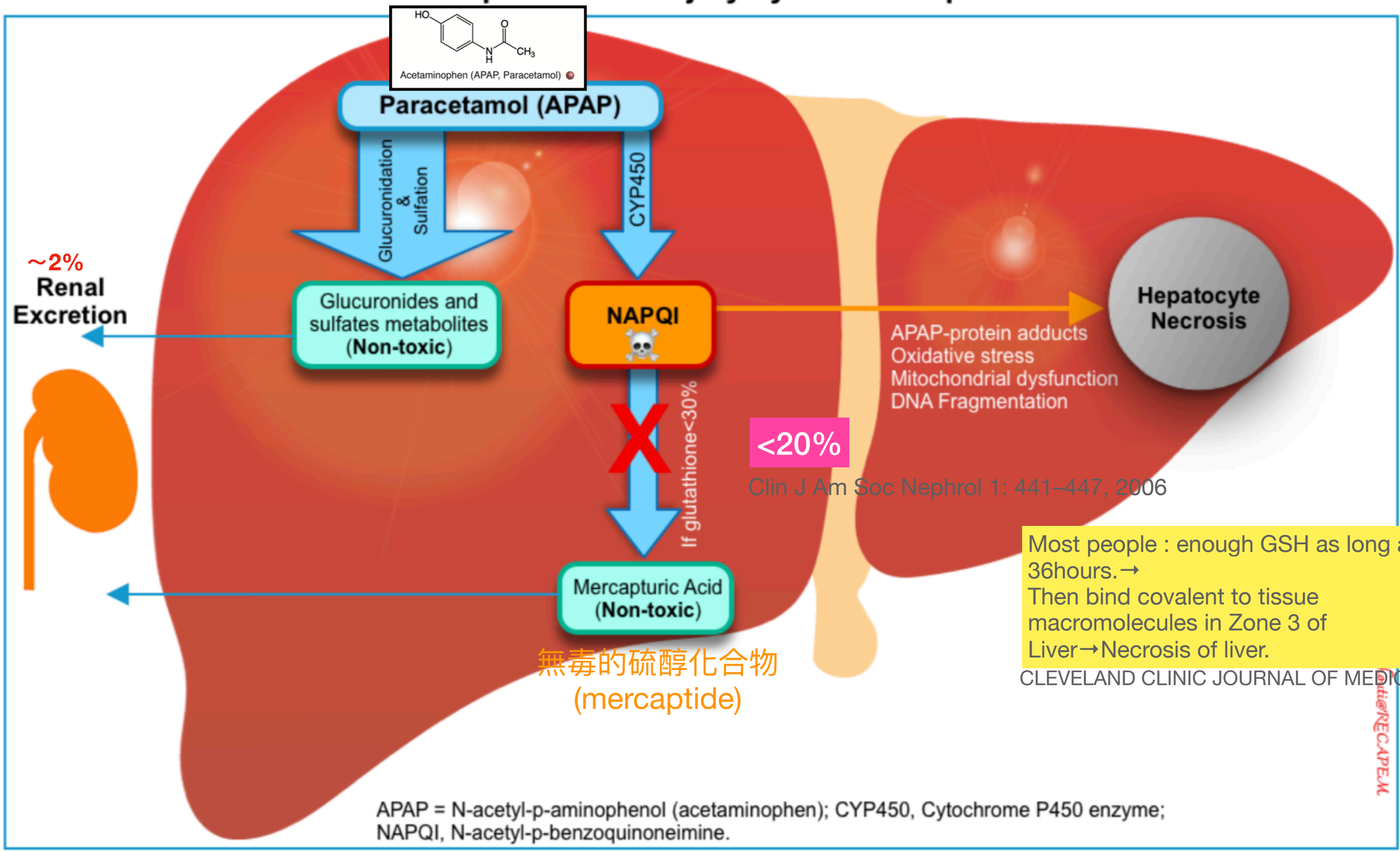


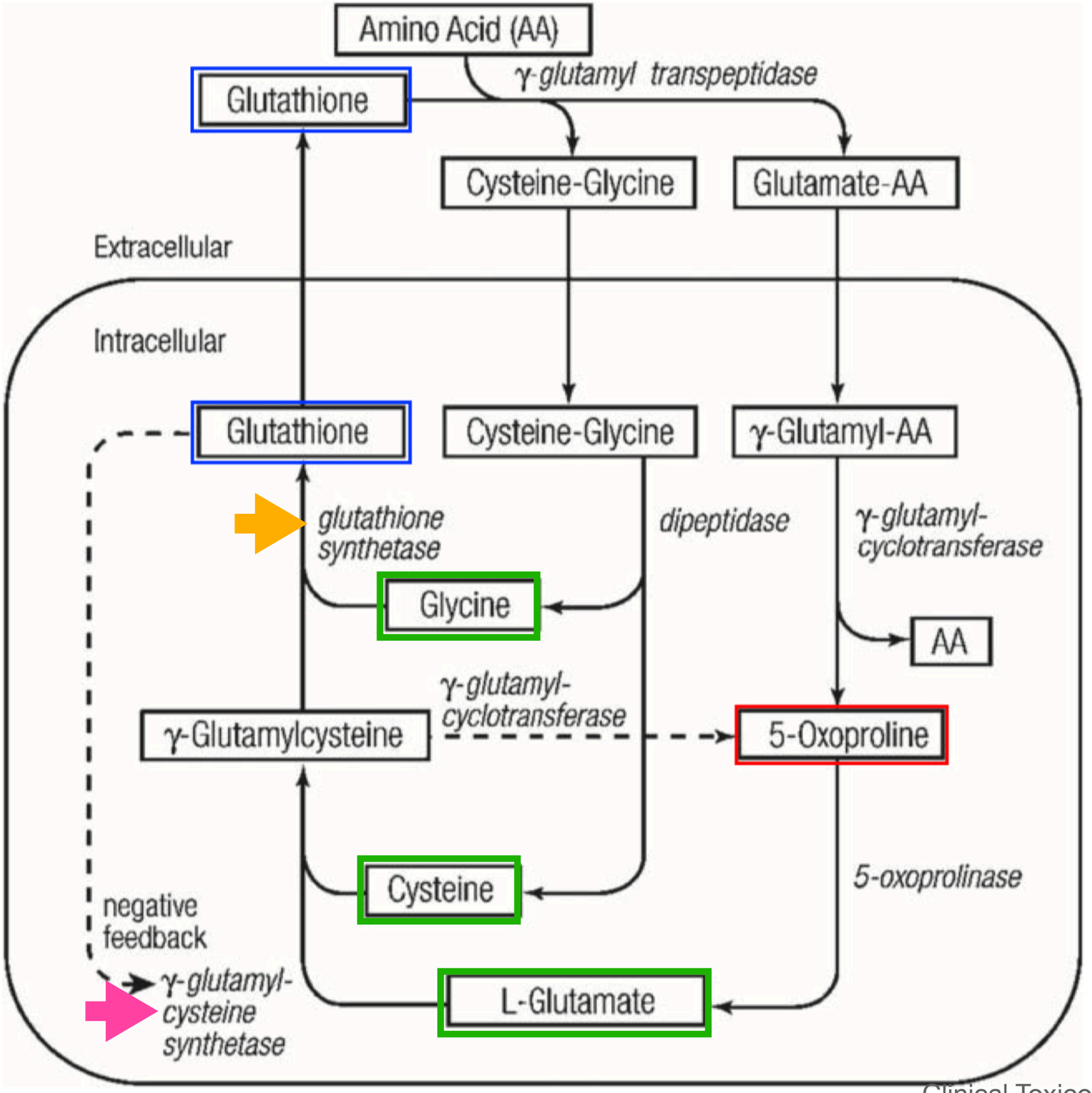
Table 1. Causes of high and normal anion gap metabolic acidosis.

Increased anion gap	Normal anion gap
• Lactic acidosis • Ketoacidosis: diabetes mellitus, starvation, alcohol use-associated • Ingestion: methanol, ethylene glycol, aspirin, toluene (if early or if renal failure), diethylene glycol, propylene glycol • D-lactic acidosis • Massive rhabdomyolysis • Pyroglutamic acidosis • Chronic kidney disease	• Toluene ingestion (if late and if renal function is preserved) • Diarrhea or other intestinal losses • Type 2 renal tubular acidosis (proximal) • After treatment of ketoacidosis • Carbonic anhydrase inhibitors • Ureteral diversion • Chronic kidney disease and tubular dysfunction (but relatively preserved glomerular filtration rate) • Type 1 renal tubular acidosis (distal) • Type 4 renal tubular acidosis (hyperaldosteronism)

S D Med. 2021 Oct;74(10):468-470

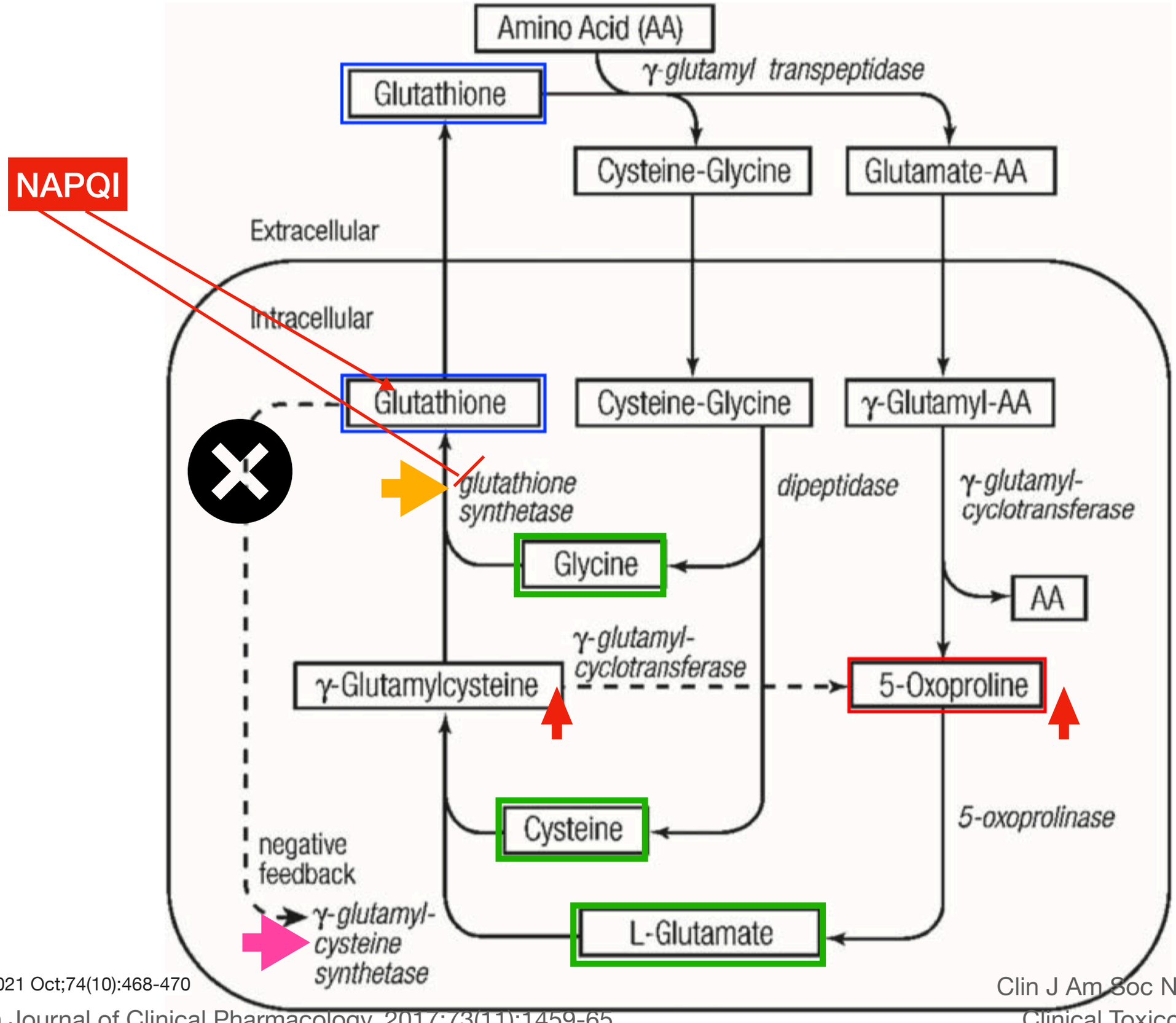
5-oxoproline (pyroglutamic acid)

Gamma-glutamyl cycle

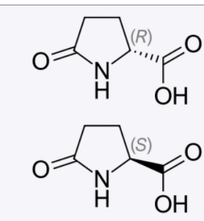


Clinical Toxicology (2013), 51, 817–827

Gamma-glutamyl cycle



Pyroglutamic acid



Pyroglutamic acid (also known as **PCA**, **5-oxoproline**, **pidolic acid**)

S D Med. 2021 Oct;74(10):468-470

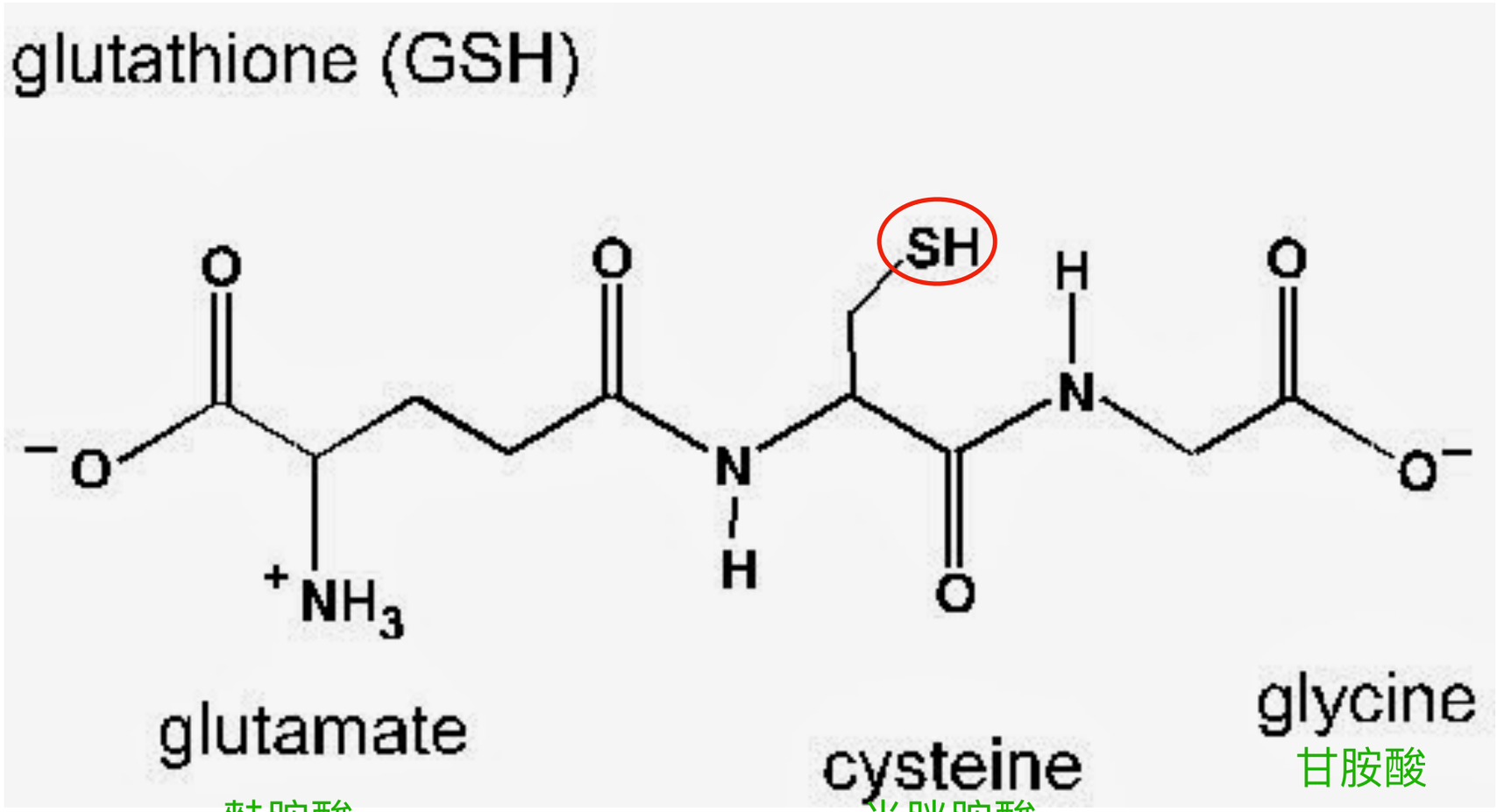
European Journal of Clinical Pharmacology. 2017;73(11):1459-65.

Clin J Am Soc Nephrol 1: 441–447, 2006

Clinical Toxicology (2013), 51, 817–827

Glutathione(GSH)

Glutathione；GSH 麩胱甘肽是由麩胺酸、胱胺酸和甘胺酸所組成的三胜肽，分子量為307，而其硫醇基與氧化還原相關。
麩胱甘肽的主要功能在於細胞內生性抗氧化的防禦，包括對抗反應氧物質（reactive oxygen species, RO）。



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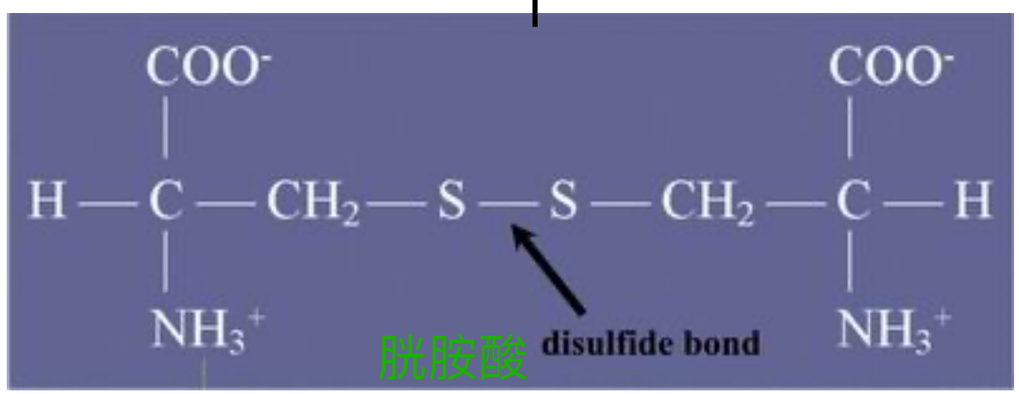
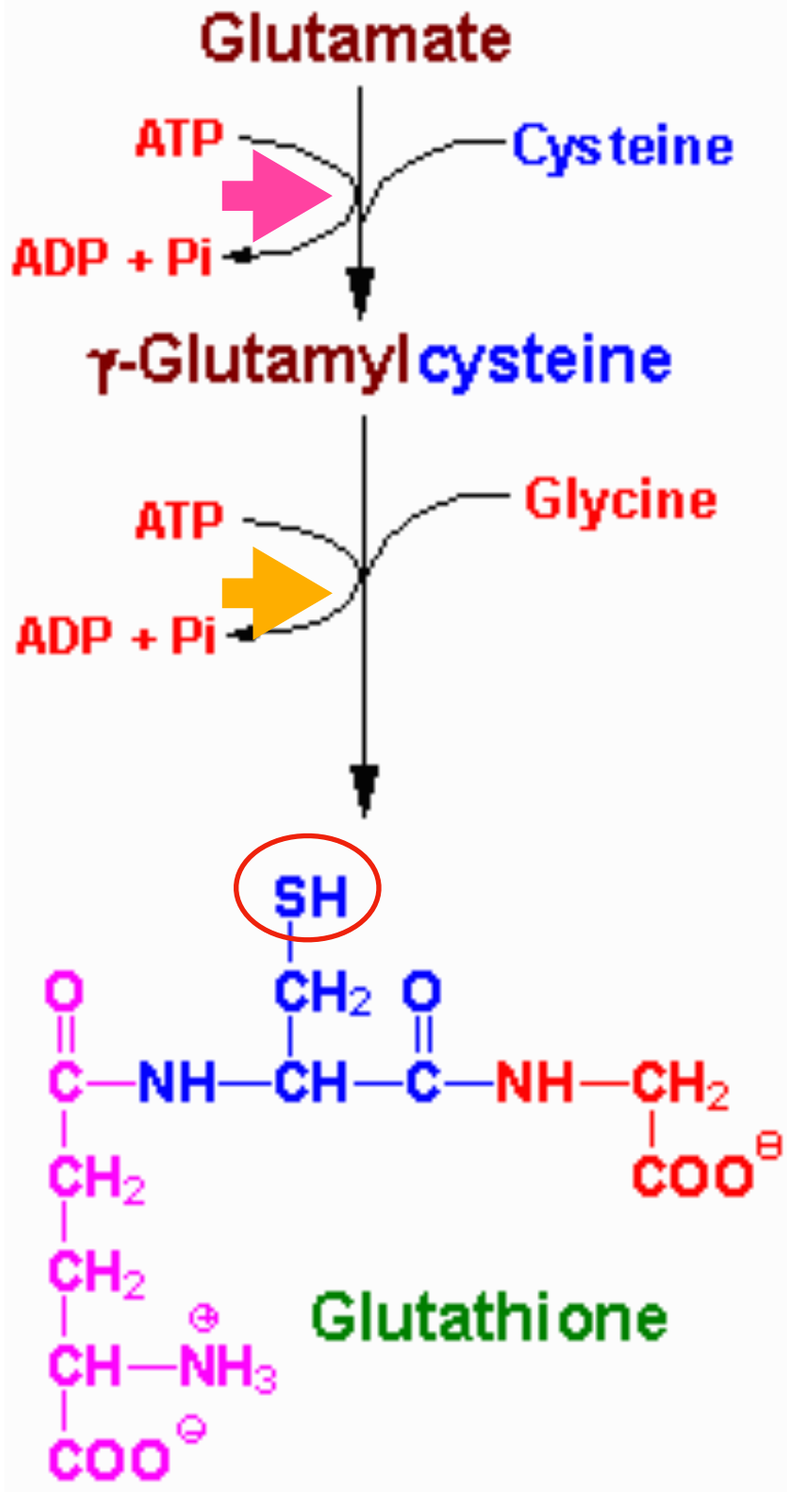
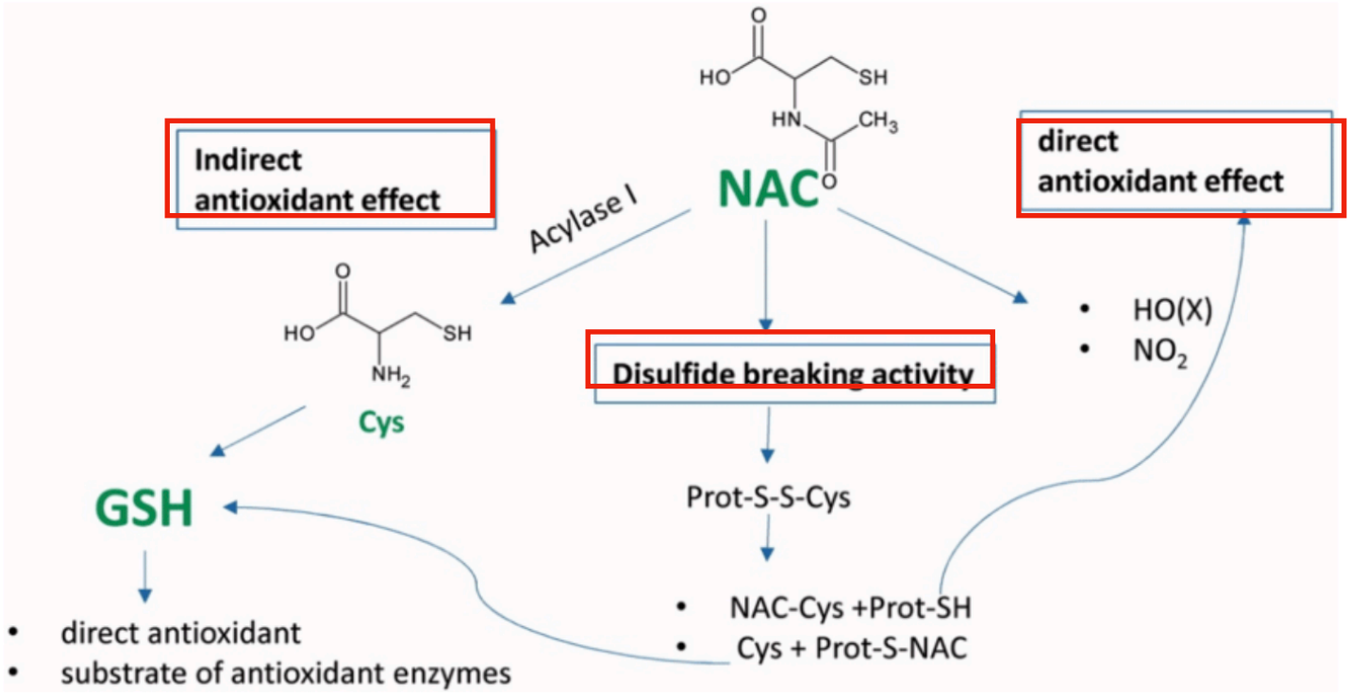
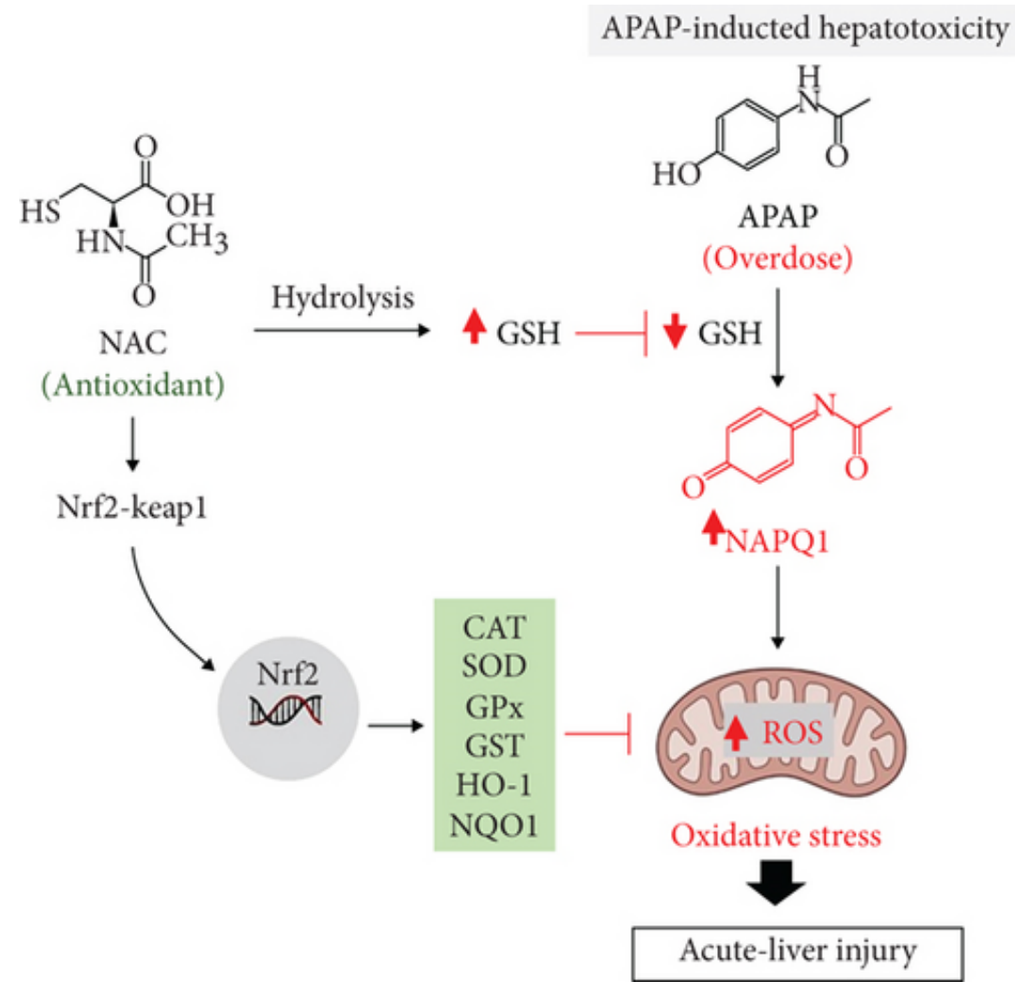


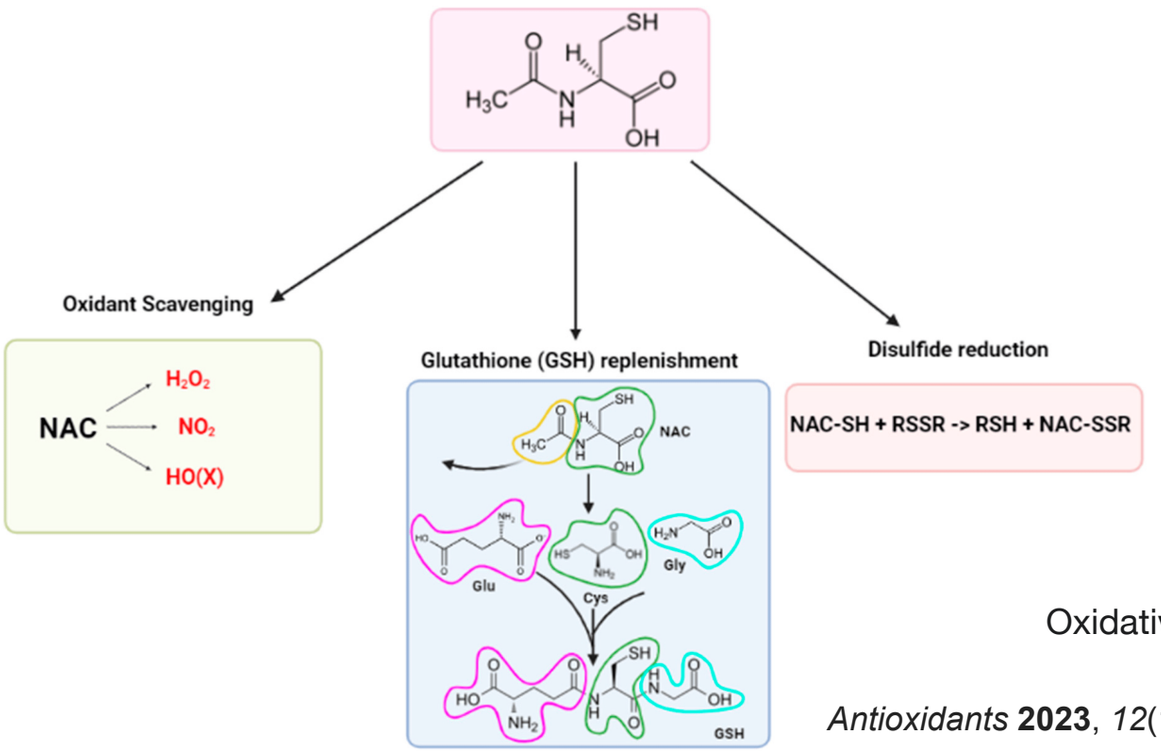


Actein (N-acetylcysteine)(NAC)

- direct antioxidant properties on oxidant species (e.g. OH •)
- indirectly as a precursor to glutathione







APAP: paracetamol/acetaminophen; NAPQI: N-acetyl-p-benzo-quinone imine; GSH: reduced glutathione; GSSH: oxidized glutathione; Nrf2: nuclear factor erythroid 2-related factor 2; Keap1: Kelch-like ECH-associated protein 1; CAT: catalase; SOD: superoxide dismutase; GPx: glutathione peroxidase; GST: glutathione s-transferase; HO-1: heme oxigenase-1; NQO1: oxidoreductase 1.

Oxidative Medicine and Cellular Longevity, 2021, 3320325, 12 pages, 2021.

Antioxidants **2023**, *12*(10), 1867

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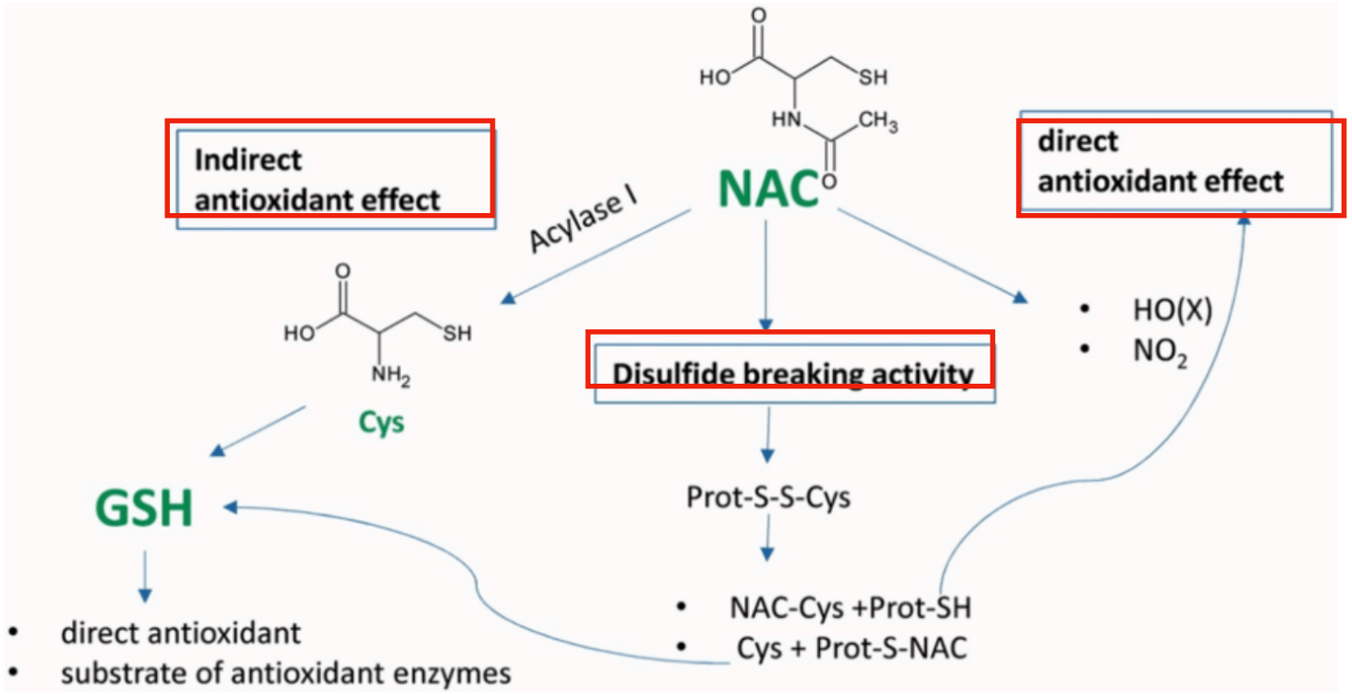

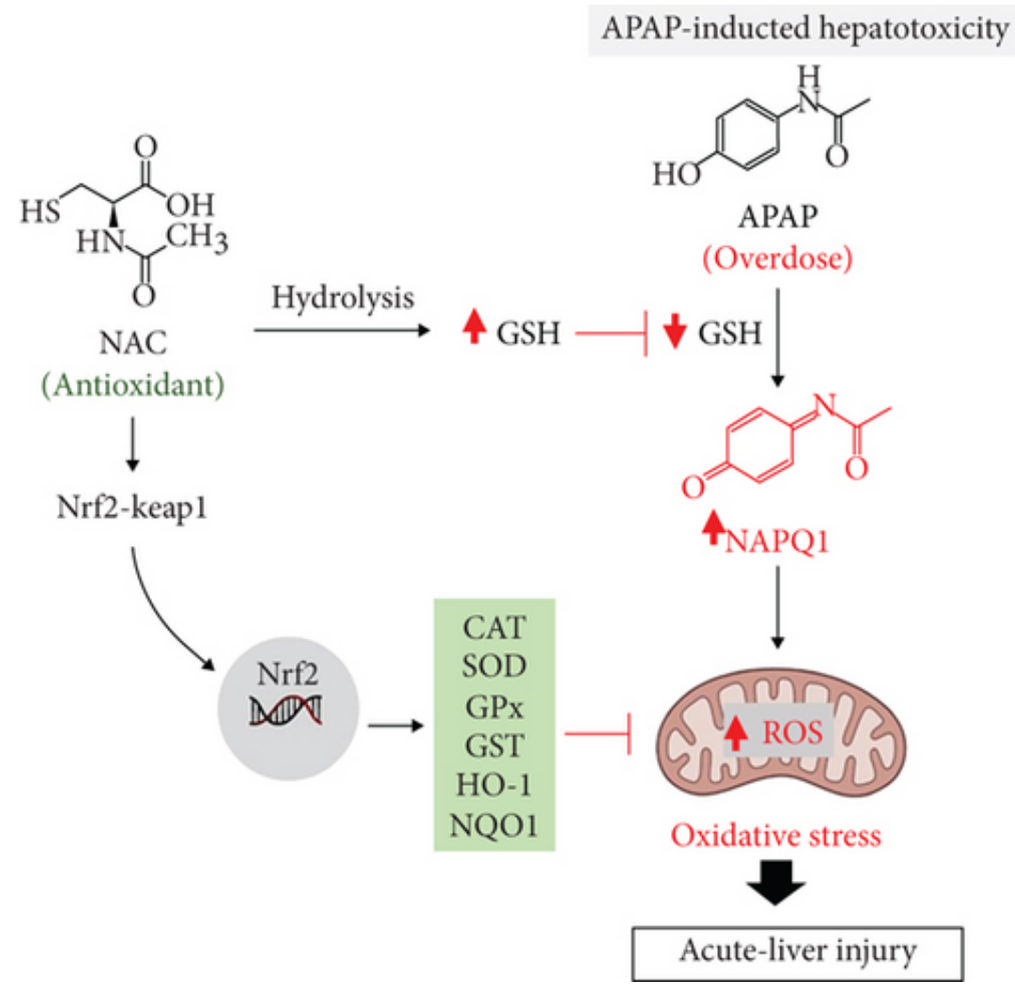

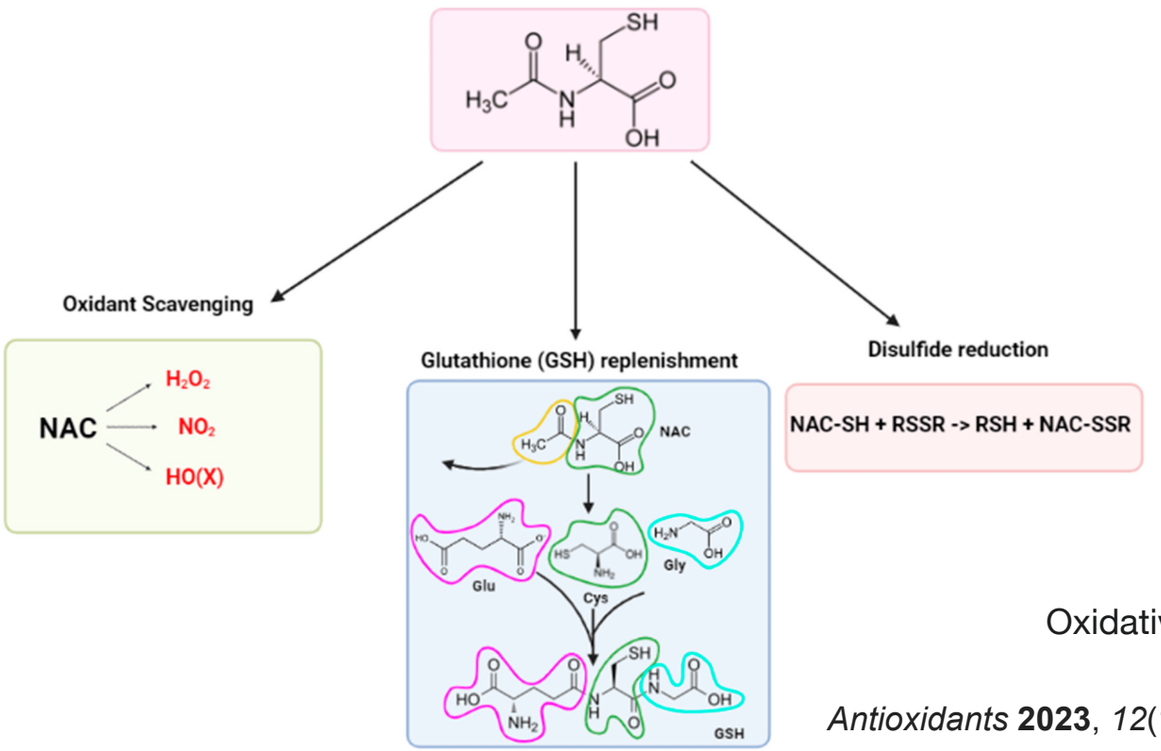

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Acetaminophen中毒症狀的臨床分期(分四期)

期別	攝入後的時間	臨床特徵
一	0.5~24小時	厭食、噁心、嘔吐、身體不適、臉色倉白、盜汗
二	24~48小時	上述的症狀緩解、右上腹疼痛和觸痛、寡尿、以及bilirubin、PT、 INR、 AST和ALT等檢檢驗值上升
三	72~96小時 (服用後的3-4天)	肝功能異常達到尖峰狀態，厭食、噁心、嘔吐、身體不適等症狀可能再出現，嚴重者引發猛暴性肝炎併發代謝性酸中毒、INR>6、腎功能異常變得較明顯
四	4~14天	可能引發寡尿性腎衰竭，猛暴性肝炎的病人可能會死亡

（16小時：ALT/AST ↑）

- AKI

- 合併有腎臟的毒性的病人可看到 BUN、Cr 上升，連同尿液分析有蛋白尿、血尿

- 但是對於多數為了控制慢性疼痛而長 期用藥的病人來說，藥物中毒的臨床分期並不明顯，必須依賴病史、用藥史和臨床症狀來做經驗性的判斷。
- 一旦發展成肝衰竭， 死亡率達 58-80%。大部分在 3-5 天死亡且可合併腦水腫、 出血、休克、敗血症等併發症。

Actein 治療 Protocol

IV

- 3 sequential infusions over a **total period of 21 hours** (For BW > 40kg):
  - Loading dose: 150 mg/kg in 200 mL of 5% dextrose (D5W), infused over 60 minutes.
  - Second infusion: 50 mg/kg in 500 mL D5W, infused over 4 hours (12.5 mg/kg/h).
  - Third infusion: 100 mg/kg in 1000 mL D5W infused over 16 hours (6.25 mg/kg/h).

Oral

- (**total** duration of treatment, **72 hours**):
  - Loading dose: 140 mg/kg
  - followed by: 17 doses of 70 mg/kg at 4 hour intervals

（如果患者在給藥後1小時內嘔吐負荷劑量或任何維持劑量，則應將患者改用靜脈製劑。）

目前並沒有研究直接去比較兩者的優劣，經驗上看起來這兩種用法都有效且差異不大。

support from McNeil Consumer Healthcare

Thanks for Your Attension~!