抗生素相關皮膚不良反應之藥師觀點與實務介入

高雄長庚醫院
童郁琇 藥師
20251008

大綱

- 抗生素相關不良反應評估重要性
- 藥師在抗生素相關皮膚不良反應的臨床觀察與評估角色
- 抗生素過敏反應類型、表徵、潛伏期及嚴重度
- 評估工具
- 檢測工具
- β-lactam抗生素、磺胺類交叉過敏
- 不良反應通報必要性與價值
- Summary
- 案例分享

抗生素過敏？還是誤標？正確辨識才是關鍵

- Allergy to penicillins accounts for the most common reported medication allergy and is a substantial and growing public health concern
- 10% to 15% of the adult population internationally has reported antibiotic allergy labels to penicillins, the most used antimicrobial class
- Up to 90% of patients with a reported penicillin allergy are not allergic
  - Patient knowledge gaps
  - Provider knowledge gaps
  - Poorer outcomes, higher costs, and longer hospital stays

J Allergy Clin Immunol Pract. 2023 Oct;11(10):3133-3145.e3.

抗生素皮膚不良反應發生風險

- 2004-2021 FDA不良事件通報系統（FAERS）
- 77,789 SCAR-related
- SCAR 佔所有 ADR 通報比例不高（約 0.54%），但其嚴重性高，死亡佔約 10%
- 抗生素通報比例最高(20.6%)

PT	Proportions of the top 10 agents									
group	1	2	3	4	5	6	7	8	9	10
SJS	Lamotrigine (12.1%)	Phenytoin (6.4%)	Acetaminophen (6.1%)	Ibuprofen (4.8%)	Allopurinol (4.7%)	Carbamazepine (4.3%)	Acetylsalicylic acid (3.7%)	Furosemide (3.4%)	TMP-SMX (3.1%)	Amlodipine (2.7%)
DRESS	Allopurinol (11.8%)	Vancomycin (9.5%)	Lamotrigine (9.0%)	Carbamazepine (5.2%)	Acetaminophen (5.1%)	Levetiracetam (4.3%)	TMP-SMX (4.1%)	Pantoprazole (3.8%)	Ceftriaxone (3.7%)	Furosemide (3.5%)
TEN	Acetaminophen (11.2%)	Furosemide (8.6%)	Lamotrigine (8.2%)	Allopurinol (7.8%)	Ibuprofen (6.5%)	Vancomycin (6.0%)	Acetylsalicylic acid (5.3%)	Omeprazole (5.1%)	Ciprofloxacin (4.9%)	Prednisolone (4.6%)
TSE	Furosemide (5.7%)	Acetaminophen (5.1%)	Allopurinol (4.6%)	TMP-SMX (4.0%)	Esomeprazole (3.7%)	Lamotrigine (3.5%)	Amlodipine (3.1%)	Pantoprazole (3.1%)	Clopidogrel (3.0%)	Vancomycin (2.9%)
EM	Acetaminophen (4.9%)	Lamotrigine (4.5%)	Acetylsalicylic acid (3.8%)	Ribavirin (3.4%)	Ibuprofen (3.4%)	Omeprazole (3.2%)	Amlodipine (2.8%)	Carbamazepine (2.8%)	Allopurinol (2.8%)	Prednisolone (2.8%)
DE	Furosemide (6.2%)	Allopurinol (5.8%)	Acetylsalicylic acid (4.4%)	Acetaminophen (4.3%)	Methotrexate (3.8%)	Omeprazole (3.5%)	Clopidogrel (3.4%)	TMP-SMX (3.4%)	Amlodipine (3.3%)	Carbamazepine (3.2%)
AGEP	Acetaminophen (8.3%)	Vancomycin (6.5%)	Furosemide (5.1%)	Amoxicillin (4.8%)	Omeprazole (4.5%)	Clindamycin (4.5%)	Ceftriaxone (4.3%)	Enoxaparin (4.1%)	Metronidazole (3.9%)	Ibuprofen (3.9%)
DB	Furosemide (6.0%)	Acetaminophen (4.9%)	Omeprazole (3.7%)	Ibuprofen (3.0%)	Acetylsalicylic acid (2.9%)	Methotrexate (2.9%)	Metformin (2.8%)	Amlodipine (2.6%)	Allopurinol (2.5%)	Simvastatin (2.5%)
SN	Methotrexate (13.6%)	Prednisone (12.8%)	Adalimumab (11.7%)	Tocilizumab (10.1%)	Etanercept (10.0%)	Rituximab (9.8%)	Infliximab (9.7%)	Sulfasalazine (9.7%)	Abatacept (9.6%)	Leflunomide (9.4%)
ER	Adalimumab (10.1%)	Etanercept (5.8%)	Acetylsalicylic acid (5.4%)	Methotrexate (4.8%)	Prednisone (4.6%)	Lenalidomide (4.6%)	Levothyroxine (4.0%)	Simvastatin (3.7%)	Omeprazole (3.6%)	Furosemide (3.5%)
DEG	Allopurinol (6.8%)	Methotrexate (6.1%)	Furosemide (5.4%)	Prednisone (5.1%)	TMP-SMX (4.8%)	Adalimumab (4.4%)	Pantoprazole (3.9%)	Vancomycin (3.5%)	Dupilumab (3.5%)	Secukinumab (3.5%)
CV	Methotrexate (10.6%)	Etanercept (9.8%)	Adalimumab (9.4%)	Tocilizumab (7.0%)	Abatacept (6.5%)	Anakinra (6.0%)	Leflunomide (5.5%)	Prednisone (5.1%)	Tofacitinib (4.9%)	Amlodipine (4.1%)
EN	Methotrexate (22.4%)	Lamotrigine (9.6%)	Acetaminophen (6.2%)	Prednisone (4.2%)	Furosemide (4.2%)	Cyclophosphamide (3.7%)	Acetylsalicylic acid (3.5%)	Methylprednisolone (3.5%)	Diclofenac (3.5%)	Carbamazepine (3.4%)
OS	Lamotrigine (10.5%)	Carbamazepine (8.0%)	Diclofenac (6.3%)	Furosemide (4.4%)	Acetylsalicylic acid (3.6%)	Amlodipine (3.6%)	Lansoprazole (2.8%)	Sulfasalazine (2.5%)	Clarithromycin (2.5%)	Zonisamide (2.2%)
STO	Ibuprofen (14.0%)	Lamotrigine (10.4%)	Acetaminophen (9.3%)	Pantoprazole (5.7%)	Pegfilgrastim (5.2%)	Ceftriaxone (5.2%)	Amoxicillin (4.7%)	Linezolid (4.7%)	Carbamazepine (4.7%)	Fluconazole (4.1%)
TSL	Aripiprazole (22.0%)	Risedronate (20.0%)	Sertraline (20.0%)	Lenalidomide (18.0%)	Bortezomib (16.0%)	Omeprazole (12.0%)	Ibuprofen (8.0%)	Acetaminophen (8.0%)	Lamotrigine (6.0%)	Dexamethasone (6.0%)
BHD	Furosemide (14.9%)	Bisoprolol (12.8%)	Daratumumab (10.6%)	Metolazone (10.6%)	Eplerenone (10.6%)	Escitalopram (10.6%)	Heparin (10.6%)	Enoxaparin (8.5%)	Warfarin (8.5%)	Acetylsalicylic acid (8.5%)
EAD	Pregabalin (42.9%)	TMP-SMX (42.9%)	Lenalidomide (42.9%)	Bortezomib (42.9%)	Thiamine (42.9%)	Daratumumab (42.9%)	Rivaroxaban (42.9%)	Dexamethasone (42.9%)	V+S (14.3%)	Baricitinib (14.3%)
SMQ	Lamotrigine (6.2%)	Acetaminophen (5.8%)	Allopurinol (5.8%)	Furosemide (4.6%)	Vancomycin (4.4%)	Ibuprofen (3.3%)	Omeprazole (3.2%)	Acetylsalicylic acid (3.2%)	Carbamazepine (3.1%)	Methotrexate (2.9%)

FIGURE 3

Top 10 agents with the highest reporting proportions at the SMQ and PT levels. AGEP, acute generalised exanthematous pustulosis; BHD, bullous haemorrhagic dermatosis; CV, cutaneous vasculitis; DB, dermatitis bullous; DE, dermatitis exfoliative; DEG, dermatitis exfoliative generalized; DRESS, drug reaction with eosinophilia and systemic symptoms; EN, epidermal necrosis; EM, erythema multiforme; EAD, erythrodermic atopic dermatitis; ER, exfoliative rash; OS, oculomucocutaneous syndrome; PT, preferred term; SCARs, severe cutaneous adverse reactions; SMQ, Standardized MedDRA Queries; STO, SJS-TEN overlap; SN, skin necrosis; SJS, Stevens-Johnson syndrome; TMP-SMX, sulfamethoxazole and trimethoprim; TSL, target skin

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Expert Opin Drug Saf. 2023 Nov 8:1-8

抗生素皮膚不良反應發生風險

- **2002-2022 Population-based, nested case-control study; Ontario, Canada**
- **21 758 older adults (median age, 75 years; 64.1% female)**

常見口服抗生素發生嚴重皮膚不良反應導致急診/住院的風險

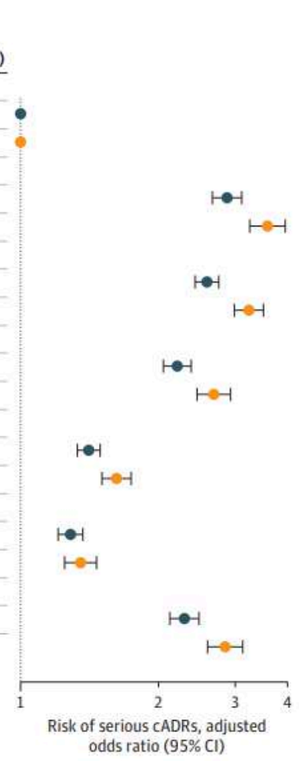
- 中位住院天數為6天
- 9.6%需轉入ICU
- 5.3%在住院期間死亡

Table 2. Crude Rate of Serious cADRs Within 60 Days of Antibiotic Prescription[a]

Antibiotic class	No. of exposures	No. of serious cADRs	Events per 1000 exposures (95% CI)
Cephalosporins	5 076 176	24 997	4.92 (4.86-4.99)
Sulfonamides	2 730 810	8780	3.22 (3.15-3.28)
Fluoroquinolones	6 825 283	16 939	2.48 (2.44-2.52)
Nitrofurantoin	3 627 644	8464	2.33 (2.28-2.38)
Penicillins	8 666 828	16 822	1.94 (1.91-1.97)
Macrolides	4 709 840	8483	1.80 (1.76-1.84)
Other antibiotics[b]	2 477 673	9786	3.95 (3.87-4.03)
All antibiotics	34 114 254	72 449	2.12 (2.11-2.14)

Figure. Comparative Risks of Serious cADRs by Antibiotic Class Using a 60-Day Latency Period (Primary Analysis) and a 30-Day Latency Period (Sensitivity Analysis)

Antibiotic class	No. (%) Cases	No. (%) Controls	Risk of serious cADRs, adjusted odds ratio (95% CI)
Macrolides			
Primary analysis (60-d latency)	2036 (9.4)	13 967 (16.1)	1 [Reference]
Sensitivity analysis (30-d latency)	1195 (7.8)	9567 (15.7)	1 [Reference]
Sulfonamides			
Primary analysis (60-d latency)	1989 (9.1)	4643 (5.3)	2.9 (2.7 to 3.1)
Sensitivity analysis (30-d latency)	1517 (9.9)	3392 (5.6)	3.6 (3.3 to 3.9)
Cephalosporins			
Primary analysis (60-d latency)	5652 (26.0)	14 224 (16.3)	2.6 (2.5 to 2.8)
Sensitivity analysis (30-d latency)	4155 (27.2)	9842 (16.1)	3.3 (3.0 to 3.5)
Nitrofurantoin			
Primary analysis (60-d latency)	2225 (10.2)	7252 (8.3)	2.2 (2.1 to 2.4)
Sensitivity analysis (30-d latency)	1714 (11.2)	5308 (8.7)	2.7 (2.5 to 2.9)
Penicillins			
Primary analysis (60-d latency)	4918 (22.6)	26 767 (30.8)	1.4 (1.3 to 1.5)
Sensitivity analysis (30-d latency)	3417 (22.4)	18 606 (30.5)	1.6 (1.5 to 1.8)
Fluoroquinolones			
Primary analysis (60-d latency)	2981 (13.7)	14 416 (16.6)	1.3 (1.2 to 1.4)
Sensitivity analysis (30-d latency)	1850 (12.1)	10 366 (17.0)	1.4 (1.3 to 1.5)
Other antibiotics			
Primary analysis (60-d latency)	1957 (9.0)	5756 (6.6)	2.3 (2.2 to 2.5)
Sensitivity analysis (30-d latency)	1427 (9.3)	4012 (6.6)	2.9 (2.6 to 3.1)



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台灣藥害救濟申請案件

(1999 –2025.8)

排名	藥品成分	案例數
1	Allopurinol	283
2	Rifampin/Isoniazid/Pyrazinamide (單方或複方)	162
3	Phenytoin	160
4	Carbamazepine	146
5	Diclofenac	110
6	Co-trimoxazole	93
7	Lamotrigine	70
8	Ibuprofen	68
9	Sulfasalazine	66
10	Mefenamic acid	63

第1～389次審議會

(1999 –2024)

排名	藥物類別	ATC編碼	筆數	百分比
1	Combinations of penicillins, incl. beta-lactamase inhibitors（例如: Amoxicillin/Clavulanate、Piperacillin/Tazobactam）	J01CR	136	14.66%
2	First-generation cephalosporins（例如: Cephalexin、Cefazolin、Cefadroxil）	J01DB	121	13.04%
3	Fluoroquinolones（例如: Levofloxacin、Ciprofloxacin、Moxifloxacin）	J01MA	118	12.72%
4	Combinations of sulfonamides and trimethoprim, incl. derivatives（例如: Co-trimoxazole）	J01EE	91	9.81%
5	Third-generation cephalosporins（例如: Ceftriaxone、Ceftazidime）	J01DD	85	9.16%

第1～381次審議會

藥師在皮膚不良反應中的角色：偵測、評估、通報、建議

ADR的偵測與通報

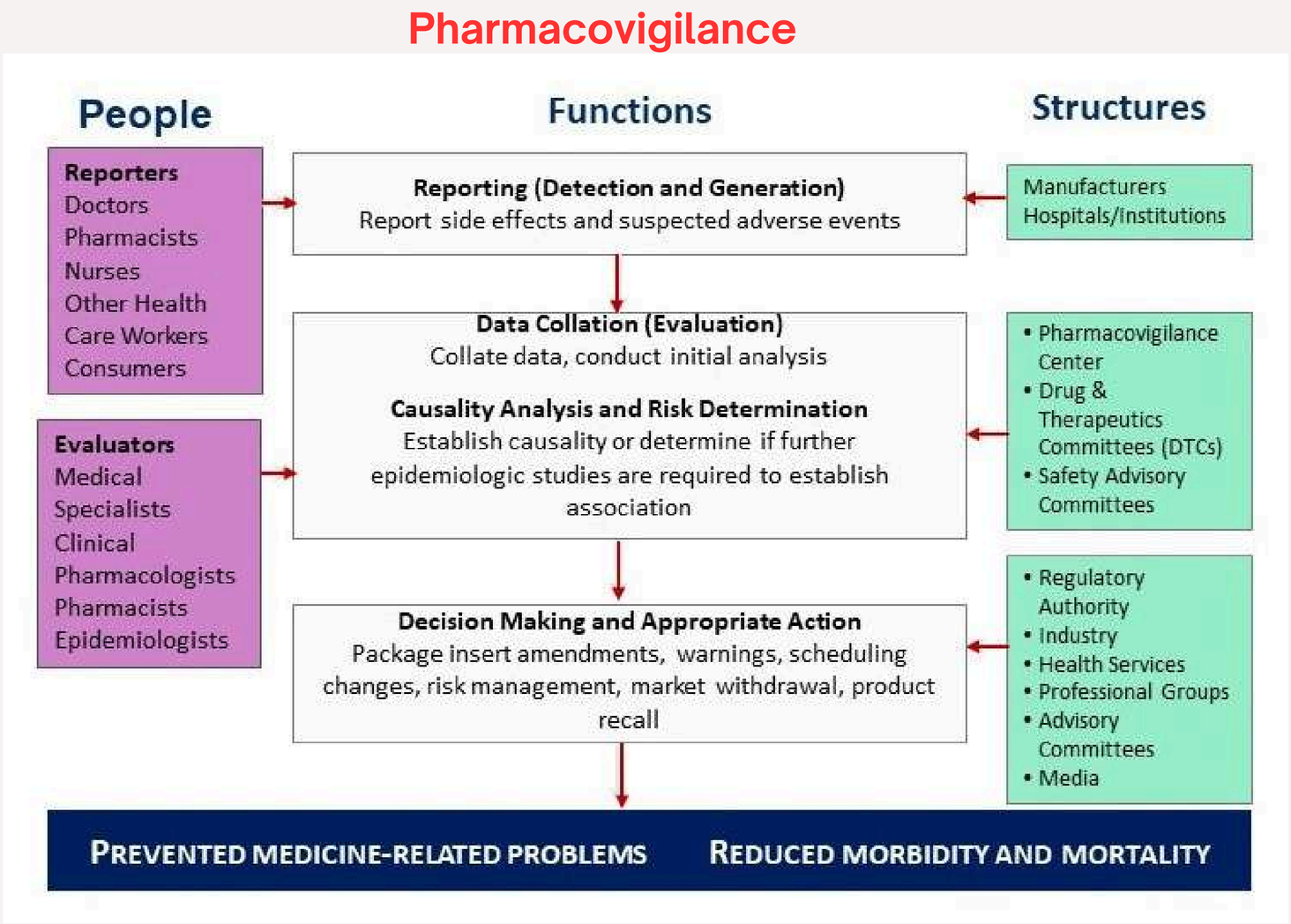
- 辨識
- 及早發現異常訊號
- ADR通報

資料收集與評估

- 協助判斷因果關係
- 降低誤標
- 辨識嚴重反應

採取/建立安全用藥策略

- 風險溝通
- 長期管理



藥師在皮膚不良反應中的角色

初步辨識與啟動通報流程

- 及早辨識疑似 ADR
- 啟動院內藥害警示流程
- 提醒醫師立即評估嚴重度

收集資料

- 核對藥物使用時間與 ADR 時序性
- 確認可疑藥物

評估與風險分層

- 協助評估病人風險
- 評估工具

檢測工具

- 評估檢測可行性與風險

停藥與替代治療

- 評估替代藥物安全性
- 提供交叉過敏資訊

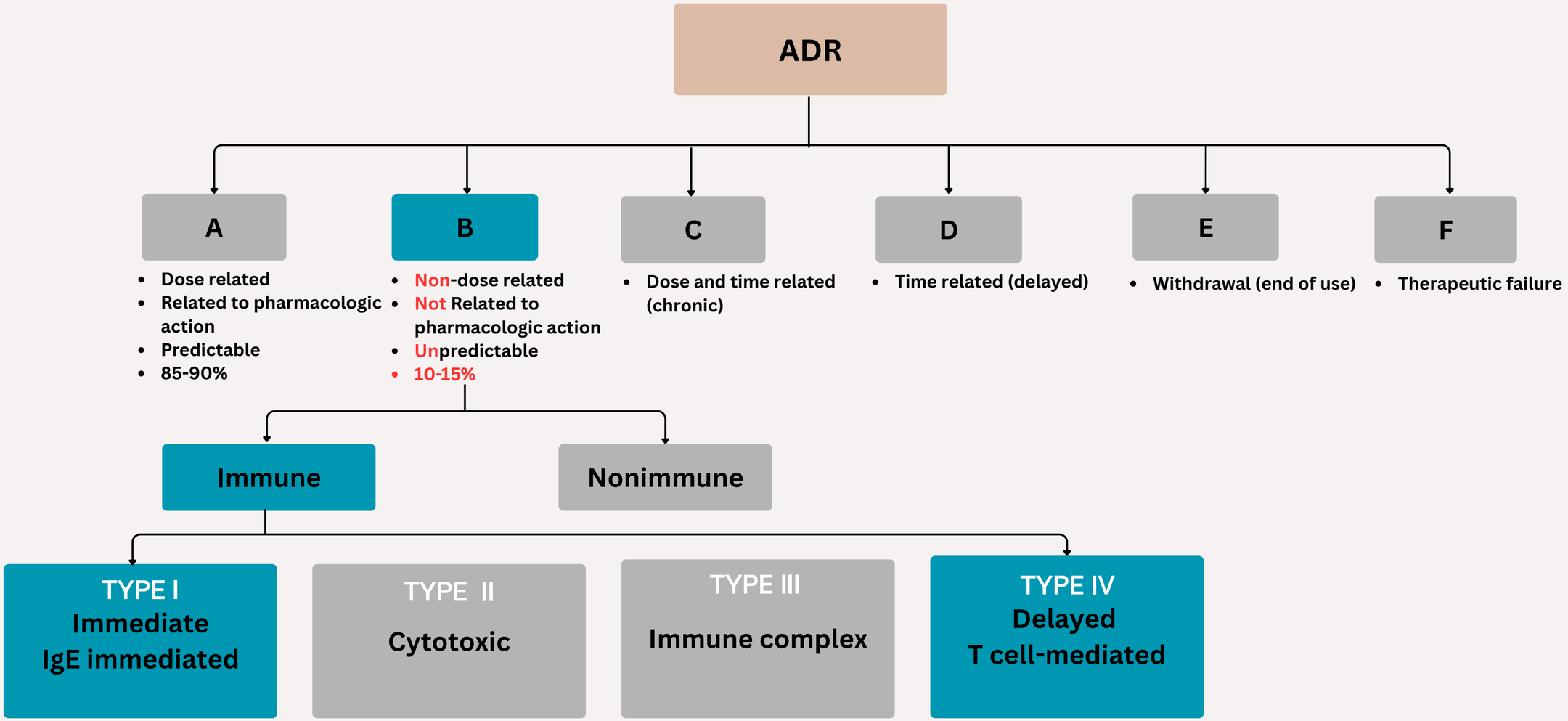
通報全國

- 完整填寫 ADR 報告
- 通報必要性與價值

風險管理

- 藥物安全小組/委員會
- 擬定對策或相關計畫
- 持續性藥物安全監控

ADR分類表現與機轉


ADR
A
Dose related
Related to pharmacologic action
Predictable
85-90%
B
Non-dose related
Not Related to pharmacologic action
Unpredictable
10-15%
C
Dose and time related (chronic)
D
Time related (delayed)
E
Withdrawal (end of use)
F
Therapeutic failure
Immune
Nonimmune
TYPE I
Immediate
IgE immediated
TYPE II
Cytotoxic
TYPE III
Immune complex
TYPE IV
Delayed
T cell-mediated

免疫引起的抗生素過敏反應-Gell and Coombs 分類

Type	Description	Pathogenesis	Onset of Reaction	Typical Clinical Findings	Commonly Associated Antibiotics
I (Immediate)	IgE-mediated hypersensitivity	Antibiotic-specific IgE binds to Fc-epsilon-RI receptors on mast cells and basophils. Subsequent antibiotic exposure leads to mast cell and basophil degranulation	<1 h	Anaphylaxis, hives, angioedema, N/V, abdominal pain, SOB, wheezing, anxiety, confusion, chest pain, palpitations, syncope, cardiac arrest	Cephs, FQs, PCNs,
II (Delayed)	Antibody-mediated hypersensitivity	Antibiotic binds to WBC, RBC, or platelet and acts as antigen leading to antibody (usually IgG or complement) mediated cell destruction	7–14 d	Hemolytic anemia, thrombocytopenia, neutropenia	Cephs, PCNs, SMX/TMP
III (Delayed)	Immune complex mediated hypersensitivity	Antibiotic and IgG/IgM bind to form immune complex activate complement	7–14 d	Serum sickness *, vasculitis	Cephs (esp cefaclor), cipro, PCNs, SMX/TMP
IV (Delayed)	Delayed type hypersensitivity	Antigen specific T-cell activation			
	IVa	Monocytic inflammation (Th1 and IFN-γ)	10–15 d	Allergic contact dermatitis	Topical neomycin, bacitracin, polymyxin
	IVb	Th2-mediated eosinophilic inflammation	2–8 wk (for DRESS)	DRESS	PCNs, Cephs, Dapsone, MinocyclineSMX/TMP, Vanco
	IVc	CD8 T cell-mediated cytotoxicity	4–28 d	SJS, TEN	FQs, Nevirapine, PCNs, SMX/TMP
	IVd	T-cell-mediated neutrophilic inflammation	24–48 h	AGEP	Ampicillin, Antifungals, FQs, SMX/TMP

常見皮膚不良反應嚴重度

<table>
<tr><td rowspan="3">Mild</td><td colspan="3">Maculopapular exanthema; Maculopapular rash</td><td rowspan="3">局部或少量、無融合、無水皰的小丘疹或斑疹</td></tr>
<tr><td colspan="3">Symmetrical drug-related intertriginous and flexural exanthema</td></tr>
<tr><td colspan="3">Fixed drug eruption macule</td></tr>
<tr><td rowspan="3">Moderate</td><td colspan="3">Urticaria</td><td rowspan="3">皮疹廣泛或融合但皮膚完整、可能伴輕微發燒或血液學變化</td></tr>
<tr><td colspan="3">Vasculitis</td></tr>
<tr><td colspan="3">Erythema multiforme</td></tr>
<tr><td rowspan="5">Severe</td><td rowspan="2">Immediate</td><td colspan="2">Anaphylactic shock</td><td rowspan="5">滲液、水皰、表皮剝脫、顯著發燒、淋巴結腫大、嗜酸性球明顯上升、肝腎或血液異常</td></tr>
<tr><td colspan="2">Red man syndrome</td></tr>
<tr><td rowspan="3">Delayed</td><td>Exfoliative</td><td>Stevens-Johnson syndrome-Toxic epidermal necrolysis (SJS/TEN)</td></tr>
<tr><td rowspan="2">Nonexfoliative</td><td>Drug reaction with eosinophilia and systemic symptoms (DRESS)</td></tr>
<tr><td>Acute generalized exanthematous pustulosis (AGEP)</td></tr>
</table>

立即型皮膚不良反應

	Mechanism	Presentation	Chronology or onset	Antibiotic examples	Diagnosis	Genetic (HLA) association[4]	Treatment	Antibiotic recommendations
Non-IgE-mediated*								
Flushing, itching, urticaria, and angio-oedema; occasionally presents like anaphylaxis	Direct mast-cell stimulation or basophil activation; MRGPRX2 implicated for certain direct mast-cell degranulators[5]	Cutaneous symptoms (most common), then respiratory symptoms (eg, wheezing), then cardiovascular symptoms (eg, hypotension)	Minutes to <1 h (typically during infusion)	Vancomycin or fluoroquinolones	History and physical exam; serum tryptase within 30 min to 1·5 h after reaction usually normal; drug challenge typically negative with lower dose (dose-dependent reaction)	..	Antihistamines alone typically suffice; epinephrine for those meeting anaphylaxis criteria; adjunctive treatment with corticosteroids and inhaled beta agonists as needed	Slow infusion or premedication with antihistamines or corticosteroids; use fewer associated drugs with similar mast-cell effects (eg, opioids)
Antibody-mediated								
IgE-mediated (type I HSR)								
Urticaria, angio-oedema, bronchospasm, and anaphylaxis	Mast-cell and basophil degranulation via IgE-crosslinking bound to the high-affinity IgE receptor (FceR1)[6]	Itching, palmar erythema, rhinitis, wheezing, urticaria, angio-oedema, or anaphylaxis	<1 h typical, but can be considered within 6 h of exposure	Penicillins or cephalosporins	History, physical exam, elevated serum tryptase (measured within 30 min to 1·5 h after reaction), skin testing, and drug challenge	..	Antihistamines; epinephrine for those meeting anaphylaxis criteria; adjunctive treatment with corticosteroids and inhaled beta agonists as needed	Desensitisation protocol for implicated drug(s); caution with use of drugs in the same class and and structurally related drugs which are potentially cross-reactive

Lancet. 2019 Jan 12;393(10167):183-198

延遲型皮膚不良反應

	Mechanism	Presentation	Chronology or onset	Antibiotic examples	Diagnosis	Genetic (HLA) association[4]	Treatment	Antibiotic recommendations
Isolated cutaneous disease¶								
Maculopapular rash	Eosinophilic inflammation (CD4 and Th2) via IL-4, IL-5, IL-13, or eotaxin (type IVb HSR)	Morbilliform rash, often with peripheral blood eosinophilia	Days to weeks (typically in second week of therapy)	Amoxicillin or sulphonamide antibiotics	History, physical exam, laboratory evaluation (eosinophilia, no organ involvement), and biopsy (severe cases only) with eosinophilic infiltrate in the dermis or variable non-specific picture	..	Antihistamines, topical corticosteroids, or systemic corticosteroids (severe cases only)	Repeat exposure to implicated drug(s) may not result in same reaction, especially after a period of unexposed time; cross-reactivity is less defined; data exists on a treat-through approach for patients requiring therapy who develop this hyper-sensitivity reaction with monitoring for signs of SCAR
Fixed drug eruption‖	Activated intraepidermal CD8 T cells release IFN gamma and cytotoxic granules	Erythematous or oedematous plaques of a round shape with gray or dusky center at same sites (often lip, tongue, face, or genitalia) with each exposure; burning and pain at involved sites	Days to weeks (within minutes on re-challenge)	Sulphonamide antibiotics or vancomycin	History, physical exam, biopsy with basal cell degeneration, pigmentary incontinence, dermal melanophages, patch testing (topical provocation), and drug challenge (systemic provocation)	..	Antihistamines, topical corticosteroids, or systemic corticosteroids (severe cases only)	Avoidance of implicated drug(s) advisable

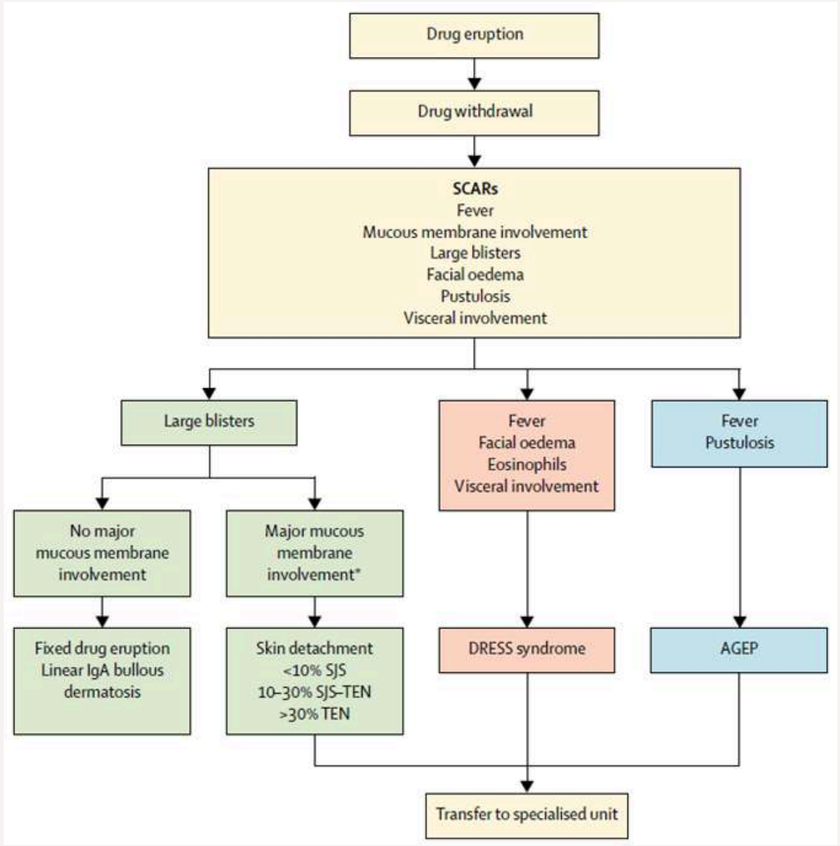
Lancet. 2019 Jan 12;393(10167):183-198

延遲型皮膚不良反應

	Mechanism	Presentation	Chronology or onset	Antibiotic examples	Diagnosis	Genetic (HLA) association[4]	Treatment	Antibiotic recommendations
(Continued from previous page)								
Systemic or multisystem disease[1,7,9]								
Drug reaction eosinophilia and systemic symptoms syndrome	CD4 (IL-4, IL-5, IL-13) and CD8 T cells implicated (release of TNF alpha and IFN gamma); primary dermal lymphocytic infiltrate	Fever, rash, peripheral blood eosinophilia, lymphadenopathy, or organ involvement (often liver or kidney)	2–6 weeks	Vancomycin, rifamycin, sulphonamide antibiotics, dapsone, or all β-lactam antibiotics	History, physical exam, laboratory (assessment of absolute eosinophil count and organ involvement), biopsy, clinical scoring RegiSCAR,†† causality assessment Naranjo,‡‡ and patch testing (may identify culprit)	HLA-B*13:01 (dapsone in southeast Asians); HLA-B*35:05 (nevirapine in southeast Asians); HLA-B*53:01 (raltegravir in African ancestry)	Immediate removal of drug; antihistamines or corticosteroids (severe cases only)	Avoidance of implicated drug(s), drugs in the same class, and structurally related drugs which are potentially cross-reactive
Stevens-Johnson syndrome and toxic epidermal necrolysis	CD8 cytotoxic T cells via perforin, granulysin, granzyme B, or FasL (keratinocyte death, type IVc HSR)	Rash with desquamation, mucosal lesions (mouth, eyes, genitals) with mucositis, or fever SJS: <10% BSA SJS–TEN overlap: 10–30% BSA TEN: >30% BSA	4 days to 4 weeks (for many antimicrobials shorter latency is typical)	Sulphonamide antimicrobials, nevirapine, antimycobacterials, macrolides, or quinolones	History (blistering rash with skin sloughing), physical exam (Nikolsky and Asboe-Hansen signs), skin biopsy with keratinocyte necrosis (from partial to full thickness) of the epidermis, and clinical scoring (SCORETEN,§§ ALDEN,¶¶ Naranjo‡‡)	HLA-C*04:01 (nevirapine in Africans)	Immediate removal of drug; aggressive supportive care in intensive care unit or burn unit setting; pulse corticosteroids, etanercept, or cyclosporine	Avoidance of implicated drug(s), drugs in the same class, and structurally related drugs which are potentially cross-reactive
Acute generalised exanthematous pustulosis	T cells via IL-8 and granulocyte-macrophage colony-stimulating factor (neutrophilic inflammation, type IVd HSR)	Acute pustular eruption characterised by widespread non-follicular sterile pustules with fever, facial oedema, or neutrophilia; 25% of patients have oral involvement	<48 h (typically within 24 h); longer latency for pristinamycin and hydroxychloroquine	Aminopenicillins, clindamycin, other β-lactams, fluoroquinolones, sulphonamides, pristinamycin, terbinafine, or hydroxychloroquine (anti-malarial)	History, physical exam, fever, laboratory evaluation showing neutrophilic leukocytosis with mild eosinophilia; skin biopsy (subcorneal pustules or intraepidermal pustules filled with neutrophils), and patch testing (to help identify culprit)	..	Immediate removal of drug, topical corticosteroids, or systemic corticosteroids (severe cases and widespread involvement)	Avoidance of implicated drug(s), drugs in the same class, and structurally related drugs which are potentially cross-reactive; drugs reintroduced may be guided by patch testing

Lancet. 2019 Jan 12;393(10167):183-198

嚴重皮膚不良反應 (SCARs)與表徵

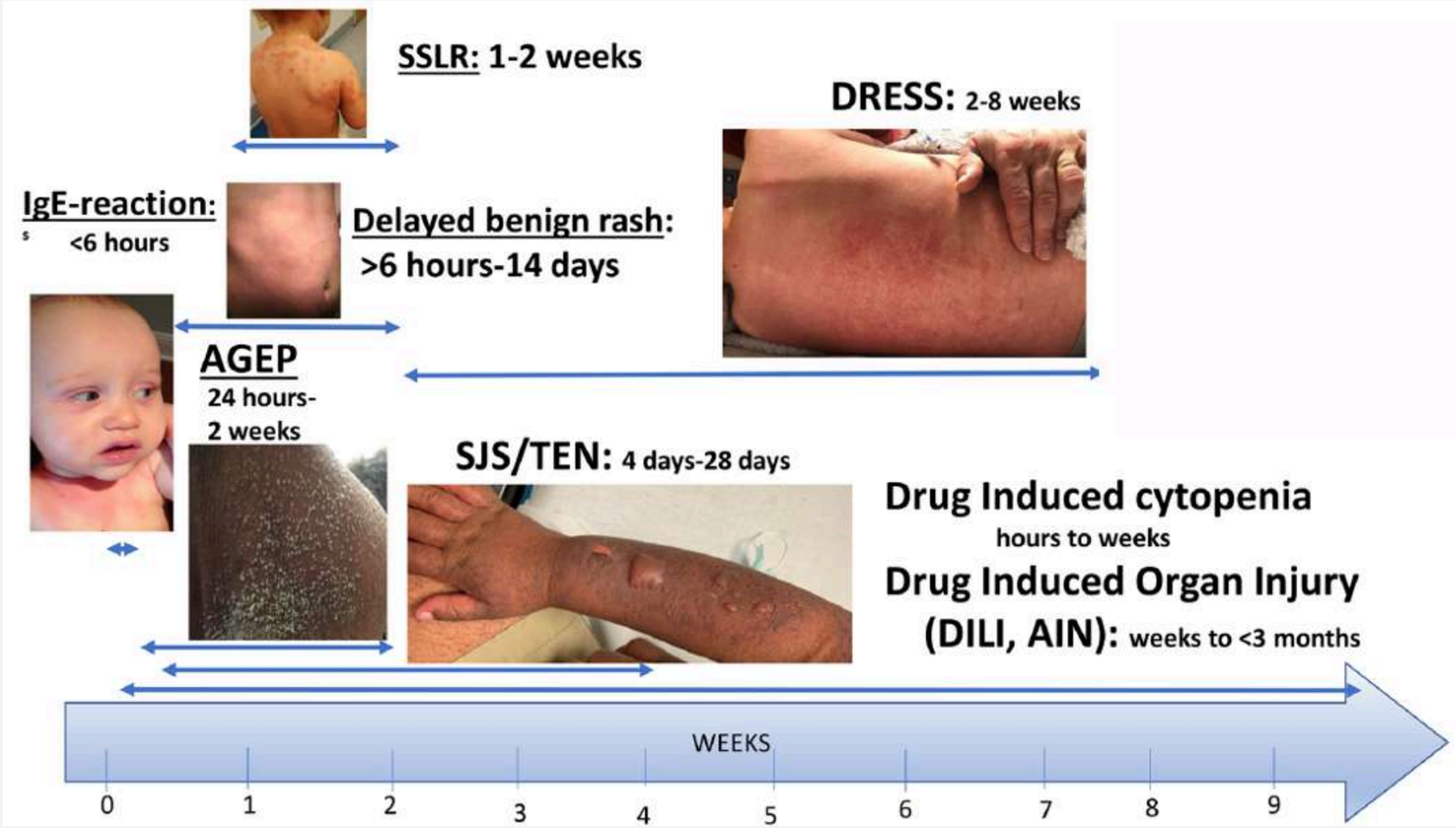


	Drug-to-SCAR interval	General symptoms*	Skin features	Laboratory values	Main organs involved	Severity score	Score system for classification	Histological features
SJS and TEN[3-5]	4–28 days	Fever ≥38°C, influenza-like syndrome, respiratory tract symptoms	Blisters, large skin detachment, confluent erythema, atypical target lesions, purpura, Nikolsky's sign; skin detachment: Stevens-Johnson syndrome <10%, toxic epidermal necrolysis ≥30%, SJS–TEN 10–30%; two or more of mucous membranes involved	Lymphopenia, transitory neutropenia, mild cytolysis, renal impairment	Ear, nose, and throat, lung, intestinal tract, liver, kidney	SCORTEN†	No‡	Full-thickness epidermal necrosis, focal adnexal necrosis, necrotic keratinocytes, mild mononuclear cell dermal infiltrate, negative direct immunofluorescence test
DRESS syndrome[6-11]	2–6 weeks	Fever ≥38°C, influenza-like syndrome	Maculopapular rash, erythroderma, facial or extremity oedema, purpura, pustules, focal monopolar mucous-membrane involvement	Eosinophilia >700 cells per µL, atypical lymphocytes, elevated transaminase concentration, impaired renal function, herpesvirus family reactivation (HHV6, HHV7, EBV, CMV), parvovirus B19 reactivation	Liver, kidney, lung, muscle, heart, pancreas, medulla, lymph nodes at two or more sites	None	Yes	Lichenoid infiltrate or eczematous pattern (spongiosis, oedema), focal necrotic keratinocytes, mononuclear infiltrate, focal eosinophil and neutrophil infiltrates, mild vasculitis
AGEP[12,13]	1–11 days	Fever ≥38°C	Intertriginous erythema, oedema, widespread non-follicular sterile pustules, post-pustular pinpoint desquamation, Nikolsky's sign, rare oral mucous-membrane involvement	Hyperleukocytosis, neutrophils ≥7000 cells per µL, mild eosinophilia	Rare: liver, lung	None	Yes	Subcorneal or intraepidermal spongiform or non-spongiform pustules with or without papillary oedema, focal necrotic keratinocytes, neutrophilic sometimes with eosinophils, mild vasculitis

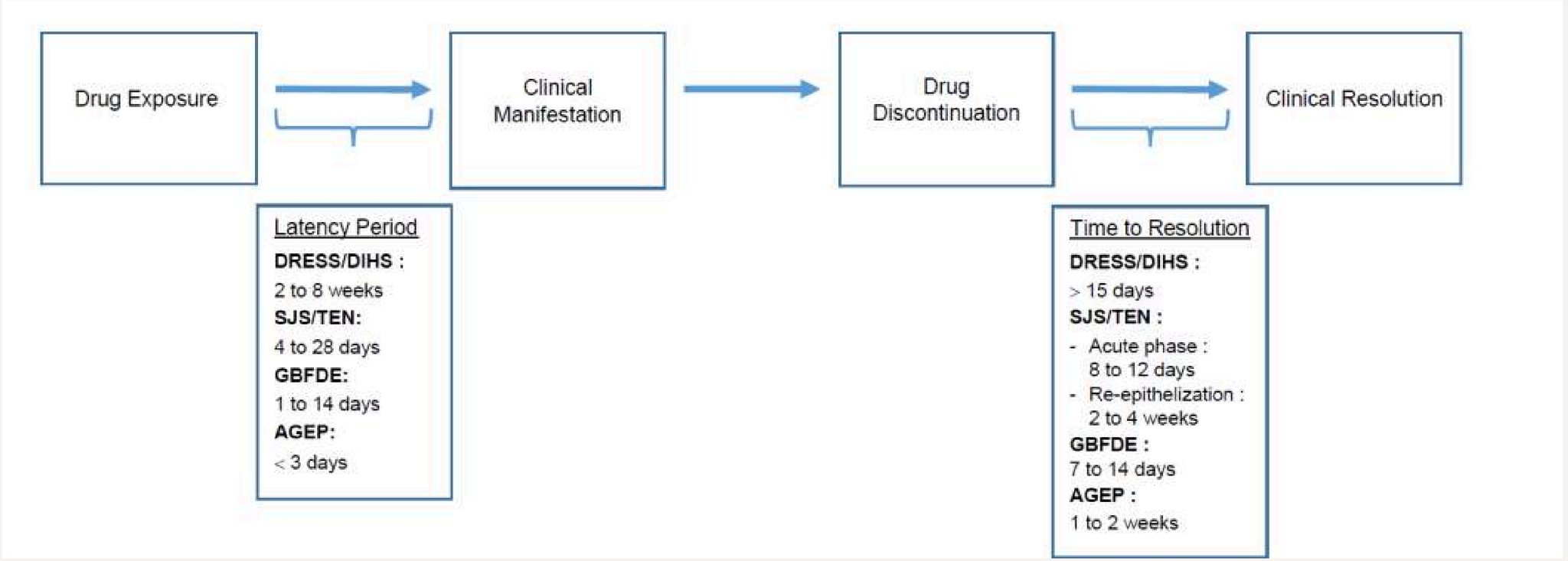
SCAR=severe cutaneous adverse reaction. SJS=Stevens-Johnson syndrome. TEN=toxic epidermal necrolysis. SCORTEN=SCORe of Toxic Epidermal Necrolysis. DRESS=drug reaction with eosinophilia and systemic symptoms. HHV=human herpesvirus. EBV=Epstein-Barr virus. CMV=cytomegalovirus. AGEP=acute generalised exanthematous pustulosis. *General symptoms can precede or occur at the same time as skin manifestations. †See appendix. ‡Not published.

Table 1: **Main clinical and histological characteristics of SCARs**

嚴重皮膚不良反應的潛伏期

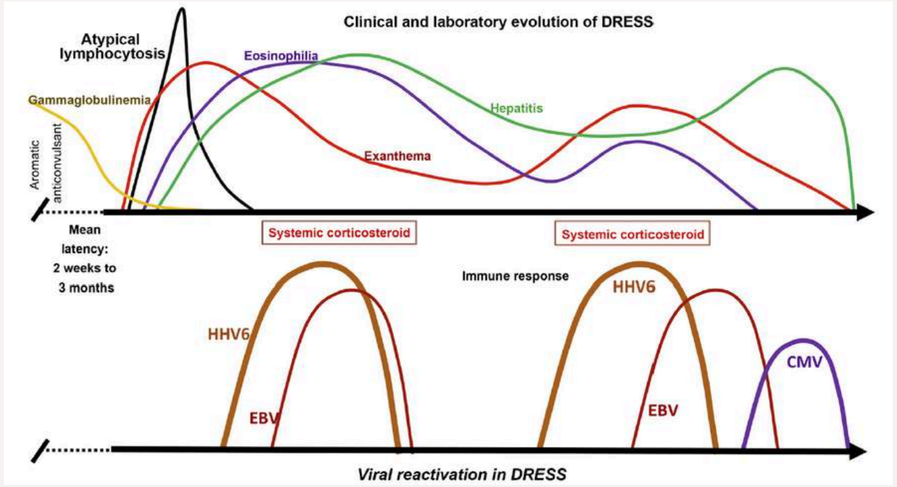


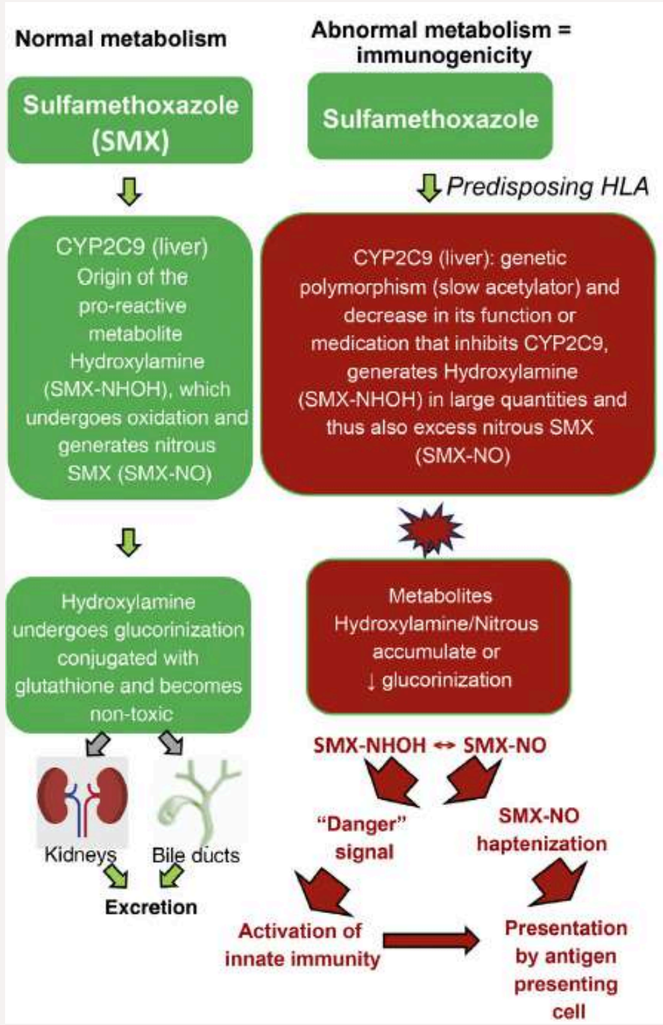
嚴重皮膚不良反應的緩解時間



DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms)

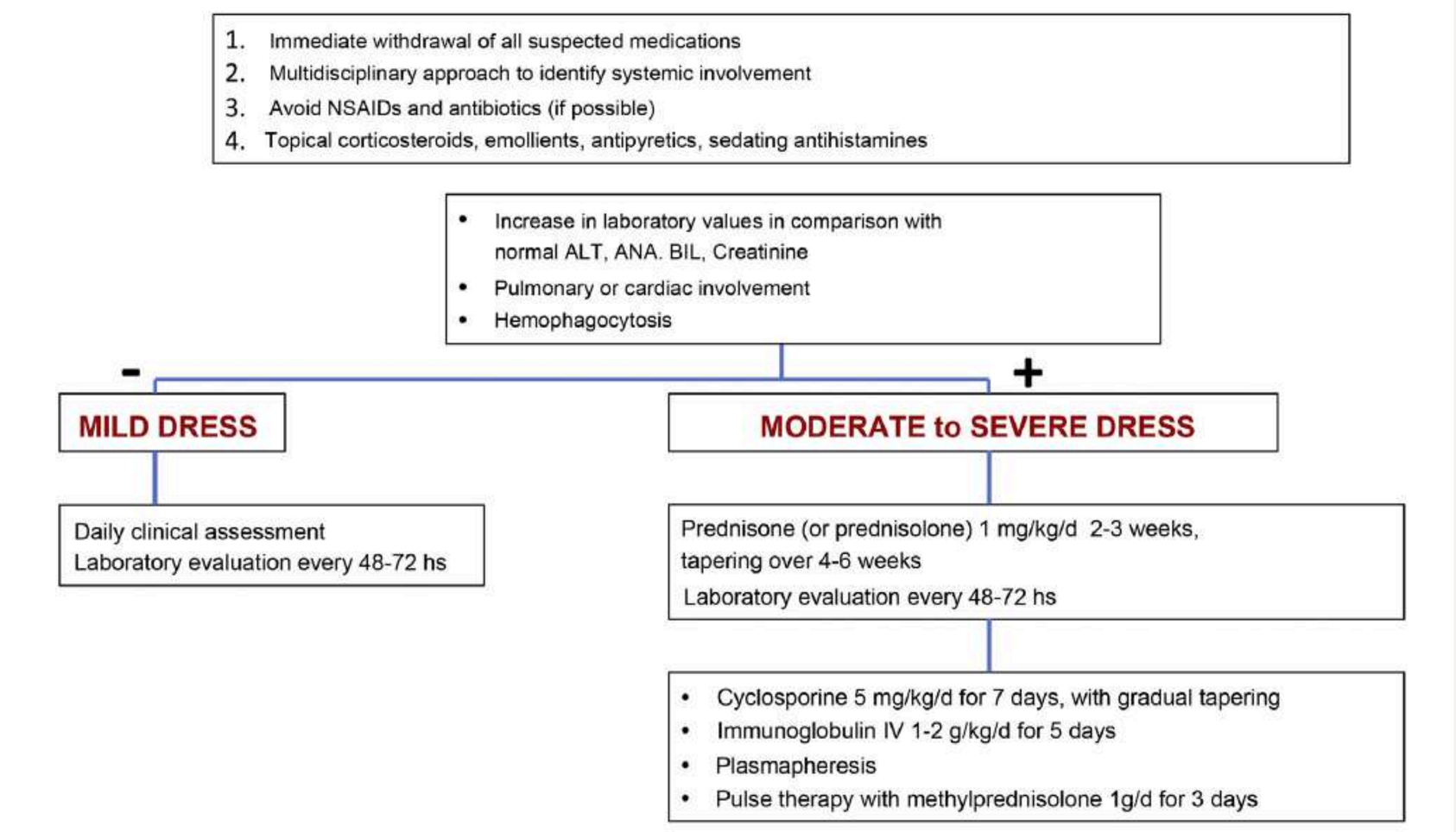
- 35% aromatic antiepileptics; other high-risk drugs: allopurinol, sulfonamides, vancomycin, minocycline, amoxicillin
- 致病機轉
  - Genetic susceptibility
  - Changes in drug metabolism pathways
  - Reactivation of viruses, particularly Human Herpes Virus 6 (HHV6)（也可見EBV、CMV)
- 約76–80%的DRESS病人對HHV-6、HHV-7或EBV呈陽性
- 90% 病程持續超過15天;20% 超過90天
- Poor prognosis: 老年、延遲停藥、多重用藥、合併CMV再活化
- 長期併發症：自體免疫疾病





An Bras Dermatol. 2025 Jan-Feb;100(1):104-120.

DRESS



An Bras Dermatol. 2025 Jan-Feb;100(1):104-120.

藥師在皮膚不良反應中的角色

收集資料

類別	收集資訊
藥物特性 (Medicinal product characteristics)	- 可疑用藥時間 - 已有文獻證據，包括該藥物的知名度或已知風險 - 正在研究的藥物，應考慮潛在藥效動力學交互作用
病人特性 (Patient characteristics)	- 基本資料：年齡、性別、遺傳背景、過敏史 - 特殊疾病患者：HIV、惡性腫瘤、SLE或其他自身免疫疾病、移植患者 - 遺傳風險因素：特定藥物相關HLA高危基因型
皮膚表現特徵 (Skin involvement characteristics)	- 皮疹出現時間 - 事件消退時間 - 皮疹描述、分布、部位與形態 - 受影響體表面積 - 是否有相同部位皮疹復發史 - 皮膚病理切片 - 皮膚檢測結果
伴隨或先行症狀 (Accompanying and/or preceding signs and symptoms)	- 口腔或生殖器黏膜受影響 - 發燒（體溫 >38°C） - 其他全身症狀 - 淋巴結腫大 - 面部水腫 - 眼部病兆
實驗室異常 (Laboratory abnormalities)	- 白血球增多 - 淋巴球增多 / 減少 - 異型淋巴球 - 嗜酸性球增多 - 血小板減少 - 內臟受影響證據 - 病毒再活化證據

藥師在皮膚不良反應中的角色

臨床常見皮膚不良反應評估工具

- **Naranjo ADR Probability Scale(廣用的藥物不良反應評估工具)**
- **ALDEN causality score(SJS/TEN 藥物不良反應評估工具)**
- **SCORTEN score(SJS/TEN – 預後評估工具)**
- **RegiSCAR score(DRESS-診斷工具)**

TABLE 1 | Clinical diagnosis and described scoring algorithms.

Clinical diagnosis	AGEP	DRESS	SJS/TEN
Disease likelihood	AGEP validation score	RegiSCAR score	None
Drug causality	Naranjo score	Naranjo score	ALDEN score Naranjo score
Mortality	None	None	SCORTEN

AGEP, acute generalized exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms; SJS/TEN, SJS/TEN, Stevens-Johnson syndrome/ toxic epidermal necrolysis. ALDEN, algorithm of drug causality for epidermal necrolysis; Naranjo score: The Adverse Drug Reaction (ADR) Probability Scale; RegiSCAR, european registry of severe cutaneous adverse reactions; SCORTEN, score of toxic epidermal necrosis.

臨床常見皮膚不良反應評估工具(Naranjo score)

Table 1-2. Naranjo ADR Probability Scale

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse event appear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that, on their own, could have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	

Total Score	ADR Probability Classification
9	Highly Probable
5–8	Probable
1-4	Possible
0	Doubtful

Adapted with permission from: Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.

- 過去是否有文獻報導?
- 不良事件是否發生於給藥後?
- 停藥或給予結抗劑後，症狀是否改善?
- 再次給予是否再發生?
- 是否有其他原因導致此次良事件?
- 給予安慰劑是否再發生?
- 血中濃度是否達到中毒劑量?
- 藥物劑量與不良事件是否呈正相關?
- 過去對同樣或類似藥物是否也產生同樣的不良反應?
- 是否有客觀的證據證明是藥品引起的?

臨床常見皮膚不良反應評估工具(ALDEN score)

Table 5 Details of the algorithm of drug causality for epidermal necrolysis (ALDEN)

Criterion	Values	Rules to apply	
Delay from initial drug component intake to onset of reaction (index day)	Suggestive +3	From 5 to 28 days	−3 to 3
	Compatible +2	From 29 to 56 days	
	Likely +1	From 1 to 4 days	
	Unlikely −1	>56 Days	
	Excluded −3	Drug started on or after the index day	
		In case of previous reaction to the same drug, only changes for: Suggestive: +3: from 1 to 4 days Likely: +1: from 5 to 56 days	
Drug present in the body on index day	Definite 0	Drug continued up to index day or stopped at a time point less than five times the elimination half-life[a] before the index day	−3 to 0
	Doubtful −1	Drug stopped at a time point prior to the index day by more than five times the elimination half-life[a] but liver or kidney function alterations or suspected drug interactions[b] are present	
	Excluded −3	Drug stopped at a time point prior to the index day by more than five times the elimination half-life[a], without liver or kidney function alterations or suspected drug interactions[b]	
Prechallenge/rechallenge	Positive specific for disease and drug: 4	SJS/TEN after use of same drug	−2 to 4
	Positive specific for disease or drug: 2	SJS/TEN after use of similar[c] drug or other reaction with same drug	
	Positive unspecific: 1	Other reaction after use of similar[c] drug	
	Not done/unknown: 0	No known previous exposure to this drug	
	Negative −2	Exposure to this drug without any reaction (before or after reaction)	
Dechallenge	Neutral 0	Drug stopped (or unknown)	−2 or 0
	Negative −2	Drug continued without harm	
Type of drug (notoriety)	Strongly associated 3	Drug of the "high-risk" list according to previous case–control studies[d]	−1 to 3
	Associated 2	Drug with definite but lower risk according to previous case–control studies[d]	
	Suspected 1	Several previous reports, ambiguous epidemiology results (drug "under surveillance")	
	Unknown 0	All other drugs including newly released ones	
	Not suspected −1	No evidence of association from previous epidemiology study[d] with sufficient number of exposed controls[c]	
		Intermediate score = total of all previous criteria	−11 to 10
Other cause	Possible −1	Rank all drugs from highest to lowest intermediate score	−1
		If at least one has an intermediate score >3, subtract 1 point from the score of each of the other drugs taken by the patient (another cause is more likely)	
Final score −12 to 10			

<0, Very unlikely; 0–1, unlikely; 2–3, possible; 4–5, probable; ≥6, very probable.

- 從第一次用藥到 SJS/TEN 發作的時間?
- 反應發生時藥物是否可能仍在體內?
- 先前使用或再暴露過?
- 停用該藥後反應是否改善?
- 該藥在文獻中是否已知會引起 SJS/TEN?風險?
- 可疑藥物不只一種?
  - 若有至少一種藥的分數 >3，
  - 表示該藥更可能是致病藥，
  - 其他藥物各自扣 1 分以反應相對可能性較低

<0, Very unlikely; 0–1, unlikely; 2–3, possible; 4–5, probable; ≥6, very probable.

臨床常見皮膚不良反應評估工具(RegiSCAR score)

Items	Score			Comments
	−1	0	1	
Fever ≧ 38.5 °C	N/U	Y		
Enlarged lymph nodes		N/U	Y	>1 cm and ≧ 2 different areas
Eosinophilia ≧ 0.7×10^9/L or ≧ 10% if WBC < 4.0×10^9/L		N/U	Y	Score 2, when ≧ 1.5×10^9/L or ≧ 20% if WBC < 4.0×10^9/L
Atypical lymphocytosis		N/U	Y	
Skin rash Extent > 50% of BSA Rash suggesting DRESS	 N	 N/U U	 Y Y	Rash suggesting DRESS: ≧ 2 symptoms: purpuric lesions (other than legs), infiltration, facial edema, psoriasiform desquamation
Skin biopsy suggesting DRESS	N	Y/U		
Organ involvement		N	Y	Score 1 for each organ involvement, maximal score: 2
Rash resolution ≧ 15 days	N/U	Y		
Excluding other causes		N/U	Y	Score 1 if 3 tests of the following tests were performed and all were negative: HAV, HBV, HCV, Mycoplasma, Chlamydia, ANA, blood culture

ANA: anti-nuclear antibody; BSA: body surface area; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; N: no; U: unknown; WBC: white blood cell; Y: yes.

<2 points: no case; 2–3 points: possible case;
4–5 points: probable case; >5 points: definite case

- **發燒 ≥38.5°C**
- **≥2個不同部位的淋巴結腫大**
- **嗜酸性球 ≥700/μL或占白血球總數 ≥10%;**
- **≥1500/μL或占白血球總數 ≥20%**
- **有非典型淋巴球**
- **紅疹超過50%身體表面積**
- **≥ 2項符合: purpuric lesions (other than legs), infiltration, facial edema, psoriasiform desquamation**
- **皮膚切片**
- **侵犯器官數目**
- **病程持續≥ 15天**
- **排除其他原因**
  - **避免將 DRESS 誤判為其他感染或免疫疾病引起的皮疹及器官侵犯**

臨床常見皮膚不良反應評估工具(SCORTEN)

Age > 40 years	1
Tachycardia > 120 bpm	1
Neoplasia	1
Initial detachment > 10%	1
Serum urea > 10 mmol/L	1
Serum bicarbonate < 20mmol/L	1
Blood glucose > 14 mmol/L	1

SCORTEN	**Mortality (%)**
0-1	3
2	12
3	35
4	58
≥ 5	90

各個評估工具特色與限制

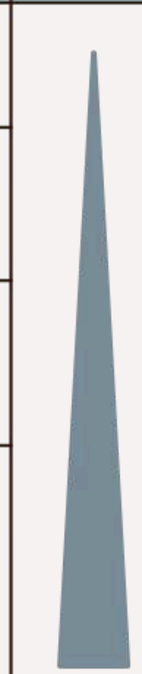
工具	評估目的	特色	限制
Naranjo	藥物不良反應因果相關	• 簡單 • 廣泛應用於臨床與文獻	• 非針對嚴重皮膚 ADR • 沒有考慮遺傳/免疫學因素 • 多藥併用時敏感度不足
ALDEN	SJS/TEN 因果相關	• 考慮潛伏期 • 過往暴露、藥物知名度、再挑戰等因素 • 為 SJS/TEN 設計，較精準	• 僅限 SJS/TEN，不適用其他皮膚 ADR • 需完整藥物暴露時程資料
RegiSCAR	DRESS 診斷	• 專門針對 DRESS 診斷	• 無法用於 SJS/TEN 或其他 SCAR；需完整臨床與檢驗檢查資料
SCORTEN	SJS/TEN 預後評估	• 可分層死亡率	• 僅能預測死亡率，不能判斷因果或診斷 • 僅適用於 SJS/TEN

藥師在皮膚不良反應中的角色

檢測工具

檢測方式	體內/外	立即型	延遲型	敏感性	特異性	時機	特色	限制
Drug challenge	體內	O (輕中度或有條件進行)	O (輕中度或有條件進行)	高	高	4-6週後	• 診斷或排除藥物過敏的黃金標準 • 需在嚴格監督下進行 • 研究顯示在低風險有良好安全性與實用性	• 嚴重過敏反應者禁忌或高度限制使用 • 抗組織胺、類固醇或免疫抑制劑可能影響結果
Skin Prick test (SPT)	體內	O	少	~30.7% (SPT + IDT)	~96.8% (SPT + IDT)	4-6週後	• 侵入性低、成本低、可快速得出結果 • SPT安全性較高，通常先做 SPT，再看是否需 IDT • IDT比 SPT 敏感但風險更高	• IDT於嚴重過敏反應者禁忌或高度限制使用 • IDT有誘發全身反應風險; 藥物濃度需標準化 • 敏感性低 • 抗組織胺、類固醇或免疫抑制劑可能影響結果
Intradermal test (IDT)	體內	O	部分			4-6週後		
Patch testing (PT)	體內	X	O	20–60% (依藥物種類差異大)	85–95%	6 週-3 個月	• 非侵入性、安全、可多藥同時測試	• 對 SJS/TEN、DRESS 等 SCARs，PT的價值與安全性需個案評估 • 敏感性有限 • 需專業判讀 • 類固醇或免疫抑制劑可能影響結果
Histamine release test	體外	O	X	30–50%	85–95%	4-6週後	• 簡單定量反應強度	• 敏感性低，現今少用 • 抗組織胺、類固醇或免疫抑制劑可能影響結果
Basophil activation test (BAT)	體外	O	X	40–70%	85–95%	4-6週後	• 可避免病人暴露藥物	• 需要新鮮血液、設備昂貴 • 類固醇或免疫抑制劑可能影響結果
Lymphocyte transformation test (LTT)	體外	X	O	60–80% (DRESS最佳)	85–95%	4–8 週內	• 可量化T cell反應	• 實驗室需求高、非標準化、假陰性常見 • 類固醇或免疫抑制劑可能影響結果
Enzyme Linked ImmunoSpot (ELISpot)	體外	X	O	70–85%	85–95%	4–8 週	• 比LTT靈敏，可偵測Th1/Th2 pattern	• 高成本、尚未廣泛應用 • 類固醇或免疫抑制劑可能影響結果

延遲型過敏反應之檢測工具與處理

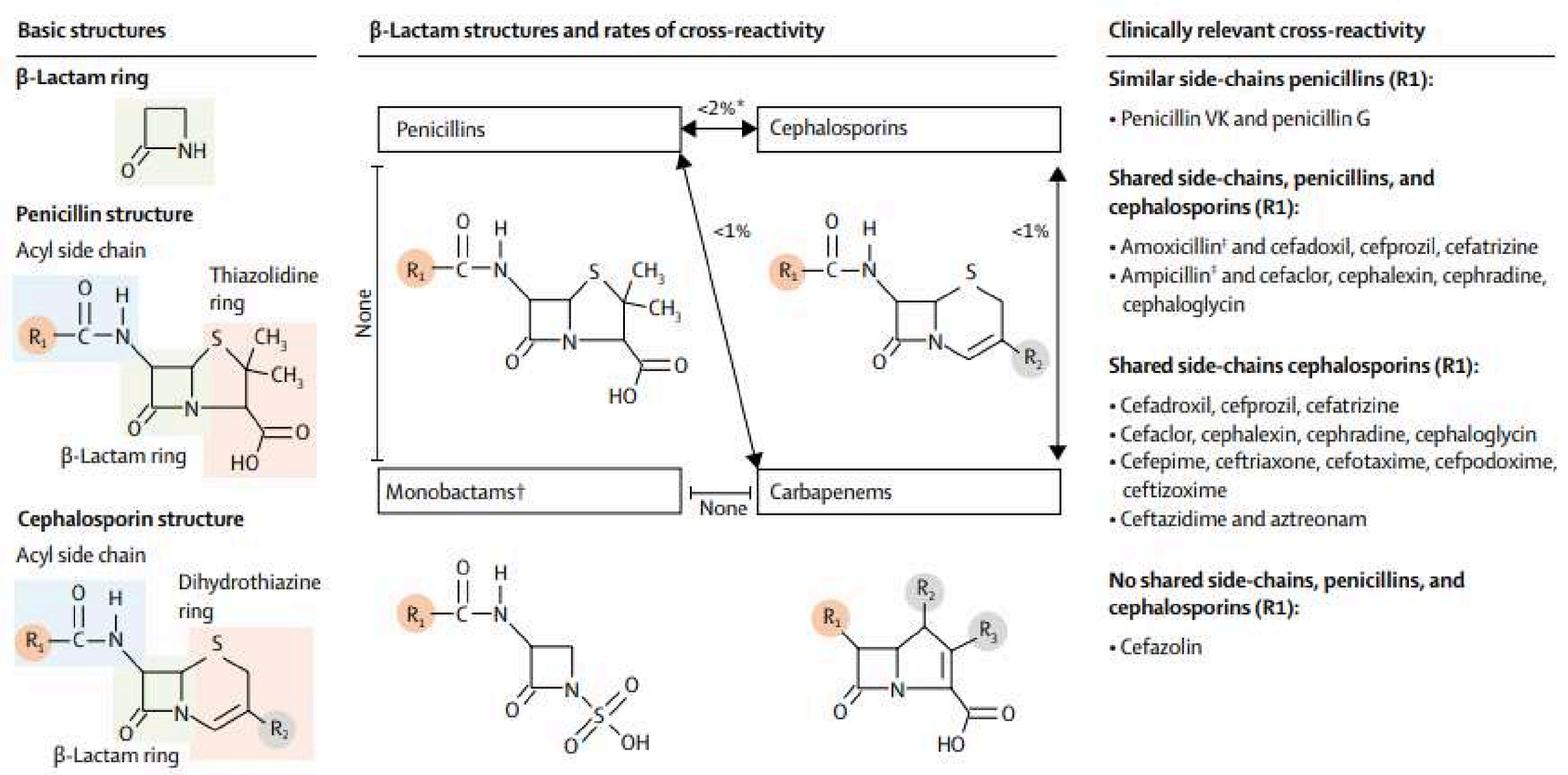
皮膚不良反應類型	發生率	致死率	體內	體外	HLA	處理方式
Maculopapular exanthem (MPE)	1–5%		IDT;PT; Drug Challenge	-	-	• Drug withdrawal • Symptomatic treatment • Treating through
AGEP	1–5/百萬人年或 1/100,000		IDT; PT; Drug Challenge*	ELISpot; LTT	-	• Drug withdrawal • Symptomatic treatment
DRESS	1/1,000–1/10,000		IDT; PT; Drug Challenge*	ELISpot; LTT	A32:01(Vancomycin) B58:01 (Allopurinol) B13:01(Dapsone) A31:01(Carbamazepine)	• Drug withdrawal • Symptomatic treatment • Systemic glucocorticoids • Cyclosporine
SJS / TEN	1/10,000–1/100,000		PT	ELISpot; LTT	B15:02 (Carbamazepine) B58:01(Allopurinol)	• Drug withdrawal • Supportive wound care • IVIG • Systemic glucocorticoids and IVIG • Cyclosporine • TNF inhibitor

*價值與安全性需個案評估

藥師在皮膚不良反應中的角色

β-lactam 抗生素交叉過敏反應（cross-reactivity）

- **同類的交叉風險：Penicillin>Cephalosporin>Carbapenem**
- **不同類的交叉風險：R1 側鏈相似性是決定性因素**



Lancet 2019; 393: 183–98

β-lactam 抗生素交叉過敏反應（cross-reactivity）

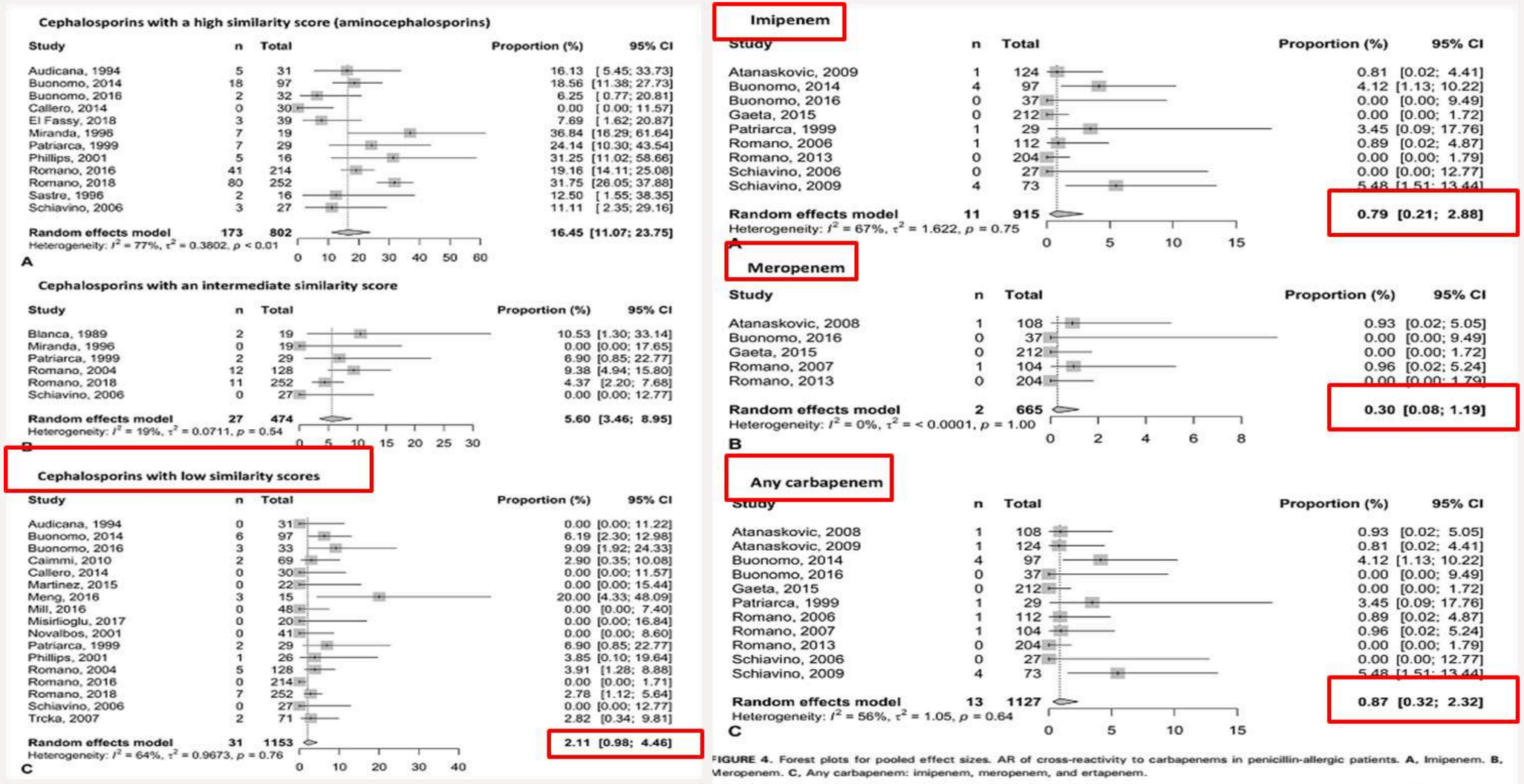
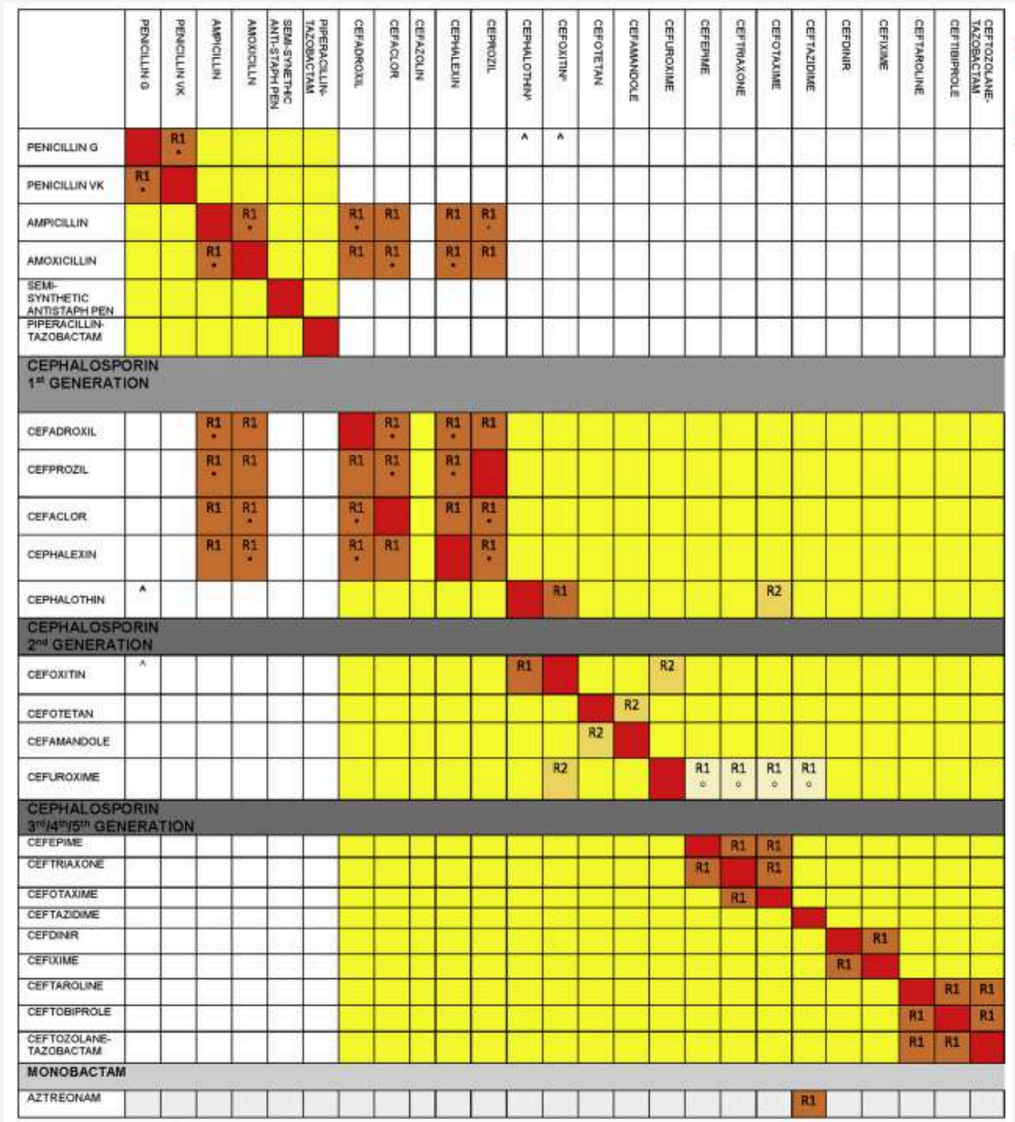


FIGURE 4. Forest plots for pooled effect sizes. AR of cross-reactivity to carbapenems in penicillin-allergic patients. A, Imipenem. B, Meropenem. C, Any carbapenem: imipenem, meropenem, and ertapenem.

J Allergy Clin Immunol Pract 2019 Nov-Dec;7(8):2722-2738.e5

β-lactam 抗生素交叉過敏反應（cross-reactivity）



Legend

^ *In vitro* data proposed cross-reactivity between cefoxitin and cephalothin based upon shared but not shared R1

Exactly the same drug

R1 – Identical R1 side chain

R1* – Almost Identical R1 side chain

R2 - Identical R2 and non-identical R1 with some cross-reactivity

R1° Non-identical R1 with some clinical cross-reactivity

Shared class specific ring but no shared side chain structure

No shared class specific ring, only shared beta-lactam ring

No shared cross reactivity with beta-lactam ring

	Cephalosporins	Penicillins						
		Penicillin G	Penicillin V	Ampicillin	Amoxicillin	Cloxacillin	Piperacillin	Ticarcillin
1st	Cefadroxil	0,371	0,220	0,618	1,000	0,179	0,060	0,333
	Cephalexin	0,592	0,333	1,000	0,618	0,208	0,043	0,371
	Cefazolin	0,176	0,110	0,099	0,088	0,078	0,032	0,088
	Cefradine	0,344	0,200	0,517	0,371	0,155	0,082	0,263
	Cephalothin	0,563	0,321	0,337	0,295	0,154	0,035	0,268
	Cefatrizine	0,371	0,220	0,618	1,000	0,179	0,060	0,333
	Cephaloridine	0,563	0,321	0,337	0,295	0,154	0,035	0,268
2nd	Cefaclor	0,592	0,333	1,000	0,618	0,208	0,043	0,371
	Cefoxitin	0,330	0,245	0,211	0,180	0,148	0,043	0,180
	Cefprozil	0,371	0,220	0,618	1,000	0,179	0,060	0,333
	Cefuroxime	0,304	0,220	0,274	0,248	0,320	0,044	0,228
	Cefamandole	0,592	0,333	0,714	0,485	0,208	0,043	0,412
3rd	Cefixime	0,110	0,110	0,098	0,157	0,219	0,084	0,138
	Cefotaxime	0,141	0,090	0,138	0,142	0,249	0,049	0,182
	Ceftazidime	0,092	0,087	0,092	0,142	0,198	0,064	0,127
	Ceftriaxone	0,141	0,090	0,138	0,142	0,249	0,049	0,182
	Cefpodoxime	0,141	0,090	0,138	0,142	0,249	0,049	0,182
	Cefdinir	0,147	0,083	0,143	0,156	0,207	0,047	0,238
	Ceftibuten	0,167	0,127	0,148	0,165	0,237	0,079	0,165
4th	Cefepime	0,141	0,090	0,138	0,142	0,249	0,049	0,182

No-similarity — Identical

A 0.000 — 1.000

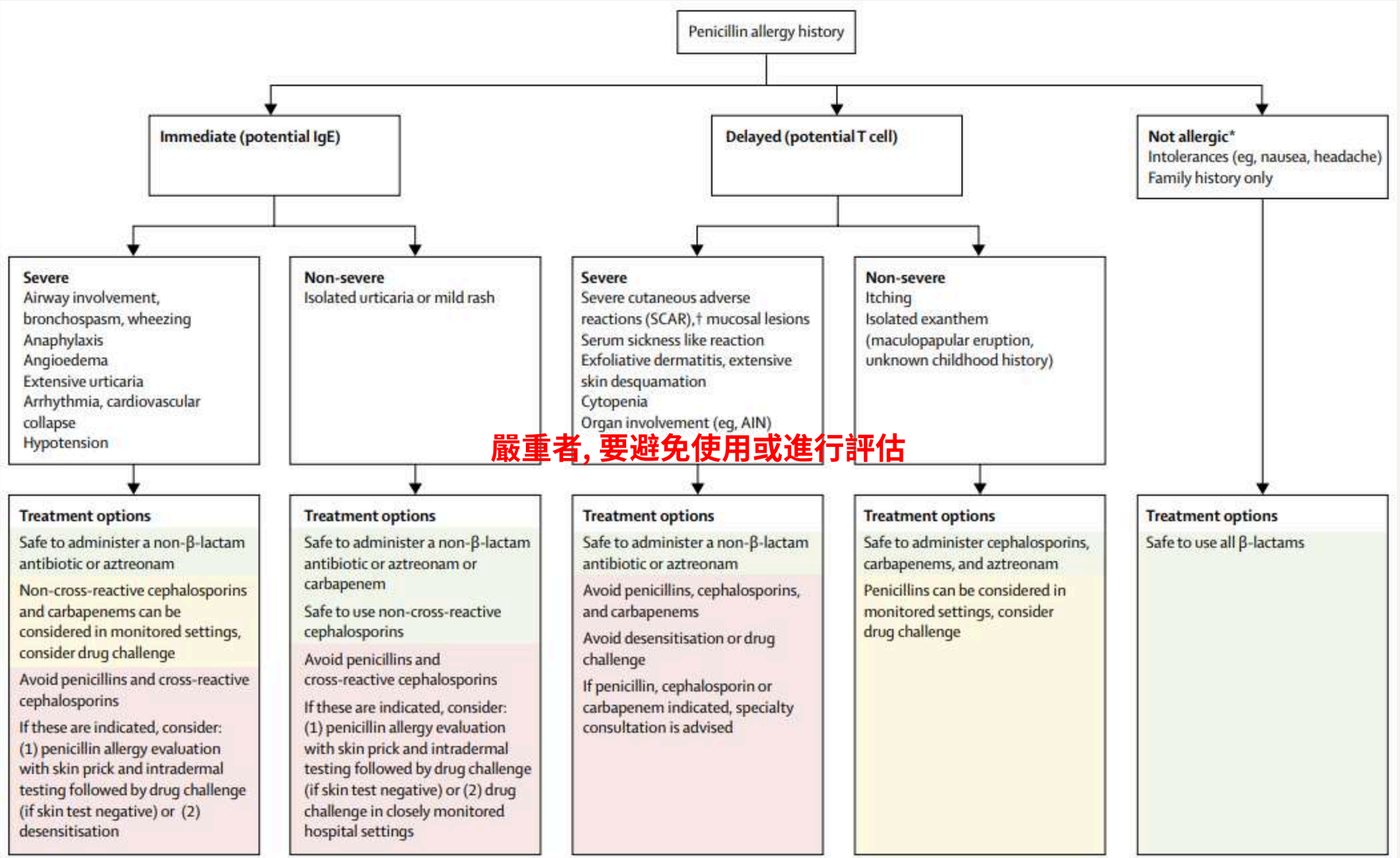
J Allergy Clin Immunol Pract. 2017 Nov-Dec;5(6):1532-1542
J Allergy Clin Immunol Pract. 2019 Nov-Dec;7(8):2722-2738.e5.

β-lactam 抗生素交叉過敏反應（cross-reactivity）

交叉過敏	立即型	延遲型
Penicillins↔Penicillins	高風險所有Penicillins共享一樣Major determinant	可發生，但資料少且差異大； 側鏈仍是重要因子，但還需考量皮膚表現類型及檢測工具
Penicillins↔Cephalosporins	整體估計低<2% (第三代以上通常 <1%；第一/二代與penicillin 側鏈相似或相同者風險較高，分別5%與2-5%)	低風險延遲型反應約2.8-31.2%
Penicillins↔Carbapenems	整體估計低<1%	資料有限，但一般認為低
Cephalosporin↔Cephalosporin	相同或高度側鏈相似者，風險可顯著上升（個別研究報告可達~10%）；若側鏈不同，交叉過敏率通常很低	資料有限，但一般認為低
Cephalosporin↔Carbapenems	整體估計低<1%	資料有限，但一般認為低
Carbapenems↔Carbapenems	資料受限	資料有限，但一般認為低
	• 研究資料較多，交叉過敏率整體偏低，但相似或相同側鏈者風險可顯著增加	• 研究受限，交叉過敏率差異較大 • 在不同研究與臨床表型間差異大，且與側鏈相似性、檢測方法密切相關

J Allergy Clin Immunol Pract. 2017 Nov-Dec;5(6):1532-1542

Penicillin過敏的處理

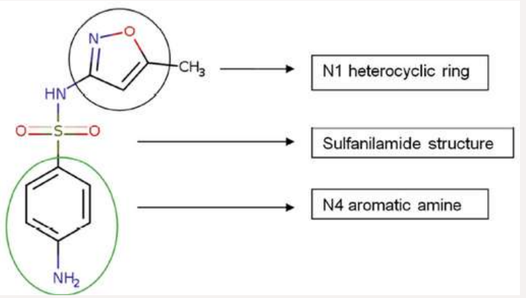


Lancet 2019; 393: 183–98

磺胺類交叉過敏反應

- **Sulfonamide為臨床常使用之藥品，也是僅次於beta-lactams常致過敏的藥品，發生率有3-8%，其中co-trimoxazole用於亞洲族群中，更是第四常見導致發生嚴重SJS/TEN之藥品**
- **Sulfasalazine和co-trimoxazole為近年藥害救濟基金會給付案中之前十名**

- 磺胺類包含三類: sulfonamide antimicrobials(高風險交叉過敏)、sulfonamide nonantimicrobials (低度風險交叉過敏)、nonsulfonamide sulfur-containing agents(不會產生交叉過敏)
- Data suggest that substitutions at the N1 and N4 positions are the primary determinants of drug allergy instead of the common sulfonamide moiety



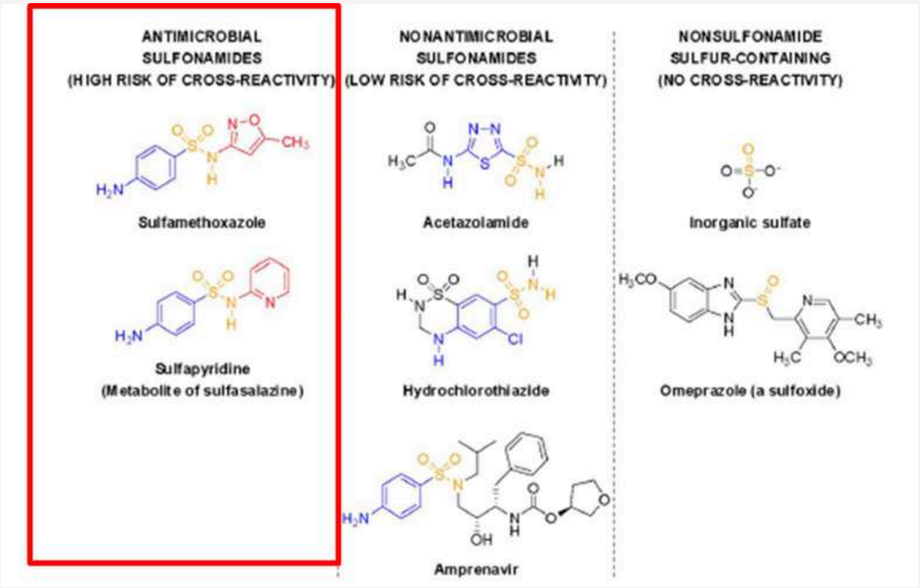
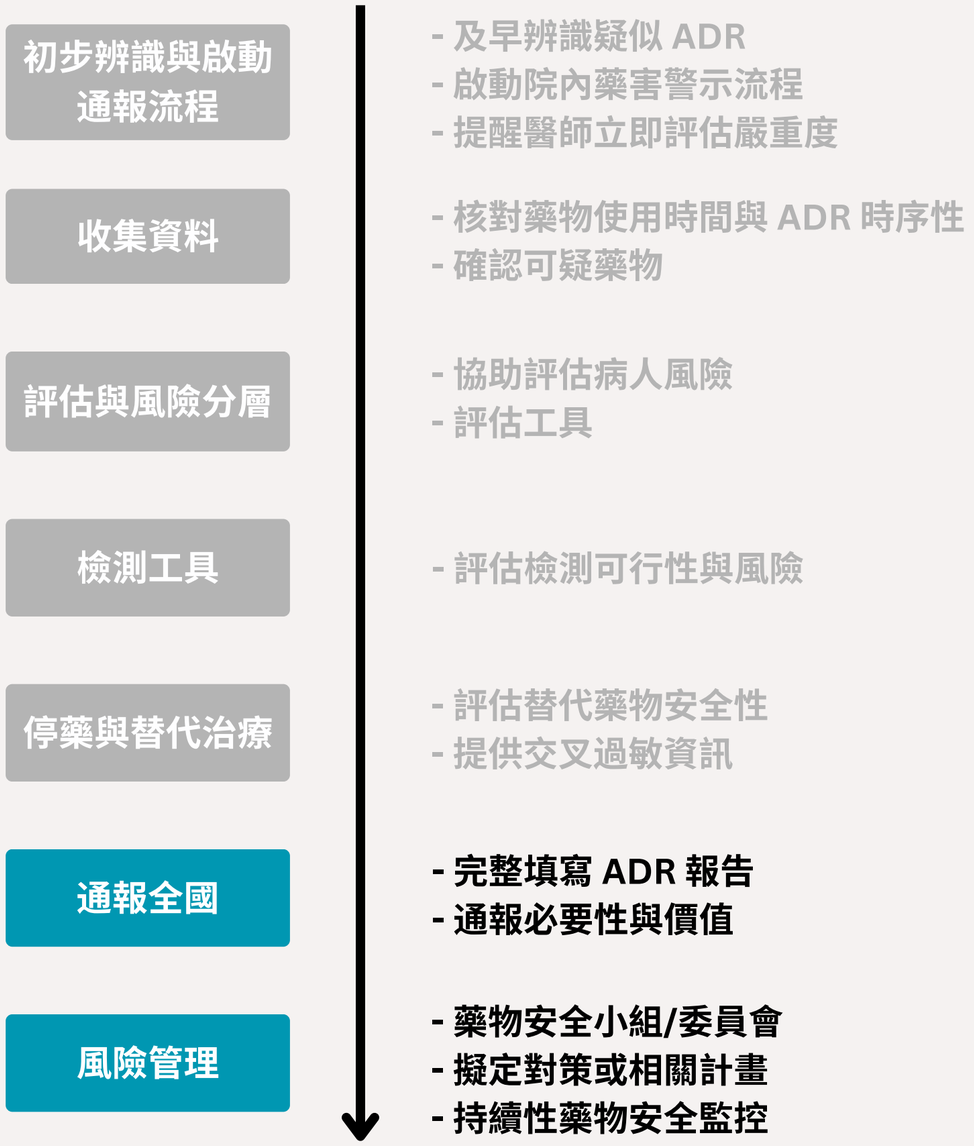


TABLE II. Drugs to avoid in patients with a history of a sulfonamide antimicrobial adverse reaction

Drug or compound	Comments
Sulfonamide antimicrobials	
• Sulfamethoxazole (oral/parenteral: cotrimoxazole, *Septra*)	Avoid all sulfonamide antimicrobials.
• Sulfasalazine (oral: *Salazopyrin*)	• Sulfasalazine should be avoided, as it is metabolized to sulfapyridine (a sulfonamide antimicrobial) and 5-ASA
• Sodium sulfacetamide (ophthalmic)	
• Silver sulfadiazine (topical: *Flamazine*)	

J Allergy Clin Immunol Pract. 2019 Sep-Oct;7(7):2116-2123
Pharmacy (Basel). 2019 Sep; 7(3): 132.

藥師在皮膚不良反應中的角色



通報ADR的必要性與價值

通報目的

- 病人安全
- 及早發現藥物風險
- 藥物安全監視
- 法規遵循

通報價值

- 建立藥物安全監測資料庫
- 改善臨床決策
- 教育與研究

何時通報

- 重度ADR
- 新發現或新藥ADR
- 反覆發生或罕見事件
- 其他臨床考量

通報要素

- 病人基本資料
- 藥物資訊（藥名、劑量、使用時間）
- ADR 描述（發生時間、嚴重程度、臨床表現）
- 結果及處理（停藥、治療）

通報迷思

- 不需完全確認因果關係才可通報
- 不需完全排除其他疾病或藥品才可通報
- 輕、中度 ADR 也應通報，尤其是新型、罕見或未上市的藥物
- 完整、具品質的通報都有其價值

藥害救濟基金會
WHO, Pharmacovigilance: Safety Monitoring of Medicinal Products, 2021
CIOMS VI, Reporting Adverse Drug Reactions, 1999
FDA MedWatch, Reporting Adverse Events and Product Problems, 2023

Summary

- 正確評估抗生素相關不良反應可減少嚴重皮膚反應與用藥風險
- 評估工具與檢測方式可輔助臨床判斷，需根據反應型態與時機選擇
- β-lactam 抗生素交叉過敏反應中，R1 側鏈相似性是決定性因素
- Re-challenge 僅限輕微皮膚反應，嚴重皮膚反應應避免再使用
- 藥師在藥物警示、通報、評估與交叉替代藥建議上扮演關鍵角色

Thank you