Severe Cutaneous Adverse Reactions (SCARs): Introduction of Gene-related Hypersensitivity

Hypersensitivity reactions could present with mild symptoms such as skin reactions, and systemic symptoms such as rash, fever and hepatitis; Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are examples of severe cutaneous adverse reactions (SCARs), with mortality rate up to 50%.

Large area ulcers and lesions are common signs of SJS and TEN.

Over 100 drugs have been implicated as possible causes of SJS, TEN and other drug-induced hypersensitivity syndromes, but are essentially confined to a small number of agents.

Main causative drugs of drug-induced hypersensitivity syndrome
- Carbamazepine
- Phenytoin
- Phenobarbital
- Zonisamide
- Lamotrigine
- Allopurinol
- Abacavir
- Nevirapine

Main causative drugs of Stevens–Johnson syndrome
- Sulphonamides
- Oxicam NSAIDs (e.g., piroxicam, meloxicam, tenoxicam)
- Carbamazepine
- Allopurinol
- Aminopenicillins
- Phenotin

Proactive measures were adopted since Sep 2008, requiring mandatory HLA (Human leucocyte antigen)-B*15:02 gene testing performed prior to prescribing Carbamazepine to new patients in HA. The decision was based on (i) High prevalence of allele in Han Chinese; (ii) Recommendation of testing from health authorities and manufacturer; and (iii) High negative predictive value of gene test for Carbamazepine-tolerant patient.

Apart from Carbamazepine and HLA-B*15:02, more recent genomic studies identifying other drug-allele relationships in developing severe cutaneous ADR include: (i) Allopurinol with HLA-B*58:01, (ii) Carbamazepine with HLA-A*31:01 and (iii) Abacavir with HLA-B*57:01.

The Hospital Authority Head Office (HAHO) recently received TWO reports developing severe adverse drug reactions after taking Allopurinol as prescribed in patients tested positive with HLA-B*5801 allele. Meanwhile, as early signs of rash and skin reactions may indicate more serious reactions such as SJS or Allopurinol hypersensitivity syndrome, healthcare professionals are advised to educate patients on early recognition of allergic reactions; on the importance of prompt withdrawal of drug at the first sign of allergic reaction like rash and to seek medical advice particularly when the drug is first prescribed.

Furthermore, healthcare professionals are encouraged to report any severe ADRs via ADR-form in AIRS and to the Department of Health for pharmacovigilance.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevalence of hypersensitivity</th>
<th>Allele associated with hypersensitivity</th>
<th>Prevalence of allele</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>Up to 5% (Mild); Up to 2% (Serious); 1 in 86000 (SJS/TEN)</td>
<td>HLA-B*5801</td>
<td>(Chinese) About 15%; (Korean) 12.2%; (Caucasians) &lt;6%</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>0.01-0.1% (Serious)</td>
<td>HLA-A*3101</td>
<td>(Chinese) 2%; (Japanese) 9%; (America) 10-15%</td>
</tr>
<tr>
<td>Abacavir</td>
<td>5%</td>
<td>HLA-B*5701</td>
<td>(Hong Kong) &gt;15%; (mainland Chinese) &lt;2%</td>
</tr>
</tbody>
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Reports of medication incidents involving known drug allergy (KDA) remains one of the top portions of serious untoward events (SUE) in HA. In 2012 (to November), over 50 cases were reported to AIRS with KDA being highlighted. These cases may involve pitfall in prescribing, dispensing and administration. By grouping these cases, we could study their underlying causes, and suggest some tips to avoid similar incidents happening again.

Aspirin was prescribed to a patient labelled with aspirin allergy

Patient with suspected allergy to Gentamicin was prescribed and given IVI Gentamicin

Panadol® was prescribed and administered to patient with known allergy to Dologesic®

Drug within the same drug group

Patient was administered IMI Ketorolac 30mg with known history of allergy to Brufen®

Patient with known history of allergy to Azithromycin was prescribed Klacid®

Brand product containing drug causing allergy

Augmentin® 1g BD PO was prescribed to a patient with known drug allergy to Penicillin

Panadol® was prescribed and given to a patient with known drug allergy to Dhamol®

Practical tips:
Before initiating any drug order, check Drug Allergy History in CMS. Do NOT administer when the drug allergy information on MAR / prescription is left blank.

Practical tips:
Extra attention may be required for unclear drug name(s), including “free-text entry” highlighted in RED, patient’s own medication and OTC products.

Practical tips:
For urgent case of drug administration, nurse could verify the prescription with pharmacy staff prior to the first dose of administration from ward stock / stock obtained outside pharmacy.

Practical tips:
Beware of cross sensitivity among different drug groups including ward stock items. Refer to the Cross-allergy reference table (available in individual hospital) if necessary.

Drug with possible cross-sensitivity

A patient with drug allergy to Zinacef® was prescribed IV 1.2g Augmentin® and two doses given
**Sharing of effective measures in minimizing medication incidents due to Known Drug Allergy**

**Kowloon East Cluster**

1. Special labels to specify “antibiotics” and “penicillin” group antibiotics

2. Establish an urgent facsimile line for receiving and vetting drug sheet for patients with drug allergy

**New Territories West Cluster**

1. Conspicuous Red Drug Allergy sticker placed immediately above the medication order on one side of the A&E sheet

2. Red button placed on patient’s wrist band for patients with known drug allergy

3. Innovative audio Drug Allergy Alert with a light-sensitive device, activated upon drawer opening for Augmentin® placed inside the Documed night cupboard

我係Augmentin, 屬於Penicillin group, 請小心檢查病人敏感歷史
The Annual Medication Safety Forum 2012, co-organized by Patient Safety & Risk Management Department (PS&RM) and Medication Safety Committee (MSC), had been successfully held on 7th November 2012. About 300 healthcare professionals participated in this meaningful event. The Forum was also incorporated into the Central Commissioned Training Programme by Quality & Safety Division, together with the Hospital Visit and Sharing Session on 6th November, as well as the workshop on Root Cause Analysis (RCA) on 8th November.

The objective of the Forum was to enlighten staff’s knowledge on Medication Reconciliation (MedRec), which is a frequently discussed issue in HA currently. Also, the Forum aimed to increase staff’s awareness on the importance of MedRec for medication safety, and to utilize MedRec as a tool to minimize related medication incidents. (The idea of MedRec was also discussed in MSB Vol. 3)

The organizing parties were honoured to have overseas guest speakers from the Institute for Safe Medication Practices (ISMP) Canada, Ms Margaret Colquhoun (Project Leader) and Ms Donna Walsh (Education Lead), to share their experience and knowledge on MedRec. Since this is a valuable platform to exchange excellent ideas amongst the 7 clusters in HA, cluster representatives were also invited to share their efforts and strategies to enhance medication safety.