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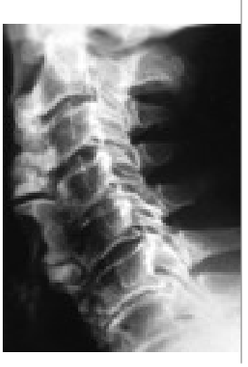

Cover Picture:
Lateral radiograph of the cervical spine radiograph.
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Editorial

Recognizing and Preventing Adverse Drug Reactions: with Particular Reference to Drug Eruptions

H L Chan

Adverse drug reactions (ADRs) are common events. In an analysis of serious ADRs defined as those that required hospitalization, were permanently disabling, or resulted in death, the overall incidence was 6.7% of hospitalized patients[1]. The incidence of fatal ADRs was 0.32% which would make these reactions between the fourth and sixth leading cause of death in 1994 in the United States[1].

Besides increasing the risk of death almost 2-fold in hospitalized patients adverse drug events is also associated with a significantly extended length of stay and increased economic burden[2]. The annual costs attributable to all events from ADRs and preventable ADRs in a 700-bed teaching hospital in the U.S. was estimated to be US$5.6 million and $2.8 million respectively[3].

Although the skin is often involved, it should be realized that ADRs are systemic reactions. An example *par excellence* is anaphylaxis where urticaria may be accompanied by facial edema, bronchospasm, and cardiovascular collapse.

Cutaneous reactions herald many ADRs. They manifest by several recognizable patterns, chief among these are the exanthemas. The next most frequent are the urticarias and the erythema multiforme/Steven's Johnson Syndrome (SJS) spectrum. Other distinctive patterns include photodermatitis, generalized exfoliative dermatitis, fixed drug eruption and toxic epidermal necrolysis.

Exanthematic eruptions are the most frequently seen. They constitute about 40 percent of the total number of drug eruptions seen in adult patients[4]. They are variously described as a toxic erythema or a maculopapular, morbilliform or rubelliform eruption. In some patients urticarial or purpuric elements may be observed. Amoxycillin (ampicillin in the past) is the most common culprit. In children, urticarias and exanthemas are just as frequent[5]. Viral exanthemas are particularly common in infancy and childhood, and there are often confused with drug eruptions. A critical approach to diagnosing cutaneous ADR is necessary[6].

Urticaria is characterized by weals, which are transient and individual lesions do not last more than 24 hours. However, a host of other factors can cause urticaria. A large number of these are idiopathic.

Erythema multiforme (EM) is as common as urticaria in adults. It is characterized by target lesions, typical and atypical[8]. An acral distribution with oro-genital involvement is often seen. When target lesions are typical, a post-infectious cause is the more likely. In EM - associated ADR the targets are usually "atypical". Fixed drug eruptions (FDE) are distinctive as the lesions recur on the same location each time the drug is administered. This is the one reaction which can be safely confirmed by a challenge test

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(in vivo) as there are no reliable in vitro tests. The most common causative drug used to be tetracycline. Now it is Bactrim (R).

Severe reaction patterns include generalized exfoliative dermatitis (GED), Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN). It is particularly important to recognise the early signs indicating when a drug eruption may be serious[7]. These include confluent erythema and skin tenderness, bullae formation and mucous membrane erosions. Fever and a general unwellness indicate a systemic reaction. The signs of anaphylaxis have been alluded to earlier.

Primary preventive measures can reduce the incidence of ADR. Avoid situations of known risk. For example if ampicillin (or amoxicillin) is used in a patient with a Epstein-Barr virus infection, a rash is almost invariable. Therefore, in someone with possible infectious mononucleosis, a different antibiotic may be chosen if one is needed. Investigations should be done and treatment given when there are clear indications for doing so. Rational prescription mandates a careful consideration of the potential benefit versus risk equation.

In no other area of medicine is the adage "prevention is better than cure" more true. Education of public, patients and physician will aid prevention[9,10]. With the completion of the human genome project and advances in pharmacogenetics, it may be possible to predict and prevent adverse events in susceptible subjects. Secondary prevention is even more important, as there might be medico-legal consequences for not doing so. For certain drug groups such as sulphonamides and anticonvulsants there is evidence that family members of patients with a positive drug allergy history has possible added risk to administration of the same drugs.

Patients who were affected by previous ADRs should have case-records clearly flagged. Community alert systems e.g. Medik Awas may be organized; patients carry a card or a bracelet or necklace with the relevant information. Some hospitals have developed computer surveillance to alert doctors and pharmacists of patients with known drug allergy. Has drug desensitisation any role in modern therapy? This was done for penicillin to treat infective endocarditis. This is now rarely necessary. We have done it when the drug is essential and when the potential benefit outweighs the risks.

ADRs are distressing to both patient and physician. When more effective and potent drugs are being developed it is inevitable in modern day practice. However, it is incumbent on us as physicians to weigh the benefits and risks of each and every therapeutic decision carefully. We need to be alert to potential adverse events and to recognise them early. Better still, if we can we should prevent them from happening. To paraphrase Beaumont and Fletcher (Love's Cure, 1647) the medicine can be worse than the malady! SMJ

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