

## Clinical Manifestation of Drug Allergy in Children

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**ABSTRACT.** In the period of January-December 18 cases of Drug Allergy were recognized, 4 cases from the allergy clinic, 8 cases were referred from outpatient clinic, 6 cases were referred from inpatient ward. The clinical manifestation varied from urticaria 5 cases (30%), Steven Johnson Syndrome 2 cases (12%), maculopapular rash 2 cases (12%), Drug fever 2 cases (12%), Fixed drug eruption 1 case (6%), exanthem 1 case (6%), Quinke's edema 5 cases (30%) consisted of 2 cases Quinke's edema only, 2 cases with urticaria, 1 case with drug fever. The underlying disease of these cases were upper respiratory tract infection 5 cases, chronic cough 2 cases, Asthma 5 cases, diarrhea 1 case cerebral abscess 1 case, Dengue Haemorrhagic Fever 1 case and Epilepsi 1 case. The mainstay of treatment was discontinuation of the offending drug. Drug substitution were given to patients necessitated continuation of drugs, antihistamines were given to patients with urticaria and Quinke's edema. Two cases with Steven Johnson syndrome received supportive treatment and hydrocortison intravenously. [*Paediatr Indones* 1999; 39:325-329]

### Introduction

It was recently estimated that the incidence of drug Allergy is increasing. As many as 0.01% to 5% of this event were reported all over the world and that a minimum of 15%-30% of hospitalized patients experience at least one drug reaction.<sup>1,2</sup> Fortunately most adverse reactions are minor and life threatening reaction are unusual. Allergic drug reactions make up 6 to 10 percent of all adverse reaction to drug.<sup>3</sup> Surprisingly little is known about the incidence of allergic reactions to individual drugs.<sup>4</sup> One of the few exceptions to this statement is penicillin, which is universally considered the most frequent cause of anaphylactic reactions. Drug allergy in children most commonly

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manifest itself in the skin, and urticaria usually account for the majority of cases. The purpose of this study is to observe the clinical manifestation of drug allergy in children on the basis of clinical criteria for drug allergy.

### Methods

The period of study was from January 1998-December 1998, patients were recruited from Allergy clinic, Pediatric outpatients clinic and inpatients ward. The clinical criteria for drug allergy were applied to establish the diagnosis.<sup>5</sup> The criteria is as follow:

1. The observed manifestations do not resemble the pharmacological action of the drug.
2. The reactions are generally similar to those which may occur with other allergens.
3. An induction period, commonly 7-10 days is required following initial exposure to the drug.
4. The reaction may be reproduced by minute doses of the drug.
5. The reaction may be reproduced by cross reacting chemical structures.
6. Blood and/or tissue eosinophilia may be present.
7. Discontinuation of the drug results in resolution of the reaction.
8. The reaction occurs in a minority of patients receiving the drug.

Positive score of 4 criteria or more justify the diagnosis of drug allergy. Clinical manifestation were described from the author observation and patients record for the resolved signs. The offending drug was estimated from the following, criteria.<sup>6</sup>

1. Multiple experiences by patient or parents.
2. Close relation between administration of the drug and symptom after considerable induction period.
3. Drug that is easily suspected of clinical reaction patterns.

### Results

During the period of January-December 1998, 18 cases of drug allergy fulfilled the criteria of drug allergy in this study: 8 patients were female and 10 patients were male aged between 3 months to 14 years. Table 1.

Urticaria and Quinke's edema accounted for the vast majority symptom in these patients. Three patients with Quinke's edema presented in combination with urticaria, the rest of two was solely presented Quinke's edema. Fever was the only systemic symptoms recognized in these patients. The underlying disease related to these symptoms are listed in Table 2.

Table 1. Age and sex distribution

Age (year)	Female	Male
0-1	1	1
1-3	2	2
3-5	2	3
5-10	1	1
>10	2	3
Total	8	10

Table 2. The relationship of presenting symptoms of Drug Allergy and the underlying disease

Symptom of drug allergy	n	Underlying disease	n
Urticaria	5	URI	2
		Epilepsi	1
		Asthma	2
Quinkes' edema+urticaria	3	Asthma	2
		Chronic cough	1
Quinkes' edema	1	Asthma	1
Quinkes' edema+Fever	1	DHF	1
Steven Johnson syndrome	2	URI	2
Fixed drug eruption	1	Chronic cough	1
Exanthema	1	Cerebral abscess	1
Maculo Popular Rash	2	URI	1
Drug Fever	1	Diarrhea	1

Drug estimated as the offending drug are listed in Table 3.

### Discussion

The diagnosis of drug allergy in this study is fully based on history and physical appearance. We believe there are few diagnostic test that can be of assistance in a drug reaction, particularly when multiple drugs are being employed. A high index of suspicion and a through history, detailing exposure to all drugs should be mandatory especially for any skin reactions.

Table 3. The offending drugs

Symptoms of Drug Allergy	The offending drugs	N
Urticaria	Codein	1
	Phenitoin	1
	Sulfa	3
Quinke's edema	Spiramycin	1
	Sulfa	1
Quinkes's edema+urticaria	Sulfa	3
Quinkes's edema+Fever	Claforan	1
Steven Johnson Syndrome	Acetyl Salicylic Acid	1
	Paracetamol	1
Fixed drug eruption	Sulfa	1
Exanthem	Chloramphenicol	1
Maculo papular rash	Amoxicillin	1
	Ibuprofen	1
Drug fever	Ampicillin	1

In this study, all drugs given to the patients, except ampicillin to patient suffer from cerebral abscess, were discontinued. Ideally, improvement following withdrawal of the drug and flare on re-exposure to the drug is the most convincing diagnostic test, but it is unsuitable for most severe forms of drug eruption.<sup>6</sup> From the literature we can find that patch testing has been usefully employed in some of the exanthematous reactions, but it has its pitfalls as a greater than 50% false negative rate. The macrophage migration inhibition factor test and the lymphocyte toxicity assay may be useful in some severe immunologically based reactions. RAST tests are of limited value for penicillin allergy. Intradermal or pick tests are useful for subsequent investigation of allergic reactions developing during general anesthesia.<sup>6</sup>

The other question may arise here is, that some symptoms may be the part of the symptoms of the underlying disease. For example in this case, fever may be the symptom of diarrhea and dengue haemorrhagic fever. Indeed it is troublesome but if fever still present outside the course of the disease, while the other symptoms has resolved, hematologic and other laboratory findings were normal, discontinuation of suspected drug result in improvement of symptom, the sequence of event would lead us to believe that drug allergy exists.

The most symptom accounted for in this study is urticaria, as solitair symptom in

5 cases and in combination with Quinke's edema in 3 cases. Urticaria is the most common manifestation of drug allergy, although similar appearances may result from non allergic mechanism, for example the reaction to codein which is believe to be a direct chemical effect to the liberation of histamin from mast cell.

The most potentially life threatening condition in this series is our patients with Steven Johnson syndrome. Widespread skin and mucous membrane involvement in these patients may lead to fluid loss and difficulty of food and fluid intake. Therefore supportive treatment with intravenous fluid and hydrocortison were given to these patients. Fixed drug eruption is so called because the lesion recurs at the same site after each administration of the causative drug, in this case is sulfamethoxazol.

The diagnosis is supported by the past history of multiple experiences with the same drug. Childhood exanthems are more likely to be infection in origin but drugs may be also implicated. Rashes usually identical to those seen in measles, and rubella in this case can be caused by Ampicillin and chloramphenicol treatment for his cerebral abscess, and cessation of the drugs may be the only way of confirming the diagnosis. Chloramphenicol was highly suspected in this patient and the cessation of this drug resulted improvement of the skin lesion.

Maculopapular rash is very common reaction in sensitive patient receiving ampicillin. Similar rashes may be seen as a reaction to a wide range of drugs including ibuprofen and amoxicillin. Other skin reactions such as lichenoid reaction, exfoliative dermatitis, photosensitivity, vasculitis, erythema nodosum, toxic epidermal necrolysis, bullous drug eruption must be born in mind to cope the possibility of drug reactions.

## References

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