Drug Eruptions at Five Institutes in Bangkok

Siripen Puavilai MD*, Nopadon Noppakun MD**,
Chasuree Sitakalin MD***, Vichit Leenutaphong MD****,
Penpun Wattanakrai MD*, Artit Nakakes MD***,
Kanokvalai Kulthanan MD****, Pravit Asawanonda MD**,
Ratsanee Akaraphan MD*****, Poohglin Tresukosol MD*****,
Puan Suthipinittharm MD****, Pitchaya Somburanasin MD*,
Somyos Charuwichitratana MD*, Natta Rajatanavin MD*

** Division of Dermatology, Department of Medicine, Ramathibodi Hospital Medical School, Mahidol University*
*** Division of Dermatology, Department of Medicine, Chulalongkorn University*
**** Division of Dermatology, Department of Medicine, Phramongkutklao Hospital and Medical College*
***** Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University*
****** Institute of Dermatology, Department of Medical Services, Ministry of Public Health*

The study was performed in five hospitals in Bangkok for a period of one year. All in- and outpatients who developed drug eruption from January to December 2001 were enrolled into the study. Physical examinations and complete history-taking were performed by one of the authors. A skin biopsy was done to confirm the diagnosis in every suspected case. Oral challenge test was performed to obtain a definite diagnosis only in some patients with informed consent.

Among 212 patients, the most common causative drugs were antimicrobial agents with cephalosporin group in the highest rank. Maculopapular rash was the most common type of drug eruption followed by urticaria and photosensitivity reaction.

It was concluded that antimicrobial agents were the predominant causative agents and maculopapular eruption was the most frequent clinical manifestation. New kinds of antimicrobial agents, anti-inflammatory drugs and lipid lowering agents could cause various patterns of drug eruption.

Keywords: *Drug eruption, Maculopapular rash, Antimicrobial agents*

J Med Assoc Thai 2005; 88 (11): 1642-50
Full text. e-Journal: *http://www.medassocthai.org/journal*

Adverse cutaneous drug reactions are common medical problems; they vary from mild to severe reactions with other organ involvement. As new drugs are released cutaneous reactions are more frequently detected. There are many risk factors for cutaneous drug reactions such as genetic susceptibility[1], immunosuppression, connective tissue disease[2], HIV infection[3,4]. Some of the reactions are preventable[3]. The aims of this study were 1) to evaluate the various clinical types of cutaneous drug eruptions 2) to identify the causative drugs 3) to analyze patients' characteristics including demographic data, previous history of drug eruptions and previous history of atopic diseases. 4) to study the changing trend of drug eruptions (if any) from previous reports due to more prescriptions of some drugs such as lipid lowering agents, nonsteroidal anti-inflammatory agents, etc.

Correspondence to : Puavilai S, Division of Dermatology, Department of Medicine, Ramathibodi Hospital Medical School, Mahidol University, Bangkok 10400, Thailand. Phone: 0-2201-1141, 0-2201-1686

Material and Method

The present study was performed at five hospitals in Bangkok: Ramathibodi Hospital Medical School, Chulalongkorn Hospital Medical School, Pramongkutklao Hospital Medical School, Siriraj Hospital Medical School and Institute of Dermatology. Data of all inpatients and outpatients diagnosed with cutaneous drug eruptions from January to December 2001

were collected. Physical examinations were performed and standardized questionnaires were completed by one of the authors. The algorithm described by Kramer et al[5] was used for assessment of the causative agents. A skin biopsy was performed in every suspected case to confirm the diagnosis. The present study was approved by the ethical committees of the five hospitals.

The criteria for diagnosis were set as follows:

1. The clinical manifestation was well accepted as adverse drug reaction to the suspected drug.
2. There was no other good alternative candidate that caused the skin lesion; the eruption was not the exacerbation or recurrence of the underlying illness.
3. Timing was as expected for adverse drug reaction of suspected medication.
4. Drug level or other data to confirm that the eruption was not from drug overdose.
5. Clinical manifestations improved suitably after dechallenge.
6. The eruption occurred after rechallenge of the suspected drug.

The inclusion criteria for the rechallenge test were as follows:

1. Benign form of cutaneous drug reaction, such as maculopapular eruption, fixed drug eruption, phototoxic or photoallergic eruption, generalized examthematous pustular eruption, lichenoid drug eruption.
2. Informed consent of the patients.
3. No pregnancy and no breast feeding.
4. No chronic or severe underlying disease, including HIV infection.
5. No allergic reaction to penicillin.
6. Age of each patient not less than 15 years.

For the present study, all patients were told to stop all the medications that they were taking within one month of drug eruptions. The rechallenge test was performed 4-6 weeks after the skin lesions had completely resolved. The most likely suspicious drug would be tested first. The test dose was one therapeutic dose of the suspected drug and one week was allowed for the reaction to develop. If no reaction occurred, the other suspected drugs would be challenged sequentially until the eruption appeared.

For definite diagnosis, all of the six mentioned criteria should be fulfilled, for probable diagnosis, 4 to 5 criteria should be obtained; and, for possible diagnosis, 1 to 3 criteria should be identified.

Results

Two hundred and twelve patients were included in the present study during a one year period. Seventy-nine (37.3%) were men, 133 (62.7%) were women and their mean age was 46.98 $\pm$ 19.23 years (range, 2 to 89 years). Forty-five patients (21.2%) had a previous history of drug reactions. Twenty-nine patients (13.7%) had a history of atopic diathesis. Sixty-four patients (30.2%) had received only one medication before the eruption occurred. One hundred and twenty-nine patients (60.8%) took multiple drugs before the appearance of drug reactions. Most of the patients (68.8%) received their medication from the five hospitals in the study (Table 1). A skin biopsy was performed in 14 patients (6.6%) to confirm the diagnosis of drug eruption.

The definite diagnosis of drug eruption was given in 6 patients (2.8%) (Table 2); a probable diagnosis was made in 73 patients (34.4%) (Table 3) and a possible diagnosis was made in 133 patients (62.7%) (Table 4).

Table 1. Sources of medications that the patients obtained

Sources	No. of the patients	Percent of the patients
Five hospitals in this study	132	62.3
Other hospitals	32	15.1
Drug stores	10	4.7
Clinics	9	4.2
Other sources	7	3.3
Five hospitals in this study plus clinics	1	0.5
Five hospitals in this study plus other sources	1	0.5
Unknown	20	9.4
Total	212	100.0

Table 2. Definite causes of drug eruptions confirmed by oral rechallenge in 6 patients

Type of drug eruption	Causative drug (number of patients with positive test)	
Maculopapular	Insulin (1) Metronidazole (1) Phenytoin (1)	Tramadol (1) Trimethoprim-sulfamethoxazole (1)
Fixed drug	Trimethoprim-sulfamelthoxazole (1)	

Table 3. Probable causes of drug eruptions in 73 patients

Type of drug eruption	Causative drug (number of patients)	
Maculopapular	Ceftriazone (7) Trimethoprim-sulfamethoxazole (5) Celecoxib (4) Imipenem+cilastatin (4) Phenytoin (4) Amphotericin B (3) Griseofulvin (3) Metronidazole (3) Sulindac (3) Cefalexin (2) Ceftazidime (2) Clindamycin (2) Cloxacillin (2) Doxycycline (2) Phenobarbital (2) Propylthiouracil (2) Roaccutane (2) Acyclovir (1) Amoxicillin (1) Amoxicillin + Clavulanate (1) Artane (1) Atenolol (1) Azithromycin (1) Carbamazepine (1) Cefazolin (1) Cefotaxime (1) Cetirizine (1) Ciprofloxacin (1) Clonazepam (1) Colchicine (1) Diflunisal (1)	Diltiazem (1) Dipotassium clorazepate (1) Eperisone (1) Ethambutol (1) Famciclovir (1) Felodipine (1) Floctafenine (1) Fosfomycin (1) Gentamicin (1) Hydrochlorothiazide (1) Hydroxyzine (1) Ibuprofen (1) Isoniazid (1) Itraconazole (1) Ketoconazole (1) Lornoxicam (1) Meropenem (1) Metformin (1) Methazolamide (1) Netilmicin (1) Nicotinamide (1) Orphenadrine citrate + Paracetamol (1) Piroxicam (1) Pyrazinamide (1) Quinine (1) Radiocontrast media (1) Rifampicin (1) Roxithromycin (1) Simvastatin (1) Sulbactam + Cefoperazone (1)
Urticaria	Ampicillin (1) Cefoxitin (1) Celecoxib (1) Cetirizine (1) Enoxaparin (1) Fenofibrate (1) Griseofulvin (1) Mefenamic acid (1)	Minocycline (1) Ofloxacin (1) Orphenadrine citrate (1) Pyrazinamide (1) Simvastatin (1) Tramadol (1) Trimethoprim-Sulfamethoxazole (1)

Table 3. (cont.)

Type of drug eruption	Causative drug (number of patients)	
Exfoliative dermatitis	Metformin (2) Diazepam (1) Doxazosin (1) Ethambutol (1) Isoniazid (1) Omeprazole (1)	Paracetamol (1) Phenobarbital (1) Phenytoin (1) Pyrazinamide (1) Radiocontrast media (1) Rifampicin (1)
Photosensitivity	Atenolol (2) Fenofibrate (1) Hydrochlorothiazide (1) Piroxicam (1)	Simvastatin (1) Tetracycline (1) Vitamin $B_{1,6,12}$ (1)
Eczematous	Cloxacillin (1) Erythromycin (1) Ketoconazole (1)	Levonorgestrel + Ethinylestradiol (1) Metformin (1) Phenobarbital (1)
Erythema multiforme	Amphotericin B (1) Nevirapine (1) Phenobarbital (1)	Phenytoin (1) Simvastatin (1) Vancomycin (1)
Fixed drug	Trimethroprim-sulfamethoxazole (2) Cloxacillin (1) Indapamide (1)	Lidocaine (1) Sulindac (1)
Stevens-Johnson Syndrome	Trimethoprim-sulfamethoxazole (2) Amoxicillin + Clavulanate (1) Doxycycline (1)	Phenytoin (1) Sulindac (1)
Acute generalized exanthematous pustulosis	Amoxicillin + Clavulanate (1) Ceftazidime (1)	Ceftriazone (1) Clindamycin (1)
Acneiform	Dexamethasone (1)	Isoniazid (1)
Angioedema	Minocycline (1)	Ofloxacin (1)
Bullous	Cloxacillin (1)	Erythromycin (1)
Hyperpigmentation	Aldactone (1)	Furosemide (1)
Lichenoid	Allopurinol (1)	Chlorpropamide (1)
Drug hypersensitivity syndrome	Phenytoin (1)	
Toxic epidermal necrolysis	Ibuprofen (1)	
Leukocytoclastic vasculitis	Ofloxacin (1)	

The three most common causative drugs were antimicrobial agents (50% of cases), antipyretic/anti-inflammatory agents (14.8%) and drugs acting on the central nervous system (10.6%) (Table 5). The most common type of drug eruptions was maculopapular eruption (55.4%) followed by urticaria (8.3%) and photosensitivity (6.4%) (Table 6). Itch was the predominant symptom occurring in 89.8% of patients who

Table 4. Possible causes of drug eruptions in 133 patients

Type of drug eruption	Causative drug (number of patients)	
Maculopapular	Trimethoprim-sulfamethoxazole (5)	Ceftriazone (1)
	Amoxicillin (4)	Diphenhydramine (1)
	Clindamycin (3)	Ethambutol (1)
	Amphotericin B (2)	Floctafenine (1)
	Aspirin (2)	Fresh frozen plasma (1)
	Baclofen (2)	Gentamicin (1)
	Dapsone (2)	Granulocyte colony stimulating factor (1)
	Fluconazole (2)	Hydrochlorothiazide (1)
	Ibuprofen (2)	Hydroxychloroquine (1)
	Naproxen (2)	Imipenem (1)
	Phenytoin (2)	Imipenem + Cilastatin (1)
	Acetaminophen (1)	Isoniazid (1)
	Alfuzosin (1)	Itraconazole (1)
	Allopurinol (1)	Nifedipine (1)
	Amikacin (1)	Ofloxacin (1)
	Amiodarone (1)	Orphenadrine citrate + Paracetamol (1)
	Amitriptyline (1)	Penicillin (1)
	Amoxicillin + Clavulanate (1)	Phenobarbital (1)
	Azathioprine (1)	Piroxicam (1)
	Bromhexine (1)	Piracetam (1)
	Budesonide (1)	Primaquine (1)
	Carbamazepine (1)	Pyrazinamide (1)
	Cefazolin (1)	Ranitidine (1)
	Cefuroxime (1)	Serratiopeptidase (1)
	Cloxacillin (1)	Sulindac (1)
	Diclofenac (1)	Terbutaline (1)
	Diosmin + Hesperidin (1)	Tolperisone (1)
		Tramadol (1)
Photosensitivity	Fenofibrate (2)	Griseofulvin (1)
	Hydrochlorothiazide (2)	Metformin (1)
	Cloxacillin (1)	Penicillin (1)
	Gemfibrozil (1)	Tetracycline (1)
	Glibenclamide (1)	Trimethoprim-sulfamethoxazole (1)
Urticaria	Amitriptyline (1)	Haloperidol (1)
	Artane (1)	Ibuprofen (1)
	Cefalexin (1)	Indomethacin (1)
	Cinnarizine (1)	Lorazepam (1)
	Dipotassium chlorazepate (1)	Paracetamol + Chlorpheniramine maleate (1)
	Fenofibrate (1)	
Eczematous	Amoxicillin (1)	Hydrochlorothiazide (1)
	Celecoxib (1)	Paracetamol (1)
	Cloxacillin (1)	Pseudoephedrine (1)
Exfoliative dermatitis	Amoxicillin (2)	Penicillin (1)
	Allopurinol (1)	Tolperisone (1)
	Ciprofloxacin (1)	
Lichenoid	Atorvastatin (1)	Isoniazid (1)
	Ethambutol (1)	Pyrazinamide (1)
	Hydroxyurea (1)	Rifampicin (1)

Table 4. (cont.)

Type of drug eruption	Causative drug (number of patients)	
Fixed drug	Amoxicillin + Clavulanate (1) Bromocriptine (1)	Interferon α-2b (1) Paracetamol (1)
Stevens-Johnson syndrome	Cefdinir (1) Cefaclor (1)	Naproxen (1) Trimethoprim-sulfamethoxazole (1)
Toxic epidermal necrolysis	Levofloxacin (1) Metronidazole (1)	Trimethoprim-sulfamethoxazole (1) Vancomycin (1)
Erythema multiforme	Ceftazidime (1) Floctafenine (1)	Piroxicam (1)
Leukocytoclastic vasculitis	Zidovudine (1) Didanosine (1)	Ritonavir (1)
Hyperpigmentation Ulcerative stomatitis medicamentosa	Methazolamide (1) Fexofenadine (1)	

Table 5. Group of drugs that caused skin lesions

Causative drugs	Percentage of the patients with drug eruption
Antimicrobial agents	50.0 %
Antipyretic/anti-inflammatory agents	14.8 %
Drugs acting on the central nervoussystem	10.6 %
Drugs acting on cardiovascular system	5.2 %
Antihyperlipidaemic agents	3.9 %
Antidiabetic agents	2.6 %
Antihistamines	1.9 %
Others	11.0 %

Table 6. Clinical type of drug eruption

Clinical type	Percentage of the patients with drug eruption
Maculopapular	55.2 %
Urticaria	8.5 %
Photosensitivity	6.6 %
Exfoliative dermatitis	6.1 %
Eczematous	3.8 %
Fixed drug	3.3 %
Stevens-Johnson syndrome	3.3 %
Erythema multiforme	2.8 %
Lichenoid	2.4 %
Toxic epidermal necrolysis	1.9 %
Acneiform	1.4 %
Acute generalized exanthematous pustulosis	1.4 %
Vasculitis	1.4 %
Hyperpigmentation	0.9 %
Aphthous stomatitis	0.5 %
Hypertrichosis	0.5 %

had maculopapular eruption. The mean duration of drug eruption of all types was 10.25 $\pm$ 7.76 days (range, 1-60 days). No serious complications were detected in these patients.

Discussion

In the present study females outnumbered males (ratio F:M = 1.7:1) in the development of cutaneous drug reaction. It is still controversial whether women are more susceptible to drug eruptions than men[3,6]. In the present study a relatively high percentage of patients (21.2%) had a previous history of drug reaction. So, it is recommended that the patients should carry a card containing data about the causative drugs and type of reactions. The history of atopic diathesis should also be considered before administration of high risk drugs because many patients (13.7%) in the present study had a history of atopic diseases. A high percentage of the presented patients (60.8%) had received multiple drugs before the eruption occurred. Drug interaction might play a role for drug eruption in some of these patients. It was difficult to determine the definite

causative drug in this group of patients without any rechallenge test. Unfortunately, only six patients agreed to oral rechallenge test. Other patients were categorized into probable and possible cause of drug eruptions. The other problem in Thailand is that sometimes the authors could not identify the name of the drugs prescribed from the clinics or some other hospitals. All the physicians and pharmacists should be responsible for written names of the drugs for all patients. The Ministry of Public Health should regulate a rule for the drug manufacturers to print code numbers on the tablets and should distribute booklets for identifying the code number of drugs to the physicians and pharmacists all over the country.

Antimicrobial agents represented the most common cause of drug eruptions similar to published studies[3,7-11]. Cephalosporins were the most common antimicrobial agents responsible for drug eruptions, followed by co-trimoxazole and amoxicillin respectively. This might be due to the many new generations of cephalosporin released into the market. The second most common cause of drug eruption was caused by antipyretic anti-inflammatory agents; in this group celecoxib and sulindac were the two most common causative drugs. The third most common group consisted of drugs acting on the central nervous system; in this group, phenytoin was the most common causative agent followed by phenobarbital.

The most common clinical manifestation of drug eruption was maculopapular eruption which is in agreement with previous studies[7-9]. The second and third most common types of drug eruption were urticaria and photosensitivity. It was interesting to have found that photosensitivity was more frequent than fixed drug eruption, Stevens-Johnson syndrome or erythema multiforme as reported previously[7,8]. This might be related to more frequent prescriptions of lipid lowering agents (a common cause of photosensitivity). For Stevens-Johnson syndrome and toxic epidermal necrolysis which are the severe forms of drug eruptions, trimethoprim-sulfamethoxazole was the most common drug responsible for these eruptions; in published reports, this drug was also recognized as one of the most common causative agents for these eruptions[12,13]. An interesting finding in the present study was toxic epidermal necrolysis from levofloxacin, rarely reported in the literature[14]. Furthermore, in the present study it was found that cetirizine and hydroxyzine caused maculopapular eruption, and cetirizine also caused urticaria. Drug eruptions from these two medications were rarely reported: only 7 cases of drug eruption from cetirizine and 10 cases from hydroxyzine. These eruptions varied from maculopapular rash to urticaria and fixed drug eruption[15-22]. One patient was reported to have morbilliform eruption from both cetirizine and hydroxyzine[22].

In the present study, it was found that the trend of drug eruptions was different to that of previous reports[7,8]. A new generation of antibiotics especially cephalosporin group has replaced penicillin group as the most common cause of drug eruption. Among the anti pyretic/anti-inflammatory agents, celcoxib (newly released within the past few years) has become the most common causative drug. Lipid lowering agents, widely prescribed nowadays, also played an important role in causing photosensitivity reaction.

In conclusion, the authors found that antimicrobial agents were the most common cause of drug eruption, with cephalosporin group being the most frequent antimicrobial agent responsible for cutaneous drug reaction. The most common clinical manifestation of drug eruption was maculopapular eruption, followed by urticaria and photosensitivity.

Acknowledgement

The authors wish to thank Ms. Suwannee Chanprasertyothin for the data analysis.

References

1. Roujeau JC, Huynh TN, Bracq C, Guillaume JC, Revuz J, Touraine R. Genetic susceptibility to toxic epidermal necrolysis. Arch Dermatol 1987; 123: 1171-3.
2. Katz J. Marmary Y, Livneh A, Danon Y. Drug allergy in Sjogren's syndrome. Lancet 1991; 337: 239.
3. Fiszenson-Albala F, Auzerie V, Mahe E, Farrinotti R, Durand-Stocco C, Crickx B, et al. A 6-month prospective survey of cutaneous drug reactions in a hospital setting. Br J Dermatol 2003; 149: 1018-22.
4. Coopman SA, Johnson RA, Platt R, Stern RS. Cutaneous disease and drug reactions in HIV infection. N Engl J Med 1993; 328: 1670-4.
5. Kramer MS, Leventhal JM, Hutchinson TA, Feinstein AR. An algorithm for the operational assessment of adverse drug rections. 1. Background, description and instruction for use. JAMA 1979; 242: 623-32.
6. Rademaker M. Do women have more adverse drug reaction? Am J Clin Dermatol 2001; 2: 349-51.
7. Puavilai S, Choonhakarn C. Drug eruptions in Bangkok: a 1-year study at Ramathibodi Hospital.

Int J Dermatol 1998; 37: 747-51.
8. Puavilai S, Kamtavee S, Chunharas A, Pongwiriyapasich S. Drug eruptions: The value of oral rechallenge test and patch test. J Med Assoc Thai 2002; 85: 263-9.
9. Sharma VK, Dhar S. Clinical pattern of cutaneous drug eruption among children and adolescents in north India. Pediatr Dermatol 1995; 12: 178-83.
10. Stubb S, Heikkila H, Kauppinen K. Cutaneous reactions to drugs. A series of in-patients during a five-year period. Acta Dermatol Venereol (Stockh) 1994; 74: 289-91.
11. Bigby M. Rates of cutaneous reactions to drugs. Arch Dermatol 2001; 137: 765-70.
12. Guillaume JC, Roujeau JC, Revuz J, Penso D, Touraine R. The culprit drugs in 87 cases of toxic epidermal necrolysis (Lyell' syndrome). Arch Dermatol 1987; 123: 1166-70.
13. Roujeau JC, Kelly JP, Naldi L, Rzany B, Stern RS, Anderson T, et al, Medication use and the risk of Stevens-Johnson syndrome or toxic epidermal necrolysis. New Engl J Med 1995; 333: 1600-7.
14. Digwood-Lettieri S, Reilly KJ, Haith Jr LR, Patton ML, Guilday RJ, Cawley M J, et al. Levofloxacin-induced toxic epidermal necrolysis in an elderly patient. Pharmacotherapy 2002; 22: 789-93.
15. Stingeni L, Caraffini S, Agostinelli D, Ricci F, Lisi P. Maculopapular and urticarial eruption from cetrizine. Contact Dermatitis 1997; 37: 249-50.
16. Ash S, Scheman AJ. Systemic contact dermatitis to hydroxyzine. Am J Contact Dermat 1997; 8: 2-5.
17. Michel M, Dompmartin A, Louvet S, Szczurko C, Castel B, Leroy D. Skin reactions to hydroxyzine. Contact Dermatitis 1997; 36: 147-9.
18. Karamfilov T, Wilmer A, Hipler UC, Wollina U. Cetirizine - induced urticarial reaction. Br J Dermatol 1999; 140: 979-80.
19. Kranke B, Kern T. Multilocalized fixed drug eruption to the antihistamine cetirizine. J Allergy Clin Immunol 2001; 106: 988.
20. Calista D, Schianchi S, Morri M. Urticaria induced by cetirizine. Br J Dermatol 2001; 144: 196.
21. Schroter S, Damveld B, Marsch WC. Urticarial intolerance reaction to cetirizine. Clin Exp Dermatol 2002; 27: 185-7.
22. Leu BL, Haw CR, Lee MH. Cutaneous drug eruption from cetirizine and hydroxyzine. J Am Acad Dermatol 2004; 50: 953-6.

การศึกษาผื่นแพ้ยาในโรงพยาบาล 5 แห่ง ในกรุงเทพมหานคร

ศิริเพ็ญ พัววิไล, นภดล นพคุณ, ชสุรี สีตกะลิน, วิชิต ลีนุตพงษ์, เพ็ญพรรณ วัฒนไกร, อาทิตย์ นาคะเกตุ, กนกวลัย กุลทนันทน์, ประวิตร อัศวานนท์, รัศนี อัครพันธุ์, พู่กลิ่น ตรีสุโกศล, ป่วน สุทธิพินิจธรรม, พิชญ สมบูรณสิน, สมยศ จารุวิจิตรรัตนา, ณัฏฐา รัชตะนาวิน

คณะผู้วิจัยได้ทำการศึกษาผู้ป่วยที่เป็นผื่นแพ้ยาทั้งผู้ป่วยนอกและผู้ป่วยในของโรงพยาบาล 5 แห่งในกรุงเทพมหานคร ระหว่างเดือนมกราคม ถึง ธันวาคม พ.ศ. 2544 ผู้ป่วยทุกรายได้รับการซักประวัติ และตรวจ ร่างกาย และตัดชิ้นเนื้อไปตรวจในกรณีที่มีปัญหาในการวินิจฉัย ผู้ป่วยบางรายที่เซ็นใบอนุญาตยินยอมจะได้รับการทดสอบโดยให้ผู้ป่วยรับประทานยาที่สงสัยเพื่อให้ทราบแน่นอนว่าแพ้ยาชนิดนั้นจริง

จากจำนวนผู้ป่วยที่ศึกษาทั้งหมด 212 ราย พบว่ายาปฏิชีวนะเป็นสาเหตุของผื่นแพ้ยาที่พบบ่อยที่สุด โดยพบว่าเป็นจากยากลุ่ม cephalosporin มากที่สุด ผื่นแพ้ยาที่พบบ่อยที่สุด คือผื่น maculopapular รองลงมาเป็นลมพิษและผื่นที่เกิดจากการแพ้แสงแดด

ผลการศึกษาสรุปได้ว่า ยาปฏิชีวนะเป็นสาเหตุที่พบบ่อยที่สุด และพบผื่นแบบ maculopapular มากที่สุด ยาปฏิชีวนะชนิดใหม่ ๆ รวมทั้งยาลดการอักเสบ และยาลดไขมันชนิดใหม่ ๆ ทำให้เกิดผื่นแพ้ยาได้หลายแบบ