# The Thai Anesthesia Incidents Study (THAI Study) of Perioperative Allergic Reactions

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***Objectives:*** *To determine the incidence, risk factors, signs, symptoms and management of perioperative allergic reactions in the Thai Anesthesia Incidents Study (THAI Study).*
***Material and Method:*** *Between February 1, 2003, and January 31, 2004, a descriptive, prospective, multicenter study was conducted in 20 hospitals across Thailand. All patients receiving anesthetic and medical agents were monitored for allergic reactions for the first 24 postoperative-hours. Signs and symptoms of suspected allergic reactions included skin reactions, wheezing and unexpected hypotension. The details of allergic reactions were reviewed and recorded.*
***Results:*** *Allergic reactions occurred in 30 of the 163,403 patients included in this study. The reaction-incidence was approximately 1 in 5,500 cases of anesthesia. Forty-eight percent of the affected patients had a history of allergic reactions. The manifestations were skin reactions, hypotension and wheezing in 38, 22 and 19 percent of the overall symptoms, respectively. Reactions were mild, moderate and severe in 40, 23 and 37 percent of the patients, respectively. The three drugs most suspected of causing the reaction(s) were antibiotics (19%), muscle relaxants (17%) and propofol (15%). All of the affected patients recovered after treatment including the one who suffered cardiac arrest because of the allergic reaction.*
***Conclusion:*** *The incidence of perioperative allergic reactions was 1 in 5,500 cases of anesthesia. History of allergies was obtained from half of the patients and the most common sign was a skin reaction. The drugs most suspected of causing an allergic reaction were antibiotics. All of the patients responded well to rescue treatment.*

***Keywords****: Allergic reactions, Anesthetic agents, Perioperative, Multicenter study*

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Having any kind of allergic reaction during anesthesia represents a potential crisis. However, the incidence of allergic reaction during anesthesia is not well documented. Data from previous studies shows that reaction-incidence ranges between 1 in 6,000 and 20,000 cases of anesthesia in Norway [1] and Australia [2], respectively. Reaction severity varies from mild to severe including death [3, 4]. The incidence of a severe reaction is reported between 1 in 10˚000 and 25˚000 cases of anesthesia with mortality being between 3.4 and 6 percent [5] . Taking a history of allergies prior to anesthesia is routinely practiced; unfortunately, such histories are unreliable for predicting the severity of a reaction [6] .

Except for a few case reports [7-9] , the incidence of allergic reactions in Thailand has not been quantified. Our objectives, therefore, were to determine the incidence, causes, signs, symptoms and management of perioperative allergic reactions in the Thai population.

## Material and Method

The Thai Anesthesia Incidents Study (THAI Study) is a multi-center study comprising 20 hospitals: 7 university, 5 tertiary-, 4 secondary-and 4 primary-

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care. The incidence of adverse events was monitored between February 1, 2003, and January 31, 2004. The THAI Study was reviewed and approved by the Institutional Ethics Review Board at each of the involved institutions.

Details of age, sex, preanesthetic conditions, anesthetic management, intraoperative events and perioperative complications within 24 hours, on consecutive patients, were recorded on a standardized form. The details of allergic reactions were recorded by the attending anesthesiologist or nurse anesthetist and verified by the site manager. The forms were then reviewed by three peer reviewers to identify the clinical risk factors, contributing factors and corrective strategies.

The definition of allergic reactions included skin reactions (cutaneous flush, rash, urticaria and angioedema), lung symptoms (wheezing and hypoxia) and cardiovascular symptoms (unexpected hypotension, dysrhythmia, and cardiovascular collapse). The severity of reactions was classified as mild, moderate and severe [4, 10]. The reaction was also rated as doubtful, suggestive, probable and highly likely according to the allergic scores (1-20) as reported by Currie *et al.* [10]. Outcome measures included the incidence of the allergic reaction, causes, signs and symptoms of the reactions and its management. Clinical risk factors, contributing factors and corrective strategies were also recorded. Data were analyzed using descriptive statistics.

## Results

### Patients:

During phase 1 of the THAI Study, 163,403 patients were monitored for signs of allergic reactions: 34 patient-incidents were reported to the study center but 4 were excluded because the allergic scores were below 3 (*i.e.* the reaction was doubtful). The remaining 30 patients were included (Table 1): 48% had a history of allergies (including one with asthma) and 32% of these had had a previous anesthetic procedure without any record of having had an allergic reaction. All of the patients had no (or an unknown) family history of allergies.

### Allergic reactions:

The reaction-incidence was approximately 1 in 5,500 cases of anesthesia. According to the allergic scores, 20 cases were suggestive, 8 probable and 2 highly likely (Figure 1). The reactions occurred in the operating room, the recovery room, or in a ward in 21, 5 and 4 cases, respectively.

The clinical symptoms of the reactions were skin reactions (38%), hypotension (22%) and bronchospasm

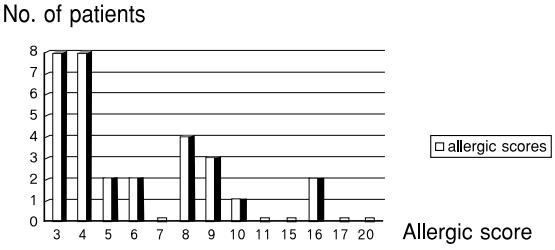


**Fig 1.** The distribution allergic scores over 3 (N= 30)

**Table 1.** Demographic characteristics and preanesthetic history

| Patient data | Number(n = 30) | % |
|---|---|---|
| Sex: | | |
| Male | 15 | 50 |
| Female | 15 | 50 |
| Age: median (range) (yr.) | 38 (6-77) | |
| History of allergies or asthma (N=23) | | |
| Yes /No | 11/12 | 48/52 |
| Family history of allergic (N=26) | | |
| No/Unknown | 14/12 | 54/46 |
| Previous anesthesia (N=28) | | |
| Yes/No/Unknown | 9/17/2 | 32/61/7 |

**Table 2.** Clinical symptoms reactions

| Clinical symptoms | N | % |
|---|---|---|
| Cutaneous: flush/rash/wheal/edema | 26 | 37.7 |
| Hypotension | 15 | 21.7 |
| Bronchospasm | 13 | 18.8 |
| Early dysrhythmia | 11 | 15.9 |
| Others | 4 | 5.8 |

(19%) (Table 2). The reaction-severity was classified as mild, moderate or severe in 40, 23 and 37 percent of the cases, respectively.

**Causal agents:**

The suspected causes of the allergic reactions included between 1 and 5 agents (Table 3). The three most common causes were antibiotics, neuromuscular blocking agents (NMBAs) and propofol (18.9, 16.9 and 15.1 percent, respectively). No incident of latex allergy was reported.

**Table 3.** Suspected causes of the allergic reactions

| Suspected cause | N | % |
|---|---|---|
| Antibiotics | 10 | 18.9 |
| Neuromuscular blocking agents | 9 | 16.9 |
| - succinylcholine | 5 | 9.4 |
| - atracurium/vecuronium/pancuronium | 4 | 7.5 |
| Hypnotics: Propofol | 8 | 15.1 |
| Opioids: pethidine/fentanyl/morphine | 6 | 11.3 |
| Gelatin | 6 | 11.3 |
| Blood and blood products | 3 | 5.7 |
| Non-steroidal anti-inflammatory drugs | 3 | 5.7 |
| Bupivacaine | 3 | 5.7 |
| Contrast media | 1 | 1.9 |
| Methergin | 1 | 1.9 |
| Protamine | 1 | 1.9 |

**Management:**

Most of the patients (95%) received appropriate medical treatment in accordance with the recorded symptoms and the severity of the reaction (Table 4). The three most common rescue medications given were corticosteroids, inotropic /vasopressor and antihistamines. The number of patients receiving respiratory support was quite high (15%) because most of them were already anesthetized and under controlled-respiration. All of the patients responded well to the rescue treatments, especially the one who experienced cardiac arrest. The four cases with only a mild reaction improved without any intervention.

According to the attending anesthesiologists, who reported the reactions, the clinical risk factors associated with the reactions ranked: 1) No (or an uncertain) history of allergic reaction; 2) No allergic history taken; 3) Emergency situation; and, 4) Unconfirmed diagnosis of the allergen(s). In addition, the three most common factors that might minimize reactions were: 1) Increased attention or care; 2) Care-givers experienced in coping with allergic reactions; and, 3) Improved communication skills among the care-givers.

**Table 4.** Medical treatment according to the symptoms and reaction-severity

| Treatment | N | % |
|---|---|---|
| Corticosteroid | 20 | 22.2 |
| Respiratory support | 14 | 15.6 |
| Inotrope and vasopressor | 13 | 14.4 |
| Antihistamine | 13 | 14.4 |
| $H_2$ antagonist | 11 | 12.2 |
| Bronchodilator | 8 | 8.9 |
| Colloid solution | 7 | 7.8 |
| No treatment | 4 | 4.4 |

## Discussion

The incidence of allergic reactions in our study was approximately 1 in 5,500 cases of anesthesia, which is similar to the 1 in 6,000 reported by Fasting and Gisvold in Norway [1]. The reactions, especially minor ones, might have been under-reported because of the large number of persons involved in the study. The reaction from gelatin might be under-reported simply because an allergic reaction and massive blood loss can both cause hypotension. However, the 11% of gelatin reactions in our study was higher than the 4% reported by Mertes *et al.* [11].

The *modus operandi* of anesthesia facilitates the rapid administration of many drugs; therefore, it is difficult to identify which specific drug(s) might have caused an allergic reaction. Notwithstanding, the two most suspected causes of reactions are antibiotics (19%) and neuromuscular blocking agents (NMBAs) (17%). In our study, the most common cause of reactions was antibiotics. Hung *et al.* [12] also reported that antibiotics caused the highest (50%) proportionof the reactions. Therefore, the standard use of antibiotics for prevention of infection in a clean surgical wound should be reconsidered because of the significant potential of an adverse reaction. Relatedly, a negative result using the test dose technique (*i.e.* starting one-third to one-fifth of the total dose) is no guarantee that a reaction will not occur. Indeed, Moss and Roizen [13] found that 90% of the reactions ocurred within 10 min of the test dose of chymopapain used for chemonucleolysis of the herniated nucleus pulposus. The incidence of allergic reaction from NMBAs in our study was lower than that reported by Mertes *et al.* [11] (58%). The difference in the reaction-rate was likely the result of their use of rocuronium whereas succinylcholine was commonly used in our study. However, both rocuronium and succinylcholine should be used with caution.

Propofol, the third most common cause of an allergic reaction, was the only hypnotic drug used because shortage of thiopental during the study period. The reaction from propofol, however, was not as severe as reported by Konarzewski and De Ath [14].

The history of allergies was taken on most of our patients, except for four. Nearly half (48%) of the patients who experienced reactions had a previous history of allergies. However, the data might not be reliable. For example, the 27% of patients who were having anesthesia for the first time would likely be unable to tell which anesthetic drug might cause them a reaction. In fact, our rate was much higher than the 18% reported by Currie *et al.* [10], perhaps because they compared the history with total reaction-symptoms whereas we compared the history with the total number of patients. Other allergic investigations are useful but may not be available at every hospital. So, although history-taking is associated with low reliability, it is still recommended because it is relatively easy, costs nothing and may yield life-saving information.

Patients who experienced reactions should avoid the same allergen in the future as, according to our experience, the reaction to succinylcholine is more severe in a second episode [9]. Porsche and Brenner [15] also reported that protamine increased risk of a reaction in a second exposure. Therefore, the causes of reaction should be investigated; either for diagnosis of the reaction or to identify the causative agent. Unfortunately, this was not done for any of the patients in our study.

## Conclusion

A 1-year survey for perioperative allergic reactions in Thailand was reported. The incidence of the reaction was approximately 1 in 5,500 cases of anesthesia (30/163,403). Allergic history was obtained in 48% of the patients. The most common sign was a skin reaction and the most commonly suspected causative drugs were antibiotics. All of the patients responded to the rescue treatment.

## Strategies to reduce risk

The three corrective strategies suggested by site managers were to: 1) Organize a center for allergy research; 2) Adopt and provide some sort of identification for patients with allergies; and, 3) Develop and implement clinical guidelines for management of allergic reactions.

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## *การศึกษาอุบัติการณ์ของปฏิกิริยาการแพ้ระหว่างการให้ยาระงับความรู้สึกในประเทศไทย*

***สมบูรณ์ เทียนทอง, ธนู หินทอง, อักษร พูลนิติพร***

***วัตถุประสงค์:*** *เพื่อทราบอุบัติการณ์ ปัจจัยเกี่ยวข้อง อาการแสดง วิธีการ และผลการรักษาของปฏิกิริยา การแพ้ที่เกิดขึ้นระหว่างการให้ยาระงับความรู้สึกในประเทศไทย (THAI Study)*

***วัสดุและวิธีการ:*** *เป็นการศึกษาแบบพรรณนาโดยเก็บข้อมูลแบบไปข้างหน้า ในผู้ป่วยทุกรายที่ได้รับยาระงับความรู้สึกโดยติดตามอาการถึง 24 ชั่วโมงหลังผ่าตัด ในโรงพยาบาลของคณะแพทยศาสตร์และของกระทรวงสาธารณสุขในทุกภูมิภาคของประเทศไทย รวม 20 แห่ง ระหว่างเดือนกุมภาพันธ์ พ.ศ. 2546 ถึงเดือนมกราคม พ.ศ. 2547 โดยอาการแสดงที่สงสัยว่าจะเกิดอาการแพ้ขึ้นได้แก่ มีผื่นตามตัว มีเสียง wheeze ในปอด และความดันโลหิตต่ำโดยไม่ทราบสาเหตุ การบันทึกรายละเอียดของผู้ป่วยจะทำเมื่อสงสัยว่าเกิดอาการแพ้ขึ้น*

***ผลการศึกษา:*** *มีผู้ป่วยที่ได้รับยาระงับความรู้สึกทั้งสิ้น 163,403 ราย มีรายงานผู้ป่วยที่สงสัยว่าเกิดอาการแพ้ทั้งหมด 30 ราย คิดอุบัติการณ์เป็น 1 : 5,500 ราย โดยผู้ป่วยร้อยละ 48 มีประวัติอาการแพ้ยาหรือสารเคมีมาก่อน อาการแสดงที่พบบ่อยคือ มีผื่นตามตัว (38%) ความดันโลหิตต่ำ (22%) และ มีเสียง wheeze ในปอด(19%) ระดับความรุนแรงที่พบแบ่งเป็นเล็กน้อย (40%) ปานกลาง (23%) และรุนแรง (37%) ยาและสารเคมีที่สงสัยว่าจะทำให้เกิดการแพ้ 3 อันดับแรกคือ ยาปฏิชีวนะ(19%) ยาหย่อนกล้ามเนื้อ(17%) และยานำสลบ propofol (15%) ผู้ป่วยในการศึกษานี้ได้รับการดูแลที่เหมาะสมและปลอดภัยทุกรายรวมทั้งผู้ป่วยหนึ่งรายที่เกิดหัวใจหยุดเต้นจากการแพ้ยาด้วย*

***สรุป:*** *อุบัติการณ์ของปฏิกิริยาการแพ้ที่เกิดขึ้นระหว่างการให้ยาระงับความรู้สึกในประเทศไทยคิดเป็น 1: 5,500 ราย โดยผู้ป่วยร้อยละ 48 มีประวัติอาการแพ้มาก่อน อาการแสดงที่พบบ่อยคือ มีผื่นตามตัว ยาและสารเคมีที่สงสัยว่าจะทำให้เกิดการแพ้มากที่สุดคือ ยาปฏิชีวนะ และยาหย่อนกล้ามเนื้อ โดยที่ผู้ป่วยได้รับการดูแลที่เหมาะสม และปลอดภัยทุกราย*