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# Anaphylaxis: lack of hospital doctors' knowledge of adrenaline (epinephrine) administration in adults could endanger patients' safety

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## KEY WORDS

*Anaphylaxis, anaphylaxis guidelines, adrenaline, epinephrine, survey, patient safety*

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## SUMMARY

*Adrenaline (epinephrine) is the first line drug to be given in anaphylaxis and can save patients' lives. Conversely, incorrect administration of adrenaline in anaphylaxis has caused patients serious harm, including death. We compared the survey results of doctors' knowledge of adrenaline administration in adults of two District General Hospitals Trusts in England and found, that from 284 Hospital Doctors, 14.4% (n=41) would administer adrenaline as recommended by published anaphylaxis guidelines. This survey comparison shows that a significant number of hospital doctors, regardless of seniority and specialty, have an educational deficit regarding correct administration of adrenaline (epinephrine) administration in adults with anaphylaxis. Multilevel strategies to educate doctors and prevent patient harm are needed. We propose a mnemonic for remembering the recommended treatment for anaphylaxis in the adult: "A Thigh 500" for Adrenaline into the antero-lateral thigh, 500 micrograms.*

## Introduction

Every hospital doctor with patient contact, who prescribes or administers medication, can potentially be involved in managing a severe anaphylactic reaction. Recent studies suggests that the prevalence and incidence of allergic disorders have increased in the last twenty years (1, 2). Even though allergic reactions are common, anaphylaxis is infrequent and fatal reactions are rare (2, 3).

On the other hand, if severe anaphylaxis occurs, there is limited time to act, especially in iatrogenic reactions: Median time to cardio-respiratory arrest is 5 minutes (3).

Adrenaline (epinephrine) is the treatment of choice and if timely administered, can save patients lives (1, 4-7). Over the last decade several surveys were conducted, suggesting a lack

of knowledge regarding the dose and administration route of adrenaline (epinephrine), mainly in junior hospital doctors' (8-11). The largest study to date shows however, that the knowledge deficit regarding junior or senior doctors in most medical and surgical specialties is equally common (12).

Disturbingly, there are now more than ten publications, citing more than 20 case reports, illustrating cardiac complications, stroke and death, caused by the incorrect administration of adrenalin to patients with true or suspected anaphylaxis treated in hospital (3, 12-23).

Motivated by the occurrence of such a critical clinical incident in their previous hospital, the authors designed this study to explore the extent of the deficit concerning hospital doctors' knowledge of adrenaline administration in the adult patient with anaphylaxis.

## Methods

A convenience sample of hospital doctors potentially involved in the treatment of anaphylaxis in two National Health Service (NHS) District General Hospital Trusts in England had been interviewed by direct questioning in 2009 (Trust A) and 2010 (Trust B). The questions addressed the knowledge of recommendations of the United Kingdom (UK) Resuscitation Council guidelines regarding the administration of adrenaline (epinephrine) in anaphylaxis in adults. (5) No prior notice had been given to doctors that a survey would be taking place and each doctor was approached individually at his working place by a single interviewer (JD). Only hospital doctors with direct patient contact were included in the survey, e.g. pathologists or researchers without patient contact were excluded. If verbal consent to conduct the survey was obtained, the doctors' answers were recorded immediately on a data collection sheet. The data collection sheets for the two surveys differed in structure, but the content of the questions regarding adrenaline (epinephrine) administration was identical. In both forms doctors' grade and specialty were noted, but not gender or age. Anaesthetists were not included in this study. On the three hospital sites of trust A the surgical specialties included: General surgery, orthopaedics and emergency department personnel, but not obstetrics and gynaecology personnel nor other surgical subspecialties.

Medical specialties included doctors from acute medicine, cardiology, gastroenterology, endocrinology and respiratory medicine. Since trust B is a much smaller hospital all the above mentioned specialties were approached and also doctors from urology and obstetrics and gynaecology, as well as consultant radiologists. The latter were grouped to medical specialties in the data analysis. The data was anonymised after collection. In each trust four consecutive working days were dedicated to collect the data. P-values were calculated to identify (significant) differences between the doctors' answers of the two trusts, using Fisher's exact test. In order to create a table to compare our results with previous similar surveys a literature search with PubMed.gov was performed, using the terms: Anaphylaxis, epinephrine, adrenaline, doctors' knowledge.

## Results

161 of 325 doctors (49.5%) in trust A (2009) and 123 of 167 doctors (73.7%) in trust B (2010) were interviewed. Out of a total workforce of 492 hospital doctors in the two trusts 284

doctors (57%) were questioned. A total of 9 doctors had declined to be interviewed (combined result). In trust B additional specialties were included: Urology (n=3), obstetrics and gynaecology (n=13), radiologists (n=6). Distributions of grades and specialties of doctors interviewed are summarized in Table 1. There was a small difference in the seniority of doctors interviewed between the two trusts, but not regarding the specialties distribution. Table 2 shows a comparison between the doctors' answers of the two trusts regarding the knowledge of recommended route of administration and correct dosage. The differences in the doctors' answers between the two trusts were mostly not significant.

Table 3 demonstrates a breakdown by grade regarding the doctors' answers in both trusts.

Table 4 shows a breakdown of answers regarding the surgical and medical specialties. Combining the results of both surveys, of 284 hospital doctors, 14.4% (n=41) would administer adrenaline as recommended by the UK Resuscitation Council guidelines from 2008 (5). 31.3% (n=89) of hospital doctors would administer the correct dose intramuscularly, albeit not all doctors would use the recommended muscle. 9.8% (n=28) of hospital doctors would administer adrenaline (epinephrine) intravenously, 11 doctors (3.9%) would use 1 milligram intravenously.

The literature search yielded eight surveys concerned with doctors' knowledge of adrenaline (epinephrine) administration guidelines for adults. Four surveys focused mainly on junior hospital doctors, three concerned Radiologists and one survey addressed General Practitioners (8-11, 24-27). Table 5 gives an overview of these studies regarding their date of publication, method of data collection, doctors' specialties and grades and the number of correct overall responses. Two studies were not included in the table because the administration route of adrenaline was not asked for in the questionnaires (11, 25). This survey comparison demonstrates that in the last decade between 5-20% of doctors of different grades and specialties knew the, at that time, recommended administration route for adrenaline (epinephrine) (Tab. 5).

**Table 1** - Hospital doctors grades and specialties

Doctors grade	Trust A (n=161)	Trust B (n=123)
Junior Doctors	48.4% (78)	39.0% (48)
Senior Doctors	51.6% (83)	61.0% (75)
Doctors Specialty		
Medical	49.7% (80)	49.6% (61)
Surgical	50.3% (81)	50.4% (62)

**Table 2** - Hospital doctors' answers regarding adrenaline (epinephrine) dosage and administration route and site

Administration route	Trust A (n=161)	Trust B (n=123)	p Value
Intra-muscular	79.5% (128)	75.6% (93)	0.475
Sub-cutaneous	11.8% (19)	5.7% (7)	0.097
Intra-venous	8.1% (13)	16.3% (20)	0.040
Not Recorded /DUA	0.6% (1)	2.4% (3)	0.319
<b>IM Administration site</b>			
Antero-lateral Thigh	31.1% (50)	43.0% (40)	0.798
Deltoid	21.7% (35)	25.8% (24)	0.661
Gluteal	19.9% (32)	21.5% (20)	0.536
Don't Know/Not Recorded	6.8% (11)	9.7% (7)	0.808
<b>Dosage</b>			
<500 mcg/0.5 mg	4.4% (7)	1.6% (2)	0.308
500 mcg/0.5 mg/0.5 ml 1:1000	37.9% (61)	26.8% (33)	0.057
1 mg	15.5% (25)	13.8% (17)	0.738
Don't Know/DUA	42.2% (68)	57.8% (71)	0.012
Correct dosage, route and site	15.5% (25)	13.0% (16)	0.611

**Table 3** - Hospital doctors' answers according to grades

Trust A (%)	Consultant (n=41)	SpR (n=42)	SHO (n=48)	FY1 (n=30)
Intramuscular Route	26 (63.4)	30 (71.4)	44 (91.7)	28 (93.3)
Antero-lateral Thigh	14 (34.1)	10 (23.8)	14 (29.2)	12 (40.0)
Adrenaline 500 mcg	10 (24.4)	19 (45.2)	28 (58.3)	4 (13.3)
Correct dosage, site and route	7 (17.1)	7 (16.7)	8 (16.7)	3 (10.0)
Trust B (%)	Consultant (n=39)	SpR (n=36)	SHO (n=26)	FY1 (n=22)
Intramuscular Route	29 (74.4)	21 (58.3)	24 (92.3)	19 (86.4)
Antero-lateral Thigh	14 (35.9)	7 (19.4)	12 (46.2)	7 (31.8)
Adrenaline 500 mcg	8 (20.5)	8 (22.2)	11 (42.3)	6 (27.3)
Correct dosage, site and route	5 (12.8)	3 (8.3)	4 (15.4)	4 (18.2)

## Discussion

This survey regarding hospital doctors' knowledge of adrenaline administration in anaphylaxis includes to date the largest number of junior and senior doctors, compared to other surveys, and embraced multiple specialties. We demonstrate in this survey that a significant percentage of hospital doctors interviewed, regardless of specialty or seniority, did not know the recommended administration dose and route for adrena-

line (epinephrine) according to recent guidelines for the treatment of anaphylaxis in adults.

This is in contrast to two previous surveys, suggesting that junior doctors have a greater lack of knowledge, than more senior doctor grades, regarding the recommended route of administration and correct dosage of adrenaline in anaphylaxis in adults (Tab. 3) (9, 10).

Overall around a third of doctors questioned would administer the correct dose via the intra-muscular route and the-

**Table 4** - Hospital doctors' answers according to specialties

Trust A (%)	Medical Specialties (n=80)	Surgical Specialties (n=81)
Intramuscular Route	65 (81.3)	63 (77.8)
Antero-lateral Thigh	25 (31.3)	25 (30.9)
Adrenaline 500 mcg	30 (37.5)	31 (38.2)
Correct dosage, site and route	12 (15.0)	13 (16.0)
Trust B (%)	Medical Specialties (n=61)	Surgical Specialties (n=62)
Intramuscular Route	53 (86.9)	40 (64.5)
Antero-lateral Thigh	23 (37.8)	17 (27.4)
Adrenaline 500 mcg	15 (24.6)	18 (29.0)
Correct dosage, site and route	8 (13.1)	8 (12.9)

**Table 5** - Anaphylaxis: Doctors' knowledge of treatment guidelines/administration of correct treatment

Authors	Year	(n =)	Country	Data collection	Doctors' specialty	Doctors' grade	Correct responses in% (n=)
Gompels et al.	2002	78	UK	Quest.	ED	SHO	5.0% (4)
Ferreira et al.	2006	100	PORT	Quest.	General Practitioners	General Practitioners	18.0% (18)
Thain et al.	2007	91	NZ	Direct Q	Multiple	HO (34), Reg (48), Cons (9)	20.0% (18)
Jose et al.	2007	95	UK	Direct Q	Not Stated	FY1/2/SHO (&%), SpR (20)	16.8% (16)
Tapping et al.	2009	105	UK	Quest.	Radiology	Cons/SpR	13.0% (14)
Lightfoot et al.	2009	235	CAN	Direct Q	Radiology	Consultant	16.0% (40)

**Glossary**

CAN: Canada; Cons.: Consultant; Direct Q: face to face questioning by an interviewer; ED: Emergency Department; Y1/2: Foundation Year 1 or 2 trainees (= post graduate year one or two trainee); HO: House Officer (= post graduate year one trainee); NZ: New Zealand; PORT: Portugal; Quest.: Questionnaire; Reg./SpR: Registrar/Specialist Registrar (senior trainees); SHO: Senior House Officer (= post graduate year two and above trainee); UK: United Kingdom

refore could be deemed safe. But not all doctors would inject into the recommended muscle and thus potentially deliver sub-optimal treatment. This applies even more to the subcutaneous route, where epinephrine absorption can be delayed up to 34 minutes (in children) and treatment could be dangerously delayed (28, 29).

Serious patients' safety concerns arise regarding the small group of hospital doctors (3.9%) that would administer a large dose (e.g. 1 mg or more) of adrenaline (epinephrine) via the intravenous route to a patient, not in cardio-respiratory arrest. Administration of adrenaline (epinephrine) in this way has shown to have potentially serious detrimental cardio-vascular effects, including death (3, 12-23).

In both hospitals convenience samples of doctors were questioned, which could have introduced a certain amount of selection bias. Also, the percentage of doctors interviewed of the total workforce of both trust was notably unequal. On the other hand, in both surveys the number of doctors questioned was high, which should guarantee a sufficient degree of representation and reduce selection bias. The small difference in the composition of the surgical and medical specialty groups between the two hospitals is unlikely to have contributed to significant selection bias. The fact that all participants were interviewed by the same person reduced interviewer bias to a minimum.

Anaesthetists and intensivists were excluded from the study. This professional group is the most frequently exposed to in-hospital anaphylaxis, since 56% of iatrogenic reactions occur in the operating theatre (3). Many anaesthetists and intensivists are well trained in giving intravenous epinephrine and would likely follow a form of “Anaphylaxis-During-Anaesthesia-Safety-Drill” (e.g. guidelines of the Royal College of Anaesthetists, United Kingdom, from 2009), which differ significantly from guidelines for non-anaesthetists (5, 30).

Nearly equally important to deliver the correct dose via the recommend route is to do so in a timely manner. Many authors agree that time is of the essence when faced with a potentially fatal allergic reaction and therefore all doctors potentially involved in the management of anaphylaxis should know the appropriate treatment and how to deliver it rapidly (3, 4, 32, 33).

One study looked at the time it takes to draw up the correct dose (for infants) of adrenaline from ampoules with needles and syringes. On average nurses needed 30–40 seconds and doctors 50 seconds (31). It is reasonable to assume that time spent to draw up adult doses would probably be in a similar range. Needless to say, that time is better not spent in trying to look for the right medication or dosage guidelines, the adrenaline, ampoules, needles and syringes, when confronted with a patient in anaphylactic shock.

Several authors have suggested in the past to introduce pre-filled syringes for intra-muscular use and store them in the resuscitation trolleys (9, 10, 23). There are cost implications to be considered, but if a fatal outcome to an (iatrogenic) anaphylactic reaction can be avoided, we feel patients’ safety should come first. A possibly less expensive alternative to consider for areas or during procedures, where anaphylaxis is likely to occur, would be to daily draw up adrenaline in the correct concentration, store it for the day and discard it at the end of the day/procedure.

Since anaphylaxis is a rare condition, many doctors may never see an anaphylactic event in their career. Maybe therefore it should not surprise that, despite the publication of several guidelines as well as studies pointing out doctors’ knowledge deficits (see Tab. 5), no significant improvements regarding anaphylaxis education of doctors have been achieved in the last decade (8–12).

Most doctors – thankfully- do not get exposed often enough to be prompted to retain over the years the information needed in this emergency. This raises the question, if widespread regular anaphylaxis education of doctors/healthcare workers of all grades and specialties is feasible and maintainable. Should not rather be relied on changes in the “hardware” (easy accessible laminated guidelines, pre-filled adrenali-

ne/epinephrine syringes etc.)?

We feel that the probable answer lies in a multi-level approach, since it is unlikely that one strategy alone is going to achieve improvement.

Like other authors before, we propose to consider the following:

*A. On a national/international level:*

1. Introduction of national registries for the collection of in-hospital anaphylaxis adverse events data.
2. Introduction of a mnemonic for remembering the recommended treatment for anaphylaxis in the adult: “A Thigh 500” for Adrenaline into the antero-lateral thigh, 500 micrograms (34).
3. Introduction of yearly mandatory answering of a short anaphylaxis questionnaire for all hospital consultants with patient contact, in order to gain Continuous Medical Education points.

*B. On a local level:*

1. Incorporation of anaphylaxis guideline training into the junior doctor training sessions, especially on induction to a new hospital/trust (11).
2. Email reminders once to twice yearly, with a multiple choice questionnaire attached, send to all doctors with patient contact. They should include 3 to 5 (multiple choice) questions regarding the administration of adrenaline.
3. The formation of an “anaphylaxis task force” consisting of a multi-disciplinary team of resuscitation officers, critical care outreach nurses, pharmacists, doctors etc. who are taking the responsibility to promote the knowledge of anaphylaxis treatment in each hospital or trust.
4. To introduce an “anaphylaxis day” per year, where members of the task force (made visible by e.g. wearing sandwich posters) visit the wards and question directly doctors and nurses about their knowledge of anaphylaxis recognition, medication and its location.
5. To introduce an easy accessible laminated guidelines chart. This could be openly displayed near the drug cupboards or resuscitation trolleys (11).
6. To place an “anaphylaxis box” (in bright colours) on resuscitation trolleys and in drug cupboards, containing the necessary medication, syringes, needles (ideally with adrenaline/epinephrine pre-filled syringes) (9, 10, 23).
7. To initiate regular audit activity regarding the subject (9).

Hopefully this study’s results and the suggestions made will be a prompt to continue the debate on this important subject, ultimately in the interest of patients’ safety.

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