LETTERS TO THE EDITOR

Intramuscular or intravenous adrenaline in acute, severe anaphylaxis?

Editor,—The consensus guidelines on the emergency medical treatment of anaphylactic reactions by the Project Team of the Resuscitation Council (UK) are an excellent guide for first medical responders, whether general practitioners or emergency department staff. They are pragmatic, safe, and emphasise the importance of first line treatment with oxygen, adrenaline (epinephrine) and fluids, and as Hughes and Fitzharris in their BMJ editorial suggest, rightly deserve to "...adorn the walls of emergency departments, general practitioners' surgeries, and outpatient clinics...". 

They are pragmatic, safe, and emphasise the importance of first line treatment with oxygen, adrenaline (epinephrine) and fluids, and as Hughes and Fitzharris in their BMJ editorial suggest, rightly deserve to "...adorn the walls of emergency departments, general practitioners' surgeries, and outpatient clinics."

The guidelines usefully remind us that a panic attack or a vasovagal syncopal episode may be confused with anaphylaxis with the danger of inappropriate treatment. Additional differentiating features not mentioned in the text suggest a faint rather than anaphylactic collapse are the rapidity of onset, maintenance of a central pulse, and prompt response to the recumbent position.

It is refreshing to see the debate over the delivery of adrenaline move forward a stage, with the subcutaneous route no longer recommended as the absorption is delayed and variable, at least in well children with a history of systemic anaphylaxis, when compared with the intramuscular route. The guidelines thus quite correctly favour the early administration of intramuscular adrenaline at a dose of 0.5 ml of 1:1000 for adults, to all patients with clinical signs of shock, airway swelling, or definite breathing difficulty. Intramuscular adrenaline given early, or when venous access is difficult and if the patient is unmonitored, is safe and effective even in less experienced hands.

Yet it is worth to note that the lifelong dogma that limits the use of intravenous adrenaline in acute, severe anaphylaxis. The introduction’s criticism of the inappropriate use of intravenous adrenaline, singling out accident and emergency department, is unjustified. It is presumably based on rare, outdated reports that include a questionnaire circulated to junior resident staff showing that in the 10% who responded there was misunderstanding about the dosage, route, and dilution of adrenaline, and a purely anecdotal letter castigating the use of intravenous adrenaline as it is "...a hazardous procedure rarely warranted in anaphylactic reactions".

As has been pointed out before, published reports on the apparent dangers of intravenous adrenaline consistently fail to emphasise that other causes such as hypoxia, hypotension, or the direct actions of the inflammatory mediators themselves released during anaphylaxis may be responsible for the cardiovascular complications. In addition, adverse outcomes to adrenaline occur when it has been given too rapidly, inadequately diluted, or in excessive dosage.

Also, the statement that intravenous adrenaline should only be reserved for profound shock or special indications, for example during anaphylaxis, is perplexing. Seventy-five per cent of anaphylactic deaths are due to anaphylaxis from upper airway oedema and hypoxia from bronchospasm, many within the first hour of onset of symptoms and only 25% from circulatory collapse. In addition, there is nothing unique about anaphylaxis during anaesthesia other than the standard model of delivery of all drugs is intravenously, and thus unexpected anaphylactic reactions may be rapid and catastrophic.

However, many of the same drugs are also used regularly in emergency medicine department and intensive care units to facilitate interventional airway care. Continuous electrocardiographic, blood pressure, and pulse oximetry monitoring are now routine in all these areas and are appropriate for the safe use of intravenous adrenaline. As Hughes and Fitzharris point out, the guidelines are somewhat vague in empirically recommending repeated intramuscular adrenaline every five minutes, or intravenous adrenaline as slowly as seems reasonable in the absence of clinical improvement or if deterioration occurs, particularly with profound shock.

Emergency medicine has come a long way in the last decade including a much higher level of senior supervision, routine access to the minimum standards of monitoring suggested above, and widespread collective expertise in managing anaphylaxis. It is now time to consider every monitored area, whether the emergency department, intensive care unit, or high dependency unit, in experienced hands low dose, high dilution intravenous adrenaline is optimal care for a patient with severe or rapidly progressive, life threatening anaphylaxis whether from shock or acute respiratory distress. Administration of 0.75–1.5 µg/kg of 1:100 000 adrenaline intravenously at 1 ml/kg per minute reverses all the life threatening effects of anaphylaxis and inhibits further mast cell mediator release by raising intracellular cyclic AMP. The 1:100 000 dilution, as the guidelines suggest, not only allows precise titration to response, but avoids inadvertent rapid or excessive dosage. In addition, the therapeutic response to the adrenaline is immediate and assured.

The Project Team of the Resuscitation Council (UK) must be congratulated on an excellent document that will undoubtedly improve first responders’ knowledge and outcome, and indeed of benefit to us all.

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Medical treatment of anaphylaxis

Editor,—We have read with grave concern the project team’s recommendations for the medical treatment of anaphylaxis and believe very strongly that the advice against using intravenous adrenaline (epinephrine) is potentially very dangerous. We also find the omission of reference to guidelines for the management of anaphylaxis in the accident and emergency (A&E) department published in the same journal as very regrettable if deliberate, or puzzling if the project team had no knowledge of their existence.

The project team’s guidelines have also failed to emphasise the relevance of grading the severity of anaphylaxis and that its treatment should be directed to the severity of the attack encountered.

We agree that the project team’s guidelines should be used by the inexperienced and invariably pre-hospital responders. We also agree that the subcutaneous route is unreliable and should be abandoned. However, to suggest that A&E seniors or supervising trainees and well supported juniors lack clinical credibility to administer high dilution intravenous epinephrine carefully titrated against response in the fully monitored patient in the resuscitation room is insulting to the specialty of A&E. It also shows that in spite of having A&E representation the project team fails to understand fundamental principles of A&E involvement in the management of the critically ill.

To suggest that patients with clinical signs of shock should be administered intramuscular epinephrine as epinephrine can be rapidly absorbed is in physiological terms most bizarre advice.

We conclude that the project team’s guidelines need urgent revision as they will lead to patients dying due to failure to urgently administer intravenous epinephrine. We will continue as we hope the majority of A&E departments will do similarly, to use the published A&E guidelines and we believe that they are currently the best available guidelines for treating anaphylaxis in the A&E department.

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Professor Chamberlain replies on behalf of the Anaphylaxis Project Team

We are grateful to Dr Brown for his kind general remarks about our consensus guidelines, and also for giving us the opportunity to clarify one sentence in our introduction. We said “There has been a vague for inappropriate use of intravenous epinephrine (adrenaline), both by paramedics and in accident and emergency departments, when epinephrine...”
(adrenaline) should have been given intramuscu-
larly.1 We believe this to be true, but it was most certainly not our intention to condemn all use of intravenous adrenaline by experi-
enced medical practitioners either in emer-
gency departments or elsewhere. In retrospect we should have been more explicit on this point. We agree totally with Dr Brown's statement that adverse outcomes for adrenaline occur when it has been given too rapidly, inadequately diluted, or in excessive dosage. We also recognise that emergency medicine has progressed a long way in the last decade with a much higher level of senior supervision and greater possibilities for treat-
ment under monitored conditions.

Our guidelines were intended specifically for those first medical responders who are inexperience in the management of this emergency. They are unlikely to have monitoring facili-
ties available. For these, cautious re-
ommendations are appropriate with intraven-
ous use of adrenaline restricted to emergencies judged to be immediately life threatening.

The examples that we gave for indications for intravenous adrenaline were clearly not intended to be comprehensive, and experi-
enced physicians in monitored areas will appropriately make their own decisions. We did mention the value of infusions of 1:10 000 adrenaline which permits titration of dose against need. It may also be worth emphasising that in asphyxia from upper airway oedema and hypoxia from severe bron-
chospasm, there are additional priorities—not really parental adrenaline—such as oxy-
genation and nebulised inhaled bronchodil-
ators. Dr Brown's comments do, of course, add to our own guidelines by making sound recommendations for expert management that was outside the remit of our article.

The concerns of Mr Gavalas and his colleagues were similar, but there seems also to be an element of misreading of our document. They say that they “believe very strongly that the advice against using intra-
venous adrenaline (epinephrine) is potentially very dangerous”. We must reiterate that we did not advise against its use, but urged only that it should be used in the most serious cases and by experienced clinicians.

Our guidelines stated in paragraph 4.4 that: “Intravenous epinephrine (adrenaline) in a dilution of at least 1:10 000...is hazardous and should be reserved for patients with profound shock that is immediately life threat-
ening and for special indications”. We also added in paragraph 5.2: “The use of epinephrine (adrenaline) by the intravenous route in the special circumstances given in paragraph 4.4 should usually be reserved for medically qualified personnel who have experience of it, who know that it must be administered with extreme care, and who are aware of the hazards associated with its use”.

The footnote to the legends state very clearly: “Consider slow intravenous (IV) ephine-
phrine (adrenaline) 1:10 000 solution. This is hazardous and is recommended only for an experienced practitioner who can also obtain IV access without delay”.

There are some practitioners who have made the habit of always using adrenaline intravenously, while others have preferred the subcutaneous route, and many are afraid to give it at all. We believe that we have given the correct guidance—that intramuscular adrenaline is the norm for the emergency treatment by first medical responders, with IV adrena-
line reserved for special and life threatening situations. This is far from advising against its use!

There is one charge to which we must plead guilty. Of course we were aware of the previous paper published in the Journal of Accident & Emergency Medicine in 1998, and it was indeed our intention to reference it together with the other specialist recommen-
dations. That omission was not deliberate, and one of us (DAG) must take responsibility for that important last minute oversight.

We do not accept that the guidelines need urgent revision. Neither does the Project Team with its wide representation accept that the recommendations were are insult-
ing to the specialty of accident and emergency. We are conscious that we all have the same aims: better and safer treatment of an important medical emergency.

Future inpatient management of patients with minor head injuries

Our department has a nurse who travels on ways of managing the patient. We do not yet know how we will resolve this issue locally, but would welcome other views on ways of managing the patient.

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Letters


3 British Association for Accident and Emergency Medicine. The way ahead: British Association for Accident and Emergency Medi-

Cycle helmets

EDITOR,—I read with horror the British Medi-
cal Association’s Board of Education and Sci-
ence conclusion that legislation to make helmets for cyclists compulsory would reduce the number of cyclists and not be in the inter-
ests of health.1

As an accident and emergency consultant for over 20 years, I have seen far too many head injuries in cyclists, some fatal. The main factor in causing most accidents is human error. I agree, as the article suggests, that cycling proficiency should be taught in all schools and the driving test modified for awareness of cyclists to other road users. The government, as suggested, should subsidise cycle helmets and promote them through the media by advertising. The car driver is not interested, but we need better cycle routes nationwide.

Our government is committed to reduce injuries from accidents (see Our Healthier Nation). The main cause of death in children is trauma. But I have personally discussed at length the benefits of wearing a helmet with children who, unhelmeted, have suffered a fractured skull in a cycle accident. Many chil-
dren still remain unconvinced! Parental con-
trol is weak. So voluntary action to increase the wearing of cycle helmets in this age group is unlikely to succeed.

My answer is that the compulsory wearing of cycle helmets is needed now. This should be integrated as part of a programme—teaching, better routes, helmet subsidies, and increased awareness through publicity. The number of cyclists may well reduce initially but more importantly head injuries will become fewer too! However, in the future, the population of cyclists naturally will then increase as cycling at last becomes safer and so even more enjoyable.

There has been successful government legislation concerning road traffic accident prevention and injury protection—for exam-
ple, the breathalyser laws, compulsory crash helmets for motorcyclists, and the seat belt laws. These are still supported by publicity. The legislation could be expanded.

We as an emergency specialty, however, have a responsibility in accident prevention and injury protection. We all need to be active, as I have been, in the local press recently highlighting, for example, the need for cyclists to wear helmets. We recognise this problem only too well.

Our department has a nurse who travels round schools talking about accident prevention and injury protection—particularly cycle
Playing in the back seat

Editor,—We read with interest the letter of Carnall D. Cycle helmets should not be compulsory. Have you put a bid in? We have. A pair of 7 year old identical twins presented to the accident and emergency (A&E) department after being involved in a head-on road traffic accident. Both had been restrained in four point child seats in the back of the car.

In the department, one was complaining of abdominal pain, the other none. On examination of the twins, both were haemodynamically unstable. Twin 1 had bruising to her abdomen, the other none. This bruising was linear in nature across her abdomen, “the seat belt sign”. She had no focal tenderness.

In view of the seat belt sign, twin 1 was admitted and an abdominal ultrasound was performed at this stage. The ultrasound showed a small amount of fluid in the pouch of Douglas, but no other free fluid or lacerations of visceral organs.

Overnight she remained painful, but haemodynamically normal. A further ultrasound was performed the next day which showed free fluid within her abdomen.

The authors reply
We also read with interest the paper by Scheinkestel et al, which was published after acceptance of our article.1 Scheinkestel’s paper was accompanied by a detailed editorial which documented a number of criticisms that preclude implementation of its findings until further data are forthcoming.2 Recommendations from poison information centres, as described in our article, have not been changed and still provide useful guidance on selecting patients for hyperbaric oxygen.

We believe that careful neurological examination, including specific testing of cognitive function, is vital in the management of patients. Physicians should use tests with which they are familiar and apply them serially to the same patient. Standardisation of formal cognitive testing for trials was beyond the scope of our clinically orientated article.


Evidence based and guideline based medicine

Editor,—Evidence based and guideline based medicine is justifiably emphasised in current accident and emergency (A&E) medicine practice. At St James’s University Hospital in Leeds, the A&E trainees participate in regular evidence based critical appraisal sessions as part of education development, and such skills are assessed in our Faculty of Accident and Emergency Medicine exit examination.

One source of valued literature is Sackett et al, particularly their appraisal cards on the subject. A hereafter card that I am particularly fond of is their appraisal card on the subject of carbon monoxide poisoning. It is worth highlighting that cognitive testing in carbon monoxide poisoning is far from standardised. Many studies utilise different screening tests, different time intervals to re-screening, and different HBO regimens. This lack of standardisation makes it difficult to compare studies and no doubt contributes to our inability to provide definitive recommendations in the management of carbon monoxide poisoning.

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References


1 Carnall D. Cycle helmets should not be compulsory. BMJ 1999;318:1505.


6 Troum S, Lane CE, Dalton ML. Surviving Boerhaave’s: this trial also included severely poisoned patients and incorporated sham treatments. This study found in 191 patients that three days of HBO (2.8 atmospheres for 60 minutes) offered no advantages compared with three days of NBO (100% oxygen for 100 minutes of 100%). Another study is continuing in the United States and the interim results have found no difference in the incidence of persistent neurological sequelae between those treated with HBO compared with NBO, although there is an increased incidence of delayed sequelae in one of the blinded treatment arms.

The authors also recommend careful neurological and cognitive re-examination. It is worth highlighting that cognitive testing in carbon monoxide poisoning is far from standardised. Many studies utilise different screening tests, different time intervals to re-screening, and different HBO regimens. This lack of standardisation makes it difficult to compare studies and no doubt contributes to our inability to provide definitive recommendations in the management of carbon monoxide poisoning.

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Letters
ards" acronym that follows Crombie’s sugges-
tion that standard questions should be used as
a filter for all papers.¹

I hope they are of use to fellow practitioners
of evidence based medicine, and further
suggestions will be gratefully received.

Standards

Stated aims?
Tests and measures appropriate?
Arithmetic (do the numbers add up?)
Design appropriate?
Model (were they considered?)
Design appropriate?
Relevance to your practice?
Different results from previous reports?
Sample size/power adequate?

Diagnosis

Diagnostic test needed?
Independent blind comparison?
Appropriate population?
Gold standard used regardless of test result?
Númerogram (2×2 table) constructable?
Sensitivity and specificity important?
Inferences possible?
Safe, cheap, and helpful?

Prognosis

Prospective study?
Representative sample?
Objective and blinded outcome criteria?
Groups adjusted for prognostic factors?
Numbers recruited and followed up ade-
quate?
Outcomes likely?
Study findings precise?
Inferences possible?
Similar patients to your own?

Guidelines

Guidelines needed?
User friendly?
Identified risks and benefits?
Decision options clear?
Evidence based decisions?
Large variations in current practice?
Implementable?
NHS benefit?
Economical?
Safe?

Therapy

Trial ethically approved?
High recruitment and follow up?
Equal treatment and assessment in each
group?
Randomised and how?
Appropriate population?
Potential benefits for patients?
End points applicable?
Absolute risk reduction/number needed to
treat?

Systematic review

Systematic search strategy?
Randomised and relevant trials?
Each trial assessed?
Valid results in all trials?
Inconsistent populations or results?
Evidence of benefit via odds ratios/number
needed to treat?
Was hypothesis satisfied by the review
results?

1 Sackett D, Richardson W, Rosenberg W, et al.
Evidence-based medicine: how to practice and teach

2 Crombie IK. The pocket guide to critical appraisal.

Weekly web review

Editor,—A noteworthy web site exists for
emergency department evidence based medi-
cine enthusiasts. The Weekly Web Review in
Emergency Medicine (www.wwrem.com/) is
dedicated to the critical analysis of current
clinical literature on topics relevant to the
practice of emergency medicine. It has a
useful rating system for each of the articles
reviewed and an archive database. It dovetails
with this journal’s journal scan and has useful
links, notably with the Centre for Evidence
Based Medicine at Oxford. I recommend it as
a useful adjunct to any emergency physician’s
continual professional development.

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Carbon monoxide poisoning

Steven Doherty

doi: 10.1136/emj.17.2.154-b

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