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.1 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 that suggest a faint rather than anaphylactic collapse are the rapidity of onset, maintenance of a central pulse, and prompt response to the recumbent position.2

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 anaphylaxis, when compared with the intramuscular route.3 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.

It is also reassuring to reappraise some of the perennial dogma that limits the use of intravenous adrenaline in acute, severe anaphylaxis. The introduction’s criticism of the inappropriate use of intravenous adrenaline, shielding out accident and emergency department involvement in the management of the critically ill 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 It is presumably based on rare, outdated reports that include a questionnaire circulated to junior resident staff showing that in the 10% who responded there was misunderstanding about the dosage,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,4 and a purely anecdotal letter castigating the use of intravenous adrenaline as it is “...a hazardous procedure rarely warranted in anaphylactic reactions”5

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.6

Also, the statement that intravenous adrenaline should only be reserved for profound shock or special indications, for example during anaesthesia, is perplexing. Seventy five per cent of anaphylactic deaths are due to asphyxia from upper airway oedema and hypoxia from bronchospasm, many within the first hour of onset of symptoms and only 25% from circulatory collapse.7 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 as an adjunct 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.8

Emergency medicine has come a long way in the last decade, and includes 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 the very monitored area, whether the emergency department, intensive care unit, or high dependency unit, in experienced hands low dose, high dilution intravenous adrenaline is as 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.9 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 important document that will undoubtedly improve first responders’ knowledge and outcome, and indeed be of benefit to us all.


LETTERS TO THE EDITOR

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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 anaphylaxis1 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 journal2 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 guidelines3 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 vogue for inappropriate use of intravenous epinephrine (adrenaline), both by paramedics and in accident and emergency departments, when epinephrine

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(adrenaline) should have been given intramuscu-
larly. 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 emergen-
cy 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 in
experienced in the management of this emer-
gency. They are unlikely to have monitoring facili-
ties available. For these, cautious rec-
ommendations are appropriate with intra-
venous use of adrenaline restricted to emer-
gencies judged to be immediately life threaten-
ing.

The examples that we gave for indications for intravenous adrenaline were clearly not in
tended to be comprehensive, and experi-
enced physicians in monitored areas will appro-
priately 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 
readily available, such as oxygenation and nebulised inhaled bronchodilators.

Dr Brown's comments do, of course, add to our own guidelines by making sound recommenda-
tions 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 intraven-
ous 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 threaten-
ing 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) epine-
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 advice—that intramuscular adrena-
line 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 (DAC) 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 are insul-
ting to the specialty of accident and emergency. We are conscious that we all have the same aims: better and safer treatment of an im-
portant medical emergency.

Future inpatient management of patients with minor head injuries

EDITOR,—We read, with interest, the letter from Pau and Buxton, regarding the need for neurosurgical referral of patients with an admittance diagnosis of minor head injury.1 We agree that these are low risk group patients. We performed an audit of patients admitted to our observation ward with the primary diagnosis of minor head injury. From October 1997 to July 1999, 668 such patients were admitted under our care. Of these patients, only two were subsequently transferred to the regional neurosurgical unit after the finding of intracranial haematoma on computed tomo-
graphy. This finding, and our general experi-
ence, leads us to agree that patients with an admittance diagnosis of minor head injury do not require neurosurgical referral, in the first instance. However, we suspect, given that only 12% of responding accident and emergency (A&E) departments (71% response rate) in the UK have on-site neurosurgical facilities,2 this practice is not widespread anyway.

Pau and Buxton's conclusion is in keeping with the recommendations of the Report of the Working Party on the Management of Patients with Head Injuries.1 One of the logistical concerns raised by this report, and highlighted in Pau and Buxton's letter, is the fact that observation wards have a finite capacity. Our current practice is that if the observation ward is full, these patients are admitted under the general surgeons, The Way Ahead docu-
ment recommends that A&E observation wards should be within, or immediately adjacent to, the A&E department. We feel that it is inevitable, when the only specialty admitting patients with isolated minor head injuries is A&E, that problems will arise when the observation ward is full. It goes against the spirit of the report of the working party to then admit these patients under other specialties, just because the observation ward is full. If these patients are to be admitted to whatever beds are within the hospital, but still under the care of A&E, we fear a major step backwards in the standards of our practice if, when a seriously ill or injured patient arrives in the A&E department at 5 am, the only A&E doctor on duty is at the far end of the hospital, assessing a head injured patient.

The recommendations of the report have provoked widespread debate and polarity of views within the specialty. It probably repre-
sents a watershed in the management of A&E departments that do not currently accept

inpatients under the care of A&E consultants.

We do not yet know how we will resolve this issue locally, but would welcome other views on ways of managing the patient.

G MCCARTHY

G QUIN

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 part of a comprehensive 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 trains schools talking about accident prevention and injury protection—particularly cycle
Playing in the back seat

EDITOR,—We read with interest the letter of fatal intra-abdominal injury associated with incorrect use of a seat belt and would like to present another aspect of seat belt misuse. 1 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 stable. 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.

It was confirmed that there was confirmed turbid fluid and this was converted to a laparotomy. Three lesions were found in her jejunum, one full thickness and two partial. A 15 cm resection of her jejunum was performed with anastomosis. She made an uneventful recovery.

On detailed questioning while in the A&E department, she stated that she had been playing a game with her twin sister and had wriggled out of her shoulder straps. This had converted her four point child seat into a lap belt. Twin 2 had remained properly restrained in her child seat.

Lap belt use has been recognised as a mechanism of blunt injury to the small bowel. The seat belt sign is associated with an increased likelihood of intestinal injury. 2 This lap belt injury in children usually occurs when children are large for their safety seats and too small for adult seat belts. 3

This case highlights the importance of the seat belt sign, but more importantly that children within their own safety seats need to be restrained properly within them. Incorrect use results in injury similar to adult lap belts.

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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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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 Faculties of Accident and Emergency Medicine exit examination.

One source of valued literature is Sackett et al, particularly their appraisal cards on the validity, importance, and applicability of a particular type of study. Lacking a photographic memory, I put forward simple acronyms that have helped me to facilitate timely and efficient appraisal for everyday use when selectively scanning relevant journals. Preceding these specific acronyms is a “stand-
ards" acronym that follows Crombie's suggestion 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?)
- Null findings (were they considered?)
- Design appropriate?
- Appropriate statistics?
- 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?
- Numerogram (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 adequate?
- Outcomes likely?
- Study findings precise?
- Inferences possible?
- Similar patients to your own?

### Guidelines

- 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?

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