BEST EVIDENCE TOPIC REPORTS

# Towards evidence based emergency medicine: Best BETs from the Manchester Royal Infirmary

**Edited by K Mackway-Jones**

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Best Evidence Topic reports (BETs) summarise the evidence pertaining to particular clinical questions. They are not systematic reviews, but rather contain the best (highest level) evidence that can be practically obtained by busy practicing clinicians. The search strategies used to find the best evidence are reported in detail in order to allow clinicians to update searches whenever necessary. Each BET is based on a clinical scenario and ends with a clinical bottom line which indicates, in the light of the evidence found, what the reporting clinician would do if faced with the same scenario again.

The BETs published below were first reported at the Critical Appraisal Journal Club at the Manchester Royal Infirmary[1] or placed on the BestBETs website. Each BET has been constructed in the four stages that have been described elsewhere.[2] The BETs shown here together with those published previously and those currently under construction can be seen at http://www.bestbets.org.[3] Four BETs are included in this issue of the journal.

- Prehospital endotracheal intubation in adult major trauma patients with head injury
- Headache in paediatric head injury
- S-100b protein levels as a predictor for long-term disability after head injury
- Aspirin and the risk of intracranial complications following head injury

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1 **Carley SD,** Mackway-Jones K, Jones A, *et al.* Moving towards evidence based emergency medicine: use of a structured critical appraisal journal club. *J Accid Emerg Med* 1998;**15**:220–222.
2 **Mackway-Jones K,** Carley SD, Morton RJ, *et al.* The best evidence topic report: A modified CAT for summarising the available evidence in emergency medicine. *J Accid Emerg Med* 1998;**15**:222–226.
3 **Mackway-Jones K,** Carley SD. bestbets.org: Odds on favourite for evidence in emergency medicine reaches the worldwide web. *J Accid Emerg Med* 2000;17:235-6.

## Prehospital endotracheal intubation in adult major trauma patients with head injury

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doi: 10.1136/emj.2005.031716

### Abstract
A short cut review was carried out to establish whether prehospital intubation was of benefit to patients with moderate to severe head injury. 4630 papers were found using the reported searches, of which 9 presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. It is concluded that prehospital intubation is associated with increased mortality in these patients.

### Clinical scenario
A 41 year old car driver was involved in a major road traffic accident, sustaining injuries to his head, a fracture of his right femur and multiple bruises on his chest. On scene he had altered sensorium and his GCS was estimated to be 5. He was intubated by the paramedics and brought to the Emergency Department. You wonder about the evidence in favour of endotracheal intubation as compared to bag and mask ventilation in trauma patients.

### Three part question
In [patients with major trauma and head injury needing airway management in prehospital setting] is [endotracheal intubation better than bag and mask ventilation] for [improved outcomes]

### Search strategies
Medline 1966-Week 4 August 2005 using the OVID interface, {Cochrane Prehospital Search filter} AND {exp Intubation, Intratracheal/ or endotracheal intubation.mp. OR ETI.mp. OR RSI.mp OR rapid sequence intubation.mp}, Embase 1980-2005 week 37, [exp Emergency Health Service/ OR exp Rescue Personnel/ OR exp Emergency Treatment/ OR exp Emergency Medicine/ OR exp Ambulance/ OR exp First Aid/ OR exp Military Medicine/] AND [intratracheal intubation.mp. OR exp Endotracheal Intubation/ OR ETI.mp. OR RSI.mp. OR rapid sequence intubation.mp. OR rapid sequence induction.mp.] LIMIT to Human, English Language, Abstracts, (adult <18 to 64 years> or aged <65+ years>) and Clinical Queries Prognosis filter – sensitive, The Cochrane Library Issue 3 2005, exp intubation, intratracheal [MeSH] AND exp Emergency Medical Services [ MeSH]

### Search outcome
4360 papers found, of which nine were relevant and of sufficient quality for inclusion. These are summarised in the table:

### Comments
Quite a few studies have been conducted to address the question of prehospital endotracheal intubation in major trauma victims needing airway management. All of them are of retrospective design and most of them show that there is increased mortality, longer transit times with prehospital endotracheal intubation. The reasons could be difficulty in ascertaining tube position, paramedic experience,

**Table 1**

| Author, country, date | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---|---|---|---|---|---|
| Winchell RJ, Hoyt DB 1997 USA | All trauma patients admitted to trauma centres in San Diego county from 1991–1995 who underwent field intubation when GCS <=8(565 were intubated and 527 were not intubated in field) | Retrospective registry based review | Scene GCS scores in intubated and non-intubated groups<br>Mortality in patients who were not intubated for whole group<br>Mortality in patients not intubated with isolated severe head injruy | No difference<br>36% versus 26% OR 1.6<br>49.6% versus 22.8% OR 3 | Retrospective design, matching may have left out several critical parameters, multivariate analysis not done, functional outcomes not compared |
| Sloane *et al* 2000 USA | All adult trauma patients who underwent prehospital RSI 1988 to 1995 (47 patients) compared with those who had RSI upon arrival to trauma resuscitation suite 1992-1995 (537 patients) as per RSI protocol | Retrospective study | Field intubation versus hospital intubation success rates<br>Attempts to reach successful intubation<br>Field intubation time versus hospital intubation time in transit<br>Field and hospital intubation immediate and long term complication<br>Field and hospital intubation pneumonia<br>Length of stay ICU and hospital field and hospital intubation<br>Mortality in field and hospital intubations in head injured subgroups | 97.9% versus 98.5%<br>No significant difference<br>25.7 mins versus 14.2 mins, $p<0.01$<br>No difference<br>28% versus 6% $p<0.001$<br>No significant difference<br>14% in field and 22% in hospital subgroups $p=0.54$ | Retrospective study, small sample of field intubation, matching not adequate esp. related to age, retrospective definition of number of attempts at intubation and record review, field patients had worse trauma severity scores, no blinding of data collector |
| Murray *et al* 2000 USA | All adult patients with severe head injury GCS <=8, head AIS score >=3 over a 3 yr period 1995-1997 who were intubated (81) in the field or non-intubated (714) or unsuccessfully intubated (57) | Retrospective study, review of trauma registry | Crude mortality figures in intubated versus non-intubated group<br>Mortality in matched groups intubated in field or non-intubated<br>Adjusted unsuccessful intubation vs nonintubated patients | 82% versus 43%, OR 1.88 (CI 1.65 to 2.15)<br>OR 1.74 (CI 1.41-2.00)<br>OR 1.53 (CI 1.15 to 1.86) | Retrospective design, matching done but certain critical parameters missed out, selection bias, only patients with more severe injuries selected for intubation |
| Eckstein *et al* 2000 USA | All adult patients from 1993 to 1995 who met trauma centre criteria, had airway intervention performed by paramedics and transported to medical centre, ETI or BVM done as per hospital policy, 93 patients had ETI and 403 BVM | Retrospective cohort study | Prehospital transit time for ETI versus BVM<br>Mortality in ETI versus BVM after adjustment for sex, mechanism and ISS,<br>Patients not receiving IV fluids mortality | 12.8 mins versus 11 mins $p=0.09$<br>93% versus 67%,OR 5.3 (CI 2.3 to 14.2)<br>OR 3.9 (CI 1.0 to 26.7) | Data obtained from paramedic field reports, retrospective study, groups compared by covariates and not true controls, effect of hyperventilation not studied, small number of patients with ETI, despite adjustment for ISS through logistic regression, ETI group had a very high mortality based on ISS, limitations of ISS, RSI not used |
| Bochichhio *et al* 2003 USA | Data collected on 191 patients admitted to a trauma centre with field GCS <=8, head Abbreviated Injury Scale >=3 who were intubated (78) in the field or intubated on arrival to hospital (113), patients who died within 48 hrs excluded | Prospective cohort study | Dispatch time field ETI versus hospital ETI<br>Field ETI versus hospital ETI<br>Field ETI versus hospital ETI respiratory complications<br>Field ETI versus hospital ETI ICU stay | $p<0.05$<br>23% versus 12.4% ($p=0.05$), OR 1.85<br>61% versus 29%, $p<0.05$<br>Longer in field ETI $p<0.005$ | Cohort study, death within 48 hrs excluded, individual paramedic bias in intubation, difference between ground and state patrol flight paramedics, lack of longterm data or functional outcomes, bias on the practice of neurosurgeon |
| Davis *et al* 2003 USA | Adult major Trauma victims with severe head injuries >18 yrs, suspected head injury by mechanism or physical findings, GCS 3–8, estimated time for transport >10 minutes, exclusion if unable to achieve IV access or needed PR before RSI | Prospective cohort study 209 patients who received ETI matched to 627 historical controls who did not | Mortality in ETI versus BVM ventilation<br>Good outcome ETI versus BVM<br>Total days in ICU ETI versus BVM<br>Total days in hospital ETI versus BVM | 33% VERSUS 24.2%, OR 1.6 (CI 1.1 to 2.2)<br>45.5% versus 57.9% OR 1.6 (1.2-2.3 CI)<br>7.1% versus 6%, non-significant<br>12.2% versus 14.5% non-significant | Cohort sudy with historical controls though matched well, GCS not used for matching as they were not consistently calculated pre-trial cohort and omitted from trial cohort as they were paralysed and intubated, higher mortality in RSI cohorts who had low pCO2, possibility of hyperventilation contributing to increased mortality, Other parameters may have been present which were unmatched in the two groups |
| Stockinger ZT, McSwain NE 2004 USA | Review of records from Dec 1999 to Sept 2002 who met level 1 trauma criteria and who received ETI or BVM ventilation | Retrospective cohort study | Overall mortality<br>Penetrating injury mortality<br>Patients receiving ETI mortality<br>Penetrating injury and ETI mortality versus blunt injury and ETI mortality<br>Penetrating injury and BVM mortality<br>Different ISS, ETI versus BVM<br>Prehospital time ETI versus BVM<br>Increasing RTS ETI versus BVM mortality<br>TRISS model actual deaths vs predicted deaths | 65.3%<br>OR 1.78 (CI 1.54 to 2.05)<br>OR 2.88 (CI 2.36 to 3.54)<br>95.8% and 78.4%, $p<0.0001$<br>53.5% $p<0.0001$<br>ETI worse than BVM $p<0.0001$<br>Longer time on ETI but only by 1.9 minutes<br>Mortality worse in ETI patients $p>0.05$<br>ETI mortality worse than BVM $p<0.05$ | Retrospective design, record review, not controlled, small number of ETI survivors to compare functional outcomes or prehospital transit time, inadequately matched groups |
| Wang *et al* Nov 2004 USA | All trauma patients > 18 years sustaining sever traumatic brain injury who were intubated in prehospital or hospital setting | Retrospective cohort study | Prehospital versus hospital intubation mortality<br>Prehospital versus hospital intubation poor neurologic outcomes<br>Prehospital versus hospital intubation functional impairment | OR of 3.99 (CI 3.21 to 4.93)<br>OR of 1.61 ( CI 1.15 to 2.26)<br>OR of 1.92 (CI 1.40 to 2.64) for moderate or severe | Non-randomised study, use of pre-existing and unvalidated registry, unvalidated functional impairment score, adjustment not done for some factors that could affect prehospital intubation, no information of course of ED airway care, Could not identify failed prehospital intubation efforts and analysis, propensity score used but matching techniques not used |
| Davis DP *et al*, 2005, USA | 13,625 patients with moderate to severe traumatic brain injury included on a country rauma registry of whom 19.3% were intubated in the prehospital environment | Observational | Mortality | Increased with prehospital intubation (OR 0.36 p < 0.001) | |

hyperventilation, transient hypoxia, or lack of sufficient pre-oxygenation prior to RSI. Prospective multi-centre randomised trials are needed to avoid the inherent problems associated with the study designs.

### ► CLINICAL BOTTOM LINE

Prehospital endotracheal intubation is associated with increased mortality in patients with moderate to severe traumatic brain injury

**Winchell RJ,** Hoyt DB. Endotracheal intubation in the field improves survival in patients with severe head injury. *Archives of Surgery* 1997;**132**:592–597.
**Sloane C,** Vilke GM, Chan TC, *et al*. Rapid Sequence Intubation in the field versus hospital in trauma patients. *J Emerg Med* 2000:**19**(3):259–64.
**Murray JA,** Demetriades D, Berne TV, *et al*. Prehospital intubation in patients with severe head injury. *J Trauma Inj Infect Crit Care* 2000;**49**:1065–70.
**Eckstein M,** Chan L, Schneir A, *et al*. Effect of prehospital advanced life support on outcomes of major trauma patients. *J Trauma Inj Infect Crit Care* 2000;**48**:643–8.
**Bochichhio GV,** Ilahi O, Joshi M, *et al*. Endotracheal Intubation in the field does not improve outcome in trauma patients who present without an acutely lethal traumatic brain injury. *J Trauma Inj Infect Crit Care* 2003;**54**:307–311.
**Davis DP,** Hoyt DB, Ochs M, *et al*. The effect of paramedic rapid sequence intubation on outcome in patients with severe traumatic head injury. *J Traum, Inj Infect Crit Care* 2003;**54**:444–53.
**Stockinger ZT,** McSwain NE Jr. Prehospital Endotracheal intubation for trauma does not improve survival over bag-valve-mask ventilation. *J Trauma, Inj Infect Crit Care* 2004;**56**:531–6.
**Wang HE,** Peitzman AB, Cassidy LD, *et al*. Out-of-hospital Endotracheal Intubation and outcome after traumatic brain injury. *Ann Emerg Med* 2004;**44**:439–50.
**Davis DP,** Peay J, Sise MJ, *et al*. The impact of prehospital endotgracheal intubation on outcome in moderate to severe traumatic brain injury. *J Trauma Infect Crit Care* 2005;**58**:933–9.

# Headache in paediatric head injury

**Report by Michelle Jacobs**
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doi: 10.1136/emj.2005.031724

**Abstract**
A short cut review was carried out to establish whether headache was a significant indicator of the severity of head injury in children. 301 papers were found using the reported searches, of which 2 presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. It is concluded that headache is not an independent risk factor for intracranial injury in children.

### Clinical scenario

A 10 year old girl has presented on several occasions since a recent head injury with a persistent headache. Clinical examination has previously been documented as normal. You wonder how significant the headache is with respect to the initial head injury.

### Three part question

In [a child with a head injury] does [the presence of headache] predict [intracranial injury]?

### Search strategies

Medline 1966- Week 4 August 2005 [exp brain injuries/ or brain injur$.mp. or exp craniocerebral trauma/ or head injur$.mp.] AND [exp headache/ or headache.mp.] AND [BestBETs Paediatric filter ] LIMIT to human AND English. Embase 1980–2005 week 37 [craniocerebral trauma.mp. OR exp Head Injury/ OR exp Brain injury/ OR brain injur$.mp] AND [exp headache/ OR headache.mp.] LIMIT to Human, English Language, Abstracts and (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) The Cochrane Library Issue 3 2005 Exp brain injuries [MeSH] OR exp craniocerebral trauma [MeSH] AND exp headache [MeSH] AND exp Child [MeSH]

### Search outcome

Altogether 301 papers were found, of which one was a meta-analysis. One further paper postdated the meta-analysis. These two papers are shown in the table.

### Comments

The consensus opinion is that the presence of headache does not correlate with the presence of or severity of intracranial injury in children. Several retrospective studies found high levels of association between extradural haemorrhage and initial presentation symptoms including headache. However, these were a highly selected group of patients and small numbers were involved.

### ► CLINICAL BOTTOM LINE

Headache does not appear to be an independent risk factor for intracranial injury in children.

**Dunning J,** Batchelor J, Stratford-Smith P, *et al*. A meta-analysis of variables that predict significant intracranial injury in minor head trauma. *Arch Dis Child* 2004;**89**:653–59.
**Chan HC,** Aasim WAW, Abdullah NM, *et al*. Characteristics and clinical predictors of minor head injury in children presenting to two Malaysian accident and emergency departments. *Singapore Med J* 2005;**46**:219–23.

**Table 2**

| Author, country, date | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---|---|---|---|---|---|
| Dunning J *et al*, 2004, UK | 1136 children reported in 4 studies | Meta-analysis | Relative risk of intracranial haemorrhage in children with headache | 1.02 (CI 0.62–1.69) | |
| Chan HC *et al*, 2005, Malaysia | 265 children aged 2–18 years admitted to hospital with head injury | Prospective cohort | Odds ratio of intracranial injury | 20.8 (CI 3.9–25.2) | Only children admitted to hospital |

# S-100b protein levels as a predictor for long-term disability after head injury

**Report by John-Paul Lomas, *House Officer***
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doi: 10.1136/emj.2005.031732

**Abstract**
A short cut review was carried out to establish whether levels of S-100b were predictive of long-term disability after head injury. 200 papers were found using the reported searches, of

**Table 3**

| Author, country, date | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---|---|---|---|---|---|
| Waterloo K *et al*, 2005, Norway | 7 patients with high S-100b after mild head injury matched with 7 patients with no detectable S-100b | Case control study | Overall cognitive function<br>Reaction time<br>Attention | No difference<br>Increased in raised S-100b group<br>Reduced in raised S-100b group | |
| Rothoerl *et al*, 1998, Germany | 30 patients with a severe head injury (GCS<=9) and 11 with minor head injury (GCS 13-15) admitted to a neurosurgical unit<br>S-100 levels measured mean 2.5 hrs after injury | Diagnostic Cohort study (4) | Glasgow Outcome Scale on discharge (Mean day 19 in severe group and mean day 1.3 in minor head injury group)<br>Detectable level of S-100 (>0.5mcg/l) | Patients with GOS 3-5 S-100 level mean 1.2mcg SD 1.8<br>Patients with GOS 1-2 (unfavourable) S-100 level mean 4.9mcg/l SD 5.3 P=0.0025<br>25 of 27 Elevated S-100 levels were found in the minor head injury group | Non-independent gold standard<br>Small, selected cohort of patients |
| Raabe A *et al*, 1999, Germany | 82 patients after severe head injury (GCS<=8)<br>s-100 taken at admission and every 24 hours | Diagnostic cohort study (2b) | Glasgow outcome score at 6 months<br>Unfavourable outcome defined as severe disability or vegetative state | For S-100 level of >2.5mcg/l, unfavourable outcome was predicted with<br>Sensitivity 44%<br>Specificity 97% | No confidence intervals presented<br>Non-consecutive |
| Woertgen *et al*, 1999, Germany | 44 patients after severe head injury (GCS score <=8)<br>S-100 taken 1-6 hrs after injury | Diagnostic cohort study (3b) | Glasgow outcome score calculated at mean 11 months after trauma (GOS 1-3 unfavourable) | For S-100 level of >2mcg/l, PCS symptoms predicted with<br>Sensitivity 95%<br>Specificity 70% | Tables 2, 3 and 4 are incorrect, with erratum printed in a later edition |
| Ingebrigtsen *et al*, 1999, Sweden | 50 patients with minor head injury and LOC (GCS 13-15) referred to Neurosurgery dept after CT scan<br>S-100 taken hourly up to 12 hours | Diagnostic Cohort study (3b) | Neuropsychological testing at 3 months (for attention, psychomotor speed, trail-making test, memory, digit span) In 36 patients<br>MRI and CT scan findings within 48hrs | 11/36 patients had S-100 >0.2mcg/l<br>There were non significant trends to reduced impairment in the S-100 negative group<br>4 of 5 patients with brain contusion had S-100 >0.4mcg/l<br>Sensitivity 80% (p=0.035) | Very small study with no sample size estimates<br>Non consecutive<br>Only 36 of 50 patients followed up at 3 months |
| Ingebrigsten *et al* 2000 Scandinavia (3 centres Sweden, Denmark, Norway) | 182 patients from 3 centres with GCS 13-15 and brief Loss of Consciousness.<br>S-100 taken on admission | Diagnostic Cohort Study (2b) | Rivermead postconcussion symptoms questionnaire score (RPQ)<br>Intracranial Pathology on CT scan at <24 hours | Patients with a positive S-100 had mean RPQ 6.0 vs 4.0 in S-100 negative group p=0.07<br>Detectable S-100 predicted intracranial pathology with: Sensitivity 90%, Specificity 65% | No sensitivities or specificities given for prediction of long term disability |
| Mussack T *et al*, 2000, Germany | 80 patients presenting with a history of minor head trauma (GCS 13-15)<br>Also 10pts with severe head injury (GCS<8)<br>S-100 taken at 0h, 6h and 24hrs post admission<br>50 patients GCS 13-15 after normal CT scan | Diagnostic study (4) | S-100 in Minor Head Trauma pts<br>Patients with Severe head Injury GCS<8 | Patients discharged <=6hrs 0.29 +/- 0.11 ng/ml<br>Patients discharged >= 24hrs 0.70 +/- 0.19 ng/ml<br>Patients subsequently admitted to ICU 5.03 +/- 3.18 ng/ml<br>5.26 +/- 1.56ng/ml | No gold standard outcome measures<br>Non consecutive<br>Results not clearly presented<br>Non significant findings between groups<br>Low number of patients |
| Herrmann *et al*, 2001, Germany | 69 patients admitted to a neurosurgical unit (mostly GCS >13)<br>S-100 taken at 1, 2 and 3 days | Diagnostic study (3b) | Intracranial pathology on CT scan at 2 weeks and 6 months, or focal neurology | At 2 weeks, S-100 of >0.14mcg/l predicted positive outcome:<br>Sensitivity 69%<br>Specificity 90%<br>At 6 month, S-100 of >0.14mcg/l predicted positive outcome:<br>Sensitivity 65%<br>Specificity 89% | Inclusion criteria for patients unclear<br>Only 29 patients followed up to 6 months |
| Chatfield DA *et al*, 2002, UK | 20 patients with severe head injury (GCS<=8) admitted to neurosurgical unit<br>s-100 on admission | Diagnostic cohort study (4) | Glasgow outcome score at 6 months after trauma (GOS 1-3 unfavourable) | Patients with GOS 1-3 S-100 mean level 2.46 +/-0.32mcg/l<br>Patients with GOS 3-5 S-100 mean level 0.6 +/-0.1mcg P<0.05 | Data not clearly presented<br>Small study<br>No cut off points or ROC curves calculated |
| Townend WJ *et al*, 2002, UK | 148 adult head injury patients (GCS 4-15) in 4 hospitals. Most had a minor head injury<br>S-100 levels taken within 6 hours of head injury | Diagnostic study (2b) | Extended Glasgow outcome score at 1 month | S-100>0.32mcg/l predicted severe disability (15 patients with GOSE<5):<br>Sensitivity 93% (63%-100%)<br>Specificity 72% (54%- 79%)<br>NPV 99% (93%-100%) | Wide confidence intervals<br>Non consecutive<br>Wide definition of head injury (including no LOC)<br>80% follow up rate |
| Spinella *et al*, 2003, USA | 27 children (<18yrs) with traumatic brain injury<br>S-100 taken within 12 hours | Diagnostic cohort study (3b) | Pediatric Cerebral performance category score (PCPC) assessed at discharge and 6 months | For s-100 level of >2.0mcg/l, unfavourable outcome was predicted with<br>Sensitivity 86%<br>Specificity 95% | Very small study<br>Confidence intervals not given<br>Non consecutive |
| Savola O & Hillbom M, 2003, Finland | 172 consecutive patients with mild head injury (GCS 13-15) | Diagnostic cohort study (2b) | Post concussional symptoms defined by Rivermead Post-Concussion Symptoms Questionnaire at 2–6 weeks | For s-100 level of >0.50mcg/l, PCS symptoms predicted with<br>Sensitivity 27%<br>Specificity 93% | No confidence intervals or sample size calculations |

which 12 presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. It is concluded that a raised level of S-100b is a marker of poorer long-term outcome after both major and minor head injury.

### Clinical Scenario

A 17 year old male presents to the Emergency Department after a road traffic accident. His GCS was 8 on arrival but an immediate CT scan showed no focal abnormality. His GCS returned to 14 after 4 hours. You are talking to his mother who is reassured that he does not need urgent neurosurgery, but she asks whether he will suffer any long term consequences from this injury. You tell her that it is difficult to predict. You have recently heard that S-100 protein measurement is available in your hospital for research purposes. You wonder whether S-100 could help predict his long term prognosis.

### Three part question

In [patients with a head injury] do [levels of S-100B protein] predict [long-term disability]?

### Search strategy

Medline 1966-Week 4 August 2005 using the OVID interface [(exp S100 Proteins/ OR s100.mp OR s-100.mp) AND (exp Brain Injuries/ OR brain injury.mp OR exp Craniocerebral trauma/ OR head inj$.mp)] Embase 1980-2005 week 37 [exp Protein S 100/ OR s100.mp OR s-100.mp] AND [exp Brain Injury/ OR brain injury.mp. OR craniocerebral trauma.mp. or exp Head Injury/] LIMIT to Human and English Language The Cochrane Library Issue 3 2005 Exp Brain injuries [MeSH] OR exp Craniocerebral trauma [MeSH] AND exp S100 proteins [MeSH]

### Search outcome

200 papers were found of which 13 were found to be relevant. Two relevant papers described the same patient population. The remaining 12 papers are shown in the table.

### Comments

All studies were under 200 patients in size and most were under 100 patients. The studies find sensitivities from 27%–95% and specificities from 70% to 97%. The reasons for this great variation in findings may in large part be due to the small sample sizes. The specificities seem to perform better than the sensitivities and thus the finding of a high S-100 may indicate that your patient is at high risk of long term disability. The cut-points for a significant S-100 level differ between studies also and are generally much higher when applied to patients after a severe head injury. Most studies agree that S-100 levels must be taken within 6 hours of head injury.

### ▸ CLINICAL BOTTOM LINE

A high S-100 level is a marker of poorer long term outcome following minor and major head injury.

**Waterloo K,** Ingebrigtsen T, Romner B, *et al.* Neuropsychological function in patients with increased serum levels of protein S-100 after minor head injury. *Acta Neurochirug* 1997;**139**:26–32.

**Rothoerl RD,** Woertgen C, Holzschuh M, *et al.* S-100 serum levels after minor and major head injury. *Journal of Trauma-Injury Infection & Critical Care* 1998;**45**:765–7.

**Raabe A,** Grolms C, Seifert V. Serum markers of brain damage and outcome prediction in patients after severe head injury. *British Journal of Neurosurgery* 1999;**13**:56–9.

**Woertgen C,** Rothoerl RD, Metz C, *et al.* Comparison of clinical, radiologic, and serum marker as prognostic factors after severe head injury. *Journal of Trauma-Injury Infection & Critical Care* 1999;**47**:1126–30.

**Ingebrigtsen T,** Waterloo K, Jacobsen EA, *et al.* Traumatic brain damage in minor head injury: relation of serum S-100 protein measurements to magnetic resonance imaging and neurobehavioral outcome. *Neurosurgery* 1999;**45**:468–75.

**Ingebrigtsen T,** Romner B, Marup-Jensen S, *et al.* The clinical value of serum S-100 protein measurements in minor head injury: a Scandinavian multicentre study. *Brain Injury* 2000;**14**:1047–55.

**Mussack T,** Biberthaler P, Wiedemann E, *et al.* S-100b as a screening marker of the severity of minor head trauma (MHT)—a pilot study. *Acta Neurochirurgica—Supplement* 2000;**76**:393–6.

**Herrmann M,** Curio N, Jost S, *et al.* Release of biochemical markers of damage to neuronal and glial brain tissue is associated with short and long term neuropsychological outcome after traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry* 2001;**70**:95–100.

**Chatfield DA,** Zemlan FP, Day DJ, *et al.* Discordant temporal patterns of S100beta and cleaved tau protein elevation after head injury: a pilot study. *British Journal of Neurosurgery* 2002;**16**:471–6.

**Townend WJ,** Guy MJ, Pani MA, *et al.* Head injury outcome prediction in the emergency department: a role for protein S-100B? *Journal of Neurology, Neurosurgery & Psychiatry* 2002;**73**:542–6.

**Spinella PC,** Dominguez T, Drott HR, *et al.* S-100beta protein-serum levels in healthy children and its association with outcome in pediatric traumatic brain injury. *Critical Care Medicine* 2003;**31**:939–45.

**Savola O,** Hillbom M. Early predictors of post-concussion symptoms in patients with mild head injury. *European Journal of Neurology* 2003;**10**:175–81.

## Aspirin and the risk of intracranial complications following head injury

**Report by Magdy Sakr, *Consultant in Emergency Medicine***
**Search checked by Libby Wilson, *Clinical Research Fellow***
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doi: 10.1136/emj.2005.031740

### Abstract

A short cut review was carried out to establish whether pre-injury aspirin increases the risk of intracranial complications following head injury. 124 papers were found using the reported searches, of which three presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. It is concluded that aspirin may increase the risk of developing intracranial complications. More research is needed.

### Clinical scenario

A 65 year old man on aspirin presents to the Emergency Department having fallen sustaining a minor head injury. You wonder whether he is at higher risk of intracranial bleeding due to aspirin.

### Three part question

In [adults with head injury] does [pre-injury aspirin] adversely [affect clinical outcome]?

### Search strategies

Medline using the OVID interface 1966- August Week 4 2005 [exp brain injuries/ OR brain injur$.mp. OR exp craniocerebral trauma/ OR head injur$.mp.] AND [exp aspirin/ OR aspirin.mp. OR exp acetylsalicylic acid/ OR antithromb$.mp.] Limit to humans and English Embase 1980–2005 week 37 [craniocerebral trauma.mp. OR exp Head Injury/ OR exp Brain Injury/ OR brain injur$.mp] AND [aspirin.mp. or exp Acetylsalicylic Acid/ OR antithrom$.mp] LIMIT to Human, English Language and (adult <18 to 64 years> or aged <65+ years>) The Cochrane Library Issue 3 2005 Exp Aspirin [MeSH] AND exp brain injuries [MeSH] OR exp craniocerebral trauma [MeSH]

**Table 4**

| Author, country, date | Patient group | Study type | Outcomes | Key results | Study weaknesses |
|---|---|---|---|---|---|
| Reymond MA *et al*, 1992, Switzerland | 189 patients with severe head injury | Retrospective Risk analysis | Chronic subdural haematoma | Aspirin is a risk factor for chronic subdural haematoma | Retrospective nature of the study |
| Mina AA *et al*, 2002, USA | 37 patients admitted with intracranial injury on anticoagulants 37 case matched patients | Retrospective case controlled | Mortality due to head injury | Higher percentage of t hose on aspirin than any other anticoagulant died | Retrospective, Subgroup analysis, and small sample size |
| Spektor S *et al*, 2003, Israel | Mild (GCS13-15) and moderate (GCS 9-12) head injuries in 231 patients >60 years old. 110 of which were on aspirin therapy | Prospective cohort study | Intracranial haemorrhage | No difference in frequency or type of ICH whether on aspirin or not | Small sample size. |
| | | | | | Mild & moderate injuries included |

## Search outcome

Altogether 103 were found in Medline and 104 in Embase. Three were relevant to the three part question, these are shown in the table below:

## Comments

There was conflicting evidence that prior chronic use of aspirin increases the risk of intracranial haemorrhage following minor head injury. However, there is some evidence to suggest that there is increased risk of chronic subdural haemorrhage. A well designed prospective cohort study with adequate sample size and follow up is needed to address such important and common problem.

## ▸ CLINICAL BOTTOM LINE

Pre-injury aspirin may increase the risk of intracranial complications following head injury. More research is needed.

**Reymond MA,** Marbet G, Radu EW, *et al*. Aspirin as a risk factor for haemorrhage in patients with head injuries. *Neurosurg Rev* 1992;**15**(1):21–25.
**Mina AA,** Knipfer JF, Park DY, *et al*. Intracranial complications of preinjury anticoagulation in trauma patients with head injury. *J Trauma* 2002;**53**(4):668–672.
**Spektor S,** Agus S, Merkin V, *et al*. Low–dose aspirin prophylaxis and risk of intracranial hemorrhage in patients older than 60 years of age with mild or moderate head injury: a prospective study. *J Neurosurg* 2003;**99**(4):661–665.