

ORIGINAL ARTICLE

Apparent life threatening events in infants presenting to an emergency department

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Objective: To describe the aetiology and outcome of apparent life threatening events (ALTE) presenting to an emergency department (ED), and to assess the value of an initial investigation protocol.

Design: A 12 month prospective study of infants under 1 year of age who presented to a children's hospital ED after an ALTE. A standardised history sheet and initial investigation protocol were used. All infants were admitted to hospital and followed up at six months.

Results: There were 65 infants recruited, median age 7 weeks. None had died at the time of writing. Diagnoses included gastro-oesophageal reflux n=17 (26%), pertussis, n=6 (9%), seizures, n=6 (9%), urinary tract infection (5), factitious illness (2), brain tumour, atrial tachycardia, persistent ductus arteriosus and opioid related apnoea. No diagnosis was reached in 15 cases (23%). Fifty seven (88%) had only one admission to hospital for ALTE. More serious diagnoses were associated with a presentation age over 2 months, abnormal initial clinical examination, and recurrent ALTE.

Conclusions: ALTEs presenting to the ED may remain as a single, unexplained event or be attributable to numerous causes, ranging from minor to serious. Knowledge of the commoner causes and factors associated with higher risk could result in a more targeted approach, improving the decision making process and benefiting both infants and parents.

An apparent life threatening event (ALTE) is defined as "an episode that is frightening to the observer and that is characterised by some combination of apnoea (central or occasionally obstructive), colour change (usually cyanotic or pallid), marked change in muscle tone, choking or gagging."¹ ALTEs are not uncommon, and infants are frequently brought to an emergency department (ED) after a "blue episode" or "funny turn". Parents are understandably anxious, however the infant often appears perfectly well by the time of arrival and thus poses a difficult dilemma.

The term ALTE is non-specific and describes a cluster of symptoms for which there may be many possible causes. The term has alarming connotations but few episodes that fulfil the definition of an ALTE require formal cardiopulmonary resuscitation. A retrospective study of similar infants in our hospital² illustrated the confusing nature of ALTEs to clinicians. Concerns linger about the link between ALTEs and the sudden infant death syndrome (SIDS), which is at best weak.

Existing literature tends to report selected groups of infants, with the risk of positive reporting bias. The purpose of this study was therefore to provide information on the outcomes of unselected infants presenting to the ED, and to assess the value of a standardised history and initial investigation protocol.

METHODS

A prospective study was performed in 65 infants under the age of one, admitted to the Royal Liverpool Alder Hey Children's Hospital after an ALTE during the 12 month period to May 1997. The age group was selected on the basis of previous data.² The ED sees approximately 67 000 children annually and receives most paediatric emergency attendances for a city of 400 000 people. A small proportion attend nearby EDs or minor injury units.

Ethical committee approval was obtained. After discussion, parents were issued with an explanatory leaflet describing the investigation protocol and a telephone contact number, and written, informed consent was gained.

Patient selection

Infants were entered into the study by the first doctor to see the infant. Infants were included if the reason for attendance was an acute, frightening event, fulfilling the accepted definition of an ALTE¹ described above. Selection was not based on duration or severity of the ALTE in order to avoid subjectivity, as recall may be unreliable by parents in a distressed state. The only group excluded was infants with a working diagnosis of febrile convulsion, a documented pyrexia, abnormal limb movements and age over 6 months old. Large numbers of such infants fulfil all three criteria, form a different age group from ALTEs, and do not present such difficulties in diagnosis or management.

Emergency attendances to the ED and patients referred directly by general practitioners to the on call inpatient services were included (these are admitted via the ED). The study required that all infants were admitted to hospital.

The standardised history and examination sheet

Demographic information, perinatal history, medical history since birth (in particular respiratory or gastro-oesophageal reflux (GOR) type symptoms), medication history for the previous 24 hours, and a record of family history of SIDS were obtained. A family history of seizures or asthma was sought, and the presence of smokers in the household. Symptoms specifically recorded included colour change, choking or vomiting, stiffness or floppiness, limb jerking, estimated duration of the episode, whether occurring while awake or asleep, the timing of the ALTE in relation to feeding, and resuscitative measures taken during the event. Routine clinical examination with the inclusion of pulse oximetry was performed.

Abbreviations: (ALTE), apparent life threatening event; ED, emergency department; SIDS, sudden infant death syndrome; GOR, gastro-oesophageal reflux; LRTI, lower respiratory tract infection

The investigation protocol

A protocol of initial investigations was followed. Subsequent investigations were performed at the discretion of the inpatient team caring for each infant. The following tests were performed as soon as possible after arrival:

- (1) Haematology: haemoglobin, leucocyte and platelet count.
- (2) Biochemistry: serum electrolytes, urea, creatinine, glucose, bicarbonate, lactate, ammonia and blood amino acids. Urine organic acids, reducing substances and toxicology for opioids, benzodiazepines, barbiturates, cannabis, cocaine, amphetamines and methadone.
- (3) Microbiology: a postnasal swab was taken for pertussis, and a nasopharyngeal aspirate for respiratory syncytial virus if secretions were present (analysed by direct immunofluorescence). A "bag" specimen of urine was "dip" tested (with strips which assay for protein, leucocyte esterase and nitrite), and sent for microscopy and culture if the "dip" test was positive.
- (4) Radiology: within the first 24 hours of admission (or immediately if indicated) a chest radiograph was performed, and within two weeks of admission (usually within 48 hours) a radioisotope milk scan was also performed. The majority of these were single phase, to observe GOR rather than pulmonary aspiration. This was because aspiration may not necessarily occur during an ALTE, and for parental convenience.
- (5) 12 Lead ECG: before discharge; analysis to include measurement of the QT_c interval.

Follow up

On entering the study, each infant was registered with the Office for National Statistics, which provides notification of deaths occurring anywhere in the country from the time of notification, until such time in the future that the authors decide to cease follow up (estimated five years).

Each infant's health visitor was contacted to see if they or their siblings were on the social services Child Protection Register and to note any particular concerns.

After hospital discharge, all investigations and discharge diagnosis were recorded. Six months later case notes were obtained for information about further hospital attendances, changes in diagnosis, and outpatient visits. For the purpose of the study the final diagnosis was that which was entered in the patient's records at this time (in some cases different from the initial discharge diagnosis).

RESULTS

Sixty five infants were recruited. The infants represented 65 of 10 743 (0.6%) of total under 1 year old attendances to the ED for the same period. Six month follow up information was obtained on 64 of 65.

Pattern of presentation

The age ranges are displayed in figure 1, and show a peak incidence of ALTEs between 1 week and 2 months. Two thirds of infants were under 10 weeks of age. The median age at presentation was 7 weeks. Mode of referral was by carer in 75%, general practitioner in 20%, other hospitals in two cases, and one each by midwife and health visitor. Thirty eight (59%) arrived by car, as is typical for this age group, and 23 (35%) by ambulance. Four were not documented. Cases were evenly distributed through the year.

Information from standardised history and examination sheet

The ALTE

Cyanosis and apnoea were the predominant presenting symptoms, occurring in 46 (71%) and 45 (70%) of infants

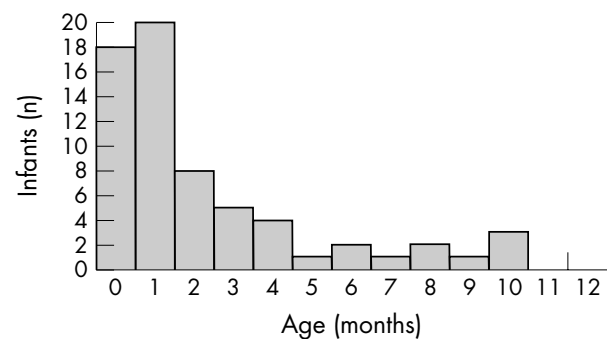


Figure 1 Age at presentation.

respectively. Difficulty in breathing occurred in 40 (62%), pallor in 33 (51%), stiffness in 30 (46%), floppiness in 28 (43%), choking in 23 (35%), red face in 19 (29%), limb jerking in 14 (22%) and vomiting in 12 (18%). None of these symptoms in particular correlated significantly with the final diagnosis: for instance limb jerking did not correlate with a final diagnosis of seizures.

Thirty eight (58%) episodes occurred while awake. A duration of more than one minute was reported in 28 (43%). Resuscitative measures taken included minor stimulation in 39 cases (60%), vigorous stimulation in seven (11%), "mouth to mouth" ventilation by parents in two, and bag-valve-mask ventilation in a further two infants. One infant was subsequently intubated. No infant required cardiac massage.

Past and family history

Twenty two infants were first born (34%), 21 (32%) were born by caesarean section and 10 (15%) were born at less than 34 weeks' gestation. A high number required treatment in a neonatal unit, compared with the 1996 figures for our region (29 000 deliveries per annum), however because of the small numbers, statistical significance was barely reached: 13 infants were admitted to the neonatal unit (20%), versus 9.3% for Mersey region, a difference of 10.7% (95% CI 1% to 20%); requirement for ventilation was 9.2% (six infants) versus 2.4%, a difference of 6.8% (95% CI 0% to 13.9%).

There was a history of respiratory symptoms since birth in 25% of infants, and GOR symptoms (recurrent possetting or vomiting) in 32%. A history of recent fever was given in 23%, and of recent upper or lower respiratory symptoms in 51%. Medication had been given within the previous 24 hours to half the infants (mainly paracetamol, vitamins or antibiotics).

A family history of asthma was present in 46% (9% not documented). A history of SIDS in first degree relatives was present in 10 cases (15.4%) although no study infant was already involved in an apnoea monitoring programme. Sixty per cent of households contained smokers (8% not documented). No infant was on the social services Child Protection Register prior to the study.

Examination findings

Thirty five infants (54%) appeared normal on routine clinical examination. Oxygen saturations of less than 95% were recorded in three infants. One of these had pertussis infection, one bronchiolitis, and the other a lower respiratory tract infection (LRTI) and patent ductus arteriosus. Of the other infants with respiratory disorder, 4 of 12 (33%) had a normal initial respiratory examination.

Cardiovascular system examination was abnormal in 10 infants: a murmur in eight (one PDA, others "innocent"), delayed capillary refill in one and atrial tachycardia in one (rate 240/min). A temperature greater than 37.5°C was recorded in 11 cases (17%).

Table 1 Positive yield of investigations in 65 infants

Investigation	Percentage abnormal	Definition of abnormal
Radio-isotope milk scan	89	Reflux through gastro-oesophageal sphincter seen on single phase scan
Chest radiograph	55	As reported by paediatric radiologist
Lactate (blood)	54	>2 mmol/l
	15	>3 mmol/l
White cell count (blood)	33	>12 cells/mm ³
Bicarbonate (blood)	20	<20 mmol/l
Urine culture	13	White cells >50 × 10 ⁵ per high powered field + pure growth of bacteria
Haemoglobin	13	<2 standard deviations for age adjusted range
Post-nasal swab	7	Culture for pertussis
Ammonia (blood)	4	>100 mmol/l
Metabolic screen: amino acids (blood)	4	
organic acids (urine)	2	
Toxicology screen (urine)	3	
Na, K, urea, creatinine and glucose (blood)	0	

Results of investigation protocol

The yield of positive results from the investigation protocol is summarised in table 1.

Although the majority of the investigations were performed, data were not fully complete. The most common reason was an inadequate volume of blood or urine obtained, or because investigations were omitted once a definitive diagnosis was apparent.

Haematology

A high proportion of infants (13%) were more than two standard deviations below the age adjusted range for haemoglobin. A raised white cell count correlated with a discharge diagnosis of infection in only 50% of cases.

Biochemistry

There were no significant findings with respect to the metabolic screen, urine reducing substances or ammonia. Eleven infants had bicarbonate levels below 20 mmol/l. Of these, four had non-specific final diagnoses, but seven had diagnoses such as sepsis or seizures. Similarly, a lactate value of over 3 mmol/l occurred in seven infants, five of whom had specific, serious diagnoses. Urine analysis for toxicology was performed on 35 infants (54%). Opioids were detected in one preterm twin with a LRTI who presented with apnoea. The general practitioner had prescribed an opioid containing cough linctus, and the parents accidentally omitted to mention it when asked about medication in the previous 24 hours on routine questioning.

Microbiology

There were seven cases of pertussis infection, three confirmed on postnasal swab, the others diagnosed by clinical symptoms and lymphocytosis. There were 14 samples taken for RSV (the majority were omitted because of lack of secretions). Only one was positive, by direct immunofluorescence.

Five infants had a urinary tract infection. Subsequent investigations for urinary tract abnormalities revealed abnormalities in two. Some blood cultures and/or lumbar punctures were ordered outside the protocol; none was positive.

Radiology

Chest radiographs were reported by a radiologist as abnormal in 28 of 51 infants, although 11 were reported as hyperinflation with no other finding. However, significant findings occurred in nine cases without any history or examination suggesting respiratory disorder.

Radioisotope milk scans were obtained in 46 infants and demonstrated GOR in 89%; however a clinical diagnosis of GOR was made in only 17 (41%) of these. The milk scan demonstrated GOR in 16 infants with other diagnoses, such as UTI, seizures or pertussis.

12-Lead ECG

Recordings were obtained in 40 infants. One infant presented in atrial tachycardia, but ECG after treatment was normal. No other abnormalities were found, in particular no prolongation of the QT_c interval.

Clinical outcome

No infant has died at the time of writing (around three years). Fifty seven infants (88%) had only one hospital admission with an ALTE, although three of those continued to have ALTEs at home. Eight infants had two or more admissions for an ALTE: all had significant underlying disorders. The commonest diagnoses are listed in table 2, and are compared with those of other authors.²⁻¹⁰

Of six infants with non-pertussis LRTI, one required ventilation because of *H influenzae* pneumonia, another had a patent ductus arteriosus, and one RSV bronchiolitis.

Six infants had seizures, one of which was a breast fed infant of African parents who had hypocalcaemia secondary to maternal vitamin D deficiency.

Two infants were diagnosed as cases of factitious illness (Munchausen's syndrome by proxy). One presented on numerous occasions with various symptoms. GOR was demonstrated on barium meal and radioisotope milk scan, but oesophageal pH studies were normal. Cranial ultrasound and an electroencephalogram (EEG) were normal. The patient underwent a Nissen's fundoplication operation, but continued to present with unwitnessed symptoms such as diarrhoea and rectal bleeding. Symptoms ceased after being placed on the Child Protection Register. The second infant was in the temporary foster care of an ex-nurse. There were three admissions for apnoea, none of which were corroborated by ward staff, including one occasion when the apnoea monitor was found to have been removed. Extensive investigations proved normal, including EEG and brain magnetic resonance imaging. On return to its natural mother the baby had no further symptoms.

One infant was diagnosed with a grade 2 temporal astrocytoma. He presented at 9 months of age with a respiratory arrest requiring bag-valve-mask ventilation. GOR was diagnosed on the basis of a barium meal and minor changes on pH studies, although endoscopy was normal and his growth was on the 90th centile. After several further severe apnoeas he underwent a Nissen's fundoplication procedure. Initial EEG had been normal, but continuous EEG recording was abnormal and magnetic resonance imaging demonstrated a tumour. After neurosurgery he has only mild visual problems and speech delay.

There was one case each of febrile convulsion, laryngomalacia (previously diagnosed) and gastroenteritis. One infant had mild cardiomegaly and hepatomegaly with developmental delay and asthma but no specific diagnosis.

Table 2 Aetiology of ALTEs (with comparison to previous work)

Study	Total patients	Patients pre-selected	Study design	Mean age (weeks)	Deaths (%)	Aetiology of ALTE (%)
Current study	65	No	Prospective	7	0	Unknown (23), GOR (25), Pertussis (9), Other LRTI (9), Seizures (9), UTI (8), Fact (3), Hypocalcaemia (1.5), Brain tumour (1.5), Opioid (1.5), Airway (1.5), SVT (1.5), PDA (1.5), gastroenteritis (1.5)
Kahn ⁴	3799	Yes	Prospective	12.8	?	Unknown (38), GOR (20), LRTI (7), Seizures (4), Fact (0.2), Hypocalcaemia (0.3), Other metabolic (1.2), Drug effect (0.2), Airway (2), Arrhythmia (0.5), CHD (0.3)
Rahilly ⁵	340	Yes	Prospective	5	1*	Unknown (15), GOR (62), Seizures (8), Fact (1.5), Hypoglycaemia (0.6), Abnormal pneumogram (8), Brain tumour (0.5), Airway (5), Oculocardiac reflex (0.9)
Ariagno ³	306	Yes	Retrospec (casenotes)	7.5	1†	Unknown (51). Did not comment on others
Dunne ⁶	132	Yes	Retrospec (casenotes)	9	2†	Excluded infants with known cause
Gray ²	130	No	Retrospec (casenotes)	9	0	Unknown (26), GOR (18), Seizures (25), Pertussis (6), Other LRTI (6), Airway (0.8)
Veere-man-Wauters ⁷	130	No	Retrospec (casenotes)	Range 2–36	2‡	Unknown (42), GOR (26), Seizures (4), Metabolic (1.5), Airway (9), Drug effect (5)
Duffy ⁸	72	Yes	Prospective	9	0	Excluded infants with known cause
Wennergren ⁹	34	Yes	Prospective	8	0	Seizures (9)
Tirosh ¹⁰	23	Yes	Prospective	30	9§	Unknown (43). 11 (48%) pathological polysomnographic studies. GOR (30); 1 case of SVT, 1 epilepsy, 1 LRTI.

GOR, gastro-oesophageal reflux; LRTI, lower respiratory tract infection; UTI, urinary tract infection; Fact, factitious illness; PDA, patent ductus arteriosus; CHD, congenital heart disease; SIDS, sudden infant death syndrome.

*Abnormal pneumogram; †SIDS; ‡GOR; §one homocystinuria, one apparent overwhelming viral infection.

Factors associated with significant disorder

Fifteen infants (23% of the study group) had no further episodes, and were given either no diagnosis, or a descriptive one (such as choke, cyanotic episode). Compared with this group, infants with either a recurrent ALTE or a definitive diagnosis were more likely to be older than 2 months at presentation, relative risk 2.87 (95% CI 1.3 to 6.8), $2p=0.009$, or have abnormal findings on initial clinical examination, relative risk 3.8 (1.6 to 9.8). There was a trend towards lower serum bicarbonate and higher lactate values in this group. Of infants aged under 2 months, with normal clinical examination and a lactate level under 2.0 mmol/l, none suffered a recurrent ALTE or was found to have a definitive diagnosis.

DISCUSSION

The definition of an ALTE¹ describes a generic set of symptoms that may have many different causes, some significant, but others simply a choking episode or “normal” infantile apnoea. The term is generally used for unexplained events and becomes superseded by a more definitive diagnosis when possible. Some clinicians reserve the term for more severe, or recurrent episodes.

The greatest difficulty for emergency physicians usually is deciding how far to pursue a diagnosis when faced with infants who appear perfectly well (54%). Parents have a high level of anxiety after such episodes and often feel unsupported by staff.¹¹ This study therefore aimed to help make an informed management plan for the non-specialist, by ascertaining the “natural history” and range of diagnoses presenting as an ALTE to the ED, and the symptoms, signs and investigations that are of most use.

Previous literature has generally been written by specialists and is of pre-selected infants, for example siblings of infants with SIDS, recurrent ALTEs, or ALTE requiring cardiopulmonary resuscitation. Diagnoses include intrapulmonary shunting,¹² upper airway disorders,^{13–15} abnormal skin perfusion,^{16,17} oculocardiac reflexes,^{5,18} cardiac conduction disorders,^{19,20} abnormal breathing regulation,²¹ abnormalities of surfactant²² or increased sweat potassium,²³ poisoning,²⁴ and inborn errors of metabolism.^{25–27}

Subsequent to our study, some practical guidelines for a general approach to the management of infants with

ALTE¹¹ were published. Our study would support their recommendation for targeted history taking, with awareness of the wide differential diagnosis. We have shown in this study and previously² that haste in making a definitive diagnosis may be seriously misleading, because diagnoses such as GOR may be coexistent but not causative. It is important to note that symptoms during the ALTE do not necessarily correlate with final diagnosis, and that recent minor symptoms are common.

The study was restricted methodologically by several factors. Firstly, it is unethical to perform invasive investigations once a definitive diagnosis has become apparent. Secondly, there were practical problems in obtaining sufficient volumes of blood, urine or respiratory secretions. Thirdly, the authors were not involved in the management of the infants beyond the ED. Lastly, given such a wide range of diagnoses in 65 infants, statistical analysis of the information is likely to reveal trends rather than unequivocal answers.

However, while many ALTEs are “innocent”, we have shown that some factors correlate with increased likelihood of significant disorders. These include presentation outside the “normal” age range for ALTE (less than 10 weeks), and recurrent ALTE.

Clinical examination should include pulse oximetry and examination alone should not be relied upon to exclude respiratory causes of ALTE: 33% of infants with respiratory disease had a normal initial respiratory examination. Chest radiography is more sensitive in this age group. In view of the risk of Munchausen’s syndrome by proxy or non-accidental injury in all infants with apnoea, examination should include fundoscopy.

We would recommend a mandatory period of inpatient observation. One reason for this is for parental reassurance. Infants are more likely to have had a complicated neonatal history, or a family history of SIDS. Our follow up information revealed high levels of anxiety in all families after an ALTE. The link between ALTEs and SIDS is, at best, weak, with mortality rates reported from zero to 13%, depending on patient selection. Apnoea alarms are often requested but many paediatricians are ambivalent about their usefulness. The family doctor and health visitor should be involved in continuing surveillance, and the family should be offered resuscitation training and a follow up visit to the hospital.

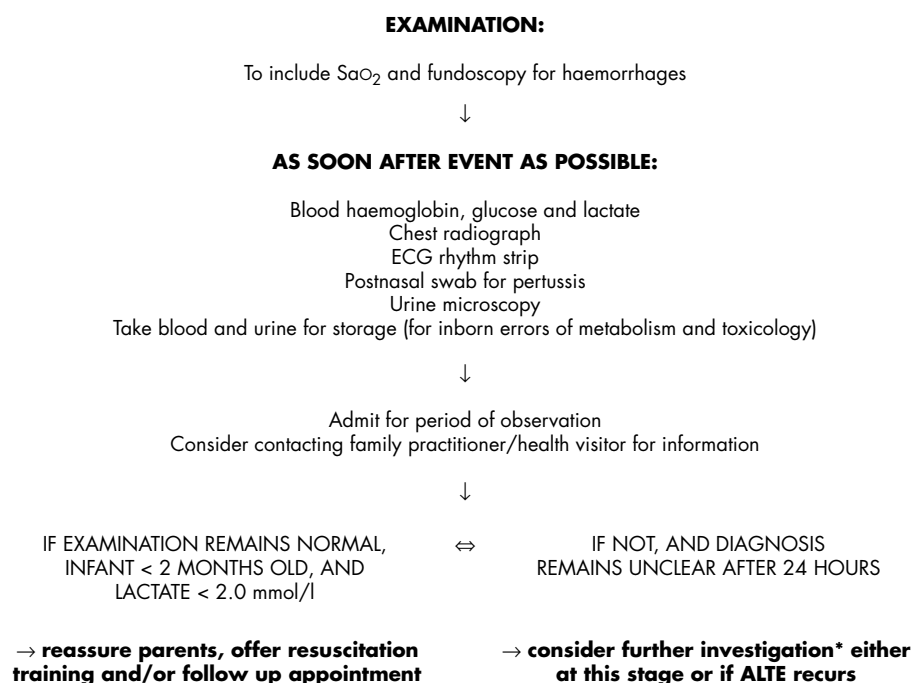


Figure 2 Suggested approach to investigation of first ALTE, if diagnosis is not apparent from general clinical history or examination.

* Further investigation should consider the following disorders: gastro-oesophageal reflux, seizures, intracranial abnormalities, hypocalcaemia, cardiac arrhythmias and upper airway disorders. Consider factitious illness if ALTE recurs.

In terms of investigation of a first ALTE, we would suggest a staged approach (fig 2). Fifteen per cent of infants were anaemic, which is in keeping with the study by Poets *et al.*²⁸ There was a trend towards higher lactate levels and low bicarbonate levels in infants with significant disease. Routine electrolytes, urea and creatinine are unlikely to be helpful.²⁹ The search for inborn errors of metabolism may not be warranted, however blood and urine samples should be collected as soon as possible, and can be stored pending a decision. It remains prudent, however, to check a blood glucose although hypoglycaemia was not encountered in our series.

Urine cultures revealed infection in five cases, making this a mandatory investigation for ALTE, given the age group. As in a previous study²⁴ we demonstrated that urine toxicology screen remains useful for picking up unsuspected drugs as a cause of apnoea.

There needs to be a greater awareness among all health care professionals of factitious illness (Munchausen's syndrome by proxy). This has been clearly implicated in ALTEs,^{16 17 24 30} and should always be considered in the differential diagnosis. Numerous investigations and one major operation were performed on the two infants in this series with Munchausen's syndrome by proxy. Neither presented with blood around the mouth, which has been highlighted as a symptom that should arouse suspicion in an ALTE,³⁰ but one was reported as having blood in the stool.

GOR should be a positive diagnosis made on the clinical picture with supportive investigations, rather than a "scapegoat" diagnosis, which may delay accurate diagnosis.

CONCLUSION

Most infants who present with an ALTE will have no further episodes, and will remain well. To predict those infants who have a significant underlying disorder the history taking and investigations need to be directed at those disorders which have been shown to cause ALTEs. For the non-specialist it is difficult to know where to start, given the large list of differential diagnoses. We have therefore designed a practical

investigation algorithm based on our findings (fig 2), although it should be validated in a larger population.

Infants may frequently be discharged from hospital without a definitive diagnosis. Most parents feel reassured by a period of observation, and it is important to empathise with their anxiety and provide adequate support. Those infants who are under 2 months of age, appear normal on clinical examination, and have a lactate level < 2.0 mmol/l are less likely to have further significant events. In these infants, doctors should explain that the risk of death is small, and should offer resuscitation training. However, if an infant is readmitted to hospital for recurrent ALTE, it should be fully investigated as the risk of significant disease is high.

Finally, all staff should be aware of the possibility of factitious illness, particularly when multiple investigations are negative.

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