Sleep apnoea during upper respiratory infection and metabolic alkalosis in infancy

F A ABREU E SILVA, U M MACFADYEN, A WILLIAMS, AND H SIMPSON

Department of Child Life and Health, University of Edinburgh, Royal Hospital for Sick Children, Edinburgh, and Department of Child Health, University of Leicester

SUMMARY Three to four hour polygraphic sleep studies were carried out in 10 infants, five with upper respiratory infection and five with metabolic alkalosis secondary to vomiting during and after recovery from illness. During upper respiratory infection, the main abnormality detected was brief ($>3<6$ seconds) or prolonged (>6 seconds) attacks of obstructive apnoea. Other indices of apnoea were similar to recovery data. Gross body movements were also increased. In infants with metabolic alkalosis indices of central apnoea were significantly increased when compared with recovery or case control data. Prolonged (>15 seconds) attacks of central apnoea and obstructive apnoea (>6 seconds) were only observed during illness. Gross body movements and periodic breathing were also increased.

These findings suggest that the functional consequences of apparently 'mild' illnesses in young infants may be greater than is generally suspected and perhaps relevant to mechanism(s) of death in sudden infant death syndrome.

Most infants have minor symptoms at some time during the early weeks of life but recover uneventfully. Several investigators observed an increased frequency of such symptoms before death in victims of sudden infant death syndrome.¹⁻⁴ Fifty nine per cent of the 145 victims of the syndrome studied by Stanton *et al* had recent symptoms, predominantly respiratory, compared with 16% of 154 controls.⁵ The questions arise whether 'minor' illnesses trigger a fatal sequence of events in a predetermined group of infants with altered responsiveness or whether age and maturity increase susceptibility in all infants from which a subgroup succumbs. The nature and severity of naturally occurring stresses that cause minor symptoms have received little attention. We have investigated the cardiorespiratory effects of natural stresses (upper respiratory tract infection and metabolic alkalosis caused by vomiting) in normal infants in the age group at risk for sudden infant death syndrome. The infants were not considered at increased risk in other aspects.

Patients and methods

Two groups of infants were studied during and after recovery from symptoms—one group with upper

respiratory infection and the other with recurrent vomiting.

Groups studied.

Group 1: respiratory tract infections

Five infants were studied during and after recovery from upper respiratory tract infection. Four were born at term after uncomplicated pregnancies and deliveries; the fifth was born at 29 weeks' gestation after premature rupture of the membranes. There were four boys and one girl, with a mean gestation of 38 weeks (range 29–41 weeks) and a mean birth weight of 2630 g (range 1290–3460 g). Mean chronological and postconceptional ages were 8 weeks (range 4–15 weeks) and 46 weeks (range 44–49 weeks), respectively, when initial studies were carried out. The mean interval between illness and recovery studies was 22 days (range 13–46 days). Initially, the infants had coryzal symptoms but were otherwise well. At follow up they were healthy and thriving. Mean rectal temperature was 36.9°C (range 36.4–37.5°C) during infection and 36.8°C (36.5–37.2°C) after recovery. There were no signs of respiratory distress on either occasion and on auscultation breath sounds were vesicular without

accompaniments. Immunofluorescent studies of nasopharyngeal secretions confirmed respiratory syncytial virus infection in one infant.

Group 2: recurrent vomiting

Five infants with a history of recurrent vomiting of duration of four to 21 days were also studied before and after pyloromyotomy for congenital hypertrophic pyloric stenosis. They had been born after uncomplicated pregnancies and deliveries. All were boys, with a mean birth weight of 3270 g (range 2690–3770 g) and a mean gestation of 39 weeks (range 36–40 weeks). Mean chronological and post-conceptual ages were 5 weeks (3–7 weeks) and 44 weeks (39–47 weeks), respectively, when initial studies were carried out. The mean interval between studies was nine days and between surgery and follow up studies was seven days (range 3–11 days).

Pyloric stenosis was suspected on clinical grounds in each infant at the time of admission to hospital and confirmed by palpation of a pyloric tumour during a test feed. In each case the degree of dehydration was judged to be less than 5% of body weight and intravenous administration of fluid and electrolytes was not deemed necessary to correct fluid and electrolyte imbalance. Table 1 gives serum electrolytes and blood urea concentrations and acid base state in individual infants when initial studies were conducted. One infant, case 1, was hypokalaemic, but otherwise electrolyte and blood urea values were remarkably normal. All infants showed moderate metabolic alkalosis. At follow up clinical recovery was apparently complete. Serum electrolyte and blood urea concentrations had become normal after treatment, and bottle feeding had been satisfactorily resumed in each case.

Infants in the above groups served as their own controls. In addition, five healthy, normal infants matched for age, sex, and postconceptional age were selected as a case control group for infants with recurrent vomiting because of the possibility that

index infants had not fully recovered from the metabolic upset associated with recurrent vomiting at the time of follow up studies.

Monitoring procedures. These have been described previously.⁶

Polygraphic sleep studies were carried out in hospital after the last evening feed, usually between 2300 and 0400 h. For follow up studies infants were re-admitted on the preceding afternoon. They were monitored in a dimly lit side room off the main ward, especially equipped for sleep studies. Ambient temperature ranged from 22–25°C. Electrodes were placed in position when the infant had settled after a feed, and nasal thermocouples were applied during periods of quiet sleep. Each infant, lightly clothed and unrestrained, was observed constantly and body movements and interventions recorded on polygraphic paper. Electroencephalogram, electro-oculogram, electromyogram, electrocardiogram, chest and abdominal movements, and nasal airflow were recorded on a Mingograf recorder at a paper speed of 10 mm per second. Sections of recording in each sleep state were also recorded at a rate of 100 mm/second to observe electroencephalogram changes more closely. Permanent records were thus available for electroencephalogram, electro-oculogram, electromyogram, electrocardiogram, nasal airflow, and chest and abdominal movements.

Data analysis. Each 30 second period (one epoch) of the record was analysed visually and sleep state coded according to the criteria of Anders *et al*⁷ and those of Rechtschaffen and Kales.⁸ The age range of the subjects was such that in some infants the transition between perinatal and 'infantile' sleep pattern⁹ might not have been completed. Individual proportions of the electroencephalogram frequencies and amplitudes during the sleep stages were used rather than absolute limits. Respiration, the variable under study, was omitted from the criteria

Table 1 Serum electrolytes and blood urea concentrations and acid base states of infants with pyloric stenosis

Case No	Serum electrolytes (mmol/l)			Blood urea (mmol/l)	Acid base state			
	Sodium	Potassium	Chloride		pH	Carbon dioxide tension (kPa)	Subtype bicarbonate ion (mmol/l)	Base excess (mmol/l)
1	138	2.4	—	5.0	7.53	7.35	40.6	+21.6
2	138	3.7	94	3.3	7.49	5.87	35.0	+11.0
3	136	3.6	86	5.6	7.49	5.70	34.0	+9.5
4	139	4.3	98	4.4	7.48	5.25	29.3	+6.6
5	138	3.4	96	3.7	7.50	5.57	30.9	+8.8

of the sleep stages. These were identified as quiet sleep, active sleep, and indeterminate sleep.

The respiration rate and heart rate were counted during the fourth, middle, and last minutes of continuous sleep for quiet and active sleep. Mean respiration rate and heart rate for each sleep state was then computed for each patient during and after recovery from illness and for each control infant. Central apnoeic pauses were defined as periods when chest and abdominal movements were absent and airflow at the nostrils had ceased for at least six seconds. Obstructive apnoea refers to periods during which there was stopping of airflow at the nostrils and continuing (often exaggerated) movements of the chest or abdomen, or both, not begun by gross body movements detected by direct observation or electromyogram recording. This latter proviso ensured that episodes of apparent obstructive apnoea begun by movement¹⁰ were excluded from analysis. The occurrence of prolonged (>15 seconds) attacks of central apnoea¹¹ and brief (>3 and <6 seconds) or prolonged (>6) attacks¹² were also noted. Indices of apnoea were assessed for central apnoeic pauses greater than six seconds. Apnoea index was defined as the duration of attacks of apnoea (seconds) during a given sleep state divided by the total duration of that sleep state expressed as a percentage. Rate of attacks of apnoea was the number of attacks of apnoea in each 100 seconds of a sleep state, and apnoea per cent was the percentage of epochs during which at least one apnoeic pause was begun. For each sleep state the mean duration of apnoeic pauses was calculated and the attack of apnoea of longest duration noted. These variables were computed for each sleep state and total sleep time. The percentage of time in each sleep state was also noted.

The occurrence and duration of periodic breathing, defined by Parmalee *et al* as two attacks of apnoea of three seconds or more within 20 seconds of each other,¹³ and gross body movements were computed in relation to sleep state and total sleep time.

Statistical analysis. The Wilcoxon matched pairs signed rank test was applied to the results obtained during and after recovery from illness in both groups of infants. The Mann-Whitney U test was applied to results obtained for infants with metabolic alkalosis and their matched case controls.

Results

Group 1: respiratory tract infections. Table 2 gives the results for apnoea variables, per cent sleep, respiration rate, and heart rate in relation to sleep

phase in the five infants during and after recovery from upper respiratory tract infection. With the exception of respiration rate, which was slightly but significantly increased after recovery, no significant differences were observed between corresponding

Table 2 Apnoea variables, per cent sleep, and respiration and heart rates in five infants during and after recovery from upper respiratory tract infection. Values are mean (SE)

	Sleep phase	During recovery	After recovery
Apnoea index	Active	0.24 (0.07)	0.69 (0.42)
	Quiet	1.10 (0.46)	0.67 (0.18)
	Indeterminate	0.33 (0.20)	1.11 (0.49)
Apnoea attack rate	Active	0.59 (0.24)	0.68 (0.23)
	Quiet	0.04 (0.01)	0.09 (0.04)
	Indeterminate	0.14 (0.06)	0.08 (0.02)
Attack of longest duration (sec)	Active	0.06 (0.04)	0.15 (0.07)
	Quiet	0.08 (0.03)	0.13 (0.05)
	Indeterminate	5.20 (1.32)	6.20 (1.83)
Mean duration of attack of apnoea (sec)	Active	5.84 (2.54)	7.68 (2.16)
	Quiet	2.80 (1.72)	4.62 (1.89)
	Indeterminate	7.22 (2.09)	7.78 (2.16)
Apnoea per cent	Active	5.09 (1.28)	5.62 (1.53)
	Quiet	4.95 (2.14)	5.63 (1.72)
	Indeterminate	2.67 (1.63)	4.30 (1.76)
Sleep per cent	Active	5.97 (1.62)	6.05 (1.60)
	Quiet	1.15 (0.36)	2.63 (1.31)
	Indeterminate	3.59 (1.58)	2.63 (0.70)
Respiration rate	Active	1.51 (0.93)	4.80 (2.09)
	Quiet	2.06 (0.79)	2.61 (0.76)
	Indeterminate	42.20 (6.58)	39.80 (5.89)
Heart rate	Active	41.80 (5.50)	52.40 (6.95)
	Quiet	38.25 (3.32)	36.95 (4.68)
	Indeterminate	32.04 (2.62)	34.20 (3.84)*
	Active	132.00 (5.74)	134.90 (5.04)
	Quiet	127.74 (4.79)	131.32 (5.29)
	Indeterminate		

*p<0.05.

Table 3 Gross body movements and periodic breathing in relation to sleep phase in five infants during and after recovery from upper respiratory infection. Values are mean (SE)

	Sleep phase	During recovery	After recovery
Body movements: Total duration (min/100 min sleep)	Active	5.68 (1.99)	1.48 (0.31)
	Quiet	0.68 (0.34)	0.63 (0.16)
	Indeterminate	58.21 (9.28)	39.10 (10.77)
No/100 min sleep	Active	12.80 (2.44)	4.01 (0.96)*
	Quiet	28 (10.18)	7 (1.59)
	Indeterminate	4 (2.13)	5 (1.88)
Periodic breathing: Total duration (min/100 min sleep)	Active	148 (14.87)	87 (14.11)
	Quiet	38 (6.71)	12 (2.46)*
	Indeterminate	0.38 (0.27)	1.31 (0.89)
No/100 min sleep	Active	1.22 (0.77)	0.83 (0.28)
	Quiet	0.59 (0.45)	0.58 (0.58)
	Indeterminate	0.75 (0.46)	1.12 (0.54)
	Active	1 (0.77)	4 (2.91)
	Quiet	3 (1.84)	3 (1.02)
	Indeterminate	2 (0.73)	2 (2.20)
	Total	2 (1.11)	4 (1.81)

*p<0.05.

variables in either active or quiet sleep. No infant had attacks of central apnoea exceeding 15 seconds. Three infants had brief (>3 and <6 seconds) or prolonged (>6 seconds) attacks of obstructive apnoea in active sleep during the course of infection, with resolution on clinical recovery. In no case did the maximum duration of an attack of obstructive apnoea exceed 10 seconds.

Table 3 gives the results for gross body movements and periodic breathing. The number and duration of movements for each 100 minutes of total sleep time was significantly increased during infection; no differences were observed in the amount of periodic breathing present.

Group 2: recurrent vomiting. Table 4 gives the results for apnoea variables, per cent sleep, respiration rate, and heart rate in relation to sleep state in the five infants during and after recovery from pyloric stenosis and in their matched controls without antecedent vomiting. Apnoea index, rate of attacks of apnoea, and apnoea per cent were significantly increased during illness, usually in both active and quiet sleep states when compared with recovery or matched control data. Similarly, the mean and longest duration of attacks of apnoea were increased during illness. Two infants had

prolonged (>15 seconds) attacks of central apnoea in both active sleep and quiet sleep (cases 1 and 5). The proportion of time spent in each sleep stage was comparable during and after illness. Respiration and heart rates were significantly lower in quiet sleep during illness than after recovery; respiration rate was reduced when compared with matched controls in both active and quiet sleep. Four infants with vomiting had prolonged (>6 seconds) attacks of obstructive apnoea in active sleep, with resolution on recovery. None of the matched control infants had either brief or prolonged attacks of obstructive apnoea.

Table 5 gives results for gross body movements and periodic breathing before and after recovery in index cases and also in matched control infants. The increase in body movements when symptoms were present did not reach significance when compared with controls, but the number of episodes and the total duration of periodic breathing were increased ($p=0.06$). Failure to reach significance in comparisons of index cases and controls is a reflection of the paucity of data available for non-parametric statistical comparisons. The Figure presents observations on periodic breathing in individual infants and illustrates the wide difference between illness and recovery data.

Table 4 Apnoea variables, per cent sleep, and respiration and heart rates in relation to sleep phase in five infants with recurrent vomiting and their matched case controls. Values are mean (SE)

Sleep phase		Infants with vomiting		Controls
		During recovery	After recovery	
Apnoea index	Active	7.00 (2.48)	0.99 (0.52)*	0.67 (0.43)*
	Quiet	8.90 (5.17)	0.91 (0.45)*	0.65 (0.27)*
	Indeterminate	9.36 (4.23)	2.57 (0.96)*	0.69 (0.44)
	Total	7.56 (3.18)	1.13 (0.56)*	0.59 (0.26)*
Apnoea attack rate	Active	0.87 (0.29)	0.13 (0.07)*	0.08 (0.04)*
	Quiet	1.05 (0.62)	0.13 (0.06)*	0.08 (0.04)
	Indeterminate	1.05 (0.47)	0.31 (0.11)	0.09 (0.06)
	Total	0.90 (0.37)	0.15 (0.07)*	0.07 (0.03)*
Attack of longest duration (sec)	Active	13.30 (1.37)	7.38 (3.15)	6.38 (1.85)
	Quiet	13.02 (0.88)	7.88 (0.46)*	5.94 (2.59)*
	Indeterminate	9.14 (2.49)	8.04 (2.13)	4.18 (1.72)
	Total	14.82 (0.58)	9.66 (1.03)*	7.38 (2.12)*
Mean duration of apnoea (sec)	Active	7.95 (0.24)	7.33 (0.32)	5.78 (1.55)
	Quiet	9.48 (0.91)	7.03 (0.26)*	5.02 (2.13)
	Indeterminate	6.87 (1.75)	6.65 (1.67)	4.18 (1.72)
	Total	8.42 (0.18)	7.37 (0.29)	6.07 (1.61)
Apnoea per cent	Active	21.28 (6.34)	3.67 (1.83)*	2.41 (1.34)*
	Quiet	25.51 (14.22)	3.34 (1.42)*	2.29 (0.99)
	Indeterminate	27.36 (11.58)	8.91 (3.19)	2.86 (1.69)
	Total	22.14 (8.35)	4.08 (1.64)*	2.15 (0.81)*
Sleep per cent	Active	50.20 (2.63)	46.60 (2.50)	45.60 (5.49)
	Quiet	38.60 (5.07)	42.00 (3.70)	44.20 (6.76)
Respiration rate	Active	25.60 (1.11)	31.40 (2.70)	37.60 (3.00)*
	Quiet	22.50 (1.76)	27.20 (1.50)*	39.40 (4.12)*
Heart rate	Active	123.40 (6.63)	129.60 (5.94)	125.10 (8.00)
	Quiet	115.20 (5.73)	126.50 (4.58)*	120.70 (7.23)

* $p<0.05$.

Table 5 Gross body movements and periodic breathing in relation to sleep phase in five infants during and after recovery from recurrent vomiting and their matched case controls. Values are mean (SE)

	Sleep phase	Infants with vomiting		Controls
		During recovery	After recovery	
Body movements:				
Total duration (min/100 sleep)	Active	4.28 (0.83)	4.36 (0.52)	6.23 (2.32)
	Quiet	1.33 (0.45)	0.84 (0.32)	1.19 (0.56)
	Indeterminate	56.27 (11.34)	43.41 (3.92)	36.76 (11.57)
	Total	8.56 (2.20)	7.78 (1.77)	6.80 (1.25)
Number/100 min sleep	Active	24 (5.46)	25 (2.13)	24 (7.72)
	Quiet	11 (3.20)	5 (4.64)	12 (5.56)
	Indeterminate	275 (128.38)	120 (9.75)	77 (24.39)
	Total	35 (10.18)	29 (5.09)	23 (4.07)
Periodic breathing:				
Total duration (min/100 min sleep)	Active	18.91 (7.43)	1.93 (1.14)	0.62 (0.50)
	Quiet	21.28 (12.58)	0.84 (0.83)	0.56 (0.25)
	Indeterminate	12.41 (6.14)	1.46 (1.16)	0.00 (0.00)
	Total	15.65 (8.01)	1.31 (0.64)*	0.62 (0.25)
No/100 min sleep	Active	25 (7.06)	5 (2.40)	2 (1.19)
	Quiet	14 (8.46)	1 (1.00)	2 (0.85)
	Indeterminate	23 (10.12)	6 (4.49)	0 (0.00)
	Total	20 (7.48)	3 (1.26)*	2 (0.65)

*p=0.06.

Figure No of episodes and total duration of periodic breathing during sleep in five infants during and after recovery from recurrent vomiting.

Discussion

These results present an opportunity to comment on the effects of natural stresses (upper respiratory infection and metabolic alkalosis) on breathing during sleep in infants, at an age when the incidence of sudden infant death syndrome is greatest.

An association between upper respiratory tract infection and sudden infant death syndrome is well documented by epidemiological and pathological studies.^{5 14-17} Several authors have reported that prolonged attacks of apnoea occur more often during upper respiratory infection in infants thought to be at increased risk for the syndrome.¹⁸⁻²⁰ In the present study no differences were observed between indices of apnoea during and after recovery from infection. Prolonged attacks of central apnoea (>15 seconds) were not observed, but brief attacks of obstructive apnoea were present in three infants in active sleep, which scarcely affected heart rate. Obstructive attacks exceeding six seconds were accompanied by bradycardia. None of the full term infants studied was thought to be at increased risk for sudden infant death syndrome on epidemiological grounds.²¹

In view of the small number of cases studied it would be misleading to generalise on the likelihood of prolonged or severe attacks of apnoea in such cases. In a retrospective study of hospital charts of 274 infants under 6 months of age with proven respiratory syncytial virus infection Bruhn *et al* reported an association between respiratory infection caused by this virus and prolonged attacks of apnoea.²² The association was strongest during the first months of life and in infants born prematurely. Mitchell *et al* reported a prospective study of the frequency and severity of attacks of apnoea in respiratory tract infections in infancy.²³ In nine infants with upper respiratory tract infection there were 121 attacks of apnoea exceeding 10 seconds (assessed by impedance pneumography), and in 8%

their duration exceeded 20 seconds. Severe bradycardia was sometimes unrelated to central apnoea. It is possible (perhaps probable) that these episodes of bradycardia resulted from attacks of obstructive apnoea not detectable by the methods they employed.

Gould *et al* described the effects of upper respiratory tract infection on twins studied polygraphically in the early months of life during two to three hour interfeed periods of sleep.²⁴ Infants with colds exhibited alterations specific for sleep state in sleep apnoea. At postconceptional ages of 40, 44, and 48 weeks the number of respiratory pauses of duration of 2.0 to 4.9 seconds and of 5.0 to 5.9 seconds for each 100 minutes of state were decreased during active and indeterminate sleep. This phenomenon did not occur at a postconceptional age of 52 weeks, suggesting that it had been modified by maturation. These authors hypothesised that the response described during the early weeks after birth was adaptive but for infants at risk for sudden infant death syndrome such adaptation could be overwhelmed, resulting in increased attacks of apnoea and sometimes sudden infant death. In our cases gross body movements were increased during the course of upper respiratory infection in relation to total sleep time (Table 3) and no differences were observed between infection and recovery values during quiet sleep. Thus arousals (as indicated by gross body movements) were increased generally and were unaffected during quiet sleep by upper respiratory infection.

In the infants with pyloric stenosis apnoea variables were significantly increased in both active and quiet sleep. Respiration and heart rates decreased in quiet sleep during the acute phase of illness when each infant had moderate metabolic alkalosis. Metabolic alkalosis of varying degree is nearly always present in such infants before surgical treatment.²⁵ In this situation the metabolic stimulus to breathing is reduced and any resulting abnormality in breathing pattern should be most obvious in quiet sleep.²⁶ Prolonged and potentially hazardous attacks of central apnoea might then result from loss of stimulus to wakefulness and/or a defect in metabolic control affecting central or peripheral chemoreceptor mechanisms. We observed prolonged attacks of central apnoea exceeding 15 seconds in two infants in both active and quiet sleep. In both infants gross body movements were increased during illness not only in relation to total sleep time but also quiet sleep, suggesting that arousal mechanisms were intact. Four of the five infants with pyloric stenosis also had attacks of obstructive apnoea during active sleep, perhaps due to loss of upper airway tone in that sleep state, possibly exaggerated by depletion

of intracellular potassium. Prolonged attacks of either central apnoea or obstructive apnoea were not observed after clinical recovery or in the matched control infants. In a previous report we did not detect these abnormalities in 11 healthy infants free of symptoms with a mean age of 48.6 weeks (range 38–63 weeks) studied on 31 occasions in the early months of life.²⁷ Thus, despite the relative paucity of control data in the present study, it seems reasonable to ascribe our findings to the effects of 'minor' illness.

Whether infants exhibiting the breathing patterns observed in upper respiratory infection and pyloric stenosis are at increased risk for sudden infant death syndrome is not known. We have observed infants with upper respiratory infection, severe metabolic alkalosis, and congenital stridor presenting with 'near miss' for episodes of the syndrome, who exhibited in even greater degree the respiratory patterns described. One such infant presented with both upper respiratory tract infection and vomiting. Pyloric stenosis was suspected clinically and confirmed at operation. It is conceivable that the summation of such stresses, perhaps of minor significance individually, influences respiratory control to produce abnormalities of breathing patterns of sufficient severity in some infants to begin the sequence that culminates in a 'near miss' episode or even sudden death. It may be unnecessary to postulate a fundamental defect in respiratory or other control mechanisms in these circumstances. Our findings support the idea that infective and metabolic stresses, manifest as 'minor' illnesses in young infants, may have respiratory consequences that are potentially profound.

We thank the parents, who allowed us to study their infants, and Mrs P Walker, who typed the manuscript.

This study was supported by the Foundation for the Study of Infant Deaths (grant no 28/HS/78).

References

- Emery JL, Crowley EM. Clinical histories of infants reported to coroner as cases of sudden infant death. *Br Med J* 1956;ii: 1518–21.
- Carpenter RG, Shaddick CW. Role of infection, suffocation and bottle feeding in cot death. *British Journal of Preventative and Social Medicine* 1965;19:1–7.
- Froggatt P. Epidemiology aspects of Northern Ireland study. In: Bergman AB, Beckwith J, Ray CG, eds. *Sudden infant death syndrome*. Seattle: University of Washington Press, 1970:32–6.
- Cameron JM, Watson E. Sudden death in infancy in Inner North London. *J Pathol* 1974;117:55–61.
- Stanton AH, Downham MAPS, Oakley JR, Emery JL, Knowelden J. Terminal symptoms in children dying suddenly and unexpectedly at home. *Br Med J* 1978;iii:1249–51.
- Abreu e Silva FA, Brezinova V, Simpson H. Sleep apnoea in acute bronchiolitis. *Arch Dis Child* 1982;57:467–72.

- ⁷ Anders T, Emde R, Parmalee A. *A manual of standardized terminology and criteria for scoring of states of sleep and wakefulness in newborn infants*. Los Angeles: UCLA Brain Information Service, BRI Publications Office, 1971.
- ⁸ Rechtschaffen A, Kales A. *A manual of standard terminology, techniques, and scoring system for states of human subjects*. Washington: National Institute of Health, 1968. (No 204.)
- ⁹ Ellingson RV. EEG of premature and full term newborn. In: Klass DW, Daly DD, eds. *Current practice of clinical electroencephalography*. New York: Raven Press, 1979:149–77.
- ¹⁰ Van Someren V, Stothers JK. A critical dissection of obstructive apnea in the human infant. *Pediatrics* 1983;**71**:721–5.
- ¹¹ Steinschneider A. Prolonged apnea and sudden infant death syndrome: clinical and laboratory observations. *Pediatrics* 1972;**50**:646–54.
- ¹² Guillemainault C, Ariagno R, Korobkin R, *et al*. Mixed and obstructive sleep apnea and near miss for sudden infant death syndrome. 2. Comparison of near miss and normal control infants by age. *Pediatrics* 1979;**64**:882–91.
- ¹³ Parmalee AH, Stern E, Harris MA. Maturation of respiration in premature and young infants. *Neuropadiatrie* 1972;**3**:294–304.
- ¹⁴ Carpenter RG, Gardner A, Pusall E, McWeeney PM, Emery JL. Identification of some infants at immediate risk of dying unexpectedly and justifying intensive study. *Lancet* 1979;ii:343–6.
- ¹⁵ Werne J. Post mortem evidence of acute infection in unexpected death in infancy. *Am J Pathol* 1942;**18**:759–69.
- ¹⁶ Bowden KM, French EL. Unexpected death in infants and young children. *Med J Aust* 1951;**1**:925–33.
- ¹⁷ Williams AL. Tracheobronchitis and sudden infant death syndrome. *Pathology* 1980;**12**:73–8.
- ¹⁸ Steinschneider A. Nasopharyngitis and prolonged sleep apnoea. *Pediatrics* 1975;**56**:967–71.
- ¹⁹ Brady JP, Ariagno RL, Watts JL, Goldman SL, Dumpit BS. Apnea, hypoxemia and aborted sudden infant death syndrome. *Pediatrics* 1978;**62**:686–91.
- ²⁰ Stevens LH. Sudden unexplained death in infancy: observations on a natural mechanism of adaption of the face down position. *Am J Dis Child* 1965;**110**:243–7.
- ²¹ Carpenter RG, Gardner A, McWeeney PM, Emery JL. Multi-stage scoring system for identifying infants at risk of unexpected death. *Arch Dis Child* 1977;**52**:606–12.
- ²² Bruhn FW, Mokrohisky ST, McIntosh K. Apnea associated with respiratory syncytial virus infection in young infants. *J Pediatr* 1977;**90**:382–6.
- ²³ Mitchell I, Barclay RPC, Railton R, Fisher J, Conely J. Frequency and severity of apnoea in lower respiratory tract infection in infancy. *Arch Dis Child* 1983;**58**:497–9.
- ²⁴ Gould JB, Lee AFS, Cook P, Morelock S. Apnea and sleep state in infants with nasopharyngitis. *Pediatrics* 1980;**65**:713–7.
- ²⁵ Degn JK, Wamberg K, Engel K, Kildberg P. Metabolic alkalosis in obstructive vomiting. *Acta Paediatr Scand* 1974;**63**:537–48.
- ²⁶ Phillipson EA. Control of breathing during sleep. *Am Rev Respir Dis* 1978;**118**:909–39.
- ²⁷ Abreu e Silva FA, MacFadyen UM, Williams A, Simpson H. Sleep apnoea in infancy. *J R Soc Med* 1985;**78**:1005–8.

Correspondence to Professor H Simpson, Department of Child Health, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65, Leicester LE2 7LX, England.

Received 24 June 1986