

Seasonality, but not prevalence of sudden infant death syndrome varies by region in mainland Britain

A.S. Douglas^{*†}, P.J. Helms⁺, I.T. Jolliffe[‡]

Seasonality, but not prevalence of sudden infant death syndrome varies by region in mainland Britain. A.S. Douglas, P.J. Helms, I.T. Jolliffe. ©ERS Journals Ltd 1999.

ABSTRACT: This study aimed to investigate whether seasonal variation in day length contributed to winter/summer variation in sudden infant death syndrome (SIDS) at different latitudes in mainland Britain.

Over 11 yrs 13,973 deaths were studied. Using appropriate analytic techniques a sine curve was fitted to monthly rates with the amplitude indicating magnitude of seasonal change.

The rate of SIDS per 1,000 live births was the same (1.73) in the north as in the south. The amplitude was a quarter less in the north (41.3%) than in the south (54.2%) ($p < 0.001$). While annual rates did not differ, the within year distribution did. The findings for seasonality of SIDS births were similar (amplitudes: north 21.3%, south 32.3%). Correlations were made between SIDS amplitude and individual environmental factors, particularly temperature and day length. These complex issues, while reported briefly, do not allow firm conclusions. In the north the winter day length is shorter, sunshine hours are less and temperature is lower, but the winter increment in SIDS is less.

The extent of seasonal variation of sudden infant death syndrome is greater in the south as compared with the colder, darker north but this has no effect on sudden infant death syndrome rates. Changing photoperiod by latitude, amongst other environmental influences, may hold clues to the aetiology of sudden infant death syndrome.

Eur Respir J 1999; 13: 95–99.

Seasonal variation is a well-known epidemiological feature of sudden infant death syndrome (SIDS) [1, 2]. In the northern hemisphere the months with the highest incidence are December, January and February and the values form a plateau during these months. Month of birth for infants who subsequently suffer SIDS is also seasonal, with the greatest risk for births in the late summer to early autumn [3, 4]. This seasonal birth risk appears to be an independent risk factor, although on multivariate analysis it is less powerful than age at death and the winter environment [4–6].

The cause of excess winter deaths in SIDS remains unidentified. Respiratory viral infection remains a prime suspect but is much debated [7, 8]. A hypothesis that in SIDS there is disturbance of airways development in combination with subclinical bronchiolitis has been proposed by MARTINEZ [9], although the present group have found no predictable relationship between features of SIDS and hospital admissions for acute bronchiolitis in infancy [10]. Of the various weather features, temperature has been examined most frequently. Disorders of or immaturity of body temperature regulation have been implicated in SIDS [11], the features of which may be compounded by intercurrent (mainly viral) respiratory diseases and parental concerns about maintaining their infant's body temperature. Because the numbers of SIDS deaths are greatest at 2–4 months of age, maturation defects are possible mechanisms. In addition to temperature regulation, maturation fail-

ure of the pineal gland and melatonin production have been hypothesized [12].

Since there are climatic differences between the north and south of mainland Britain, seasonality of SIDS was examined in different geographical areas from Scotland in the north to Devon and Cornwall in the south.

University Depts of *Medicine and Therapeutics, [†]Child Health and [‡]Mathematical Sciences, University of Aberdeen, Aberdeen, UK.

Correspondence: P.J. Helms, University Dept of Child Health, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, UK, Fax: 44 1224663658

Keywords: Geographic season seasonality sudden infant death syndrome

Received: April 23 1998
Accepted after revision September 3 1998

Supported by the Scottish Cot Death Trust. A.S.D. was also supported by the Maryland Medical Research Institute.

[†]A.S. Douglas died on November 15, 1998, P.J. Helms and I.T. Jolliffe acknowledge the support and encouragement of his widow Mrs C. Douglas.

Subjects and methods

Patients

Month of birth and month of death from SID (International Classification of Diseases (ICD) 9th Revision (798.0)) were obtained from the Office of Population, Censuses and Survey for England and Wales (OPCS) and the General Register Office for Scotland for the years 1982–1992. In order to maintain confidentiality, the month of birth and month of death, but not the exact day of birth and death, were provided. Those diagnosed as SIDS in the first month of life were included. The diagnosis of SIDS is dependent on *post mortem* examinations by experienced pathologists and is very tightly controlled by law. In this series of 13,973 cases, those deaths in 1982 with a birth date in 1981 were excluded. The data were examined as a whole and by each Regional Health Authority (RHA) in England and Wales, and in Scotland. The rate of SIDS deaths per 1,000 live births was used throughout.

Statistical methods

The technique described by HALBERG *et al.* [13] (cosinor analysis) was used, which has been used in previous work [14] and critically reviewed [15]. This is equivalent to fitting a cosine or sine curve to the data and can also be implemented using standard statistical software. This sine wave function was fitted to the monthly data (for both month of death and month of birth), identifying the goodness of fit and establishing the timing and magnitude of the fluctuation. For each set of monthly data the annual peak position (acrophase) and the extent of seasonal variation (amplitude) were calculated. Amplitude was expressed as a percentage above the monthly mean.

Methods

Data were grouped by the 15 RHA in England and Wales (before the 1995–96 reorganization), with Scotland making up the 16th geographical area with photoperiod (day length). Weather data were obtained from the UK Meteorological Office for weather stations in or close to the main populations in each of these regions. For the 11-yr period monthly averages were available for temperature and hours of bright sunshine.

Unpaired t-tests were used to compare values of rates and seasonal amplitudes in eight northern regions with eight southern regions. Linear regression was used to relate rates and amplitudes of death to latitude, although conclusions based on linear regression had to be tentative because the eight areas in the south had only a very small variation in latitude. Similar comparisons were made with the climatic variables.

Results

The numbers and rates of SIDS per 1,000 live births are given in parenthesis in each region. In the north were Scotland (1,466: 2.03), Northern (706: 1.60), Yorkshire (1,067: 1.99), North-Western (1,236: 2.00), Mersey (612: 1.71), Trent (823: 1.24), West Midlands (1,233: 1.57) and East Anglia (484: 1.75). In the south were Wales (638: 1.56), Oxford (579: 1.54), North West Thames (832: 1.55), North East Thames (860: 1.44), South-Western (957: 1.69), Wessex (827: 2.09), South West Thames (700: 2.25) and South East Thames (953: 1.78). The north and south division was an approximate latitude line of 52°. Wales was placed in the south because the majority of the population lives in the southerly areas (fig. 1).

Using an unpaired t-test, mean SIDS rates were not significantly different between the north (1.73) and the south (1.73). The standard deviations were 0.27 in the north and 0.29 in the south. Table 1 and figure 2 show that the rates in the south were higher in the winter and lower in the summer compared with the north. Rates in summer (June, July and August) and winter (December, January and February) were compared for the eight northern regions (24 values) and the eight southern regions. Using an unpaired t-test the mean summer rate was greater in the north (eight regions) than in the south (eight regions) and the winter rate was lower in the north than the south, although not reaching significance. Comparisons were also made between the four most northerly regions and the four most

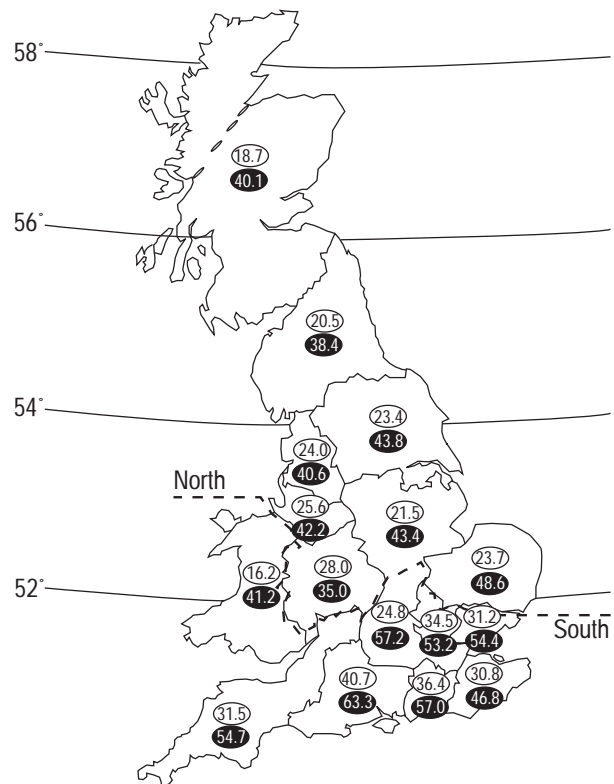


Fig. 1. – Amplitude of sudden infant death syndrome: births and deaths in the 16 regions used in the study. Within each region the amplitude of death is given in a black background, and that of births on a white background. The division between the eight "northern" and eight "southern" regions is shown as a dotted line.

southerly regions and the differences were significant (table 1). These differences are also shown in figure 2a alongside a comparison of annual change in photoperiod (fig. 2b).

Amplitudes of death month and birth month were lower in the north (*e.g.* for deaths: Scotland 40%; Northern Health Authority in England 38%) than in the south (South-Western 55%; Wessex 63%) and are shown for all regions in figure 1. In the eight northern regions the mean±SD death amplitude was 41.3±4.04%, compared with 54.2±6.77% for the south. The corresponding values for birth amplitudes were 21.3% and 32.2%. Both of these amplitude comparisons were statistically significant in an unpaired t-test ($p < 0.001$).

Table 1. – Incidence of sudden infant death syndrome in summer and winter (rates per 1,000 live births)

	Summer	Winter
Eight regions north	1.13±0.26	2.48±0.44
Eight regions south	0.93±0.25	2.67±0.58
Comparison of 24 rates ⁺	$t=2.79, p<0.01$	$t=1.30, p=NS$
Four most northerly regions*	1.24±0.25	2.69±0.25
Four most southerly regions [†]	1.02±0.23	3.10±0.25
Comparison of 12 rates [‡]	$t=2.27, p<0.05$	$t=2.73, p<0.05$

Data are shown as mean±SD. ⁺: t-test; *: Scotland, Northern, North-Western, Yorkshire; [†]: South-Western, Wessex, South West Thames, South East Thames.

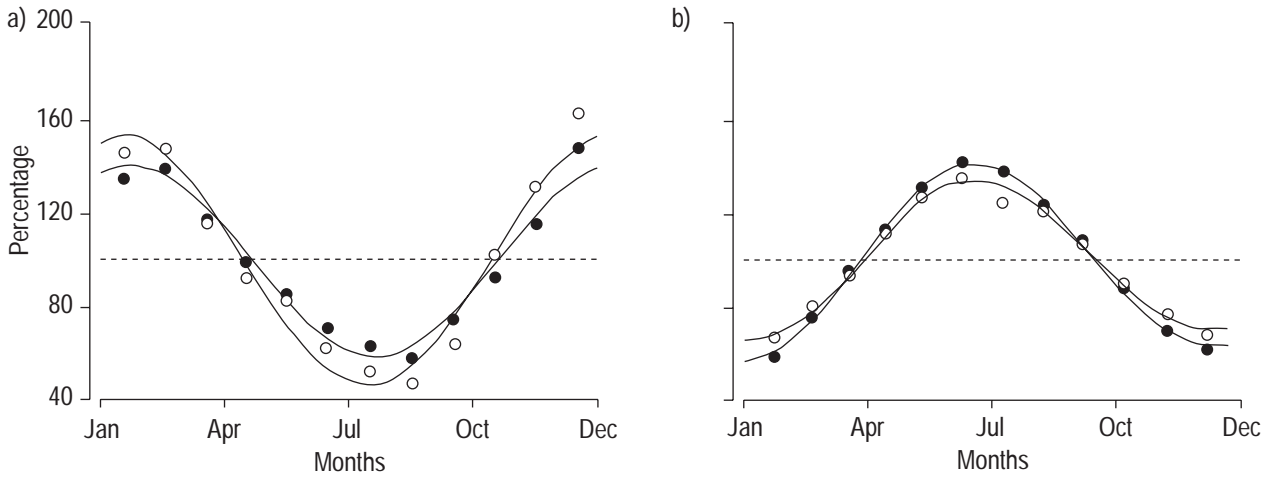


Fig. 2. – Comparison of rates of sudden infant death syndrome (SIDS). The ordinate is the percentage of a) the mean monthly rate and b) the mean photoperiod (hours of day length). Amplitude north (55°; ●)=41.3%, south (30°; ○)=54.2%; $r=0.98$, $p<0.001$; b) amplitude north (●)=39.7%, south (○)=32.1%; $r=0.98$, $p<0.001$. In the north, where the day length in winter was shorter than in the south, the SIDS rate was lower. In the summer, with longer days, the rate was higher in the north. - - - : Annual mean.

Figure 3a shows a scattergram of death amplitude plotted against latitude and there appeared to be an inverse relationship between the two ($r=-0.76$, $p<0.001$). Birth amplitude gave a similar result ($r=-0.72$, $p<0.001$). However, these linear regressions should be interpreted with caution as the eight southern regions had similar latitude values, causing a bunching of results at 50–52° and two horizontal lines fitted separately through the two groups of eight regions provided a similar quality of fit to the data.

Figure 3b shows a scattergram of the SIDS rates (SIDS per 1,000 live births) against latitude with no suggestion of any relationship ($r=0.07$, $p=NS$). Annual means of temperature and sunlight hours for the eight northern regions and eight southern regions were significantly different (table 2). Latitude and photoperiod data are also shown in table 2. On cosinor analysis, SIDS rates and day length suggested an inverse relationship in the north/south comparison (fig. 2). In contrast, there was no clear suggestion of any such relationship among SIDS rates on the amplitude of environmental temperature ($r=0.49$) or sunshine hours

($r=0.29$). Regression gave no evidence for a linear relationship when regional amplitudes of death were regressed on amplitudes of climatic features. The amplitude of death in each of the regions decreased with increased amplitude of photoperiod ($r=-0.76$ and $p<0.001$), the same result (with the same reservations) as the comparison with latitude already shown in figure 3a.

Discussion

There appears to be a variation in the amplitude of seasonality of SIDS deaths (and births) between the south and the north of mainland Britain, but without differences in annual rates. To the authors' knowledge this is the first examination of SIDS in this respect. The finding of a decreased extent of seasonal variation for SIDS in the north compared with the south would, at first sight, be contrary to common expectation. Because most SIDS deaths occur under 4 months of age, no one infant is exposed to all

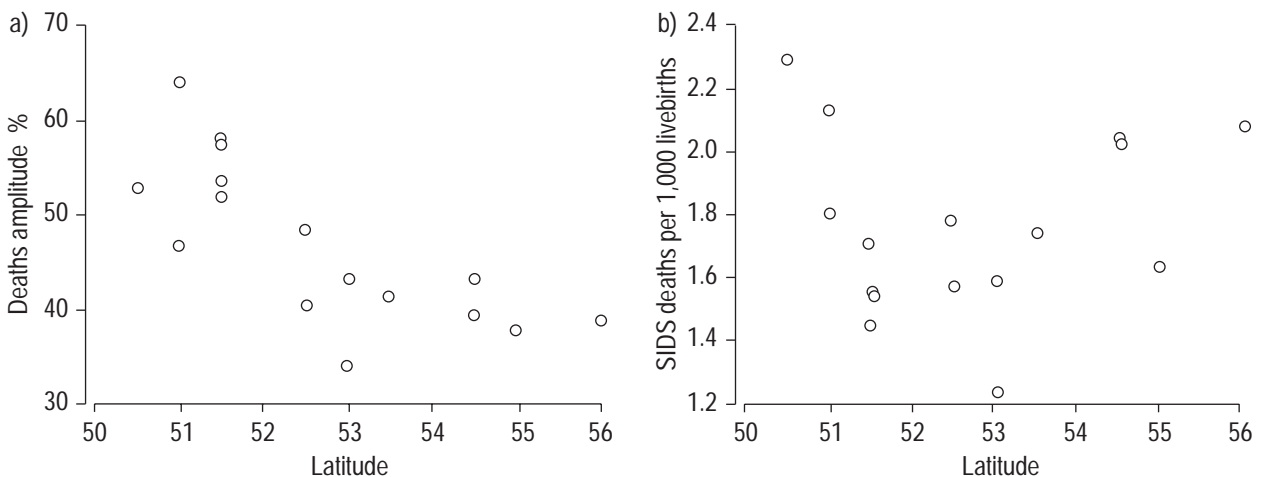


Fig. 3. – Scattergrams of comparison of latitude with a) amplitude of death and b) rates of sudden infant death syndrome (SIDS). In (a) seven of the eight southern regions are bunched together below 52° latitude and no linear regression line has been illustrated. There was no significant correlation in (b).

Table 2. – Annual means of temperature, sunlight hours and photoperiod in the northern and southern regions

	North (low amplitude)		South (high amplitude)		p-value
Annual comparison	Higher	54°	Lower	51.4°	<0.01
Latitude	Colder	9.49	Warmer	10.42	<0.001
Temperature °C	Less	1598	More	1776	
Annual sunshine h					
Winter/summer comparison					
Day length min					
December	Shorter	435	Longer	463	
January	Shorter	474	Longer	500	
February	Shorter	591	Longer	606	
June	Longer	1029	Shorter	996	
July	Longer	995	Shorter	965	
August	Longer	908	Shorter	879	

seasons of the year and the results reflect the experience of the group.

For mortality from all causes in a whole population there is an increase in the winter [16, 17]. In the northern hemisphere the acrophase (peak) of total population mortality is fixed to January [18] and the amplitude is minimal near the equator reaching maximal values in mid-latitude. As latitude increases towards the North Pole the amplitude declines, so that in Scandinavia it is only one-third of that in the Mediterranean area. ASCHOFF [18] has also examined seasonality of all births and found the maximal amplitude to be at about 20–25° latitude. Some of these issues on latitude have been confirmed in a single country, Chile, which is unique in that it spans a large range of latitude (19–53°), while having similar geographical and social features throughout its length [19, 20]. These observations on the influence of latitude on births and whole population mortality may or may not be relevant to SIDS. The latitude changes in Britain are small and these findings would need to be replicated for the whole hemisphere. The amplitudes of seasonality of deaths and births in SIDS reported here are much greater than for total mortality or births [18] and, hence, the mechanisms might be different.

The question of environmental variables, such as climatic conditions, and their relationship to these findings have not been emphasized. In addition to the concerns about the representativeness of single weather stations for each of the 16 regions, the latitude differences in temperature and sunshine hours are small in Britain, although mean values are lower in the north than in the south (table 2). The amplitude of temperature and sunshine hours is broadly similar throughout Britain, while the amplitude of photoperiod is greater in the north.

Despite these concerns, the seasonality of SIDS deaths and births is different between the north and south of mainland Britain and remains to be explained. The dividing line (approximately 52° latitude) chosen was bordered by Wales, Oxford and two northern London Metropolitan regions. Wales rather than East Anglia was chosen to be included in the south because its main population is in the southern coastal fringe. The land mass of Wales extends further north than East Anglia. The inclusion of East Anglia in the south and Wales in the north substantially in-

creased the difference between north and south (data not shown). While the authors have no explanation for this finding, it tends to strengthen the results.

Some environmental influences are likely to cause the observed variation in SIDS. Since the annual rates are the same between north and south, these influences produce their effects by redistributing deaths in different proportions throughout the year without changing the total annual numbers. There are relatively more summer deaths in northern regions and fewer in winter, compared with southern regions (fig. 2).

The observation that the amplitude of photoperiod (but not of temperature or sunshine hours) appears to be associated with amplitude of SIDS suggests a possible role for the photoneuroendocrine axis in the pathogenesis of SIDS, while recognizing that associations do not provide proof of causation.

Melatonin is secreted by the pineal gland in response to darkness. Most SIDS deaths occur during sleep, although not necessarily during darkness [21]. It may be of relevance that the normal sleep pattern concentrated at night is established around the second month of life, the time of greatest risk of SIDS [22]. The amplitude of photoperiod (but not of temperature or sunshine hours) differs between north and south and could be associated with the observed amplitude difference of SIDS. There is an extensive literature on diurnal and seasonal changes in melatonin [23–31]. Studies of daily melatonin rhythm show a phase delay of melatonin secretion in winter compared with summer of 1–2 h [26, 29], whereas quantitative melatonin seasonal differences are debated. There are suggestions of pineal immaturity in SIDS, and WEISSBLUTH and WEISSBLUTH [12] have hypothesized that SIDS is associated with impaired maturation of the photoneuroendocrine system. In support of this hypothesis, melatonin levels in the cerebrospinal fluid have been found to be significantly lower in SIDS infants than in controls at autopsy [25]. However, any relationship between photoperiod and SIDS must remain highly speculative.

Despite the fall in the incidence of sudden infant death syndrome the epidemiological feature of seasonality is still present [32]. The present study was mainly concerned with the seasonality of sudden infant death syndrome before the major fall in incidence following the adoption of the supine sleeping position and these findings could, therefore, be relevant in the pursuit of aetiology.

Acknowledgements. The authors thank J. Rawles, who prepared the cosinor programme. The authors are grateful to the staff of the Medical Library and Dept of Medical Illustration of Aberdeen and to R.G. Carpenter of the London School of Hygiene and Tropical Medicine for their co-operation. M. Burnett and N. Duncan undertook repeated typing of the manuscript and R. Gupta extracted the data. T.M. Allan co-operated in this work and provided bibliographic guidance. M. Moffat undertook some of the computing work.

References

1. Wakley T. Infants found dead in bed. *Lancet* 1853; i: 103.
2. Allan TM, Douglas AS, eds. *Seasonal Variation in Health and Diseases*. London, Mansell, 1994; pp. 67, 341, 348, 363.

3. Thomas CC, ed. Sudden Death in Infancy. Springfield IL, Thomas, 1968; pp. 7–10.
4. Osmond C, Murphy M. Seasonality in the sudden infant death syndrome. *Paediatr Perinat Epidemiol* 1988; 2: 237–245.
5. Centre for Disease Control. Seasonality of SIDS – United States 1980–87. *MMWR* 1993; 39: 891–895.
6. Douglas AS, Gupta R, Helms PJ, Jolliffe IT. Month of birth as an independent variable in SIDS. *Paediatr Perinat Epidemiol* 1977; 11: 57–66.
7. Fleming KA. Viral respiratory infection and SIDS. *J Clin Pathol* 1992; 45: 29–32.
8. Bajanowski T, Brinkmann B. Pulmonary viral infections in SIDS. In: Rognum TO, ed. Sudden Infant Death Syndrome. Oslo, Scandinavian University Press, 1995; pp. 199–202.
9. Martinez FD. Sudden infant death syndrome and small airway occlusion. Facts and a hypothesis. *Paediatrics* 1991; 87: 190–198.
10. Gupta R, Helms PJ, Jolliffe IT, Douglas AS. Seasonal variation in sudden infant death syndrome and bronchiolitis – a common mechanism? *Am J Respir Crit Care Med* 1996; 154: 431–443.
11. Nelson EAS, Taylor BJ, Weatherall IL. Sleeping position and infant bedding may predispose to hyperthermia and the sudden infant death syndrome. *Lancet* 1989; i: 199–200.
12. Weissbluth L, Weissbluth M. Sudden infant death syndrome: a genetically determined impaired maturation of the photoneuroendocrine system. A unifying hypothesis. *J Theoret Biol* 1994; 1167: 13–25.
13. Halberg F, Johnson EA, Nelson W, Runge W, Southern R. Autorhythmometry – procedure for physiological self measurements and their analysis. *Physiol Teacher* 1972; 1(4): 1–11.
14. Russell D, Douglas AS, Allan TM. Changing seasonality of birth – a possible environmental effect. *J Epidemiol Commun Hlth* 1993; 47: 362–367.
15. Minors DS, Waterhouse JM. Analysis of biological time series. In: Arndt J, Minors DS and Waterhouse JM, eds. *Biological Rhythms in Clinical Practice*. London, Wright, 1989; pp. 272–293.
16. Douglas AS, Al-Sayer H, Rawles JM, Allan TM. Seasonality of disease in Kuwait. *Lancet* 1991; 337: 1393–1397.
17. Douglas AS, Allan TM, Rawles JM. Composition of seasonality of disease. *Scot Med J* 1991; 36: 76–82.
18. Aschoff J. Annual rhythms in man. In: Aschoff J, ed. *Handbook of Behavioural Neurobiology*. New York, Plenum Press, 1981; pp. 475–487.
19. Hajek ER, Gutierrez JR, Espinosa G. Seasonality of conception in human populations in Chile. *Int J Biometeor* 1984; 25: 281–291.
20. Hajek ER, Gutierrez JR, Espinosa G. Seasonality of mortality in human populations of Chile as related to a climate gradient. *Int J Biometeor* 1984; 28: 29–38.
21. Golding J, Limerick S, MacFarlane A. Sudden Infant Death. London, Open Books 1985; pp. 33–35.
22. Kleitman N, Engleman TG. Sleep characteristics of infants. *J Appl Physiol* 1953; 6: 269–282.
23. Attansio A, Rager K, Gupta D. Otogeny of circadian rhythmicity for melatonin, serotonin and N-acetylserotonin in humans. *J Pineal Res* 1986; 3: 251–256.
24. Wauldhauser G, Wieszenbacher G, Tatzler E, et al. Alterations in nocturnal serum melatonin in humans with growth and ageing. *J Clin Endocrinol Metab* 1988; 63: 648–652.
25. Sturmer WQ, Lynch HJ, Deng MH, Gleason RE, Wurtman RJ. Melatonin concentrations in the sudden infant death syndrome. *Forensic Sci Int* 1990; 45: 171–180.
26. Arendt J. Melatonin and the Mammalian Pineal Gland. London, Chapman and Hall, 1995; pp. 66–107.
27. Bojkowski C, Arendt J. Annual changes in 6 sulphatoxymelatonin excretion in man. *Acta Endocrinol* 1988; 117: 470–476.
28. Hofman MA, Swaab DF. Diurnal and seasonal rhythms of neuronal activity in the suprachiasmatic nucleus of humans. *J Biol Rhythms* 1993; 8: 283–293.
29. Laakso ML, Porkka-Heiskanen T, Alila A, Sternberg D, Johansson G. Twenty-four hour rhythms in relation to natural photoperiod: a field study in humans. *J Biol Rhythms* 1994; 9: 470–476.
30. Sparks LF, Hunsaker JC. The pineal gland in sudden infant death syndrome: preliminary observations. *J Pineal Res* 1988; 5: 111–118.
31. Reppert SM, Klein DC. Transport of maternal (³H)-melatonin to suckling rats and the fate of (³H)-melatonin in neonatal rats. *Endocrinology* 1978; 102: 582–588.
32. Douglas AS, Allan TM, Helms PJ. Seasonality and the sudden infant death syndrome during 1987–9 and 1991–3 in Australia and Britain. *BMJ* 1996; 312: 1381–1383.