THE DEVELOPMENT OF TEMPERATURE AND HEART RATE RHYTHMS IN BABIES

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DEDICATION

I dedicate this thesis to Oliver John Bullock who spent the first thirty-eight weeks of life in front of a visual display unit, and whose imminent arrival spurred me on to complete the draft copy. His life heightens my awareness of the tragedy of Sudden Infant Death Syndrome and the need to prevent all suffering in children.

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CONTENTS

CHAPTER ONE

INTRODUCTION

Introduction

"Mum and Dad I'm growing up!" This is a perpetual cry from teenagers, but perhaps if babies could talk they would shout it, too. Often parents continue, for months, to care for their growing child in a manner more appropriate to a newborn baby.

Researchers and health professionals have also occasionally assumed that processes studied in neonates will be the same three months later.

The first six months of life are, however, a period of great change. In many respects the six month old is more like an adult than a neonate.

This thesis examines two aspects of development occurring at this time; the appearance of body temperature and heart rate rhythms.

Body Temperature

"La fixite du milieu interieur" was first expounded by Claude Bernard and the principle taught for many years. Humans as homoeotherms have internal body environments that are stable or constant within a narrow range, despite fluctuations in the external environment, but they are not 'fixed' or static as Bernard suggested.

Homoeotherms have developed an endothermic method of maintenance of body temperature rather than being dependent upon an external heat source, so they have the ability to keep their core temperature constant within a range of, at the most, $2^{o}C$, in environments varying by up to $50^{o}C$. Conversely, poikilotherms who have probably adapted well to scanty food resources, have few control mechanisms and their core temperature changes according to the environment. If their behavioural actions are inadequate their core temperature may fall in cooler temperatures, for example at night, with resultant slowing of

metabolism, responses and movements.

When comparing these two methods of temperature control, those animals who are independent of changes in the physical conditions of their environment and are able to maintain a constant body temperature probably have the advantage, especially at night. Thus the homoeotherm who has constant responses at all times is able to catch his food when the poikilotherm is too slow to escape. Higher body temperature also enhances the digestion and absorption of food into the circulation and consequently nerve cells receive energy more quickly and are capable of functioning more rapidly.

There are disadvantages to maintaining a constant core temperature, however. In order to produce the faster metabolism, necessary for the maintenance of this high body temperature, homoeotherms need to catch and eat more food, and if the core temperature cannot be maintained within its narrow limits, death or injury results. In humans body temperature is normally between 36^{o}C and 38^{o}C. Temperatures above 39^{o}C produce cerebral responses and discomfort so that action is taken to cool down, but if this temperature persists, cramps, from the loss of sodium and chloride in sweat, rapid breathing and dehydration occur. These are reversible, but if above 41^{o}C for any length of time heat exhaustion and brain damage result, and over 43^{o}C heat stroke with sudden cessation of sweat, loss of consciousness, hypotension, circulatory, renal and hepatic failure and convulsions occur, sometimes resulting in death. The human brain needs a constant temperature to function at its peak and homoeotherms keep brain temperature stable in preference to other areas of the body. In particular the needs of temperature regulation take priority over circulatory equilibrium. This is a factor which has been implicated in the surprising survival of children who have fallen into frozen rivers and lakes. Generally, however, in waters below 10^{o}C the redistribution of heat within the body leads to such a fall in core temperature that survival time can be measured in minutes. The minimum environmental temperature, at which survivial is possible, is difficult to

calculate. Many factors, such as wind chill factor, how wet the person becomes, tiredness, hunger and activity interact with each other. Edholm (1978) also reports on the effects of acclimatisation of people. There is an individual variation in environmental temperature at which frost bite begins to occur. For these reasons, most studies have investigated the minimum body temperatures at which a person can survive. At a body temperature of 33°C temperature regulation fails, at 29°C - 31°C consciousness is lost and below 30°C glucose is metabolised slowly, breathing is depressed and the heart rate is very slow. Death occurs at body temperatures below 25°C, unless it has been deliberately induced and controlled in patients undergoing surgery.

In adult humans the core or body temperature is taken as that of the internal organs, particularly the viscera, liver and brain. The temperature of these central organs is determined by their own heat production, their insulation and by the temperature and rate of blood flow through them. At rest the core temperature measures between 36°C - 37.5°C.

Homoeotherms have a well developed ability to regulate temperature or keep body temperature within a constant range because of the existence of protection mechanisms which defend the temperature of the body core and overcome some of the disadvantages discussed. Humans also have the added advantage of being one of the few species who can manipulate their environment, or create microenvironments which control ambient temperature, using such factors as air conditioning, fire and clothing, enabling them to concentrate on other matters.

Measurement of Clothing and Bedding Insulation

Unlike animals who utilise their fur for variable insulation, man has to use materials, fabrics and skins of other animals. The insulation of clothing depends upon the air trapped between the fibres of the fabrics and between the layers of clothing. Still air is an effective insulator, but natural convection currents carry heat away; these currents can be reduced by creating 'dead air', either by making the spaces narrow or by filling them with materials like cotton wool or feathers, which immobilises the trapped air. The greater the thickness of this filling the better the insulation, and therefore it is important that the filling recovers quickly and completely when compressed. Feathers are more suitable as a form of insulation for this reason. Cold weather clothing also benefits from a windproof and waterproof outer layer, but this in itself may cause problems; plastic is a good material, but this is impermeable to the water vapour that is lost from sensible and insensible evaporation, and it condenses on the inner surface. When clothing becomes soaked, the dead air is displaced by water, which has a much higher thermal conductivity, and the insulation is therefore reduced and more heat is lost by evaporation (Edholm and Weiner, 1981).

Until the early 1980's insulation was measured by 'clo units', an average of 25-30mm of material providing 4.0-4.5 clo units; (Burton and Edholm, 1955). Today, however, the thermal properties of materials are measured in 'togmeter values'. It is a unit of thermal resistance, and the value is defined as ten times the temperature difference, in degrees Celsius, between the two surfaces of a fabric when the heat flux through it is equal to 1 watt/m^2. All items of clothing and duvets can be given a tog value using methods described in the British Standards 4745 (1986) and 5335 (1984).

Thermoregulation

Humans need to thermoregulate, or utilise their protection mechanisms, if the environment they are in is not "thermoneutral". The neutral thermal environment is when ambient temperature is such that man need not alter his metabolic rate or insulation in order to keep his core temperature constant (Motil and Blackburn, 1973). This is clinically measured as being when oxygen consumption and evaporative water loss are both at a minimum (Stern, 1977). The temperature of a neutral environment is not a fixed figure, however; if metabolism is increased by exercise or a large meal the ambient temperature needs to be lower and if clothing is removed the ambient temperature needs to be higher. The temperature which is considered thermally neutral also varies for different species; dogs increase their metabolism if the ambient temperature rises above or falls below 24^{o}C, whereas the range of temperatures in which the arctic fox can control his temperature by other means is -25^{o}C to +20^{o}C (Dayson, 1970). For naked adult humans at rest the thermo-neutral zone is between 25^{o}C and 30^{o}C (Stern, 1977).

Passive heat is produced by the basal metabolic rate which is about 80W in adults and increases to between 150W to 300W of heat depending on posture. Passive heat is lost by insensible evaporation, radiation and conduction; 20% of heat is lost through water loss from the skin, lungs and in urine, 67% from radiation, which is dependent on the surface temperature of the surrounding solid objects, and 10% from conduction which is a function of the temperature of the object on which a person is resting, so more heat is lost in this way when laying down rather than standing.

When an imbalance between heat produced and heat lost, or the 'heat in' and the 'heat out', occurs, active thermoregulation takes place in order to maintain a

stable core temperature. Heat must be actively lost if the 'heat in' exceeds 'heat out'. Exercise is the most common way metabolism and heat production increase to a maximum of 1.8KW. The consumption and digestion of food also increases heat production. In humans the primary mechanisms which enable us actively to lose heat are behavioural; insulation is reduced by removing clothing or convection improved by fanning the skin or standing in a cool breeze, which removes the layer of air around the body acting as an insulator. Other behavioural responses are bathing in cool water or placing a cold object next to the skin, which improve heat loss from conduction.

The body automatically reduces insulation if behavioural responses are not taken or are not sufficient. Fat, which acts as an insulator, is by-passed by the blood, and by increasing the circulation of blood into the capillary network the temperature of the surface of the skin is raised and there is a consequent dissipation of heat. This is peripheral vasodilatation. The process of heat loss is also helped by increased sweating; the sweat glands become active and secrete sweat onto the surface of the body, which evaporates and in the process cools the skin. Evaporation in the form of sweating is an important method for dissipating heat, but the body seems to have a defense mechanism against sweating too much during sustained exposure to a warm environment; dehydration can inhibit evaporative water loss, and at all times sweating will increase to a maximum and then decrease to a lower level (sweating fatigue) unless the skin is wiped dry (Cabanac, 1975).

When the ambient temperature is too low and the 'heat out' outweighs 'heat in' or heat production, again the first line of defence for humans is behavioural. Insulation is improved by adding clothing, and heat lost by conduction or radiation is reduced by moving to a warmer spot. Alternatively the heat produced by the metabolism is increased by exercise or eating.

If these actions are not sufficient the body naturally improves the insulating properties of fat by ensuring blood circulation to the capillaries in the dermis is

kept to a minimum by the process of vasoconstriction. Insulation is also improved by piloerection and consequent raising of body hair, which creates dead space and metabolism and heat are increased by the physical method of muscle contraction and shivering.

In human adults an additional mechanism which produces heat, non-shivering thermogenesis, occurs at a 'critical' ambient temperature. The primary chemothermogenesis mechanism is activated by the thyroid and works on the liver to increase metabolism and therefore produce heat. Another mechanism is mediated sympathetically and acts on brown fat.

Thermoregulation in Infants

Much of the research into temperature control in infants has been on premature neonates, because it has been known for some time that low body temperature decreases the chances of survival (Budin, 1900), and assistance may be needed to maintain a constant temperature (Blackfan and Yaglou, 1933). The problems of pre-term babies are exacerbated by them being physically small and immature, but studies on full term neonates have suggested that they, too, do not have the same thermoregulatory mechanisms as adults. Neonates have less thermal capacity, or ability to hold heat within the body than adults, as their surface area/body mass ratio is greater; the body mass of the neonate may be only approximately 5% of the adult, but their surface area is about 15% (Adamson and Towell, 1965). Heat production per unit surface area in an environment free of thermal stress has been found to increase with postnatal age (Hey and Katz, 1970). Body insulation is less efficient than adults, as babies have less white fat. The insulation of their body tissues is only between a third and one half as good as in adult life (Hey and O'Connell, 1970). As maintaining a stable body temperature is probably more difficult, babies have actively to thermoregulate more often.

Babies have a higher basal metabolic rate per unit area than adults (Hill and Rahimtulla, 1965) so passive heat production is higher, but passive heat loss may also be greater. Heat loss from conduction will be large if the baby is laid on a cold surface or even if he is placed in cool sheets; these will absorb the body heat until their temperature has increased. Heat loss from radiation may also be increased if the baby is in a room which is warm, but the external walls or windows are cold. Infants are also affected by draughts and wind, and more heat will be lost from evaporation if babies are wet. Increased passive heat loss from the lungs occurs if the baby has breathing difficulties and consequent increased respiratory rate. The neutral thermal environment is also higher for babies and they require warmer conditions in order to prevent active thermoregulation. Hey and O'Connell's (1970) research on full term babies during the first few days of life found that if the babies were dressed in a terry nappy, vest and long nightie, wrapped in a brushed cotton sheet and covered with two cotton blankets (calculated tog value = 6.6), oxygen consumption and evaporative water loss were at a minimum in an environment of 25°C. This room temperature could fall to 19°C or rise to 31°C before it had a comparable effect on the babies' metabolic rates as a 2°C variation from the neutral thermal environment, of 32°C- 34°C, for naked newborn babies (Hey and Katz, 1970 and Stern, 1977). Hey and O'Connell found that when a baby is naked his heat production must increase by 35% if there is a fall of 2°C in ambient temperature, and a rise of 2°C causes pyrexia.

It would appear that if there is an inbalance between 'heat in' and 'heat out' infants' active thermoregulatory mechanisms are less efficient than adults. Their behavioural responses are limited to reducing insulation by kicking covers off, putting hands and feet outside the bedclothes or adopting the 'sun-bathing posture', which exposes as much of the body to air as possible (Rutter and Hull, 1979). Otherwise babies depend on being able to communicate discomfort by restlessness or crying, because they are reliant on their carers to increase

fluid intake or reduce insulation. If these responses are not sufficient neonates can reduce insulation by vasodilatation and, contrary to former beliefs, it appears that babies are able to sweat from quite a young age and therefore increase evaporative heat loss (Hey and Katz, 1969).

If 'heat out' exceeds 'heat in' babies face similar problems. They are unable to increase insulation by behavioural means, although their ability to adapt posture develops with age. Body insulation is improved slightly by vasoconstriction, but having less surface fat this is not as effective as in adults. Crying, kicking and other exercise also increases the metabolic rate and therefore heat production, but neonates have a limited ability to increase metabolic rate by shivering.

Infants' primary mechanism of active heat production is non-shivering thermogenesis, which is probably more efficient in babies than adults. The 'critical' ambient temperature at which babies utilise this mechanism is much higher than adults at 18^{o}C (Schiff, Stern and Leduc, 1966). This is activated by sympathetic nerves and the main chemical reaction is one where adipose tissue lipase or 'brown fat' stores are activated by noradrenaline excretion which increases metabolic activity and oxygen consumption and therefore heat production (Rizack, 1964). It is called brown fat because of its rich vascular supply, and can be found in newborn humans both internally and at the body surface (Stern, 1977). Infants who die in the first months of life and have suffered from malnutrition, but have not been exposed to cold, show a depletion in white fat stores but relative intactness of the brown fat stores. In contrast, infants who die well nourished, but exposed to cold, show a depletion of the brown fat stores, with the white fat relatively intact, although weight gain is slower in newborns exposed to cold (Heim, Kellermayer and Dani, 1968). The gradual disappearance of the brown fat stores within the first year of life also correlates well with the clinical appearance of babies' ability to shiver when cold (Stern, 1977).

Consequences of Thermal Imbalance in Babies

A number of studies have shown significantly higher mortality rates in premature and sick infants who were not nursed in controlled thermoneutral environments (Silverman, Fertig and Berger, 1958 and Buetow and Klein, 1964). Newborn babies may also be easily 'stressed' if the ambient temperature is raised above the neutral zone. Adams, Fujiwara, Spears and Hodgman (1964) demonstrated an increase in oxygen consumption in newborn premature infants at temperatures of 36-38^{o}C; their respiratory rate increased by 34% and respirations were shallow and irregular. This reaction has also been seen in full term neonates, although they only had slightly elevated rectal temperatures (Adamsons, Gandy and James, 1965). Conversely, Grausz (1968) reported a 30% decrease in oxygen consumption at an ambient temperature of 40^{o}C compared to 35^{o}C. When studying babies in a warm environment, however, Sulyok, Jequier and Prod'Hom (1973) suggest that respiratory rate does not correlate well with metabolic rate, so increased oxygen consumption may not be an indication of metabolic stress, but a thermoregulatory response to rising body temperature.

Babies experience breathing difficulties if they are re-warmed too quickly or are exposed to a very warm environment. 'Heat-induced apnoea' has been reported as being more common if babies are maintained in environments heated in response to skin temperatures below 36.5^{o}C rather than 36^{o}C, and Perlstein, Edwards and Sutherland (1970) report a higher proportion of apneoic spells occurring during rises in incubator temperatures.

Babies' survival rate is also lower if the environment is too cold, and this is an area that has been studied extensively, prompting great advances in neonatal care, particularly the development of the incubator (Budin, 1900) and the overhead heater on the delivery room recovery trolley.

Mann and Elliot (1957) report a survival rate of less than 50% if babies' body temperatures fall to between 27-32^{o}C, and if the face is suddenly cooled, for

example by plunging into cold water, bradycardia and decreased respiration occur immediately. Motil and Blackburn (1973) report that cold stress with consequent acidosis leads to decreased pulmonary blood flow, right to left shunting, hypoxia and accumulation of ketone bodies. Cold stress also stimulates a rise in the metabolic rate and consequent need to increase oxygen consumption by increasing respiration rate. Schiff, Stern and Leduc (1966) suggest that hypothermia may influence other systemic responses of the neonate with resulting secondary hypoglycaemia. Additional possible complications are kernicterus at lower levels of serum bilirubin (Stern, 1977), diarrhoea (Hey and Katz, 1969) and tachycardia (Goodlin and Horowitz, 1971). Glass, Silverman and Sinclair (1968) suggest that there is a retardation in weight gain in babies who have been exposed to prolonged cold stress.

If the low ambient temperatures overwhelm the babies' ability to thermoregulate, death from Neonatal Cold Injury Syndrome often follows (Egan, Illingworth and MacKeith, 1969).

When the findings about neonates' thermoregulatory mechanisms are transferred to the studies of older babies, who on the face of it are not greatly physically different, although slightly larger and able to sweat and shiver more, it is hardly surprising that in the past researchers have considered the main problems of temperature control are related to becoming too cold. One of the objectives of this study is to measure heart rate, oxygen saturation and sweating at the same time as rectal temperature, skin temperature and environmental conditions, in order to assess whether those conditions considered to be excessively hot or cold for neonates have any measurable affect on the physiological mechanisms of older babies.

The Role of the Hypothalamus

The hypothalamus is thought to be the principal centre for integration of mechanisms concerned in the regulation of body temperature, although the behavioural responses indicate the cerebral cortex also plays an important role. Information concerning the temperature of the surface of the body is sent to the hypothalamus via thermal receptors in the skin, and changes in the temperature of the blood perfusing the hypothalamus itself are detected by receptors there (Keele, Neil and Joels, 1982). The vasomotor centre in the medulla oblongata is also thought to be extremely sensitive to the temperature of blood, and when this and the hypothalamus sense change, the hypothalamus via the nervous systems modifies muscular and glandular activity, cutaneous circulation, sweat secretion and pulmonary ventilation. In some animals temperature regulatory responses have also been elicited by changes in spinal cord temperature, but its role is uncertain in humans although implicated in the mechanisms of sweating (Cabanac, 1975).

One theory about the thermoregulatory role of the hypothalamus is that the preoptic region acts as a 'thermostat' regulating the activities of the posterior hypothalamic regions, which in turn integrate the mechanisms responsible for heat loss or heat conservation and production. If the hypothalamic temperature rises above or falls below a 'set point', or range of values, the 'thermostat' switches the thermoregulatory mechanisms on, and active thermoregulation occurs. This 'thermostat' has also been described as a Continuous Proportional Controller, rather than implying a simple 'on-off' mechanism, because the magnitude of the thermoregulatory response that is induced is directly related to the extent to which the temperature varies from its 'pre-set' value (Keele, Neil and Joels, 1982). Cabanac and Massonnett (1977) also argue that there is no 'dead band' around the set point where the body does not need to thermoregulate, but that the mechanisms are permanently active.

The Role of Skin Receptors

Thermosensors have been found in the skin on the chest, nose, nipples, abdomen and anterior surface of the arm (Keele, Neil and Joels, 1982), and in the central nervous system, particularly the spinal cord (Hensel, (1981). The warm receptors in the skin respond to temperatures above, and the cold receptors to temperatures below, body temperature. There are four times as many cold spots as warm (Ganong, 1985). Other nerve endings in the skin respond to touch and pain.

The temperature sensitive organs are unmyelinated fibres which respond to the absolute temperature of the skin at the site of the receptors and not to the gradient of temperature between deep subcutaneous tissue and the surface. The cold receptors respond to temperatures between 10°C and 35°C, with maximum frequency between 25°C and 30°C. The warm receptors discharge at temperatures between 35°C and 45°C, with a maximum frequency between 38°C and 43°C. Sudden cooling or heating produces a rapid, high response.

At extremes of temperatures, the sensations felt are not those of warmth or coolness, but pain. 'Heat pain', which begins at temperatures of 45°C, is a sharp pain localised in the outermost skin surface. 'Cold pain', which can be induced by persistent temperatures below 17°C, has a dull character, is poorly localised and radiates intensely into the surrounding areas (Hensel, 1973). The picture is complex, however, as it is not known whether these sensations are produced by the cold and warmth receptors, or different ones, as they are all naked nerve endings. Ganong (1985) speculates that pain receptors may sub-serve the temperature receptors, if the heat is above 45°C, because it feels painful, and if the heat continues, tissue damage occurs. In contrast, Keele, Neil and Joels (1982) write that at these high temperatures, the warmth receptors do not respond but the cold receptors respond briskly. Hensel (1981) believes that if the skin is exposed to persistent cold, the sensation felt probably does not arise from

the thermoreceptors, but the result of blood vessel spasms.

As it is the temperature of the subcutaneous tissue that determines the response, a cool metal object feels colder than a wooden one of the same temperature. The metal conducts the heat away more rapidly, cooling the subcutaneous tissue to a greater degree. If the skin temperature is between 20°C and 40°C there is an adaptation to the sensation, so it feels thermally neutral.

Controlled Changes in Body Temperature

In certain circumstances the 'thermostat' or 'set point' value is altered, so that the hypothalamus instigates temperature regulating mechanisms either above or below the normal range of temperatures. This occurs because it is advantageous to alter the core value in a controlled manner in order to increase efficiency or aid other mechanisms of the body (Hammel, 1968).

Circadian rhythms of body temperature probably developed to reduce the metabolic cost of maintaining a high core temperature, with consequent demands for food, at times when it was not necessary, for example whilst asleep, usually at night.

Circadian Rhythms

The Concise Oxford Dictionary defines circadian as occurring once per day. It is from the Latin circa = about and dies = day. For decades scientists have been investigating the circadian rhythms of humans, and many functions of the body exhibit daily cycles (for reviews see Conroy and Mills, 1970). The most obvious of these are the sleep-wakefulness cycle and feeding, but it has been shown that, for example, respiration, hormones, heart rate and temperature also have circadian rhythms (figures 1:1 and 1:2).

Much research has been carried out on adults in order to discover when the

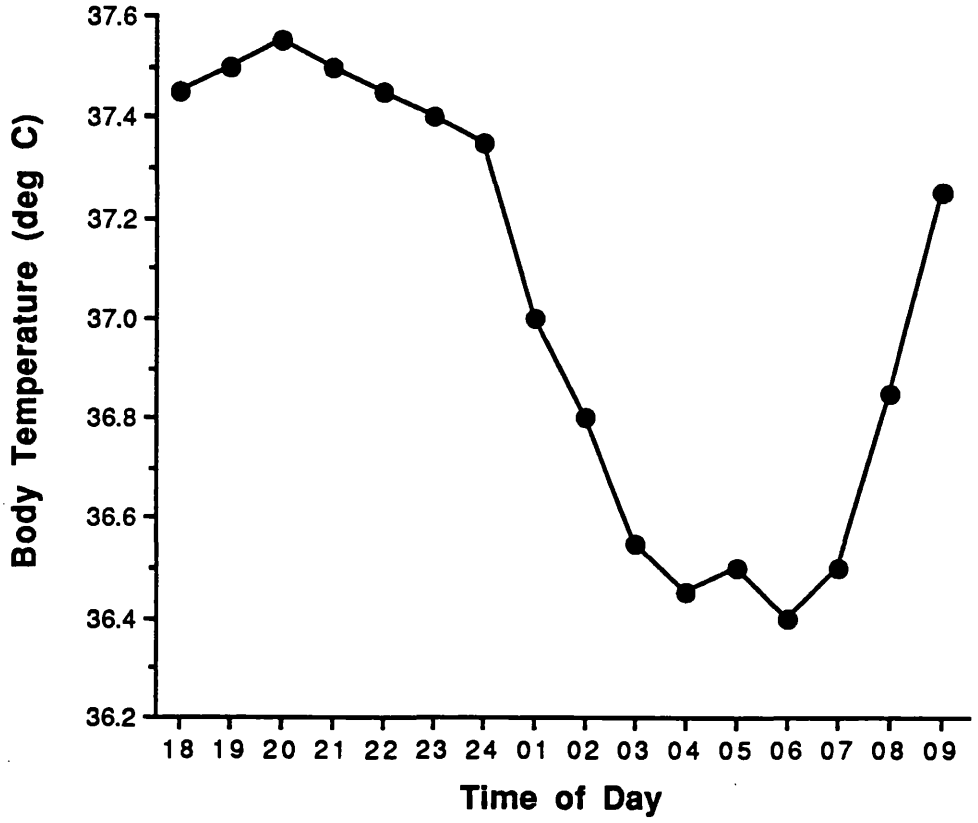


Figure 1:1 Minors and Waterhouse's data on the daily changes in adult deep body temperature, illustrating a night-time fall and daytime rise. Measurements were made hourly over a single 24 hour period, and the data represent the means from four subjects.

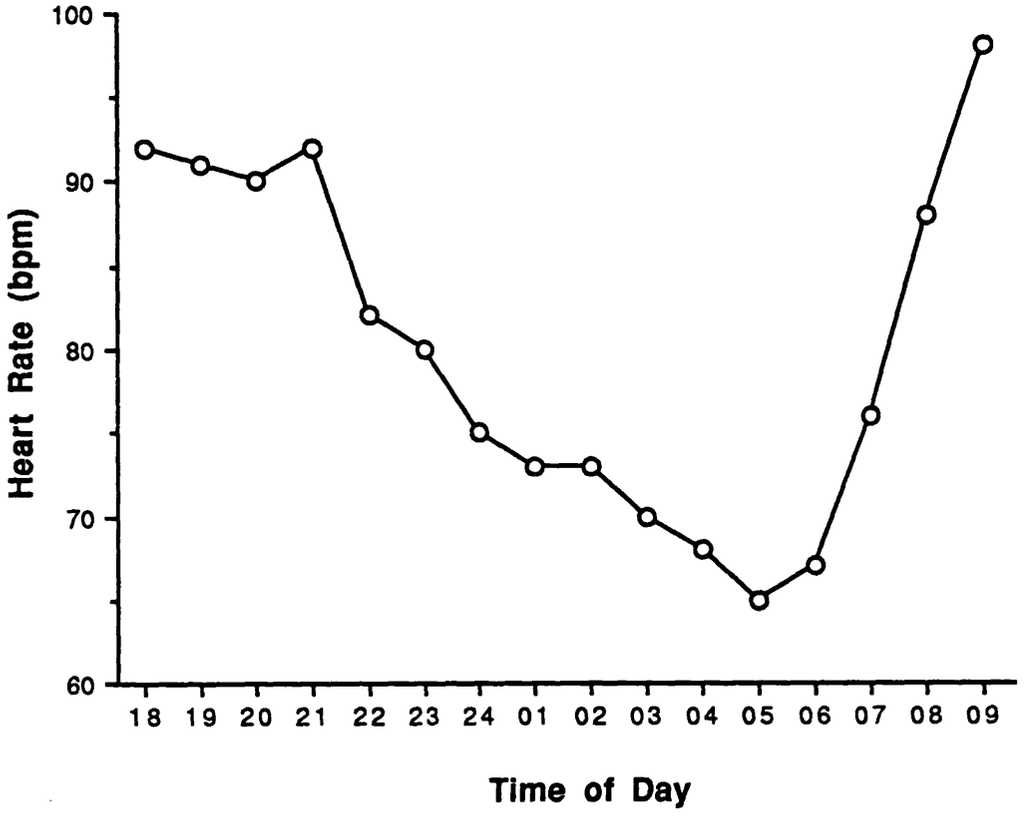


Figure 1:2 Minors and Waterhouse's data on the daily changes in adult heart rate, illustrating a decrease in rate at night and an increase during the day. Measurements were made hourly over a single 24 hour period, and the data represent the means from four subjects.

rhythms occur during twenty-four hours, and whether they are endogenous (originating from within) and therefore consistent despite changes in the external environment, or exogenous (originating from the outside) and cued by zeitgeber (literal translation = time givers), for example darkness, clock time or normal daily routines (Minors and Waterhouse, 1981).

Circadian Rhythms of Body Temperature

The earliest records of the diurnal variation of temperature are generally attributed to A Gierse (1842) or J Davy (1845), and since then most of the research on rhythms has studied the circadian periodicity of temperature and whether or not it is endogenous.

A number of approaches indicate that deep body temperature is the most independent or endogenously controlled rhythm (for reviews see Czeisler, 1978 and Conroy and Mills, 1970). Under experimental conditions the temperature circadian rhythm varies less from day to day than the sleep-wakefulness cycle (Wever, 1979), respiratory variables (Schaefer, Kerr and Buss, 1979), many hormones and the secretion of urinary constituents (see Conroy and Mills, 1970), indicating that the temperature rhythm is not produced or influenced by these other factors, but conversely may control those circadian rhythms.

Control of Circadian Rhythms of Body Temperature

Circadian rhythms, particularly body temperature, are not merely passive responses to the daily changes in the environment, although they may be influenced by them. If humans are isolated from external cues, and the rhythms are allowed to "free run", most of the rhythms initially increase to twenty-five hours, but if the free running state continues for some time internal desynchronisation occurs. All the rhythms that have been studied, apart from

the temperature cycle which continues to run over about twenty-five hours, free run over different time periods (for example the sleep-wakefulness cycle extends to thirty-three hours). These results have led researchers to conclude that each rhythm is predominantly driven by a particular pace-maker, but each pace-maker is coupled to others to ensure internal synchronisation (Groos, 1983). Generally, however, circadian rhythms have only been studied concurrently with daytime/night-time and not other rhythms.

Little is known about what controls body temperature rhythms, although much research has been undertaken. In adults the pattern appears to be due more to a cyclical change in the extent of heat loss rather than a change in metabolic heat production. This conclusion has been drawn because variations in heat loss mechanisms, such as cutaneous blood flow which is measured by skin temperature, are almost mirror images of the rectal temperature cycle (Hildebrandt, 1974). Attempts to correlate temperature curves with variations in energy metabolism have also been unsuccessful; the cycle is the same in active and inactive people and in fasting as well as people eating regularly (Conroy and Mills, 1970). This argument does not consider the effects of sleep on metabolism which almost halves the heat produced and is paralleled by a lower body temperature. Temperature, too, cannot solely be due to the change in the extent of heat loss as the temperature rhythm would presumably change in different climates, because of variations in ambient temperature (Adam and Ferres, 1954 and Halberg, Reinhardt and Bartter, 1969).

Despite extensive research on animals in an attempt to find the role of the higher nervous centres and which part of the brain is responsible for maintenance of the temperature rhythm, results have been ambivalent and most researchers conclude that there is either an unspecified independent mechanism in the body, or that once again it is the hypothalamus which not only controls thermoregulation, but also influences circadian rhythms (for reviews see Conroy and Mills, 1970 and Minors and Waterhouse, 1981).

Endogenous / Exogenous Components of Circadian Rhythms

Much attention has been given to answering whether circadian rhythms of the body originate from within and are therefore independent of the environment, or whether they are cued by 'zeitgeber' and vary according to what is happening outside the body. Generally it is concluded that most of the rhythms are endogenous, but strongly influenced by other rhythms and zeitgeber (Aschoff, Gerecke and Wever, 1967).

In adults there is a remarkably constant phase relationship between each rhythm and the environmental light-dark cycle (Groos, 1983). If a rhythm is synchronous with a cycle like this it is said to be entrained by the environment, although it may be maintained in the absence of environmental variables. Examples of rhythms which are controlled by events or zeitgeber are sleeping and eating; they are cued by clock time, although not one specific time (people do not all eat and sleep at the same hour). Other rhythms are thought to be correlated, although no exact or causal link has been found. Certain hormones are released in specific sleep stages (Daly and Evans, 1974). For example human growth hormone is associated with sleep stages 3 and 4 of Slow Wave Sleep (Takahashi, Kipnis and Daughaday, 1968), thyroid stimulating hormone measures peak values at the onset of sleep with a fall in the morning (Beck, Reinhardt, Kendel and Schmidt-Kessen, 1976), cortisol secretion is stimulated during Rapid Eye Movement Sleep and prolactin secretion is inhibited during REM sleep (Minors and Waterhouse, 1981).

A number of experiments indicate that the rhythm of deep body temperature, perhaps more than other rhythms, has a largely endogenous component (Aschoff, 1960 and Czeisler, 1978). These studies have attempted to exclude normal exogenous influences by keeping subjects in permanent daylight or darkness, isolating or fasting them whilst remaining in bed or imposing a non-24 hour day. Research has also been carried out on people flying across time

zones or working night shifts.

When adults are isolated from external cues, the rhythm of deep body temperature does not disappear, but continues with a decreased amplitude and a period of twenty-five hours (Colin, Timbal and Bontelier, 1968 and Czeisler, 1978). Subjects who travel across time zones gradually change their rhythms over a period of about three days (Elliott, Mills and Minors, 1972), although individual adaptation to 'changing' days varies (Reinberg, 1970) and children appear to adapt more quickly (Sasaki, 1964). Night-shift workers alter their circadian rhythms, too, although not always completely, suggesting that they are still influenced by light and darkness (Conroy and Mills, 1970). Food intake, however, does not appear to influence the temperature circadian rhythm (Reinberg, 1975).

Minors and Waterhouse (1981) suggest that although the endogenous component of the temperature rhythm is marked, an exogenous component is present too. They cite Kleitman and Kleitman's study in 1953 which showed a number of temperature peaks in accord with the number of activity periods. Other studies have shown that environmental temperature change prior and subsequent to sleep onset inhibits slow wave sleep and dampens the normal circadian fall in core body temperature (Bonegio, Driver, King, Laburn and Shapiro, 1988).

In contrast cardiac rhythms are generally considered exogenous (for reviews see Conroy and Mills, 1970 and Minors and Waterhouse, 1981). The main arguments for this are that Kleitman and Ramsaroop (1948) found that when times of sleep and activity were shifted this was quickly accompanied by an adaptation of heart rate, and Kleitman and Kleitman (1953) suggest that heart rate quickly entrains to an eighteen or twenty-eight hour day. The parallelism between heart rate and temperature is also used clinically as part of assessment for the presence of fever, suggesting that heart rate is influenced by temperature.

Minors and Waterhouse (1981), however, once again cite research that illustrate that there may be an endogenous component to heart rate (Wertheimer, 1974, Reinberg, 1970 and Halberg et al, 1970). These studies found that the cardiac rhythm cannot be solely attributed to rhythms of food intake or activity, because when posture and meal times were regulated, the amplitude of the heart rate rhythm decreased, but did not disappear. Conroy and Mills (1970) citing Levine et al's 1967 study on a comatose girl also report that rhythms of heart rate persist when a person is in coma.

Heart rate, therefore, appears to be mainly governed by habit, increasing during activity and decreasing during rest and sleep, but if these major influences are absent it is largely determined by body temperature.

One method of discovering the endogenous/exogenous component of circadian rhythms has always been to study the development of these rhythms in babies, so hereditary factors and the influence of environmental variables can be compared. Results may still be inconclusive, however, as fetuses are not isolated from the external environment and may be influenced by the circadian rhythms of their mothers. Oestriol in maternal blood, which is a hormone of fetal-placental origin, shows a circadian rhythm during the last days of pregnancy (Mills, 1975). Mirmiran and Kok (1991) in their study of pre-term babies suggest that a biological clock is present in fetuses from twenty-two weeks gestation, which is entrained by the mother's rhythms, because in premature babies who are exposed to the constant conditions of the Special Care Baby Unit 50% still exhibit rhythms of heart rate and temperature. Hellbrügge (1960) reports that temperature rhythms develop more slowly in premature infants, but this may be either a slower maturation of the babies' ability to respond to environmental rhythmicity or a later maturation of some inherent mechanism (Minors and Waterhouse, 1981).

Mills (1975) agrees that the development of rhythmicity in individual babies must represent a combination of genetic potential, a maturation process in the

brain and varying influences in the environment. He cites Martin-du-Pan's study (1974) of a baby kept in constant daylight, fed on demand and not exposed to other environmental cues, whose temperature rhythm developed independently of these external variables. Again Hellbrügge's conclusions are similar. He suggests that human beings have an inborn circadian periodicity of nearly 24.4 hours, and after the organ functions and regulative mechanisms are fully developed, zeitgeber adjust the inborn periodicity to the twenty-four hour day. He concludes that rhythms are spontaneous and are later synchronised by day/night twenty-four hour periodicity; the process being one where monophasic day-night or circadian rhythms originate out of polyphasic or ultradian cycles. This would appear to be derived from observations of feeding and sleeping, however.

Much of the previous research studied circadian rhythms in relation to clock time, so that measurements were made four hourly or once during the day and once at night, but this may not be the best method. Most rhythms are at least influenced by lightness and darkness, activity and rest, and it is therefore preferable to measure them in relation to other events such as bedtime, meals or exercise. This study will try to discover how the rhythm of rectal temperature with sleep develops before four months of age, and monitoring will be continuous overnight, studying babies both cross-sectionally as a group and longitudinally as individuals.

Minors and Waterhouse (1981) and Anderson, Petersen and Wailoo (1990) have emphasised the importance of the effect of sleep by illustrating that, both in adults and children, there is a decrease in body temperature associated with sleep, even when taken during the daytime. The fall associated with sleep could be the exogenous element of the temperature rhythm which is superimposed on the endogenous circadian rhythm resulting in a greater fall once every twenty-four hours, usually at night.

Advantages of Circadian Rhythms

There are remarkably constant phase relationships between physiological rhythms and the light-dark cycle, so the main theory for the existence of circadian rhythms is that they have physiological and evolutionary advantages. Constant, high body temperature aids muscular and mental efficiency, but has to be off set against the high metabolic cost, so a decrease associated with sleep (when the animal is not eating) reduces energy requirements, but the modest size of the fall does not jeopardise escape from predators. The twenty-four hour period of the earth's rotation sets a natural time base. This theory is reinforced by nocturnal animals having peak temperatures at night (Minors and Waterhouse, 1981), and in extreme environments such as the Arctic, where the twenty-four hour days or nights mean it is advantageous to be able to respond immediately at all times, creatures exhibit weak circadian rhythms (Conroy and Mills, 1970).

Development of Circadian Rhythms

Studies on infants of circadian rhythms of temperature and other physiological functions that are present in adults are comparatively few, especially since the 1970's. Those by Mills (1975), Minors and Waterhouse (1981) and Hellbrügge (1960) conclude that although fetuses are subjected to circadian influences via their mothers, circadian rhythms are not present at birth or in the first few weeks of life, but develop some time over the first year (see pages 19 and 20 for further discussion). These studies have usually been analysed by comparing the daytime maximum reading and the night-time minimum, or by analysis of a graph of readings taken at regular intervals (usually four hourly) using a sine curve, which defines a rhythm in terms of amplitude and phase. They conclude that the increase in range is caused by a daytime increase with some functions

and a night-time decrease in others.

The first objective of this study is to monitor temperature and heart rate at minute intervals during the night to discover how the rhythms develop with sleep.

Temperature Rhythms

Newborn babies respond to infection by pyrexia, and have some thermoregulatory mechanisms, but it is generally agreed that there is no controlled changing on a daily basis of the 'set point' of body temperature by the hypothalamus, and neonates therefore do not exhibit a circadian rhythm of temperature.

Of all the functions, development of circadian rhythms of temperature has been studied the most extensively, perhaps because it is one of the easiest physiological measurements to monitor and because of the importance of thermoequilibrium in the body. The most famous reviews are from Hellbrügge (1960), Conroy and Mills (1970) and Minors and Waterhouse (1981), and the latter authors particularly emphasise the advantages in clinical assessment of knowing normal or abnormal body temperatures at a given time of day or age. Their studies looked at the averaged rectal temperature of a group of babies at given ages and concluded that a rhythm is not present in the first week of life, but then a small daytime rise and night-time fall is seen, the amplitude of which gradually increases until three years of age.

Jundell (1904) was the first to make systematic attempts to study the development of the body temperature in infants. He obtained four hourly rectal temperature recordings over several days for one hundred children up to five years of age, and reported that no significant diurnal variation was seen during the first few weeks, but a rise in daytime temperature was seen by the end of the second month; by six months the rhythm was clearly evident and during the

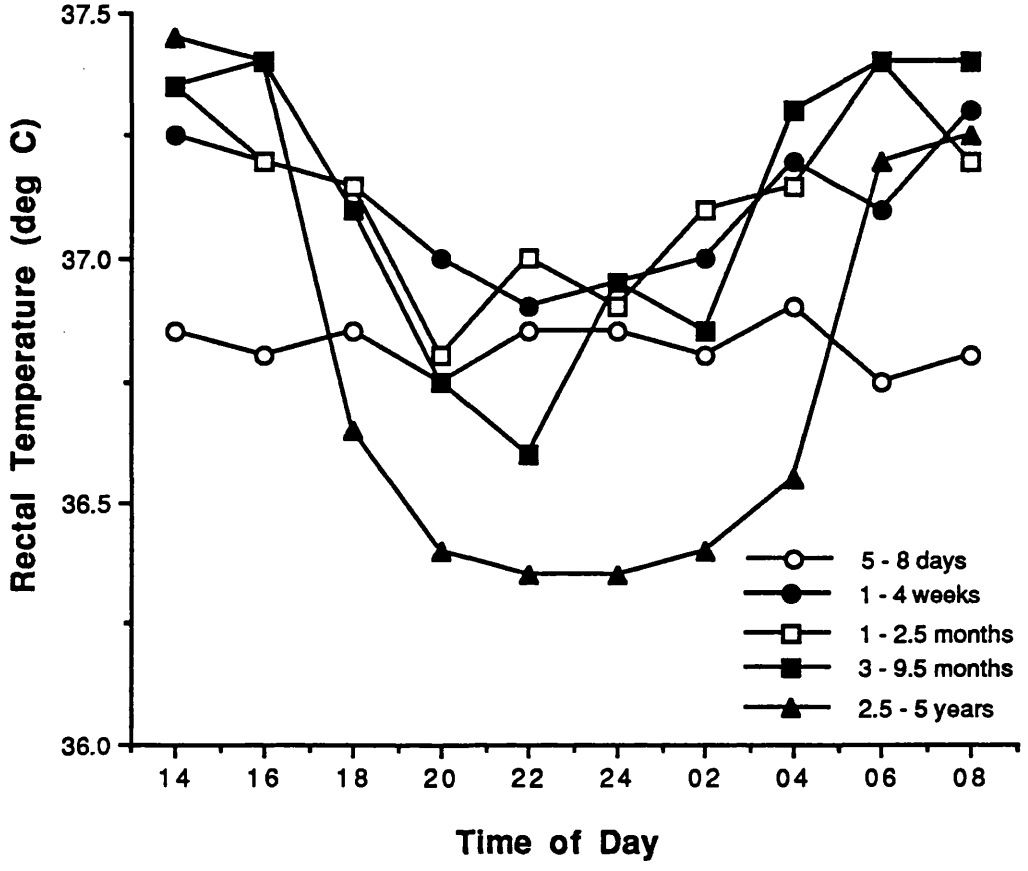


Figure 1:3 Jundell's data on the development of circadian rhythms of body temperature in relation to age. Four hourly readings taken from two different groups of 3 - 18 infants observed over two to eleven days

second year of life became fully established (figure 1:3). Many of the cross-sectional studies and reports carried out since Jundell's original work have been based on his results (Kleitman, Titelbaum and Hoffman, 1937 and Hellbrügge, 1960 (figure 1:4)). The results are probably blurred and distorted by studying different types of babies as a group, for example a wide age distribution, and using averaged data.

Two studies have monitored individual babies longitudinally, Mullin (1939) and Parmalee (1961). Mullin recorded body temperature every two hours for 4 to 5 successive days about once a month. He showed the development of a definite diurnal cycle from a spread of about 1^{o} Fahrenheit at birth to one of 3^{o} Fahrenheit by the eleventh month. He commented that this was manifested by a progressive lowering of the minimum level at night, with practically no change in the maximum temperature reached during the daytime, and also reported that from six months the body temperature curve became progressively more regular with less and less varying distribution of the readings at corresponding times on successive days. Parmalee monitored the temperature and other rhythms of a single child up to eight months of age, and reached similar conclusions.

A rhythm of electrical skin resistance is another indication of circadian thermoregulation, or the periodic changing of the hypothalmic set point. Electrical resistance falls as sweat increases and therefore is an indirect measure of the intensity of sweating and thus the utilisation of heat loss mechanisms. Hellbrügge (1960) reports that the rhythm of electrical skin resistance is present during the first week of life, and the amplitude slowly enlarges during the first year. Bruck (1961) found that full term newborn babies were able to sweat if ambient temperatures were as high as $35^{o}C$ - $37^{o}C$ and rectal temperature $37.5^{o}C$ - $37.9^{o}C$, and this has been confirmed by Hey and Katz (1969) who observed thermoregulatory sweating in the first ten days of life, if the ambient temperature exceeded $34^{o}C$ and rectal temperature $37.2^{o}C$. They also suggested that the threshold body temperature for sweating decreases and

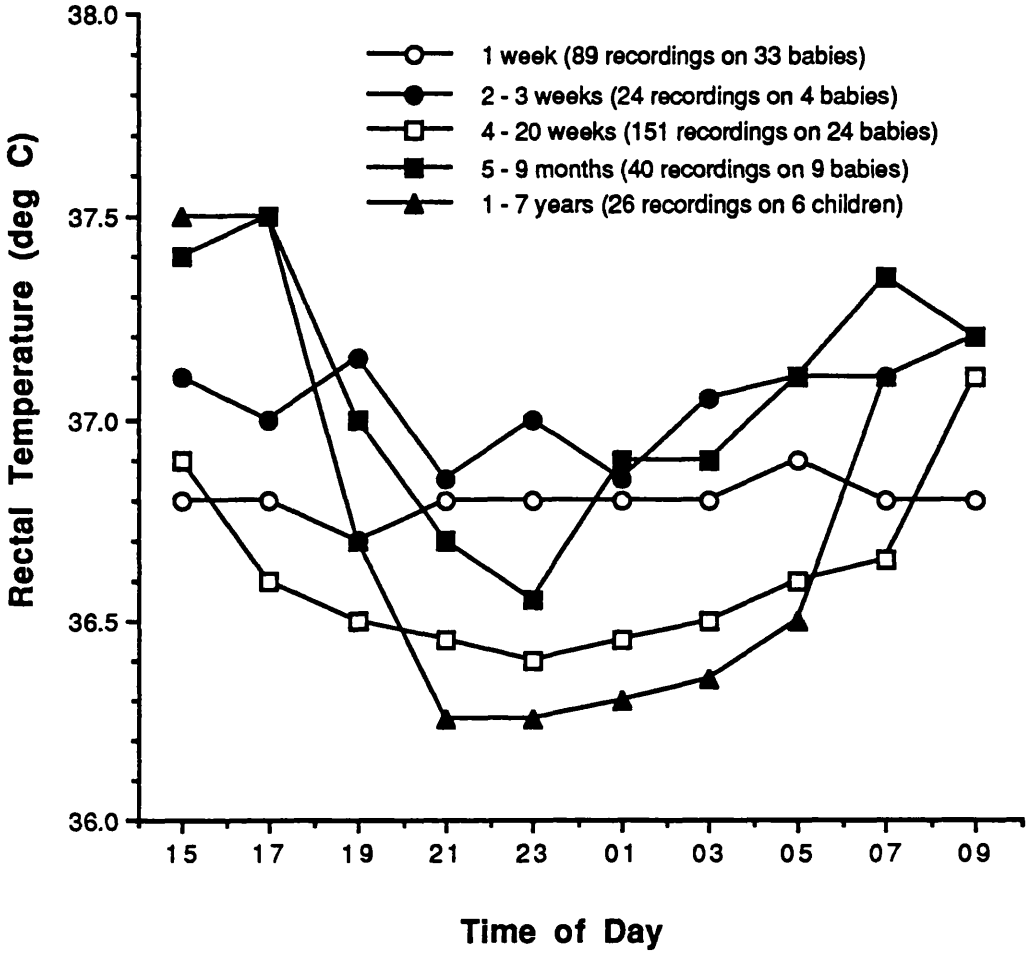


Figure 1:4 Hellbrügge's data on the day and night levels of rectal temperature. Averaged data of babies studied cross-sectionally.

maximal sweat reaction increases with postnatal age. An objective of this study is to monitor electrical skin resistance as a measure of sweating.

Little is known about whether the temperature rhythm develops as a result of exposure to external rhythms, or as a result of a maturation process in the infant, but Hellbrügge (1960) reported that premature infants developed their temperature rhythm slowly over the first three months, suggesting that a maturation process in the baby plays some part. It is difficult to discover Hellbrügge's definition of 'prematurity', although presumably none of the babies was born before 30 weeks gestation. More recent research indicates that prematurity does not delay development of temperature and heart rate circadian rhythms. Thomas (1991) reports that three out of five pre-term infants studied demonstrated a cyclic pattern of abdomen temperature, and this was not a reaction to incubator temperature. D'Souza, Tenreiro, Minors, Chiswick, Sims and Waterhouse (1992) showed that circadian rhythms of heart rate and skin temperature were present in some infants of extreme prematurity, and that if there was some delay, felt that poor medical condition may have contributed to it. They conclude that pre-term infants appear to benefit from exposure to alternating periods of light and darkness in the Intensive Care Unit.

This research aims to assess whether development is affected by gestational age.

Pulse Rate and Blood Pressure Rhythms

In adults circadian rhythmicity of pulse rate is considered to be largely exogenous especially as it rapidly adapts to abnormal time schedules. Minors and Waterhouse (1981) suggest that it is governed mainly by habit, increasing during activity and decreasing during rest and sleep. In the absence of other major influences, however, as in subjects kept under constant conditions, pulse rate is probably determined by body temperature (Kleitman and Kleitman, 1953). Pulse rate is one rhythm that has been studied antenatally and shown to be

constant during both day and night (Hellbrügge, Lange and Rutenfranz, 1956). Studies of the mean rate postnatally suggest that there are significant differences between day and night-time values from between four and twenty weeks of age, and these become more pronounced from that age onwards. This development is a result of lower night-time rates, not raised values during the day; for example the average night-time rate between the fifth and eighth month is 120 beats per minute, and between the eleventh and twenty-first month, 100 beats per minute (Hellbrügge, 1960 (figure 1:5)). Other researchers have commented on an increasing trend in heart rate up to about four weeks of age, before a fall is seen from that age onwards (Richards, Alexander, Shinebourne, deSwiet, Wilson and Southall, 1984 and Harper, Hoppenbrouwers, Sterman, McGinty and Hodgman, 1976).

A circadian rhythm in blood pressure has been detected in children aged four to fourteen years (Hellbrügge, Lange, Rutenfranz and Stehr, 1964).

The development of rhythms of blood pressure and heart rate is probably influenced by the combined effects of the temperature rhythm and, initially by the pattern of feeding, and later by the development of a circadian pattern of rest and activity.

Rhythms of Urine and Urinary Constituents

Hellbrügge (1960) suggests that urine excretion, potassium and sodium excretion all show significantly different levels at night than during the day from about four weeks of age, but phosphate, creatinine, chloride and creatine excretion do not show a circadian variation until the sixteenth month. Other writers contend, however, there is no evidence that clearly separates the development of rhythms of flow and individual electrolytes (Mills, 1975). It has been suggested that urinary flow is secondary to one of fluid intake, but babies receiving four hourly feeds with the night feed omitted still have an urine flow that falls prior

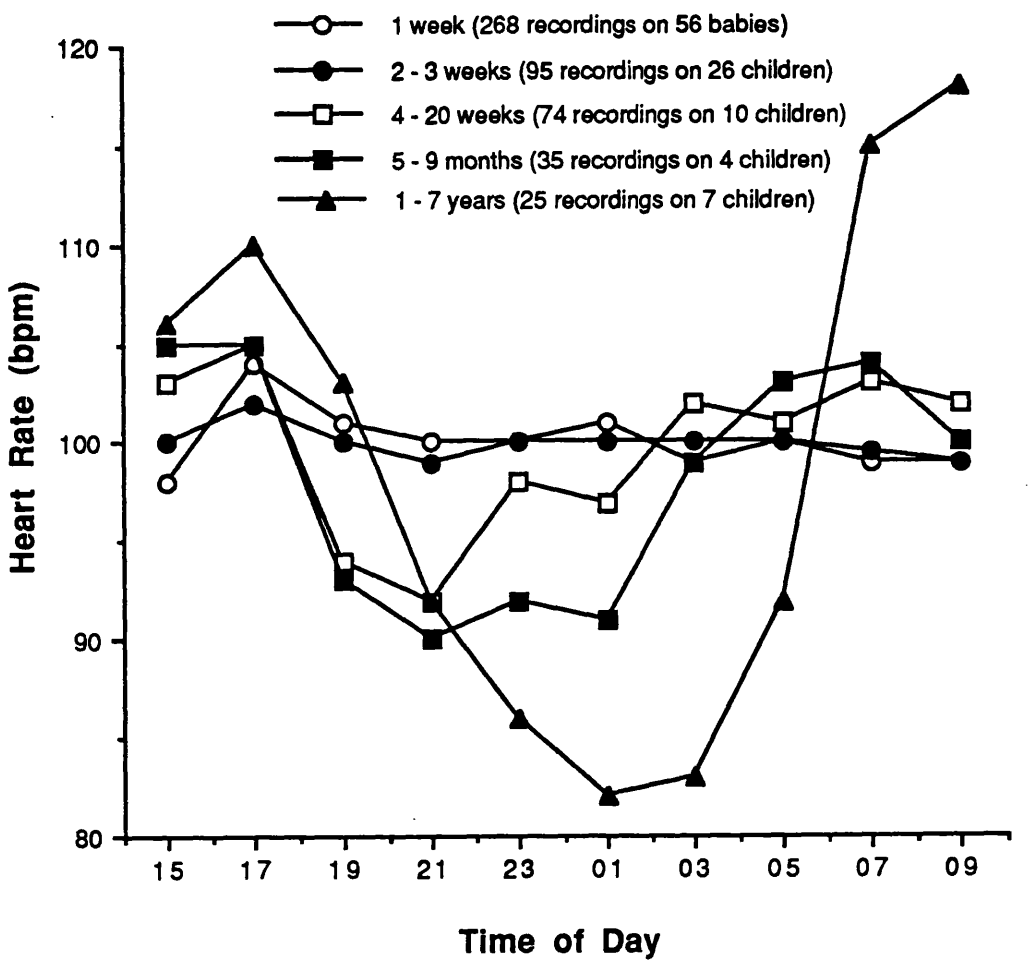


Figure 1:5 Hellbrügge's data on day and night levels of children's heart rate. Averaged data of cross-sectional studies.

to the last evening feed and rises before the first morning one.

Rhythms of the Adrenals, Pineal Gland and Growth Hormone

Work on these rhythms has been scarce, possibly because of difficulties taking many plasma samples over twenty-four hours, and results have been inconclusive. Generally, however, it has been demonstrated that there are ultradian variations, or episodic excretions, in the plasma, of cortisol and melatonin that develop over the first two years of life, but a circadian rhythm of growth hormone secretion has not been demonstrated in babies (Zurbrugg, 1976 and Martin-du-Pan and Vollenweider, 1967).

Rhythms of Sleep-Wakefulness, Activity and Feeding

These rhythms possibly have the most effect on other rhythms, and in turn are greatly influenced by exogenous factors such as light and darkness, how much attention a baby receives and whether feeding is at regular intervals (for example, four hourly) or on demand. Various studies, particularly that of Martin-du-Pan (1974) demonstrate that a rhythmic environment is not a prerequisite for the development of circadian rhythms in babies, but external factors are important in synchronising infants to an adult pattern. Martin-du-Pan observed two babies who were demand fed and kept in constant light, and reported that by the seventh week sleep periods became longer at some times of the day than others. By about nine weeks most sleep was between 06.00 hours and 15.00 hours, presumably because of the lack of cues as to the alternation of day and night. At about twelve weeks the babies were exposed to the normal light/dark cycle, and within nine days had altered to demanding four feeds at more conventional hours and sleeping from 19.30 hours to 05.00 hours. The interpretation is that the circadian clock can develop independently of external

synchronisers.

Sleep Stage Rhythms

Initially during a sleep cycle there is a progressive reduction in muscle activity which is accompanied by a gradual slowing, but increase in amplitude, of Electro-Encephalogram (EEG) waves. This Quiet, Non-Rapid Eye Movement (NREM) or Slow Wave Sleep (SWS) has been divided into four stages; Stage One is characterised by fast, low amplitude EEG activity, but skeletal muscle activity is not noticeably different from that of a person when resting and awake; Stage Two is marked by the appearance of 'sleep spindles' or bursts of alphalike waves on the EEG, and muscle activity is greatly reduced. In Stages One and Two the sleeper is easily aroused. In Stage Three sleep deepens and 'sleep spindles' are superimposed on EEG waves of slower frequency and increased amplitude and Stage Four is associated with a high threshold for awakening and the EEG readings consist solely of slow high-voltage waves. SWS is followed by Rapid Eye Movement (REM) sleep which is a phase with rapid irregular movements of the eyes, gross body movements, occasionally against a background of decreased muscle tone, and quickening of heart and respiratory rates, accompanied by low voltage, fast and irregular EEG activity. Sleep is deeper in this stage, despite the EEG readings being those normally associated with wakefulness, and these observations have led to the term 'paradoxical sleep'. Dreaming occurs during REM sleep and it has been argued that it is necessary for mental well being, because if a person is repeatedly aroused in the REM stage they become irritable and on subsequent nights have more periods of REM sleep.

In adults Slow Wave Sleep is the predominant sleep phase and appears normally at the onset of sleep. A period of fifteen minutes of Rapid Eye Movement sleep follows after about 75-100 minutes and the two forms alternate regularly throughout the sleep period. Towards morning the SWS periods shorten and

REM sleep increases.

At birth REM sleep occupies about 50% of the time asleep, the remainder being classed as 'indeterminate sleep' rather than quiet sleep, because the distinction between the different stages is not as clear in the neonate as in adults. By two years of age the amount of REM sleep decreases to about 20% of the time asleep, the value found in young adults (Webb, 1974). The length of the sleep stage cycle also increases considerably from about 50 minutes at birth to about 75 minutes by four years of age. A circadian variation in the tendency for REM sleep to occur has also been illustrated by Sostek, Anders and Sostek (1976), the lowest amount occurring in the afternoon.

Webb (1974) writes that babies do not manifest Slow Wave Sleep until one to three months of age and when it is present there is circadian pattern, a finding also found in adults.

In summary, it would seem reasonable to presume that three processes interact during the development of circadian rhythms in babies. These are:

1. The maturation of an endogenous clock
2. The ability to respond to synchronisers
3. The direct effect of external rhythms

Researchers have also commented on the importance of the rhythms themselves and the timing of their development. Neonates may not have circadian rhythms because they are unable (possibly due to immaturity) to respond to their new external environment and rhythms (Minors and Waterhouse, 1979). The normal infant then passes through a sequence of maturation that develops over the first few months of life concurrently with the nervous system and other functions, including better control of temperature. There may be a 'critical period', or possibly several critical stages, before functional stability is established and during which thermoregulation mechanisms and controlled changes in temperature may not be complete.

Hoppenbrouwers, Jensen and Hodgman (1979) write of a cluster of dynamic changes during development, stating that the first three months of life are characterised by dramatic increases in quiet sleep and oxygen saturation levels and decreases in active sleep, heart and respiratory rate, incidence of apneoa and periodic breathing. This is followed by a period from three to six months of relative stability of these functions.

These dynamic changes appear to develop correctly and at the appropriate rate in the majority of babies, but it is possible that occasionally one function changes before another or that some rhythms do not develop at all. If this occurs and/or the physiological functions are challenged during this critical period, perhaps by infection, cold or heat stress, malnourishment or lack of sleep, the consequences of underdevelopment or misaligned development may be grave. Delayed maturation and misaligned development may be caused by several factors, including biochemical imbalances, genetic abnormalities, adverse maternal influences or trauma. By studying babies longitudinally it will be possible to correlate information about the baby and any delay in rhythm development.

Evidence to support the theory of a critical period has been provided by work carried out on premature babies and babies who have suffered an apneoic attack that was considered severe enough to be fatal if resuscitation had not taken place ("Near-SIDS Infants"), on babies who have subsequently died ("Future-SIDS") and on brothers and sisters of babies who have died from Sudden Infant Death Syndrome ("Subsequent Siblings") (for review see Guntheroth, 1989).

Premature babies are delayed achieving normal levels of quiet sleep and their temperature rhythms and sleep-wakefulness cycles may be slower to develop (Hellbrügge, 1974), although information about the extent of prematurity and delay is not available. Near-SIDS have demonstrated delay in their maturation of sleep, too, and up to three months of age have more REM sleep and less quiet sleep than normal controls, and in the age group three to six months have fewer

body movements during REM sleep (Guilleminault and Coons, 1983). Conversely, Hoppenbrouwers, Jensen and Hodgman (1979) suggest that Subsequent Siblings have sleep and other circadian cycles that develop earlier than the control population.

Leistner, Haddad, Epstein, Lai, Epstein and Mullins (1980) report that Near-SIDS have heart rates 5-10% faster and their heart rate variability is 10-45% smaller than controls and Kelly, Golub, Carley and Shannon (1986) and Southall, Stevens, Franks, Newcombe, Shinebourne and Wilson (1988) report that Future-SIDS have a higher heart rate. Harper et al (1982) (cited by Guntheroth, 1989) write, too, that Subsequent Siblings have a higher mean heart rate during quiet sleep in the first six months and during the waking state after three months of age.

Fever

This is another controlled change in body temperature. Fever is generally thought to be a consequence of an elevation in the regulated internal body temperature. von Liebermeister (1875) (cited by Keele, Neil and Joels, 1982) first postulated that the 'set point' of body temperature is, by the action of pyrogens, shifted to a higher, but still regulated level so that at febrile temperatures thermoregulation in response to heating and cooling the body is just as precise as normal, and the usual diurnal variation in body temperature is still present (Keele, Neil and Joels, 1982). Pyrogens are fever producing substances; the term was first introduced by Burdon Sanderson in 1876 to describe substances which produced fever that had been extracted from putrefying meat. Pyrogens occur mainly in bacteria, particularly Gram-negative bacteria and mammalian tissues, but are also present in viruses and endotoxins. Pyrogens themselves cause a rise in temperature, but they also react with polymorphonuclear leucocytes to produce endogenous pyrogens (including interleukin-1), which

appear to be more potent and specific in their action (Keele, Neil and Joels, 1982). In the initial stages of fever a rigor or shivering occurs which increases heat production and the skin vessels are constricted, minimising heat loss. A rapid rise in temperature and blood pressure therefore takes place. When the body temperature has reached its new height (sometimes up to 42^{o}C), the cutaneous vessels relax, the skin is flushed and the blood pressure falls. Once the fever has run its course, the temperature falls, marked sweating occurs and heat loss is now greater than heat production.

Drugs such as Paracetamol and Aspirin reduce body temperature in infection induced fever, but they do not reduce normal body temperature nor hyperthermia due to high environmental temperatures. They probably act by antagonising the action of pyrogens on the hypothalamus and thus 're-set the thermostat', so the temperature returns to normal by increased vasodilatation and sweating. Cortisone and its related products are also antipyretics, but their mode of action is unknown.

There are probably a number of reasons for fever, although the benefits are uncertain. Many micro-organisms grow best within a narrow range of temperature and a rise in temperature would therefore inhibit growth, and elevated body temperature increases antibody production. Artificially induced hyperthermia has been successful in the treatment of neurosyphilis, slowed the growth of a number of tumours and been beneficial in the treatment of some diseases (Ganong, 1985). Fever with illness is a sign that the body has mounted a defence reaction to stress, in this case bacteria or virus, by increasing metabolic activity and is an indication for the sick person to rest and seek treatment. Infection is considered to be an important source of thermal stress so another objective is to study the effects of natural infection and immunisation on rectal temperature, heart rate and sweating.

Sudden Infant Death Syndrome (SIDS)

In the past those children dying suddenly and unexpectedly were swamped numerically by the large numbers of children dying as a result of infection and malnutrition, but during the 1980's in the western World, Sudden Infant Death (SID) was the major cause of death of children between one month and one year old, accounting for 21% of all deaths of babies in that age range. These children usually die at home or on the way to hospital, and at post-mortem there may either be no signs of any abnormality at all, minor abnormalities but no indication of a specific disease process, or evidence of disease not considered severe enough to have caused death.

The definition, therefore, of Sudden Infant Death Syndrome is the sudden death of any infant which is unexpected by history and in whom a thorough necropsy examination fails to demonstrate an adequate cause of death (Beckwith, 1970). In America a recent revision only includes babies under one year (National Institute of Health, USA, 1989) and in this country since 1986 only the post neonatal figures have been published, although 5% of deaths occur in the first month (Limerick and Gardner, 1992). Correspondence between Limerick, Gardner and Gordon (1992) discusses the interpretation by coroners of 'unexpected' and 'adequate cause' and an updated definition may possibly be reached in 1994.

In the late 1980's and early 1990's SIDS has accounted for about two deaths per thousand live births in the United Kingdom, a rate reflected in Leicestershire, which with fluctuations, has been the same for at least the past forty years. However it is difficult to compare statistics, as definitions and reported causes of deaths have varied during this time. In 1992 the national rate was reported to be 0.7 per 1000 live births.

Babies dying suddenly and unexpectedly have been considered a distinct cause of death since biblical times (1 Kings, Chapter 3, Verse 19), but it was judged to be as

a result of overlaying or deliberate suffocation. During the mid to late nineteenth century French doctors attributed the cause to "congestion of the lungs", and then in the early 1900's German doctors expounded that the deaths were due to an enlarged thymus obstructing the upper airways or creating pressure on the vagus nerve. This theory remained popular for a number of years, mainly because the only other autopsy specimens available were from children dying from infection or malnutrition, in both of whom the thymus becomes involuted and small. Thus those children dying from SIDS had a normal size thymus, but in comparison it looked larger. During the 1920's there was a return to the view that these deaths were due to suffocation, and as a result autopsies became compulsory in England. "Cause unknown" was unacceptable to the Registrar of Births and Deaths, but as coroners did not wish to give further distress to bereaved parents, "Infection" particularly "Pneumonia" was often given as the reason for death (for historical review see Golding, Limerick and Macfarlane, 1985).

Since the 1960's research and theories have expanded, but still no exact causative mechanisms are known.

Epidemiology of Sudden Infant Death Syndrome

The epidemiology of SIDS has been studied extensively and there are a number of factors which have been shown repeatedly to be related to the syndrome, although causal links have not been proved. Unfortunately much of the research relies on studying the babies and their families after a death has occurred. The findings on the babies at post-mortem may be changes after death or 'normal', for example the size of the thymus (see previous section). Results also rely on parents' and professionals' recall of a very traumatic event, characteristics and care of the baby in the past and seeking records of events perhaps a number of months before the baby died. This mode of research may be

limited, but as often as possible it is backed up by information collected about babies who subsequently die from SIDS. In this study prospective data about the families and care of the babies will be collected.

Unless otherwise specified the following statistics are taken from Golding, Limerick and Macfarlane's (1985) research and reports.

The majority of deaths occur between the ages of four and twenty weeks, with a peak incidence between eight and twelve weeks; nearly 80% occur in babies under six months of age. Boys are at greater risk than girls and the age distribution is different; 45% of male deaths occur between the ages of eight to fifteen weeks, whereas only 36% of female deaths occur then.

It is generally believed that the deaths happen whilst the babies are asleep at night in their 'cots' or 'cribs', and although it is difficult to estimate time of death, 50% are thought to occur between midnight and 8am, 36% between 8am and 4pm and 14% between 4pm and midnight. As Golding, Limerick and Macfarlane point out, however, these figures may be misleading, because they imply the majority of babies are not seen for sometime before they die, whereas their research suggested that over 50% of deaths occur between the time the baby is first seen in the morning and 9pm.

In all countries babies are more likely to die in the winter than the summer months, and in this country the highest risk is to babies born from September to November and the lowest risk is to babies born in March and April. Studies have also suggested that those months with the lowest night temperatures and/or the least number of hours of sunshine are the ones with the highest rates of SIDS. There have also been positive associations with average wind speed, the number of days with snow and relative humidity, but no verified evidence that the weather on the days immediately preceding death is correlated with the deaths.

Social factors about the babies and their families have also been studied and SIDS is more common in cities than urban and rural areas, and in infants living

in poor quality housing (Knowlden, Keeling, Nicholl, Emery, Harris, Oakley, Stanton and Huber, 1984).

Those babies born in the lower social classes are at increased risk compared to those born into the upper social classes, but what this means is difficult to interpret, as there are also social class trends for diet, smoking, the likelihood of the mother to breast feed, the attitude of the mother to child rearing, income, leisure activities, education and type of housing (Black, Morris, Smith and Townsend, 1982 and Kraus, Greenland and Bulterys, 1989). If the father is unemployed or in the armed forces, or the mother is unmarried, there is also a detrimental effect on the risk to the baby.

A relationship with SIDS has also been shown when the mother is under twenty years old (Babson and Clarke, 1983), if she smokes (Bergman and Weisner, 1976) or is addicted to opiates or has had a number of previous pregnancies, particularly with an inter-partum interval of less than six months (Kraus, Greenland and Bulterys, 1989). Height of the mother has also been studied, and if she is under 5 feet 1 inch or over 5 feet 6.5 inches the baby is at increased risk. Studies of the ethnic origin of the parents (as determined by the country in which they were born) have shown that babies of West Indian and Irish Republic mothers are at increased risk of SIDS and those of Asian mothers at decreased risk, which has been paralleled by a lower mortality from respiratory causes (Balarajan, Raleigh and Botting, 1989).

When the pregnancy is studied, those babies who die are more likely to have been born after a short second stage of labour, perhaps because of the higher parity of their mothers, and the mothers are more likely to have had an infection during pregnancy, particularly one of the urinary tract (Carpenter, Gardner, Jepson, Taylor, Salvin, Sunderland, Emery, Pursall and Roe, 1983) or influenza.

An increasing risk has been illustrated with a shorter gestation and smaller birth weight, and interestingly pre-term babies die at an older average post-natal age than full term infants (Ponsonby, Dwyer and Jones, 1992). There is

also a possible relation to postnatal growth, particularly static weight or weight loss before death (Williams, Taylor, Ford and Nelson, 1990). Twins and triplets are at increased risk, and in addition, if one twin dies the remaining sibling is at greatly increased risk for four weeks (Smialek, 1986) and then his risk is increased by a factor of three, the same as any subsequent sibling of a baby who has died. There are no data, however, to support a genetic component to SIDS (Peterson, Sabotta and Daling, 1986).

The babies often have a larger than average number of admissions to hospital and a possible increased incidence of illness in their lifetimes (Carpenter, 1988 and Watson, Gardner and Carpenter, 1981). These statistics, however, are taken from known visits to the GP and hospital, or from recall, when minor illnesses might be considered more important if the baby subsequently dies.

Infection is often implicated in SIDS, however, so one objective is to study the effects of natural infection and immunisation on rectal temperature, heart rate and sweating and to assess whether parental care alters at this time.

Recently much publicity has been given to the larger proportion of babies dying from SIDS whose usual sleeping position is prone rather than lateral and supine (Fleming, Gilbert, Azaz, Berry, Rudd, Stewart and Hall, 1990 and Beal and Finch, 1991), and the dramatic decrease in deaths following a national campaign advocating avoiding the prone sleeping position (Foundation for the Study of Infant Death).

Research into the epidemiology of SIDS has aimed to compile a number of 'risk factors' that added together hopefully identify those babies at increased risk of SIDS (Carpenter and Emery, 1974, Oakley, Tavare and Stanton, 1978, Carpenter, Gardner, Pursall, McWeeny and Emery, 1979 and North, Petersen and Wailoo, 1991 (unpublished data)). The common factors in all these predictive or scoring system approaches are low birth weight (caused by prematurity or dysmaturity) or admittance to Special Care Baby Unit, young maternal age, high maternal parity and short inter-partum interval, maternal smoking, male babies and

multiple births as well as a subjective view of the home conditions. Many of these factors may be related to each other, for example maternal smoking has shown to be correlated with smaller babies (Butler, Goldstein and Ross, 1972), and high maternal parity is associated with short inter-partum interval and short second stage of labour (Carpenter and Emery, 1974).

As social factors and care of the baby have been implicated in the aetiology of SIDS the second objective is to collect as much information as possible about the parents and family, ante-, peri- and post-natal history, living conditions, and care of the babies being studied, and to assess whether they correlate with any of the other factors studied.

Recent recommendations from the Foundation for the Study of Infant Death are based on these and other studies on babies at increased risk of SIDS, and reports from research in England, Hong Kong, The Netherlands, Tasmania and New Zealand. They advise that SIDS may be reduced by breast feeding, avoiding the prone sleeping position and not smoking (Lee, Chan, Davies, Lau and Yip, 1989, de Jonge, Engelberts, Koomen-Liefting and Kostense, 1989, Dwyer, Ponsonby, Gibbons and Newman, 1991 and Taylor, 1991).

General Hypotheses about SIDS

Over the years there have been a number of theories about why babies die suddenly and unexpectedly, and it is widely believed that SIDS is not an expression of a single cause and effect, but a multifactorial phenomenon. Below there is brief outline of some of the main theories that have been discussed over the past twenty to thirty years.

One of the reasons expounded in the 1970's, which may explain some of the infant deaths during this time, was hypernatraemia, probably as a result of high levels of sodium in artificial feeds and weaning foods or the mixing of over concentrated milk feeds. A further theory related to feeds, is that in a family

with a history of allergy, the baby may be sensitised to cows' milk protein which causes gastro-intestinal reflux and inhalation leading to death by anaphylaxis (Parrish, Barrett, Gunther and Camps, 1960).

Another group of theories that has been studied is whether babies dying from SIDS have a deficiency or excess of some trace elements, vitamins or hormones, for example selenium and vitamin E, vitamin C and thiamine.

Babies with older siblings and mothers who smoke are at increased risk of SIDS in the winter months, and they are also more likely to develop infections, particularly those of the upper respiratory tract. Respiratory syncytical virus, botulism and cytomegalo virus have been cited as the most likely organisms. Some researchers believe that the babies are dying because of an immature immune system which cannot prevent a rapidly fulminating infection, or that the babies have an allergic reaction to the micro-organism which results in anaphylactic shock. Researchers in Sheffield have also discovered a limited number of babies with an inherited enzyme (MCAD) defect which prevents them using the full reserves of body energy at times when it is needed most, for example when fighting an infection (Voet and Voet, 1990).

There are many theories about respiratory causes of SIDS, as Near-SIDS are resuscitated from an apneoic attack and episodes of non-breathing have been studied extensively in premature babies. Recurrent apnoeic episodes tend to occur more often in babies with certain patterns of light sleep and if they have a respiratory tract infection (Guilleminault, Peraita, Sonquet and Dement, 1975), and evidence suggests that nerve constriction and compression following trauma to the brainstem and cervical spinal cord, possibly as a result of a difficult birth, retard development of the respiratory nervous system (Banks, Beck, Columbus, Gold, Kinsinger and Lalonde, 1987).

The simplest theory is that there is a mechanical obstruction to breathing; this may be internally, for example if obligatory nose breathers (20% of babies) have blocked noses, and cannot resort to mouth breathing, or if the weight of the jaw,

tongue and soft palate block the airways, perhaps because of the sleeping position; and externally obstruction may be deliberate or by soft pillows and mattresses.

Low levels of surfactant in the lungs has also been propounded as a cause; surfactant decreases the surface tension in the alveoli of the lungs and helps stop the lungs collapsing. Babies dying from SIDS have the same levels as premature babies dying from respiratory distress syndrome.

Other theories have studied babies' reactions to levels of carbon dioxide, and conclude that babies dying from SIDS may have a decreased response to high levels of carbon dioxide (Shannon and Kelly, 1977 and Parks, Paton, Beardsmore, Macfadyen, Thompson, Goodenough and Simpson, 1989). In addition it has been observed that during REM sleep the respiratory drive and rhythm appear to be unaffected by sensory input, so if hypoxia occurs at this time the baby is less likely to react appropriately (Simpson, Pallot, Thomas, Swaminathan and Beardsmore, 1991). The carotid body normally responds strongly to hypoxia, hypercapnia and acidosis by increasing respiratory drive. At post-mortem some SIDS victims have elevated levels of carotid body dopamine, an amine known to depress ventilation in animals (McKeever, Vaughan, Pallot, Simpson and Beardsmore, 1991). Perhaps SIDS victims do not react to hypoxia in the same way as controls.

Under consideration, too, is whether the heart stopping is primary or secondary. Studies have shown that part of the electrical conducting system of the heart alters soon after birth, and during this period of alteration the baby may be more susceptible to abnormal rhythms. Other researchers have analysed electrocardiogram readings and shown that Subsequent Siblings and Future-SIDS have a prolonged QT interval (Southall, Arrowsmith, Stebbins and Alexander, 1986). Another theory relates to the 'oculo-cardiac' response or vagal nerve stimulation slowing the heart beat; this is elicited by applying pressure to the eyeballs, and it is possible that the baby's head pressing down on the cot

initiates this response. Two further hypotheses are that ventricular arrhythmia may be caused by acute hypokalemia induced by hyperventilation and that the prone position causes the ventricles of the heart to fall forward and prevents filling of the heart, leading to arrhythmia or cardiac arrest.

Other theories in the national press over the past few years are that electromagnetic fields play a part (Coghill, 1990) and that fire retardant cot mattresses can give off poisonous fumes if a chemical reaction to urine takes place (Richardson, 1990 and Turner (Department of Health), 1991).

Thermoregulation, Circadian Rhythms and Sudden Infant Death Syndrome

When the importance of body temperature and thermoregulation are considered, and the extensive research studied, it is hardly surprising that many hypotheses about Sudden Infant Death Syndrome are based on theories about the malfunction of temperature control; for example the controlled 'set point' of temperature being fixed too high or too low by the hypothalamus or extreme responses by the thermoregulatory mechanisms to the environment.

For many years the theories were mainly based on the idea that babies suffer from hypothermia, or that perhaps in a cold environment babies' metabolisms increase to excessively high levels. These conclusions were drawn from Budin's discovery that premature babies have a better chance of survival at higher ambient temperatures, and his consequent development of the incubator.

Researchers have also been concerned that babies should be in a thermoneutral environment (see **page eight**) and there are recommendations about clothing, bedding and room temperature. For older babies, Stanton (1984) recommends a room temperature of $18^{0}C$ if the baby is wearing vest, nappy and nightie and is covered with a sheet and three blankets (calculated tog value 9.4). The Foundation for Sudden Infant Death (FSID) offer guidance about bedding assuming the baby is clothed in nappy, vest and babygro. (The description here

is followed by an estimate of the total tog value of clothing and bedding). It is advised that a baby is covered with a sheet and four layers of blankets (11.4) in a room temperature of 15°C, a sheet and three to four layers of blankets ((9.4) in an ambient temperature of 18°C, a sheet and two to three layers of blankets (7.4) in an environmental temperature of 21°C, a sheet and one layer of blanket (5.4) in a temperature of 24°C and a sheet only (3.4) in 27°C. One objective of this study is to measure the amount of coverings on babies and the temperature of the room in which they are sleeping.

The role of temperature is implicated because deaths from SIDS are more likely to occur in the late autumn and winter (McGlashan and Grice, 1983), a fact shown poignantly in the very cold winter of 1986 when there was a national increase in the incidence of SIDS (Gordon, 1989 and Prentice, 1988). It is feasible that if the baby's face is wet and exposed to cold air or winds his heart and respiration will cease because the dive reflex is exhibited, which is a sudden reduction in heart rate and breathing. This seems an unlikely cause for all but a few deaths. There have been no reports of unexplained deaths under these circumstances, and the majority of babies die at home. The dive reflex, however, may be a possible result of regurgitation leading to milk or acid in the pharynx (A. Davies - Involvement of upper airway chemoreflex in sudden infant death. FSID grantholders meeting, Cambridge, 1992).

The autumn/winter trend is generally attributed to the cold weather, but Guntheroth (1989) also points out that it often correlates with the school terms when older children are more likely to have infections, and cites the seasonal variation of SIDS in Hawaii which is not characterised by cold weather, but by school schedules.

In 1974 Robert Dallas postulated that very high temperature might play a part, and others suggested that the association with cold weather may be because babies are more heavily wrapped and kept in warmer home environments at these times (Stanton, 1984 and Bacon, Bell, Clulow and Beattie, 1991). Again

during the winter illness in young children increases, particularly upper respiratory tract infections. Infection increases body temperature, and in the presence of fever the body's natural control mechanisms are disturbed in order to fight the organisms and protect the body (for discussion see Campbell, 1989). Many babies (in some studies up to 80% (Pfeifer, 1980)) who were classified as dying from SIDS have had extremely high rectal temperatures several hours after death (Sunderland and Emery, 1981 and Bacon, Scott and Jones, 1979).

Theories relating to high temperature and SIDS can be divided into two groups, although the reasons may overlap and interrelate with each other. The first group infers an inherited or acquired disposition to react abnormally to infection or high ambient temperatures, so that the 'set-point' is either not controlled or is fixed at an abnormal level, and the second expounds that extreme environmental conditions combine to overwhelm the baby's thermoregulatory mechanisms, so that the baby either does not regulate its temperature, or its responses are inappropriate.

Within the first group is Sunderland and Emery's theory (1981) that SIDS and febrile convulsions both have a common causal mechanism (thermolabile cerebral ischaemia), and age of the baby determines which reaction occurs. There is a cross-over in the age at which SIDS and febrile convulsions occur; the peak incidence of SIDS being before six months of age, whereas febrile convulsions at that age are rare, but 3-4% of children have one between the ages of six months and six years (Stanton, 1984). Babies, therefore are less likely to have convulsions with fever, but if they do the severity is greater. No other link has been found between SIDS and febrile convulsions, however; there is no relation between admissions for febrile convulsions and SIDS and Barry (1981) calculated that if the causal mechanism was similar, siblings of victims of SIDS would have a risk of 20% of suffering from febrile convulsions, but only 2 out of 164 siblings were admitted to hospital with them. Sociological factors have

consistently been correlated with SIDS, but these are not associated with febrile convulsions.

In Australia, Denborough, Galloway and Hopkinson (1982) postulate that there may be a connection with the disease Malignant Hyperpyrexia, a disorder of the muscles which causes a sharp rise in temperature under anaesthetic. They found that five out of fifteen parents of babies dying from SIDS had malignant hyperpyrexia. No other studies have been reported.

Other researchers have concluded that SIDS is caused by an abnormally high temperature, possibly because of a genetic disposition for the hypothalamus to raise the 'set-point' temperature too high in response to a brief viral infection, although they also state that the reaction may be because of concurrent viral or bacterial infection, nutrition, season and social conditions.

Apnoeic episodes have been associated with rapid increases in ambient temperature, and in a study of babies who had a history of cyanotic episodes, the most prolonged and severe periods of apneoa were in conjunction with an upper respiratory tract infection, and presumably concurrent raised temperature (Stanton, Scott and Downham, 1980 and Stanton, 1984).

A combination of infection and environmental overheating is the main theory in the second group. In the past health education has concentrated on the problems of preventing low temperature and hypothermia, and parents are encouraged to feel that the amount of bedding and clothing provided is a measure of their care and love. Maternity units are very warm and babies are provided with warm clothing and often swaddled, which gives parents an impression of good parental care, and the practice is continued at home. This is not necessary after the first few days, and in fact full term babies of more than a month have a greater body mass to surface area ratio, and are quite efficient at generating and conserving heat (Downham and Stanton, 1981). Research has indicated that there is a small group of mothers who are particularly concerned about keeping their babies warm (Nicoll and Davies, 1986), and it has been suggested that

parents judge the amount of bedding they put on their babies by the apparent temperature outside the home, rather than the temperature in the bedroom (Bacon, Bell, Clulow and Beattie, 1991). Therefore, if it is frosty or snowy outside, it "feels" colder and more bedding may be used, even though the temperature is constant in the home, or the thermostat on the heating may be turned up. Occasionally adult bedding is used on babies' cots or beds and consequently may be folded many times to fit. When babies are unwell traditional practice often prevails, too; 'old wive's' advise keeping well wrapped up in bed with a hot water bottle and hot drinks and 18.8% of parents in Newcastle reported that they would keep a baby warmer if it was ill (Bacon, Bell, Clulow and Beattie, 1991). If babies are uncomfortable, they are usually unable to alter their environmental conditions to any great extent by themselves, although if their coverings allow it, will change position or expose limbs to the air. Bacon, Bell, Clulow and Beattie (1991) propound that crying generates heat, so, rather than trying to communicate their discomfort to their carers, many babies have what may be a fatal instinct to remain silent. Empirically it seems that babies are more likely to be restless and cry if cold, and remain quiet if warm. Mestyan, Jarai and Fekete (1968) also report that warmth has a tranquilising effect. This is under normal conditions, however, not excessive heat.

These hypotheses about babies dying are based on necropsy findings that rectal temperature is frequently still raised many hours after death, and often the babies or their cots have indications of visible sweating (Stanton, 1984 and Beal, 1983). Some of the factors associated with SIDS have also been found to be correlated with higher levels of insulation, for example when the mother is younger or in a lower social group, during the winter and at night. Fleming, Gilbert, Azaz, Berry, Rudd, Stewart and Hall (1990) in their retrospective study noted that SIDS victims over seventy days old were more likely to be more heavily wrapped and virus positive than the control babies.

Bacon, Scott and Jones (1979) report a series of case histories where children were mildly ill as reported by the parents, but with no focal point of infection, and were also considered to have been in warm conditions; they suffered from convulsions, shock and death from heatstroke. Some illnesses generate high temperatures, with the only symptoms being changes in behaviour which are hard to recognise and interpret, and are not usually considered life threatening, for example urinary or ear infection. In other cases of SIDS where the babies have been judged to be more heavily wrapped than normal, findings at post-mortem indicate either infection or histological changes in the small intestine compatible with heatstroke (Stanton, Scott and Downham, 1980). Incidents of this type of death have been reported when babies have been left in cars in warm weather or incubators were too near windows in the sunshine. In addition there are empirical observations that often outdoor clothes, especially hats, are left on in warm shopping centres and indoors if the baby is asleep on arrival at home.

These theories assume that SIDS and heatstroke are a continuation of the same reaction and that the professionals assessment of 'over-wrapped' is correct. Over-wrapping cannot be the sole cause for SIDS, or even consistently detrimental to all babies' health, however, as 33% of parents cover their babies more heavily than recommended by researchers (Nicoll and Davies, 1986), and therefore this practice is much more common than the incidence of SIDS. Anderson, Wailoo and Petersen (1990) also report that 'over-wrapping' does not influence night-time rectal temperature. Just because many parents do it without apparent harm coming to their baby, however, does not necessarily infer that it is the safest practice, and an objective of this study is to assess whether parental choice of clothing and wrapping differs according to the gestation and age of the baby, and whether this has any effect on skin temperature.

Allied to this hypothesis is the theory that if a baby is consistently cared for in

an excessively warm environment it may suffer thermal stress, particularly if it also has an infection or series of infections (Nelson, Taylor and Weatherall, 1989 and Ponsonby, Jones, Lumley, Dwyer and Gilbert, 1992). One response to thermal stress is to raise heart rate in order to increase circulation, which aids peripheral vasodilatation and sweating, so that normal body temperature is maintained. These may not be 'cheap' thermoregulatory responses for babies as inferred by some physiologists. Studies in monkeys suggest that if the heart rate is raised continually it ultimately results in left ventricular failure (Engel and Talon, 1989). The composition of sweat depends on the rate and duration of sweating, but if babies sweat profusely their comparatively small body mass may not be able to compensate for, or replace, the amount of water and sodium chloride that can be lost very quickly, and cardiac function may be affected (Campbell, Dickinson, Slater, Edwards and Sikora, 1984). Post-mortem results do not always reinforce this theory, although there is a suggestion that the pulmonary oedema often seen may be a sign of heart failure. This study will measure heart rate, oxygen saturation and sweating at the same time as rectal temperature, skin temperature and environmental conditions, in order to assess whether those conditions considered to be excessively hot or cold, and therefore causing thermal stress, have any measurable affect on physiological mechanisms.

A third theory is that SIDS occurs as a result of a malfunction in the developmental process of temperature regulation and the maturation of other physiological functions such as respiration, heart rate and hormone secretion (Hoppenbrouwers and Hodgman, 1992, Goldberg, Hornung, Yamashita and Wehrmacher, 1986 and see **General Hypotheses**). This delay may be a consequence of hereditary factors, either genetic or as a result of intrauterine conditions, maturity at birth or environmental conditions.

A number of factors such as infection, an excessively warm environment or desynchronisation of various developmental mechanisms may combine at

certain key ages of development, so the baby is unable to cope.

This research is based on studying these last two hypotheses (that consistent exposure to a warm environment may cause thermal stress and that there may be a malfunction in the developmental process of thermoregulation) plus whether there are any connections with the 'risk factors' discussed previously. It has grown from previous work which answered questions about the amount of coverings on babies, and what effect these differences have on rectal and skin temperatures of babies whilst sleeping. These previous studies suggest that by three to four months of age babies have developed a distinctive circadian variation in rectal temperature associated with sleep, which is not present at birth and is unaffected by thermal environment (Anderson, Wailoo and Petersen, 1990). Going to sleep or bedtime is considered to be an important environmental measure rather than clock time, which is the variable used by other researchers when studying circadian rhythms, and other events such meals and exercise are also taken into account.

There is no doubt that temperature regulation and cycles are important mechanisms which have been implicated in the pathology of both infants and adults. The process of development may be important, too, as unlike other circadian rhythms, such as sleeping and eating, it appears that the temperature rhythm does not 'grow out' of ultradian rhythms, as suggested by Hellbrügge (1960).

Finally there may be implications from the interrelation between temperature, which is not simply an endogenous day-night rhythm, and genetic, internal and environmental factors.

Objectives of the Study

The first objective of this study is to discover how the rhythms of sleeping rectal temperature and heart rate develop before four months of age, whether other changes occur afterwards and how this development is affected by gestational age. The methods used must be able to monitor continuously overnight and study babies both cross-sectionally as a group and longitudinally as individuals.

The second objective is to study social factors and care of the baby as these have been implicated in the aetiology of SIDS. As much information as possible should be collected about the parents and family, ante-, peri- and post-natal history, living conditions, and care of the babies being studied, and to assess whether they correlate with any of the other factors studied.

The third objective is to assess whether parental choice of clothing and wrapping differs according to the weather, gestation and age of the baby, and whether these have any effect on skin temperature.

The fourth objective is to measure heart rate, oxygen saturation and sweating at the same time as rectal temperature, skin temperature and environmental conditions, in order to assess whether those conditions considered to be excessively hot or cold, and therefore causing thermal stress, have any measurable affect on physiological mechanisms.

The fifth objective is to study the effects of natural infection and immunisation on rectal temperature, heart rate and sweating and to assess whether parental care alters at this time, because infection is considered to be an important source of thermal stress and is often implicated in SIDS.

CHAPTER TWO

METHODOLOGY

Study Design

Over the first year of life circadian rhythms of bodily functions develop (Hellbrügge, 1960 and Mills, 1975) and recent research in Leicester indicates that by four to six months of age babies have developed a pattern of temperature change throughout the day and night (Wailoo, Petersen, Whittaker and Goodenough, 1989 and Anderson, Petersen and Wailoo, 1990). This is primarily affected by sleep, but feeds and infection also exert characteristic influences (Wailoo, Petersen and Whittaker, 1990 and Rawson, Petersen and Wailoo, 1990).

Initially this study was designed to record the night-time sleeping body temperatures of babies at intervals from birth to nine months of age thus discovering information about babies studied cross-sectionally. The babies were of varying gestational ages and monitored at home and in hospital. This was to confirm the existence of a temperature pattern in all babies, and to assess the mean age at which, and how the temperature pattern changes.

Analysis of the early data indicated that in full term babies a pattern or rhythm 'developed' or matured at a mean age of twelve weeks; this is a consistent rhythm which is stable for some months and similar to the adult pattern, but development occurred at different ages in individual babies. A second study was therefore designed to monitor full term babies at much shorter intervals longitudinally from five to eighteen weeks of age. An assessment could therefore be made of the exact age of the temperature changes in a series of individual babies, and characteristics of those babies, their families and environments studied.

Recording Schedule

In the cross-sectional study babies were monitored at about four weekly intervals from birth to nine months of age. Most of the babies were recruited to the study at birth, others at an older age and a few were monitored just once or twice at random. The recordings were planned so that there were equal numbers of babies in given two week age groups, although no baby's temperature was recorded more than six times. All of the monitorings were for an average of fifteen hours each, starting one to three hours before the baby settled to sleep, and finishing half to two hours after morning waking.

For the longitudinal study babies were monitored at one to two weekly intervals from five to eighteen weeks of age. For each baby there was a series of recordings of temperature and heart rate over the period of changing temperature patterns, and it was possible to pin-point, within two weeks, the age of any significant change.
The length of the overnight recordings was the same as the first study.

Ethical Permission

Ethical permission was sought and given by the Ethical Committee of Leicestershire Area Health Authority.

Recruitment of Subjects

At first mothers of newborn babies were approached on the post-natal ward and asked if they would allow their baby to be monitored overnight on the ward or Special Care Baby Unit (SCBU), and then at two to four weekly intervals at home. If possible monitoring began immediately, but some babies did not join the

study until an older age.

Recruiting took place at about three monthly intervals, so that each group was monitored through different seasons. Compliance was one in four.

On a given day as many mothers as possible were approached on the ward, but there was some filtering by ward staff, especially on SCBU; for example it was requested that anxious mothers or very ill babies were not asked. Parents who agreed to monitoring tended to be those who were in-patients longer as one objective was that the first monitoring was on the ward, and occasionally very well motivated parents would spontaneously volunteer. This method of recruiting also meant that there was some clustering of birth days.

In the second part of the study babies were recruited at about four weeks of age at home. All parents of babies born within a given time span in an area of Leicestershire were approached and their permission sought. The period of these monitorings spanned all seasons. Compliance was one in three.

This method of recruiting eliminated many of the problems of the initial study, and was also more successful. A broader range of families agreed to the monitoring as discussion of the research was on a more personal basis with fathers present, although none of the babies was premature. The area of Leicester chosen had a wide variety of types of housing etc, but obviously this second group of babies did not come from as wide a geographical area as the first study.

Examples of the recruiting letters and consent form are in the Appendix (1).

Equipment

The study was designed and equipment chosen, so that various physiological functions were able to be monitored continuously, in a range of environments and without interfering with the baby's usual routine and care, including visits outside the home. It was imperative that the apparatus was portable, robust, safe, reliable and unimposing to the family, so that it could be left for long periods of time without professional supervision.

Temperature

Body temperature was recorded from four different sites simultaneously, using thermistors provided by Grant Instruments, Cambridge.

Rectal Temperature

A soft rectal temperature probe which was inserted 5cm from the anal margin was felt to be the most practical method for recording body temperature, was not intrusive and did not appear to cause any distress to the babies. Whilst in situ, the readings were consistent, and recordings were reproducible for each individual baby and across the range of subjects. The probe measures 5cm length x 2mm diameter and is attached to the recording apparatus by two-core pvc cable. The manufacturers state the range available for recording is -50°C to +150°C with a tolerance in the 0°C to 70°C range of 0.1°C, and a response time of 0.8 seconds. The thermistors are guaranteed for three years.

All probes used in this study were calibrated and standardised against a Total Immersion E-mil Gold Line mercury thermometer, and were correct to 0.15°C for all measurements, and correct to 0.05 for the range 35.5°C - 40°C (figure 2:1). The probes were immersed in a Grant Instruments' Water Bath which was heated slowly and readings taken from all the probes every 0.5°C as measured by the

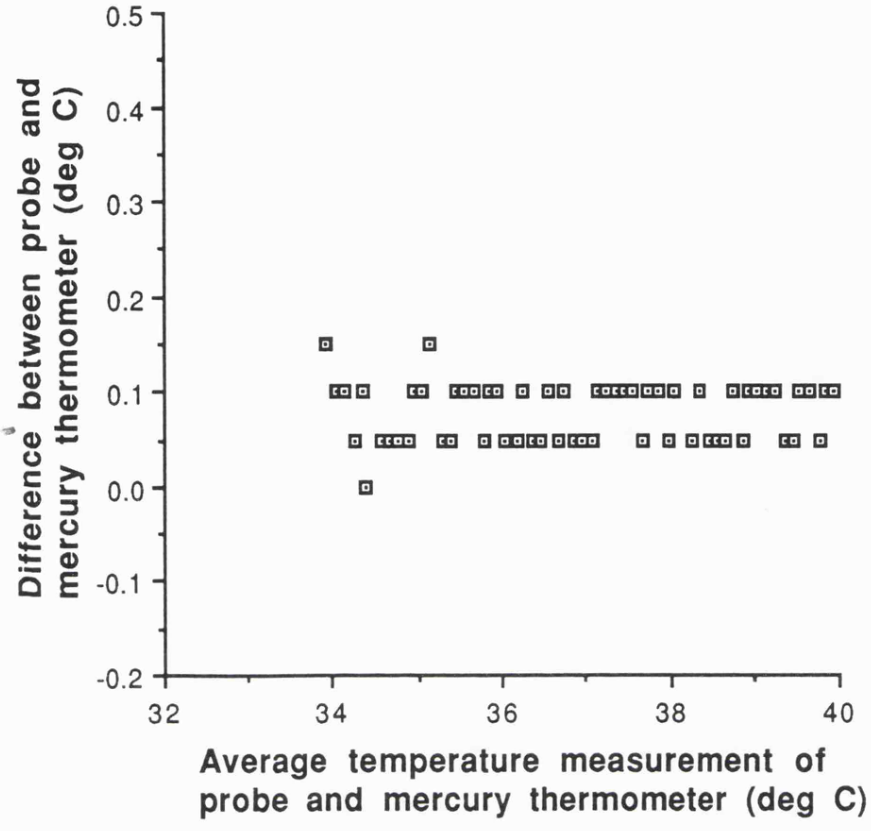


Figure 2:1 Bland and Altman (1986) analysis of rectal probe and mercury thermometer measurements, showing they were correct to within 0.15°C

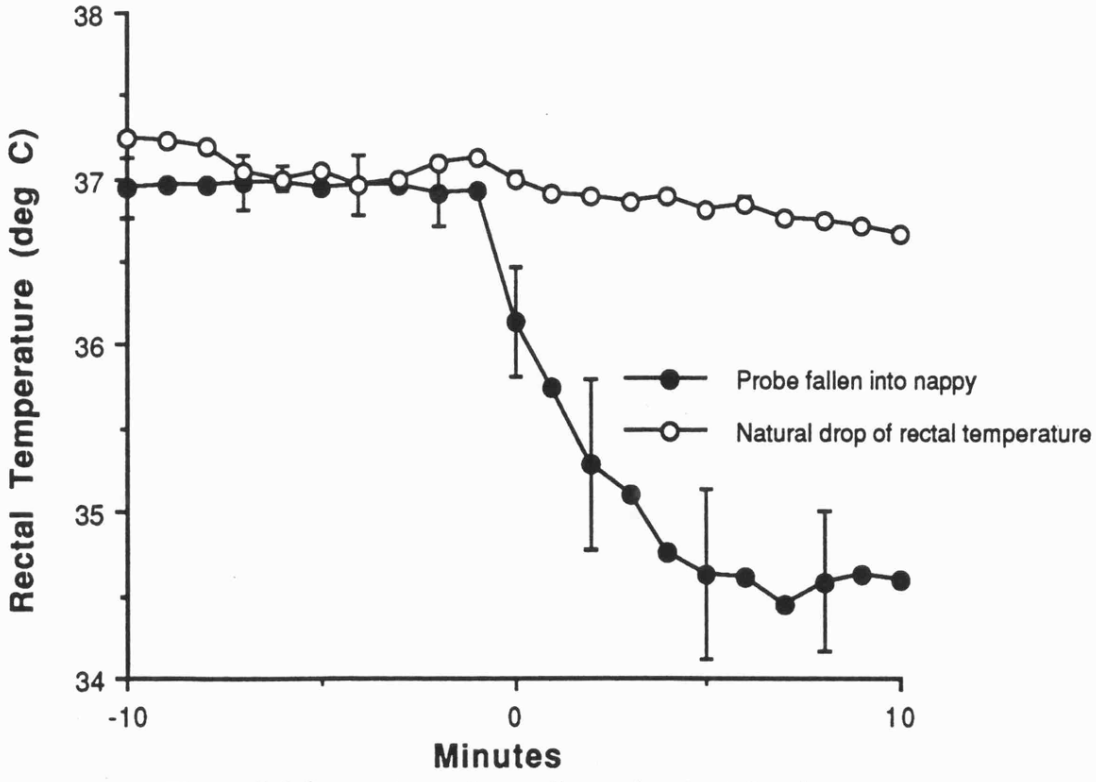


Figure 2:2 Comparison of recordings of probe fallen from rectum into nappy and largest fall seen physiologically

mercury thermometer, and then readings were also recorded as the water cooled. Blemished data from monitorings were easily recognisable, as they were either as a result of apparatus failure or the probe becoming dislodged. Figure 2:2 compares the rate of temperature fall when the probe drops from the rectum into the nappy and the most rapid fall in temperature that has been recorded physiologically. The values are completely disparate, and the temperature recorded in the nappy is much lower than any rectal temperature recorded. Figure 2:3 charts the five second readings of a simulated falling of the probe into the air. These changes are more rapid and greater than those seen physiologically. Figure 2:4 is seven examples of recordings illustrating that there is a weak positive correlation between rectal temperature taken overnight, and the buttock skin temperature under the nappy, taken at the same time. These readings indicate, however, that buttock temperature is usually much lower (about 2°C) than normal levels of rectal temperature, so if the probe fell from the rectum without the parents' knowledge the change in recorded temperature would be quicker than that seen physiologically and easily spotted when the readings were analysed.

Any data, therefore, which showed a decrease in rectal temperature greater than 0.5°C/1 minute or went below 35.8°C were discarded.

Skin Temperature

Surface probes, which are 3mm wide and 8.5mm long epoxy coated copper with a sensor on the back of the disc were attached to various sites on the body.

In the first study forehead temperature was taken as an indirect measure of heat lost from the head. This is an area which may be the avenue for up to 80% of heat loss from radiation and convection at an air temperature of 30°C (Scopes, 1975) and Keele, Neil and Joels (1982) also write that heat loss from a bare head in an environmental temperature of -4°C may amount to half the total resting heat production in man. The readings were not analysed as they appeared to be

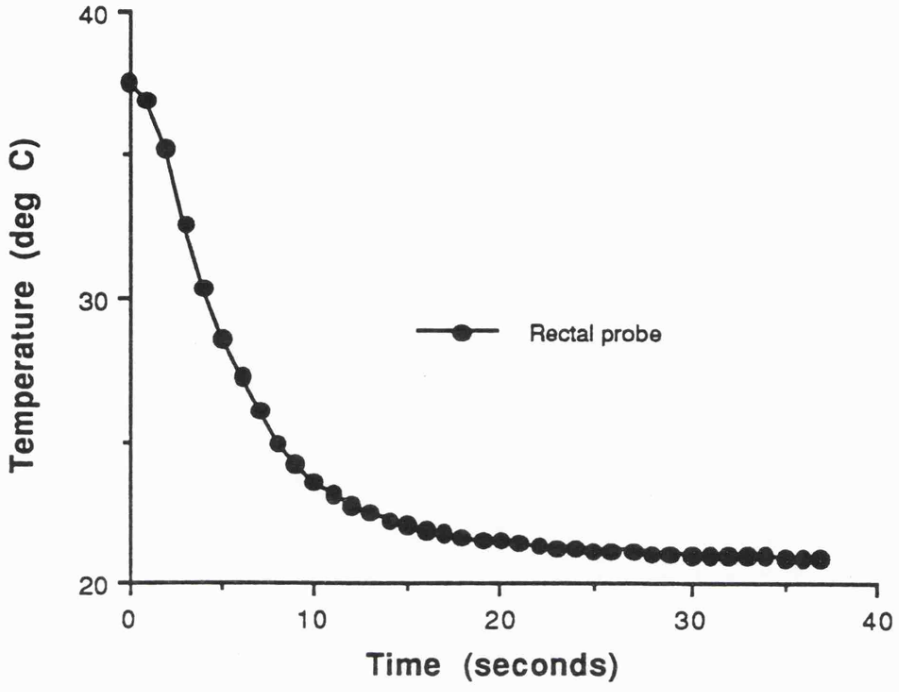


Figure 2:3 Cooling of probe from water 38° C (rectal temperature) to water 21° C (air temperature)

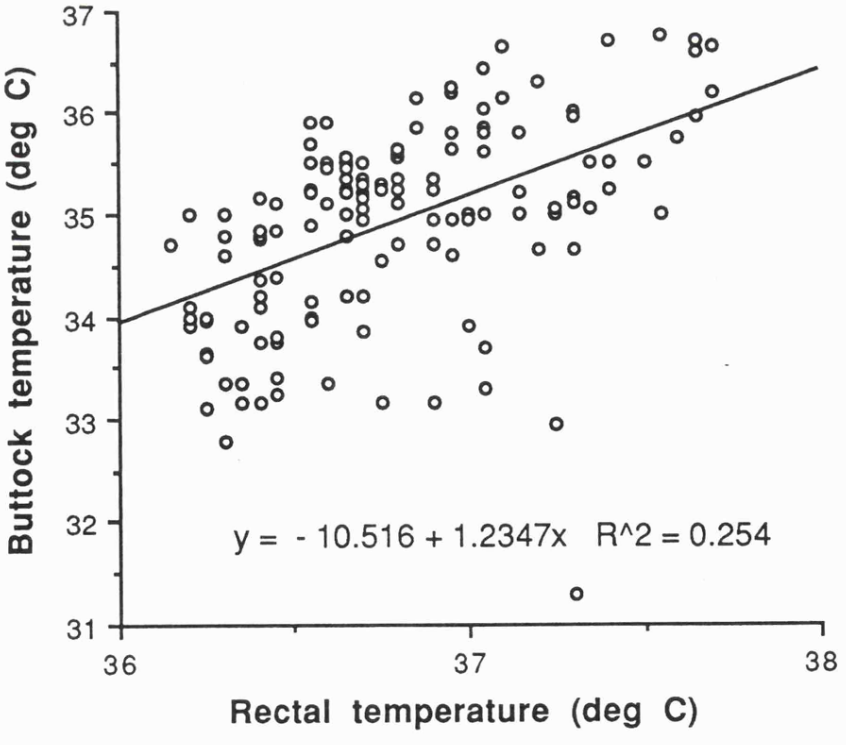


Figure 2:4 Comparison of rectal and buttock temperatures of seven babies, showing the 2°C difference in values

influenced by ambient temperature as well as the baby's temperature and often were inconsistent because the thermistor was not acceptable to either the babies or their parents and was dislodged or removed.

Abdominal and peripheral skin temperatures were taken in order to assess the role of vasodilatation in thermoregulation. Initially the probe was sited to the left of the umbilicus and then on the right shin. Only data from the right shin were used, as the numbers of readings from the abdomen were too small.

All probes were calibrated and standardised against a Total Immersion mercury thermometer in the same way as the rectal probe and were correct to between 0.05°C and 0.1°C.

Data were excluded if the change in temperature measured was greater than 0.5°C/1 minute indicating that the thermistor had become detached.

Ambient Temperature

A stainless steel probe with a response time of three seconds was used to record environmental temperature near the baby; whilst the baby slept this was usually at the cot side.

The probes and cable were attached to the baby using 3M Mefix tape. This was found to cause the least discomfort and remained in place even if wet. Tests carried out on adults showed that the tape did not influence the value of the temperature recorded by more than 0.05°C

Heart Rate and Oxygen Saturation

The equipment available to monitor heart rate and oxygen saturation is not as portable as the temperature monitoring equipment because of size, weight and inability to function for long periods on batteries. Dräger's Nellcor Oxymeter N-200E, however, was transported to the home with reasonable ease, and then

positioned and connected to the electricity supply near to the place where the baby slept for the longest period, usually the cot.

The N-200E receives a heart rate signal from two sources; direct electro-cardio graphic (ECG) input is from a conventional three-lead ECG cable positioned in the standard limb configuration. The machine indicates when it locates an ECG signal where the R-wave is between 0.5 and 2.0 millivolts, and uses this to identify the pulse and synchronise the saturation measurements. Secondly the oxiband oxygen transducer is attached to the baby's foot or toe using a disposable adhesive wrap which maintains appropriate positioning. The sensor is electro-optical and contains two low-voltage, low intensity light emitting diodes (LEDs) as light sources (one red light and one infrared) and one photodiode as a light receiver. When the light from the LEDs is transmitted through the blood and tissue components, a portion of both the red and infrared light is absorbed by the blood and by each tissue component. The photodiode in the sensor measures the light that passes through without being absorbed, and this measurement is used to determine how much red light and infrared light is absorbed. With each heartbeat, a pulse of oxygenated arterial blood flows to the sensor site. This oxygenated haemoglobin differs from deoxygenated haemoglobin in the relative amount of red and infrared light that it absorbs, so the oxymeter uses those measurements to determine the percentage of functional haemoglobin that is saturated with oxygen. At each beat the saturation and pulse rate measurements are recalculated.

The N-200E has an automatic calibration mechanism, so that it calibrates itself whenever it is turned on, at periodic intervals thereafter, and whenever a new sensor is connected. All the instruments were tested and passed by the hospital Medical Physics' Department before use.

The oxymeter has two intrinsic memories. A trend memory stores up to twelve hours of heart rate data, sampled every second and averaged every five seconds, and an alternative higher resolution event memory stores up to one hour of

oxygen saturation, pulse rate and pulse amplitude data, sampled once a second. These readings were not used, however, as on average only six hours of data were retrievable, and the graphs produced were not suitable for the type of analysis required.

The advantages of this means of measurement were that the sensors were lightweight and non-invasive, and there was no heat source to burn the baby. The sensitivity of the instrument changed automatically to accommodate a wide range of tissue thickness and skin pigmentation.

The disadvantages were that the sensor was easily moved or dislodged, and excessive movement of the baby appeared to produce artefactual changes. Tests on the equipment also showed that, if the sensor was well attached, the oxygen saturation apparatus measured correctly even when the baby moved. If the sensor was loose, however, the readings may not always have been reliable. The instrument was able to accommodate to some of this because it double checked the pulse rate reading taken at the toe with the heart rate recorded via the ECG cable, which was taken as correct. Data about oxygen saturation were not used, however, for two reasons. The transducer which was fixed to the toe was damaged, resulting in unreliable readings. Whilst being repaired heart rate was monitored using the chest leads. There were, therefore, insufficient readings of oxygen saturation. On the few recordings obtained, a reduction in oxygen saturation was coupled with an increase in heart rate or recorded movement of the baby, indicating that the reduction may have been as a result of the baby moving or crying, rather than a physiological fall in the oxygen saturation level due to decreased or abnormal respiration of the baby.

The Data Loggers

Grant Squirrel Data Loggers, type 1201, were chosen because they fulfilled the criteria required of the monitoring equipment; they are reasonably light and

small, and therefore portable, and can be left for a number of hours without supervision. The loggers measure 18cm x 12cm x 6cm and weigh 0.98kg including batteries. Date and time can be set on the machine and were checked before each monitoring. The manufacturers state that the clock is correct to within one second in twenty-four hours, but during use it was found to be correct to five seconds in twenty-four hours. Whenever possible the time of events recorded by the parents and the logger clock were compared and this rarely differed by more than five minutes.

The logger can be used at temperatures between -30^{o}C and +65^{o}C with a relative humidity of 95%, and the range available for recording is -50^{o}C to +150^{o}C with a resolution in the range of -25^{o}C to +105^{o}C of 0.05^{o}C, or a DC voltage of -20V to +20V with a resolution of 1mV.

The logger is manufactured so that it is safe, and there is no possibility of danger or interference from electrical current as it has battery power. A low battery warning is displayed when the internal batteries are down to a third of their original capacity, but in order to avoid problems relating to power supply the batteries were changed once they were down to half their life.

Before use all the data loggers were inspected and tested by the hospital Medical Physics' Department.

Whilst in use the logger was placed within a cardboard box in a carrier bag and thus withstood the rigours of most homes, and helped the baby and logger to be transported easily whilst attached to each other. In this way some protection was also afforded against accidental and inquisitive tampering. If the control buttons on the logger are pressed whilst recording is taking place, the only possible outcomes are for logging to stop or data to be erased completely. Tampering with a logger occurred only once, whilst a baby was being monitored on the hospital Special Care Baby Unit - but never in a home.

The timing of each individual recording of temperature, heart rate etc within the period of monitoring can be altered and set from two seconds. After initial

recordings at ten second intervals, temperature and heart rate were recorded every minute.

The temperature probes and N-200E were connected to the logger. Temperature was recorded as a true reading in degrees centigrade (°C), and the oxygen saturation and heart rate as a voltage measurement; the true value was then calculated by multiplying the oxygen saturation reading by ten, and dividing the heart rate reading by four. Each logger has 19,000 memory slots, and each set of readings use one slot per channel. An average individual night-time recording, reading every minute over fourteen hours on three channels would therefore use 2,520 memory slots.

Social and Health Data

In order to be able to study trends and individual differences between those babies whose temperature and heart rate were recorded, data about the babies' health, care and social conditions, and data about the health and situation of their families were collected from various sources throughout the period of monitoring.

Perinatal and Social Data

Perinatal and social data were collected from the maternity notes and mothers were asked about their recollection of the pregnancy and birth.

Information collected:

Postcode of family home

Married status of mother

Occupation of the head of household

Smoking of either or both the parents

Age of parents

Number of siblings

Age of siblings

Family history of febrile convulsions

Complications of pregnancy

Complications of labour and delivery

Apgar score and onset of respirations

Admittance to Special Care Baby Unit (SCBU)

Date of birth

Gestation

Birth weight

Method of feeding at birth

Sleeping position in the first week

Problems or illness in the first week

Occupation of the head of household was used to determine social class as defined by the Registrar General's classification (Office of Population and Surveys, 1980).

Data Collected at Time of Monitoring

At every visit information was also obtained from the care givers about the general health of the family and the baby's care and development.

Information collected:

Age and weight of the baby

Feeding regimens

Age of weaning

Sleeping position

Dates of illness

Dates of immunisation

Type and amount of heating

Type and position of cot

Illness in the family

Information Obtained from the Health Diary

Parents kept health diaries of illness in their baby and any treatment or medicine that was prescribed or given.

Information collected:

Type of illness (symptoms)

Age of the baby at time of illness

Duration of illness

Whether seen by GP

Admittance to hospital

Prescribed medicines

Family remedies used

Reaction to immunisation and whether paracetamol given.

Diary

Whilst the baby was being monitored the parents kept a detailed diary of their baby's activities.

Events recorded:

Time and length of sleeps

Nappy and clothing changes

Periods of crying

Time of being placed in cot

Time and type of feed

Bowel movements

Times of play

The parents were also asked the next morning to comment on their child's health and behaviour the previous night.

Togmeter Values

A note was made of the clothing and wrapping of the baby, so that a "tog value" could be calculated, using values provided by the Shirley Institute, Manchester.

Item of clothing	Tog value
Nappy	2.0
Babygro	1.0
Cardigan	1.0
Sleep suit	2.0
Dress	4.0
Vest	0.2
Socks	0.2

Item of bedding	Tog value
Sheet	0.2
Airtex blanket	1.5
Woollen blanket	2.0
Duvet	9.0
Pram quilt	4.0
Sleeping bag	9.0

See Appendix (2) for examples of the forms used.

Analysis of the Data

The recordings from the Squirrel Data Loggers were downloaded as soon as possible onto an IBM PC using software provided by Grant Instruments, Cambridge. The crude data were printed numerically showing the date and time of each channel reading.

The software is able to graph data, but not in detail, so data were extracted at fifteen minute intervals and graphed by hand. The time of sleeps and feeds etc were then superimposed. Any blemished data were excluded using the criteria given previously.

The social and health data, along with details of the baby's care were entered onto a MacIntosh Apple 4th Dimension database, and calculations carried out using the Excel, Cricket Graph, Deltagraph and Statworks programmes.

Statistical Analysis

Various statistical tests were used and are summarised below:

Mean The addition of all the numbers in a set, and then division of that total by the number of items in the set.

Median The middle number of a series of numbers arranged in order.

Mean Deviation A number which indicates how much, on average, the scores in a distribution differ from a central point.

Standard Deviation A measure derived from the sum of the squared differences between the original data and their mean value.

Standard Errors The square root of the sample variance divided by the sample size.

Correlation A means of specifying precisely the extent to which variables are associated.

Significance Level The probability of rejecting the null hypothesis when it is true.

Chi-square Test A test to measure whether the values of one variable are associated with particular values of another.

Student's T-test A comparison of the average of two groups to determine the probability that any differences between them are real and not due to chance.

Two way Analysis of Variance with repeated measures Partitions the variablility, in the sample as a whole, into components attributable to different affects (Hays,1969 and Keppel, 1991).

Statistical advice given by Associate Professor Graham Pollard

Head, Mathematics and Statistics Program

Associate Dean, Canberra University, Australia

CHAPTER THREE

CROSS-SECTIONAL ANALYSIS OF RECTAL TEMPERATURE DATA

In order to assess the changes in babies' rectal temperature patterns over the first nine months of life, a number of babies were monitored at least once during that time, and at monthly intervals if possible. The data collected comprised eight to ten recordings for every two week age group.

During the twelve months observations were made on 48 babies aged from birth to nine months, and 133 periods of night-time temperature data were collected. Probes were lost on a further ten occasions. Nine babies were monitored on at least six occasions, 12 five times, 5 four times, 7 three times and 15 once or twice. Most of the recordings over the age range four to sixteen weeks formed part of a series on individual babies of at least four.

There were 27 males and 21 females, and the mean (+-SEM) birth weight was 3090.4 (116) grams. The average (+-SEM) age of the mother was 28.27 (0.89) years; 20 were first children and 13 had two or more siblings. The babies were classified according to the social class of the main wage earner in the family; unfortunately the lower social classes in Leicestershire were under-represented, but the range was present (see Appendix (3)); seventeen parents were in social classes 1 and 2 (35%), twenty-four in 3 and 4 (50%) and seven in 5 and 6 (14.5%) (Office of Population and Surveys, 1980). There was smoking in twelve of the households. Twenty-two of the babies lay prone in their cots overnight. Thirty-three of the mothers breast fed at birth, and twenty-five continued beyond the first six weeks.

The data are studied cross-sectionally in this chapter.

Gestational Age

Hey and Mount (1967) and Hill and Rahimtulla (1965) suggest that premature babies have difficulty thermoregulating and Hellbrügge (1960) concludes that physiological functions develop later in premature infants compared to those born at term. Babies were, therefore, recruited with gestational ages varying from 28 to 42 weeks, although only six were 33 weeks or below. Seven were between 34 and 37 weeks gestation and thirty-five between 38 and 42. The mean (+-SEM) gestation was 38.23 (0.47) weeks.

All the results are given using chronological age.

Thermal Environment

As discussed in the **Introduction** one effect on a baby's body temperature and thermoregulatory mechanisms may be that of the environment in which it is sleeping.

Figure 3:1 shows the mean tog values and maximum and minimum room temperatures of the babies when divided into two week age groups up to the age of six months. The data for the ten babies 0-2 weeks old are mainly readings made in hospital, including four on the Special Care Baby Unit (SCBU), where ambient temperatures were often high and babies lightly wrapped.

A simple calculation of the thermal environment can be made by adding the minimum room temperature (that recorded four hours from bedtime) and the tog value of the baby's clothing and wrapping (Clulow, 1987 - personal communication). Using this formula babies during the first two weeks of life were kept in a cooler thermal environment (mean (+-SEM)=28.98 (2.80)) than those babies up to one month of age at home who were kept in warmer rooms and covered in more insulation (mean (+-SEM)=31.84 (5.37)), although this does not reach significance. Babies below 36 weeks gestation in SCBU were cared for in a mean thermal environment of 32.11 (3.0) up to four weeks of age, which is only slightly higher than term babies at home. This is contrary to the instinctive

Figure 3:1

Averaged (+-SEM) tog and room temperature for the two week age groups 0-6 months.

15 minute recordings taken in hospital and at home. 133 observations on 48 babies.

Age (weeks) Number (n) of babies	Tog value	Room min (deg C)	Room max (deg C)	Thermal environment
0-2 (n=18)	7.41(0.79)	21.46(0.55)	24.58(0.55)	28.87
2-4(n=11)	13.83(1.34)	19.12(0.94)	23.59(0.53)	32.95
4-6 (n=12)	11.34(1.80)	18.21(0.75)	22.28(0.69)	29.55
6-8 (n=10)	8.90(1.71)	18.83(0.75)	23.15(0.64)	27.73
8-10(n=11)	10.61(1.44)	17.03(0.66)	22.43(0.62)	27.64
10-12(n=10)	11.39(1.35)	19.11(0.67)	22.75(0.51)	30.50
12-14(n=13)	10.69(1.52)	16.10(1.00)	20.18(0.94)	26.80
14-16(n=12)	11.71(1.74)	17.58(0.95)	22.50(0.73)	29.29
16-18(n=7)	9.39(1.75)	18.12(0.51)	22.24(0.72)	27.51
18-20(n=13)	10.80(0.73)	18.54(0.58)	22.20(0.62)	29.34
20-22(n=6)	10.08(3.17)	20.98(1.82)	24.59(1.52)	31.06
22-24(n=10)	12.17(0.96)	15.33(1.88)	20.91(0.52)	27.50

feeling that parents have that maternity units are warmer than homes, but illustrates that many care givers have taken to heart the implied suggestion that it is important to keep their new baby warm, and in a consistently high ambient temperature, not just when changing or bathing.

From about six weeks of age the way parents dressed their baby at night, and the temperature they maintained in their homes, did not vary greatly from family to family, or on different nights for the same baby. The amount of coverings and room temperatures did not change significantly as the babies grew, although parents did appear to make slight adjustments to their babies wrapping depending on the ambient temperature (see 6-8 weeks and 22-24 weeks) and season. Premature babies were kept in similar thermal environments.

All these environments are cooler than those recommended for newborn babies. Although still in the range suggested by Hey and O'Connell, they often feel uncomfortably warm to adults. Up to six weeks of age, and on some occasions afterwards, however, the thermal environments are higher than those recommended by Stanton, and at all times the babies were dressed and wrapped in more clothes and bedding than recommended by the FSID for the ambient temperature of the room (see **Introduction**).

Rectal Temperature

Averaged night-time rectal temperature data from one hour before sleep to eight hours after bedtime, for the same two week age periods are presented in figure 3:2, and figure 3:3 illustrates selected two week periods of the same data in line graph format.

During the first two weeks of life rectal temperature varied little overnight, and babies appeared to thermoregulate well, as the thermal environment in which they slept did not influence their rectal temperature, and there were only slight fluctuations of about 0.03^{o}C for feeds and nappy changes.

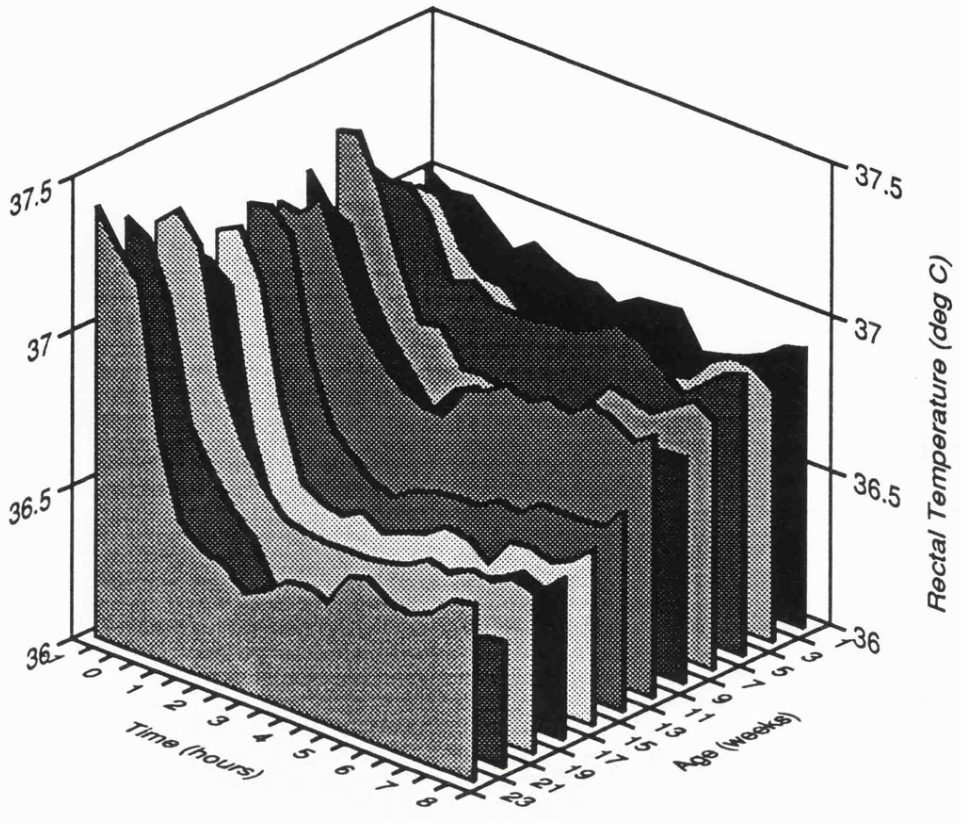


Figure 3:2 The mean rectal temperatures of 133 over night recordings on 48 babies, taken at fifteen minute intervals from one hour before sleep to eight hours afterwards. The babies are divided into 12 two week age groups from birth to six months

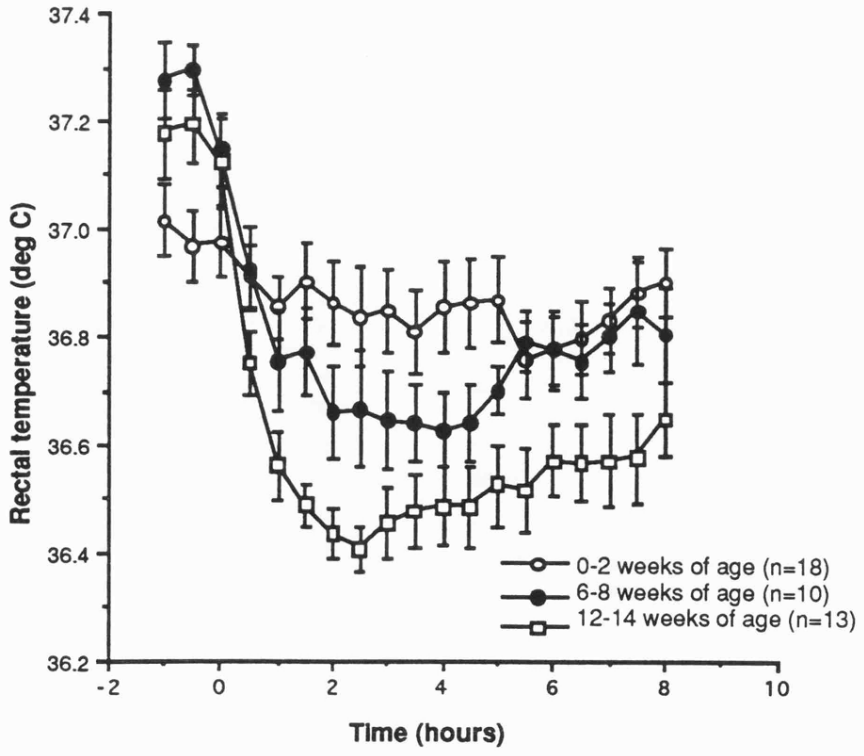


Figure 3:3 Averaged night-time rectal temperatures showing standard errors for three age groups illustrating the development of the rectal temperature rhythm with sleep up to 14 weeks of age. Recordings were analysed every 15 minutes from one hour before sleep to eight hours afterwards.

By six weeks of age rectal temperature was over 37°C at bedtime and fell to about 36.8°C half to one hour later, which is the pattern illustrated by Anderson, Petersen and Wailoo (1990) for daytime sleeps in babies of three to four months of age (figure 3:4). Figure 3:5 indicates that the first changes in the pattern were at about four weeks of age when the babies' rectal temperatures fell to below 36.8°C one to two hours after bedtime. Then, in babies over six weeks of age compared to younger infants, this was followed by a significantly higher rectal temperature one to half an hour before bedtime ($p < 0.01$ Student's t-Test) (figure 3:6). Night-time rectal temperature patterns remained constant from around six weeks to about twelve to fourteen weeks of age.

At about twelve weeks of age the most significant change in the night-time sleeping rectal temperature rhythm occurred; the babies' temperature was significantly lower all night than the two weeks previously ($p<0.004$ at two hours and $p<0.013$ at five hours, Student's t-Test) and reached a minimum of 36.5°C or below (figure 3:7). The pattern, too, was significantly different between day and night-time sleeps ($p<0.001$, Student's t-Test), and may be the introduction of a circadian rhythm or controlled change at night of rectal temperature. The change in temperature was sudden and dramatic, occurring within one to two weeks.

This night-time pattern of rectal temperature continued until at least six months of age (figure 3:8), and was similar to the adult rhythm, although perhaps falling to lower values (Hellbrügge, Lange, Rutenfranz and Stehr, 1964).

The average age for rectal temperature to fall below 36.5°C with night-time sleep was twelve weeks, although this varied considerably in individual babies. Figure 3:9 shows the minimum rectal temperature recorded at various ages of five different babies. All the babies' rectal temperatures fell to below 36.5°C within a two week period, but one baby exhibited this change between seven and eight weeks and another not until thirteen to fourteen weeks of age. The range between which this occurred was six to sixteen weeks.

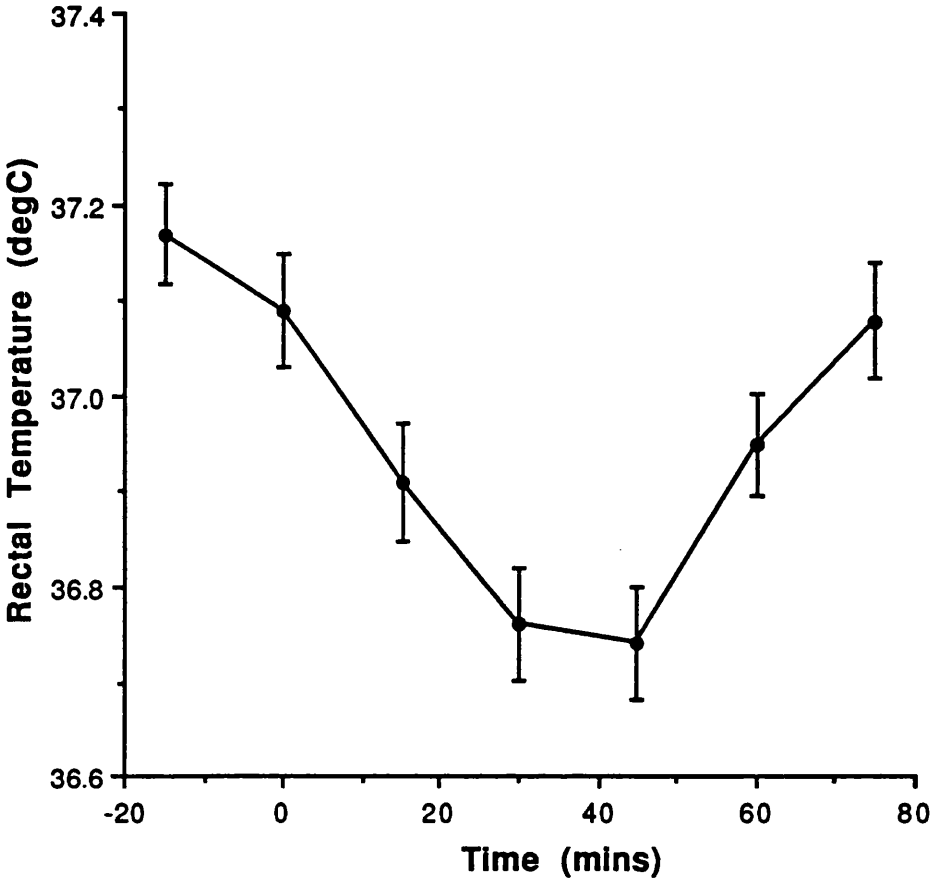


Figure 3:4 Anderson's data on the rectal temperature pattern during daytime sleeps for three to four month old babies. The data is the mean of the fifteen minute recordings on 70 babies.

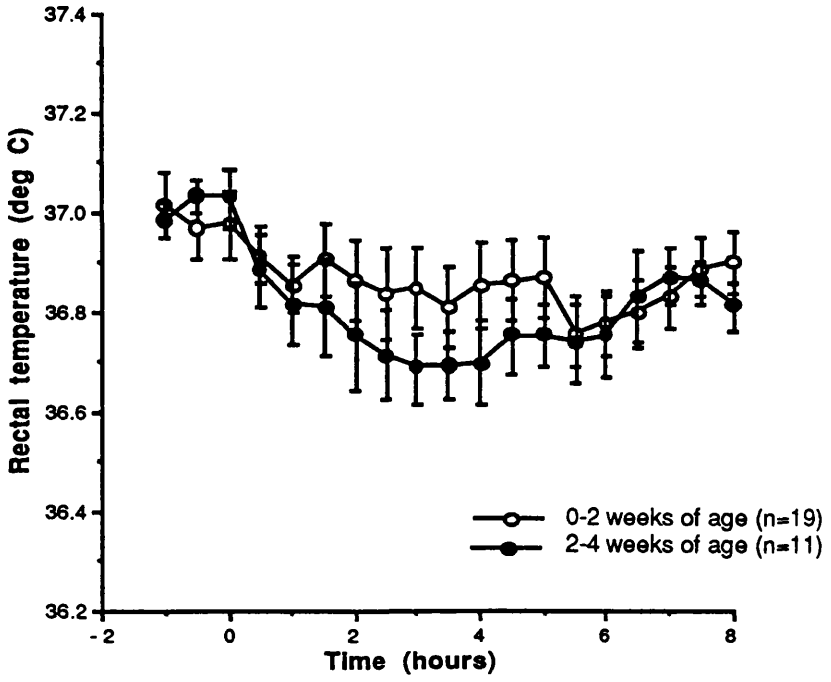


Figure 3:5 Averaged rectal temperature with standard errors, illustrating the fall to below 36.8° C two hours after bedtime at four weeks of age

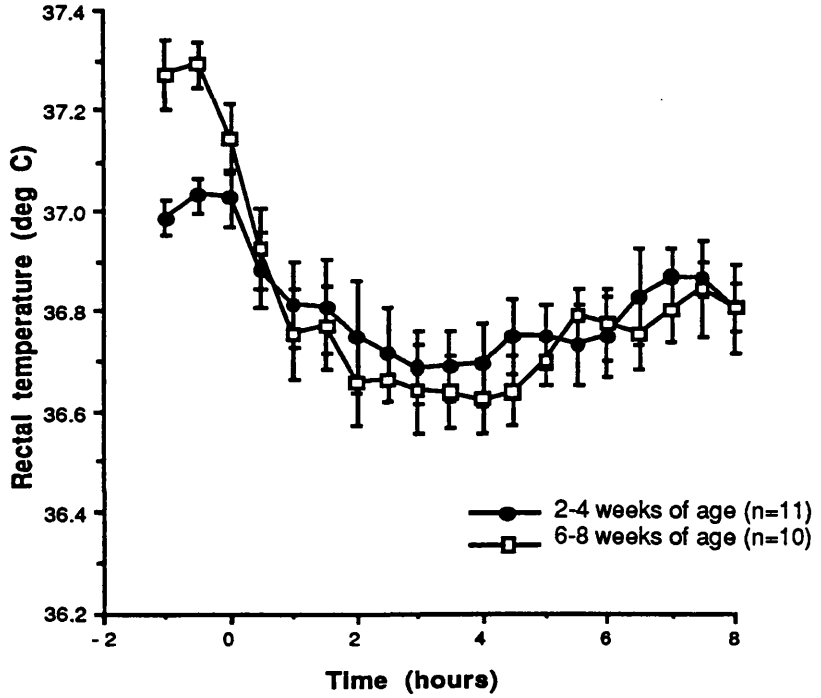


Figure 3:6 Averaged rectal temperature with standard errors, illustrating the higher rectal temperature at bedtime of babies over six weeks of age

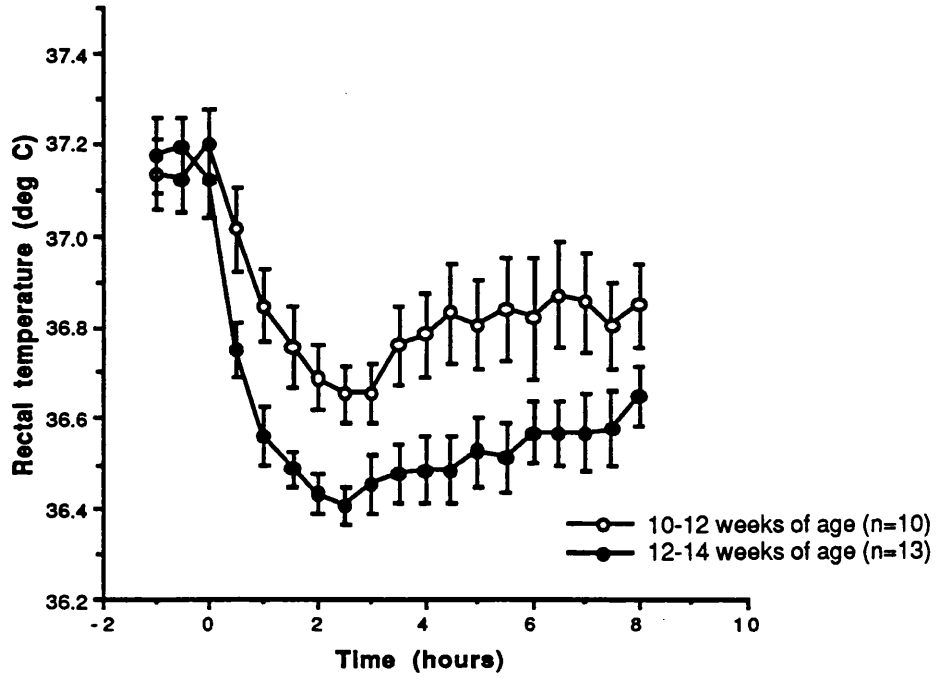


Figure 3:7 Averaged rectal temperature with standard errors, illustrating the constancy of the night time pattern from 6-12 weeks of age and the deeper pattern which dramatically appears about 12 weeks of age

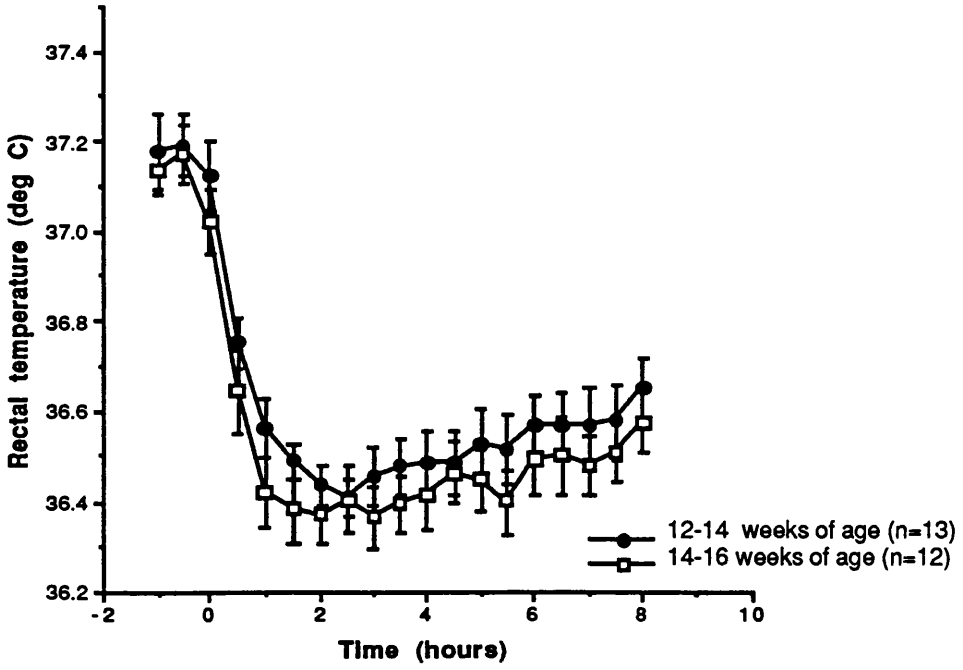


Figure 3:8 Averaged rectal temperature with standard errors, illustrating the constancy of rectal temperature after 12-14 weeks of age

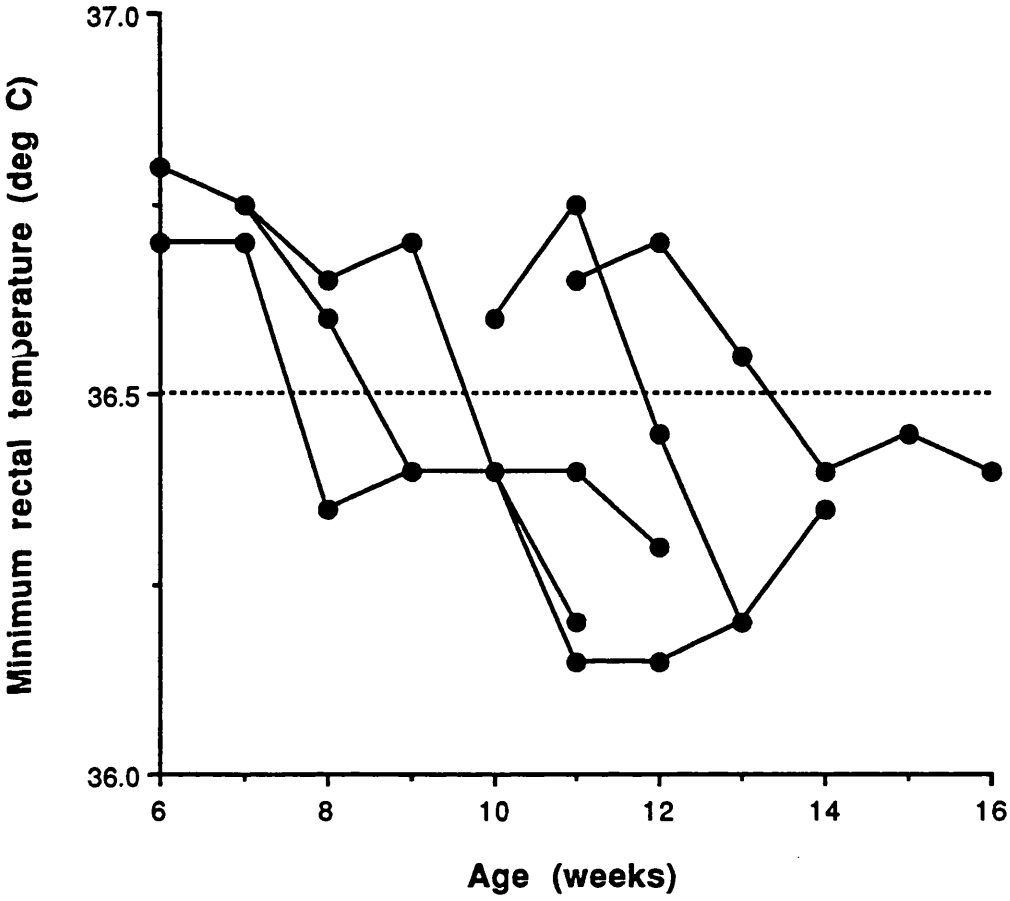


Figure 3:9 The minimum rectal temperature of individual babies illustrating the differences in age at which the night time rectal temperature fell below 36.5°C

Sleep Duration

Sleep patterns develop over the first few months of life too (see **Introduction**). In adults high ambient temperatures may decrease the total duration of sleep, particularly Slow Wave Sleep (SWS) (Bonegio, Driver, King, Laburn and Shapiro, 1988), indicating that the period of change in babies' sleep patterns may be influenced by their environment.

As rectal temperature was monitored during sleep, sleep duration was also recorded. The time used for analysis was the longest unbroken period of night-time sleep, or the length of time after the baby was put down to sleep before it disturbed its parents. In older babies the first part of the recording usually corresponded to the longest sleep period.

Figure 3:10 shows the mean sleep duration of babies, in the two week age categories, correlated with the minimum rectal temperature of those babies on the same nights. As sleep duration increased the minimum night-time rectal temperature fell. As expected from observations and parents' reports, sleep duration also increased as the babies became older, but was not significantly affected by the other recorded factors. There were trends, however, that indicated babies slept longer in slightly cooler environments, and in their own rooms. Babies over sixteen weeks also appeared to sleep longer if they were lying on their fronts. These trends are difficult to interpret, however, as babies might not sleep longer or better in their own rooms, but may just disturb their parents less.

Unfortunately the results do not indicate whether sleep and temperature rhythms develop independently, or are controlled or influenced by one another. The controlled fall in rectal temperature was dependent on the baby sleeping at night, as it corresponded to the baby going to sleep, not clock time. A fall is exhibited during daytime sleeps, but not to such a great extent (Anderson, Petersen and Wailoo, 1990). Rectal temperature rhythm development was not

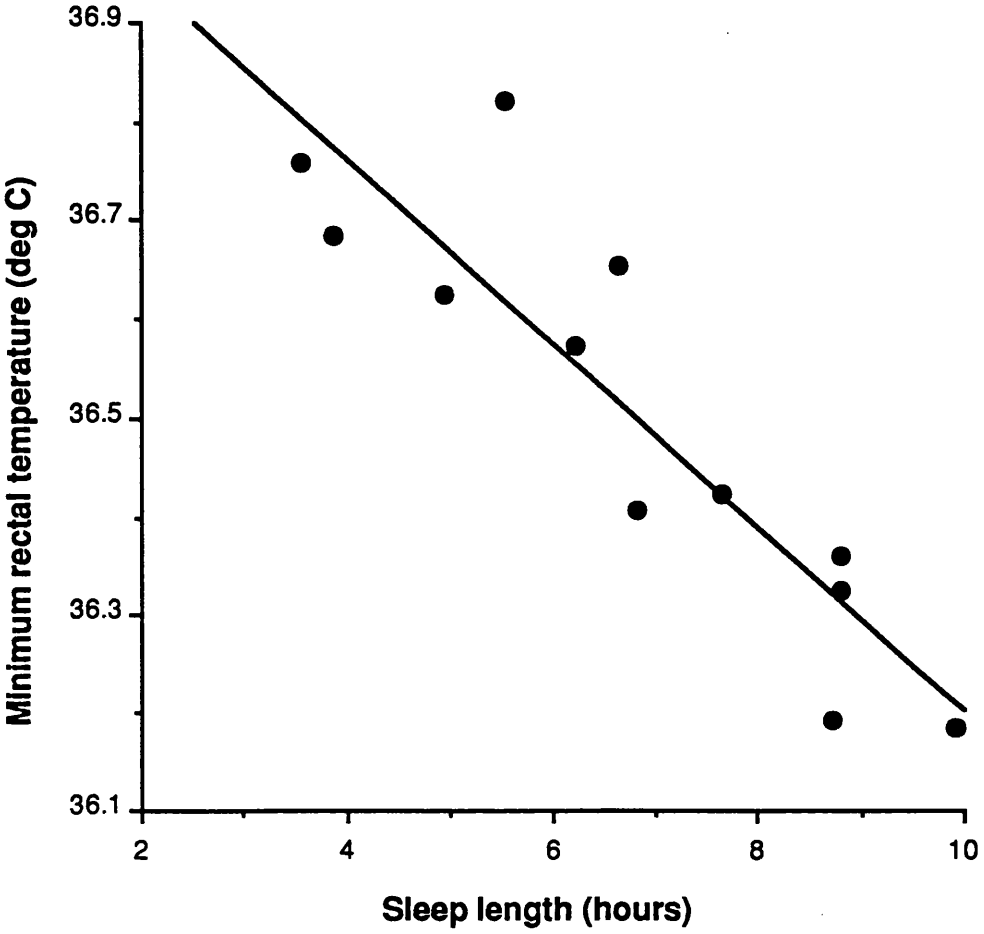


Figure 3:10 Mean sleep duration compared to the mean rectal temperatures of all the babies divided into two week age groups, up to six months of age. 133 observations on 48 babies. Correlation coefficient = 0.802, $p<0.001$

reliant, however, on the baby sleeping for a minimum amount of time, and sleeping through the night did not guarantee that the baby's rectal temperature fell below 36.5°C.

Summary of Cross-Sectional Studies of Rectal Temperature

1 Newborn babies were kept in slightly cooler environments than recommended by Hey and Katz, and older babies slept in slightly warmer environments than advised by Stanton and the FSID, especially at home.

2 Sleeping rectal temperature was lower than daytime values from two weeks of age, and at about twelve weeks old, minimum rectal temperature suddenly fell from 36.8^{o}C to 36.5^{o}C with night-time sleep.

3 Mean sleep duration increased as the babies became older, and as sleep duration increased minimum night-time rectal temperature fell.

CHAPTER FOUR

LONGITUDINAL STUDIES OF RECTAL TEMPERATURE

The cross-sectional analysis suggested that the greatest change in babies' rectal temperature patterns occurs on average at twelve weeks old, but there were considerable individual differences.

A further thirty babies were therefore studied, at weekly intervals from six to twenty weeks of age, in order to assess the exact age at which the minimum rectal temperature fell below 36.5^{o}C with night-time sleep in individual babies, and to examine the process and related factors in more detail.

Twenty-six subjects yielded sufficient data, a total of 231 nights of recording. It was not possible to assess the age of greatest change for the other four babies as they did not have a complete series of recordings, either because of technical problems or family illness.

The mean (+-SEM) gestational age of the twenty-six babies was 39.9 (0.3) weeks, with all but one born between 38 and 42 weeks and none before 36 weeks. Premature babies were not studied, because although the cross-sectional study data indicated that their rectal temperature patterns were similar to full term babies and they developed the rhythm at ages within the normal range, the numbers studied were small and it would be necessary to monitor larger numbers more closely to draw worthwhile conclusions.

The birth weight averaged 3471(95) grams, and 50% were boys. The mean maternal age was 27.3 (0.91) years, and the social class distribution was close to that in Leicestershire (Appendix 3), although only two fathers were unemployed; six of the babies had parents in occupational groups 1 or 2 (16.5%), and seven in groups 5 or 6 (27%) (Office of Population and Surveys, 1980). Nine were first children, fourteen had one sibling and three had two or more siblings. There was smoking in ten of the households. Sixteen of the babies laid lateral or supine in their cots and one baby slept in his parents' bed. Eighteen of the babies were breast fed at birth and thirteen continued after six weeks of age.

Sleeping Rectal Temperature

The twenty-six babies were each monitored successfully on average eight times, fourteen being monitored between five and seven times, and twelve between eight and fourteen times. Each baby's rectal temperature was recorded from one hour before sleep, at least eight hours into the night and usually to one hour after waking, and the parents were asked to keep a record of their baby's activities. The longest interval between an individual's recordings was three weeks, but there were sufficient data in all cases to be able to calculate within one week when the baby's rectal temperature first fell below 36.5°C with night-time sleep. Studying the night-time rectal temperatures of individual babies on a weekly basis indicated that the change from a nightly minimum rectal temperature of about 36.8°C to one below 36.5°C was abrupt, happening between one week and the next, and irreversible, unless the baby was incubating an infection or had been immunised (see **Chapter Ten**). Figures 4:1 and 4:2 are of two different babies, showing a series of night-time recordings of rectal temperature around the age at which their rectal temperature first fell below 36.5°C. Figure 4:1, a breast fed baby, first exhibited this minimum at nine weeks of age and the pattern continued thereafter with only slight changes from eleven weeks of age when the middle-of-the-night feed was discontinued. Figure 4:2, a bottle fed baby, first exhibited the minimum rectal temperature later at twelve weeks of age, but once again the pattern remained afterwards and was irreversible. Figure 4:3 shows the distributions of minimum rectal temperatures, before and after the week in which they first fell below 36.5°C with sleep, in babies who were well around the time of recording Only one of the twenty-six babies had a minimum rectal temperature above 36.5°C without having any signs of illness after the week in which it first fell below that level.

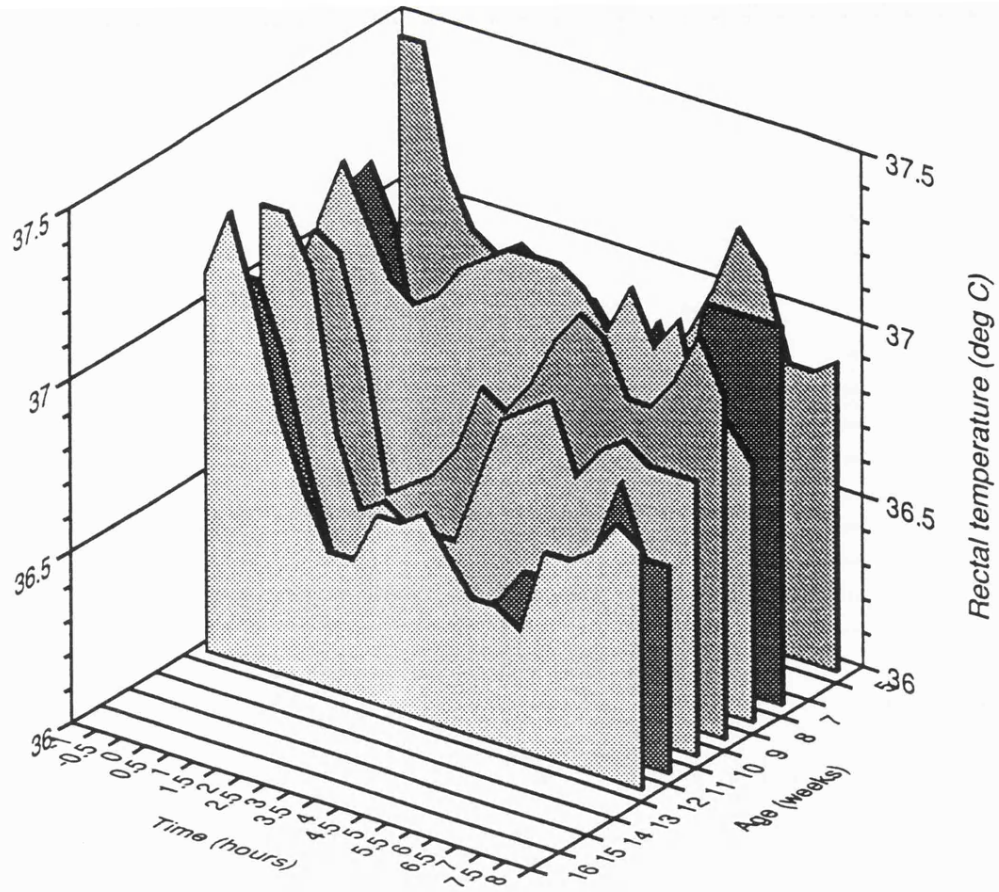


Figure 4:1 Seven over night recordings at fifteen minute intervals of a breast fed baby's rectal temperature, illustrating the abrupt and irreversible fall in her rectal temperature with sleep at nine weeks of age.

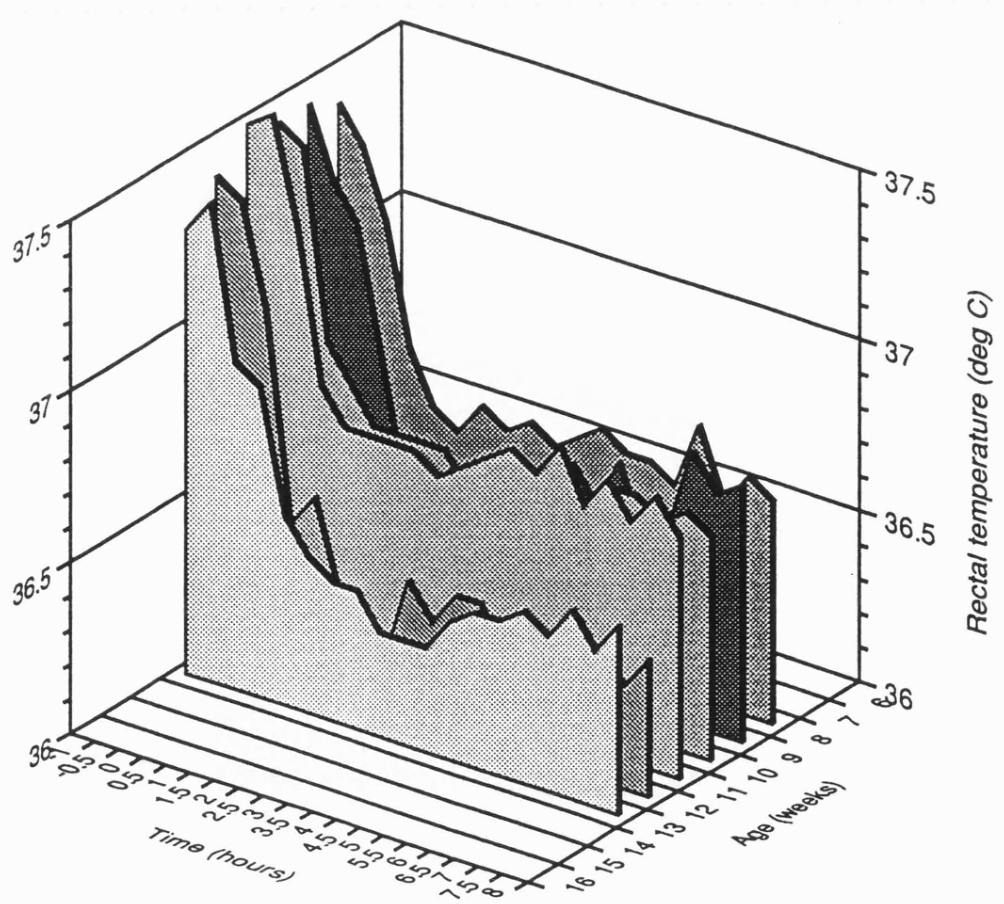


Figure 4:2 Six over night recordings at fifteen minute intervals of a bottle fed baby's rectal temperature, illustrating the abrupt and irreversible fall in his rectal temperature with sleep at twelve weeks of age.

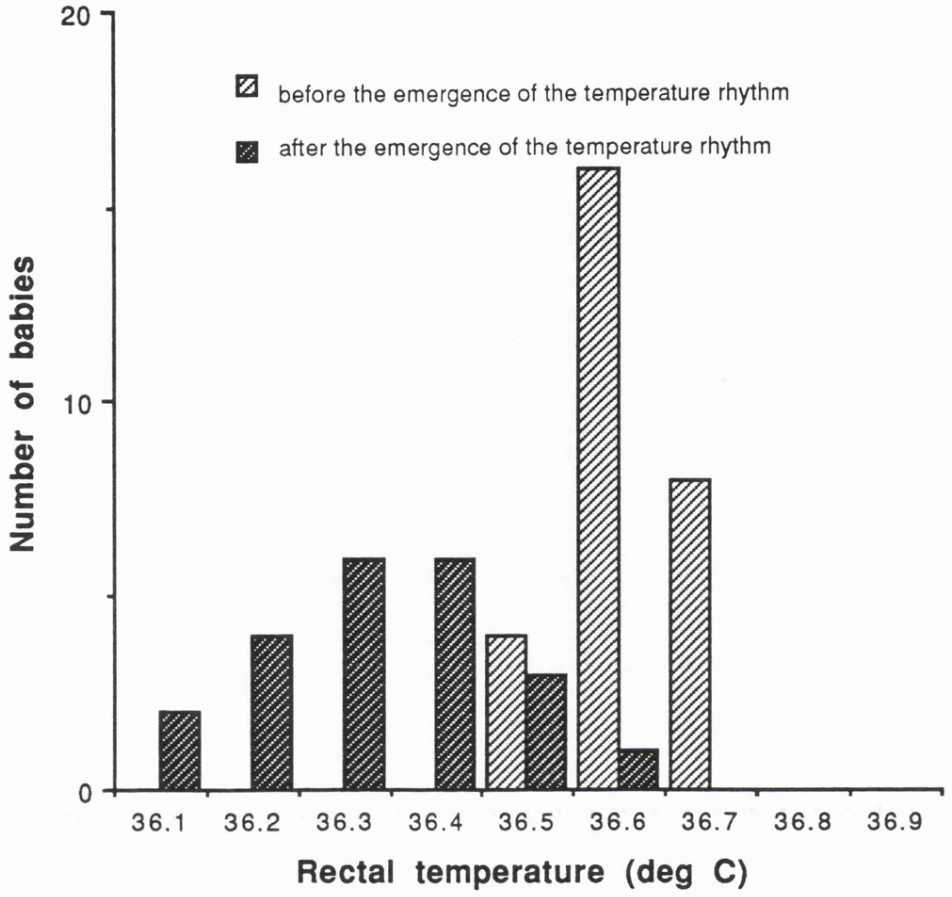


Figure 4:3 The distributions of minimum rectal temperatures before and after the first week they fell below 36.5°C with night-time sleep. 58 recordings on 23 babies before, and 65 recordings of 25 babies afterwards.

From these data, an hypothesis of a three stage process of rectal temperature development was formulated. These stages were chosen because they were distinct and easily recognisable patterns which occurred in all babies, and were irreversible.

The Three Stage Developmental Process of Night-Time Rectal Temperature Rhythms

1. Neonatal Stage Lasts from birth to about two to four weeks of age. The rectal temperature remains stable during sleep, at a level just below daytime levels.

2. Pre-rhythm Stage The baby's rectal temperature is above 37^{o}C in the evening and falls to about 36.8^{o}C with night-time sleep, rising only when the baby wakes for a feed in the night or in the morning; this stage lasts anything from four to fourteen weeks.

3. Mature Stage The rectal temperature rhythm is considered to be established or mature when a minimum rectal temperature of below 36.5^{o}C is achieved with night-time sleep. This usually occurs within one week, but at different ages in individual babies.

In this study the transition from the second to third stage is analysed in detail. As the greatest change in rectal temperature occurred then, this development was an easily recognisable phenomenon and had a wide age distribution. The beginning of the third stage or the week of the first appearance of a rectal temperature below 36.5^{o}C was studied and compared with the mean rectal temperature patterns for the two weeks before and the two weeks afterwards. The abrupt and irreversible nature of the change is illustrated in figure 4:4. This distinctive pattern would be masked by using chronological age.

Figure 4:5 shows the distribution of chronological ages at which the change from the second to third stage occurred. The mean (+-SEM) age was 11.1 (0.5) weeks. Twelve of the babies changed or matured between seven and eleven weeks old (inclusive) and fourteen between twelve and sixteen weeks.

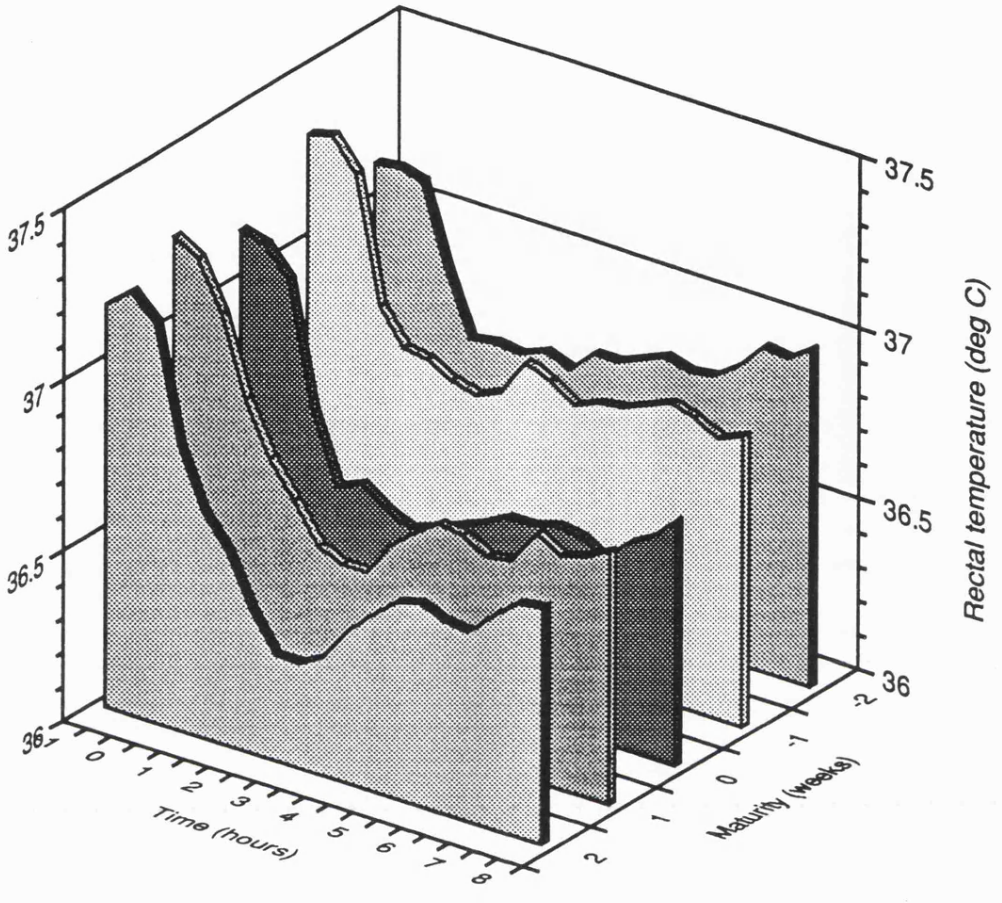


Figure 4:4 Averaged fifteen minute recordings, of sleeping rectal temperature on 26 babies, during the two weeks before the rhythm appeared, the week the change occurred, and the two weeks afterwards, illustrating the abrupt and irreversible fall of rectal temperature with night-time sleep.

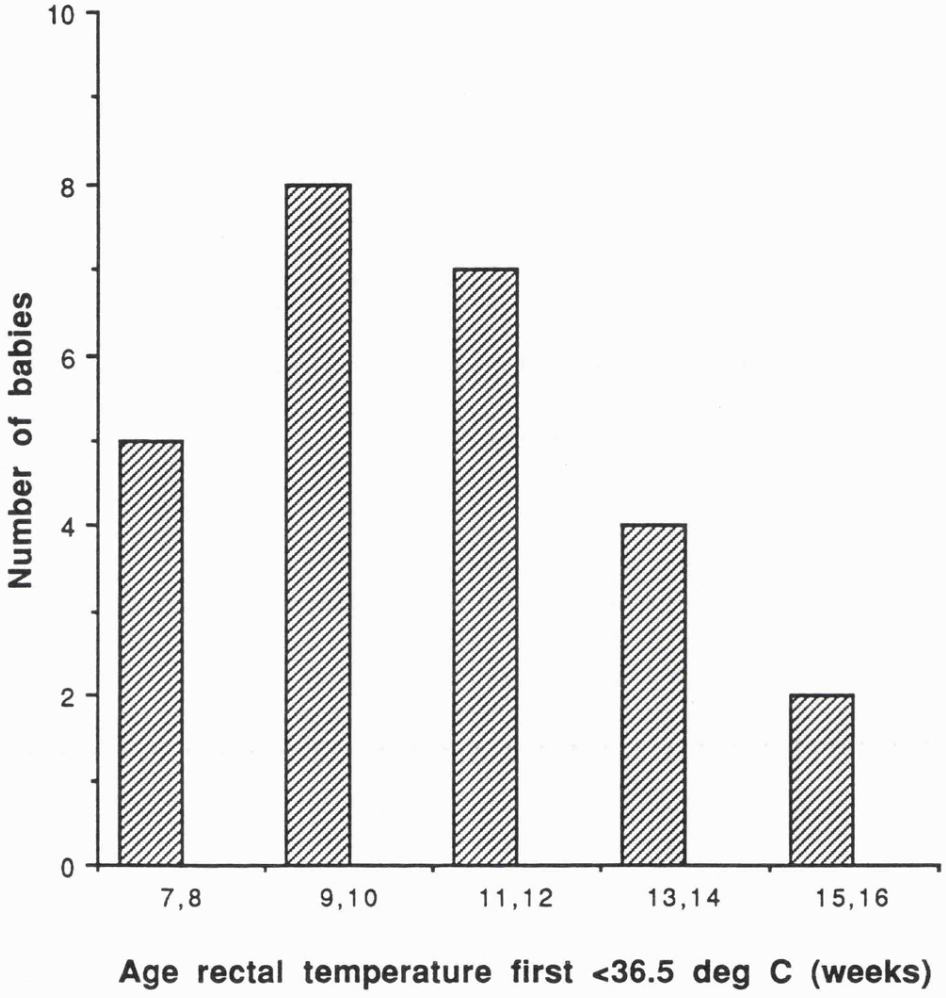


Figure 4:5 The distribution of ages at which the change from the second to third stage occurred (when the night-time minimum rectal temperature fell below 36.5°C). In the 26 babies studied the age of this abrupt transition ranged from seven to sixteen weeks.

Summary of Longitudinal Studies of Rectal Temperature

1 There is a three phase process of rectal temperature development: **1 The Neonatal stage,** from birth to two to four weeks of age, is when the rectal temperature remains fairly stable during sleep. **2 The Pre-rhythm stage,** which may last from four to fourteen weeks, is when the baby's rectal temperature is raised above 37°C before sleep in the evening, falls to about 36.8°C with sleep and rises when the baby awakes. **3 The Mature stage**, occurring at varying ages in different babies, is when a minimum rectal temperature of below 36.5°C is achieved with night-time sleep.

2 The changes in the temperature pattern from the second to the third stage occurred between one week and the next, and in well babies were irreversible.

3 The mean age (+-SEM) at which the changes occurred was 11.1 (0.5) weeks, but the range was from 7 to 16 weeks.

CHAPTER FIVE

FACTORS ASSOCIATED WITH THE AGE AT WHICH RECTAL TEMPERATURE PATTERNS DEVEELOPED

The twenty-six babies were divided into two groups by using the age at which their rectal temperature first fell below 36.5^{o}C with sleep or 'matured' (see **Chapter Four** for definition). There were twelve babies whose sleeping rectal temperature pattern changed between seven and eleven weeks old, and fourteen who did not achieve this until twelve to sixteen weeks of age. Aspects of the babies' health and care were then compared. Examples of factors studied are gestational age of the baby, method of feeding, at birth and during the study period, and sleeping environment. Those social factors examined included the mother's age and social class. Those that were significant are discussed below.

Method of Feeding

The babies who developed a 'mature' temperature rhythm before twelve weeks of age were significantly more likely to have been breast fed at birth (χ^2= 5.26, $p<0.025$), and for at least six weeks afterwards (χ^2= 5.56, $p<0.025$). Assessed slightly differently, the mean (+-SEM) chronological age for the change in the sleeping rectal temperature for babies who were always bottle fed was 12.33 (0.52) weeks, whereas those breast fed for at least six weeks changed at 10.07 (0.74) weeks, a significant difference ($p<0.01$, Student's t-Test).

Growth

There was a clear relationship between the weekly rate of weight gain, up to twelve weeks of age, and the age of temperature rhythm maturation. Average rate of weight gain was calculated by subtracting the baby's birth weight from the baby's weight at twelve weeks of age and dividing by 12.

Figure 5:1 illustrates the correlation (correlation coefficient = 0.513, $p<0.01$) between the average weekly weight gain and the age at which the baby's rectal temperature first fell below 36.5^{o}C with sleep; this shows that the babies gaining weight most rapidly developed their rhythm later than the slower growing babies.

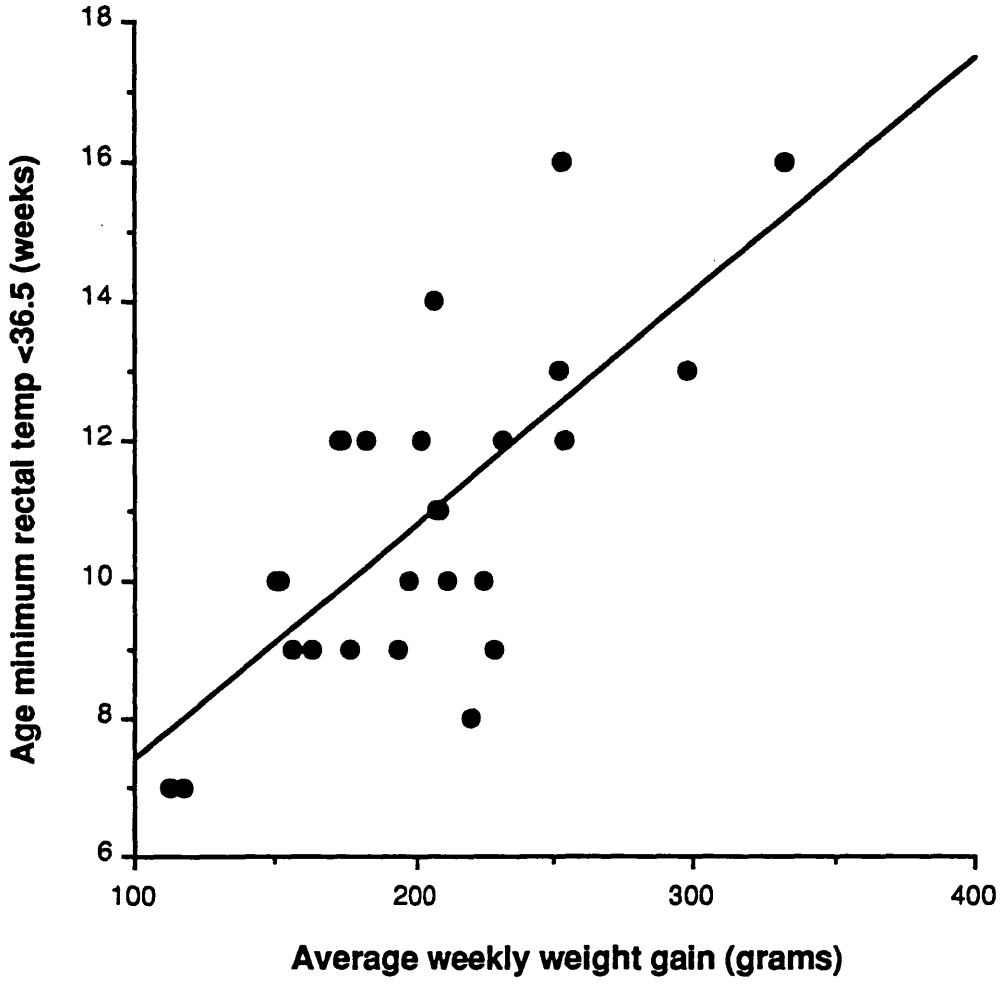


Figure 5:1 Individual baby's weekly growth rate against the age at which their rectal temperature first fell below 36.5°C with night-time sleep. Slower growing babies were younger changing from stage two to stage three.
Correlation Coefficient = 0.513, $p<0.01$

The correlation between growth and temperature rhythm maturation might be related to the method of feeding; breast fed babies may only have taken what was required at each feed. Other facets of the child's care may be implicated, too, for example how often and why the baby is fed; to prevent crying some parents may have fed their baby, rather than play with or cuddle it. Alternatively it may be a hereditary phenomena, influenced by parental genes or maternal smoking during pregnancy. Not enough data were collected to see whether maternal smoking was significantly correlated with poor or rapid weight gain, but weekly weight gain was not related to birth weight, indicating that it was not a result of the premature or dysmature babies exhibiting 'catch-up' growth, or the genetically large babies continuing to grow rapidly.

Sex and Birth Order

Girls developed their rhythms significantly earlier than boys. The mean (+-SEM) age for girls to first exhibit a rectal temperature below 36.5^{o}C with sleep was 10.23 (0.59) weeks and for boys 11.92 (0.44) weeks ($p<0.02$, Student's t-Test). First children developed their rectal temperature rhythm earlier than second or subsequent children. The mean age (+-SEM) for first children was 10.11 (0.74) weeks and for second or subsequent children 12.58 (0.42) weeks ($p<0.05$, Student's t-Test). Method of feeding seemed to have a strong effect on the timing of development, but there was no significant correlation between this and sex of the child or birth order.

Sleeping Position

Babies who normally slept prone were significantly more likely to develop their rhythms after eleven weeks of age (χ^2= 5.51, p<0.025). They were, however, also more likely to be second or subsequent children (χ^2 = 4.34, p<0.05).

Interestingly, babies who normally lay in the prone position were more likely to sleep on average for more than six hours at night (ages six to twelve weeks), than those who normally slept in a lateral or supine position (χ^2= 5.92, p<0.025).

Position of Cot

Those babies who had their own bedrooms, compared with those who slept in their parents' room or in the lounge were significantly more likely to develop their temperature rhythm earlier (χ^2= 3.88, p<0.05). Where a baby slept was also associated with social class; children were more likely to have their own room if their parents were classified as being in the upper three social classes (χ^2 = 6, p<0.025).

There was a strong trend, close to significance, for babies of parents in the non-manual occupation groups to develop an established rectal temperature rhythm earlier than those from families in the manual groups. No association could be found, however, between social class and type of feed.

Age of Mother

The mothers of the babies who developed their temperature rhythm before twelve weeks of age were older (28.5 (1.14) years) compared with those babies who changed their pattern later (25.9 (1.41) years). Older mothers, however, were also significantly more likely to breast feed until their babies were at least six weeks of age; the mean age of mothers who breast fed was 29.77 (3.61) years, whereas the mean age of mothers who bottle fed their babies was 24.85 (4.36) years (p< 0.004, Student's t-Test).

Season and Environment

The time of year that the baby was born and the room temperature and tog value of clothing and bedding in which the baby slept did not differ significantly between the two groups.

Gestation of the Baby

The data were also analysed correcting for the small differences in gestational age between the babies, and all the factors which are significant with chronological age remain when the ages are corrected to a forty week gestation.

In conclusion, both breast feeding and laying a baby supine or lateral were significantly associated with earlier 'maturing' of a rectal temperature rhythm, as were being a first child and female. Numbers were not great enough to reach significance, but those parents who smoked were more likely to have babies who developed their rhythms later, a trend which was probably associated with social class, as indicated by other measurements of social standing, such as age of mother and position of cot. Infection, too may also have played a part in households where parents smoke. Unfortunately, only univariate analysis was appropriate, as the numbers were small.

These results suggest that earlier maturing may be beneficial to the baby, or that delayed or later maturing is detrimental. Those factors that correlate with later development are also those that North, Petersen and Wailoo (1991-personal communication) have shown to be associated with an increased risk of SIDS. Unpublished data are also beginning to indicate that babies considered to be at increased risk of SIDS, using these criteria, have delayed maturing of their temperature rhythm (Jackson, Pratt, Milner, Petersen and Wailoo, 1992-personal communication).

Summary of Factors Associated with the Age at which Rectal Temperature Rhythms Developed

1 The age of the change in rectal temperature rhythm depended on the type of care the baby received and social factors relating to the mother and family.

2 Earlier development of an established sleeping rectal temperature pattern was associated with breast feeding, slower average weight gain to twelve weeks of age, older mothers, first children, higher social class, girls and laying supine or lateral.

3 Later development of an established rectal temperature pattern was correlated with bottle feeding, faster weight gain, younger mothers, laying prone, second or subsequent children, lower social classes and boys.

4 Babies who changed their sleeping rectal temperature pattern later shared characteristics with those babies who have been shown to be at increased risk of SIDS.

CHAPTER SIX

CROSS-SECTIONAL ANALYSIS OF HEART RATE DATA

The previous chapters have established that sleeping rectal temperature rhythms alter with age. Other physiological functions were studied in order to see whether they are affected in similar ways. Heart rate rhythms may be closely aligned to those of rectal temperature (Hellbrügge, 1960), and increased heart rate is a sign of thermoregulatory responses and possibly thermal stress. One objective of this part of the study was to assess if the ability to thermoregulate and maintain a consistently lower rectal temperature with sleep might cause stress under some circumstances and consequently raise heart rate. The studies on rectal temperature illustrated that the age of maturation is unaffected by thermal environment, but did not answer questions about whether babies have to "work" harder physiologically to keep their body temperature constant in certain conditions such as warmer rooms, being covered in more clothing and bedding, colder environmental conditions or when suffering from an infection with or without a fever. Patterns of heart rate were therefore studied in order to assess whether they are determined by body temperature, the baby's age or other circumstances. In this chapter the data are analysed cross-sectionally, and the association between the mean chronological age of the babies and the sleeping heart rate is discussed.

Heart rates were monitored at the same time as rectal, skin and ambient temperature in fifteen babies cross-sectionally and twenty-four babies longitudinally. Of the thirty-nine babies, nineteen were males, thirteen were first children and eight had two or more siblings with the average (+-SEM) age of the mother being 27.6 (0.86) years. Their mean birth weight was 3464.49 (80.9) grams and the mean gestation 39.77 (0.24) weeks. The range of social classes in Leicestershire was represented (see Appendix (3)); thirteen parents were classified as being in the upper non-manual social classes, fifteen in the lower manual classes and one father was unemployed (Office of Population and Surveys, 1980). There was smoking in twelve of the households and twenty-four babies were breast fed at birth.

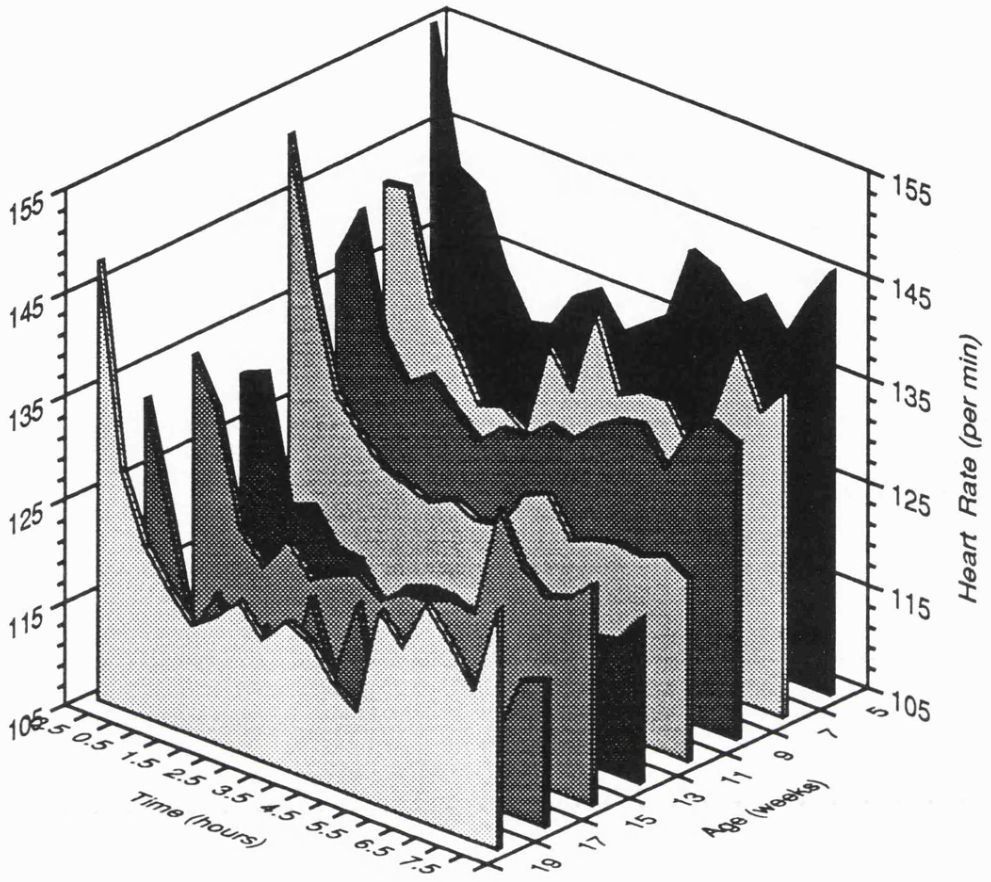
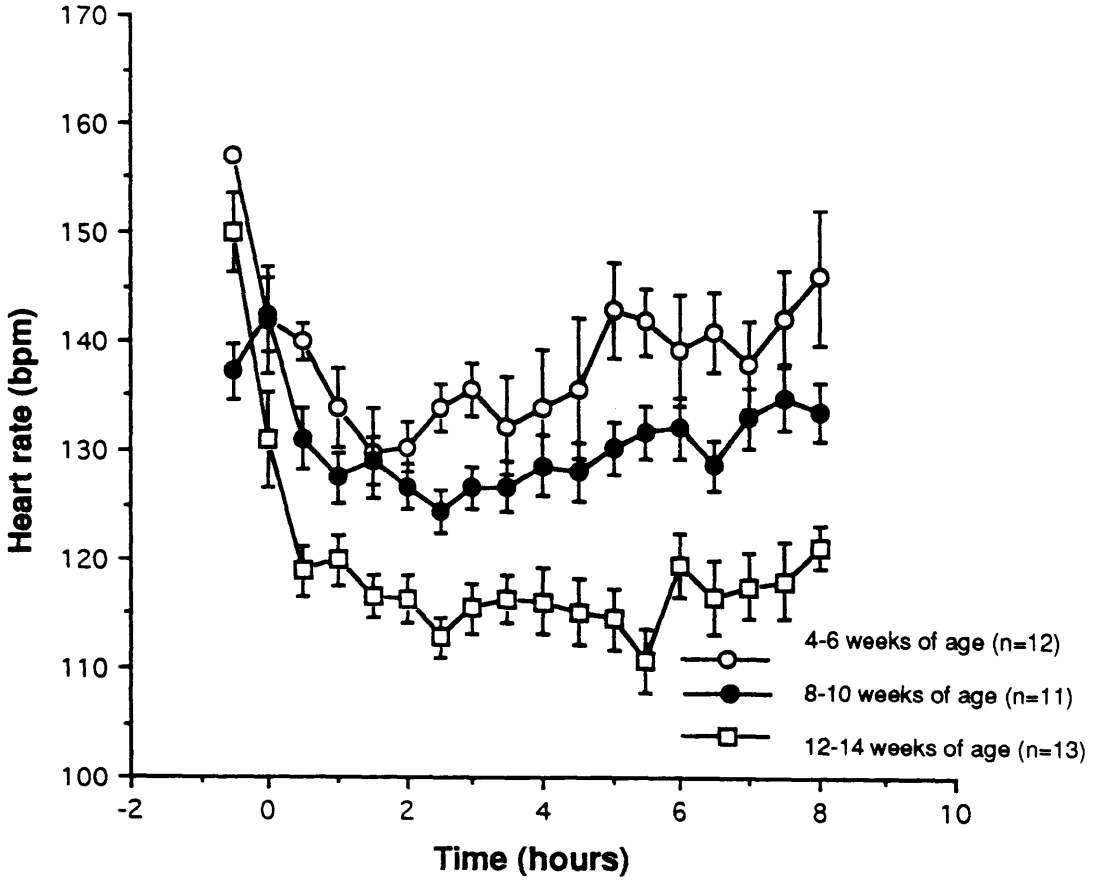


Figure 6:1 The means of fifteen minute recordings on 24 babies divided into two week age groups from four to twenty weeks of age. At about twelve weeks of age the night-time sleeping heart rate fell below 115 bpm.

The heart rate readings taken at minute intervals during the night from one hour before sleep until eight hours into the night were grouped into two-week age groups. The mean value for every half an hour throughout the night was then calculated for each age group.

Figure 6:1 shows the averaged heart rate data from typical night sleeps of all the babies divided into two week periods from four to twenty weeks of age. As with rectal temperature, the heart rate fell with sleep from an early age, but the minimum consistently remained above 125 beats per minute. Then over a two week period there was a sudden slowing of heart rate with night-time sleep of more than twelve beats per minute (bpm), the second week having the greater fall of about eight beats per minute to a minimum value below 115 bpm. Similarly to rectal temperature patterns all the recordings taken after this age suggested that in the child's normal sleeping environment and unless the child was ill, this pattern was irreversible.

Figure 6:2 confirms these findings. At any age the pattern of night-time sleeping heart rate could be superimposed on the pattern of night-time sleeping rectal temperature. Keele, Neil and Joels (1982) report that a 10 bpm rise in pulse rate accompanies a 0.5^{o}C rise in rectal temperature in adults. The heart rate patterns of the sleeping babies were, therefore, what would be expected if heart rate is directly related to rectal temperature; the change in heart rate from one week to the next (8bpm) corresponded to the fall in rectal temperature of 0.4^{o}C.


170
160
150
140
130
120
110
100
Heart rate (bpm)
-2
0
2
4
6
8
10
Time (hours)
4-6 weeks of age (n=12)
8-10 weeks of age (n=11)
12-14 weeks of age (n=13)

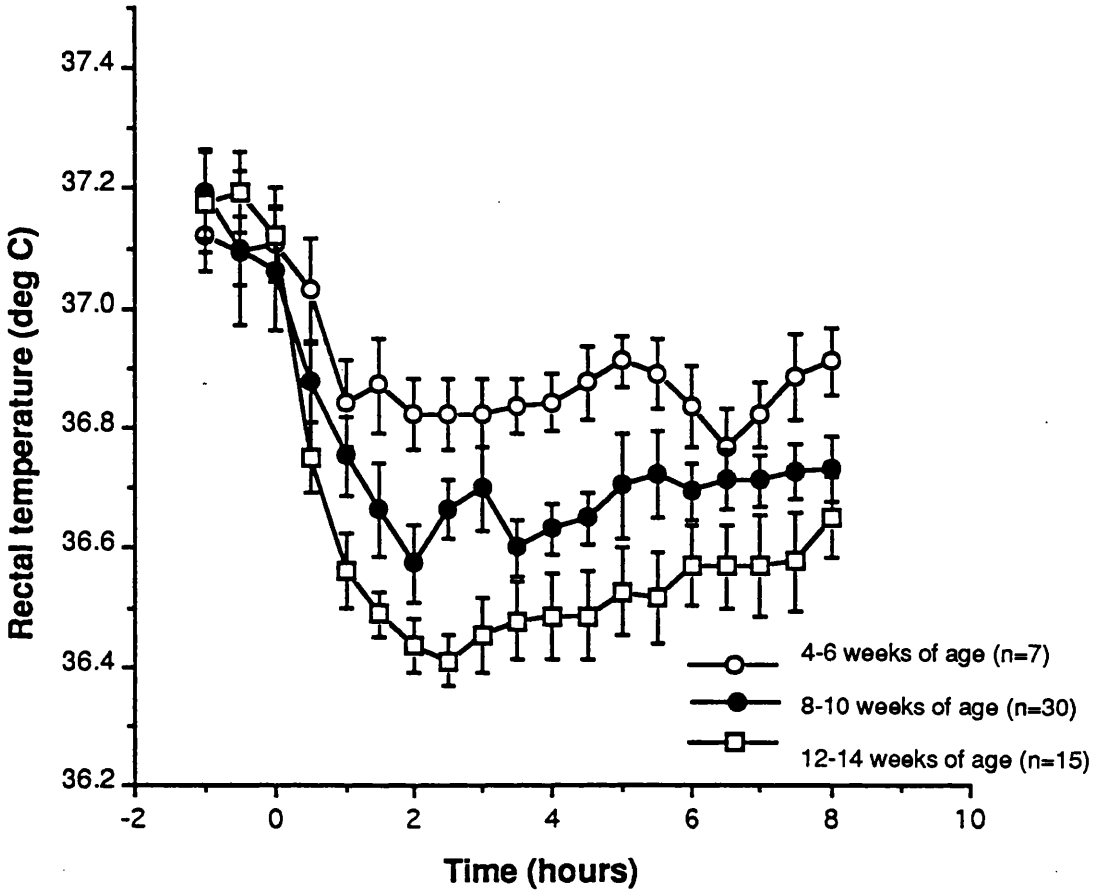


Figure 6:2 Averaged fifteen minute recordings, with standard errors, of night-time rectal temperature and heart rate. Three different age groups of babies, illustrating that heart rate can be superimposed on rectal temperature values.

Summary of Cross-Sectional Analysis of Heart Rate Data

1 Heart rate slowed with night-time sleep from an early age.

2 It was on average at about twelve weeks of age that the heart rate suddenly fell to below 115 beats per minute with sleep.

3 The slowing in heart rate mirrored the fall in rectal temperature until the age of eighteen weeks.

CHAPTER SEVEN

LONGITUDINAL STUDIES OF HEART RATE

Twenty-four babies were monitored at one to two weekly intervals between the ages of six to sixteen weeks, a total of ninety-four recordings. There were technical problems, or the period of recording was not long enough, on a further eighteen occasions. There were at least five valid recordings on nine babies and three to four on the remaining fifteen. All the babies had enough data to be able to calculate the week when the minimum rectal temperature fell to below 36.5°C with sleep (see **Chapter Four**), and there were heart rate data for the weeks around this time of change.

Thirteen of the babies were male, eight were first children and twelve had one sibling with four having two or more siblings. The mean (+-SEM) birth weight was 3436.25 (99.6) grams, the average gestation 39.87 (0.29) weeks and the mean maternal age 26.92 (0.95) years. The mean of the social classes represented was 4 with six babies having parents in classes 1 or 2 and ten in 5 or 6 (see Appendix (3) for Leicestershire distribution). There was smoking in eight of the households and fifteen babies were breast fed at least for the first six weeks of life.

The babies' heart rates slowed by about ten beats per minute at the same age as the minimum rectal temperature fell by 0.4°C - 0.5°C to below 36.5°C. Figure 7:1 plots the minimum rectal temperature of individual babies before and after development or change in the pattern of the temperature rhythm against the minimum heart rate recorded for the same night's sleep. The minimum rectal temperature was usually reached two to three hours after bedtime and coincided with the minimum heart rate.

These data confirm that there was quite a dramatic slowing of the heart rate with sleep over a period of two weeks and this coincided with the change in rectal temperature and at all times the curves could be superimposed (see **Chapter Six**).

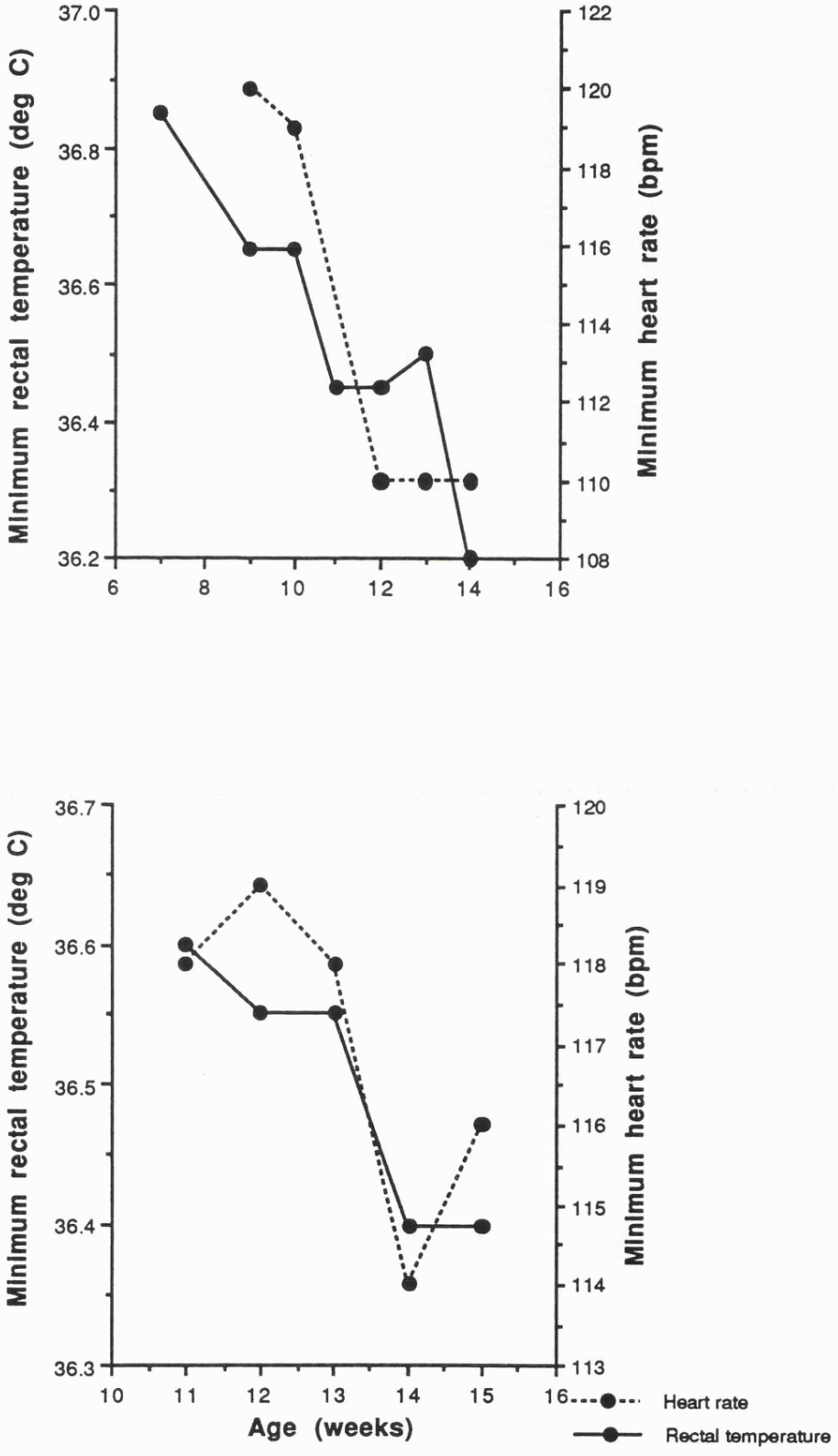


Figure 7:1 A longitudinal series of the minimum night-time rectal temperatures and heart rates recorded on two babies studied at fifteen minute intervals over night. The abrupt fall of temperature to below 36.5°C, and the slowing of heart rate to below 115 bpm occurs at the same time in individual babies, but at varying ages for different infants.

The age, therefore, at which the minimum heart rate slowed to below 115 beats per minute with sleep varied for individual babies, and the factors correlated with this change were the same as those associated with the developing of the rectal temperature pattern. The numbers were smaller, but it can be inferred that babies who were breast fed, had a slower average weight gain to twelve weeks of age and lay supine or lateral slowed their heart rate to a lower level with sleep at a younger age, and those babies who had younger mothers, older siblings and were boys in the lower social classes did not slow their heart rate with sleep until they were older.

Summary of Longitudinal Heart Rate Studies

1 The development of a heart rate rhythm or a slowing of the rate to below 115 beats per minute with sleep occurred at the same age as the change or 'maturing' of rectal temperature.

2 Changes in the rhythm appearing at a younger age seemed to be associated with social factors such as older mothers who were classified as being in the higher social classes, breast feeding, sleeping lateral or supine, first children and girls.

3 Changes in the rhythm appearing at an older age seemed to be correlated with features of infant care such as bottle feeding, boys, second or subsequent children and sleeping prone.

CHAPTER EIGHT

ASPECTS OF CARE AND HEALTH OF THE BABY AFFECTING THE NIGHT-TIME MINIMUM OF RECTAL TEMPERATURE

In the previous chapters characteristics of babies were correlated with the age at which their rectal temperature first fell below 36.5°C, and their heart rate slowed to below 115 beats per minute with sleep, and the conclusion drawn that those babies, who were older when their temperature and heart rate rhythms developed a distinct pattern, also shared characteristics of parental care and social standing with those babies who have been shown to be at increased risk of Sudden Infant Death Syndrome (see **Introduction**).

In order to study the data further and in an attempt to assess whether the earlier appearance of an established rectal temperature rhythm is beneficial or the later development harmful, the data were studied by dividing, not by age, but by those recordings made when the babies' rectal temperature rhythms were in stage two (before the babies' rectal temperature patterns developed) and those recorded afterwards, when the patterns were in stage three. The range of babies' ages was considerable both in stage two (the pre-rhythm stage) and stage three (the post-rhythm stage) groups.

Various factors about the babies and their care were compared in both the 'pre-rhythm' and 'post-rhythm' groups, in order to assess whether these factors had any influence on the minimum rectal temperature attained with sleep, or the shape of the night-time rectal temperature curve. As there are a number of graphs, they are presented at the end of the chapter.

The data are also presented in a slightly different manner from the earlier chapters, as the results indicated that the time of most change in the night-time rectal temperature curve is when the baby is going to sleep and during the first four hours of sleep. Waking up, therefore, may also be a time of change in the temperature curve and consequently a period of vulnerability, so the last four hours of sleep and the first hour of waking were analysed. Analysing the data in this way has the added advantage of avoiding distortion of the figures by differences in the babies' sleep lengths or middle-of-the-night feeds, which

would temporarily affect the rectal temperature and heart rate.

In order to compare infant care, the babies were divided into two distinct groups for each factor, and the mean rectal temperature values in stage two and stage three calculated for both of these groups. Thus the average night-time rectal temperature curves for each group were plotted and compared for the two weeks before the rectal temperature reached a minimum of below 36.5^{o}C and for the two weeks afterwards.

Statistical Analysis

Two way Analysis of Variance with repeated measures was used to assess the difference between the two curves, for the first four hours of the night, and the last four hours before waking.

Creation of Groups for Comparison

The social and health factors studied were the ones that had been shown to be significantly different between babies who were later or earlier developing an established sleeping rectal temperature pattern (see **Chapter Five**), and were therefore, factors which are correlated with an increased risk of dying from Sudden Infant Death Syndrome.

Sleeping Position

Babies in stage two of their development were divided by their sleeping position, one group laying prone and the other supine or lateral. Prone is defined as having the ventral surface of the trunk in symmetrical contact with the mattress cover, irrespective of head position. Lateral is having either the left or right side of the trunk in contact with the mattress covering, and the humerus of both arms flexed at the shoulder joint. Supine is having the dorsal surface of the trunk in symmetrical contact with the mattress cover.

Method of Feeding

Those babies who were breast fed until six weeks of age comprised one group, and those bottle fed another.

Unfortunately, not all factors were as distinct or as easy to divide as method of feeding or *sex of the child*, as often there were a range of things that had happened or values reached. In these cases the mean rectal temperatures of the groups at the extremes of these values were compared. The creation of groups in this way for analysis excludes some of the data, but inclusion would reduce the power of the technique and add random variation.

Weight Gain up to Twelve Weeks of Age

The babies' average weekly weight gain from birth to twelve weeks of age was calculated by subtracting their birthweight from their weight at twelve weeks and dividing by 12. In order to be able to study two distinct groups the third of the babies who gained weight most rapidly and the third who were the slowest growing were compared.

The Thermal Environment

The thermal environment was studied in three ways; 1. *room temperature* (degrees centigrade), which was taken as the ambient temperature recorded four hours into the night which in the majority of cases was the same as the minimum room temperature taken during the recording; 2. the *quantity of clothing and wrapping* on the baby which was measured in units of tog and; 3. the *total of room temperature and coverings*, which was calculated by the simple addition of the two values.

The groups whose rectal temperatures were plotted were selected by arranging the room temperature or tog values linearly and excluding those around the median value and studying the first and last third. Thus in a group of fifty-eight babies where twenty babies slept in rooms with a minimum ambient temperature four hours into the night of between 7.5°C and 17.2°C, nineteen

babies slept in rooms with a minimum ambient temperature measuring between 17.3°C and 19.25°C and nineteen were in rooms with a minimum temperature of between 19.3°C and 27.5°C. The middle group (those in rooms of between 17.3°C and 19.25°C) were excluded from the analysis of the effect of ambient room temperature on rectal temperature, and the other two groups' rectal temperature patterns plotted and compared.

Illness

Infectious illness, particularly upper respiratory tract infections, cause acute raising of body temperature, so all episodes of infectious and other illnesses were noted. The majority of infectious illnesses were upper respiratory tract infections, sometimes with a cough, and others included ear infections and gastroenteritis. Candida albicans, eczema, milk allergy and conjunctivitis were also common, but were not included in the analysis.

The number of episodes of infectious illness up to twelve weeks of age was recorded; eight babies had no recorded history of illness, nineteen had one episode and twelve babies had two recorded episodes of illness. None of the children had more than two episodes of illness up to twelve weeks of age. The two groups studied consist of those children who had two episodes of illness compared to those who had none.

The rectal temperatures used to plot these graphs excluded any recordings that were taken at the time of obvious illness, and were, as far as it is possible to assess, 'infection-free' recordings.

Black, Morris, Smith and Townsend (1982) suggest that an increased incidence of illness is correlated with other social and health factors about the family. These were also studied.

'Pre-' and 'Post' Rhythms or Before and After the Change in Sleeping Rectal Temperature Patterns

Figure 8:1 shows the mean rectal temperature of all the babies monitored longitudinally, in the last two weeks of stage two and the first two weeks of stage three, for the hour before bedtime and the first four hours of the night and for the last four hours of sleep and an hour after waking up. The rectal temperature was similar before going to sleep and after waking up in both stages, which suggests that the rectal temperatures of awake babies varied very little, both pre- and post-rhythm development. By one and a half hours into the night, however, the post-rhythm babies' rectal temperature was lower than the pre-rhythm babies, and remained so until two hours before waking (Two way Analysis of Variance with repeated measures, $F= 87.98$ with 1, 416 df, $p<0.001$ and 33.72 with 1, 416 df, $p<0.001$).

Sleeping Position

Figure 8:2 illustrates that before the babies' rectal temperature rhythms were developed there was no consistent significant difference between those laying prone and those laying supine or lateral.

The night-time rectal temperature pattern of sleeping babies after the rhythm was developed was also unaffected by sleeping position (figure 8:3).

Method of Feeding

During the first four hours of the night in stage two there was a significant difference in rectal temperature patterns between those babies who were breast fed for more than six weeks, and those who were bottle fed (Two way Analysis of Variance with repeated measures, $F=6.19$ with 1, 232 df, $p<0.025$). This is probably accounted for by the significant rise in the breast fed babies' temperature in the middle of the night ($p<0.05$ at 3.5 hours after bedtime, Student's t-Test), which may be a result of waking for a feed. This is shown in

figure 8:4.

Figure 8:5 illustrates that once the babies' rectal temperature pattern had developed (stage three) method of feeding still affected the level of temperature over the last four hours of the night. Breast fed babies were significantly warmer (Two way Analysis of Variance with repeated measures, $F=11.40$ with 1, 368 df, $p<0.001$).

Weight Gain of the Baby up to Twelve Weeks of Age

There was no difference, in stage two, of the night-time rectal temperature pattern of faster growing babies compared to slower growing babies (figure 8:6). Differences were seen, however, in stage three or post-rhythm. Figure 8:7 illustrates that the slower growing babies' night-time rectal temperatures were significantly higher over the last four hours of the night (Two way Analysis of Variance with repeated measures, $F=5.82$ with 1, 232 df, $p<0.025$).

The Thermal Environment

The age of transition from stage two to stage three appeared to be unaffected by the thermal environment in which the babies slept, but environment did influence the night-time rectal temperature pattern of babies whilst they were in stage two, or before the rhythm had changed.

The greatest influence on rectal temperature in stage two was a combination of more coverings and higher room temperature than the median. Figure 8:8 compares the mean rectal temperatures of those babies, in stage two of their development, who slept in the highest total combination of coverings and ambient temperature, and those in the lowest. Interestingly, the rectal temperature of the babies in the former group fell to a significantly lower level, more quickly, in the first part of the night, than those in less coverings and cooler rooms (Two way Analysis of Variance with repeated measures, $F=16.78$ with 1, 448 df, $p<0.001$). However, they then warmed significantly much more

quickly, and to a higher level at the end of the night (Two way Analysis of Variance with repeated measures, F=25.67 with 1, 448 df, p<0.001). There was no significant difference between the two groups in stage three (figure 8:9), indicating that post-rhythm the room temperature and amount of clothing and wrapping did not continue to influence babies' rectal temperatures, a finding also discussed by Anderson, Petersen and Wailoo (1990).

Raised room temperature in itself appeared to have little or no effect, as there was no difference in the mean rectal temperatures of the babies kept in warmer as opposed to colder rooms.

In stage two the rectal temperature pattern, over the first four hours of the night, was unaffected by more clothing and wrapping on the babies, but again it did influence their rectal temperature significantly around the time of waking. Figure 8:10 illustrates how babies, before the change in the rectal temperature rhythm, who had more clothing and wrapping on them were significantly warmer for the last four hours of the night (Two way Analysis of Variance with repeated measures, F=21.98 with 1, 114 df, p<0.001). This influence continued in stage three of development. The amount of coverings the baby had on did not significantly affect their night-time sleeping rectal temperature, but it was higher for the last four hours of the night (Two way Analysis of Variance with repeated measures, F=5.93 with 1, 240 df, p<0.025)(figure 8:11).

Illness

Analysis suggests that infection not only affected rectal temperature acutely (see **Chapter Ten**), but also influenced the night-time pattern of rectal temperature long term, both pre- and post-rhythm.

Babies in stage two of their development who had a history of two episodes of illness had a higher rectal temperature all night, and warmed significantly more quickly than those with none (Two way Analysis of Variance with repeated measures, F= 4.82 with 1,88 df, p<0.05)(figure 8:12).

Babies' night-time rectal temperatures were also affected in stage three, often a number of weeks after the reported episodes of illness. When compared with babies who had no recorded history of illness, those babies with a history of two episodes of illness cooled more slowly when going to sleep, and were significantly warmer all night (Two way Analysis of Variance with repeated measures, $F=6.45$ with 1,88 df, $p<0.025$ and $F=9.25$ with 1, 88 df, $p<0.01$)(figure 8:13).

Those babies with a higher incidence of illness were significantly more likely to be second or subsequent children ($\chi^2 = 6.983$, $p<0.01$), and although the numbers were small, there was also a trend for them to be bottle fed and have parents who smoked.

Sex of the Child, Social Class of the Family and Position of the Cot

Although sex of the baby, where it slept and the social class of its family were correlated with the age of transition from stage two to stage three of the night-time rectal temperature rhythm, these factors did not appear to affect the babies' patterns of rectal temperature at any time.

Discussion

The significant differences in pattern between the slower growing and faster growing babies were not seen in stage two, but in stage three of their rectal temperature rhythm, which is surprising, because in many of the babies the age at which the rate of growth was calculated (up to 12 weeks) coincided with them being in stage two. The slower growing babies may have been given a different type or quantity of food; for example they might have had solid food or a larger milk feed before bedtime or when they woke up. Unfortunately information about quantities of food was not collected but there was no indication that at this stage of their development the slower growing babies either fell asleep whilst being fed or woke in the middle-of-the-night for a feed, which may have affected their rectal temperature readings.

The slower growing babies were more likely to be breast fed (see **Chapter Four**), who also had significantly higher temperatures, both in stage two and stage three. This again is puzzling as, on average, breast fed babies developed the temperature rhythm at a younger age than bottle fed babies, and artificial milk presumably requires more energy to digest, creates more waste, and therefore produces more heat and raises body temperature higher than breast milk. One possible explanation is that post-rhythm breast fed babies were weaned on to artificial feeds, and their metabolism increased to cope with the different digestive processes. This seems unlikely, however, as although the quantity of food may have increased, the amount of protein would probably be about the same, and this raises metabolic rate more than carbohydrates. Breast fed babies may be slower growing and have a higher basic metabolic rate, utilising energy (food) to maintain a higher rectal temperature, rather than for growth.

In some babies warming-up before waking was more rapid, and their rectal temperature reached higher levels, than others, indicating that under some conditions the morning raising of body temperature may reach pathological levels. The most likely combination of factors to contribute to this, both in

stage two and stage three, are warm rooms with lots of bedding and a history of infection. The higher values of rectal temperature recorded at this time, however, were not always significant and studies need to be carried out on temperatures after waking.

Conclusions

Some babies may not only be later in reaching stage three, or changing their rectal temperature rhythm, and consequently are older when their temperature falls below 36.5°C whilst asleep, but, if kept in certain conditions, will also have consistently higher levels of rectal temperature than their contemporaries, regardless of age. In stage two, warmer rooms and more clothing and wrapping increased the night-time rectal temperature whilst asleep and in stage three, if the baby was breast fed, slower growing or had a history of upper respiratory tract infections this influenced the night-time rectal temperature pattern.

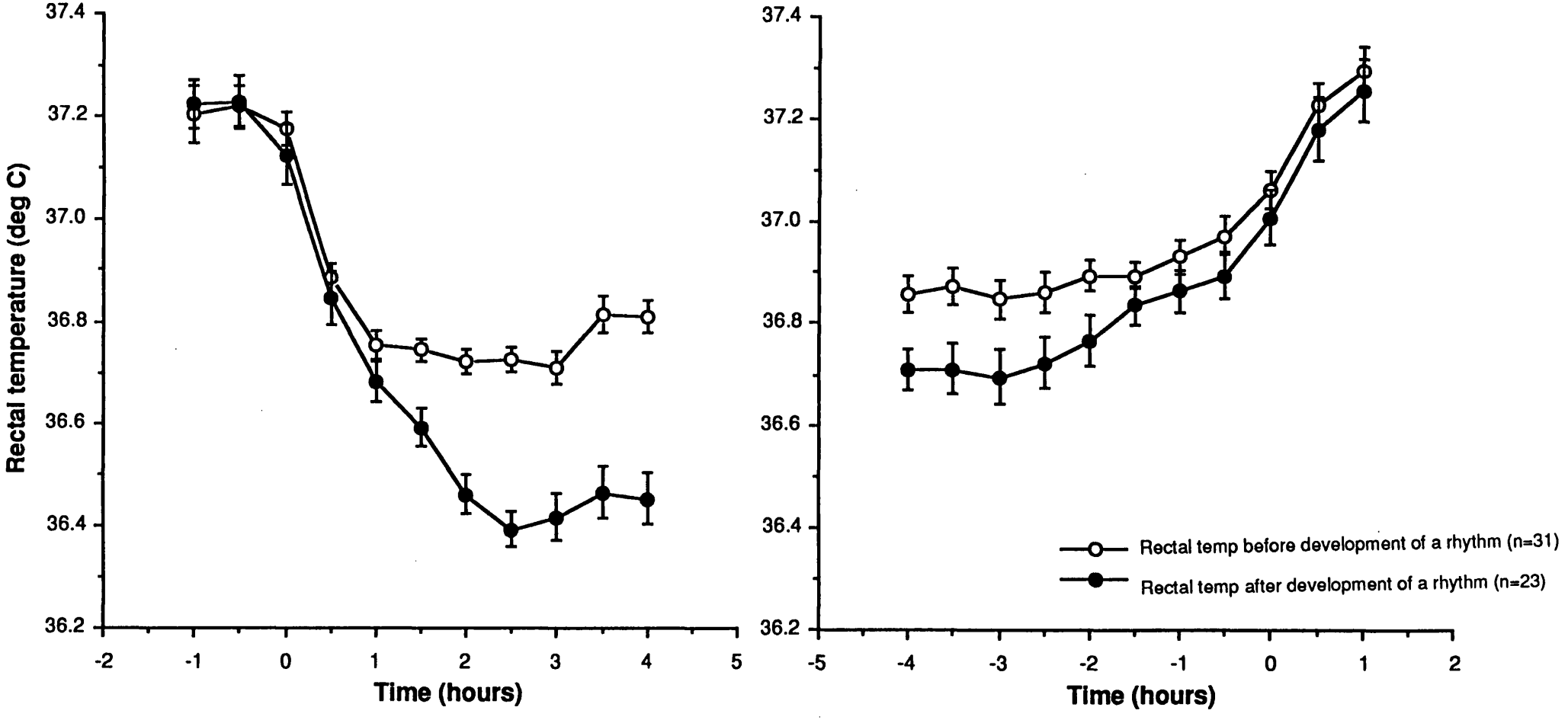


Figure 8:1 Averaged rectal temperature for the two weeks 'pre-maturity' and two weeks 'post-maturity'

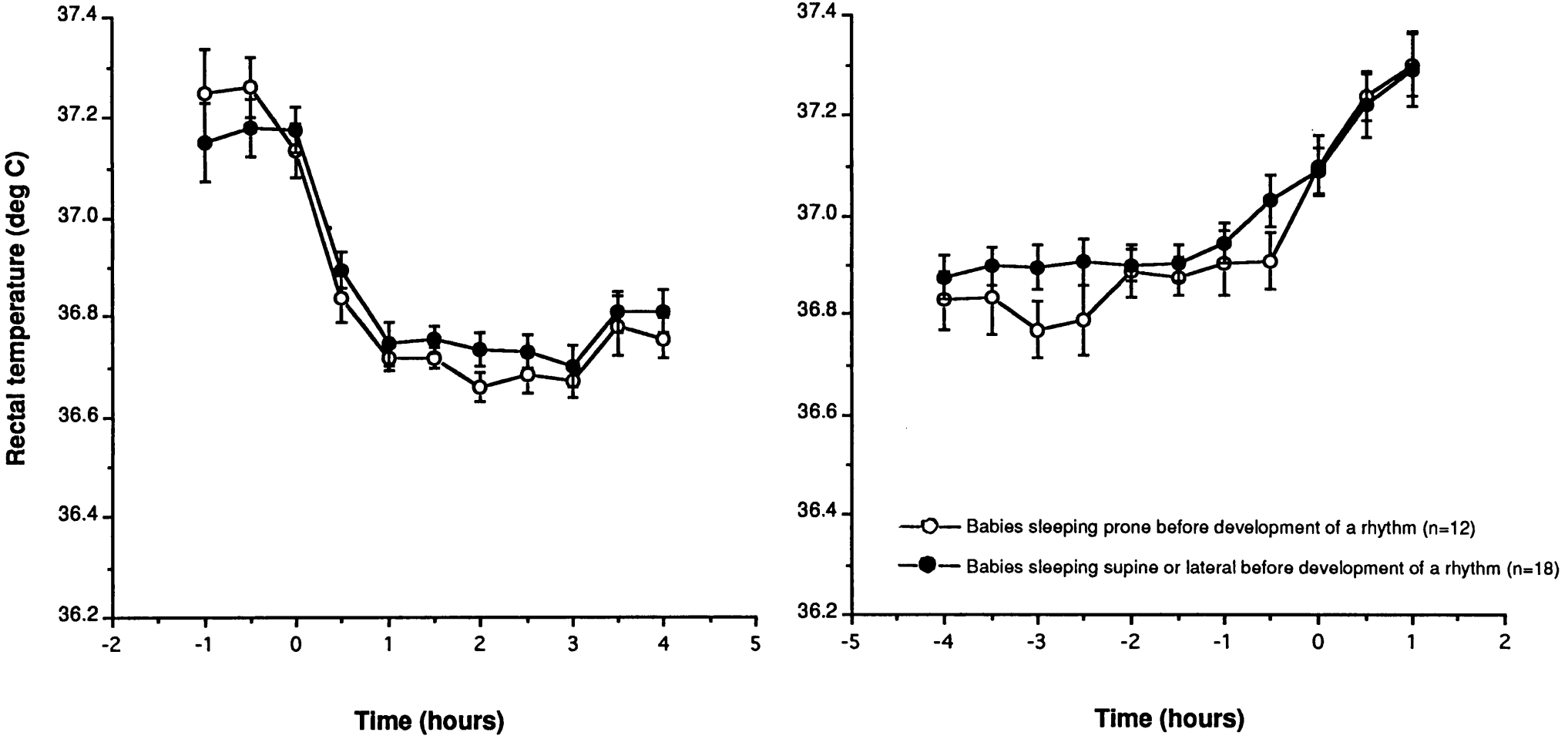


Figure 8:2 Averaged rectal temperature of babies before maturity comparing sleeping postion

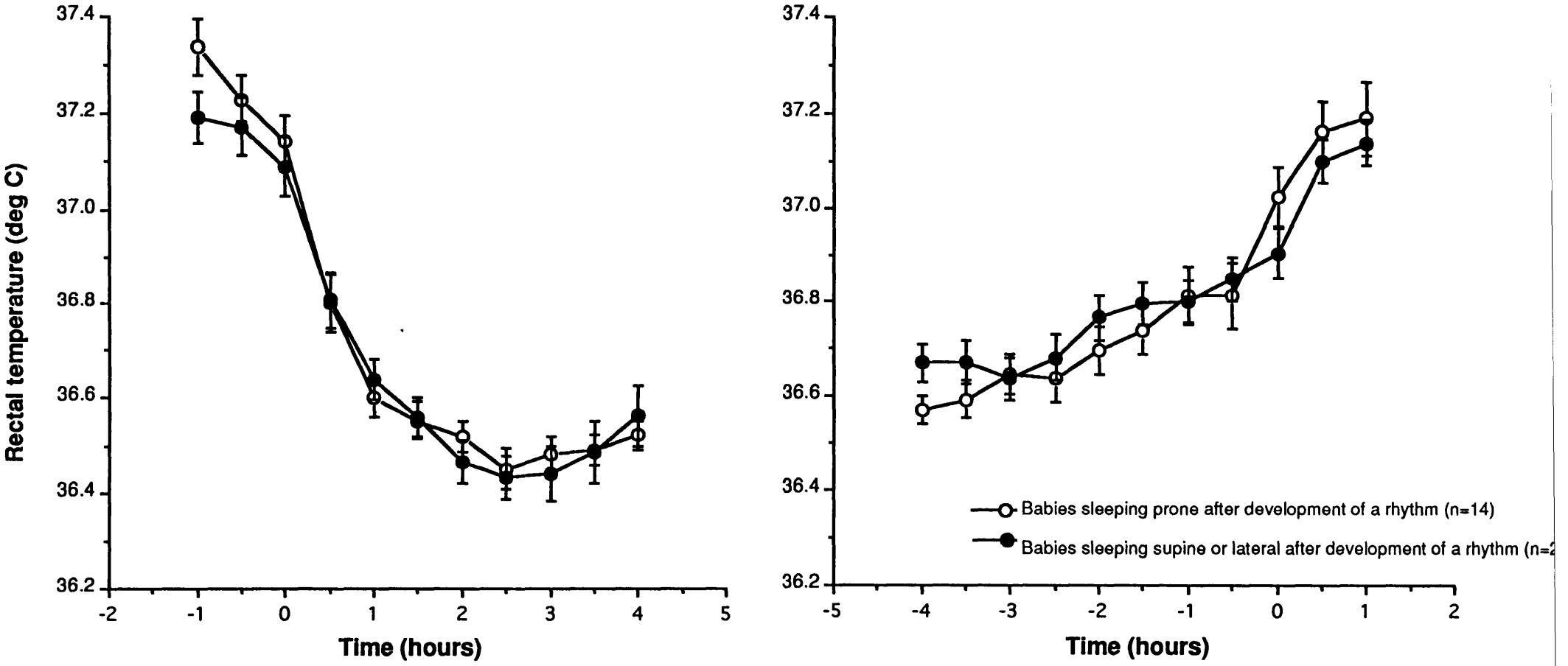


Figure 8:3 Averaged rectal temperature of babies after maturity comparing sleeping position

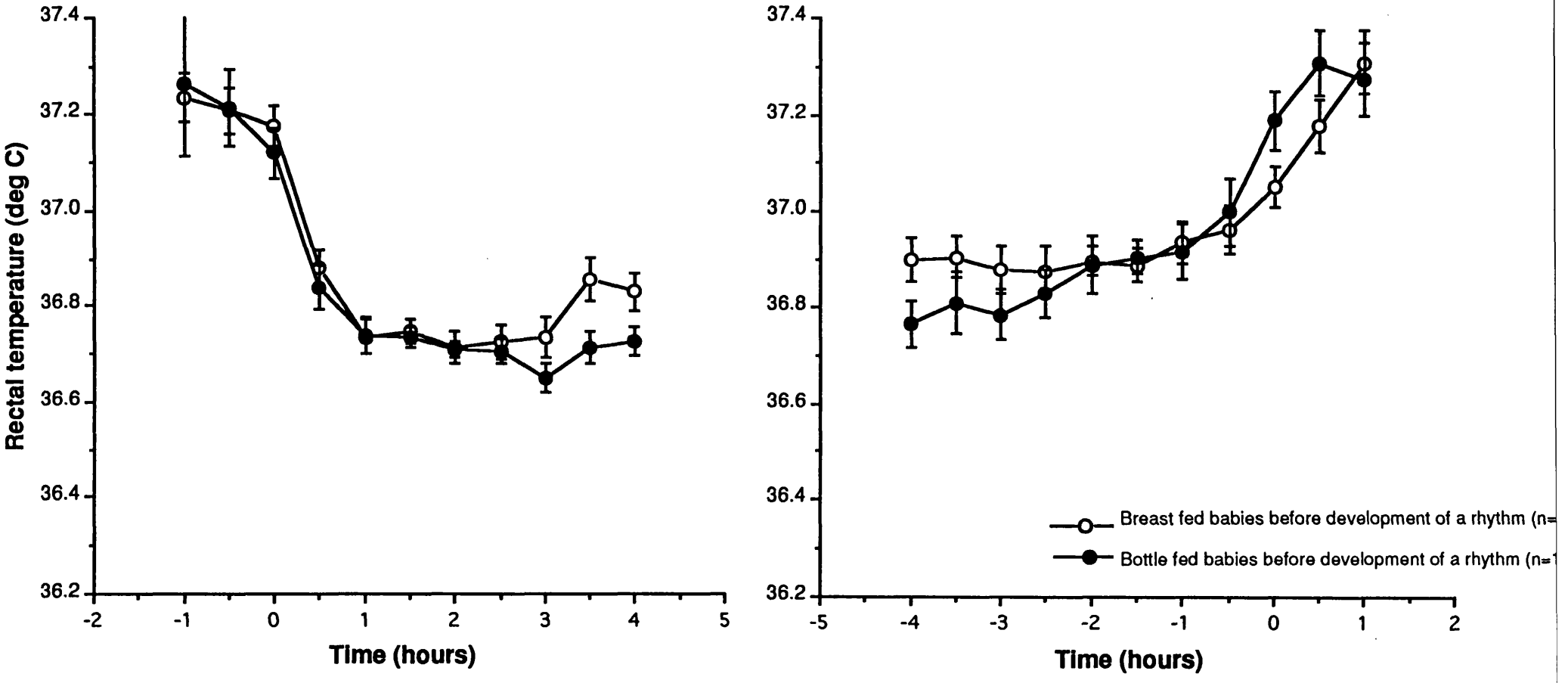


Figure 8:4 Averaged rectal temperature of babies before maturity comparing method of feeding

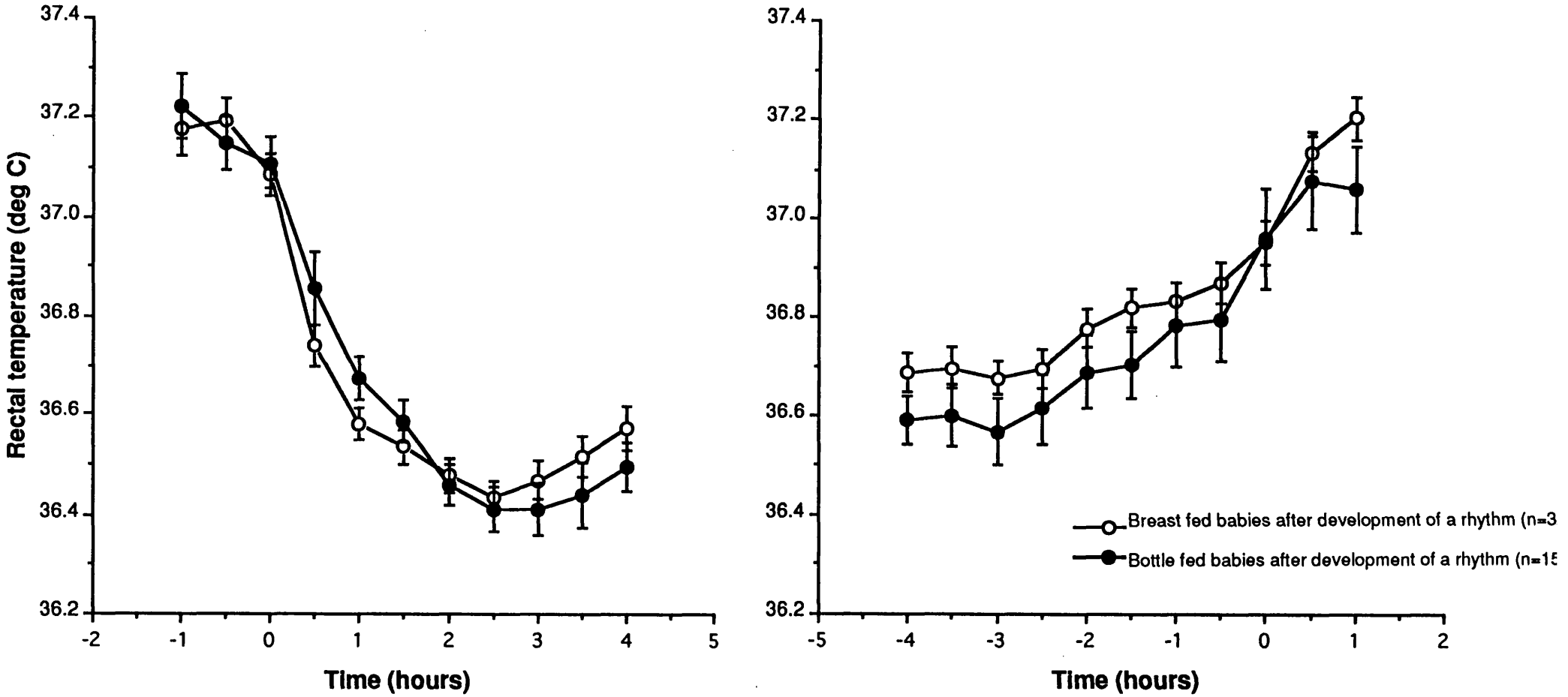


Figure 8:5 Averaged rectal temperature of babies after maturity comparing method of feeding

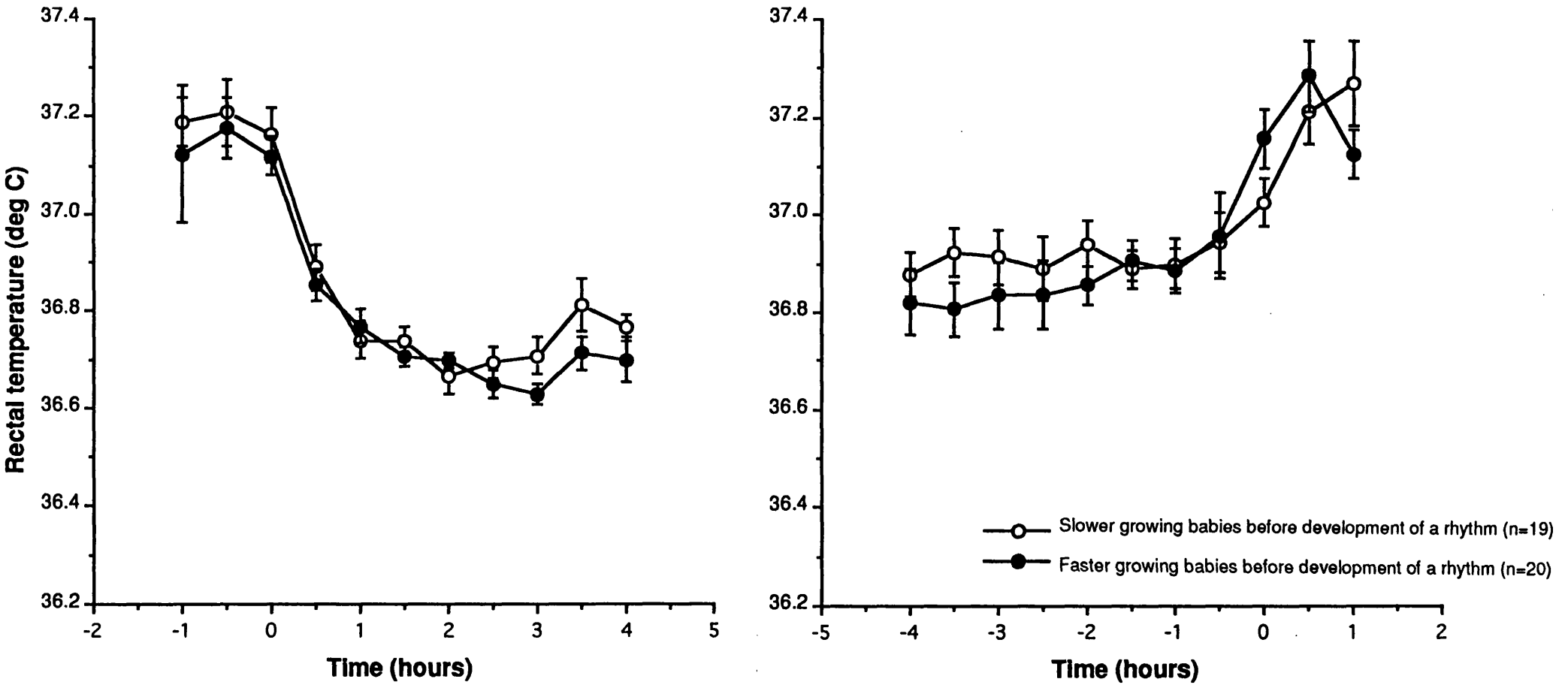


Figure 8:6 Averaged rectal temperature of babies before maturity comparing mean weekly weight gain

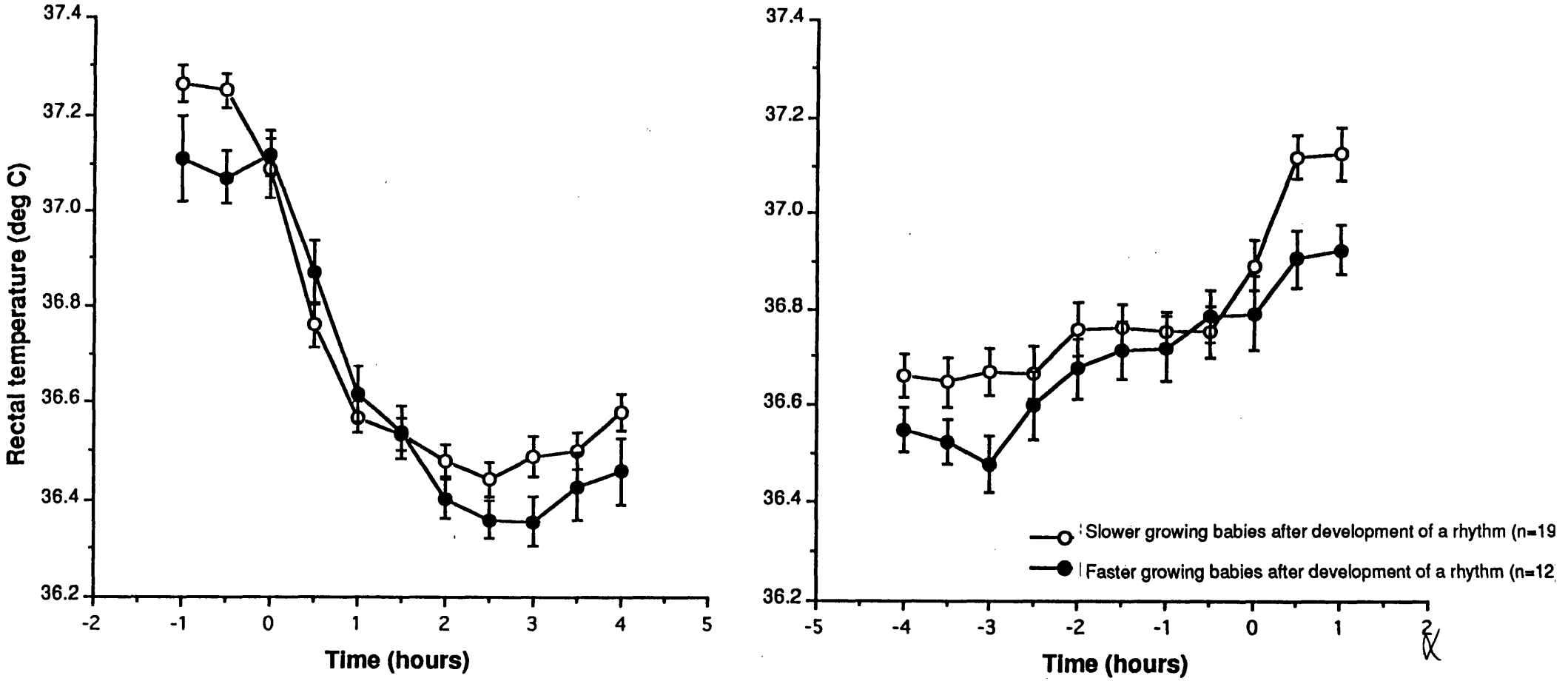


Figure 8:7 Averaged rectal temperature of babies after maturity comparing mean weekly weight gain

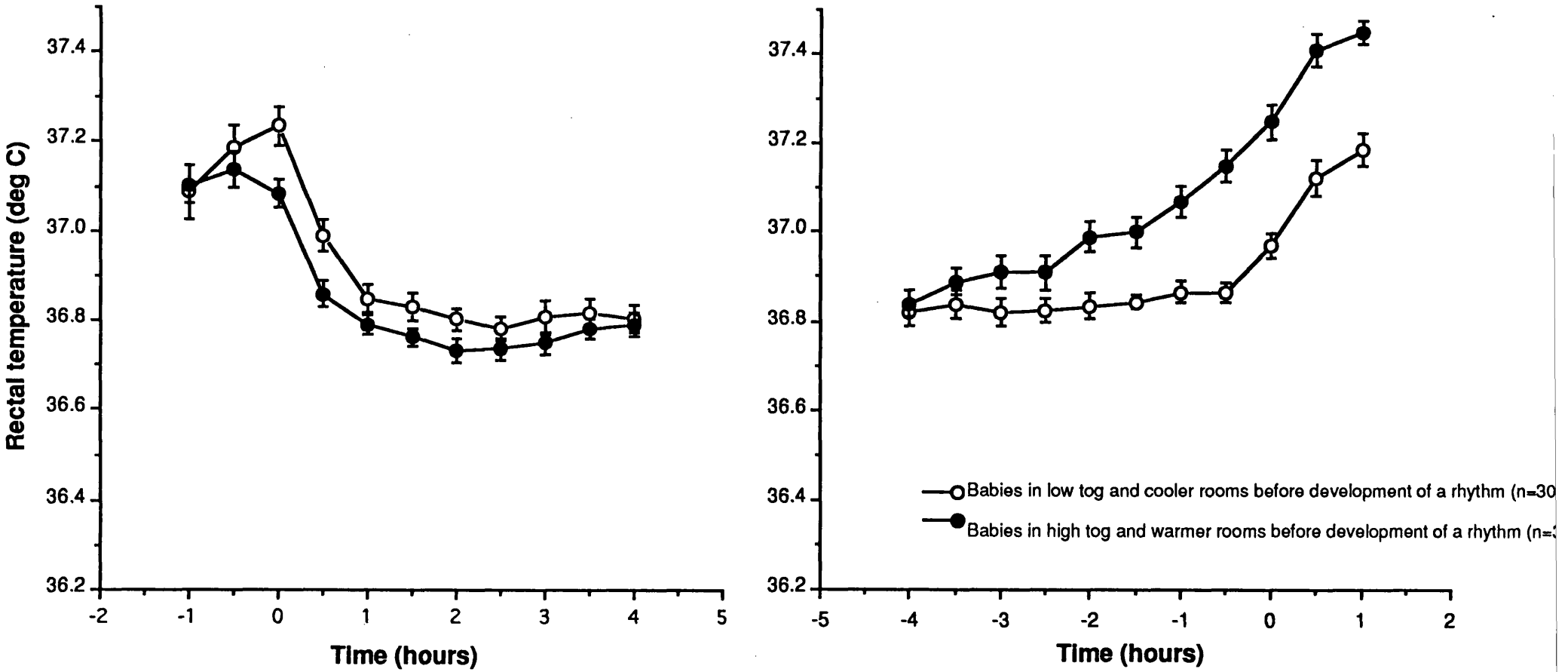


Figure 8:8 Averaged rectal temperature of babies before maturity comparing thermal environment

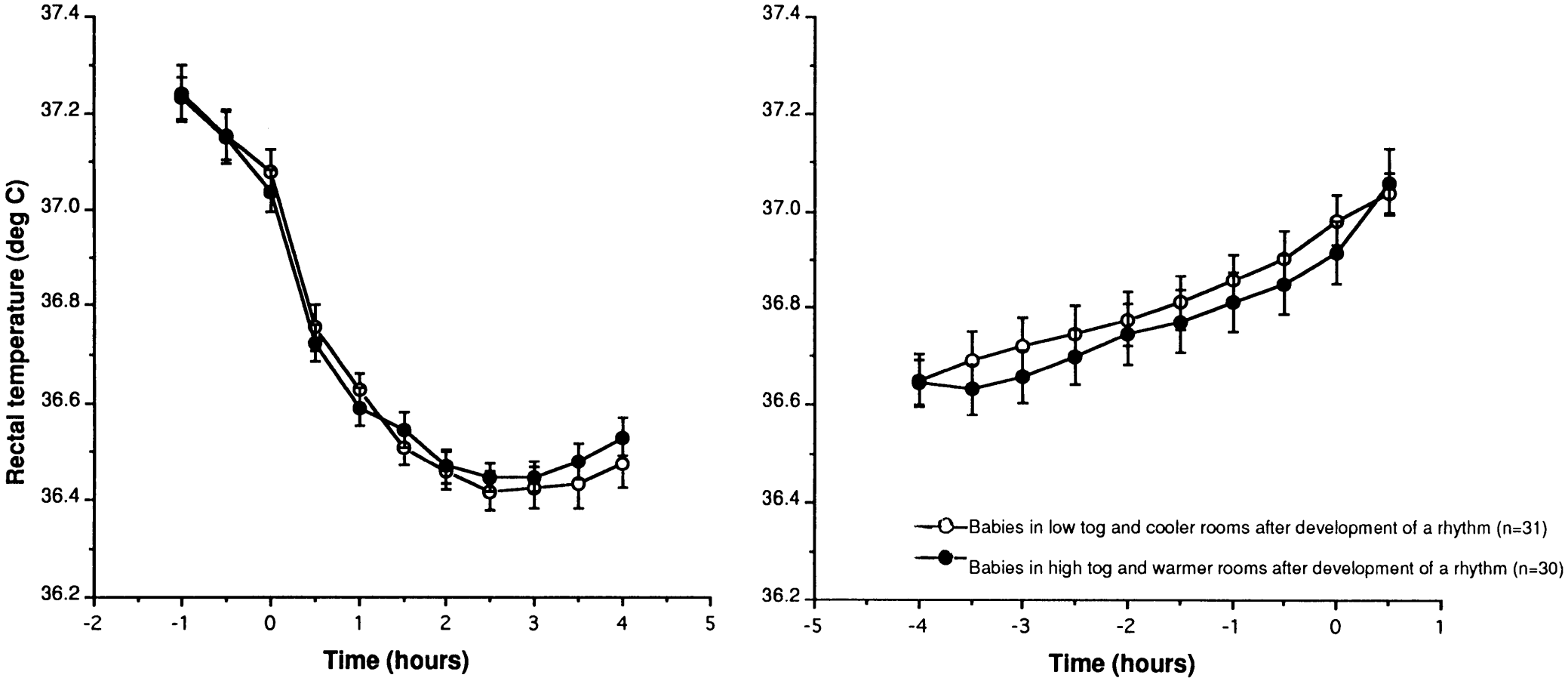


Figure 8:9 Averaged rectal temperature of babies after maturity comparing thermal environment

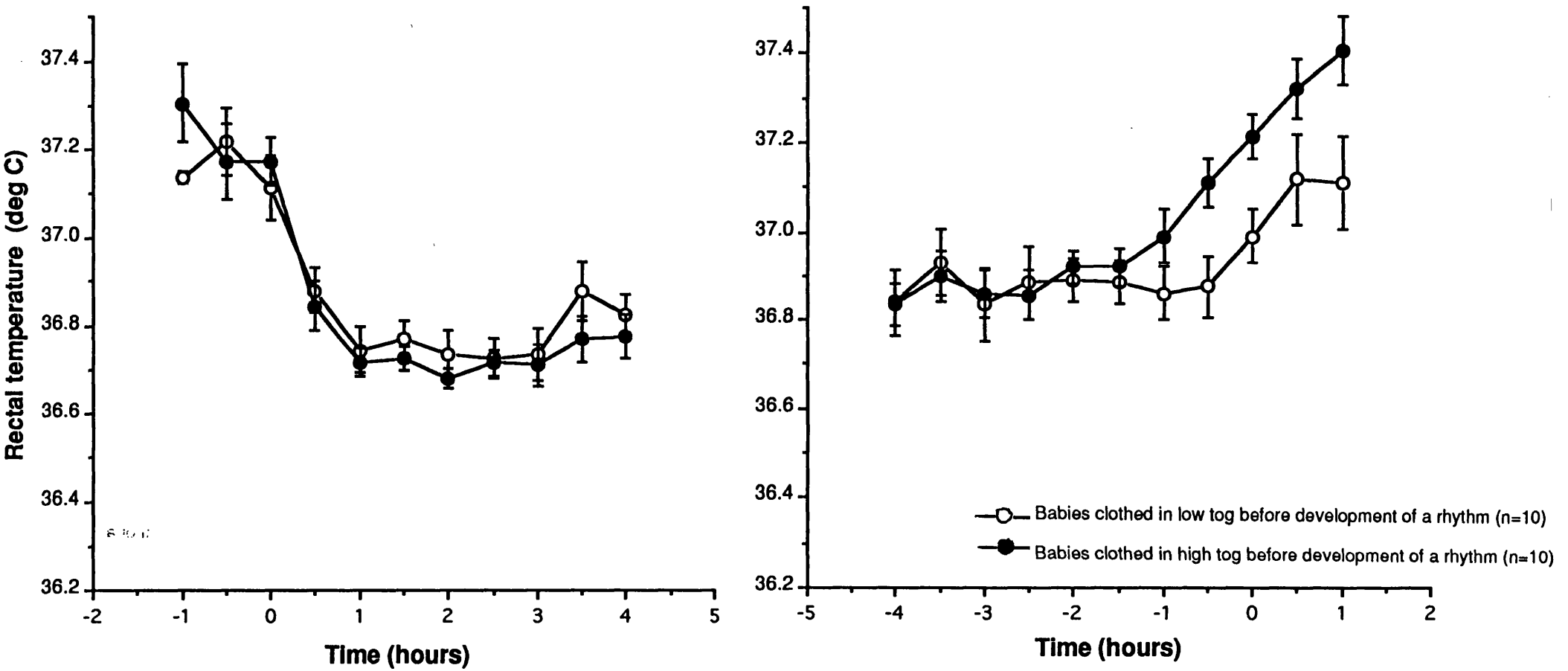


Figure 8:10 Averaged rectal temperature of babies before maturity comparing levels of clothing and bedding

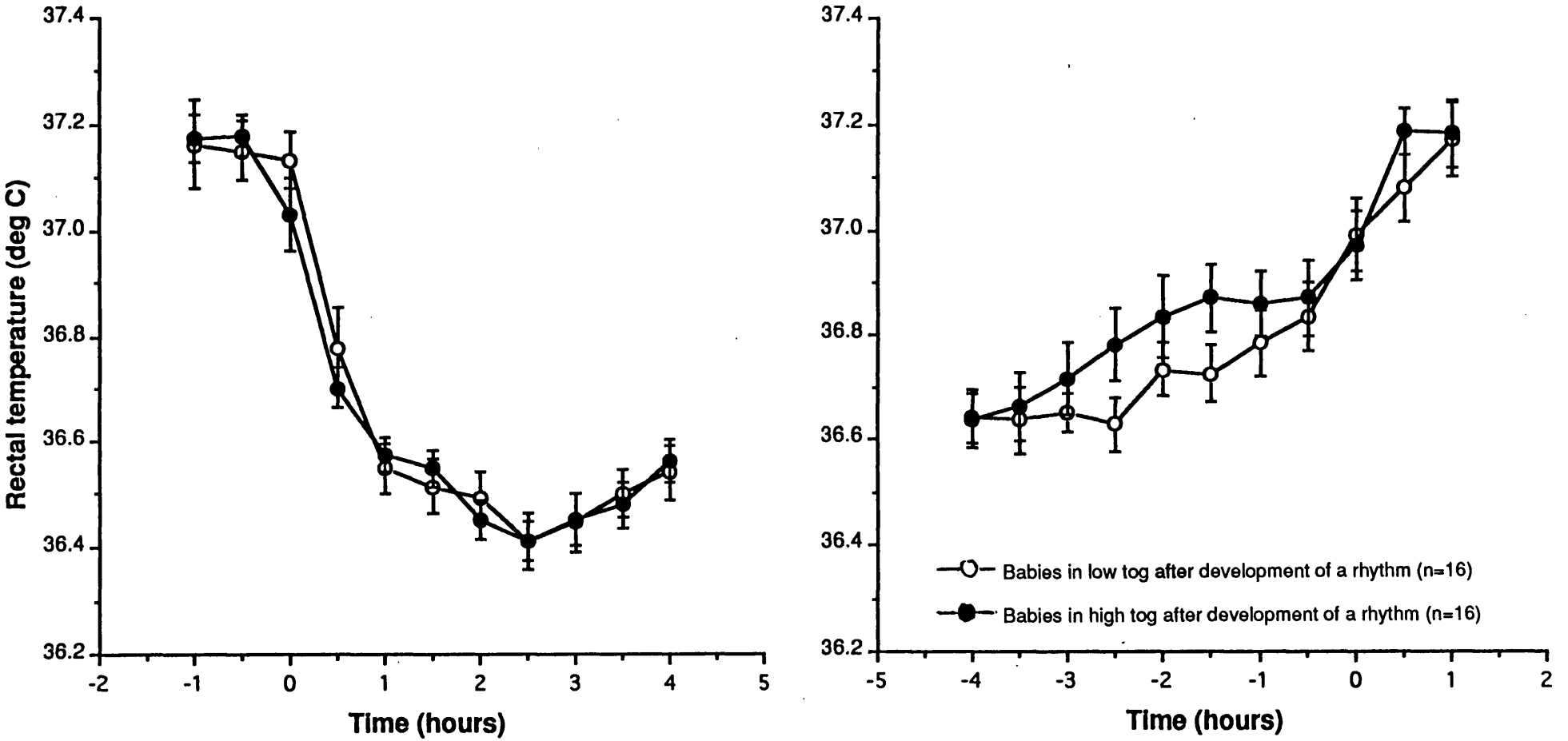


Figure 8:11 Averaged rectal temperature of babies after maturity comparing level of clothing and bedding

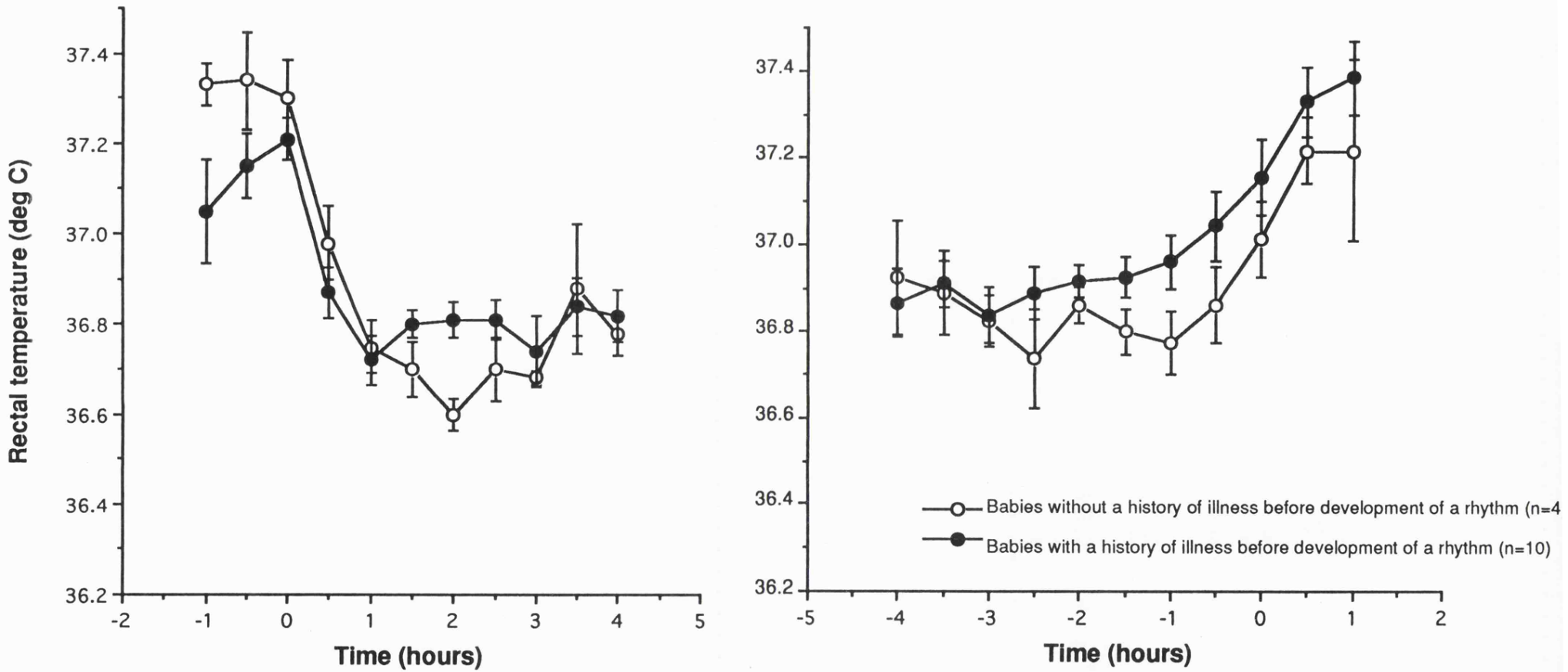


Figure 8:12 Averaged rectal temperature of babies before maturity comparing incidence of illness

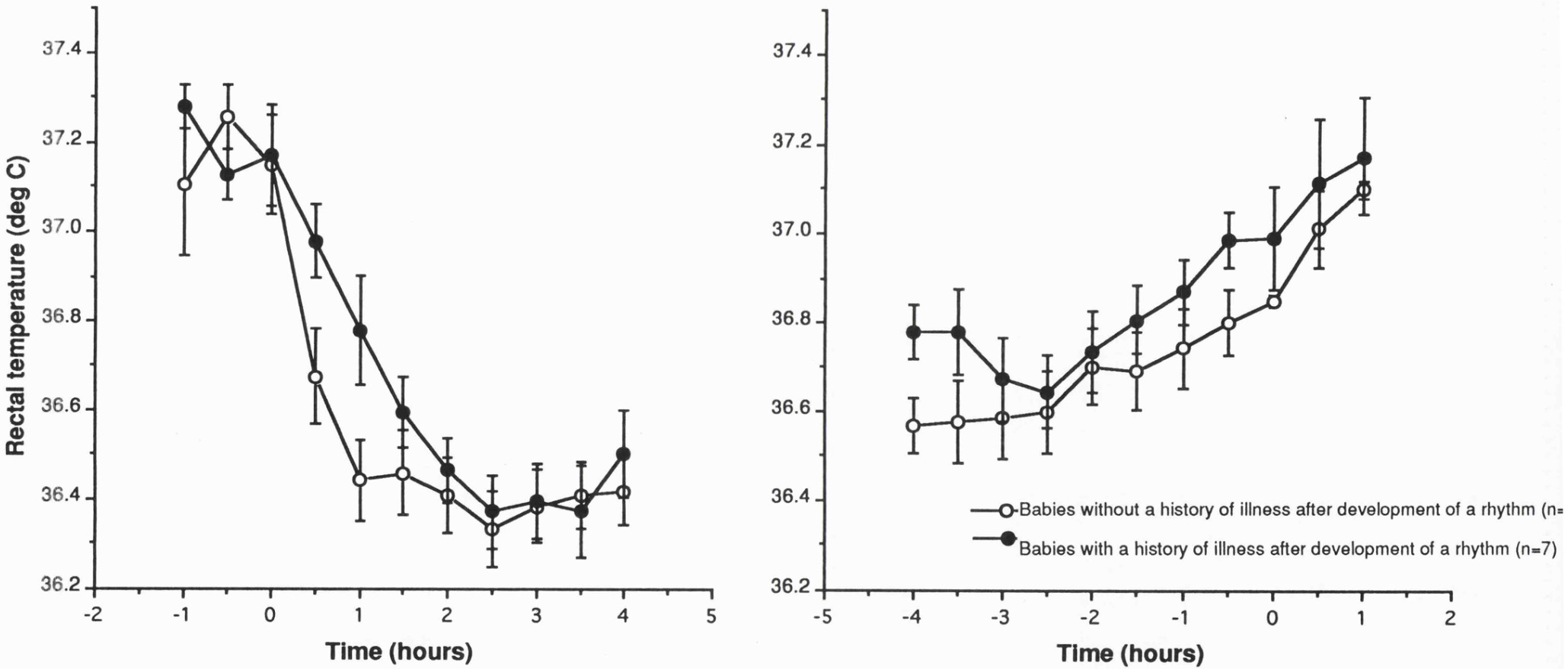


Figure 8:13 Averaged rectal temperature of babies after maturity comparing incidence of illness

Summary of Aspects of Care and Health of the Baby Affecting the Night-Time Minimum of Rectal Temperature

1 A warmer thermal environment raised the night-time rectal temperature pattern of babies over the last four hours of the night, and after waking.

2 Breast fed babies have a higher rectal temperature for parts of the night in stage two of the rhythm. Once in stage three or 'post-rhythm' development, breast fed babies, slower growing babies and children who suffered two episodes of illness before twelve weeks of age had higher rectal temperature patterns than their contemporaries, particularly for the latter part of the night.

CHAPTER NINE

ASPECTS OF CARE AND HEALTH OF THE BABY AFFECTING THE NIGHT-TIME MINIMUM OF HEART RATE

Heart rate was analysed in the same way as rectal temperature. Rather than using the age of the baby the data were compared in stages two and three of the rectal temperature, which were before and after the night-time rectal temperature fell to below 36.5°C and the heart rate slowed to below 115 bpm with sleep. The data were then graphed and studied for the four hours after bedtime, and for the four hours before the baby awoke. As there are a number of graphs they are presented at the end of the chapter.

The babies were also divided into groups using the same formulae as for the temperature readings, and analysed using the Two way Analysis of Variance with repeated measures (see **Chapter Eight**).

'Pre' and 'Post' Rhythms

As with rectal temperature there was a dramatic difference between night-time heart rate in stage two and stage three. Figure 9:1 illustrates the significant difference between the heart rate for the two weeks pre-rhythm when compared to the two weeks immediately post-rhythm; all through the night the heart rate was on average ten beats per minute higher before the pattern of rectal temperature changed with night-time sleep, than afterwards (Two way Analysis of Variance with repeated measures, $F=57.83$ with 1, 368 df, $p<0.001$ and 39.79 with 1,368 df, $p<0.001$).

Sleeping Position of the Baby

The babies' heart rate in stage two was unaffected by sleeping position (figure 9:2), a finding similar to that of the affect of sleeping position on rectal temperature.

Figure 9:3 illustrates, however, that in stage three those babies sleeping prone had significantly higher heart rates for the four hours before waking (Two way Analysis of Variance with repeated measures, $F=18.48$ with 1, 216 df, $p<0.001$).

Method of Feeding

In stage two, heart rate patterns with sleep were not influenced by whether the babies were breast fed or bottle fed for the first six weeks of life (figures 9:4), findings in contrast to the studies on rectal temperature curves. Figure 9:5 illustrates, however, the significantly higher heart rate of breast fed babies in stage three for the first four hours of the night (Two way Analysis of Variance with repeated measures, $F=9.00$ with 1, 192 df, $p<0.01$).

Weight Gain

Babies' average weekly weight gain was associated with different heart rate patterns whilst asleep at night in stage two, but not stage three. This finding is in contrast to the rectal temperature analysis.

In stage two the slower growing babies had significantly faster heart rates for the first four hours of sleep (Two way Analysis of Variance with repeated measures, $F=16.73$ with 1, 136 df, $p<0.001$)(figure 9:6).

The graphs (figure 9:7) of the babies' heart rates in stage three illustrate that although the breast fed babies' heart rate was higher, this was not significant.

Illness in the Baby

Unfortunately, the amount of heart rate data collected was very small. The mean heart rates of those babies who had suffered two episodes of illness before twelve weeks of age were compared with those who had none, and from the small amount of data collected, it would appear that there were no long term effects on the night-time patterns of heart rate from previous illness, in either stage two or stage three, a finding once again contrary to the rectal temperature curves.

The Thermal Environment

Analysis of the effect of thermal environment on heart rate was calculated in the same three ways as for rectal temperature (see **Chapter Eight).**

As expected from the analysis of the rectal temperature patterns, the largest affect on heart rate rhythms was from a combination of high room temperature and higher levels of clothing and wrapping. Those babies in stage two who were dressed in more clothing and bedding and in warmer rooms had heart rates that slowed significantly more quickly, and to a lower level, over the first four hours of the night, than those with less coverings and in cooler rooms (Two way Analysis of Variance with repeated measures, $F=6.79$ with 1, 240 df, $p<0.01$). Their heart rate also continues at a significantly lower level for the rest of the night (Two way Analysis of Variance with repeated measures, $F= 25.67$ with 1, 240 df, $p<0.001$)(figure 9:8).

In stage three this trend continued and those babies in more clothing and wrapping and a higher room temperature had lower heart rates all through the night, although this was not significant (figure 9:9).

Figure 9:10 illustrates that, in stage two, the effect of clothing and wrapping alone was similar to that of a combination of coverings and room temperature, as those babies who were more heavily wrapped had significantly lower heart rates all through the night (Two way Analysis of Variance with repeated measures, $F=6.48$ with 1, 208 df, $p<0.025$ and $F=8.52$ with 1, 208 df, $p<0.01$).

Figure 9:11 shows that in stage three those babies in more clothing and bedding had significantly lower heart rates for the first four hours after bedtime (Two way Analysis of Variance with rpeated measures, $F=6.60$ with 1, 208 df, $p<0.025$). Similarly to the results of the studies on rectal temperature, the night-time patterns of heart rate in babies both pre- and post-rhythm were unaffected by ambient temperature alone (figures 9:12 and 9:13).

Discussion

These results reinforce the hypothesis that the breast fed and slower growing babies had higher metabolisms or were more active during sleep and unable to lay down as much energy for growth. Perhaps, however, they had less slow wave or quiet sleep until later in the night. Goldie (1964 - cited by Scopes, 1966) reports that the rate of oxygen consumption is always higher in the light phase of sleep (REM sleep), the mean difference being an increase of 15%. Beck, Reinhardt, Kendel and Schmidt-Kessen (1976) report, too, that the phasic secretion of growth hormone is associated with slow wave sleep stages three and four during the first two cycles of sleep. These may account for the babies growing more slowly. Other studies, however, have reported that growth hormone is not secreted in the same way in babies (for review see Minors and Waterhouse, 1981).

Sleep staging and analysis of metabolism by measurement of oxygen consumption were not done in this study, so further work needs to be carried out in order to test these hypotheses.

In contrast to expectations, those babies in warmer thermal environments had lower heart rates. Perhaps this was an indication of deeper sleep, which reinforces many parents' perceptions and old wives' tales that babies sleep better if well-wrapped. No correlation could be found between lower heart rates and sleep duration in this study.

Conclusions

It appears that heart rate is primarily influenced by the body temperature. Often the patterns of heart rate and temperature reacted similarly to a factor about the baby. Slower growth, for example, was associated with higher temperature and heart rate, and in stage three, breast fed babies had both higher rectal temperatures and heart rate. At other times, however, the patterns did not appear to be synchronised, perhaps indicating the effect of exogenous influences

on heart rate. Warmer thermal environment was associated with a lower rectal temperature and heart rate for the first four hours of the night, but with a higher temperature, and lower heart rate, for the second four hours. Temperature, too, was unaffected by laying prone, but raised the heart rate in stage three. Other studies (Petersen, Anderson, Lodemore, Rawson and Wailoo, 1991), however, report that after development of the rectal temperature rhythm, those babies laying prone tended to warm faster towards the end of the night, which is when heart rates were raised in this study. The higher rectal temperature reached significance from six hours after bedtime in babies laying prone in rooms over 18^{o}C, and covered in more than 15 tog.

Future research should consider that ambient temperature alone appeared to have little affect on heart rate, and additional measurements of thermal environment, such as clothing or humidity should be taken.

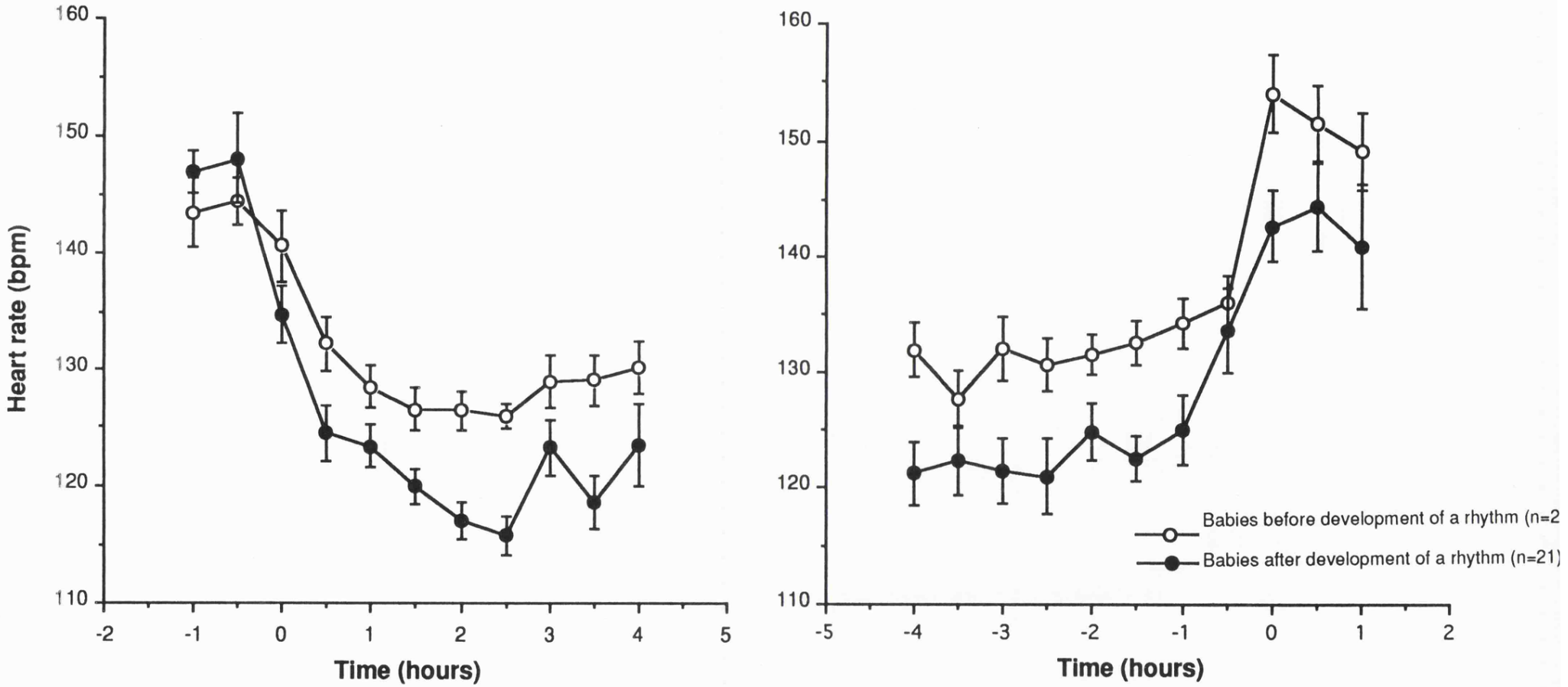


Figure 9:1 Averaged heart rate for babies before and after maturity of the temperature rhythm

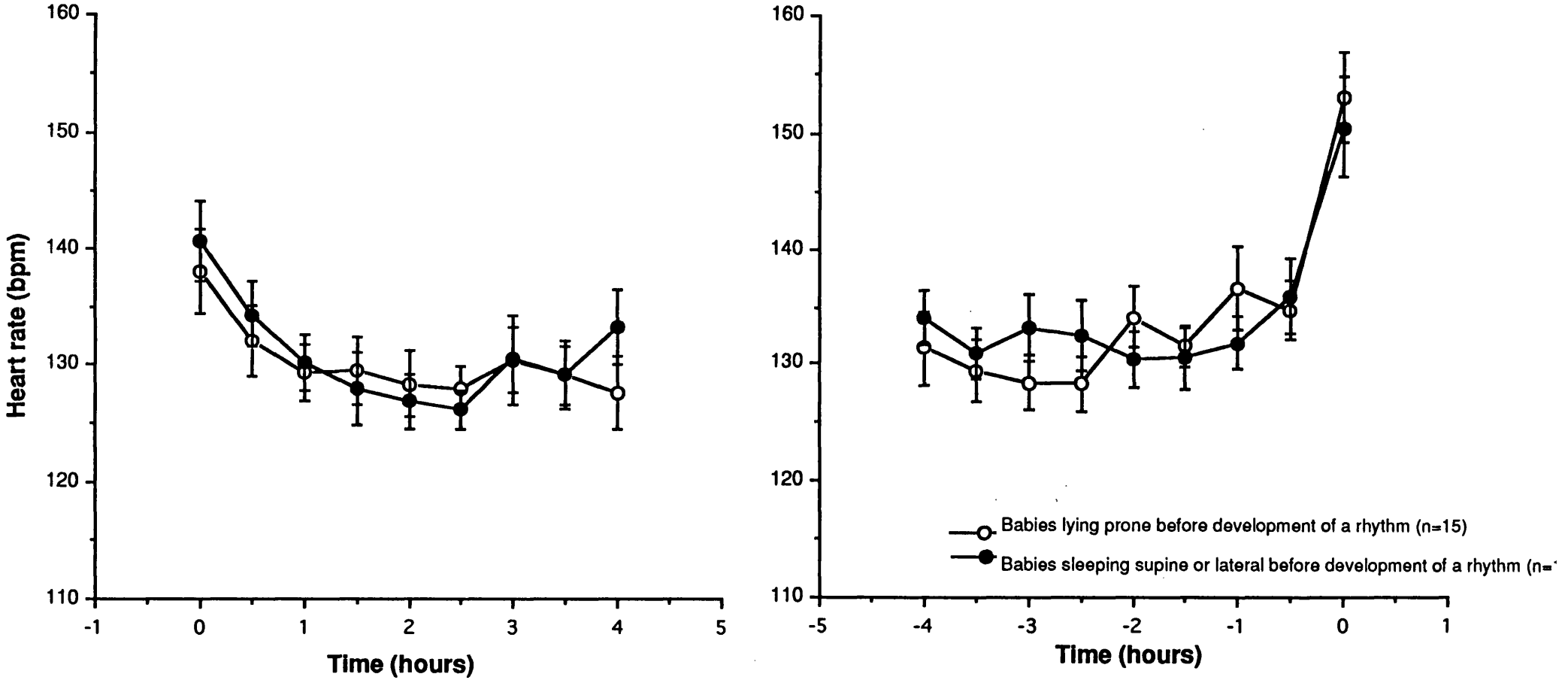


Figure 9:2 Averaged heart rate of babies before maturity comparing sleeping position

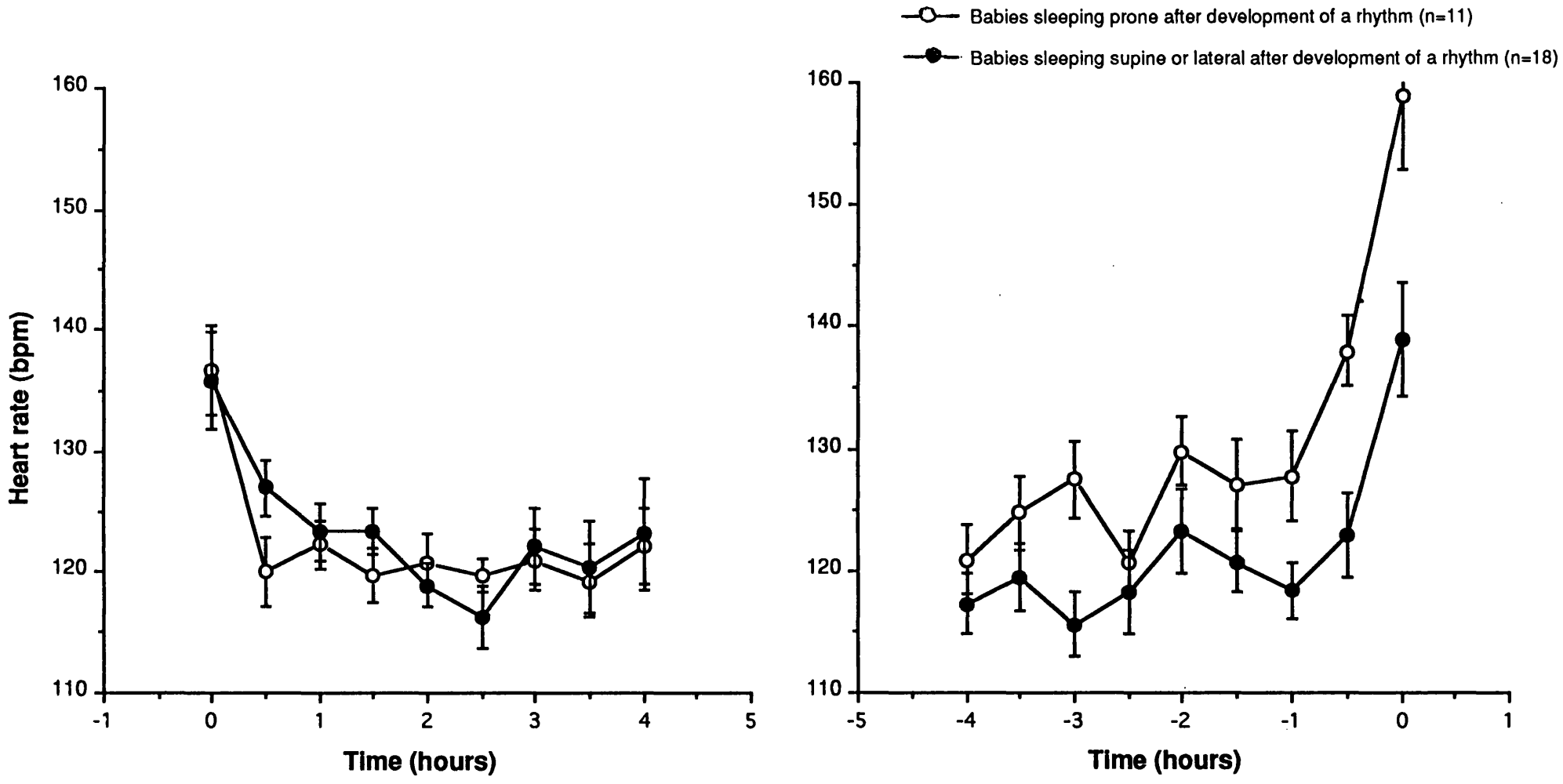


Figure 9:3 Averaged heart rate of babies after maturity comparing sleeping position

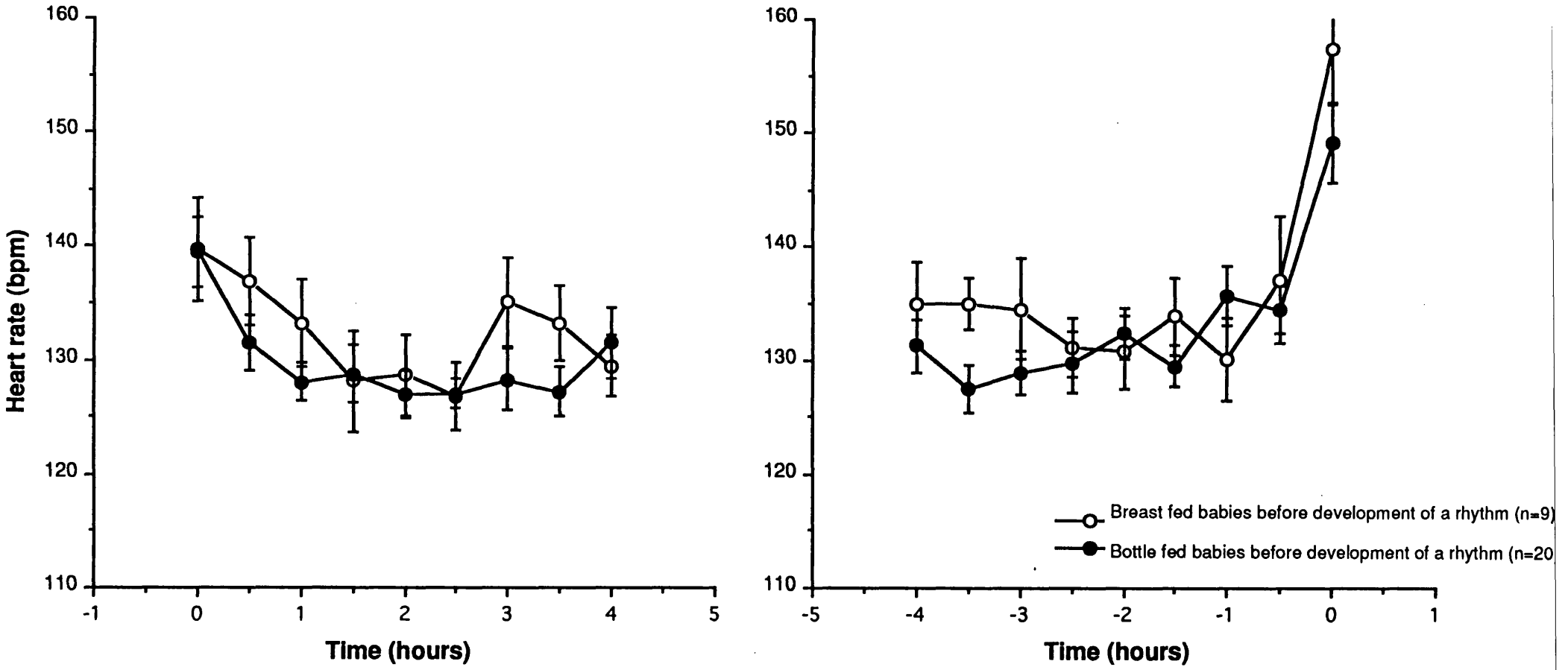


Figure 9:4 Averaged heart rate of babies before maturity comparing method of feeding

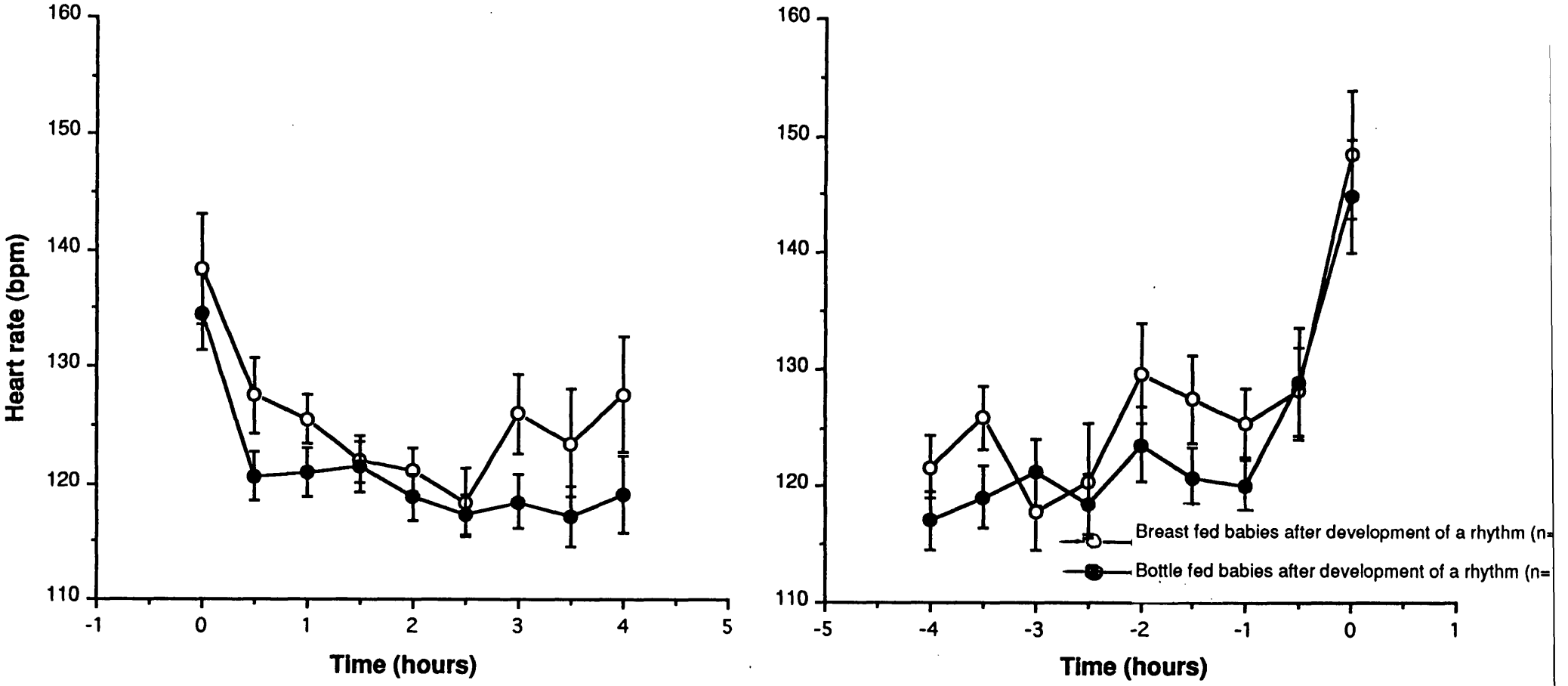


Figure 9:5 Averaged heart rate of babies after maturity comparing method of feeding

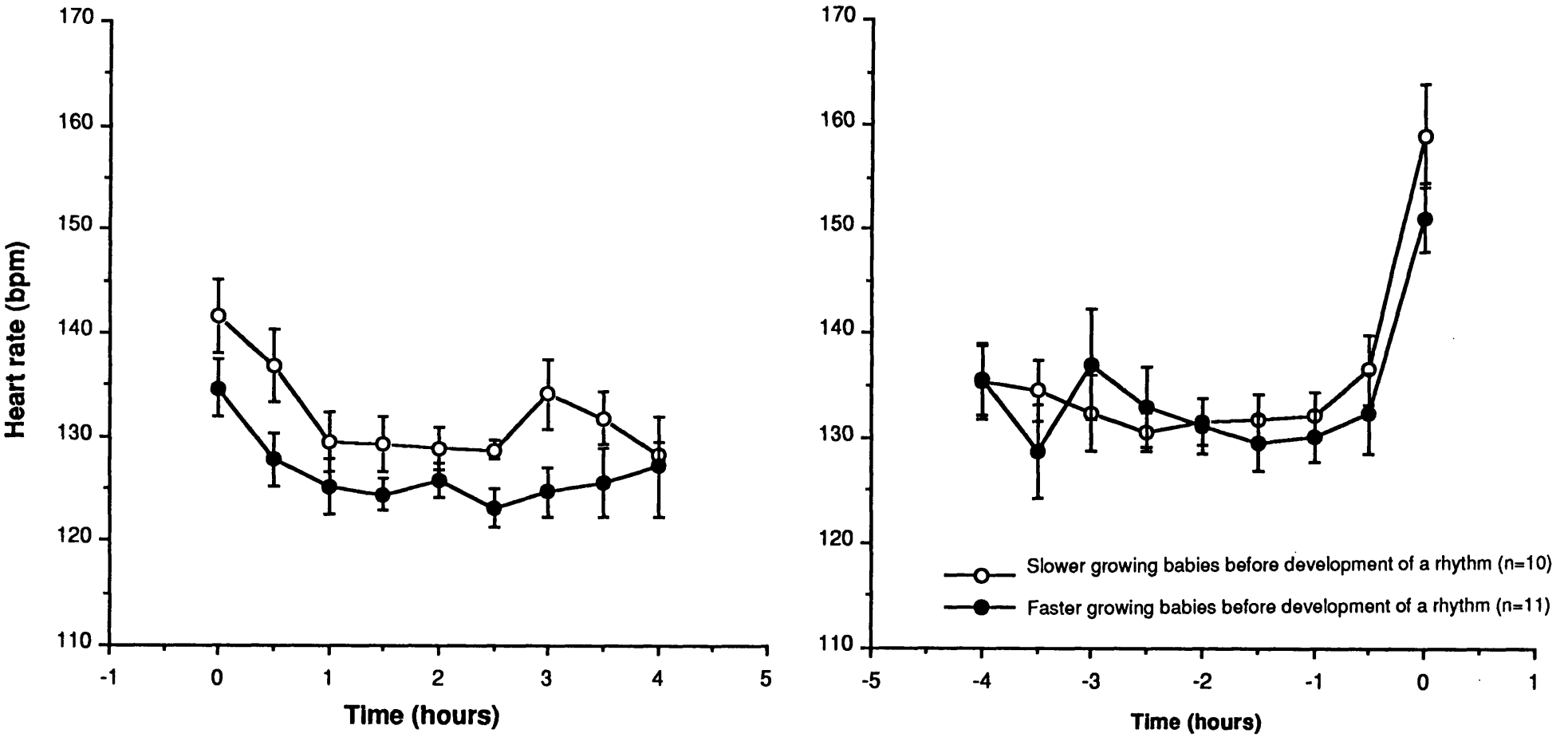


Figure 9:6 Averaged heart rate of babies before maturity comparing mean weekly weight gain

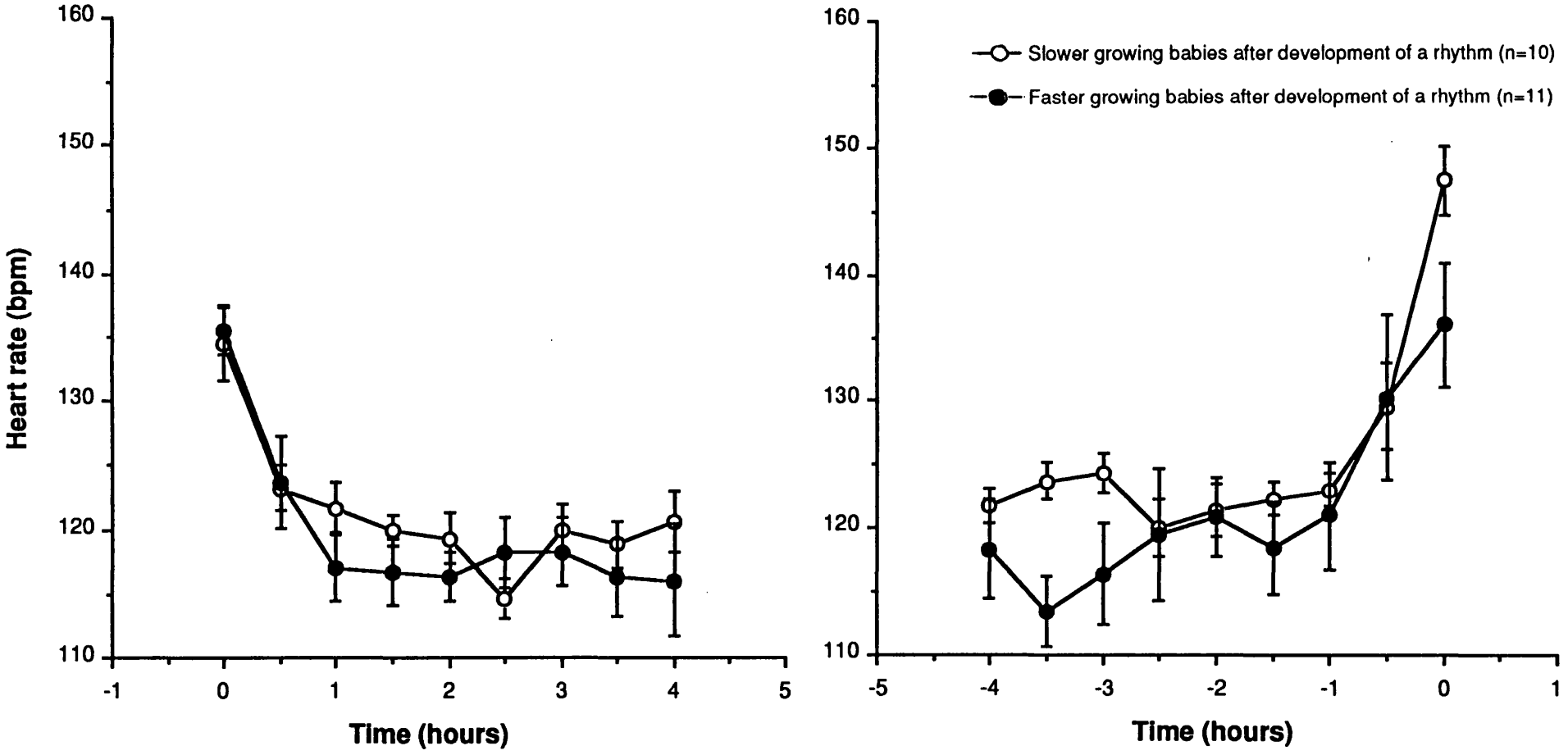


Figure 9:7 Averaged heart rate of babies after maturity comparing mean weekly weight gain

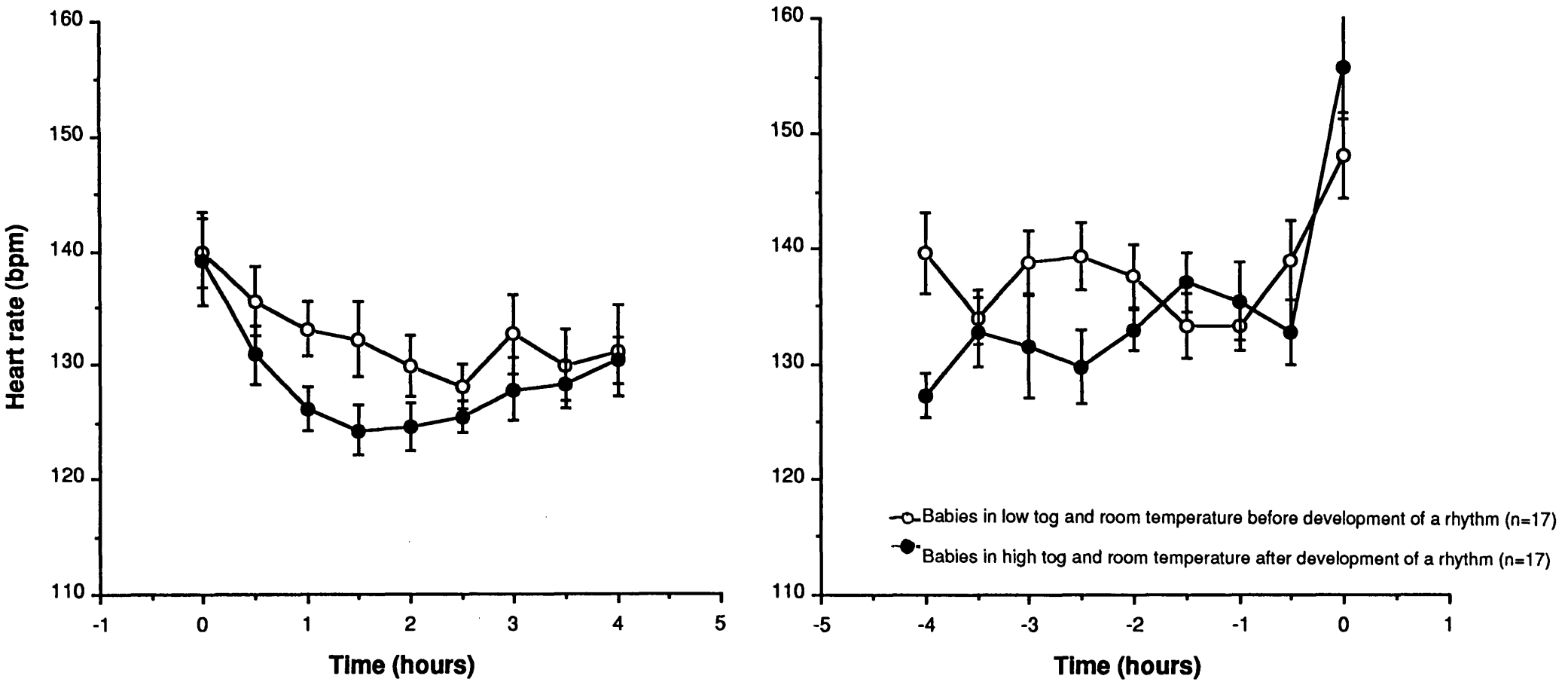


Figure 9:8 Averaged heart rate of babies before maturity comparing thermal environment

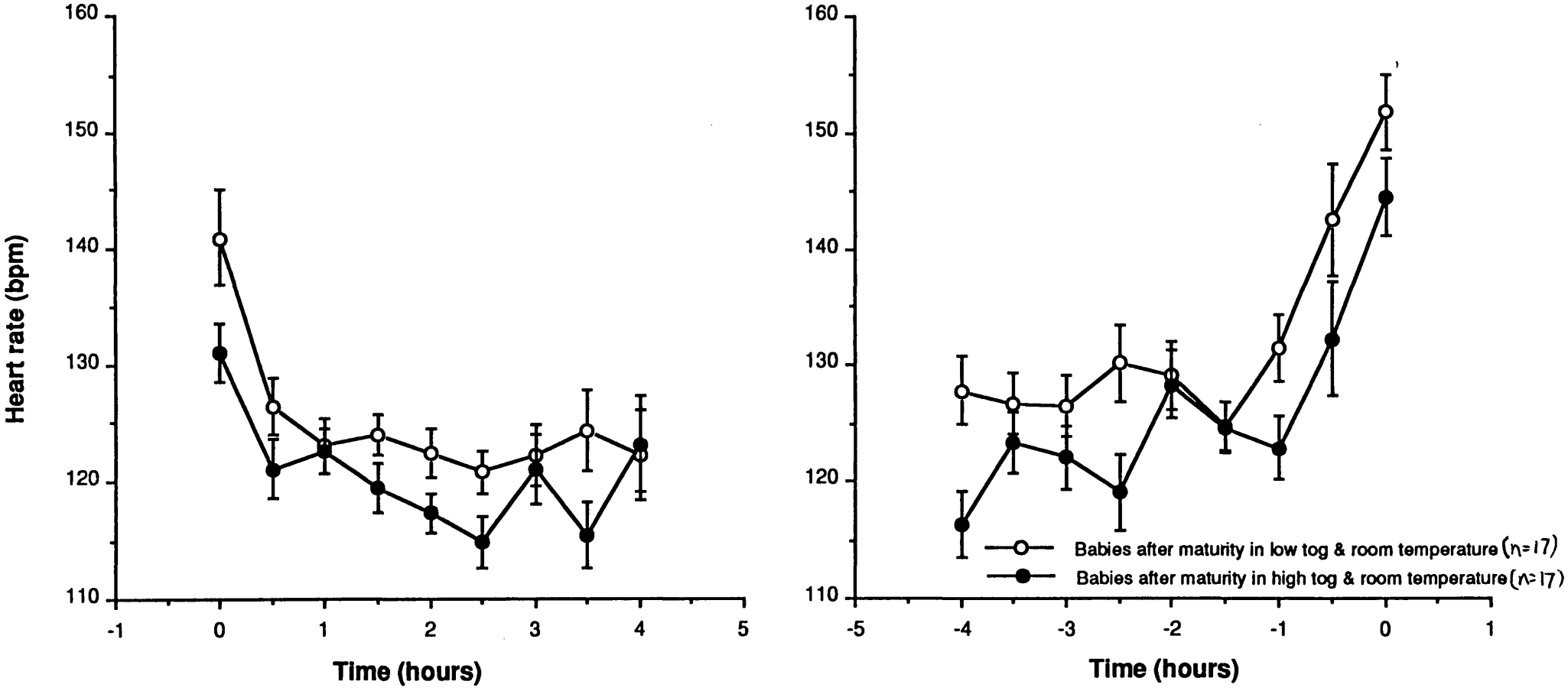


Figure 9:9 Averaged heart rate for babies after maturity comparing thermal environment

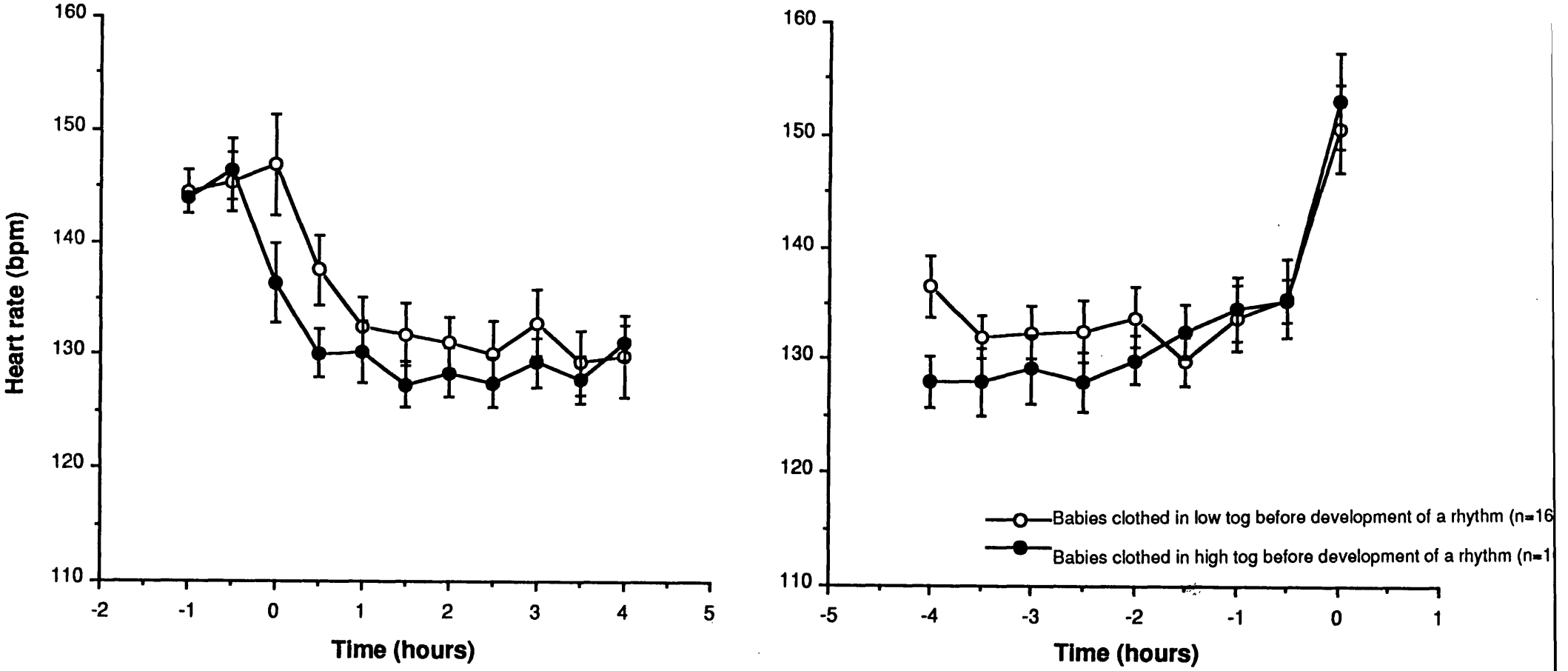


Figure 9:10 Averaged heart rate for babies before maturity comparing level of clothing and bedding

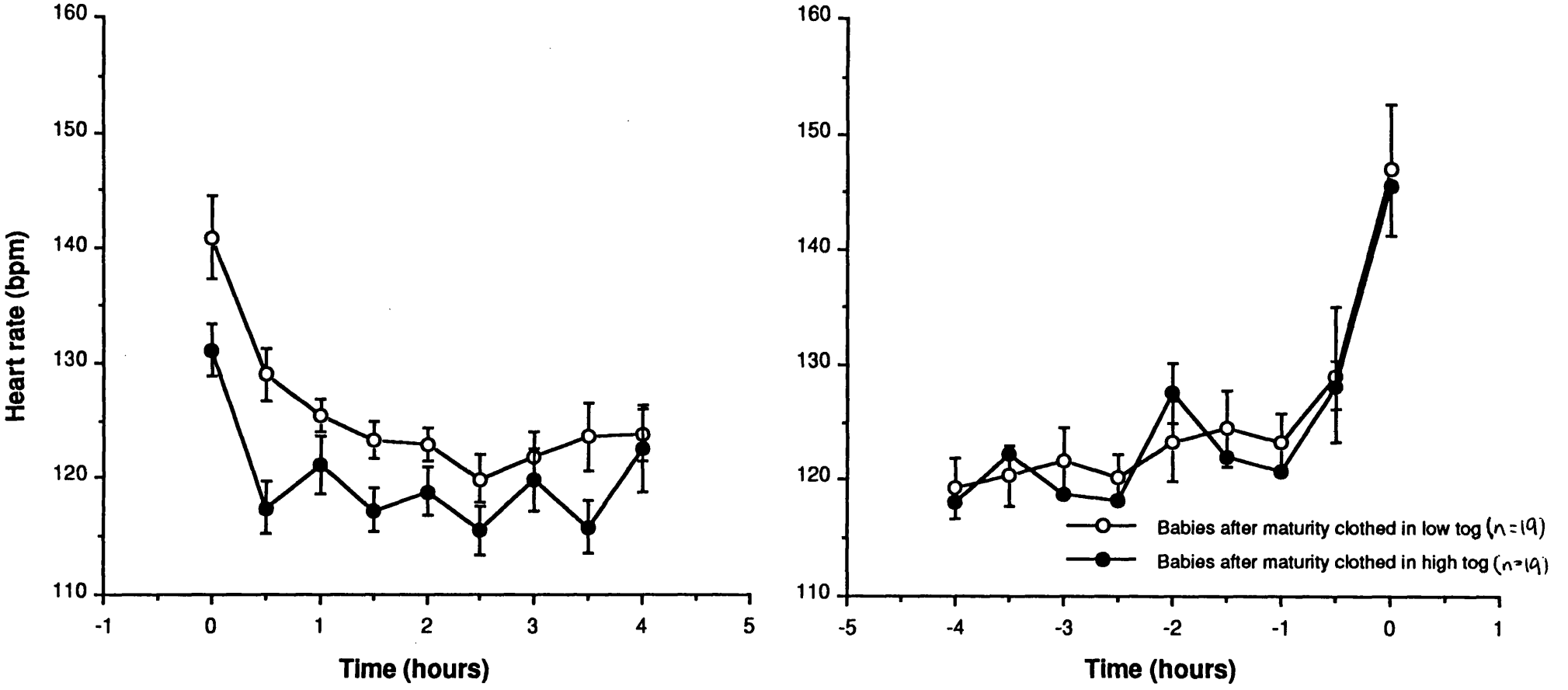


Figure 9:11 Averaged heart rate of babies after maturity comparing level of clothing and bedding

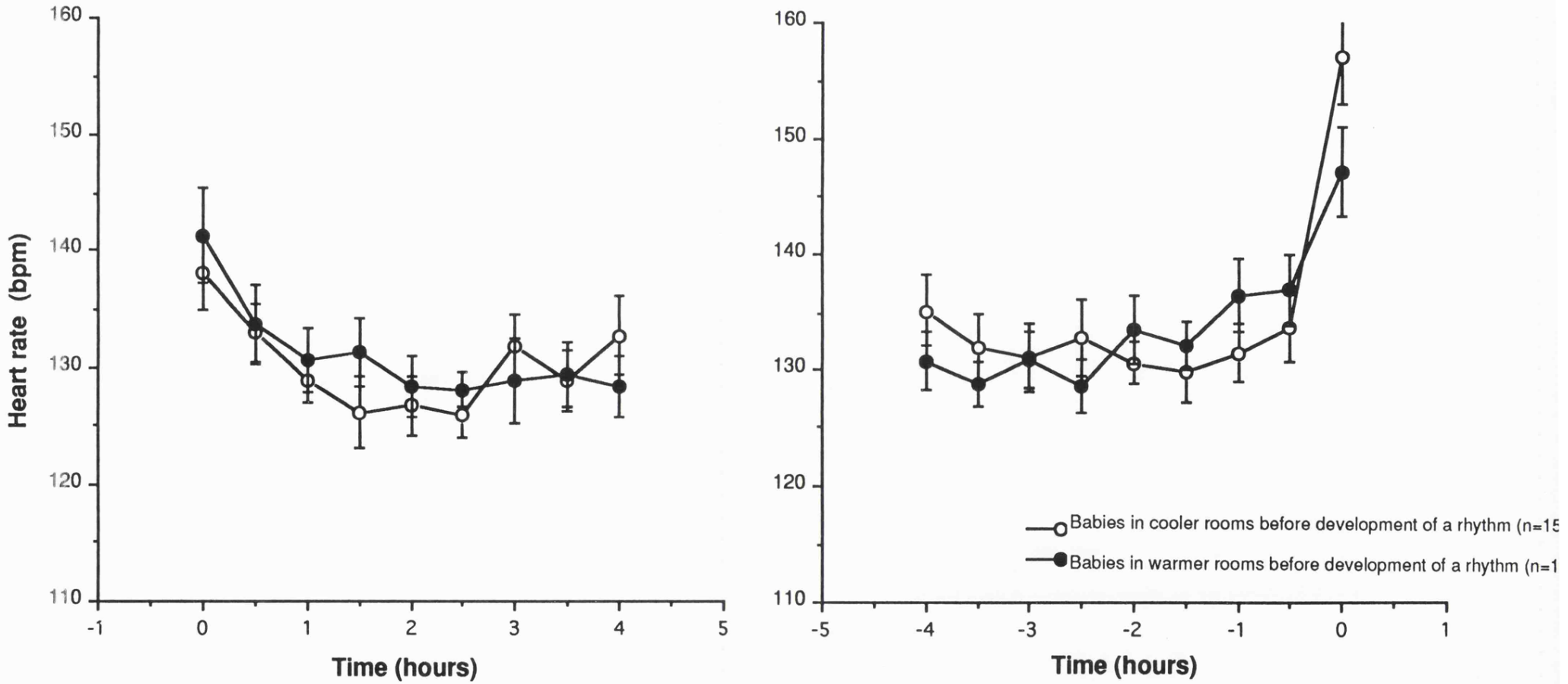


Figure 9:12 Averaged heart rate of babies before maturity comparing minimum room temperature

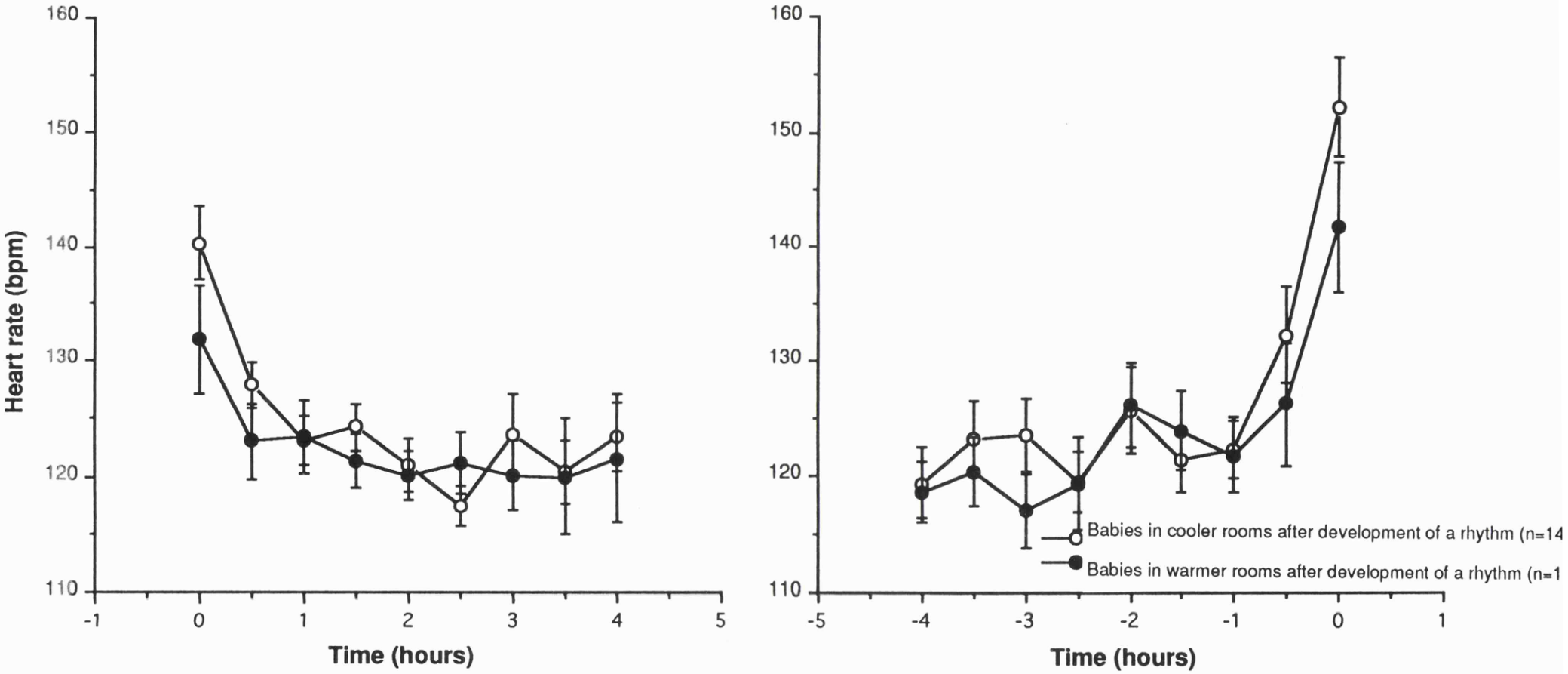


Figure 9:13 Averaged heart rate of babies after maturity comparing minimum room temperature

Summary of Aspects of Care and Health Affecting Heart Rate

1 During stage two of their development or pre-rhythm, slower growing babies had a faster heart rate for the first few hours of the night.

2 In stage three or post-rhythm those babies laying prone had higher heart rates towards the end of the night, and breast fed babies had higher heart rates for the first four hours of the night.

3 Babies, both before and after the development of the rhythm, who were in warmer thermal environments had slower heart rates, sometimes significantly so, for parts of the night.

CHAPTER TEN

THE EFFECT OF IMMUNISATION AND ILLNESS ON RECTAL TEMPERATURE

Illness is known to have an effect on babies' temperatures, although little is known about infants' controlled responses to infection. Immunisation with diphtheria, pertussis, tetanus and polio sometimes raises a baby's temperature (Rawson, Petersen and Wailoo, 1990) and parents often report that their child is feverish the night after an injection.

Immunisation and natural illness are assumed to produce similar reactions, as parts of the triple injection are live vaccines. These are controlled doses of infection aimed at stimulating the body to produce its own antibodies, and thus confer 'immunity', as the body is quickly able to replicate the antibodies if exposed to the disease. Natural illness varies in severity, and is therefore not 'controlled' in the same way as vaccine induced infection.

Illness in the Baby

On a number of recordings, the baby either had symptoms of the beginning of an infectious illness or developed an infection, usually of the upper respiratory tract, the following day.

Twenty of these babies exhibited a characteristic change in their temperature pattern; after the initial fall of rectal temperature with sleep their temperature rose to above 37^{o}C remaining there all night, often returning to normal levels the next morning when the baby awoke. Figure 10:1 compares the mean rectal temperatures of a group of babies about three months of age who had no signs of illness with those who were incubating an infection. Other infants, who appeared to have similar symptoms to the twenty babies above, did not have a different temperature pattern from the nights when they were apparently well.

Analysis of these data and the assessment of "illness" were difficult as this was on the number of symptoms present and not on culture of bacteria or virus.

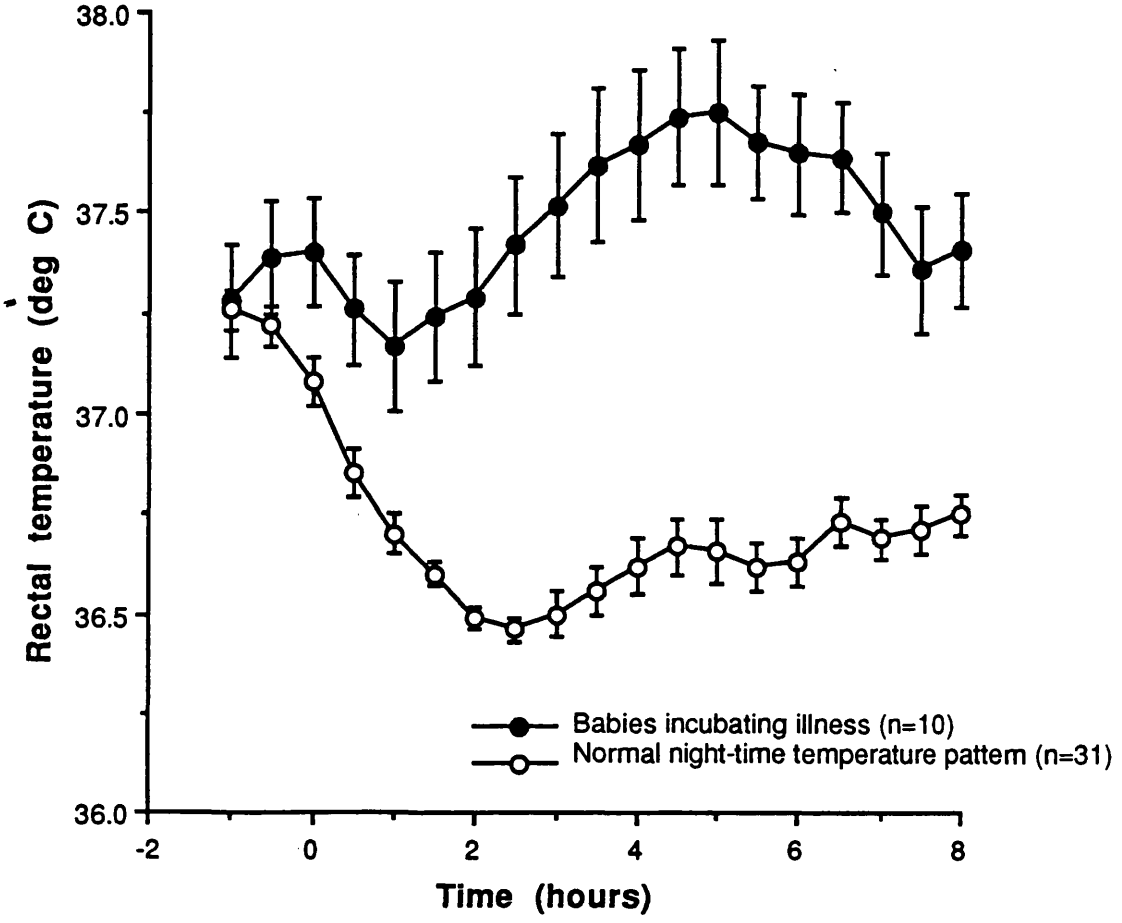


Figure 10:1 Averaged rectal temperature data comparing the night-time rectal temperature pattern of healthy babies and those babies incubating an illness

Immunisation with the First Dose of Diphtheria, Pertussis, Tetanus and Polio

In order to examine the effects of a 'controlled dose' of infection, babies have been monitored before and after their first immunisation against diphtheria, pertussis, tetanus and polio given routinely at twelve weeks of age (some data from D. Rawson).

Not all babies exhibited a 'reaction' to the immunisation; in Rawson, Petersen and Wailoo's (1990) study, by four hours into the night, only half the babies were over two standard deviations above the mean rectal temperature of non-immunised babies at that time. Similarly not all babies exhibited a change in temperature pattern with apparent illness. If the mean values of rectal temperature after immunisation are plotted, however, the curve is comparable to that of some babies incubating an infection. Figure 10:2 illustrates the significant differences between the mean rectal temperatures of babies the nights before and after immunisation; afterwards the babies' rectal temperatures fell with sleep, but only to just below 37^{o}C ($p<0.01$, Student's t-Test from two hours after bedtime).

Interestingly, often those babies who had a raised rectal temperature the first night post-immunisation were not the same children whose parents reported being irritable, restless or hot that night.

Factors Which May Influence How Much a Baby "Reacts" to Immunisation

Research has not yet been carried out on the comparative effects of immunisation on babies who are either 'earlier' or 'later' changing their rectal temperature rhythm. Some indication of the differences between each group may be seen, however, by dividing babies who were monitored post-immunisation, into those who breast fed and those bottle fed, one of the major factors shown to be correlated with the timing of individual baby's development of rectal temperature (see **Chapter Five**).

When these two groups were compared, both groups exhibited a reaction to the

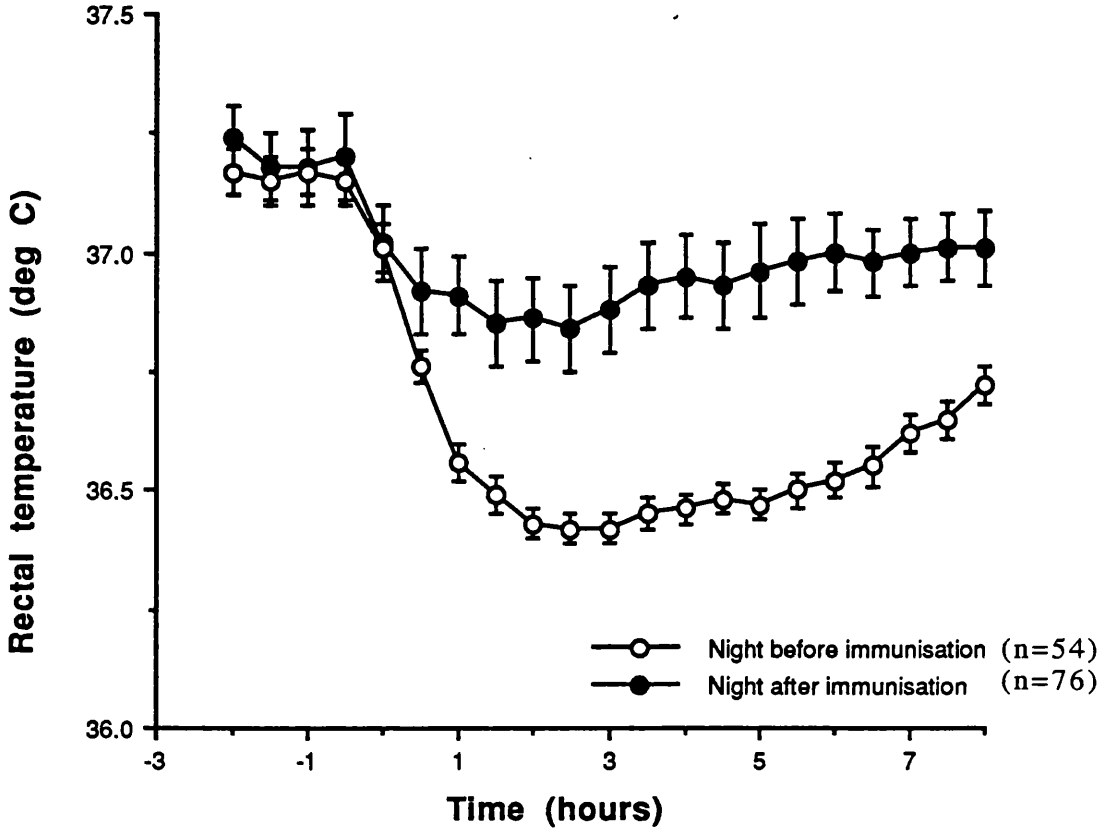


Figure 10:2 Averaged rectal temperature of babies the night before and the night after immunisation

vaccine, but it was the group of bottle fed babies who were significantly more likely to have higher rectal temperatures which rose near to or above 37°C ($p<0.05$ four hours after bedtime, Student's t-Test). Figure 10:3 reinforces the findings discussed in **Chapter Eight** that suggested method of feeding has no effect on the temperature curve of well babies at the same stage of night-time rectal temperature development. After immunisation, however, whether the baby breast or bottle fed did influence the level of rectal temperature and presumably the level of reaction, too. Rawson, Petersen and Wailoo (1990) also report that those babies who exhibited a rectal temperature above the median were of significantly lower birth weight ($p<0.02$, Student's t-Test) and tended to belong to social classes 4 and 5.

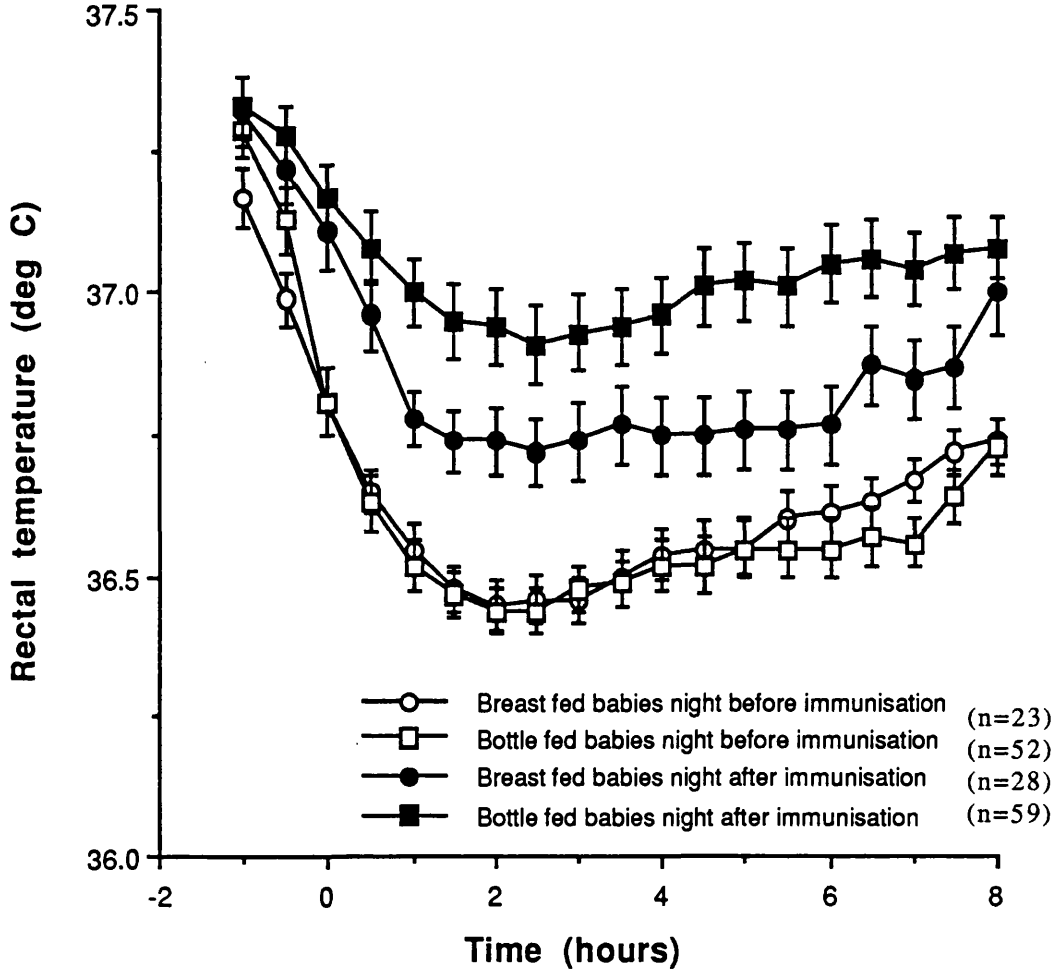


Figure 10:3 Averaged rectal temperatures comparing breast fed and bottle fed babies the night before and the night after their first immunisation

Summary of the Effect of Immunisation and Illness on Rectal Temperature

1 Some babies exhibited a characteristic night-time rectal temperature pattern when they were incubating an upper respiratory tract infection.

2 Over half of the babies exhibited a similar rectal temperature pattern the first night after their first diphtheria, pertussis, tetanus and polio immunisation.

3 Bottle fed babies and babies of lower birth weight were significantly more likely than breast fed babies to have a higher rectal temperature post-immunisation.

CHAPTER ELEVEN

MEASUREMENTS OF SKIN TEMPERATURE

In order that the mechanisms of temperature regulation in babies may be understood more and some attempt made to measure indications of thermal stress, the babies' skin temperatures were also monitored. Possible sites that may be important are those areas which are known to be channels of heat loss, particularly the forehead and limb peripheries, namely the shin. During the period of research, and at the same time as the babies' rectal temperature and heart rate were monitored, their forehead, abdomen or shin temperatures were recorded.

There were not enough data on forehead temperature readings, either because the apparatus failed, the probe was dislodged by the baby's movements and hands, or was removed by parents because they either felt the baby was uncomfortable or disliked the appearance of the probe, which gave the impression their baby was unwell. Brown, Dove, Tuffnell and Ford (1992) also found that forehead temperature did not correlate well with any other site of measurement.

The abdomen temperature measurements were also not used, as no pattern or consistency could be seen across the readings or within individual babies. Analysis of the sound data indicated that the abdomen temperatures were possibly influenced by the position of the nappy, type of clothing, what the baby slept on and their sleeping position, although not all the results obtained could be accounted for by the variations in clothing and bedding. The abdomen temperature measurements were therefore not analysed further.

Shin Temperature

Shin temperature was recorded during the longitudinal studies of rectal temperature. Data were collected on twenty-four babies who were monitored on a weekly basis from six to twenty weeks of age. 231 recordings were analysed.

Figure 11:1 illustrates that after babies fell asleep their shin temperature rose, remained constant over-night and fell again when the baby awoke. This was in direct contrast to the pattern of rectal temperature (Figures 11:1 and 11:1a).

In stage two of the development of rectal temperature, the shin temperature pattern rose more quickly and to a higher level than in stage three ($p<0.002$ at 1.5 hours, $p<0.032$ at 2 hours, $p<0.006$ at 4 hours and $p<0.002$ at 4.5 hours after bedtime, Student's t-Test). Figure 11:1 illustrates this and indicates that skin or peripheral temperatures were not direct reflections of rectal temperature, because otherwise the levels of shin temperature would have been lower pre-rhythm than post-rhythm as the rectal temperature was at a higher level during that time.

Shin Temperature and Clothing and Bedding

Both before and after the change in the sleeping rectal temperature pattern, leg temperature appeared to be unaffected by the amount of clothing and bedding on the babies. The group of babies was divided into three by the total amount of clothing and bedding that covered them, and the group around the median was excluded from analysis. Two groups of eight babies were therefore studied and the mean shin temperature of each group plotted both in stage two and stage three. The babies in the 'low tog group' were covered in clothes and bedding ranging from 4.9 to 9.6 tog value, and the babies in the 'high tog group' were covered in clothes and bedding ranging from 12.2 to 23.2 total tog value. Figures 11:2 and 11:3 graph the data from the 'higher tog' compared to the 'lower tog' group, and illustrate that there was no difference in shin temperature between the two groups when studied both pre- and post-rhythm.

Other studies in adults (Czeisler, 1978) report that their rectal temperatures lower at night in a way that is almost a complete inversion of their tip of

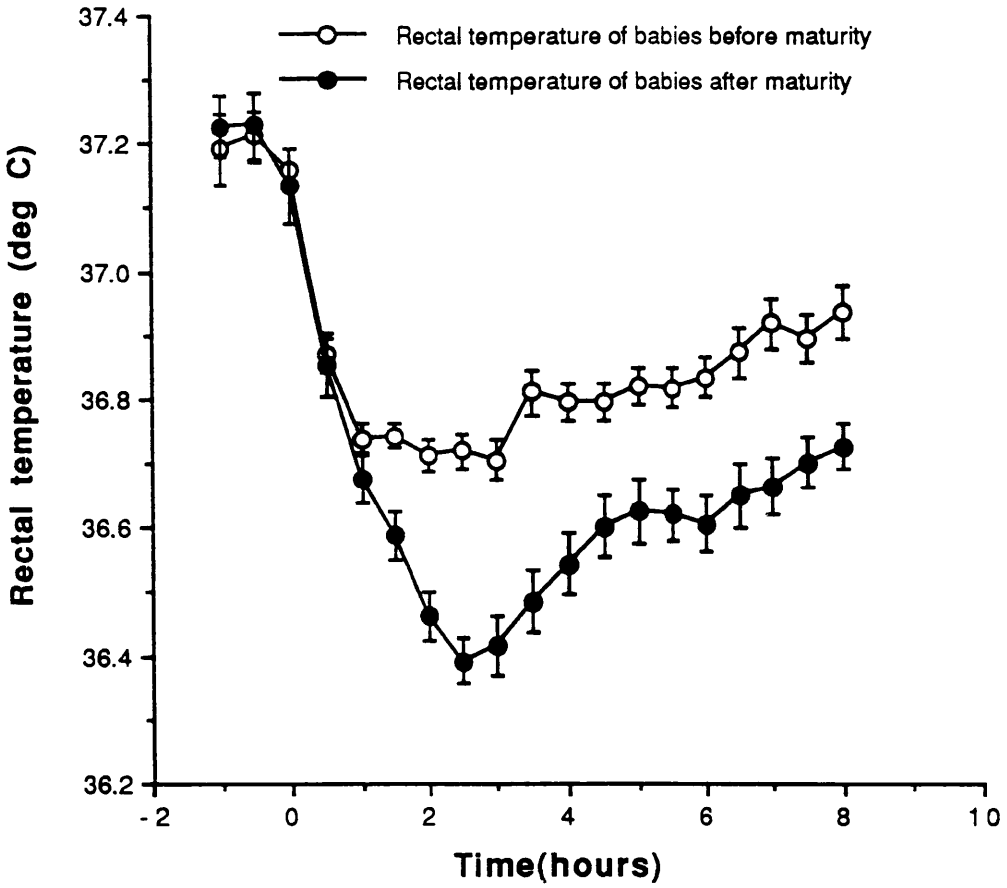


Figure 11:1a The mean rectal temperatures (+-SEM) of fifteen minute recordings on babies, comparing the night-time pattern, before and after the rectal temperature first fell below 36.5°C with sleep. 31 observations on 24 babies before, and 38 observations on 26 babies afterwards.

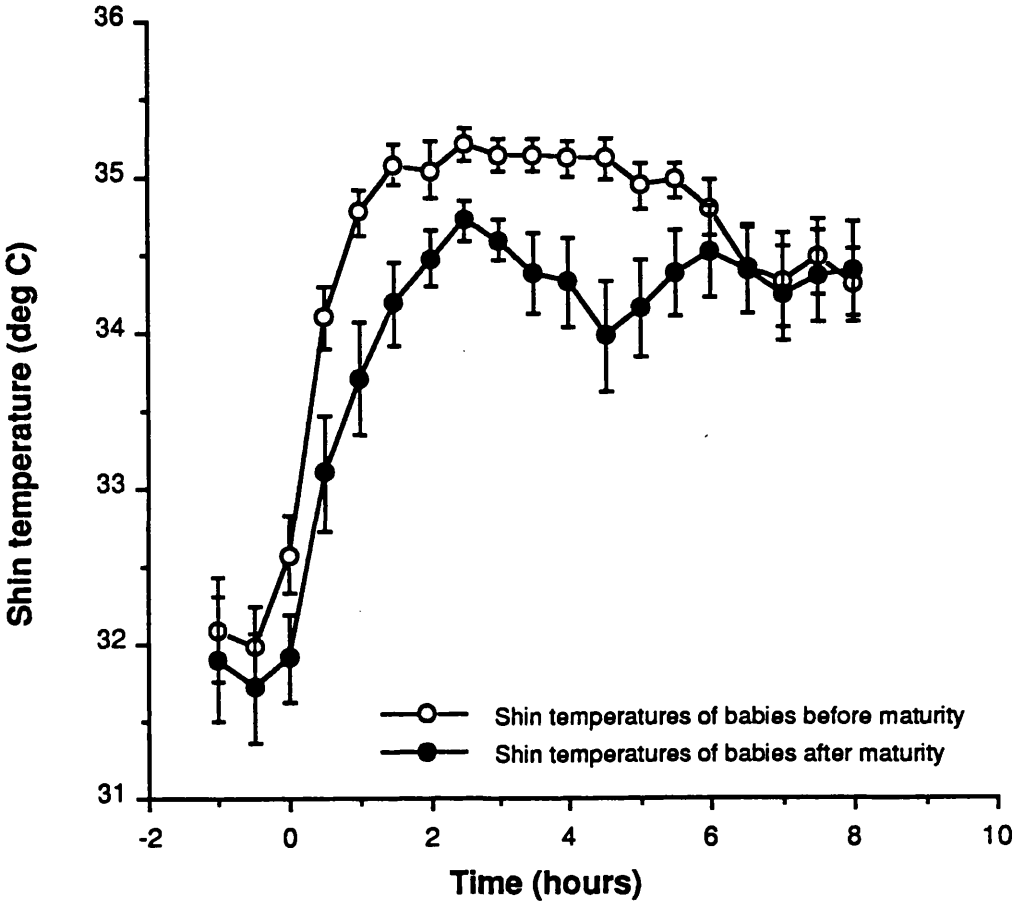


Figure 11:1 The mean shin temperatures (+-SEM) of fifteen minute recordings on babies, comparing the night-tme pattern, before and after the rectal temperature first fell below 36.5°C with sleep. 31 observations on 24 babies before, and 38 observations on 26 babies afterwards.

finger measurement. He concludes that this finger tip temperature is a measure of peripheral vasodilatation or vasoconstriction, and that adults primarily control their circadian rhythm of body temperature by heat loss mechanisms. The effect of bedding on the finger tip temperature measurements was discounted as the subjects slept with their hands outside the bedcovers. Peripheral vasodilatation cannot be the only heat loss mechanism at night, however, as the amplitude of the body temperature rhythm is the same in tropical and arctic conditions (Cabanac,1975).

Alternatively, Kerslake (1991) hypotheses from studies on objects monitored in laboratory conditions, that when babies are put to bed their heat loss is higher because the cool bedclothes absorb heat. This would be reflected by a skin temperature reading that gradually increases to a certain level as the bedclothes warm up, and then stabilises until the baby is removed from the cot.

From the results of this study it is difficult to conclude what the leg temperature was measuring. Figure 11:2 may illustrate that in stage two babies needed to vasodilatate more in order to lower their rectal temperature to the appropriate night-time level, or their shin temperature may have been affected more by the amount of clothing and bedding at this stage than in stage three.

In order to answer these questions, further studies need to be carried out with more data, greater analysis of the type and placing of bedding and clothing and a record kept of leg position.

For the above reasons and the possibility that shin temperature would offer no further information than rectal temperature alone, only rectal temperature results will be discussed.

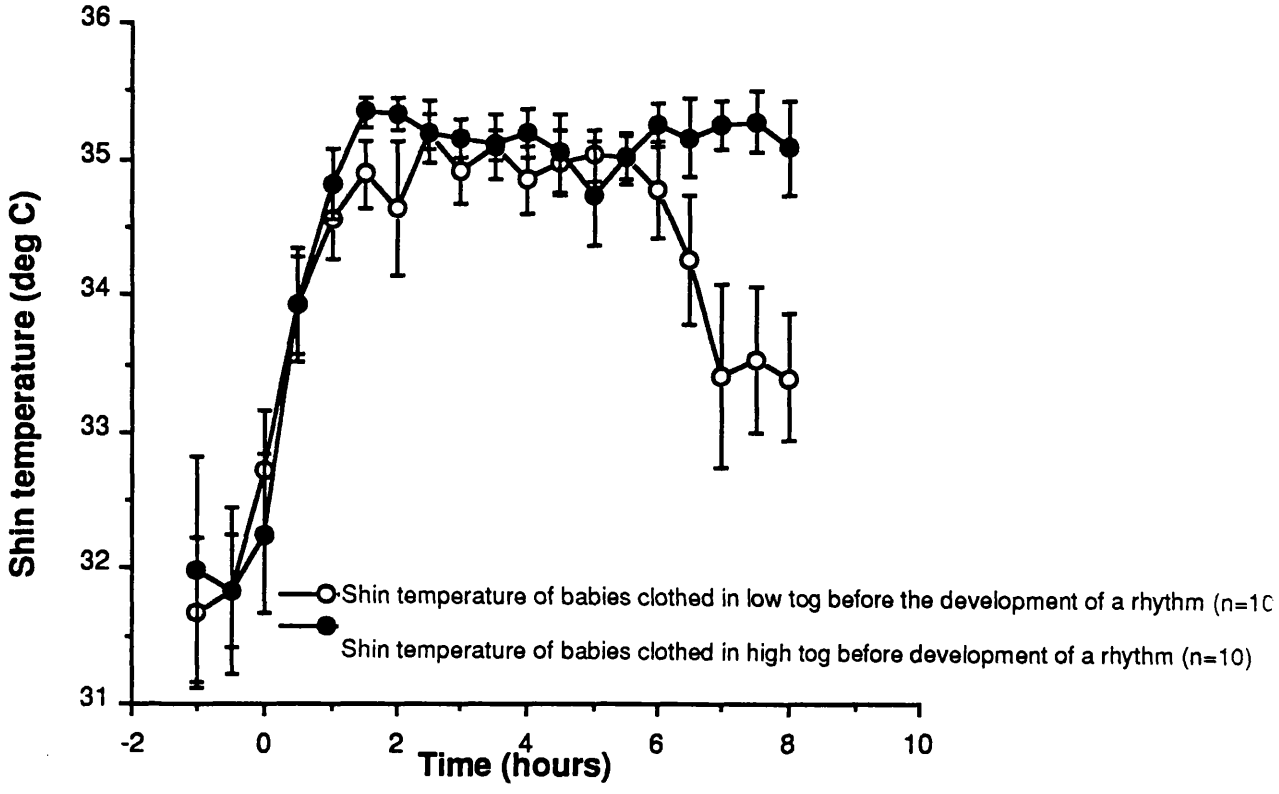


Figure 11:2 Mean shin temperature of babies before maturity comparing tog value of clothing and bedding

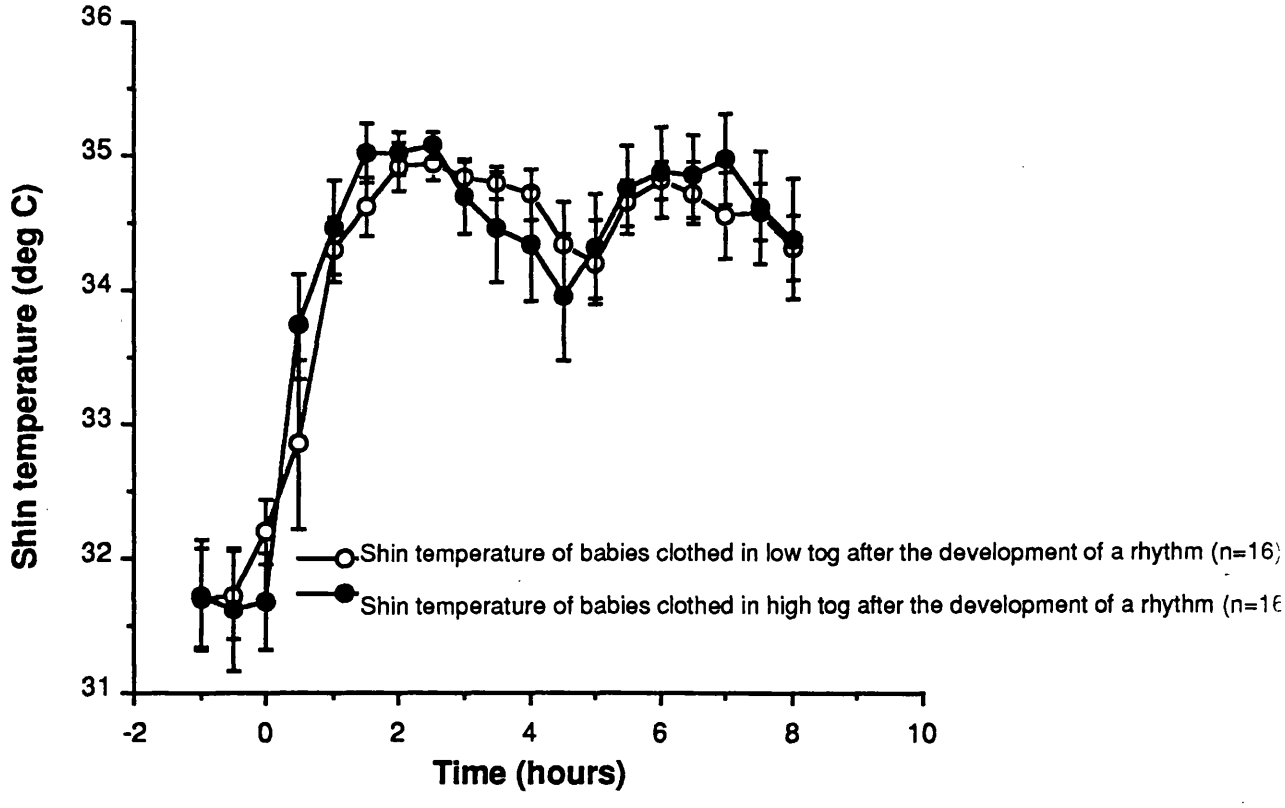


Figure 11:3 Mean shin temperature of babies after maturity comparing tog value of clothing and bedding

Summary of Measurements of Skin Temperature

1 Babies' shin temperatures rose with sleep, remained constant overnight and dropped when the baby awoke.

2 The pattern of shin temperature appeared to be an inversion of the rectal temperature curve.

3 Before the change in the sleeping rectal temperature pattern shin temperature rose more quickly and to a higher level than after maturity.

4 Shin temperature appears to be unaffected by the amount of clothing and bedding covering the baby.

CHAPTER TWELVE

A CASE HISTORY

On one occasion during the months of monitoring, a baby was accidentally left on an electric blanket which was switched on for the first two hours of sleep, and it was possible to examine the effects this had on his rectal temperature and heart rate.

The second child of Kenyan-Asian parents, his birthday is in February. He was born by normal delivery at 38 weeks gestation and weighed 2610 grams. The baby was breast fed for ten weeks with a supplement of cow's milk and baby rice in a bottle from seven weeks of age.

Father was a British Telecom engineer who was not working at the time of monitoring because of a broken leg. The family lived in a one bedroomed council flat which was sparsely furnished; the parents and children slept in the bedroom, which had areas of damp on the walls, and a paternal aunt slept on a bed in the lounge.

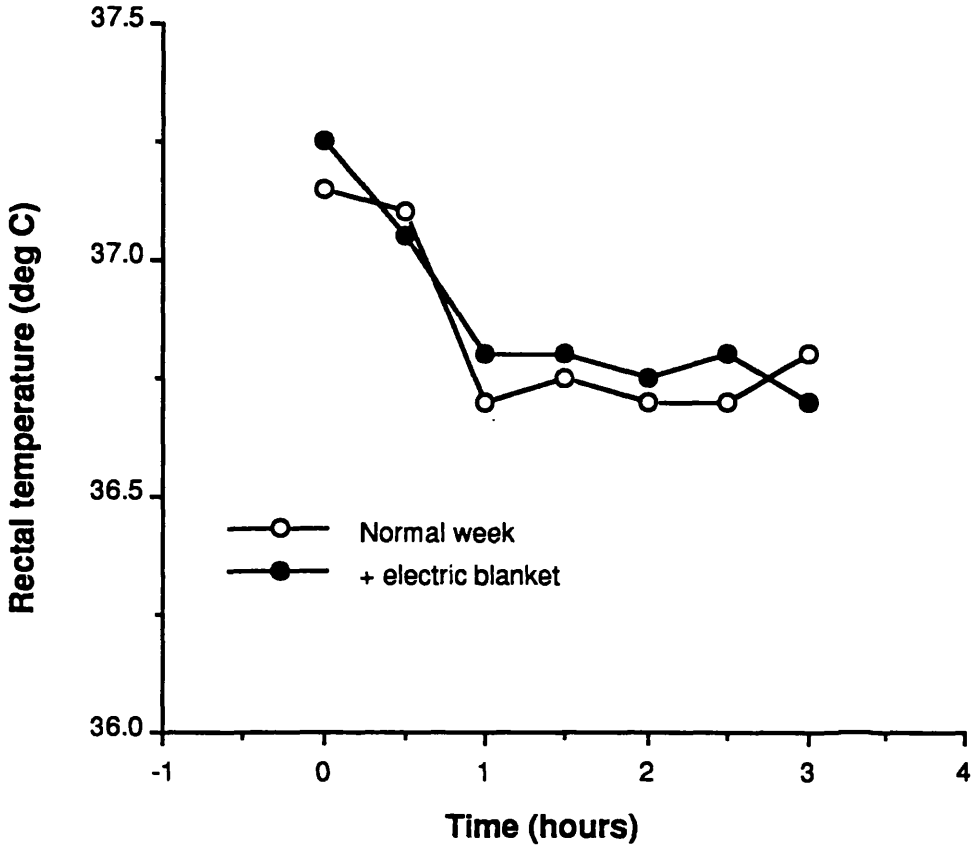
Usually the baby wore a nappy, vest and babygro (estimated tog = 3.2 tog), and when put to sleep in a buggy/carry-cot in the bedroom, was placed on his side or back. Until ten weeks of age he was wrapped in a double shawl and covered with two blankets (estimated tog value = 7) at which age his coverings were reduced to one blanket (tog value = 2). The mean room temperature of all the recordings, apart from the night to be described, was 17°C.

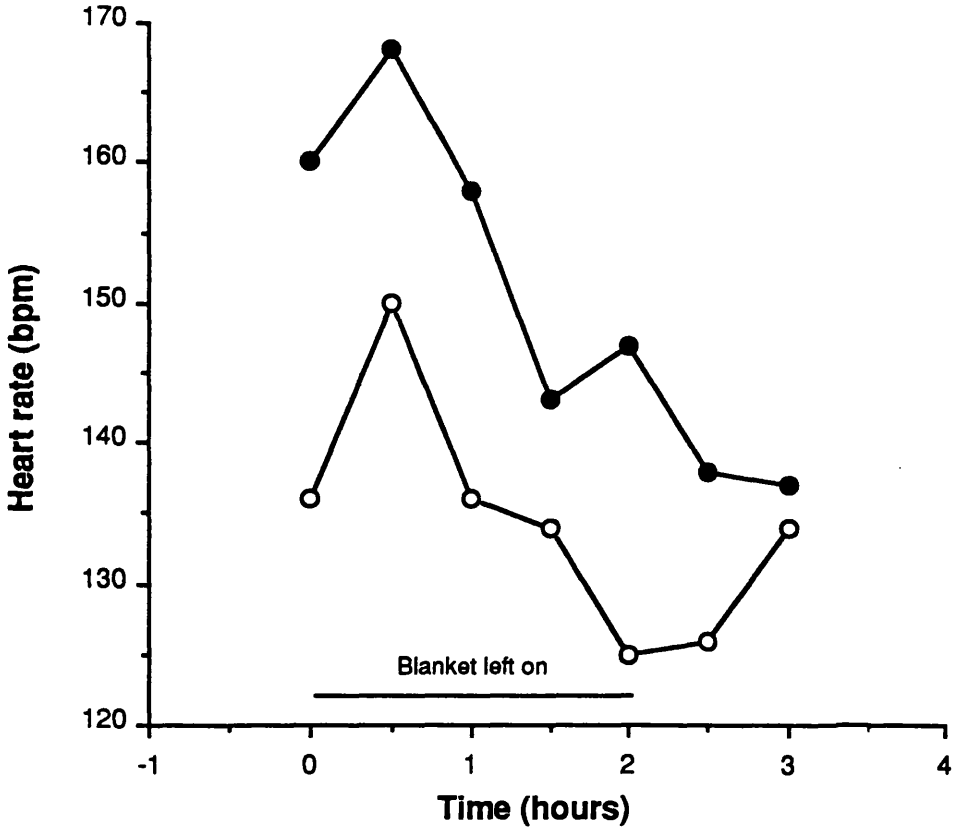
At about two weeks of age the baby developed a cold and suffered from snuffles until seven weeks of age. At ten weeks old he was seen by the General Practitioner again because of an upper respiratory tract infection and colic, and was prescribed paracetamol and infacol, as well as the nose drops given previously. Despite quite a lot of illness in the family over the ensuing weeks, the baby only developed vague symptoms and a slight cough at about seventeen weeks of age, which was treated with paracetamol. He was routinely immunised with diphtheria, pertussis, tetanus and polio at twelve and sixteen weeks old; his mother reported that the night after vaccination she gave him paracetamol and he had no obvious reaction to the injection and slept well.

At thirteen weeks of age, whilst the baby was still in his 'pre-rhythm' stage of rectal temperature, he was not placed in his carry-cot, but for two hours was left on his parents' bed laying on an electric blanket which was switched on. He was dressed in nappy, vest and babygro and covered with one blanket (estimated tog value = 5.2), and during that time the ambient temperature probe which was also resting on the bed recorded temperatures ranging from 30.5°C to 47.65°C.

Unfortunately the heart rate monitor was disconnected after the baby had been asleep for three hours, but the rectal temperature and heart rate were studied for the first three hours of the night, including the time spent on the electric blanket, and compared to the preceding week's readings.

The baby's rectal temperature showed no significant difference from a normal week's recordings (figure 12:1), but his heart rate was consistently higher for the time he was on the blanket and for half an hour afterwards, although still slowing with sleep (figure 12:2). His parents stated that the baby was not distressed or more restless than usual that night and he did not appear to suffer any after effects.





Figures 12:1 and 12:2 Comparison of rectal temperature and heart rate readings the week before and the week of sleeping on an electric blanket.

CHAPTER THIRTEEN

DISCUSSION

In the past limited data have been collected about babies' circadian rhythms and control of temperature. The prime aim of this study was to collect information about normal babies and the development of their temperature rhythms up to nine months of age, and to investigate indications of abnormalities which may be detrimental to them. Some objectives were not achieved, but other facts were discovered that had previously been unexplored. I will discuss the objectives, and how far they were achieved, and also postulate about the implications the results have for general child care and the aetiology of Sudden Infant Death Syndrome.

The **first objective** was to study the development of body temperature rhythms with sleep, and the effect of endogenous and exogenous factors, primarily gestation, on this.

Are Rectal Temperature Measurements the Best?

Rectal temperature measurements were used, not only because the readings are reproducible within infants and across the babies monitored, but also because obtaining rectal temperature is practical and non-invasive, and therefore acceptable to both babies and their parents. Rectal temperature is also widely assumed to be a correct index of the blood temperature to which the hypothalamic thermoregulatory receptors are exposed. Various studies have shown that rectal temperature is not as accurate as the temperatures taken in the subclavian artery, oesophagus and tympanic membrane (Aikas, Karvonen, Prironen and Ruosteenoja, 1962 and Poole and Stephenson, 1977), and the ideal method would be to use zerogradient thermometers, which measure the temperature of the tympanic membrane whilst accounting for heat lost via the aural meatus. However these sensors are probably impractical, possibly

dangerous and unethical to use on babies at home, because they are sited close to the ear drum and have an electrical heating element.

Oral and axilla temperature are other possible methods for measurement of body temperature. Oral temperature in the mornings in adults is 36.3°C - 37.1°C (+- 1.96 standard deviation), and has shown to be closely correlated and have a response time that is similar to other deep body measurements, but it is subject to technical error, such as the effect of hot or cold drinks and whether the person is breathing with their mouth open. An oral thermometer also cannot be left in situ.

In 1977, Buntain, Pregler, O'Brien and Lynn found that, using a glass thermometer, axilla temperature correlated well with rectal temperature, but still concluded, that when using an electric probe, axillary temperature may not be the most precise method. Morley, Hewson, Thornton and Cole (1992) compared axillary and rectal temperatures of children at home and in hospital using glass thermometers and found no consistent correlation, with a range difference of 3°C. The upper daytime limit for rectal temperature was 37.9°C and for axillary 37.2°C. When used in hospital to detect high temperatures, axillary temperature had a sensitivity of 73% compared to rectal temperature. They conclude that axillary temperature is imprecise and the risk of perforation using rectal thermometers is less than one in two million.

The principal drawback with rectal temperature is that it is slower to respond to variations in blood temperature, possibly because of the insulation of the body mass, but otherwise it has changes, and records values, similar to the other temperatures (Aikas, Karvonen, Prironen and Ruosteenoja, 1962). In fact, Nadel and Horvath (1970) in their comparison of rectal temperature and the only other practical method of recording body temperature, the tympanic temperature, conclude that in a steady state rectal temperature may be more informative than using the tympanic membrane, because the latter is influenced by ambient temperature.

Day (1941) illustrated that body temperature change is a gradual process, so monitoring at minute intervals illustrates the trend without the data becoming too bulky, and sampling the readings at fifteen minute or half an hour intervals does not affect the picture produced.

How do Temperature and Heart Rate Rhythms Develop?

As already shown by Hellbrügge (1960), Mills (1975) and Minors and Waterhouse (1980) babies in the present study did not exhibit a fall in rectal temperature with sleep in the first week of life, and at between two to four weeks of age there was only a small fall in the night-time value. The results also confirm that on average by twelve weeks of age night-time patterns of temperature and heart rate are significantly different from daytime values in all babies. A discovery from this work, however, is that the main step in the process of rhythm development is not gradual, as previously assumed, but abrupt and irreversible, occurring between one week and the next. The development is described in stages:

1. Neonatal Stage Lasts from birth to about two to four weeks of age. The rectal temperature remains stable during sleep, at a level just below daytime levels.

2. Pre-rhythm Stage When the baby's rectal temperature is above 37^{o}C in the evening and falls to about 36.8^{o}C with night-time sleep, rising only when the baby wakes for a feed in the night or in the morning. This stage lasts anything from four to fourteen weeks.

3. The Post-Rhythm Stage The rectal temperature pattern is considered to be developed when a minimum rectal temperature below 36.5^{o}C is achieved with night-time sleep. This usually occurs within one week, but at different ages in individual babies.

The abruptness of the development was probably not seen by Hellbrügge, Mills, Minors and Waterhouse because they studied information from babies divided

into age groups of a week or more, which would average out the results, and their studies were mainly cross-sectional.

The longitudinal studies suggest that the timing of pattern development varies in individual babies. The age at which a circadian rhythm of rectal temperature first appeared ranged from seven to sixteen weeks with a mean of about eleven weeks old, but an age to within one week could be ascribed to each baby, and the pattern was similar in all babies. The only observed occasions when this pattern was sometimes not seen 'post-rhythm' were when a baby had an infectious illness or after immunisation.

The longitudinal studies of Mullin and Parmalee were four hourly readings at up to a few months interval, so any change was interpreted as being gradual, and comparisons could not be made between infants as they were only on one or two babies.

Hellbrügge (1960) reports that rectal temperature continues to fall further with sleep until a baby is at least two years old. Not enough babies were monitored after six months of age in this study for conclusions to be reached about the rhythms of older babies. Although there was some indication of a lower minimum body temperature in older babies, the mean rectal temperature curve at twenty weeks of age was similar to those plotted at twelve weeks and not dissimilar to the adult pattern (Minors and Waterhouse, 1981). Hellbrügge's data was probably distorted by using clock time rather than bedtime, so that the averaged rhythm continued to change as babies began going to bed at a similar time. A 'mature' rhythm was not evident until the two year olds went to bed at about the same hour.

Heart rate rhythms also developed in the same manner and at the same age as rectal temperature rhythms and at all times could be superimposed onto the rectal temperature pattern. The heart rate is defined as being in stage three when it slows to below 115bpm with night-time sleep. This cannot be said to be completely 'mature', however, as heart rate continues to fall for several years

after infancy (Hellbrügge, Lange, Rutenfranz and Stehr, 1964, Mills, 1975 and Minors and Waterhouse, 1981).

There were not enough data on premature babies to give any conclusive information about the effect of gestational length on the development of rhythms. It would appear, however, that if the baby is over 35 weeks gestation, the development of the rhythms is not affected. More extensive research on babies with low Apgar scores and a slightly shorter mean gestation (38.85 weeks) discovered the average age of temperature rhythm development was thirteen weeks. Although this is later than heavier full term babies, who had straightforward deliveries (Williams, 1992-personal communication), this is probably more to do with the traumatic birth, as reflected by the higher incidence of caesarian births, and the low Apgar score, than with gestational age.

The **second objective** of the study was to collect information about the babies' birth, social conditions, health and care and to correlate this with any alterations in temperature and heart rate rhythms and the age at which they were first exhibited.

What Factors about the Baby Correlate with the Development of Temperature and Heart Rate Rhythms?

A number of factors were collected and studied in relation to circadian rhythms of temperature and heart rate. A new, significant finding, with far reaching implications for child care, is that parental and family factors and the way in which a baby is treated affect physiological development.

This study found that earlier development of temperature and heart rate rhythms is correlated with belonging to the upper social classes, the baby

having its own room and an older mother, being breast fed and growing more slowly than average, sleeping supine or lateral, being a girl and a first child. Which of the factors is primary and which secondary is open to question. Multivariate analysis was not possible, as the sub-groups would be too small. Many of the factors, however, are interrelated. Having a bedroom just for the baby is almost definitely associated with social class, as is the age of the mother. Age of the mother may also be associated with the desire to breast feed and the ability and confidence to continue over many weeks. Slower rate of growth may relate to breast feeding and being female. Sleeping position might be influenced by whether the baby is the first or subsequent child. The association between sleeping position and being a second or subsequent child has also been reported elsewhere. In the Netherlands, 10.8% of first born and 20.7% of second born infants slept prone (Engelberts, de Jonge and Kostense, 1991).

The factors studied are those recorded in the maternity notes and general observations, so there are many more areas that could be studied in order to pin-point what it is that influences the development of the rhythms.

Are Circadian Rhythms in Babies Influenced Exogenously or Endogenously?

By studying the development of heart rate and temperature circadian rhythms, some clues may be provided about their causal nature. In this study there are indications that both endogenous and exogenous factors play a role.

Endogenous Components

Perhaps the greatest indication that the rectal temperature rhythm is primarily endogenous is that the fall to below 36.5^{o}C only occurred with night-time sleep,

and the pattern for sleeps of the same duration during the day were distinctly different. This is despite babies being fed, an activity which might be expected to raise temperature, before all the night-time sleeps although not necessarily before daytime sleeps.

The same pattern is seen for heart rate, although no daytime data were collected in this study. Keele, Neil and Joels (1982) report a change of ten beats per minute for every 0.5^{o}C variation in body temperature, and this was seen during these recordings. It would appear heart rate is primarily influenced by body temperature, especially in the absence of other variables such as activity and feeding, a conclusion reached by Minors and Waterhouse (1981). In adults, Kleitman and Ramsaroop (1948) showed that heart rate and body temperature curves can be closely superimposed except when a post-prandial rise in pulse rate occurs.

There are other indications that the development of circadian rhythms originates from within the baby, although it is difficult to separate genetic and environmental factors. On average, girls exhibited stage three of the temperature and heart rate rhythms earlier than boys. Girls' genetic make-up may be such that their maturational processes are more developed or that they grow more slowly than boys. They may, however, also be treated differently in subtle ways and receive more of the appropriate stimulation, which in some way affects the maturational process. Boys might gain weight faster because they are changed to bottle feeding more readily, perhaps because the parents believe they are hungrier and should be bigger. Many psychological studies have observed behavioural differences in babies and studied whether these sex differences are hereditary or acquired as a result of parental handling and expectations (for reviews see Hilgard, Atkinson and Atkinson, 1975) and conclude it is very difficult to differentiate, because parental care may respond to the baby's own demands. The age and social class of the mothers might be an indication of parental care and attitudes, although they could equally be signs

of nutritional status or other physical properties of the mother which are transmitted to the fetus in utero.

If the rhythms are influenced by exogenous factors, the development of the rhythms would presumably be affected by the temperature outside the body. In this study the thermal environments in which the babies slept did not affect the timing of rhythm development. Conversely, however, thermal environment did influence the shape or amplitude of the temperature and heart rate patterns before circadian rhythms were established, which may indicate external factors affect circadian rhythms.

Exogenous Components

Other results from this research indicate that there is an exogenous component to temperature and heart rate rhythms. Lowering of the babies' temperature and heart rate was dependent on the time they went to sleep even if this varied from day to day. This suggests that the rhythms are not cued by clock time or darkness, but the correlation with night-time sleep, rather than daytime sleeps, indicates that darkness may influence the rhythms or type of sleep, and that they are therefore not totally independent. In stage two the degree of fall was correlated with the length of sleep, but not all babies had settled into a regular sleep pattern at the time of the change in the sleeping rectal temperature rhythm, and, once the circadian rhythm was established in individual babies, the length of sleep did not influence the rectal temperature pattern. In fact, breast fed babies, who often wake for a middle-of-the-night feed, were more likely to develop their rhythms earlier, and babies who slept prone were more likely to sleep longer from six to twelve weeks of age, but were later developing their rhythms. This correlation between sleeping position and sleep length has not been reinforced elsewhere. In Tasmania, Dwyer, Ponsonby, Gibbons and Newman (1991) found that at one month of age the length of consecutive hours

sleep and total duration of sleep in twenty-four hours did not differ between prone and non-prone infants.

This research indicates that exogenous factors do influence the age at which individual babies first exhibit circadian rhythms of temperature and heart rate. How parents care for their baby may greatly influence physiological as well as behavioural and psychological development. The factors associated with earlier development of temperature and heart rate rhythms have one characteristic in common; they are, or could be, related to the amount of attention and stimulation the baby receives. It is impossible to 'prop-breast feed', so breast feeding ensures that the baby has the mother's undivided attention and close contact; when lying on its back or side the baby is able to observe its environment more easily and interact with 'passers-by'; empirical reports suggest that first children receive more attention than subsequent children from their parents and other adults. It might also be assumed that older mothers in higher social classes are better educated about the need to talk and play with their baby, have more time to do so and better facilities with easier access, for example the use of a car. Interaction is different with babies of opposite sexes (Hilgard, Atkinson and Atkinson, 1975) and perhaps the less boisterous, more intimate play that parents have with girls helps maturational processes.

If the baby is over 35 weeks gestation, it appears that rectal temperature rhythm development is not affected by being pre-term. This suggests that it is not an endogenous maturity that is important, but time outside the womb. Perhaps it is a traumatic delivery, an external factor, which affects the baby and its circadian rhythm development endogenously (Williams, 1992-personal communication). In my study the number of children who had difficult births was insufficient for analysis but Williams' hypothesis is reinforced by North, Petersen and Wailoo's (1991) studies on thirty sets of twins. In fourteen pairs one baby developed its rectal temperature rhythm significantly earlier than its

twin, and the only correlation found was that the later developer had difficulties at birth, with a consequent lower Apgar score (personal communication). D'Souza, Tenreiro, Minors, Chiswick, Sims and Waterhouse (1992) also raise the possibility that the poor medical condition of some of the pre-term babies they studied may have contributed to the delayed onset of their circadian rhythms.

Rhythm development appears to be a combination of the maturation of an endogenous clock and the ability to respond to 'zeitgeber' such as light and darkness, attention, feeds and quietness and other environmental rhythms. Social factors and parental care probably influence the endogenous clock's ability to respond to external cues, because although they did not prevent the development of rhythms (all babies exhibited circadian rhythms eventually) they did affect the age at which the change in the rectal temperature pattern occurred.

The **third objective** was to assess whether parental choice of clothing and bedding differs according to the gestation and age of the baby, and whether this has any effect on the skin temperature.

What are the Best Methods for Assessing Thermal Environment?

Togmeter values were used to measure objectively the amount of coverings placed on the babies by parents. They are a generally recognised method for measuring the amount of insulation provided by clothing and bedding. It is not clear, however, how much allowance should be made for the areas of the body left exposed, for example head and hands; the age of the clothing and bedding, and how many times it has been washed; and whether the type of mattress and underbedding is important. Researchers, therefore, calculate tog value in different ways (Fleming, 1990, Bacon, 1991 and Wailoo, 1991). It appears

reasonable to take into account an exposed head, as much heat is lost from this area, especially in babies. Throughout all this research none of the babies wore a hat, so all babies were able to lose heat from their heads. Kerslake (1991) points out that allowance should also be made for curvature effects of thick clothing and the fit of bedclothes, and that the insulation of bedclothes of given thermal resistance depends on the size of the body insulated. He writes that the difference between thick bedclothes (10 tog), and very thick bedding (30 tog), is less than the variation in insulation which may be caused by draping, or the way the bedding fits around the body. Posture is important, too, as a baby lying curled up under tucked-in blankets has different thermal properties from one lying spread out. By curling up, an infant can more than double the effective insulation of bedclothes.

Given the complexities of accounting for these variables, and the observation that even very young babies are not static throughout the night, it would appear that accurate calculations about the level of insulation are so complicated that it is only possible to undertake them in a laboratory. The simple addition of the average tog values of the individual items of clothing and bedding was probably as effective and certainly more practical than using complicated formulae. Parental observation would have become time consuming, and interfered with the babies' normal routines, if it was detailed enough to record movement of hands in and out of the bedclothes or posture.

The estimated tog value gives an indication of the type of parental care, whether they believed it important to wrap their baby up well, or tended to keep their baby cool. It was possible to calculate if parents varied coverings depending on ambient temperature and the presence of illness.

Although Motil and Blackburn (1973) state that conductive heat loss through contact with blankets and mattress accounts for less than 5% of the total, it would appear that loss of heat through the mattress is not negligible (Kerslake, 1991). Recent studies in New Zealand (Taylor, 1991) indicate that the use of

under-sheepskins may compromise the baby, and in the case history (**see Chapter Eleven**), it was the high temperature of the blanket that the little boy lay on which appeared to raise his heart rate. More detailed analysis of the effect of bedding could have been carried out if information had been collected about the mattress and underbedding.

In order to assess the total thermal environment, room temperature was monitored. Ambient temperature recordings were of the air temperature near the baby, measured every minute throughout the night. Mount (1966) writes that although air temperature is easily measured, by itself it is by no means a complete index of the thermal environment. As a metal probe was used it may have been affected by convection (for example if the window was left open) and conduction (if resting on a solid object such as the mattress). Air temperature may have been different from the ambient temperature which is influenced by radiation, for example, if the baby was in a warm room but sleeping next to a cold wall. During this study no note was made of the position of the probe and whether it hung inside or outside the cot, although the difference between these two temperatures could be considerable. Another disadvantage of having a single probe to measure ambient temperature, is that there is no record of relative humidity, which affects the heat loss and gain from the body (Rutter and Hull, 1979). Ambient temperature is very difficult to measure accurately and more conclusive results may be reached by studying ambient temperature more extensively. As with tog values of insulation, however, air temperature is a good indicator of the warmth of the room without too much intrusion into everyday life, and provides information for general categories for analysis.

All analysis that took place considered the room temperature at four hours into the night.

The simple addition of the two interval scales, of tog and degrees Celsius, is not mathematically correct. It does, however, give an indication of whether the babies were in warm or cool environments.

How Do Parents Choose Clothing, Wrapping and Temperature of their Baby's Room, and Does the Thermal Environment Affect the Baby?

Up to four weeks of age babies at home were kept in slightly warmer environments than those in hospital. Even those babies on Special Care Baby Units were only in marginally warmer conditions unless in incubators. From six weeks of age, however, all babies were kept in similar total environments regardless of age or gestation. Although there were individual differences, parents appeared to make only slight adjustments to clothing and bedding depending on the temperature or season, and little, if any, if the baby was unwell.

The effect of clothing, wrapping, bedding and ambient temperature on skin temperature is discussed in **Chapter Ten**, but no conclusions reached. When studying rectal temperature, however, babies who slept under more clothing and bedding and in higher room temperatures than average, had significantly higher temperatures before rhythm development, for the latter part of the night, than those babies in lower amounts of clothing and wrapping and cooler rooms. This was significantly so during waking up, and remains significant if thermal environment is assessed by coverings alone. Studies in adults suggest that ambient temperature does not affect the presence of the rhythm, but does dampen the normal circadian fall in temperature with sleep (Bonegio, Driver, King, Laburn and Shapiro, 1988). Those findings were not confirmed in this study, as the rhythm of temperature was unaffected by air temperature alone, and, after the development of the rectal temperature rhythm, thermal environment did not influence the degree of fall of the babies' rectal temperature as they were going to sleep. For the four hours before waking, however, after development of the rhythm, the rectal temperatures of babies with more coverings were slightly raised, although this may be a result of increased activity rather than more coverings.

It has always been assumed that a baby will be stressed if it is nursed in conditions that are not thermo-neutral, therefore the **fourth objective** was to measure physiological reactions to the environment.

Is There Evidence of Thermal Stress?

Stanton (1984) believes that thermal environment may affect babies' thermoregulatory mechanisms at certain stages of their development, and this might be detrimental to them. From this study, stage two of the rhythm may be defined as a 'vulnerable' period and the higher rectal temperature of babies sleeping in more clothing and bedding and warmer rooms, at this time, may be an indication of thermal stress. However, Sulyok, Jequier and Prod'Hom (1973) argue that body temperature alone is not a good indication of thermal stress as it only alerts us to situations in which the stress has become so severe that the baby's normal thermoregulatory mechanisms have been at least partially overpowered.

The neutral thermal environment is defined as the environmental temperature at which metabolism, as reflected by oxygen consumption, is minimal yet sufficient to maintain the body temperature (Stern, 1977). Scopes (1966) argues that true basal metabolic rates are almost impossible to assess in babies, as they are always digesting one feed or actively anticipating the next. However, generally it is accepted that oxygen consumption is quantitatively related to heat production (Adamsons, 1966). Heat balance, or heat production, storage and loss, is used in most studies of metabolism rather than body temperature alone.

The neutral thermal environment of naked full term neonates up to ten days old is between 32^{o}C and 34^{o}C (Hey and Katz, 1970 and Stern, 1977). Hey and O'Connell's work (1970) concludes that for a baby who is clothed in a short

woollen vest, a large towelling nappy and a long cotton night-dress the optimum environment is 28°C. If the baby is nursed clothed, in a cot with bedding (lightly swaddled in a flannelette sheet placed on a thick linen-covered waterproof mattress and covered by two layers of cotton blanket), the optimum environment is 25°C. In their study insulation against heat loss was little affected by birth weight, but heat production was affected by both birth weight and age, so newborn babies weighing under two kilograms require higher temperatures.

Calculations on thermo-neutral environments have generally been on neonates, so it is difficult to extrapolate to older babies. It has been suggested that older infants are more comfortable in cooler conditions, however (Motil and Blackburn, 1973), and recommendations about ambient temperatures and wrappings have been made by Stanton (1984) and the Foundation for Sudden Infant Death (1992) (**see page 41**). On the nights of monitoring the babies were in a wide range of thermal environments, but only the baby, who on one occasion slept on an electric blanket, was in conditions outside the neutral thermal zone for clothed and covered neonates (discussed at the end of the section). The measurement of 'thermal environment' can be calculated in various ways, but it would appear that some older babies were in slightly cooler total environments than those recommended for neonates and some in marginally warmer conditions, but generally most were in the range advised by Stanton and the FSID.

A few babies were in more clothing and bedding, but lower ambient temperatures than average, a situation which provides a similar total thermal environment to average coverings and a high environmental temperature, using the simple formula of adding tog values and minimum room temperature together. Hey and O'Connell (1970) feel this exposes the babies to cold stress; they found if a baby is naked and the surroundings cold enough to increase body heat production by 50%, the baby wakes and cries, but if dressed the baby

continues to sleep quietly, even in comparatively cool conditions. They concluded that the limit for heat production in a full-term cot nursed infant is at an ambient temperature of 10-15^{o}C, and if nursed in conditions below this the baby may suffer cold stress but not call attention to it. They also showed that if exposed to the cold, a naked infant's rectal temperature falls, but a clothed baby's temperature rises. This is possibly because the thermoregulatory centre is receiving messages from a naked, cold head, and, in anticipation of the body becoming colder, stimulates heat production. It is difficult to reach conclusions, therefore, about the higher rectal temperature of babies in stage two, who were in more clothing and wrapping. It may be the room temperature was too cold. However, a more significantly different rectal temperature pattern is seen if both the room temperature and coverings are above average, which indicates that it is warm conditions that raise rectal temperature, not a cold room.

Other responses to cold stress in babies are vaso-constriction and shivering, increased respiration rate (Stern, 1977) and a slight retardation in weight gain (Motil and Blackburn, 1973). No correlation between slower growing babies and colder environments was found in this study.

If babies are exposed to an excessively warm environment, the responses seen are change of posture and sweating (Rutter and Hull, 1979) and an increase in cutaneous blood flow and respiration rate (Sulyok, Jequier and Prod'Hom, 1973).

Metabolic rate could not be assessed in this study by oxygen consumption or heat balance, and there were insufficient data on sweating and oxygen saturation. Heart rate was monitored successfully, however, and the data discussed here.

Heart rate was recorded every minute to monitor the trend which was reproducible across all babies and within individuals. More detailed

monitoring would be interesting as there is much beat-to-beat variability with heart rate (Leistner, Haddad, Epstein, Lai, Epstein and Mellins, 1980). Acute incidents during sleep, such as a short dip in the heart rate due to a respiratory pause or perhaps a brief tachycardia, are not noted with trend recordings. Other studies also suggest that individual heart beats have varying structures in different babies, the QT interval being studied in particular (Southall, Arrowsmith, Stebbins and Alexander, 1986).

Without more complicated and bulky machinery and detailed analysis it would be difficult to extend the knowledge about heart rate. In this study basic questions about heart rate and its circadian rhythm have been answered, and future studies may be able to study the beat-to-beat variability more fully.

Thermal environment influenced the shape or amplitude of heart rate patterns before the circadian rhythms were established. Those babies in more clothing and wrapping and warmer rooms and those babies who were just more heavily clothed and covered had a greater slowing of heart rate, although their rectal temperatures, after an initial greater fall, were generally higher towards the end of the night. Perhaps those babies in cooler thermal environments were suffering from some cold stress and needed to increase their metabolism, and therefore their heart rate, in order to maintain body temperature. This is reinforced by the analysis of weekly weight gain in babies in stage two of the rhythm. Slower growing babies had higher heart rates, perhaps indicating that they were cold stressed, and therefore had a slight retardation in weight gain (Motil and Blackburn, 1973 and Hey and Mount, 1967). Smaller babies may have a higher basic metabolic rate, however, because in stage three they have a higher rectal temperature at night as well as a faster heart rate.

Conversely, the results may indicate that warmth, and particularly clothing and wrapping, also provide comfort and in some way help the baby to sleep more soundly, something which is frequently reported by parents. Sleep staging was not done in this study, and no connection could be found between

the amount of clothing and wrapping, room temperature and sleep duration of the babies. Other studies, however, have looked at type of sleep and environmental conditions. Hey and O'Connell (1970) conclude that sleep is a doubtful indicator of thermal stress, because swaddled infants continue to sleep quietly even in environments that are comparatively cold enough to wake a naked baby. Mestyan, Jarai and Fekete (1968) also comment on this tranquillising effect of a warm environment and Sulyok, Jequier and Prod'Hom (1973) write that at the beginning of sweating there is a sharp fall in metabolic rate. Rutter and Hull (1979) report that as babies approach the point of sweating spontaneous activity usually ceases.

On the one occasion in which a baby must surely have been thermally stressed because of the high temperature of the blanket on which he was lying, it appears that a raised heart rate is a good measure of thermal stress, which not only alters at the time of the insult, but may take many hours to recover. The baby maintained a normal rectal temperature, but his heart rate was higher than average, although still slowing with sleep. In studies of average children at home, however, heart rate may not be a sensitive enough measure of heat stress as it only quickens under extreme conditions.

The **fifth objective** was to to assess whether parental care alters if their baby has a natural infection or immunisation and to study the effects of these on rectal temperature, heart rate and sweating.

How do Rectal Temperature and Heart Rate Change with Infection and Immunisation?

Sweating was not assessed because of technical problems, and, after immunisation and with illness, there were insufficient recordings of heart rate. This was often because parents felt unable to cope with extra wires and equipment if they thought their baby was going to be irritable and restless.

Post-immunisation recordings are of a known entity, because a measured dose of the immunisation has been given within the previous twelve hours, and therefore level of reaction can be assessed. This was not possible with natural infection as no formal categorisation of 'illness', by the taking of swabs or scoring of symptoms by something like Morley's 'Baby-Check' system, was undertaken (Morley, Thornton, Cole, Fowler, Tunnacliffe, Walker and Green, 1991). Subjective assessments were used and reinforced Black, Morris, Smith and Townsend's (1982) conclusions that babies with a higher incidence of illness are more likely to be second or subsequent children and also bottle fed and have parents who smoke.

Some babies exhibit a characteristic night-time rectal temperature pattern when incubating an upper respiratory infection, a pattern which 50% of babies exhibit the first night after their first diphtheria, pertussis, tetanus and polio immunisation (Rawson, Petersen and Wailoo, 1990). In this study parents did not appear to alter the environment, from the normal sleeping conditions, of ill or immunised babies in order to counteract raised temperature, although paracetamol or other medicines from the doctor may have been given.

Bottle fed babies were significantly more likely than breast fed babies to have a higher rectal temperature post-immunisation. These results suggest one or both of two things:

1. Bottle fed babies belonged to the group who generally developed their night-time rectal temperature rhythm later, that is after eleven weeks of age. This

delay in the age at which the rectal temperature pattern changes may in some way affect their response to immunisation. Alternatively, there may be a period around the age of temperature rhythm development, where the baby responds differently to illness or immunisation (usually given at twelve weeks of age).

2. Breast milk may contain an ingredient which improves the babies' temperature control, which is why they were younger when their rectal temperature rhythm developed. Melatonin, which is present in breast milk, but not formula preparations, has been cited as an entrainer of circadian rhythms by some researchers (Reppert, Duncan and Goldman, 1985) and is secreted in adults by the pineal gland in response to light and darkness. Minors and Waterhouse (1981) observed that blind people do not develop circadian rhythms at the same time and to the same amplitude as sighted people. Many researchers (Addy, 1976, Gunther M, 1975 and Stanway and Stanway, 1983) have written about the beneficial affects of breast feeding in the prevention of infection, primarily because of the immunity conferred to the baby by the mother. Little is known, however, about whether breast milk offers protection from the effects of infection or whether it enables babies' thermoregulatory mechanisms to respond more appropriately.

It appears that night-time rectal temperature patterns are not only affected acutely at the time of infection, but are also influenced in the long term, both in stage two and stage three. Perhaps infection compromises babies' temperature control for quite long periods and may alter their thermoregulatory responses to other stresses. The data are difficult to quantify as the numbers were small, the ill babies may not have been assessed by myself, another Health Visitor or General Practitioner (GP) and no swabs were taken or their temperature recorded at the time; the type of illness and degree of severity was assessed by the varying subjective reports of the parents. Some of the babies were seen by a GP and medication prescribed, but parents have different thresholds for

visiting their GP (Black, Morris, Smith and Townsend, 1982), and GPs have varying thresholds for prescribing.

How Does Thermal Environment Affect Heart Rate, Breathing and Sleep State?

'Fever' is a controlled change in body temperature and probably beneficial to humans, but raised temperature may 'stress' infants in some way, as shown by the baby on the electric blanket. His heart rate rose despite his rectal temperature being normal. Higher than average room temperature and more clothing did not usually raise heart rate; on the contrary it was lowered both before and after development of the rhythm. Perhaps environmental temperature needs to be excessive, and in combination with a fever before thermoregulatory mechanisms are stressed. Unfortunately, sweating, another indication of active and possibly stressful thermoregulation, was not successfully measured using electrical skin resistance.

The mean slower heart rate of babies who slept in a warm thermal environment may indicate more slow wave or deeper sleep, perhaps a result of being comfortable. Guilleminault, Peraita, Sonquet and Dement (1975) report that the longest apneoas, with pronounced oxygen desaturation, occur with quiet sleep and are of the central (non-obstructive) type. Newman, Frost, Bury, Jordon and Phillips (1986) found arousal after partial nasal obstruction less frequent in quiet, rather than rapid eye movement (REM) sleep, with the ability to arouse from REM sleep improving after two months of age. Guntheroth (1989) concludes that the longest apneoic episodes are in quiet sleep and are more common in premature babies and 'near-SIDS'.

Guntheroth (1989) contends that apneoa may be the pathway to SIDS and cites studies that illustrate an increase in apneoic episodes when the central nervous system is depressed by, for example, alcohol (in children perhaps by that in gripe water or the phenothiazine in cough mixture) (McGinty and Harper, 1974).

Guilleminault and Coons (1983) write that sleep deprivation in adults causes a significant increase in the mean number of apneoic episodes during quiet and REM sleep, and significantly prolongs apneoa during REM sleep. In babies the most common disruption to sleep must be illness, particularly coughs and colds, although teething and colic as well as family late nights may also be disturbing. Parental anxiety, particularly with Subsequent-Siblings or after a 'near-miss' episode may also influence sleep state. In the presence of infection muramyl peptide and interleukin-1 are derived from bacterial walls, too. These increase the duration and depth of quiet sleep, produce fever and activate the immune system (Guntheroth, 1989). Frequent 'respiratory pauses' as opposed to apneoic episodes are seen in all children during REM sleep and the incidence increases with infection (Guilleminault, Peraita, Sonquet and Dement, 1975 and Abreu e Silva, Williams, MacFadyen and Simpson, 1985). Stevens (1965) (cited by Guntheroth, 1989) reports that if babies are susceptible to apneoa, rapid rises in ambient temperature are provocative and that the febrile state increases the risk of apneoa. Guntheroth (1989) hypothesises that during the fetal period, 65% of the time near term is spent in apneoa, so arousal from it is a learned response or maturational process, and some immature infants may 'accept' apneoa. Two out of five newborn monkeys failed to resume respiration spontaneously after the stimulus that induced apneoa was removed, but when re-tested at an older age had no problems.

Bradycardia is an essential part of the oxygen conserving reflex (Guntheroth, 1989) and develops if apneoa is present for more than thirty seconds (Daily, Klaus and Meyer, 1969 and Deuel, 1973 (cited by Guntheroth, 1989)). Cardiac monitoring, therefore, is probably superior to apneoa monitoring, as both upper airway apneoa and central apneoa produce bradycardia, whereas obstructive apneoa does not trigger the pneumographic alarm.

Unfortunately bradycardic heart rate is not defined, so it is difficult to assess whether the significantly slower heart rates in some groups of babies in this

study could be construed as pathological. Sleep staging, assessment of respiration and the incidence of apneoic episodes were not monitored successfully as it was not possible to prove the reliability of the readings, so therefore comparisons of sleep state, apnoeic episodes and heart rate were not made.

Is Above Average Heart Rate Harmful?

Engel and Talon (1989) illustrate that if non-human primates are subjected to consistent tachycardia, death ensues. Guntheroth (1989), however, believes it unlikely that raised heart rate is fatal without previous symptoms, as babies have a great ability to tolerate tachycardia; congestive failure does not occur for twelve to twenty-four hours and death is uncommon. 'Future-SIDS' have a higher mean heart rate as do 'Near-SIDS' and Subsequent-Siblings of babies who have died. This is perhaps a result of parental anxiety (for a review see Guntheroth, 1989). This has implications for those babies in cooler rooms and less clothing, however, perhaps indicating that they thermoregulate more in order to keep warm. It also reinforces the theories that prone sleeping position and/or babies' growth velocity are detrimental to babies, or an indication of problems (Williams, Taylor, Ford and Nelson, 1990). It does not, however, correspond to views about the benefits of breast feeding. Breast fed babies also have higher heart rates.

In this study, because of the uncertainty in interpretation of the skin temperature readings, it was not possible to assess whether the changed heart rate was due to vasodilatation or vasoconstriction

Are There Associations between Rectal Temperature and Heart Rate Circadian Rhythms and Sudden Infant Death Syndrome?

Babies who developed their temperature and heart rate rhythms after eleven weeks of age share characteristics with babies who, by various processes and scoring systems, are considered at increased risk of Sudden Infant Death Syndrome (SIDS) Being a boy, a second or subsequent child, having parents belonging to the lower social classes or a young mother, and sleeping prone have consistently been associated with increased risk of SIDS, although no causal connection has been found. Various hypotheses have also been expounded about whether 'temperature' either of the baby or the environment may be a factor in SIDS (see **Introduction**).

The data reinforce some of these theories, but although many of the babies shared characteristics with infants who have died from SIDS they were also healthy and survived. A single causal mechanism for SIDS is therefore ruled out.

If babies slept in a warmer room and more clothing in stage two of the rhythm their temperature fell as low as those in cooler thermal environments, but as they awoke, and just after waking, they had significantly higher rectal temperatures. The babies' rectal temperature might become higher still as they continue to wake, become more active and are fed, so babies in excessively warm environments, either in the short term or over long periods, may suffer acutely or be chronically affected. During the incident when a baby was on the heated electric blanket (**Chapter Eleven**) his rectal temperature did not rise and was no higher than his normal curve, which follows findings that have been reported about babies, after development of the sleeping rectal temperature rhythm, by Anderson, Petersen and Wailoo (1990). Unfortunately he was not monitored all night, so it is impossible to say whether his rectal temperature rose to higher than normal levels upon waking in the morning.

If the hypothesis is taken further, the risk of a hot environment may be minimal unless the baby is suffering from an infectious illness or has had many episodes of infection. Infection is more likely in second or subsequent children, and when ill, many children exhibit an acutely raised rectal temperature. Bottle fed babies may also have a greater reaction to infection than breast fed babies because they exhibit a higher mean rectal temperature after immunisation. Children who are repeatedly ill may therefore be subjected to a number of nights of abnormally high temperature, particularly if bottle fed, and in stage three continue to have consistently higher rectal temperatures at night than those babies who have no history of illness. If they also sleep in a warmer environment these babies could conceivably have night-time rectal temperatures 0.1°C - 0.2°C higher than their contemporaries, even when well, although they are no later developing their temperature rhythms.

Another group of theories about SIDS is that babies have 'critical periods' in their development when they are more vulnerable to external influences, or when it is important that maturational processes coincide (Hawdon, Ward Platt and Aynsley Green, 1991). The inability to mount a metabolic response to stress or immaturity of systems may contribute to Sudden Infant Death Syndrome. Harper, Hoppenbrouwers, Sterman, McGinty and Hodgman (1976) describe their results on heart rate studies in stages; in the first months of life, neuronal maturation appears to favour increased cardiac regulation during sleep. From about four months a second stage emerges, characterised by an increase, and then a decrease in rate and variability. Then after this, there is a stage indicative of mature regulatory control. These stages appear to coincide with those described for temperature in this study.

If stage two is considered as a critical or transitional period, then those babies who remain at this stage for longer, sometimes twice as long as their contemporaries, may be at greater risk. Their night-time rectal temperature may be 0.5°C higher for many more weeks and their heart rate 8-12 bpm faster

when asleep. Additionally, if they sleep in a warmer environment their temperature may be higher still. From the comparisons of bottle feeders and breast feeders, the late developers' reaction to illness or immunisation, during stage two, may also be greater than the earlier developers. It seems possible that stage two is a vulnerable period, but why do some babies succumb to SIDS at this time?

Temperature and heart rate rhythms develop at the same age but it is still uncertain whether the rhythms occur independently of each other or are causally related. The body may be unable to cope if one develops before the other and desynchronisation occurs. Another possibility is that some babies do not develop circadian rhythms, and consistently high rectal temperatures and heart rates have dire consequences.

This transitional phase must also be important for other circadian rhythms of the body, for example hormone excretion. This study did not monitor these and could not answer whether these rhythms are normally synchronised with heart rate and temperature. However, it is possible that any associations between features of babies who die from SIDS and development of temperature and heart rate rhythms may be coincidental. Perhaps SIDS is the result of the malfunction of another circadian rhythm which is normally synchronised with temperature and heart rate.

In order to answer the questions posed more fully, further research is needed to study premature babies more extensively and to compare their rhythms with those of full term babies. Confirmation that babies who are selected as being at increased risk of SIDS are later developing their rhythms needs to be sought, and more comparisons made of their night-time patterns of temperature and heart rate in different environments, for example, when they have an infection. To achieve this a consistent classification system for illness is needed and infection cultured when present in the baby.

More detailed recording of both skin temperature and measurement of water evaporation from the skin would help quantify 'thermal stress', and monitoring of the babies' movements and sleep state may be beneficial. Finally, knowledge about body temperature and synchronisation between other circadian rhythms and their development should be investigated.

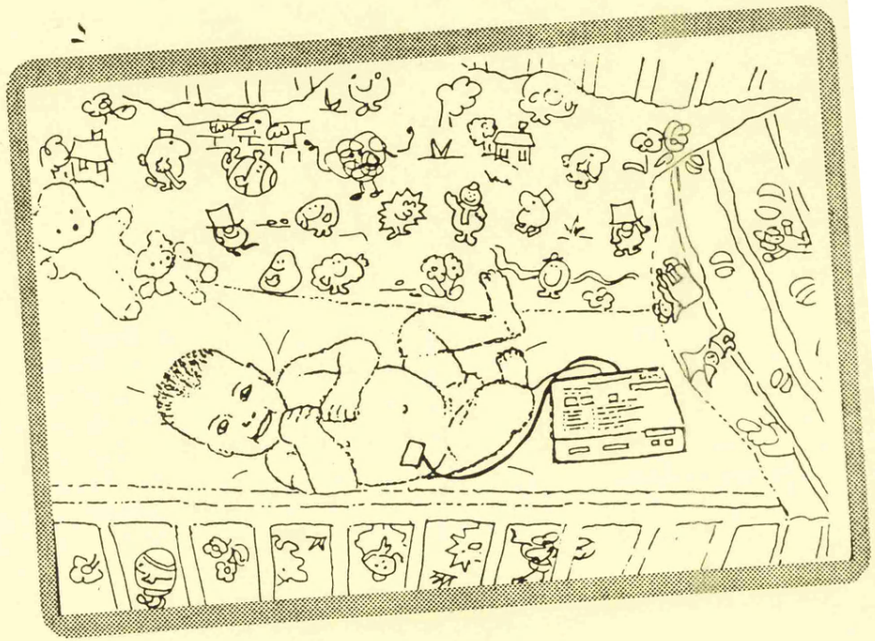
It seems likely that the early development of circadian rhythms, with consequent lower temperature and heart rate, is preferable. This means Health Visitors, Midwives, Community Doctors, General Practitioners and other health personnel should advocate that mothers breast feed and give their babies as much attention as possible, put them down to sleep in the supine or lateral position and avoid extremes of ambient temperature and wrapping. Advice about the thermal environment, however, should take into account that there is a wide range of 'normal' for babies. What is important is that the wearing of hats and other outdoor clothes when inside should be avoided, electric blankets, adult bedding and clothing should not be used and freedom of movement, especially of the head and arms, should be encouraged. Parents should be informed that, in an average home, the ambient temperature varies very little from night to night. In order to reduce the possibility of infection parents should not smoke or should at least restrict smoking to outside the baby's environment.

This study is the first step, the foundation for further research, as it provides information about the care of babies, their health and environment, as well as temperature and heart rate rhythms. It illustrates that as with all bodily processes, such as walking and talking, there is a wide range of normal development. Clues about what is abnormal have also been disclosed, providing points of reference for intervention, more stringent monitoring or treatment in order to prevent SIDS.

Our children do grow up more quickly than we think or perhaps wish, and often parents do not respond as rapidly. However, babies have great adaptive qualities which generally enable them to survive healthily despite environmental conditions and parental care, rather than because of them.

APPENDIX ONE

Could you help ?



During the last four years, doctors and health visitors in the Department of Child Health at Leicester Royal Infirmary have been carefully monitoring the body temperatures and heart rate of babies to find out whether they become too hot or too cold whilst sleeping. The results so far have been very encouraging.

By understanding how babies normally control their temperatures, we will hopefully be able to answer previously unexplained questions about childhood illness.

We are now hoping to monitor more babies, both at home and in hospital, and we are asking for your help.

Your baby's temperature and heart rate would be taken overnight in a very safe, simple way, which does not affect their sleep or care. Sometimes we also film babies in their cots.

A Health Visitor may approach you at the ante-natal clinic, on the ward, at home or at your G.P.'s surgery to explain the study further. If you are interested, please fill in the enclosed form and leave it with Sister or your family Health Visitor or leave a message at the telephone number provided.

Telephone numbers:
(0533) 585682
(0533) 585773

Health visitors; Liz, Donna, Marion and Rachel.

TMENT OF
HEALTH

AD OF
RTMENT
H SIMPSON
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UNIVERSITY OF LEICESTER

SCHOOL OF MEDICINE · CLINICAL SCIENCES BUILDING
LEICESTER ROYAL INFIRMARY · P O BOX 65 · LEICESTER LE2 7LX · ENGLAND

Dear Parent

Over the past four years doctors and health visitors in the Department of Child Health at Leicester Royal Infirmary have been carefully monitoring the body temperature and heart rate of babies at home in order to find out whether they get too hot or too cold. Many babies have taken part and the techniques used are safe and simple. Results so far have been very encouraging, and it is likely that they will lead to improvements in the care of babies.

We now wish to extend our studies and request your help by allowing your baby to take part in the project.
A Health Visitor will contact you to explain what is involved, so that you may decide whether or not you wish your baby to participate. If, however, you feel you are unable to be part of the project, please return the tear-off strip as soon as possible.

Thanks for your help.

Yours sincerely

Marion Lodemore
Health Visitor

Dr M.P. Wailoo
Senior Lecturer

Tel: 585682 or 585773

I regret I am unable to take part in this project

Name: Baby's name:

Address: Date of birth:

APPENDIX TWO

PRIMARY INFORMATION(1)

NAME **FILE NUMBER**

ADDRESS D.O.B.

MALE/FEMALE

POSTCODE

MOTHER'S NAME
UNIQUE NO.\HOSP.
AGE
OCCUPATION
GENERAL HEALTH
NO. PREVIOUS PREGNANCIES
SMOKER/NON-SMOKER

FATHER'S NAME
AGE
OCCUPATION
SOCIAL CLASS
GENERAL HEALTH
SMOKER/NON-SMOKER

SIBLING'S NAME
D.O.B.
GENERAL HEALTH

SIBLING'S NAME
D.O.B.
GENARAL HEALTH

SIBLING'S NAME
D.O.B.
GENERAL HEALTH

SIBLING'S NAME
D.O.B.
GENERAL HEALTH

FAMILY PETS:

FAMILY HISTORY OF FEBRILE CONVULSIONS- YES/NO
FAMILY MEMBER:

BIRTH DETAILS:

GESTATIONAL AGE
BIRTH WEIGHT
CENTILE
APGAR SCORE

TYPE OF DELIVERY:
NSD
ELECTIVE LSC
INDUCED
BREECH
FORCEPS
EMERGENCY LSC
ARM

LENGTH OF SECOND STAGE
ONSET OF RESPIRATIONS
COMPLICATIONS

PRIMARY INFORMATION(2)

ILLNESS AT BIRTH:

JAUNDICE
APNEOA ATTACKS
CONVULSIONS
DIFFICULTY ESTABLISHING FEEDING
INFECTION TYPE
OTHER

CONGENITAL ANOMALIES

FEEDING AT BIRTH: BREAST BOTTLE

MIXED NASOGASTRIC

SLEEPING POSITION AT BIRTH: PRONE SUPINE LATERAL

PREVIOUS ILLNESS:

TYPE	DATE	DURATION	TREATMENT

HOME CONDITIONS

BABY'S NAME **FILE NUMBER**
LOG NUMBER

TYPE OF HOUSE:	DETACHED	BUNGALOW
	TERRACE	FLAT
	BEDSIT	SEMI-DETACHED
	COUNCIL	OWNER OCCUPIED
	HOUSING ASSOCIATION	
HEATING:	CENTRAL HEATING	STORAGE HEATERS
	GAS FIRES	OPEN FIRE
	ELECTRIC FIRE	OTHER
HEATING IN ROOM WHERE BABY SLEEPS	RADIATOR	ELECTRIC FIRE
	FAN HEATER	WALL HEATER
	OTHER	
ROOM INSULATION	CAVITY WALL INSULATION	
	DOUBLE GLAZING	
	CARPET	

ANY PROBLEMS WITH HOUSING

PLEASE DRAW DIAGRAM SHOWING POSITION OF COT IN ROOM, RELATIONSHIP TO HEATER ETC AND VENTILATION:

DIARY OF CHILD HEALTH

NAME

DATE OF BIRTH

Please record if your baby is unwell, off their food, or behaving differently from normal.
Include visits to your G.P. or hospital, medicines prescribed and any immunisations that they have been given.
Thank you.

Week 1

Week 2

Week 3

Week 4

Week 5

Week 6

Week 7

Week 8

Week 9

Week 10

ANY COMMENTS

ADDITIONAL INFORMATION

BABY'S NAME **LOG NUMBER**

WEIGHT DATE

CENTILE AGE/D.O.B.

FEEDING

BREAST	WEANING FOODS	AGE OF WEANING
BOTTLE	FAMILY FOODS	FREQUENCY OF SOLIDS
BABY RICE		DATE OF CHANGE
		METHOD OF FEEDING

SLEEPING POSITION

PRONE		PRONE	BEDDING POSITION
SUPINE	TO	SUPINE	IN MORNING: ON/OFF
LATERAL		LATERAL	

CLOTHING

DAYTIME	DESCRIPTION	TOG	NIGHTTIME	DESCRIPTION	TOG
NAPPY			NAPPY		
VEST			VEST		
SOCKS			BABYGRO		
BABYGRO			NIGHTIE		
CARDIGAN			CARDIGAN		
MITTS			SLEEPSUIT		
DRESS			SOCKS		
BONNETT			OTHER		
SHIRT					
OTHER					

BEDDING	DESCRIPTION	TOG	DESCRIPTION
SHEET			BUMPERS
SHAWL			SHEEPSKIN
			MATTRESS
DUVET			WATERPROOF
BLANKET			OTHER

PILLOW

TYPE OF COT WHICH ROOM

DOOR: OPEN/CLOSED/AJAR **WINDOW:** OPEN/CLOSED
HEAT: HOUSE - TIME ROOM - TIME

IMMUNISATION HISTORY

TYPE				
DATE	1 / /	2 / /	3 / /	4 / /

REACTION(if any)

ACTIVITY SHEET

BABY'S NAME
LOG NUMBER

PLEASE WRITE DOWN THE ACTIVITIES OF YOUR BABY WHILST HE/SHE IS ON THE MONITOR. THESE MAY INCLUDE:

SLEEP
FEEDS
NAPPY CHANGE
CLOTHING CHANGE
WASHES
PLAYTIMES
HOW YOU FEEL YOUR BABY IS (ANY SICKNESS, ILLNESS OR REACTION TO IMMUNIZATION)
ANY MEDICATION GIVEN TO YOUR BABY, INCLUDING GRIPE WATER, INFACOL AND PARACETAMOL

DATE	TIME	ACTIVITY

APPENDIX THREE

Social Class Distribution in Leicestershire

Percentage of Leicestershire population from the 1981 Census

Group One (Professional ieLawyer/Doctor/Accountant)	**2.6%**
Group Two (Professional ieTeacher/Nurse/Manager)	**12.7%**
Group Three (Skilled Non-Manual ieClerk)	**8.6%**
Group Four (Skilled Manual ieElectrician/Plumber)	**29.7%**
Group Five (Semi-Skilled ieMachine Operator/Lorry Driver)	**16.4%**
Group Six (Unskilled ieLabourer)	**4.5%**
Group Seven (Unemployed)	**22.1%**
Armed Forces	**3.5%**

BIBLIOGRAPHY

PREVIOUS PUBLICATIONS

Lodemore M.R., Petersen S.A. and Wailoo M.P. 1991 Development of night time temperature rhythms over the first six months of life.
Arch Dis Childh;**66**;521-524

Petersen S.A, Anderson E.S., Lodemore M.R., Rawson D. and Wailoo M.P. 1991 Sleeping position and rectal temperature.
Arch Dis Childh;**66**:976-979

Lodemore M.R., Petersen S.A. and Wailoo M.P. 1992 Factors affecting the development of night-time temperature rhythms.
Arch.Dis.Childh;**67**:1259-1261

REFERENCES

Abreu e Silva F.A., Williams A., MacFadyen U.M. and Simpson H. 1985 Sleep apnoea in infancy.
Journal of the Royal Society of Medicine;78:1005-1007

Adam J.M. and Ferres H.M. 1954 Observations on oral and rectal temperature in the humid tropics and in a temperate climate.
Journal Physiology;125:21

Adams F.H., Fujiwara F., Spears R. and Hodgman J. 1964 Temperature regulation in premature infants.
Paediatrics;**33**:487

Adamson K., Gandy G.M. and James L.S. 1965 The influences of thermal factors upon the oxygen consumption of the newborn infant.
J Paediatr;**66**:495

Adamsons K.Jr. and Towell M.E. 1965 Thermal homeostasis in the fetus and newborn.
Anesthesiology;**26**:531

Adamsons K. Jr. 1966 The role of thermal factors in fetal and neonatal life.
Pediatr. Clin.North Am;13:599

Addy D.P. 1976 Infant feeding: a current view.
Br Med J; **1**:1268-1271

Aikas E., Karvonen M.J., Pironen P. and Ruosteenoja R. 1962 Intramuscular, rectal and oesophageal temperature during exercise.
Acta Physiol Scand;**54**:366-370

Anderson E.S., Wailoo M.P. and Petersen S.A. 1990 Use of thermographic imaging to study babies sleeping at home.
Arch Dis Childh;**65**:1266-1267

Anderson E.S., Petersen S.A. and Wailoo M.P. 1990 Factors influencing the body temperature of 3-4 month old infants at home during the day.
Arch Dis Childh;**65**:1308-1310

Aschoff J. 1960 Exogenous and endogenous components in circadian rhythms.
Cold Spr Harb Symp Quant Biol;**25**:11-28

Aschoff J., Gerecke U. and Wever R. 1967 Desynchronization of human circadian rhythms.
Jap J Physiol;**17**:450-457

Babson S.G, and Clarke N.B. 1983 Relationship between infant death and maternal age.
J Paediatr;**103**:391-3

Bacon C.J., Bell S.A., Clulow E.E. and Beattie A.B. 1991 How mothers keep their babies warm.
Archives of Disease in Childhood;**66**:627-632

Bacon C., Scott D. and Jones P. 1979 Heatstroke in well-wrapped infants.
The Lancet;Feb 24:422-425

Balarajan R., Raleigh S.V. and Botting B 1989 Sudden infant death syndrome and postneonatal mortality in immigrants in England and Wales.
Br Med J;**298**:716-720

Banks B.D., Beck R.W., Columbus M., Gold P.M., Kinsinger S. and Lalonde M.A. 1987 Sudden infant death syndrome: a literature review with chiropractic implications.
Journal of Manipulative and Physiological Therapeutics;vol.10:no.5

Beal S.M. 1983 Some epidemiological factors about sudden infant death syndrome in South Australia.
Tildon J. T., Roeder L. M. and Steinschneider A. (eds) Sudden Infant Death Syndrome. Academic Press, New York. 1983;15-28

Beal S.M. and Finch C.F. 1991 An overview of retrospective case-control studies investigating the relationship between prone sleeping position and sudden infant death syndrome.
J Paediatr Child Health;**27**:334-339

Beck U., Reinhardt H., Kendel K. and Schmidt-Kessen W. 1976 Temperature and endocrine activity during sleep in man.
Arch Psychiat Nervenkr;**222**:245-256

Beckwith J.B., 1970 Epidimiology. Bergman A.B., Beckwith J.B. and Ray C.G. (eds). Sudden Infant Death Syndrome. Washington: University of Washington Press:18

Bergman A.B. and Weisner L. 1976 Relationship of passive smoking to sudden infant death syndrome.
Pediatrics;**58**:665-8

Black D., Morris J.N., Smith C. and Townsend P. 1982 Inequalities in Health: The Black Report. Townsend P. and Davidson N. (eds). Penguin books

Blackfan K.D. and Yaglou C.P. 1933 The premature infant. A study of the effects of atmospheric conditions on growth and on development.
American Journal of Diseases of Children;**46**:1175

Bland J.M. and Altman D.G. (1986) Statistical methods for assessing agreement between two methods of clinical measurement.
The Lancet;**i**;307-310

Bonegio R.G.B., Driver H.S., King L.M., Laburn H.P. and Shapiro C.M. 1988 Circadian temperature rhythm blunting and sleep composition.
Acta Physiol Scand;133 supplementum **574**:44-47

Brown P.J., Dove R.A., Tuffnell C.S. and Ford R.P.K. 1992 Oscillations of body temperature at night.
Arch Dis in Childh;**67**:1255-8

Bruck K. 1961 Temperature regulation in the newborn infant.
Biol Neonat;**3**:65

BS4745 1986 Methods for the determination of thermal resistance of textile materials. London. British Standards Institute.

BS5335 1984 Specification for continental quilts. London. British Standards Institute.

Budin P. 1900 Le nourrisson, alimentation et hygeine des enfants debiles - enfants nes a terme.
Octave Poin, Paris (ed)

Buetow K.C. and Klein S.W. 1964 Effect of maintenance of "normal" skin temperature on survival of infants of low birth weight.
Pediatrics;**34**:163

Buntain W.L., Pregler M., O'Brien P.C. and Lynn H.B. 1977 Axillary versus rectal temperature: a comparative study.
J Lousiana State M Soc;vol 129:no 1

Burton A.C. and Edholm O.G. 1955 Man in a Cold Environment.
Publ. Arnold, London

Butler D.R., Goldstein H. and Ross E.M. 1972 Cigarette smoking in pregnancy: its influence on birth weight and mortality.
Br Med J; **2**:127

Cabanac M. 1975 Temperature regulation.
Ann Rev Physiology:415-439

Cabanac M. and Massonnett B. 1977 Thermoregulatory responses as a function of core temperature in humans.
J Physiol;**265**:587-596

Cambell E.J., Dickinson C.J., Slater J.D.H., Edwards C.R.W. and Sikora K. (Eds) 1984 Clinical Physiology. Fifth Edition. Blackwell Scientific Publication

Cambell M.J. 1989 Sudden infant death syndrome and environmental temperature: further evidence for a time-lagged relationship.
The Medical Journal of Australia;vol.151, Oct 2:365-367

Carpenter R.G. and Emery J.L. 1974
Sudden Infant Death Syndrome:91-96
Robinson R.B. (ed). FSID, London

Carpenter R.G., Gardner A., Pursall E., McWeeny P.M. and Emery J.L. 1979 Identification of some infants at immediate risk of dying unexpectedly and justifying intensive study.
Lancet;18 August:343-346

Carpenter R.G., Gardner A., Jepson M., Taylor E.M., Salvin A., Sunderland R., Emery J.L., Pursall E. and Roe J. 1983 Prevention of unexpected death. Evaluation of the first seven years of the Sheffield intervention programme.
The Lancet;2 April:723-727

Carpenter R. 1988 Preventing unexpected infant deaths by giving extra care to high risk infants.
Health Visitor;**61**:238-240

Coghill R. 1990 Killing fields. The biophysical evidence.
Electronics World and Wireless World;Feb:112-118

Colin J., Timbal J. and Boutelier C. 1968 Rhythm of the rectal temperature during a six month free-running experiment.
J Appl Physiol;**25**:170-176

Conroy J.T.W.L. and Mills J.N. 1970 Human Circadian Rhythms.
Publ. J and A Churchill, London

Czeisler C.A. 1978 Human circadian physiology; internal organization of temperature, sleep-wake and neuroendocrone rhythms monitored in an environment free of time cues.
Phd. thesis, Stanford University

Daily W.J., Klaus M. and Meyer H.B. 1969 Apnea in premature infants: monitoring incidence, heart rate changes and an effect of environmental temperature.
Pediatrics;**43**:510

Daly J.R. and Evans J.I. 1974 Daily rhythms of steroid and associated pituitary hormones in man and their relationship to sleep.
Adv Steroid Biochem Pharmacol;**4** :61-110

Davy J. 1845 On the temperature of man.
Phil Trans;**2**:319-333

Day R. 1941 Regulation of body temperature during sleep.
Amer J Dis Child;**61**:734
Dayson H. 1970 A Textbook of General Physiology. Vol.One, Fourth Edition

Denborough M.A., Galloway G.J. and Hopkinson K.C. 1982 Malignant hyperpyrexia and sudden infant death.
The Lancet;Nov 13:1068-1069

Downham M.A.P.S. and Stanton A.N. 1981 'Keep cool baby': the risks of overheating in young babies.
The Health Visitor; vol 54

D'Souza S.W., Tenreiro S., Minors D., Chiswick M.L., Sims D.G. and Waterhouse J. 1992 Skin temperature and heart rate rhythms in infants of extreme prematurity.
Arch Dis Childh;**67**:784-788

Dwyer T., Ponsonby A.L., Gibbons L.E. and Newman N.M. 1991 Prone sleeping position and SIDS: evidence from recent case-control and cohort studies in Tasmania.
J Paediatr Child Health;**27**:340-343

Edholm O.G. 1978 Man - Hot and Cold.
publ. Edward Arnold

Edholm O.G. and Weiner J.S. 1981 Thermal Physiology.
Principles and Practice of Human Physiology;chapt 3:170.
Publ Academic Press, London

Egan D.F., Illingworth R.S. and MacKeith R.C. 1969 Developmental Screening, 0-5 years.
Publ.by E. and S. Livingstone

Elliott A.L., Mills J.N. and Minors D.S 1972 The effect of real and simulated time zone shifts upon the circadian rhythms of body temperature, plasma 11-hydroxycorticosteroids and renal excretion in human subjects.
J Physiol;**221**:227-257

Engel B.T. and Talon M.I. 1989 The role of the sympathetic nervous system in the regulation of diurnal hemodynamic patterns.
Acta Physiologica Scandinavica;136,suppl584:14

Engleberts A.C., de Jonge G.A. and Kostense P.J. 1991 An analysis of trends in the incidence of sudden infant death in The Netherlands 1969-1989.
J Paediatr Child Health;**27**:329-333

Fleming P.J., Gilbert R., Azaz Y., Berry P.J., Rudd P.T., Stewart A. and Hall E. 1990 Interaction between bedding and sleeping position in the sudden infant death syndrome: a population based case-control study.
Br Med J;**301**:85-89

Froggatt P., Lynas M.A. and MacKenzie G. 1971 Epidemiology of sudden unexpected death in infants ("cot death") in Northern Ireland.
Brit.J.Prev.Soc.Med;25:119

Ganong W.F. 1985 Review of Medical Physiology.
Twelfth Edition;chapter 14. Lange Medical publ.

Gierse A. 1842 Quaemiam sit ratio caloris organics.
Dissertation, Halle

Glass L., Silverman W.A. and Sinclair J.C. 1968 Effect of the thermal environment on cold resistance and growth of small infants after the first week of life.
Pediatrics;**41**:1033

Godlin R.C. and Horowitz M. 1971 Thermal effects on heart rate of the neonate.
Am J Obstet Gynecol;**110**:674

Goldberg J., Hornung R., Yamashita T. and Wehrmacher W. 1986 Age at death and risk factors in sudden infant death syndrome.
Aust Peaediatr J;**22** (suppl 1):21-8

Golding J., Limerick S. and Macfarlane A. 1985 Sudden Infant Death. Patterns, Puzzles and Problems.
Open Books Publishing Company, England

Gordon R.R. 1989 Trends in unexpected deaths in Sheffield (letter).
The Lancet;Jan 14:106

Gordon R.R. 1992 What counts as cot death?
British Medical Journal;**304**:1508

Grausz J.P. 1968 The effect of environmental temperature changes on the metabolic rate of newborn babies.
Acta Pediat Scand;**57**:98

Groos G.A. 1983 Circadian rhythms and the circadian system.
Adv Biol Psychiat;vol 11:1-9

Guilleminault C. and Coons S. 1983 Sleep states and maturation of sleep: a comparative study between full-term normal and near-miss sudden infant death syndrome infants.
Sudden Infant Death Syndrome; pg401:Tildon J. T., Roeder L.M. and Steinschneider A. (eds). Academic Press, New York

Guilleminault C., Peraita R., Sonquet M. and Dement W.C. 1975 Apneoas during sleep in infants: possible relationship with sudden infant death syndrome.
Science;190:677

Gunther M. 1975 The neonates immunity gap, breast feeding and cot death.
The Lancet;Feb 22:441-442

Guntheroth W.G. 1989 Crib Death. The Sudden Infant Death Syndrome.
Second Edition. Futura Publishing Company, New York

Halberg F., Reinhardt J. and Bartter F.C. 1969 Agreement in endpoints from circadian rhythmometry on healthy human beings living on different continents.
Experientia;**25**:106-112

Hammel H.T. 1968 Regulation of internal body temperature.
Annu Rev Physiol;**30**:641

Harper R.M., Hoppenbrouwers T., Sterman M.B., McGinty D.J. and Hodgman J. 1976 Polygraphic studies of normal infants during the first six months of life. 1. Heart rate and variability as a function of state.
Pediat Res;**10**:945-951

Hawdon J. M., Ward Platt M.P. and Aynsley Green A. 1991 Postnatal metabolic adaptation - the effects of gestation and feeding.
Foundation for Sudden Infant Death conference. Cambridge, Sept. 1991

Hays W.L. 1969 Statistics.
Publ. Holt, Rinehart and Winston, London

Heim T., Kellermeyer M. and Dani M. 1968 Thermal conditions and the mobilization of lipids from brown and white adipose tissue in the human neonate.
Acta Paediatr Sci Hung;**9**:109-120

Hellbrügge T. 1960 The development of circadian rhythms in infants.
Cold Spring Harbour Symposium Quantitative Biology;**25**:311-323

Hellbrügge T. 1974 The development of circadian and ultradian rhythms of premature and full-term infants.
Schering L E, Halberg R and Pauly J E (eds). Chronobiology:339-341.Tokyo, Igaku Shoin

Hellbrügge T., Lange J. and Rutenfranz J. 1956 Uber die Entwicklung von tagesperiodischen Veranderungen der Pulsfrequenz im Kindesalter.
Zscher Kunderhk;**78**:703-22

Hellbrügge T., Lange J.E., Rutenfranz J. and Stehr K. 1964
Circadian periodicity of physiological functions in different stages of infancy and childhood.
Annals New York Academy of Sciences;**117**:361-373

Hensel H. 1981 Thermoreception and temperature regulation.
London Academic Press. Monographs of the Physiological Society;**38**

Hey E. 1971 The Care of Babies in Incubators.
In Recent Advances in Paediatrics;171-215: Churchill

Hey E. 1975 Thermal neutrality.
Br.Med.Bull;31:69-74

Hey E.N. and Katz G. 1969 Evaporative water loss in the newborn baby.
J Physiol;**200**:605

Hey E.N. and Katz G. 1970 The optimum thermal environment for naked babies.
Archives of Disease in Childhood;**45**:328-333

Hey E.N. and Mount L.E. 1967 Heat losses from babies in incubators.
Arch Dis in Childh;**42**:75

Hey E.N. and O'Connell B. 1970 Oxygen consumption and heat balance in the cot-nursed baby.
Arch Dis in Childh;**45**:335-343

Hildebrandt G. 1974 Circadian variations of thermoregulatory response in man.
Schering L E, Halberg F and Pauly J E (eds) Chronobiology:234-240. Tokyo, Igaku Shoin

Hilgard E.R., Atkinson R.C and Atkinson R.L. 1975 Introduction to Psychology. Sixth Edition.
Harcourt Brace Jovanovich Inc., New York

Hill J.R. and Rahimtulla K.A. 1965 Heat balance and the metabolic rate of new-born babies in relation to environmental temperature; and the effect of age and weight on basal metalbolic rate.
J Physiol;**180**:239-265

Hoppenbrouwers T., Jensen D and Hodgman J. 1979 Respiration during the first six months of life in normal infants. II The emergence of a circadian pattern.
Neuropadiatrie;**10**:264-280

Hoppenbrouwers T. and Hodgman J.E. 1992 Is SIDS precipitated by a cluster of dynamic changes during development?
Clinical Research;**40**:67

Illingworth R.S. 1972 The Development of Infants and Young Children: Normal and Abmormal.
5th edition; Livingstone, Edinburgh

de Jonge G A., Engleberts A.C., Koomen-Liefting A.J.M. and Kostense P.J. 1989 Cot death and prone sleeping position in The Netherlands.
Br Med J;**298**:722

Jundell 1904 Uber die nykthemeralan Temperaturschwankungen im 1. Lebensjahre des Menschen.
Jb Kinderheilth;**59**:521-619

Keele C., Neil E. and Joels N. 1982 Samson Wright's Applied Physiology. Thirteenth Edition. Oxford Medical Publications.

Kelly D.H., Golub H., Carley D. and Shannon D.C. 1986 Pneumograms in infants who subsequently died of sudden infant death syndrome.
J.Peduatr;109:249

Keppel G. 1991 Design and Analysis. A Researchers Handbook.
Prentice Hall. Englewood Cliffs, N.J.

Kerslake D. McK. 1991 The insulation provided by infants' bedclothes.
Ergonomics;Vol 34 no 7:893-907

Kleitman N. and Kleitman E. 1953 Effect of non-24-hour routines of living on oral temperature and heart rate,
J Appl Physiol;**6**:283-291

Kleitman N. and Ramsaroop A. 1948 Periodicity in body temperature and heart rate.
Endocrinology;**43**:1-20

Kleitman N., Titelbaum S. and Hoffman H. 1937 The establishment of the diurnal temperature cycle.
Amer J Physiol;**119**:48-54

Knowelden J., Keeling J., Nicholl J.P., Emery J.L., Harris F., Oakley J.R., Stanton A.N. and Huber J. 1984 A Multicentre Study of Post-neonatal Mortality.
Medical Care Research Unit. University of Sheffield

Kraus J.F., Greenland S. and Bulterys M. 1989 Risk factors for sudden infant death syndrome in the US collaborative perinatal project.
Int J Epidmiol;**18**:113-20

Lee N.N.Y., Chan Y.F., Davies D.P., Lau E. and Yip D.C.P. 1989 Sudden infant death in Hong Kong: confirmation of low incidence.
Br Med J;**298**:721

Leistner H.L., Haddad G.G., Epstein R.A., Lai T.L., Epstein M.A. and Mellins R.B. 1980 Heart rate and heart rate variability during sleep in aborted sudden infant death syndrome.
Journal Pediatr;97:51

Limerick S.R., Gardner A. 1992 What counts as cot death?
British Medical Journal;**304**:1176

Lobban M.C. 1967 Daily rhythms of renal excretion in arctic-dwelling Indians and Eskimos.
Q J Exp Physiol;**52**:401-410

Mann T.P. and Elliot R.I.K. 1957 Neonatal cold injury due to accidental exposure to the cold.
Lancet;**1**:229-234

Martin-du-Pan R. and Vollenweider L. 1967 L'apparition du Rhythme Circadian des 17-hydrosysteroides chez le Nourrissons. Sa Modification sons L'effet de la Consommation de Corticosteroides.
Praxis;56:138-144

Martin-du-Pan R. 1974 Some clinical applications of our knowledge of the evolution of the circadian rhythms in infants.
Schering L E , Halberg F and Pauly J E (eds). Chronobiology. Tokyo, Igaku Shoin:342-347

McGinty D.J. and Harper R.M. 1974 Sleep Physiology and SIDS: Animal and Human Studies.
In SIDS (ed.Robinson R.R.):201. Publ.The Canadian Foundation for the Study of Infant Deaths

McGlashan N. D. and Grice A.C 1983 Sudden infant deaths and seasonality in Tasmania, 1970-1976.
Soc Sci Med;vol 17 no 13:885-888

McKeever P., Vaughan K., Pallot D.J., Simpson H. and Beardsmore C. 1991 Carotid body catecholamines in experimental animals, sudden infant death syndrome infants and infants dying of other known causes.
Foundation for Sudden Infant Death Conference, Cambridge, Sept, 1991

Mestyan J., Jarai I. and Fekete M. 1968 The total energy expenditure and its components in premature infants maintained under different nursing and environmental conditions.
Pediatric Research;2:161

Mills J.N. 1973 Biological Aspects of Circadian Rhythms.
Publ. by Plenum Press, London and New York

Mills J.N. 1975 Development of circadian rhythms in infancy.
Chronobiolia;**2**:363-371

Minors D.S. and Waterhouse J.M. 1979 The effect of maternal posture, meals and time of day on fetal movements.
Br J Obstet Gynaecol;**86**:717-723

Minors D.S. and Waterhouse J.M. 1980 Development of Circadian Rhythms in Infancy.
Scientific Foundations of Paediatrics:980-997

Minors D.S. and Waterhouse J.M. 1981 Circadian Rhythms and the Human.
Publ. by Wright. PSG, Bristol, London and Boston

Mirmiran M. and Kok J. H. 1991 Circadian rhythms in early human development.
Early Human Development;**26**:121-128

Morley C.J., Thornton A.J., Cole T.J., Fowler M.A., Tunnacliffe J.M., Walker K.A. and Green S.J. 1991 Baby Check. The Baby Illness Research Project.
University of Cambridge. Dept. of Paediatrics

Morley C.J., Hewson P.H., Thornton A.J. and Cole T.J., 1992 Axillary and rectal temperature in infants.
Arch Dis in Childh;**67**:122-125

Motil K.J. and Blackburn M.G. 1973 Temperature regulation in the neonate.
Clinical Pediatrics;Nov:634-639

Mount L.E. 1966 Basis of heat regulation in homeotherms.
Br.Med.Bull.;22:84-87

Mullin J.J. 1939 Development of the diurnal temperature and motility patterns in a baby.
Amer J Physiol;126:589

Nadel E.R., 1977 Problems with Temperature Regulation during Exercise.
Nadel E R (ed). Academic Press Inc.

Nadel E.R. and Horvath S.M. 1970 Comparison of tympanic membrane and deep body temperatures in man.
Life Sciences;vol 9 no 15

Nelson E.A.S., Taylor B.J. and Weatherall I.L. 1989 Sleeping position and infant bedding may predispose to hyperthermia and the sudden infant death syndrome.
Lancet;**1**:199-201

Newman N.M., Frost J.K., Bury L., Jordan K. and Phillips K. 1986 Responses to partial nasal obstruction in sleeping infants.
Aust.Paediatr.J;**22**:111

Nicoll A. and Davies L. 1986 How warm are babies kept at home?
Health Visitor;**59**,4:113-114

Oakley J.R., Tavare C.J. and Stanton A.N. 1978 Evaluation of the Sheffield system for identifying children at risk for unexpected death in infancy.
Archives of Disease in Childhood;53:649-652

Office of Population and Surveys 1980 Classification of Occupations. HMSO, London

Orr U.C., Stahl M.L., Duke J., McGaffree M.A., Toubas P., Mattice C. and Kraus H.F. 1985 Effect of sleep state and position on the incidence of obstructive and central apneoa in infants.
Pediatria;75:832

Parks Y.A., Paton J.Y., Beardsmore C.S., Macfadyen U.M., Thompson J., Goodenough P.C. and Simpson H. 1989 Respiratory control in infants at increased risk for sudden infant death syndrome.
Arch Dis Childh;**64**:791-797

Parmalee A.H. Jr. 1961 Sleep patterns in infancy. A study of one infant from birth to eight months of age.
Acta Paediat;**50**:160-170

Parrish W.E., Barrett A.M., Gunther M. and Camps F.E. 1960 Hypersensitivity to milk and sudden infant death in infancy.
Lancet;2:1106

Perlstein P.H., Edwards N.R. and Sutherland J.M. 1970 Apnea in premature infants and incubator air temperature changes.
N Engl J Med;**282**:461

Peterson D.R., Sabotta E.E. and Daling J.R. 1986 Infant mortality among subsequent siblings of infants who died of sudden infant death syndrome.
J Ped;**108** no 6 :911-914

Pfeiffer K.C. 1980 Significance of rectal temperature and environmental studies in sudden infant death syndrome.
Dt Med Wschr;**105:**1065

Ponsonby A-L., Jones M.E., Lumley J., Dwyer T. and Gilbert N. 1992 Sudden infant death syndrome: factors contributing to the difference in incidence between Victoria and Tasmania;**156**:252-4

Ponsonby A-L., Dwyer T. and Jones M.E. 1992 Sudden infant death syndrome: seasonality and the biphasic model of pathogenesis.
Jour of Epidemiol and Commun Health;**46**:33-37

Poole S. and Stephenson D. 1977 Core temperature: some shortcomings of rectal temperature measurements.
Physiology and Behaviour. Vol 18:203-205
Pergamon Press and Brain Research Publ.

Prentice T. 1988 Cot deaths on the increase.
The Times;March 18

Rawson D., Petersen S.A. and Wailoo M.P. 1990 Rectal temperature of normal babies the night after first diphtheria, pertussis and tetanus immunisation.
Archives of Disease in Childhood;**65**:1305-1307

Reinberg A. 1970 Evaluation of circadian dyschronism during transmeridian flights.
Stud Gen;**23**:1159-1168

Reinberg A. 1975 Circadian changes in the temperature of human beings.
Bibl Radiol;**6**:128-139

Reppert S.M., Duncan M.J. and Goldman B.D. 1985 Photic influences on the developing mammal.
in Photoperiodism, Melatonin and the Pineal;116-128:Ciba Foundation Symposium 117

Richards J.M., Alexander J.R., Shinebourne E.A., deSwiet M., Wilson A.J. and Southall D.P. 1984 Sequential 22 hour profiles of breathing patterns and heart rate in 110 full-term infants during the first six months of life.
Pediatrics;**74,no5**:763-777

Rizack M. 1964 Activation of epinephrine-sensitive lipolytic activity from adipose tissue by adenosine 3-5 phosphate.
J Biol Chem;**239**:385-392

Rutter N. and Hull D. 1979 Water loss from the skin of term and preterm babies.
Arch Dis in Childh;**54**:858-868

Rutter N. and Hull D. 1979 Response of term babies to a warm environment.
Arch.Dis.in Childh;54:178-183

Sasaki T. 1964 Effect of rapid transpostion around the earth on diurnal variation in body temperature.
Proc Soc Exp Biol, N Y;**115**:1129-1131

Schaefer K.E., Kerr C.M. and Buss D. 1979 Effect of 18-h watch schedules on circadian cycles of physiological functions during submarine patrols.
Undersea Biomed Res:S81-S90

Schiff D., Stern L. and Leduc J. 1966 Chemical thermogenesis in newborn infants: catecholamine excretion and the plasma nonesterified fatty acid response to cold exposure.
Pediatrics;**37**:577

Scopes J. 1966 Metabolic rate and temperature control in the human baby.
Br.Med.Bull;22:88-91

Scopes J.W. 1975 in Neonatology, Pathophysiology and Management of the Newborn.
Gordon B. and Avery J.B. (eds);Lippincott Co.Philidelphia, Toronto

Shannon D.C. and Kelly D. 1977 Impaired regulation of alveolar ventilation and the sudden infant death syndrome.
Science;**197**:367-368

Silverman W.A., Ferrtig J.W and Berger A.P. 1958 The influence of the thermal environment upon the survival of newly born premature infants.
Pediatrics;22:876

Simpson H., Pallot D., Thomas D., Swaminathan S. and Beardsmore C. 1991 Does the peripheral chemoreceptor response differ in identical and non-identical twins?
Foundation for Sudden Infant Death Conference, Cambridge, Sept 1991

Smialek J.E. 1986 Simultaneous sudden infant death syndrome in twins.
Pediatrics;**77** no 6:816-821

Sostek A. M., Anders T.F. and Sostek A.J. 1976 Diurnal rhythms in 2- and 8-week old infants: sleep-waking state organisation as a function of age and stress.
Psychosom Med;**38**:250-256

Southall D.P., Arrowsmith W.A., Stebbins V. and Alexander J.R. 1986
QT interval measurements before sudden infant death syndrome.
Arch.Dis.Childh;61:327

Southall D.P., Stevens V., Franks C.I., Newcombe R.G., Shinebourne E.A. and Wilson A.J. 1988 Sinus tachycardia in term infants preceding sudden infant death.
Eur.J.Pediatr;147:74

Stanton A.N. 1984 Overheating and cot death.
The Lancet;Nov 24:1199-1201

Stanton A.N., Scott D.J. and Downham M.A.P.S. 1980 Is overheating a factor in some unexpected infant deaths?
The Lancet;May 17:1054-1057

Stanway A. and Stanway P. 1983 Breast is Best.
Pan books, London

Stern L. 1977 Thermoregulation in the newborn infant: physiologic and clinical considerations.
Acta Pediatr.Belg;30:3-14

Sulyok E., Jequier E. and Prod'Hom L.S. 1973 Thermal balance of the newborn infant in a heat-gaining environment.
Pediat Res;**7**:888-900

Sunderland R. and Emery J.L. 1981 Febrile convulsions and cot death.
The Lancet;ii:176-178

Takahashi Y., Kipnis D.M. and Daughaday W.H. 1968 Growth hormone secretion during sleep.
J Clin Invest;**47**:2079-2090

Taylor B.J. 1991 A review of epidemiological studies of sudden infant death syndrome in Southern New Zealand.
J Paediatr Child Health;**27**:344-348
Taylor B. and Wadsworth J. 1987 Maternal smoking during pregnancy and lower respiratory tract illness in early life.
Arch Dis Childh;**62**:786-791

Thomas K.A. 1991 The emergence of body temperature biorhythm in preterm infants.
Nursing Research;**40**:2

Turner P. (chairman) 1991 Sudden infant death (SIDS): report of the expert working group enquiring into the hypothesis that toxic gases evolved from chemicals in the cot mattress covers and cot mattresses are a cause of sudden infant death.
Great Britain, Dept.of Health;London HMSO

Voet D. and Voet J.G. 1990 in Biochemistry.
622-624:Wiley, New York

Wailoo M.P., Petersen S.A., Whittaker H. and Goodenough P. 1989 Sleeping body temperatures of 3-4 month old infants.
Arch Dis Childh;**64**:596-599

Wailoo M.P., Petersen S.A. and Whittaker H. 1990 Disturbed nights and 3-4 month old infants: the effects of feeding and thermal environment.
Arch Dis Childh;**65**:499-501

Watson E., Gardner A. and Carpenter R.G. 1981 An epidemiological and sociological study of unexpected death in infancy in nine areas of southern England. 11 Symptoms and patterns of care.
Med Sci Law;**21**:89-98

Webb W. 1974 The rhythms of sleep and waking.
Schering L E, Halberg F and Pauly J E (eds). Chronobiology. Tokyo, Igaku Shoin:482-486

Wever R. 1979 The circadian system of man. Results of experiments under temporal isolation.
Berlin Spring Verlag

Williams S.M., Taylor B.J., Ford R.P.K. and Nelson E.A.S. 1990 Growth velocity before sudden infant death.
Archives of Disease in Childhood;**65:**1315-1318

Zurbrugg R.P. 1976 Hypothalamic-pituitary-adrenocortical regulation: a contribution to its assessment, development and disorders in infancy and childhood with special reference to plasma circadian rhythm.
Monographs in Paediatrics;vol 7. Basel:Karger