Analysis of Respiratory Rate and the Respiratory Cycle in Infants and Children using an Optical Sensor

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1995.
Statement of Sources

I declare that the material contained within this thesis submitted for the Bachelor of Medical Science degree, is my own personal work unless otherwise acknowledged. This work has not been submitted for assessment or publication at any other University or Institution.

Anthony Herbert.

Anthony Herbert
Acknowledgments

I would like to thank my co-supervisors for assistance throughout the year I was undertaking this project. Professor John Pearn, of the Department of Child Health, University of Queensland, was a great source of inspiration and encouragement. Dr Stephen Wilson, of the Centre for Magnetic Resonance, University of Queensland, freely offered advice about the direction of the project throughout the year. I am also grateful for his technical skill in developing and maintaining the fibre optic sensor and the computer software required to make it operate.

Dr Paul Francis, of the Department of Respiratory Medicine, Royal Children's Hospital, Brisbane, has been a great help throughout the year in discussing research methods and findings. Dr Claire Wainwright, of the same department, has also been of assistance in suggesting and discussing ideas, as well as allowing me to test some of the children in her own study. Mr Barry Dean provided assistance with working with computers and respiratory function tests.

The staff at the Mater Children's Hospital Sleep Laboratory, Brisbane, assisted with comparing the optical sensor with a respiratory inductive plethysmograph. I would like to thank Dr Brent Masters, Ms Jane Brass and Professor Brian Hill for ideas and assistance in doing this. Dr Gina Benchetrit, of the Laboratoire de Physiologie, La Tronche, France, provided the computer program, *McAster Version 2.8*. Dr Graham Huxham, of the University of Queensland's Department of Physiology and Pharmacology, helped me with using this program on the Apple Macintosh Computers.

Dr Vic Siskind, of the Department of Social and Preventive Medicine, University of Queensland, provided very helpful statistical advice. Mrs Huiqi Pan, of the Institutes of Education and Child Health, University of London, provided the *Grostat* program which allowed me to develop centile charts. Professor John Biddulph, of the Department of Child Health, University of Queensland, assisted by proof-reading the thesis and offering advice about improvements which could be made.

The clinical nurse consultants in the various wards of the Royal Children's Hospital, Brisbane, assisted with finding children with various respiratory diseases. In particular I would like to thank Sisters Ramm, Kruck, Buyes and Nichol and all of their nursing staff. I am also grateful to Dr Simon Latham, Dr Ken Armstrong, Ms Janelle Lugge and the nursing staff of the
Riverton Centre, Clayfield, for providing me with access to infants at this centre. Dr Tim Donovan supervised my work in the Royal Women's Hospital, Brisbane.

Many children and their parents assisted by participating in the project. There are numerous childcare centres and kindergartens which allowed me to test children aged less than six years. The directors of these centres received an extra administrative burden by distributing and collecting parent information and consent forms. In particular, I would like to thank staff at the Peter Pan, Peter Rabbit, Silky Oaks, Mowbray House, Margaret Cribb, Lady Gowrie, Alexandra Hills and Wilston Child Care Centres. I would also like to thank the staff at St Thomas', Herston, General Gordon and Belmont Kindergartens.

Principals and staff at schools were also accommodating in allowing me to test children during class time. These schools included Redlands College, Anglican Church Grammar School, St Ambrose School and the Mansfield Christian Outreach College. Various youth groups and clubs allowed me to test children in their groups such as the East Brisbane After-school Care, Wynnum and Bayside Boy's Brigade, Ipswich Church of England Boys' Society, Mt Gravatt, Slack's Creek and Algester Girls' Friendly Societies and the Manly Sea and Birkdale Scouts. Mrs Alison Corcoran assisted with testing the primary school children.

I would also like to thank the Department of Child Health and Centre for Magnetic Resonance at the University of Queensland for providing the resources for this work to proceed. The Head of Department, Dr Bill McWhirter, and office staff, Ms Ethyl Brown, Ellen Donovan and Janet Pullen, at the Department of Child Health have been of great help when any problem arose. This project was funded by the Asthma Foundation of Queensland (through the Rex Death Asthma Foundation Scholarship), Charles Ferdinand Marks and Elizabeth Gray Marks Prize, William Nathaniel Robertson Scholarship and the Australian Medical Association - JG Hunter Scholarship.

Finally I am indebted to my family, in particular my parents, for both encouragement and support to pursue this research project.
Abstract

Elevated respiratory rates have been described in several disease states, such as pneumonia, asthma and bronchiolitis. Despite this there are few studies defining the range of respiratory rates found in healthy children. Almost all of those which have been published have limitations and shortcomings in terms of methodology. The present study observed respiratory rates in healthy children and children with respiratory disease. The current research project had several aims.

The primary aim of the study was to construct centile curves for respiratory rate (RR) by age. A newly developed optical respiratory sensor was used for this purpose. This sensor placed no restrictions on respiratory excursions and provided a novel approach to studying breathing patterns in children. The sensor was found to measure respiratory rate accurately and to measure inspiratory time and expiratory time in healthy subjects. Healthy children in this study were obtained from maternity wards, childcare centres and schools. Informed consent was obtained from all parents of children. Respiratory rates observed in 343 awake and 94 sleeping children were used to create the reference ranges for healthy children.

Respiratory rates were significantly higher when children were awake compared to when they were asleep (p < 0.01, unpaired t test). During quiet sleep, RR (±SD) decreased from 41.4 (±4.1) bpm in newborn infants to 19.5 (±2.7) bpm in children aged 2.0 - 2.9 years. In awake children, RR measured in children ranged from 59.3 (±9.8) bpm to 16.9 (±4.5) bpm, in children aged 0 - 0.49 and 12.0 - 12.99 years respectively.

A secondary aim was to examine the sub-components of the respiratory cycle in both health and disease. Age did not have an effect on the fractional inspiratory time (T/i / Ttot) in children older than two weeks. T/i / Ttot was 0.40 (±0.04) in sleeping children aged from two weeks to 3.5 years and 0.41 (±0.03) in awake children aged from two to twelve years.

The centile charts for RR were useful in detecting disease, in particular pneumonia and asthma. All sleeping children with pneumonia in the study (6/6) had a RR higher than the 95th centile for healthy children. Seventy-eight per cent (7/9) of sleeping and 75% (9/12) of awake children with asthma who were younger than seven years of age also had respiratory rates above the 95th centile for healthy children. Respiratory rate correlated with body temperature in sleeping children with pneumonia (r = + 0.83, p<0.05), oxygen saturation levels in sleeping children with asthma (r = - 0.72, p<0.05) and peak expiratory flow rates in awake children with asthma (r = - 0.45, p<0.05).
Fractional inspiratory time ($T_i / T_{TOT}$) in children with asthma and bronchiolitis was not significantly different to the values observed in healthy children. Children with cystic fibrosis (CF) had a significantly increased mean $T_i / T_{TOT}$ value of 0.44 (±0.03) ($p<0.05$, unpaired $t$ test). These measurements of respiratory timing reflect alterations primarily in the contribution of the abdominal compartment to breathing.

It was concluded:

1. The centile charts for respiratory rate should be helpful as an aid to detecting abnormal respiratory rates in children, especially those with pneumonia. The data obtained in this thesis will allow abnormalities in rate to be quantified.

2. The newly developed optical sensor was an appropriate respiratory transducer, capable of measuring respiratory rate and detecting apnoea in health and disease. Further work in the analysis and practical application of the timing indices measured by the sensor in disease is needed.
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Abbreviations

CF  cystic fibrosis
EEG  electroencephalogram
FEV$_{1.0}$  forced expiratory volume in one second
FRC  functional residual capacity
pO$_2$  partial pressure of oxygen
pCO$_2$  partial pressure of carbon dioxide
PEFR  peak expiratory flow rate
Pm$_{0.1}$  mouth occlusion pressure 0.1 s after onset of inspiration
RR  respiratory rate
T$_I$  inspiratory time
T$_E$  expiratory time
T$_I$/T$_{TOT}$  fractional inspiratory time
T$_{TOT}$  total respiratory cycle duration
TLC  total lung capacity
V$_T$  tidal volume
V$_E$  expired minute ventilation
Introduction

Background to Thesis

Respiratory rates are routinely measured in the wards and emergency departments of hospitals. The significance of this sign was recognised as early as Hippocrates who noted that rapid respirations were a "sign of pain or inflammation in parts above the diaphragm" (Hippocrates in Hooker et al., 1989). Many modern authors and textbooks also emphasise the importance of this clinical sign. One textbook describes tachypnoea as "the most common alteration in breathing and the most important clue to pulmonary dysfunction" (Avery and First, 1989).

Marked increases in respiratory rate, or tachypnoea, have been found in such varying conditions as pneumonia, sepsis, salicylism, bronchiolitis and acute asthma (Krieger, 1964; Temple, 1981; Selbst, 1985; Kesten et al., 1990; Singhi et al., 1994a). Low respiratory rates or bradypnoea are unusual and may indicate brainstem dysfunction as seen in Arnold-Chiari malformation or brain tumour (Brouillette, 1992). Respiratory rate has a role in the evaluation of a number of clinical conditions such as: asthma, burns, communicable diseases, cough, croup, diabetic ketoacidosis, diarrhoea, eye infection, fever, head injury, ingestion of poison or drugs, seizure, sore throat, vaginal bleeding and vomiting (Barkin and Rosen, 1990).

It is argued that careful observation of breathing movements usually gives a more reliable indication of the severity of a respiratory infection in a child than auscultation with a stethoscope (WHO, 1988). Acute respiratory infection, along with malnutrition and diarrhoea, have been identified as the most important causes of death in children world wide. It is estimated that each year 3.6 million deaths from acute respiratory infection occur throughout the world (UNICEF, 1993). Death due to acute infection of the lower respiratory tract is due to pneumonia and bronchiolitis, with pneumonia accounting for 75% of these deaths (WHO, 1981). Children under five years of age and those from developing countries are at greatest risk (WHO, 1981).

The World Health Organisation (WHO) defines a chest infection as severe if there is a combination of cough, chest indrawing, cyanosis and difficult breathing (WHO, 1991). Rapid breathing is defined as 50 breaths per minute (bpm) or more in children aged two to twelve months and 40 bpm or more in children aged one to five years (WHO, 1991). In the absence of rapid breathing, or cyanosis, or inability to drink, or chest indrawing, the case can be
considered mild and only supportive measures are indicated (WHO, 1991). Clearly respiratory rate is considered a simple and valuable clinical sign in evaluating this important cause of mortality, especially in areas where radiological and bacteriological facilities are not readily available. While this is of great use to primary health workers managing respiratory infections in developing countries, it should also be of use in developed countries in outpatient settings (Rusconi et al., 1994).

A substantial increase has been noted in hospital admissions for acute asthma in children (Kerem et al., 1991). An Australian study has found the prevalence of the diagnosis of "asthma" to be 17.5% in children aged from five to twelve years of age (Bauman et al., 1992). Mortality associated with asthma can be linked to underestimation of the severity of the fatal event by both relatives and medical practitioners, with a resulting delay in referral to hospital (Kerem et al., 1991). It is therefore important to optimise both the clinical and laboratory assessment of asthma, so the most appropriate treatment can be given to patients promptly. It has been found that the pre-treatment respiratory rate in acute asthma correlates with measurements of peak expiratory flow rate (PEFR) and forced expiratory volume in one second (FEV\(_1\)) (Kesten et al., 1990). Respiratory rate is therefore a simple clinical sign which can be helpful in assessing the severity of asthma in children.

Respiratory rate has also proven to be a sensitive indicator of other diseases. In cystic fibrosis, respiratory rate has been found to correlate with airway obstruction, hyperinflation, reduced arterial oxygenation and rib cage-abdominal incoordination (Browning, D'Alonzo and Tobin, 1990). Respiratory rate has been found to be a good predictor of weaning outcome in mechanically ventilated patients. Patients who failed a weaning trial had higher respiratory rates than patients who were successfully weaned (Meek and Tyler, 1985).

Despite the above mentioned examples and the emphasis placed on the importance of respiratory rate as a clinical sign, other authors negate its importance. One study of respiratory rate concluded that the routine measurement of respiratory rates in hospital wards was an "expensive tribute to tradition" (Kory, 1957). The author found that measuring respiratory rate rarely affected the clinical management of a patient and that there was an overall lack of proficiency and enthusiasm on the part of hospital staff in its measurement. It has been argued that the practical importance of respiratory rate is not very great in assessing lung function. "Deficiencies of the data should not have a serious effect and this may explain the paucity of studies" (Polgar and Promadhat, 1971). The poor reputation of respiratory rate as a clinical sign
may be partly due to inaccuracy in its measurement (Browning, D'Alonzo and Tobin, 1990). Recently, the need for detailed studies of respiratory rate with sound research methods has been highlighted (American Thoracic Society/European Respiratory Society, 1993). Longitudinal studies of respiratory rate are especially needed.

Focus of Thesis

One reason for undertaking a study of respiratory rate in health and disease was to investigate, on a scientific basis, the value of measuring respiratory rate in a paediatric population. If the measurement of respiratory rate was found to be a sensitive indicator of disease, then this may give more impetus to paying greater attention to this clinical sign. Its value in diagnosing disease, evaluating therapeutic responses and monitoring the progress of chronic disease could be assessed. Such a study would also enhance understanding of the effects of growth on respiratory physiology.

Another reason for undertaking this study of respiratory rates was to define reference ranges more accurately. Unless serial determinations are made on the same patient to detect deterioration or improvement, the interpretation of respiratory rate in a patient depends upon a knowledge of respiratory rates in healthy persons of the same sex and appropriate age range (Cassels and Morse, 1962). Normal values for respiratory rate are often poorly defined in textbooks and some authors fail to cite studies to support their suggested reference ranges. For example, one textbook, *Emergency Pediatrics*, defines abnormal respiratory rates as listed in Table 1 (Barkin and Rosen, 1990).

Table 1 - Abnormal Respiratory Rates by Age (Barkin and Rosen, 1990)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Abnormal Respiratory Rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2</td>
<td>&lt; 15 or &gt; 40</td>
</tr>
<tr>
<td>2 - 5</td>
<td>&lt; 10 or &gt; 30</td>
</tr>
<tr>
<td>&gt;5</td>
<td>&lt; 5 or &gt; 25</td>
</tr>
</tbody>
</table>
A number of studies of respiratory rate which are quoted in other textbooks have methodological limitations. Having accurate reference ranges or percentile charts of respiratory rates for healthy children would make defining abnormal or clinically significant respiratory rates easier. The range of normal values may also vary with geographic and ethnic factors, thus giving another reason for undertaking a study in Brisbane.

Defining the respiratory rate in children with conditions that alter the respiratory rate, in particular respiratory disease, would also help to determine the overlap in values of respiratory rate in health and disease. Thus the sensitivity and specificity of respiratory rate as a clinical sign could be assessed.

Respiratory rate is traditionally counted by observing chest movements with a timer. This method is affected by observer error and can be compromised if chest movements are rapid, small or masked by general body movements. Nevertheless, it is a readily available and cost effective method. A respiratory sensor which detected chest wall motion was considered an effective way of obtaining reference ranges for respiratory rate, since most measurements made in clinical medicine are based on observation of chest wall movements. A sensor also had the advantages of being able to minimise human error and record movements over longer periods.

A respiratory sensor which monitored chest wall motion had been developed at the University of Queensland's Centre for Magnetic Resonance. It seemed an appropriate tool to determine reference ranges for respiratory rate measured by chest wall movement in children. Added to this, the sensor was able to produce a waveform pattern of breathing. The pattern of tidal breathing has been suggested as a sensitive indicator of lung mechanics (American Thoracic Society/European Respiratory Society, 1993).

The exact nature of the waveforms produced by the sensor and how closely these correlated with the timing of volume changes in the lung could also be further investigated. One way of quantifying the respiratory waveform is to partition the respiratory cycle into inspiratory and expiratory phases. This allows inspiratory time (T_i), expiratory time (T_e) and total time for one respiratory cycle (T_{TOT}) to be calculated. The RR could be measured by the sensor for a number of minutes. This allowed analysis of breathing patterns for the presence of frequencies, other than that associated with the respiratory rate. A mathematical technique called the Fast Fourier Transform was used for this purpose.
The following aims for this study were formulated, recognising the need for further studies of respiratory rate.

Aims of Thesis

1. To evaluate and investigate the use, shortcomings and practical application of a respiratory sensor which detects chest wall movement. These studies were to be undertaken in both a bedside (hospital) and field (community) setting.

2. To develop percentile charts of respiratory rate for age and sex in normal children - such as for potential use in clinical medicine, in pre-hospital care (first-aid) and for reference in respiratory research.

3. To study respiratory rates and wave-form patterns of the respiratory cycle in some selected paediatric respiratory diseases. Research studies were undertaken on children diagnosed with pneumonia, cystic fibrosis, bronchiolitis and asthma.

4. To study indices of the respiratory cycle and their relationship, if any, to age and to selected respiratory diseases.

5. To examine breathing patterns (approximately 3 minutes in duration) for frequencies or oscillations other than the respiratory rate. The Fast Fourier Transform Method was to be used in this analysis.
Part I

Review of Literature
Chapter 1

Respiratory Rate in Health and Disease

1.1 Introduction

"The frequency of the respirations varies in different individuals, and at different ages, and is so much influenced by the conditions of the body and the mind at the time, even when the individual is in perfect health, that it is a much more difficult matter to determine their average frequency than may at first be imagined " (Reid, 1847).

While respiratory rate (RR) is simple to measure with a watch, its interpretation is difficult since the act of measuring it can alter a person's breathing pattern (American Thoracic Society/European Respiratory Society, 1993). Measurement of respiratory rate in children is made more difficult because of lack of cooperation. The protocol of any research which examines how respiratory rate changes with age needs to be carefully scrutinised so that sources of variability associated with its measurement can be identified.

1.2 Factors Affecting Measurement of Respiratory Rate

Factors to consider in measuring respiration in children include the duration of the observation period, differences in states of arousal and environmental surroundings. Recordings under hyperthermic or hypothermic conditions may increase respiratory and metabolic rate (Brouillette, 1992). If respiratory rate is to be measured in sleeping children, sleep state should be noted since respiratory rate is higher and more variable in active sleep when compared to quiet sleep (Hathorn, 1974; Curzi-Dascalova, Lebrun and Korn, 1983). Studies of respiratory rate in subjects sedated with chloral hydrate need to be carefully evaluated, since some studies found this to reduce respiratory rate (Tepper et al., 1986).

The method of obtaining respiratory rate may also affect the results. For example respiratory rates measured with stethoscopes or respiratory monitors record higher respiratory rates when compared to respiratory rates obtained with observation alone (Berman, Simoes and Lanata, 1991). This may be due to the detection of small breaths not appreciated when observing chest or abdominal movements. It is also possible that touching an infant with a stethoscope or hand may cause an increase of agitation that raises the respiratory rate (Berman, Simoes and Lanata, 1991). If respiratory monitors are to be used it is important that there is a normal environment with minimal parental limitations and a minimum of attachments to the child during testing so that the child is comfortable (Cross, 1949; Richards et al., 1984). The child should not be touched or disturbed during the observation period (Waring, 1980).
1.3 Methods of Measuring Respiratory Rate

A number of authors note that the most reliable and reproducible rate is the sleeping respiratory rate (Polgar and Promadhat, 1971; Dworkin, 1992). For infants in particular this should be during quiet sleep (American Thoracic Society/European Respiratory Society, 1993). This however is impractical in an emergency situation and for older children who may not sleep at all during the day. However it is possible for parents to monitor sleeping respiratory rate. A special form can be supplied to parents if RR is to be counted and recorded at home. Waring (1980) recommends three separate one-minute counts at night after the child has gone to sleep.

In a baby, respiratory rate should be timed for a full minute before it is disturbed or undressed (Meadow and Smithells, 1991). The measurement is meaningless if the baby is crying (Meadow and Smithells, 1991). Simoes et al. (1991) found that two 30 second counts added together give an accurate value of respiratory rate when compared to values obtained from an impedance pneumogram.

Respiratory rate can usually be measured by observing or feeling chest movements. Some studies, however, note difficulty with measuring respiratory rate by observation alone or placing hands on the child's chest (Valman, Wright and Lawrence 1983; Morley et al., 1990). Other methods of monitoring respiration include capnography, monitoring nasal thermal changes, respiratory inductance plethysmography, graphite rubber strain gauges and air filled capsules taped to the abdominal wall.

Instrumental recordings are desirable because of the difficulty of obtaining reliable counts by human observation over long periods of time (Polgar and Promadhat, 1971). However, electronic monitoring is not always practical in a clinical setting and is also subject to limitations. For example, movements can distort the respiratory tracings of sensors which detect chest wall motion (Rusconi et al., 1994). Respiratory apparatus placed on the face can decrease the RR of subjects (Gilbert et al., 1972). This is a limitation of studies performed with pneumotachographs and spirometers.

1.4 Reference Values for Respiratory Rate

Textbooks vary on reference values for respiratory rate. Table 1.1 displays reference ranges for respiratory rate quoted by two textbooks. No reference was made to the studies from which these results may have been obtained from.
Table 1.1 - Respiratory Rate Reference Ranges in Two Textbooks

<table>
<thead>
<tr>
<th>Author and Textbook</th>
<th>Age (yr)</th>
<th>RR (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dworkin (1992)</td>
<td>newborns</td>
<td>30 - 75</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>6 - 12 mo</td>
<td>22 - 31</td>
</tr>
<tr>
<td></td>
<td>1 - 2</td>
<td>17 - 23</td>
</tr>
<tr>
<td></td>
<td>2 - 4</td>
<td>16 - 25</td>
</tr>
<tr>
<td></td>
<td>4 - 10</td>
<td>13 - 23</td>
</tr>
<tr>
<td></td>
<td>10 - 14</td>
<td>13 - 19</td>
</tr>
<tr>
<td>Marks et al. (1992)</td>
<td>birth - 6 mo</td>
<td>45</td>
</tr>
<tr>
<td>Pediatric Handbook</td>
<td>6 mo - 3 yr</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>4 - 7</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>8 - 10</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>11 - 12</td>
<td>20</td>
</tr>
</tbody>
</table>

The studies of respiratory rate in humans can be categorised by the age range being studied. This includes neonates, infants, children, adolescents and adults. Respiratory rate can also be monitored over a short period (such as for a few minutes) or over an extended period (such as in a sleep study).

1.5 New Born Babies

Many respiratory adaptations occur at birth and throughout the first year of life. Table 1.2 shows the results of some studies performed on newborns. Hunger, temperature changes and handling of the infant will increase RR (Avery and Normand, 1965). Most studies of respiration in newborn infants agree that respiratory rate is higher and more variable during active sleep (Bolton and Herman, 1974; Hathorn, 1974; Finer, Abroms and Taeusch, 1976). Some studies used a body plethysmograph (Cross, 1949; Bolton and Herman, 1974; Hathorn, 1974). Other studies used a face mask which may change the RR (Finer, Abroms and Taeusch, 1976).
Table 1.2 - Studies of Respiratory Rate in Neonates

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (days)</th>
<th>Number</th>
<th>RR ±SD (bpm)</th>
<th>Range (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quiet Sleep</td>
<td>Active Sleep</td>
</tr>
<tr>
<td>Cross (1949)</td>
<td>0 - 13</td>
<td>36 (16M, 20F)</td>
<td>28.64 ± 5.20</td>
<td>14 - 51</td>
</tr>
<tr>
<td>Cook et al. (1955)</td>
<td>0 - 7</td>
<td>35</td>
<td>33.8 ± 6.57</td>
<td>23 - 51</td>
</tr>
<tr>
<td>Ashton and Connolly (1971)</td>
<td>3 (mean)</td>
<td>22 (12M, 10F)</td>
<td>44.9 ± 10.3</td>
<td>53.9 ± 11.1</td>
</tr>
<tr>
<td>Bolton and Herman (1974)</td>
<td>1 - 7</td>
<td>14 (8M, 6F)</td>
<td>46.4 ± 11.0</td>
<td>59.5 ± 12.7</td>
</tr>
<tr>
<td>Hathorn (1974)</td>
<td>0 - 1</td>
<td>20 (10M, 10F)</td>
<td>39.5</td>
<td>55.7</td>
</tr>
<tr>
<td>Finer, Abroms and Taeusch (1976)</td>
<td>0 - 2</td>
<td>10 (5M, 10F)</td>
<td>50 ± 11</td>
<td>62 ± 12</td>
</tr>
<tr>
<td>Aarimaa and Valimaki (1988)</td>
<td>Term (37 - 41 wk GA)</td>
<td>22 (14M, 8F)</td>
<td>46.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-term (27 - 36 wk GA)</td>
<td>21 (11M, 10F)</td>
<td>49</td>
<td></td>
</tr>
</tbody>
</table>

There is a diminution of RR with increasing time since the last feed in sleeping infants (Bolton and Herman, 1974). This could account for Cross (1949), who measured RR 1.5 to 3.5 hours after a previous feed, obtaining lower RR values than Bolton and Herman (1974), who measured RR within two hours of a feed. Cross (1949) also observed smaller RRs than Hathorn (1974). This could be due to Hathorn (1974) measuring RR during quiet sleep which was close in time to periods of active sleep. In contrast, Cross (1949) measured infants when they had been "quiescent" for at least 20 minutes. They were therefore closer to a condition of minimal oxygen consumption.

Respiratory rate was measured hourly in many neonates with a compressible abdominal sensor in another study (Valman, Wright and Lawrence, 1983). One per cent of apparently normal infants had a raised RR greater than 60 bpm. The main reason for observing RR was to detect group B streptococcal infections that can be rapidly progressive and cause an increased RR. Infants with a RR greater than 60 bpm persisting for more than one hour were transferred
to a special care unit. This occurred in 1.0% (29/2789) infants who passed through the postnatal ward of a hospital. Four of these infants had group B streptococcal infections and one child had hypoplastic heart failure. Another nine infants had increased RRs for only a few minutes. Nineteen infants had an increased RR for a considerable time and received antibiotics. Most of these were attributed to failure of lung fluid resorption.

Aarimaa and Valimaki (1988) found no difference in RR between healthy term and preterm newborn babies. However, the variability in RR was less in the term infants when compared to the preterm infants. Gestational age therefore affects respiratory control.

### 1.6 Respiratory Rate in Infants Studied for an Extended Time

These studies are usually performed for at least three hours on infants and are summarised in Table 1.3. RR is increased in active sleep when compared to quiet sleep. There is also an intermediate sleep stage where RRs are between those of active and quiet sleep (Curzi-Dascalova, Gaudebout and Dreyfus, 1981; Curzi-Dascalova, Lebrun and Korn, 1983). Hoppenbrouwers et al. (1979) demonstrated the emergence of a circadian pattern in RRs in full-term infants aged up to six months. RRs decreased between 10:00 PM and 4:00 AM.

Hoppenbrouwers et al. (1978) found RRs were highest and most variable in the first week of life and declined rapidly to three months. RRs continued to decline up to six months of age. Katona and Egbert (1978) found RRs were faster in preterm infants throughout the first six months of life. It is therefore important to consider a child's gestational age when studying RRs.

Curzi-Dascalova, Gaudebout and Dreyfus (1981) found RR to slow during a cycle of sleep. RR was also slower during subsequent sleep cycles. The choice of period in sleep to record RR will therefore affect the measurement obtained. Respiratory pauses will also affect the calculation of RR. While respiratory pauses of three seconds duration were possible during quiet sleep, they were more prominent during active sleep. This is one reason measurement of RR in quiet sleep is preferable.

Richards et al. (1984) measured RR for 22 continuous hours in infants aged up to six months. There was loss of data during the day when the infants were active. RR increased gradually from birth to two weeks of age (not significant). After four weeks of age, RR and the spread of values between individuals decreased with age. There was also an increase in the duration of quiet sleep with age.
1.7 Respiratory Rate and the Sudden Infant Death Syndrome

The value of respiratory rate as an indicator for Sudden Infant Death Syndrome (SIDS) is controversial. Some studies have found increased RRs in siblings of infants who died of SIDS (SSIDS) in specific age groups (Hoppenbrouwers et al., 1977; Hoppenbrouwers et al., 1980). However, other studies have not shown significant differences between controls and SSIDS (Southall et al., 1987).

Pneumograms of future SIDS victims have been reported to show an increase in RR when compared to controls (Shannon et al., 1987). In contrast, other studies have found no difference in RR between infants who later died of SIDS and control infants (Southall et al., 1986; Kahn et al., 1992). The different findings of the studies related to SIDS may be due to the sources of variability in measuring RR and large inter-individual variability of RR in infancy.

1.8 Respiratory Rates in Infants Studied for a Short Time

Studies performed over the shorter term in children usually monitor tidal breathing over a few minutes. These studies of children are usually performed during sleep and are summarised in Table 1.3. Some studies have found no gender differences in RR (Tepper et al., 1986; Morley et al., 1990; Rusconi et al., 1994; Yau and Fang, 1994). In contrast, Hoppenbrouwers et al. (1979) found the mean RR in infant girls to be 4.7 to 5.9 bpm less than in boys. Respiratory rate is increased in awake and calm children compared to sleeping children (Morley et al., 1990; Rusconi et al., 1994). Most studies observe respiratory rate to decrease with age especially in the early months of life (Rusconi et al., 1994).

Taussig, Harris and Lebowitz (1977) studied children aged from three months to six years of age. Most of the children aged less than three years were asleep and wore face masks. Children older than three years were awake and used mouthpieces. RR was calculated by counting respirations during a helium dilution test. This test itself may have affected the RR.
### Table 1.3 - Studies of Respiratory Rate in Infants and Toddlers
(Sleeping unless stated otherwise)

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (mo)</th>
<th>Number</th>
<th>RR ± SD (bpm)</th>
<th>Range (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taussig, Harris and Lebowitz (1977)</td>
<td>3</td>
<td>34</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td></td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Hoppenbrouwers et al. (1978)</td>
<td>0.25</td>
<td>8</td>
<td>38.2 ± 8.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td>25.1 ± 3.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
<td>24.0 ± 4.2</td>
<td></td>
</tr>
<tr>
<td>Gaultier et al. (1979)</td>
<td>0</td>
<td>52</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td>44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
<td>39</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td></td>
<td>34</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Curzi-Dascalova, Gaudebout and Dreyfus-Brisac (1981)</td>
<td>2 - 10 d</td>
<td>22</td>
<td>Quiet Sleep</td>
<td>35.6 ± 7.6</td>
</tr>
<tr>
<td></td>
<td>2 - 5 wk</td>
<td>11</td>
<td></td>
<td>49.4 ± 10.9</td>
</tr>
<tr>
<td></td>
<td>6 - 10 wk</td>
<td>14</td>
<td></td>
<td>45.6 ± 11.1</td>
</tr>
<tr>
<td></td>
<td>11 - 18 wk</td>
<td>10</td>
<td></td>
<td>38.0 ± 10.2</td>
</tr>
<tr>
<td>Richards et al. (1984)</td>
<td>1-3 d</td>
<td>110</td>
<td>40.3 ± 7.9</td>
<td>28.2 - 64.7</td>
</tr>
<tr>
<td></td>
<td>4-7 d</td>
<td></td>
<td>42.6 ± 15.9</td>
<td>26.7 - 117.5</td>
</tr>
<tr>
<td></td>
<td>0.25 - 0.5</td>
<td></td>
<td>45.1 ± 8.4</td>
<td>26.8 - 64.9</td>
</tr>
<tr>
<td></td>
<td>1 - 1.49</td>
<td></td>
<td>38.5 ± 6.2</td>
<td>28.3 - 57.5</td>
</tr>
<tr>
<td></td>
<td>1.5 - 2</td>
<td></td>
<td>37.1 ± 5.8</td>
<td>26.7 - 49.2</td>
</tr>
<tr>
<td></td>
<td>2.4 - 4.5</td>
<td></td>
<td>31.1 ± 5.6</td>
<td>20.7 - 40.4</td>
</tr>
<tr>
<td></td>
<td>4.7 -7.1</td>
<td></td>
<td>27.3 ± 3.6</td>
<td>20.7 - 36.8</td>
</tr>
<tr>
<td>Tepper et al. (1986)</td>
<td>0</td>
<td>117</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td>38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td></td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Litscher et al. (1993)</td>
<td>1.5</td>
<td>19</td>
<td>37.2 ± 5.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>14</td>
<td>30.1 ± 4.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>19</td>
<td>24.1 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>Yau and Fang (1994)</td>
<td>0.3</td>
<td>22</td>
<td>Awake</td>
<td>60.4 ± 13.2</td>
</tr>
<tr>
<td></td>
<td>1.9</td>
<td>31</td>
<td></td>
<td>39.7 ± 6.1</td>
</tr>
<tr>
<td></td>
<td>3.8</td>
<td>20</td>
<td></td>
<td>35.3 ± 6.4</td>
</tr>
<tr>
<td></td>
<td>6.0</td>
<td>11</td>
<td></td>
<td>31.1 ± 5.8</td>
</tr>
<tr>
<td>Rusconi et al. (1994)</td>
<td>0 - 1.9</td>
<td>104</td>
<td>Awake</td>
<td>48.0 ± 9.1</td>
</tr>
<tr>
<td></td>
<td>2 - 5.9</td>
<td>106</td>
<td></td>
<td>44.1 ± 9.9</td>
</tr>
<tr>
<td></td>
<td>6 - 11.9</td>
<td>126</td>
<td></td>
<td>39.1 ± 8.5</td>
</tr>
<tr>
<td></td>
<td>12 - 17.9</td>
<td>177</td>
<td></td>
<td>34.5 ± 5.8</td>
</tr>
<tr>
<td></td>
<td>18 - 23.9</td>
<td>65</td>
<td></td>
<td>32 ± 4.8</td>
</tr>
<tr>
<td></td>
<td>24 - 29.9</td>
<td>79</td>
<td></td>
<td>30 ± 6.2</td>
</tr>
<tr>
<td></td>
<td>30 - 35.9</td>
<td>61</td>
<td></td>
<td>27.1 ± 4.1</td>
</tr>
</tbody>
</table>
A regression equation for RR according to age in months (m) was determined by Taussig, Harris and Lebowitz (1977):

$$RR = 31.61 - 0.09 \times m$$ \hspace{1cm} (1.1)

This equation failed to show any change in respiratory rate in the first year of life.

Tepper et al. (1986) examined the growth and development of the lung throughout the first year of life in 125 healthy infants. Some children went to sleep spontaneously while others were sedated with chloral hydrate. Length (height) was found to correlate more closely with respiratory parameters than weight or age. Tidal volume increased and respiratory rate decreased with increasing length.

Morley et al. (1990) measured RR in infants aged less than six months. This was done by listening to breath sounds either with a stethoscope or when putting warm hands on the children's chests. The act of placing hands or a stethoscope on the children's chests may have affected their respiratory rates. Respiratory rate was counted for three 15 second periods and averaged. For awake children, the average RR was 61 bpm. Sleeping children had an average respiratory rate of 42 bpm. Mean respiratory rates for each of the first six months of life was similar.

Rusconi et al. (1994) assessed respiratory rate in 618 infants and children aged from fifteen days to three years of age. Half the sample of children were seen in day care centres while the other half were children in hospital without respiratory disease. Exclusion criteria included the presence of chronic or severe illness, a history of fever and respiratory findings suggesting a respiratory infection in the previous two weeks. Children older than one year were assessed while they played quietly. In 50 subjects, RR measurement was repeated 30 to 60 minutes after the initial recording and found to be quite consistent. RRs obtained by Rusconi et al. (1994) were similar to RRs measured with continuous electronic monitoring in other studies over prolonged time (Hoppenbrouwers et al., 1978; Curzi-Dascalova, Gaudebout and Dreyfus-Brisac, 1981; Richards et al., 1984) but lower than the RRs reported by Morley et al. (1990).

1.9 Studies of Respiratory Rate in Older Children and Adolescents

After early childhood, respiratory rate slowly declines reaching normal adult values by adolescence (Brouillette, 1982). Relatively few studies of respiratory rate have been performed in older children. A study of RR values obtained in children, aged one to seven years, by Marks, South and Carlin (1993) is presented in Table 1.4.
Table 1.4 - Study of Respiratory Rate in Children

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (years)</th>
<th>Number</th>
<th>RR ± SD (bpm)</th>
<th>2.5% - 97.5% Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Awake</td>
<td>Asleep</td>
<td>Awake</td>
</tr>
<tr>
<td>Marks, South and Carlin (1993)</td>
<td>1 - 1.9</td>
<td>17 (10M, 7F)</td>
<td>27 (14M, 13F)</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>2 - 2.9</td>
<td>45 (21M, 24F)</td>
<td>39 (18M, 21F)</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>3 - 3.9</td>
<td>59 (26M, 33F)</td>
<td>37 (18M, 19F)</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>4 - 4.9</td>
<td>68 (42M, 26F)</td>
<td>20 (12M, 8F)</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>5 - 5.9</td>
<td>53 (30M, 23F)</td>
<td>----</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>6 - 6.9</td>
<td>51 (27M, 24F)</td>
<td>----</td>
<td>21</td>
</tr>
</tbody>
</table>

In the study by Marks, South and Carlin (1993), 293 awake and 123 sleeping children were observed by a single investigator. RR was counted for two thirty-second periods using a nasal thermistor attached to the children's cheeks. The children were distracted with a story while they sat quietly. Thermistry was made more difficult in nasally obstructed children and failed in some of these children. Those children who were unwilling to have a story read to them, or who became upset when the probe was attached to their cheek, were not tested. This included 50 per cent of children in the 12 to 24 month age range.

The children were tested at day care centres, kindergartens and schools. Some sick children were included in this sample. A questionnaire inquiring of any rhinorrhoea, coughs, fever, sore throats, or wheezes in the preceding 24 hours was issued. A history of asthma, wheezy bronchitis or recurrent bronchitis was also noted. The presence of past or current respiratory symptoms, or the sex of the children, did not affect RR significantly. RR declined with increasing age and was lower when children were asleep compared to when they were awake. No differences were observed in RR between quiet and active sleep states using behavioural criteria.

A number of studies of RR have been performed on both children and adolescents. These are summarised in Table 1.5 and 1.6 and discussed.
### Table 1.5 - Studies of Respiratory Rate in Awake Children and Adolescents

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (years)</th>
<th>Number</th>
<th>RR ± SD (bpm)</th>
<th>Range (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetelet (1842)</td>
<td>0</td>
<td>300</td>
<td>44</td>
<td>23 - 70</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td></td>
<td>26</td>
<td>27 - 68</td>
</tr>
<tr>
<td></td>
<td>15 - 20</td>
<td></td>
<td>20</td>
<td>- 32</td>
</tr>
<tr>
<td>Robinson (1938)</td>
<td>5.7 - 6.5</td>
<td>8 M</td>
<td>23.5</td>
<td>18 - 28</td>
</tr>
<tr>
<td></td>
<td>8.2 - 12.6</td>
<td>10 M</td>
<td>17.8</td>
<td>11 - 22</td>
</tr>
<tr>
<td></td>
<td>13 - 15.9</td>
<td>11 M</td>
<td>15.4</td>
<td>11 - 22</td>
</tr>
<tr>
<td></td>
<td>16 - 19.9</td>
<td>12 M</td>
<td>13.2</td>
<td>5.5 - 25</td>
</tr>
<tr>
<td>Iliff and Lee (1952)</td>
<td>* 0 - 0.9 (102M, 95F)</td>
<td></td>
<td>3 ± 8</td>
<td>30 ± 6</td>
</tr>
<tr>
<td></td>
<td>* 1 - 1.9</td>
<td></td>
<td>26 ± 4</td>
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<tr>
<td></td>
<td>* 2 - 2.9</td>
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<td>25 ± 4</td>
<td>25 ± 3</td>
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<td>15 - 15.9</td>
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<td>16 - 16.9</td>
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<td></td>
<td>17 - 17.9</td>
<td></td>
<td>16 ± 3</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>Hooker et al. (1992)</td>
<td>0 - 0.9</td>
<td>32</td>
<td>39 ± 11</td>
<td>22 - 65</td>
</tr>
<tr>
<td></td>
<td>1 - 1.9</td>
<td>32</td>
<td>30 ± 6</td>
<td>16 - 46</td>
</tr>
<tr>
<td></td>
<td>2 - 2.9</td>
<td>25</td>
<td>28 ± 4</td>
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<td>3 - 3.9</td>
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<td>16 - 34</td>
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<td>4 - 4.9</td>
<td>26</td>
<td>27 ± 5</td>
<td>20 - 36</td>
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<td></td>
<td>5 - 5.9</td>
<td>28</td>
<td>23 ± 5</td>
<td>14 - 32</td>
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<td></td>
<td>6 - 6.9</td>
<td>11</td>
<td>25 ± 5</td>
<td>18 - 36</td>
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<td>7 - 7.9</td>
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<td>24 ± 6</td>
<td>15 - 40</td>
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<td>8 - 8.9</td>
<td>28</td>
<td>21 ± 5</td>
<td>12 - 34</td>
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<td>9 - 9.9</td>
<td>25</td>
<td>22 ± 4</td>
<td>17 - 36</td>
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<td></td>
<td>10 - 10.9</td>
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<td>21 ± 4</td>
<td>16 - 28</td>
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<td>11 - 11.9</td>
<td>24</td>
<td>21 ± 3</td>
<td>15 - 26</td>
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<td></td>
<td>12 - 12.9</td>
<td>23</td>
<td>21 ± 4</td>
<td>16 - 32</td>
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<td>13 - 13.9</td>
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<td>21 ± 4</td>
<td>16 - 30</td>
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<td></td>
<td>14 - 14.9</td>
<td>29</td>
<td>20 ± 4</td>
<td>14 - 28</td>
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<td>15 - 15.9</td>
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<td>21 ± 3</td>
<td>16 - 28</td>
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<td></td>
<td>16 - 16.9</td>
<td>25</td>
<td>20 ± 4</td>
<td>14 - 32</td>
</tr>
<tr>
<td></td>
<td>17 - 17.9</td>
<td>18</td>
<td>20 ± 4</td>
<td>16 - 28</td>
</tr>
</tbody>
</table>
Quetelet (1842) studied 300 children with ages ranging from birth to 20 years. This study is limited in that only three age groups were covered in detail. No mention of the method of counting RR is made. Robinson (1938) studied 51 male children and adolescents. This is the only study to mention the social situation of the children tested. The sample was divided into several groups. Five to seven year old children formed one group and belonged to middle class families. Children aged from eight to twelve years lived at an orphanage and children aged from 13 to 19 years attended a private school at Cambridge. By 17 years of age the boys' RR had reached adult levels. Younger boys had higher lung ventilation in relation to body weight at rest in comparison with post-adolescent boys and adults. This was achieved in part by breathing with higher respiratory rates.

Iliff and Lee (1952) performed a significant study of respiratory rates, pulse rates and rectal temperatures in children aged from two months to 18 years of age. This study is frequently quoted in textbooks such as Nelson's Textbook of Pediatrics (Behrman, 1992) and the Harriet Lane Handbook (Rowe, 1987). It was a longitudinal study that followed 102 boys and 95 girls. From this sample 1859 measurements of RR were made on boys and 1459 on girls. Children under 18 months of age were tested while they were sleeping. No observation of what sleep state the children were in was made. Between 18 months and three years of age, respirations were counted when children were either awake or asleep. No differentiation between whether the children were awake or asleep was made. Children over three years of age were tested early in the morning, when they were fasting and awake.

Respirations were counted for at least 30 seconds by visual observation. The children were involved in a metabolism study that required them to lie down. They were rested and unaware their RR was being counted. The children in this study lived at high altitude (Denver, Colorado) and the lower oxygen partial pressure may have affected their breathing patterns (Rusconi et al., 1994).

Hooker et al. (1992) observed 434 children in an emergency department, with ages ranging from two weeks to 18 years. RRs were counted for 60 seconds. Children with cardiorespiratory problems, elevated temperatures (>38°C) or who were crying were excluded. Limitations of this study relate to the other illnesses of the children who were sampled and anxiety associated with the surrounding emergency department.

RRs ranged from 65 bpm in a child, aged four months, to 12 bpm in a child, aged 14 years. Below one year of age, the respiratory rate varied greatly from 22 bpm to 65 bpm. RR
fell into adult ranges by eight years of age. Female patients had higher RRs than male patients but this was not statistically significant. The authors concluded that the large range of "normal" RRs made it difficult to identify "abnormal" RRs.

Studies of RR values observed in adolescent subjects only are shown in Table 1.6. Tabachnik et al. (1981a) found RR to be 15.3 (±1.6) bpm in adolescent during non-REM (non rapid eye movement) sleep. RR increased to 16.4 (±1.5) in REM (rapid eye movement) sleep and to 17.4 (±1.3) in awake children. These findings were in contrast to Carskadon et al. (1978) who found no change in RR between non-REM and REM sleep.

### Table 1.6 - Studies of Respiratory Rate in Awake Adolescents

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (years)</th>
<th>Number</th>
<th>RR ± SD (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock and Soley (1939)</td>
<td>11 - 12.9</td>
<td>100</td>
<td>M 16.3±0.4</td>
</tr>
<tr>
<td></td>
<td>13 - 14.9</td>
<td></td>
<td>M 17.0±0.2</td>
</tr>
<tr>
<td></td>
<td>15 - 16.9</td>
<td></td>
<td>M 15.6±0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F 16.1±0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F 15.6±0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F 15.2±0.3</td>
</tr>
<tr>
<td>Cassels and Morse (1962)</td>
<td>12 - 17</td>
<td></td>
<td>M 15.6±3.0</td>
</tr>
<tr>
<td>Tabachnik et al. (1981a)</td>
<td>15 (mean)</td>
<td>9 (4M, 5F)</td>
<td>17.4 ± 1.3</td>
</tr>
<tr>
<td>Tabachnik et al. (1981b)</td>
<td>12 (mean)</td>
<td>20 (9M, 11F)</td>
<td>19.7 ± 6.2</td>
</tr>
</tbody>
</table>

### 1.10 Studies of Respiration in Adults

Hutchinson (1849) published observations in 1890 adult subjects. Ninety-two percent of this sample had a respiratory rate between 16 and 24 bpm, while one third had a respiratory rate of 20 bpm. Mead (1960) observed respiratory rates in 75 individuals seated at a public gathering and found the mean to be between 16 and 18 bpm. Other studies of RR in adults are summarised in Table 1.7.

Hooker et al. (1989) studied RR in 110 emergency department patients. Patients with cardiorespiratory problems, elevated temperatures and pregnant women were excluded. The mean respiratory rate was 20.1 (± 4.0) bpm. Women had a mean RR of 20.9 bpm that was 1.5
bpm significantly higher than that seen in men. Litscher et al. (1993) found RR in 10 sleeping adults to be 14 (±1.8) bpm.

### Table 1.7 - Studies of Respiratory Rate in Awake Adults

<table>
<thead>
<tr>
<th>Author</th>
<th>Age Range (years)</th>
<th>Number</th>
<th>RR (bpm) M</th>
<th>RR (bpm) F</th>
<th>Range (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetelet (1842)</td>
<td>20 - 25</td>
<td>Approx. 150</td>
<td>18.7</td>
<td>17</td>
<td>14-24</td>
</tr>
<tr>
<td></td>
<td>25 - 30</td>
<td></td>
<td>16.0</td>
<td>----</td>
<td>15-21</td>
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<tr>
<td></td>
<td>30 - 50</td>
<td></td>
<td>18.1</td>
<td>19</td>
<td>11-23</td>
</tr>
<tr>
<td>Robinson (1939)</td>
<td>20 - 29</td>
<td>11</td>
<td>11.4</td>
<td>8-15</td>
<td></td>
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<tr>
<td></td>
<td>32 - 38</td>
<td>10</td>
<td>13.3</td>
<td>9-16</td>
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<tr>
<td></td>
<td>41 - 48</td>
<td>10</td>
<td>15.5</td>
<td>12-21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 - 57</td>
<td>9</td>
<td>12.4</td>
<td>4-24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>59 - 71</td>
<td>8</td>
<td>11.8</td>
<td>8-16</td>
<td></td>
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<tr>
<td></td>
<td>73 - 76</td>
<td>3</td>
<td>13.7</td>
<td>13-14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>91</td>
<td>1</td>
<td>11.0</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Shock and Soley (1939)</td>
<td>18 - 27</td>
<td>86 (46 M, 40 F)</td>
<td>14.0 ± 0.3</td>
<td>14.7 ± 0.5</td>
<td>14.4 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>27 - 43</td>
<td></td>
<td>13.7 ± 0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bendixen, Smith and Mead (1964)</td>
<td>26-27 (mean)</td>
<td>28 (16M, 12F)</td>
<td>16 ± 3.5</td>
<td>F</td>
<td>19 ± 2.9</td>
</tr>
<tr>
<td>Tobin et al. (1983a)</td>
<td>20 - 50</td>
<td>47</td>
<td>16.7 ± 2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 - 81</td>
<td>18</td>
<td>16.8 ± 2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hooker et al. (1989)</td>
<td>38 (mean)</td>
<td>100 (57 M, 43F)</td>
<td>18.4 ± 3.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 1.11 Determinants of Respiratory Frequency in Healthy Individuals

Respiratory rate is set at a particular frequency that is least costly in terms of the average force or tension developed by the respiratory muscles (Mead, 1960). Alternatively, some argue RR observed in humans is least costly in terms of respiratory work (Otis, Fenn and Rahn, 1950). At low RRs, large tidal volumes are required to maintain ventilation. To achieve a large tidal volume, the muscle forces required to overcome the elastic recoil of the lungs and thorax are increased (Waring, 1980). This is inefficient in terms of the elastic work which must be performed. On the other hand, deadspace ventilation is increased when an elevated RR is maintained. Total ventilation must therefore be increased if alveolar ventilation is to be maintained at high RRs. This increased ventilation requires increased muscle force and rate of
work to overcome the increased flow-resistance of the respiratory system. Normal breathing occurs as a compromise between these two extremes of reduced and elevated RRs (Avery and Normand, 1965).

Mead (1960) derived an equation for this optimal RR. It is a function of the ratio of alveolar ventilation to dead space ventilation ratio and the time constant of the respiratory system (τ). The time constant is dependent upon the resistance and the compliance of the respiratory system. The principal site of receptors responsible for frequency adjustment is believed to be in the lung, with vagal afferent nerves carrying the information to the central nervous system (Avery and Normand, 1965).

1.12 Effects of Disease on Respiratory Rate

Respiratory rate is a simple and non-invasive clinical sign which can be observed in sick children. A repeat respiratory rate count for infants under two months of age when the initial count is 60 or higher is recommended (Berman, Simoes and Lanata, 1991). Morley et al. (1990) found no correlation of RR with the presence or severity of a lower respiratory tract infection (LRTI). Since Morley et al. (1990) observed mostly awake infants, sleeping RR is probably a more sensitive indicator of disease.

1.12.1 Lower Respiratory Tract Infection

Respiratory rate has a role in diagnosing, deciding the severity of and management of pneumonia. For example, under WHO protocols, RR is considered abnormal if it exceeds 50 bpm in children aged two to twelve months, or 40 bpm in children aged one to five years (WHO, 1991). RR should be considered in the light of other signs such as cough, nasal flaring, intercostal indrawing, decreased alertness, poor feeding, grunt and fever (WHO, 1981; Morley et al., 1990).

Campbell et al. (1989) in a community-based study found that in children, aged from one to four years, a fever of greater than 38.5°C or a RR greater than 60 bpm were the most accurate clinical signs of lower respiratory tract infections (LRTI). Fever, refusal to breastfeed and vomiting were the best predictors in infants. In a hospital-based study, a RR greater than 50 bpm in infants under 12 months of age and greater than 40 bpm in children aged from one to three years were good indicators of LRTI (Cherian et al., 1988). A summary of sensitivity and specificity of RR as an indicator of LRTI (mainly pneumonia) is presented in
Table 1.8. Sensitivity is defined as the percentage of children who have a LRTI and a respiratory rate above a cut-off respiratory rate. Specificity is the percentage of healthy children whose respiratory rate is below this level. Sensitivity may be different in community based studies because the severity of the disease is lower than that in the hospital setting.

Table 1.8 - Sensitivity and Specificity of Respiratory Rate in Lower Respiratory Tract Infection

<table>
<thead>
<tr>
<th>Author/s</th>
<th>Age</th>
<th>Threshold RR (bpm)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campbell et al., (1989)</td>
<td>1-4 yr</td>
<td>60</td>
<td>60%</td>
<td>73%</td>
<td>Community</td>
</tr>
<tr>
<td>Lucero et al. (1990)</td>
<td>&lt;5 yr</td>
<td>50</td>
<td>54%</td>
<td>84%</td>
<td>Hospital (children presenting with a cough)</td>
</tr>
<tr>
<td>Berman, Simoes and Lanata (1991)</td>
<td>&lt;3 mo</td>
<td>60</td>
<td>62%</td>
<td>63%</td>
<td>Hospital (children presenting with a cough)</td>
</tr>
<tr>
<td>Singhi et al. (1994a)</td>
<td>&lt;2 mo</td>
<td>60 (and/or chest indrawing)</td>
<td>85%</td>
<td>97%</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

RR proved to be a good discriminator between 400 children with diagnosed pneumonia (based on radiological findings) and 454 children diagnosed with upper respiratory tract infection. The children were aged between two months and five years and RR thresholds varied according to the age of the children (Singhi et al., 1994b).

RR is also a good indicator of pneumonia in adult subjects. In a study of acute admissions to a geriatric unit, 19 out of 21 patients diagnosed with lower respiratory tract infections had a RR above 24 bpm on the day of diagnosis. This rise in RR actually preceded the clinical diagnosis of a chest infection by three to four days (McFadden et al., 1982).

1.12.2 Hypoxaemia

Although RR is a useful predictor of respiratory infection in young infants, it does not correlate well with hypoxaemia (O'Dempsey and Todd, 1993). The presence of subcostal retractions is a more useful predictor of hypoxaemia (Berman, Simoes and Lanata, 1991). Subcostal retractions suggest severe pneumonia due to loss of elasticity in the lungs. A child
with chest indrawing may not have fast breathing because the RR can fall when the pneumonia becomes severe and the child becomes exhausted (WHO, 1993). A child with chest indrawing is at higher risk of death from pneumonia than a child with fast breathing without chest indrawing (WHO, 1993).

However, other studies have found RR to correlate well with hypoxaemia in diseases such as cystic fibrosis (CF) and pneumonia (Browning, D'Alonza and Tobin, 1990; Onyango et al., 1993). In children with symptoms of respiratory infection aged three to eleven months, Onyango et al. (1993) found a RR of greater than or equal to 70 bpm and grunting retractions were the best clinical signs for hypoxemia. In older children a RR of greater than or equal to 60 bpm was the best predictor (Onyango et al., 1993). Increases in ventilation during experimentally induced hypoxia have also been found to be due to increases in RR rather than tidal volume (Rebuck, Rigg and Saunders, 1976).

1.12.3 Febrile Illness

Ventilation is affected by environmental and body temperatures (Cooper and Veale, 1986). An increase in RR of 2.5 bpm per degree Celsius in children less than five years of age has been found (Campbell, Byass, and O'dempsey, 1992). This may account for some false positive diagnoses of pneumonia in children with a cough, difficult breathing, raised RR and fever.

Temperatures of children with a fever and raised RR were reduced with an antipyretic medication in a study by O'dempsey et al. (1993). This resulted in an average reduction in RR of 3.7 bpm per degree Celsius that temperature was reduced. The children were diagnosed with either pneumonia or malaria, and there was no difference in response between these groups (O'dempsey et al., 1993). RR was still elevated after the axillary temperature returned towards normal. Therefore, fever was not the sole cause of increased RR in these conditions.

In contrast to these findings, one study found febrile infants with pneumonia to have similar RRs to those who were not febrile (Singhi et al., 1994a). A poor correlation between rectal temperature and RR in awake infants has also been reported (Morley et al., 1990).
1.12.4 Bronchiolitis

Tachypnoea, with RR above 50 bpm, is a well described feature of bronchiolitis (Wohl, 1990). Krieger (1964) studied 24 infants with bronchiolitis within 24 hours of admission to hospital. RRs ranged from 36 to 88 bpm. The mean RR of 62 bpm during sleep was higher than the mean for normal children of 35 bpm.

Silva, Brezinova and Simpson (1982) found the mean RR to be 29.6 bpm during quiet sleep and 33.4 bpm during active sleep in 16 infants with acute bronchiolitis. Respiratory Syncytial Virus (RSV) was isolated in nine and adenovirus in one infant. The infants were studied breathing air during quiet sleep. This restricted the study to a time when oxygen therapy was no longer considered necessary for the infants. The infants were studied again approximately one month later and the mean RR had reduced to 26.5 bpm during quiet sleep and 29.6 bpm during active sleep. The increase in RR caused by bronchiolitis occurring in this study is very different to that found by Krieger (1964) and may be due to differences in the severity of the illness affecting the respective samples.

Mulholland, Olinsky and Shann (1990) found that RR on admission to hospital in 60 infants with bronchiolitis did not predict severity of illness. The presence of crackles and cyanosis was most closely related with the severity of illness. The severity of illness was judged by blood gas analysis and pulse oximetry. RR was not associated with arterial blood gas results or pulse oximetry. No distinction was made between sleeping and awake children in this study.

Others argue RRs greater than 60 bpm are associated with a reduction of arterial O₂ and elevation of CO₂ tension (Wohl, 1990). In 32 children with RSV infection, causing pneumonia, bronchiolitis, or a combination of these conditions, cyanosis was the best indicator of hypoxaemia. An increase in RR correlated with lower arterial oxygen saturation (SaO₂) determinations (r = -0.49) (Breese Hall, Hall and Speers, 1979).

Morley et al. (1990) found the mean respiratory rate in 51 babies with bronchiolitis to be 65 bpm. This was only four bpm higher than the RR observed in healthy babies. Only one baby with bronchiolitis was asleep. The studies that observe sleeping children appear to show more significant differences in RR between children diagnosed with bronchiolitis and normal children. Apnoeas have been found to occur in infants with bronchiolitis and this should be considered when measuring RR in these children (Bruhn, Mokrohisky and McIntosh, 1977; Silva, Brezinova and Simpson, 1982).
1.12.5 Asthma

Hyperventilation is a characteristic of acute asthma. There is debate over whether hyperventilation is achieved by rapid, shallow or slow, deep breathing in asthma (Camazine, 1983; Macklem, and Roussos, 1983). In children with mild to moderate asthma, Tanaka et al. (1990) found RR to be 25.5 (±10.7) bpm during attacks and 18.4 (±5.0) bpm between attacks. Kerem et al. (1991) found RR and dyspnoea to be inversely correlated with measurements of forced expiratory volume in one second (FEV$_{1.0}$) and oxygen saturation levels in children with acute asthma. However, the degree of accessory muscle use was a better predictor of the severity of asthma.

Kesten et al. (1990) assessed breathing patterns in spontaneous severe asthma in adults treated in the emergency department. At the time of initial presentation, the mean initial FEV$_{1.0}$ was 43 (±16) per cent of the predicted value. Inverse correlations between RR and several indicators of air flow including FEV$_{1.0}$, peak expiratory flow rates (PEFR) and flow at 50% of vital capacity ($V_{50}$) were found. One hour after inhalation of nebulised sympathomimetic and/or anticholinergic drugs, the mean RR had slowed from 26.8 (±6.8) to 20.6 (±4.3) bpm. The RR was still higher than controls who had a mean RR of 17.8 (±4.3) bpm. Following therapy, RR no longer correlated with any indicators of flow (such as FEV$_{1.0}$). Connet and Lenney (1993) found oxygen saturation in children with asthma to be poorly correlated with RR on admission to hospital. Hillman, Prentice and Finucane (1986) also found no significant relationship between FEV$_{1.0}$ and RR in acute asthma.

1.12.6 Cystic Fibrosis

RR was measured, using a respiratory inductive plethysmograph, in 11 patients with cystic fibrosis. Their ages ranged from 17 to 29 years (Browning, D'Alonzo and Tobin, 1990). The mean RR was 26.4 bpm compared to the mean RR of 17.1 bpm observed in control subjects. RR was related to a number of indices of respiratory function. These included airway resistance ($r = +0.76$), hyperinflation - functional residual capacity / total lung capacity - ($r = +0.52$) and FEV$_{1.0}$ ($r = -0.60$). There was also a relationship between arterial O$_2$ tension and RR ($r = -0.59$).

In infants, sedated with quinalbarbitone, Phelan (1968) found the mean RR in children with CF aged from one to six weeks to be similar to that of healthy children (see Table 1.9).
Children with CF, aged from 20 to 30 weeks, did have an elevated mean RR (45.3 bpm) when compared to the RR of healthy children (35.5 bpm).

**Table 1.9 - Respiratory Rates in Healthy Infants and Infants with Cystic Fibrosis**

(Phelan, 1968)

<table>
<thead>
<tr>
<th>Children</th>
<th>Age Range (wk)</th>
<th>number</th>
<th>RR (±SD) bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>1 - 6 weeks</td>
<td>9</td>
<td>49.7 (±16.8)</td>
</tr>
<tr>
<td></td>
<td>20 - 30 weeks</td>
<td>4</td>
<td>35.5 (±3.4)</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>1 - 6 weeks</td>
<td>8</td>
<td>43.7 (±13.0)</td>
</tr>
<tr>
<td></td>
<td>20 - 30 weeks</td>
<td>13</td>
<td>45.3 (±11.1)</td>
</tr>
<tr>
<td></td>
<td>40 weeks</td>
<td>7</td>
<td>46.8 (±5.6)</td>
</tr>
</tbody>
</table>

1.12.7 Other Diseases

RR is affected by many other diseases. For example, Morgan et al. (1984) found higher RR in infants with bronchopulmonary dysplasia (57.6 ± 4.6 bpm) compared to the RR of controls (48.9 ± 1.4 bpm). In children, aged from four to nine years, with congenital heart disease, the RR was 28.3 bpm in seven children with cyanosis and 19.8 bpm in eight acyanotic children (Cassels and Morse, 1962). Fever, acidosis, dehydration and malnutrition affect RR and also need to be considered when assessing sick children (Berman, Simoes and Lanata, 1991).
Chapter 2
Breathing Patterns and Respiratory Indices

2.1 Introduction

Respiration is controlled by an automatic metabolic control system located in the brainstem. Added to this is a behavioural or voluntary control system located in supramedullary structures of the brain (Mador and Tobin, 1991). While the metabolic control system exerts the predominant control during resting breathing, respiration can be overridden by behavioural factors. The control system and activity of receptors may also be modified by immaturity, sleep state and drugs (Henderson-Smart, 1994). The pattern of breathing is changed by exercise, reflexes (e.g. swallowing, coughing or sneezing) and expressive behaviour (e.g. speaking, singing and laughing) (Thews, 1989). This suggests a complex regulatory mechanism exists for respiration.

The characteristics of the ventilatory cycle, in terms of RR and tidal volume, are less variable within a subject than between subjects (Shea et al. 1987a). Under identical conditions the characteristics of ventilation differ from subject to subject which leads to the idea of "personnalité ventilatoire" (i.e. ventilatory personality) (Shea and Guz, 1992). Similarity between the breathing patterns of identical twins suggests a genetic basis for the determination of breathing patterns (Shea et al., 1989).

Several factors determine the breathing pattern of an individual. These relate to central nervous system (CNS) mechanisms, mechanical afferents from the lungs, central and peripheral chemoreceptors, forebrain influences and the respiratory musculature. Feldman et al. (1990) argue a set of neuronal elements in the medulla generate the "kernel" of the rhythm. This pattern generation system is embedded within a layered hierarchy of other control elements as shown in figure 2.1. These elements modify the "kernel's" behaviour, but do not change its basic organisation. Some speculation exists about whether the organisation of the "kernel" is changed between states (e.g. sleep and wakefulness).

Berger, Mitchell and Severinghaus (1977) have divided the respiratory control system into three elements. These include the controller (brainstem and higher centres), effector (muscles, lungs and upper airways) and various sensors. A schematic diagram of the system is displayed in figure 2.2. Other factors such as temperature and hormones can also influence this system.
Figure 2.1 - Reductionist hypothesis for generation of the respiratory pattern (Feldman et al., 1990).

Figure 2.2 - Diagram showing different elements of the Respiratory Control System (adapted from Berger, Mitchell and Severinghaus, 1977).
2.2 Ventilation

The expired minute ventilation required for normal gas exchange can be represented by the following equation (Milic-Emili, Whitelaw and Grassino, 1981):

$$V_E = V_T \times RR$$  \hspace{1cm} (2.1)

where $V_E$ is the expired minute ventilation and $V_T$ the tidal volume.

A given ventilation can be obtained with the same frequency and tidal volume but with different airflow and phase duration (Milic-Emili, Whitelaw and Grassino, 1981). Consequently it is useful to partition ventilation into indices of neurochemical drive and respiratory timing as shown in equation 2.2.

$$\dot{V}_E = \frac{V_T}{T_I} \times \frac{T_I}{T_{TOT}}$$  \hspace{1cm} (2.2)

The index for neurochemical drive is the mean inspiratory flow ($V_T / T_I$) and the index for timing is fractional inspiratory time or duty cycle ($T_I / T_{TOT}$) (Milic-Emili and Grunstein, 1976). These indices reflect different central mechanisms. Several reflexes and other influences affect $T_I$ and $T_E$ (and therefore $T_I / T_{TOT}$) without influencing $V_T / T_I$. Increases in chemical drive cause increases in $V_T / T_I$, with only secondary effects on timing (Milic-Emili, Whitelaw and Grassino, 1981).

2.3 Respiratory Timing

The timing index ($T_I / T_{TOT}$) can be calculated from values of respiratory volume change or neural activity (Clark and Euler, 1972). Inspiratory time ($T_I$) is defined as the time from rapid volume change at the onset of a breath to peak volume of an inspiration as shown in figure 2.3. $T_E$ is defined as the interval between the termination of one inspiratory phase and the onset of the next (see figure 2.3). $T_{TOT}$ is the sum of $T_I$ and $T_E$. In healthy humans, the time of expiration is determined in part by the time of the preceding inspiration (Clark and Euler, 1972; Newsom Davis and Stagg, 1975). During quiet breathing $T_I$ is approximately 50 to 70% of $T_E$ (Chemiack and Longobardo, 1986). Decreases in respiratory period are achieved primarily by shortening $T_E$ (Gautier, Remmers and Bartlett, 1973).
During expiration, the potential energy stored in the respiratory system from the preceding inspiration is dissipated. The time required for passive collapse of the paralysed respiratory system is shorter than that observed during a normal expiration (Gautier, Remmers and Bartlett, 1973). This retarded collapse is due to upper airway resistance and antagonistic contraction of the diaphragm (Gautier, Remmers and Bartlett, 1973). Laryngeal resistance fluctuates synchronously with breathing due to phasic contraction of the laryngeal muscles (Bartlett, Remmers and Gautier, 1973).

2.4 Central Mechanisms

Rhythmic activity of specialised neurones in the medulla and pons control the breathing movements of the thorax and diaphragm. These neurones discharge automatically as part of the "central pattern generator" (Mitchell and Berger, 1981; Thews, 1989). The medulla is the site of the dominant respiratory oscillator (Mitchell and Berger, 1981).

There are two compact groups of respiratory neurones in the medulla. One group associated with inspiration is called the dorsal respiratory group. Respiratory phase switching and perhaps primary respiratory pattern generation may reside here. Output from these neurones is found to have a distinct rising phase or "ramp" (Younes and Remmers, 1981). There is also an off-switch mechanism by which their activity is terminated (Younes and Remmers, 1981). There is also a collection of both inspiratory and expiratory cells called the ventral respiratory group in the medulla and a pneumotaxic centre in the pons. The pneumotaxic centre
may have a role in setting the threshold for various inputs that can terminate inspiration and prolong expiration (Mitchell and Berger, 1981).

The respiratory control centre compares arterial levels of carbon dioxide (CO₂) and oxygen (O₂) with desired values for these substances. It also uses information fed back from mechanoreceptors in the thorax and stretch receptors in the lung to change the pattern of ventilation. The respiratory controller then manipulates the respiratory muscles, setting a new pattern of inspiratory and expiratory duration if necessary (Chemiack and Longobardo, 1994). For example, hypercapnia and hypoxia augment the rate of rise of the inspiratory "ramp" described previously (Younes and Remmers, 1981).

Through close association with reticular neurones, various non-specific factors that activate the reticular system also activate the respiratory neurones. Touch may play a role in stimulating respiratory drive through this mechanism (Henderson-Smart, 1994). Cutaneous stimulation causes a marked stimulation of breathing in the newborn (Henderson-Smart, 1994). Factors that cause non-specific central nervous system depression such as drugs can reduce the drive to breathe (Henderson-Smart, 1994). Finally, automatic mechanisms may be temporarily overridden by volitional control via the corticobulbar and corticospinal pathways (Knox, 1979).

2.5 Mechanical Afferents from the Lungs

Afferent activity from pulmonary mechanoreceptors and stretch receptors is transmitted along the vagus nerve. Inspiration is believed to be terminated by a group of medullary off-switch neurones, which are activated when their input reaches a critical threshold (Clark and Euler, 1972). The afferent discharges of the pulmonary stretch receptors which increase as the lungs expand act additively with gradually increasing central activity to end inspiration. An increase in tidal volume therefore shortens inspiratory time when the stretch receptors are functioning and the vagus nerve is intact (Clark and Euler, 1972).

Vagally mediated reflexes do not exert a major influence in healthy humans but may be important in disease (Clark and Euler, 1972). Stretch receptors are not stimulated until tidal volume is increased to about twice its usual level in humans (Clark and Euler, 1972). If lung inflation is sustained then inspiration is inhibited and the classic Hering-Breuer reflex is observed particularly in newborns (Henderson-Smart, 1994). During expiration, lung inflation produces expiratory prolongation (called the Hering Breuer prolongation reflex) since pulmonary stretch
receptors are stimulated by distension of the lungs (Mitchell and Berger, 1981; Widdicombe, 1981).

2.6 Central and Peripheral Chemoreceptors

Central and peripheral chemoreceptor discharge will stimulate respiratory activity and increase ventilation. This occurs when neural and muscular compensating mechanisms are unable to prevent blood gas tensions from rising.

During hypercapnia, signals originate from both peripheral (carotid body) and central chemoreceptors (medulla), resulting in an increase in mean inspiratory flow and tidal volume. Inspiratory time may decrease or not change significantly while expiratory time decreases (Cunningham, Robbins and Wolff, 1986). With hypoxia, a peripheral component associated with stimulation of the arterial chemoreceptors interplays with a central component which causes a depression of respiratory activity. There is a net increase in inspiratory flow with shortening of both inspiratory time ($T_i$) and expiratory time ($T_e$) (Younes and Remmers, 1981).

In vagotomised humans with an intact chemoreceptor system, the effect of hypercapnia on $T_i$ is minimal (Younes and Remmers, 1981). Therefore, the chemoreceptor regulatory system may affect timing indirectly by its effect on tidal volume. Changes in tidal volume are detected by mechanoreceptors and relayed through the vagus nerve.

2.7 Other Respiratory Reflexes

Irritant receptors (or rapidly adapting stretch receptors) are stimulated by the inhalation of chemical irritants such as histamine. They are also stimulated by abrupt changes in the rate of inspiratory airflow and lung collapse (Widdicombe, 1981). The receptors located deep in the lungs lead to tachypnoea but do not lead to secretion of mucus. This is in contrast to those in the trachea and large bronchi which cause coughing, bronchoconstriction and secretion of mucus (Widdicombe, 1981). In animals, these receptors cause tachypnoea by shortening $T_e$ and have a role in the pathogenesis of asthma (Widdicombe, 1981).

Alveolar J-type receptors respond primarily to pulmonary congestion (Widdicombe, 1981). They have an important role in modifying breathing patterns in diseases such as pneumonia (Thews, 1989). J-receptor stimulation reduces both $T_i$ and $T_e$ thereby increasing RR (Armstrong and Luck, 1974).
2.8 Respiratory Muscles

The diaphragm is the principal muscle associated with inspiration (Goldman et al., 1994). The thoracic wall contains two functionally distinct layers of respiratory muscles - the internal intercostals (expiratory) and external intercostals (inspiratory). The muscles of the anterior and lateral abdominal wall can also assist with expiration. Expiration is usually passive, but the abdominal wall expiratory muscles can be recruited during hypercapnia and in conditions such as in asthma (Gautier, Remmers and Bartlett, 1973; Hillman, Prentice and Finucane, 1986).

The rib cage and abdomen make up two parallel pathways which allow change in the volume of the thorax (Konno and Mead, 1967; Goldman et al., 1994). During respiration in healthy subjects, the rib cage and diaphragm usually move synchronously (Tobin et al., 1983a; Goldman et al., 1994).

Breathing in a healthy subject occurs at a fractional inspiratory time (i.e. $T_i/T_{TOT}$) of about 0.4. (Grassino and Bellemare, 1981). Fatigue occurs more rapidly when a subject breathes at duty cycle of 0.6 compared to a duty cycle of 0.3. Mechanisms may exist where an optimal breathing pattern that prevents fatigue (i.e. a low fractional inspiratory time) is achieved by trial and error. Diseases where greater pressures must be generated by the diaphragm predispose to fatigue.

The intrinsic control of breathing movements involves spinal reflexes originating from muscle spindles in the respiratory musculature. When the muscles encounter difficulty, the spindles are activated and cause a reflex increase in contraction of the muscle. This reflex can respond to momentary changes in resistance and compliance of the lungs (Thews, 1989).

2.9 Forebrain Influences

The cerebral cortex plays a major role in the regulation of breathing. It is possible that "comfort" or a minimisation of unpleasantness is a factor that affects the way that patients with lung disease breathe when awake (Anthonisen and Cherniack, 1981). Wakefulness produces a stimulus to breathe even after hyperventilation removes any chemical influences upon breathing (Fink, 1961; Shea and Guz, 1992). It seems there is either a tonic or phasic input into respiratory neurones provided by wakefulness, perhaps by the reticular activating system or the forebrain.

Cognitive activities (such as thought and emotion) also modulate breathing patterns. Feleky (1916) found $T_i$ and $T_E$ varied with different emotions such as laughter, pleasure, anger,
pain and fear. Mador and Tobin (1991) studied the effects of four conditions of altered mental activity on the breathing pattern. These included increased auditory and visual stimulation (watching television), increased cognitive activity (performing mental arithmetic), noxious stimulation (staring at a bright light) and various stages of sleep. During audiovisual stimulation and mental arithmetic, a rise in minute ventilation was achieved entirely by an increase in RR. A rise in ventilation during noxious stimulation was due to an increase in both RR and tidal volume. There were no consistent alterations in $T_i / T_{TOT}$.

These changes with mental activity could be due to differences in regional activity of the cerebral cortex, such as metabolism in the primary and associative visual cortex. Behavioural tasks also increase the level of alertness and stimulate the reticular activating system. Thus an increase in the level of arousal may lead to increases in RR and respiratory drive (Mador and Tobin, 1991). These factors needed to be considered when carrying out the current research project.

2.10 Sleep

Sleep consists of two very different states - slow-wave sleep (SWS) and rapid eye movement sleep (REM). SWS refers to slow-wave "synchronised" electroencephalogram (EEG) patterns that characterise this state (McGinty and Szymusiak, 1994). This state is also called non-REM (NREM) sleep or in infants, quiet sleep. It is further divided into stages one, two, three and four based on details of the EEG pattern, with stages three and four being the deeper states. It is characterised by reduced total metabolism. There is also reduced activity in a majority of brain neuronal sites and a reduction in cerebral metabolism (McGinty and Szymusiak, 1994). During stage four sleep the breathing pattern is very regular, which reflects a vegetative endogenous rhythm controlled entirely by the "automatic" brainstem respiratory controller (Shea et al., 1990) (see figure 2.4a).

REM sleep is characterised by "desynchronised" EEG patterns and is sometimes called active sleep in infants. During REM sleep, cerebral blood flow and metabolism are increased to waking levels (McGinty and Szymusiak, 1994). Most neuronal sites in the brain exhibit increased discharge. Overall metabolism as measured by oxygen consumption remains low (McGinty and Szymusiak, 1994). Respiratory studies conducted during REM sleep reveal rapid and irregular RRs (Lydic and Baghdoyan, 1994) (see figure 2.4b).
During sleep, the partial pressure of carbon dioxide (pCO₂) increases, while the partial pressure of oxygen (pO₂) is reduced (Chemiack and Longobardo, 1994). Decreased metabolic demand during sleep, a reduction in body temperature and sleep itself are responsible for this reduction in alveolar ventilation and RR (Krieger, 1989; Goldman et al. 1994; McGinty and Szymusiak, 1994). One study found a decrease in RR occurred with sleep in adolescents due to increases in both Tᵢ and Tₑ while the ratio of Tᵢ / Tₜₒᵢₜ was not significantly affected by sleep state (Tabachnik et al., 1981a). Variable changes in Tᵢ / Tₜₒᵢₜ found by other studies during sleep suggests fluctuations may occur at random (Krieger, 1989).
The amount of time spent in each stage of sleep changes with age (Anders, 1978). Anders (1978) found that between two and nine months of age, time spent in quiet sleep increased from 30% to 50%. Simultaneously, time spent in active sleep decreased from 54% to 40%. These factors would need to be considered when observing respirations in sleeping infants.

2.11 Hormonal Influences

The decrease of alveolar pCO₂ during pregnancy reflects in part a hormonal influence on breathing (Lyons, 1976). Ventilation is also increased during the luteal phase of the menstrual cycle. Stimulation of respiration is related to progesterone levels. The primary effect is central (Lyons, 1976; Hickey and Severinghaus, 1981).

Francis (1981) found male children to have higher $T_i/T_{TOT}$ values than females while rebreathing CO₂. Jammes et al. (1979) found no sex-related differences for $T_i$ and $T_e$ in subjects aged from 6 to 70 years. Jammes et al. (1979) used a spirometer with a CO₂ absorber and O₂ regulator. This may account for the different $T_i/T_{TOT}$ values found by these studies.

Noxious stimuli can activate the autonomic nervous system leading to the release of catecholamines (Mador and Tobin, 1981). This can change the respiratory pattern. This could be one possible mechanism by which cognitive processes and emotional stimuli alter respiration.

2.12 Studies of Respiratory Timing in Healthy Subjects

Gaultier et al. (1981) studied mouth occlusion pressure ($P_m_{0.1}$) and breathing patterns in children, aged from four to 16 years, and adults with a face mask. Both $V_T/T_i$ and $P_m_{0.1}$, which reflect central inspiratory drive, corrected for weight, decreased up to the age of 13 years. $T_i/T_{TOT}$ did not change with age and was between 0.4 and 0.5 in most individuals. This was due to $T_i$ and $T_e$ increasing proportionately with age.

Jammes et al. (1979) also used a spirometer to measure $T_i/T_{TOT}$ and found it to decrease minimally with age according to the following equation:

$$\frac{T_i}{T_{TOT}} = 0.46 - (0.01 \times \text{age})$$  (2.3)

Tobin et al. (1983a) the mean $T_i/T_{TOT}$ value to be 0.42 in adult subjects using a respiratory inductive plethysmograph (RIP). $T_i/T_{TOT}$ did not change with age, but the breathing pattern
was more irregular in elderly subjects. Other studies obtained different values for $T_I/T_{TOT}$. These include 0.37 in awake and 0.39 during NREM sleep in adolescents and 0.36 and 0.35 in male and female young adults respectively (Bendixen, Smith and Mead, 1964; Tabachnik et al. 1981a).

In newborn babies, $T_I/T_{TOT}$ was between 0.46 and 0.47 during sleep, in studies using a respiratory inductive plethysmograph (RIP) or a pneumotachograph with a face mask (Stick et al., 1992; Finer, Abroms and Taeusch, 1976). Yau and Fang (1994) also found $T_I/T_{TOT}$ to be 0.47 (±0.03) at birth. $T_I/T_{TOT}$ had decreased to 0.42 (±0.03) at four and six months of age in this study.

Neonates and infants are different from adults in that the functional residual capacity (FRC) is dynamically maintained above the mechanically determined relaxation volume of the respiratory system. This helps to prevent collapse and increases forces available for expiration. This can be achieved by actively interrupting expiration and initiating inspiration before passive deflation of the respiratory system is complete (Hershenson, 1992). This results in a reduction in $T_E$ and increase in RR (Agostoni and Hyatt, 1986). Expiratory braking, using the laryngeal adductors, and post-inspiratory activity of the diaphragm are alternative ways of maintaining resting lung volume (Kosch et al., 1988; Henderson-Smart, 1994). The decrease in rate of lung deflation and increase in end-expiratory volume with braking may elicit a reflex prolongation of $T_E$ (Kosch et al., 1988). Infants can alternate between these different mechanisms. This may account for both increased and reduced $T_I/T_{TOT}$ values being observed at this age (Kosch et al., 1988).

2.13 Studies of Respiratory Timing in Subjects with Respiratory Disease

Children with various disease states (such as bronchopulmonary dysplasia, cilia abnormalities and cystic fibrosis) have been found to have reduced $T_I/T_{TOT}$ values (Gaultier et al., 1982). $T_I/T_{TOT}$ was found to be reduced in male adolescent subjects with cystic fibrosis (CF) during rebreathing experiments (Francis, 1981). No such change was observed in female subjects. Browning, D'Alonzo and Tobin (1990) found $T_I/T_{TOT}$ was similar in adult patients with CF compared to controls. They did however find increased mean inspiratory flow values ($V_I/T_I$) and rib cage asynchrony in the patients with CF. This study used a RIP which would cause less interference with breathing than a facemask or mouthpiece.
Tobin et al. (1983b) found $T_I / T_{TOT}$ to be reduced in adult patients diagnosed with chronic obstructive pulmonary disease (COPD). This included hypercapnic and normocapnic patients. Other studies have found lower values of $T_I / T_{TOT}$ in patients with COPD with hypercapnia only (Sorli et al., 1978).

### 2.13.1 Asthma

A prolonged expiration is often listed as a clinical feature of asthma (Bierman and Pearlman, 1990). A prolonged and difficult expiration has been identified as a feature of acute life-threatening asthma or status asthmaticus (Phelan, Landau and Olinsky, 1990). Some studies have even used the inspiratory to expiratory ratio as an index of asthma severity in assessing the efficacy of drugs, such as theophylline (DiGiulio et al., 1993).

In adult subjects with acute asthma, $V_I / T_I$ has been found to be increased, while $T_I$ and $T_I / T_{TOT}$ were found to be reduced when compared to normal subjects (Kassabian, Miller and Lavietes, 1982; Tobin et al., 1983b; Hillman, Prentice and Finucane, 1986). Asai et al. (1990) also found $T_I / T_{TOT}$ was reduced but observed no change in $T_I$ in a study of children. With bronchodilator therapy, inspiratory drive decreased while the alteration of respiratory timing persisted. It was argued persistent obstruction of small airways may have accounted for the reduced $T_I / T_{TOT}$ after the treatment period in this study. In severe attacks following treatment, $T_E$ was still prolonged three to six days after the attack (Asai et al., 1990). Prolongation of expiration decreased with improving $FEV_{1.0}$ values in a number of the children with asthma in this study.

In the study by Asai et al. (1990), $T_E$ increased during the attack. Another study of children found $T_E$ to decrease during a mild asthmatic attack. However, the ratio of $T_E$ to $T_I$ increased with $T_I / T_{TOT}$ being 0.37 during the attack and 0.39 after recovery (Tanaka et al., 1990). No change in timing during asymptomatic periods in both adults and children has been found (Tobin et al., 1983b; Asai et al., 1990). The notion that the severity of the asthmatic attack will determine timing changes is supported by $T_I / T_{TOT}$ increasing disproportionately with $FEV_{1.0}$ ($r = +0.47, p < 0.01$) (Hillman, Prentice and Finucane, 1986).

Francis (1981) found $T_I / T_{TOT}$ to be reduced in male children with asthma $(0.44 \pm 0.03)$ compared to healthy male subjects $(0.49 \pm 0.02)$ during rebreathing experiments. Measuring $T_I / T_{TOT}$ during a rebreathing experiment is different to measuring $T_I / T_{TOT}$ during tidal breathing. However, in the study by Francis (1981) $T_I / T_{TOT}$ remained constant during the
rebreathing experiments. In contrast to Hillman, Prentice and Finucane (1986), no significant correlation between $T_I / T_{TOT}$ and percent predicted FEV$_{1.0}$ was found by Francis (1981). It was speculated the reduction in timing may have been caused by increased irritant receptor activity (Derenne, Macklem and Roussos, 1978; Francis, 1981).

2.13.2 Bronchiolitis

Textbooks also describe prolonged expiration as a feature of bronchiolitis (Wohl, 1990). Krieger (1964) found infants with bronchiolitis did not show prolongation of the expiratory phase, but had a normal or higher than normal inspiratory/expiratory time ratio (i.e. $T_I / T_{TOT}$ was increased). Phelan, Williams and Freeman (1968) did not find any change in the $T_I / T_E$ ratio either during the acute phase of the disease (0.72) or after recovery (0.71). There was however a marked change in the pattern of expiratory flow during the acute stage of the illness. Seidenberg et al. (1989) found $T_I / T_{TOT}$ to be significantly smaller in five infants with bronchiolitis who did not compensate with hyperinflation (0.382) compared to nine infants who were hyperinflated (0.426).

2.13.3 Pneumonia

In patients with pneumonia, $V_T / T_I$ and $T_I / T_{TOT}$ were found to be similar to healthy subjects while RR was increased in a study by Kassabian, Miller and Lavietes (1982). Supplementary oxygen did not alter this ventilatory pattern. The tidal volume increased with recovery.

2.13.4 Pulmonary Oedema

Butler and Hills (1979) have calculated the inspiratory time to expiratory time ratio between 40% and 90% of tidal volume. This ratio, the gamma index, falls as inspiration shortens with pulmonary oedema and pulmonary venous embolisation. It has possible applications in predicting the onset of pulmonary oxygen toxicity in divers (Butler and Hills, 1979).
2.14 Time to Maximum Expiration

The ratio of time to reach peak tidal expiratory flow to total expiratory time ($T_{pef}/T_E$ or alternatively $T_{me}/T_E$) correlates with conventional measurements of airway obstruction (Morris and Lane, 1981). It has also been found to predict the development of wheezing respiratory illness during the first year of life (Martinez et al., 1991). Dynamic compression of the airways during tidal breathing causes the largest flows to occur early in the expiratory cycle (American Thoracic Society/European Respiratory Society, 1993). This accounts for a reduced $T_{pef}$ in airways obstruction. Expiratory airflow is also slowed with obstruction. Therefore, $T_E$ may be increased to allow exhalation to be completed (American Thoracic Society/European Respiratory Society, 1993). Both these factors cause $T_{pef}/T_E$ to be reduced in the presence of airways obstruction.

More recently, Clarke, Aston and Silverman (1994) have found $T_{pef}/T_E$ to be an insensitive index when compared to other indices of airway obstruction in children. RR appeared to affect $T_{pef}/T_E$. It may be more advantageous to analyse $T_{pef}$ and $T_E$ separately, particularly in young children where RR changes rapidly with age.

2.15 Low Frequency Oscillations in the Breathing Patterns

Although the breathing pattern in adults was regular, Priban (1963) observed small, recurring changes in the rate and depth of breathing. The average length of these changes measured three to four breaths. It is possible these short term patterns reflect the behaviour of a respiratory control mechanism. Feedback which regulated RR (or tidal volume) so that the average tension developed by the respiratory muscles was at a minimum, could explain these changes (Priban, 1963). Alternatively these oscillations could be generated independently by a central mechanism.

Feedback involving blood gases require a longer time course, and involve oscillations that are 12 to 20 breaths in duration (Priban, 1963). Waggener et al. (1982) have observed cycles of 50-60 breaths and 16-20 breaths duration in sleeping infants. The 16-20 breath cycle was thought characteristic of the control loop mediated by the carotid body chemoreceptors and is probably associated with periodic breathing. The low frequency loop of 50-60 breaths duration may be mediated by medullary chemoreceptors. Apnoeas were related to some of these oscillations.
Hathorn (1978) showed periodic fluctuations, varying from 6.7 to 12.5 seconds, in both rate and depth of breathing in the newborn. These oscillations were more prominent in active sleep compared to quiet sleep. Hathorn (1978) concluded they were compatible with the respiratory feedback control system, with a time-lag representing the lung-chemoreceptor circulation time.

2.16 Spectral Analysis of the Breathing Pattern

A periodically changing signal, such as the breathing pattern, can be recreated as a Fourier series. This is the sum of many sine and cosine waves each having a different frequency, amplitude and phase (Bendat and Piersol, 1980). A Fast Fourier Transform (FFT) is a mathematical tool, which can resolve a wave form into its individual frequency components. Nugent and Finley (1983) performed spectral analysis using the Fast Fourier Transform technique on the breathing pattern of ten healthy full term infants. Two to three hours of respirations were analysed. The spectra revealed a low-frequency component to the breathing pattern with a frequency of 0.076 (±0.023) Hz. This was approximately equal to the frequency of periodic breathing when this occurred. The respiratory frequency was also present in the spectra at 0.60 Hz (i.e. 36 bpm). It was concluded periodic breathing was an exaggeration of an underlying slow variation in the amplitude of respiration that is present in regular breathing.

Patients with significant pulmonary dysfunction (COPD and respiratory insufficiency) have been found to have rhythmical oscillations of $T_p$, $T_e$ and tidal volume that do not differ from healthy subjects (Siegelova and Kopecny, 1983; Siegelova, 1988).
Part II

Materials and Methods
Chapter 3

Subjects and Experimental Protocol

3.1 Subjects

Healthy Children

This study of respiratory rates was cross-sectional in nature. This type of study has some disadvantages when compared to a longitudinal study in that a longitudinal study provides a lower variance and gives more precision in estimates of temporal change (Hibbert et al., 1989). However, a cross-sectional study could be done in a much shorter period than a longitudinal study. The sample of the present study needed to be large, and also representative of the population from which it was chosen. For this study, the city of Brisbane was chosen as representative of urban communities within Australia. Within Brisbane, children were tested in at least four disparate geographical areas. These areas had the added advantage of being convenient locations.

To provide raw data from which the centile charts for RR could be derived, 343 children without a history of respiratory disease were tested when they were awake and 103 children were tested while they were asleep. There was some overlap of these groups, with 31 children tested when sleeping also tested when they were awake. Tables 3.1 and 3.2 shows the age span and number of children tested. Three children aged between one and six months were born more than three weeks before term (40 weeks). These children still remained in this age group after correction for prematurity.

<p>| Table 3.1 - Age Span and Number of Healthy Children Tested While Awake |
|------------------------|------------------------|</p>
<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Number Tested</th>
<th>Age Span (yr)</th>
<th>Number Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 0.9</td>
<td>18 (12M, 6F)</td>
<td>8.0 - 8.9</td>
<td>47 (24M, 23F)</td>
</tr>
<tr>
<td>1.0 - 1.9</td>
<td>14 (6M, 8F)</td>
<td>9.0 - 9.9</td>
<td>20 (13M, 7F)</td>
</tr>
<tr>
<td>2.0 - 2.9</td>
<td>19 (11M, 8F)</td>
<td>10.0 - 10.9</td>
<td>31 (22M, 9F)</td>
</tr>
<tr>
<td>3.0 - 3.9</td>
<td>26 (8M, 18F)</td>
<td>11.0 - 11.9</td>
<td>14 (5M, 9F)</td>
</tr>
<tr>
<td>4.0 - 4.9</td>
<td>30 (13M, 17F)</td>
<td>12.0 - 12.9</td>
<td>11 (4M, 7F)</td>
</tr>
<tr>
<td>5.0 - 5.9</td>
<td>27 (15M, 12F)</td>
<td>13.0 - 19.9</td>
<td>7 (5M, 2F)</td>
</tr>
<tr>
<td>6.0 - 6.9</td>
<td>32 (14M, 18F)</td>
<td>20.0 - 25.0</td>
<td>13 (13M, 0F)</td>
</tr>
<tr>
<td>7.0 - 7.9</td>
<td>34 (13M, 21F)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3.2 - Age Span and Number of Healthy Children Tested During Sleep

<table>
<thead>
<tr>
<th>Age Span (yr)</th>
<th>Number Tested</th>
<th>Age Span (yr)</th>
<th>Number Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6.99 d</td>
<td>11 (5M, 6F)</td>
<td>1.0 - 1.99</td>
<td>20 (12M, 8F)</td>
</tr>
<tr>
<td>7.0 d - 0.99 mo</td>
<td>4 (2M, 2F)</td>
<td>2.0 - 2.99</td>
<td>23 (15M, 8F)</td>
</tr>
<tr>
<td>2.0 - 5.99 mo</td>
<td>19 (7M, 12F)</td>
<td>3.0 - 4.5</td>
<td>11 (8M, 3F)</td>
</tr>
<tr>
<td>6.0 - 11.99 mo</td>
<td>15 (7M, 8F)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

An attempt was made to test twenty healthy children without respiratory disease in each age group. This was achieved in most, but not all age groups. Testing sleeping infants was limited by the time-consuming process of waiting for the children to go to sleep. In contrast, it was easier to test many older children when they were awake.

Another 217 children who were tested in the community were excluded from data used to create centile curves for RR in healthy children. This included children with a history of respiratory diseases such as asthma, pneumonia, croup, bronchiolitis and hyaline membrane disease. These children were excluded because data on children, free from even minimal lung disease, is vital if it is to be used as a baseline for studying sick children (Hibbert et al., 1989). Children with a history of bronchiolitis in infancy have been found to have persisting abnormalities in pulmonary mechanics (Kattan, Klens and Lapierre, 1977). A history of respiratory disease may therefore affect lung function in children. Seventy-four per cent (161/217) of the children excluded had a history of a present or past condition labelled as "asthma". Children with cardiac disease were also excluded from the healthy control group. Thirty-four per cent (217/632) of all children tested in the community setting were excluded from the healthy group of children.

**Sick Children**

Children with respiratory disease were tested in the wards of the Royal Children's Hospital, Brisbane, at the bedside. This was done with the approval of the Clinical Nurse Consultants of the respective wards. Consulting the registry of admissions in the Accident and Emergency Department helped in finding children with acute respiratory disorders. The main clinical condition studied was asthma. A smaller sample of children with pneumonia, bronchiolitis and cystic fibrosis were also studied.
All those with bronchiolitis were diagnosed by a paediatrician and fulfilled the criteria set by Mulholland, Olinsky and Shann (1990) of acute onset of respiratory distress and wheeze in a child less than 15 months of age. Respiratory syncytial virus (RSV) bronchiolitis was confirmed by the fluorescent antibody test on nasopharyngeal aspirate.

Children with asthma fulfilled the criteria of recurrent wheezing responsive to bronchodilators and were diagnosed by a paediatrician (DiGuilfo et al., 1993). Acute pneumonia was defined as acute inflammatory infiltration of the lungs. This was evident as lobular, segmental or lobar consolidation on chest radiographs (Phelan, Landau and Olinsky, 1990). The diagnosis of cystic fibrosis was made by a paediatrician during the earlier years of life. Some infants and toddlers with CF were monitored in the hospital's pulmonary function laboratory during sleep. These children were sedated with chloral hydrate as part of an unrelated research study which had obtained ethical approval to do this.

### 3.2 Setting

All new born babies were tested in the maternity wards of the Royal Women's Hospital, Brisbane. This was done at the discretion of the Clinical Nursing Consultants of the respective wards. Infants, aged between two weeks and one year of age were tested at a short term residential centre. Mothers with babies experiencing feeding or sleeping difficulties stayed with their children at this centre.

Most children aged between six months and six years of age were recruited from child care centres and kindergartens throughout Brisbane. These centres were located in four disparate geographical areas. Another two centres, one at a university servicing staff and students, and another in the city, included children not confined to the geographical area surrounding the centre. Children aged five years and above were sampled from four schools, one after-school centre, and various youth and scout groups. Private schools were selected because these schools gave quicker administrative approval for the project.

Another group of children tested were inpatients and siblings of inpatients at the Royal Children's Hospital, Brisbane. These children were without significant cardiorespiratory disease, or were siblings of inpatients. Some children were also tested in their homes. A group of young adult males, aged between 18 and 25 years, also had their breathing monitored at the hospital. The characteristics of the sample (excluding absent and non-compliant children) are summarised in Table 3.3.
Table 3.3 - Source of Population for Obtaining Reference Ranges for Respiratory Rate

<table>
<thead>
<tr>
<th>Source (approximate numbers)</th>
<th>Healthy Children</th>
<th>Children with Respiratory Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternity Ward</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Residential Centre</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Children's Hospital</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Child's Personal Home</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Child Care Centres/ Kindergartens</td>
<td>127</td>
<td>77</td>
</tr>
<tr>
<td>Primary School Aged Children (schools, youth clubs)</td>
<td>210</td>
<td>135</td>
</tr>
<tr>
<td>Medical Students</td>
<td>13</td>
<td>----</td>
</tr>
<tr>
<td>Total = 632</td>
<td>415*</td>
<td>217</td>
</tr>
</tbody>
</table>

* Thirty-one children were tested while they were awake and while they were asleep.

3.3 Ethical Considerations

Ethical approval was obtained from both the Royal Children's Hospital Ethics Committee and the Royal Women's Hospital Ethics Committee, Brisbane (see Appendix 1). Written consent was obtained from both children tested within the community and those within the hospital. The person in authority at the school, childcare centre or youth club was approached through a letter (see Appendix 2).

After approval was given, letters containing both a parent information sheet and a parent consent form were sent via the teacher (or leader/childcare provider) to parents. An example of an information sheet and consent form given to parents is also shown in Appendix 2. The children of parents who had returned forms were then tested. Many people were involved in this liaison process with the children and parents. This accounted for some variability in the response rates of parents and children consenting to the test.

Response rates varied from 25.0% (29/116) to 89.6% (26/29) at different schools and 29.6% (16/54) to 73.3% (22/30) at different childcare centres. About 1220 children received an invitation to participate in the study, resulting in a response rate of 52% approximately (632/1220). This figure excludes absent children and children who refused or were not able to participate in the study (approximately 30 children in each of these two groups). The latter group included sleeping children who woke up during the testing process, children who refused to participate possibly due to stranger shyness and children unable to lie still.
The parent consent forms contained a few brief questions. Parents were asked whether their child had suffered from any respiratory illness and the date of birth of their child. This allowed children to be divided into two groups so that the sample of healthy individuals could be readily identified. This group could also be compared with children who did have a history of present or past respiratory disease. More detailed questions, such as a family history of respiratory disease or the presence of any smokers in the household, were not included. This was done to make this consent form simple for parents to complete and maintain a high response rate. A question concerning medications the children may have been on was added in the second half of the research project. Some drugs are known to affect RR\(^1\) (Hickey and Severinghaus, 1981). Within the hospital setting the procedure was explained to parents. They were asked to read the information sheet and then sign a consent form (see Appendix 3).

Informing the parents and children about the research could bias this research to some extent, as the children knew their breathing was being monitored. This is an example of the Hawthorne effect, where individuals may change their behaviour if they are aware of someone taking an interest in them (Drever and Wallerstein, 1974). Naturally, both parent's and child's informed consent must take priority over this consideration. This problem mainly concerned older, awake children. Its effect was reduced by leaving most of the explanation about how the sensor worked until after the experiment was completed. Pre-test information given to the children aimed to reduce their anxiety by explaining where the sensor would be applied, that it would not be painful and that they would need to lie still. The fact that their breathing was being monitored was given a low key role in this discussion and the words "breathing rate" or "respiratory rate" were avoided.

3.4 Questionnaire

A questionnaire (see Appendix 4) containing more detailed questions than those previously discussed was issued to a selected sample of the children in the study. All parents of children within two groups (one class at a school and one class at a kindergarten) regardless of their response to the study were issued with this questionnaire. Questions related to the presence of any current upper or lower respiratory tract symptoms, history of respiratory

\(^1\)Narcotics and benzodiazepines will depress ventilation. Hypnotic doses of barbiturates (e.g. pentobarbitone) have little effect on ventilation. Other drugs such as noradrenaline, aminophylline and salicylates are examples of drugs that stimulate respiration.
disease and family history of respiratory disease. There were several reasons for the inclusion of this more detailed questionnaire.

The first was to determine if there was any difference between the group of children and parents who agreed to participate in the research study and those who did not. Such groups are known to differ, at least for some types of research. Harth, Johnstone and Thong (1992) found a difference in the psychological profiles of parents who volunteered their children for medical research compared to parents who did not. They concluded that the informed consent procedure had a psychosocial "filter" effect resulting in more socially disadvantaged groups being involved in medical research. To this end, a further question relating to parents' perception of risk relating to their child's involvement in the research was also included. It was also possible that parents with a family history of respiratory disease, or of a certain socio-economic status, would take greater interest in the study and therefore cause bias within the sample.

Secondly, the questionnaire served to show how similar the sample that responded was to the Brisbane population. The questionnaire was given to a sample of children tested at childcare centres and schools for this purpose. Some studies deal with the problem of socio-economic status by studying children in a wide range of schools to ensure all socioeconomic groups are represented (Hibbert et al., 1989). This was not possible in this study as the testing procedure was time consuming. This limited the number of schools and childcare centres that could be involved.

A method of determining socio-economic status based on parental occupation was used. Daniels (1983) argued that occupational prestige is an accurate measure of social status. While "class lines are blurred and confused" in Australia, division of the sample into several categories based on parental occupation was appropriate (Daniels, 1983). The Australian Standard Classification of Occupations (ASCO) provided a detailed description and categorisation of occupations (Australian Bureau of Statistics, 1991a - see appendix 5). When both parents worked, the occupation that was highest on a scale of occupational prestige created by Daniels (1983) was chosen. The occupations of parents of children in this sample were then compared with data for the general Brisbane region (Australian Bureau of Statistics, 1991b).

The questionnaire's third purpose was to evaluate the presence of any recent respiratory symptoms in children, including upper respiratory tract infections (URTI). The questions were similar to those of Marks, South and Carlin (1993) and included sore throat, breathlessness,
cough, fever, "runny nose" and night cough. Children without any respiratory disease and no recent upper respiratory tract infection were compared to those without respiratory disease but who had symptoms of an upper respiratory tract infection. A recent respiratory tract infection was defined as one or more of the following: "runny nose", fever, cough and sore throat.

3.5 Experimental Protocol

Body weight, height and axillary temperature were recorded at the time of testing. Axillary temperature was measured with a digital thermometer (Safety 1st, Chestnut Hill, USA). Body weight was measured with bathroom scales (Salter, Kent, England) in most children. No medical examination was done on the children, since this would have increased their anxiety (Marks, South and Carlin, 1993). However, noisy breathing and rhinorrhea were readily observed. The ambient temperature was measured with a digital thermometer during the second half of the project. The temperature of the hospital's air conditioning system was set at 23°C. Except for newborn infants, children were not tested within half an hour of eating food. Ashton and Connolly (1971) have suggested that the metabolic stimulus of food can change RR. Food may also alter the position of the diaphragm.

Most children under three years of age were monitored during their daily nap. A smaller proportion were tested when they were awake (see figure 3.1). This was due to these children being more readily upset, unable to lie still and less able to co-operate. If the children were unable to lie still, movement artefact was recorded on top of the respiratory signal. This made it difficult to count respirations. An attempt was made to score the sleep state of sleeping children based on behavioural criteria. Table 3.4 summarises the general findings of breathing patterns in the two main sleep states (Hathorn, 1974; Stefanski et al., 1984).

Table 3.4 - Summary of Features of Quiet and Active Sleep

<table>
<thead>
<tr>
<th>Sleep State</th>
<th>Facial Features</th>
<th>Extremities</th>
<th>Respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quiet</td>
<td>Eyes closed. Flaccid &quot;rag doll&quot; appearance</td>
<td>Body movements limited to startles*</td>
<td>Regular</td>
</tr>
<tr>
<td>Active</td>
<td>Rapid eye movements may be seen beneath lids Frowns, smiles Frequent oral activity (e.g. chewing, sucking) Eyes may occasionally open and close</td>
<td>Small body movements are seen (often of extremities) Slow intermittent writhing movements Limb twitches and tremors. Jerky startles Whimpers</td>
<td>Irregular</td>
</tr>
</tbody>
</table>

* A startle is a sudden contraction of many muscles lasting a few seconds with an immediate return to a relaxed posture.
Figure 3.1 - A photograph showing the sensor applied to a cooperative and awake infant. Because infants were easily upset, only a small number were tested when they were awake.

Scoring of sleep state based on behavioural criteria was limited without an electroencephalogram (EEG), electrooculogram and electromyogram (Marks, South and Carlin, 1993). Another way of describing the sleep patterns is that of regular and non-regular breathing patterns. Regular breathing patterns are signified by episodes of at least one minute in duration where abdominal wall movement waveform is steady in rate and amplitude. A regular breathing pattern is highly correlated with a state of quiet sleep (Stebbens et al., 1991). Periods not conforming to this definition, and those in which the pattern is disrupted by body movements, sighs, or apnoeic pauses are classified as irregular. Examination of the respiratory patterns, therefore, provided an additional source of information when scoring sleep state.

Awake children were sedentary for at least ten minutes before measurement of their breathing patterns commenced. Ten minutes seemed an appropriate rest period, since most children were not engaging in strenuous activities before this time. One study found it took just
15 minutes for the average RR in a group of children to decrease to resting levels after maximal exercise (Salvadori et al., 1993).

The optical sensor was placed on the child's chest at least five minutes before monitoring began. This allowed time for adjustment. Some researchers have allowed an adjustment period of 15 minutes, while others started recording the moment the respiratory waveform looked regular (Mador and Tobin, 1991; Marks, 1994 personal communication). In the present study, the sensor was hidden under the children's clothing so that they would not focus attention on the sensor or their breathing pattern. The sensor was usually applied with tape (Micropore; 3M, St. Paul, Mn, USA) (see figure 3.2). Double-sided tape (3M, St. Paul, Mn, USA) was used on infants if the sensor was affixed before they went to sleep. No children were observed to have allergic reactions to the tape.

The breathing pattern was recorded for approximately five minutes in both awake and sleeping children. Less data was obtained from children who were unable to lie still, since movements distorted the respiratory waveform. A mean amount 4.18 (±2.2) minutes of breathing pattern that was recorded was suitable for counting respirations in awake subjects. In sleeping children, an average of 6.9 (±4.2) minutes of recorded data was suitable for counting respirations.

The supine position was the researcher's preferred position for all children. This was because the posture of the children may have affected RR. The functional residual capacity (FRC) is decreased in the supine position compared to the upright posture (Goldman et al., 1994). Some sleeping children preferred to sleep prone or on their side. Attempts were made to move the children to the supine position, but this was not always possible. Sometimes children would wake if they were moved and would not go back to sleep. Alternatively, they would quickly revert to their preferred position. The sensor was then placed on the children's side and an adequate respiratory waveform was obtained.

Reducing external environmental stimuli was important in establishing a resting state in awake children (Mador and Tobin, 1991). Awake children were occupied with a story book. This had several advantages. For younger children, it decreased the anxiety associated with the testing procedure and provided an incentive to participate. It also prevented them from getting bored, thus helping them to lie still. Most importantly it distracted them from focussing on their breathing. Children under five were read a story (Monty Mouse Looks for An Adventure\textsuperscript{1}). One

\textsuperscript{1}Fossard E. \textit{Monty Mouse Looks for An Adventure}. Melbourne: Childerset, 1976.
disadvantage of this was that the investigator was beside the children during the testing (see fig 3.3).

Figure 3.2 - The optical sensor being applied to the lower chest of a girl, aged nine years, with Micropore tape.
Children older than six years read a book (Where's Wally?1 - see figure 3.4). The children turned pages infrequently since this book contained detailed pictures. This was important since movement of limbs has been found to increase RR. This is due to stimulation of joint receptors and muscle spindles (Agostoni and D'Angelo, 1976). The five year old age group represented a transition period in the testing procedure with 27 children tested at childcare centres read the story (The Adventure's of Monty Mouse) and 23 tested at schools read the book (Where's Wally).

Figure 3.3 - A boy, aged four years, being read a story while his breathing was being monitored.

External stimuli and fluctuations in level of alertness were reduced by giving each subject the same material to focus on during the experiment. Shea et al. (1987b) used blindfolds and earmuffs to achieve a baseline level of brain activity for their respiratory experiments. This was inappropriate for children since any theoretical benefit would be counterbalanced by

apprehension or fear, resulting in larger artefacts. Reading has been found to increase the RR by about six per cent (Shea et al., 1987b). Auditory stimulation had a similar effect (Shea et al., 1987b). To investigate the effects of reading on respiration, some children were tested while they rested quietly, and also while they were reading. This was done in both older children (who had only visual stimulation) and younger children (who had both auditory and visual stimulation). Children were instructed to keep their eyes open since RR is reduced when the eyes are closed (Shea et al., 1987b). This also prevented the children from falling asleep.

The children did not view their breathing pattern on the monitor until after the testing had been completed. Children at the schools were tested in a quiet room. A female assistant was always present when primary school aged girls were tested. This was done for ethical reasons and out of courtesy to the children. It also reduced anxiety associated with adjustment of clothing. Most children had to lift up the lower part of their shirt for the sensor to be applied. Testing at childcare centres was done in a quiet corner of a room in clear view of staff. This

Figure 3.4 - A boy, aged eleven years, reading a book (*Where's Wally?*) while his breathing was being monitored.

The children did not view their breathing pattern on the monitor until after the testing had been completed. Children at the schools were tested in a quiet room. A female assistant was always present when primary school aged girls were tested. This was done for ethical reasons and out of courtesy to the children. It also reduced anxiety associated with adjustment of clothing. Most children had to lift up the lower part of their shirt for the sensor to be applied. Testing at childcare centres was done in a quiet corner of a room in clear view of staff. This
seemed an important way of preventing the anxiety that might occur if young children were moved to an isolated room with a stranger. The sensor was wiped between uses when new born babies or children with infection were tested.

Children in hospital were normally tested at their bed, usually with their parents present. Additional clinical measurements were sometimes made on these children including pulse oximetry. A number of pulse oximeters were used including a Criticare 503 Pulse Oximeter (Criticare, Wau Kesha, WI, USA) and Ohmeda Biox 3740 Pulse Oximeter (Ohmeda, Boulder, CO, USA). A Wright's Peak Flow Meter (Clement Clarke International, London, U.K.) was used to obtain peak expiratory flow rates (PEFR) values in 20 children. A portable pneumotachometer (Welch Allen Pneumocheck, Skaneateles Falls, NY, USA) was used to obtain lung function values at the bed side in eight asthmatic children. For children with CF, recent spirometry values obtained from the hospital's Pulmonary Function Laboratory (Vitalograph Pneumotachometer, Birmingham, U.K.) were noted.
Chapter 4
The Optical Respiratory Sensor and Analysis of Data

4.1 Background

The respiratory sensor used in this study was an angular displacement optical sensor. The sensor had previously been used in magnetic resonance imaging (MRI) of the abdomen (Wilson et al., 1993). Periodic movement of abdominal organs with respiration during MRI produces a loss of image clarity (Wilson et al., 1993). However, the acquisition of the image can be synchronised to a period of minimal motion within the respiratory cycle. The respiratory sensor was initially developed for this application.

This optical sensor was considered advantageous in the paediatric setting for several reasons. The sensor was made of plastic and attached to an optical fibre that used light for detecting motion. Therefore, there was no risk of electrical shock. It was small and simple to use and caused minimal inconvenience to the subject. There was no risk of infection because the sensor was non-invasive.

The sensor imposed no restrictions to respiratory excursions, since it did not encircle the chest. Other respiratory devices that encircle the chest, such as strain gauges, may increase the external elastic resistance to breathing. In conscious subjects this is known to increase RR (Cherniack and Altose, 1981). The ease of application of the sensor was another advantage. This was particularly the case when testing sleeping children, as it could be applied while the children were sleeping, often without waking them. For these reasons, the sensor was considered an appropriate device for undertaking a study of breathing patterns in children.

4.2 Components of the Optical Sensor

The sensor consisted of a plastic hinge device as shown in figures 4.1 and 4.2. Embedded within this hinge was a loop of optical fibre. Two "sensor tubes" were positioned at the pivot point of the hinge. They consisted of flexible vinyl tubes, with internal reflective surfaces, and were connected to the loop of optical fibre. A 660nm LED (red) light source was optically coupled into one end of the loop. As the hinge device moved to and fro with respiration, the sensor tubes were bent and straightened. This modified the internal reflection of light within the sensor tubes. A phototransistor at the other end of the loop converted these changes in light signal to a voltage signal. The components of the sensor are listed in Appendix 6.
Figure 4.1
The optical respiratory sensor. Two sensor tubes are positioned at the pivot of an optical fibre loop. This is supported by a plastic hinge. When applied to the lower costal margin abdominal respiratory movements bend the hinge. This modulates the intensity of light transmitted in the optical fibre loop (Wilson et al., 1993 - diagram used with permission).

Figure 4.2
Photograph of the optical fibre respiratory sensor. A smaller form of this sensor was used to observe the breathing patterns of newborn infants. The sensor was affixed to the chest wall with adhesive tape. It was connected to a two metre long fibre optic cable. This in turn was connected to a small interface unit which contained the light source and phototransistor.
The phototransistor, optical light source, amplifier and a filtering device were all contained within a custom built interface unit. The interface unit was connected to the hinge device by a one mm single core, step index polymer optical cable which was two metres long. There was no risk of electrical shock to the children. The voltage signal was amplified and converted to a digital signal by an analogue to digital converter (PC-LPM-16 Multifunction I/O Board, National Instruments, Austin, TX). The zero and gain of the amplifier were arbitrarily adjusted so that the waveforms caused by respiratory motion used a substantial part of the display screen.

This signal could be displayed and recorded by a computer (386DX33 A4 Systems Tower or 386 Toshiba T3200SX Laptop) using a computer program written in Turbo C Version 2.0 (1989) (see figure 4.3). Data points were sampled every 43.04 ms. The sampling rate was increased to 20 ms for young children who were breathing rapidly.

Figure 4.3
Photograph of breathing pattern of an infant, aged seven months, as seen on the computer monitor. Twenty-six seconds of breathing pattern is shown.

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1 The interface unit was designed and built by Dr S.J. Wilson, Centre for Magnetic Resonance, University of Queensland.

2 This computer program, called Display, was written by Dr S.J. Wilson, Centre for Magnetic Resonance, University of Queensland.
As the tube was initially bent, there was a large reduction of light passing through it. With further bending of the tube, the attenuation of the light signal became less. Therefore depending of the placement of the sensor on the chest, the changes in light signal would not always be linearly related to angular displacement of the hinge device. The sensor detected little rib cage contribution to breathing since it primarily measured the rise and fall of the abdomen. These two factors limits its ability to give an accurate measurement of volume change in the lung. Since the focus of the study was to obtain RR and timing indices in children, the ability to calibrate for volume changes was not considered essential.

There was insignificant attenuation of the light signal using the two metre optical cables. An advantage of this is that the interface unit and computer could be placed some distance away from the children (see figure 4.4).

Figure 4.4
Photograph illustrating the two metre length of optical cable. This connected the sensor applied to a child's chest with a small interface unit. This in turn was connected to a computer.
4.3 Application of the Sensor  

One half of the hinge was applied to the lower costal margin. This was fixed compared to the other end of the hinge, which was attached to the abdominal wall (see figure 4.5). The sensor primarily detected the rise and fall of the abdomen. This was because during respiration in the supine posture, the contraction of the diaphragm displaces the abdominal wall outwards more than the rib cage (Goldman et al., 1994). During tidal breathing in healthy subjects, the majority of the volume displacement of the lung is accounted for by abdominal movements (Konno and Mead, 1967). The mechanics of operation of the sensor may differ in certain diseases, such as acute asthma, where an increased contribution of the rib cage to tidal volume has been observed (Tanaka et al., 1990). The half of the hinge attached to the lower costal margin was less stable in such cases. With increased contribution of the rib cage compartment to tidal volume, the signal could become more complex.

Figure 4.5  
Photograph showing the sensor applied to an eight year old boy's chest. Abdominal movements associated with respiration moved the hinge device. The sensor worked equally well with the optical fibres directed upwards (as in this picture) or downwards.
The same mechanical principles moved the hinge device when the sensor was placed either upright or inverted on the children's chest. Placing the sensor inverted on the children's chest required less manipulation of clothing. This was therefore the preferred position. To reduce the effect of the apex beat of the heart, the sensor was placed on the right side of the chest.

4.4 Comparison of the Optical Sensor with Other Respiratory Transducers

Visual observation by experienced personnel will always be an important method of monitoring respiration. It is also a useful way of evaluating a respiratory sensor's ability to measure RR (Vegfors et al., 1992). RRs obtained by visual observation for two mintues were compared with those of the optical sensor in 13 subjects.

The waveform pattern of the optical sensor was also compared to patterns obtained from a respiratory inductive plethysmograph (Respitrace®, Ambulatory Monitoring, Inc., Ardsley, NY) and a water-sealed spirometer. A comparison of the timing of events (such as onset of inspiration and expiration) in the respiratory cycle was of particular interest.

The water-sealed spirometer (9L Respirometer, Warren and Collins, Braintree, Mass) is considered a reference standard for respiratory volume measurement (Hanning and Spence, 1982). It consisted of a counterbalanced, cylindrical bell which was immersed in water. This bell was connected to the subject's airway by a mouthpiece and tubing. The bell rose and fell as it was filled with air during exhalation and emptied during inspiration. There may be some lack of precision with such a spirometer due to inertia of the bell. The bell's displacements were recorded on a moving chart. The optical sensor was applied when a subject, wearing a nose clip, breathed into the mouth piece (see figure 4.6). Two young adult subjects participated in this experiment.

The respiratory inductive plethysmograph (RIP) or Respitrace® consists of two elastic bands that encircle the rib cage and abdomen. Insulated coils of wire are sewn into the bands. Self-inductance of the coils and the frequency of connected oscillators change with cross-sectional changes in area of the rib cage and abdomen. It is arguably the "gold standard" among the non-invasive respiratory transducers that detect thoracic wall movement (Hanning and Spence, 1982). Stick et al. (1992) found the mean difference between $T_1 / T_{TOT}$ calculated from a pneumotachograph and Respitrace® was 0.04 ($\pm 0.024$) in 19 sleeping neonates. Some
The authors state estimates of respiratory timing from Respitrace® are within 0.1 seconds when compared to a spirometer (Shea and Guz, 1992). In the present study, comparisons between the optical sensor and Respitrace® were made on an infant and two children, aged four and nine years.

Figure 4.6
Photograph illustrating a male subject breathing into a spirometer (recording onto the drum) at the same time that the optical sensor (recording data into the laptop computer) was applied to his chest.
Figure 4.7
A four year old boy with Respitrace® bands applied to his chest and abdomen. The optical sensor is also applied to the right hand side of his chest.

The sensor was also used with a Sensor Medics 2600 system (Anaheim, CA, USA). This device consisted of a pneumotachograph that measured flow. Children in these experiments were usually sedated with chloral hydrate, as part of an unrelated research study. The breathing pattern was recorded by the optical sensor at the same time as the children's respiration was being monitored with the pneumotachograph using a face mask. Since the Sensor Medics 2600 system analysed eight breaths, eight breaths obtained from the optical sensor were also analysed. These were compared with the values obtained by the pneumotachograph. Since the breaths chosen for analysis by the Sensor Medics 2600 system were not always consecutive, the breaths measured by the two devices were not always the same. Nine children with CF and three other children were involved in this part of the study.
4.5 Analysis of Data

Respiratory Rates

All data were analysed off-line on an IBM compatible personal computer (386DX33 - A4 Systems or 486DX66 - Byte Pro). The respiratory signals could be played back in 30 second epochs using a computer program compiled in Turbo C Version 2.0 (1989)\(^1\). Curzi-Dascalova, Gaudebout and Dreyfuss-Brisac (1981) found pauses did not have a large effect on RR in infants. Despite this, pauses between respirations lasting longer than four seconds were excluded from analysis in the present study. The signal was disregarded if there was movement artefact or if the quality of the waveforms was poor. Two measures of RR were made. The respirations counted in the first two 30 second epochs of data were added together. The average RR for the total duration of recording was also calculated.

Timing Indices

The inspiratory and expiratory times (\(T_i\) and \(T_e\)) were calculated on an Apple Macintosh 2SI computer using available software called MacAster Version 2.8 (1994). It detected peaks and troughs in the respiratory waveform as shown in figure 4.8 (Eberhard, 1992). The peak in the respiratory waveform corresponded to the end of an inspiration, while the trough corresponded to the end of expiration. Troughs also corresponded to the start of the next inspiration. Data were filtered using a weighted average according to equation 4.1:

\[
D_i = (0.08 \times D_{i+2}) + (0.22 \times D_{i+1}) + (0.40 \times D_{i}) + (0.22 \times D_{i-1}) + (0.08 \times D_{i-2}) \quad (4.1)
\]

where \(i = 2, \ldots, n - 3\); \(n\) is the number of points which was analysed; and \(D\) is the displacement value of the optical sensor.

Breaths were analysed one at a time. A breath was discarded if it was not representative of the total sample of breaths (e.g. a sigh). The peaks and troughs detected by the computer program could be adjusted manually if they did not correlate with the "true" start of inspiration or expiration. An adjustable threshold could be set to correspond to the relative size of the breaths. This excluded noise from the signal.

\(^1\)This computer program, called Fread, was written by Dr S.J. Wilson, Centre for Magnetic Resonance, University of Queensland.
Breathing pattern of a 22 year old male. The troughs, or nadirs, at points 1, 3, 5, 7 and 9 mark the start of inspiration and end of the previous expiration. The peaks, or zeniths, at points 2, 4, 6, 8 and 10 mark the start of expiration and end of inspiration.

The values of $T_i$, $T_e$ and $T_{TOT}$ obtained were saved in a computer spreadsheet file and analysed statistically using a spreadsheet program Quattro Pro for Windows Version 5.0 (1992). Stick et al. (1992) analysed 10 breaths in 19 newborn babies with Respitrace® and obtained a small spread of $T_i / T_{TOT}$ values with a SD of 0.03. Based on this, ten breaths were analysed in the present study.

Other methods of defining the various points in the respiratory waveform exist (Frank Scott, Studley Data Systems, Oxford, UK, personal communication 1994). While formally $T_e$ is terminated by the onset of inspiration, this may not coincide with the end of the active expiratory process (Cunningham, Robbins and Wolff, 1986). An expiratory pause is a period of absent flow between the end of expiration and the start of the next inspiration. It may be prominent in individuals breathing with a slow RR (Cunningham, Robbins and Wolff, 1986).

In the present study, this pause was included as part of $T_e$. It was difficult to define the start of an expiratory pause using the optical sensor, which measured chest wall movements. It was possible flow may have continued after abdominal motion had ceased. This was a limitation of the present study. Fig. 4.9 illustrates expiratory pauses present in the breathing
pattern of a girl, aged four years. The pause is not associated with all breaths in this tracing but when present has a large effect on $T_1/T_{TOT}$.

![Graph showing breathing pattern](image)

**Figure 4.9**
Breathing pattern of a girl, aged four years. The horizontal lines mark expiratory pauses in the breathing pattern. Expiratory pauses were included as part of the expiratory time in the present study. The small fluctuations in the waveform during the expiratory pauses are caused by cardiac contractions ("heart bumps") detected by the sensor.

The derivative of the displacement signal obtained by the optical sensor could also be obtained using the *MacAster Version 2.8* (1994) program. The formula used to do this was:

$$S_i = \frac{D_{i+1} - D_{i-1}}{2 \Delta t}$$

(4.2)

where $\Delta t$ is the time interval between the two successive samples, $i$ is the number of the data point being analysed, $D$ is displacement, and $S_i$ the slope or derivative of the signal at point $i$. It was possible the differentiated signal may have been related to flow (Eberhard, 1992).

**4.6 Spectral Analysis**

A power spectrum represents distribution of the energy of a signal among its various sinusoidal frequency components. A Fast Fourier Transform (FFT) was performed on 1024 points of respiratory waveform data using *Quattro Pro for Windows Version 5.0* (1992). This corresponded to approximately three minutes of data. The mean of the data series was
subtracted from each data point. The data was also windowed to reduce leakage (Loring and Bruce, 1986). A cosine window function, as shown in equation 4.3, was used for this purpose.

\[ W_i = 0.5 \times (1 - \cos \frac{2 \pi i}{n}) \times D_i \]  

(4.3)

where \( n \) is the number of points in the series (1024 in the current study), \( D_i \) the displacement value at point \( i \), and \( W_i \) the "windowed" value. The Nysquist frequency, which is the highest frequency that can be analysed using this technique, was 11Hz (or 697 bpm) in the present study. The Nysquist frequency \( (f_n) \) is defined by the following equation:

\[ f_n = \frac{1}{2 \times SR} \]  

(4.4)

where \( SR \) is the sampling rate (in seconds).

The FFT produced a set of complex numbers. The absolute values of these complex numbers were squared and plotted against frequency to give the power spectrum. Values were smoothed using a non-weighted moving average. Since the Fourier series in this study contained 1024 points, the 512th point corresponded to the Nysquist frequency. The frequency of all other points could be calculated as a proportion of this Nysquist frequency.

The spectral analysis of the breathing pattern is usually associated with a fundamental frequency corresponding to the RR. There may also be harmonic frequencies present in the spectrum, which are multiple integers of the fundamental frequency (Bachy et al., 1986). These harmonics become prominent as the waveform becomes less sinusoidal (Diggle, 1990).

The width of the peak corresponding to the RR (i.e. the fundamental frequency) gives a measure of dispersion in respiratory frequency around the mean RR (Gordon et al., 1984).

The spectrum of the breathing pattern also consists of low frequency oscillations (Nugent and Finley, 1983). In the present study, spectral analysis was performed on a few children to detect low frequency oscillations in the breathing pattern. The approach to spectral analysis used in this study is quite simplistic and may be statistically biased (Loring and Bruce, 1986).
4.7 Statistical Analysis

Data, unless otherwise stated, were presented as mean (± standard deviation). Most statistical analyses were performed using Quattro-Pro for Windows Version 5.0 (1993). On occasions, logarithmic transformation was used before performing statistical tests to make the data more normally distributed (Bland, 1987).

An analysis of variance with two factors (age and gender) was used to find if there was a significant difference in RR between boys and girls. To achieve the same number of children in each age group, seven awake and six asleep boys and girls were randomly selected from each age group1.

The unpaired \( t \) test was used to find out if there were significant differences between groups (such as healthy children and children tested in the community who had a past and/or present history of respiratory disease). To compensate for the effect of age each child's individual RR was divided by the mean RR for healthy children (appropriate for each child's age). The paired \( t \) test was used to determine differences in RR made on the same group of children but under different conditions (asleep versus awake; reading versus non-reading). The chi-squared test was used to compare categorised data. This related to data obtained from the questionnaire. A computer program, Minitab Version 5.1.1 (1986), was used for this purpose. Since the groups were small (with at least one expected frequency less than five), Yates' correction was performed on the chi-squared value obtained.

Correlation coefficients (Pearson's \( r \)) were calculated to detect a relationship, if any, between RR and: age; body weight; height (length); axillary temperature and ambient temperature. When analysing the effect of axillary and ambient temperatures on RR, RR was standardised for age. To standardise RR for age, each child's RR was divided by the mean RR for healthy children for that child's respective age.

The method of Bland and Altman (1986) was used to assess the agreement between the optical sensor and other methods of measuring the breathing pattern. The other methods included counting RR by visual observation and measuring \( T_1 / T_{TOT} \) with a pneumotachograph. The mean (d) and standard deviation (s) of the differences in values obtained by the optical sensor and the other method (i.e. measurement a - measurement b) were calculated. This allowed the 95% "limits of agreement" (d ± 2s) between the two methods to be calculated. If the "limits of agreement" are not clinically important, the methods can be considered

---

1 A random number table was used for this purpose.
comparable. This method was also used to compare RRs obtained by adding together two thirty-second counts and the RRs obtained by counting for the total test period.

The repeatability of measuring RR was assessed using a similar method in eight pre-school and five school aged children. The mean of the differences between the first and second RR measurements was calculated. This value should be zero (Bland and Altman, 1986). The 95% "coefficient of repeatability" is twice the SD of the differences.

The RR of children with respiratory disease was presented as Z-scores (Weinbach and Grinnell, 1991). In the present study, the z-score was defined by the following equation:

\[
Z\text{-score} = \frac{\text{observed RR (child with disease)} - \text{predicted RR}}{\text{SD}}
\]

(4.5)

The predicted RRs were based on age appropriate data obtained from healthy children in the present study. Z-scores show the deviation in RR from predicted RRs in healthy subjects. The units are standard deviations (SD). A similar method has been used in other respiratory studies (Cassels and Morse, 1962; Desager et al., 1994). The main reason for using this method was to minimise the effect of age on RR. This meant that all children with a certain disease could be analysed as a whole group despite their different ages.

The sensitivity and specificity of RR to detect pneumonia, in children aged 6.0 - 11.99 months, and bronchiolitis, in children aged from 1.0 to 5.99 months, were also calculated. Sensitivity and specificity are defined in equations 4.6 and 4.7.

\[
\text{Sensitivity (\%)} = \left( \frac{\text{Number of True Positive (TP) decisions}}{\text{Number of actually positive cases}} \right) \times 100
\]

(4.6)

\[
\text{Specificity (\%)} = \left( \frac{\text{Number of True Negative (TN) decisions}}{\text{Number of actually negative cases}} \right) \times 100
\]

(4.7)

In relation to RR, a true positive decision occurred when a child with respiratory disease had a RR above a designated threshold, which was used to discriminate between health and disease. A true negative decision occurred when a healthy child had a RR below this threshold RR. The sensitivity increases and specificity decreases as this threshold value of RR is reduced (Metz, 1978). With a decrease in specificity, the false negative rate increases. These changes in sensitivity and false negative rate were presented graphically as a receiver operating...
characteristic (ROC) curve (Metz, 1978; Cherian et al., 1988). The false positive fraction (x-axis) is plotted against sensitivity (y-axis) as shown in the theoretical ROC curve in figure 4.10.

![ROC Curve Diagram](https://via.placeholder.com/150)

**Figure 4.10**
A conventional ROC curve. If the test provides useful information, the points on the ROC curve must be above a line joining the lower left to upper right corners of the graph (Metz, 1978).

In this study, the false positive fraction (also equivalent to \[100 - \text{specificity}\]) was the percentage of children who were healthy but had a RR above the threshold RR for detecting disease. A clinical test is able to detect disease, if its ROC curve is closer to the top left-hand corner of the ROC graph (Metz, 1978).

### 4.8 Construction of Centile Curves

The centile charts were constructed according to the method of Rasbash, Pan and Goldstein (1992). A computer program, *Grostat II* (1992), was used to perform the calculations associated with this method. This method was also used by Rusconi et al. (1994) to construct centiles for RRs in children, aged from birth to three years. The methods are outlined in more detail by Healy, Rashbash and Tang (1988) and Pan, Goldstein and Yang (1990).

Some problems were encountered when attempting to construct centile curves. The SD of RR varied with age. A logarithmic transformation was used in an attempt to equalise SDs and variances across all age groups. Rusconi et al. (1994) found the logarithmic transformation to be useful for this purpose in relation to RR.

The data were sorted into ascending order according to age and displayed on a scatter diagram. A "box" was superimposed on the left-hand side of the diagram and contained a fixed
proportion of data points. For awake children, the size of this "box" was 34 and for sleeping children, the size was 10. A least squares regression of RR on age was calculated and fitted to the points in the box. The residual\(^1\) of each data point was calculated and sorted in order of size. Centiles (5, 25, 50, 75 and 95 in the current study) were then plotted against the median values of the RR in the "box". The box was then moved to the right by three points and the process described above was repeated. This occurred until all data points had been used. Some data (half the size of the "box") were lost in the extreme age ranges. For this reason, newborns and young adults were included in the study. This meant that fewer values of the area of interest (children aged between one month and twelve years of age) would be excluded from analysis.

The raw centiles obtained were very irregular and needed to be smoothed. This was done by fitting polynomial functions to the observed centiles. A cubic equation characterised the data for sleeping children, aged from birth to one year, and awake children, aged from one to three years:

\[
\log_{10} RR_i = a_{0,i} + a_{1,i} + a_{2,i}t^2 + a_{3,i}t^3
\]  

(4.8)

where \( t \) denoted age in years and \( \log_{10} RR_i \) the smoothed curve for the \( i \)th percentile. The method for obtaining the values for the co-coefficient of equation 4.8 (\( a_0, a_1, a_2 \) and \( a_3 \)) is presented in Appendix 7.

For awake children, aged from three to thirteen years, and sleeping children, aged one to three years, the raw centiles were fitted by a quadratic equation:

\[
\log_{10} RR_i = a_{0,i} + a_{1,i} + a_{2,i}t^2
\]  

(4.9)

The method of obtaining the co-efficients of equation 4.9 is also presented in Appendix 7. For sleeping and awake children, the two polynomials were joined at the ages of one and three years respectively. The smoothed centile curves and raw data were also superimposed. This was done to assess how representative the smoothed curves were of the raw data. These curves were chosen because they appeared to fit the data well and showed smooth changes with age.

\(^1\)The residual is the difference between the observed value and expected value (in this case the value obtained from the regression equation).
An examination of outliers was made because it is justifiable to exclude these values if an explanation for their deviation from other values can be made (Royston, 1991).
Part III

Results
Chapter 5

Evaluation of an Optical Sensor

5.1 Introduction

The optical sensor used in this research project had not been used to determine respiratory rates or fractional inspiratory time previously. Therefore it was necessary to establish the accuracy and precision of the sensor. This involved comparing the respiratory rate and respiratory waveform obtained by the optical sensor with that obtained by other methods such as visual observation.

5.2 Accuracy of Sensor in Measuring Respiratory Rate

The RR obtained by counting respirations with a stop watch for two minutes was subtracted from the RR obtained by the optical sensor for the same two minutes. This was done in a selection of subjects in the population which was studied. Table 5.1 shows the mean difference between the two methods was 0.12 amongst 13 individuals. Fig. 5.1 shows that the difference between the two methods was not affected by the RR. The 95% limit of agreement (mean ± 2 SD) between the two methods was -1.28 to 1.04 bpm. This meant that 95% of RR values obtained by the optical sensor were within approximately one bpm of the RR measured by visual observation, which was clinically acceptable.

<table>
<thead>
<tr>
<th>Initial</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Awake(A)/Sleeping(S)</th>
<th>RR measured by observation</th>
<th>RR measured by optical sensor</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.A.</td>
<td>7 mo</td>
<td>M</td>
<td>S</td>
<td>29</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>T.G.</td>
<td>6 mo</td>
<td>F</td>
<td>S</td>
<td>24</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>J.H.</td>
<td>9 mo</td>
<td>M</td>
<td>S</td>
<td>22</td>
<td>21.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>J.K.</td>
<td>10 mo</td>
<td>M</td>
<td>S</td>
<td>29</td>
<td>28.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>H.T.</td>
<td>1</td>
<td>F</td>
<td>S</td>
<td>20</td>
<td>19</td>
<td>-1</td>
</tr>
<tr>
<td>N.L.</td>
<td>1</td>
<td>M</td>
<td>S</td>
<td>24.5</td>
<td>24.5</td>
<td>0</td>
</tr>
<tr>
<td>N.C.</td>
<td>2</td>
<td>M</td>
<td>S</td>
<td>19</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>R.C.</td>
<td>3</td>
<td>F</td>
<td>A</td>
<td>26</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>C.O.</td>
<td>4</td>
<td>F</td>
<td>A</td>
<td>24.5</td>
<td>23.5</td>
<td>-1</td>
</tr>
<tr>
<td>K.S.</td>
<td>4</td>
<td>F</td>
<td>A</td>
<td>16</td>
<td>16.5</td>
<td>0.5</td>
</tr>
<tr>
<td>L.H.</td>
<td>5</td>
<td>F</td>
<td>A</td>
<td>21.5</td>
<td>21</td>
<td>-0.5</td>
</tr>
<tr>
<td>A.R.</td>
<td>5</td>
<td>F</td>
<td>A</td>
<td>21.5</td>
<td>22</td>
<td>0.5</td>
</tr>
<tr>
<td>J.P.</td>
<td>22</td>
<td>M</td>
<td>A</td>
<td>22</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td>23</td>
<td>22.88</td>
<td>-0.12 (0.58)</td>
</tr>
</tbody>
</table>
5.3 Comparison of Optical Sensor with Other Respiratory Sensors

5.3.1 Respiratory Inductive Plethysmograph (RIP)

The Respiratory Inductive Plethysmograph (RIP) (otherwise known as Respitrace®) is widely used in sleep studies (Brouillette, 1992). It could be considered the "gold standard" method for measuring chest and abdominal wall movements. Comparisons of the optical sensor and abdominal tracing of Respitrace® obtained from a nine year old girl are shown in figure 5.2. The shape of the waveforms were very similar and the optical sensor gave an accurate measurement of abdominal excursion and RR. The inspiratory and expiratory times also appeared similar. The Respitrace® chest recording continued to decrease after both the abdominal Respitrace® and optical sensor recording showed an expiratory pause. This suggested it was possible for air to be exhaled after the abdominal compartment had ceased moving.

Figs 5.3 shows similar abdominal Respitrace® and optical sensor tracing obtained in a six month old infant with chronic neonatal lung disease. Despite paradoxical inward chest wall motion shown on the chest Respitrace® tracing, the optical sensor and abdominal Respitrace® tracing were very similar. The waveform pattern at the end of the recording differed slightly suggesting further work needs to be done in investigating the accuracy of the optical sensor in young children.
Figure 5.2
Comparison of Respitrace® and the optical sensor in a nine year old girl, with spina bifida.
The optical sensor was sensitive to movement artefact and required children to lie still. Fig 5.4 illustrates the poor signal obtained by both sensors in a four year old boy who was unable to lie still. Movement artefact is especially a problem when testing infants who cannot understand requests to lie still.

**Figure 5.3**
Comparison of Respitrace® and the optical sensor in a six month old infant.

**Figure 5.4**
Comparison of Respitrace® and optical sensor in a four year old boy. There is significant artefact in both tracings due to body movement.
5.3.2 Comparisons with a Water-sealed Spirometer

The relationship between abdominal motion measured by the optical sensor and an accurate measure of volume changes in the lung were also investigated. The main reason for this was to determine if inspiratory and expiratory times determined by body surface measurements (such as with the optical sensor) were similar to those obtained from direct measurement of air volume movement (such as with the spirometer). Figures 5.5, 5.6 and 5.7 show that the onset and offset of both inspiration and expiration coincide in both spirometer and optical sensor. There is thus good agreement between the two methods of measuring the breathing pattern.

![Optical Sensor](image)

![Spirometer](image)

**Figure 5.5**
Comparison of spirometer and optical sensor in a 23 year old male. The tracing went off scale during a large breath.
Figure 5.6
Comparison of spirometer and optical sensor in a 20 year old male.

Figure 5.7
Comparison of spirometer and optical sensor in the same 20 year old male.
5.3.3 Comparison with a Pneumotachograph

Eight breaths analysed by a pneumotachograph were compared with eight breaths obtained by the optical sensor at a similar period in time. As shown in Table 5.2 the means of the differences of values for $T_{TOT}$ and $T_I / T_{TOT}$ obtained by the two methods are quite small being 0.04 and 0.01 respectively. The SD of the difference in $T_I / T_{TOT}$ obtained by the optical sensor and pneumotachograph was 0.04. The limits of agreement between the two methods for $T_I / T_{TOT}$ was -0.07 to 0.09. Fig 5.8 shows that the differences between the two methods was greater when $T_I / T_{TOT}$ was lower (i.e. when expiration is relatively longer than inspiration).

![Graph showing relationship between $T_I / T_{TOT}$ measured with a pneumotachograph and the optical sensor (y-axis) and the average value of $T_I / T_{TOT}$ (x-axis).]

The mean difference in $T_E$ obtained by both methods was 0.09s. This was larger than the value obtained for $T_I$ which was 0.01s. This suggests inspiratory airflow measured by a pneumotachograph coincides more closely with outward motion of the abdomen than does expiratory airflow with inward motion of the abdomen.

The measurements made by both sensors were not performed on the same breaths in the results in Table 5.2. However in two subjects the same breaths were recorded by both pneumotachograph and optical sensor (see Table 5.3). In both subjects $T_I / T_{TOT}$ measured by the optical sensor was similar to the pneumotachograph.
### Table S2 - Comparison of Optical Sensor with a Pneumotachograph

<table>
<thead>
<tr>
<th>Diff</th>
<th>Optical</th>
<th>Pneumotachograph</th>
<th>Diff</th>
<th>Optical</th>
<th>Pneumotachograph</th>
<th>Diff</th>
<th>Optical</th>
<th>Pneumotachograph</th>
<th>Diff</th>
<th>Optical</th>
<th>Pneumotachograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.00</td>
<td>0.04</td>
<td>100</td>
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<td>100</td>
<td>0.00</td>
<td>0.04</td>
<td>100</td>
<td>0.00</td>
<td>0.04</td>
</tr>
<tr>
<td>90</td>
<td>0.00</td>
<td>0.07</td>
<td>90</td>
<td>0.00</td>
<td>0.07</td>
<td>90</td>
<td>0.00</td>
<td>0.07</td>
<td>90</td>
<td>0.00</td>
<td>0.07</td>
</tr>
<tr>
<td>80</td>
<td>0.00</td>
<td>0.09</td>
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<td>10</td>
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<td>0</td>
<td>0.00</td>
<td>0.18</td>
<td>0</td>
<td>0.00</td>
<td>0.18</td>
<td>0</td>
<td>0.00</td>
<td>0.18</td>
</tr>
</tbody>
</table>

*Denotes a breach and a result of 8.*
Table 5.3 - Breaths Observed by Optical Sensor and Pneumotachograph Simultaneously

<table>
<thead>
<tr>
<th>Subject</th>
<th>Optical Sensor</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Pneumotachograph</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{TOT}$ (s) ± SD</td>
<td>$T_{i}$ (s) ± SD</td>
<td>$T_{E}$ (s) ± SD</td>
<td>$T_{i}/T_{TOT}$ ± SD</td>
<td>$T_{TOT}$ (s) ± SD</td>
<td>$T_{i}$ (s) ± SD</td>
<td>$T_{E}$ (s) ± SD</td>
<td>$T_{i}/T_{TOT}$ ± SD</td>
<td></td>
</tr>
<tr>
<td>1 (8 breaths analysed)</td>
<td>1.43 ± 0.09</td>
<td>0.57 ± 0.05</td>
<td>0.86 ± 0.08</td>
<td>0.4 ± 0.03</td>
<td>1.33 ± 0.09</td>
<td>0.56 ± 0.03</td>
<td>0.77 ± 0.07</td>
<td>0.42 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>2 (4 breaths analysed)</td>
<td>1.76 ± 0.07</td>
<td>0.67 ± 0.05</td>
<td>1.09 ± 0.04</td>
<td>0.38 ± 0.02</td>
<td>1.78 ± 0.08</td>
<td>0.63 ± 0.02</td>
<td>1.15 ± 0.06</td>
<td>0.35 ± 0.01</td>
<td></td>
</tr>
</tbody>
</table>

5.4 Quality of Signal Obtained by the Optical Sensor

Overall the signal obtained by the optical sensor was of high quality and respiratory waveforms were easily recognised. The sensor was able to detect apnoea. Figure 5.9 shows the breathing pattern recorded in an infant aged two weeks. When placed on this child, the sensor was able to demonstrate cyclic fluctuations in tidal volume and frequency, interrupted by periods of apnoea, related to periodic breathing (Nugent and Finley, 1983). The sensor was also easily applied to young children. Figs 5.10 and 5.11 show a 7 month old infant sleeping with the sensor applied to his chest and the subsequent breathing pattern obtained.

![Figure 5.9](image)

Breathing pattern of a two week old infant during periodic breathing.
Figure 5.10
Seven month old infant with sensor applied to lower chest. This was done without waking the infant. The tracing obtained is shown in figure 5.11.

Fig 5.11
Respiratory waveform signal obtained from optical sensor in a sleeping seven month old infant in the supine position.
The sensor was also able to measure rib cage movements if positioned correctly on the upper part of the chest (see figures 5.12a and 5.12b). Rib cage recordings were not further investigated in this study, since the addition of a rib cage sensor would have made children more aware that their respiration was being monitored. This also would have added to the technical complexity of the experiments. The supine posture was preferred when applying the sensor. However, tracings could be obtained in the lateral and prone postures. Figure 5.13 shows the respiratory signal obtained from one infant in three positions of sleep. The shape of the waveforms differed slightly in each posture.

**Figure 5.12a**  
Respiratory tracing obtained by application of the sensor to the rib cage of a six year old boy, with acute asthma.

**Figure 5.12b**  
Respiratory tracing obtained by application of sensor to the abdomen of a six year old boy, with acute asthma.

**Figure 5.13**  
Breathing pattern of infant in three different positions - supine (bottom), lateral (middle) and prone (top).
Chapter 6
Analysis of Respiratory Rate and the Respiratory Cycle in Healthy Children

6.1 Introduction

A large sample (343 awake and 94 sleeping subjects) was used to create centiles for respiratory rate in healthy subjects. The signal recorded by the optical sensor also allowed calculation of inspiratory and expiratory times. A questionnaire helped to characterise attributes of the voluntary sample studied.

6.2 Respiratory Rates in Healthy Children

The RRs observed in 343 healthy awake subjects, including 20 adolescents and young adults, are summarised in the scatter diagram figure 6.1. RR was highest in infants and fell rapidly until the age of three years. The mean values and other statistical measures for each age group are summarised in Table 6.1. There was a greater spread of the data points in the younger age groups. This was reflected in the higher SD observed in the younger age groups.

Figure 6.1
Scatter diagram illustrating changes in respiratory rate with age in awake healthy subjects.
Table 6.1  -  Respiratory Rate in Awake Healthy Subjects

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Median Respiration Rate (RPR)</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 - 0.4</td>
<td>9.1</td>
<td>3.14</td>
<td>7.7</td>
</tr>
<tr>
<td>0.5 - 1.4</td>
<td>1.56</td>
<td>2.52</td>
<td>4.7</td>
</tr>
<tr>
<td>1.5 - 2.9</td>
<td>2.46</td>
<td>5.0</td>
<td>7.6</td>
</tr>
<tr>
<td>3.0 - 4.4</td>
<td>3.62</td>
<td>6.5</td>
<td>9.1</td>
</tr>
<tr>
<td>4.5 - 5.9</td>
<td>4.79</td>
<td>8.9</td>
<td>11.6</td>
</tr>
<tr>
<td>6.0 - 7.4</td>
<td>5.96</td>
<td>11.2</td>
<td>13.7</td>
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<td>7.5 - 8.9</td>
<td>7.13</td>
<td>13.5</td>
<td>16.0</td>
</tr>
<tr>
<td>9.0 - 10.4</td>
<td>8.30</td>
<td>15.8</td>
<td>18.3</td>
</tr>
<tr>
<td>10.5 - 11.9</td>
<td>9.47</td>
<td>18.1</td>
<td>20.6</td>
</tr>
<tr>
<td>12.0 - 13.4</td>
<td>10.64</td>
<td>20.4</td>
<td>22.9</td>
</tr>
<tr>
<td>13.5 - 14.9</td>
<td>11.81</td>
<td>22.7</td>
<td>25.2</td>
</tr>
<tr>
<td>15.0 - 16.4</td>
<td>12.98</td>
<td>25.0</td>
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</tr>
<tr>
<td>16.5 - 17.9</td>
<td>14.15</td>
<td>27.3</td>
<td>29.7</td>
</tr>
<tr>
<td>18.0 - 19.4</td>
<td>15.32</td>
<td>29.6</td>
<td>32.1</td>
</tr>
<tr>
<td>19.5 - 20.9</td>
<td>16.49</td>
<td>31.9</td>
<td>34.3</td>
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<td>20.0 - 21.4</td>
<td>17.66</td>
<td>34.2</td>
<td>36.7</td>
</tr>
<tr>
<td>21.5 - 22.9</td>
<td>18.83</td>
<td>36.5</td>
<td>38.9</td>
</tr>
<tr>
<td>22.0 - 23.4</td>
<td>20.00</td>
<td>38.8</td>
<td>41.3</td>
</tr>
<tr>
<td>23.5 - 24.9</td>
<td>21.17</td>
<td>41.1</td>
<td>43.6</td>
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<tr>
<td>24.0 - 25.4</td>
<td>22.34</td>
<td>43.4</td>
<td>45.9</td>
</tr>
<tr>
<td>25.5 - 26.9</td>
<td>23.51</td>
<td>45.7</td>
<td>48.2</td>
</tr>
</tbody>
</table>

Respiratory Rate measured for two thirty-second periods.

Note: Respiratory Rate averaged over 30 sec.
Two methods of measuring RR are presented in Table 6.1. RRs obtained by adding the respirations registered by the sensor for the first two thirty second periods of recording were calculated. RR was also measured by averaging the respirations counted over the total recording time. The mean of the differences between measuring RR using these alternative methods was 0.279 bpm. This showed there was little systematic difference (or bias) between the two methods. The standard deviation of the differences was 1.59 and the 95% limit of agreement was between -2.9 and 3.2 bpm. The RR measured by adding respirations counted for two thirty-second periods was used for analysis in this study. This is the way RR is most likely to be counted in a clinical setting.

Table 6.2 and figure 6.2 summarise the RRs observed in children, aged from birth to 4.5 years, during quiet sleep. The most significant change in RR occurs between birth and one year of age. The spread of data points was larger in children aged from 1.0 to 5.99 months (SD 7.18). While 103 children were tested, nine children had temperatures greater or equal to 37°C or some other condition (such as receiving certain medications) which could alter their RR. These children's RRs were excluded from the data used to calculate reference ranges for healthy children.

![Figure 6.2](image)

**Figure 6.2**
Scatter diagram illustrating changes in respiratory rate with age in sleeping healthy children.
Table 6.2 - Respiratory Rates in Healthy Subjects during Quiet Sleep

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>0 to 2.95</th>
<th>3.0 to 4.5</th>
<th>4.5 to 7.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8 yrs</td>
<td>19.3</td>
<td>19.4</td>
<td>21.2</td>
</tr>
<tr>
<td>2 yrs</td>
<td>20.3</td>
<td>20.2</td>
<td>21.8</td>
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<td>2.5 yrs</td>
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<td>23.2</td>
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<td>5 yrs</td>
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<td>6 yrs</td>
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<td>26.7</td>
</tr>
<tr>
<td>7 yrs</td>
<td>26.8</td>
<td>26.8</td>
<td>28.9</td>
</tr>
<tr>
<td>8 yrs</td>
<td>28.1</td>
<td>28.1</td>
<td>30.2</td>
</tr>
</tbody>
</table>

Median Respiratory Rate was 4.5 breaths per minute (BPM) with a range of 3.4 to 5.6 BPM. The table includes data for ages ranging from 1.8 to 7.0 years.
The mean of the differences between RRs obtained for two thirty-second periods and for the total time of recording was 0.34 in sleeping children. The SD of the differences was 1.22 and the 95% limit of agreement was between -2.1 and 2.8 bpm. Counting respirations for two thirty-second periods therefore seemed an appropriate method of measuring RR. For children, aged from birth to one year only, the mean of the differences was 0.659 and the SD was 1.53. The 95% limit of agreement was therefore -2.40 to 3.72 suggesting the difference between the two methods is greater in young children who have higher RRs.

There was no significant effect of sleeping position with the RR (standardised for age) giving an average of 1.0 in 81 supine children and an average of 0.98 in 15 prone children (p = 0.29, unpaired t test). To standardise for age, each individual RR was divided by the mean RR for that particular age. Figures 6.3a and 6.3b show the wide range of RR values in humans, with a RR of 42 bpm in a sleeping neonate and 18 bpm in an awake young adult.

A comparison of respiratory rates during periods of quiet (regular) and active (irregular) sleep is presented in Table 6.3. This comparison is limited as there were occasions when an infant seemed in quiet sleep but had an irregular breathing pattern. In these cases, the sleep state was classified as active. The RR was higher during active sleep in children aged up to one year. The highest difference - six bpm - was seen in infants aged up to one month (p = 0.02, paired t test).
Table 6.3 - Comparison of Respiratory Rates during Regular and Irregular Breathing

<table>
<thead>
<tr>
<th>Age (mo)</th>
<th>n</th>
<th>mean RR ± SD (bpm) Regular Breathing</th>
<th>mean RR ± SD (bpm) Irregular Breathing</th>
<th>Difference (bpm)</th>
<th>p-value (paired t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 0.99</td>
<td>11</td>
<td>41.7 (±4.2)</td>
<td>47.7 (±6.2)</td>
<td>6.0</td>
<td>0.02</td>
</tr>
<tr>
<td>1 - 5.99</td>
<td>14</td>
<td>33.2 (±8.3)</td>
<td>36.7 (±14.6)</td>
<td>3.5</td>
<td>0.2</td>
</tr>
<tr>
<td>6.0 - 11.99</td>
<td>3</td>
<td>21.3 (±2.4)</td>
<td>23.2 (±2.0)</td>
<td>1.9</td>
<td>0.05</td>
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</table>

Thirty-one children had their breathing monitored while they were awake and asleep. RR was greater when children were awake as shown in Table 6.4 and figure 6.4. Figure 6.4 shows that there was a greater reduction in RR during sleep in younger subjects. Figures 6.5 and 6.6 show breathing patterns of two children, aged five months and two years, when awake and asleep. The RR was also more irregular when awake, especially in the infant.

Table 6.4 - Comparison of Awake and Sleeping Respiratory Rates in the Same Subjects

<table>
<thead>
<tr>
<th>Age (mean) years</th>
<th>Number</th>
<th>RR (bpm) Awake</th>
<th>RR (bpm) Asleep</th>
<th>p (paired t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 0.99 (0.32)</td>
<td>8</td>
<td>52.3</td>
<td>34.5</td>
<td>0.002</td>
</tr>
<tr>
<td>1.0 - 2.99 (1.57)</td>
<td>12</td>
<td>30.7</td>
<td>22.4</td>
<td>0.00002</td>
</tr>
<tr>
<td>2.00 - 4.5 (2.85)</td>
<td>11</td>
<td>26.2</td>
<td>19.4</td>
<td>0.00002</td>
</tr>
</tbody>
</table>

Figure 6.4
Mean respiratory rates in the same subjects when awake and asleep.
6.3 Variables Influencing Respiratory Rate

An investigation of factors which affected respiratory rate with growth was performed. Variables analysed included height, body weight, axillary temperature and ambient temperature. No significant correlation was found between RR (standardised for age) and axillary temperature in sleeping ($r = +0.15$, not significant) or awake children ($r = +0.03$, not significant) (see figures 6.7a and 6.7b). There did, however, appear to be an effect of axillary temperature on RR in some sleeping infants. For example, in non-identical twins aged 11 months tested on the same night, one child had a normal temperature of 36°C and RR of 23 bpm, while the other twin had a temperature of 37.9°C and a RR of 29 bpm. There was some correlation of ambient temperature with RR in awake children ($r = +0.32$, $n = 112$, $p < 0.01$), but no significant correlation in sleeping children ($r = -0.003$, $n = 56$, not significant). This data is displayed in figures 6.8a and 6.8b.
Respiratory rate was negatively correlated with age ($r = -0.76$, $p < 0.01$), body weight ($r = -0.80$, $p < 0.01$) and height (length) ($r = -0.83$, $p < 0.01$) in sleeping children, aged from birth to 4.5 years. The partial correlation coefficient between RR and height standardised for age ($r_{RH,H}$) was -0.53, while the partial coefficient between RR and age standardised for height ($r_{RA,H}$) was 0.08 in the sleeping children. This suggested height (length) had a greater effect than age on RR in younger children.

In awake subjects, aged from 2.0 to 12.99 years, RR was negatively correlated with age ($r = -0.58$, $p < 0.01$), height ($r = -0.54$, $p < 0.01$) and weight ($r = -0.44$, $p < 0.01$). The partial correlation coefficient between RR and age standardised for height ($r_{RA,H}$) was -0.26 while the partial correlation coefficient between RR and height standardised for age ($r_{RH,A}$) was +0.07. This suggested age had a greater influence in determining RR in the older, awake subjects.
Figures 6.9a and 6.9b show the relationship between RR (standardised for age) and time of day that testing occurred. Most asleep children were tested between midday and three o'clock in the afternoon. Most awake children were tested between the hours of nine o'clock and five o'clock during the day. There was no significant correlation between RR and the time of testing.

Figure 6.9a
Scatter diagram showing poor relationship between respiratory rate and time of testing in asleep children \( (r = +0.06, \text{ not significant}) \).

Figure 6.9b
Scatter diagram showing poor relationship between respiratory rate and time of testing in sleeping children \( (r = -0.01, \text{ not significant}) \).

Tables 6.5 and 6.6 show values for RRs obtained for awake and sleeping children tested in the community with a history (past or present) of respiratory disease. Most children in this group had a history of asthma. Responses to the question "Has your child suffered from any respiratory illness (e.g. asthma) in the past?" did not always indicate whether the child still had asthma. Therefore, it was not possible to discriminate between children with past or present histories of respiratory illness. Some children also had a history of pneumonia, croup or bronchiolitis.

The RR (standardised for age) showed no significant difference between children with a history of respiratory disease and healthy children. This was when children were asleep \( (p = 0.63, \text{ unpaired } t \text{ test after logarithmic transformation}) \) and awake \( (p = 0.64, \text{ unpaired } t \text{ test after logarithmic transformation}) \).
Table 6.5 - Respiratory Rate of Sleeping Children with a History of Respiratory Disease (Past or Present) Tested in the Community

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
<th>Median</th>
<th>Mean RR in healthy children (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 0.99</td>
<td>26.1</td>
<td>9</td>
<td>4.2</td>
<td>28</td>
<td>24.1</td>
</tr>
<tr>
<td>1 - 1.99</td>
<td>20.6</td>
<td>11</td>
<td>4.39</td>
<td>20</td>
<td>22.9</td>
</tr>
<tr>
<td>2 - 2.99</td>
<td>20.1</td>
<td>7</td>
<td>1.35</td>
<td>20</td>
<td>19.8</td>
</tr>
</tbody>
</table>

Table 6.6 - Respiratory Rates of Awake Children with a History of Respiratory Disease (Past or Present) Tested in the Community

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
<th>Median</th>
<th>Mean RR in healthy children (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 0.99</td>
<td>41.7</td>
<td>3</td>
<td>15.01</td>
<td>41</td>
<td>45.5</td>
</tr>
<tr>
<td>1 - 1.99</td>
<td>30.2</td>
<td>4</td>
<td>1.50</td>
<td>30</td>
<td>31.9</td>
</tr>
<tr>
<td>2 - 2.99</td>
<td>29</td>
<td>10</td>
<td>4.35</td>
<td>28</td>
<td>26.7</td>
</tr>
<tr>
<td>3 - 3.99</td>
<td>24.9</td>
<td>12</td>
<td>3.48</td>
<td>25</td>
<td>25.4</td>
</tr>
<tr>
<td>4 - 4.99</td>
<td>23.6</td>
<td>22</td>
<td>2.80</td>
<td>23</td>
<td>23.5</td>
</tr>
<tr>
<td>5 - 5.99</td>
<td>21.0</td>
<td>23</td>
<td>3.83</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>6 - 6.99</td>
<td>20.2</td>
<td>32</td>
<td>3.43</td>
<td>20.3</td>
<td>20.4</td>
</tr>
<tr>
<td>7 - 7.99</td>
<td>19.5</td>
<td>14</td>
<td>4.45</td>
<td>18</td>
<td>20.6</td>
</tr>
<tr>
<td>8 - 8.99</td>
<td>18.5</td>
<td>23</td>
<td>3.70</td>
<td>19</td>
<td>19.7</td>
</tr>
<tr>
<td>9 - 9.99</td>
<td>20.7</td>
<td>22</td>
<td>3.97</td>
<td>20.5</td>
<td>20.5</td>
</tr>
<tr>
<td>10 - 10.99</td>
<td>19.9</td>
<td>18</td>
<td>3.22</td>
<td>19.5</td>
<td>18.7</td>
</tr>
<tr>
<td>11 - 11.99</td>
<td>19.1</td>
<td>7</td>
<td>3.53</td>
<td>17</td>
<td>16.9</td>
</tr>
<tr>
<td>12 - 12.99</td>
<td>17.5</td>
<td>4</td>
<td>2.89</td>
<td>17.5</td>
<td>16.9</td>
</tr>
<tr>
<td>13 - 19.9</td>
<td>16.7</td>
<td>3</td>
<td>0.58</td>
<td>17</td>
<td>13.9</td>
</tr>
</tbody>
</table>

The different values of RR for asleep and awake male and female children are presented in Tables 6.7 and 6.8. A two-way analysis of variance (factors: age and sex) showed no significant effect of gender on respiratory rate when awake (p=1.00) or asleep (p= 0.81).

Table 6.7 - Respiratory Rates in Sleeping Children According to Gender

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 6.99</td>
<td>45.0</td>
<td>5</td>
<td>5.05</td>
<td>39.8</td>
<td>6</td>
<td>2.93</td>
</tr>
<tr>
<td>7.0d - 0.99 mo</td>
<td>40.5</td>
<td>2</td>
<td>4.95</td>
<td>42.5</td>
<td>2</td>
<td>7.78</td>
</tr>
<tr>
<td>1.0 - 5.99 mo</td>
<td>32.4</td>
<td>7</td>
<td>5.44</td>
<td>35.6</td>
<td>12</td>
<td>8.36</td>
</tr>
<tr>
<td>0.5 - 0.99</td>
<td>24.7</td>
<td>7</td>
<td>3.55</td>
<td>24.1</td>
<td>8</td>
<td>2.64</td>
</tr>
<tr>
<td>1.0 - 1.99</td>
<td>23.7</td>
<td>12</td>
<td>4.47</td>
<td>21.5</td>
<td>8</td>
<td>2.73</td>
</tr>
<tr>
<td>2.0 - 2.99</td>
<td>19.5</td>
<td>15</td>
<td>2.9</td>
<td>20.4</td>
<td>8</td>
<td>3.42</td>
</tr>
<tr>
<td>3.0 - 4.5</td>
<td>18.9</td>
<td>8</td>
<td>2.36</td>
<td>20.3</td>
<td>3</td>
<td>3.21</td>
</tr>
</tbody>
</table>

90
Table 6.8 - Respiratory Rates in Awake Children According to Gender

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
<th>Mean RR (bpm)</th>
<th>n</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td></td>
<td></td>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 0.99</td>
<td>56.2</td>
<td>12</td>
<td>14.63</td>
<td>56.3</td>
<td>6</td>
<td>9.81</td>
</tr>
<tr>
<td>1.0 - 1.99</td>
<td>31.7</td>
<td>6</td>
<td>7.17</td>
<td>32.1</td>
<td>8</td>
<td>7.74</td>
</tr>
<tr>
<td>2.0 - 2.99</td>
<td>28.0</td>
<td>11</td>
<td>2.72</td>
<td>24.9</td>
<td>8</td>
<td>2.03</td>
</tr>
<tr>
<td>3.0 - 3.99</td>
<td>25.8</td>
<td>8</td>
<td>2.31</td>
<td>25.2</td>
<td>18</td>
<td>3.86</td>
</tr>
<tr>
<td>4.0 - 4.99</td>
<td>23.5</td>
<td>13</td>
<td>4.88</td>
<td>23.5</td>
<td>17</td>
<td>4.05</td>
</tr>
<tr>
<td>5.0 - 5.99</td>
<td>21.5</td>
<td>15</td>
<td>3.09</td>
<td>22.7</td>
<td>12</td>
<td>4.27</td>
</tr>
<tr>
<td>6.0 - 6.99</td>
<td>21.4</td>
<td>14</td>
<td>3.23</td>
<td>19.7</td>
<td>18</td>
<td>3.82</td>
</tr>
<tr>
<td>7.0 - 7.99</td>
<td>20.7</td>
<td>13</td>
<td>3.99</td>
<td>20.6</td>
<td>21</td>
<td>3.49</td>
</tr>
<tr>
<td>8.0 - 8.99</td>
<td>19.7</td>
<td>24</td>
<td>3.21</td>
<td>19.7</td>
<td>23</td>
<td>3.35</td>
</tr>
<tr>
<td>10.0 - 10.99</td>
<td>18.2</td>
<td>22</td>
<td>3.28</td>
<td>19.8</td>
<td>9</td>
<td>3.73</td>
</tr>
<tr>
<td>11.0 - 11.99</td>
<td>17.0</td>
<td>5</td>
<td>3.67</td>
<td>16.8</td>
<td>9</td>
<td>3.9</td>
</tr>
<tr>
<td>12.0 - 12.99</td>
<td>16.0</td>
<td>4</td>
<td>4.55</td>
<td>17.4</td>
<td>7</td>
<td>4.69</td>
</tr>
</tbody>
</table>

Table 6.9 presents the results of an experiment examining the effect of reading on RR. For pre-school children, a decrease in RR of 1.0 bpm was observed during rest after the children were read a story (consisting of both visual and auditory stimulation) (p=0.04, paired t test). There was no difference, however, when pre-school children rested first and then were read a story. For school aged children, reading a book (visual stimulation only) had no significant effect on RR regardless of whether the children rested or read first. Young adults (medical students) showed a significant increase in RR of 2.2 bpm with reading after an initial rest period (p=0.0003, paired t test).

Table 6.9 - Effect of Reading on Respiratory Rate

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>n</th>
<th>Mean reading RR (bpm)</th>
<th>Mean resting RR (bpm)</th>
<th>Mean time of testing (min.)</th>
<th>Difference (reading RR - resting RR)</th>
<th>Significance (paired t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading followed by no reading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-school</td>
<td>3-5</td>
<td>18</td>
<td>23.4 (2.3)</td>
<td>22.4 (2.0)</td>
<td>3.0</td>
<td>1.0</td>
<td>p = 0.04</td>
</tr>
<tr>
<td>School</td>
<td>5-13</td>
<td>72</td>
<td>19.5 (4.0)</td>
<td>19.9 (3.6)</td>
<td>3.5</td>
<td>0.2</td>
<td>p = 0.16</td>
</tr>
<tr>
<td>No reading followed by reading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-school</td>
<td>3-5</td>
<td>33</td>
<td>22.3 (3.6)</td>
<td>22.0 (3.0)</td>
<td>3.5</td>
<td>0.3</td>
<td>p= 0.26</td>
</tr>
<tr>
<td>School</td>
<td>5-13</td>
<td>31</td>
<td>19.2 (2.86)</td>
<td>19.2 (3.13)</td>
<td>3.5</td>
<td>0</td>
<td>p = 0.79</td>
</tr>
<tr>
<td>Medical Students</td>
<td>19-24</td>
<td>8</td>
<td>15.0 (4.5)</td>
<td>12.8 (4.3)</td>
<td>6.0</td>
<td>2.2</td>
<td>p = 0.0003</td>
</tr>
</tbody>
</table>
6.4 Centile Charts

Raw centiles were obtained as outlined in the methods section. The raw centiles for RR for sleeping children, aged from birth to 4.5 years, were affected by some elevated RR values. Some of these children had axillary temperatures greater than 37°C at the time of testing. An axillary temperature of 37.0°C indicated a core temperature of 37.5 to 38°C and suggested these children were febrile. As a result, all sleeping children who had an axillary temperature of greater than 37°C were excluded from the analysis (see Table 6.10). A infant on medication which may affected respiration and an infant who had recently had a general anaesthetic were also excluded. In older awake children, however, elevated temperatures did not affect the RR. These children were not excluded from this data analysis.

Table 6.10 - Sleeping Children excluded from Data Used to Construct Centile Charts

<table>
<thead>
<tr>
<th>Initial</th>
<th>Age (yr)</th>
<th>RR (bpm)</th>
<th>Temp (°C)</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.K.</td>
<td>0.003</td>
<td>50</td>
<td>37.3</td>
<td>Temperature</td>
</tr>
<tr>
<td>A.N.</td>
<td>0.18</td>
<td>34</td>
<td>37.5</td>
<td>Temperature</td>
</tr>
<tr>
<td>K.G.</td>
<td>0.48</td>
<td>24</td>
<td>37.5</td>
<td>Receiving phenobarbitol</td>
</tr>
<tr>
<td>B.D.</td>
<td>0.86</td>
<td>32</td>
<td>---</td>
<td>Recovering from anaesthetic</td>
</tr>
<tr>
<td>M.L.</td>
<td>0.99</td>
<td>29</td>
<td>37.9</td>
<td>Temperature</td>
</tr>
<tr>
<td>S.M.</td>
<td>1.08</td>
<td>30</td>
<td>37.1</td>
<td>Temperature</td>
</tr>
<tr>
<td>G.M.</td>
<td>1.18</td>
<td>29</td>
<td>37.5</td>
<td>Temperature</td>
</tr>
<tr>
<td>N.L.</td>
<td>1.56</td>
<td>24</td>
<td>37.4</td>
<td>Temperature</td>
</tr>
<tr>
<td>L.L.</td>
<td>2.02</td>
<td>27</td>
<td>37.3</td>
<td>Temperature</td>
</tr>
</tbody>
</table>

A cubic equation was fitted to the raw centiles for RR in children who were asleep, aged from birth to one year of age, and children who were awake, aged from one to three years. A quadratic equation fitted the raw centiles in sleeping children, aged from one to three years, and awake children, aged from three to thirteen years. The polynomial equations representing the 50th and 95th centiles are superimposed on scatter diagrams of the raw data (after logarithmic transformation) in figures 6.10a and 6.10b. These polynomial equations were chosen because they appeared to fit the data and showed smooth changes with age. Due to the method of creating the centile curves, the data at the extremes of ages are not represented (e.g. sleeping children older than three years and awake children older than thirteen years).
Figure 6.10a
The polynomial equations that describe the 5th, 25th, 50th, 75th and 95th centiles for respiratory rate superimposed upon a scatter diagram of respiratory rate data (after logarithmic transformation) for healthy awake subjects, aged 0 to 25 years.
Scatter Diagram and Centiles for Respiratory Rate

The polynomial equations that describe the 5th, 25th, 50th, 75th and 95th centiles for respiratory rate superimposed upon a scatter diagram of respiratory rate data (after logarithmic transformation) for healthy sleeping subjects, aged 0 to 4.5 years.
Figures 6.10a and 6.10b suggest the curves are representative of the data. However, there were eleven points in the RR data for awake children which were on or above the 95th centile and eighteen points on or below the 5th centile. This suggested some asynchrony was present. This could be caused by some children breathing slowly and deeply due to their awareness of being observed. The equations for the 50th and 95th centile are shown in figure 6.11. These equations were calculated from general equations using the normal equivalent deviate (see Appendix 8). The completed centiles are shown in figures 6.12a and 6.12b.

### Sleeping Children, aged zero to one year

**Equation for median:**  
\[
\log_{10} RR = 1.6305 - 0.4112 t + 0.017280 t^2 + 0.1096 t^3 
\]  
(1)

**Equation for 95th centile:**  
\[
\log_{10} RR = 1.7159 - 0.4396 t + 1.6721 t^2 + 0.1096 t^3 
\]  
(2)

### Sleeping Children, aged one to three years

**Equation for median:**  
\[
\log_{10} RR = 1.4033 - 0.06626 t + 0.009213 t^2 
\]  
(3)

**Equation for 95th centile:**  
\[
\log_{10} RR = 1.4720 - 0.06127 t + 0.009213 t^2 
\]  
(4)

### Awake Children, aged one to three years

**Equation for median:**  
\[
\log_{10} RR = 1.8443 - 0.3232 t + 0.08029 t^2 - 0.006982 t^3 
\]  
(5)

**Equation for 95th centile:**  
\[
\log_{10} RR = 2.07187 - 0.4149 t + 0.09661 t^2 - 0.006982 t^3 
\]  
(6)

### Awake Children, aged three to thirteen years

**Equation for median:**  
\[
\log_{10} RR = 1.5092 - 0.037037 t + 0.0011707 t^2 
\]  
(7)

**Equation for 95th centile:**  
\[
\log_{10} RR = 1.5899 - 0.030745 t + 0.0011707 t^2 
\]  
(8)

**Figure 6.11**  
Equations describing the 50th centile (median) and 95th centile for respiratory rates in awake and asleep children (t denotes the age in years).
Fig. 6.12a

Respiratory Rate Centile Chart

Awake Boys and Girls Aged 1-13 Years
Respiratory Rate Centile Chart
Sleeping Boys and Girls Aged 0-3 Years

Fig. 6.12b
6.5 Repeatability of Measurement of Respiratory Rate

Respiratory rate was measured on two occasions in five school and eight pre-school aged children who were awake, as shown in Table 6.11. The mean of the differences in the RR counted for two thirty-second periods on the two occasions was 1.0 bpm for the younger children and 1.5 bpm for the older children. The RR measured on the second occasion was higher. It is possible that the children's experience of having their respiration measured on the first occasion may have influenced the measurement of their RR's on the second occasion. However, 1.0 to 1.5 bpm was not a large change in RR.

The 95% coefficient of repeatability (SDx2) for RR measured over two thirty-second periods was 3.7 bpm for school aged children and 4.0 bpm for pre-school aged children. This variability occurred despite attempts to keep the protocol for testing children uniform. However, the children's RR were not always observed at the same time of day. Figure 6.13 shows there to be no relationship in the differences between the pairs of RR measurements and the RR itself. There were two outlying values that increased the 95% coefficient of repeatability. Apart from these two values, all other subjects had similar RR's on the two different days of measurement.

![Graph showing relationship between difference in respiratory rate measured on two occasions (y-axis) and the mean of these RR's (x-axis).](image)

**Figure 6.13**
Graph showing relationship between difference in respiratory rate measured on two occasions (y-axis) and the mean of these RR's (x-axis).
Table 6.11 - Repeatability of Measurements of Respiratory Rate in Awake Children

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Pre-school Aged (1.0-1.8y)</th>
<th>School Children (2.0-4.0y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>16</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>18</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>20</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>22</td>
<td>2</td>
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</tr>
<tr>
<td>24</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>26</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>28</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>30</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>32</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>34</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>36</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>38</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>40</td>
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<td>2</td>
</tr>
<tr>
<td>42</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>44</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>46</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>48</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>50</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>52</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>54</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>56</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>58</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>60</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

RR (b) - Respiratory rate measured for total test period.
RR (a) - Respiratory rate measured for two thirty-second periods.
6.6 Respiratory Timing Indices

Table 6.12 shows the mean inspiratory time \( T_I \), expiratory time \( T_E \), total respiratory cycle duration \( T_{TOT} \) and fractional inspiratory time \( T_I / T_{TOT} \) observed in sleeping children. Appendix 9 contains each subject's individual results. Newborn infants had a mean \( T_I / T_{TOT} \) of 0.44 (±0.04). This was significantly higher than the value of 0.40 (±0.04) observed in sleeping children, aged from two weeks to 3.5 years (\( p < 0.05 \), unpaired \( t \) test). Overall, however, there was no significant effect of age on \( T_I / T_{TOT} \) (\( r = -0.24 \), not significant, see fig. 6.14). A positive correlation existed between values of \( T_I \), \( T_E \), and \( T_{TOT} \) with age (\( r \) being +0.89, +0.86 and +0.89 respectively, \( p < 0.01 \)). \( T_{TOT} \) would be expected to increase with age since RR decreases with age. This is because \( T_{TOT} \) is inversely related to the RR, as shown in the following equation:

\[
RR = \frac{60}{T_{TOT}}
\]  

(6.1)

There was also a positive correlation between \( T_I \) and \( T_E \) (\( r = +0.93 \), \( p < 0.01 \)).

<table>
<thead>
<tr>
<th>Age Range (yr)</th>
<th>n</th>
<th>( T_{TOT} \pm SD ) (s)</th>
<th>( T_I \pm SD ) (s)</th>
<th>( T_E \pm SD ) (s)</th>
<th>( T_I/T_{TOT} \pm SD )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1.99 wk</td>
<td>10</td>
<td>1.30 ± 0.27</td>
<td>0.57 ± 0.10</td>
<td>0.73 ± 0.18</td>
<td>0.44 ± 0.04</td>
</tr>
<tr>
<td>2.0 wk - 3.5 yr</td>
<td>15</td>
<td>2.25 ± 1.02</td>
<td>0.90 ± 0.42</td>
<td>1.35 ± 0.63</td>
<td>0.40 ± 0.04</td>
</tr>
</tbody>
</table>

Figure 6.14
Scatter diagram showing relationship between age and fractional inspiratory time \( T_I / T_{TOT} \) in sleeping healthy children.
Measurements of the components of the respiratory cycle in healthy awake children, aged between two and twelve years, and young adults are shown in Table 6.13. Each subject's individual results are listed in Appendix 9. Both groups had similar values for $T_i / T_{TOT}$ with the mean being 0.41 for awake children, aged 2 to 12 years, and 0.42 for awake young adults. This difference was not significant ($p = 0.59$, unpaired $t$ test). Age had no significant effect on $T_i / T_{TOT}$ as demonstrated in figure 6.15 ($r = +0.12$, not significant). As with sleeping children, there was a positive correlation between age and $T_{TOT}$ ($r = +0.68$, $p < 0.01$, see figure 6.16). There was also a positive correlation between $T_i$ and $T_e$ in awake children ($r = +0.82$, $p < 0.01$, see figure 6.17). There was a difference of 0.01 in the mean $T_i / T_{TOT}$ between awake and sleeping children, which was not significant ($p = 0.38$, unpaired $t$ test).

Table 6.13 - Respiratory Timing Indices in Awake Children

<table>
<thead>
<tr>
<th>Age Range (yr)</th>
<th>n</th>
<th>$T_{TOT}$ ± SD (s)</th>
<th>$T_i$ ± SD (s)</th>
<th>$T_e$ ± SD (s)</th>
<th>$T_i / T_{TOT}$ ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0 - 12.99</td>
<td>38 (13M, 25F)</td>
<td>2.77 ± 0.56</td>
<td>1.14 ± 0.23</td>
<td>1.63 ± 0.34</td>
<td>0.41 ± 0.03</td>
</tr>
<tr>
<td>19.0 - 23.99</td>
<td>8 (8M, 0F)</td>
<td>3.93 ± 1.00</td>
<td>1.64 ± 0.73</td>
<td>2.14 ± 0.46</td>
<td>0.42 ± 0.05</td>
</tr>
<tr>
<td>Both groups</td>
<td>46 (21M, 25F)</td>
<td>2.97 ± 0.78</td>
<td>1.21 ± 0.32</td>
<td>1.72 ± 0.46</td>
<td>0.41 ± 0.03</td>
</tr>
</tbody>
</table>

Figure 6.15
Graph showing relationship between age and fractional inspiratory time ($T_i / T_{TOT}$) in healthy awake subjects.
A single breath obtained from a newborn infant during sleep is shown in fig 6.18a. The fractional inspiratory time ($T_I/T_{TOT}$) is 0.46, reflecting the higher value of $T_I/T_{TOT}$ found in this age group. In comparison, a single breath from a seven month old infant during sleep had a $T_I/T_{TOT}$ value of 0.38 (see figure 6.18b). Fig 6.19a shows a typical breath obtained from an awake 12 year old girl, with a $T_I/T_{TOT}$ value of 0.40. An expiratory pause reduced the $T_I/T_{TOT}$ value obtained, as shown in figure 6.19b where a $T_I/T_{TOT}$ of 0.32 was observed.
6.7 Spectral Analysis

Approximately three minutes of data was analysed using the Fast Fourier Transform method. Fig 6.20 displays the breathing pattern of an awake seven year old girl. The power spectrum of this breathing pattern showed a large peak (the fundamental frequency) at approximately 0.42 Hz (see figure 6.21). This corresponded to the RR. Low frequency oscillations are also present with peaks occurring at 0.1 Hz (this oscillation had a period of 10s). Another peak occurred at 0.2 Hz. This could be the harmonic of the former oscillation or alternatively an independent oscillation. The breathing pattern in figure 6.20 showed minimal movement artefact. This means movement artefact is a less likely cause of these low frequency oscillations.

![Figure 6.20](image)

Breathing pattern of an awake girl, aged seven years, which was analysed using the Fast Fourier Transform method.
Figure 6.21
Power spectrum of the breathing pattern of an awake girl, aged seven years. The fundamental frequency appears to be at 0.42 Hz or 25 bpm. Some low frequency oscillations are also present.

Figures 6.22 and 6.23 show the power spectrum of the breathing patterns of a girl, aged three years, and a young adult, aged 22 years, when awake. There is a large peak (the fundamental frequency) which corresponds to the RR (e.g. 0.40 Hz or 24 bpm in the girl, aged three years). Low frequency oscillations are also present at 0.1 Hz. The width of the fundamental frequency is narrower in the older subject which may reflect a more mature respiratory control system.

Figure 6.22
Power spectrum of breathing pattern of an awake three year old girl.

Figure 6.23
Power spectrum of breathing pattern of an awake 22 year old male.

The breathing patterns of one pair of identical twins, aged two years, measured during quiet sleep, are illustrated in figure 6.24. The power spectrum of these patterns show the
twins's fundamental frequency and low frequency oscillations to be almost the same (see figures 6.25a and 6.25b). This supports the idea that there is some degree of genetic determination of breathing patterns.

![Figure 6.24](image)

Breathing patterns of one pair of female identical twins, aged two years, during sleep.

![Figure 6.25a](image)

Power spectrum of twin 1.

![Figure 6.25b](image)

Power spectrum of twin 2.

The power spectrum of the breathing pattern of a two week old infant, during periodic breathing, while asleep, is shown in figure 6.26a. This breathing pattern was illustrated in figure 5.9, chapter 5. There is a significant low frequency oscillation present at 0.1 Hz related to the bursts of breathing and apnoea associated with the periodic breathing. This peak was markedly reduced when the infant was breathing with a regular pattern during sleep (see figure 6.26b). The peak associated with the RR (approximately 0.8 Hz) is also more prominent during regular breathing.
In contrast to the prominent low frequency oscillation observed during periodic breathing, no low frequency oscillations were observed in a subject who was being ventilated. The ventilated subject's breathing pattern is shown in figure 6.27a and the power spectrum is shown in figure 6.27b. There is no significant peak in the low frequency region at 0.1 Hz. This would be expected since a ventilator would keep the respirations at a constant rate. Oscillations due to feedback mechanisms would not be present since the ventilator would not respond to these in the same way as the respiratory control centre does. The breathing pattern is not very sinusoidal. The frequency corresponding to the respiratory rate of approximately
0.2 Hz (i.e. a RR of 10 - 12 bpm) is the largest peak. The other peaks present are the harmonics associated with the RR. These were prominent because the breathing pattern associated with the ventilator was not sinusoidal in shape.

6.8 Questionnaire

The questionnaire allowed further investigation of the population studied in this project. The effects of a recent upper respiratory tract infection and a family history of asthma on respiratory rate were also investigated.

Comparison of Participants and Non-participants

All children in one kindergarten class and in one primary school class, regardless of their participation in the research project, were issued with the questionnaire. All children in the kindergarten group (21/21) returned the questionnaire, while 75% (21/28) of the primary school group responded to the questionnaire. Since this analysis depended on all children returning a form, the kindergarten group only was studied.

Most parents felt there was no risk associated with the testing procedure with no parents responding with "yes" and one parent responding "maybe" to the question "Do you think there is any risk to your son/daughter participating in this type of medical research?" Based on this questionnaire, there did not appear to be a difference in the perception of risk between parents who allowed their children to participate in the research study and those who did not. These results are shown in Table 6.14.

Table 6.14 - Perception of Risk Related to Breathing Research Study by Parents of Kindergarten Children

<table>
<thead>
<tr>
<th>Group</th>
<th>Yes</th>
<th>No</th>
<th>Maybe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>0</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Non-participants</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 6.15 shows there was a greater percentage (42%) of children who participated in the study with a first degree relative who had respiratory disease compared to children who did not participate in the study (22%). When a history of respiratory disease in a second degree relative was included this difference was reduced to 6% which was not statistically significant (Chi square test with Yate’s correction).

Table 6.15 - Presence of a Family History of Respiratory Disease in Participating and Non-Participating Children

<table>
<thead>
<tr>
<th>Group</th>
<th>Family History (First Degree Relative)</th>
<th>Family History (Second Degree Relative)</th>
<th>No Family History</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>5 (42%)</td>
<td>1 (8%)</td>
<td>6 (50%)</td>
</tr>
<tr>
<td>Non-participants</td>
<td>2 (22%)</td>
<td>2 (22%)</td>
<td>5 (56%)</td>
</tr>
</tbody>
</table>

A comparison of the occupations, arranged in categories, of the parents of children who participated in the research with those who did not is made in Table 6.16. When both parents worked, the occupation with the highest status, based on a scale created by Daniels (1983), was used. A more detailed outline of the groups of occupations was provided in appendix 5. In both groups, parents came from managerial/administrator and professional groups. Sixty-seven percent of the parents who allowed their children to participate were from the professional group compared with 44% who did not allow their children to participate (not significant, chi square test with Yates’ correction). There was a relative lack of other groups which could be related to demographic factors associated with the kindergarten surveyed.

Table 6.16 - Comparison of Parent's Occupations of Participating and Non-participating Children

<table>
<thead>
<tr>
<th>Occupation of Parents</th>
<th>1 - managers/administrators</th>
<th>2 - professionals</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6 - sales persons personal service workers</th>
<th>7</th>
<th>8</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>2</td>
<td>8</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>1</td>
</tr>
<tr>
<td>Non-participants</td>
<td>3</td>
<td>4</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>1</td>
</tr>
</tbody>
</table>

The categories of occupations include: 1. managers/administrators; 2. professionals; 3. para-professionals; 4. tradespersons; 5. clerks; 6. salespersons and personal service workers; 7. plant and machine operators and drivers; 8. labourers and related workers; and 9. inadequately described or not stated.
Survey of a Sample of the Children Participating in the Research

Questionnaires were also issued to a sample of the children who participated in the project for further analysis. Response rates to the questionnaire were 83.3% (20/24), 80.8% (21/26) and 100% (12/12) at two childcare centres and a kindergarten; 100% from a youth group (13/13); 91.6% (22/24) at an after-school care centre and 56% (20/36) at a school.

An analysis of the effect of recent upper respiratory tract infection (URTI) and a family history of asthma on RR was made. An upper respiratory tract infection was defined as the presence of a cough, fever, sore throat or runny nose in the absence of any known respiratory disease, in a similar way to the study of Marks, South and Carlin (1993). In pre-school children, the mean RR standardised for age was found not to differ significantly between 16 pre-school children with the symptoms of an URTI and 12 without an URTI (p=0.95; unpaired \( t \) Test).

Some difference in RR between children with and without a family history of asthma was found in pre-school children (see table 6.17). The difference in mean RR standardised for age of 5% was not statistically significant (p=0.27, unpaired \( t \) Test). There was no significant difference in RR between primary school children with and without a family history of asthma (p=0.85, unpaired \( t \) test). Children with a history of respiratory disease or current upper respiratory tract symptoms were excluded from this analysis.

### Table 6.17 - Effect of Family History of Asthma on Respiratory Rate

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-school Children</th>
<th>School Children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>RR (standardised for age)</td>
</tr>
<tr>
<td>No Family History</td>
<td>15</td>
<td>94.9%</td>
</tr>
<tr>
<td>Family History</td>
<td>18</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 6.18 shows the occupations of parents who responded to this questionnaire. This can be compared with the percentage of people in Brisbane amongst the various categories of occupation. Amongst the pre-school children, there is an over-representation of parents in the professional and para-professional groups, and lack of other groups. Amongst the school age children, there is a better distribution of parent's occupations of the children in the breathing study when compared to the general population.

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Sub-total</th>
<th>Sub-total</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Brisbane Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Australian Bureau of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistics, 1991b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30,618</td>
<td>3,900</td>
</tr>
<tr>
<td>Sub-total</td>
<td>3,061</td>
<td>390</td>
</tr>
<tr>
<td>Youth Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>School</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>After-school Care</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Kindergarten</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Child Care Centre (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Child Care Centre (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sub-total</td>
<td>26</td>
<td>49</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 6.18 - Children in Breathing Research Study Sorted According to Parent's Occupation.
Some of the comments and concerns parents made relating to the research project are listed in Appendix 10. The concerns related to the anxiety or harm which may be caused by the testing procedure and the child's interaction with a stranger. Positive responses were also received with a number of parents fully supporting any form of research which helps children and being interested in the results of the study.
Chapter 7
Analysis of Respiratory Rate and Cycle in Children with Respiratory Disease

7.1 Introduction

The effect of respiratory disease on respiratory rate was examined. Diseases studied included pneumonia, bronchiolitis, cystic fibrosis (CF) and asthma in the current study. An examination of inspiratory time, expiratory time and fractional inspiratory time in disease was also made. Reference to results found in healthy children was made to find out the usefulness of respiratory rate as an indicator of the presence and severity of respiratory disease.

7.2 Pneumonia

All children in the present study diagnosed with pneumonia (n = 6) were found to have elevated RR when asleep. The mean Z-score (the number of SDs above the predicted RR for healthy children) was +4.75 (see Table 7.1). The RR was also higher than the ninety-fifth centile for healthy children in all cases. Severity of the illness had a role in influencing the level of increase in RR. One child aged eight months, whose breathing pattern is shown in figure 7.1, had a RR that was 17.3 bpm above the 95th centile. This child had severe pneumonia with an associated pleural effusion. In contrast, another child, aged nine months, with no evidence of laboured breathing had a RR 0.1 bpm above the 95th centile. There was a positive correlation between these children's Z-scores for RR and their body temperatures (r=+0.83, p<0.05) as shown in figure 7.2.

Figure 7.1
Breathing pattern of a sleeping female infant, aged eight months, with pneumonia.
Table 7.1 - Respiratory Rates in Sleeping Children with Pneumonia

<table>
<thead>
<tr>
<th>Abbreviations: R - right; L - left; LL - lower lobe; ML - middle lobe; RSY - respiratory syncytial virus.</th>
</tr>
</thead>
<tbody>
<tr>
<td>§ Denotes receiving oxygen therapy.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mean Time (±SD)</th>
<th>R</th>
<th>LL</th>
<th>ML</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patchy consolidation</td>
<td>38.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>Dehydrated</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>Collapse/consolidation</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>RML consolidation</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>RML, RML and RML consolidation</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>RML and RML consolidation</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
<tr>
<td>RML consolidation, RML and RML consolidation</td>
<td>39.5 + 0.8</td>
<td>26.4</td>
<td>36.5</td>
<td>27.7</td>
<td>0.2</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Note: Data collected during the test period.
The RR measure over a one minute period in the sleeping children, by adding two thirty-second counts, was similar to that measured for the total test period (mean time 6.1 minutes). The 95% limit of agreement (i.e. mean ± 2 SD) was -3.19 to 1.69 bpm, which was clinically acceptable given these children's high RRs.

The RR obtained in four of the sleeping children with pneumonia aged between 6.0 and 11.99 months and RR observed in healthy children, aged between 6.0 and 11.99 months, is shown in Table 7.2. The sensitivity and specificity for various RR thresholds are also shown. A threshold RR of 28 bpm gave a sensitivity of 100% and a specificity of 85% for the detection of pneumonia. The significance of these values is limited by the small number of subjects in the study. The data is summarised in the ROC curve illustrated in figure 7.3. When the points are close to the top left-hand corner of the graph, the clinical test is considered an efficacious one.

<table>
<thead>
<tr>
<th>RR in children with pneumonia</th>
<th>RR in healthy children</th>
<th>RR threshold (bpm)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>28, 40, 42, 45.</td>
<td>20, 20, 23, 23, 23, 24, 24, 24, 24, 25, 26, 29, 30.</td>
<td>≥ 20</td>
<td>100% (4/4)</td>
<td>0% (0/13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 28</td>
<td>100% (4/4)</td>
<td>85% (11/13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 29</td>
<td>75% (3/4)</td>
<td>85% (11/13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 30</td>
<td>75% (3/4)</td>
<td>92% (12/13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 31</td>
<td>75% (3/4)</td>
<td>100% (13/13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 28</td>
<td>0% (0/4)</td>
<td>100% (13/13)</td>
</tr>
</tbody>
</table>

Figure 7.2
Relationship between body temperature and increase in RR (Z-score) in sleeping children with pneumonia.
In awake children with pneumonia, there was also a marked increase in RR. Table 7.3 shows the mean Z-score to be 2.39. Figure 7.4 shows the rapid respirations due to pneumonia in a boy, aged four years. Sixty-seven per cent (6/9) of cases were above the 95th centile for RR in healthy children. The three cases below the 95th centile were only marginally so. Two of these cases were unusual in that they were of a more chronic nature involving *Bordetella pertussis* infections. Excluding these two cases, 86% (6/7) of cases were above the 95th centile threshold. There was a poor correlation of increases in RR with body temperature in these children ($r = -0.16$, not significant).
Table 7.3 - Respiratory Rates in Awake Children with Pneumonia

<table>
<thead>
<tr>
<th>Abbreviations:</th>
<th>L - Left</th>
<th>R - Right</th>
<th>LL - Lower Lobe</th>
<th>ML - Middle Lobe</th>
<th>UL - Upper Lobe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Mean</td>
<td>Median</td>
<td>25th Percentile</td>
<td>75th Percentile</td>
<td>95th Percentile</td>
</tr>
<tr>
<td>Temperature</td>
<td>36.5°F</td>
<td>36.3°F</td>
<td>36.0°F</td>
<td>36.8°F</td>
<td>37.0°F</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>122 bpm</td>
<td>120 bpm</td>
<td>115 bpm</td>
<td>125 bpm</td>
<td>130 bpm</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>22 L/min</td>
<td>20 L/min</td>
<td>15 L/min</td>
<td>24 L/min</td>
<td>26 L/min</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>98%</td>
<td>97%</td>
<td>95%</td>
<td>99%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Note: Additional columns and rows may be present in the table.
Due to the rapid breathing and asynchronous chest wall movements associated with pneumonia, timing indices are not presented. The optical sensor detected some subcostal indrawing associated with an expiratory grunt in an infant, aged eight months (see figure 7.5).

![Figure 7.5](image)

Breathing pattern of an 8 month old girl diagnosed with pneumonia. The dark lines mark the parts of the trace which coincided with an expiratory grunt.

### 7.3 Cystic Fibrosis

RR was also elevated in nine awake children diagnosed with cystic fibrosis (see Table 7.4). There was an average increase of 1.99 SDs above the predicted RR (i.e. mean Z-score). Fig 7.6 illustrates an elevated RR present in a male, aged 16 years, with CF. There was a poor correlation between FEV$_{1.0}$ as a percentage of the predicted value, and the Z-score ($r = -0.13$, not significant). There was a positive correlation between age and Z-score for RR ($r = +0.67$, $p < 0.05$). RR measured over two thirty second periods was similar to the RR averaged over the total test time, with the 95% limit of agreement being -3.17 to 3.55 bpm.

![Figure 7.6](image)

Breathing pattern in male, aged 16 years with cystic fibrosis, demonstrating a RR of 32 bpm.
<table>
<thead>
<tr>
<th>Patient</th>
<th>RR (bpm)</th>
<th>RR (a)</th>
<th>Difference (bpm)</th>
<th>z-score</th>
<th>HR (b)</th>
<th>SD</th>
<th>Date of Test</th>
<th>Age (y)</th>
<th>Date of Birth</th>
<th>Initial</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. S.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>L. T.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>B. S.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>T. I.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>B. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>G. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>T. B.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>E. M.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>B. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>G. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>T. B.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>E. M.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>B. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>G. C.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>T. B.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
<tr>
<td>E. M.</td>
<td>105</td>
<td>103</td>
<td>2</td>
<td>-1.41</td>
<td>2.74</td>
<td>25</td>
<td>06-Jul-83</td>
<td>8.5</td>
<td>14-Nov-83</td>
<td>G</td>
<td>M</td>
</tr>
</tbody>
</table>

Table 7.4 - Respiratory Rates in Awake Children with Cyclic Pneumonia

Excluded from analysis of correlation between RR and FEV1.0 percent predicted as primary function test performed two months prior to measurement of RR.
Table 7.5 presents RRs observed ten sleeping infants and toddlers diagnosed with cystic fibrosis. These children were sedated with chloral hydrate as part of an unrelated research study performed by a different researcher. Sixty percent (6/10) had an increase in RR of at least one SD above normal, with three children having increases of two or more SDs. These changes in RR may signify dysfunction in the lungs at this early age. A child, aged eight weeks, had a RR of 54 bpm and a Z-score of 3.93. Forty-four percent of children (4/9) had a RR above the 95th centile. However, three of the children had RRs within the range observed in healthy children. These children's lungs may have been affected less by the disease at this age. There was no significant change in RR after the administration of salbutamol sulfate (Ventolin) in seven children (p = 0.57, unpaired t test). The Z-score before salbutamol sulfate (Ventolin) was 0.14 and changed to 0.37 after its administration.

Table 7.5 - Respiratory Rates in Sleeping Infants and Toddlers with Cystic Fibrosis

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Date of Birth</th>
<th>Age (yr)</th>
<th>Ht (m)</th>
<th>Wt (kg)</th>
<th>RR(a) * (bpm)</th>
<th>Z-score (SD)</th>
<th>RR (95th Centile) (bpm)</th>
<th>RR (b) * (bpm)</th>
<th>Z-score</th>
<th>Time (min)</th>
<th>RR (bpm)</th>
<th>Z-score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.M.</td>
<td>M</td>
<td>20-Jul-94</td>
<td>0.09</td>
<td>0.474</td>
<td>2.43</td>
<td>35</td>
<td>-0.06</td>
<td>47.5</td>
<td>35</td>
<td>1</td>
<td>42</td>
<td>0.92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R.P. *</td>
<td>M</td>
<td>14-Mar-94</td>
<td>0.16</td>
<td>0.51</td>
<td>3.93</td>
<td>54</td>
<td>2.59</td>
<td>44.3</td>
<td>43.9</td>
<td>3</td>
<td>38</td>
<td>0.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H.L.</td>
<td>M</td>
<td>02-Jul-94</td>
<td>0.17</td>
<td>0.57</td>
<td>4.8</td>
<td>47</td>
<td>1.62</td>
<td>43.9</td>
<td>47.3</td>
<td>3</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.E.</td>
<td>F</td>
<td>30-Mar-94</td>
<td>0.25</td>
<td>0.56</td>
<td>4.63</td>
<td>31</td>
<td>-0.61</td>
<td>40.7</td>
<td>32.3</td>
<td>3</td>
<td>27</td>
<td>-1.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.W.</td>
<td>M</td>
<td>12-Apr-94</td>
<td>0.31</td>
<td>0.65</td>
<td>5.52</td>
<td>31</td>
<td>-0.61</td>
<td>38.6</td>
<td>30.5</td>
<td>4</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.</td>
<td>F</td>
<td>10-Jan-94</td>
<td>0.42</td>
<td>0.616</td>
<td>5.62</td>
<td>45</td>
<td>1.34</td>
<td>35.1</td>
<td>41.7</td>
<td>3.5</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.W.</td>
<td>F</td>
<td>13-Jul-93</td>
<td>0.75</td>
<td>0.713</td>
<td>9.06</td>
<td>24</td>
<td>-1.59</td>
<td>28.3</td>
<td>24</td>
<td>5</td>
<td>28</td>
<td>-1.03</td>
<td></td>
<td>Rhinorhoea</td>
</tr>
<tr>
<td>Z.H.</td>
<td>F</td>
<td>31-Jul-92</td>
<td>1.8</td>
<td>0.844</td>
<td>13.1</td>
<td>40</td>
<td>5.13</td>
<td>24.6</td>
<td>42.3</td>
<td>3</td>
<td>26</td>
<td>2.43</td>
<td></td>
<td>Mild Asthma</td>
</tr>
<tr>
<td>B.S.</td>
<td>M</td>
<td>21-Jan-92</td>
<td>2.17</td>
<td>0.844</td>
<td>11.3</td>
<td>24</td>
<td>1.69</td>
<td>24.1</td>
<td>24.2</td>
<td>6</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.W.</td>
<td>F</td>
<td>07-Feb-91</td>
<td>3.52</td>
<td>0.89</td>
<td>12.2</td>
<td>25</td>
<td>2.13</td>
<td>§</td>
<td>24.5</td>
<td>4</td>
<td>21</td>
<td>0.64</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Denotes child not sedated with chloral hydrate.
† RR (a) - respiratory rate measured for two thirty-second periods.
† RR (b) - respiratory rate measured for total test period.
‡ GOR - gastro-oesophageal reflux.
§ Since the centile chart for sleeping healthy children finished at three years, the 95th centile for RR could not be calculated for this child's age.

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Table 7.6 displays $T_i$, $T_e$, $T_{TOT}$ and $T_i/T_{TOT}$ calculated in nine awake children with CF. The mean $T_i/T_{TOT}$ is 0.44 (±0.03), which was higher than the value of 0.41 (±0.03) obtained in 46 healthy subjects aged from 2 - 23 years ($p = 0.02$, unpaired t Test). There was no significant correlation between airways obstruction, as measured by $FEV_{1.0}$ (per cent of predicted value) and $T_i/T_{TOT}$ ($r = +0.14$, not significant - see figure 7.7). This correlation excluded the subject whose $FEV_{1.0}$ was measured two months before the breathing test was performed. Figure 7.7 showed that some children (particularly those with higher $FEV_{1.0}$ per cent predicted values) had larger values of $T_i/T_{TOT}$ such as 0.47, 0.47 and 0.48.

Table 7.6 - Indices of the Respiratory Cycle in Awake Children and Adolescents with Cystic Fibrosis

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>$T_i$ ±SD (s)</th>
<th>$T_e$ ±SD (s)</th>
<th>$T_{TOT}$ ±SD (s)</th>
<th>$T_i/T_{TOT}$ ±SD</th>
<th>$FEV_{1.0}$ (L)</th>
<th>$FEV_{1.0}$ % pred.</th>
<th>Days between measurement of $FEV_{1.0}$ and $T_i/T_{TOT}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.B.</td>
<td>M</td>
<td>16.44</td>
<td>0.94 ±0.15</td>
<td>1.18 ±0.12</td>
<td>2.12 ±0.23</td>
<td>0.44 ±0.04</td>
<td>1.12</td>
<td>34</td>
<td>1</td>
</tr>
<tr>
<td>C.S.</td>
<td>F</td>
<td>12.1</td>
<td>0.89 ±0.10</td>
<td>1.25 ±0.15</td>
<td>2.13 ±0.20</td>
<td>0.41 ±0.03</td>
<td>0.3</td>
<td>13</td>
<td>-64</td>
</tr>
<tr>
<td>S.S.</td>
<td>F</td>
<td>8.51</td>
<td>1.17 ±0.17</td>
<td>1.27 ±0.26</td>
<td>2.44 ±0.34</td>
<td>0.48 ±0.06</td>
<td>0.7</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td>B.L.</td>
<td>F</td>
<td>15.02</td>
<td>1.41 ±0.16</td>
<td>1.8 ±0.42</td>
<td>3.21 ±0.47</td>
<td>0.44 ±0.06</td>
<td>1.05</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>B.S.</td>
<td>M</td>
<td>15.74</td>
<td>0.96 ±0.13</td>
<td>1.45 ±0.16</td>
<td>2.41 ±0.21</td>
<td>0.4 ±0.04</td>
<td>1.56</td>
<td>49</td>
<td>1</td>
</tr>
<tr>
<td>P.G.</td>
<td>M</td>
<td>16.86</td>
<td>0.9 ±0.09</td>
<td>1.29 ±0.25</td>
<td>2.19 ±0.25</td>
<td>0.42 ±0.05</td>
<td>0.84</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>L.H.</td>
<td>M</td>
<td>11.7</td>
<td>0.8 ±0.12</td>
<td>1.01 ±0.20</td>
<td>1.81 ±0.23</td>
<td>0.44 ±0.06</td>
<td>1.05</td>
<td>51</td>
<td>-1</td>
</tr>
<tr>
<td>L.T.</td>
<td>F</td>
<td>11.27</td>
<td>1.06 ±0.24</td>
<td>1.19 ±0.18</td>
<td>2.25 ±0.36</td>
<td>0.47 ±0.05</td>
<td>0.60</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>B.C.</td>
<td>M</td>
<td>18.52</td>
<td>1.04 ±0.07</td>
<td>1.18 ±0.10</td>
<td>2.22 ±0.16</td>
<td>0.47 ±0.02</td>
<td>2.49</td>
<td>56</td>
<td>1</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td></td>
<td></td>
<td>1.02 ±0.18</td>
<td>1.29 ±0.22</td>
<td>2.31 ±0.38</td>
<td>0.44 ±0.03</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 7.7
Graph showing relationship of $FEV_{1.0}$ (% predicted) and fractional inspiratory time ($T_i/T_{TOT}$).
Figures 7.8 and 7.9 show individual breaths obtained from two different awake subjects with CF. Figure 7.8 demonstrated a normal \( T_i / T_{TOT} \) of 0.43. The other child's breath represented a more prolonged expiration, resulting in a \( T_i / T_{TOT} \) of 0.38. However, this child had a mean \( T_i / T_{TOT} \) of 0.41 ± 0.03 when ten breaths were analysed. The shapes of the curves in figures 7.11 and 7.12 were different, which could be an area of further investigation.

![Figure 7.8](image)

**Figure 7.8**
Single breath obtained from a male with cystic fibrosis, aged 16 years. \( (T_i / T_{TOT} = 0.43) \).

![Figure 7.9](image)

**Figure 7.9**
Single breath obtained from a female diagnosed with cystic fibrosis, aged 12 years. \( (T_i / T_{TOT} = 0.38) \).

### 7.4 Bronchiolitis

Bronchiolitis had varied effects on RR in infants with bronchiolitis, as shown in Table 7.7. Eighty per cent (8/10) of sleeping children, aged from birth to seven months, had RSV infection confirmed by microbiological tests. The mean Z-score for RR of the ten cases of bronchiolitis was +0.63. There was large variation with five infants having negative Z-scores and one infant having a Z-score of 4.60.

RR measured by adding respirations counted for two thirty-second periods together was similar to the average RR measured over the test period (mean time ten minutes). The mean of the differences between the two methods was 0.19. The 95% limit of agreement was -5.81 to 6.19 bpm, which seemed acceptable given these children are breathing at elevated RR (mean of 37 bpm). There was no significant difference in RR between sleeping children receiving oxygen and those breathing room air (0.43 and 1.05 SDs respectively, \( p = 0.70 \), unpaired \( t \) test). Infants receiving oxygen therapy had lower oxygen saturation compared to children breathing room air (94.7% and 97.2% respectively).
Table 7.7 - Respiratory Rates in Sleeping Children with Bronchiolitis

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (mo)</th>
<th>RR(a) † (bpm)</th>
<th>Z-score (SD)</th>
<th>RR - 95th Centile (bpm)</th>
<th>RR(b) † (bpm)</th>
<th>Diff RR (a)-(b)</th>
<th>Time Measured (min.)</th>
<th>O₂ Saturation (%)</th>
<th>RSV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.L.</td>
<td>F</td>
<td>0</td>
<td>53</td>
<td>2.11</td>
<td>50.44</td>
<td>52.4</td>
<td>0.6</td>
<td>4.5</td>
<td>93 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.M.</td>
<td>M</td>
<td>1</td>
<td>32</td>
<td>-0.46</td>
<td>46.57</td>
<td>33.1</td>
<td>3.5</td>
<td>44</td>
<td>100 +</td>
<td></td>
<td>Born at 36 weeks</td>
</tr>
<tr>
<td>C.R.</td>
<td>M</td>
<td>1</td>
<td>49</td>
<td>1.83</td>
<td>45.66</td>
<td>46.7</td>
<td>2.3</td>
<td>7</td>
<td>97 *</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>D.H.</td>
<td>M</td>
<td>2</td>
<td>23</td>
<td>-1.67</td>
<td>43.09</td>
<td>22.2</td>
<td>0.8</td>
<td>8</td>
<td>96 +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.C.</td>
<td>M</td>
<td>2</td>
<td>41</td>
<td>0.75</td>
<td>43.09</td>
<td>41.4</td>
<td>-0.4</td>
<td>5.5</td>
<td>93 *</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>V.V.</td>
<td>F</td>
<td>2</td>
<td>44</td>
<td>1.16</td>
<td>42.28</td>
<td>50.8</td>
<td>-6.8</td>
<td>4.5</td>
<td>89 *</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>C.P.</td>
<td>F</td>
<td>2</td>
<td>30</td>
<td>-0.73</td>
<td>41.88</td>
<td>31.7</td>
<td>-1.7</td>
<td>11</td>
<td>98 +</td>
<td></td>
<td>Born at 27 weeks</td>
</tr>
<tr>
<td>B.F.</td>
<td>F</td>
<td>2</td>
<td>30</td>
<td>-0.73</td>
<td>41.88</td>
<td>26.4</td>
<td>3.6</td>
<td>7</td>
<td>100 *</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>T.J.</td>
<td>M</td>
<td>2</td>
<td>31</td>
<td>-0.59</td>
<td>41.88</td>
<td>31.5</td>
<td>-0.5</td>
<td>8</td>
<td>96 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.D.</td>
<td>M</td>
<td>7</td>
<td>37</td>
<td>4.60</td>
<td>29.83</td>
<td>36.5</td>
<td>0.5</td>
<td>6</td>
<td>95 +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td>37</td>
<td>0.63 ±9.5</td>
<td>29.83 ±1.87</td>
<td>36.5 ±3.00</td>
<td>6.0 ±3.00</td>
<td>10.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Denotes receiving oxygen therapy
† RR (a) - respiratory rate measured for two 30s periods.
RR(b) - respiratory rate measured for total test period.

Forty per cent of the sleeping infants (4/10) had RRs above the 95th centile for healthy sleeping children. An example of a breathing pattern that was not elevated is shown in fig. 7.10. A suggestion of a correlation, although not significant, between Z-scores for RR and oxygenation existed (r = -0.42, not significant, see figure 7.11). Episodes of apnoea were also observed in some children with bronchiolitis as shown in figures 7.12 and 7.13.

**Figure 7.10**
Breathing pattern of a sleeping female infant, aged two months, with bronchiolitis. Her RR was about 26 bpm.
Figure 7.11
Relationship between respiratory rate (Z-score) and oxygen saturation in sleeping infants with bronchiolitis.

Figure 7.12
Breathing pattern of a sleeping infant, aged two months (uncorrected for prematurity), with bronchiolitis. There was a significant episode of apnoea present. This infant was born prematurely at 27 weeks of gestation, which would also be a causative factor for this apnoea.

Figure 7.13
Breathing pattern of another sleeping infant, aged two months, with bronchiolitis. Pauses in breathing lasting about 5 - 10 seconds are present.
Table 7.8 shows the sensitivity and specificity of different RR thresholds for detecting bronchiolitis in sleeping infants, aged between 1.0 and 5.99 months. A RR of 30 bpm or greater gave a sensitivity of 87.5% and specificity of 11.85%. In contrast, a RR of 41 bpm or greater resulted in a specificity of 82% but the sensitivity was only 37.5%. The ROC curve shows that when the sensitivity is high, there is also a high false positive rate (see figure 7.14). Therefore, RR was a poor indicator of bronchiolitis in the sample of children observed.

Table 7.8 - Sensitivity and Specificity of Different Respiratory Rates Measured During Sleep in Identifying Bronchiolitis (in children aged from 1.0 to 5.99 months)

<table>
<thead>
<tr>
<th>Threshold RR (bpm)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal 57, 44, 41, 40, 37, 36, 35, 34, 33, 32, 31, 30, 29, 27.</td>
<td>23</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>Bronchiolitis 49, 44, 41, 32, 31, 30, 23.</td>
<td>30</td>
<td>87.5% (7/8)</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>62.5% (5/8)</td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>50% (4/8)</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>37.5% (3/8)</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>37.5% (3/8)</td>
</tr>
<tr>
<td></td>
<td>41</td>
<td>37.5% (3/8)</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>25% (2/8)</td>
</tr>
<tr>
<td></td>
<td>58</td>
<td>0% (0/8)</td>
</tr>
</tbody>
</table>

Figure 7.14
ROC curve for respiratory rate as an indicator of bronchiolitis, in sleeping children aged from 1.0 to 5.99 months.
The respiratory rate in awake infants with bronchiolitis is shown in Table 7.9. These children had large RRs, with a mean RR of 60 (±8.0) bpm. However, the healthy infants had similar RRs, with healthy children aged from birth to 5.99 months having a mean RR of 59.29 (±9.82). Consequently, the Z-scores for awake children with bronchiolitis were not high, with a mean value of + 0.17.

Table 7.9 - Respiratory Rates in Awake Children Diagnosed with Bronchiolitis

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (mo)</th>
<th>RR(a) † (bpm)</th>
<th>Z-score (SD)</th>
<th>RR(b) † (bpm)</th>
<th>Diff. RRa-b</th>
<th>Time (min.)</th>
<th>O₂ Sat. (%)</th>
<th>RSV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.R.</td>
<td>M</td>
<td>1</td>
<td>62</td>
<td>0.28</td>
<td>60</td>
<td>2</td>
<td>4</td>
<td>98</td>
<td>+</td>
</tr>
<tr>
<td>B.F.</td>
<td>F</td>
<td>2</td>
<td>49</td>
<td>-1.05</td>
<td>49</td>
<td>0</td>
<td>1</td>
<td>100*</td>
<td>+</td>
</tr>
<tr>
<td>B.F.</td>
<td>F</td>
<td>2</td>
<td>69</td>
<td>0.99</td>
<td>70</td>
<td>-1</td>
<td>1.5</td>
<td>94</td>
<td>+</td>
</tr>
<tr>
<td>T.H.</td>
<td>M</td>
<td>4</td>
<td>55</td>
<td>-0.44</td>
<td>60.2</td>
<td>-5.2</td>
<td>4</td>
<td>97</td>
<td>-</td>
</tr>
<tr>
<td>N.D. ‡</td>
<td>M</td>
<td>6</td>
<td>65</td>
<td>1.07</td>
<td>65</td>
<td>0</td>
<td>1</td>
<td>95</td>
<td>+</td>
</tr>
</tbody>
</table>

Mean ±SD

* Denotes receiving oxygen therapy.
† RR (a) - RR measured for two 30 s periods.
RR (b) - RR measured for total test period.
‡ N.D., aged six months, was compared with the healthy children, aged from 6.0 to 11.99 months. This explains why his RR is similar to other children, but his Z-score is larger.

Table 7.10 shows the T₁, Tₑ, and T₁/Tₜₒₜ values measured by the optical sensor in nine sleeping infants with bronchiolitis. The mean T₁/Tₜₒₜ obtained was 0.43 (±0.06). This was not significantly different to the value of 0.41 (± 0.03) observed in ten healthy infants, aged between 2.0 weeks and 11.99 months (p=0.36, unpaired t test). T₁/Tₜₒₜ ranged from 0.35 to 0.50 (see figure 7.15). Forty-four per cent (4/9) infants with bronchiolitis had T₁/Tₜₒₜ values greater than 0.45, compared to 10 % (1/10) of the healthy infants aged between 2.0 weeks and 0.99 years.

There was no significant correlation between T₁/Tₜₒₜ and oxygen saturation (r = - 0.31, not significant). Although not statistically significant, there was a suggestion of a positive correlation between Tₜₒₜ and oxygen saturation (r = + 0.52, not significant). There was also a suggestion of a negative correlation between Tₜₒₜ and T₁/Tₜₒₜ (r = - 0.62, not significant). It is possible that as the RR increases (i.e. Tₜₒₜ decreases), T₁/Tₜₒₜ may also increase. There was also a correlation between T₁ and Tₑ (r = + 0.94, p < 0.01).
Table 7.10 - Components of the Respiratory Cycle in Sleeping Infants with Bronchiolitis

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Date of Birth</th>
<th>Age (yr)</th>
<th>( T_{TOT} ) ± SD</th>
<th>( T_i ) ± SD</th>
<th>( T_e ) ± SD</th>
<th>( T_i/T_{TOT} ) ± SD</th>
<th>( O_{s,a,t.} (%) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.L.</td>
<td>F</td>
<td>13-Jun-94</td>
<td>0.03</td>
<td>1.12 ± 0.2</td>
<td>0.42 ± 0.05</td>
<td>0.71 ± 0.22</td>
<td>0.38 ± 0.07</td>
<td>93 *</td>
</tr>
<tr>
<td>C.R.</td>
<td>M</td>
<td>26-Apr-94</td>
<td>0.13</td>
<td>1.29 ± 0.19</td>
<td>0.61 ± 0.06</td>
<td>0.67 ± 0.14</td>
<td>0.48 ± 0.04</td>
<td>97 *</td>
</tr>
<tr>
<td>D.H.</td>
<td>M</td>
<td>22-Apr-94</td>
<td>0.19</td>
<td>2.62 ± 0.16</td>
<td>1.01 ± 0.05</td>
<td>1.61 ± 0.17</td>
<td>0.39 ± 0.03</td>
<td>96</td>
</tr>
<tr>
<td>J.C.</td>
<td>M</td>
<td>29-Mar-94</td>
<td>0.19</td>
<td>1.22 ± 0.09</td>
<td>0.6 ± 0.08</td>
<td>0.63 ± 0.08</td>
<td>0.49 ± 0.05</td>
<td>93 *</td>
</tr>
<tr>
<td>V.V.</td>
<td>F</td>
<td>29-Dec-93</td>
<td>0.21</td>
<td>0.98 ± 0.18</td>
<td>0.49 ± 0.07</td>
<td>0.49 ± 0.12</td>
<td>0.5 ± 0.04</td>
<td>89 *</td>
</tr>
<tr>
<td>C.P.</td>
<td>F</td>
<td>22-Mar-94</td>
<td>0.22</td>
<td>1.45 ± 0.31</td>
<td>0.69 ± 0.14</td>
<td>0.76 ± 0.2</td>
<td>0.48 ± 0.04</td>
<td>98</td>
</tr>
<tr>
<td>B.F.</td>
<td>F</td>
<td>17-Apr-94</td>
<td>0.22</td>
<td>1.83 ± 0.34</td>
<td>0.73 ± 0.18</td>
<td>1.09 ± 0.2</td>
<td>0.4 ±  0.05</td>
<td>100 *</td>
</tr>
<tr>
<td>T.J.</td>
<td>M</td>
<td>06-Apr-94</td>
<td>0.22</td>
<td>1.95 ± 0.24</td>
<td>0.67 ± 0.09</td>
<td>1.28 ± 0.19</td>
<td>0.35 ± 0.03</td>
<td>96 *</td>
</tr>
<tr>
<td>N.D.</td>
<td>M</td>
<td>29-Oct-93</td>
<td>0.65</td>
<td>1.74 ± 0.09</td>
<td>0.69 ± 0.06</td>
<td>1.05 ± 0.09</td>
<td>0.4 ±  0.03</td>
<td>95</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>1.58</td>
<td>±0.51</td>
<td>±0.66</td>
<td>±0.92</td>
<td>±0.43</td>
<td>±0.06</td>
</tr>
</tbody>
</table>

* Denotes receiving oxygen therapy

Figure 7.15
Graph showing relationship between fractional inspiratory time \( (T_i/T_{TOT}) \) and age.

Figures 7.16a and 7.16b illustrate single breaths from two different infants. One breath showed a reduced \( T_i/T_{TOT} \). The other breath showed an increased \( T_i/T_{TOT} \) with shortening of the expiratory phase.
Figure 7.16a
A single breath obtained from a sleeping male infant, aged two months, with bronchiolitis. It shows a prolonged expiration ($T_e/T_{TOT} = 0.30$).

Figure 7.16b
A single breath obtained from a sleeping female infant, aged two months, with bronchiolitis. It shows a reduced $T_e/T_{TOT}$ value of 0.51.

It was possible that displacement measured by the optical sensor was related to volume changes in the lung. It was speculated that the slope of the displacement-time waveform obtained by the sensor could give an indication of respiratory airflow. This was because flow ($Q$) is defined as volume change ($V$) divided by time ($t$). The slope of the displacement-time curve was obtained by differentiating it. An example of such curves are shown in figures 7.17a and 7.17b. They represent the breathing patterns obtained from sleeping infants with bronchiolitis.

Figure 7.17a
Waveform resulting from differentiation of the displacement signal of a sleeping infant with bronchiolitis. Rapid rise to peak during expiration is seen at points 4 and 8.
Figure 7.17b
Waveform resulting from the differentiation of the displacement-time signal obtained from an infant with bronchiolitis. A rapid rise to the peak can be seen during expiration at point 4.

Inspiration occurred when these curves were positive and expiration when they were negative. Both show a rapid rise to the peak value during expiration. The sensor may therefore have detected the rapid rise to peak expiratory flow, known to occur in obstructive disease. A differentiated signal obtained from a healthy neonate is shown in figure 7.18. There was no rapid rise to the peak value during expiration. The waveform, in contrast to the children with bronchiolitis, was also more sinusoidal in shape.

Figure 7.18
Waveform resulting from differentiation of displacement signal obtained from the optical sensor in a healthy neonate.
7.5 Asthma

The transient nature and reversibility of asthma, the different patterns of progression and recovery of children and the varied times of presentation to hospital meant that this group of children studied was not homogeneous. The state of the children's asthma would have been influenced by the administration of medications, such as salbutamol sulfate (Ventolin), and receiving oxygen.

Respiratory rates were observed in 12 sleeping children, aged between 10 months and six years, as shown in Table 7.11. RR was on average 3.11 SDs above the mean RR for healthy children. Seventy-eight per cent (7/9) of the children aged less than three years had RRs that were greater than the 95th centile for healthy children. Due to the centile chart finishing at three years, children older than three years could not be included in this analysis. RR was inversely related to oxygen saturation ($r = -0.72$, $p < 0.05$, see figure 7.19).

Table 7.11 - Respiratory Rates in Sleeping Children with Asthma

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr.)</th>
<th>Days after admission into hospital</th>
<th>RR(a) (bpm)</th>
<th>Z-score (SD)</th>
<th>RR 95th centile (bpm)</th>
<th>RR(b) (bpm)</th>
<th>Time (min)</th>
<th>$O_2$ Sat. (%)</th>
<th>Medication ‡ Before (B) or After(A) Ventolin</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.K.</td>
<td>M</td>
<td>1.8</td>
<td>----</td>
<td>31</td>
<td>2.55</td>
<td>24.6</td>
<td>32</td>
<td>3</td>
<td>96</td>
<td>V (2), At, S, I</td>
</tr>
<tr>
<td>B.U.</td>
<td>M</td>
<td>1.3</td>
<td>----</td>
<td>49</td>
<td>7.71</td>
<td>25.6</td>
<td>52.4</td>
<td>5</td>
<td>91</td>
<td>V (2), S, P, Ab</td>
</tr>
<tr>
<td>X.Y.</td>
<td>F</td>
<td>5.8</td>
<td>1</td>
<td>29</td>
<td>3.63</td>
<td>27.8</td>
<td>10</td>
<td>93*</td>
<td>V (1), At, S, P</td>
<td></td>
</tr>
<tr>
<td>S.B.</td>
<td>M</td>
<td>4.2</td>
<td>2</td>
<td>30</td>
<td>4.28</td>
<td>32.1</td>
<td>17.5</td>
<td>91</td>
<td>V (2), S, P</td>
<td></td>
</tr>
<tr>
<td>T.H.</td>
<td>M</td>
<td>2.5</td>
<td>0</td>
<td>27</td>
<td>2.81</td>
<td>23.8</td>
<td>26</td>
<td>6</td>
<td>94</td>
<td>V (1.5), S, I</td>
</tr>
<tr>
<td>G.S.</td>
<td>F</td>
<td>1.7</td>
<td>1</td>
<td>24</td>
<td>0.54</td>
<td>24.8</td>
<td>23.6</td>
<td>6</td>
<td>98</td>
<td>V (3), At, S</td>
</tr>
<tr>
<td>C.S.</td>
<td>M</td>
<td>6.0</td>
<td>0</td>
<td>36</td>
<td>6.68</td>
<td>35.3</td>
<td>9</td>
<td>94*</td>
<td>V (1), At, S, P</td>
<td></td>
</tr>
<tr>
<td>C.I.</td>
<td>M</td>
<td>1.3</td>
<td>1</td>
<td>35</td>
<td>3.7</td>
<td>25.6</td>
<td>33.1</td>
<td>4.5</td>
<td>95</td>
<td>V (3), S, P</td>
</tr>
<tr>
<td>T.W.</td>
<td>M</td>
<td>1.0</td>
<td>0</td>
<td>32</td>
<td>2.84</td>
<td>26.3</td>
<td>35.1</td>
<td>4.5</td>
<td>98</td>
<td>V (2), S</td>
</tr>
<tr>
<td>J.W.</td>
<td>F</td>
<td>1.0</td>
<td>3</td>
<td>24</td>
<td>0.54</td>
<td>26.3</td>
<td>25</td>
<td>2</td>
<td>----</td>
<td>V (3)</td>
</tr>
<tr>
<td>J.R.</td>
<td>M</td>
<td>1.2</td>
<td>----</td>
<td>26</td>
<td>1.12</td>
<td>25.8</td>
<td>28.2</td>
<td>6</td>
<td>----</td>
<td>V (2), At, S</td>
</tr>
<tr>
<td>A.Z.</td>
<td>F</td>
<td>0.9</td>
<td>2</td>
<td>27</td>
<td>1.03</td>
<td>26.8</td>
<td>26</td>
<td>11</td>
<td>----</td>
<td>V, S, P</td>
</tr>
</tbody>
</table>

* Denotes receiving oxygen.

† RR (a) - Respiratory rate measured for two thirty second periods.

RR (b) - Respiratory rate measured for total test period.

RR (95th centile) - Respiratory rate corresponding to the 95th centile for RR for total test period.

‡ Medication abbreviations: V - salbutamol sulfate (Ventolin), At - ipratropium bromide (Atrovent), S - steroid treatment; P - Paracetamol (Panadol), Ab - antibiotic, I - sodium cromoglycate (Intal).

Numbers in brackets indicate time between Ventolin treatment in hours.
Table 7.12 summarises the RRs observed in awake children with asthma, aged from 1.0 to 16 years. A more comprehensive table of results can be found in Appendix 11. There was a marked increase in RR, with a mean Z-score for all awake children with asthma of 2.00. The increase was highest in children aged from 1.0 to 6.99 years, with the RR increased to 3.03 SDs above predicted. The mean Z-scores ranged from 1.5 to 1.8 in the older groups (7.0 - 9.9 yrs, 10.0 - 12.99 years, and 13.0 - 16.99 years). There were no significant differences in Z-scores between the groups, except between children aged from 1.0 to 6.99 years and from 13.0 to 16.99 years (p = 0.05, unpaired t test).

<table>
<thead>
<tr>
<th>Age Range (mean) yr</th>
<th>n</th>
<th>Days after admission to hospital ±SD</th>
<th>RR(a) (bpm) ±1SD</th>
<th>Range of RR (a) (bpm)</th>
<th>Z-score of RR(a) (SD)</th>
<th>RR(b) (bpm) ±SD</th>
<th>Diff. RR (a) - (b) ±SD</th>
<th>Test Time (min)</th>
<th>O₂ sat. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 - 6.7 (4.4)</td>
<td>12 (8m, 4f)</td>
<td>2.3 ± 2.2</td>
<td>35.5 ±10.3</td>
<td>22 - 56</td>
<td>3.03</td>
<td>34.1 ±9.2</td>
<td>1.43 ±1.60</td>
<td>4.4</td>
<td>94.2±2.19</td>
</tr>
<tr>
<td>7.2 - 9.8 (8.5)</td>
<td>11 (9m, 2f)</td>
<td>1.8 ± 1.7</td>
<td>25.6 ±7.5</td>
<td>11 - 38</td>
<td>1.60</td>
<td>25.3 ±7.6</td>
<td>0.3 ±1.87</td>
<td>5.9</td>
<td>96.4±2.17</td>
</tr>
<tr>
<td>10.2 - 12.8 (11.5)</td>
<td>14 (9m, 5f)</td>
<td>1.7 ± 1.5</td>
<td>24.2 ±5.0</td>
<td>18 - 34</td>
<td>1.80</td>
<td>23.6 ±7.0</td>
<td>0.51 ±3.20</td>
<td>5.5</td>
<td>95.5±1.61</td>
</tr>
<tr>
<td>13.1 - 16.6 (14.3)</td>
<td>11 (8m, 3f)</td>
<td>2 ± 1.5</td>
<td>20.5 ±4.3</td>
<td>14 - 26</td>
<td>1.51</td>
<td>21.5 ±4.0</td>
<td>-1.01 ±1.93</td>
<td>6.3</td>
<td>95.6±2.13</td>
</tr>
<tr>
<td>1.0 - 16.6</td>
<td>48 (34m, 14f)</td>
<td></td>
<td></td>
<td></td>
<td>2.00</td>
<td></td>
<td>0.50 ±2.15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* RR (a) - Respiratory rate measured for two 30 s periods.
RR (b) - Respiratory rate measured for total test period.
Seventy-five per cent (9/12) of awake children with asthma aged from 1.0 to 6.7 years had RRs over the 95th centile for healthy children. Thirty-six per cent (4/11) of awake children with asthma, aged from 7.0 to 9.99 years, and 43% (6/14) aged from 10.0 to 12.99 years, had RRs above the 95th centile for healthy children. Therefore, a large proportion of children older than 7.0 years did not have markedly increased RRs. The centile charts finished at 13.0 years of age, so the RR of children aged 13.0 and older could not be compared with the 95th centile for healthy children.

RR was measured for two thirty second periods was similar to that measured for the total test period. The SD of the difference between these two methods was less than two in all age groups, except the children aged from 10.0 to 12.99 years. For all awake children with asthma, the 95% limit of agreement between these two different methods of measuring RR was -3.8 to 4.8 bpm. This was larger than the 95% limit of agreement for healthy awake children which was -2.9 to 3.2 bpm.

No statistically significant correlation was found between arterial oxygen saturation and the Z-score for RR (r = -0.31, not significant, n = 32, see figure 7.24). The data of the eleven children who were receiving oxygen were excluded from this analysis while five children did not have their oxygen saturation levels measured. An inverse relationship existed between PEFR (as per cent of predicted value) and the Z-score for RR in 20 children who had their PEFR measured (r = -0.45, p < 0.05, n = 20, see figure 7.21). The values for PEFR measured in twenty children are listed in Appendix 11.

![Figure 7.20](image-url)

**Figure 7.20**
Relationship between peak expiratory flow rate (as a percentage of the predicted value) and RR (Z-Score).
Table 7.13 shows the $T_I$, $T_E$, $T_{TOT}$ and $T_I/T_{TOT}$ values obtained by the optical sensor in 25 awake children with asthma. A mean fractional inspiratory time ($T_I/T_{TOT}$) of 0.40 (±0.04) observed in subjects with asthma was not significantly different to the value of 0.41 (±0.03) ($p = 0.10$, unpaired $t$ test). Age did not affect the $T_I/T_{TOT}$ values in the healthy subjects. Therefore, all awake healthy subjects aged from two to twenty-three years were used as a comparison (n=46).

Table 7.13 - Indices of the Respiratory Cycle in Awake Children and Adolescents with Acute Asthma

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Days in hospital</th>
<th>$T_I$ ± SD (s)</th>
<th>$T_E$ ± SD (s)</th>
<th>$T_{TOT}$ ± SD (s)</th>
<th>$T_I/T_{TOT}$ ± SD</th>
<th>O2 sat. (%)</th>
<th>PEFR (L/min.)</th>
<th>PEFR % pred.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.C.</td>
<td>M</td>
<td>7.21</td>
<td>3</td>
<td>0.90 ± 0.25</td>
<td>1.36 ± 0.39</td>
<td>2.26 ± 0.60</td>
<td>0.4 ± 0.04</td>
<td>98</td>
<td>280</td>
<td>113</td>
</tr>
<tr>
<td>M.R.</td>
<td>M</td>
<td>7.61</td>
<td>1</td>
<td>1.01 ± 0.15</td>
<td>1.25 ± 0.11</td>
<td>2.25 ± 0.19</td>
<td>0.44 ± 0.04</td>
<td>94</td>
<td>120</td>
<td>44</td>
</tr>
<tr>
<td>L.B.</td>
<td>M</td>
<td>8.45</td>
<td>0</td>
<td>0.88 ± 0.07</td>
<td>1.37 ± 0.17</td>
<td>2.49 ± 0.14</td>
<td>0.35 ± 0.04</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R.D.</td>
<td>F</td>
<td>9.75</td>
<td>1</td>
<td>0.99 ± 0.09</td>
<td>1.63 ± 0.15</td>
<td>2.62 ± 0.17</td>
<td>0.38 ± 0.03</td>
<td>100</td>
<td>250</td>
<td>90</td>
</tr>
<tr>
<td>P.E.</td>
<td>F</td>
<td>9.83</td>
<td>6</td>
<td>1.04 ± 0.23</td>
<td>1.22 ± 0.21</td>
<td>2.26 ± 0.38</td>
<td>0.46 ± 0.05</td>
<td>98</td>
<td>340</td>
<td>106</td>
</tr>
<tr>
<td>L.H.</td>
<td>F</td>
<td>10.76</td>
<td>5</td>
<td>0.77 ± 0.09</td>
<td>0.98 ± 0.18</td>
<td>1.75 ± 0.23</td>
<td>0.44 ± 0.03</td>
<td>98</td>
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<td></td>
</tr>
<tr>
<td>D.W.</td>
<td>M</td>
<td>11.02</td>
<td>1</td>
<td>0.86 ± 0.10</td>
<td>1.14 ± 0.19</td>
<td>2 ± 0.18</td>
<td>0.43 ± 0.03</td>
<td>94</td>
<td>300</td>
<td>96</td>
</tr>
<tr>
<td>H.D.</td>
<td>M</td>
<td>11.4</td>
<td>1</td>
<td>1 ± 0.17</td>
<td>1.35 ± 0.20</td>
<td>2.34 ± 0.26</td>
<td>0.42 ± 0.06</td>
<td>95</td>
<td>270</td>
<td>80</td>
</tr>
<tr>
<td>J.R.</td>
<td>F</td>
<td>11.5</td>
<td>0</td>
<td>1.2 ± 0.18</td>
<td>1.96 ± 0.16</td>
<td>3.16 ± 0.21</td>
<td>0.38 ± 0.05</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.L.</td>
<td>M</td>
<td>11.7</td>
<td>0</td>
<td>1.18 ± 0.31</td>
<td>1.5 ± 0.20</td>
<td>2.67 ± 0.37</td>
<td>0.43 ± 0.07</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.B.</td>
<td>M</td>
<td>11.74</td>
<td>1</td>
<td>1.65 ± 0.34</td>
<td>3.16 ± 0.65</td>
<td>3.12 ± 0.73</td>
<td>0.35 ± 0.04</td>
<td>96</td>
<td>300</td>
<td>84</td>
</tr>
<tr>
<td>B.R.</td>
<td>M</td>
<td>11.85</td>
<td>3</td>
<td>1.04 ± 0.13</td>
<td>1.58 ± 0.29</td>
<td>2.62 ± 0.37</td>
<td>0.4 ± 0.04</td>
<td>96</td>
<td>330</td>
<td>96</td>
</tr>
<tr>
<td>C.O.</td>
<td>M</td>
<td>11.97</td>
<td>1</td>
<td>1.04 ± 0.13</td>
<td>1.84 ± 0.28</td>
<td>2.88 ± 0.29</td>
<td>0.36 ± 0.05</td>
<td>96</td>
<td>260</td>
<td>77</td>
</tr>
<tr>
<td>S.D.</td>
<td>M</td>
<td>12.15</td>
<td>1</td>
<td>0.95 ± 0.13</td>
<td>1.66 ± 0.22</td>
<td>2.62 ± 0.30</td>
<td>0.36 ± 0.03</td>
<td>94</td>
<td>260</td>
<td>70</td>
</tr>
<tr>
<td>N.F.</td>
<td>M</td>
<td>13.67</td>
<td>2</td>
<td>1.28 ± 0.18</td>
<td>1.9 ± 0.26</td>
<td>3.18 ± 0.19</td>
<td>0.4 ± 0.06</td>
<td>95</td>
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<td></td>
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<tr>
<td>M.A.</td>
<td>M</td>
<td>14.07</td>
<td>1</td>
<td>1.06 ± 0.09</td>
<td>1.91 ± 0.22</td>
<td>2.97 ± 0.27</td>
<td>0.36 ± 0.03</td>
<td>96</td>
<td>280</td>
<td>73</td>
</tr>
<tr>
<td>S.M.</td>
<td>M</td>
<td>14.6</td>
<td>1</td>
<td>1.23 ± 0.41</td>
<td>1.95 ± 0.58</td>
<td>3.17 ± 0.95</td>
<td>0.38 ± 0.05</td>
<td>96</td>
<td>301</td>
<td>67</td>
</tr>
<tr>
<td>M.H.</td>
<td>M</td>
<td>15.04</td>
<td>1</td>
<td>1.08 ± 0.30</td>
<td>1.85 ± 0.39</td>
<td>2.92 ± 0.65</td>
<td>0.37 ± 0.04</td>
<td>91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.B.</td>
<td>M</td>
<td>15.22</td>
<td>1</td>
<td>0.93 ± 0.14</td>
<td>1.14 ± 0.32</td>
<td>2.07 ± 0.42</td>
<td>0.46 ± 0.05</td>
<td>97</td>
<td>520</td>
<td>87</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td>1.6</td>
<td>1.62 ± 0.19</td>
<td>2.60 ± 0.40</td>
<td>0.40</td>
<td>94</td>
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<td></td>
</tr>
</tbody>
</table>

| Children receiving oxygen therapy |

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Days in hospital</th>
<th>$T_I$ ± SD (s)</th>
<th>$T_E$ ± SD (s)</th>
<th>$T_{TOT}$ ± SD (s)</th>
<th>$T_I/T_{TOT}$ ± SD</th>
<th>O2 sat. (%)</th>
<th>PEFR (L/min.)</th>
<th>PEFR % pred.</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D.</td>
<td>F</td>
<td>5.79</td>
<td>0</td>
<td>0.72 ± 0.06</td>
<td>0.68 ± 0.07</td>
<td>1.4 ± 0.1</td>
<td>0.52 ± 0.03</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.S.</td>
<td>M</td>
<td>6.7</td>
<td>0</td>
<td>0.81 ± 0.07</td>
<td>1.11 ± 0.12</td>
<td>1.91 ± 0.17</td>
<td>0.42 ± 0.02</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.F.</td>
<td>M</td>
<td>9.14</td>
<td>1</td>
<td>0.73 ± 0.13</td>
<td>0.83 ± 0.16</td>
<td>1.56 ± 0.26</td>
<td>0.47 ± 0.05</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.W.</td>
<td>F</td>
<td>13.82</td>
<td>2</td>
<td>0.87 ± 0.07</td>
<td>1.15 ± 0.1</td>
<td>2.03 ± 0.11</td>
<td>0.43 ± 0.03</td>
<td>92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.C.</td>
<td>M</td>
<td>9.83</td>
<td>1</td>
<td>0.78 ± 0.16</td>
<td>1.08 ± 0.24</td>
<td>1.86 ± 0.28</td>
<td>0.42 ± 0.08</td>
<td>96</td>
<td>140</td>
<td>45</td>
</tr>
<tr>
<td>L.A.</td>
<td>F</td>
<td>10.72</td>
<td>4</td>
<td>0.88 ± 0.11</td>
<td>1.47 ± 0.28</td>
<td>2.35 ± 0.32</td>
<td>0.38 ± 0.05</td>
<td>97</td>
<td>200</td>
<td>64</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td>1.6</td>
<td>1.05 ± 0.07</td>
<td>1.85 ± 0.34</td>
<td>0.44</td>
<td>94</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The values for $T_1/T_{TOT}$ in the awake subjects with asthma, who were not receiving oxygen, ranged from 0.35 to 0.46. Amongst these subjects, 31.6% (6/19) had a $T_1/T_{TOT}$ value equal to or less than 0.37. In contrast, 10.9% (5/46) of healthy awake subjects had a $T_1/T_{TOT}$ value less than or equal to 0.37. This suggests the distribution of data in the group of subjects with asthma was skewed. Figures 7.21 and 7.22 show single breaths obtained from two different individuals with acute asthma. One shows a prolonged expiration while the other has a normal time for expiration.

![Figure 7.21](image1)  
Figure 7.21  
A breath obtained from a 11 year old boy with acute asthma, showing a prolonged expiration ($T_1/T_{TOT} = 0.31$)

![Figure 7.22](image2)  
Figure 7.22  
A breath obtained from an eight year old boy with acute asthma, showing a normal length of expiration ($T_1/T_{TOT} = 0.40$)

Using the data from Table 7.13 and excluding children who were receiving oxygen, no significant relationship between $T_1/T_{TOT}$ and oxygen saturation was found ($r = +0.14$, $n = 19$, not significant). There was also no significant correlation between per cent predicted PEFR and $T_1/T_{TOT}$ ($r = +0.20$, $n = 13$, not significant). Children receiving oxygen had a $T_1/T_{TOT}$ value of 0.44 (±0.05) compared to the mean value of 0.40 (±0.05) in those who were not (p = 0.08, not significant, unpaired $t$ test). $T_{TOT}$ was inversely related to $T_1/T_{TOT}$ ($r = -0.63$, $n = 25$, $p < 0.01$). This suggests that when $T_{TOT}$ is smaller and RR is larger (since RR = $60/T_{TOT}$), $T_1/T_{TOT}$ will also tend to be larger. There was also a relationship between $T_1$ and $T_E$ ($r = +0.87$, $n = 25$, $p < 0.01$).

In eight children, $FEV_{1.0}$ was measured at the same time their breathing pattern was being observed (see Table 7.14). Four children were tested twice, so that 12 measurements were made in total. Although not significant, there was a suggestion of a correlation between $FEV_{1.0}$ (as a percentage of predicted) and $T_1/T_{TOT}$ ($r = +0.43$, $n = 12$, not significant, see figure...
7.23). There was no significant relationship between the Z-Score for RR and FEV\textsubscript{1.0} values (r = -0.19, n=12).

![Graph showing relationship between FEV\textsubscript{1.0} (% pred.) and T\textsubscript{1} / T\textsubscript{TOT.}](image)

**Table 7.14 - Respiratory Timing Indices and Lung Function Parameters in Awake Children with Asthma (including FEV\textsubscript{1.0} and PEFR)**

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Day of Illness</th>
<th>RR (a) * (bpm)</th>
<th>RR (b) * (bpm)</th>
<th>Time (min.)</th>
<th>PEFR (L/min.)</th>
<th>PEFR % pred.</th>
<th>FEV\textsubscript{1.0} (L)</th>
<th>FEV\textsubscript{1.0} % pred.</th>
<th>T\textsubscript{1} / T\textsubscript{TOT} ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.C.</td>
<td>M</td>
<td>9.83</td>
<td>1</td>
<td>34</td>
<td>4.15</td>
<td>33.6</td>
<td>4.5</td>
<td>140</td>
<td>45</td>
<td>0.69</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>22</td>
<td>0.46</td>
<td>23.2</td>
<td>7</td>
<td>120</td>
<td>39</td>
<td>0.71</td>
<td>34</td>
</tr>
<tr>
<td>D.W.</td>
<td>M</td>
<td>11.02</td>
<td>1</td>
<td>30</td>
<td>3.56</td>
<td>26.6</td>
<td>3.5</td>
<td>300</td>
<td>96</td>
<td>1.49</td>
<td>73</td>
</tr>
<tr>
<td>J.B.</td>
<td>M</td>
<td>11.74</td>
<td>18</td>
<td>0.3</td>
<td>12.2</td>
<td>8</td>
<td>300</td>
<td>84</td>
<td>1.28</td>
<td>51</td>
<td>0.35 ± 0.04</td>
</tr>
<tr>
<td>C.O.</td>
<td>M</td>
<td>12</td>
<td>1</td>
<td>24</td>
<td>1.59</td>
<td>21</td>
<td>3</td>
<td>260</td>
<td>77</td>
<td>1.49</td>
<td>65</td>
</tr>
<tr>
<td>S.D.</td>
<td>M</td>
<td>12.2</td>
<td>1</td>
<td>29</td>
<td>2.71</td>
<td>28.1</td>
<td>10</td>
<td>260</td>
<td>70</td>
<td>1.21</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>22</td>
<td>1.14</td>
<td>21.7</td>
<td>10</td>
<td>370</td>
<td>100</td>
<td>2.35</td>
<td>89</td>
</tr>
<tr>
<td>D.B.</td>
<td>M</td>
<td>16.6</td>
<td>19</td>
<td>1.15</td>
<td>24</td>
<td>9</td>
<td>520</td>
<td>87</td>
<td>3.22</td>
<td>64</td>
<td>0.46 ± 0.05</td>
</tr>
<tr>
<td>B.R.</td>
<td>M</td>
<td>11.9</td>
<td>OPD †</td>
<td>15</td>
<td>-0.52</td>
<td>15.3</td>
<td>7.5</td>
<td>330</td>
<td>96</td>
<td>1.78</td>
<td>78</td>
</tr>
<tr>
<td>L.A.</td>
<td>F</td>
<td>10.7</td>
<td>1</td>
<td>24</td>
<td>1.55</td>
<td>23.8</td>
<td>4.5</td>
<td>260</td>
<td>83</td>
<td>0.92</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPD †</td>
<td>23</td>
<td>1.25</td>
<td>20.3</td>
<td>6</td>
<td>340</td>
<td>109</td>
<td>1.73</td>
<td>88</td>
</tr>
</tbody>
</table>

* RR (a) - RR measured over two thirty second periods.
RR (b) - RR measured over total test period.
† OPD denotes tested as an outpatient.

Changes in RR in children who were tested twice are shown in figures 7.24 and 7.25. A detailed table of these results is presented in Appendix 12. There was little change in RR in children who were tested on consecutive days (see figure 7.24). However, there was a reduction in RR in all subjects, except one, who were tested at least two days apart (see figure 7.25).
Figure 7.24
Changes in respiratory rate in children with asthma observed on consecutive days.

Figure 7.25
Changes in respiratory rate occurring in children with asthma observed over two to seven days.

Figure 7.26 illustrates the changes in the fractional inspiratory time in awake children tested on two occasions. In two children there was an increase in $T_1 / T_{TOT}$ (0.06 and 0.07). The other children showed a reduction or no change in $T_1 / T_{TOT}$. This could be associated with lack of improvement in their asthma or possibly due to the oxygen therapy two of these children received. Figures 7.27a and 7.27b show single breaths obtained from a 12 year old boy with asthma on two occasions. The mean $T_1 / T_{TOT}$ for ten breaths for this subject increased from 0.36 ($\pm 0.03$) to 0.43 ($\pm 0.04$) over a four day period. Simultaneously, his FEV$_{1.0}$ (per cent of predicted) increased from 46% to 89%.

Figure 7.26
Changes in fractional inspiratory time ($T_1 / T_{TOT}$) in awake children with asthma. The children were tested on two occasions. Dashed lines indicate the subjects who were receiving oxygen during the first test. The number of days between tests is also shown.
Figures 7.27a and 7.27b show a decrease in RR and increase in $T_i / T_{TOT}$ that occurred as a girl, aged 12 years, recovered from an acute episode of asthma. At the same time, her lung function improved as shown by the increases in the PEFR and FEV$_{1.0}$ values. In some cases, therefore, $T_i / T_{TOT}$ increased with improving lung function. In contrast, the fractional inspiratory time ($T_i / T_{TOT}$) of a boy, aged nine years, was 0.47 when his RR was 38 bpm during an acute episode of asthma (see figure 7.29) and decreased to 0.42 when his RR had reduced to 22 bpm with recovery.

Figure 7.28a
Changes in respiratory rate and FEV$_{1.0}$ which occurred in a 12 year old girl recovering from an acute episode of asthma.

Figure 7.28b
Changes in fractional inspiratory time and PEFR which occurred in a 12 year old girl recovering from an acute episode of asthma.
Figure 7.29
Breathing pattern of a boy, aged nine years, during an acute episode of asthma. He had an elevated RR of 38 bpm.
Part IV

Discussion
Chapter 8
Respiratory Rate and the Respiratory Cycle in Childhood in Health and Disease

8.1 Introduction

The results obtained in this study were dependent upon the reliability of the optical sensor used to record breathing patterns. Comparison of this sensor with other methods of observing breathing patterns showed this sensor to be appropriate in the investigation of respiratory rate in children. Respiratory rate, for several reasons, declined rapidly during the early years of life and after this decreased gradually to adult values. There was a marked increase in RR in children with pneumonia, CF and asthma, with inconsistent changes in bronchiolitis. Both the severity of the cases studied and the pathophysiological mechanisms associated with each disease could account for these variations. The pathophysiological mechanisms associated with each disease could also account for the fractional inspiratory times \( T_1/T_{TOT} \) observed.

8.2 Optical Sensor

The optical sensor gave values for respiratory rate that were similar to those obtained by visual observation. The waveform shape of the breathing pattern was similar to that of the respiratory inductive plethysmograph (Respirac®) and water sealed spirometer in relation to \( T_1 \) and \( T_E \). The 95% limits of agreement between the pneumotachograph and optical sensor for \( T_1/T_{TOT} \) was -0.07 to 0.09. The differences may have been increased by the inability to know the exact breaths which the Sensor Medics 2600 system had analysed. This range is greater than the 95% limit of agreement of -0.016 to 0.064 between a pneumotachograph and Respirac® observed by Stick et al. (1992).

Digit preference (i.e. the tendency to select round numbers) and bias towards choosing a value closer to "normal" are limitations of measuring RR by visual observation (Hanning and Spence, 1982). The sensor could therefore provide accurate measures of respiratory rate, without the influence of human error, for creating the reference ranges.

Hanning and Spence (1982) have described twelve characteristics of the "ideal" respiratory monitor (see Table 8.1). The optical sensor fulfilled eight of these. The sensor was unable to give an accurate volume measurement since it did not measure the rib cage contribution to breathing. The sensor observed apnoea and hypopnoea, but in its present form
would be unable to provide any indication of airway obstruction or thoracoabdominal
incoordination.

Table 8.1 - The Requirements of the Ideal Respiratory Monitor
(Hanning and Spence, 1982)

<table>
<thead>
<tr>
<th>Attributes Possessed by Optical Sensor</th>
<th>Attributes Lacking in Optical Sensor</th>
</tr>
</thead>
<tbody>
<tr>
<td>No resistance to respiration</td>
<td>Accurate stable volume measurement</td>
</tr>
<tr>
<td>Minimal deadspace</td>
<td>Easy calibration</td>
</tr>
<tr>
<td>No influence on respiratory patterns</td>
<td>Unaffected by gas composition and</td>
</tr>
<tr>
<td>Robust</td>
<td>humidity</td>
</tr>
<tr>
<td>Sterilisable</td>
<td>Provide warnings of:</td>
</tr>
<tr>
<td>Easily Applied</td>
<td>- airway obstruction</td>
</tr>
<tr>
<td>Acceptable to subject and user</td>
<td>- thoracoabdominal incoordination</td>
</tr>
<tr>
<td>(no need for electrical isolation, portable)</td>
<td></td>
</tr>
<tr>
<td>Potentially inexpensive</td>
<td></td>
</tr>
<tr>
<td>Provide warnings of:</td>
<td></td>
</tr>
<tr>
<td>- apnoea</td>
<td></td>
</tr>
<tr>
<td>- hypopnoea</td>
<td></td>
</tr>
</tbody>
</table>

Most of the advantages of this sensor, as outlined in Table 8.1, make it very appropriate
for investigating breathing patterns. These include the ease with which it could be applied,
particularly to a paediatric subject, and minimal deadspace and resistance imposed on
respiration. Using an optical fibre to detect abdominal motion also had a number of
advantages. No electrical wires were attached to the children. There was therefore no risk of
electric shock or need to isolate an electric source. The non-laser light used could not harm
the children (e.g. cause burns). However, allergic reactions to adhesive tape needed to be
carefully observed. Another advantage of the sensor was its compact size, which made it very
portable. There is potential for the sensor to receive its light source from a battery powered
light. This would reduce its size and increase its portability further. The cost of producing the
sensor is potentially quite low.

The use of a face mask has been found to decrease RR and increase tidal volume
(Gilbert et al., 1972). This could be due to stimulation of trigeminal receptors on the face. An
increase in awareness of breathing also occurs with a face mask (Western and Patrick, 1987).
The face mask may also increase dead space and resistance to breathing and change the balance
between nasal and oral breathing (Cohn et al., 1982; Western and Patrick, 1988). The optical
sensor could be placed on the abdomen and imposed little resistance to respiratory excursions. Therefore, it avoided the problem of altering the breathing pattern associated with using a face mask or increasing elastic resistance with a band surrounding the chest.

8.3 Healthy Children
8.3.1 Respiratory Rates

Measuring respiratory rate over two thirty second periods was similar to the RR measured for the total test period (approximately five minutes) with the 95% limit of agreement between the two methods for healthy awake subjects being -2.9 to 3.2 bpm. These results are in agreement with Simoes et al. (1991) who concluded that one minute's counting of respiration, either at a stretch or in two blocks of thirty second intervals, is probably the optimum method for counting RR in a clinical situation.

The RR differed slightly when measured on the same awake subjects on different days. Difficulty controlling external environmental stimuli during, and varying activities of the subjects preceding the breathing study, may account for this. The mean of the differences in RR measured on the two occasions was 1.0 bpm in school children and 1.5 bpm in pre-school aged children. The 95% coefficient of repeatability was 3.7 bpm for school aged children and 4.0 bpm for pre-school aged children.

The large intersubject variability of RR and similarity of RR in the same individual measured twice supports the idea that each individual has a distinct breathing pattern (personality of ventilation) (Shea and Guz, 1992). This may be related to a variation in the set-point of the chemical control of breathing. Subjects who breathe slowly and deeply have a lower ventilatory sensitivity to CO₂ (Shea and Guz, 1992).

A sudden change in temperature (such as when a person is suddenly immersed in cold water) or other noxious stimuli results in a gasp and change in breathing pattern (Cooper and Veale, 1986). It is possible, therefore, that placement of a stethoscope on a child's chest could have altered the children's breathing pattern (Cooper and Veale, 1986). The RRs obtained in the present study differed in certain age groups to those observed by Rusconi et al. (1994) with a stethoscope. For example, the mean RR obtained in the present study for infants, aged six to twelve months and observed in behavioural quiet sleep, was 24.1 (±2.81) bpm. In contrast, Rusconi et al. (1994) found the RR for this age to be 29.6 (±7.0) bpm. However, Rusconi et al. (1994) found the RR in children aged less than six months when asleep to be similar to the present study (see Table 1.3 and Table 6.2).
RRs were found to be higher in awake infants in the present study when compared to the findings of Rusconi et al. (1994). For example, in the present study infants aged 0 - 5.99 months had a mean RR of 59.3 (± 9.82) bpm. Rusconi et al. (1994) found infants, aged 0 - 1.9 months, to have a lower mean RR of 48.0 (± 9.1) bpm. The agitation caused by attaching the optical sensor onto very young infants may account for this difference. This effect may have been minimised by the age of one year, as both studies observed similar RRs in awake children older than one year. The present study found the RR for awake children aged two to three years to be 26.7 (± 2.87). Rusconi et al. (1994) found children aged from 2.0 to 2.5 and 2.5 to 3.0 years to have RR of 30.0 (± 6.2) and 27.1 (± 4.1) bpm respectively.

Respiratory rates measured by Marks, South and Carlin (1993) were very similar to the present study with very little differences in the values obtained. For example, the present study found the mean RR to be 26.7 bpm in awake and 19.8 bpm in sleeping children, aged 2.0 - 2.99 years. Marks, South and Carlin (1993) found the RR to be 27 bpm in awake and 20 bpm in sleeping children of the same age. Both studies used respiratory sensors rather than the placement of a stethoscope on the chest to measure respiratory rate. While not allowing for a rest period, Marks, South and Carlin (1993) waited until the children's breathing patterns appeared regular. In contrast to the current study, Marks, South and Carlin (1993) also used data obtained from children with a history of respiratory disease to create their reference ranges.

Both studies also involved close contact with the children. This is a limitation since respiratory rates could have been altered due to a stranger effect, as the researchers were not known to the children. This also led to some children refusing to participate in both studies. The present study had some strengths absent in the study by Marks, South and Carlin (1993). Marks, South and Carlin (1993) used a thermistor which may have drawn attention to breathing and possibly stimulated facial trigeminal receptors. However, the thermistor was advantageous in other respects, since it required no manipulation of clothing and its readings were not affected by movement artefact. One reason for both of these studies determining similar RRs would be that the populations studied were Australian. Birth weights, nutrition, activity levels, genetic and other factors can affect RR (Berman, Simoes and Lanata, 1991).

The RR values measured in this study for awake children aged four years and older were lower than those measured in children from a paediatric emergency department (Hooker et al., 1992). This would be due to the increased stresses associated with an emergency department and the presence of non-respiratory illnesses within this population. Children aged
less than two years had higher RRs in the present study compared to Hooker et al. (1992). This could be explained by the agitation caused by placement of the optical sensor on the children's chest. Non-specific stimuli are believed to have a larger effect on breathing and its variability in younger children (Henderson-Smart, 1994).

It was difficult to make a comparison of values for young children with the study by Iliff and Lee (1952). They did not make a differentiation between sleep states in children aged up to 18 months and did not note whether the children were awake or asleep between the ages of 18 months and three years. The values for the older children, aged three and above, were very similar to the present study. Iliff and Lee (1952) found the RR in awake six year old children to be 21 (± 3) bpm, while the present study found a RR of 20.4 (± 3.62) bpm. The children were unaware their RR was being observed, which is an advantage of the study by Iliff and Lee (1952).

Ten sleeping neonates were found to have a mean RR of 41.4 (±4.09) bpm in the current study. This differed to the findings of Cross (1949) who observed a RR of 28.64 (± 5.20) bpm and Cook et al. (1955) who observed a RR of 33.8 (±6.57) bpm in neonates. The results were more similar to the findings of Bolton and Herman (1974) and Hathorn (1974) who obtained RRs of 46.4 (±11.0) bpm and 39.5 bpm during quiet sleep respectively. These latter two studies measured RR closer to feeds and periods of active sleep. This was also the case in the present study which may account for the similar RRs obtained.

The mean RR observed in awake teenagers and young adults was 14.2 (±4.17) bpm in the current study. This was less than that obtained by most other published studies. For example, Tobin et al. (1983a) found RR to be 16.7 (±1.7) bpm in subjects aged between 20 and 50 years using a respiratory inductive plethysmograph. The values obtained were, however, similar to the RR obtained by Shock and Soley (1939) for 18 to 27 year old subjects.

Centile curves for RR were obtained by smoothing the raw centiles with polynomial equations as outlined in chapter 4. This allowed the curves to show smooth changes with growth ignoring random fluctuations. While cut-off values for RR are appropriate in the examination of children with acute disease, they are inefficient ways of presenting data. Centile curves may prove helpful in the first few months of life. A rapid decline in RR limits the use of cut off values to define normality (Rusconi et al., 1994).

The curves obtained from the present study have certain advantages over centile curves previously reported in the literature. Iliff and Lee (1952) did not discriminate between whether children aged between 18 months and three years were awake or asleep. Marks, South and
Carlin (1993) created 95% reference ranges for children aged from one to seven years. The study by Rusconi et al. (1994) covered the age range from birth to three years and used a stethoscope to obtain this data. The age of children in these latter two studies are not as comprehensive as in the present study.

A decrease in the variability of RR between individuals was observed with increasing age. The weakening and disappearance of reflexes (such as the Hering-Breuer reflex) and maturation of neuronal connections occur during infancy. These may occur at different rates in children accounting for the variability in RR (Rigatto, 1989; Rusconi et al., 1994). The haemoglobin dissociation curve changes as foetal haemoglobin is replaced by adult haemoglobin. This would affect oxygen delivery to tissues (Rusconi et al., 1994). This may also account for the variability of RR in young children, since this change may occur at different rates.

There was a rapid decline in RR up to about three years of age in awake children and up to one year of age in sleeping children. Changes in the central neurogenesis of the breathing rhythm could account for this, such as the inspiratory-expiratory phase-switching mechanism (Polgar and Weng, 1979). Alternatively, changes in ventilatory drive caused by peripheral afferents (such as lung receptors and arterial chemoreceptors) could account for RR changes with age (Jammes et al., 1979). In healthy humans, the partial pressure of O\textsubscript{2} decreases in arterial blood with age but the partial pressure of CO\textsubscript{2} rises. Such variations in arterial blood composition could modify ventilatory drive via chemoreceptor afferents and have an effect on RR (Jammes et al., 1979).

Alternatively, the respiratory centres may detect changes that occur in the mechanical properties of the lung with development, such as changes in compliance and resistance (Jammes et al., 1979). The shape of the lung resistance versus age curve and RR versus age curve are very similar. This suggests decreases in lung resistance may play some role in the decreases in RR with age (Jammes et al., 1979). Jammes et al. (1979) observed that an inverse relationship between tidal volume and T\textsubscript{1} mediated by the vagus nerve is least evident between the ages of 20 and 40 years. RR is also lowest in this age group. Lung stretch receptor afferents may exert less of an inhibitory influence on inspiratory excursions in this age group. This would allow greater tidal volumes to develop and therefore a slower RR (Jammes et al., 1979).

The elastic recoil pressure of the lung increases with growth resulting in a decrease in chest wall compliance (Fisher and Mortola, 1981; Hershenson et al., 1990; Hershenson, 1992).
Motor activity such as sitting, crawling and walking stiffens the rib cage by increasing the bulk of intercostal and abdominal muscles. Ongoing mineralisation of the rib cage also stiffens the chest wall (Hershenson, 1990). With these changes in compliance, the RR at which the force developed by the respiratory muscles is least may decrease with age (Mead, 1960).

Total metabolism increases with size, while body metabolism per unit mass decreases with age and size (Shock and Soley, 1939; Mortola, 1987). Infants and small children therefore have a higher metabolic rate per unit mass than older children and adults. This is caused by the larger oxygen requirements associated with a decreased ability to regulate temperature and the processes that accompany rapid tissue growth at these ages (Hill, 1959; Polgar and Weng, 1979). Tidal volume increases linearly with body weight in young children and is therefore smaller in younger children (American Thoracic Society/European Respiratory Society, 1993). The increased demand for oxygen per body weight in the young child is therefore met by an increase in RR (Worthington, Young and Altringham, 1991). Thus, there are a number of different reasons for RR to decrease with increasing age.

In the present study, RR was found to correlate most closely with height (length) in sleeping children aged from birth to 4.5 years. This could be due to height (length) being a better reflection than age of the stage of development and lung size of the children (Gaultier et al., 1979). Tepper et al. (1986) found RR to decrease and tidal volume to increase with increasing length. Length, when compared to age and weight, was the most important variable in determining these values in the study by Tepper et al. (1986). In the current study, age correlated most closely with RR in the awake subjects (r = -0.54, p < 0.01). This group of children included older subjects aged up to 12.99 years.

Respiratory rates were higher in awake children compared to sleeping children. Synaptic transmission of sensory information throughout the thalamus and cerebral cortex is enhanced during states of waking and active sleep compared to quiet sleep (Steriade, 1989). The absence of a drive to breathe associated with being awake, a decrease in the metabolic rate and decrease in body temperature explain this reduced RR (Douglas, 1989; Krieger, 1989; McGinty and Szymbusia, 1994). Ventilation is also decreased as a direct result of the state of sleep itself (Krieger, 1989).

RR was also higher and more variable during active (or irregular) sleep when compared to periods of quiet (or regular) sleep. In children aged from 0 to 0.99 months, RR was 6 bpm higher during active sleep compared to quiet sleep in the present study. In agreement, Hoppenbrouwers et al. (1978) found RR to be 7.4 bpm higher during active sleep compared
to quiet sleep in children aged one month. This could be due to the altered state of central nervous system function in this state and other factors, such as increased cerebral blood flow and metabolism (Douglas, 1989). There is also increased oxygen consumption and muscular activity during active sleep (Bolton and Herman, 1974). The behavioural respiratory control systems are also activated by the REM sleep processes (Krieger, 1989). These observations were only measured in children aged less than one year, as these children were frequently observed to be in active sleep. Behavioural criteria was used to judge sleep state, which may limit these findings.

Other factors such as the gender of the children, time of day of testing and the presence of past respiratory disease had minimal effects on RR. The tests in the present study were conducted for a short time. Therefore, this study was unlikely to pick up changes in RR due to a circadian rhythm. The minimal effect of a history of respiratory disease suggests RR is a poor indicator of past and asymptomatic respiratory disease. This agrees with Marks, South and Carlin (1993) who found a history of airway obstruction did not affect RR. The present and other studies of RR have found gender not to affect RR (Hooker et al., 1992; Rusconi et al., 1994). Hormonal influences associated with puberty may cause differences in RR in adolescents (Cassels and Morse, 1962). This could not be investigated in this study since males were predominantly tested in the adolescent and early adult years. The position of sleeping of children, either supine or prone, did not appear to affect the RR. This agrees with the study by Kahn et al. (1993).

Respiratory rate could be increased in children with higher core temperatures due to an increased metabolic rate (Guyton, 1986). Heat also affects the hypothalamus, respiratory neurones in the medulla and respiratory receptors (Cooper and Veale, 1986). Despite this, in the present study there was no effect of axillary temperature on RR in awake children. However, some sleeping children who had axillary temperatures above 37°C did have increased RRs.

Ambient temperature did not significantly affect RR in sleeping children in the present study. This could be due to these children being well rugged during testing. There was also a small range of ambient temperatures in which these children were tested. In older awake children there was a larger range of ambient temperatures in which the children were tested. Ambient temperature was positively correlated with RR in these children \( r = +0.32, p < 0.01 \). There is believed to be an integrated interplay of superficial and deep temperatures in respiratory regulation which may account for this relationship (Cooper and Veale, 1986).
other postulated reason for the elevated RRs observed in neonates and infants is their tendency to pant. This is a mechanism for losing heat and may play a prominent role when infants are awake (Dejours, 1966; Morely et al., 1990). It may also account for the positive correlation between ambient temperature and RR observed in older awake children.

Mental activity increases respiratory rate from a resting basal level in adult subjects (Mador and Tobin, 1991). In the current study of children, RR decreased by one bpm in children aged three to five years during rest after they had been read a story (p < 0.05, paired t test). There was no significant differences in RR in older children (aged 5 to 13 years) between when they were resting quietly and receiving mental stimuli (reading a book). Without using ear muffs and blindfolds it was impossible to eliminate all visual and auditory stimuli in the external environment. Despite the small change in RR observed in the younger children, the use of books was considered advantageous since this standardised the level of stimulation each child received. When testing medical students, there was an increase in RR of 2.2 bpm when reading a book compared to resting. This could be due to the ability of these subjects to relax more during the testing procedure.

8.3.2 Respiratory Timing

The present study found a significant difference between $T_i / T_{TOT}$ in sleeping neonates and children aged up to three years (0.44 ±0.04 and 0.40 ±0.04 respectively, p < 0.05, unpaired t test). In infancy the outward recoil of the chest wall is small while the inward recoil of the lung is marginally lower than in the adult (Bryan and Wohl, 1986). The static balance of these forces results in an FRC that is 10% of the TLC. This low FRC is incompatible with stability of the terminal airways and adequate gas exchange. Therefore, the FRC is dynamically maintained at 40% of the TLC (Bryan and Wohl, 1986). This can be achieved by a shortened expiratory duration or by retarding expiratory airflow (Agostoni and Hyatt, 1986; Kosch et al., 1988; Hershenson, 1992). The higher $T_i / T_{TOT}$ values observed in neonates could be explained by them actively maintaining their FRC. A similar change in $T_i / T_{TOT}$ values in children of this age was also observed by Yau and Fang (1994).

In awake subjects $T_i / T_{TOT}$ in children and young adults was 0.41(±0.03) and 0.42 (±0.05) respectively (no significant difference, unpaired t test). These values were similar to those measured by Tobin et al. (1983a) who obtained a value of 0.42 (±0.03) using a respiratory inductive plethysmograph. The lack of change in $T_i / T_{TOT}$ with age in awake children agrees with Jammes et al. (1979) and Gaultier et al. (1981). Therefore, inspiratory and
expiratory time change proportionally with growth in awake children. A positive correlation existed between $T_i$ and $T_E$. The length of inspiration plays a significant role in determining the length of the subsequent expiration (Clarke and Euler, 1972).

$T_i$ is shorter than $T_E$ for several reasons. The pressure generated during expiration results from the elastic recoil pressure stored in the respiratory system during the preceding inspiration (Milic-Emili, Shee and Ploisongsang, 1987). Due to the braking action of the laryngeal and inspiratory muscles acting early in expiration, flow during expiration is reduced. This increases the expiratory time (Milic-Emili, Shee and Ploisongsang, 1987). This is advantageous because RR is increased by removing these impediments and shortening $T_E$. RR can therefore be increased without extra expiratory muscle activity or increase in end-expiratory lung volume (Milic-Emili, Shee and Ploisongsang, 1987).

The sizes of the airways are narrower during expiration resulting in a greater resistance to airflow (West, 1990; Yau and Fang, 1994). Negative intrapleural pressures keep the airways open during inspiration while positive intrapleural pressures during expiration narrow the airways. Unless greater flows are generated in expiration, it takes a longer time for the inspired volume of air to move through the narrower airways during expiration. A low $T_i / T_{TOT}$ also allows a relatively long resting period for the inspiratory muscles which counterbalances fatigue (Mortola, 1987).

Jammes et al. (1979) found no influence of gender on $T_i$ and $T_E$ values observed during tidal breathing. However, Francis (1981) found females to have reduced $T_i / T_{TOT}$ values during a rebreathing test when compared to males. This was attributed to progestational hormonal differences. In the present study, most adolescents and young adults were males, so this was not further explored. This may be a limitation of the timing indices calculated for healthy children, as more female data was analysed in the older age group.

### 8.3.3 Spectral Analysis

Examining the frequency components of the breathing pattern, using spectral analytic techniques, showed the RR and a low frequency oscillation of approximately 0.1 Hz. This corresponds with a cycle time of 10 seconds. It may be associated with feedback from the respiratory muscles (Priban, 1963). This oscillation could also originate from the central respiratory control centre. It is less likely to be associated with a chemoreceptor feedback loop since this would probably have a larger cycle time. These oscillations were absent in a child who was being ventilated, where feedback mechanisms would not exert an effect. The spectral
analysis of the breathing patterns of identical twins were very similar. This supports the finding that there is a genetic basis to the generation of the human breathing pattern (Shea et al., 1989).

8.3.4 Questionnaire

The questionnaire provided some information about the characteristics of the sample in this study. The perception of risk associated with the experiments did not differ significantly between parents who allowed their children to participate and those who did not. This seems to exclude this as a reason for parents not allowing their children to participate in the research. A large proportion of children who participated in the study had a first degree relative with asthma (42%) compared to children who did not participate (22%). When second degree relatives were included, the difference between the groups decreased to 6%. One study of children with asthma, also using an informed consent process to recruit subjects, found no significant difference in social attributes or frequency of reported asthma between a random sample of non-respondents and the study population (Riha, 1990).

The most prevalent occupations of parents of children in the study were managers/administrators and professionals, suggesting some social groups were under-represented in the population studied. This could be due to many children being contacted through child care centres and private schools. Only one previous study of RR has noted the social factors of the children sampled (Robinson, 1938).

The parents who allowed their children to participate in the study commented on the benefits they could see associated with medical research. A similar finding was observed in a study of parents' participation in the controlled trial of a new asthma drug (Harth, Johnstone and Thong, 1992). Children with symptoms of a recent upper respiratory tract infection had similar RR to healthy children, in agreement with Marks, South and Carlin (1993).
8.4 Children with Respiratory Disease

8.4.1 Respiratory Rates

Elevated RRs were observed in children with pneumonia, cystic fibrosis and asthma and some of the children with bronchiolitis. Pneumonia appeared to elevate RR to the highest levels.

Pneumonia

There was a large elevation of respiratory rate in sleeping children with pneumonia. The mean difference between the RR measured in these children and predicted RR for healthy children was 4.7 SDs. All these sleeping children had RRs above the 95th centile RR for healthy children. Respiratory rate was also significantly elevated in awake children diagnosed with pneumonia, with a mean Z-score of 2.39. Eighty-six percent of these subjects (6/7 - excluding two children with Bordetella pertussis infections) had a RR above the 95th centile for RR in normal awake children.

There was a significant positive correlation of RR in sleeping children with pneumonia and central temperature (r = 0.83, p < 0.05). Fever could be one direct cause of tachypnoea, or alternatively both fever and tachypnoea could reflect another physiological change associated with infection, such as cytokine production. This remains to be determined (O'dempsey et al., 1993). Ventilatory sensitivity to hypercapnia and hypoxia is also increased with an increase in temperature (Cooper and Veale, 1986).

The raised RR in pneumonia is not dependant upon hypoxemia, since RR can be elevated without this influence (Anthonisen and Cherniack, 1981). The tachypnoea may be mediated by non-myelinated fibres serving J-receptors in the affected lungs (Anthonisen and Cherniack, 1981). The compliance of the lungs is decreased in pneumonia. This is explained by consolidation and increased rigidity in unconsolidated areas of the lung due to congestion (Marshall and Christie, 1954). The optimal RR where work is at a minimum is increased because of reduction in compliance of the lungs (Marshall and Christie, 1954; Anthonisen and Cherniack, 1981).

Cystic Fibrosis

RR was also elevated in awake subjects, aged between 8 and 18 years, with cystic fibrosis. The mean increase in RR was 1.99 SDs above the mean for healthy children of a similar age. The Z-scores were positively correlated with age (r = 0.67, p < 0.05), suggesting
RR provided an indication of decreasing lung function associated with increasing age. No significant relationship between FEV\textsubscript{1.0} and RR was observed in the present study, in contrast to the findings of Browning, D'Alonzo and Tobin (1990). They also found correlations between RR and arterial oxygenation and hyperinflation. Therefore, a number of mechanical and chemical stimuli may interact to produce the elevated RR in CF.

Stimulation of pulmonary sensory receptors, probably via the vagus nerve, by excessive lung inflammation and mucus production may be responsible for the elevated RR in CF (Browning, D'Alonzo and Tobin, 1990). Hyperinflation, where breathing occurs on the upper, less compliant portion of the pulmonary pressure-volume curve, may act as an elastic load which also predisposes to tachypnoea. This may also activate pulmonary stretch receptors and chest wall afferents which may contribute to the elevated RR (Browning, D'Alonzo and Tobin, 1990). Tachypnoea predisposes to hyperinflation in patients with airways obstruction, because the associated shortening of expiratory time provides insufficient time for complete emptying of the lungs. This results in an increase in end-expiratory lung volume, which is itself may be a stimulus for increased RR (Browning, D'Alonzo and Tobin, 1990).

Some sleeping infants and toddlers with CF who were monitored had elevated RRs suggesting lung changes occur at an early age. Sixty percent (6/10) had increases of at least one SD above the mean RR for healthy children. Three children, aged eight weeks, 1.8 and 3.5 years, had RRs two SDs above predicted. Phelan (1968) also found infants, aged from 20 to 30 weeks, to have elevated RRs. Forty-four percent (4/9) of sleeping infants and toddlers in the current study had a RR above the 95th centile for healthy children.

**Bronchiolitis**

Some sleeping children diagnosed with bronchiolitis had elevated RRs, with one child having a Z-score of 4.60. However, half the children (5/10) had negative Z-scores (i.e. a RR less than the mean RR for healthy children). Forty per cent (4/10) of children with bronchiolitis had RRs above the 95th centile for healthy children. This could be due to these children having a milder form of the disease. Alternatively, by testing children one to two days after they were admitted to hospital it is possible the severity of their disease could have improved with time and supportive treatment. Silva, Brezinova and Simpson (1982) found RR was increased by 3.1 bpm at the time of illness compared to one month after the illness when the children had recovered. Their study had a similar delay of one to two days in testing the infants.
Six sleeping children with bronchiolitis were receiving oxygen therapy in the present study. This may have reduced their RRs. Despite this, there was some suggestion of a correlation between RR and oxygen saturation ($r = -0.42$, not significant). Breese Hall, Hall and Speers (1979) found a similar correlation that was significant ($r = -0.49$). The hypoxaemia is caused by a mismatch of ventilation and perfusion (Wohl, 1990).

The low RRs could also be explained by fatigue. Mulholland, Olinsky and Shann (1990) found a trend for children with lower respiratory rates to have high $\text{PaCO}_2$ values. It is argued a low RR may be a sign of incipient respiratory failure (Mulholland, Olinsky and Shann, 1990). Tidal volume has been found to vary in infants with bronchiolitis. This may be due to the variable extent to which retractive forces limit respiration associated with a reduction in compliance (Krieger, 1964). This could also explain the variation in RR values found. While a high RR is theoretically inefficient in diseases associated with increased resistance to air flow, a rapid RR can compensate for a reduced tidal volume. Episodes of apnoea would not account for the reduced RRs observed in the present study since they were excluded when calculating RRs.

The mean RR in awake children with bronchiolitis, aged from 1.0 to 6.99 months, was $60.0\ (\pm8.0)$ bpm. This was similar to the RR of $59.3\ (\pm9.8)$ bpm observed in healthy infants, aged from birth to 5.99 months. The elevated RR in the healthy children may have been associated with agitation associated with the testing procedure. These findings agree with Morley et al. (1990) who found little difference in RR between awake healthy children and awake children with bronchiolitis.

**Asthma**

Respiratory rate was also increased in children with asthma. Seventy-eight per cent (7/9) of sleeping children, aged from birth to six years, had RRs above the 95th centile for healthy children. The RR was also inversely related to oxygen saturation in these children ($r = -0.72$, $p < 0.05$). This suggests hypoxemia plays some role in the elevation of RR.

In awake children, aged from one to sixteen years, the youngest children had the highest $Z$-scores (3.03) compared to children aged 7 to 9.9 years, 10 to 12.9 years and 13 to 16.9 years (1.60, 1.80 and 1.51 respectively). Seventy-five per cent (9/12) of awake children aged from 1.0 to 6.9 years had a RR above the 95th centile for normal children. Thirty-six per cent (4/11) of children aged from 7.0 to 9.9 years and 43% (6/14) children aged from 10 to 12.99 years had RRs above the 95th centile for RR for normal children (see Appendix 11). A significant
proportion of the older children therefore had RRs less than the 95th centile for healthy children.

The optimal RR for those with asthma, in terms of lung mechanics, is believed to be less than normal (Hedstrand, 1971). This is because less work is required for passing air slowly through obstructed airways, since this avoids turbulence. However, Macklem and Roussos (1983) dispute this and argue turbulence contributes very little to the work of breathing in asthma, particularly when obstruction occurs in peripheral airways.

The exact mechanism for the increase in RR observed in asthma may be vagally mediated, but is not clearly established in human beings (Macklem and Roussos, 1983). Obstruction is believed to have a significant role in the elevated RR associated with asthma (Anthonisen and Chernicack, 1981). This is supported in the present study by the correlation between PEFR and RR which was found in awake children with asthma ($r = -0.45$, $p < 0.05$). Due to obstruction, subjects with asthma may have to breathe at low tidal volumes and high RRs close to total lung capacity where the airways are open as wide as possible. This helps to maintain flow rates and ventilation (Hedstrand, 1971).

However, methacholine challenge tests, which can cause bronchoconstriction in well people with asthma, induce an increase in ventilation largely by increasing tidal volume rather than RR (Mathieu and Sartene, 1987; Kesten et al., 1990). It is possible increases in RR in acute asthma could be due to the more severe airway obstruction associated with this situation. Release of inflammatory mediators could also contribute to alterations in breathing patterns in asthma (Kesten et al., 1990). Histamine induced bronchoconstriction and anaphylaxis are associated with tachypnoea mediated by irritant receptors in animals (Anthonisen and Chernicack, 1981).

The effects of hypoxaemia on RR are not believed to be as significant since there is no measurable effect on RR in patients given supplemental oxygen (Kesten et al., 1990; Freedman, Mangura and Lavuetes, 1983). In the present study, a significant correlation between the Z-score for RR and oxygen saturation was found only in sleeping children, aged from one to six years. The factors associated with hyperinflation causing an increased RR in CF may also have a role in asthma.
8.4.2 Respiratory Timing in Disease

Fractional inspiratory time (T₁/Tₜₒₑ₅) was measured in children with cystic fibrosis, bronchiolitis and asthma. Rapid RRs and asynchronous chest wall motion made it difficult to calculate accurate values of T₁/Tₜₒₑ₅ in children with pneumonia. Therefore, the respiratory waveforms from these children were not analysed. The values for T₁/Tₜₒₑ₅ obtained in sleeping children with bronchiolitis were compared with values obtained from ten healthy sleeping infants aged from 2.0 weeks to 11.99 months. The T₁/Tₜₒₑ₅ values obtained in awake subjects with CF and asthma were compared with the T₁/Tₜₒₑ₅ observed in 46 healthy awake subjects. Age did not have an effect on T₁/Tₜₒₑ₅ in healthy subjects, so no account of age was made for in this comparison. The healthy subjects ranged in age from two to 23 years.

Cystic Fibrosis

The fractional inspiratory time in awake subjects with CF was 0.44 ± 0.03. This was significantly higher than the value of 0.41 ± 0.03 measured in healthy children (p = 0.02, Student's t test). These findings differ to previous research. Browning, D'Alonzo and Tobin (1990) measured T₁/Tₜₒₑ₅ to be 0.403 (± 0.140) in patients with CF. In contrast to the present study, this value was not significantly different to the value they obtained in healthy subjects. Francis (1981) during rebreathing experiments in adolescents found T₁/Tₜₒₑ₅ to be reduced in adolescents with CF when compared to healthy subjects. Francis (1981) during rebreathing experiments in adolescents found T₁/Tₜₒₑ₅ to be reduced in adolescents with CF when compared to healthy subjects.

The present study found no significant correlation between FEV₁.₀ and T₁/Tₜₒₑ₅ which was in agreement with Francis (1981). It is possible that factors other than obstruction may be responsible for alterations in respiratory timing. The hyperinflation and tachypnoea associated with CF may cause a reduction in Tₑ (Browning, D'Alonzo and Tobin, 1990). This could account for the increased T₁/Tₜₒₑ₅ values observed.

Bronchiolitis

When comparing nine sleeping infants with bronchiolitis with 10 normal infants, no significant differences were observed in T₁/Tₜₒₑ₅ values (0.43 ± 0.06 and 0.41 ± 0.03 respectively, p = 0.36, Student's t test). These values are similar to those of Phelan, Williams and Freeman (1968) who measured Tₑ/Tₑ to be 0.72 (or a T₁/Tₜₒₑ₅ ratio of 0.42) during the acute phase of the illness and Seidenberg et al. (1986) who found T₁/Tₜₒₑ₅ to be 0.426 (±0.03) in infants with bronchiolitis who were not hyperinflated. In contrast, Krieger (1964), observed
a reduction in expiratory time in children with bronchiolitis. A $T_i / T_e$ ratio of 0.93 was observed which would be associated with a larger $T_i / T_{TOT}$ value of 0.48.

Inflammatory obstruction, and possibly muscle spasm, of the bronchioles cause an increased flow resistance in bronchiolitis (Krieger, 1964; Wohl, 1990). This occurs particularly during expiration and leads to retention of air and hyperinflation (Phelan, Williams and Freeman, 1968; Seidenberg et al., 1989). A reduction in dynamic compliance of the lungs is observed due to the higher lung volumes at which breathing is occurring. An increase in non-elastic resistance also occurs due to resistance not being uniform throughout the lung (Phelan, Williams and Freeman, 1968; Wohl, 1990)

This reduced compliance may have contributed to the rapid expiration and shortened expiratory time observed by Krieger (1964). The airways are also distended with hyperinflation. This would reduce the effect of obstruction and also affect respiratory timing in bronchiolitis (Krieger, 1964). This could account for the increase in $T_i / T_{TOT}$ over 0.45 in 44% (4/9) of infants with bronchiolitis compared to 10% (1/10) of healthy infants in the present study.

Children who do not compensate by hyperinflation or hyperventilation may maintain ventilation by spending more time on expiration (Seidenberg et al., 1989). Seidenberg et al. (1989) found $T_i / T_{TOT}$ to be 0.382 (±0.04) in five children with bronchiolitis who were not hyperinflated. One child in the present study did have a reduced $T_i / T_{TOT}$ value of 0.35. It could be speculated that the children without hyperinflation could compensate by decreasing their fractional inspiratory time.

Asthma

There was no significant difference between $T_i / T_{TOT}$ in the awake children with asthma and the healthy subjects (0.40 ± 0.04 and 0.41 ± 0.03 respectively, $p = 0.10$, unpaired $t$ test). However, the distribution of data appeared to be skewed in the group of subjects with asthma who were not receiving oxygen. Amongst these subjects, 31.6% (6/19) had a $T_i / T_{TOT}$ value equal to or less than 0.37 compared to 10.9% (5/46) of the healthy subjects. Other studies have shown a reduction in $T_i / T_{TOT}$ in children and adults with asthma (Tobin et al., 1983b; Asai et al., 1990). A suggestion of a correlation between $T_i / T_{TOT}$ and FEV$_{1.0}$ values, although not significant, was noted in the present study. Hillman, Prentice and Finucane (1986) observed a positive correlation between these values ($r = + 0.47$, $p < 0.01$) and suggested the prolongation of expiration may be related to increases in airway obstruction.
It is possible trapped gases associated with obstruction may activate stretch receptors which are known to shorten $T_i$ and prolong $T_e$ (Clark and Euler, 1972; Knox, 1973; Sorli et al., 1978; Gaultier et al., 1982). A reduction in $T_i / T_{TOT}$ could also be due to exposure of irritant receptors to endogenous chemicals (Derenne, Macklem and Roussos, 1978; Sorli et al., 1978; Francis, 1981). However, other authors have proposed these receptors increase RR by decreasing $T_e$ (Widdicombe, 1981). Smaller $T_i / T_{TOT}$ values are advantageous in that there is greater rest time for the inspiratory muscles (during expiration) which helps to delay the onset of respiratory muscle fatigue (Bryan and Wohl, 1986). A prolonged expiration also helps to reduce the effects of expiratory flow limitation by allowing more time for air to be expired through the narrowed airways (Pride and Macklem, 1986).

An increase in FRC results when inspired air cannot be fully expired. This gives a stronger elastic recoil on expiration and increases the calibre of the airways reducing the effects of obstruction (Engstrom, 1964; Woolcok and Read, 1965). This may explain why $T_i / T_{TOT}$ was not reduced in all subjects in the present study. An inverse relationship between $T_i / T_{TOT}$ and $T_{TOT}$ was found in awake children with asthma ($r = -0.63$, $p < 0.01$) in the current study. It is possible that children with higher RRs (or lower $T_{TOT}$ values) have higher values of $T_i / T_{TOT}$. To maintain an elevated RR the expiratory limb of the respiratory cycle needs to be truncated. This is caused by the inspiratory drive demanding the next inspiration (Morris and Lane, 1981).

$T_i / T_{TOT}$ ranged from 0.35 to 0.46 in the children with asthma not receiving oxygen in the present study. This could be due to responses to treatment, particularly bronchodilators. Ipratropium bromide is known to decrease $T_e$ and $T_e / T_i$ (Asai et al., 1991). In the present study, children who were receiving oxygen therapy had a $T_i / T_{TOT}$ value of 0.44 ($\pm 0.05$) in contrast to those who were not ($T_i / T_{TOT} = 0.40 \pm 0.05$) ($p = 0.08$, Student's $t$ test). This difference, although not statistically significant, could be due to children receiving oxygen having more severe asthma, or possibly the effect of oxygen itself.

The present study did not show a significant correlation between $T_i / T_{TOT}$ and oxygen saturation levels. In agreement with this, Hillman, Prentice and Finucane (1986) observed changes in $T_i / T_{TOT}$ in the absence of hypoxia or hypercapnia. This could be due to the respiratory timing being independent of central respiratory drive. A lack of correlation between $T_i / T_{TOT}$ and indices reflecting central drive (such as mean inspiratory flow and the mouth occlusion pressure after 0.1s) during rebreathing experiments supports this (Francis, 1981).
Comparison of Factors Affecting Timing in Different Respiratory Diseases

The alterations in lung mechanics in asthma are transient and fluctuant, while the changes in CF are chronic and more stable. This may also account for differences in timing between these two disease states. Subjects with CF were found to have significantly higher values of $T_i / T_{TOT}$ compared to children with asthma ($p = 0.002$, unpaired t test). This could be due to adaptation, possibly central, to an unchanging degree of airways obstruction (Francis, 1981). It could also be due to a lesser degree of irritant receptor activity in CF (Francis, 1981). Infants need to actively maintain their FRC either by shortening their expiratory time or retarding their expiration using laryngeal adductors and post-inspiratory diaphragmatic activity (Agostoni and Hyatt, 1986). This may be another factor influencing timing in children with bronchiolitis, which is not present in the older children with CF and asthma.

It has been suggested that the measurement of timing indices may be a useful method of evaluating the degree of airway obstruction in disease (Asai et al., 1990). However, the optical sensor used in this study detects the abdominal contribution to respiration only. Therefore care needs to be taken when considering the clinical significance of the timing indices measured by the optical sensor, particularly in respiratory disease.

### 8.4.3 Analysis of Sensitivity and Specificity of Respiratory Rate

Sensitivity and specificity were calculated for different RR thresholds, in children with pneumonia and bronchiolitis. Children with pneumonia were aged 6.0 to 11.99 months and were sleeping. Children with bronchiolitis were also sleeping and aged from 1.0 to 5.99 months. These age groups were chosen since they contained the largest proportion of children with each respective disease. The analysis is limited since the population of sick children came from a hospital and the population of healthy children came predominantly from the community. Nevertheless, it seemed worthwhile to investigate how useful RR was in differentiating between health and disease.

A respiratory rate of 28 bpm gave a sensitivity of 100% and specificity of 85% for sleeping children with pneumonia. In bronchiolitis, a threshold RR of 30 bpm or greater gave a sensitivity of 87.5% but a specificity of only 11.8%. A ROC (receiver operator characteristic curve) plots false positive diagnoses (X-axis) against sensitivity (Y-axis). A clinical test performs well when the ROC curve is closest to the top left corner of ROC space (Metz, 1978).
The ROC curves (see figures 7.3 and 7.14) show RR fulfilled this criterion for the detection of pneumonia but not for bronchiolitis. The usefulness of RR as a clinical sign in detecting pneumonia has been confirmed by other studies (Singhi et al., 1994a; Singhi et al., 1994b).
Chapter 9
Conclusions, Limitations and Suggestions for Further Work

9.1 Conclusions

The primary aim of this study was to obtain centile charts for respiratory rate in both sleeping and awake healthy children. Centile charts for RR were made for sleeping children, aged from birth to three years, and for awake children, aged from one to thirteen years. These charts are presented in figs. 6.12a and 6.12b. An analysis of variance showed sex of the children had no effect on RR. Centiles combining both female and male data were therefore created.

There were several other conclusions made in relation to breathing patterns in children. These are as follows:

1. The optical sensor used in the study was a very accurate way of measuring RRs when compared to visual observation. The waveform pattern obtained using the sensor was very similar to the patterns obtained from a respiratory inductive plethysmograph and water-sealed spirometer. This would support its accuracy in measuring $T_I$, $T_E$, $T_{TOT}$ and $T_I / T_{TOT}$ in healthy children. The sensor's accuracy in measuring these values in children with respiratory disease has not been fully established. The fractional inspiratory time measured by the optical sensor varied somewhat with that measured by a pneumotachograph in infants and toddlers.

2. RR decreased with age from birth in healthy children. In sleeping children most change occurred between birth and one year of age. This was also where RR varied most between subjects. In awake children, RR appeared to decline rapidly up until the age of about three years. Small changes occurred after this age.

3. Adding the respirations obtained in two thirty-second periods was an accurate method of counting RR. The 95% limit of agreement between measuring RR as just described and counting respirations for the total test period (approximately five minutes) was between -2.9 and 3.2 bpm for awake children. Similar findings were found for children with bronchiolitis, pneumonia, asthma and cystic fibrosis. The 95% co-efficient of
repeatability for RR measured on two occasions was approximately five bpm. This shows there is some variability in RR when measured on two occasions.

4. The effects of a number of different variables on RR were explored in this study:

A child's sleeping posture (supine or prone) did not appear to affect RR. Larger RRs were observed in awake children. RRs were also higher during periods of irregular (active) sleep in infants. A history of respiratory disease (past or present) did not significantly affect the RR of children tested in the community.

No significant correlation between axillary temperature and RR was found in awake \( r = +0.03 \) or sleeping children \( r = +0.15 \). However, some sleeping children with temperatures above 37°C did have elevated RRs. Ambient temperature had some effect on RR in awake children \( r = +0.32, p < 0.01 \).

Respiratory rate was more closely correlated with age than weight or height in awake healthy children, aged from two to twelve years \( r = -0.58, p < 0.01 \). However in the sleeping children, RR was more closely correlated with height \( r = -0.93, p < 0.01 \). The children in this group were aged from birth to four years. Height could be a better indication of neurodevelopmental status in such a group.

5. Cognitive activity had a minimal effect on RR in children aged from three to five years. A decrease in RR of one bpm was observed in these children as they rested after being read a story. There was no significant changes seen in older children aged from 5-13 years who read the book themselves. It was concluded that reading the younger children a story and giving the older children a book was advantageous in that it distracted them from thinking about their breathing. It also appeared to reduce anxiety and boredom that could be associated with the testing procedure. In older subjects, aged from 19 to 24 years, reading did have an effect on RR by increasing it by two bpm.
6. Spectral analysis of the breathing patterns allowed examination of the frequency components of the breathing pattern. There was a significant peak at the frequency corresponding to the RR. Some low frequency oscillations were also noted, especially at the frequency of 0.1Hz. It is possible they were the consequence of feedback mechanisms, possibly related to the respiratory muscles.

7. Children with pneumonia had significantly elevated RRIs with the mean increase in RR in sleeping children being 4.75 SDs above the RR obtained in healthy children. There was a close correlation between RR and body temperature in sleeping children with pneumonia (r = + 0.83, p < 0.05). For awake children the increases in RR averaged 2.4 SDs above the mean RR for healthy children.

8. Awake subjects with cystic fibrosis also had significantly elevated RRIs. The mean Z-score for RR was 1.99. Some infants and toddlers diagnosed with CF, who were sleeping, also had increased RRIs. Sixty percent of these children had a Z-score for RR of at least one.

9. Bronchiolitis had a variable effect on RR in this study. The mean Z-score for RR was 0.63 in sleeping infants with bronchiolitis. Half the children (5/10) had RRIs lower than the mean RR for healthy children, while one child had a RR that was 4.6 SDs above the mean RR for healthy children appropriate for age. Awake RRIs for children, aged from one to six months, averaged 60.0 (± 8.0) bpm. This was not different from the value obtained for healthy children aged from birth to 5.99 months of 59.3 (±9.8) bpm.

10. Respiratory rates were increased in children diagnosed with asthma in both sleeping children, aged from one to six years, and in awake children, aged from one to seventeen years, by 3.11 and 2.00 SDs above the mean RR for healthy children respectively. RR was negatively correlated with oxygen saturation in sleeping children diagnosed with asthma (r = - 0.72, p < 0.05) and PEFR in awake children (r = - 0.45, p < 0.05). RR therefore reflects these alterations in pulmonary function.
It was still possible for a child with asthma to have a RR which was in the range of that for healthy children. RR should therefore never be used as the sole basis for excluding serious disease. This conclusion is supported by another study by Kerem et al. (1991).

11. The fractional inspiratory time ($T_I / T_{TOT}$) was found to be $0.44 \pm 0.04$ in sleeping neonates and $0.40 \pm 0.04$ in sleeping infants aged from 2.0 weeks to 3.5 years. For awake children and young adults the mean $T_I / T_{TOT}$ was $0.41 \pm 0.03$. Age did not have an effect on fractional inspiratory time in awake subjects and sleeping subjects older than two weeks. A positive correlation existed between $T_I$ and $T_E$. The larger $T_I / T_{TOT}$ values observed in neonates may have been associated with their active maintenance of FRC at this age.

12. The different diseases had variable effects on fractional inspiratory time. The fractional inspiratory time in awake children with CF was $0.44 \pm 0.02$. This was significantly higher than the value for healthy subjects ($p = 0.02$, Student's $t$ test). There was no significant difference between $T_I / T_{TOT}$ in the awake children with asthma ($0.40 \pm 0.04$) and the healthy subjects ($p = 0.10$, Student's $t$ test). However, the distribution of data appeared skewed in the subjects with asthma who were not receiving oxygen therapy. Of these subjects, 31.6% (6/19) had $T_I / T_{TOT}$ values less than or equal to 0.37 compared with 10.9% (5/46) of the healthy subjects. Some children with acute asthma had increased $T_I / T_{TOT}$ values, reflecting a reduction in $T_E$ relative to $T_I$. There are physiological explanations for both reduced and increased fractional inspiratory times in children with asthma.

When comparing nine sleeping infants with bronchiolitis with the 10 healthy sleeping infants, no significant differences were observed in $T_I / T_{TOT}$ values. A larger SD for the children with bronchiolitis suggests there was a larger spread of data in this group. It is possible different mechanisms associated with this disease may either increase or decrease $T_I / T_{TOT}$. 

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13. The centile charts appeared to be useful in discriminating children with disease. All sleeping children with pneumonia had a RR greater than the 95th centile for healthy children. Eighty-six per cent of awake cases with pneumonia (6/7 - excluding two Bordetella pertussis infections) had RR's greater than the 95th centile for healthy children. Only 40% (4/10) of sleeping children with bronchiolitis had RR's above the 95th centile. Forty-four percent (4/9) of sleeping infants and toddlers diagnosed with cystic fibrosis had RR's above the 95th centile while asleep. Since the centile chart finished at 13 years of age, no analysis of the older awake adolescents with CF was made. The charts were more useful in identifying pneumonia than bronchiolitis.

Seventy-eight per cent (7/9) of sleeping children, aged from 1.0 to 6.0 years, with asthma had RR's over the 95th centile. Seventy-five per cent (9/12) of awake children, aged from one to 6.99 years also had RR's above the 95th centile. Respiratory rate appears to be a good indicator of respiratory dysfunction in this age group. The centile charts should be helpful for both parents and physicians when assessing the state of asthma in children of this age. Thirty-six per cent (4/11) of awake subjects with asthma, aged from 7.0 to 9.99 years, and 43% (6/14) of awake subjects with asthma, aged from 10.0 to 12.99 years, had RR's above the 95th centile. A significant number of children with acute asthma therefore had RR's within the range of healthy children amongst this older age group.

9.2 Limitations of Study

The findings of this study were limited somewhat by the population that volunteered to participate in the study. Examination of the occupations of parents of children involved in the study does show that there is an over-abundance of certain occupational groups and a lack of others. Obtaining children from the childcare centres and predominantly private schools would help to account for this.

In relation to sleeping children, it was difficult to judge sleep state from behavioural criteria alone. Muscle arousals evident on an electromyogram may not always be observed with the naked eye (Marks, South and Carlin, 1993). Litscher et al. (1993) have observed that physiological and behavioural activities recorded during sleep are not easily classified into two
groups. This is because a large amount of sleep appears poorly organised and has mixed features. The distinctions between active and quiet sleep in this study are therefore quite crude.

Awake children were informed about certain aspects relating to the breathing study before their respirations were observed. This may have caused the children to alter their breathing patterns. This is a limitation of any study that observes breathing patterns in children, unless the experiments are performed without telling the subject that their breathing is being monitored.

In relation to the children examined in the hospital, the study was limited by lack of homogeneity in the degree of acuteness and severity of disease affecting the children. Decisions about admission of children into hospital are influenced by many factors including the social needs of the patient population, the availability of medical facilities both in the community and the hospital, and the level of experience of the doctor who makes the assessment (Connet and Lenney, 1993).

There are two important limitations that must be considered in relation to the optical sensor. A source of error relates to compression and decompression of thoracic gas which is most evident at high RRs. Changes in air flow direction can cause changes in alveolar pressure. These in turn can cause a change in thoracic gas volume that is not associated with any net movement of air (i.e. airflow). This occurs most at the changeover between inspiration and expiration. This can result in smaller $T_I$ and larger $T_E$ values being obtained than what would be observed with a pneumotachograph (Stagg, Goldman and Newsom Davis, 1978).

Incoordination between abdominal motion, chest wall motion and respiratory air flow may also lead to some errors of measurement by the respiratory sensor. "Paradoxical" outward motion of the abdominal wall during early expiration and paradoxical inward motion of the abdominal wall during early inspiration has been described in patients with acute exacerbations of chronic obstructive pulmonary disease and nocturnal asthma in non-REM sleep. This results in a biphasic abdominal movement (Issa and Sullivan, 1985; Goldman et al., 1994). If this was the case, the sensor would not give an accurate indication of airflow.

Other studies have found the anterior-posterior abdominal diameter was in phase with respired volumes in subjects with asthma. Rib cage motion lagged behind abdominal motion during both inspiration and expiration in asthma (Ringel et al., 1983; Hillman, Prentice and Finucane, 1986; Hershenson, 1992). Low inspiratory pleural pressures and an abnormal distribution of muscle forces acting on the rib cage resulted in this phase lag of the rib cage (Hillman, Prentice and Finucane, 1986). The sensor may provide an accurate measurement of
timing in respiratory disease if these findings are correct. Multiple degrees of freedom of motion of the chest wall exist during obstructive episodes (Ringel et al., 1983). Therefore, the conclusions relating to timing indices in respiratory disease in this study are made with caution. The sensor should nevertheless provide accurate measurements in health.

9.3 Suggestions for Future Research

There are several areas that this study has touched upon which could be explored in more depth in the future. These include:

1. The use of the sensor as a diagnostic tool in different aspects of medicine could be further explored. For example the sensor was able to detect apnoea in sleeping infants. The sensor was only trialed for short periods in this study (a duration of 20 minutes at the most). The accuracy of the recording it gives over a longer period could be investigated. Reducing the size of the hardware that the sensor requires would also assist with this.

2. The extent to which the displacement signal corresponds with volume changes in the lung could also be further explored. If this signal was closely correlated with volume, then the signal could be differentiated to give a flow signal. This would allow indices such as $T_{pef}$ (time to peak expiratory flow) to be calculated. Some examples of this were shown in the results section. The differentiated signal in children with bronchiolitis did show a rapid rise to the peak expiratory flow value. Making adaptations to the optical sensor so it could measure rib cage excursions would assist in detecting asynchrony between the abdomen and rib cage. This could also allow volume changes to be more accurately measured.

3. Breathing can be described as chaotic in that it is not entirely regular and varies in complex patterns. This is the result of many inputs and corrections (Donaldson, 1992; Yamashiro and Kryger, 1993). It has been argued that periodic breathing and certain disease states may result from a loss of the "chaos" of normal physiological control (Yamashiro and Kryger, 1993). Denton and Diamond (1991) have proposed several different techniques that could be used to examine the extent to which the breathing patterns obtained in the present study were "chaotic".
Part V

Summary, Appendices and Bibliography
Summary

Introduction

This study has obtained reference ranges and centile curves of respiratory rate for healthy children. An examination of the literature highlighted the need for this research. The literature also highlighted several ways of analysing the respiratory waveform. There are some potential sources of error when examining the breathing patterns of human subjects. Care needed to be exercised in analysing such data, particularly with a newly developed respiratory sensor. The respiratory rate, and other features of the breathing pattern which the sensor measured, proved to be helpful in distinguishing between health and disease.

Overview of Thesis

The widespread use of respiratory rate as an indicator of pulmonary dysfunction and aims of the study were prefaced in the introduction. A diverse group of diseases manifest changes in respiratory rate such as pneumonia, sepsis, bronchiolitis and acute asthma. There is some speculation in the literature as to the usefulness of respiratory rate as a clinical sign. This study aimed to create centile charts for respiratory rate in children. Another aim involved examining whether respiratory rate could distinguish healthy children from those with respiratory disease. Simultaneously, other features of the breathing pattern, such as the timing of events in the respiratory cycle and spectral analysis could be executed. An evaluation of the optical respiratory sensor was another purpose of the study.

The thesis was divided into five parts. Part one, consisting of chapters one and two, contained the review of literature. Chapter one reviewed the literature on the measurement of respiratory rate in both healthy and sick children. A lack of studies of respiratory rate in awake children throughout childhood and in sleeping children past the age of one was observed in the literature. Relatively few studies have detailed the exact changes in respiratory rate in diseases such as asthma, pneumonia and bronchiolitis. Most studies though did report an increase in RR, particularly in pneumonia. Some attempt in the past has been made to find out what factors influence the respiratory rate in both health and disease, including both chemical and mechanical stimuli.

The focus of chapter two was a review of the literature on methods of investigating and analysing the shape of the waveform pattern associated with respiratory movements. Breathing patterns can be detected by a large number of different sensors. Sensors can measure respiratory airflow and volume change or chest wall movements. The respiratory optical sensor
used in the present study fits into this latter category. There were few studies defining the
effect of respiratory disease on fractional inspiratory time \( (T_i / T_{TOT}) \), particularly in children.

The experimental protocols and their rationale were outlined in part two of the thesis,
containing chapters three and four. Chapter three discussed the population studied. This
chapter also dealt with areas of difficulty such as in defining sleep states and achieving a resting
state in awake subjects. Obtaining consent from parents and children and a representative
sample from Brisbane's population of children were other significant obstacles. Chapter four
focused on the respiratory sensor used in the study and methods of analysis done on the
respiratory waveforms obtained from this sensor. This included calculating inspiratory times
and expiratory times, which are dependent upon the definitions used to describe them.
Statistical analysis used in the study and a method to construct centile charts is described.

Part three of the thesis outlined the results of this research study in three chapters.
Results associated with comparing the optical sensor with other available methods of studying
respiration were presented in chapter five. Methods of comparison included visual observation,
a pneumotachograph, a spirometer and a respiratory inductive plethysmograph. It was
important to identify how accurate the sensor was in detecting respiratory excursions. This was
the first time this sensor has been used for respiratory research purposes.

Chapter six reviewed the results obtained from studies of healthy children. A centile
chart showing respiratory rate changes with age is an important outcome of the thesis. Two
charts were presented since sleeping respiratory rates differed from awake respiratory rates (see
figs 6.12a and 6.12b). The method of counting RR used to obtain the centile chart involved
counting respirations over two thirty-second periods. This was found to give a similar RR to
that obtained by counting respirations for the total time of testing which was usually five
minutes. An investigation of other factors that might influence RR, such as temperature and
a history of respiratory disease, was also undertaken. There was minimal effect of age on the
fractional inspiratory time \( (T_i / T_{TOT}) \). Low frequency oscillations were observed in the spectral
analysis of the breathing patterns also presented in this chapter.

Chapter seven looked at the changes in RR and fractional inspiratory time in children
with various respiratory diseases. These diseases included pneumonia, cystic fibrosis,
bronchiolitis and asthma. Respiratory rate was markedly elevated in children with pneumonia,
when they were both awake and asleep. A RR of 28 bpm gave a sensitivity of 100% and
specificity of 85% for detecting pneumonia in sleeping children. There was also a significant
correlation between RR and temperature in these children \( (r = + 0.83, p < 0.05) \). Children with
cystic fibrosis also had elevated RRs. These included mostly older subjects (aged from eight to eighteen years) and some younger children (aged from one month to three years). Some children with bronchiolitis had elevated RRs, but the majority did not. Most young children, diagnosed with asthma, aged up to six years had increased RRs which were higher than the 95th centile for healthy children. An elevated RR was observed in both sleeping and awake children of this age. However, in older children aged from seven to sixteen years there was significant variation in RR values obtained. Some children with asthma did not have elevated RRs.

The changes in fractional inspiratory time ($T_1/T_{TOT}$) in respiratory disease were also examined in this chapter. It appeared $T_1/T_{TOT}$ was elevated in the older awake subjects with cystic fibrosis compared to healthy subjects. There was no overall difference in $T_1/T_{TOT}$ between healthy children and children with asthma or bronchiolitis. However, forty-four percent (4/9) of infants with bronchiolitis had $T_1/T_{TOT}$ values greater than 0.45 and 32% (6/19) of subjects with asthma had $T_1/T_{TOT}$ values which were below 0.37. It is possible that stretch or irritant receptors may be responsible for the alteration in fractional inspiratory time in asthma. These values were based on measurements made with the optical respiratory sensor. Therefore they might not correlate exactly with airflow since the sensor detected movement of the abdominal compartment of respiration mainly.

The final two chapters of the thesis, contained in part four, discussed the results, conclusions and limitations associated with the present study. Some findings were discussed in chapter eight. The decrease in RR with age might have been due to changes in mechanical properties of the respiratory system (such as compliance and resistance), chemical factors and changes in metabolic rate with growth. The larger RRs observed in subjects when they were awake compared to when they were asleep could be accounted for by factors such as the reduced metabolism associated with sleep and a stimulus to breathe which is associated with being awake.

The centile charts are a very efficient way of presenting RR data, particularly in the younger ages where RR tends to change rapidly. The advantages of the centile charts obtained in the present study, particularly in the age ranges covered, were also discussed in chapter eight. The results obtained in this study are very similar to those of Marks, South and Carlin (1993) who also conducted a study of respiratory rates in Australian children. The ages of children in the study by Marks, South and Carlin (1993) ranged from one to seven years. Data from children with a history of respiratory disease were not excluded when constructing the
reference ranges for RR by Marks, South and Carlin (1993). The present study used data from children with no history of respiratory disease.

Chapter eight also considered the reason for the elevated RRs observed in diseases such as asthma and pneumonia. The influence of lung receptors, such as irritant and J receptors, was discussed. The changes in mechanical properties (such as increased airway resistance) of the lungs might also account for some changes in RR. The variable changes of RR in bronchiolitis could have been due to some children having reduced RRs caused by fatigue. Alternatively, these cases could have been milder forms of the disease processes. One limitation of the study was the heterogeneity of the study population in relation to severity of disease and treatment regimens. This was particularly so in the case for asthma.

Changes in $T_e/T_{TOT}$ were also explored in chapter eight. Several different factors can conceivably alter respiratory timing. These include the action of stretch receptors in prolonging expiration and breathing at higher lung volumes. A balance also needs to be made between truncating the expiratory limb of the respiratory cycle to maintain an elevated RR and prolonging expiration so that inspired air can be expelled and fatigue does not occur.

The conclusions of this study were presented in chapter nine. The accuracy and precision of the respiratory sensor in measuring RR was confirmed. Another finding was the rapid decrease in RR on the centile charts observed in the early years of life. The centile charts were particularly helpful in discriminating healthy children from children with pneumonia or children with asthma aged up to six years. This was for both awake and asleep children.

The limitations of the study were also discussed in chapter nine. These included the lack of representation of certain social groups in the sample and problems associated with measuring breathing patterns which can be consciously controlled. While the optical sensor should give an accurate indication of abdominal respiratory movements, there are some arguments against linking the timing values obtained from the optical sensor with air flow. Suggestions for future research were also made and included investigation of the possible use of the sensor as an apnoea monitor.
Appendix 1

Letters written to and received from the Ethics Committees of the Royal Children's Hospital and Royal Women's Hospital, Brisbane.
To the Ethics Committee. Royal Children's Hospital.

Next year beginning January 1994, I plan to undertake a Bachelor of Medical Science project within the University of Queensland's Department of Child Health. I am writing to request ethical approval of my project entitled "Respiration in children: analysis using a fibre optic sensor".

The project will involve the use of adhesive sensors about the size of an adult finger. These sensors will be stuck on to the lower chest of children using micropore tape. The sensors are small, unobtrusive, painless and pose no risk to the children as they are composed entirely of plastic. They use visible light as a means of determining motion and there is no risk of electrical shock.

It is planned children in the hospital without respiratory disease, ages ranging from 6 months to 15 years, will be studied. Some of the older children may need to be obtained from the community (e.g. Scout/Youth Groups).

The time taken to obtain the data using the sensor will take no longer than 30 minutes to perform. This will generate a set of normal respiratory rates for different ages, which will then aid in deciding if an individual has a significantly elevated respiratory rate (as in diseases such as pneumonia and asthma).

The next part of the project will involve testing the respiration of children in the hospital who have asthma or pneumonia. The waveform pattern obtained will provide further information about the pulmonary mechanics of the disease. The time of inspiration and time of expiration vary with diseases such as asthma. Obtaining this data has applications to both the diagnosis and assessment of treatment of disease. The device in this project provides a ready means of obtaining such information.

If the device proves successful in a clinical setting, it may be used in other areas of medicine (e.g. magnetic resonance imaging, sleep studies). Throughout the project I will be supervised by Dr Steven Wilson, from the Centre for Magnetic Resonance, and Prof John Pearn, from the Department of Child Health. All consideration will be given to the welfare of the children participating in the study. Enclosed is a proposed information sheet and consent form, which will be used when explaining the project to parents.

Yours faithfully,
Anthony Herbert.
To the Ethics Committee Members, Royal Women's Hospital,

August 12, 1994

At present I am undertaking a Bachelor of Medical Science project within the University of Queensland's Department of Child Health. I am writing to request ethical approval to monitor the breathing patterns of some new born babies, using a newly developed fibre optic sensor.

The sensor is about the size of a finger. It is attached to the lower chest of children using micropore tape. The sensor is small, unobtrusive, painless and poses no risk to the children as the sensor is composed entirely of plastic. It uses visible light as a means of determining motion and there is no risk of electrical shock.

I have already tested about 300 children, with ages ranging from 2 weeks to 13 years. It would be good to test about 10-20 new born babies to give me data from birth right up to the teenage years.

This would generate reference ranges for normal respiratory rate in new born babies. Measuring respiratory rates has been found to be valuable in detecting Lancefield group B Streptococci infections in babies. We would also be able to assess the practicality of using the sensor on this age group, as it has possible uses an apnea monitor.

I am supervised by Dr Stephen Wilson, from the Centre for Magnetic Resonance, and Prof John Pearn, from the Department of Child Health. All consideration will be given to the welfare of the children participating in the study. Enclosed is a proposed information sheet and consent form, which will be used when explaining the project to parents. I have also attached a copy of my methodology and the ethical approval obtained from the Royal Childrn's Hospital.

Yours faithfully,
Anthony Herbert.
RESPIRATION IN CHILDREN: ANALYSIS USING A HIGH-RESOLUTION FIBRE OPTIC SENSOR

Breathing patterns are an important clue to pulmonary dysfunction. This project will involve the use of risk-free stick-on sensors (about the size of an adult finger). This has been developed at the Centre for Magnetic Resonance at the University of Queensland. It enables the pattern of breathing of children to be fed into a computer. This data can later be analysed to determine respiratory rate and characteristics of waveform.

Part A) The initial part of the project will involve determining mean respiratory rates for normal individuals at different ages (e.g. throughout the early years of life and generation of percentile distributions). The device will provide a better means of obtaining this data since it can monitor respiration continuously and is also unobtrusive and unlikely to cause children to alter their respiratory patterns, a flaw which is a criticism of much previous research in this area.

Part B) Respiratory rate has been found to be an important predictor of severity and prognosis of various disease such as pneumonia and asthma. Therefore the second part of the project will involve determining if the waveform pattern of respiration produced by various diseases could provide further information about the cause (e.g. which infection) and severity of the disease.

It is likely that this study will be limited to one or two disease processes (e.g. asthma or lower respiratory tract infections). Both respiratory rate and inspiration/expiration ratios have been used to assess the severity of asthma and monitor subsequent treatment, so analysis of the waveform pattern may be of clinical value. Having mean respiratory rates for normals would also be of value.

Finally, the project will determine if the device is practical in a clinical setting. This has implications for further use (e.g. high resolution magnetic resonance imaging, sleep studies, breathing patterns following drowning).
Mr. Anthony Herbert,
60 Prospect Street,
WYNNUM NORTH. Q. 4178.

Dear Mr. Herbert,

Respiratory wave-pattern and breathing research project
Department of Child Health and Centre for Nuclear Magnetic
Resonance, University of Queensland

The Ethics Committee of the Royal Children’s Hospital has approved your project in full. Colleagues join with me in sending all best wishes for this important work, on the study of the chest movements and breathing patterns of children in health and disease.

It will be necessary also, as a separate enterprise, to apply for permission to pursue this study, from the administrative point of view, in the Royal Children’s Hospital. The approving authority is Dr. Rod Davison, the Chief Executive Officer for the Children’s Sector of the Brisbane North Region, to whom I will send a copy of this letter to help with communication. I would ask that you write directly to him in this context.

Members of the Ethics Committee join with me in sending all best wishes to you for your important research.

Kindest regards,

[Signature]

Professor John Pearn,
Chairperson,
Ethics Committee,
Royal Children’s Hospital.

cc. Ethics Committee files (Professor John Pearn)
Ethics Committee files - Office of the C.E.O. Children’s Sector, Brisbane North Region, C/- Lady Norman Wing, Royal Children’s Hospital.
Members of the Ethics Committee.
Dr. R. McCrossin, Medical Superintendent, Royal Children’s Hospital, Herston.
22 December, 1993 (Wed)

Mr Anthony Herbert
60 Prospect Street
WYNNUM NORTH Q 4178

Dear Mr Herbert

Thank you for your letter of 16 December 1993 requesting approval to undertake a Bachelor of Medical Science project within the Royal Children's Hospital in 1994.

I am pleased to advise that such approval has been granted subject to the standard rules and regulations. Professor Pearn will advise you of these as and when required.

Your project sounds quite interesting, and I wish you every success with it.

Yours sincerely

Dr Bob McCrossin
Medical Superintendent
WRP:AMP

31 August 1994

Mr A Herbert
Dept of Child Health
University of Queensland,
ROYAL CHILDREN’S HOSPITAL

Dear Mr Herbert

RE: PROTOCOL 94/21 "RESPIRATORY WAVE PATTERN AND BREATHING RESEARCH PROJECT"

It is advised that on the recommendation of the Research Ethics Committee, the Chief Executive Officer, Royal Womens Hospital has approved your request provided the concerns of the Committee as advised hereunder are addressed.

All investigations must be carried out according to the "Declaration of Helsinki 1976" as subsequently modified and the latest statement by the National Health and Medical Research Council to which you as the research worker must adhere. Should a copy of the 'Declaration of Helsinki 1976' as subsequently modified be required, please request a copy from the Secretary, Research Ethics Committee.

Attached is a letter listing some matters specified by the National Health and Medical Research Council to which you as the research worker must adhere.

You are required to provide a report on any pilot study and the outcome of the study at the completion of the trial or annually if the trial continues for more than 12 months.

If the results of your project are to be published, an appropriate acknowledgment of the Hospital should be contained in the article. Copies of all publications resulting from the study should be submitted to the Chief Executive Officer.

'Please ensure that a copy of any publication that results from this project is forwarded to the Herston Medical Library for future reference'.
You are required to sign the duplicate copy attached of this approval stating that you will follow all the conditions of this approval and return same to the Secretary, Research Ethics Committee, Womens Health Sector.

Should you have any problems, please liaise directly with the Chairman of the Research Ethics Committee, Sir Raymond Hoffenberg, early in your programme.

Yours faithfully

for CHIEF EXECUTIVE OFFICER
WOMENS HEALTH SECTOR
Appendix 2

An example of an offertory letter to a childcare centre and the information sheet and consent form given to parents.
Anthony Herbert
365 5386 (W)
396 4354 (H)


The Co-ordinator,
The Silky Oak's Child Care Centre,
218 Manly Rd,
Manly. 4179

Dear Mrs Gorrie,

I am writing to you to ask you to consider allowing some simple research to be carried out on the children at the Silky Oaks's Child Care Centre. My name is Anthony Herbert and at present I am undertaking a research project within the University of Queensland's Department of Child Health. This project is called "Respiratory wave pattern and breathing research project" and focuses on children aged 0 to 10 years.

The research will provide information which will assist in the diagnosis and treatment of diseases such as asthma and pneumonia. Would you please consider allowing us to enlist some of the healthy children at your centre in the project. This will enable us to compare the breathing patterns of normal children with those with disease.

We will also be able to obtain average respiratory rates for the various ages. This would have direct application to First Aid situations in the community.

We would only involve children whose parents are informed about the research (see the proposed parent information sheet enclosed) and have signed a parent consent form. The research will involve the use of adhesive sensors about the size of an adult finger. The sensors are small, unobtrusive, painless and pose no risk to the children as they are composed entirely of plastic. They use visible light as a means of determining motion and there is no risk of electrical shock.
The time taken per child would be about 10 minutes (although this may vary per child). It would be preferable if the measurements could be done after the children were rested (if this is possible). The welfare of the children will be my first priority at all times. I will also comply with the parent’s and your staff’s wishes.

I am supervised by Dr Steven Wilson, from the Centre for Magnetic Resonance, and Prof John Pearn, from the Department of Child Health. You may contact them or myself if you are willing to let us work at your centre or if you want to know more information.

Thank you for considering my request. If you are willing to work with us it would be necessary to discuss the details of this project with you in person.

Yours faithfully,
Anthony Herbert.
Parent Information Sheet on Breathing Research Project

Dear parent,

The Department of Child Health at the University of Queensland is conducting research into the breathing patterns of children. We would request your consideration of allowing your child to participate in this simple project. This research will provide valuable information about breathing in children, and has direct application to the diagnosis and treatment of diseases such as asthma, pneumonia and bronchiolitis.

The project involves applying a small finger sized sensor on your child’s chest. It will involve minimal inconvenience to your child and is not painful. The device is made of plastic and is attached to an optical fibre which uses light as a means of determining motion. Therefore there is no risk of electrical shock.

The time the device will be applied will be short (approx. 10 - 15 minutes). Throughout this course of time, all consideration will be given to the welfare of your child. If you are willing to allow your child to participate could you please sign the consent form and return it.

Yours faithfully,
Anthony Herbert.

Parent Consent Form

I have read the parent information sheet.
I also understand I am free to withdraw my child from this study at any time.

I hereby give permission for my child, ________________________________

, to participate in the research analysing breathing patterns in children.

Has your child suffered from any respiratory illnesses (e.g. asthma) in the past?
If so what ________________________________

What is your child’s birthdate? ____________

Signed ___________________________ Date ____________
Appendix 3

Information sheet used in the Royal Children's Hospital and Royal Women's Hospital, Brisbane. The consent form used in the Royal Children's Hospital (shown first) differed slightly to that used in the Royal Women's Hospital.
Parent Information Sheet on Breathing Research Project

Dear parent,

The Department of Child Health at the University of Queensland is conducting research into the breathing patterns of children. We would request your consideration of allowing your baby to participate in this simple project. This research will provide information about breathing in children, and has direct application to the diagnosis and treatment of diseases such as pneumonia and bronchiolitis.

The project involves applying a small finger sized sensor on your child's chest. It will involve minimal inconvenience to your child and is not painful. The device is made of plastic and is attached to an optical fibre which uses light as a means of determining motion. Therefore there is no risk of electrical shock.

The time the device will be applied will be short (approx. 10-15 minutes). Throughout this course of time, all consideration will be given to the welfare of your child.

Yours sincerely,

Anthony Herbert

Department of Child Health,
University of Queensland.

(Ph 396 4354/365 5268)
Parent Consent Form

I have read the parent information sheet and the procedure has been explained to me by ____________________________.

I also understand I am free to withdraw my child from this study at any time.

I hereby give permission for my child, ____________________________,

to participate in the research analysing breathing patterns in children.

Signed ________________________ Date ________
Parent Consent Form

I have read the parent information sheet and the procedure has been explained to me by ________________________.

I give permission for my child, ________________________, to participate in the research analysing breathing patterns in children.

Parent/Guardian
Signature: ________________________ Date:_______

Witness: ________________________ Date:_______

Investigator's
Name: ________________________ Date:_______
Appendix 4

A questionnaire containing more detailed questions given to a sample of parents of children in the study. Some parents of children who did not participate in the study were also issued with this questionnaire.
Participation in Medical Research

Dear Parent,

The Department of Child Health at the University of Queensland is undertaking a study of breathing patterns in children. As you will recall, you would have received an "Information and Consent" form relating to this study.

To interpret the results of this study, we need to know parents' attitudes to their children's involvement in medical research and if those children who participated in the study are representative of all children in the kindergarten. We would be very grateful if you could complete the attached questionnaire. We require returned forms from all children who received a breathing test as well as all children who were not tested for a complete result. No names will be used in any publication of this data. Apart from returning this questionnaire, no further testing will be required.

We thank you for your help in this study.

Yours faithfully,

Anthony Herbert

Department of Child Health, University of Queensland.
(396 4354 / 365 5268)
Medical Research Questionnaire

Please tick the appropriate response.

1. Did you receive the "Information and Consent" form relating to the breathing research project?
   yes [ ] no [ ]

2. Was your child born prematurely?
   yes [ ] no [ ]
   If yes, by how many weeks? ..........

3. Has your child ever experienced any of the following in the past week?
   - sore throat [ ]
   - breathlessness [ ]
   - cough [ ]
   - fever [ ]
   - wheeze [ ]
   - runny nose [ ]
   - night cough [ ]

4. Has your child suffered from any major respiratory illnesses in the past?
   - Asthma [ ]
   - Bronchiolitis [ ]
   - Cystic Fibrosis [ ]
   - Pneumonia [ ]
   - Croup [ ]
   - Other [ ]
   If yes, does he/she still suffer from this condition?
   Yes [ ] No [ ]

5. Is there a family history of any respiratory disease in your family?
   - Asthma [ ]
   - Bronchiolitis [ ]
   - Cystic Fibrosis [ ]
   - Other [ ]
   If so, who? .................................................................

6. Parent(s) occupation ..................................................
   .................................................................

7. Does any one in the household smoke?
   yes [ ] no [ ]

8. Do you think there is any risk to your son/daughter participating in this type of medical research?
   yes [ ] no [ ] maybe [ ]

Comments:
Appendix 5

Australian Standard Classification of Occupations

The Australian Standard Classification of Occupations (ASCO) was used to determine socio-economic status. The major categories of occupations are outlined (Australian Bureau of Statistics, 1991a).

Occupations

1. Managers and Administrators:
   legislators and government appointed officials, general managers, specialist managers, farmers and farm managers, managing supervisors sales/service, managing supervisors other business.

2. Professionals:
   natural scientists, building professionals, health diagnosis and treatment practitioners, school teachers, other teachers and instructors, social professionals, business professionals, artists and related professionals

3. Para-professionals:
   medical and science technical officers and technicians, engineering and building associates and technicians, air and sea transport technical workers, registered nurses, police.

4. Tradespersons:
   metal fitting and machining tradespersons, other metal tradespersons, electrical and electronic trades persons, building tradespersons, printing tradespersons, vehicle tradespersons, food tradespersons, amenity horticultural tradespersons, marine construction tradespersons.

5. Clerks:
   stenographers and typists, data processing and business machine operators, numerical clerks, filing, sorting and copying clerks, material recording and dispatch clerks, receptionists, telephonists and messengers.

6. Salespersons and personal service workers:
   investment, insurance and real estate salespersons, sales representatives, sales assistants, tellers, cashiers and ticket salespersons.

7. Plant and machine operators and drivers:
   road and rail transport drivers, mobile plant operators.

8. Labourers and related workers:
   trades assistants and factory hands, agricultural labourers and related workers, cleaners, construction and mining labourers.

9. Other:
   inadequately described.
Appendix 6

Components of Optical Respiratory Sensor
(Wilson et al., 1993)

A. Vinyl tubing, No 2, Portex Ltd, High St, Hythe, Kent CT216JL.

B. Optical Fibre, Duplex polymer cable, Cat. 368-053, RS Components.

C. Optical fibre plug, Cat. 456-598, RS components.

D. Emitter - GaAsP LED SE 4355, Honeywell Optoelectronics, 830 East Arapaho Rd, Richardson Texas, 75081.

E. Detector, Photodarlington MEL12, Microelectronics, 38 Hung To Rd, Kwun Tong, Kowloon, Hong Kong.
Appendix 7

Method for Determining Coefficients of Quadratic and Cubic Equations
(Rashbash, Pan and Goldstein, 1992)

The smoothed values of the \( r \)th percentile represented by a quadratic equation can be written as:

\[
y_i = a_{0,i} + a_{1,i}t + a_{2,i}t^2
\]  
(1)

and for a cubic equation can be written as:

\[
y_i = a_{0,i} + a_{1,i}t + a_{2,i}t^2 + a_{3,i}t^3
\]  
(2)

where \( y_i = \log_{10}(RR)_i \) and \( t = \text{age} \).

It was beneficial for each centile to interrelate in a smooth way with the other centiles. This was achieved by modelling the coefficients \( (a_0, a_1, a_2, \text{and } a_3) \) as polynomial functions of the normal equivalent (NED) which corresponded to the \( r \)th centile. For the 3rd centile \( Z_3 = -1.88 \); the 50th centile \( Z_{50} = 0 \); for the 95th centile \( Z_{95} = 1.645 \).

For the quadratic equations, linear equations described \( a_0 \) and \( a_1 \) and \( a_2 \) was a constant:

\[
a_{0,i} = b_{0,0} + b_{0,i}Z_i
\]  
(2)

\[
a_{1,i} = b_{1,0} + b_{1,i}Z_i
\]  
(3)

\[
a_{2,i} = b_{2,0}
\]  
(4)

The final model for the \( r \)th centile can be summarised as:

\[
\log_{10}(RR)_i = (b_{0,0} + b_{0,i}Z_i) + (b_{1,0} + b_{1,i}Z_i)t + b_{2,0}t^2
\]  
(5)

For the cubic equations, a quadratic equation described \( a_0 \), linear equations described \( a_1 \) and \( a_2 \) while \( a_3 \) was constant:

\[
a_{0,i} = b_{0,0} + b_{0,i}Z_i + b_{0,2}Z_i^2
\]  
(6)

\[
a_{1,i} = b_{1,0} + b_{1,i}Z_i
\]  
(7)

\[
a_{2,i} = b_{2,0} + b_{2,i}Z_i
\]  
(8)

\[
a_{3,i} = b_{3,0}
\]  
(9)

The final model for the \( r \)th centile can be summarised as:

\[
\log_{10}(RR)_i = (b_{0,0} + b_{0,i}Z_i + b_{0,2}Z_i^2) + (b_{1,0} + b_{1,i}Z_i)t + (b_{2,0} + b_{2,i}Z_i)t^2 + b_{3,0}t^3
\]  
(10)
Appendix 8

General Equations from which Centile Curve Equations Can be Calculated

In the following equations, $Z_i$ is the normal equivalent deviate corresponding to the $i$th centile.

The equation for any centile can be obtained using these equations, provided the normal equivalent deviate corresponding to the $i$th centile is known. For example, for the 50th centile, $Z_{50} = 0$, and for the 95th centile, $Z_{95} = 1.645$.

Equation for sleeping children aged 0 to 1 year
\[
\log_{10} RR = (1.6305 + 0.051935 Z_i) + (-0.4112 - 0.017270 Z_i) t + (0.017280 + 0.010149 Z_i) t^2 + 0.1096 t^3
\]  
(1)

Equation for sleeping children aged 1 to 3 years
\[
\log_{10} RR = (1.4033 + 0.041786 Z_i) + (-0.066258 + 0.003029 Z_i) t + 0.009213 t^2
\]  
(2)

Equation for awake children aged 1 to 3 years
\[
\log_{10} RR = (1.8443 + 0.13834 Z_i) + (-0.32323 - 0.055706 Z_i) t + (0.080288 + 0.0099218 Z_i) t^2 - 0.0069819 t^3
\]  
(3)

Equation for awake children aged 3 to 13 years
\[
\log_{10} RR = (1.5092 + 0.04904 Z_i) + (-0.037037 + 0.0038248 Z_i) t + 0.0011707 t^2
\]  
(4)
## Appendix 9

### Respiratory Timing Indices in Healthy Subjects

#### A. Respiratory Timing Indices in Healthy Sleeping Children

<table>
<thead>
<tr>
<th>Initial</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>$T_{TOT} \pm SD$ (s)</th>
<th>$T_1 \pm SD$ (s)</th>
<th>$T_2 \pm SD$ (s)</th>
<th>$T_1/T_{TOT} \pm SD$</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.K.</td>
<td>0.003</td>
<td>M</td>
<td>1.05 ± 0.28</td>
<td>0.43 ± 0.07</td>
<td>0.62 ± 0.22</td>
<td>0.42 ± 0.05</td>
</tr>
<tr>
<td>J.N.</td>
<td>0.005</td>
<td>F</td>
<td>1.52 ± 0.16</td>
<td>0.63 ± 0.06</td>
<td>0.89 ± 0.12</td>
<td>0.40 ± 0.03</td>
</tr>
<tr>
<td>M.T.</td>
<td>0.005</td>
<td>F</td>
<td>1.08 ± 0.12</td>
<td>0.44 ± 0.05</td>
<td>0.64 ± 0.10</td>
<td>0.41 ± 0.04</td>
</tr>
<tr>
<td>L.W.</td>
<td>0.005</td>
<td>M</td>
<td>1.21 ± 0.22</td>
<td>0.62 ± 0.11</td>
<td>0.59 ± 0.12</td>
<td>0.51 ± 0.04</td>
</tr>
<tr>
<td>M.T.</td>
<td>0.005</td>
<td>F</td>
<td>1.01 ± 0.15</td>
<td>0.51 ± 0.07</td>
<td>0.50 ± 0.06</td>
<td>0.50 ± 0.06</td>
</tr>
<tr>
<td>L.W.</td>
<td>0.005</td>
<td>M</td>
<td>1.09 ± 0.07</td>
<td>0.51 ± 0.03</td>
<td>0.57 ± 0.07</td>
<td>0.47 ± 0.03</td>
</tr>
<tr>
<td>L.D.</td>
<td>0.008</td>
<td>M</td>
<td>1.42 ± 0.13</td>
<td>0.56 ± 0.07</td>
<td>0.85 ± 0.14</td>
<td>0.40 ± 0.06</td>
</tr>
<tr>
<td>N.S.</td>
<td>0.008</td>
<td>M</td>
<td>1.20 ± 0.11</td>
<td>0.51 ± 0.05</td>
<td>0.69 ± 0.08</td>
<td>0.43 ± 0.03</td>
</tr>
<tr>
<td>T.T.</td>
<td>0.008</td>
<td>F</td>
<td>1.61 ± 0.14</td>
<td>0.71 ± 0.04</td>
<td>0.90 ± 0.14</td>
<td>0.44 ± 0.04</td>
</tr>
<tr>
<td>S.C.</td>
<td>0.014</td>
<td>M</td>
<td>1.78 ± 0.14</td>
<td>0.73 ± 0.08</td>
<td>1.05 ± 0.09</td>
<td>0.41 ± 0.02</td>
</tr>
<tr>
<td>J.S.</td>
<td>0.05</td>
<td>M</td>
<td>1.60 ± 0.09</td>
<td>0.64 ± 0.05</td>
<td>0.96 ± 0.06</td>
<td>0.40 ± 0.02</td>
</tr>
<tr>
<td>E.M.</td>
<td>0.1</td>
<td>F</td>
<td>0.99 ± 0.15</td>
<td>0.46 ± 0.06</td>
<td>0.53 ± 0.15</td>
<td>0.47 ± 0.07</td>
</tr>
<tr>
<td>S.H.</td>
<td>0.1</td>
<td>F</td>
<td>1.65 ± 0.16</td>
<td>0.69 ± 0.11</td>
<td>0.96 ± 0.08</td>
<td>0.42 ± 0.03</td>
</tr>
<tr>
<td>A.N.</td>
<td>0.18</td>
<td>F</td>
<td>1.43 ± 0.42</td>
<td>0.43 ± 0.14</td>
<td>0.89 ± 0.30</td>
<td>0.38 ± 0.04</td>
</tr>
<tr>
<td>L.P.</td>
<td>0.32</td>
<td>F</td>
<td>0.91 ± 0.09</td>
<td>0.33 ± 0.03</td>
<td>0.57 ± 0.08</td>
<td>0.37 ± 0.03</td>
</tr>
<tr>
<td>S.B.</td>
<td>0.4</td>
<td>F</td>
<td>0.94 ± 0.08</td>
<td>0.41 ± 0.06</td>
<td>0.53 ± 0.05</td>
<td>0.44 ± 0.04</td>
</tr>
<tr>
<td>M.S.</td>
<td>0.43</td>
<td>M</td>
<td>1.92 ± 0.16</td>
<td>0.74 ± 0.09</td>
<td>1.18 ± 0.10</td>
<td>0.38 ± 0.03</td>
</tr>
<tr>
<td>I.A.</td>
<td>0.6</td>
<td>M</td>
<td>1.96 ± 0.11</td>
<td>0.8 ± 0.09</td>
<td>1.16 ± 0.09</td>
<td>0.41 ± 0.04</td>
</tr>
<tr>
<td>T.G.</td>
<td>0.73</td>
<td>F</td>
<td>2.59 ± 0.10</td>
<td>1.01 ± 0.07</td>
<td>1.58 ± 0.07</td>
<td>0.39 ± 0.02</td>
</tr>
<tr>
<td>A.P.</td>
<td>0.94</td>
<td>F</td>
<td>2.67 ± 0.35</td>
<td>1.10 ± 0.11</td>
<td>1.57 ± 0.30</td>
<td>0.42 ± 0.05</td>
</tr>
<tr>
<td>M.P.</td>
<td>1.61</td>
<td>M</td>
<td>3.04 ± 0.14</td>
<td>1.36 ± 0.08</td>
<td>1.68 ± 0.14</td>
<td>0.45 ± 0.03</td>
</tr>
<tr>
<td>M.S.</td>
<td>1.7</td>
<td>F</td>
<td>3.38 ± 0.31</td>
<td>1.06 ± 0.11</td>
<td>2.32 ± 0.33</td>
<td>0.31 ± 0.04</td>
</tr>
<tr>
<td>T.P.</td>
<td>2</td>
<td>M</td>
<td>3.74 ± 0.20</td>
<td>1.49 ± 0.12</td>
<td>2.25 ± 0.19</td>
<td>0.4 ± 0.03</td>
</tr>
<tr>
<td>R.D.</td>
<td>3.27</td>
<td>M</td>
<td>3.40 ± 0.27</td>
<td>1.41 ± 0.21</td>
<td>1.99 ± 0.18</td>
<td>0.41 ± 0.05</td>
</tr>
<tr>
<td>D.D.</td>
<td>3.27</td>
<td>M</td>
<td>3.67 ± 0.27</td>
<td>1.54 ± 0.12</td>
<td>2.12 ± 0.23</td>
<td>0.42 ± 0.03</td>
</tr>
<tr>
<td><strong>Mean ± S.D.</strong></td>
<td></td>
<td></td>
<td><strong>1.80 ± 0.93</strong></td>
<td><strong>0.73 ± 0.36</strong></td>
<td><strong>1.06 ± 0.58</strong></td>
<td><strong>0.42 ± 0.04</strong></td>
</tr>
</tbody>
</table>

#### B. Respiratory Timing Indices in Healthy Awake Young Adults

<table>
<thead>
<tr>
<th>Initial</th>
<th>Ag (yr)</th>
<th>Sex</th>
<th>$T_{TOT} \pm SD$ (s)</th>
<th>$T_1 \pm SD$ (s)</th>
<th>$T_2 \pm SD$ (s)</th>
<th>$T_1/T_{TOT} \pm SD$</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.M.</td>
<td>19</td>
<td>M</td>
<td>5.6 ± 0.65</td>
<td>2.12 ± 0.37</td>
<td>3.48 ± 0.58</td>
<td>0.38 ± 0.06</td>
</tr>
<tr>
<td>J.W.</td>
<td>21</td>
<td>M</td>
<td>3.86 ± 0.47</td>
<td>1.55 ± 0.25</td>
<td>2.31 ± 0.36</td>
<td>0.40 ± 0.04</td>
</tr>
<tr>
<td>A.K.</td>
<td>21</td>
<td>M</td>
<td>2.86 ± 0.44</td>
<td>1.45 ± 0.22</td>
<td>1.40 ± 0.27</td>
<td>0.51 ± 0.03</td>
</tr>
<tr>
<td>J.P.</td>
<td>22</td>
<td>M</td>
<td>2.72 ± 0.12</td>
<td>1.06 ± 0.07</td>
<td>1.66 ± 0.08</td>
<td>0.39 ± 0.02</td>
</tr>
<tr>
<td>S.M.</td>
<td>22</td>
<td>M</td>
<td>4.00 ± 0.60</td>
<td>1.41 ± 0.19</td>
<td>1.41 ± 0.19</td>
<td>0.36 ± 0.07</td>
</tr>
<tr>
<td>P.G.</td>
<td>22</td>
<td>M</td>
<td>3.72 ± 0.46</td>
<td>1.59 ± 0.29</td>
<td>2.13 ± 0.30</td>
<td>0.43 ± 0.04</td>
</tr>
<tr>
<td>P.W.</td>
<td>22</td>
<td>M</td>
<td>5.09 ± 0.78</td>
<td>2.22 ± 0.54</td>
<td>2.87 ± 0.54</td>
<td>0.44 ± 0.03</td>
</tr>
<tr>
<td>P.D.</td>
<td>23</td>
<td>M</td>
<td>3.61 ± 0.37</td>
<td>1.71 ± 0.31</td>
<td>1.9 ± 0.18</td>
<td>0.47 ± 0.05</td>
</tr>
<tr>
<td><strong>Mean ± S.D.</strong></td>
<td></td>
<td></td>
<td><strong>3.93 ± 1.00</strong></td>
<td><strong>1.64 ± 0.73</strong></td>
<td><strong>2.14 ± 0.73</strong></td>
<td><strong>0.42 ± 0.05</strong></td>
</tr>
</tbody>
</table>
### C. Respiratory Timing Indices in Awake Children

<table>
<thead>
<tr>
<th>Initial</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>$T_{TOT} \pm SD$ (s)</th>
<th>$T_i \pm SD$ (s)</th>
<th>$T_E \pm SD$ (s)</th>
<th>$T_i/T_{TOT} \pm SD$</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.P.</td>
<td>2</td>
<td>M</td>
<td>1.96 ± 0.18</td>
<td>0.79 ± 0.09</td>
<td>1.17 ± 0.11</td>
<td>0.40 ± 0.02</td>
</tr>
<tr>
<td>S.W.</td>
<td>2</td>
<td>M</td>
<td>1.63 ± 0.20</td>
<td>0.79 ± 0.13</td>
<td>0.84 ± 0.13</td>
<td>0.48 ± 0.05</td>
</tr>
<tr>
<td>A.S.</td>
<td>2</td>
<td>M</td>
<td>2.06 ± 0.23</td>
<td>0.97 ± 0.10</td>
<td>2.06 ± 0.23</td>
<td>0.47 ± 0.04</td>
</tr>
<tr>
<td>N.S.</td>
<td>2</td>
<td>F</td>
<td>2.30 ± 0.41</td>
<td>0.93 ± 0.21</td>
<td>1.37 ± 0.26</td>
<td>0.40 ± 0.05</td>
</tr>
<tr>
<td>S.S.</td>
<td>2</td>
<td>F</td>
<td>2.30 ± 0.19</td>
<td>0.94 ± 0.17</td>
<td>1.37 ± 0.11</td>
<td>0.41 ± 0.05</td>
</tr>
<tr>
<td>M.W.</td>
<td>2</td>
<td>F</td>
<td>2.18 ± 0.42</td>
<td>0.91 ± 0.12</td>
<td>1.27 ± 0.32</td>
<td>0.42 ± 0.04</td>
</tr>
<tr>
<td>A.L.</td>
<td>3</td>
<td>F</td>
<td>1.99 ± 0.24</td>
<td>0.88 ± 0.12</td>
<td>1.11 ± 0.16</td>
<td>0.44 ± 0.03</td>
</tr>
<tr>
<td>W.H.</td>
<td>3</td>
<td>M</td>
<td>2.62 ± 0.25</td>
<td>1.07 ± 0.12</td>
<td>1.55 ± 0.23</td>
<td>0.41 ± 0.05</td>
</tr>
<tr>
<td>C.B.</td>
<td>3</td>
<td>F</td>
<td>2.26 ± 0.29</td>
<td>0.93 ± 0.09</td>
<td>1.33 ± 0.23</td>
<td>0.41 ± 0.03</td>
</tr>
<tr>
<td>A.C.</td>
<td>3</td>
<td>F</td>
<td>2.82 ± 0.26</td>
<td>1.08 ± 0.09</td>
<td>1.74 ± 0.20</td>
<td>0.38 ± 0.02</td>
</tr>
<tr>
<td>J.C.</td>
<td>3</td>
<td>F</td>
<td>2.83 ± 0.44</td>
<td>1.09 ± 0.21</td>
<td>1.74 ± 0.33</td>
<td>0.39 ± 0.05</td>
</tr>
<tr>
<td>C.B.</td>
<td>3</td>
<td>F</td>
<td>2.10 ± 0.23</td>
<td>0.88 ± 0.08</td>
<td>1.22 ± 0.19</td>
<td>0.42 ± 0.03</td>
</tr>
<tr>
<td>C.M.</td>
<td>4</td>
<td>F</td>
<td>3.76 ± 0.47</td>
<td>1.50 ± 0.21</td>
<td>2.25 ± 0.43</td>
<td>0.40 ± 0.06</td>
</tr>
<tr>
<td>S.K.</td>
<td>4</td>
<td>M</td>
<td>1.81 ± 0.12</td>
<td>0.81 ± 0.08</td>
<td>1.01 ± 0.09</td>
<td>0.45 ± 0.03</td>
</tr>
<tr>
<td>M.G.</td>
<td>4</td>
<td>F</td>
<td>2.76 ± 0.36</td>
<td>1.04 ± 0.25</td>
<td>1.72 ± 0.17</td>
<td>0.37 ± 0.04</td>
</tr>
<tr>
<td>C.G.</td>
<td>5</td>
<td>F</td>
<td>2.94 ± 0.25</td>
<td>1.30 ± 0.18</td>
<td>1.64 ± 0.19</td>
<td>0.44 ± 0.05</td>
</tr>
<tr>
<td>R.H.</td>
<td>5</td>
<td>F</td>
<td>3.73 ± 0.77</td>
<td>1.52 ± 0.41</td>
<td>2.22 ± 0.51</td>
<td>0.41 ± 0.07</td>
</tr>
<tr>
<td>N.W.</td>
<td>5</td>
<td>M</td>
<td>2.92 ± 0.32</td>
<td>1.17 ± 0.09</td>
<td>1.76 ± 0.29</td>
<td>0.40 ± 0.04</td>
</tr>
<tr>
<td>P.R.</td>
<td>5</td>
<td>F</td>
<td>2.20 ± 0.35</td>
<td>0.85 ± 0.14</td>
<td>1.35 ± 0.29</td>
<td>0.39 ± 0.06</td>
</tr>
<tr>
<td>K.T.</td>
<td>5</td>
<td>F</td>
<td>2.68 ± 0.28</td>
<td>0.98 ± 0.23</td>
<td>1.70 ± 0.22</td>
<td>0.36 ± 0.07</td>
</tr>
<tr>
<td>S.H.</td>
<td>6</td>
<td>F</td>
<td>2.71 ± 0.15</td>
<td>1.10 ± 0.11</td>
<td>1.61 ± 0.09</td>
<td>0.41 ± 0.03</td>
</tr>
<tr>
<td>P.I.</td>
<td>7</td>
<td>M</td>
<td>3.31 ± 0.38</td>
<td>1.32 ± 0.21</td>
<td>1.99 ± 0.23</td>
<td>0.40 ± 0.03</td>
</tr>
<tr>
<td>R.L.</td>
<td>7</td>
<td>M</td>
<td>2.77 ± 0.10</td>
<td>1.06 ± 0.07</td>
<td>1.71 ± 0.14</td>
<td>0.38 ± 0.03</td>
</tr>
<tr>
<td>J.C.</td>
<td>7</td>
<td>F</td>
<td>2.46 ± 0.23</td>
<td>1.09 ± 0.15</td>
<td>1.37 ± 0.23</td>
<td>0.45 ± 0.06</td>
</tr>
<tr>
<td>S.T.</td>
<td>7</td>
<td>M</td>
<td>2.99 ± 0.46</td>
<td>1.09 ± 0.14</td>
<td>1.90 ± 0.43</td>
<td>0.37 ± 0.05</td>
</tr>
<tr>
<td>E.T.</td>
<td>7</td>
<td>F</td>
<td>3.53 ± 0.57</td>
<td>1.42 ± 0.41</td>
<td>2.11 ± 0.29</td>
<td>0.40 ± 0.06</td>
</tr>
<tr>
<td>B.E.</td>
<td>8</td>
<td>M</td>
<td>2.46 ± 0.38</td>
<td>0.95 ± 0.14</td>
<td>1.51 ± 0.29</td>
<td>0.39 ± 0.04</td>
</tr>
<tr>
<td>C.H.</td>
<td>8</td>
<td>M</td>
<td>2.93 ± 0.17</td>
<td>1.12 ± 0.10</td>
<td>1.81 ± 0.14</td>
<td>0.38 ± 0.03</td>
</tr>
<tr>
<td>P.J.</td>
<td>8</td>
<td>M</td>
<td>3.26 ± 0.32</td>
<td>0.83 ± 0.09</td>
<td>1.43 ± 0.28</td>
<td>0.37 ± 0.05</td>
</tr>
<tr>
<td>M.C.</td>
<td>9</td>
<td>F</td>
<td>3.29 ± 0.65</td>
<td>1.56 ± 0.33</td>
<td>1.73 ± 0.37</td>
<td>0.47 ± 0.04</td>
</tr>
<tr>
<td>C.G.</td>
<td>11</td>
<td>F</td>
<td>3.18 ± 0.46</td>
<td>1.26 ± 0.19</td>
<td>1.92 ± 0.38</td>
<td>0.4 ± 0.05</td>
</tr>
<tr>
<td>S.L.</td>
<td>11</td>
<td>F</td>
<td>3.53 ± 0.36</td>
<td>1.45 ± 0.14</td>
<td>2.08 ± 0.44</td>
<td>0.42 ± 0.08</td>
</tr>
<tr>
<td>Y.K.</td>
<td>11</td>
<td>F</td>
<td>2.92 ± 0.18</td>
<td>1.13 ± 0.05</td>
<td>1.79 ± 0.11</td>
<td>0.39 ± 0.02</td>
</tr>
<tr>
<td>J.L.</td>
<td>11</td>
<td>M</td>
<td>3.70 ± 0.47</td>
<td>1.41 ± 0.16</td>
<td>1.8 ± 0.43</td>
<td>0.44 ± 0.06</td>
</tr>
<tr>
<td>B.C.</td>
<td>11</td>
<td>F</td>
<td>2.94 ± 0.41</td>
<td>1.38 ± 0.29</td>
<td>1.56 ± 0.21</td>
<td>0.47 ± 0.05</td>
</tr>
<tr>
<td>J.D.</td>
<td>11</td>
<td>F</td>
<td>2.85 ± 0.21</td>
<td>1.28 ± 0.14</td>
<td>1.57 ± 0.14</td>
<td>0.45 ± 0.03</td>
</tr>
<tr>
<td>B.W.</td>
<td>12</td>
<td>F</td>
<td>3.24 ± 0.61</td>
<td>1.20 ± 0.13</td>
<td>2.03 ± 0.49</td>
<td>0.38 ± 0.03</td>
</tr>
<tr>
<td>J.A.</td>
<td>12</td>
<td>F</td>
<td>3.18 ± 0.36</td>
<td>1.44 ± 0.18</td>
<td>1.74 ± 0.23</td>
<td>0.45 ± 0.03</td>
</tr>
<tr>
<td><strong>Mean ± S.D.</strong></td>
<td></td>
<td></td>
<td><strong>2.77 ± 0.56</strong></td>
<td><strong>1.14 ± 0.23</strong></td>
<td><strong>1.63 ± 0.34</strong></td>
<td><strong>0.41 ± 0.03</strong></td>
</tr>
</tbody>
</table>
Appendix 10

Comments Made by Parents Relating to Research Project

The following comments were made by parents in a questionnaire in relation to the breathing research study (see Appendix 4).

Pre-school children:

"Depends entirely on methods used and quality of supervision."

"We don't know what procedures and tests will be administered to our son. What sort of risk - spread of infection from other participants or researchers, physical damage or discomfort due to testing situation, administration or equipment."

"Sarah was very excited about having been tested. Said 'a nice person measured me. It was fun.'"

"If this type of research will help children I'm all for it."

"It would be interesting to learn of the results of the study."

"Because I don't know the details of what the research entails."

"Please advise of procedures that can cause harm."

"Would like feedback."

"Unsure of the person conducting the research and therefore Daniel may have been upset. However, this was not the case in this instance as staff were on hand to ensure that the children were not upset."

"I'd like to know what the research is intended to do (i.e. findings) Will it involve research over a prolonged period i.e. reassessing the child over time."

School Children

"Shalveen's asthma was really bad until he started using "Buteyko breathing techniques" in which he has learnt to breathe in and out through his nose always. Would he be asked to breath using mouth if he does participate in your research (main concern)."

"I hope you get some positive outcomes."

"The child was happy to help this time but doesn't want to help any more."

"Anything done in the interest of children's health has my support. Well done."
Appendix 11

Detailed respiratory rate data in awake subjects with asthma aged from 1.0 to 16.99 years.

Key:

* Denotes receiving oxygen.

† RR(a) - Respiratory rate measured for two thirty second periods.
RR(b) - Respiratory rate measured for total test period.
RR(95th centile) - Denotes RR corresponding to the 95th centile for healthy children (appropriate for age).

‡ Medication abbreviations:
  V - salbutamol suflate (Ventolin), At - ipratropium bromide (Atrovent), S - steroid treatment; P - Paracetamol (Panadol), Ab - antibiotic, I - sodium cromoglycate (Intal).
Numbers in brackets indicate time between Ventolin treatment in hours.
### Table: Respiratory Rates in Awake Children with Asthma Aged 1.0 to 6.99 Years and 7.0 to 9.99 Years

<table>
<thead>
<tr>
<th>Initial Sex</th>
<th>Age (y)</th>
<th>Days after admission (0h)</th>
<th>Z-score (SD)</th>
<th>RR (A)</th>
<th>RR (B)</th>
<th>Diff RR Time to Ventil (min)</th>
<th>Ventil used</th>
<th>Before (A) PEFR</th>
<th>After (A) PEFR</th>
<th>PEFR%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>7-10</td>
<td>3</td>
<td>±2.29</td>
<td>1.04</td>
<td>1.90</td>
<td>±6.3</td>
<td>B</td>
<td>280</td>
<td>113</td>
<td></td>
</tr>
<tr>
<td>Subject</td>
<td>Oral (a)</td>
<td>Nasal (b)</td>
<td>RR (a)</td>
<td>T (a)</td>
<td>PEFR (b)</td>
<td>PEFR % (b)</td>
<td>Admissions</td>
<td>Days Alive (b)</td>
<td>Z-score</td>
<td>PEFR and SD</td>
</tr>
<tr>
<td>---------</td>
<td>----------</td>
<td>-----------</td>
<td>--------</td>
<td>-----</td>
<td>---------</td>
<td>-----------</td>
<td>------------</td>
<td>----------------</td>
<td>---------</td>
<td>--------------</td>
</tr>
<tr>
<td>D.B.</td>
<td>A</td>
<td>87</td>
<td>5.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D.H.</td>
<td>B</td>
<td>1.5</td>
<td>6.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Note: Table contains data on respiratory rates in awake children with asthma aged 10.0 - 12.99 years and 13.0 - 16.99 years.*
Appendix 12

Changes in respiratory rates and other respiratory parameters (including PEFR, FEV₁₀) occurring in children who were tested on two or more occasions.
### Table 12: Table Showing Changes in Respiratory Indices in Subjects with Asthma Treated on Two Occasions

<table>
<thead>
<tr>
<th>Initial Sex</th>
<th>Age (y)</th>
<th>Initial FEV1 % predicted</th>
<th>Final FEV1 % predicted</th>
<th>Initial PEFR (L/min)</th>
<th>Final PEFR (L/min)</th>
<th>Initial Reactive Airways Disease Score</th>
<th>Final Reactive Airways Disease Score</th>
<th>Initial Reaction (Z) score</th>
<th>Final Reaction (Z) score</th>
<th>Initial Reaction (P) score</th>
<th>Final Reaction (P) score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4.6</td>
<td>3.6</td>
<td>3.6</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>-3</td>
<td>-3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>4.6</td>
<td>3.6</td>
<td>3.6</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>-3</td>
<td>-3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>4.6</td>
<td>3.6</td>
<td>3.6</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>-3</td>
<td>-3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>4.6</td>
<td>3.6</td>
<td>3.6</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>-3</td>
<td>-3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: The table contains data on changes in respiratory indices in subjects with asthma treated on two occasions. The data includes initial and final values for FEV1, PEFR, and reactive airways disease scores.
Appendix 12 (con.) - Table Showing Changes in Respiratory Indices in Subjects with Asthma Tested on Three Occasions

<table>
<thead>
<tr>
<th>Initial</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Day of Illness</th>
<th>R.R. one min. (bpm)</th>
<th>Z-score (SD)</th>
<th>R.R. total time (bpm)</th>
<th>Time (min.)</th>
<th>T1 / Ttot</th>
<th>O2 Sat. (%)</th>
<th>PEFR (L/min.)</th>
<th>FEV1.0 (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.F.</td>
<td>M</td>
<td>9.14</td>
<td>1</td>
<td>38</td>
<td>5.38</td>
<td>41.5</td>
<td>6</td>
<td>0.47</td>
<td>97*</td>
<td>200</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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* Denotes receiving oxygen therapy

---- Denotes value not measured or calculated


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