A critical approach to the detection and measurement of infantile apnoea in preterm and high-risk infants

---0000---

VIVIENNE HAZEL VAN SOMEREN

---0000---

A thesis submitted for the Degree of Doctor of Medicine
University of Edinburgh
1984
ABSTRACT

There are two forms of infantile apnoea: central apnoea, in which respiratory efforts cease, and obstructive apnoea, in which respiratory efforts continue, but no air flow results. No study of infantile apnoea can be considered complete unless the methods used allow detection of both phenomena. In the current work, this was achieved by devising a polygraphic monitoring system incorporating both respiratory movement and airflow detectors. The latter required a unique facial appliance to maintain the sensors within the airstreams of the infant. The system was refined by the incorporation of electronic methods for speeding up the detection of the apnoeas present on the trace.

However, identification of apnoeic episodes proved to be only a beginning. A considerable amount of work on the interpretation and quantification of the data was required before the system could be used to compare apnoea rates in different groups of subjects. In particular, the polygraphic definition of obstructive apnoea was critically examined and found to include much normal movement, as well as true obstructive apnoea, indicating that previous work based on the usual polygraphic definition of obstructive apnoea has overestimated its importance.

The methods were then used to determine the rates of central and obstructive apnoea in various groups of infants. Fourteen full-term infants who had suffered a "near miss" cot death were studied both clinically and polygraphically. A subgroup of these infants which could be defined clinically was found to show an unusually high rate of central, but not obstructive, apnoea.
Using similar methods, preterm infants, whose airways resistance was iatrogenically increased by naso-enteric feeding tubes, exhibited higher scores for central apnoea and lower TcPO₂ levels than those in whom the nose was left free.

The significance of these brief respiratory pauses is not known, but the evidence that they result from increased oscillations in an unstable control system was reviewed and the complex relationship between apnoea and hypoxia, whereby each can be either cause or effect, was discussed.

Throughout the work, new insights were gained from a critical reappraisal of the work of others. In the difficult field of infantile apnoea and SIDS, judicious co-operation between investigators is the avenue most likely to lead to significant advances.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>1</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>3</td>
</tr>
<tr>
<td>INDEX OF FIGURES AND TABLES</td>
<td>8</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>12</td>
</tr>
<tr>
<td>CHAPTER ONE - INFANT APNOEA: BACKGROUND AND AIMS OF THE PROJECT</td>
<td>14</td>
</tr>
<tr>
<td>EARLY CLINICAL OBSERVATIONS</td>
<td>15</td>
</tr>
<tr>
<td>LABORATORY OBSERVATIONS</td>
<td>19</td>
</tr>
<tr>
<td>THE AIMS OF THE PROJECT</td>
<td>23</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>25</td>
</tr>
<tr>
<td>CHAPTER TWO - INFANT APNOEA: METHODS OF DETECTION, DATA STORAGE AND RETRIEVAL</td>
<td>30</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>31</td>
</tr>
<tr>
<td>AIRFLOW DETECTION</td>
<td>31</td>
</tr>
<tr>
<td>(a) THE BUTTERFLY PLATE</td>
<td>31</td>
</tr>
<tr>
<td>(b) NASAL THERMISTORS</td>
<td>33</td>
</tr>
<tr>
<td>IMPEDANCE PNEUMOGRAPHY</td>
<td>41</td>
</tr>
<tr>
<td>ELECTROCARDIOGRAM</td>
<td>42</td>
</tr>
<tr>
<td>RECORDING APPARATUS</td>
<td>42</td>
</tr>
<tr>
<td>THE APNOEA DETECTOR</td>
<td>42</td>
</tr>
<tr>
<td>RECORDING OF HEART RATE</td>
<td>46</td>
</tr>
<tr>
<td>THE COMPLETED SYSTEM</td>
<td>47</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>50</td>
</tr>
<tr>
<td>CHAPTER THREE - A CLOSER LOOK AT OBSTRUCTIVE APNOEA</td>
<td>52</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>53</td>
</tr>
</tbody>
</table>
1. **DETECTION OF EXPIRED CO₂ AT THE MOUTH RECORDED IN NORMAL NEONATES** .................................................. 54
   - **INTRODUCTION** .................................................. 54
   - **METHODS** ...................................................... 55
   - **RESULTS** ....................................................... 55
   - **CONCLUSION** .................................................. 57

2. **OESOPHAGEAL PRESSURES RECORDED IN INFANTS WITH SUSPECTED UPPER AIRWAYS OBSTRUCTION** .......................... 57
   - **INTRODUCTION** .................................................. 57
   - **METHODS** ...................................................... 57
   - **RESULTS** ....................................................... 59
     - i. True Obstructive Apnoea .................................... 59
     - ii. False Obstructive Apnoea ................................ 59
     - iii. Movement .................................................. 59

3. **DIRECT OBSERVATION OF AN INFANT WITH DEFINITE UPPER AIRWAY OBSTRUCTION** ........................................ 63
   - **INTRODUCTION** .................................................. 63
   - **METHODS** ...................................................... 65
   - **RESULTS** ....................................................... 65
   - **DISCUSSION** .................................................. 67
   - **REFERENCES** .................................................. 70

4. **CHAPTER FOUR - QUANTITATIVE ANALYSIS OF APNOEA RATES** ................................................................. 72
   - **INTRODUCTION** .................................................. 73
   - **THE DEVELOPMENT OF THE SCORING SYSTEM** .............. 73
   - **INTER-OBSERVER VARIABILITY** ................................ 77
   - **METHODS** ...................................................... 79
CHAPTER SIX - THE EFFECT OF NASOENTERIC TUBES ON THE INCIDENCE OF APNOEA AND TcPO2 LEVELS IN PRETERM INFANTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRODUCTION</td>
<td>114</td>
</tr>
<tr>
<td>STUDY 1: A CLINICAL TRIAL TO COMPARE NASOENTERIC TUBE-FEEDING WITH OROENTERIC TUBE-FEEDING USING THE PALATAL APPLIANCE</td>
<td>118</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>118</td>
</tr>
<tr>
<td>METHODS</td>
<td>119</td>
</tr>
<tr>
<td>Clinical</td>
<td>119</td>
</tr>
<tr>
<td>Polygraphic Monitoring</td>
<td>120</td>
</tr>
<tr>
<td>RESULTS</td>
<td>122</td>
</tr>
<tr>
<td>Clinical</td>
<td>122</td>
</tr>
<tr>
<td>Polygraphic</td>
<td>122</td>
</tr>
<tr>
<td>CONCLUSION</td>
<td>125</td>
</tr>
<tr>
<td>STUDY 2: FURTHER EXAMINATION OF THE EFFECTS OF THE PASSAGE AND REMOVAL OF NASOENTERIC TUBES ON APNOEA AND PO2</td>
<td>128</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>128</td>
</tr>
<tr>
<td>RESULTS</td>
<td>129</td>
</tr>
<tr>
<td>CONCLUSIONS</td>
<td>129</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>132</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>134</td>
</tr>
<tr>
<td>CHAPTER SEVEN - DISCUSSION</td>
<td>135</td>
</tr>
<tr>
<td>1. THE LOW INCIDENCE OF TRUE OBSTRUCTIVE APNOEA IN ALL THE INFANTS STUDIED</td>
<td>136</td>
</tr>
</tbody>
</table>
INDEX OF FIGURES AND TABLES

CHAPTER ONE

No Figures or Tables.

CHAPTER TWO

FIGURE 1: The butterfly plate and airflow sensors in situ.
2: Infant at the breast wearing butterfly plate.
3: Protection of eyes and nostrils prior to the taking of an impression for the manufacture of the butterfly plate.
4: Showing taking of impression for manufacture of butterfly plate and protection of the nasal airway during the procedure.
5: Plaster model of the infant's face.
6: Pressure moulding of the appliance.
7: Cutting grooves in the surface of the trimmed butterfly plate.
8: The finished appliance with sensors in the grooves.
9: Central apnoea preceded by what appears to be obstructive apnoea.
10: Apnoea detection.
11: Analysis of ECG.
12: The data recorded using the final system.

CHAPTER THREE

FIGURE 1: Showing some air movement at the mouth, but none at the nose during a yawn.
FIGURE 2: True obstructive apnoea.
3: False obstructive apnoea.
4: Movement artefact.
5: Respiratory and body movements.

TABLE 1: Subjects studied using oesophageal balloons.
2: Results of oesophageal balloon studies.

CHAPTER FOUR

FIGURE 1: Cardiac artefact appearing on thermistor trace during central apnoea.
2: Other artefact appearing on thermistor trace during central apnoea.
3: Apnoea scoring.
4: Venn diagram showing the relationship between the apnoea counts derived from three different methods of monitoring respiration.

TABLE 1: No. of studies in which the scores of 2 observers differed considerably.
2: Reasons for disagreement between observers over record of Baby A.
3: Reasons for disagreement between observers over record of Baby B.
4: Reasons for the differences in apnoea counts derived using different methods of recording respiration.

CHAPTER FIVE

TABLE 1: Results of polygraphic monitoring and follow-up data in Group 1: Near Misses (asymptomatic).
TABLE 2: Clinical details and results of polygraphic monitoring in Group 2: Near Misses (associated symptoms).

3: Clinical details and results of polygraphic monitoring in Group 3: Premature Near Misses.

4: Clinical details and results of polygraphic monitoring in Group 4: Infants with Upper Airway Symptoms.

5: Studies comparing central apnoea in near misses and controls.

6: Studies comparing central apnoea in sibs and controls.

7: Studies of apnoea rates in normal infants.

8: Summary of rates of mixed and obstructive apnoea in the literature.

CHAPTER SIX

FIGURE 1: The palatal appliance viewed from its glossal surface.

2: The appliance *in situ*.

3: The sickness score in use.

4: The effect of removing established nasoenteric tube(s) on TcPO$_2$, periodic breathing and apnoea.

TABLE 1: Clinical characteristics and clinical outcome in Study 1.

2: Results of polygraphic monitoring carried out 3 and 7 days after entry into the trial.

3: Clinical characteristics of infants monitored 7 days after entry into the trial.
TABLE 4: Summary of changes induced by insertion or removal of nasogastric tube(s).

CHAPTER SEVEN

No Figures or Tables.

APPENDIX ONE

FIGURE 1: Showing infant positioned for impression-taking within the incubator.

2: First impression being taken with silicone putty in special tray.

3: First impression complete.

4: Second impression.

5: Plaster model of palate and gums.

6: Palatal surface of acrylic base plate with grooves and feeding tubes.

7: The final blue-lined appliance ready for use.
ACKNOWLEDGEMENTS

The work described in this thesis was undertaken while holding the post of Research Fellow in the Neonatal Research Group of the Joint Academic Department of Child Health at The London Hospital Medical College. The author was responsible for the design and execution of the studies, but has received help from many sources.

I owe most to Professor K. W. Cross, who has been concerned about the problem of nasal obstruction in the infant for many years. Dr. J. K. Stothers has given up a great deal of his time to practical help with a screwdriver and discussion of methods and results. His advice on the preparation of the manuscript was invaluable. Miss S. J. Linnett and Miss E. R. Carter, the research nurses involved in the project, provided help not only with preparing the babies, but also with the analysis of the large amounts of data produced.

Many members of the Physiology Department have also contributed. In particular, Mr. T. G. Barnett designed and built much of the electronic equipment. Dr. M. K. S. Hathorn has provided a great deal of advice on computing, statistics and analysis. Dr. P. G. Sullivan and Mr. H. Haringman, of the Department of Paediatric Orthodontics, designed and built the facial and palatal prostheses used. I am also indebted to Mrs. Irene Sampson, who has typed the manuscript.

I am grateful to the medical and nursing staff at The London Hospital, and especially to the many parents who allowed me to study their babies.
Finally, I would like to acknowledge the financial help received from the Foundation for the Study of Infant Deaths, who made the project possible.
CHAPTER ONE

---00000---

INFANT APNOEA: BACKGROUND AND AIMS OF THE PROJECT
The study of infant apnoea began more than one hundred years ago with clinical observations on cyanotic attacks in the newborn. Physiological studies of the patterns of infantile breathing began just before the turn of this century, but for the next 70 years, the clinical and physiological lines of enquiry proceeded separately. Then, with the development of measuring techniques suitable for use in the sick infant, joint clinical and physiological studies became possible. In the course of reviewing these more recent studies, one area still requiring examination was delineated. This forms the first part of the thesis. In the second part, the techniques developed are applied to some clinical problems.

**EARLY CLINICAL OBSERVATIONS**

Isolated apnoeic spells, which may cause cyanotic attacks in otherwise healthy infants, had received little formal attention before the clinical work of Illingworth, published in 1957. However, the presence of cyanotic attacks has been recognised for more than one hundred years, although at first they were noted chiefly in infants with pre-existing respiratory distress.

Thus, Evanson and Maunsell in their paediatric textbook of 1842 describe exacerbations of cyanosis, but not cyanotic or apnoeic attacks arising de novo. Under the heading "Cyanosis" they write:

"This term is applied to a morbid appearance of the skin, in which it assumes a blue, purple or leaden colour and which is occasionally observed in newborn infants. The change in colour is particularly remarkable in the lips, cheeks and nails, and is generally accompanied with reductions of temperature, and paroxysms of difficult respiration, during which the blueness"
becomes deeper and extended over the surface of the body - the pulse stops, the extremities become cold and syncope resembling death often occurs."

These authors were aware of two causes of cyanosis, namely congenital heart disease and "imperfect filling of the lungs". By the latter, they meant a partial continuation of the lungs in their foetal condition.

In contrast, Budin (1907), who did so much to place the management of premature infants on a sound footing, was well aware of the problem of isolated cyanotic attacks which he attributed to underfeeding.

"Almost from the time I undertook the direction of the department for weaklings at the Maternite, I was greatly impressed, not only by the facility with which they become fatally chilled, but also by a curious clinical phenomenon of which, till then, I had had little experience. I observed that a few days after their admission, infants frequently had attacks of cyanosis. They suddenly became blue, as if part of the milk they had taken had passed into their air passages and was choking them. If assistance was not immediately rendered, they died.

In search for the possible cause of these cyanotic attacks, I noticed that, as a rule, infants, in whom they occurred, were underfed."

Budin's taking note of these sudden attacks reflects the obsessional attention to detail which characterised his work and enabled him to rear premature infants successfully at a time when the infant mortality in Paris was such that any newborn child had less chance than a man of ninety of living for a week.

However, Reuss (1921), writing on the premature child, dismissed Budin's views and, like Evanson and Maunsell, emphasised the contribution of atelectasis to the development of cyanosis.
He felt that imperfect functioning of the respiratory centre was responsible for the atelectasis and also for the apnoeic spells seen in the same infants. He lays no stress on sudden attacks of apnoea or cyanosis in otherwise healthy infants, but says:

"The gaseous exchanges are very insufficient and excess of carbonic acid in the blood results, which for its part is unable to stimulate the inexcitable respiratory centre. Finally the cyanosed child entirely ceases to breathe, only after an astonishingly long interval (a minute or more) the threshold of stimulation is passed and breathing again takes place, the condition resembles the mechanism of Cheyne-Stokes breathing."

Two years later, Still published the first article to be concerned exclusively with isolated apnoea in apparently well infants. He published his detailed clinical description under the title "Attacks of Arrested Respiration in the Newborn" in order to draw attention to a previously unrecognised phenomenon.

"The individual attacks come on without any apparent reason, .... The onset is absolutely silent, there is no crying, no struggling, no stridor, no apparent distress, the infant simply ceases to breathe and apparently, as a rule, this cessation is abrupt and complete .... A very striking feature of all of them was the perfectly healthy colour of the infant during the intervals between attacks. The actual attack was accompanied by more or less cyanosis, and this occurred so nearly simultaneously with the arrest of respiration that it was difficult to say which came first, cyanosis or arrest of respiration .... The heart continues to beat steadily for some time after respiration has ceased."

In spite of this clear description, the problem received little general attention in the next 20 years, although there are isolated references to it. Cyanotic attacks were attributed chiefly to intracranial haemorrhage, atelectasis and congenital heart disease with some speculation on the role of an enlarged
thymus⁶,⁷,⁸. The character of the respiration during cyanotic attacks and apnoea as a cause of cyanosis were scarcely considered.

Thus, when Illingworth began to consider the problem of cyanotic attacks in the newborn, various ideas of causation existed, but there had been no systematic attempt to assess either the frequency of such attacks or the relative importance of the different causes suggested.

Illingworth reported the incidence of cyanotic attacks among all the babies seen in one maternity hospital over 8 years. This averaged 15.5 per 1,000. Sixty per cent of attacks occurred in the 10% of infants who were premature. There was also an association with birth asphyxia. Of those who died, a third had atelectasis and a third intracranial haemorrhage, but similar proportions were observed in babies dying without having cyanotic attacks. He found diagnosis in individual cases to be almost impossible, but suggested that obstruction of the respiratory tract by mucus, attacks of apnoea and convulsions were the principal causes. He concluded:

"The difficulties of making a correct clinical diagnosis are emphasised, and the need for further research is indicated."

In the same year (1957), Miller⁹ studied apnoeic spells in premature infants from a different standpoint. During the course of a study on respiratory rates, he noted that apnoeic spells lasting longer than one minute occurred in 30% of the infants between 1,000 and 1,750 g and were associated with a high mortality. He formed the clinical impression that severe attacks of apnoea were more likely to occur if the respiratory rhythm became
highly irregular with frequent periods of shorter apnoea. He therefore set up a study using both clinical and laboratory methods to determine the relationship between irregular respiratory rhythms and prolonged apnoea. This study, published in 1959, was the first to use laboratory methods specifically to study apnoea and marked the beginning of a period of intense investigation into the subject.

LABORATORY OBSERVATIONS

The development of laboratory methods of studying neonatal respiration had begun in the nineteenth century, but little progress had been made by 1890, when Eckerlein reviewed the literature and presented his own results. Initial studies by Gorham, Quetelet, Mignot and Monti were confined to respiratory rate determined by simple observation. The first measuring device was a tambour on the epigastrium, used by Rennembaum in 1884 to record respiratory rate. Eckerlein himself used a face mask and spirometer to measure tidal volume. Even in the one-minute periods of observation allowed by his rebreathing system, he noted periodicity in the only premature infant studied. Similarly, Eckstein and Rominger, using a mask and spirometer to measure minute volume, made the incidental observation of periodic respiration in both the premature infants studied, with some apnoeic spells lasting as long as ten seconds.

Salmi and Vuori were the first investigators to concern themselves primarily with the respiratory patterns of the prematurely born. Since they were not interested in respiratory volumes, they were able to use a much simpler technique than that
of Eckstein and Rominger. The apparatus consisted of a hollow belt which encircled the chest or abdomen of the child. The movements of air within the belt were recorded on a kymograph. This method had the great advantage of minimal disturbance to the subjects, who were studied in their own beds for periods of up to 20 minutes. "Cheyne-Stokes breathing", not precisely defined, was noted in 12 of the 14 premature infants studied. In addition, prolonged apnoea (70 seconds) was noted in an infant who subsequently died. This high prevalence of periodic breathing in premature infants was confirmed by Peiper\textsuperscript{15} and Raiha and Salmi\textsuperscript{16} using similar techniques.

The development of the trunk plethysmograph, in which resting infants could remain for 30 minutes or more, allowed detailed study of respiratory patterns as well as measurement of tidal volume; many valuable observations have been made using the method. Periodic breathing was noted by Deming and Washburn\textsuperscript{17} in 30\% of term infants and by Wilson, Long and Howard\textsuperscript{18} in 75\% of premature infants. The latter also noted that periodic breathing could be induced by hypoxia and abolished by hyperoxia. Howard and Bauer\textsuperscript{19} found that this was also true in term infants. The effect of hypoxia and hyperoxia on respiratory patterns were confirmed by Graham et al\textsuperscript{20}, Cross and Warner\textsuperscript{21}, and Cross and Oppe\textsuperscript{22} using similar methods.

However, although the trunk plethysmograph had proved useful for examining periodic breathing in healthy preterm infants over a short period of time, it could not be used in the case of sick infants for long periods. For a plethysmograph study, the infant must be taken from his incubator and enclosed in a box with only
the face or neck protruding. The adequacy of the seal around the
tace or neck is vital and if this is compromised by movement of
the baby, the observation comes to an end, so that a study of
minutes rather than hours is feasible.

Miller et al\textsuperscript{10} therefore turned to a pneumographic technique
derived from small animal work for their study of respiratory
instability and apnoea in preterm infants. The apparatus consist¬
ed of hollow corrugated tubes placed on the abdomen and connected
by a Y piece to an air tambour. The records were made on a
tymograph. Using this apparatus, the authors confirmed Miller's
previous impression that prolonged apnoea was more likely to occur
in those infants with frequent shorter apnoeas and in those with
the respiratory distress syndrome. Although the method was simple
and non-invasive, it was also cumbersome and no further studies
were done with this kind of pneumograph.

However, the study of apnoea did proceed with other devices
to detect chest movement. The application of impedance pneumo¬
graphy to the newborn represented a considerable advance\textsuperscript{23}. This
method is based on the principle that volume changes within an
electrical field during breathing are accompanied by changes in
electrical resistance. Thus electrical signals are produced, with
the advantage that they can be displayed on an oscilloscope,
recorded on paper by a pen recorder, or on magnetic tape. The
method was used by Daily, Klaus and Meyer\textsuperscript{24} in their study which
examined the incidence of apnoea in premature infants and its
relationship to bradycardia, cyanosis, periodic breathing and
changes in environmental temperature.

21
Following the work of Daily et al, there was an explosion of interest in apnoea in preterm infants. Although a few studies relying on clinical observation were published, the bulk of the work that followed used laboratory methods to define respiratory patterns and the occurrence of apnoeic spells. Impedance pneumography was the most popular method\textsuperscript{25-29}, but other devices for recording chest movement were also used and some investigators chose instead to monitor nasal airflow using thermistors\textsuperscript{30,31}, a screen flowmeter\textsuperscript{32} or expired CO\textsubscript{2}\textsuperscript{33}.

At the same time, because of widespread use of similar techniques, particularly in sleep research, it was appreciated that periods of apnoea also occurred in adults and older children during sleep\textsuperscript{34,35,36}. Steinschneider, who with Lipton, Groschen and Richmond had been studying the the cardiac and respiratory responses of infants to minor stimuli\textsuperscript{37}, suggested that an exaggeration of the normal tendency to apnoea during sleep might be the cause of the sudden infant death syndrome (SIDS). His initial report of excessive apnoea, detected using a thoracic strain gauge and a single nasal thermistor, in older infants with cyanotic attacks and their sibs\textsuperscript{38}, lent weight to this suggestion and a number of centres began to study the incidence of apnoea in infants at risk for SIDS and normal controls.

By this time, adult sleep research had already established that there was more than one kind of apnoea. During the course of a study of the Pickwickian syndrome, characterised by periods of apnoea during sleep and daytime hypersomnolence, Gastaut et al\textsuperscript{39} had used both a thoracic strain gauge to detect chest movement and a thermopile in front of the nose and mouth which would respond to
airflow, to determine the respiratory pattern. They found that there were two kinds of apnoea: central apnoea, during which there was no respiratory effort as well as no airflow, and obstructive apnoea, with continuing respiratory movements but no airflow. Obstructive apnoea has since been reported by other investigators using similar techniques in adults\textsuperscript{40}, children\textsuperscript{36}, infants\textsuperscript{41} and, more recently, premature infants\textsuperscript{42}.

THE AIMS OF THE PROJECT

Because of the existence of obstructive apnoea, no study of infantile apnoea can now be considered complete unless the methods used allow detection of both kinds of apnoea. This makes studies much harder to do, as reliable means of monitoring both respiratory effort and the resulting airflow must be found. Simple, non-invasive indicators of respiratory effort are available and easy to use, although, unfortunately, they are all affected by movements which are not purely respiratory.

Monitoring of airflow is more difficult; an airflow sensor must be accurately positioned within the airstreams of a non-cooperative subject. To overcome this problem, a facial plate was devised by Cross and Sullivan\textsuperscript{43} and is fully described in the next chapter.

The aims of the current work were to combine airflow detection using this device with respiratory movement detectors and thus to create a polygraphic recording system capable of detecting both central and obstructive apnoea. This system was then to be used to study closely and properly the respiratory patterns of infants thought to be at high risk of SIDS and also to evaluate
the effect of oroenteric as against nasoenteric tube-feeding on
the respiratory patterns of preterm infants.
REFERENCES


CHAPTER TWO

INFANT APNOEA: METHODS OF DETECTION,
DATA STORAGE AND RETRIEVAL
INTRODUCTION

A brief outline of the system used to detect both central and obstructive apnoea was given at the end of Chapter One. In this section, the components of the recording system are described in detail, together with the methods used to speed up identification of the apnoeas present on the traces.

AIRFLOW DETECTION

(a) THE BUTTERFLY PLATE

Since most infants breathe exclusively through their noses\(^1\), the detection of airflow requires the presence of sensors in the nasal airstreams. Some device must therefore be fixed to the face of the subject. This is undesirable because it is uncomfortable, and more important, stimulation of the trigeminal area may alter respiratory patterns\(^2\). The current work began with the development, in conjunction with dental colleagues, of a facial appliance to locate airflow sensors reliably, comfortably and without actually touching the nares or lips.

The device, called "The Butterfly Plate", is a biologically inert acrylic plate, moulded to the shape of the face, covering the malar regions and the nasal bridge and thus butterfly shaped. Grooves are set into the surface and provide a snap fit for the airflow sensors, which are located in the nasal airstreams (Fig. 1). The device is fixed to the skin with double-sided adhesive tape. Neither the face plate nor the sensors touch the sensitive perioral skin. Because it is located on the fixed malar regions, its position is little affected by facial movements and
FIG. 1: The butterfly plate and airflow sensors in situ. (The nasogastric tube is for feeding.)
it can remain in situ, without special attention, for long periods during sleep, or even feeding (Fig. 2).

To make a plate, an impression is taken of the nose and cheeks of the infant. First, the nostrils and eyes of the subject are protected (Fig. 3). Then, the impression is obtained (Fig. 4). From this a plaster model is made for use as a template (Fig. 5). Next the appliance is formed on the model by pressure moulding (Fig. 6). It is then trimmed to shape and grooves are cut into the surface to provide a snap fit for the airflow sensors (Figs. 7 and 8). At first, each face plate was individually made using an impression of the subject's face. Later, when a bank of appliances had been built up, it was found that most subjects could be fitted from stock.

(b) **NASAL THERMISTORS**

The methods available for monitoring airflow include screen flowmeters, CO₂ sensors and temperature-sensing devices. A face mask is necessary for a screen flowmeter, which was not therefore considered suitable. CO₂ meters have the disadvantage of an appreciable lag time. Instead, an electrical method of sensing the temperature of the inspired and expired air was chosen, using thermistors. These are non-metallic semiconductors (Radio Spares stock no. 151-237) with a resistance which alters quickly with temperature. Resistance is easily measured with a modified Wheatstone bridge circuit. Expired gases are usually at about 35.6°C. Therefore, if a subject inhales room air at, say, 29°C, regular swings of 6°C are produced during the respiratory cycle.
FIG. 2: Infant at the breast wearing butterfly plate.
FIG. 3: Protection of eyes and nostrils prior to the taking of an impression for the manufacture of the butterfly plate.
FIGS. 4(a) and (b): Showing taking of impression for manufacture of butterfly plate and protection of the nasal airway during the procedure.
FIG. 5: Plaster model of the infant's face.
FIG. 6: Pressure moulding of the appliance.
FIG. 7: Cutting grooves in the surface of the trimmed butterfly plate.

FIG. 8: The finished appliance with sensors in the grooves.
There are theoretical problems with thermistors\textsuperscript{4} which had to be considered and, where possible, overcome. These problems were tackled with ingenuity by Mr. Barnett, Electronics Engineer. Firstly, the response of thermistors to temperature changes is not quite linear. Additional small resistances in the measuring circuit were used to linearise the response. However, as the thermistors were operating over only 10\% of their range, the deviation from strict linearity was, in any case, small. A second theoretical difficulty is that the current passing through the thermistor results in some additional heating. This effect was minimised by using a measuring circuit with a current of only 100 microamps. The use of thermocouples, rather than thermistors, would have avoided these problems, but produced others. Thermocouples require a reference junction and high-quality amplification. Because of this and because our existing electronic expertise was mainly with thermistors, this method of airflow detection was adopted.

These theoretical problems were dwarfed in practice by two factors. Firstly, in every subject it was noted that the size of the airflow signal was dependent on the exact position of the sensor within the airstream. However, the greatest difficulties arose when monitoring very low birth weight infants; the signals obtained were tiny and of poor quality. This was puzzling until it was remembered that these infants were being nursed in incubators at up to 35.5\textdegree{}C. Therefore, the inspired and expired gases were at virtually the same temperature and the thermistors were indicating not temperature changes, but velocity effects. With this one exception, the thermistors produced a reliable qualitative indication of airflow.
IMPEDEANCE PNEUMOGRAPHY

Monitoring of airflow alone will detect apnoea, but will not distinguish between central and obstructive episodes. For this purpose, a detector of respiratory movements is necessary. There are several non-invasive methods available, including strain gauges, magnetometers and electrical impedance plethysmography. The latter was available for incorporation into the monitoring system. The instrument used was the Healthdyne Infant Monitor from Oxford Intruments.

The basis of impedance pneumography is that the resistance of an electrical conductor changes with its volume. Thus, changes in volume of the chest with respiration should, in theory, be reflected in changes in chest impedance. Unfortunately, there are difficulties in applying electrical engineering theory to physiological measurement. The theory is based on a cylinder of constant length, containing homogeneous tissue and varying only in area. The chest bears little resemblance to such a cylinder. In addition, it is not clear whether the current travels through the middle of the chest, in which case the method might measure volume change, or around the chest wall, when it would reflect instead dimensional changes. Finally, Hill et al produce evidence that electrode factors may be dominant and suggest that impedance changes are chiefly artefacts arising from movement at the skin/electrode interface.

There are therefore sound reasons why the impedance pneumogram cannot be used to measure respiratory volumes. However, it
remains an adequate movement detector, its role in the current work.

**ELECTROCARDIOGRAM**

The final component of the system was a standard ECG obtained from the same Healthdyne Infant Monitor as the impedance signal.

**RECORDING APPARATUS**

The data were recorded simultaneously onto magnetic tape using a 7 channel analogue tape recorder (Racal Store 7). This machine allowed recording and replaying to be performed at various speeds. Using the slowest recording speed, 12 hours of recording could be stored on one tape. The data were replayed onto oscilloscopes (Gould and Scopex) and either 4 or 6 channel pen recorders (Hewlitt Packard).

**THE APNOEA DETECTOR**

The simultaneous recording of nasal airflow and chest movement allows the detection of apnoeas of two types: those with and those without chest movement. Figure 9 shows a 4-second apparently obstructive apnoea, followed by a 7-second central apnoea. The data shown constitutes a minute fraction of a 12-hour recording. The hard copy in the Figure was obtained by replaying the tape at 8 times its original recording speed onto an oscilloscope and identifying the pauses in airflow by eye. A short segment of data, including the pause, was then replayed onto the printer. This proved time consuming and, possibly, not quite accurate. It was
FIG. 9: Central apnoea preceded by what appears to be obstructive apnoea.
felt that some automatic means of detecting pauses in airflow should be devised.

Low-voltage, biphasic signals recorded by instruments such as thermistors are usually accompanied by high noise levels due mainly to inadequate sensing and movement artefact. In addition, the airflow signals are subject to the addition of cardiac artefact: a regular oscillation produced when the column of air in the airways is agitated by the movement of the heart. This is very prominent when breathing is interrupted with the glottis open.\(^7\)

In these circumstances, the human eye and brain distinguish between breaths and pauses using pattern recognition. Attempts to reproduce this process using digital computers have not, so far, been particularly successful, although a great deal of work has been done on the problem. It was therefore decided to attempt apnoea detection using relatively simple analogue methods. The equipment used was designed and built by Mr. T. G. Barnett.

The basis of the apnoea detector lay in the antilog amplifiers used to improve the signal-to-noise ratio\(^8\). These produce non-linear amplification of the thermistor signal, such that signals larger than one volt are increased in size and those smaller than one volt are reduced. Thus the breathing signal is amplified, whilst the noise is suppressed. A trigger level is then set on the handled signal such that both inspiration and expiration are detected. If no breathing is detected for a period of 5 seconds or more, a marker voltage is emitted and an alarm sounds. The process is illustrated in Figure 10, in which the thermistor signal shows obvious cardiac artefact.
Fig. 10  Apnoea Detection

Thermistor Signal → DC amp × 2 → non linear amp → Handled Signal on which trigger is set → no trigger for 5 secs → Apnoea Spike
There was little theoretical basis for the choice of 5 seconds as the minimum length of pause to be designated as apnoea. Other investigators have used 2, 3, 6 or 10 seconds. Because of the interest in the connexion between short and long apnoeas, I wished to include reasonably short spells. On the other hand, at low respiratory rates it becomes difficult to distinguish between a long expiration and a short pause. This difficulty is compounded by the distortion of the original biological signal by electrical handling (e.g. AC coupling) designed to minimise baseline drift. These distortions become an important source of potential errors if very short pauses are to be examined.

Once the 5-second apnoea had been detected by the device, the marker voltage was recorded on line, using a separate channel of the magnetic tape. For analysis, the tape was replayed at 30 times the original recording speed and stopped when a marker spike was seen on the oscilloscope. The data from the marked incident were then transferred to paper for detailed study. No attempt was made to count the apnoeas automatically, without studying the incident in detail; the device was used as an aid to apnoea detection, not for complete analysis. In this capacity it functioned well, speeding up apnoea detection with very few false negatives.

**RECORDING OF HEART RATE**

A heart rate meter was built using similar principles. The ECG obtained from the Healthdyne monitor is subject to a great deal of noise. The signal is improved by passage through a low pass filter and a pair of antilog amplifiers. The handled ECG has a
single clear R wave which triggers a marker spike. This spike is used as the input voltage to an instantaneous frequency meter which emits a voltage inversely proportional to the RR interval, averaged over 3 beats. The resulting heart rate "histogram" is recorded on line on another channel of the magnetic tape. Tachycardia and bradycardia can be sensed and will trigger auditory and electrical alarms. The handling of the ECG is illustrated in Figure 11.

THE COMPLETED SYSTEM

The sensing devices, tape recorder, apnoea detector and heart rate meter were arranged in one large rack which could be taken into the ward or special care unit. Eventually, 6 channels of the magnetic tape were used: for thermistors (2), chest impedance, ECG, apnoea spike and heart rate, as illustrated in Figure 12.

The final system was very robust in use. The face plate ensured that the thermistors remained in situ. The nature of the electrical circuits used meant that no adjustments were needed during recording. Thus no interference with the subject was required after the sensors had been applied and no special supervision was needed, even for 12-hour recordings. The infant could be picked up, comforted, fed and changed while recording continued - a considerable advantage.
Fig. 11 Analysis of ECG
FIG. 12: The data recorded using the final system. The "handled" thermistor signal is included here for completeness, but was not usually recorded.)
REFERENCES


CHAPTER THREE

--00000--

A CLOSER LOOK AT OBSTRUCTIVE APNOEA
INTRODUCTION

Obstructive apnoea is defined by many investigators\(^1,^2,^3\) simply as continued chest or abdominal movement without airflow movement. There are two assumptions implied by this definition: that all such movement is a reflection of respiratory effort, and that all airflow has stopped when the sensors cease to record it.

As soon as the first infants had been studied using the current system, it became obvious that these assumptions must be questioned. It seemed likely that the same pattern of continued chest movement without airflow might be produced by normal body movement.

These reservations about the true nature of polygraphically defined obstructive apnoea have important implications. There is a great deal of circumstantial evidence to suggest that upper airway obstruction may be responsible for at least some cases of cot death. The Sudden Infant Death Syndrome (SIDS) is more common in babies with coryza symptoms\(^4\). Intrathoracic petechiae are often found in such infants at post mortem\(^5\) and might result from the large intrathoracic pressure swings which occur if the infant has struggled against a closed airway. Patency of the infant airway is precarious. Most infants are exclusively nose breathers\(^6\) and the anatomy of the infant nasopharynx, with the relatively high position of the hypopharyngeal structures, may contribute to this by making mouth breathing difficult\(^7\).

Because of the possible role of upper airway obstruction, some authors studying the respiratory patterns of infants at risk of SIDS have looked for obstructive as well as central apnoea in
the course of polygraphical monitoring during sleep. For instance, Guilleminault et al.\(^1\) found that the only difference between a "Near Miss" and a control group was an increased frequency of short (3 to 10 second) periods of mixed and obstructive apnoea in the high risk group.

It was decided to examine episodes of polygraphically defined obstructive apnoea (POA) critically in an effort to determine whether true obstruction, that is, inspiratory efforts against a closed upper airway, was really present. Therefore, in selected infants, additional data were recorded during polygraphic monitoring in an attempt to determine the nature of possible obstructive episodes. Three separate investigations, addressing different aspects of the problem were carried out.

1. DETECTION OF EXPIRED CO\(_2\) AT THE MOUTH
RECORDED IN NORMAL NEONATES

INTRODUCTION

Monitoring of ventilation is often confined to nasal airflow alone\(^2,3\). Whilst it is clear that the undisturbed neonate is a nose breather\(^6\), it has also been shown that a proportion of young infants whose airway is blocked in the laboratory can establish mouth breathing\(^6,7,8,9\). Therefore, the available evidence does not rule out the possibility of intermittent short episodes of mouth breathing giving a false impression of obstructive apnoea, particularly when a short period of movement interrupts an otherwise regular respiratory pattern.
METHODS

Polygraphic monitoring was carried out in 4 normal newborns for 2 hours each. In addition to nasal thermistors, chest impedance and ECG, airflow at the mouth was recorded continuously. Initial attempts to detect the airflow that must occur with crying and yawning failed. Both a bead thermistor, such as was used for nasal airflow, and a narrow diameter CO₂ sampling cannula failed to register any mouth breathing at all. This difficulty was thought to be due to the large area and hence relatively low flow at the mouth compared to the nose. To overcome the problem, a soft funnel was attached to the end of the CO₂ cannula. When held over the mouth, this served the dual purpose of collecting all the expired CO₂ from the mouth and separating the mouth from the nose. This method was therefore capable of detecting mouth breathing.

Episodes of possible obstructive apnoea, that is chest movement, with no nasal airflow, lasting 5 seconds or more, were identified and the presence or absence of mouth breathing was noted.

RESULTS

Fifty-four episodes of POA were identified from a total of 8 hours of recording. In fifty, there was no airflow at the mouth, but on four occasions, POA was associated with a brief increase in CO₂ at the mouth. However, in all of these instances, the infant was either crying or yawning. A yawn is illustrated in Figure 1.
Mouth Breathing during a yawn

FIG. 1: Showing some air movement at the mouth, but none at the nose during a yawn.
CONCLUSION

Although isolated short episodes of mouth breathing did occur in these normal infants, this did not present any real difficulty in interpretation of most episodes of POA.

2. OESOPHAGEAL PRESSURES RECORDED IN INFANTS WITH SUSPECTED UPPER AIRWAYS OBSTRUCTION

INTRODUCTION

Any device recording deformation of the chest (impedance or inductance pneumogram, magnetometer or strain gauge) will obviously detect gross body movement as well as purely respiratory activity. Further information is required to differentiate between these phenomena and can be provided by measurements of oesophageal pressure^10. If the oesophagus is relaxed, the pressure within it reflects intrapleural pressure. In these circumstances, respiratory efforts produce negative intracoesophageal pressure swings.

METHODS

In 3 infants in whom pathological obstruction was suspected on clinical grounds, oesophageal pressure was recorded by a balloon attached to a pressure transducer. In addition, nasal thermistors, chest impedance and ECG were recorded. Clinical details of the subjects are given in Table 1. Episodes of POA were identified as described above and then classified according to the pattern of oesophageal pressure swings.
### TABLE 1: Subjects studied using oesophageal balloons

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>BIRTH WEIGHT (kg)</th>
<th>GESTATION (weeks)</th>
<th>AGE AT STUDY (days)</th>
<th>CLINICAL PROBLEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.23</td>
<td>29</td>
<td>51 68</td>
<td>Recurrent apnoea</td>
</tr>
<tr>
<td>2</td>
<td>3.5</td>
<td>40</td>
<td>19</td>
<td>Apnoea and gastro-oesophageal reflux</td>
</tr>
<tr>
<td>3</td>
<td>3.7</td>
<td>39</td>
<td>48</td>
<td>Near miss SIDS</td>
</tr>
</tbody>
</table>
RESULTS

Sixty-six episodes of POA were identified in traces obtained from the 3 infants with suspected obstruction. These were found to be associated with three different patterns of oesophageal pressure changes which could be interpreted as true obstructive apnoea (Fig. 2), false obstructive apnoea (Fig. 3) and movement artefact (Fig. 4).

i. True Obstructive Apnoea (Fig. 2)

The baseline of the oesophageal pressure record was stable, with a clearly visible cardiac artefact. It was thought that this artefact was a reliable indication that the oesophageal wall was relaxed and that intraoesophageal pressures reflected those in the thorax. The negative deflections seen therefore represented inspiratory efforts. These were not matched by airflow and true obstruction was considered to be present.

ii. False Obstructive Apnoea (Fig. 3)

Again the oesophageal wall was relaxed, but no intrathoracic pressure change was noted in spite of a chest impedance deflection. This pattern occurred without obvious movement and gave a totally false impression of obstruction.

iii. Movement (Fig. 4)

The oesophageal pressure was chiefly positive, punctuated by some negative swings. The pattern was not that of a peristaltic wave, and was associated with obvious body movement. Any negative
FIG. 2: Oes. = oesophageal pressure, chest imp. = chest impedance, HR = heart rate.
False Obstructive Apnoea

FIG. 3: Oes. = oesophageal pressure, chest imp. = chest impedance, HR = heart rate.
FIG. 4: Movement artefact. Oes. = oesophageal pressure, chest imp. = chest impedance.
swings were matched by some airflow. There was no cardiac artefact on the baseline of the airflow trace, suggesting that the airway may have been closed (11), so that in one sense the infant was obstructed. However, this is "voluntary" obstruction, occurring as he raises intrathoracic pressure to stiffen the trunk during movement and the significance of this phenomenon must be very different from that of the true obstruction defined above.

The number of episodes of POA falling into each category, the length of the episodes, and the associated heart rate and impedance patterns are given in Table 2. It is clear that true obstruction was characterised by longer episodes with a more regular chest impedance pattern than false obstruction or movement and that bradycardia tended to occur. This slowing was noted within a few seconds of the first obstructed breath.

Of the 3 infants with suspected obstruction investigated, virtually all of the episodes of true obstruction were found in the preterm infant, in whose case the obstructive episodes were not associated with much movement and were not apparent to the observer.

3. DIRECT OBSERVATION OF AN INFANT

WITH DEFINITE UPPER AIRWAY OBSTRUCTION

INTRODUCTION

Because episodes of possible obstruction are brief and relatively infrequent, they are normally difficult to detect by direct observation. However, the opportunity arose to study one infant
TABLE 2: Results of Oesophageal Balloon Studies

<table>
<thead>
<tr>
<th>TYPE OF EPISODE</th>
<th>FIG. NO.</th>
<th>NO.</th>
<th>NO. ≥ 10 SECS</th>
<th>NO. WITH HR &lt; 90/MIN</th>
<th>NO. WITH REGULAR IMPEDANCE PATTERN</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Obstructive Apnoea</td>
<td>2</td>
<td>25</td>
<td>10</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>False Obstructive Apnoea</td>
<td>3</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Gross Movement</td>
<td>4</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
with right-sided choanal atresia and very frequent obstructive episodes. Orotracheal intubation was required to maintain an adequate airway for a few days, but when studied on the seventh day of life, he was mouth breathing via a Brooke's airway.

METHODS

Airflow at the mouth, chest movement and ECG were monitored for 30 minutes and frequent periods of POA were noted. Because of his relatively slow respiratory rate and sternal recession, his respiratory efforts were easily detected and distinguishable from body movements by an observer, who coded a further channel of magnetic tape accordingly. The episodes of POA were then identified and the observer's comments noted.

RESULTS

The majority of episodes of POA in this infant were associated with inspiratory efforts as judged by the observer. The chest impedance pattern of these episodes was regular. However, it was noted that some of the longer episodes were terminated by gross body movements, during which inspiratory efforts ceased. This type of episode is illustrated in Figure 5. Such a combination of respiratory and body movement within one episode was much more common than in the preterm infant with frequent obstructive apnoea. From these mixed episodes, it could be seen that inspiratory efforts were associated with a much more regular impedance pattern than gross movements.
FIG. 5: RM = respiratory movement, BM = body movement, chest imp. = chest impedance.
DISCUSSION

The polygraphic definition of obstructive apnoea has been critically examined for possible sources of error, particularly mouth breathing and movement artefact. The methods used to examine this technical question involved intensive scrutiny of the records of few babies, some with a definite abnormality. Large numbers are not necessary for the identification of problems. On the contrary, it is the need to process large amounts of cumbersome polygraphic data which has led to the use of simple definitions, such as the one under scrutiny.

The results support the general impression that mouth breathing is not a major source of confusion in the majority of apparently healthy newborn infants. This is fortunate, as airflow at the mouth is difficult to monitor satisfactorily. As discussed above, it was found that a face mask was necessary to do this. Since this will be in contact with the sensitive perioral skin, it may alter respiratory pattern as well as annoying the baby. It is also difficult to keep in place. For most normal infants, nasal monitoring should suffice, but the fact that some infants can mouth breathe if sufficiently stressed (like the infant with choanal atresia who eventually established unaided mouth breathing at the age of ten days) should be remembered. However, since performing this study, brief checks for the presence of mouth breathing in older "Near Miss" SIDS infants have been made with negative results. Special efforts to check for and monitor mouth breathing may still be needed in individual cases.
A more serious source of error arose because the chest impedance deflections did not necessarily correspond with respiratory movements. In some instances (those of false obstructive apnoea), there was no obvious explanation for the impedance deflections. The chief source of confusion, however, was movement with the glottis closed during sleep. This finding has been confirmed by Abu-Osba et al. who studied respiratory patterns during movement in the preterm infant using similar methods to those used here. They describe expiratory obstruction, which they call a "Valsalva Breath", and distinguish it from inspiratory obstruction. The polygraphic pattern of those "valsalva breaths" is identical to that of the movement artefact described here. The initial suspicion that POA included both pathological obstruction and normal body movement therefore proved to be well founded. Since these events must have very different significance, it is essential to differentiate between them.

The results suggest that close scrutiny of the trace may help in making this distinction. The longer episodes, with early bradycardia and a regular chest impedance pattern, are more likely to result from true obstruction. Unfortunately, even after close inspection, some doubt will remain, particularly about shorter episodes, and there is no easy way of resolving this uncertainty. Since it was observed that one of the subjects had many mixed episodes of obstruction and movement, portions of the record with obvious movement artefact cannot simply be eliminated. Oesophageal manometry is too invasive and skilled a technique to be used for long studies and would destroy the simplicity of the system, its chief merit. It might be thought that changes in TcPO₂ would
help distinguish between true obstructive apnoea and movement artefact, but, in fact, TcPO_2 falls in both situations, at least in preterm infants (12). Therefore, in the work that follows, true obstructive apnoea was distinguished from movement artefact by careful examination of the four-channel trace alone.

In broader terms, it would appear that research groups who have failed to differentiate between true respiratory and other body movements must have over-reported the incidence of obstructive apnoea. Their conclusions regarding its frequency in the various categories of infants considered at risk must therefore be treated with caution.
REFERENCES


CHAPTER FOUR

--00000--

QUANTITATIVE ANALYSIS OF APNOEA RATES
INTRODUCTION

A detailed description of how apnoea is identified from the recordings and classified into three types has been given in Chapters Two and Three. The next problem was to devise a standard method of expressing the amount of apnoea exhibited by a particular infant in order to make valid comparisons of the incidence of apnoea between subjects. Once a scoring method suitable for the recording system used had been developed, interoperator variability was critically examined, as were the effects of modification to the electronic equipment on the final scores.

THE DEVELOPMENT OF THE SCORING SYSTEM

Because it was considered necessary to look at short apnoeas, whilst avoiding the difficulties of interpretation posed by extremely short pauses (Chapter Two), an apnoea was defined as a period of no airflow lasting at least 5 seconds. It was considered as beginning when airflow stopped, usually in expiration, and as ending with the resumption of airflow. Sometimes it was difficult to decide whether small signals indicated a breath or not. The convention adopted was to ignore both low frequency "wobbles" with an amplitude of less than 25% of the thermistor signal of the previous breath and obvious cardiac artefact. The application of this convention is illustrated in Figures 1 and 2.

Apnoeas between 5 and 10 seconds in length were frequent, whilst those over 10 seconds were comparatively rare. Therefore, for scoring purposes, all episodes were categorised as either up to 10 seconds or 10 seconds or more.
Cardiac Artefact appearing on Thermistor trace during Central Apnoea

Nasal Thermistors

Chest Impedance

ECG

FIG. 1: During a central apnoea, artefact appears on the thermistor trace. Although it produces signals more than 25% of the size of the first breath after the apnoea, it is obviously in time with the ECG and is therefore cardiac artefact, which is ignored.
Other Artefact appearing on Thermistor trace during central Apnoea

Nasal Thermistors

Chest Impedance

ECG

FIG. 2: The low-frequency, low-amplitude "wobbles" seen on this thermistor trace are not cardiac artefact. The deflection at A is more than 25% of the size of the preceding breath and would therefore be considered as another breath. The deflection at B is less than 25% of the preceding and following breaths and would therefore be ignored.
From the thermistor signal, the nature of the impedance signal and the presence or absence of bradycardia, the apnoea could then be classified as central, true obstructive or movement artefact using the criteria described in Chapter 3.

Periodic breathing is very common in premature and newborn infants. Its presence results in a large number of short central apnoeas which are obvious during the analysis of the trace. However, a separate indicator of periodic breathing was considered necessary. A common definition of periodic breathing is "a sequence of 2 or 3 apnoeic pauses separated by less than 20 seconds". This definition is too wide, for it includes runs of short apnoea where the alternation of breaths and pauses has no discernable pattern. Periodic breathing was therefore defined more strictly and was only scored if there were 3 or more apnoeas within one minute, one of which was at least 5 seconds long and the basic pattern of breaths and pauses was regular.

In preterm infants of less than 36 weeks gestation, behavioural states, which are known to affect the respiration of full term infants, are not fully organised. Since much of the work that follows was done in preterm infants, the usual state concept was not applied. However, movement of the infant is associated with apnoea at any age; movement artefact type apnoeas occur during activity, which may then be followed by a central apnoea. It was therefore necessary to try to distinguish between quiet periods and those disturbed by movement. Thus, after examining the impedance and ECG records for obvious sustained movement artefact, the whole record was divided into "quiet" and "disturbed" periods. No portion of the trace was excluded because it contained move-
ment, however gross. Although this is the practice of some investigators\textsuperscript{2}, it inevitably leads to the exclusion of many apnoeas. For instance, in some preterm infants at least 50\% of the trace would be discarded.

When the work began, it was already clear that normal and abnormal infants were more likely to be distinguished by the number rather than the length of their apnoeas\textsuperscript{5,6}. Accordingly, apnoeas were counted and the scores were expressed as the number of each type of episode per hour of quiet or disturbed trace. The completed scoring system for apnoeas is illustrated in Figure 3.

Periodic breathing is rather different. An infant with a lot of periodic breathing will have not only more, but also longer episodes than one with little\textsuperscript{2}. To allow for both these factors, periodic breathing was expressed as seconds of periodic breathing per hour of quiet or disturbed trace.

**INTER-OBSERVER VARIABILITY**

The completed system did require that the observer use his judgement, particularly in the classification of apnoeas and in deciding which portions of the trace were quiet and which disturbed. Since this constituted a potential source of errors, inter-observer variability was studied systematically. First, the overall agreement between two observers independently scoring the same records was assessed. Then, the reasons for discrepancies were studied in detail.
FIG. 3: Apnoea scoring
METHODS

Fourteen 2-hour studies carried out on 7 preterm infants were analysed separately by 2 observers (V.V.S. and E.C.) and the resulting scores were compared. Since each of the 14 studies gave rise to 14 separate apnoea scores, there were 196 (14 x 14) pairs of scores included in the analysis. Unfortunately, there is no satisfactory statistical way of assessing the inter-observer variation in this study. A correlation coefficient is meaningless because there is naturally a very strong association between the values obtained by the two observers. Analysis of variance is the method of choice for looking at inter-observer variation when the data follow a normal distribution, but it is hardly valid when only 2 observers are involved and the data are non-parametric. In the absence of an appropriate statistical method, the number of important discrepancies was noted.

The records of the two infants in whom there was least agreement were then identified. The scoring process was divided into 4 separate components and the discrepancies between the observers in each one were examined. These were:

1. Finding the apnoeas and printing them out.
2. Deciding from the printout if the apnoeas were 5 seconds or more in length.
3. Classification of apnoeas into different types.
4. Allocation to "quiet" or "disturbed" periods of trace.
RESULTS

The agreement between the observers was very good: in 85% of comparisons they differed by less than 10%. In only 9.2% of the 196 instances did they differ by as much as 30% (see Table 1).

The results of the detailed examination of the way the 2 observers handled the traces of the infants on whom they agreed least are presented in Tables 2 and 3.

There was little difficulty in identifying apnoeas for printing. However, there was considerable disagreement over the exact length of apnoeas, especially in the case of Baby A. The observers had printed the trace out at different amplifications, so that on the more amplified printout, "wobbles" were more likely to be interpreted as breaths, thus interrupting apnoeas. This is not strictly an observer factor, but it does illustrate how small differences in the trace can lead to large differences in interpretation. Where both observers scored from technically similar printouts, agreement was greatly improved, but some difficulty remained which could only be resolved by obsessional attention to measuring the exact length of episodes.

Classification of apnoeas led to surprisingly little trouble. There was good agreement about differentiating between true obstructive apnoea and movement artefact, because the criteria described in Chapter Three were rigorously applied. There was some difficulty in the case of Baby A in differentiating pure central apnoea from movement artefact. This infant was particularly restless and the impedance method is sensitive to even small movements. One observer had tended to disregard small disturbances of
TABLE 1: No. of studies in which the scores of 2 observers differed considerably

<table>
<thead>
<tr>
<th>DESCRIPTION OF APNOEA</th>
<th>NO. WHERE DIFFERENCE $\geq 10%$</th>
<th>NO. WHERE DIFFERENCE $\geq 30%$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>QUIET PORTIONS OF TRACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central apnoea 5-9 s</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Movement artefact 5-9 s</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>True obstruction 5-9 s</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Periodic breathing</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td><strong>DISTURBED PORTIONS OF TRACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central apnoea 5-9 s</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Movement artefact 5-9 s</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>True obstruction 5-9 s</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\geq 10$ s</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Periodic breathing</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>29 (14.8%)</td>
<td>18 (9.2%)</td>
</tr>
</tbody>
</table>

14 different kinds of apnoea were scored in 14 subjects; therefore, the total no. of comparisons was 196.
<table>
<thead>
<tr>
<th>AGREE NO. OF EPISODES</th>
<th>DISAGREE NO. OF EPISODES</th>
<th>COMMENT ON DISCREPANCIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Printing out</td>
<td>189</td>
<td>3</td>
</tr>
<tr>
<td>Scored as &gt; 5 s</td>
<td>73</td>
<td>75</td>
</tr>
<tr>
<td>Scored as &gt; 5 s using same printout</td>
<td>141</td>
<td>47</td>
</tr>
<tr>
<td>Classification of apnoeas</td>
<td>133</td>
<td>8</td>
</tr>
<tr>
<td>Classification of trace into quiet and disturbed</td>
<td>701 ft</td>
<td>350 ft</td>
</tr>
</tbody>
</table>
TABLE 3: Reasons for disagreement between observers over record of Baby B

<table>
<thead>
<tr>
<th></th>
<th>AGREE NO. OF EPISODES</th>
<th>DISAGREE NO. OF EPISODES</th>
<th>COMMENT ON DISCREPANCIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Printing out</td>
<td>127</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Scored as &gt; 5 s</td>
<td>104</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Classification of apnoeas</td>
<td>82</td>
<td>22</td>
<td>Mainly due to disagreement over significance of small impedance signals during apnoea</td>
</tr>
<tr>
<td>Classification of trace into quiet and disturbed</td>
<td>800 ft</td>
<td>200 ft</td>
<td></td>
</tr>
</tbody>
</table>
the impedance pattern, whilst the other had scored apnoea with minimal impedance changes as movement artefact. This problem would only be expected with particularly active infants.

The observers found it difficult, at times, to agree on whether a given portion of trace should be considered "quiet" or "disturbed". There was no obvious objective means of improving the distinction.

In summary, there were two main contributions to the differences in the scores of these infants, who were picked to represent the worst case. The first was a difficulty in deciding on the exact length of an apnoea, which was made worse if the tapes were not identically reproduced. The second problem, which made a bigger difference to the overall scores, was that of allocating a given episode to a "quiet" or "disturbed" period.

In fact, during the course of the clinical trial reported in Chapter Six, no significant differences between the apnoea rates during "quiet" and "disturbed" periods were found.

**THE EFFECT OF MODIFICATIONS OF THE ELECTRONIC EQUIPMENT:**

**COMPARISON OF TWO METHODS OF MONITORING RESPIRATORY MOVEMENT**

The electronic equipment used can only provide an indirect indication of the physiological events taking place and the resulting signals must always be interpreted with caution. In particular, many factors interfere with the impedance method. A false impression that respiratory movement is being made may arise from the presence of movement or cardiac artefacts (Chapter Three and Ref. 6). On the other hand a thoracic respiration detector may fail to register abdominal breathing7. The effect of these
factors on the final apnoea score was assessed from 8 recordings, during which 2 methods of recording respiration were used simultaneously.

METHODS

In 8 preterm infants, respiratory movement was recorded using both chest impedance and a pressure capsule on the abdomen, based on the one described by Wright. Thermistors and ECG were recorded as before. The pressure capsule was attached to the skin in the hypochondriacal region, on a spot which obviously moved with respiration. A 100-foot portion of tape, representing about 20 minutes recording time, was randomly selected from each tape for printing out. Pauses of 5 seconds or longer, detected by either thermistors, impedance or pressure capsule, were identified and inspected. It was noted whether all 3 methods agreed that apnoea was present, or whether one method was at odds with the others. If this was the case the reason for the discrepancy was noted.

RESULTS

The apnoea counts varied considerably according to the recording method used. The 3 methods agreed in 27 out of 88 episodes. The final apnoea counts were 71 for thermistors alone, 33 for impedance alone and 55 for the capsule alone. The relationship between the apnoea counts derived by each method is illustrated by the Venn diagram in Figure 4 and the reasons for the differences are set out in Table 4. There were 2 main problems: firstly, where true obstruction or movement artefact occurred, the thermistors indicated no airflow, while the other channels indic-
FIG. 4: Venn diagram showing the relationship between the apnoea counts derived from three different methods of monitoring respiration.

- **N** = apnoeas on thermistor trace
- **C** = apnoeas on chest impedance trace
- **A** = apnoeas on abdominal capsule trace
- **NnC** = apnoeas on thermistor and impedance traces
- **NnA** = apnoeas on thermistor and abdominal traces
- **AnC** = apnoeas on abdominal and impedance traces
- **NnCnA** = apnoeas detected by all 3 methods
TABLE 4: Reasons for the differences in apnoea counts derived using different methods of recording respiration

<table>
<thead>
<tr>
<th>ALL 3 METHODS AGREE</th>
<th>27</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCREPANCIES</td>
<td></td>
</tr>
<tr>
<td>Thermistors no signal, other signals continue</td>
<td></td>
</tr>
<tr>
<td>True obstruction</td>
<td>3</td>
</tr>
<tr>
<td>Movement artefact</td>
<td>20</td>
</tr>
<tr>
<td>Poor thermistors</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>31</td>
</tr>
<tr>
<td>Thermistors respiratory type signal, others no signal</td>
<td>4</td>
</tr>
<tr>
<td>Impedance no signal, others continue</td>
<td></td>
</tr>
<tr>
<td>Impedance malfunction</td>
<td>2</td>
</tr>
<tr>
<td>Impedance signal, others no signal</td>
<td></td>
</tr>
<tr>
<td>Movement artefact</td>
<td>10</td>
</tr>
<tr>
<td>True obstruction not detected by capsule</td>
<td>2</td>
</tr>
<tr>
<td>Impedance malfunction</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>13</td>
</tr>
<tr>
<td>Pressure capsule no signal, others continue</td>
<td></td>
</tr>
<tr>
<td>Bad capsule function</td>
<td>2</td>
</tr>
<tr>
<td>Thoracic respiration</td>
<td>1</td>
</tr>
<tr>
<td>Other channels affected by movement</td>
<td>6</td>
</tr>
<tr>
<td>Other channels affected by artefact</td>
<td>1</td>
</tr>
<tr>
<td>True obstruction not detected by capsule</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>11</td>
</tr>
<tr>
<td>TOTAL DISCREPANCIES</td>
<td>61</td>
</tr>
<tr>
<td>TOTAL EPISODES</td>
<td>88</td>
</tr>
</tbody>
</table>
ated continuing movement; secondly, the impedance signal was much more easily distorted by movement artefact than the capsule. Inspection of the impedance and thermistor traces together then lead to the scoring of movement artefact, whilst the combination of thermistor and capsule traces suggested central apnoea. Surprisingly few discrepancies appeared to have occurred because the infant exhibited solely thoracic or abdominal respiration. Therefore, in the case of central apnoea, more discrepancies arose for technical than physiological reasons.

CONCLUSIONS

The final apnoea scores achieved using the current methods may be considerably affected by modifications in the equipment used, as well as by inter-observer variation. To reduce these effects, the recording and scoring procedures were altered as follows:

1. Traces were not amplified after recording and before scoring.
2. Since use of the capsule as the only indicator of respiration would result in a falsely high central apnoea rate, wherever possible impedance was used to record breathing movements, in spite of its limitations.
3. The attempt to divide the records into quiet and disturbed periods was abandoned, because it proved to be the source of considerable error and, since there was no significant difference between the scores obtained during
quiet and disturbed periods, it provided no useful information.
REFERENCES


CHAPTER FIVE

---00000---

CLINICAL HISTORY AND LABORATORY OBSERVATIONS
IN HIGH-RISK INFANTS
INTRODUCTION

Since the original suggestion, made by Steinschneider\(^1\), that apnoea might be responsible for the sudden infant death syndrome (SIDS), a great deal of effort, on both sides of the Atlantic, has gone into studying the incidence of apnoea in controls and infants at increased risk of SIDS. To date, these studies have produced conflicting results: some find an increase in central apnoea in at-risk infants\(^2-6\), some find less than in controls\(^7\) and others find no differences between the groups\(^8,9\). Some of the studies have also looked at obstructive apnoea and thus the controversy has extended to whether central or obstructive apnoea is more important\(^8\). These studies are reviewed in more detail in the discussion at the end of this chapter.

By the time the current work began in January 1981, local clinicians were well aware of the interest in apnoea and SIDS and wished to refer patients, who had had "near miss" episodes, for evaluation. In view of the large number of studies already in existence, I did not want to undertake a formal study of "near misses" and controls, but I did wish to have the opportunity of examining these patients, particularly with regard to the amount of obstructive apnoea they experienced.

SUBJECTS AND METHODS

Twenty-six patients were referred for evaluation: 17 were thought by the referring clinician to have suffered a "near miss" episode and a further 9 had symptoms suggestive of upper airway difficulties.
The term "near miss for SIDS" can be useful if not interpreted too literally. It is usually used to describe infants found unexpectedly collapsed by their attendants, who believe that the child would probably have died, but for their intervention. The label is based, not on an objective description, but on the subjective emotional response evoked in the observer.\(^{10}\)

However, although some "near miss" infants do go on to suffer a cot death, it cannot be assumed that all of these events really are aborted cot deaths. This difficulty has produced understandable dissatisfaction with the expression "near miss" and the alternative of "infantile apnea syndrome"\(^{12}\) has recently been adopted in the United States. This encompasses the "near miss" group and other infants who have excessive apnoea, discovered during investigation.

Both terms are imperfect because they imply that more is known about the phenomena of sudden unexplained collapse and death than is actually the case. To me, the term "infantile apnea" is the least satisfactory, because it suggests that these infants collapsed because of apnoea, when, in fact, there is evidence both for and against the apnoea hypothesis in SIDS. I shall therefore adopt the term "near miss" to describe the infants who were referred because of a sudden episode of collapse which remained unexplained after the initial clinical evaluation.\(^{13}\)

In all 26 infants, the clinical history was retaken by me. It was found that the infants fell naturally into 4 groups, based on the history alone.
GROUP 1: NEAR MISSES, OTHERWISE ASYMPTOMATIC

This group contained 7 full term infants, who had been found pale or blue and floppy or stiff, without warning, at a time when they were probably asleep, and had, according to their attendants, needed vigorous stimulation or formal resuscitation. Most had been found by their mothers, who could not be sure whether they were breathing or not. It was not therefore presumed that this group had definitely been apnoeic.

GROUP 2: NEAR MISSES, ASSOCIATED SYMPTOMS

In this group were 7 full term infants, also referred following a near miss episode. In these subjects, the event had been preceded by vomiting or crying, had occurred in an infant already ill for other reasons, or had some of the characteristics of a fit. However, in no case was a definite cause for the event identified.

GROUP 3: PREMATURE NEAR MISSES

Three premature babies who had had cyanotic attacks were referred. In one case, the attacks were associated with a blocked nose, in another they occurred following discharge from a neonatal unit after a very difficult neonatal course, and in the third they were initially unexplained (see below).

GROUP 4: INFANTS WITH UPPER AIRWAY SYMPTOMS

There were 6 preterm and 3 term infants with various upper airway symptoms, chiefly stridor.
Clinical investigations on all 26 infants were undertaken by the referring clinician. In most of the near misses, these consisted of chest x-ray, 12 lead ECG, routine EEG, blood glucose, urea and electrolytes and a full blood count. An infection screen was performed, if indicated. Unfortunately, very few barium swallow examinations for gastro-oesophageal reflux were made. Many of the infants from Group 4 with upper airway difficulties had laryngoscopy performed.

In each case, a polygraphic study was carried out, usually for 12 hours overnight. The records were scored as already described. In view of the confusion in the literature about the range of normal, the referring clinician was only informed that the record was abnormal if apnoeas of 15 seconds or longer were seen or if obstructive apnoea occurred more than once or twice. However, the clinician was informed of all the apnoea rates. Further management, including the decision to use theophylline therapy or provide a home monitor, was decided by the referring clinician.

Two years after the study began, follow-up information on the subjects was sought by examining hospital case notes or by sending a brief questionnaire to the referring clinician.

The clinical history, apnoea rates and follow up information on each subject were then put together. The data were examined to see if there were any differences between the groups. The statistical significance of any difference was assessed using the Mann Whitney U Test, because the data were non parametric.
RESULTS

The clinical details of each infant, with the results of his polygraphic study and available follow-up information, are presented in detail in Tables 1 to 4. The results can be summarised as follows:

CLINICAL INVESTIGATIONS

In Group 1, the negative history was reflected in the normal investigation results; in no case was a possible explanation found. One infant in Group 2, who had vomited before her collapse, was found to have gastro-oesophageal reflux, but investigations were unhelpful in the rest of Group 2 and in Group 3. In Group 4, a diagnosis of subglottic stenosis was made in 4 preterm infants with stridor while laryngomalacia was found in both term infants who were stridulous. Other diagnoses in this group were unilateral choanal atresia, chronic snuffles and permanent tracheostomy.

APNOEA RATES

Central Apnoea

No central apnoea lasting 15 seconds or more was seen in any infant, indeed most of the central apnoeas were less than 10 seconds long. These short apnoeas were much more common in Group 1 (median 9.4 per hour) than in Group 2 (median 3.4 per hour) or Group 4 (median 0.65 per hour). The differences between Groups 1 and 2 and Groups 1 and 4 were highly significant (p = 0.018 and
TABLE 1: Results of polygraphic monitoring and follow-up data in Group 1: Near Misses (asymptomatic)

<table>
<thead>
<tr>
<th>NO.</th>
<th>AGE</th>
<th>SEX</th>
<th>TIME (days) SINCE EPISODE</th>
<th>LENGTH OF RECORD (hrs)</th>
<th>POLYGRAPHIC MONITORING</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CENTRAL APNOEA no/hr</td>
<td>MOV. ARTEFACT no/hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5-9 s</td>
<td>≥ 10 s</td>
</tr>
<tr>
<td>11</td>
<td>13/7</td>
<td>F</td>
<td>9</td>
<td>12.09</td>
<td>9.6</td>
<td>1.5</td>
</tr>
<tr>
<td>10</td>
<td>2/52</td>
<td>M</td>
<td>4</td>
<td>11.80</td>
<td>9.4</td>
<td>0.2</td>
</tr>
<tr>
<td>25</td>
<td>2/52</td>
<td>F</td>
<td>6</td>
<td>2.96</td>
<td>9.1</td>
<td>0.3</td>
</tr>
<tr>
<td>15</td>
<td>1/12</td>
<td>F</td>
<td>7</td>
<td>11.92</td>
<td>6.3</td>
<td>0.2</td>
</tr>
<tr>
<td>2</td>
<td>6/52</td>
<td>M</td>
<td>1</td>
<td>8.32</td>
<td>9.9</td>
<td>0.2</td>
</tr>
<tr>
<td>31</td>
<td>10/52</td>
<td>F</td>
<td>10</td>
<td>8.1</td>
<td>3.7</td>
<td>0</td>
</tr>
<tr>
<td>27</td>
<td>5½/12</td>
<td>M</td>
<td>5</td>
<td>13.08</td>
<td>1.1</td>
<td>0</td>
</tr>
<tr>
<td>Median</td>
<td>1/12</td>
<td>F</td>
<td>6</td>
<td>11.8</td>
<td>9.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

ABBREVIATIONS: movt. = movement, PB = periodic breathing, devp. = development, N = normal

*Episodes XI/wk continued until death. PM-SIDS*
<table>
<thead>
<tr>
<th>NO.</th>
<th>AGE</th>
<th>SEX</th>
<th>HISTORY</th>
<th>TIME (days) SINCE EPISODE</th>
<th>LENGTH OF RECORD (hrs)</th>
<th>POLYGRAPHIC MONITORING</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CENTRAL APNOEA no/hr</td>
<td>MOVIT ARTEFACT no/hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5-9 s ≥ 10 s</td>
<td>5-9 s ≥ 10 s</td>
</tr>
<tr>
<td>29</td>
<td>1/7</td>
<td>F</td>
<td>Cyanotic attacks during feeds</td>
<td>1</td>
<td>2.36</td>
<td>0.8 0 5.5 0</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>3</td>
<td>2/52</td>
<td>F</td>
<td>URTI</td>
<td>3</td>
<td>7.09</td>
<td>3.4 0 3.5 0.6</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>4</td>
<td>3/52</td>
<td>F</td>
<td>Vomiting → apnoea</td>
<td>4</td>
<td>4.55</td>
<td>4.0 0.2 2.4 0</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>28</td>
<td>6/52</td>
<td>M</td>
<td>Crying + collapse</td>
<td>28</td>
<td>11.8</td>
<td>3.4 0 0.4 0</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>26</td>
<td>2/12</td>
<td>M</td>
<td>Severe viral illness → collapse</td>
<td>35</td>
<td>11.8</td>
<td>0.4 0 0 0</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>22</td>
<td>5/12</td>
<td>F</td>
<td>? Febrile fit</td>
<td>21</td>
<td>8.01</td>
<td>4.5 0 0.4 0.1</td>
<td>0 0.1 0</td>
</tr>
<tr>
<td>13</td>
<td>9/12</td>
<td>M</td>
<td>? Febrile fit</td>
<td>5</td>
<td>11.0</td>
<td>0.6 0 0.4 0.1</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>Median</td>
<td>6/52</td>
<td></td>
<td></td>
<td>21</td>
<td>8.01</td>
<td>3.4 0 2.4 0</td>
<td>0 0 0 0</td>
</tr>
</tbody>
</table>

**ABBREVIATIONS:** Movt. = movement, URTI = upper respiratory tract infection, PB = periodic breathing, Devp. = Development, N = normal
<table>
<thead>
<tr>
<th>NO</th>
<th>B.WT (g)</th>
<th>GEST. (wks)</th>
<th>PN AGE (wks)</th>
<th>SEX</th>
<th>TIME (days) SINCE EPISODE</th>
<th>LENGTH OF RECORD (hrs)</th>
<th>CENTRAL APNOEA no/hr</th>
<th>MOVT. ARTEFACT no/hr</th>
<th>OBSTRUCTIVE APNOEA no/hr</th>
<th>PB s/hr</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>1840</td>
<td>32</td>
<td>4</td>
<td>M</td>
<td>2</td>
<td>5.48</td>
<td>20.6</td>
<td>0.2</td>
<td>33.9</td>
<td>3.8</td>
<td>1.3</td>
</tr>
<tr>
<td>24</td>
<td>2000</td>
<td>34</td>
<td>4</td>
<td>M</td>
<td>4</td>
<td>8.66</td>
<td>1.8</td>
<td>0</td>
<td>2.0</td>
<td>0.1</td>
<td>0.2</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>
<td></td>
</tr>
<tr>
<td>16</td>
<td>2175</td>
<td>34</td>
<td>4</td>
<td>F</td>
<td>2</td>
<td>48.24</td>
<td>2.1</td>
<td>0.1</td>
<td>1.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**ABBREVIATIONS:** Gest. = gestational age, PN Age = postnatal age, Movt. = movement, PB = periodic breathing, URTI = upper respiratory tract infection
<table>
<thead>
<tr>
<th>NO</th>
<th>GEST AGE</th>
<th>PN AGE</th>
<th>SEX</th>
<th>HISTORY</th>
<th>POLYGRAPHIC MONITORING</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LENGTH OF RECORD (hrs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CENTRAL APNOEA no/hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5-9 s</td>
<td>≥ 10 s</td>
</tr>
<tr>
<td>18</td>
<td>26</td>
<td>6/52</td>
<td>M</td>
<td>Stridor C</td>
<td>3.80</td>
<td>0.5</td>
</tr>
<tr>
<td>14</td>
<td>27</td>
<td>2/12</td>
<td>M</td>
<td>Tracheostomy C</td>
<td>2.83</td>
<td>1.4</td>
</tr>
<tr>
<td>9</td>
<td>28</td>
<td>7/12</td>
<td>M</td>
<td>Stridor</td>
<td>6.96</td>
<td>0.6</td>
</tr>
<tr>
<td>21</td>
<td>28</td>
<td>7/12</td>
<td>M</td>
<td>Stridor</td>
<td>4.4</td>
<td>2.9</td>
</tr>
<tr>
<td>17</td>
<td>30</td>
<td>1/12</td>
<td>F</td>
<td>Stridor</td>
<td>12.3</td>
<td>0.7</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>1/7</td>
<td>M</td>
<td>Unilateral choanal atresia</td>
<td>Very short</td>
<td>++</td>
</tr>
<tr>
<td>20</td>
<td>40</td>
<td>5/52</td>
<td>M</td>
<td>Stridor</td>
<td>11.9</td>
<td>0</td>
</tr>
<tr>
<td>19</td>
<td>40</td>
<td>6/52</td>
<td>F</td>
<td>Stridor</td>
<td>15.9</td>
<td>0.4</td>
</tr>
<tr>
<td>8</td>
<td>40</td>
<td>6/52</td>
<td>F</td>
<td>Chronic snuffles</td>
<td>7.11</td>
<td>0</td>
</tr>
</tbody>
</table>

**ABBREVIATIONS:** Gest. = gestation, PN Age = postnatal age, Movt. = movement, Devp. = development, N = normal, + = died, OA = obstructive apnoea, PB = periodic breathing, C = on caffeine at time of recording
p < 0.002 respectively). However, the difference between Groups 2 and 4 did not quite reach statistical significance (p = 0.06).

Movement Artefact

There were no significant differences between the groups for movement artefact apnoeas. However, close inspection of the data revealed that these apnoeas were more common in those preterm subjects from Groups 3 and 4 who had not yet reached their expected date of delivery. The median for all preterm infants in the study was 6.35 episodes per hour, that for the term subjects 0.8 per hour. This difference was significant (P = 0.02)

Obstructive Apnoea

Obstructive apnoea was a rarity; more than 0.1 episodes per hour were seen in only 4 infants, all had been preterm. Severe or prolonged episodes were observed in only 2 infants. The first (no. 6) suffered from unilateral choanal atresia, the second (no. 16) exhibited infrequent prolonged episodes, in spite of an anatomically normal airway. Eventually, a great deal of circumstantial evidence accumulated to suggest that the child's mother was repeatedly occluding the airway. Obstructive apnoea was not a feature of either of the full term near miss groups.

CLINICAL FOLLOW-UP

Follow-up information was obtained on 16 of the 26 infants. There was one death, attributed to SIDS, in Group 1. The remainder of that group were healthy and had not experienced further episodes. Most of those in Group 2 were doing well, although one
infant had gone on to develop definite febrile convulsions. In Group 3, the infant who had prolonged obstructive apnoea, probably induced by the mother, sustained severe brain damage. Thus, of the 13 near miss infants followed up, one died and one suffered severe neurological handicap. The outcome in Group 4 depended on the severity of the underlying problems.

DISCUSSION

From this study of near miss and other symptomatic infants, two results stand out: the high central apnoea rate in the asymptomatic near miss group and the paucity of obstructive apnoea in the study as a whole.

Since there are no normal controls, it is difficult to interpret the difference in central apnoea rates between the two groups of near misses. Does Group 1 show too much apnoea or Group 2 too little? To try to resolve this problem, the results from the present study were compared with those in the literature. Comparisons between studies are difficult, because of variation in the selection of patients, the details of recording technique and the methods of quantitating results. In addition, as discussed in Chapter 4, small differences in interpretation can result in large differences in apnoea rates. In view of all these factors, it is hardly surprising that there are differences of opinion as to whether near miss infants have more or less apnoea than controls.

With all these reservations in mind, studies of near misses, siblings of SIDS infants and controls in the literature were scrutinised and any using methods similar to those employed here
were analysed in detail. The methods of selection of patients and of making the recordings were noted. The authors' mean or median apnoea rates were converted, where possible, to the number of central apnoeas, lasting 5 seconds or more, per hour of total sleep time. To do this, results from REM and NREM sleep were averaged where necessary. In addition, if the authors had examined apnoeas of 6 seconds or more, the apnoea count was doubled, as 2 separate investigators note that apnoeas $>5$ seconds are roughly twice as common as those $>6$ seconds$^{14,15}$. The results of these manipulations are presented in Tables 5 (near misses and controls), 6 (sibs of SIDS and controls) and 7 (normals only).

Once the scores have been standardised in this way, the agreement between investigators is remarkable. The range of apnoea rates for controls is from 2.2 to 5.5 per hour and averages around 4.5 per hour. The range for near misses is a little higher - from 3.0 to 7.1 per hour. Nogues and Samson-Dollfus$^2$ found the only significant difference between near misses and controls, which was confined to 2-5 second apnoeas. The range for sibs is also higher than that for controls - from 3.9 to 9.1. In this case, significant differences were found for 5 second apnoeas by 2 sets of investigators$^5,6$. The finding of Hoppenbrouwers et al$^7$ that sibs experience less apnoea than controls was confined to 2-5 second apnoeas.

Thus, the evidence is that there is slightly more apnoea in high-risk infants than in controls. When the current results are compared with those reported, it can be seen that the median apnoea rate in Group 2, the symptomatic near misses, at 3.4 per hour, is well within the control range, whilst that of Group 1,
TABLE 5: Studies comparing central apnoea in near misses and controls.

<table>
<thead>
<tr>
<th>INVESTIGATORS</th>
<th>DEFINITION OF NEAR MISS</th>
<th>AGE</th>
<th>METHODS</th>
<th>TIMING</th>
<th>CENTRAL APNOEAS &gt; 5 seconds/hr</th>
<th>AUTHORS' CONCLUSIONS RE CENTRAL APNOEA &gt; 5 or 6 secs</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guilleminault et al, 1979*</td>
<td>Blue, limp, apnoeic during sleep. Resus req.</td>
<td>3/52 - 6/12</td>
<td>Airflow, chest movt, EEG</td>
<td>24 hrs</td>
<td>4.92</td>
<td>7.14</td>
<td>NM = controls</td>
</tr>
<tr>
<td>Nogues and Samson-Dollfus, 1979²</td>
<td>Found blue at least once</td>
<td>2/12 - 1 yr</td>
<td>?</td>
<td>Day/evening short</td>
<td>3.9</td>
<td>3.0</td>
<td>NM = controls</td>
</tr>
<tr>
<td>Guilhaume et al, 1981¹</td>
<td>Apnoea/cyanosis req. resus. No obvious cause</td>
<td>2.7 mo</td>
<td>Airflow, chest movt. EEG</td>
<td>Night</td>
<td>2.2</td>
<td>6.2</td>
<td>NM &gt; controls</td>
</tr>
<tr>
<td>Hodgman et al, 1982²</td>
<td>Apnoea/colour change req. intervention</td>
<td>5/52</td>
<td>Airflow, chest movt, EEG</td>
<td>12 hrs night</td>
<td>4.8</td>
<td>3.4</td>
<td>NM = controls</td>
</tr>
</tbody>
</table>

ABBREVIATIONS: resus. = resuscitation, req. = required, movt. = movement, NM = near misses
<table>
<thead>
<tr>
<th>INVESTIGATORS</th>
<th>AGE</th>
<th>METHODS</th>
<th>TIMING</th>
<th>CENTRAL APNOEA &gt; 5 seconds/hr</th>
<th>AUTHORS' CONCLUSIONS RE CENTRAL APNOEA &gt; 5 or 6 secs</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nogues and Samson-Dollfus, 1979</td>
<td>2/12 - 1 yr</td>
<td>?</td>
<td>Day/evening</td>
<td>3.9</td>
<td>Sibs = controls</td>
<td>For 2-5 secs sibs &gt; controls</td>
</tr>
<tr>
<td>Hoppenbrouwers et al, 1980</td>
<td>1-6/12</td>
<td>Airflow, chest movt, EEG</td>
<td>12 hrs night</td>
<td>5.02</td>
<td>Sibs = controls</td>
<td>Sibs &lt; controls for all 2-5 sec pauses</td>
</tr>
<tr>
<td>Guilhaume et al, 1981</td>
<td>2.7 mo</td>
<td>Airflow, chest movt, EEG</td>
<td>Night</td>
<td>2.2</td>
<td>Sibs &gt; controls</td>
<td>But p &gt; 0.1</td>
</tr>
<tr>
<td>Kelly et al, 1982</td>
<td>2-14/52</td>
<td>Imp only</td>
<td>All night home</td>
<td>4.45</td>
<td>Sibs &gt; controls</td>
<td>Longitudinal study. Difference only sig at 2 wks of age</td>
</tr>
<tr>
<td>Flores-Guevara et al, 1982</td>
<td>1-17/52</td>
<td>?</td>
<td>Daytime</td>
<td>5</td>
<td>Sibs &gt; controls</td>
<td>Longitudinal study. Difference only sig from 6-9 wks</td>
</tr>
</tbody>
</table>

ABBREVIATIONS: Movt. = movement, Sig. = significant, Imp. = chest impedance
TABLE 7: Studies of apnoea rates in normal infants

<table>
<thead>
<tr>
<th>INVESTIGATORS</th>
<th>AGE</th>
<th>METHODS</th>
<th>TIMING</th>
<th>CENTRAL APNOEA ≥ 5 seconds/hr</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoppenbrouwers, 1977&lt;sup&gt;11&lt;/sup&gt;</td>
<td>0-6/12</td>
<td>Airflow, Chest impedance, EEG</td>
<td>12 hrs</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>Gould et al, 1977&lt;sup&gt;15&lt;/sup&gt;</td>
<td>40-52/52 PCA</td>
<td>Airflow, EEG, No chest movt.</td>
<td>Daytime</td>
<td>5.5</td>
<td>All twins. ? Some premature</td>
</tr>
<tr>
<td>Stein et al, 1979&lt;sup&gt;17&lt;/sup&gt;</td>
<td>0-12/52</td>
<td>Impedance only</td>
<td>24 hrs</td>
<td>4.4</td>
<td>Authors' original Figure included much waking time. After study of their 24 hr profiles of apnoea, rates were doubled to give values for sleep time alone.</td>
</tr>
</tbody>
</table>

ABBREVIATION: PCA = Post-Conceptual Age
the silent near misses, at 9.4 per hour, is higher than that of any other near miss group examined. The median apnoea rate for Groups 1 and 2 together is 3.85, which lies in the control range.

Thus, there may well be a proportion of the infants, usually described as near misses, who do experience more apnoea than normal, but most studies have failed to bring this out. There are at least two reasons why this might be so. Firstly, since the near miss group is clinically heterogeneous, it might be expected that the incidence of apnoea varies from one subgroup to another. Secondly, it is possible that the more elaborate recording techniques provide a non-specific stimulus which reduces apnoea rates. Comparisons between the current study and that of Kelly and Shannon provide some support for both suggestions. (This study is not included in Table 5 as it dealt entirely with periodic breathing.)

Kelly and Shannon found differences between their near misses and controls as large, and as significant, as the differences found here between Groups 1 and 2. The methodology of this study has much in common with that used here. The authors seem to have been more selective than usual in defining a near miss infant and the infants were studied using a relatively simple system: impedance pneumography in the home.

The authors exclude infants with gastro-oesophageal reflux from the near miss group. Silva et al have suggested that infants with reflux can be distinguished from those without by the presence of symptoms, such as vomiting or choking. If that is so, then Group 1, who had no symptoms, probably had no gastro-oesophageal reflux and hence were similar to Kelly and Shannon's near
miss group. In that case, it is not surprising that they share a high apnoea rate.

The literature on obstructive apnoea in controls and at risk patients is even more confusing than that dealing with central apnoea. The reported results differ by factors of up to 100 (see Table 8). The explanation appears to lie in the difficulty of distinguishing obstructive apnoea from movement artefact, which forms the subject matter of Chapter 3. Certainly, those who appear, from the definitions of obstructive apnoea cited in their methods sections, to use the least strict definitions, find the most obstructive apnoea. The current results give lower rates than those found by any other group, with the exception of Kahn et al\textsuperscript{19}, whose definition is the most exclusive.

Since it is likely that Guilleminault et al\textsuperscript{8} have scored as obstructive apnoea episodes more likely to represent movement artefact, it is interesting to compare their mixed and obstructive apnoea rate of 1.84 episodes of 6-10 seconds per hour in near miss infants aged 6 weeks with the movement artefact apnoea rate found in Groups 1 and 2 (0.6 and 2.4 episodes per hour). The similarity is striking.

In spite of their differing rates of obstructive apnoea, Guilleminault et al\textsuperscript{8} and Kahn et al\textsuperscript{19} agree that short obstructive episodes are more common in near miss infants than in controls. In the current study, obstructive apnoea was so rare in both term near miss groups that it is difficult to envisage any control group showing significantly less obstruction.

Even in Group 4, little obstructive apnoea was found, although many of the subjects were known to suffer from incomplete
### TABLE 8: Summary of rates of mixed and obstructive apnoea in the literature

<table>
<thead>
<tr>
<th>INVESTIGATORS</th>
<th>DEFINITION OF OBSTRUCTIVE APNOEA</th>
<th>LENGTH OF APNOEA secs</th>
<th>NO. OF MIXED/OBSTRUCTIVE APNOEAS/HR</th>
<th>AUTHORS' CONCLUSIONS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CONTROLS</td>
<td>NEAR MISSES</td>
<td>SIBS OF SIDS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C</td>
<td>NM</td>
<td></td>
</tr>
<tr>
<td>Guilleminault et al, 1979</td>
<td>Continued chest/abdominal movt. No airflow</td>
<td>6-10</td>
<td>0.38</td>
<td>1.54</td>
<td>--</td>
</tr>
<tr>
<td>Hoppenbrouwers et al, 1980</td>
<td>No airflow with identifiable respiratory excursions, not preceded by movt.</td>
<td>≥ 6</td>
<td>0.6</td>
<td>--</td>
<td>0.18</td>
</tr>
<tr>
<td>Guilhaume et al, 1981</td>
<td></td>
<td></td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Kahn et al, 1982</td>
<td>Continued chest movt. but no airflow. Excluding those preceded by another apnoea or movt.</td>
<td>≥ 2</td>
<td>0.01</td>
<td>0.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Flores-Guevara et al, 1982</td>
<td>No airflow, continued chest/abdominal movt.</td>
<td>≥ 2</td>
<td>&lt; 1.2</td>
<td>&lt; 1.2</td>
<td>&lt; 1.2</td>
</tr>
</tbody>
</table>
obstruction. The technique used detects only episodic complete obstruction and provides no useful information even in severe incomplete obstruction.

There were no significant differences between any of the groups on the movement score, but the finding that movement was more common in preterm infants is in keeping with previous reports that preterm babies move more, both in and out of the uterus, than full term infants\textsuperscript{20,21}.

Finally, the follow-up data indicate that the prognosis for most near miss infants is good. This is in agreement with other work; Southall\textsuperscript{11}, reviewing the literature on this subject, noted 12 deaths from a total of 845 near miss infants.
REFERENCES


CHAPTER SIX

--00000--

THE EFFECT OF NASOENTERIC TUBES ON THE INCIDENCE OF APNOEA AND TcPO2 LEVELS IN PRETERM INFANTS
INTRODUCTION

It is common, though not universal, clinical practice to feed preterm infants through nasoenteric tubes. Although it is well established that partial nasal obstruction increases airways resistance and may reduce ventilation\(^1\), it is not known what effect this manoeuvre might have on the precarious first days of life of preterm infants. The alternative, that of oroenteric feeding, is not generally used as many centres find it difficult to secure oral tubes. Frequent tube displacement then interrupts the feeding regime, with the result that inadequate volumes of feed are administered\(^2\) and the infant runs the risk of milk aspiration.

A palatal appliance was devised by Sullivan to overcome those problems\(^3,4\). The device is illustrated in Figures 1 and 2. In its final form, it consisted of a small acrylic base plate, lined with silicone impression material and with two grooves cut into the glossal surface to hold the feeding tubes. Like an adult denture, it remained in situ because it had been shaped using the palate and gums as a template and was therefore an exact fit. Standard orthodontic impression techniques were used in its manufacture, which is described in detail in Appendix 1.

Two impressions were needed for the manufacture of each device. These were carried out with the infant lying across the incubator on his back with the neck extended. He was positioned by myself or a paediatric nurse who observed his condition throughout. Intravenous lines and monitoring equipment were not disturbed and he breathed additional oxygen if necessary. The
FIG. 1: The palatal appliance viewed from its glossal surface, formed by the acrylic base plate. The blue silicone impression material which forms the palatal surface is seen through the base plate. The two feeding tubes are securely located within their grooves.
FIG. 2: The appliance in situ, securing a single orogastric feeding tube.
infants tolerated the procedure well. Even in the smallest and most immature subjects there was only a transient bradycardia and fall in TcPO₂ on insertion of the special tray loaded with impression material. These resolved within ten seconds and for the remainder of the two minutes required for the material to polymerise, the infant's condition remained stable.

In theory, oroenteric feeding using the device ought to be superior to nasoenteric feeding. However, neonatal care has been bedevilled by the uncontrolled introduction of treatments which work well in theory, but have unforeseen disadvantages in practice. The most notable example is oxygen, over-enthusiastic use of which resulted in an epidemic of retrolental fibroplasia⁵.

The device was therefore introduced cautiously into the Neonatal Unit of The London Hospital (Whitechapel) and evaluated in two separate studies. The first was a randomised controlled trial in which conventional nasoenteric feeding was compared with oroenteric feeding using the appliance. In the second, the effect of passing and removing nasogastric tubes on the incidence of apnoea and PO₂ levels was assessed.

**STUDY 1**

**A CLINICAL TRIAL TO COMPARE NASOENTERIC TUBE-FEEDING WITH OROENTERIC TUBE-FEEDING USING THE PALATAL APPLIANCE**

**INTRODUCTION**

Other investigators have documented the consequences of acute nasal obstruction in the laboratory¹. However, the effects of chronic nasal obstruction in the clinical situation have not been
examined. This part of the study was designed to compare clinical and physiological data in two groups of infants, those with and those without chronic iatrogenic nasal obstruction, with the aim of determining the usefulness of the appliance in practice.

METHODS

Clinical

Forty-four preterm infants requiring tube-feeding were randomly allocated to one of two groups. A separate sealed envelope was provided for each infant entering the trial and was opened as soon as the clinical decision that enteric feeding should be started had been made. Each group of four envelopes contained equal numbers of control and experimental instructions, thus keeping the two groups matched for size throughout the trial. The first "appliance" group was to receive exclusively oroenteric tube feeding with the aid of the appliance, and the second "control" group nasoenteric tube feeding. Ethical permission from the hospital was obtained and parental consent was sought. Unfortunately, two members of the "treatment" group were excluded because a parent was not available to discuss the baby's entry into the trial, leaving 20 patients in the appliance group and 22 in the control group.

Once the appropriate gastric and, in some cases, jejunal tubes had been passed, further management, including the volume, type and timing of feeds was decided by the medical and nursing staff of the Neonatal Unit. The appliances allocated were worn until either breast or bottle feeding had been established. The
mouth was frequently and carefully inspected for local complications. Full records were made of the subsequent course, including weight gain and sickness score. The latter was an index devised to reflect the number of neonatal problems experienced by each baby and was heavily weighted by the need for, and duration of, oxygen therapy and mechanical ventilation. The use of this score is illustrated in Figure 3.

Because of the large variation in the study population, a clear-cut clinical difference between the groups was not expected. It was felt that more subtle benefits might be conferred on those infants fitted with the oral appliance and accordingly, respiratory monitoring was undertaken to look for differences such as an altered incidence of apnoea or periodic breathing.

**Polygraphic Monitoring**

The infants were studied using the techniques and scoring system described in Chapters Two to Four. Each recording lasted approximately four hours and took place in the afternoon or early evening. Thirty-eight studies were carried out on 29 of the infants on the 3rd and/or 7th day after entry into the trial. Fifteen members of the appliance group were studied, 6 on the 3rd day, 2 on the 7th day and 7 on both occasions. Fourteen controls were monitored, 7 on the 3rd day, 5 on the 7th and 2 twice. The two main reasons for failure to study were either that the infant was too ill to undergo unnecessary procedures or that parental consent for recording was withheld.

Since the data were not normally distributed, all comparisons between the groups were made using the Mann-Whitney U-test.
ILLNESS SCORE

<table>
<thead>
<tr>
<th>Condition</th>
<th>ENTRY</th>
<th>WEEK 1</th>
<th>WEEK 2</th>
<th>WEEK 3</th>
<th>WEEK 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.M.D.</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic P.D.A.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic Infection</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.E.C.</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed collapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson-mikity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other important condition(s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>specify 1. Exchange transfusion</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑FiO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;24 hrs</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation &lt; 24 hrs</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(exclude &lt; 7 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>resuscitation &lt; 14 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>include CPAP) &lt; 21 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FIG. 3: The sickness score in use. Before entry into the trial, this infant suffered from mild hyaline membrane disease and severe ABO incompatibility. Later, he developed sepsis and necrolising enterocolitis and required a period of artificial ventilation.
RESULTS

Clinical

The clinical effects of the appliance were assessed in the whole group of 42 infants. No side-effects or complications were associated with use of the appliance. In particular, there was no evidence of increased oral infection or ulceration of the oral mucosa in the treated group. Adequate volumes of feed were received by both groups; on the seventh day of the trial, the treatment group received a mean of 184 mls/kg/24 hrs, and the controls 187 mls/kg/24 hrs.

Comparison of the groups revealed no significant differences on entry into the trial in birthweight, gestational age, postnatal age or sickness score. Furthermore, there was no significant difference in the apparent clinical outcome, as evidenced by change in sickness score between the two groups (Table 1).

Weight gain was calculated in the 37 babies who remained in the trial for at least 14 days. During the first 7 days after randomisation, the appliance group gained weight whilst the control group lost. This difference was just statistically significant. There was no difference between the groups in the rate of weight gain in the second week of the trial.

Polygraphic

The results of the respiratory monitoring carried out on the third and seventh day after entry into the trial in 29 of the infants are summarised in Table 2. There were no significant differences between the groups three days after entry into the
TABLE 1: Clinical characteristics of patients and clinical outcome in Study 1. Values are expressed as median and (interquartile range)

<table>
<thead>
<tr>
<th>CLINICAL CHARACTERISTICS</th>
<th>APPLIANCE GROUP</th>
<th>CONTROL GROUP</th>
<th>P MANN-WHITNEY U TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight (kg)</td>
<td>N = 20</td>
<td>N = 22</td>
<td>NS</td>
</tr>
<tr>
<td>1.42 (1.28 - 1.74)</td>
<td>1.37 (1.32 - 1.76)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>31.0 (30.0 -33.0)</td>
<td>32.0 (31.0 -34.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Postnatal Age (days)</td>
<td>6.0 (2.5 -12.5)</td>
<td>2.0 (1.0 - 6.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Sickness score at entry</td>
<td>4.0 (1.5 - 6.0)</td>
<td>2.0 (0 - 4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>OUTCOME</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final sickness score</td>
<td>N = 20</td>
<td>N = 22</td>
<td>NS</td>
</tr>
<tr>
<td>5.0 (1.5 - 8.0)</td>
<td>2.5 (1.0 - 6.0)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Weight Gain 0-7 days</td>
<td>N = 17</td>
<td>N = 20</td>
<td></td>
</tr>
<tr>
<td>(g/kg/24 hrs)</td>
<td>8.3 (0 - -15.1)</td>
<td>0.6 (-8.6 -+8.5)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Weight Gain 8-14 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g/kg/24 hrs)</td>
<td>12.3 (10.2 -17.1)</td>
<td>13.6 (9.8 -18.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>
TABLE 2: Results of polygraphic monitoring carried out 3 and 7 days after entry into the trial. Values are expressed as median and (interquartile range)

<table>
<thead>
<tr>
<th>Periodic Breathing (secs/hr)</th>
<th>3 DAYS</th>
<th>7 DAYS</th>
<th>P MAN-WhITNEY U TEST</th>
<th>3 DAYS</th>
<th>7 DAYS</th>
<th>P MAN-WhITNEY U TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>APPLIANCE GROUP N = 13</td>
<td>0 (0-16)</td>
<td>0 (0-20)</td>
<td>NS</td>
<td>0 (0-20)</td>
<td>303 (81-1051)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>CONTROL GROUP N = 9</td>
<td>0 (0-571)</td>
<td>0 (0-20)</td>
<td>NS</td>
<td>0 (0-20)</td>
<td>19.4 (12.0-24.0)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>APNOEAS (no/hr)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Central apnoea 5-9 secs</td>
<td>4.1 (1.7-5.0)</td>
<td>3.9 (1.1-32.9)</td>
<td>NS</td>
<td>4.1 (1.7-3.2)</td>
<td>19.4 (12.0-24.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Central apnoea &gt; 10 secs</td>
<td>0 (0-1.2)</td>
<td>0 (0-0)</td>
<td>NS</td>
<td>0 (0-0)</td>
<td>1.4 (1.0-4.9)</td>
<td>= 0.05</td>
</tr>
<tr>
<td>Movement artefact 5-9 secs</td>
<td>4.9 (4.5-9.9)</td>
<td>4.1 (2.0-9.1)</td>
<td>NS</td>
<td>4.5 (2.9-12.3)</td>
<td>17.1 (15.1-17.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Movement artefact &gt; 10 secs</td>
<td>0 (0-1.8)</td>
<td>0 (0-0)</td>
<td>NS</td>
<td>0 (0-0.6)</td>
<td>2.3 (1.9-5.6)</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>True obstruction 5-9 secs</td>
<td>0 (0-0.3)</td>
<td>0 (0-0)</td>
<td>NS</td>
<td>0 (0-0.3)</td>
<td>0.5 (0.1-1.7)</td>
<td>NS</td>
</tr>
<tr>
<td>True obstruction &gt; 10 secs</td>
<td>0.2 (0-0.3)</td>
<td>0 (0-0.6)</td>
<td>NS</td>
<td>0 (0-0.3)</td>
<td>0.3 (0-1.6)</td>
<td>NS</td>
</tr>
</tbody>
</table>
trial, but it can be seen that after seven days clear differences emerged with the control group showing significantly more periodic breathing, central apnoea and movement than the treated group. Naturally an infant with a lot of periodic breathing also had a high score for central apnoea. However, when isolated short apnoeas were scored separately, the significant difference between the groups at seven days remained. Overall, there were very few episodes of true obstructive apnoea in either group and no significant differences between the groups.

The frequency of neonatal apnoeic spells is affected by many variables. Among the infants monitored after 7 days, there were no significant differences in birth weight, gestational age, postnatal age, amount of illness experienced or exposure to caffeine to account for the observed differences in apnoea rates (see Table 3).

CONCLUSION

The appliance provided a satisfactory method of retaining oroenteric tubes as judged by the adequate volumes of feed administered and the absence of side-effects or complications associated with its use.

Oroenteric tube-feeding using the appliance appeared to confer some clinical benefit in that early weight gain was better in the appliance group. However, it is possible that this difference was due not to the appliance, but to a small, statistically insignificant difference between the groups at age of entry into the trial. The changes in weight in the first week of life are so large that a difference in age of only one or two days makes a big
TABLE 3: Clinical characteristics of infants monitored 7 days after entry into the trial. Values are expressed as median and (interquartile range)

<table>
<thead>
<tr>
<th></th>
<th>APPLIANCE GROUP N = 9</th>
<th>CONTROL GROUP N = 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight (kg)</td>
<td>1.38 (1.3-1.64)</td>
<td>1.35 (1.11-1.39)</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>31.0 (30.0-32.0)</td>
<td>31.0 (29.0-33.0)</td>
</tr>
<tr>
<td>Postnatal Age (days) at time of study</td>
<td>12 (11-19)</td>
<td>11 (10-16)</td>
</tr>
<tr>
<td>Sickness Score on entry</td>
<td>5 (4.0-6.0)</td>
<td>2 (1.5-5.5)</td>
</tr>
<tr>
<td>Receiving caffeine</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
difference to the expected weight gain. Thus, if the control group had entered the trial just before the end of the usual period of neonatal weight loss, whilst the treatment group had entered just after, the observed differences in weight gain could be accounted for.

To exclude this possibility, the postnatal age at which weight loss ceased was determined for the 37 infants who remained in the trial at least 14 days. The results which did not differ significantly were median 7 days (interquartile range 5-15) for the appliance and 5 days (4-6) for the control group. The number of infants entering the trial aged 5 days or less was 7 (of 17) in the appliance and 13 (of 20) in the control group. These proportions did not differ significantly \( (X^2 = 1.25, 0.25 < p < 0.50) \).

Therefore, since the proportion of infants entering the trial whilst still losing weight was similar in the two groups and, furthermore, the pattern of the early weight loss was unaffected by appliance use, the improved early weight gain in the treatment group was considered to be a beneficial effect of the appliance.

The effect of the appliance on apnoea rates was considerable. By 7 days after entry into the trial, the infants with nasal tube(s) experienced 10 times as much apnoea as those without, as well as appearing more restless.

A weakness of Study 1 was the low number of infants who were monitored on the seventh day. In fact, the 2 groups of infants monitored on the seventh day did not differ significantly, either from each other, or from the larger groups from which they came in birth weight, gestational age, postnatal age or sickness score.
In spite of this, it is still possible that some bias arose because some infants in each group could not be monitored.

Accordingly, a second study was set up to see if the apparent effect of the appliance on apnoea rates could be demonstrated using a different approach.

**STUDY 2**

**FURTHER EXAMINATION OF THE EFFECTS OF THE PASSAGE AND REMOVAL OF NASOENTERIC TUBES ON APNOEA AND PO<sub>2</sub>**

**INTRODUCTION**

To avoid the difficulties encountered in carrying out clinical trials, this study was designed so that each infant acted as his own control, whilst the effect of passing or removing naso-enteric tubes on apnoea rates and PO<sub>2</sub> levels was assessed.

The same kind of monitoring, but with the addition of transcutaneous PO<sub>2</sub> (TcPO<sub>2</sub>) was used. The TcPO<sub>2</sub> sensor (Radiometer TM-204) remained on the same skin site throughout the 4-hour period of each study.

Seven parenterally fed infants who had not had any nasal tubes in situ for at least 12 hours were studied for 2 hours before and 2 hours after insertion of a nasogastric tube, required for feeding. The first feed was not given until completion of the study.

In each case, the apnoea rates and median TcPO<sub>2</sub> in each half of the study were computed and the significance of any changes associated with the insertion of nasal tubes were assessed using the Wilcoxon matched-pairs signed-ranks test.
Data from 7 further infants were handled in the same way. These infants, who had had nasoenteric tube(s) in situ for several days, were monitored for 2 hours before and 2 hours after the removal of the tube(s), which usually took place after a feed, the regime being 2-3 hourly.

RESULTS

No significant changes in apnoea measures or TcPO$_2$ were seen after the insertion of a nasal tube, but, removing nasal tube(s) that had been in situ for some days caused a statistically highly significant rise in TcPO$_2$ associated with a significant fall in the incidence of central apnoea and periodic breathing (Fig. 4 and Table 4). Removal of the tubes did not affect the movement artefact or true obstruction scores.

The most dramatic clinical difference was seen in a 28-week gestation, 1,020 g, male infant suffering from apnoea of prematurity. He was found to be apnoeic for 24% of the recording time whilst two nasal tubes were in situ and was being considered for artificial ventilation. Removal of the tubes resulted in an immediate stabilisation of his condition and a 50% reduction in the proportion of time spent apnoeic.

CONCLUSIONS

The results of this study support the conclusion drawn from the clinical trial, namely that nasal feeding tubes cause a chronic increase in the incidence of apnoea. This is associated with a fall in TcPO$_2$ levels.
FIG. 4: The effect of removing established nasoenteric tube(s) on TcPO₂, periodic breathing and apnoea.
TABLE 4: Summary of changes in periodic breathing, apnoea rates and TcPO₂ induced by insertion or removal of nasogastric tube(s)

<table>
<thead>
<tr>
<th></th>
<th>INSERTION OF TUBE N = 7</th>
<th>REMOVAL OF TUBE(S) N = 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodic breathing</td>
<td>NS</td>
<td>Reduced p &lt; 0.05</td>
</tr>
<tr>
<td>All central apnoea</td>
<td>NS</td>
<td>Reduced p &lt; 0.05</td>
</tr>
<tr>
<td>All movement artefact</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>All true obstruction</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TcPO₂</td>
<td>NS</td>
<td>Increased p &lt; 0.01</td>
</tr>
</tbody>
</table>
DISCUSSION

Both studies therefore provide, in different ways, evidence for the same conclusion, namely that nasal feeding tubes increase the rate of central apnoea and periodic breathing considerably but that this phenomenon appears slowly over several days. It appears that the infant can compensate for the increased work of breathing only for a time. Other investigators have shown the consequences of acute nasal obstruction in the laboratory. Our results suggest that the chronic obstruction produced in the clinical situation also has a measurable, detrimental effect.

Most of the apnoeas observed during monitoring were short and self-limiting and it could be argued that this is a small price to pay for securing the feeding tube accurately without costly orthodontic aid. The significance of such short respiratory pauses is still uncertain, but there exists considerable evidence indicating that periodic breathing and short apnoeas can be produced by hypoxia\textsuperscript{6,7}. Our results from Study 2 certainly support the notion of an inverse relationship between pO\textsubscript{2} changes and changes in the rates of apnoea and periodic breathing, although it is not possible to say which is cause and which effect. This link between apnoea and hypoxia strongly suggests that the control group in Study 1 was less well oxygenated than the appliance group, which must be considered undesirable.

Neither of the studies was designed to delineate the group of infants least able to bear the burden of increased airways resistance with the accompanying apnoea and reduction in pO\textsubscript{2} which were documented, but the results do suggest that the smaller infant,
suffering from either lung disease, pre-existing apnoea or hypoxia, will be least able to cope with this additional problem. Since the appliance enables oroenteric feeding to be carried out simply and without side-effects, these infants need no longer be burdened with nasal feeding tubes.
REFERENCES

CHAPTER SEVEN

--00000--

DISCUSSION
The original aim of this work was to devise and apply a polygraphic recording system capable of detecting both central and obstructive apnoea in the human infant. This has been fulfilled. The final techniques were simple and the system proved robust enough for everyday use, in the laboratory, the children's wards and the Neonatal Intensive Care Unit of The London Hospital, Whitechapel.

Many other research groups have used similar polygraphic systems for the detection of apnoea, which appears at first sight to be a straightforward task. However, it soon became obvious that a considerable amount of further work on interpretation and quantification of the data was required. Only when this had been done was it possible to compare the apnoea rates of various groups of infants in different clinical situations.

As a result of the work reported in the earlier chapters of this thesis and the scrutiny of the literature required for the discussion of other authors' work (Chapter Five), four recurring themes emerge. They are obviously interrelated but it is proposed to examine them separately.

1. **THE LOW INCIDENCE OF TRUE OBSTRUCTIVE APNOEA IN ALL THE INFANTS STUDIED**

As soon as the first recordings of possible obstructive apnoea had been made, it was apparent that the same pattern of absent airflow and continuing chest movement might be produced both by obstructive apnoea and normal body movements. The two phenomena could not be distinguished without the aid of further information which was therefore obtained from measurements of
expired CO₂ at the mouth and oesophageal pressure, as well as careful clinical observation (Chapter Three). The studies showed conclusively that obstructive apnoea and movement may, indeed, produce similar polygraphic patterns, but that careful inspection of the trace enables the distinction to be made with some confidence.

When analysing the records of the 69 infants who took part in the investigations described in Chapters Five and Six, this distinction was always made, and true obstructive apnoea was found to be very rare. Frequent natural episodes occurred in just one preterm infant, who had choanal atresia (Chapter Three). The more prolonged episodes which occurred in another older child were produced by deliberate airway obstruction by her mother (Chapter Five). In some preterm infants, brief episodes were seen at the end of a period of central apnoea (Chapters Five and Six). This pattern of mixed apnoea is well described in preterm subjects and is more likely to occur during longer spells\(^1,\)\(^2\). However, the present results suggest that the vast majority of the short episodes of apnoea occurring in otherwise well preterm infants do not contain an obstructive element.

Very little obstructive apnoea occurred in the near-miss infants studied, although there is a great deal of speculation about the role of obstructive apnoea in SIDS. In fact, there is only one polygraphic study which provides any evidence that obstructive apnoea may be important in SIDS. This is the study of Guillemainault et al\(^3\), who found more mixed and obstructive apnoea in near-miss cases than in controls. However, as this group does not appear to have differentiated between true respiratory and
other body movements, their conclusions must be treated with caution (Chapters Three and Five). In the course of the current work, obstructive apnoea was so unusual that no significant differences between groups of infants were found.

2. THE SIGNIFICANCE OF THE INCREASED FREQUENCY OF SHORT CENTRAL APNOEAS FOUND IN THE PRETERM INFANTS WITH PARTIAL NASAL OBSTRUCTION AND A MINORITY OF NEAR-MISSES FOR SIDS

There was definite evidence of an increase in short central apnoea, not only in some of the near-miss infants, but also in preterm infants with iatrogenic nasal obstruction, in whom apnoea was accompanied by a fall in TcPO₂ and reduced early weight gain (Chapter Six).

In spite of a decade of intense interest in the subject, the significance of these brief respiratory pauses is unknown, although they are often thought to be due to imperfect control of respiration. It is easy to see that periodic breathing, which involves 'regular' alternations of breaths and pauses, may be the result of oscillations in an unstable control system. This attractive idea is not new, having been elegantly expressed in 1909 by Douglas and Haldane⁴ writing of Cheyne-Stokes breathing:

"It is evidently a phenomenon analogous to the 'hunting' often produced by the governor of an engine; and what is remarkable is not that it should occur, but that its occurrence should be so unusual under normal conditions."

A more recent application of control theory to periodic breathing has been lucidly expounded by Cherniak and Longobardo⁵.
It is more difficult to fit apparently isolated apnoeas into such a system. However, the new digital filtering techniques make it possible to identify oscillations that are not immediately apparent to the naked eye. Using this approach in infants, Waggener et al. have described several oscillations in ventilation occurring simultaneously, but with different cycle times. Apparently random apnoeas can then be related to these hidden oscillations. Thus, both classical periodic breathing and isolated apnoeas can be considered as manifestations of increased oscillations in a feedback control system.

From the model of Cherniak and Longobardo, a disturbing force will cause oscillations if the system is either slow to respond to stimuli, oversensitive or insufficiently damped. Evidence that each of these 3 characteristics of the ventilatory control system alters during the first 6 months of life was found by Fleming et al. in their study of ventilatory oscillations and apnoea in response to the stimulus of a sigh. Other factors which are known to induce apnoea experimentally, such as hypoxia and nasal obstruction (Chapter Six), also offer a stimulus, either chemical or reflex, to the respiratory centre.

The comment that the studies of both Fleming and Waggener are purely descriptive does not imply criticism. The complex interaction between apnoea and only one of the above variables, namely hypoxia, is illustrated by observations made on one of the preterm infants taking part in Study 2 of Chapter Five. During regular breathing in air, the infant had a TcPO₂ of 90 mm Hg, which fell to 50 mm Hg following 2 apnoeas which lasted longer than 15 seconds within one minute. Following this disturbance, the respirat-
ory pattern changed to periodic breathing with a regular recurrence of 5-6 second central apnoeas and TcPO$_2$ of around 75 mm Hg. This continued for 20 minutes and TcPO$_2$ did not rise to 90 mm Hg until after regular breathing had been resumed. Thus, although it seems likely that the infants in these studies with most central apnoea also had the lowest levels of PaO$_2$, it is impossible to know which was cause and which effect. The fact that hypoxia can be, at different times, either the cause or the result of apnoea highlights the complexity of the changes in the physiology of respiration which underly the changing oscillatory patterns.

3. AN OVERVIEW OF THE CLINICAL AND POLYGRAPHIC FINDINGS IN NEAR-MISS INFANTS

A combined clinical and polygraphic approach (Chapter Five) suggested that the increase in central apnoea observed in near-miss infants is confined to a subgroup which can be identified by the clinical history alone. The 14 full-term near-miss infants studied could be divided into 2 groups. The group with essentially negative clinical findings had increased central apnoea, while the apnoea rates in the symptomatic group were normal. In the latter, a number of medical conditions of questionable significance, including gastro-oesophageal reflux, were found. Kahn et al. have also looked at both clinical and polygraphic data with similar results. In their series, infants who had a severe near-miss episode, not associated with other symptoms and with negative findings on investigation, were those most likely to exhibit excessive central apnoea. In addition, they were more likely to have further frightening episodes. Thus, the classification
arrived at here would seem to have predictive, as well as descriptive, value.

If one accepts (albeit with some of the reservations discussed in Chapter Five) that many near-miss infants really did have a narrow escape from death, then the present work provides some support for the hypothesis that apnoea may cause a proportion of SIDS deaths. Of course, apnoea seen in near-miss cases could be the result and not the cause of the near-miss episode. However, siblings of SIDS infants, who have not had any incident, but do form a group at increased risk of SIDS, also show a little more short apnoea than controls (Chapter Five). This similarity between the near-miss and sibling groups provides further support for a link between central apnoea and SIDS. However, although real, the association is not a strong one. In a large prospective study of normal babies\textsuperscript{10}, only 2 of the 14 who subsequently suffered SIDS showed excessive short apnoea and none showed prolonged central apnoeas.

Disturbingly, child abuse was found to be the cause of the near-miss episodes in one infant, whose records, made while the mother was alone with the infant, showed prolonged obstructive apnoea. Suspicions were also aroused of the role of child abuse in 2 other clinically negative cases, including the only one who died, apparently of SIDS. Interestingly, those infants were the only members of Group 1 who did not show high frequencies of central apnoea. Although child abuse was suspected in 3 out of 17 cases, its role in near-miss for SIDS has received scant attention, there being only isolated case reports in the literature\textsuperscript{11,12}. The reason is probably that most investigators have
concentrated on the apnoea hypothesis and have looked at the polygraphic, rather than the clinical, findings in these infants. Thus, careful examination of all the available data, rather than blind scoring of polygraphic traces, has led to a new and disturbing conclusion.

4. THE NEED FOR MORE CRITICAL EXAMINATION OF ALL POLYGRAPHIC DATA

Throughout the current work it was found that constructive criticism of polygraphic data led to interesting conclusions. The analysis of obstructive apnoea, described in Chapter Three, which was based on the careful examination of the records of just 8 infants, called into question the results of some large polygraphic programmes. It also illustrated the major problems of polygraphic studies. The data is voluminous and the interpretation of individual incidents is often difficult. To overcome these difficulties, rigid definitions of phenomena have been used and are sometimes incorporated into computer programs for detecting and counting events. While this approach has the advantage of avoiding observer bias and rendering complex data manageable, the current work has shown that, where large amounts of polygraphic data are processed in this way and apnoeas detected automatically and uncritically, the resulting apnoea indices may be very misleading. This is particularly true for obstructive apnoea, but the work described in Chapter Four suggests that it also applies to central episodes.

Although the definition of central apnoea is not controversial, differences in recording technique and interpretation can
still affect the final scores, sometimes considerably. However, the bewildering array of apnoea indices in use causes far more confusion than these purely technical factors. At first sight, different research groups appear to produce widely differing conclusions. When the apnoea scores are expressed in a standardised fashion, as in Chapter Five, it is obvious that much of this confusion is more apparent than real.

These problems of interpretation and quantification have been recognised before to a more limited extent. A meeting of all the research groups investigating the possible relationship between prolonged apnoea and SIDS was held in 1978 and made some recommendations to improve comparability of results among investigators, but although recording methods were discussed in detail, the analysis of the records was not tackled. In spite of its limitations, this report was useful and many of its recommendations have been followed.

However, the standardised approach has its own problems. Firstly, whilst the factors which affect apnoea scores can be considered unimportant where two groups of infants are studied using the same techniques by the same workers, they cannot be totally ignored when inter-laboratory comparisons are made. Thus, the growing trend to use control values found by others, perhaps working thousands of miles from where the data on abnormal infants is collected, is to be condemned. More important than this is the danger that the recommended techniques become the only accepted ones so that past errors are perpetuated and criticism and new ideas are stifled.
Despite these reservations, studies in infant apnoea will be more fruitful if investigators share their experience, pool ideas, and acknowledge the common ground that does exist. However, they must retain just the right amount of healthy scepticism whilst doing so.
REFERENCES


APPENDIX ONE

--oo0oo--

MANUFACTURE OF THE INTRA-ORAL APPLIANCE

147
The intra-oral appliance consisted of an acrylic base plate lined with silicone impression material and with grooves cut into its surface to hold the feeding tubes. It was manufactured like an adult denture, using standard orthodontic impression techniques. Each impression was obtained in the same way, with the infant lying across the incubator on his back, with the neck extended (Fig. 1). The nurse or paediatrician holding the baby watched his condition and the readings of the cardiac and TcPO$_2$ monitors. Occasionally, a brief episode of bradycardia occurred when the impression material was first put into the mouth. This always resolved within 10 seconds. Additional oxygen by face mask was only necessary in infants already being nursed in oxygen. Initially, 3 impressions were needed in the manufacture of each device; later, it required only 2. There were 4 stages in the manufacture of the appliance:

1. **OBTAINING THE IMPRESSIONS FOR THE BASE PLATE**

The first impression was taken using silicone putty (Optosil* Bayer) on a small spatulate special tray (Figs. 2 and 3). Using this as a base, a second impression was taken using an addition curing silicone material (Reprosil* Bayer), to which a plaster model was poured (Figs. 4 and 5). When a number of appliances had been made, it proved possible to design a series of special trays, in which a single impression could be taken using Reprosil*, regular grade.
FIGURE 1: Showing infant positioned for impression-taking within the incubator.
FIGURE 2: First impression being taken with silicone putty in special tray.
FIGURE 3: First impression complete.
FIGURE 4: Second impression.
FIGURE 5: Plaster model of palate and gums
2. **APPLIANCE CONSTRUCTION**

The acrylic appliance was formed on the plaster model of the palate and gums using a pressure-moulding technique. Grooves were then constructed on the glossal surface to provide a snap fit for the feeding tubes (Fig. 6). Thus, the tubes could be inserted into and removed from the grooves, so that the appliance could be taken out for inspection or cleaning without dislodging the tubes.

3. **LINING THE APPLIANCE**

To improve the final fit, the base plate was fitted with a temporary handle and used as a special tray to take a final impression of the infant's palate using Reprosil*, regular body. Finally, the excess impression material was trimmed and the appliance was ready for use (Fig. 7).

The impression materials used were chosen for their speed of hardening (2-3 minutes in an incubator) and their lack of toxicity. This was particularly important for the material used to make the lining, which formed an integral part of the device, and remained in contact with the oral mucosa for weeks.

4. **RELINING THE APPLIANCE**

After about 2 weeks, the appliance began to fit less adequately because of changes in palatal shape due to growth. When this happened, the old lining was removed and replaced using fresh impression material. With relining, a single base plate could last for 6 to 8 weeks.
FIGURE 6: Palatal surface of acrylic base plate with grooves and feeding tubes
FIGURE 7: The final blue-lined appliance ready for use.
Thus, latterly 2 impressions were required for the initial manufacture of each plate. These were well tolerated by the infant, but were expensive in orthodontic time. In addition, the bench stages required a skilled technician. The technique was therefore not cheap, an additional reason for undertaking a detailed evaluation of its role (Chapter Six).
REFERENCES