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Management of Neonatal Respiratory Failure

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The major cause of respiratory failure in the neonatal period is surfactant deficient hyaline membrane disease (HMD). Extensive reviews of the pathophysiology and management of this condition exist (e.g. Farrell and Avery, 1975; Roberton, 1976), but this article concentrates on the management of respiratory failure by continuous positive airways pressure (CPAP) and intermittent positive pressure ventilation (IPPV).

In 1973, the last year for which figures are available, the deaths of 1,208 infants in this country were attributed to HMD (Registrar General, 1976). In addition, many infants whose death was attributed to twinning, asphyxia and immaturity were probably also suffering from HMD. A truer incidence of fatal HMD is therefore nearer 2,000 cases a year, representing approximately 1 for every 350 live births. In the British Birth Survey (Chamberlain *et al.*, 1975), the majority of infants with HMD had no other major pathological finding at postmortem, whereas more recently (Table 1) most infants who die from HMD have some other condition, particularly an intraventricular haemorrhage (IVH). The disappearance of deaths from uncomplicated HMD has lowered the overall mortality due to this condition in our unit to approximately 1 in 600 live births. This fall in mortality has been due largely to the enormous improvement in the

Table 1. Causes of death in infants with respiratory distress syndrome (Personal Series 1972-76)

Hyaline membrane disease	6[1]
Hyaline membrane disease and intraventricular haemorrhage	21[2]
Hyaline membrane disease and infection	4[3]
Hyaline membrane disease and bronchopulmonary dysplasia	4
No postmortem	5
Total	40

[1] One case with bilateral tension pneumothorax and one with pulmonary haemorrhage.
[2] One with early histological changes of bronchopulmonary dysplasia.
[3] *E. coli* x 3, *H. influenza* x 1.

last few years in the techniques available for managing respiratory failure in the neonate.

CONTINUOUS POSITIVE AIRWAYS PRESSURE (CPAP)

Although Thibeault *et al.* (1967) showed that CPAP improved the respiratory performance of very low birthweight infants suffering from recurrent apnoea, it was the study of Gregory and his co-workers (1971) that initiated its widespread use.

CPAP is a technique in which a pressure is applied to the airways of a spontaneously breathing patient. The pressure splints the alveoli open by preventing the airways pressure falling to atmospheric at end expiration. This minimises atelectasis, and the intrapulmonary right-to-left shunt, and thus improves arterial oxygenation (Gregory *et al.*, 1971; Baum and Roberton, 1974). There are numerous synonyms for CPAP, partly depending on the technique of application, and partly resulting from authors' attempts to provide some unifying phrase to describe the method, irrespective of the technique used to apply it (Table 2).

Table 2. Synonyms for continuous positive airways pressure (CPAP)

Continuous distending pressure	CDP
Continuous inflating pressure	CIP
Continuous negative pressure	CNP
Continuous negative external pressure	CNEP
Continuous negative airways pressure	CNAP
Continuous positive transpulmonary pressure	CPTP

Gregory *et al.* (1971) initially used an endotracheal tube to administer CPAP, but because of the understandable unwillingness of many paediatricians to intubate infants, many other techniques have been tried (Table 3). Many have

Table 3. Techniques for applying CPAP

Technique	Reference
Endotracheal tube	Gregory *et al.* (1971)
Head box	Gregory *et al.* (1971); Dunn (1974)
Negative pressure – incubator adaptation	Chernick and Vidyasagar (1972)
– chamber	Fanaroff *et al.* (1973)
Face chamber	Ahlström *et al.* (1976)
Head bag	Barrie (1972)
Nasal prongs – single	Boros and Reynolds (1975)
– double	Kattwinkel *et al.* (1973)
Face mask	Rhodes and Hall (1973)

major disadvantages in that their use restricts access to part of the infant, requires a comparatively tight neck seal, and results in considerable manipulation of the patient. For this reason nasal prongs or a face mask are now widely used.

Several controlled trials of the technique have been reported, comparing the use of CPAP with traditional methods of therapy in HMD (Fanaroff *et al.*, 1973); Rhodes and Hall, 1973) and comparing intervention with CPAP early or late in the disease (Gerard *et al.*, 1975; Mockrin and Bancalari, 1975; Durbin *et al.*, 1976; Allen *et al.*, 1977). The results of these trials have been most interesting, and perhaps a little surprising. They do not show a dramatic improvement in survival when CPAP is used; the improvement tends to achieve significance only at the 5 per cent level (Allen *et al.*, 1977). The trials do show that the duration of the illness is less, the duration of exposure to high inspired oxygen tensions is less,

Table 4. Reported results of the use of CPAP in HMD
(Data from Ackerman *et al.*, 1974; Ahlström *et al.*, 1976; Allen *et al.*, 1975, 1977; Baum and Roberton, 1974; Boros and Reynolds, 1975; Caliumi-Pellegrini *et al.*, 1974; Chernick and Vidyasagar, 1972; Dunn, 1974; Durbin *et al.*, 1976; Fanaroff *et al., sr,1973; Gerard et al.*, 1975; Gregory *et al.*, 1971; Gupta *et al.*, 1974; Harris *et al.*, 1976; Kamper *et al.*, 1974; Kattwinkel *et al.*, 1973; Krouskop *et al.*, 1975; Mockrin and Bancalari, 1975; Outerbridge *et al.*, 1972; Rhodes and Hall, 1974; Risemberg *et al.*, 1974. Papers recording series of less than 10 infants not included.)

Birthweight	Infants receiving CPAP	Number progressing to IPPV	Number of deaths*
1001-1500 g	73	39	30
1501-2000 g	95	18	9
2001-2500 g	74	10	4
>2500 g	45	11	2
No birthweight data	246	75†	48
Total	533	153	93

* All infants who died received IPPV.
† In the study of Caliumi-Pellegrini *et al.* this data was not available but the number of infants on CPAP and dying are included in the relevant columns.

and, if IPPV is subsequently required, it can be carried out at lower peak inspiratory pressures (Allen *et al.*, 1977).

The results of CPAP therapy published in English are shown in Table 4. Two important points emerge: first, 28.5 per cent of infants requiring CPAP subsequently require IPPV, and secondly, in infants weighing less than 1,500 g, this figure increases to 53.5 per cent with a very high associated mortality.

One of the reasons for the comparatively poor results from CPAP may be the increased incidence of pneumothorax. The complete list of complications of

CPAP is shown in Table 5. Many of them are only likely to occur through inexperience and incorrect use of the apparatus, such as drawing the neck seal too tight, but the increased incidence of pneumothorax has been observed in all

Table 5. Complications of CPAP

Complication	Reference
Air leak ↑ x 3-4	
Pneumothorax	Yu *et al.* (1975)
Pneumomediastinum	Hall and Rhodes (1975)
Interstitial emphysema	Baum and Roberton (1974)
Neck excoriation	Krauss and Marshall (1975)
Brachial palsy	Turner *et al.* (1975)
Intracranial haemorrhage	Vert *et al.* (1973)
Cardiovascular. ↓ venous return etc. (in recovery phase)	Powers and Swyer (1975)
Local trauma to nose	Roberton (personal observation)

centres, and there can be no doubt that the development of a tension pneumothorax considerably worsens the prognosis for any infant with HMD (Ogata *et al.*, 1976). If we take the overall view, noting the high incidence of pneumothorax and of subsequent IPPV, the potential for other serious complications such as intracranial haemorrhage, and the comparatively small improvement in mortality, it is clear that the best results can be obtained only when the infants receiving CPAP are nursed in an intensive care unit in which pneumothorax will be rapidly recognised and treated, and in which facilities for IPPV exist. One can only endorse the words of Stahlman and Cotton (1975): 'The proper use of CPAP or CNP requires frequent and alert monitoring of arterial blood gases and pH, and attention to all the other details of nursing and medical care which newborn infants with RDS demand. It is not a panacea . . .'.

There is still no certain answer to the question of when to start CPAP during the course of an infant's illness. Many experts have settled for starting CPAP when the infant requires 60 per cent oxygen to keep his PaO_2 greater than 60 torr, at which stage the benefits of CPAP are thought to outweigh the dangers.

There are indications for CPAP other than its use early in HMD. Most important, it can be used for 'weaning' infants with severe HMD off the ventilator (Cumarasamy *et al.*, 1973; Baum and Roberton, 1974). It has also proved very successful in controlling pulmonary oedema in a variety of situations including pulmonary haemorrhage (Trompeter *et al.*, 1975), patent ductus in the very low birthweight infant (Roberton, 1974), and after cardiac surgery (Hatch *et al.*, 1973). It is also very successful in regularising the respiration in very low birthweight infants suffering from the recurrent apnoea syndrome (Thibeault *et al.*, 1967; Speidel and Dunn, 1976), though with the use of theophylline

derivatives in this condition CPAP is rarely required (Kuzemko and Päala, 1973; Aranda *et al.*, 1976).

INTERMITTENT POSITIVE PRESSURE VENTILATION (IPPV)

Some form of positive pressure respiration is required for an infant with HMD when CPAP fails to achieve satisfactory oxygenation, or when apnoea or irregular gasping respirations supervene. In our unit, the most frequent indication for starting IPPV is apnoea or irregular gasping respirations. We ventilate for deteriorating blood gases only if the PaO_2 falls to less than 30 torr or when there is a marked increase in $PaCO_2$ without compensation sufficient to keep the pH greater than 7.25.

The successful application of IPPV in HMD is one of the major improvements in neonatal care in the last five years. It requires the full facilities of a neonatal intensive care unit, and should be attempted only if the unit can provide the facilities and cover listed in Table 6. Without doubt the most important item on

Table 6. Facilities essential in a neonatal unit before undertaking long-term IPPV

1. Adequate staff	Medical: Resident SHO full time
	Nursing: Trained cover – at night especially
2. Monitoring facilities	Heart rate, ECG
	BP, preferably continuous
	PaO_2 or TcO_2 – preferably continuous
3. Skilled technique	Umbilical artery catheter maintenance
	Accurate i.v. fluid homeostasis
	i.v. feeding
	Pneumothorax diagnosis and treatment
4. Laboratory services	Daily biochemistry – ultramicro-methods
	Frequent blood gas analyses with immediate results
	Haematology – frequent FBC
	– frequent transfusions
	Frequent bacteriological control
5. Warmth	
6. Adequate ventilator	

that list is adequate nursing cover at night and at weekends. As a result of work done at University College Hospital, London (Reynolds, 1975), we now have a much fuller understanding of how to ventilate infants with HMD. However, to ventilate as they suggest requires a sophisticated ventilator with the capabilities listed in Table 7, which table also shows the suggested ventilator settings for starting IPPV in any infant with HMD. There is no need to try to work out the infant's minute volume, or indulge in other sophisticated calculations of how much gas to deliver to the infant in unit time. The ventilator should be set up as shown, and subsequent adjustments made in the light of blood gas analyses.

Table 7. Specifications for the ideal ventilator for the neonate with HMD

Specifications	Initial settings
Rate 10-60	40
F_IO_2 0.21-1.0	0.8
Inflation pressure 10-60 cm H_2O	25 cm H_2O
Positive end expiratory pressure (PEEP) 0-10 cm H_2O	5 cm H_2O
I : E Ratio 1 : 3 - 3 : 1	2 : 1
Good humidifier	ON

In addition, the ideal ventilator should be compact, silent, have the facility to apply CPAP at the flick of a switch, and have all the above settings independently variable.

All infants can be ventilated in the long term through an endotracheal tube; it does not seem to matter whether an oral or nasal tube is used, and, although frightening histological changes are reported in the trachea of such infants (Joshi *et al.*, 1972), long-term sequelae such as subglottic stenosis are very rare. Tracheostomy is never indicated in routine care.

In the initial phases of IPPV, feeding by nasogastric tube should be abandoned, since the feeds are virtually never absorbed, and fluid balance should be maintained by parenteral fluids or i.v. feeding. Once an infant becomes stable on IPPV after 48 to 72 hours of illness, and it looks likely that prolonged IPPV will be required, tube feeds may be started; they are usually well tolerated.

Although we do not routinely administer antibiotics to infants with HMD on IPPV, a retrospective study of such infants showed that 90 per cent received antibiotics, usually started before or shortly after IPPV was begun (Roberton, 1976).

Maintenance of blood volume and haematocrit is of great importance in infants on IPPV and end expiratory pressure (Morgan *et al.*, 1969; Quist *et al.*, 1975). Frequent recordings of packed cell volume and blood pressure should be taken, and hypertension of less than 40 mmHg systolic, or haematocrit of less than 40 per cent, should be treated with appropriate blood or plasma transfusion.

We do not routinely use sedation for infants on IPPV as we can usually take over the infant's ventilation completely. However, a few infants, especially those weighing over 2 kg persistently 'fight' the ventilator, and it becomes possible to ventilate them at lower pressures and achieve better oxygenation after they have been sedated.

There are many other important practical points in the nursing care of these infants. The nurse should not be mesmerised by the battery of monitoring apparatus, and must remember the importance of good clinical observation. Does the infant look pink (or yellow), is his chest moving at all and if it is, is the movement in phase with and/or due to the ventilator? She must also be taught to

use the monitors correctly, since not only does this ease her job, but the infant is spared unnecessary handling and manipulation, which, it is increasingly recognised, virtually always causes a fall in PaO_2 (Huch *et al.*, 1976). Furthermore, whenever procedures such as sucking out an endotracheal tube are necessary, the monitors should be watched. A rapidly falling heart rate or PaO_2, or a rising blood pressure are sure indications that the infant is not benefiting from the procedure, which should be stopped at once.

Once the infant improves on IPPV, indicated by a falling oxygen requirement and lower ventilator pressures, attempts can be made to change over to CPAP. It is not usually worth attempting this until the infant is on 50 per cent oxygen or less, with peak airway pressures on the ventilator of 20 cm of water.

Table 8. Overall published results for IPPV in HMD
(Data from Adamson *et al.*, 1968; Baden *et al.*, 1972; Ballard *et al.*, 1973; Blake *et al.*, 1973; Bomsel *et al.*, 1973; Brown *et al.*, 1973; Buckfield and Malcolm, 1972; Cooke *et al.*, 1967; Cumarasamy *et al.*, 1973; Daily *et al.*, 1971; Delivoria-Papadopoulos *et al.*, 1965; Dinwiddie *et al.*, 1974; Fitzhardinge *et al.*, 1976; Ganderan *et al.*, 1974; Gupta *et al.*, 1974; Heese *et al.*, 1970; Hunt, 1974; Johnson *et al.*, 1974; Linsao *et al.*, 1970; Martin-Bouyer *et al.*, 1970; Meyer *et al.*, 1974; Murdock *et al.*, 1970; Pusey *et al.*, 1969; Reynolds, 1970; Reynolds and Taghizadeh, 1974; Roloff *et al.*, 1973; Silverman *et al.*, 1967; Stahlman *et al.*, 1971; Stern *et al.*, 1970; van Reken *et al.*, 1974; plus ventilated cases drawn from CPAP literature in Table 4.)

Infants ventilated	2709
Survivors	1029
% Survival	38

The published results for IPPV in neonates with HMD give a depressing picture of the survival rate (Table 8). The data in this table exclude a few reports from the early 1960s describing the very early work in this field. The overall survival rate is only 38 per cent. Table 9 shows results broken down by birthweight from those studies where this information was given. It can be seen that the results are particularly poor in infants with a birthweight of less than 1,500 g. Analysis of these results surprisingly does not show a general trend towards improving survival rates in recent years. However, Cumarasamy *et al.* (1973) and Blake *et al.* (1973)

Table 9. Published results of survival by birthweight in HMD treated with IPPV.

Birth weight (kg)	Infants ventilated	Survivors	%
1001-1500 g	446	106	23.8
1501-2000 g	168	88	52.4
2001-2500 g	105	71	67.6
>2500 g	75	53	70.6
Total	794	318	40

Table 10. Improved results now possible in HMD treated by IPPV

Birth weight (kg)	Published results Cambridge 1976				*P*
	Total IPPV	Survivors	Total IPPV	Survivors	
1001-1500 g	446	106	21	10	<0.02
1501-2000 g	168	88	9	9	<0.01
2001-2500 g	105	71	3	3	N.S.
>2500 g	75	53	2	2	N.S.
Total	794	318	35	21	<0.001

have reported better figures than the averages shown in Table 9, and our own results in Cambridge for 1976 also show an improving and much more hopeful picture (Table 10).

A small number of infants who have received IPPV develop a severe progressive pulmonary fibrosis in which higher and higher ventilator pressures are required to achieve adequate gas exchange. The infant eventually dies with severely fibrosed lungs and cor pulmonale. The pulmonary condition has been labelled broncho-pulmonary dysplasia (BPD). Initially, this was attributed to the use of high inspired oxygen concentrations. However, there were several problems with this hypothesis, particularly the fact that histologically BPD looks different from experimental pulmonary oxygen toxicity in animals, and significant BPD was only found in infants who had received intermittent positive pressure via an endotracheal tube at pressures in excess of 30 cm of water (Roberton, 1976). Reynolds and Taghizadeh (1974) have shown that by reducing the peak airways pressure used the incidence of BPD has dramatically fallen in their unit, despite liberal oxygen usage. Furthermore, it has been shown that long-term abnormalities in pulmonary function are associated with previous IPPV rather than exposure to high inspired oxygen concentrations (Bryan *et al.*, 1973; Stocks and Godfrey, 1976).

OTHER CAUSES OF RESPIRATORY FAILURE

Table 11 lists the other neonatal illnesses in which respiratory failure developed and IPPV was required: HMD is plainly the major cause of neonatal respiratory failure. With the exception of infants receiving IPPV for recurrent apnoea, who have lungs of normal compliance and whose apnoea is the result of failure of the central control of respiration, most neonatal conditions requiring IPPV have a gloomy prognosis. Congenital malformations such as diaphragmatic hernia which require high pressure IPPV before surgical repair, do not do well, nor do infants whose septicaemia is so severe that they require IPPV. In some of the infants ventilated initially because of severe birth asphyxia, IPPV was withdrawn when it became apparent that there was severe CNS damage. However, it is always worth ventilating infants who are apnoeic after severe birth asphyxia, since Scott (1976)

Table 11. Survival following IPPV in different neonatal conditions (Oxford and Cambridge 1972-76).

Condition	Total IPPV	Survivors	% Survival
HMD	114	64*	56*
Birth asphyxia	20	5	25
Infection	20	4	20
Congenital malformation	19	–	0
Recurrent apnoea	6	6	100
Rhesus incompatibility	4	2	50
Massive pulmonary haemorrhage	2	1	50
Meconium aspiration	1	1	100
Miscellanea	6	–	0
Total	192	83	43

* Includes 5 post-neonatal deaths.

has shown that the majority of such infants who survive are neurologically intact.

Only two infants are listed who suffered from massive pulmonary haemorrhage, but several infants included under birth asphyxia or HMD had a massive pulmonary haemorrhage as a complication of their primary illness. Many of these have survived, confirming our hopes of an improved prognosis for this condition (Trompeter *et al.*, 1975). We have successfully ventilated only one infant for meconium aspiration. Severe forms of this condition seem to be much more common in North America where even with IPPV the mortality is high (Vidyasagar *et al.*, 1975). In Britain we have no experience in ventilating tetanus neonatorum, but in many parts of the world this is a major cause of respiratory failure in the neonate. With the modern management of tetanus, the prognosis for these infants is much improved (Smythe *et al.*, 1974).

It is apparent that many infants with respiratory illness so severe that IPPV is required in the neonatal period can be resuscitated successfully. Indeed, as Table 10 suggests, the overall prognosis has become better in the last year or two and, particularly in infants with HMD, it is now fair to say that death from respiratory failure alone should be the exception rather than the rule. However, to achieve such results, the recommendations made in the recent government circular (DHSS, 1976) need to be implemented as a matter of urgency, so that the facilities enumerated in Table 6 can be made generally available to all low birthweight infants, and not just to the few infants who have the good fortune to be born in or transferred to one of the recognised neonatal intensive care units.

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THE MARCH OF PROPERTY

The Duke of Newcastle paid £17,500 for the entire lands of Marylebone manor in 1708. He gave them to his daughter and heiress, Henrietta. Her husband, Edward Harley, Earl of Oxford, delighted by this windfall, set up as a property developer. The inhabitants of his new houses were pleased to have the entertainments made available by the opening of Marylebone Gardens. The cottagers just north of the estate did not like the intrusion on their privacy. One put on his gate a notice reading 'Steel Traps and Spring Guns ALL OVER these grounds. N.B. Dogs trespassing will be shot'.

Harley died in 1741, three years after the gardens were opened. The estate passed to his daughter, Margaret, whose husband, the Duke of Portland, continued the building programme. However, the gardens of Marylebone still flourished and Thomas Arne of *Rule Britannia* fame was made the music master. But the builders took over in 1778 and the pleasure gardens disappeared under Devonshire Place and bits of Wimpole, Devonshire and Beaumont streets. In the last years of the gardens a small spa was opened, peddling medicinal water from a dubious well. The modern medical inhabitants of this area might like to know that the waters were said to be good for indigestion and nervous and scorbutic disorders. Maybe we still need them around there.