The Early Use of Neonatal Continuous Positive Airway Pressure (CPAP) in Bristol*

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In the 1960s, and indeed into the 1970s, respiratory distress syndrome (RDS) of the newborn was by far the commonest cause of death among normally formed infants. It affected 20% of preterm infants (about 1% of all infants) and had a mortality of around 40% even in major centres(1). Death was caused by hypoxaemia from secondary resorption atelectosis due to lack of pulmonary surfactant, usually within 2 – 3 days of birth. For non-neonatologists these babies were almost invariably preterm, adopting a frog position (Fig 1) and exhibiting respiratory distress soon after birth with rapid respiration, inspiratory retraction and expiratory grunting. They became oedematous and cyanosed. Radiologically their lungs demonstrated a ground-glass appearance and biochemically they showed mixed respiratory and metabolic acidosis, and often hypoxaemia in spite of supplemental oxygen.

Fig 1. A premature newborn baby with respiratory distress syndrome.

In 1966-67 I was fortunate to spend a year at the Cardiovascular Research Institute (CVRI) in San Francisco (Fig 2). The Head of Neonatology at that time was the late Abe Rudolph on a flight from Vienna to London. Abe was Head of the Cardiovascular Research Institute, George Gregory (Fig 3), then representing a group of paediatricians from Cape Town, South Africa(2). In brief, he showed that if you prevented a baby with RDS from grunting by passing an endotracheal tube down through its vocal cords, then its arterial oxygen tension fell dramatically.

Fig 2. The University of California Cardiovascular Research Institute was on the 13th floor of Moffat Hospital, San Francisco, seen in the background.

As a result of these observations, a young anaesthetist at the Cardiovascular Research Institute, George Gregory (Fig 3), then argued that if grunting represented the baby’s defence against alveolar collapse, why not save the baby all the effort of expiring against a closed glottis? Why not let the baby breathe with a continuous positive pressure in its airway? Against expert advice that this would be dangerous, he pursued this approach and the outcome of treating their first 20 severe RDS babies using continuous positive airway pressure (CPAP) was duly reported in the June issue of the New England Journal of Medicine in 1971(3).

In August 1971 I found myself sitting next to Dr. Abe Rudolph on a flight from Vienna to London. Abe was Head of the Cardiovascular Division of the CVRI in San Francisco and he told me of Gregory’s work, news of which had still not reached the UK. He also told me that he was kicking himself for being among those who had warned George Gregory against using the new technique. Because of this conversation, as soon as I got back to Bristol I asked my lecturer, John Thearle, to request the Medical Physics Department in Bristol to help us to set up our own apparatus for administering CPAP. The San Francisco group had preferred to use an endotracheal tube for supplying CPAP but I favoured using a less-invasive head-box which we named after Gregory. Our apparatus (Fig 4) was completed in time for our next case of severe RDS at the beginning of October, 1971. To the best of my knowledge this baby was the first in Europe with RDS to be treated with CPAP.

Fig 3. Dr. George Gregory of San Francisco (1980).

Fig 4. The apparatus using a Gregory box to deliver continuous positive airway pressure (CPAP) to infants with respiratory distress syndrome (1971).

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Fig 5. The first infant treated in the Gregory box in October, 1971 (see text).

By the age of nine hours it had been possible to reduce the ambient oxygen to room air and his pH had risen to 7.33. CPAP was cautiously reduced and finally discontinued on the 4th day. His further progress was uneventful.

The dramatic response of this moribund premature infant to CPAP was the most exciting event I had ever witnessed. At that time some 2000 preterm infants were dying from RDS in the UK every year within three days of birth. I felt that no time should be lost in spreading the word. So for the only days of birth. I felt that no time should be wasted in establishing its effectiveness.

The indications for using CPAP which we developed in those early days were as follows:

1. Clinical and radiological signs of severe RDS.
2. Spontaneous regular respiration.
3. A PaO2 below 45 mm Hg at 3 - 4 hours, when the ambient oxygen was 40% or more.
4. An ambient oxygen greater than 60% required to prevent hypoxaemia defined as a PaO2 below 45 mm Hg.

The immediate effect that CPAP had on the arterial oxygen tension of the first four infants that we treated, without changing the ambient oxygen concentration, may be seen in Fig 6. The improved oxygenation is obvious in each case.

In March 1972 we presented the use of CPAP in our first six cases of severe RDS to the Paediatric Research Society meeting at St. Thomas’ Hospital. Somewhat to my surprise I was quite heavily criticised for advocating a new technique without a randomised controlled trial. I defended myself by drawing attention to the rationale of the method, and its dramatic success in San Francisco and now in Bristol. I said I was not prepared to withhold such a life-saving technique from a dying infant, any more than I would be prepared to chuck alternative people out of an aeroplane with or without a parachute in order to prove that there was a significant difference in outcome. Two years later two reports of controlled trials of CPAP aimed at establishing its effectiveness were accompanied by an editorial in the Journal of Pediatrics criticising the authors for unethical practice in conducting RCTs against a background of the available evidence. Meanwhile we continued to have success with the Gregory box until in 1975 we switched to using CPAP nasal prongs for ease of nursing the baby. Our RDS statistics for the period October 1971 to December 1973 in the University Department in Bristol were as follows:

1. Approximately 9500 births.
2. 77 (0.8%) cases of significant RDS.
3. 25 cases (33%) treated in the Gregory box.
4. 4 deaths (6.5%) among the whole series of infants with RDS.

The immediate effect that CPAP had on the breathing pattern of infants with RDS (Fig 8). We showed, using impendence pneumography on ten babies with RDS, that CPAP had an immediate effect on the characteristics of respiration; from being very disorganised it became at once regular in both rate and depth.

The speed with which the breathing pattern changed suggested a reflex mechanism. We also showed that a sudden reduction in the airway pressure through discontinuation of the CPAP was frequently followed by apnoea, regular breathing restarting with the reintroduction of the CPAP. These observations suggested to us that CPAP provided a respiratory drive in babies with RDS, probably mediated through the Hering-Breuer inflation reflex.
A year later in 1976 we published another paper in the Lancet with the title: Use of nasal CPAP to treat severe recurrent apnoea in very preterm infants. It was based on the study of five infants. One of them, a baby boy was born by the breech at 28 weeks gestation following an APH and cord prolapse. His complications after birth included primary atelectasis and a patent ductus arteriosus. At the age of 51 hours he commenced having repeated and severe apnoeic attacks. The record of his transcutaneous arterial oxygen tension (Fig 9) shows the repeated apnoeic attacks as drops in the trace.

These intermittent falls, as you see, were abolished on the application of CPAP 2mm Hg pressure. There were no further apnoeic attacks during the next thirty-eight hours, after which the CPAP was discontinued. Once again we postulated that CPAP provided a respiratory drive by reflexly stimulating pulmonary stretch receptors. Ten years after our first case treated with CPAP, that is in 1981, I reviewed our first fifty cases treated in the Gregory box. Unfortunately I have been unable to find either the file relating to the follow-up or the paper I gave on my findings to the Bristol Perinatal Club that year. But I can clearly remember that among the some 41 or more cases I was able to review, there was only one child with a neurological disability serious enough to require special schooling.

As an addendum it is of interest that Gregory and his colleagues were not the first to use CPAP in the treatment of respiratory distress of the newborn. The technique was actually first described by Austrian and German paediatricians as early as 1909 and 1911. The over-pressure apparatus used by Englemann for delivering CPAP via a face mask before the Great War may be seen in Fig 10. Although the technique was actually described in an English translation of Von Reuss’ book Diseases of the Newborn published in 1921, it was not picked up in Britain and America and appears also to have been subsequently forgotten on the Continent. Thus we are reminded once more of the importance of a knowledge of the past and the history of medicine.

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