ARTERIAL BLOOD GAS TENSIONS IN ACUTE DISEASE OF LOWER RESPIRATORY TRACT IN INFANCY

BY

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In infants under the age of 1 year bronchiolitis is the commonest clinical syndrome of acute disease of the lower respiratory tract necessitating admission to hospital (Morrison *et al.*, 1957). This condition may be recognized clinically by the presence of a severe cough, recession of the chest wall, a tachypnoea of up to or exceeding 100 breaths a minute, and little or no fever. Sometimes there is cyanosis, and fine adventitious sounds can usually be heard over both lung fields. Chest radiographs are often normal or there may be areas of emphysema, collapse, or consolidation (Hubble and Osborn, 1941; Garrow and Fawcett, 1953; Heycock and Noble, 1956, 1962; Morrison *et al.*, 1957; Disney *et al.*, 1960).

In this age group it is not possible to distinguish clearly between bronchiolitis and bronchopneumonia (Heycock and Noble, 1956, 1962; Morrison *et al.*, 1957; Disney *et al.*, 1960) or acute bronchitis. No attempt has therefore been made to classify the cases studied here into these three clinical categories.

Morrison (1955) has investigated the oxygen saturation of "arterialized" capillary blood, using the method of Hytten and Cherry (1951), and concluded that infants with disease of the lower respiratory tract may have considerable hypoxia.

Because it has not been shown that capillary blood gas measurements give an accurate estimate of the arterial values, and there is evidence (Cooper and Smith, 1961) that in some circumstances the measurement of capillary carbon-dioxide tension may give a misleading result, direct arterial sampling, an established technique in the management of respiratory disease in the adult, has been employed in the present investigation, which is concerned with the changes in arterial oxygen (Po_2) and carbon-dioxide (Pco_2) tensions in 12 babies with acute disease of the lower respiratory tract, and the effect of oxygen administration on these tensions. In this way an assessment could be made of the respiratory abnormality present in each baby, and the effect of oxygen therapy could be observed.

Material

The 12 infants, aged 5 weeks to 7 months, were admitted to hospital between November, 1961, and March, 1962; seven were male and five female. All had abnormal signs over both lung fields and nine of them had the typical features of bronchiolitis as described above. Of the others, Case 4 had, in addition to the signs of widespread airway obstruction, a fever of 104°F . (40°C), a consolidated left upper lobe, and acute otitis media; Case 5 had coarser sounds on auscultation than the more typical bronchiolitis; and Case 8 was admitted moribund, with a rectal temperature of 108°F . (42.2°C), shallow irregular respiration, cyanosis, heavily infected sputum, and a

chest radiograph showing widespread consolidation with peripheral emphysema.

Treatment included humidified oxygen for all the babies except Case 12; sedatives in small doses (phenobarbitone, promethazine, and chloral), bronchodilators (isoprenaline by atomizer, adrenaline, and ephedrine), antibiotics when indicated, and steroids in Cases 6 and 8, who also required parenteral fluids, tracheostomy, bronchoscopic aspiration, and mechanically assisted ventilation. All the babies recovered.

Method

The respiratory rate was counted for one minute before arterial sampling and a note made of whether the baby appeared to be centrally cyanosed, as judged by an examination of the mucous membranes of the mouth. Lighting conditions were not uniform, since the infants were studied at different times of day and night, but the observations were made by one person.

The technique of brachial-artery puncture was as follows: The dead space of a 5-ml. glass syringe and short No. 4 gauge needle was filled with heparin. The skin over the brachial artery in or just above the cubital fossa was anaesthetized with 2% procaine, using a very fine needle, which was then advanced slightly to deliver a drop of anaesthetic near the artery itself. This manoeuvre caused little disturbance. After about two minutes the arm was held extended by pressing the baby's wrist against the flat surface of the cot or incubator with the hypothenar region of the right hand, while the sampling syringe was held between the thumb and first two fingers of the same hand. The left hand was therefore free to palpate the brachial artery and prevent movement of the upper arm. The needle was guided into the artery as it lay under the left forefinger. Arterial blood could be distinguished from venous since it spontaneously pushed up the barrel of the syringe. After removal of the needle, pressure was applied over the artery for several minutes.

In one baby the arm became discoloured and the radial artery impalpable after a sample was taken; 10 minutes later, however, the limb appeared normal and the pulse returned. Apart from this, no ill-effect was noted in any infant except for some small haematomata. The radial arteries remained palpable and the limbs moved normally afterwards.

Fifty-six samples of arterial blood were obtained from the 12 babies—51 from the brachial and five from the femoral arteries. No sample was taken until the baby had been breathing air or the required gas for half an hour or more. In experiments where the infant breathed 100% or 40% oxygen the gas was supplied through a disposable "polythene" facemask (adult size) applied tightly round the baby's face and fully distended at a flow-rate of 71 to 91 per minute. The oxygen concentration inside the masks of infants similarly arranged was checked with a Beckman D2 oxygen analyser calibrated against known gases, and was never lower than 94% when 100% oxygen was supplied or 37% when 40% oxygen was used. These levels were reached within two minutes of the masks being put in position. No sedative was given to any baby for four hours before sampling. Blood was not taken unless the baby was in a quiet state, and many attempts had to be postponed or abandoned owing to restlessness or crying.

Blood samples were stored in iced water and analysed within three hours. The gas tensions were estimated

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directly by bubble equilibration (Riley *et al.*, 1957). The standard gas mixtures and correction factors employed were those suggested by Bradley *et al.* (1956) and by Semple and Young (1959). Where the measured P_{O_2} was greater than 100 mm. Hg the result is reported as >100 mm. Hg, as the method is inaccurate at oxygen tensions above this level (R. H. Shepard, personal communication, 1962). No correction to the P_{O_2} or P_{CO_2} was required for the presence of the heparin in the sampling syringe, as had also been found by Oliver *et al.* (1961). Duplicate estimations were performed on 40 samples and single estimations on 16. When duplicate readings were taken the results agreed to within 4 mm. Hg. Three ml. of blood sufficed for two estimations and 1.75 ml. for one for both P_{O_2} and P_{CO_2} .

The normal values for the P_{O_2} and P_{CO_2} of arterial blood in babies of this age-group are unknown, although there is no reason to believe that after the first few weeks of life they differ from those in the adult. Normal mean values are therefore assumed to be about 95 mm. Hg for P_{O_2} and 40 mm. Hg for P_{CO_2} (*Handbook of*

Showing the Respiratory Rate Just Before Sampling; the Arterial Carbon-dioxide and Oxygen Tensions on Successive Days; and the Respiratory Rate and Gas Tensions After Breathing 100% Oxygen for 30 Minutes

Case No. Age, Sex	Day	Cyanosis	Breathing Air			Breathing 100% O_2		
			Resp. Rate per min.	P_{CO_2} mm. Hg	P_{O_2} mm. Hg	Resp. Rate per min.	P_{CO_2} mm. Hg	P_{O_2} mm. Hg
1 2/12 F	1 9 11	+	72	68.9	33.9	82	55.7	>100
			52	37.7	78.8			
			53	38.1	72.0			
2 2/12 M	2 5 16 20	+	60	53.5	69.2	64	70.5	>100
			80	64.1	47.8			
			45	42.1	67.5			
			25	41.2	82.7			
3 5/12 M	2 7	—	60	46.3	71.6			
			30	42.2	81.6			
4 7/12 M	2 9	—	42	40.9	70.0			
			27	37.7	85.5			
5 3/12 M	2 9	—	44	46.5	74.4			
			35	41.6	84.4			
6 4/12 M	3 11 20 40 58	+	60	44.6	70.2	60	46.1	>100
			64	57.2	65.3			
			65	37.3	67.5			
			40	40.3	86.7			
			36	40.6	82.7			
7 9/52 F	1 14 19 23	+	60	42.9	58.1	55	50.6	>100
			57	42.8	66.2			
			45	40.6	72.5			
			27	39.7	81.5			
8 3/12 M	21 42 47 55 63 111	+	40	44.6	47.6	32	50.0	>100
			48	45.1	39.4			
			50	45.7	51.6			
			—	40.0	58.6			
			42	38.5	78.0			
			31	36.1	96.4			
9 2/12 M	2 5 9 11	+	63	46.6	61.2	56	49.5	>100
			58	40.4	77.3			
			48	37.8	81.2			
			31	42.7	92.3			
10 3/12 F	1 2 5 7 9 11	+	51	40.1	72.3	62	51.9	>100
			—	45.3	58.7			
			61	50.9	51.9			
			52	51.6	66.2			
			55	44.5	63.7			
11 5/52 F	3 6 9 13	+	62	50.3	57.7	53	50.3	>100
			63	51.0	57.2			
			42	48.8	62.0			
			38	37.0	93.3			
12 2/12 F	2 5 9 13	—	68	60.6	62.6			
			48	41.7	68.2			
			32	37.4	75.8			
			42	38.3	95.1			

The readings obtained immediately before the administration of the oxygen are the adjoining ones in the preceding columns.

Respiration, 1959). Measurements of the arterial gas tensions in six normal babies, and in most of the cases studied here who had recovered from their chest infections, support the validity of this assumption.

Results

It can be seen from the Table that hypoxia (P_{O_2} less than 75 mm. Hg) occurred in all the babies at some stage of their illness and that very low oxygen tensions were recorded in several. The lowest reading was in Case 1, with a P_{O_2} of 33.9 mm. Hg shortly after admission. (No samples were taken from Cases 6 or 8 during the worst part of their illnesses.) Four of the babies had considerable CO_2 retention, with readings of above 57 mm. Hg (Cases 1, 2, 6, and 12), and in two infants (Cases 10 and 11) the arterial P_{CO_2} (51.6 and 51.0 mm. Hg) was just above the upper limit of the usually accepted normal range (48 mm. Hg).

In general the high carbon-dioxide tensions occurred in those infants with the lowest oxygen tensions; however, Case 8 had a normal P_{CO_2} , at the same time as a very low P_{O_2} on three occasions in the course of his illness.

The clinical assessment of the severity of the illness depends largely upon the presence or absence of cyanosis and upon the respiratory rate. For this reason a correlation has been attempted between these observations and the blood gases.

In Fig. 1 the 16 observations of cyanosis are separated from the 30 in which cyanosis was absent, and the two groups are plotted against the arterial oxygen tension. It can be seen that cyanosis was not necessarily present with oxygen tensions of as low as 60 mm. Hg, and that there is an overlap of 13.7 mm. Hg between the two

Fig. 1.—Correlation of the clinical assessment of cyanosis with the oxygen tension of the arterial blood. Cases 3, 4, 5, and 12 were never clinically cyanosed.

groups; however, their means differ significantly ($P < 0.01$). Morrison (1955) has suggested that restlessness is a better sign of hypoxia than cyanosis in infancy, and some of the babies in this series were restless while they were in a hypoxic state; but as might be expected the most severely ill infants were stuporous at the height of their illnesses (Cases 1, 6, and 8).

Fig. 2 shows the result of plotting P_{O_2} against the respiratory rate, and a fairly good correlation has been found between these variables ($r = -0.8401$), the respiratory rate rising as the P_{O_2} falls. The results obtained from Case 8 are shown by open circles, and on the same three occasions on which low oxygen tensions were

found in the presence of normal carbon dioxide tensions in this baby the respiratory rate appeared low by comparison with the other infants.

In Fig. 3 the respiratory rate has been plotted against the PCO_2 and it is evident that with rates of up to 60 breaths a minute the PCO_2 has shown little increase. At this point the PO_2 has usually fallen to about 60 mm. Hg.

FIG. 2.—Oxygen tension plotted against respiratory rate. ($\text{PO}_2 = 115.49 - 0.9200 \text{ R.R.}$)

FIG. 3.—Carbon-dioxide tension plotted against respiratory rate.

Fig. 4 shows the serial readings obtained during the illness of Case 12, who had uncomplicated bronchiolitis with a normal chest x-ray picture and negative sputum culture. (This baby was not given oxygen therapeutically.) The PCO_2 has returned to normal before the PO_2 or the respiratory rate. This sequence of events appears to be usual.

FIG. 4.—Oxygen and carbon-dioxide tensions, and the respiratory rate (plotted as the average of the readings recorded on the temperature chart in each 24 hours), in Case 12, uncomplicated bronchiolitis, on successive days of illness.

It can be seen from the Table that administering 100% oxygen for 30 minutes to eight babies caused, in general, a slight fall in the respiratory rate and a rise in PCO_2 . The mean respiratory rates before and after oxygen-breathing were 65 and 60 breaths per minute respectively and the mean PCO_2 50.7 and 52.8 mm. Hg. These differences are small because of the inclusion of the results from Case 1, in whom comparatively large changes occurred in the opposite directions; the respiratory rate rising from 72 to 82 breaths per minute and the PCO_2 falling from 68.9 to 55.7 mm. Hg. Oxygen-breathing caused an increase in arterial PO_2 to above 100 mm. Hg in all eight infants, and in two of them (Cases 9 and 10) 40% oxygen similarly raised the PO_2 to above 100 mm. Hg from 61.2 and 72.3 mm. Hg respectively.

Discussion

With attention to positioning and local anaesthesia, arterial puncture has proved safe and practicable in these infants. Because samples of blood taken during restlessness and crying might have given misleading results, the procedure was often postponed, but with patience a satisfactory sample could nearly always be obtained. Repeated observations were also possible, and one baby had three samples taken within two hours.

All the babies had hypoxia, and when this was severe carbon-dioxide retention was also present (except in Case 8). The most important mechanism responsible for these changes is likely to be an alteration in the ventilation:perfusion ratios of the lungs, which would be consistent with the pathological finding of bronchiolar obstruction previously reported in infants dying from similar illnesses (Hubble and Osborn, 1941; Dugdale and McGeorge, 1960; Disney *et al.*, 1960). In addition, inadequate alveolar ventilation may occur as a result of a decrease in tidal volume associated with the extreme tachypnoea often seen in these babies, and sometimes from the depressive effects of severe hypoxia upon the central nervous system. Since the airways are narrow it is to be expected that babies under the age of 1 year would be particularly vulnerable to the effects of airway obstruction; also, the thoracic cage is soft and much respiratory effort may be used in retracting the chest wall rather than in moving air into the alveoli. The fact that the arterial PO_2 rose to above 100 mm. Hg on breathing oxygen suggests that a veno-arterial shunt is not a major factor in the production of the gas-tension abnormalities, although it is possible that in the most severely hypoxic infants an increase in pulmonary vascular resistance causing shunting of blood through the foramen ovale was corrected by oxygen administration (James and Rowe, 1957). A diffusion defect would not cause the observed retention of carbon-dioxide.

The presence or absence of cyanosis has been found to correlate fairly well with the arterial PO_2 and infants with tensions of below 58 mm. Hg were always cyanosed. The observation of cyanosis depends upon a number of factors, including the amount of circulating reduced haemoglobin, the thickness of the tissues, and the skin blood-flow, and it is important to realize that serious hypoxia can occur without cyanosis.

Although breathing oxygen did not correct the tachypnoea, the respiratory rate is, in general, a fairly good guide to the degree of hypoxia when the baby is breathing air, the rate rising as the PO_2 falls. However, too much reliance must not be placed on this observa-

tion, since Case 8 had a comparatively slow rate at the same time as severe hypoxia (Fig. 3), and in Case 1 the rate increased further on oxygen-breathing, probably owing to correction of hypoxic depression of the respiratory centre.

Breathing oxygen always caused a rise in arterial P_{O_2} to above 100 mm. Hg; the slight rise in P_{CO_2} which usually occurred was in the expected direction but of no clinical significance, and should not lead to hesitation in administering oxygen therapy.

Summary

A study is reported of the arterial oxygen and carbon-dioxide tensions of 12 babies, aged 5 weeks to 7 months, with acute disease of the lower respiratory tract.

Sampling from the brachial artery, an established technique in the adult, has proved to be a safe procedure in this age-group. The method employed is described.

All the babies had hypoxia, and in some cases this was very severe; in six of them there was evidence of carbon-dioxide retention. It is likely that these abnormalities were primarily due to uneven ventilation: perfusion ratios in the lungs, resulting from airway obstruction.

Cyanosis and the respiratory rate are both fairly good clinical indices of the severity of the hypoxia in most cases. However, there are occasions when these observa-

tions may be seriously misleading, and they must be interpreted with caution.

The administration of 100% oxygen to breathe for 30 minutes always caused an increase of arterial oxygen tension to above 100 mm. Hg. No clinically significant rise in carbon-dioxide tension was produced.

I am grateful to Dr. B. D. R. Wilson and Dr. D. G. Cottom for allowing me to study their patients; to Professor A. C. Dornhorst, Dr. S. J. G. Semple, and Dr. I. M. Young for their advice and criticism; and to Dr. G. I. C. Ingram for his help with the statistics.

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INFLUENCE OF ANAESTHESIA ON THE INCIDENCE OF MATERNAL MORBIDITY, NEONATAL ASPHYXIA, AND PERINATAL MORTALITY

BY

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General anaesthesia is nowadays responsible for only a small number of maternal deaths, and this number is diminishing; thus there were 19 maternal deaths in England and Wales due to the complications of anaesthesia in 1954, but only eight in 1957 (Walker *et al.*, 1957, 1960). However, general anaesthesia is probably responsible for a much greater amount of maternal morbidity, possibly for some perinatal deaths, and it may increase the incidence of neonatal asphyxia; but accurate information is lacking, and this is essential if the risks to mothers and babies associated with obstetric operations are to be reduced. Information that will enable the advantages and disadvantages of various anaesthetic techniques to be assessed is required, so that the safest anaesthetic can be chosen to suit the circumstances. The problems involved in obtaining this information are complicated (Crawford, 1962), since the type of anaesthetic must be correlated with the experience of the anaesthetist, the time taken for the induction, as well as with the post-operative state of the mother and the condition of the baby at birth. The indications for and the nature of the operative assistance must also be considered in addition to other factors, such as associated maternal disease, the length of labour, the presence of toxæmia, etc. An attempt has therefore been made to evaluate the advantages and disadvantages of local analgesia and general anaesthesia of three different types by assessing the incidence of maternal morbidity, neonatal asphyxia, and perinatal mortality.

Method of Inquiry

The analysis is based on the records of all the patients delivered in St. Thomas's Hospital and on the records of those women delivered with operative assistance in the General Lying-In Hospital from August 1, 1959, to December 31, 1960. The same obstetric and anaesthetic team was responsible for the management of patients in both hospitals. The relevant data were entered on punch-cards, which were completed at the delivery of each patient.

The nature of the anaesthetic used was determined by the preference of the individual anaesthetist, taking into consideration the condition of the patient. A survey of the case records showed that there was no difference between the various groups with regard to the incidence of associated maternal disease, toxæmia, the length of labour, or the time and amount of analgesic drugs given during labour. If pudendal nerve block was used, it was induced by the obstetrician. Three different types of general anaesthetic were employed.

1. Anaesthesia was induced with cyclopropane and oxygen, with the patient's whole body tilted head up; after relaxation had been obtained with intravenous suxamethonium, a cuffed endotracheal tube was passed. The anaesthetic was maintained with nitrous oxide and oxygen, and, if necessary, further doses of suxamethonium (Wylie and Churchill-Davidson, 1960).

2. Anaesthesia was induced with the minimum quantity of intravenous sodium thiopentone which was just sufficient