Scientific Basis for Current Perinatal Care*

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We are witnessing the birth of a new era in paediatrics and obstetrics; the era of the foetus and the newborn. Many of the more challenging clinical problems of the past have been reduced to almost routine care as a result of our improved understanding of water and electrolyte balance, the introduction of many public health measures, particularly extensive immunization programmes, and the advent of antibiotics. On the other hand, infant mortality has changed little during the past 20 years. While this mortality is considered by some to be a hard-core residue, the great variability found amongst institutions, communities, and countries, as well as preventable tragedies identified from time to time, suggest that the hard-core has not yet been reached. Realization that the responsiveness of an infant at birth correlates with subsequent neurological development has added urgency and direction to this challenge. Data from approximately 14,000 live born infants in the Collaborative Child Development Program, recently published (Drage, Kennedy, Berendes, Schwarz, and Weiss, 1966), indicate that even in infants whose condition at birth is excellent the incidence of neurological deficit is 1.4%. In the mature weight group there was nearly a fourfold increase in significant neurological damage at 1 year if the infant was only mildly depressed. Unfortunately one has no way of knowing whether the damage occurred before labour, or was the result of labour and delivery.

At the same time that our awareness of neonatal mortality and morbidity has become more acute, a wealth of new information on the physiology of the foetus and newborn derived from both animal experiments and human investigations has opened fresh horizons suggesting different approaches to infant care and questioning some of our most time-honoured concepts. In this new era, the principle of watchful waiting is rapidly disappearing, being replaced by active investigations with frequent blood sampling for multiple analyses; even the foetus can be studied. Acute experiments where a foetal lamb is removed from the uterus have been followed

by long-term observations where the foetus is replaced into the uterus together with catheters, electrodes, and electronic transmitters, without the pregnancy being interrupted. From the lamb we have passed to the primate. In some experiments K. Adamsons has removed the foetus from the uterus twice in one week, the pregnancy continuing until the state of viability. We have now been able to study even the human foetus during complete intrauterine exchange transfusion, serial acid-base values, haematocrit, and heart rate being monitored directly.

Foetal Acid-base State and Birth Asphyxia

Until recently the foetus was considered to thrive in a low oxygen environment during intrauterine life, his blood being also acidotic and hypercapnic. This concept was largely derived from analysis of cord blood at delivery, where healthy vigorous infants have oxygen saturations in the region of 20% and tensions of carbon dioxide averaging 54 mm. Hg.

Because of the wide range of values, we proposed a number of years ago that cord blood reflected a variable interference with maternal or foetal perfusion of the placenta during labour and delivery causing foetal asphyxia (James, Weisbrot, Prince, Holaday, and Apgar, 1958; James, 1960) and that the highest values which were observed more nearly approached the normal intrauterine environment. Direct sampling from the foetus *in utero* by means of chronically implanted catheters has borne out this concept.

Simultaneous foetal and maternal samples from the rhesus monkey (Adamsons, James, Towell, and Lucey, 1965b) indicate that the transplacental gradient for PCO_2 is 5 mm. Hg or less and for pH, 0.02-0.04 pH units, foetal pH being between 7.37 and 7.40. At a PO_2 of 40 mm. Hg and a pH of 7.37, the foetal arterial blood is approximately 80% saturated. The transplacental gradient for PCO_2 , pH, and PO_2 are likely to vary somewhat between species, particularly with regard to PO_2 ; but for pH and PCO_2 , maternal and foetal values in the sheep and rhesus monkey appear to be quite similar.

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FIG. 1.—Changes in oxygen saturation and pH in apnoeic newborn puppies. (From James, 1960.)

E. Saling's introduction of a technique for sampling capillary blood from the foetal scalp has provided further evidence of the way in which foetal blood gases and pH change as labour advances (Saling, 1962). There is a fall in oxygen saturation and pH, particularly during the second stage of labour. The pH in both the umbilical artery and umbilical vein at birth is usually lower than in the scalp sample immediately before delivery, suggesting that capillary blood which flows readily from the scalp during uterine contractions is meaningfully close to foetal arterial blood, and is a reliable indication of the foetal state. The average pH in healthy infants just before delivery is 7.24. A significant correlation exists between low pH during the first stage of labour and a clinically depressed infant at birth. Consequently if foetal pH falls below 7.2 and there is any indication of a further decline, we recommend prompt delivery, either *per vaginam* if the cervix is fully dilated or by caesarean section.

During complete asphyxia, pH falls and PCO_2 rises rapidly. In five minutes pH can fall from 7.35 to 6.9 and PCO_2 rise from 40 to 90 mm. Hg. These changes have been monitored in both newborn puppies and monkeys asphyxiated at birth (James, 1960; Adamsons, Behrman, Dawes, Dawkins, James, and Ross, 1963; Adamsons, Behrman, Dawes, James, and Koford, 1964) (Fig. 1). Because pH continues to fall after oxygen levels are zero, reflecting a continuing anaerobic metabolism, measurement of pH has proved to be a more useful

indication of a period of asphyxia than the measurement of either oxygen saturation or tension. The fall in pH is due to the accumulation of both volatile and non-volatile hydrogen ion donors, namely CO_2 and fixed organic acids. With the cessation of asphyxia and the establishment of normal pulmonary exchange, CO_2 can be removed quite rapidly; pH, however, returns to normal at a slower rate due to the presence of fixed acids. The rate at which the foetus recovers from an asphyxial episode *in utero* might be more rapid if the placenta readily transferred hydrogen ion to the mother. Placental capacity in this regard has not yet been determined.

Asphyxia present at birth could arise in a number of ways. Maternal perfusion of the placenta is reduced and may even cease with strong uterine contractions. The operative procedure of caesarean section itself can impair uterine blood flow; it may be accompanied by pressure on the inferior vena cava by the heavy gravid uterus or by depression of the myocardium by potent inhalation anaesthetic agents. We have monitored changes in foetal and maternal pH and PCO_2 in pregnant monkeys during hysterotomy under fluothane anaesthesia and following recovery (Adamsons *et al.*, 1965b) (Fig. 2). During the operative procedure the foetus becomes acidotic in comparison with the mother, but two hours later foetal and maternal values are quite close. Maternal hyperventilation may also have an adverse effect. This was first observed by Moya while attempting to reduce foetal acidosis at elective caesarean section by lowering the maternal

FIG. 2.—Changes in the maternal-foetal gradient for pH and P_{CO_2} in the rhesus monkey during hysterotomy and 2 hours later. ● foetus; ○ mother. (From Adamsons et al., 1965b.)

PCO_2 (Moya, Morishima, Shnider, and James, 1965). In Fig. 3, the condition of four groups of infants at birth has been plotted against maternal pH. In those mothers where the pH was above 7.6 or the PCO_2 below 18 mm. Hg, the infant was not only hypoxic and acidotic but also depressed. Morishima hastened to investigate this phenomenon in pregnant guinea-pigs (Morishima, Moya, Bossers, and Daniel, 1964; Morishima, Daniel, Adamsons, and James, 1965). Her experiments confirmed our clinical observations. The foetal acidosis which developed during maternal alkalosis appeared to be caused by a reduction in uterine blood flow. The unresponsive state of infants at birth following maternal hyperventilation is without doubt due to asphyxia and not because CO_2 has been washed out of the baby's blood before birth, as has been claimed (Holmes, 1963).

At this junction I would like to consider briefly

FIG. 3.—Proportion of depressed infants in relation to maternal pH at elective caesarean section, during progressive maternal hyperventilation. (From Moya et al., 1965.)

the possibility of treating the acidotic foetus before delivery. Although the maternal acid-base state will be reflected in the foetus, more profound degrees of foetal acidosis are caused predominantly by foetal hypoxia or asphyxia. The currently favoured treatment for foetal hypoxia and one that is routinely employed for foetal distress is administration of high concentrations of oxygen to the mother. However, it is rarely remembered that the additional amount of oxygen carried in solution is small, once the maternal blood is fully saturated. At a PO_2 of 700 mm. Hg it only amounts to 1.4 ml. O_2 /100 ml. blood. To deliver this additional oxygen in any significant amount to the foetus, either maternal or foetal blood flow to the placenta must be increased. This strikes at the root of the problem; the hypoxia is usually caused by a reduction in blood flow to the placenta, either maternal or foetal.

Because of the difficulties in obtaining a successful chronic catheter preparation, three-quarters of our experiments have on the average yielded after operation an acidotic and hypoxic foetus (Adamsons et al., 1965b). In the monkey foetus a PO_2 of 30 mm. Hg was associated with a progressively increasing metabolic acidosis and deterioration of the foetus over a period of hours. It appears that the acidosis is due to impaired perfusion of the intervillous space rather than to an adverse effect of the operative procedure on the foetal circulation, since the foetuses have not been hypotensive. In many respects this preparation represents conditions existing in clinical practice when administration of oxygen to the mother is considered as a therapeutic measure. Even raising the maternal PO_2 to values as high as 600 mm. Hg resulted in no, or only trivial increase in foetal PO_2 (1-2 mm. Hg). Correction of the acidosis by direct infusion of base

FIG. 4.—Recovery from birth asphyxia. Changes in acid-base state during first 24 hours of life in healthy infants. Curves showing carbon dioxide tension are spaced logarithmically. Upper quadrilateral represents range of normal arterial values for the adult. Lower quadrilateral represents range of maternal arterial values. (B) = Umb. art. av. at birth, $N = 21$. (1) = During 1 hour av., $N = 10$. (3) = Av. at 3 hr., $N = 7$. (●) = 24 hr. av., $N = 14$. (○) = Individual at 24 hr. Broken lines indicate ± 1 SD. (From Weisbrot *et al.*, 1958.)

into the foetus produced only a brief and temporary improvement; this was invariably followed by a rebound, the foetus becoming more acidotic than previously. It seems, therefore, that if the basic cause for hypoxia cannot be corrected, neither oxygen to the mother nor infusion of base directly to the foetus will be of benefit.

Following delivery the healthy infant recovers from this mild-to-moderate degree of asphyxiation during the first few hours of life (Weisbrot, James, Prince, Holaday, and Apgar, 1958). When serial acid-base values of the infant's arterial blood are plotted on the Davenport nomograph (Fig. 4), it may be seen that by 24 hours of age the infant adjusts to the same level as the mother before the onset of labour.

What has this to do with treatment of the infant in the perinatal period? An understanding of the normal internal environment of both foetus and newborn, and a knowledge of the mechanisms whereby a normal acid-base balance is achieved after birth, form the cornerstone for a rational approach to postnatal care. The fact that the foetus is neither hypoxic nor acidotic during development raises important questions regarding his tolerance to hypoxia, and the urgency of resuscitation. While it is widely believed that the central nervous system of the newborn human infant can survive a far greater asphyxial insult than that of the adult, evidence for this is inadequate or irrelevant. Many of the experiments were carried out on rats (which Professor McCance calls reagents). The adult monkey will continue to gasp during asphyxia for nearly as long as the newborn provided the circula-

tion does not collapse (G. S. Dawes, L. S. James, and B. Ross, unpublished data), and in the infant monkey, as will be mentioned later, the duration of gasping closely parallels maintenance of intact cerebral function (Adamsons *et al.*, 1963; Dawes, Hibbard, and Windle, 1964; Daniel, Dawes, James, Ross, and Windle, 1966b).

The gradual deterioration of the foetus when only moderate hypoxia is present over a period of hours also raises questions of how much hypoxia he can tolerate, and whether anaerobic metabolism can supply sufficient energy to maintain intact cellular function. Several conditions are necessary for this to take place, including an adequate source of substrate from either the mother or the foetus, a relatively normal pH, and a means of dispersing excess acid products. If oxygen supply from the mother is limited due to a reduced maternal blood flow to the placenta, the maternal supply of glucose is also likely to be limited, and the foetus himself does not have unlimited reserves of carbohydrate. Furthermore, the enzymatic reactions involved in the breakdown of glucose to lactate appear to be pH-dependent. Therefore, unless the foetus has some special mechanism for excreting or metabolizing the lactate, the accumulation of this end-product during periods of hypoxia will lower the pH and gradually bring the anaerobic metabolism of glucose to a halt.

Respiratory Responses During Asphyxia and Resuscitation

The predictable nature of cardiovascular, respiratory, and biochemical changes that occur during

asphyxia, under controlled conditions, have permitted the evaluation of various modalities of treatment in a quantitative fashion. In collaboration with G. S. Dawes and the late M. Dawkins, we have been able to study newborn monkeys at special facilities in Puerto Rico (Adamsons *et al.*, 1963, 1964; Daniel *et al.*, 1966b).

During the initial phase of asphyxia, respiratory efforts increase in depth and frequency for up to three minutes. This is followed by an apnoeic period which has been termed primary apnoea lasting for approximately one minute. Rhythmic gasping then begins and is maintained at a fairly constant rate of about six gasps per minute for several minutes. The gasps finally become weaker and slower and their cessation marks the beginning of secondary apnoea. Mean time to the last gasp under our particular experimental condition was 8.5 minutes. When the relation between duration of gasping and gestational age, body weight, initial temperature, rate of fall of body temperature, and initial pH was subjected to multiple regression analyses, Ross found that the initial pH at the beginning of asphyxia at a given environmental temperature was the principal determinant, followed in importance by initial temperature, body weight, gestational age, and cooling rate, the last two being not of sufficient merit (Ross, Dawes, James, and Adamsons, 1964).

In this series of experiments asphyxia was continued for 10, 12.5, or 15 minutes before commencing resuscitation by positive pressure ventilation. There was a linear relation between the duration of asphyxia after the last gasp and the time taken to reinitiate gasping and breathing following resuscitation (Adamsons *et al.*, 1964). In the newborn monkey, for each minute after the last gasp that artificial ventilation is delayed there is a further delay of two minutes before gasping begins and four minutes before rhythmic breathing is established. Thus, if asphyxia were continued for 7 minutes after the last gasp, it would take approximately 14 minutes of artificial ventilation before the animal would start to gasp again, and approximately 28 minutes to establish spontaneous breathing. This indicates that the longer artificial ventilation is delayed during secondary apnoea, the longer will it take to resuscitate the infant.

If pH is maintained during the course of asphyxia by infusion of alkali, the duration of gasping is significantly prolonged (Adamsons *et al.*, 1963) (Table). After resuscitation, gasping begins again sooner. Furthermore, when the brains of these animals were studied at a later age, those in whom

pH had been maintained showed little evidence of cellular damage (Dawes *et al.*, 1964).

TABLE
Effect of Alkali Treatment on Resuscitation of Asphyxiated Monkeys

Time (min.) to Last Gasp	Untreated	Treated
	8.54 ± 0.20	12.14 ± 0.24
From ventilation to first gasp	9.0 ± 1.9	0.16 ± 0.1
" " to breathing	25.1 ± 4.6	7.1 ± 1.3

We do not know whether infusion of base during artificial ventilation will also reduce brain damage, but it does shorten the time for gasping and spontaneous breathing to start again, suggesting that there might be some protective effect (Adamsons *et al.*, 1964). The beneficial effect could be due to correction of the metabolic acidosis. Artificial ventilation can successfully remove CO₂, but the metabolic acidosis, due largely to lactic acid, remains if base is not infused (Fig. 5a and b).

The effects of correcting pH are probably several. As noted above, anaerobic glycolysis is pH-dependent and proceeds at a very slow rate at any pH below 7.0. With severe acidosis the oxygen dissociation curve for haemoglobin flattens and moves to the right, thus reducing the quantity of O₂ carried at a given tension; restoration of normal pH restores the oxygen carrying capacity. The myocardium becomes unresponsive to sympathomimetic amines under conditions of severe hypoxia and acidosis; restoration of pH restores this responsiveness causing cardiac output to increase and blood pressure to rise. The way in which correction of pH alone can raise blood pressure and heart rate, once gasping efforts have ceased, is shown in Fig. 6 (Daniel, Dawes, James, and Ross, 1966a); pH was corrected by 0.5 M THAM, infused one minute after the last gasp. In this infant monkey, gasping started again spontaneously shortly after the blood pressure rise, and the animal continued to improve; finally, spontaneous breathing was established. This contrasts sharply with the infusion of lobeline—which appeared to accelerate circulatory collapse. Nikethamide had a similar disastrous effect, and neither drug caused the animals to gasp when given during secondary apnoea. Finally, and most important is the influence of pH on pulmonary vascular resistance; asphyxia and acidosis cause intense pulmonary vasoconstriction (Colebatch, Dawes, Goodwin, and Nadeau, 1965).

Hypothermia and Resuscitation

Using the asphyxiated newborn monkey as a model we have been able to study the effects of

FIG. 5A, B.—Changes in P_{CO_2} and base deficit in the newborn rhesus monkey during asphyxia and following resuscitation. ○—○ animals treated by ventilation alone; ●—● animals treated by ventilation together with infusion of THAM. (From Adamsons et al., 1964.)

hypothermia during resuscitation (Daniel *et al.*, 1966b). At first we cooled the animals one minute after gasping had stopped, by which time the circulation has already collapsed and blood pressure and heart rate were both low. Under these circumstances the animals cooled very slowly, and we found it difficult or impossible to resuscitate them. In no instance did cooling reinstate gasping.

FIG. 6.—Observations on two immature foetal monkeys delivered by caesarean section and asphyxiated by tying the umbilical cord; the head was covered by a bag containing a small quantity of saline. Drugs were injected during secondary apnoea, one minute after the last gasp. Injections of alkali (Tris) in A caused a rapid rise in heart rate (indicated by the numerals above the arterial pressure record in beats/min.) and after 25 seconds the monkey began to gasp again (the consequent disturbances can just be detected in the pressure record). Injection of lobeline (2 mg./kg.) in B caused the arterial pressure to fall more rapidly; heart rate continued to decrease and there were no further respiratory efforts. Time scales in seconds. (From Daniel *et al.*, 1966a.)

We then cooled a group of animals during the course of asphyxia (after 6.5 minutes of asphyxiation), and compared the cardiovascular and respiratory responses with a control group. We were also able to make comparisons with a similar group of animals in which alkali was infused at 6.5 minutes. Blood pressure was slightly better maintained in the cooled animals compared with the controls. The time to last gasp was, however, not significantly different, neither was the time to the onset of spontaneous breathing following resuscitation altered. When the brains of these animals were examined, we could not distinguish between those animals treated with hypothermia and the control group, both having a similar distribution and degree of cellular damage. This was in marked contrast to the minimal brain damage in the group receiving alkali. From these experiments it was concluded that hypothermia during resuscitation did not offer any advantages over conventional techniques.

Metabolic Responses to Cold Stress after Birth

It is difficult to prevent the infant from losing heat postnatally, principally because his surface area is relatively large, wet, and poorly insulated. Deep body and skin temperatures fall at a rate of 0.1°C. and 0.3°C. per minute, respectively, following delivery (Gandy, Adamsons, Cunningham, Silverman, and James, 1964; Adamsons, Gandy, and James, 1965a); the calculated heat loss is approximately 200 cal./kg. minute, assuming that 50% of body mass is at deep rectal temperature and 50% at skin temperature.

FIG. 7A.—The relation between oxygen consumption and deep body (rectal) temperature of newborn human infants under a variety of thermal environmental conditions.

FIG. 7B.—Oxygen consumption of newborn human infants as a function of the gradient between body surface (skin) and environmental temperatures (ΔT_{S-E}). The surrounding radiant surfaces are within $\pm 2^\circ \text{C}$. of the corresponding ambient air temperature. The regression line refers to ΔT_{S-E} between 1.5 and 15°C . (From Adamsons *et al.*, 1965a.)

Although the healthy newborn infant has a brisk metabolic response to cold stress by 30 minutes of age, being able to increase his oxygen consumption two or three times above basal levels if an adequate stimulus is applied, it is not known whether this response is present immediately after birth when he is hypoxic and acidotic. In newborn animals, strong hypoxic stimuli to the chemoreceptors will inhibit or impair the thermogenic response to cold (Mott, 1961). However, the initial heat loss exceeds the maximal observed heat production at 30 minutes of age by a factor of 3, indicating that, irrespective of the infant's metabolic rate, there will always be a fall in body temperature under the usual delivery room conditions.

Once the infant is placed in an environment which is warmer than his skin temperature, metabolic rate promptly falls to basal levels, even though deep body temperature is still subnormal (Adamsons *et al.*, 1965a). We were unable to demonstrate any relation between deep body temperature and oxygen consumption (Fig. 7a). However, when oxygen consumption was related to the temperature gradient between skin and environment (Fig. 7b), a good correlation was obtained. This gradient between skin and environment is the one to which the skin thermal receptors are exposed and appears to be the principal determinant of metabolic rate for the newborn.

Once pulmonary function is established and the infant is no longer hypoxic, continued exposure to a

heat-losing environment will stimulate metabolic rate and aggravate the metabolic acidosis present at birth (Gandy *et al.*, 1964). Data from two groups of infants studied by Gandy demonstrate this phenomenon (Fig. 8). In one group, body temperature was maintained by an infrared lamp. The other group was exposed to room temperature (25°C). The differences in deep body temperature and degree of metabolic acidosis at 2 hours of age were significant. However, the postnatal rise in pH was similar—the metabolic acidosis in the cooler infants being compensated for by an increase in alveolar ventilation. If an infant exposed to a cold environment is unable to increase alveolar ventilation because of central nervous system depression, meconium aspiration, or immaturity, the pH will fall.

How might these observed responses relate to optimal treatment? For the newborn infant whose skin temperature during foetal life is nearly 38°C ., the initial cold stimulus must be intense; this could play an important role in the onset and maintenance of ventilation, the initial cold stress stimulating the reticular formation which, as in the adult, increases the excitability of the respiratory neurones, making them more responsive to chemoreceptor stimuli arising as a result of birth asphyxia. It has been claimed that undue warming inhibits breathing postnatally; this observation, however, requires more careful documentation.

Impairment of the metabolic response to cold at

FIG. 8.—Changes in colonic temperature, pH, and excess acid in 2 groups of mature human newborns maintained in a warm environment (●) or exposed to room temperature (○). (From Gandy et al., 1964.)

birth, while resulting in a greater fall in body temperature, would at the same time lead to a conservation of energy stores under circumstances when it is quite impossible for the infant to raise his metabolic rate sufficiently to maintain body temperature.

After the infant has been dried and placed in a heat-gaining environment such as close to the mother's skin, in a warm nest, under a radiant heat lamp, or in a warm blanket, he will gradually rewarm. Provided that the environment is warmer than skin temperature he will rewarm again at basal metabolic rate, since oxygen consumption is predominantly determined by the thermal gradient between body surface and environment and not by the absolute values of either skin or core temperatures. If this is done, body temperature will rise gradually toward normal at approximately 1.5°C . per hour. In deciding which environmental temperature would be optimal for warming a cold infant it is important to bear in mind the gradient between skin and environment once normal body

temperature has been reached. From our data it appears to be about 34°C . for the mature, naked infant, provided that wind velocity is low and relative humidity is about 50%. These conclusions are made on the assumption that it is desirable to maintain a basal metabolic rate during the neonatal period.

In this light, the initial cold stress if not unduly prolonged might not be harmful and might even be of value in establishing and maintaining normal respiration. Continued exposure to cold after the infant is well oxygenated, however, could be harmful, stimulating metabolic rate and causing a metabolic acidosis. The environmental temperature which is optimal for growth and development of the newborn has yet to be defined. It will probably vary, depending upon the degree of maturity and condition of the infant. Possibly a neutral environment is not the best. The foetus develops and matures at a temperature of 38°C . On the other hand, some constant mild thermal stimulus or cold stress might even be beneficial, and could account for differences in certain physiological measurements between American and British babies.

Respiratory Distress Syndrome and Artificial Ventilation

Artificially assisted or controlled ventilation for infants with respiratory distress syndrome is receiving increasing attention. In a gasping immature infant monkey, assisted ventilation was found to increase oxygen consumption quite dramatically (Fig. 9). The lower spirometer tracing records a gasping pattern of breathing and the oxygen consumption. During artificial ventilation, monitored on the upper tracing, oxygen consumption increased threefold. Both respiratory rate and oxygen consumption were higher when the infant was again allowed to breathe spontaneously. However, a controlled study of the use of artificial ventilation during respiratory distress by Silverman and co-workers has so far failed to show any improvements in survival rate (Silverman, Sinclair, Gandy, Finster, Bauman, and Agate, 1967).

Before dismissing artificial ventilation, the difficulties in management should be emphasized. It is a real *tour de force* to carry one of these infants through such a course, running the gauntlet of aspiration, obstructed airway, misplaced endotracheal tube, severe jaundice with exchange transfusions, etc. The difficulties are almost inversely related to the infant's size. We have no knowledge of how high pressures, necessary to expand lungs becoming increasingly stiff, might affect a failing circulation.

Added to this is the problem of oxygen. The

FIG. 9.—Influence of controlled ventilation on respiration and oxygen consumption of an immature rhesus monkey (see text).
(From Dawes, G. S., James, L. S., and Ross, B., unpublished data.)

FIG. 10a.—Acute hyaline membrane disease in an 8-hour-old premature infant. Fine granular densities fill both lungs, with air-filled bronchi standing out ('air-bronchogram' sign).

FIG. 10b.—Chronic hyaline membrane disease in 3-week-old premature infant, with re-expansion of some areas of pneumonia-atelectasis in other sites. Necropsy confirmation of beginning resorption of hyaline membranes. (From Berdon, W. E., and Baker, D. H., 1966, *Pediat. Clin. N. Amer.*, 13, 1017.)

chest x-ray films of an infant, weighing 800 g., in a negative pressure ventilator reproduced in Fig. 10a and 10b, show a picture typical of hyaline membrane at 3 days of age. Six weeks later, still in an artificial ventilator, the lungs were grossly abnormal, with patchy areas of emphysema, consolidation, and collapse. Whether this picture is the inevitable sequel to hypoxic damage of the alveolar lining during the early phases of the syndrome, whether it is due to repeated chest infection, so difficult to avoid with prolonged intubation, or whether it is actually caused by the high concentration of oxygen necessary to maintain arterial Po_2 even at 40 mm. Hg, is not known. The microscopical appearance of lung sections is somewhat similar to that produced by oxygen poisoning. It seems there are many questions still to be answered.

Conclusion

I would like to suggest that the paediatrician should take a leading role in this new era of perinatal care. Departmental barriers between paediatrics and obstetrics are falling by the wayside. The foetus, isolated and neglected for so long, is now accessible for diagnostic procedures and treatment. Sampling of capillary blood from the foetal scalp during labour is an important new technique offering a direct method of monitoring foetal welfare, and I hope it will soon gain widespread acceptance.

Our initial efforts at intensive and heroic therapy are likely to be met with frustration and discouragement as we see mentally retarded children survive. However, with persistence we should ultimately reach the stage of knowing whom to treat, when, and how, in order that intact survival be achieved.

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