

The viable child

The Croonian Lecture 1988

DAVID HULL, MB, FRCP, FRCOG, *Professor of Child Health,
Department of Child Health, University Hospital, Queen's Medical Centre, Nottingham*

The major achievement of neonatal medicine has been in the care of the prematurely born infant. More and more infants born at earlier and earlier gestation are surviving. There is and always will be a limit as to what current skills and technology can achieve and thus a dilemma on how to care for those infants born on the edge of viability. The limit in 1988 is most conveniently defined as infants born before 28 weeks gestation. This definition is useful, but it is artificial: intra-uterine development does not march to a strict timing, and will vary from one infant to another and between different body systems within any individual infant.

Some infants born before 28 weeks gestation survive intact, others are left permanently damaged and many die. If they had remained within a favourable uterine environment most would have survived intact. I propose to explore the question as to how far we are able, or might be able to provide such an environment outside the womb. That must precede the wider and perhaps more important debate as to whether it would be proper for us to attempt to do so.

The question of artificially sustaining the life of a newborn infant is not new. The minutes of the meeting of the Royal Society on 27 January, 1663 [1] read:

Dr Merret acquainted the Society that he had received information from Naples, concerning a person, who had an art of keeping newborn infants alive without respiration, for a good while. It was thought very desirable to have further enquiry made into this matter, both as to the truth of fact, and the way of performing it, viz. whether it was done by hindering the closure of the foramen ovale, which is supposed to shut soon after the birth of the animal.

Mr Croune suggested an experiment of keeping a new cast puppy in warm milk to see how long it would live so without air. He was desired to be curator of this experiment, . . .

Dr Croone, as he was later addressed, was the first Registrar of the Royal Society and as such was usually required to perform the experiments; the minute continues:

. . . and to remember the experiment, with which he had been formally charged, of making a carp live for a good while in air.

At that time the Fellows of the Society, which included Boyle, Hooke and Wren, were very interested in how various animals were able to live in different environments. Dr Croone recorded having observed small eels

wriggling in the belly of a larger one, he made the 'first reasoned attempt based on observation and illustration, to establish the corporeal existence of the preformed foetus in the unincubated egg' [2] and made numerous observations on the characteristics of the egg shell to determine how the developing chick survived.

Ten years earlier in 1651 Harvey [3] was asking a similar question in relation to man:

How does it happen that the foetus continues in its mother's womb after the seventh month?, seeing that when expelled after this epoch, not only does it breathe, but without respiration cannot survive one little hour, whilst . . . if it remains in utero it lives in health and vigour more than two months longer without the aid of respiration at all.

Their primary problem was how could life be maintained without breathing, and therein lies the central problem of the previable child.

Viability

There has been much discussion in recent years amongst those on high committees concerned with preparing the law of the land as to the meaning of viability. The *Shorter Oxford English Dictionary* defines viable as 'capable of living, able to maintain a separate existence' but quotes by way of example: 'Such deformity of the female pelvis as will absolutely preclude the birth of a viable child, 1881', and in so doing it illustrates the problem, for in that example it is the *skill of the obstetrician* which determines whether the child is viable or not. The viability of the child has always been a major consideration for obstetricians and it often influences their action. They, and others, sometimes speak of the viable fetus but that can be confusing, for more often than not the fetus is viable as a 'fetus'; the question is ability to maintain a separate existence.

On the basis of general experience, already known 300 years ago to Harvey, it was thought that infants born before seven months were unable to breathe and that they invariably died. Thirty years ago, as a house obstetrician, along with many others, I completed proformas for the National Perinatal Study. It was the practice then to admit all women in labour before 28 weeks gestation to the gynaecological ward. Infants born at such a stage were not expected to live and they did not. The study showed that prematurity was a major cause of perinatal deaths, that survival of infants born before 28 weeks was

very rare, and the survival of infants born between 28 to 31 weeks and 32 to 35 weeks was around 40 and 75 per cent respectively.

At this time the viability of the children born early depended on *their inherent capacity* to establish adequate gaseous exchange; the limit of viability was thought to be determined by the structural and functional development of the lung. Over the next fifteen years, fetal and neonatal research blossomed. Much of the work was on animals, but there were attempts to study the human fetus and newborn, including the maintenance of fetal and neonatal life using external oxygenators [4-6]. Inevitably, there was concern; the Secretary of State for the Social Services asked the College of Obstetricians and Gynaecologists to advise. Their report in 1972 on 'The Use of Fetuses and Fetal Material for Research' [7] recommended that in future a fetus over 20 weeks gestation should be considered viable. That provoked McCance [8] in the closing chapter of a book edited by Austin on *The mammalian fetus in vitro* to observe:

Very very few fetuses of less than 28 weeks are viable, or can be made so at the present time and this decision will create a shadowy period of eight weeks during which many abortions will necessarily be performed on fetuses that are certainly not viable, yet in which their use for research of any kind may become illegal. Yet this is the very material on which most valuable work can and should be done. Only the paediatrician on the spot can decide whether a fetus is likely to be viable or not, and only the investigator whether an experiment would be justifiable or not. No ethical committee can decide

These are strong and wise words, but times were changing fast, as Professor McCance wrote, neonatal medicine was already beginning to have its impact. Opportunities were lost and we have now to act without understanding.

The techniques of modern neonatal care are essentially modifications of approaches used to sustain life at any age, namely respiratory support, fluid and nutrient maintenance, the correction of metabolic fluctuations, and infection control. The success of some of these approaches has been questioned [9], and there is no doubt that some innovations did more harm than good [10]; nevertheless there can be no doubt that some infants now survive when previously they would not. The benefits were first seen in the 33 to 36 week and then the 28 to 32 week gestation band.

With modern neonatal care the determinants of viability have changed yet again, for it is now not only the skills of the obstetricians and the inherent characteristics of the infants but also *the abilities and resources* of those who attended them after birth which determine whether the infants survive or not.

Current position

The most satisfactory data that I am aware of on the survival of infants born at different gestations in this country at this time is that collected by Dr Wariyar under the direction of Dr Hey and colleagues in the Northern

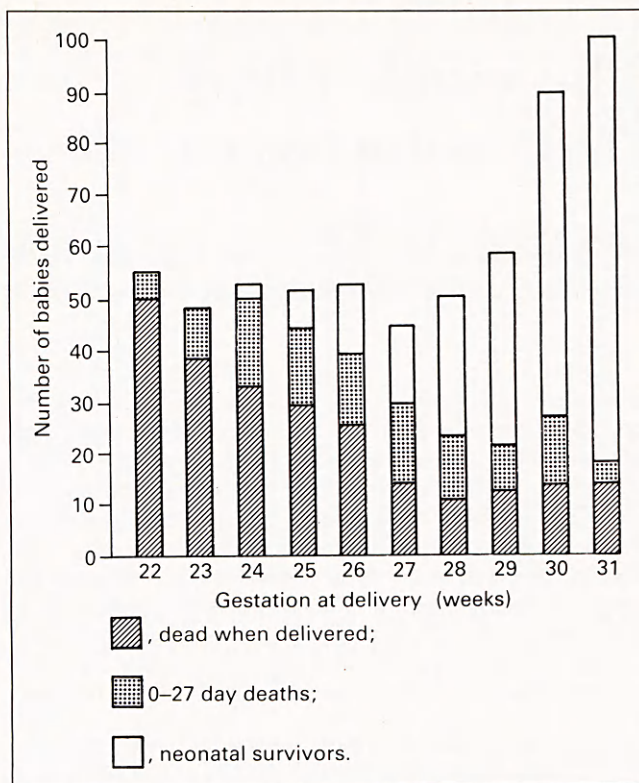


Fig. 1. The effect of gestation on survival amongst all babies born at 22 to 31 weeks gestation in the Northern Region in 1983 (including late miscarriages). Unpublished survey data collected by Dr U. Wariyar in connection with the follow-up survey of all survivors.

Regional Health Authority [11] (Fig 1). Our own experience in Nottingham over the last five years, with respect to survival of live born infants below 28 weeks gestation, suggests that the survival rates have remained unchanged and that they are of the same order as those in similar units across the world.

Thus, whilst there will be technical advances which will increase the effectiveness of the methods used and, one hopes, will also reduce their intrusiveness, it seems unlikely that such developments will achieve much success in those infants whom they currently fail, particularly the very immature and those with congenital defects incompatible with independent life such as heart defects in which only heart transplantation offers any hope of life. Disorders of immaturity are now responsible for over 50 per cent of neonatal deaths. The causes of death in Nottingham in 1985, classified by main neonatal pathology (Table 1), give a rough indication of the numbers involved for a service to around 10,000 births per year, with tertiary responsibility for around a further 5,000 births per year. Although the number of infants born alive under 28 weeks gestation is relatively low, it is greater than those who might benefit, for example, from infant heart transplantation.

Neonatal intensive care has not been an unqualified

Table 1. Primary causes of neonatal deaths, Nottingham Neonatal Service, 1985

Gestation	Immaturity	Lung failure	Bowel failure	Congenital abnormalities	Others	
24-25	9	3	—	—	—	
26-27	2	5	—	1	—	
28-29	—	10	1	—	—	
30-31	—	7	—	—	—	
32+	—	—	—	20	10	
	11	25	1	21	10	Total 68

success. Initially, the percentage of survivors under 32 weeks gestation with severe residual brain damage was high, in some studies as much as 30 per cent. There is some evidence that the percentage of those who have severe disability is falling [12], but whether that is due to better obstetric care prior to birth or neonatal care after is difficult to resolve; no doubt both play a part. Our current experience suggests that around 10 per cent of infants born in the 28-32 week period have a major disability, and between 15 and 20 per cent of those born before 28 weeks gestation are similarly disabled. The handicap rates are higher the shorter the gestation and they are highest in those requiring most intensive care. On the other hand, severe disability is not inevitable even in those who survive having been born at 24 weeks gestation [13]. Some of the 'graduates' of neonatal units have irreparable brain damage; they and others often have chronic lung disorders [14]. Re-admission rates of these children to paediatric wards in the first year of life are high [15]. Many require hernia operations and most have skin scars to mark the sites of life support intervention used to support their existence. In the majority, the scars are trivial, but in 10 per cent they are not [16]. Their parents, far from having the joys of parenthood, experience weeks of worry and face an uncertain future. If they had to pay for treatment, most would be in debt [17]. As it is, their need to visit and to remain committed and confident is a severe drain on their financial, emotional and family resources. In these circumstances, we have to consider the challenging question of whether we should have a selection procedure to respect a family request or consider the wider issues. We are equally bound to investigate alternative forms of care; in particular, is it possible to create an artificial environment like that of the inside of the uterus, to gain vascular access, to perform the function of the placenta and to maintain life without causing damage.

Creating a uterine environment

The fetus is bathed in water which contains a trace of salt, is sterile, is held at a temperature close to 37°, and is dark but not silent.

Temperature

There is limited information on the thermoregulatory responses of infants under 28 weeks gestation. What there is suggests that such infants have no thermoregulatory

capacity either to increase heat production on cold exposure or to increase heat loss by sweating in hot environments. They need to be incubated like a chicken in an egg [18]. Furthermore, the physical characteristic of the under 28 week infant is such that the surrounding temperature must be close to the desired body temperature (36.5-37°C). This is not so for the term infant. The fetus at term runs a deep body temperature 0.5-1°C above maternal temperature and the placenta acts to exchange heat back to the mother. The reason is that the fetus has a higher metabolic rate per kg than the mother, and at term a non-porous skin and a generous layer of subcutaneous fat provide thermal insulation.

It was whilst studying the poor thermal control of the very immature infant that we became aware of one of their unique characteristics [19]. Their skin is not water-tight, it is but two to three cells thick and without keratin. Thus, when these infants emerge into air cooler than 37°C or lower than 100 per cent humidity, they lose water and with the evaporation of water from their exposed surfaces they lose heat. Clearly, the amount they lose will depend on the environmental conditions; nursing them, as was the practice in the past, at 25 to 30°C at under 50 per cent humidity and withholding fluid for 48 hours ensured that none would survive. The environment into which immature infants are placed is critical and warmth itself is not enough.

Birth appears to induce accelerated skin maturation, keratin is produced and the skin becomes water-tight earlier than it would have done if the baby had remained *in utero*. The mechanisms of this response are not known; in particular it is not known whether the maturation is a response to the birth itself or the conditions in which the infant is nursed. In effect, nurses document the skin's maturation by recording the infant's body temperature and the incubator settings (temperature and humidity) required to maintain that temperature. Any attempt to provide an 'artificial uterus' would have to document this development. However, in units which rely on incubators rather than radiant heaters, the environmental conditions that are initially necessary to keep the infant's body temperature around 37°C, namely, fully humidified air at 37°C, already approach the characteristics of the water envelope from which the infant emerged.

Watery envelope

Might it help to keep the infants submerged—at least partially? The underlying question is, do infants in mid-

gestation exchange body fluids with amniotic fluid and, if they do, does it serve a purpose? We know the fetus passes urine into the amniotic fluid. Might it release waste products through the skin? Whilst it may, and that in turn may provide a larger sink to modulate changes, any net loss from the uterine contents passes across the placental membranes into the maternal circulation. Thus, if the permeability of the infant's skin is to be explored as a temporary organ of excretion, its use for that purpose would be contrived rather than physiological.

To date, there have been few studies on the outward passage of electrolytes and chemicals through the immature infant's permeable skin; there is more information on the transfer of drugs into the baby, for example to deliver amniophylline to encourage the infant to keep breathing [20].

Sterility

Bacterial colonisation is not an essential requirement for life, it is not needed for intestinal digestion. Animals have been reared in sterile conditions for many years. Infants have been reared in sterile environments in one or two exceptional circumstances. This arrangement was thought desirable at one time in the management of infants with combined immune deficiency. One such infant was born at University College Hospital and maintained in a special sterile plastic tent in Great Ormond Street Hospital for a few days until it was determined that the child did not have the condition [21]. A child that did have the deficiency was reared in a sterile environment for 7 months in Ulm and, we were told, came to no harm [22].

It is exceptional for immature infants nursed under current methods not to become infected and not to require broad spectrum antibiotics for long periods. There would seem to be good grounds, if we are concerned with quality of survival, at least for those delivered by Caesarean sections, to consider maintaining a sterile environment for the early critical weeks.

Physical stimuli

Sound and light seem less important. Provided the noise level is kept within a reasonable range of decibels and frequency consistent with borborygmi and arterial flow noises, little harm or benefit should follow [23]. Light is more problematic for, no doubt, birth induces changes on the coverings of the eye as it does on the skin, and we are only too well aware of the vulnerability of the retina. Many animals are born with sealed eyelids. Experiments with newborn rabbits showed that ambient temperature contributed to the time when the eyelids parted. The temperature of the cornea affects its rate of growth. So we have much to learn, and there may be virtue in initially 'working in the dark'. Damaging jaundice currently forces us to use massive 24-hour light exposure. This cannot be accepted as an ideal solution. When the infant achieves full independence, breathing and feeding with minimal support, the evidence suggests that it is important to introduce the cycle of day and night [24].

Providing an 'artificial uterus' and introducing the infant to the wider world as he or she matures, in effect a controlled birth, does seem to be a practical proposition. It is certainly easier than the other aspect of creating a fetal world, namely replacing the placenta.

Performing the functions of the placenta

To the fetus, the placenta is an organ for gaseous exchanges for the absorption of nutrients, for the metabolism of some chemicals, and for the excretion of waste products. Whilst the maternal uterine-placental arrangement determines what is available to the fetus, the fetus does elect within that restraint to take what it wants. The placenta presents oxygen to the fetus and secretes carbon dioxide, it presents glucose, fatty acids, longer chain desaturated fatty acids possibly linked to phospholipids, and a selection of amino acids and all the essential nutrients. It is possible that the fetus can reject excess energy as fatty acids. Theoretically, an approximate estimation of the net fluxes can be made from analyses of umbilical venous arterial differences and the fetus' metabolic rate and accretion rates. It is the delivery systems which are the problem. Animal studies give us no encouragement to try and use the infant's own placenta by placing it in a suitable medium to mimic the maternal blood supply.

Gaseous exchange through the immature lung

The dramatic event at birth is the occlusion of the umbilical cord and the cessation of the umbilical circulation. This has two immediate and irreversible effects: the newborn infant, like any other animal, has a very limited oxygen store and needs an alternative supply to survive, and the heart and circulation must adjust, and that adjustment means opening the pulmonary circulation.

The Select Committee on the Infant Life (Preservation) Bill (HL) 1988 concluded from all the advice they were given that:

A child which leaves the womb prematurely has no chance of survival if the lungs are insufficiently developed to enable its blood to be oxygenated. Until the completion of about 24 weeks pregnancy, the lungs are incapable of expanding, so that the unborn child is unable to survive if removed from the womb.

The same argument was applied to infants of 28 weeks. What has changed? Firstly, infants below 28 weeks are now expected to survive. Expectation alone seems to be an important factor, but it also means that they are delivered with care and tended from the moment of birth, and kept in an environment which stresses them least and maintains their hydration. Asphyxia, hypothermia and dehydration are not allowed to compromise whatever lung function the infant achieves. Secondly, the infant's respiratory performance is sensitively supported with a controlled supply of oxygen, the maintenance of a functional residual capacity and augmentation of tidal volume. The more delicate and sensitive the support, and the least invasive, the better the results.

A great deal is now known about the structural development of the lung in relation to gestation and the factors that induce functional maturation prior to birth [25-28]. Early interpretations of the pathogenesis of lung disorders in immature infants have not always been helpful. Too much was ascribed to immaturity alone rather than the effects of asphyxia, trauma, haemorrhage, aspiration and infection on the immature lung, incomplete in structure and with very limited reserve capacity. Most neonatologists have now observed with delight an infant of 26 weeks gestation breathe adequately and survive without ventilator support. Idiopathic respiratory distress syndrome, surfactant deficiency, hyaline membrane disease are not the inevitable consequences of being born too soon.

Profound changes occur in the structural development of the lung between 22 and 28 weeks gestation: they change from the canalicular to the sacular stage. The practical question is: can useful gaseous exchange be achieved through an elaborate respiratory tree without air sacs?

The lungs of the newborn marsupial when it first enters the pouch are thin walled sacs lined by an epithelial layer with capillaries beneath; they are devoid of bronchioles, alveolar ducts and alveoli which develop later [29]. Yet the pouch young achieve adequate gaseous exchange. Thus, during the development of marsupials, alveolar sacs are not a prerequisite for gaseous exchange.

The techniques that facilitate lung ventilation and are successful in the care of an infant of 32 to 36 weeks gestation may well be inappropriate in infants under 28 weeks gestation, both to achieve gaseous exchange, and because of the damage they cause. At present, we appear to have the uncomfortable option of death due to hypoxia or life with prolonged oxygen dependency and permanent lung damage. There are very few studies of the gaseous exchange (oxygen consumption) and lung function of infants under 28 weeks and it is questionable if we should continue as we are without further studies. A recent multicentre study in the US [14] reported that lung damage, as indicated by oxygen dependency, was lowest in the unit that did not vigorously ventilate from birth, had the lowest rates of tracheal intubation and mechanical assistance, and never used muscle relaxants. Lantos *et al.* [30] concluded that cardiac pulmonary resuscitation in babies of very low birthweight was a futile therapy and recommended that it should not be used in very low birthweight infants until it had been validated. In a retrospective analysis of Nottingham figures, it was found that, once a very immature infant required artificial ventilation and developed a pneumothorax, death or survival with severe permanent brain damage were the only outcomes. These are but three observations which illustrate the limitations of our current approaches and apply in particular in the care of infants born before 28 weeks. The survival of an infant of 440 g born at 25 to 26 weeks gestation was ascribed to an approach described as 'minimal intervention' [31]. The bronchial tree and its branches provide a surface where significant gaseous exchange might occur, without forced lung inflation and high pressure ventilation.

It may be possible to oxygenate the infant via the lungs

using a liquid medium containing perfluorchemical-based blood substitutes. Clarke and Gollan [32] showed that mice survived suspended in liquid containing perfluorchemicals saturated in oxygen. There is no obvious reason, from present knowledge, why the bronchial tree should not be cleared of fluid and gas introduced. However, it may be that the premature introduction of a gas-liquid interface in the bronchial tree itself interferes with its normal development and predisposes to bronchopulmonary dysplasia. This is another area in need of exploration.

Gaseous exchange through the skin

The finding that the immature infant's skin is so permeable raises the possibility that the infant's surface may be used for gaseous exchange. Evans and Rutter [33] demonstrated that oxygen enters and carbon dioxide is lost through the skin, and recently Cartlidge and Rutter [34] showed that central arterial oxygen pressure increases when the gas surrounding the infant is changed from air to 90 per cent oxygen. The extent to which hyperbaric oxygen might augment this effect remains to be explored.

Once we understand more of determining and limiting factors, cutaneous and respiratory tree exchanges may be sufficient to support the infant's needs over the critical early 2 or 3 weeks, without resorting to external oxygenation membranes or high pressure ventilation. The implications are considerable.

Gaseous exchange through external membranes

With the development of bypass cardiac surgery, extra corporeal membrane oxygenation (ECMO) became available as a support system for newborn infants with respiratory failure. Between 1965 and 1975 it was tested on fetal animals. The major problems then centre round achieving adequate flow and avoiding haemorrhages and disturbed fluid balance due to the anticoagulants and perfusates used. Nonetheless, ECMO was tentatively tried in the UK and elsewhere within a clinical setting including premature infants with severe respiratory failure, but with little if any success [6]. It is again being promoted in some units in the US for the management of infants with persistent pulmonary hypertension from whatever cause [35-37]. Criteria for its use have been based on a retrospective analysis [38], and the results of a randomised controlled trial have been published [39]. It has only been used when all else, ie aggressive ventilation with high pressures and oxygen concentrations, induced alkalosis, respiratory paralysis, tolazaline, dopamine, sodium bicarbonate bolus therapy etc has failed. In these studies, infants of low birthweight have in the main been excluded because of the increased risk of intracranial bleeding. As the authors warn, the therapy is not without risks such as haemorrhagic complications [40] and the adverse effects of ligation of the common carotid artery and internal jugular vein when these have been used to gain vascular access. ECMO is only used as a last resort. Should it be re-evaluated in this country? Given the current indications, a unit serving a 5,000 delivery rate

would possibly consider its use once a year. A system so infrequently employed would be dangerous. If it were indicated, then at the most, three or four units in major population areas would be needed, with agreed criteria for referral and excellent transfer arrangements.

A special case has been made for the use of ECMO in infants with diaphragmatic hernia [41]. It has been our experience in Nottingham that active management to stabilise the infant before surgery has improved survival, but whether the use of ECMO would improve it still further would need to be demonstrated [42].

External membranes as presently used support oxygenation, they do not replace lung alveolar exchanges altogether. It would seem that there are still insurmountable problems to establishing the placental function of gaseous exchange with an extracorporeal system alone for the support of infants under 28 weeks gestation. Nevertheless, the possibility of using the technology to buy time for infants under 28 weeks will continue to be explored.

On the question of vascular access, there would seem to be grounds to reconsider the use of the umbilical vein. The umbilical cord of the 28-week infant is surprisingly and comparatively large. With appropriate maintenance and protection, this purpose-designed vascular access might be used to far greater effect and with less risk and pain than peripheral stabs and long lines.

Reducing oxygen requirements

The tolerance of newborn mammals, including the human infant, to hypoxia, hypothermia and trauma has been known for many years. Whether the infant born under 28 weeks gestation has the same tolerance is not known nor can it be assumed. In the past, clinicians have sought to buy time immediately after birth by reducing the infant's oxygen requirement by such techniques as cooling and so induce a kind of torpor. That method foundered in term-asphyxiated infants because it failed in its primary objective of cooling the infant rapidly. It would be much easier to cool a 24–28 week infant; in fact, it is very difficult to avoid it to some extent, and at this gestation the argument to avoid the thermogenic challenge does not apply. It might, therefore, be tempting to re-examine the position, so as to buy time to set up more elaborate support systems, but that would only be justified after extensive animal investigation. The alternative would be the immediate availability over 24 hours of a highly skilled technically equipped team to initiate all systems at birth. Such an arrangement might be possible for babies born by section but it would not be so easy for precipitate vaginal delivery after haemorrhage.

Fluids and nutrition

Swyer [43] began a recent review article on neonatal nutrition with words that express the general feeling of confidence of neonatologists in the care of healthy infants born after 28 weeks gestation:

Over the last 20 years, there have been major advances in life support techniques for the newborn, especially in facilitating

lung gas exchange. As a result, the gut and the achievement of adequate nutrition have replaced the respiratory and central nervous system as the more important in infant survival of all except perhaps the lowest birthweight infants (<750 g).

Whilst a high blood flow is required to deliver oxygen, the same is not true for nutrients. The net flux to the infant might be estimated from umbilical cord a-v differences and the effects of daily increments of nutrients on the fetal tissues. The aim would be to deliver the net flux in the daily water requirement via an i.v. line. At present, neither our knowledge nor food technology has advanced to the point where we can do this entirely satisfactorily for older infants. However, there is no doubt we can maintain life and achieve acceptable increments on parenteral feeding alone.

Much of our knowledge on placental flux is based on animal studies and on the performance of the human placenta near term. The situation in mid-gestation may be different in many respects. It is certainly different with regard to fatty acid transfer when the rate of fatty acid deposition is negligible compared to the levels it reaches towards term.

It is still the usual practice to encourage early feeding to give known and unknown factors not included in the intravenous programme. Many infants under 28 weeks gestation who survive in the first week or two of life have major problems in the third and fourth week with bowel disorders and undernutrition. The range of oral feeds available is widening. There is great need to evaluate what may and may not be appropriately introduced into the immature bowel to assist its maturation without causing harm, and to support the infant's nutrition.

Nutrition during the weeks 20–28 may be a great deal more critical than it is during the 28–40 week period simply because that is the time when the brain grows rapidly and neurones are forming. Asphyxia and undernutrition at this time may have subtle long-lasting effects which will not be revealed by a two-year or even a five-year evaluation for severe handicap, blindness, deafness, cerebral palsy, mental retardation. At the present we simply do not know.

Conclusions

If we are to maintain the life of very immature infants artificially with sophisticated support systems then we need to know a great deal more about the infants themselves and we need to evaluate carefully every step we take in our efforts to help. Trying harder with the current approach which has been effective in more mature infants is probably not going to be good enough; we are likely to go on as we are, saving some after a frightening struggle and losing others. With this predictable outcome, parents must be given the option of making another infant. Many 'viable' fetuses are aborted at 18 weeks, yet for an infant born six weeks later a struggle begins which is painful and stressing to the infant and the parents. The immediate outcome is uncertain, and remains so for those who survive. In my view, the time has

come when some national group should take on the responsibility for collecting all the data and monitoring clinical practices and innovations, with a view to taking a stand on what is necessary and acceptable and what is not so in the care of infants on the edge of viability.

More importantly, there is a need for research, both on animals and on the infants themselves. We need to make sensitive, detailed observations, accepting all the ethical restraints, on how they live, to try and discover why they are damaged or die.

Acknowledgements

I am grateful to all my friends and colleagues in Nottingham for the help they have given me in the preparation of this article and in many other ways over the years.

References

- Birch, T. (1956-7) *The history of the Royal Society of London*, Vol. 1. p.180.
- Cole, F. J. (1944) *Early theories of sexual generation* p.47. Oxford: Oxford University Press.
- Harvey, W. (1651) *De Generatione Animalium*.
- Chamberlain, G. (1968) An artificial placenta. *American Journal of Obstetrics and Gynecology*, **100**, (5), 625.
- McNaughton, M. C. (1973) Extracorporeal maintenance of small human fetuses. In *The mammalian fetus in vitro* (Ed C. R. Austin) London: Chapman and Hall.
- Walker, C. H. M. and Danesh, J. N. Z. (1973) Extracorporeal circulation for the study of the preterm fetus. In *The mammalian fetus in vitro* (Ed C. R. Austin). London: Chapman and Hall.
- Report of the Advisory Group (1972) *The uses of fetus and fetal material for research*. London: HMSO.
- McCance, R. A. (1973) The road ahead. In *The mammalian fetus in vitro* (Ed C. R. Austin). London: Chapman and Hall.
- Maddock, C. R. (1987) A population-based evaluation of sustained mechanical ventilation of newborn babies. *Lancet*, **ii** 1254.
- Silverman, W. A. (1980) *Retrolental fibroplasia: a modern parable*. New York: Grune and Stratton.
- Wariyar, U. (1985) In *Collaborative survey of perinatal and late neonatal mortality*. Northern Regional Health Authority Report.
- Yu, V. (1987) On deciding care for the extremely premature baby. *Maternal and Child health*, **12**, 158.
- Weindling, A. M. and Cooke, R. W. I. (1988) The outcome for infants of less than 28 weeks gestation. Paper presented to British Paediatric Association Meeting, April 1988.
- Avery, M. E., Tooley, W. H., Keller, J. B. *et al.* (1987) Chronic lung disease in low birth weight infants: a survey of eight centers. *Pediatrics*, **79**, 26.
- Skeoch, C., Rosenberg, K. and Turner, T. (1987) Very low birthweight survivors: illness and readmission to hospital in the first 15 months of life. *British Medical Journal*, **295**, 579.
- Cartlidge, P. H. T., Fox, P. E. and Rutter, N. (1988) Personal communication.
- Ryan, S. Sics, A. and Congdon, O. D. (1988) Cost of neonatal care. *Archives of Disease in Childhood*, **63**, 303.
- Wheldon, A. E. and Hull, D. (1983) Incubation of very immature infants. *Archives of Disease in Childhood*, **58**, 504.
- Rutter, N. and Hull, D. (1979) Water loss from the skin of term and preterm infants. *Archives of Disease in Childhood*, **54**, 858.
- Evans, N. J., Rutter, N., Hadgraft, J. and Parr, G. (1985) Percutaneous administration of theophylline to preterm infant. *Journal of Paediatrics*, **107**, 307.
- Barnes, R. D., Fairweather, D. V. I., Holliday, J. *et al.* (1969) A germfree infant, *Lancet*, **i**, 268.
- Teller, W. (1974) Personal communication.
- Wolke, D. (1987) Environmental neonatology. *Archives of Disease in Childhood*, **62**, 987.
- Mann, N. P., Haddow, R., Stokes, L., Goodley, S. and Rutter, N. (1986) Effect of night and day on preterm infants in a newborn nursery: randomised trial. *British Medical Journal*, **293**, 1265.
- Langston, C. and Fagan, D. G. (1978) *Recent advances in neonatal pulmonary disease in lung*. IAP Monograph No. 19. Baltimore: Williams and Wilkins Co.
- Dunhill, M. S. (1982) The problem of lung growth. *Thorax*, **37**, 561.
- Hislop, A. A., Wigglesworth, J. S. and Desai, R. (1986) Alveolar development in the human fetus and infant. *Early Human Development*, **63**, 1.
- Langston, C., Kida, K., Reed, M. and Thurlbeck, W. M. (1984) Human lung growth in late gestation and in the neonate. *American Review of Respiratory Disease*, **129**, 607.
- Hill, J. P. O. and Hill, W. C. O. (1955) The growth stages of the pouch young of the mature cat (*Dasyurus viverrinus*) together with observations on the anatomy of the newborn young. *Transactions of the Zoological Society of London*, **28**, 349.
- Lantos, J. D., Miles, S. H., Silverstein, M. D. and Stocking, C. B. (1988) Survival after cardiopulmonary resuscitation in babies of very low birth weight. Is CPR futile therapy? *New England Journal of Medicine*, **318**, 91.
- Pleasure, J. R., Dhand, M. and Kaur, M. (1984) What is the lower limit of viability? Intact survival of a 440 g infant. *American Journal of Disease in Childhood*, **138**, 783.
- Clarke, L. C. and Gollan, F. (1966) Survival of mammals breathing organic liquids equilibrated with oxygen at atmospheric pressure. *Science*, **1**, 1755.
- Evans, N. J. and Rutter, N. (1987) Percutaneous respiration in the newborn infant. *Journal of Pediatrics*, **108**, 282.
- Cartlidge, P. H. T. and Rutter, N. (1988) Percutaneous oxygen delivery to the preterm infant. *Lancet*, **i**, 315.
- Bartlett, R. H., Andrews, A. F., Toomasian, C. C. P., Haiduc, N. J. and Gassaniga, M. D. (1982) Extracorporeal membrane oxygenation for newborn respiratory failure: Forty-five cases. *Surgery*, **92**, 425.
- Andrews, A. F., Klein, M. D., Toomasian, J. M., Roloff, D. W. and Bartlett, R. H. (1983) Venovenous extracorporeal membrane oxygenation in neonates with respiratory failure. *Journal of Pediatric Surgery*, **18**, 339.
- Krummel, T. M., Greenfield, L. J., Kirkpatrick, B. V. *et al.* (1984) The early evaluation of survivors after extracorporeal membrane oxygenation for neonatal pulmonary failure. *Journal of Pediatric Surgery*, **19**, 585.
- Beck, R., Anderson, K. D., Pearson, G. D. *et al.* (1986) Criteria for extracorporeal membrane oxygenation in a population of infants with persistent pulmonary hypertension of the newborn. *Journal of Pediatric Surgery*, **21**, 297.
- Bartlett, R. H., Roloff, D. W., Cornell, R. G. *et al.* (1985) Extracorporeal circulation in neonatal respiratory failure. A prospective randomized study. *Pediatrics*, **76**, 479.
- Sell, L. L., Cullen, M. L., Whittlesey, G. C. *et al.* (1986) Haemorrhagic complications during extracorporeal membrane oxygenation: prevention and treatment. *Journal of Pediatric Surgery*, **21**, 1087.
- Hardesty, R. L., Griffith, B. P., Debski, R. F., Jeffries, M. R. and Borovetz, H. S. (1981) Extracorporeal membrane oxygenation. *Journal of Thoracic and Cardiovascular Surgery*, **81**, 556.
- Cartlidge, P. H. T., Mann, N. P. and Kapila, L. (1986) Preoperative stabilisation in congenital diaphragmatic hernia. *Archives of Disease in Childhood*, **61**, 1226.
- Swyer, P. R. (1987) New perspectives in neonatal nutrition. *Biology of the Neonate*, **52**, Suppl. 1, 4.