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Neonatal management and safe discharge of late and moderate preterm infants

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SUMMARY

Late and moderate preterm infants form the majority of admissions for prematurity to special care neonatal nurseries. Although at risk for acute disorders of prematurity, they do not suffer the serious long term risks and chronic illnesses of the extremely premature. The special challenges addressed here are of transition and of thermal adaptation, nutritional compensation for postnatal growth restriction, the establishment of early feeding, and the avoidance of post-discharge jaundice or apnea. These 'healthy' premature infants provide challenges for discharge planning, in that opportunities may be available for discharge well before the expected date of delivery, which should be pursued. Barriers to early discharge are rigid conservative protocols and unwarranted investigations; facilitators of discharge are individualized care by nurses expert in cue-based feeding, early management of the thermal environment, support of family preferences and encouragement of mother–baby interactions. Safe discharge depends on recognizing these opportunities and applying strategies to address them.

1. Introduction

The definitions of moderate and late preterm infants are accepted as infants of 32 and 33 and of 34, 35 and 36 weeks respectively. This review addresses management issues particular to prematurity but does not address in detail the disease-specific interventions of intensive care. The management issues of premature infants addressed here will be confined to discussing the selection of infants for admission to special or intensive neonatal care units (hereafter called special care nurseries) and their preparation for discharge in industrialized countries with established maternity and neonatal intensive care services.

The birth weights of this population overlap with infants of very low and even extremely low birth weight (Table 1).[1] Most morbidity of prematurity is related to gestational age, but some challenges (such as the maintenance of thermal homeostasis or the re-establishment of growth) are related to size at birth. Moderate preterm infants form a continuum with very preterm infants (<32 weeks' gestation) and will therefore occasionally require discharge plans usually applied to this group of smaller infants. Neonatal follow-up programmes do not routinely enrol infants >32 weeks' gestation, and infants with chronic lung disease requiring home oxygen are rarely included this group. Infants of >32 weeks' gestation are not ordinarily at risk of retinopathy of prematurity.[2,3]

Aspects of discharge related to more extreme prematurity will not be addressed here.

2. Triage at birth

2.1. The delivery room

A resuscitation physician or team, with appropriate equipment, capable of assessing the newborn, of establishing an airway and of achieving thermal neutrality must be present. If the birth is anticipated the team should have reviewed the maternal antenatal record and should be, in particular, knowledgeable as to the estimated gestational age and the confidence with which this has been estimated, and to the use of antenatal steroids, the estimated fetal weight and the presence or absence of maternal drugs or infection. Resuscitation and its controversies will not be addressed here, other than to say that the risks of respiratory depression and distress are much higher in this population than at term. There is no prerequisite for prophylactic surfactant, added oxygen or antibiotics and a minimal-handling, expectant approach may be taken, with close attention to thermal homeostasis.

2.2. Post-delivery triage of the premature infant

A decision must be made to admit the baby either to a special care nursery or to a postnatal ward, which in practice includes a decision either to separate the baby from the mother or to maintain the mother–infant dyad. Admission to a special care

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Table 1
Distribution of birth weight by gestational age for singletons. Approximated from the data of Kramer et al.[1]

Gestational age (weeks)	Median birth weight (g)	Cumulative percentage below birth weight limits						
		<1000 g	<1250 g	<1500 g	<1750 g	<2000 g	<2250 g	<2500 g
32	1862	1%	5%	16%	38%	65%	86%	96%
33	2081	0%	1%	6%	19%	41%	67%	87%
34	2313	0%	0%	2%	7%	21%	44%	69%
35	2553	0%	0%	0%	2%	8%	22%	45%
36	2795	0%	0%	0%	1%	3%	9%	23%

nursery is generally required for infants who need incubator care, cardiorespiratory monitoring, assessment of adaptation or management of the complications of prematurity. This triage is specific to institutions and depends greatly on nursing skills and resources allocated to postnatal wards and the availability of pediatric expertise. Early separation can be usefully delayed if delivery room staff has the resources to monitor premature infants with their mothers and has the skills to manage the neonatal environment with skin-to-skin contact and early breast-nippling.[4,5] The stable maintenance of an axillary temperature in the range 36.7–37.3 °C, the absence of respiratory distress and the presence of resources for ongoing surveillance are prerequisites for a prolongation of maternal–infant contact in the delivery room; skin-to-skin contact requires continued surveillance of the infants by nursing staff.[6] Blood sugar screening in the delivery room is of unclear benefit and the consequences of intervention unevaluated; screening for hypoglycemia is advocated for preterm infants at 1½ to 2 h of age.[7,8]

The abilities and benefits to the mother of continued shared care with their infants must also be addressed. Exhausted mothers or those recovering from anesthesia cannot be expected to participate in infant care, but innovative and individualized strategies (sometimes involving other family members) may reduce separation and support the early establishment of breastfeeding. Limitation of nursing resources and medical skills in the delivery room and postnatal wards reduces the safety of individualized triage decision-making; in these circumstances clear guidelines must be imposed which determine the criteria that will permit admission of the infant to the postnatal ward.

3. Admission to and early management in the special care nursery

Many special care nurseries have universal admission protocols for premature infants, which include incubator care and cardiorespiratory monitoring. An early medical assessment, including review of the maternal perinatal history, birth events and physical examination of the newborn should determine whether an infant is to be admitted for care limited to observation of adaptation or for specific investigation and management of disorder of prematurity (such as respiratory distress). For many infants, where there are no risk factors for infection and no signs of delayed adaptation or cardiorespiratory disease, management can be confined to observation, establishment of feeding, monitoring and care of the thermal environment.

The admission process must not result in additional morbidity or prolonged hospital stay. There is no place for 'routine' investigations such as blood sampling; in the presence of low disease prevalence (risk) such pursuits generate a high rate of false-positive results which frequently result in further investigation, intervention and prolongation of stay. Likewise there is no role for routine blood culture or recourse to antibiotics; these strategies must be reserved for infants in whom there is a defined risk of perinatally acquired infection from the maternal history or clinical findings. The requirement for blood sugar measurements on admission and at selected intervals thereafter is inescapable,[8] but these must be limited by protocol or to response to clinical suspicion of hypoglycemia; repeated unsolicited estimations lead to false-positive observations, further confusion and unwarranted intervention.

4. Establishing thermoneutrality

All caregivers should have a good understanding of the components of the thermal environment.[9] In order to facilitate observation, incubator placement may be a prerequisite for admission in some units, in which case great care must be exercised not to overheat larger infants. Thermoneutrality can be assumed if the axillary temperature is between 36.7 and 37.3 °C.[10]

5. Early feeding

The importance of the establishment of very early nutrition has recently been recognised, with the goal of establishing, so far as the constraints of fluid allowances permit, full nutrition within the first 2–5 days of life.[11,12] Whereas these discussions have focused more on extremely low birth weight infants, the nutritional deficiencies of moderate and late preterm infants must be similarly addressed, as these infants have been born before the major part of fetal growth has been completed. The special needs of the small-for-dates preterm have long been recognised, but all premature infants including those born of appropriate size-for-dates suffer from postnatal growth restriction attributable to the prolonged delay in re-attaining birth weight characteristic of the preterm infant.[13]

Feeding should be fully enteral where possible, often by gavage, and should be the expectation in infants of >1500 g birthweight. Mother's milk will generally not be immediately available, and human milk banks are not universally accessible, in which case an individualized decision must be taken, preferably with the mother, to feed with infant formula, using additional maternal colostrum or milk as it comes available, or to feed by an intravenous route. Early enteral feeding and advancement are not risk factors for necrotizing enterocolitis.[14–16] Trophic feeding may be introduced when full enteral tolerance cannot be achieved, and it may accelerate the achievement of full feeding.[16,17] Where intravenous feeding is unavoidable, amino acids and lipids should be introduced as soon as these are available in fully supportive quantities.[12,18,19]

6. Ongoing care and preparation for discharge

Safe discharge of late preterm infants has been addressed in reviews[20,21] but including moderate premature infants requires the consideration of an expanded profile of precedent conditions. Despite the greatly increased morbidity of the late preterm as compared with the term infant[20,22] there is still a considerable proportion of infants who appear sufficiently stable at birth to be managed in a low risk newborn nursery and discharged according

to protocols offered to healthy term infants. Discharges at 2–5 days of age can be characterized as 'low risk' newborn discharges; in recent years there has been an increase in discharges within 2 days (and sometimes within hours) of birth. These have been termed 'early' discharges. To qualify for early discharge American[23] and Canadian[24] guidelines specify that an infant must be term (i.e. ≥37 weeks' gestation). British guidelines do not apply this limitation to early discharge,[25] preferring instead to stress the individualized decision-making for all mother–infant dyads concerning discharge.

Infants who experienced some of the morbidities of prematurity, such as respiratory distress, cannot be discharged until their requirements for intensive care support have been addressed.

Moderate preterm infants, even if free of otherwise serious morbidity of prematurity, do not qualify for 'low risk' newborn discharges and will always have to be demonstrably physiologically stable enough for the home environment. Guidelines specific to this group of infants are not available, but may be adapted from those made for smaller infants.[26,27] Infants born at 32–34 weeks tend to go home before due date, as they have had time to recover from early complications and opportunities for early feeding and parental planning can be addressed.[28]

7. Conditions required for discharge

Conditions for discharge include infant, community and family factors. Preterm infants must be breathing room air without respiratory embarrassment or interruption, feeding adequately to establish and maintain weight gain, and capable of maintaining thermal homeostasis without stress in the receiving environment. These achievements depend in part on physiological maturation, and they tend to mature together in individual infants.[29] A further condition, which applies to late preterm infants who may qualify for 'term' discharge, is that the metabolic adaptations of early postnatal life are either complete or provided for.

8. Resolution of jaundice

All newborn infants should now be screened for hyperbilirubinemia, but current guidelines address late preterm but not moderate premature infants.[30] Phototherapy is very effective at reducing high levels of bilirubin and has few adverse effects,[31] but it disturbs maternal access and impedes nursing care. Unless there are clear indications to the contrary (such as established hemolysis or early jaundice) bilirubin measurements should be made when phototherapy is likely to be effective and the predictive power of the test greatest (i.e. at >24 h of age).

The preterm infant has a slower rise in serum bilirubin than the term infant, reaching its peak at 4–9 days.[32] Moderate and late premature infants are at greater risk for kernicterus[33]; more conservative levels for phototherapy, currently undefined, should be used for these infants.[34] Moderate premature infants, with their more prolonged admissions, can more readily receive phototherapy, but the late preterm infant is at risk of discharge before the peak bilirubin has been reached or even before the bilirubin has risen to moderate risk values. Late preterm infants who are breastfeeding are at particular risk of kernicterus[35] or extreme hyperbilirubinemia,[36] and this complication can be avoided by ensuring adequate post-discharge supervision for all infants who are not known to be both free of jaundice and in a low risk category from earlier screening.

9. Maintenance of thermal homeostasis

Infants must be adapted to the thermal environment of the home to achieve a successful discharge. Several trials, combined in a Cochrane review,[37] have confirmed the feasibility of transfer of medically stable infants to a cot at 1600 g (as compared with 1800 g) for infants of ≥32 weeks' gestation. Furthermore, early transfer to a cot is associated with greater weight gain and earlier discharge. The larger and more recent of these trials[38,39] took place in nursery temperatures of 24 °C with humidities approaching 50%, with infants dressed in light clothing with single blankets. Possibly the reported increased weight gain reflects a more optimal self-regulated thermal environment for these dressed infants than is provided by an incubator. It is important not to exceed the thermal insulation described in these and other studies[40]; overbundling is associated with sudden infant death syndrome.[41]

Current guidelines for term infants cared for at home suggest that the infant should be lightly clothed for sleep,[40] and the room temperature should be kept comfortable for a lightly clothed adult.[42]

10. Establishment of feeding to discharge

Enteral feeding is often delayed by respiratory and other illnesses. Late and moderate preterm babies may retain the premature patterns of poor suck, swallow and breathing coordination,[43] as well as reflux or poor satiety associated with slow gastric emptying.[44] Staged, timed introduction of scheduled feeds of predetermined volume has traditionally been achieved by prolonged gavage feeding. There is now substantial evidence that early maturation of sucking may be accelerated by the early cue-based introduction of suckling feeding 'on demand' (where the infant controls the timing) and 'ad libitum' (where the infant controls the amount).[45] The skilled recognition of and response to infant signs of hunger and satiety can result in successful infant-cued feeding at or before 32 weeks' gestation and a shortened length of stay.[46] Non-nutritive sucking may be used as either a tool for cue recognition or as an infant training technique and may also contribute to the earlier establishment of feeding.[47] For breastfeeding infants, a staged sequence from feeding expressed milk by gavage or bottle may be safely combined with early breast nippling to achieve early infant-cued and maternally responsive breast-nipple feeding.

11. Goals and content of feeding

The practice of staged increases in feeds in the first week to life to achieve a goal of 150 ml/kg/day have changed little from the original 2½ oz/lb/day from which this number was derived. Models of ideal postnatal weight gain are based on estimates of fetal growth combined with growth rates of healthy term infants.[11,48] From 32 to 50 weeks postconceptional age (pca) these idealized weight gains can be approximated by a daily weight gain of 30 g/day. Weight gain is close to linear, despite feeding being increased on a per bodyweight basis, because the energy and nutrient costs of weight gain increase with postnatal age.[11,49,50] Matching the fetal rate of weight gain may not be enough, as this does not compensate for the prolonged postnatal delay in weight gain experienced by the more preterm infants, who may, despite establishing 'adequate' rates of weight gain, be discharged below the tenth centile for weight at discharge.[11–13] This 'postnatal growth restriction' can only be addressed by strategies designed to increase nutrient intake to the maximum tolerated.[50] Recommended protein intakes for infants >1200 g are ≥3.6 g/kg/day with a protein:energy ratio of 2.8.[11] Strategies for achieving these goals include fortification of human milk with commercial fortifiers, the use of high nutrient preterm formulas, and the addition of protein sources to the limit of metabolic tolerance, as defined by urea levels.[51] Weight gain goals of ≥35 g/day may be achieved with such strategies. Some concern has been addressed that rapid weight gain in infancy is associated with adverse outcomes in adult life[52]; clarification of this

dilemma must await further long term follow-up of early feeding trials, but as previous enriched nutritional intervention was predominantly focused on increased energy intake, resulting in excess growth of fat mass,[53] it may be that re-establishing lean body mass with high protein:energy and phosphate:energy ratios will address this concern.

12. Feeding beyond discharge

Full enteral feeding is generally a prerequisite for discharge, although in specific circumstances infants may be discharged with gavage feeds.[54] In most circumstances safe tolerance and retention of feeds and at least a reasonable expectation of weight gain are requirements for discharge home. High nutrient post-discharge formulas are available,[55,56] as are human milk fortifiers[57]; their use has not been fully evaluated or compared to a strategy of fully liberalizing infant intake to demand.[58]

13. Respiratory stability

Respiratory stability depends on complete recovery from respiratory illness and the absence of apnea of prematurity. Well preterm and term infants have median pulse oximetry readings in excess of 97% after the first days of life[59,60] (partly because pulse oximeters may read errantly high in the range 97–100%). When additional oxygen therapy has been withdrawn, oximetry readings should be $\geq$93% when the infant is asleep or quietly awake in room air for a least one night prior to discharge.[61]

14. Apnea of prematurity

Apnea of prematurity increases in frequency and severity with decreasing gestational[62] and postconceptional age,[63] and is a particular component of discharge planning for the moderate preterm. Apnea may persist well beyond term,[29] but this phenomenon is far more common in very premature infants and rare for infants born at or after 32 weeks' gestation.[63,64] The required apnea/bradycardia-free interval that safely defines this period has been estimated conservatively at 8 days[64] where apnea is defined as apnea for >20 s, bradycardia <60 bpm or oxygen saturation of <80%, not provoked by feeding. Infants who have apnea of increasing frequency or a new episode beyond an 8-day apnea-free interval are likely to be manifesting new illnesses, such as infection.[64] There is a reassuring tendency for apnea for all infants to resolve by 44 weeks' pca.[65] Apnea at home is a frightening event which usually leads to emergency readmission, but it rarely results in mortality and does not appear to be a predictor of sudden infant death syndrome.[65,66] Families should be so reassured and instructed on the simple stimulatory techniques required to resolve such an event; their knowledge of access to emergency services should be reviewed on discharge. Caffeine has been used on an ambulatory basis, but its discontinuation may require readmission for monitoring.[26,67]

15. Resources for care: transition between hospital and home resources

The resources that are provided by ongoing hospitalization of an infant are facility-based, health profession-based and physician-based; discharge may take place when these are no longer required. Health profession support includes individualized expert patient care from nursing and allied health professions. The physician, in most systems, provides medical expertise as intermittent care, and generally bears the responsibility for the decision to discharge to the community. Expert continuous nursing care and observation is the cornerstone of evaluation of readiness for discharge. The community, on the other hand, generally includes a highly variable (but often superior) home environment, family care which may be continuous, community health resources which can be intermittent, and physician resources which require access and often transport.

A supportive home environment is an opportunity for earlier discharge which should be seized. The convalescent preterm infant is at increased risk of infection, but more so of serious nosocomial bacterial infection in a hospital nursery than of a sibling-acquired viral infection in a well-managed home. Continuous observation of the infant may be more effectively and reliably conducted (and reported) by a parent supported by an extended family than by a nurse sharing responsibilities with other sicker infants and working intermittent shifts. Marked improvements in feeding may follow discharge.[68]

Merritt et al.[25,69] have critically reviewed strategies for effecting safe, early discharge of very low birth weight infants that can be applied to moderate and late preterm infants. Parent involvement, empowerment and education[70] can and should be used to reduce the length of hospital stay where the opportunity arises.

16. Anticipating discharge

Safe discharge of a healthy infant is the primary goal of neonatal care, and plans should be clear and documented from admission. Parents should be expected to plan for discharge home from the time of birth, and this date should be estimated with them soon after admission; if there are uncertainties, these should be explicit and the estimation repeatedly adjusted. Planning for discharge following premature birth is more difficult for parents than it is for institutions, as it may involve adjustment of parental leave, changes in domestic planning, recruitment of family support, earlier acquisition of baby needs, and changes or improvements to housing. Maternal medical needs, twins or other multiples, and parental separation or discord may further impede timely discharge. A nurse discharge specialist or team can evaluate and address parenting skills and confidence, community resources, and access to health care and resources. These evaluations and arrangements are time-consuming and require excellent coordination and communication skills, but may be expected to be cost-effective.[69]

Attention must be paid to the safe transport of the infant to the community. Recommendations for car seat use for premature infants should be applied.[26]

17. Types of discharge

Hospital discharge may take the following forms:

1. Complete discharge home with support from local community care services (health visitors, family doctor appointments).
2. Provisional discharge home with ongoing daily management by hospital personnel, which may include daily blood testing and management (for example, in hyperbilirubinemia or anemia) or monitoring (e.g. weight gain).
3. Suspended discharge, where a hospital admission ('bed') is maintained for the infant who goes home 'on a pass', usually with a daily return for evaluation or care. The hospital staff retains the responsibility although not the direct administration of infant care.
4. Rooming in or placing the baby under family care in accommodation within the hospital, supervised by hospital staff, is an important step in evaluating and managing the infant with the family outside the directly monitored environment of the nursery.

Institutions should recognize and develop flexibility in discharge arrangements with a view to making opportunities for safe, earlier but sometimes graduated discharge available. The following is a list of requirements for safe discharge of the moderate or late preterm infant, modified from a plan for the very low birth weight infant.[26]

1. Sustained or anticipated weight gain sufficient to attain antenatal growth expectations.
2. Stable feeding and infant cue-driven feeding patterns.
3. Stable temperature when lightly clothed at room temperature.
4. A scheduled immunization plan.
5. Nutritional supplementation, where indicated, to include iron, vitamin D or fortification.
6. Review of requirements for retinal fundoscopy (generally limited to infants of $\leq$32 weeks' gestation).
7. Written copy of discharge summary for parents to share with medical care services.
8. Satisfactory evaluation of, or education of, parenting skills.
9. Review of medications with parents.
10. Home environment evaluation and availability of community support services.
11. Community-based home or office assessment within 48 h of discharge.

Practice points

- Moderate and late preterm infants are increasingly vulnerable to disorders of prematurity with decreasing gestational age.
- An individualized approach to care (expecting different babies to respond in different ways) leads to safe, earlier discharge in selected infants.
- Otherwise-healthy preterm babies should be evaluated at 1600 g for selected transfer from an incubator to a cot.
- Otherwise-healthy preterm babies should be evaluated early for early oral feeding and satiety cuing; selected infants may be nipple fed from 32 weeks on.
- Some stable preterm babies will do better at home and be safer and more successfully fed than in a nursery environment.
- Individual review of metabolic tolerance should be used to maximize and optimize nutrient intakes to achieve weight gains sufficient to compensate for the postnatal malnutrition of the premature.
- Discharge plans and expectations should be shared with parents and community resources from the day of admission.
- Discharge, and preparation for discharge, may take many forms and should be flexible, with easy recourse to readmission or to suspended discharge schemes.

Research directions

- More on cue-based feeding: does recognition of early satiety signals lead to better weight gain or avoidance of later onset obesity or metabolic syndrome?
- Does early servocontrol lead to earlier or later successful response to transfer from incubator to cot?
- What are the long term neurodevelopmental and physical health outcomes of early aggressive adaptive feeding of the preterm newborn?
- Is the body composition of the preterm newborn at term due date predictive of body habitus in later childhood?
- Can we safely identify full vascularization of the preterm retina? If so, can we release our restraints on higher levels of oxygen in respiratory therapy?
- How effective is replacement of breast milk with formula in the treatment of prolonged hyperbilirubinemia in the breast-fed, late preterm infant?
- When should phototherapy be applied or discontinued in the prevention of exchange transfusion or kernicterus in otherwise-healthy preterm infants?
- Are blood glucose levels in otherwise-healthy preterm infants predictive of anything, and should they be treated?

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