Policies and Practice in Neonatal Nursing Related to Nutrition

EVA-LOTTA FUNKQUIST
Dissertation presented at Uppsala University to be publicly examined in Rosén-salen, Akademiska sjukhuset, ing 95/96, Uppsala, Friday, October 29, 2010 at 09:15 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

The aim of these studies was to increase knowledge about hospital feeding routines in high-risk neonates. A retrospective medical chart review procedure was used to study routines at the neonatal units of two Swedish hospitals. In Papers I and II, the sample (Uppsala n=21 and Umeå n=21) comprised of small for gestational age (SGA) infants, in Papers III (Uppsala n=64 and Umeå n=59) and IV (n=127), the samples comprised of appropriate for gestational age (AGA) infants.

Paper I indicated large enteral/oral milk volumes rendered i.v. administration of glucose unnecessary, reduced weight loss and helped SGA infants regain birth weight earlier. More rapid postnatal growth did not remain up to 18 months with corrected age in any growth variable (Paper II).

In Paper III, effects were compared whether the infants’ volume of breast milk intake in hospital was estimated by “clinical indices” or determined by test-weighing. Infants treated in hospitals where test-weighing was practised attained exclusive breastfeeding at an earlier postmenstrual age (PMA), and they were discharged at an earlier PMA. However, the two study units were similar regarding the proportion of infants attaining exclusive breastfeeding. Paper IV revealed preterm AGA infants with higher standard deviation scores (SDS) at birth had more negative changes from birth to discharge for all growth variables.

Conclusions: Papers I and II indicated that early initiation of enteral/oral feeding with proactive increases in milk volume was beneficial short term. No evidence was found for a proactive nutrition regimen with initial large volumes of milk resulting in a different pattern of growth up to the corrected age of 18 months. Test-weighing before and after breastfeeding might help infants to attain exclusive breastfeeding at an earlier PMA (study III). Finally, preterm AGA infants with higher SDS at birth are at higher risk of inadequate growth during their hospital stay (study IV).

Keywords: breastfeeding, nutrition, preterm infants, SGA

Eva-Lotta Funkquist, Uppsala University, SE-75185 Uppsala, Sweden. Department of Women's and Children's Health, Pediatrics, Akademiska barnsjukhuset, ing. 95 nbv, Uppsala University, Uppsala, Sweden.

© Eva-Lotta Funkquist 2010

ISSN 1651-6206
ISBN 978-91-554-7894-0
urn:nbn:se:uu:diva-130316 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-130316)
Men Lovis stod där lugn. Hon tog barnet ifrån honom och la det till sitt bröst, och sedan var där ingen gråt mer.

_Ur Ronja Rövardotter av Astrid Lindgren_
List of studies

This thesis is based on the following studies. The studies are referred to in the text by the Roman numerals.


IV  Funkquist E-L, Tuvemo T, Jonsson B, Serenius F, Nyqvist KH. Preterm appropriate for gestational age infants: size at birth explains subsequent growth (accepted for publication in *Acta Paediatrica*).
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA</td>
<td>appropriate for gestational age</td>
</tr>
<tr>
<td>CPAP</td>
<td>continuous positive airway pressure</td>
</tr>
<tr>
<td>GA</td>
<td>gestational age</td>
</tr>
<tr>
<td>HC</td>
<td>head circumference</td>
</tr>
<tr>
<td>IUGR</td>
<td>intra-uterine growth retardation/restriction</td>
</tr>
<tr>
<td>NEC</td>
<td>necrotising enterocolitis</td>
</tr>
<tr>
<td>PMA</td>
<td>postmenstrual age</td>
</tr>
<tr>
<td>PNA</td>
<td>postnatal age</td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
</tr>
<tr>
<td>SDS</td>
<td>standard deviation score</td>
</tr>
<tr>
<td>SGA</td>
<td>small for gestational age</td>
</tr>
<tr>
<td>VLBW</td>
<td>very low birth weight</td>
</tr>
</tbody>
</table>
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>9</td>
</tr>
<tr>
<td>Being born preterm</td>
<td>9</td>
</tr>
<tr>
<td>Being born SGA or IUGR</td>
<td>9</td>
</tr>
<tr>
<td>Extra-uterine growth retardation</td>
<td>10</td>
</tr>
<tr>
<td>Being born both SGA and preterm</td>
<td>10</td>
</tr>
<tr>
<td>Regimens for enteral feeding in neonatal care</td>
<td>11</td>
</tr>
<tr>
<td>Nutrition and growth among preterm infants</td>
<td>11</td>
</tr>
<tr>
<td>“Catch-up”, good or bad?</td>
<td>12</td>
</tr>
<tr>
<td>Breastfeeding in Sweden</td>
<td>13</td>
</tr>
<tr>
<td>Benefits of breast milk feeding for high-risk neonates</td>
<td>13</td>
</tr>
<tr>
<td>Breastfeeding in neonatal care – a challenge</td>
<td>14</td>
</tr>
<tr>
<td>Evidence-based support for breastfeeding of high risk neonates</td>
<td>15</td>
</tr>
<tr>
<td>Breast milk expression</td>
<td>15</td>
</tr>
<tr>
<td>Early permissive breastfeeding support</td>
<td>15</td>
</tr>
<tr>
<td>Kangaroo Mother Care</td>
<td>15</td>
</tr>
<tr>
<td>Supplementation strategies</td>
<td>15</td>
</tr>
<tr>
<td>Nipple shield</td>
<td>16</td>
</tr>
<tr>
<td>Test-weighing</td>
<td>16</td>
</tr>
<tr>
<td>Westernised caretaking style</td>
<td>16</td>
</tr>
<tr>
<td>Discourse – the truth-telling of a phenomenon</td>
<td>17</td>
</tr>
<tr>
<td>Professionals still have underlying conceptions</td>
<td>18</td>
</tr>
<tr>
<td>Research problems</td>
<td>19</td>
</tr>
<tr>
<td>Aims</td>
<td>21</td>
</tr>
<tr>
<td>The specific aims</td>
<td>21</td>
</tr>
<tr>
<td>Materials and methods</td>
<td>23</td>
</tr>
<tr>
<td>Subjects</td>
<td>23</td>
</tr>
<tr>
<td>Studies I and II</td>
<td>23</td>
</tr>
<tr>
<td>Studies III and IV</td>
<td>24</td>
</tr>
<tr>
<td>Ethics</td>
<td>24</td>
</tr>
<tr>
<td>Design</td>
<td>24</td>
</tr>
<tr>
<td>Infant and maternal data</td>
<td>25</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>25</td>
</tr>
</tbody>
</table>
Background

Being born preterm
The WHO definition of being preterm is birth before 37 weeks of gestation. Between 5% (in developed countries) and 25% (in developing countries) of all infants are born preterm [1]. Preterm deliveries are often subdivided into: extremely preterm (<28 weeks), very preterm (28–31 weeks), moderately preterm (32–33 weeks), and late preterm (34–36 weeks) [2].

Being born SGA or IUGR
There are several definitions of being born small for gestational age (SGA). One common definition is birth weight and/or length below the 10th percentile [3]. Another definition is birth weight and/or birth length below -2 standard deviations (SD) for gestational age (GA) [4]. Being born SGA does not mean having suffered intra-uterine growth retardation (IUGR), even though these terms are often used interchangeably. For IUGR infants, the full in utero growth potential was not achieved, whereas, SGA infants might be genetically small and yet never have suffered foetal malnutrition [5].

SGA infants can be divided into two different types. Type I have suffered malnutrition early in pregnancy and are symmetrically small. These infants will remain light and short and will not score well in mental development tests [6]. Ninety percent of SGA infants are type II and appear to have reversible growth retardation. They are asymmetrically small and will catch-up postnatally, if given adequate nutrition [7].

IUGR can lead to a series of endocrinological, metabolic, and physiological adaptations that allow the foetus to survive [8]. This foetal adaptation to malnutrition appears associated with an increased risk of developing the metabolic syndrome, which includes insulin resistance, glucose intolerance, dyslipidaemia, and hypertension [9]. Barker’s et al [10] findings suggest that these survival mechanisms are associated with increased risk of death from coronary heart disease, whereas, some studies indicate even stronger association with continued poor weight gain during the first year of life [10, 11].
Extra-uterine growth retardation

Postnatal growth failure in preterm infants is described as a universal problem [12]. When discharged from hospital, many preterm infants show extra-uterine growth retardation for the parameters weight, length and head circumference (HC). Infants born with low GA and critically ill are more growth restricted [13]. This malnutrition is hypothesized to increase the risk of developing the metabolic syndrome. Children, born preterm, but not SGA, have for instance a reduction in insulin sensitivity [14] and young men are at risk of high blood pressure if born at a low GA [15]. Although avoiding extra-uterine growth retardation appears a worthwhile goal, teenagers, born preterm and given high-nutrient preterm formula early in life, are often more insulin resistant than preterm infants given a lower nutrient diet [16]. Breast milk feeding protects against the metabolic syndrome (also among preterm infants) possibly due to the slower growth in breast fed infants [17].

Being born both SGA and preterm

Infants born preterm have often suffered poor intrauterine growth [18]. Moreover, infants who suffer poor intrauterine growth more often experience perinatal problems [19]. Therefore, it is hard to know whether poor growth and poor neuro-cognitive outcomes within this group are due to illness severity after preterm birth or due to poor intrauterine growth. Some authors claim neonatal complications may have a larger detrimental effect on cognitive development of preterm infants, than being born SGA or appropriate for gestational age (AGA). In one study [20], very low birth weight (VLBW) for GA was not associated with increased risk of low intellectual performance. In contrast, the same study indicated low birth weight constitutes an increased risk for low intellectual performance among infants born term [20]. Moreover, infants born preterm can show poor postnatal weight gain, but accelerated head growth [21].

When infants are born preterm, growth in length and HC appears important for later intellectual performance; therefore, high-energy nutrient intake for SGA preterm infants is often suggested for promoting HC catch-up growth and for preventing negative consequences of under nutrition [22]. Infants born both SGA and preterm are thin, but appear at risk of increased adiposity immediately after birth. Therefore, quality of growth, rather than weight gain might be an important issue for these infants [23].
Regimens for enteral feeding in neonatal care

Despite the common practice of applying a 3-hourly feeding schedule in neonatal care, scientific support for this practice is lacking [24]. It may be assumed more frequent feeds could be advantageous, as this is similar to the specific human breastfeeding pattern, which means feeding frequency up to several times an hour [25, 26]. Preterm VLBW infants who are initially fed continuously with nasogastric tube display better growth rate than infants fed according to a 3-hourly schedule [27]. Moreover, preterm infants can be completely breastfed with an adequate weight gain at a low postmenstrual age (PMA), if semi-demand/ frequent breastfeeding is practiced [28].

There is a lack of consensus on appropriate feeding volumes. One commonly suggested measure for full enteral/oral feeding with formula or breast milk is 150–180 ml/kg and day from when the infant is 9 days old [29-32]: this measure has remained basically unchanged during recent decades. Even though it is often claimed infants born SGA have a greater energy requirement than AGA infants, there is no consensus regarding a desirable norm for feeding volumes, even for these infants. One suggested measure is 200 ml/kg, but not until the infant is 14 days old [30]. A reason for this strategy may be that SGA infants are less tolerant to enteral feeding than AGA infants are [33, 34] and that the concern increasing feeding volumes could cause necrotising enterocolitis (NEC) [35]. However, it is still unclear which specific feeding strategies affect the risk of NEC [36].

Nutrition and growth among preterm infants

Measurements of growth include weight, length and HC. Even though weight gain is a poor indicator for growth, as it provides no information about body composition, it is the most commonly used method. However, optimal growth for the preterm infant remains undefined. Postnatal growth among these infants is often compared with foetal intrauterine growth and a common target for weight gain during the 3rd trimester is 15 g/kg/day [37]. However, this might be unrealistic, as preterm birth is often the end result of a complicated pregnancy and preterm infants are often small and ill [12]. It has been advocated that all preterm infants develop postnatal growth failure during the first weeks of life [38].

The addition of protein to breast milk appears to contribute to more rapid growth among VLBW infants, whereas fat supplementation does not appear to influence growth [39]. Better linear catch-up growth in SGA infants has been found in infants given protein-enriched formulas [40]. It is generally agreed human milk requires enrichment with protein when given to VLBW infants [41] and analysis of the mother’s own milk is recommended due to
large variation in the inter- and intrapersonal concentration of protein and fat [42].

Experts focus much attention on the effects of nutrient-enriched feedings on infants’ growth and development. Infants fed with expressed human milk, fortified with calories, protein and minerals have increased growth during hospital stay [43]. However, there is a lack of randomised studies on breastfed preterm infants’ growth and development versus preterm infants fed with fortified breast milk [44] or enriched formulas [45] after discharge. Furthermore, experts also conclude there is no strong evidence for the positive effects of nutrient-enriched formulas after discharge on growth rates or development during the first 18 months post-term [46]. At the same time, unfortified human breast milk may not be appropriate nutrition for preterm infants, as breastfed infants have shown poorer weight gain than formula fed infants after discharge [47]. Nevertheless, there is evidence from low income countries that preterm infants, who were exclusively breastfed, have attained weight comparable to intra-uterine growth rates [48-50].

“Catch-up”, good or bad?

Catch-up means increase towards the population mean in weight, length or HC. Barker et al. concluded in 1989 [10] that increasing weight gain during the first year of life could prevent the development of ischemic heart disease in men in later life. However, this conclusion has been challenged, and other researchers advocate caution in interpreting rapid growth per se as a positive result because diets promoting faster neonatal growth increase the risk for later cardiovascular disease [16]. Weight “catch-up” in childhood may be a part of the metabolic syndrome leading to type 2 diabetes, high blood pressure and overweight later in life [51, 52]. It has been suggested the costs for the offspring are especially marked if nutrition improves after birth [53].

However, another, outwardly controversial finding, the so-called linear catch-up growth of children born SGA (who are not given growth promotion nutrition) is associated with a lower risk of overweight, and not associated with an increased risk of high blood pressure [54].

Lucas [55] concludes breast milk provides protection against the metabolic syndrome, but raised the question of why. Lucas and Singhal speculates the reason may be that infants with breast milk as their source of nutrition gain weight more slowly thereby, acquiring protection against the metabolic syndrome [55, 56]. In the study in which Barker et al. demonstrated an association between high weight gain during the first year of life and protection against early death in cardiovascular illness, a very high proportion of the sample had been breastfed (92%), and the protection was better in individuals who had been breastfed [10]. However, this sample also consisted of infants who, by current diagnostic criteria, had not suffered
intrauterine growth retardation. It is possible rapid weight gain in these children during their first year of life is associated with advantages related to health later on in life.

There is evidence early diet might influence later performance in developmental tests. Breastfeeding is for instance associated with higher scores for infants’ cognitive development than formula feeding [57]. For preterm neonates, better psychomotor development, is observed among those given early growth promotion nutrition [58]. This effect has not been determined for term SGA infants [59]. Instead, SGA infants with linear catch-up growth (but not given growth promotion nutrition) present better intellectual performance as young adults [60].

Breastfeeding in Sweden

The World Health Organization (WHO) defines a goal for breastfeeding, with the aim of supporting children’s optimal growth, development and health. Infants should be exclusively breastfed for 6 months and thereafter, receive complementary foods while breastfeeding up to two years of age or beyond [61]. In Sweden, the goal is defined as exclusive breastfeeding for 6 months and thereafter, up to one year or beyond. However, there are no international or Swedish national guidelines for optimal breastfeeding of preterm or SGA infants.

Sweden can be defined as a breastfeeding culture. Most people have a positive attitude to breastfeeding and during the study period approximately 90% of all infants were fully breastfed at the age of one week and approximately 75% (at the age of 2 months), 60% (at 4 months), and 15% (at 6 months) were being fully breastfed [62]. This general positive attitude towards breastfeeding can be attributed to several circumstances in the Swedish society. For instance, Swedish mothers are entitled to leave of absence from work, with 80% of their salary, for about a year after the child’s birth. Furthermore, all hospitals were certified as “Baby-Friendly” between 1992 and 1995 and although the Baby-Friendly Hospitals Initiative is targeted at mothers of healthy full-term infants, there appears to be “spill-over effects” in neonatal care [63].

Benefits of breast milk feeding for high-risk neonates

For the mother, the ability to supply her own milk to a critically ill preterm infant may be an important psychological experience that enhances bonding. Mothers who breastfeed their preterm infant consider it a rewarding experience that outweighs the effort [64].
In the western society, mothers who elect to breastfeed, and do so successfully, form a socially privileged subgroup and this might influence the results in studies on the effects of breastfeeding. However, preterm infants’ intake of nutrients is strictly monitored and is not always dependant on successful breastfeeding.

Feeding with breast milk is associated with many benefits of particular importance for preterm infants. For instance, lower rates of infections, sepsis and meningitis [65], NEC [66], and retinopathy of prematurity [67] are reported. Breast milk may also reduce the risk of allergic disease among these infants [68].

After adjustment for parental factors, breastfeeding is associated with higher scores for infants’ cognitive development than formula feeding [57]. Preterm infants are born at a stage of rapid brain growth. Data from studies on this subgroup also indicate a beneficial effect of human milk on neurodevelopment [69]. Moreover, the beneficial effects of breast milk for cognitive development also apply to term SGA infants [59].

Lucas [55] concludes breast milk provides protection against the metabolic syndrome. A lower proportion of infants born preterm who received expressed breast milk developed this syndrome than preterm infants who never received breast milk. Breast milk feeding during a short period, such as a one month, makes a difference. There is a dose-response effect: the more breast milk, the better protection is.

Breastfeeding in neonatal care – a challenge

Even though it is important, breastfeeding is maintained to a lower extent among infants born preterm or/and SGA [70-72]. Successful breastfeeding is possible in these groups [73], but presents unique challenges [72, 74]. The mother must establish and maintain milk production while feeling fear for the infant’s health and the transition from gavage/bottle or cup to breastfeeding. Preterm infants do not always take well to the breast and a common concern is whether the infant is taking enough milk at the breast. Aggressive feeding with high milk volumes, enriched breast milk or formulas can be hypothesised as exerting a negative influence on mothers’ emotional experience of breastfeeding. In industrialised, western societies, with a mechanistic notion of supplying nutrition via breastfeeding, it is common for mothers to be concerned regarding milk volumes and adequacy of breastfeeding [75, 76]. Supplementation on medical indications in postpartum wards does not appear to negatively affect breastfeeding, whereas, supplementation without any indication has negative effects [77].
Evidence-based support for breastfeeding of high risk neonates

Hospital feeding routines can be obstacles to successful breastfeeding. Conceivable support components for successful breastfeeding of high-risk neonates are described below.

Breast milk expression

Mothers of infants admitted for neonatal care should be supported in initiating breast milk expression 6 hours post delivery, and continue regular and frequent (seven times per 24 hours) expression. The most effective technique is to combine gentle manual massage with breast pump expression [78, 79].

Early permissive breastfeeding support

Nutritive sucking, verified by test-weighing, has been observed in infants as early as 30 weeks GA [73]. Therefore, guidelines for initiation of breastfeeding in preterm infants should be based on cardio-respiratory stability rather than current PMA, postnatal age (PNA) or weight, and that a mature sucking pattern is not necessary for achievement of full breastfeeding [73]. Moreover, in another study [80], the breastfeeding experience, rather than maturity, appeared to play a role in preterm infants’ suckling behaviour.

Kangaroo Mother Care

In the Kangaroo Mother Care method, which was launched in Colombia 1978, breastfeeding together with skin-to-skin contact are key components [81]. Settings that utilise this method for low birth weight infants have high breastfeeding rates at discharge [82].

Supplementation strategies

For stable preterm infants, cup feeding is possible from about 29 weeks [83]. As exclusion of bottle feeding is a recommendation for the transition from full enteral feeding to breastfeeding, cup feeding can be considered as the first choice when the infant does not take enough milk from the breast [84]. However, because of the infant’s illness, milk is often initially given by tube, and the presence of an indwelling feeding tube is associated with smaller volumes of milk intake when infant is fed orally [85]. Therefore, breastfeeding establishment in infants, in need of some tube feeding, might be enhanced by insertion and removal of a new tube for occasional intermittent supplementation.
Nipple shield

Preterm infants with difficulties in latching on to or staying fixed at the breast can be helped if the mother uses a nipple shield when breastfeeding. Milk consumption increases with the use of a nipple shield through helping the infant to stay awake long enough at the breast and by acting as a milk collector [86].

Test-weighing

In one study [87], test-weighing with electronic scales before and after breastfeeding was found to be a reliable method for assessing infant milk intake. However, in another study [88], electronic scales were found to be too imprecise for assessing milk intake in infants. Nevertheless, in some neonatal units, this method is used until full breastfeeding is established, as staff consider it important to have control of the volume of breastfed infants’ milk intake [89, 90]. An alternative strategy is “clinical indices”, commonly defined as the determination of the milk volume ingested by observing the suckling behaviour of the infant and the reduced distension of the breast after nursing. However, this method is unreliable and it is impossible for nursing staff and mothers to accurately assess the infants’ milk intake through merely making a breastfeeding observation based on the so called “clinical indices” [91].

One argument against the use of test-weighing is the common assumption among nursing staff that test-weighing is stressful for mothers; therefore, this method should not be applied as a routine. However, in a comparison of mothers applying test-weighing during the transition to full breastfeeding with mothers who did not, no differences were determined in mothers’ confidence in their ability to attain well-functioning breastfeeding [92].

Another argument against test-weighing is that mothers look forward to the experience of breastfeeding as times of closeness and reciprocity, not merely as a means for feeding the infant. A focus on the volume of milk intake through scheduled breastfeeding and test-weighing before and after breastfeeding, constitute additional risks for making breastfeeding appear as a fulfilment of a duty and associated with feelings of guilt and shame if the duty cannot be fulfilled successfully [93].

Westernised caretaking style

When the emergence of modern medicine, authorities began to show interest in controlling how mothers took care of their children. With the acceptance of the principles of asepsis towards the end of the 19th century, physicians made efforts to apply the principles of a healthy lifestyle to infants and
breastfeeding [94]. Breastfeeding was one of several components in children’s upbringing that paediatricians considered should be regulated. After an international conference (the Milk Drop Conference) in Brussels in 1907, Swedish paediatricians disseminated the recommendation that mothers should nurse their children five times a day, at fixed hours: 6 and 10 am and 2, 6, and 10 pm [94].

The idea that women ought to regulate breastfeeding and the fact that this practice became reality can be understood from a philosophical perspective. In his book "Discipline and punish", the philosopher Michel Foucault [95] describes his view of how the discipline of citizens in Western societies has changed. His conclusions can be summarised as follows: up to the 17th and 18th centuries, punishment in the judicial system was extremely cruel and based on the principle of retribution. When such methods of punishment no longer succeeded in controlling popular unrest, the nature of penalties changed. Imprisonment evolved as a method of controlling the citizens. A new doctrine of discipline emerged as a combination of the sciences of penalties, mental phenomena, and education.

According to Foucault, this doctrine of discipline permeates the entire Western society. In modern society, the previous method of control, based on forcible management and severe sanctions, has been replaced by a carefully thought-out method for managing an organisation. The prison concept has become the model for the whole of society. In the same way as prisoners are separated from the surroundings and placed in prisons, children are placed in schools and sick people in hospitals etc. The power exercised is total and multidimensional. The time of the subordinate persons is regulated in detail. The older method of management for attaining discipline was brutal, but, as Foucault suggests, at the same time it allows a certain degree of freedom. However, this does not influence everybody and as it is oppressive, it brings forth resistance and empathy for the oppressed.

Discourse – the truth-telling of a phenomenon

Foucault’s criticism of science is radical [96]. According to his opinion, science creates the order needed to make it appear as truth by forming alliances with other authorities. Foucault’s definition of “discourse” is: all statements which, when brought together, forms the idea of a phenomenon. Foucault argues if you want to scrutinise a discourse, you should not look for underlying meanings or intentions in what was said, on the contrary, you should ask why certain statements are made and others remain untold. Each separate, minute statement must be scrutinised, by examination of its agreement with other statements, of the conditions required for its existence, and which other statements it excludes. In this fashion, new associations and new forms of regularity will be discovered, which would not be discovered
by traditional methods of analysis. Foucault is of the opinion that every scientific discipline serves as a principle of control, ensuring what is produced inside its domain does not diverge from the mutually agreed scientific structure of opinions. In order for something to be “true”, it must be included in “the truth”, viz. “included in the discourse”.

Professionals still have underlying conceptions

Foucault’s ideas assist in comprehending some aspects of modern medicine. For instance, modern medicine actually disregards evidence concerning infant feeding. Children living in original cultures are breastfed according to a continuous suckling strategy, which means an average frequency of nursing of four times per hour, and weaning does not take place until the age of three or four years [26]. Up to the 19th century, childcare in Sweden was compatible with this intuitive socialisation. The care was directed at the child’s needs, and the child’s requirements of comfort and physical contact were met both on a conscious and a subconscious level [97]. The medicine breastfeeding discourse is still valid. In a study of inherent ideas on sleep and diet consultations [98], demand breastfeeding is defined as: infants are allowed to feed as often as they want (perhaps once an hour) during the first weeks after birth, but are expected to gradually develop a circadian rhythm with intervals between feeds of several hours during the night and three to four hours during the day. This pattern should preferably emerge spontaneously as a natural developmental process that is a component of the mother-child relationship. Once a more regular feeding regimen is established, the mother will have more time for other activities and life in general will become easier. One of the study participants described it as follows:

“If she has a child who still demands breastfeeding every hour it is very hard, but if the child more automatically passes into some type of self-regulation when the mother breastfeeds every three or four hours, and the mother likes this, and there are no great difficulties either during the night or the daytime, then there is no problem.” [98]: p. 141.

Selection of this perspective on breastfeeding pattern presupposes exclusion of other disciplines and disregard of scientific knowledge. The concept of scheduled breastfeeding is a culturally specific phenomenon that has only existed for a very brief time, and is only practiced among mothers with a westernised style of caretaking and may be one of several explanations why breastfeeding duration is short in many industrialised countries. In breastfeeding observations in African children, Konner and Worthman [26] found that breastfeeding frequency increased with increasing age of the child. During the 12 hours of observation, a boy at the age of 14 days
suckled 36 times and a boy at the age of 18 months 75 times. Although this feeding pattern may partly be explained by cultural differences, it also provides evidence breastfed children cannot be expected to show a predictable developmental pattern that ‘matures’ into feeding with intervals of 3-4 hours. The main opinion of the participating health care staff in the study on the way breastfeeding ought to be controlled [98] still concords with the opinions expressed by paediatricians several decades ago. The participants’ statements showed that one idea that has disappeared is that four-hour breastfeeding intervals contribute to making the child hardy, a common opinion several decades ago. The same participants emphasised empathy for the mother: they believed nobody can manage breastfeeding every other hour and that the mother has other tasks that need attending to. This is also an expression of the linear time concept. Time is something you can accumulate. It is hardly probable that a woman in earlier farming societies had fewer tasks to perform; however, her cyclical time concept explains why she did not think she could accumulate time by postponing tasks.

In contrast, paediatricians at the beginning of the 20th century were not of the opinion that a scheduled breastfeeding pattern would emerge automatically. The origin of the belief in such a pattern is found in a desire to solve social problems through child-rearing methods based on science and to contribute to the creation of the new and eagerly desired free, egoistic and fighting individual [94]. Policies developed by male paediatricians extinguished the female ‘silent knowledge’ about child rearing that developed at an early date and was passed from generation to generation. By stressing the importance of empathy for the mother in modern consulting, the component of overt coercion disappears. This is an important principle for the development of the disciplinary modern society in the sense that it makes the mother transform herself and her child in the desired direction through voluntary and active compliance with recommended activities. This regulated schedule formed the concept of “normality” in the breastfeeding pattern in modern society [98] and still influences how infants born preterm or SGA are fed in neonatal care. Biologically incongruent schedules have become the norm for both feeding volumes and feeding intervals [30, 99]. Thus, it is necessary to perform critical examinations of hospital feeding routines.

Research problems

- Evidence for appropriate feeding volumes for high-risk preterm and SGA neonates are lacking.
- Research on growth among high-risk neonates who are exclusively breast milk fed during hospital stays and after discharge is scare.
• Swedish hospitals apply various regimens for nutrition in connection with mothers' establishment of breastfeeding. Possible differences between hospitals in feeding progress, proportion of infants attaining exclusive breastfeeding, and weight patterns between infants treated according to different policies have not been investigated.

• Poor growth among preterm AGA infants during their hospital stay and throughout infancy appears to be universal problem and advances in neonatal care do not seemingly change this situation. However, preterm infants are a heterogeneous group and may have different nutrition requirements.
Aims

The overall aim of these studies was to increase knowledge of the effects of hospital feeding routines on successful breastfeeding and growth in high-risk neonates.

The specific aims

I  To evaluate the weight patterns of infants born SGA, related to two different feeding regimens during their stay in hospital.

II  To evaluate the growth during the first 18 months CA of life of infants born SGA, related to two different feeding regimens during the infants’ hospital stay.
   Research questions:
   1. Were there any differences in growth between SGA infants treated at two neonatal units that applied different feeding regimens during their hospital stay?
   2. Were there any differences in growth between SGA infants born at various gestational ages?

III  To compare effects on breastfeeding and weight gain of preterm infants, depending on whether the volume of breast milk intake when suckled in hospital was estimated by “clinical indices” or determined by test-weighing.
   Research questions:
   Were there any differences between infants treated at two neonatal units that applied test-weighing or did not apply test weighing as the basis for prescribing supplementation in:
   1. feeding progress?
   2. establishment of breastfeeding?
   3. weight-pattern before discharge?
   4. PNA and PMA and weight at discharge?
IV To evaluate growth up to 18 months corrected age among preterm AGA infants whose mothers initiated breastfeeding during the infants’ hospital stay.
Research questions:
1. What were the rates of loss in weight and in standard deviation scores (SDS) for weight, length and HC in the infants during their hospital stay and what factors explained these changes?
2. Which changes in SDS did these infants show in weight, length and HC from discharge up to a CA age of 18 months?
3. Did duration of breastfeeding affect the infants’ later growth?
Materials and methods

Subjects

The infants who participated in the four studies of this thesis were treated at the neonatal units at University Hospital, Uppsala, Sweden, and at the Norrland University Hospital in Umeå, Sweden. They were born in the catchment area, assessed by the attending neonatologist as need of neonatal care and discharged alive (Table 1). Eligibility criteria were absence of serious illness or congenital abnormality seriously affecting feeding tolerance, such as NEC, severe asphyxia, periventricular leucomalacia, intraventricular haemorrhage grades III and IV, severe cardiac illness, chronic lung disease or chromosomal abnormality. Furthermore, the infant should have a Swedish-speaking mother who intended to breastfeed. Determination of GA at birth was based on ultrasound examination at 16–18 weeks. Infants transferred to another hospital before discharge home were excluded.

Studies I and II

The sample comprised all SGA infants, born consecutively in Uppsala between December 2000 and November 2001, and in Umeå between December 2000 and May 2002, who were admitted to the neonatal intensive care unit of the respective hospital. Furthermore, the infant should not have received parenteral intra-venuous (i.v.) nutrition. Eight infants in Uppsala and seven infants in Umeå were excluded because of illness (six received parenteral i.v. nutrition in each hospital). A couple of twins in Uppsala were excluded because their mother did not speak Swedish and one infant in Umeå because the mother stated she did not want to breastfeed. One infant in each hospital had been given an incorrect SGA diagnosis but were retained as a borderline case of SGA. This generated a sample of 21 infants treated at the Uppsala neonatal unit and 21 infants in Umeå (Table 1). Of the 42 infants, 20 were born preterm (<37 weeks), 10 at each hospital.
Studies III and IV

The sample comprised all preterm AGA infants born consecutively at the two hospitals, between December 2000 and February 2002 (Uppsala), and between June 2000 and March 2002 (Umeå), who were admitted to the neonatal intensive care unit of the respective hospital. One infant in Uppsala was excluded because the mother did not speak/understand Swedish. Five infants in Uppsala and three in Umeå were excluded because the mother stated that she did not want to breastfeed. The criteria for inclusion in study III were GA over 28 and below 36 weeks. Three infants in Uppsala and six in Umeå were excluded because of illness. This generated a sample of 123 infants, 64 treated in Uppsala and 59 in Umeå. In study IV, an inclusion criterion was GA at birth below 36 weeks: five infants in Uppsala and eight in Umeå were excluded because of illness. This generated a sample of 127 infants, 67 treated in Uppsala and 60 in Umeå (Table 1).

Table 1. Study infants.

<table>
<thead>
<tr>
<th>Study</th>
<th>SGA or AGA born in hospital</th>
<th>Mother did not want to breastfeed</th>
<th>Excluded because of illness</th>
<th>Mother did not speak Swedish</th>
<th>Study infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>U* N**</td>
<td>U N</td>
<td>U N</td>
<td>U N</td>
<td>U N</td>
</tr>
<tr>
<td>Studies I and II</td>
<td>31 29</td>
<td>1 8</td>
<td>7 2</td>
<td>21 21</td>
<td></td>
</tr>
<tr>
<td>Study III</td>
<td>73 68</td>
<td>5 3</td>
<td>3 6</td>
<td>64 59</td>
<td></td>
</tr>
<tr>
<td>Study IV</td>
<td>78 71</td>
<td>5 3</td>
<td>5 8</td>
<td>67 60</td>
<td></td>
</tr>
</tbody>
</table>

* Uppsala University Hospital, ** Norrland University Hospital in Umeå

Ethics

The design and procedures were approved by the research ethics committees of the medical faculties at both Uppsala University (code: 01-492) and Umeå University (code: 01-380), Sweden.

Design

A retrospective, descriptive and comparative procedure was used to assess high-risk infants’ growth and the consequences of different nutritional regimens at the neonatal units of two Swedish hospitals: University Hospital in Uppsala and Norrland University Hospital in Umeå. The neonatal units were chosen because of the consistent medical care approach at each unit, with the exception of the nutrition interventions, which rendered comparisons possible.
Infant and maternal data

Relevant background data on mothers and information on infants’ growth and feeding during their stay in hospital were obtained by chart review of hospital medical records. Data on breastfeeding, supplementary feeding and growth after discharge from hospital were obtained through a questionnaire completed by the mothers when the infant was around two years old, and, in the case of unanswered questionnaires, from child health care medical records.

Statistical methods

For the statistical calculations, the Standard Statistical Package for Social Sciences (SPSS), versions 11–15, was used. The chi-square test, Fisher’s exact test, Student’s t-test and the Mann-Whitney U-test were used for inter-group comparisons. In correlation analyses, Spearman’s rho and Pearson correlation were used. Multiple linear stepwise backward and forward regression analysis was also applied. For testing within group changes, the Wilcoxon test was applied. The level of significance was set at \( p<0.05 \).

Growth charts

Infants were considered AGA if born with birth weight within two SD for GA, according to Marsal et al. [4] and SGA if they had a birth weight below \(-2\) SD. This reference is used in Sweden in clinical practice to determine adequacy of intrauterine growth. In studies II and III, Niklasson et al.’s [100] adjusted Swedish reference standards for size at birth were used to assess growth up to 40 weeks PMA, and in study II, Swedish reference standards were used for growth after 40 weeks PMA [101]. In study IV, Niklasson et al.’s [102] reference from the 24th week of gestation to 24 months chronological age was used to assess growth.

Outcome measurements

Growth

In study II, growth in SDS was studied during the infants’ hospital stay and at the corrected age of 40 weeks, and 2-, 4-, 6-, 12- and 18-months corrected age. In study IV, growth in SDS was studied during hospital stay and at the
corrected age of 40 weeks, 2-, 6- and 18-months. Windows for corrected ages (CA) are presented in Tables 2 and 3.

**Table 2.** Windows for CA, study II.

<table>
<thead>
<tr>
<th>CA</th>
<th>n</th>
<th>Range</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 weeks</td>
<td>42</td>
<td>38.43 to 42.71</td>
<td>40.43</td>
</tr>
<tr>
<td>2 months</td>
<td>41</td>
<td>1.2 to 3.1</td>
<td>2.1</td>
</tr>
<tr>
<td>4 months</td>
<td>38</td>
<td>2.9 to 5.3</td>
<td>4.2</td>
</tr>
<tr>
<td>6 months</td>
<td>40</td>
<td>5.1 to 7.4</td>
<td>6.3</td>
</tr>
<tr>
<td>12 months</td>
<td>39</td>
<td>9.8 to 14.4</td>
<td>11.9</td>
</tr>
<tr>
<td>18 months</td>
<td>34</td>
<td>15.2 to 24.5</td>
<td>18.2</td>
</tr>
</tbody>
</table>

**Table 3.** Windows for CA, study IV.

<table>
<thead>
<tr>
<th>CA</th>
<th>n</th>
<th>Range</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 weeks</td>
<td>125</td>
<td>37.89 to 42.14</td>
<td>40.00</td>
</tr>
<tr>
<td>2 months</td>
<td>125</td>
<td>1.1 to 2.9</td>
<td>2.0</td>
</tr>
<tr>
<td>6 months</td>
<td>116</td>
<td>5.0 to 6.9</td>
<td>5.9</td>
</tr>
<tr>
<td>18 months</td>
<td>87</td>
<td>15.2 to 20.8</td>
<td>17.3</td>
</tr>
</tbody>
</table>

**Milk volume**

In study I, the volume of milk and total volume of fluid during the first days of life was calculated from the medical records. In order to minimise the interruption in growth already started in utero, Uppsala hospital adopted a proactive nutrition policy. This stipulated that all term and preterm SGA infants, who could tolerate it, were to be prescribed a total daily volume of 100 mL/kg per day on the day of birth, 150 mL/kg on day 1, and 200 mL/kg on day 2. The latter daily volume was maintained until the infant reached what was considered by the attending neonatologist to be an adequate weight gain (usually 15–20 g/kg/day).

In Umeå hospital, the nutrition procedure was the same for all infants, including SGA infants: commencing with 65 mL/kg per day on the day of birth and gradually increasing to 170 mL/kg per day by day 9.

**Milk intake**

In study III, infants’ milk intake via breastfeeding was assessed in two different ways. At Uppsala hospital, all infants were test-weighed before and after breastfeeding. At Umeå hospital, the volume of ingested milk was assessed according to “clinical indices” and the infants were only weighed once daily.

When breastfeeding was initiated and there were signs of milk ingestion (audible swallowing or fresh milk obtained by aspiration during verification of feeding tube position), infants in Uppsala were weighed before and after feeding to determine the amount ingested. Reduction of supplementation
was based on the infant’s progress in milk intake, verified by test-weighing and the daily weight.

Both units had the same routine for obtaining daily weight: the infant was placed naked on electronic scales. Receiving blankets etc. used during weighing and feeding tube and other equipment attached to the infant were subtracted from the weight with an accuracy of 1 or 5 g (depending on type of scales). All nursing staff was trained in performing weighing in a consistent way. In Umeå, the daily volume of supplementation was determined from the infant’s observed latching on, suckling and swallowing behaviour at each breastfeeding session and daily weight gain.
Results

Study I

Significant differences between Uppsala and Umeå were determined regarding volume of milk and total volume of fluid (milk and 10% i.v. glucose) given during the first three days of life (Figure 1-2). A larger proportion of infants at Umeå (71%), than at Uppsala (29%), were given 10% i.v. glucose ($p<0.013$). No statistical differences in the proportion of infants with at least one bout of hypoglycaemia (B-glucose <2.5 mmol/L) were noted at the the hospitals, (Uppsala 57% and Umeå 86%).

Infants in Uppsala weighed less at a younger age and had smaller weight loss (Table 4). GA at birth ($p<0.001$) and hospital ($p<0.009$: $R^2=0.52$) were important factors for the percentage of weight loss on regression analysis, with a combined dataset for both hospitals and independent variables hospital, birth weight SDS, GA at birth, continuous positive airway pressure (CPAP) treatment (in days) and milk intake on day 3. Infants in Uppsala regained birth weight earlier (after 4 days) than infants in Umeå (after 8 days) (Table 4). Infants in Uppsala attained full enteral feeding earlier (median 0 days post-partum) than those in Umeå (median 3 days post-partum: $p<0.004$). No difference in the rate of infants discharged with full breastfeeding was identified, 71% in Uppsala and 67% in Umeå.

Table 4. Lowest weight, weight loss percent, regain of birth weight and weight and age at discharge: median (range).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Uppsala ($n=21$)</th>
<th>Umeå ($n=21$)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest weight, days</td>
<td>2 (0-4)</td>
<td>3 (0-7)</td>
<td>0.024</td>
</tr>
<tr>
<td>Weight loss, %</td>
<td>2.2 (0-7.5)</td>
<td>4.7 (0-12.9)</td>
<td>0.029</td>
</tr>
<tr>
<td>Regain birth weight, days</td>
<td>4 (0-10)</td>
<td>8* (0-14)</td>
<td>0.023</td>
</tr>
<tr>
<td>Weight at discharge, grams</td>
<td>2225 (1850-3114)</td>
<td>2240 (1994-2711)</td>
<td>0.890</td>
</tr>
<tr>
<td>Age at discharge, days</td>
<td>16 (6-47)</td>
<td>15 (9-66)</td>
<td>0.820</td>
</tr>
</tbody>
</table>

*missing data = 2
Figure 1. Milk volumes and total volume of fluid (milk and i.v. glucose) at 1 day old.

Figure 2. Milk volumes and total volume of fluid (milk and i.v. glucose) at 3 days old.
Study II

Despite lower weight loss in Uppsala, infants did not display better subsequent catch-up growth. At 40 weeks, PMA and 2-, 4-, 6-, 12- or 18-months corrected age; there were no differences between the two hospitals in SDS for weight, length or HC. When the data sets from the two hospitals were combined and split into two groups, preterm (i.e., born at less than 37 weeks gestation) and term infants, there was no difference in weight SDS at birth between the groups. However, when comparing weight SDS at 40 weeks PMA, preterm infants had less negative weight SDS (Table 5). Correlation analysis indicated low GA at birth was related to higher weight ($r=-0.46$, $p=0.002$) and weight SDS ($r=-0.39$, $p=0.010$) at 40 weeks PMA.

There were no statistical differences between preterm and term infants in birth length SDS or length SDS at 40 weeks PMA. However, at 40 weeks PMA, infants with low GA at birth had higher length SDS, GA at birth was negatively correlated with length SDS ($r=-0.35$, $p=0.030$) and SDS for length at 18 months ($r=-0.49$, $p=0.004$).

There were no differences in HC SDS between preterm and term infants at birth. At 40 weeks PMA, preterm infants had less negative HC SDS (Table 5). The lower the GA was at birth, the larger the HC was at PMA 40 weeks (GA correlated negatively with HC ($r=-0.55$, $p<0.001$) and with HC SDS at 40 weeks PMA, ($r=-0.66$, $p<0.001$). After 40 weeks PMA, infants with higher GA at birth showed greater improvement in head growth, as the improvement in HC SDS from 40 weeks to 4 months corrected age correlated positively with GA at birth ($r=0.42$, $p=0.016$).

At the time of discharge 29 (69%) and at the PNA of 2 months 26 (62%) of the infants were breastfed fully. There was no significant correlation between duration of full breastfeeding and any parameters of infant growth during the first 18 months of life.

Table 5. Median weight, length and HC SDS at birth and 40 weeks PMA in preterm and term infants.

<table>
<thead>
<tr>
<th>Preterm/term n</th>
<th>Preterm Md (range)</th>
<th>Term Md (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>20/22</td>
<td>-2.6 (-3.7 to -1.8)</td>
<td>-2.5 (-3.9 to -1.8)</td>
</tr>
<tr>
<td>Length</td>
<td>20/22</td>
<td>-1.7 (-4.3 to -0.2)</td>
<td>-2.3 (-3.1 to -1.4)</td>
</tr>
<tr>
<td>HC</td>
<td>19/22</td>
<td>-1.1 (-2.3 to 1.0)</td>
<td>-1.5 (-2.3 to 0.5)</td>
</tr>
<tr>
<td>40 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>20/22</td>
<td>-1.6 (-2.9 to -0.4)</td>
<td>-2.3 (-3.9 to -0.5)</td>
</tr>
<tr>
<td>Length</td>
<td>17/21</td>
<td>-1.5 (-3.0 to 0.3)</td>
<td>-1.8 (-3.2 to -0.6)</td>
</tr>
<tr>
<td>HC</td>
<td>19/22</td>
<td>-0.1 (-1.3 to 0.9)</td>
<td>-1.0 (-2.6 to 0.2)</td>
</tr>
</tbody>
</table>
Study III

The first day with a record of milk intake in connection with breastfeeding occurred at an earlier PMA among infants in Uppsala, with a (median of 34 weeks + 5 days) than at Umeå (35 weeks + 2 days: \(p<0.001\)), assessed by test-weighing at Uppsala and by “clinical indices” at Umeå.

The infants at Uppsala attained exclusive breastfeeding at an earlier median PMA (35 weeks + 6 days) than at Umeå (36 weeks + 3 days: \(p<0.010\)), i.e. they were four days less mature (Table 6). There were no significant differences in infants’ PNA on this day, (median PNA 13 days at Uppsala and 12 days at Umeå) (Table 6), or in the days from the first record of nutritive suckling at the breast to attainment of exclusive breastfeeding, with an interval of eight days for infants at Uppsala and seven days at Umeå.

There were no significant differences between the two hospitals regarding the proportion of infants exclusively breastfed at discharge: most infants at both hospitals had attained this competence, 88% in Uppsala and 81% in Umeå.

In order to explore the influence of maternal and infant factors on the infants’ PMA on attaining exclusive breastfeeding, a regression analysis was performed on a combined sample of the two units with the independent variables hospital, GA at birth, days with CPAP treatment, twin, smoking/non-smoking mother, and mother with/without university education. Two factors contributed significantly to attainment of exclusive breastfeeding at a lower PMA: lower GA at birth (\(p<0.001\)) and fewer days of CPAP treatment (\(p<0.002\)) (R\(^2=0.229\)). Infants with lower GA and fewer days of CPAP treatment attained exclusive breastfeeding earlier. The same factors were also examined in a logistic regression analysis regarding explanation of exclusive breastfeeding before discharge. Having a university-educated mother (\(p<0.043\)) (R\(^2=0.063\)) was the only significant factor for progression to exclusive breastfeeding before discharge.

The infants in Uppsala were discharged at a lower PMA (36 weeks + 5 versus 37 weeks + 1 day: \(p<0.005\)), with discharge occurring from a PMA of 33 weeks + 4 days in Uppsala versus 34 weeks + 4 days in Umeå. There was no significant difference in the infants’ age on this day, which was median (range) 18 (7-58) days in Uppsala and 20 (7-67) days in Umeå. No significant differences between the units were found regarding weight at discharge, with a median (range) of 2,550 (1,740-3,410) g in Uppsala and 2,639 (2,025-3,216) g in Umeå.
### Table 6. PNA and PMA when infants attained full enteral, oral and breastfeeding.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Uppsala (n=64)</th>
<th>Umeå (n=59)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNA (md/range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteral feeding</td>
<td>0 (0-11)</td>
<td>2 (0-16)</td>
<td>0.039</td>
</tr>
<tr>
<td>Oral feeding</td>
<td>12 (1-55)</td>
<td>12 (0-61)</td>
<td>NS</td>
</tr>
<tr>
<td>Breastfeeding*</td>
<td>13 (3-56)</td>
<td>12 (3-61)</td>
<td>NS</td>
</tr>
<tr>
<td>PMA (md/range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteral feeding</td>
<td>34.00 (29.00-36.14)</td>
<td>35.00 (30.14-36.29)</td>
<td>0.001</td>
</tr>
<tr>
<td>Oral feeding</td>
<td>35.71 (32.57-37.86)</td>
<td>36.43 (34.28-38.00)</td>
<td>0.001</td>
</tr>
<tr>
<td>Breastfeeding*</td>
<td>35.86 (32.57-38.00)</td>
<td>36.43 (34.28-38.86)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

*Uppsala n=56 and Umeå n=48

**Study IV**

The changes in standard deviation scores during the infants’ hospital stay were -0.9 for weight, -0.3 for length and -0.5 for HC. Infants with higher weight, length and HC SDS at birth had higher losses from birth to discharge, as change in SDS from birth to discharge correlated negatively with birth SDS ($p<0.001$ for all three growth parameters). This is illustrated for weight, length and HC SDS in Figure 3 A-C.

When the data set was stratified into infants born after a GA of <32 weeks, 32-33 weeks and 34-35 weeks, the statistical analysis indicated no statistically significant differences between these three groups for changes in weight SDS from birth to discharge (Table 7). When infants were grouped according to three groups: infants born with a birth weight SDS <-1, between 0 and -1, and >0, the infants with the lowest birth weight SDS had the lowest loss in SDS during their hospital stay (Table 7).

All three GA groups (<32, 32-33 and 34-35) had positive changes in weight, length and HC SDS between discharge and a CA of 2 months. The most preterm group displayed better gain in length SDS from discharge to 6 months, but not subsequently up to 18 months (Table 7). Statistical analyses of the three birth weight SDS groups (<-1, between 0 and -1, and >0) indicated infants with the lowest birth weight SDS had the greatest acceleration in growth between discharge and 2 months CA (Table 7).

Months of full breast milk feeding/ breastfeeding correlated negatively with length SDS at 6 months ($r=-0.23$, $p=0.013$); that is, the longer the duration of breastfeeding, the shorter the infant was. Months of any breastfeeding correlated negatively with length SDS at 6 months ($r=-0.26$, $p=0.006$) and 18 months ($r=-0.28$, $p=0.014$). No other significant correlation between duration of full or any breastfeeding and any parameter of infant growth during the first 18 months of life was identified.
Figure 3. Correlation between weight, length and HC SDS at birth and changes from birth to discharge.

A. Weight standard deviation score (SDS) at birth and change in weight SDS from birth to discharge ($n=127$, $r=-0.44$, $p<0.001$).

B. Height standard deviation score (SDS) at birth and change in height SDS from birth to discharge ($n=122$, $r=-0.46$, $p<0.001$).

C. Head circumference (HC) standard deviation score (SDS) at birth and change in HC SDS from birth to discharge ($n=117$, $r=-0.70$, $p<0.001$).

Filled circles: gestational age below 32 weeks, open circles: gestational age 32-35 weeks.
Table 7. Changes in weight, length and HC SDS from birth to 18 months, where data are stratified into GA 25-31, 32-33, 34-35 weeks and into birth weight SDS: <-1, between -1 and 0, and >0.

<table>
<thead>
<tr>
<th>GA</th>
<th>Delta: median (range) SDS</th>
<th>n</th>
<th>A: 25-31 weeks</th>
<th>n</th>
<th>B: 32-33 weeks</th>
<th>n</th>
<th>C: 34-35 weeks</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge - birth</td>
<td>Weight</td>
<td>24</td>
<td>-0.9 (-2.9 to 0.8)</td>
<td>27</td>
<td>-1.0 (-2.6 to 0.2)</td>
<td>76</td>
<td>-0.9 (-2.8 to 0.3)</td>
<td>A/C: 0.019, B/C: 0.007</td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>22</td>
<td>-0.5 (-2.6 to 1.1)</td>
<td>26</td>
<td>-0.7 (-2.2 to 1.7)</td>
<td>74</td>
<td>0.0 (-1.9 to 3.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>21</td>
<td>-0.4 (-1.4 to 0.7)</td>
<td>23</td>
<td>-0.6 (-2.0 to 0.6)</td>
<td>73</td>
<td>-0.4 (-2.5 to 1.5)</td>
<td></td>
</tr>
<tr>
<td>2 months - discharge</td>
<td>Weight</td>
<td>24</td>
<td>1.5 (-1.1 to 2.9)</td>
<td>27</td>
<td>1.1 (-2.9 to 3.3)</td>
<td>74</td>
<td>1.6 (-0.3 to 3.3)</td>
<td>B/C: 0.011</td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>24</td>
<td>0.8 (-0.9 to 2.2)</td>
<td>25</td>
<td>0.9 (-2.0 to 2.7)</td>
<td>73</td>
<td>0.9 (-1.8 to 2.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>24</td>
<td>1.0 (0.0 to 2.8)</td>
<td>23</td>
<td>0.7 (-0.9 to 1.6)</td>
<td>68</td>
<td>0.9 (-1.7 to 2.2)</td>
<td></td>
</tr>
<tr>
<td>6 months - discharge</td>
<td>Weight</td>
<td>24</td>
<td>1.3 (-1.2 to 2.5)</td>
<td>23</td>
<td>0.8 (-0.8 to 3.0)</td>
<td>69</td>
<td>1.2 (-0.3 to 3.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>22</td>
<td>1.1 (-1.8 to 3.2)</td>
<td>23</td>
<td>0.3 (-1.9 to 2.8)</td>
<td>66</td>
<td>0.8 (-1.8 to 3.0)</td>
<td>A/B: 0.043</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>21</td>
<td>1.0 (-0.9 to 2.4)</td>
<td>20</td>
<td>0.6 (-0.4 to 2.9)</td>
<td>56</td>
<td>0.8 (-1.1 to 2.4)</td>
<td></td>
</tr>
<tr>
<td>18 months - discharge</td>
<td>Weight</td>
<td>19</td>
<td>0.9 (-1.0 to 3.3)</td>
<td>20</td>
<td>0.7 (-2.0 to 2.9)</td>
<td>48</td>
<td>0.8 (-1.1 to 2.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>19</td>
<td>1.0 (-1.5 to 3.7)</td>
<td>17</td>
<td>1.1 (-1.1 to 2.7)</td>
<td>42</td>
<td>0.4 (-2.3 to 2.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>14</td>
<td>0.0 (-1.1 to 2.0)</td>
<td>13</td>
<td>0.3 (-1.0 to 1.3)</td>
<td>27</td>
<td>0.3 (-0.8 to 2.1)</td>
<td></td>
</tr>
<tr>
<td>Birth weight</td>
<td>Delta: median (range) SDS</td>
<td>n</td>
<td>A: SDS &lt;-1</td>
<td>n</td>
<td>B: SDS 0 to -1</td>
<td>n</td>
<td>C: SDS &gt;0</td>
<td>P value</td>
</tr>
<tr>
<td>Discharge - birth</td>
<td>Weight</td>
<td>24</td>
<td>-0.3 (-1.7 to 0.8)</td>
<td>56</td>
<td>-0.9 (-2.9 to 0.1)</td>
<td>47</td>
<td>-1.2 (-2.6 to 0.0)</td>
<td>A/B and A/C: &lt;0.001, B/C: 0.035</td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>23</td>
<td>0.1 (-2.2 to 1.5)</td>
<td>54</td>
<td>-0.4 (-2.1 to 3.0)</td>
<td>45</td>
<td>-0.3 (-2.6 to 1.7)</td>
<td>A/B: 0.036</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>21</td>
<td>-0.1 (-0.8 to 1.5)</td>
<td>54</td>
<td>-0.6 (-1.9 to 0.6)</td>
<td>42</td>
<td>-0.6 (-2.5 to 0.8)</td>
<td>A/B: &lt;0.001, A/C: 0.002</td>
</tr>
<tr>
<td>2 months - discharge</td>
<td>Weight</td>
<td>24</td>
<td>1.9 (0.0 to 3.3)</td>
<td>55</td>
<td>1.4 (-2.9 to 3.3)</td>
<td>46</td>
<td>1.3 (-1.6 to 3.2)</td>
<td>A/C: 0.012</td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>24</td>
<td>1.3 (-0.5 to 2.7)</td>
<td>54</td>
<td>1.0 (-2.0 to 2.6)</td>
<td>44</td>
<td>0.6 (-1.4 to 2.8)</td>
<td>A/C: 0.003</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>22</td>
<td>1.0 (0.0 to 2.2)</td>
<td>52</td>
<td>0.8 (-0.7 to 2.8)</td>
<td>41</td>
<td>0.8 (-1.7 to 1.8)</td>
<td>A/C: 0.035</td>
</tr>
<tr>
<td>6 months - discharge</td>
<td>Weight</td>
<td>22</td>
<td>1.5 (-0.4 to 2.8)</td>
<td>52</td>
<td>1.1 (-1.2 to 3.5)</td>
<td>42</td>
<td>1.0 (-0.8 to 3.0)</td>
<td>A/C: 0.048</td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>21</td>
<td>1.0 (-0.5 to 2.8)</td>
<td>50</td>
<td>0.7 (-1.8 to 3.2)</td>
<td>40</td>
<td>0.4 (-1.9 to 3.0)</td>
<td>A/C: 0.001</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>21</td>
<td>0.7 (-0.7 to 2.4)</td>
<td>42</td>
<td>0.8 (-0.9 to 2.4)</td>
<td>34</td>
<td>0.6 (-1.1 to 2.9)</td>
<td></td>
</tr>
<tr>
<td>18 months - discharge</td>
<td>Weight</td>
<td>16</td>
<td>0.9 (-0.5 to 2.5)</td>
<td>41</td>
<td>0.9 (-1.0 to 3.3)</td>
<td>30</td>
<td>0.7 (-2.0 to 2.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Length</td>
<td>15</td>
<td>1.1 (-1.5 to 3.2)</td>
<td>38</td>
<td>1.0 (-2.3 to 3.7)</td>
<td>25</td>
<td>-0.1 (-1.6 to 1.8)</td>
<td>A/C: 0.002, B/C: 0.002</td>
</tr>
<tr>
<td></td>
<td>HC</td>
<td>11</td>
<td>0.4 (-1.1 to 1.2)</td>
<td>26</td>
<td>0.4 (-0.6 to 2.1)</td>
<td>17</td>
<td>0.0 (-1.0 to 1.2)</td>
<td>B/C: 0.035</td>
</tr>
</tbody>
</table>
Discussion

Methodological considerations regarding all studies

Small sample size
In studies I and II, the small sample size was a major limitation. The choice of this sample size is explained by the performance of the study in a country with a small population and a low annual admission rate at neonatal intensive care units. In order to reach the study sample size, the data collection included all infants meeting inclusion criteria born during one year (Uppsala) and one-and-a-half years (Umeå). The choice of study settings was to ensure all study infants were treated according to the same clinical guidelines relevant for the study purpose.

Randomisation
Randomisation is always the preferable design for controlling sources of bias. However, infant feeding presents many ethical issues, therefore, randomisation is not always feasible, especially when it concerns mother-infant pairs in a setting in which breastfeeding is considered the norm (Sweden can be defined as a breastfeeding culture [62]). The study units were chosen because of the similar medical care approach and because both hospitals are regional, university hospitals. However, lack of randomisation could result in discrepancy between the groups. For instance, in study III, infants in Uppsala were born at a lower GA and a larger proportion of the mothers were delivered by caesarean section, whereas, a larger proportion of the mothers in Umeå had a university education.

Retrospective cohort
Research based on review of medical records can suffer from incomplete data; however, in these studies, the extent of missing data was limited. Asking mothers to recall post-discharge feeding practice could be a source of bias, but mothers has been found able to provide accurate reports of emotionally charged perinatal experience in comparison to information from medical records [103].
Observational tools
The assessment of “clinical indices” of infants’ milk intake at the hospital in Umeå was not guided by any standard observational tool and the nurses had not received any training in which inter-observer reliability was tested. This is the clinical reality in many neonatal units all over the world. Furthermore, the method is unreliable, as it has been demonstrated it is impossible for nursing staff and for mothers to make an accurate assessment of infants’ milk intake [91].

Weighing and measuring
When the infants were weighed, multiple scales were used and weighing was performed by different nurses. However, the scales were regularly calibrated to produce accurate weights and all weighing and measurements of length and HC were made by trained nurses.

Experience of breastfeeding
The studies did not include any emotional or relational assessment of how the mothers perceived their breastfeeding experience and the routines in the process of establishing exclusive breastfeeding, through test-weighing or clinical indices. An investigation of this issue should be based on mothers’ own reports of their experience of hospital policies and practices related to nutrition, feeding and breastfeeding in neonatal care.

Growth charts and definitions of SGA and AGA
Infant born preterm have often suffered poor intrauterine growth [18]. Therefore, construction of growth charts and assessment of their growth are complicated issues [104], as all growth charts can be assumed to have limitations.

There are different definitions of being born SGA or AGA and the definition chosen for this thesis has limitations. Lubchenco et al.’s curves [3] are often used internationally and infants with a birth weight below the 10th percentile are considered SGA and AGA between 10th and 90th percentiles. In clinical practice in Sweden, the diagnosis criterion for SGA, according to Marsal et al. [4], is birth weight below -2 SD for GA. This means the Swedish diagnosis criterion is narrower than that of Lubchenko et al., meaning that fewer infants are defined as SGA according to the Swedish diagnosis criterion.
Discussion of the separate studies

Study I

In neonatal care, sufficient scientific support for various nutrition regimens used in practice is often lacking [24]. For feeding volumes, one commonly suggested measure for full enteral/oral feeding with formula or breast milk is 150–180 ml/kg and day [32] on day nine [99]. This target volume may be too low and the common policies for advancement in feeding volumes too slow to sustain adequate growth [105].

In study I, SGA infants tolerated larger volumes than commonly thought possible, and large feeding volumes during the first days of life reduced weight loss and helped infants regain their birth weight earlier. Fewer infants with early proactive feeding required i.v. glucose treatment, and despite differing nutrition policies at the hospitals, there were no differences in breastfeeding rate and exclusivity on discharge. SGA infants do not tolerate enteral feeding as well as AGA infants [33, 34]. Nevertheless, the infants at Uppsala appeared to tolerate large milk volumes. This was unexpected, as the proportion of preterm infants was almost 50% and rapid increase in milk volume given enterally to preterm infants is usually considered unrealistic by clinicians. One plausible explanation for the tolerance could be the application of a two hourly feeding schedule up to a weight of 1500 g. in Uppsala, compared with 1200 g. in Umeå.

To summarise, early initiation of enteral/oral feeding with proactive increases in milk volume may be beneficial in short-term. Such a feeding regimen may render i.v. administration of glucose unnecessary and reduce weight loss in SGA infants. Conversely, nutrition intervention for promoting rapid catch-up growth might be associated with adverse outcome in later life and lead to adult obesity rather than an increase in height [55].

Study II

In study II, the rapid postnatal growth in study I was not maintained at 40 weeks, 2-months, 4-months, 6-months, 12-months or 18-months corrected age in any growth variable. However, the preterm infants had an early catch-up in weight and HC and had less negative SDS than infants born at term at 40 weeks. At the corrected age of 18 month, infants with low GA at birth had less negative length SDS. It must be considered positive that prematurity was not associated with poor growth in these SGA infants. No evidence was found in the present study for a proactive nutrition regimen with initial large volumes of milk resulting in a different pattern of growth up to the corrected age of 18 months. Of all infants born in Sweden in 2001, 92% at the age of one week and 80% at the age of two months were fully breastfed [62]. In this
study of SGA infants, the rate of full breastfeeding at discharge was 69% and 62% at PNA of two months. This demonstrated the need for targeting mothers of SGA infants with special breastfeeding support, because of the additional advantages of breast-milk feeding for these infants [59, 106, 107]

Study III
Successful breastfeeding is feasible and worth striving for in preterm infants [73], but presents a challenge for the mother [72]. The mother must establish and maintain lactation while feeling anxious for her infant’s health and survival, and then, manage the transition to breastfeeding from gavage or cup/bottle. Test-weighing before and after breastfeeding or gradual reduction of supplementation after breastfeeding, with the use of “clinical indices”, were both determined as applicable regimens. Mothers could be encouraged to choose either of them; even though it is possible test-weighing might help infants to attain exclusive breastfeeding at an earlier PMA. Most infants in Uppsala (where test-weighing was applied) attained exclusive breastfeeding and were discharged from hospital while they were still preterm, with an earliest PMA at attainment of exclusive breastfeeding of 32 weeks and 4 days. It is likely exclusive breastfeeding of an infant at such a low maturational level would not be possible unless professionals and the mother were convinced (through test-weighing) that the infant was receiving sufficient milk.

Study IV
Studies report poor growth among preterm AGA infants during hospital stay [13] and throughout infancy [108, 109]. Advances in neonatal care do not appear to change this circumstance [108]. In study IV, preterm AGA infants born with high SDS at birth were at higher risk of inadequate growth during their hospital stay. A possible explanation for this might be infants with higher SDS at birth have more stable intrauterine growth and are therefore more sensitive to environmental factors, whereas, those with a lower SDS are more resistant to inadequate nutrition. This also agrees with the findings in our study that the infants who had the lowest SDS at birth, a group that included infants born at a GA of <32 weeks, had accelerated growth during their hospital stay. Thus, infants’ SDS should be included in the clinical data used as a basis for prescription of nutrition in hospital and after discharge in order to prevent both underfeeding and overfeeding.

Research on nutrition after discharge focuses primarily on the connection between nutrient-enriched formulas and infants’ growth and development. However, there is no strong evidence for the positive effects of these nutrient-enriched formulas on growth rates or development during the first 18 months post term in preterm infants [46].
After discharge and to CA of 2 months the AGA infants displayed increments in SDS as high as, or higher than, the loss from birth to discharge, irrespective of being fed exclusively with breast milk, exclusively with standard formulas, or with mixed feeding. This supported the adequacy of exclusive breastfeeding for AGA preterm infants after discharge.

Future research

Preterm infants often receive inadequate nutrition during their hospital stay. Postnatal growth failure in preterm infants can be assumed as partly attributed to inappropriate (too long) feeding intervals and inadequate volumes during the hospital stay. Future studies should investigate the effect of more frequent feeds and earlier advancement of feeding volumes adapted to the individual infant’s tolerance (both of volumes fed and the pace and mode of administration) on preterm infants’ growth pattern. The effect of extended parent-infant skin to skin contact (kangaroo mother care) on infants’ growth and breastfeeding should also be explored.

Paediatricians might treat IUGR infants with adaptive slow growth as suffering postnatal growth failure. Therefore, another research topic that needs to be addressed is how to provide IUGR infants with appropriate nutrition in order to prevent an overfeeding situation (with large milk volumes and/or enrichment) with the negative consequences this might imply.

The effects of hospital nutrition policies and practices on the duration of exclusive and partial breastfeeding have not been in focus and need to be highlighted in future research to avoid undesired consequences.

Sammanfattning på svenska

Forskning har visat att spädbarns nutrition de första veckorna kan påverka deras hälsa som vuxna decennier senare. Barn som vårdas på neonatalavdelningar är ofta högriskbarn som har visat sig vara särskilt sårbara för felaktig nutrition. Trots det saknas ofta vetenskapligt stöd för de nutritionsrutiner som följs inom neonatalvården. Matmängder, matningsintervall och amningsstöd har utformats i ett medicinskt paradigm, där vissa vetenskapliga aspekter kommit i skymundan. Syftet med den här avhandlingen var att öka kunskapen om sjuhusrutinernas inverkan på amning och tillväxt hos underburna och lågviktiga barn.

En retrospektiv, deskriptiv, och jämförande undersökning gjordes med hjälp av journalgranskning för att undersöka nutritionsrutiner på neonatalavdelningarna på Akademiska sjukhuset i Uppsala och Norrlands universitetssjukhus i Umeå.
Urvalet i studie I och II bestod av underburna och fullgångna
tillväxthämmade barn som föddes konsekutivt i respektive sjukhus
upptagningsområde (Uppsala n=21 och Umeå n=21). I studie III (Uppsala 
n=64 and Umeå n=59) och IV (n=127) bestod urvalet av konsekutivt födda
underburna, men inte tillväxthämmade barn.

Vi visade i studie I att på Akademiska sjukhuset, där stora höjningar av
den enterala matmängden praktiserades de första dygnen, fick en lägre andel
barn intravenös behandlig med glukos. De stora matmängderna gjorde att
viktförlusten minskade och att barnen nådde födelsevikten fortare.

Studie II visade att den här snabbare neonatalev tillväxten inte bestod vid
40 veckor, 2 månader, 4 månader, 6 månader, 12 månader eller 18 månader
korrigerad ålder. Däremot hade underburna barn på båda sjukhusen liknande
tillväxtacceleration i vikt oavsett matmängd.

I studie III jämfördes det underburna barnets väg till full amning. På det
ena sjukhuset skedde detta med hjälp av vägning före och efter amning och
på det andra genom gradvis minskning av tillmatningen genom tolkning av
barnets amningsbeteende. Det visade det sig att barnen som behandlades på
avdelningen där testvägning praktiserades nådde full amning vid lägre
mognadsålder och också skrevs ut från sjukhuset vid lägre mognadsålder.
Däremot var det ingen skillnad mellan sjukhusen i andelen barn som nådde
full amning, ålder på barnen då detta skedde eller i viktutveckling under
sjukhusvistelsen.

Studie IV visade att underburna barn som inte var tillväxthämmade och
födda med högre standardavvikelsepoäng (m.a.o.: var större för sin ålder)
hade större förlust i standardavvikelsepoäng från födelsen till utskrivning. 
Efter utskrivning hade barnen återtagit hela förlusten eller mer därtill vid 2
månaders korrigerad ålder.

Slutsatser: Tidig höjning av enteral mat kan ha medicinska fördelar i ett
kort perspektiv. Stora mjölkändamanger under de första dagarna ledde
emellertid inte till ett annorlunda tillväxtmönster fram till 18 månader
korrigerad ålder. Testvägning före och efter amning eller gradvis minskning
av tilläggsmatningen genom tolkning av barnets amningsbeteende är båda
möjliga vårdrutiner för att nå full amning. Mammor kan uppmuntras att välja
vilken de vill av dem, även om testvägning kan hjälpa underburna barn att nå
full amning vid en lägre mognadsålder. Slutligen, underburna barn med
högre standardavvikelsepoäng för vikt, längd och huvudomfång löper större
risk för förlust i standardavvikelsepoäng under sjukhusvistelsen. Därför
borde hänsyn tas till standardavvikelsepoäng då mat ordineras till
underburna barn. Detta för att undvika både övergödning och undernutrition
av underburna barn.
Acknowledgements

I want to express my thanks to all of you who made this thesis possible, especially I say thank you to:

Kerstin Hedberg Nyqvist - for being such an extraordinary person. For being so generous with your time, ideas and support and for having courage.

Torsten Tuvemo - for your unique way of saying “aah… interesting”.

Björn Jonsson - because you are such a clever statistician.

Fredrik Serenius - for generously inviting me to Umeå.

Maria Haglund och Magnus Näslund - for help with data collection and for acceptance of payment in bullpåsar.

Barbro Westerberg - for commitment to my needs on the PC.

Lena Lööf - for being so tall and always letting me hide behind you.

Ylva Thernström Blomqvist, Gunn Engvall and Helena Volgsten - for sustained support during a PhD student’s rollercoaster journey and Ylva, also thanks for all small details.

Maud Marsden, Max Brandt and Susan Pajuluoma - for your linguistic skills.

My colleagues at 95 F and especially to: Sandra Olsson, Edji Nimmerstam, Lena Kjellberg, Sol-Britt Eriksson, Lisa Strömbeck, Anna Nyström, Maria Hagstedt, Maria Jansdotter, Karin Holmgren, Ann-Sofie Wahlberg, Sara Fälldt, Hedvig Strand, Wandee Larsson, Siriwan Ellenius, Tzieghe Kifle, Ann-Britt Eriksson, Lise Llerena and Maria Palmkvist - for many years of joyful cooperation in breastfeeding issues also when the wind blows.

Ingmarie Emilsson - for always, straightforwardly, signing my frequent leave applications.

Tula Nyström, Charlie Karis, Anna and Andreas Marcström, Marit Olanders, Lotta Sigge, Paola Oras and Heidi Aalto - for all these endless breastfeeding discussions.

Berit Funkquist - for teaching me not to believe what people say just because I should.
Pia Funkquist - for teaching me to never give up a good fight.

Lisa and Nisse Nyborg - for all you taught me about breastfeeding.

Gunnar Nyborg - for always letting me be who I am.

The Gillbergska Foundation, the Solstickan Foundation, the Birth Foundation, the Goljes Memorial Foundation, the Swedish Association of Pediatric Nurses and Pampers - for financial support.

Also thanks to the mothers - who, despite their situation as parents of a small child, devoted time to answering questionnaires.
References

[8] Gray IP, Cooper PA, Cory BJ, Toman M, Crowther NJ. The intrauterine environment is a strong determinant of glucose tolerance during the neonatal period, even in prematurity. J Clin Endocrinol Metab 2002;87:4252-6.


Acta Universitatis Upsaliensis

Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 597

Editor: The Dean of the Faculty of Medicine

A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)