Benefits and Challenges of the Use of Human Milk for Premature Infants

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- Dr. Rhine has indicated that he has nothing to disclose

Talk Objectives

- Review the benefits of human milk for all infants
- Describe the role of human milk in meeting the unique physiologic and nutritional needs of premature infants
- Share strategies for optimizing the use of human milk for premature infants
- Review nutritional monitoring of premature infants

Clinical Impact of Human Milk for Term Infants–Short-term

- Respiratory – URI (60% reduction), LRI (72-77% reduction), RSV bronchiolitis (74% reduction)
- SIDS – 36% reduction
- Otitis media – 23-50% reduction (77% reduction in recurrent OM)
- Allergies – atopic dermatitis (27-42% reduction)
- GI – gastroenteritis (64% reduction)

AAP. Pediatrics 2012;129(8):e827–e841.

Clinical Impact of Human Milk for Term Infants–Long-term

- GI – celiac disease (52% reduction); inflammatory bowel disease (31% reduction)
- Allergy – asthma (26-40% reduction)
- Obesity – 24% reduction
- Diabetes –Type 1 (30% reduction); Type 2 (40% reduction)

AAP. Pediatrics 2012;129(8):e827–e841.

Clinical Impact of Human Milk for Term Infants–Long-term

- Cancer – leukemia (15% reduction AML, 20% reduction ALL)
- Cardiovascular – reduced BP by 3.2 mmHg - more than weight loss (2.8 mmHg), alcohol reduction (2.1 mmHg), salt restriction (1.3 mmHg), exercise (0.2 mmHg)
- Neurodevelopmental outcomes – improved IQ scores and teacher ratings
- Maternal benefits include reduction in diabetes, HTN, breast and ovarian cancer

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Gold Standard of Growth for Premature Infants

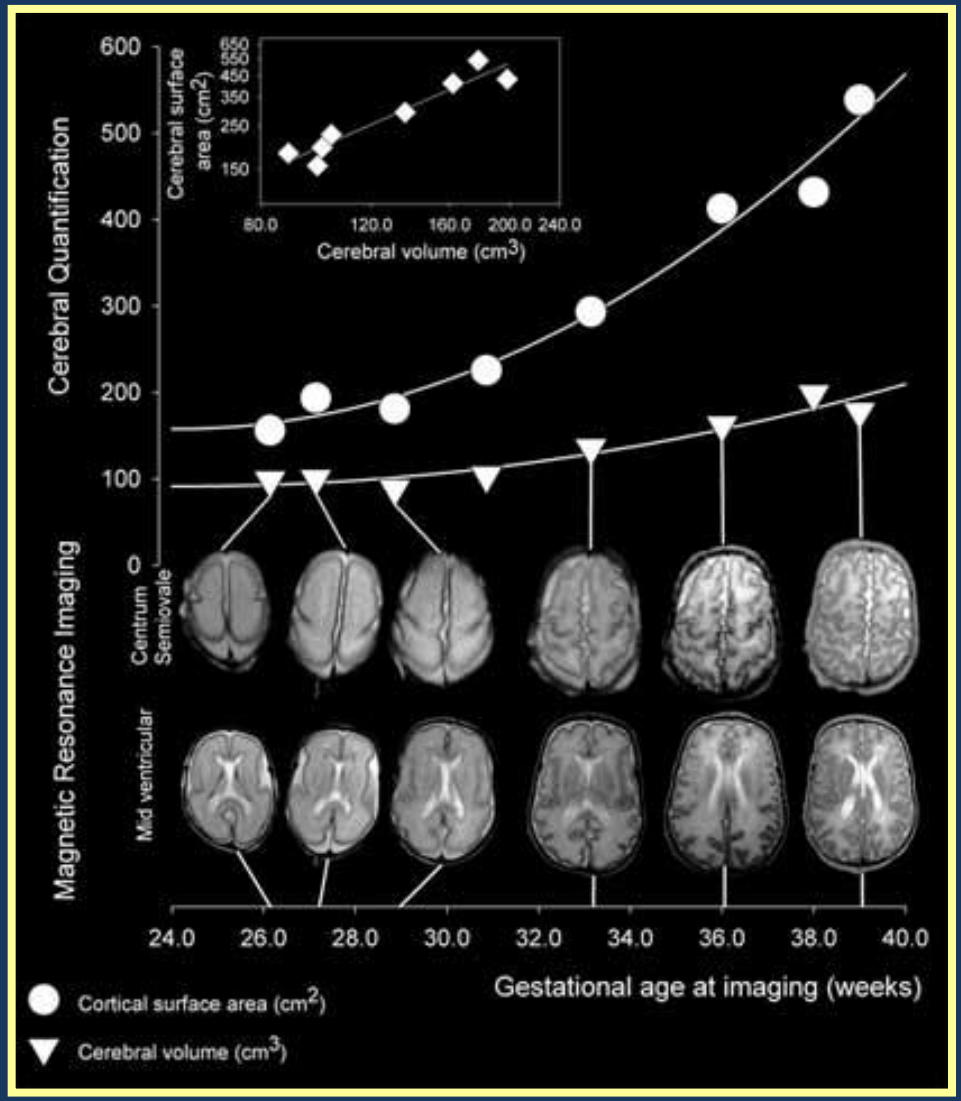
- The ideal goal of providing nutrition to premature infants is to approximate the *in utero* growth of a normal fetus of the same post-conceptional age
  - Body weight and length
  - Body composition and organ development

AAP Committee on Nutrition (2009). Nutritional needs of the preterm infant. In R.E. Kleinman (ed), ***Pediatric Nutrition Handbook*** (pp. 79-104). Elk Grove Village, IL: American Academy of Pediatrics.

Unique Nutritional Aspects of the Premature Infant

- Higher organ: muscle mass ratio
- Higher rate of protein synthesis and turnover
- Greater oxygen consumption during growth
- Higher energy cost due to transepidermal water loss
- Higher rate of fat deposition
- Prone to hyperglycemia
- Higher total body water content

Unique Nutritional Aspects of Premature Infants-Brain Growth



Brain growth over 8 weeks:

At 28 wks.	100% Increase
At term	40% Increase
At 3 mo.	25% Increase

Kapellou O, et al. PLoS Med 2006;3(8):e265.

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Preventing Feeding-Related Morbidities in Premature Infants

- Necrotizing enterocolitis
- Osteopenia/rickets of prematurity
- Vitamin and mineral deficiencies
- Feeding intolerance
- Prolonged TPN and related cholestasis
- Nosocomial infections
- Prolonged hospitalization

Optimal Growth of Premature Infants Influences Long-term Health and Disease

- Premature infants receiving breast milk are less likely to have excessive growth
- Adverse effects of excessive growth acceleration:
  - Obesity
  - Elevated blood pressure
  - Insulin resistance and diabetes
  - Cardiovascular mortality

Gillman M, et al. Arch Pediatr Adol Med 2011;165:993-8.
Ben-Shlomo Y, et al. Hypertension 2008;52(4):638-44.
Forsen T, et al. Ann Intern Med 2000;133(3):176-82.
Eriksson JG et al. BMJ 1999;318(7181):427-31.

Clinical Benefits of Human Milk for Preterm Infants

- Improve Host Defense – reduced infections
- Promote Gastrointestinal Development
- Provide Special Nutritional Needs
- Improve Neurodevelopmental Outcome
- Support Physically & Psychologically Healthier Mother

Human Milk Provides Protection from Infection in Premature Infants

OUTCOME	Fortified BM	Formula
Oxygen Rx (days)	19	33
NEC	1.6%	13%
Late-onset sepsis	31%	48%
NEC or sepsis	31%	54%

Schanler et al. Pediatrics 1999;103(6):1150.

GI Benefits of Human Milk for the Premature Infant

- Gastrointestinal development
  - Reduces intestinal permeability faster
  - Induces lactase activity
  - Multiple factors to stimulate growth, motility and maturation of the intestine
  - Human milk empties from the stomach faster than artificial milks
  - Less residuals and faster realization of full enteral feedings

Nutrition of Premature Infants: Cognitive Development

- Many studies have evaluated impact of receiving breast milk (especially fortified) on cognitive development, specifically higher IQ or Bayley score (MDI improved 0.53 per 10ml/kg/day of breast milk)
- Benefit was strongest for children of low birth weight and in males
- Improvement in developmental achievements associated with breast milk persisted at least through adolescence
- Postnatal growth lag and suboptimal HC associated with neurological and sensory handicaps and poor school performance

Vohr et al. Pediatrics 2006;118(1):e115-e123.
Anderson JW et al. Am J Clin Nutr. 1999 ;70(4):525-35.
Isaacs WB et al. Pediatr Res. 2010;67(4):357-62 .

Human Milk Fortification

- Expressed human milk has variable nutritional content, and does not provide adequate nutrition for premature infants
- Must fortify human milk to provide adequate energy, protein, minerals and vitamins for the growing premature infant
- Starting fortifier before being on full feeds (40-100 ml/kg/day total fluids) will allow for transition from parenteral to enteral nutrition without accumulating deficits

Human Milk Fortification

	HM	Pro	Sim	Enf
Energy (kcal)	67	83	79	81
Protein (g)	1.4	2.3	2.3	2.5
Carbohydrate (g)	6.6	7.3	8.2	7.0
Fat (g)	3.9	4.9	4.1	4.9
Calcium (mg)	25	110	138	115
Phosphorus (mg)	13	59	78	63
Osmolality[§]	290	<360*	385	325

*estimated

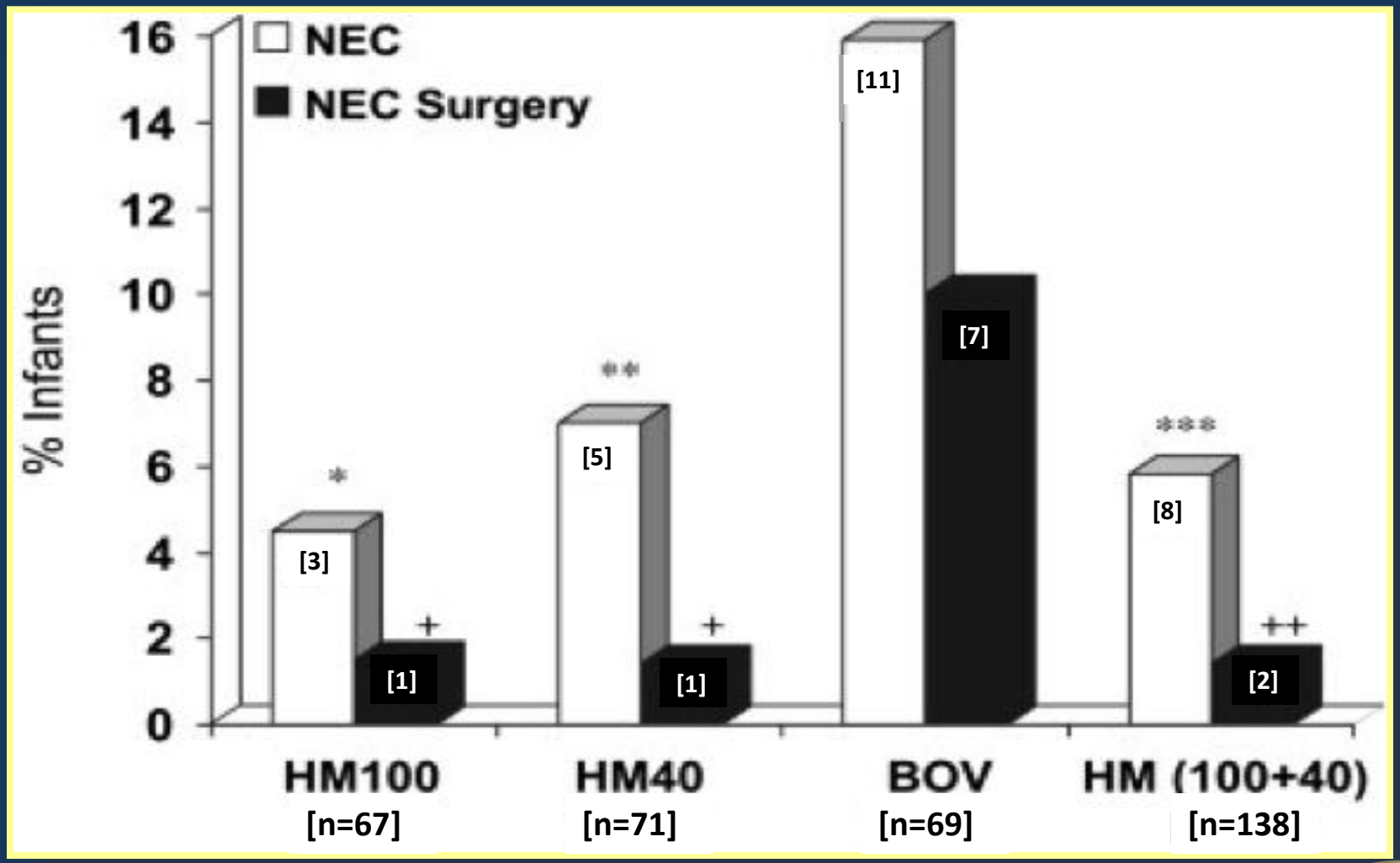
HM=Human Milk; Pro=Prolacta; Sim=Similac; Enf=Enfamil

Human Milk Fortification

- Babies randomized to receive human milk-based fortifier had 50% reduction in medical NEC ($p<0.03$) and 90% reduction in surgical NEC ($p<0.007$) compared to bovine-based
- No difference in feeding intolerance or NEC in those infants receiving human milk-based fortifier starting at 40 mL/kg/day of feeds vs. 100 mL/kg/day

Sullivan et al. J Pediatr 2010;156(4):562-7.

Reduced NEC with HM-Based Fortifier



Sullivan et al. J Pediatr 2010;156(4):562-7.

Human Milk-Based Fortifier Cost/Benefits

- Recent cost analysis predicts savings of 3.9 NICU days and $8,167 per patient, based on cost estimates of medical and surgical NEC within California 2007 dataset
- Factors that influence costs include patient selection, duration of fortifier use, and baseline NEC rate
- Calculator program to estimate unit-specific costs/benefits available at vtoxford.org NICQpedia
- Estimated cost per patient at LPCH=$3,750

Ganapathy et al. Breastfeeding Medicine 2012;7(1):29-37.

Use of Human Milk for Premature Infants- Optimizing Commitment

- Need to start education around human milk and pumping before delivery–by Obstetrical Services and during Neonatology consultations
- Hospital policy support of WHO/UNICEF Ten Steps to Successful Breastfeeding (<5% of hospitals support 9-10 steps) for all babies
- Resource allocation includes facilitating breast pump availability, appropriate milk storage
- Post partum and NICU staff education and support of breastfeeding and pumping, as directed by adequate lactation consulting services

AAP. Pediatrics 2012;129(8):e827–e841.

Human Milk Availability- Recent Studies

- Best way of optimizing milk production is a combination of hand expression and breast pump
  Morton et al. J Perinatology 2009;29:757.
- This combination also increases the caloric content of human milk available to premature infants
  Morton et al. J Perinatology 2012;32:791-6.
- Bundle of practices to improve breast milk availability can be found at cpqcc.org – these were associated with relative 13% improvement in % of VLBW infants being sent home on breast milk
  AAP. Pediatrics 2012;130(6):e1679-e1687.

Challenges to the Use of Mother's Breast Milk for Premature Infants

- Neonatal transports
- Maternal diseases/colonization
- Maternal medications
- Concerns about CMV
- Safety of transport and storage of maternal milk

Alternatives to Specialty Fortifiers

- Protein fortifiers-liquid formulation recently available; lack many nutrients including Ca^{+2} and phosphorus that may be necessary for optimal fortification of breast milk
- Thickeners-recent warning by FDA against use of Simply Thick thickener for VLBW infants due to association with NEC; expressed concern that xantham gum may affect GI flora

FDA Expands Caution About Simply Thick. (2012). Retrieved from FDA.gov http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm256250.htm

Nutritional Care/Outcomes in Premature Infants-LPCH at Stanford

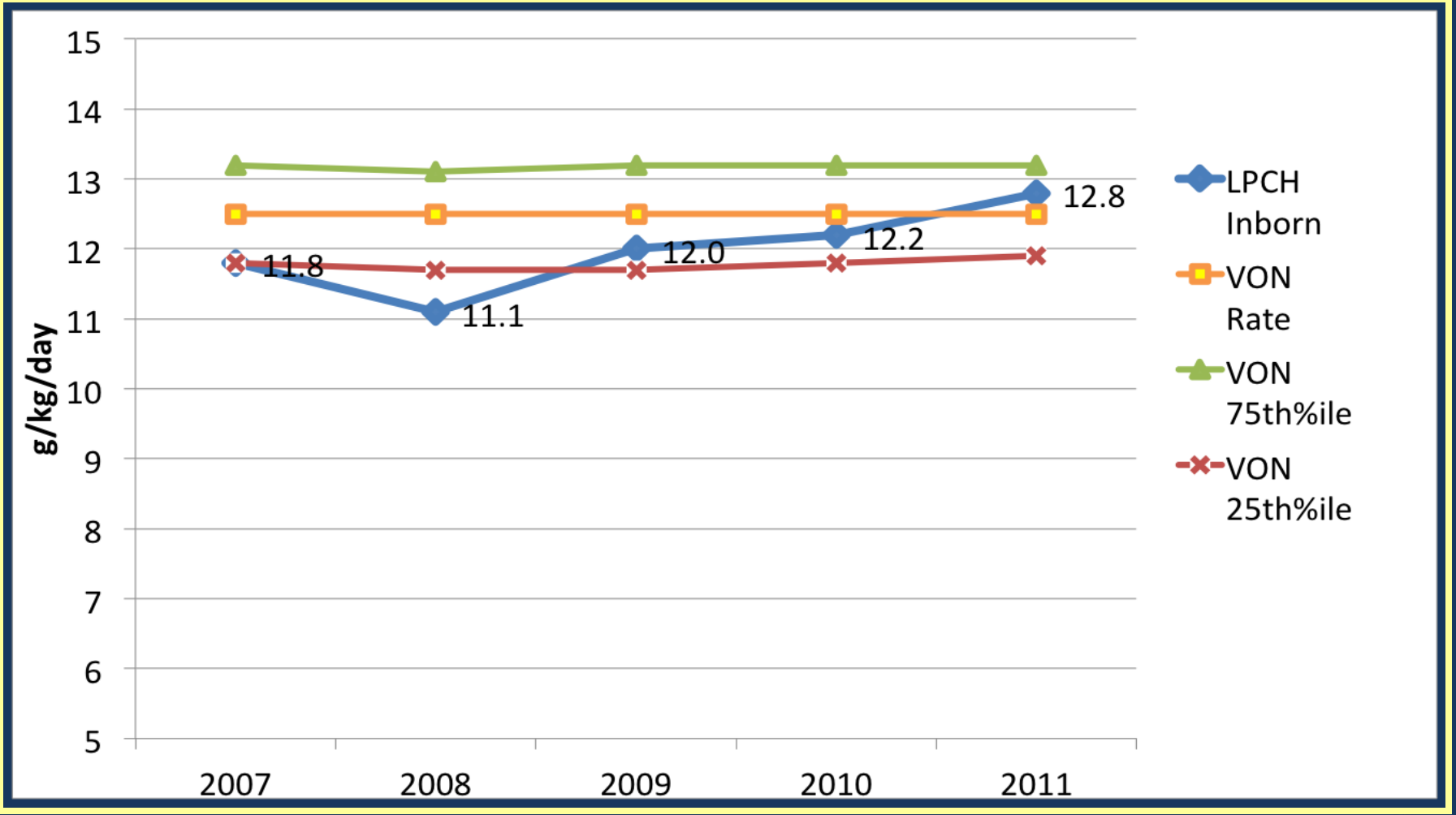
- Feeding pathway and nutrition bundle used at Stanford described by McCallie et al.
- Encourage use of human milk and fortification
- "Early" TPN
- GI priming/trophic feeds
- Defined feeding advance schedule
- Standardized fortification
- Consensus around residuals, feeding intolerance

McCallie et al. J Perinatol 2011;31(Suppl 1):S61-7.

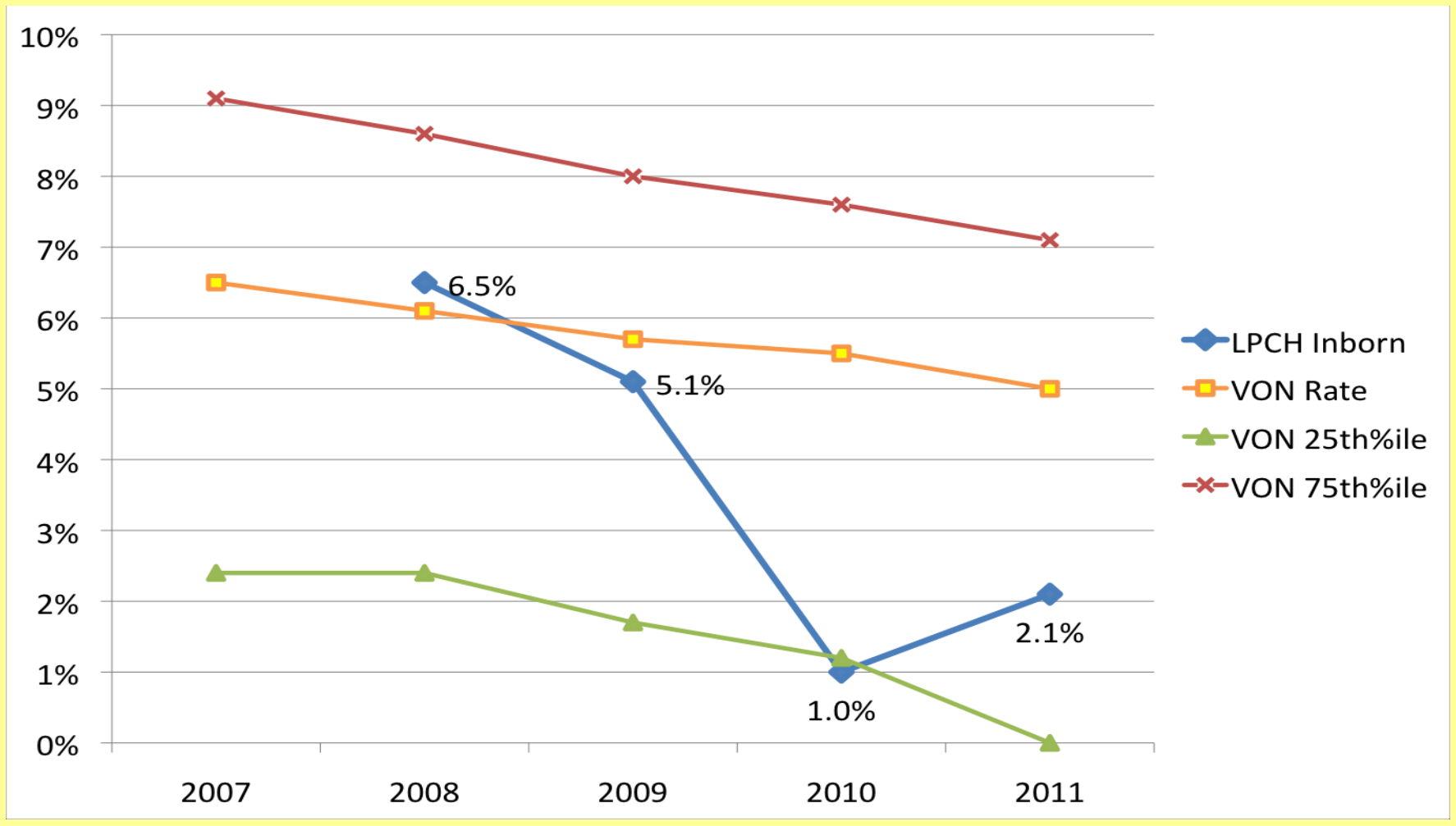
Human Milk Use and Fortification at LPCH

- Over 90% of the mothers of our VLBW infants provide breast milk; if mother's milk not available, we recommend banked breast milk
- Per FDA recommendations, we seek to avoid powdered fortifier products, which until recently limited options
- In past 2+ years we have used Prolacta fortifier up to 1500 gm/34-35 weeks gestational age, then transitioned to other liquid fortifiers
- 85% of inborn VLBW infants are discharged on at least some breast milk

LPCH vs. VON
Inborn Growth Velocity



LPCH vs. VON
Inborn NEC



Nutritional Practices Supporting Breast Milk-Individual Patient Level

- Careful monitoring of nutrition
  - Intake-fluid volume, calories, protein
  - Growth-measuring weight, length (using board), head circumference
- Adjust intake volume to anticipate growth instead of reacting to decreases in growth rate
- Track breast milk production- use pumping log
- No definitive evidence about selection and benefits of nutrition lab monitoring, e.g. alkaline phosphatase

Nutritional Practices Supporting Breast Milk-Individual Patient Level

- Should aim for weight gain of 15-18+ gm/kg/day during growth phase after weight nadir
- Premature infants being discharged home should have careful follow-up of their nutrition and growth
- Nutritional supplementation for premature infants should be continued for 3-6 months to optimize growth and development

Nutritional Practices Supporting Breast Milk-NICU Level

- Average weight gain for VLBW infants*
- NEC rate for VLBW infants*
- Track and benchmark percentage of babies starting on human milk (mom's or banked)
- Track and benchmark percentage of babies discharged on human milk*
- Other nutritionally-related measures include day of first feed, TPN days, length of stay*

* Data available on VON, Pediatrix NICU databases

Alternatives to Mother's Breast Milk

- Banked breast milk-usually in conjunction with HMBANA milk bank
  - Usually selected population for use, e.g. VLBW infants
  - Informed assent/consent should be obtained describing pros and cons of donated milk compared to formulas
- Special premature formulas-superior to term formulas as far as growth; nutritional content better meets the needs of premature infants

Summary

- Nutrition is critically important for the optimal growth and development of premature babies
- Ideal food for premature infants is mother's breast milk that should be fortified, or donated breast milk (fortified prn), or else premature specialty formula
- Successful use of breast milk depends on institutional promotion and support and maximizing availability
- Should have standardized approach based on providing optimal nutrition, mainly human milk for premature infants; at Stanford this has been associated with improved growth velocity and reduced NEC