Infant nutrition is not and never has been based on static or well established rules and methods. Nowhere are ever changing principles truer than in observations of nutrition and feeding practices of premature infants.

Premature infants have been born and have survived since the dawn of history. MacDuff who killed MacBeth was a premie. Little record of early feeding practices of these infants is available. Assumption is made that most of the infants who lived must have been fed human milk, since mortality of term infants fed artificial milks, at least in foundling hospitals, approached 100%. Not all of this abhorrent mortality, however, can be ascribed to infant feeding practices alone, since it is known that much of the failing to thrive of these infants was related to their isolation and lack of stimulation.

In the Papyrus Ebers (Egypt 1550 B.C.) breast feeding and methods of increasing secretion are discussed. Wet nurses were utilized in the 4th century B.C. in Egypt. Soranus in Rome (100 A.D.) recommended testing a drop of breast milk by placing it on the fingernail.[1] If it retained its form, it was supposedly easy to digest. By the 16th century, written references recommended nursing 2-3 years, even though paps were used beginning in the 3rd month. Nonetheless, Holt and others in the early 20th century recommended that no solids be given before the 10th month.[2]
After improvements were made in modifying other animal milks so that they were reasonable substitutes for mother's milk, attempts were made to feed premature infants artificial formulas. Following the appreciation of sanitation, pasteurization and causes of infectious diseases, around the turn of the century, a host of different formulas were developed, each purporting to have special benefits for the term infant, and some especially recommended for preterm infants. Ruebner and Huebner[3] developed a calorimetric method of determining nutritional needs and this was applied to premature infants.

In spite of the concern of Rotch[4] of Boston that human milk was inadequate for term as well as preterm infants, the first milk bank was established in Boston in 1910 and was used until about 1950, especially for the nourishment of preterm infants. Many of the vitamins had been identified by 1940 and these were used as supplements, much as had been prescribed for term infants. Many of those who cared for premature infants recommended human milk with or without other supplements.

In the late 1930's, Gordon and Levines studied premature infants by balance techniques and confirmed Holt's findings that they absorbed cow's milk fat poorly. Gordon and Levine then recommended a high protein diet for low birth weight infants which became a standard for premature infants for about a decade.

In the early 1950's, Kagan et al.[6] noted that premature infants could thrive on cow's milk altered to contain vegetable fat, and Barness et al.[7] noted an increased morbidity and mortality in premature infants fed high protein diets. Morbidity and mortality both decreased when the protein of cow's milk was derived largely from whey.[8]

Debate of the necessity of onset of premature feedings existed until about 1960. Hess[9] had recommended withholding feedings for several days. Holt[10] and Smith[11] supported this view by claiming that the edema of premature infants must disappear before beginning feedings, lest the infant aspirate. However, Haworth[12] had noted that hyperbilirubinemia and hypoglycemia were lessened when the first feeding was offered in the first 12 hours, a practice recommended today.

Until 1950, few metabolic studies in premature infants could be performed without extreme difficulty because of the very high mortality rate of low birth weight infants. With improved technology, particularly relating to isolation procedures, more infants lived and, with the advances in respiratory support, long-term studies were more frequent. As these studies have progressed, data have accumulated on the nutritional needs of premature infants, so far largely based on and limited to growth rates. An early goal was a rate of weight gain as rapid as possible to limit hospital stay, since it was recognized that the spread of infection was more hazardous in the hospital than at home.

One of the problems concerning premature feedings was related to the mode of supplying both food and water. Droppers which were recommended by Hess[9] and others depended on the infant's ability to swallow and many infants died from aspiration of the feeding. Tube feedings were instituted, mainly through intermittent gavage, with a lowering of morbidity. Debate persists as to the best method of tube feeding, with certain advantages ascribed to intermittent gavage and placement of the tube in a
transpyloric position or in the stomach.

Parenteral nutrition was limited largely to glucose, base, and water, until purified amino acid mixtures were developed in the late 1960's and intravenous fat mixtures in the past decade. These promise to provide data on which to base better nutrition for infants.[13]

Caloric requirements of premature infants were estimated by Gordon and Levines to be about 150 cal/kg/day, not too different from those recommended by Hill et al. [14] and Sinclair et al. [15] At the same time, the extra requirements of the stressed infant were recognized and present recommendations continue to be about 110 to 150 cal/kg/day. Hardy and Goldstein recommended supplying these calories in concentrated liquids to shorten hospital stay.[16]

Estimates of water requirements were first based on those of term infants. Term infant requirements, however, were based on knowledge obtained from progress of infants fed breast milk. Since few premature infants could feed directly from the breast, modifications and estimates varied widely. Metabolic studies have related water requirements to weight, as well as to surface area, and recommendations now are similar to those for the term breast fed infant, with the recognition that heat, cold, stress or phototherapy increase requirements.

Water requirements must be met, while high caloric intake seems desirable. Therefore, an optimal caloric density of formulas continues to be of concern. Recent reports express disagreement in regard to fluid intake early in the life of premature infants, particularly those afflicted with respiratory distress and heart failure, or in those in whom the re-opening of a ductus arteriosus due to large water intakes may be detrimental.

Protein requirements have been reestimated periodically, since 1869, when Beidert stated that cow's milk protein was needed for term infants.[17] Preparations of fresh or banked human milk were used until the studies of Gordon and Levine were published. The protein content of human milk was estimated at 1.2-1.5 gm/100 ml, so that a baby consuming about 150 ml was calculated to be receiving about 2.25 gm/kg/day. The Gordon and Levine formulas supplied 5-10 gm/kg/day.

Present recommendations[13] include a protein requirement of 2.25-5 gm/kg/day, the higher number clearly not obtainable from breast milk with a protein content of 1.5 gm/100 ml. This led many to believe that human milk was insufficient in protein for human infants, a concept which was anathema to those believing that human milk was the optimal food for all infants. This controversy has been partially resolved by the findings of Atkinson et al. [18] and Gross et al. [19] that the milk of mothers delivering preterm contains a higher protein content than that of mothers delivering at term.

That the quality of the protein of human milk is different from and superior to that obtained from cow's milk or other sources of protein has been suggested. Among the differences noted to be of probable importance is the higher content of cystine and taurine in human milk, as documented by Gaull and co-
Part of the debate surrounding protein requirements occurred secondary to the recognition that fat absorption was limited in small infants. This was especially noted in infants weighing less than 1500 gm and in infants fed fats which were largely saturated.

Tidwell and co-workers\[21\] showed that fat absorption was relatively good when infants were fed human milk fat or fat with similar concentration of unsaturated fats. Additional studies gave good indication that polyunsaturation of fats and distribution of fatty acids on triglycerides increased fat absorption, so that premature infants could obtain 40-50% of their calories from fats, a dietary distribution similar to that of human milk.

While polyunsaturated fats appear to be better absorbed than saturated or mono-unsaturated fats, a high intake of polyunsaturated fats was found to be associated with a hemolytic anemia responsive to vitamin E\[22\] and apparently was made worse by the presence of iron in the feeding.\[23\] This has led to concern regarding the amount of iron which should be in the formula, as well as the onset of iron-containing feedings to prevent anemia. Most human milks contain about 11-13% polyunsaturated fats.

It has been appreciated for at least 40 years that certain fats are essential. Linoleic acid certainly appears to be essential and is included in all presently formulated diets for premature infants. Linolenic and arachidonic acids may also prove to be limited, though present evidence indicates that premature infants can make these as well as several other long-chain polyunsaturated fatty acids found in human milk. Since these are precursors of prostaglandins, further work is necessary to qualify the need of these nutrients for prostaglandin metabolism.

Medium chain triglycerides have been added to formulas with a consequent increase in fat absorption in low birth weight infants. Concomitantly, calcium and nitrogen absorption have increased.\[24\]

Interest in carbohydrate content of formulas is of recent vintage. Almost any monosaccharide or disaccharide was considered satisfactory, since stool losses of reducing substances were not great. Lactose such as in breast milk, dextrin-maltose, sucrose and glucose appeared to be equally satisfactory. Developmental studies by Auricchio and others\[25\] indicate that maltase and sucrose reach mature values at the end of the second trimester, while lactase does not reach these levels until term. In addition, some have suggested a relationship between high osmolality of the diet and necrotizing enterocolitis. For the past decade, attempts have been made to relate the type of carbohydrate with elimination of some diseases and various glucose polymers have again been used for premature feedings.

For a time, soy isolate formulas enjoyed some popularity in premature feeding. Some felt that soy protein might be less allergenic than cow's milk protein. It now appears that soy is highly allergenic. In addition, the lack of carnitine in vegetable proteins may contribute to errors of fat metabolism. Interest in minerals for premature infants extends back at least 75 years. Early studies in the prevention of rickets included addition of calcium and phosphorus to the diet. Parks and others recommended calcium
supplements but concluded that rickets could not be prevented. Others have recommended increased vitamin D and new studies may support the concept that the premature infant has decreased ability to hydroxylate vitamin D.[26]

Interest also extends to copper, zinc and other trace minerals. These may be limited in human milk, but may be present in higher quantities in premature than in term milk. Data are needed to establish mineral requirements, for differing growth rates, of all the minerals recognized as essential.[13]

Philosophically, proponents of breast milk feedings for term infants suggest advantages of similar feedings for preterm infants. The lower osmolality and anti-infective properties of human milk have been documented.[27] The recognition that the young of other mammals die if not given colostrum lends support to the unique advantages of milk of homologous species for their infants. Indication that foreign proteins can be absorbed by the young and that compatible proteins may improve the gastrointestinal barrier[28] stimulates the search for better feedings than are now readily available.

The understanding of nutritional requirements of the premature infant is presently in its infancy. Each item of the diet-water, calories, carbohydrate, fat, minerals and vitamins—is evaluated separately. Modes of feeding vary. Sources of nutrients are surrounded by debate. Function of a warm and loving caretaker is in conflict with rules and regulations of a high-risk nursery. Optimal rates of growth are being studied. Outcome of the infant at some finite period, such as 5 or 7 years, has been suggested as a true test of nutritional adequacy; but even this is subject to variables such as innate endowment, stimulation and challenge during the post hospital period, and the resiliency of the human constitution. Some more quantitative method of evaluation must be developed, lest we continue groping and debating.

REFERENCES


