PARENTERAL feeding in which all nutrients are given intravenously was shown by Wilmore and Dudrick\(^1\) to have sustained growth at a near-normal rate in an infant. Height, head circumference, and development progressed at normal rates for 44 days. Normal weight gain and skeletal growth also has occurred in puppies fed intravenously for 10 months.\(^2\) A number of studies\(^3\)–\(^7\) have shown that nutritional needs sufficient to promote wound healing, improve general status, cause a gain in body weight, and support positive nitrogen balance can be met for periods in excess of 1 year entirely by parenteral alimentation. The mean daily weight gain in a recent report\(^8\) was 18 gm for infants in the first 2 months of life. This rate of gain is at the 5th percentile for normal breast-fed infants during the first 2 months of life.\(^8\)

The preferred method of infusion has been the insertion of a silastic catheter through either a subclavian or jugular vein into the superior vena cava, with scrupulous attention paid to the prevention of sepsis from skin bacteria.\(^2\) Insertion into other veins has been associated with a much higher complication rate.\(^5\),\(^10\) The infused solution\(^7\) has provided about 80% of the needed calories as glucose and 20% as either Amigen (a hydrolysate of casein) or Aminosol (a hydrolysate of beef fibrin).\(^*\) Minerals and vitamins have been added to these solutions. Plasma has been infused in some, but not all, patients 1 to 2 times weekly in an effort to provide essential fatty acids and trace minerals.

Certain observations can be made from the experience to date:

1. Glucose utilization will increase and will, in most instances, be sufficient to meet caloric requirements in the absence of significant fat intake;\(^2\)
2. A glucose-amino acid mixture can support linear growth, an increase in head circumference, and a gain in weight;\(^1\)
3. By inference, the infused amino acid peptide mixture permits normal synthesis of protein by tissues, although plasma amino acid patterns may differ considerably from normal;\(^11\)–\(^13\)
4. Loss of infused glucose and amino acids in the urine is usually trivial;\(^4\)
5. Short-term (35 days) clinical results, when there are no complications, are impressive.\(^1\)–\(^7\)

Most of the reports involving the pediatric age group are from surgeons treating newborn infants who have major anomalies of the gastrointestinal tract. The infant reported by Wilmore and Dudrick\(^1\) had massive bowel resection and died after 22 months of heroic efforts at therapy. Many of the infants have had lesser, but heretofore high-risk, anomalies of the bowel and have received from 10 to 35 days of parenteral feeding. The use of parenteral feeding in the hands of those who have established special programs has undoubtedly improved the survival rate of infants with such major anomalies. Infants requiring parenteral nutrition much beyond 35 days have an increase in the incidence of complications,\(^8\) and their survival rate probably is low.

Several recent studies were undertaken to determine whether survival and growth rates of low birth weight newborn infants, including premature infants and infants small for gestational age, are improved by parenteral alimentation. Many of the clinical results of these studies and complications were reported informally before an open symposium held in Atlantic City.\(^14\) Limited data from metabolic studies also were presented.

To develop some recommendations concerning parenteral alimentation, the Committee on Nutrition reviewed the literature, reports of Committee members who are

\(^*\) Protein hydrolysates are approximately 50% free amino acids and 50% undefined peptides.
working in this field, and reports recalled from the Atlantic City meeting. The recommendations take into account the discrepancies between complications and clinical gains in the various reports reviewed. These discrepancies appear to be the result of, to a great extent, the degree of program development and, to a lesser extent, the type of patient selected for parenteral alimentation. The complications cited so far include, in approximate order of importance:

1. Sepsis, including fungal and bacterial: The major contribution in the technique of Dudrick was the method of catheter insertion and care which reduced the incidence of infection. Nonetheless, infection is the most frequent, serious complication, even where ideal conditions prevail. Reports from other hospitals, where special programs were instituted, record a high rate of sepsis. Anecdotal information has reinforced the reasonable assumption that the infection rate is prohibitive in hospitals not making special provisions for preventing infection.

2. Extravasation: Solution and catheter accidents constitute a second category of complications. These again vary in proportion to the experience, energy, and organization directed to the program in a given institution. However, it is fair to surmise that the rate of complications in institutions where considerable effort is expended is still high.

3. Hyperglycemia associated with osmotic diuresis, dehydration, and a hyperosmolar state: This complication arises when the rate of glucose infusion exceeds the rate of glucose utilization. The resulting osmotic diuresis can lead to dehydration and either hyper- or hyponatremia, depending on the ratio of salt to water in the intake and output. Using the formula originally proposed, these problems are infrequent in full-term infants with normal liver and kidney function. Either osmotic diuresis or hyperglycemic hyperosmolality is apt to be a more important problem in the low birth weight infant and the child with renal insufficiency or liver disease. Decreased glucose utilization may develop in a patient who becomes septic. Errors in setting delivery rate can induce one or more of these complications.

4. Volume overload and heart failure: These problems have been cited as a complication in low birth weight infants where infusion rate exceeds renal excretory capacity for salt and water resulting in volume expansion. This complication is more likely in smaller infants in whom infusion rate per kilogram of body weight is likely to be highest, particularly if there is immature kidney function or renal anomalies.

5. Metabolic acidosis: There is little information on acid-base status in most reports. The detailed studies of Filler and his associates do not mention acidosis developing during treatment. The use of a metabolic mixture, providing 20% of calories as amino acids, may induce metabolic acidosis. Heird and his associates noted the development of hyperchloremic acidosis—which was a result of the high content of amino acid hydrochlorides in the essential amino acid solution—in premature infants on a glucose-free amino acid mixture.

6. Abnormal plasma aminograms: Abnormal aminograms have been reported in some, but not all, infants receiving Aminosol or Amigen. Although no adverse effects have been noted associated with these abnormal aminograms, amino acid imbalances may have an adverse effect which is not clinically apparent. Loss of amino acids in urine is slight, but there is little or no information on peptide loss. Positive nitrogen balance has been documented.

7. Bone abnormalities: Two reports of abnormal roentgenographic changes in bone have been recorded. Rickets developed in one patient during prolonged parenteral feeding. The nature and significance of the bony changes in the second report are uncertain. Disuse or deficiency in a trace element such as zinc may have caused these changes because parenteral alimentation was prolonged.

8. Hypophosphatemia: Glucose administration will produce hypophosphatemia and a defect in red cell metabolism.
9. Liver necrosis: Two deaths from liver necrosis have been reported.\(^2\) Liver necrosis may be related to catheter placement and the infusion of hypertonic glucose directly into the liver.

10. Vitamin and trace mineral deficiencies: Nutrient deficiencies always are possibilities when semi-synthetic diets are used as a sole source of nutrition. Deficiencies in folic acid, vitamin D, vitamin K, magnesium, and copper have been reported.

In addition to these cited complications, a number of uncertainties remain:

1. In a relatively short-term use of parenteral feeding (2 to 4 weeks), weight gain often is used as an index of growth. Weight gain under these conditions may be the result of an expansion of extra-cellular fluid volume rather than growth as a gain in cell mass. A true measure of growth is not necessarily determined by a change in weight.

2. This type of artificial feeding during so crucial a period of development may induce deficiencies that will emerge only later, particularly in terms of brain growth and function. The absence of essential fatty acids in the nutrient mixture, hypophosphatemia, and abnormal plasma aminograms are of particular concern.

3. The use of this regimen in small infants (<1,500 gm) may increase the risk of death in a group whose survival rate would be better without this therapy.

4. Metabolic variation of genetic origin is more prevalent than many appreciate. Infants with such variations would be at an undetermined risk from parenteral feeding until their precise tolerance and requirements are known.

The Committee on Nutrition recommends the use of parenteral alimentation only where experience in its use can be accumulated and monitoring techniques directed to the prevention of complications are available at all times. For infants with intolerance to food whose life is threatened, it is hoped that results from different centers can be pooled to determine the ultimate effectiveness of this technique over a short time. Despite the theoretic appeal of parenteral alimentation for low birth weight infants, its therapeutic efficacy—both in terms of survival and long-term development—must be proved before it becomes an accepted form of therapy.

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