The Use of Intravenous Fat Emulsions in Preterm Infants

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The first intravenous fat (IVF) preparation used to any great extent in the United States was made from cottonseed oil and marketed under the trade-name of Lipomul®. A great deal of experience was gained with the use of this emulsion and, in fact, an entire symposium was published reviewing the data regarding this agent (*Metabolism*, 6:591–831, 1957). Lipomul® was withdrawn from the market in 1965 because of numerous reports of toxicity, including "the fat-overloading syndrome", hemorrhagic tendencies, and liver damage. The toxic accumulation of fat observed with Lipomul® was attributed to its large particle size (1 μ in diameter), and possibly the emulsifying agent, pluronic F-68 (46,76).

In 1961 Schuberth and Wretlind described the use of a parenteral fat emulsion made from soybean oil (65), and in 1981 Wretlind reported that in Sweden over 1.6 million units of this emulsion, Intralipid®, were infused with only 8 cases of suspected untoward reaction. In only one case was a causal relationship probable (79).

After Intralipid® had been used extensively in Europe and Canada, it was finally approved by the FDA for use in the United States in 1975. In 1979 Liposyn® became available in the United States, and, more recently, a third fat preparation, Travamulsion®, has also been released for use.

Intralipid® and Travamulsion® contain soybean oil as a base, while Liposyn® is made from safflower oil. Each product uses purified egg phospholipid as an emulsifier, each contains glycerin to make the solutions isotonic, and, when metabolized appropriately, each will yield 1.1 cal./ml.

Table 1 lists the make-up and notes the differences in each of the products. The particle size of Intralipid® is 0.5 μ while those of Liposyn® and Travamulsion® are 0.4 μ. Both Intralipid® and Travamulsion® contain linolenic acid in significant amounts—8% and 6% respectively; less than 0.5% of this fatty acid is found in Liposyn®. Until recently, linolenic acid deficiency had been recognized only in trout (80) and rats (41), but a 6-year-old child who had received a linolenic-free diet for 5 months developed neurological symptomatology including numbness, weakness, leg pain, and blurring of vision (37). Her symptoms disappeared when she was given linolenic acid via an infusion.
TABLE 1. IVF emulsions (10%)

<table>
<thead>
<tr>
<th></th>
<th>Intralipid®</th>
<th>Liposyn®</th>
<th>Travamulsion®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base</strong></td>
<td>Soybean oil</td>
<td>Safflower oil</td>
<td>Soybean oil</td>
</tr>
<tr>
<td><strong>Glycerin content</strong></td>
<td>2.25%</td>
<td>2.5%</td>
<td>2.25%</td>
</tr>
<tr>
<td><strong>Osmolarity (mOsmoles/l)</strong></td>
<td>280</td>
<td>300</td>
<td>270</td>
</tr>
<tr>
<td><strong>Particle size (micron)</strong></td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Fatty acid composition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>54%</td>
<td>77%</td>
<td>56%</td>
</tr>
<tr>
<td>Oleic acid</td>
<td>26%</td>
<td>13%</td>
<td>23%</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td>9%</td>
<td>7%</td>
<td>11%</td>
</tr>
<tr>
<td>Linolenic acid</td>
<td>8%</td>
<td>0.5%</td>
<td>6%</td>
</tr>
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</table>

of Intralipid®. Thus, one must be cautious in using Liposyn® as the only source of fat for patients receiving long-term parenteral nutrition (10).

Both Liposyn® and Intralipid® are available as 10% and 20% solutions, but Travamulsion® is available only as a 10% solution. To date, experience with the 20% emulsions has been limited in the United States (10), and most reports evaluating this solution have emanated from Europe (78). Two additional soybean preparations are available, Intrafat® (Japan) and Lipofundin-S® (Germany), and a cottonseed oil emulsion, Lipiphysan®, is available in France.

METABOLISM OF INTRAVENOUS FAT

The metabolic pathway for the IVF emulsions is similar to that of naturally occurring chylomicrons. The clearance takes place near the capillary endothelial cells, primarily in adipose tissue and muscle, and is dependent upon the activity of lipoprotein lipase to hydrolyze the circulating protein-bound triglyceride (7,30). The free fatty acids thus liberated can enter adipose tissue, where they are reesterified to triglycerides and stored, or they can be utilized as metabolic fuel in the heart, skeletal muscle, or liver. In the liver, free fatty acids can also be converted to very low density lipoproteins (VLDL), which in turn can be secreted into the plasma.

The clearance of lipid can be enhanced with the concurrent use of heparin, dextrose, or insulin. Adequate calories derived from carbohydrates are necessary for free fatty acids to be oxidized through the citric acid cycle. If there is inadequate carbohydrate to fuel the citric acid cycle, oxidation of fatty acids does not progress properly, and ketone body formation is accelerated. Insulin enhances triglyceride clearance and tissue uptake through lipogenesis and decreases the release of free fatty acids from adipose tissue.

USE OF INTRAVENOUS FAT IN PRETERM INFANTS

While a great deal of experience has been accumulated with the use of IVF in laboratory animals and adult humans, it has been only within the last 10
years that any data have been generated regarding the use of these preparations in preterm infants (11,28,29,47). With the use of IVF, it has become possible to provide the infants with a more balanced nutritional regimen, to avoid the problems of essential fatty acid deficiency, and, at the same time, to allow physicians to utilize peripheral rather than large-caliber central veins to infuse nutriments parenterally. The major stimulus for the use of IVF was provided by the work of Cashore and co-workers, who demonstrated that infants given glucose, casein hydrolysate, and IVF regain their birthweights by 8–12 days of age and grow at approximately the same rate they would have, had they remained in utero (11).

In addition, physicians recognize that infants receiving parenteral nutrition that is free of fat soon develop signs and symptoms of fatty acid deficiency (26,31,35,36). This is especially true in small prematurely born infants and infants who are small for gestational age, as they often have less than 1% of their body weight as fat. Essential fatty acids are necessary for a large number of important physiological functions, including the maintenance of membrane integrity (26,49), prostaglandin synthesis (44,58), wound healing, immunocompetency (35), and integrity of the central nervous system (36). Often the signs and symptoms of fatty acid deficiency are not recognized readily, and, in some infants, these signs can occur within several days to a week of being on a fat-free intake (23). In addition to a reduced rate of growth, these infants demonstrate a characteristic scaly dermatitis, which at times can develop into a weeping erythematous rash, impaired wound healing, decreased resistance to infection, abnormal platelet aggregation, and thrombocytopenia, as well as increased fragility of red cells (22). Laboratory documentation of fatty acid deficiency consists of monitoring the ratio of eicosatrienoic to arachidonic acid (triene/tetraene ratio), and a ratio of 0.4 or greater is indicative of essential fatty acid deficiency (34).

In the past, in order to prevent fatty acid deficiency in infants receiving parenteral nutrition, physicians provided some fat enterally whenever that was possible, or else they infused fresh frozen plasma which had been drawn from a suitable donor who had ingested a high-fat meal prior to the collection. While this technique, at times, could transiently reverse essential fatty acid deficiency, the long-term effectiveness was minimal, and the plasma provided few, if any, calories for the infant. In addition, attempts to prevent the essential fatty acid deficiency with use of medium-chained triglycerides were also unsuccessful (33). One-half to 1.0 g/kg/day of IVF is adequate to prevent essential fatty acid deficiency.

IVF preparations have also been shown to provide protein-sparing effects similar to those demonstrated with intravenous glucose, and have resulted in infants demonstrating a marked improvement in nitrogen retention (59). In fact, an infusion of glucose and amino acids, as well as intravenous fats, would seem to be the preferred way of providing a balanced nutritional intake. With the use of IVF the amount and concentration of glucose needed for infusion
can be decreased, the need to use a large-caliber vessel for infusions can be obviated, and the fat emulsion itself seems to offer a protective effect to the blood vessel through which the solution is infused.

Because the fat emulsion breaks down if mixed with hypertonic solutions, the fat must be administered separately, usually through a Y-connector attached as near as possible to the point of entry of the catheter or needle into the vein. The infusion is usually best tolerated if given as a constant infusion over 24 hr.

In most situations the infusion of fat need not exceed 2 g/kg/day. Thus, if IVF is given to infants receiving 12.5% dextrose and 2.0% amino acids, the fat will provide 24% of the calories if the glucose-amino acid solution is infused at the rate of 100 ml/kg/day (75 cal./kg/day); 20% of the total calories if the rate is 120 ml/kg/day (85 cal./kg/day); and 17% of the calories if the rate is 150 ml/kg/day (105 cal./kg/day). This type of caloric distribution may be appropriate for the preterm infant, even though the contribution of fat to total caloric intake is less than that found in most formulas, including breast milk. Data from the studies of Riechman and co-workers show that very-low-birth-weight infants, who are fed enterally an infusion wherein the fat makes up greater than 50% of the total calories, have a much greater fat content in their body composition than they would have had had they remained in utero (32% vs. 10%-12%) (57).

In very-low-birth-weight infants or infants who have severe respiratory disease, where fluid restriction is desired, the lipids can be given as a 20% solution rather than as a 10% solution. On occasion an increased amount of IVF may be desired or indicated, especially if a greater caloric intake is necessary; however, it is unusual for more than 3 g/kg/day to be infused into very-low-birth-weight infants.

TOLERANCE OF IVF IN PRETERM INFANTS

Although normal term infants are able to tolerate and metabolize IVF at rates similar to those of adults, preterm infants are unable to tolerate the fats as well (18,60). Studies by Shennan and co-workers (60), as well as by Filler and co-workers (18), suggest that immature infants metabolize IVF slowly, at rates that are approximately one-third those of mature infants. The incidence of hyperlipidemia in infants who are less than 33 weeks gestation and who weigh less than 1,500 g is triple or quadruple that of mature infants (18). Interestingly, these immature infants increase their capabilities to tolerate IVF after the first week or two of extrauterine life (54,55).

Similarly, infants who are small for gestational age (SGA) also have a decreased rate of utilization of IVF compared with infants who are appropriate for gestational age (AGA) (2,29,50). Often the incidence of decreased tolerance in SGA infants is greater than that found in preterm infants who are AGA, and concentrations of triglycerides and free fatty acids in serum following
infusions of IVF are two to three times greater than that found in preterm infants who are AGA (1).

In addition, infants who are hypoxic, acidotic, septic, or who have intercurrent illnesses, have intolerances for IVF even at rates of infusion that had been tolerated before these problems became evident (9).

Thus, while infants who are AGA can metabolize 0.15 g/kg/hr (3.6 g/kg/day), very immature infants and infants who are SGA may accumulate plasma lipids at this rate, and slower rates of infusion are necessary for these patients (29).

The reason for this impaired rate of infusion has been thought to be due to decreased activity of lipoprotein lipase as well as decreased amounts of adipose tissue present in these infants. Dhanireddy and co-workers have demonstrated that immature infants of 25 and 26 weeks gestation have about one-third of post-heparin lipolytic activity as compared with infants of more than 27 weeks gestation (15). This is indirect evidence that the activity of tissue lipoprotein lipase is also decreased. Data in humans are lacking, but studies in laboratory animals show that the activity of lipoprotein lipase in lungs follows a developmental pattern that is very low in activity in the immediate newborn period and increases as the animal matures (32).

Although heparin has been shown to release lipoprotein lipase from tissue and enhance the clearance of IVF in the serum of patients receiving Intralipid®, (29) Coran and co-workers have shown that the addition of 150 IU/kg/day of heparin did not significantly alter the rate of clearance of fat from the serum of immature infants (13). Recently, Zaidan and co-workers (81) have shown that continuous intravenous administration of 1 U/ml of heparin to very-low-birth-weight infants receiving Intralipid® enhanced the clearance of triglycerides from serum, but at the same time appreciably increased the concentration of free fatty acids in serum. Thus, the routine addition of heparin to IVF solutions has not been completely evaluated, especially in the very-low-birth-weight infants.

**COMPLICATION OR ADVERSE REACTIONS**

The incidence of complication or adverse reactions of IVF is low even in the preterm infant if the rate of infusion does not exceed 0.15 g/kg/hr. However, there are numerous complications, actual and theoretical, that should be anticipated if IVF is to be used.

**Allergic Manifestations**

Allergic manifestations, painful extremities, fever, headaches, and vomiting have been described in older infants, children, and adults; these complications, however, are difficult to recognize and assess in preterm infants (38). Eosinophilia is not an uncommon finding in infants (6), but it may be due to a variety of factors, such as ingestion of cow's milk protein, frequent blood transfusions, cutaneous applications of various dermatological preparations, and oral and
parenteral infusions of pharmacological agents. Thus, documentation of allergic reaction to IVF in preterm infants is difficult, if not impossible.

Cholestasis

Cholestasis is a complication frequently encountered in infants receiving total parenteral nutrition (TPN), and the longer the infant receives TPN, the greater likelihood that cholestasis will be encountered (66). It was hoped that the use of IVF would decrease the incidence of cholestasis; unfortunately, this is not the case. Conversely, the use of IVF has not resulted in an increased incidence of cholestasis in these infants. The pathophysiological factors that are responsible for the development of cholestasis in the affected infants are incompletely understood at present.

Fat-Overloading Syndrome

The fat-overloading syndrome, consisting of hyperlipemia, fever, liver damage, and coagulopathy, which was described primarily in adults, has been encountered infrequently, if at all, in infants and children (4,48). This is due primarily to the fact that infants are given relatively small amounts of IVF as compared with adults.

Impaired Utilization of Glucose

Rapid infusions of IVF have caused hyperglycemia in infants receiving glucose and amino acid solutions at rates that they had tolerated prior to the time the IVF was given. In recently reported studies, infusions of IVF at rates of 0.5 g/kg/hr for 2 hr, and even at rates of 0.25 g/kg/hr, have resulted in glucose intolerance in low-birth-weight infants (75). Mechanisms by which hyperglycemia has been produced is not completely understood, but a significant increase in the concentration of plasma insulin occurs during the infusion of IVF, mitigating the hypothesis that insulin activity is depressed. Whether the IVF reduces the rate of glycolysis or enhances gluconeogenesis has not been elucidated in these patients.

Impairment of Pulmonary Function

Greene and co-workers were the first to note the relationship between IVF-induced hyperlipemia and decreased pulmonary function (27). They noted a decrease in pulmonary membrane diffusion at rest, and also following exercise, in normal healthy adults. In addition, they demonstrated that rabbits infused with Intralipid® had erythrocytes coated with lipid particles in their lungs. Friedman and co-workers reported two infants of low-birth-weight who received IVF and had fat globules in their alveolar macrophages and capillaries at necropsy (25). Levene and co-workers described fat accumulation in the lungs of eight prematurely born infants who expired in the neonatal period and who had received a 20% solution of IVF (42). The maximum rate of
infusion of fat in seven of eight of these infants had exceeded 0.15 g/kg/hr, but the mean rate of infusion exceeded 0.15 g/kg/hr in only one infant. Andersen and co-workers performed postmortem examinations not only of preterm infants who had received IVF, but also of those who had received only intravenous glucose and human milk enterally (3). They found similar findings to those reported by Levene and co-workers in both groups of infants, and they felt that pulmonary accumulation of fat could occur in infants whether they received fat enterally or parenterally. Dahms and Halpin suggested that lipid deposition in pulmonary walls was probably derived from IVF, but occurred in vessels that had been damaged secondary to pulmonary hypertension, chronic lung disease, or congenital heart disease (14).

Sun and co-workers demonstrated a reduction in PaO\textsubscript{2} in term infants when given 1 g/kg of Intralipid\textsuperscript{®} over a 15-min period (69). Although they could demonstrate no alteration in pulmonary function per se, Pereira and co-workers were able to detect a significant decrease in PaO\textsubscript{2} in preterm infants given 1 g/kg of fat emulsion over a 4-hr period (55). This drop in PaO\textsubscript{2} was more pronounced in infants less than a week of age than in older preterm infants and seemed to be correlated with increased concentrations of both triglycerides and free fatty acids in plasma. We have also noted significant drops in P\textsubscript{Tc}O\textsubscript{2} in patients who receive IVF emulsions, especially in those with severe cardio-pulmonary disease.

In classic studies carried out in an anesthetized sheep model, McKeen, Brigham, and others showed that the reduction in arterial PO\textsubscript{2} during and following the infusion of fat emulsions in amounts that were usually given to humans was not due to hyperlipidemia (45). They clearly demonstrated that the IVF was associated with an increase in pulmonary lymphatic flow, an increase in pulmonary arterial pressure, and a decrease in arterial oxygen tension. While treatment with heparin cleared the serum of triglyceride, it did not affect the increased pulmonary lymphatic flow, the increased pulmonary arterial pressure, or the fall in PaO\textsubscript{2}. However, pretreatment of the animals with indomethacin, a potent inhibitor of prostaglandin synthesis, prevented these changes.

It appears that infusions of fat emulsions to preterm infants are associated with an increase in the rate of pulmonary lymphatic flow, and this in turn increases pulmonary arterial pressure, which may cause a decrease in PaO\textsubscript{2}. In infants with chronic lung disease or heart disease who already have increased lung water and increased pulmonary lymphatic flow, infusions of IVF even at rates of less than 0.15 g/kg/hr may potentiate an already undesirable condition. Not only does the PaO\textsubscript{2} decrease, but, in patients who become relatively hypoxic, fat is poorly metabolized, and plasma triglycerides and free fatty acids may remain elevated for a prolonged period of time and potentiate this vicious cycle of events. This creates a very difficult clinical situation, because as one tries to provide adequate calories for infants with chronic lung or heart disease, the solution used to provide the calories may potentiate the hypoxia and lead to acidosis as well.
INTRAVENOUS FAT IN PRETERM INFANTS

Diminished Immune Responsiveness Secondary to IVF

Deposition of fat in the macrophages of the reticuloendothelial system of infants who have received IVF has been noted by a number of investigators (40,52,74). Fischer and co-workers showed that IVF impaired bacterial clearance and enhanced bacterial virulence in mice and inhibited chemotaxis of human neutrophils in an in vitro situation (19,20).

Palmblad et al. could not demonstrate that IVF affected the function of neutrophils of adults (51), and English and co-workers showed that chemotaxis inhibition was due to the glycerol in the Intralipid® preparation (17). This inhibition was probably a result of "hypotonic shock." They also noted that lipid emulsions would have had to have been administered at an "inordinately high rate to cause transient inhibition of circulating neutrophil function" (17).

Generation of Free Bilirubin by Metabolites of IVF

Although the IVF emulsions themselves have been shown not to displace bilirubin from albumin circulating in plasma (71,72), there has been some concern that liberation of free fatty acids during hydrolysis of IVF might displace albumin-bound bilirubin. If infants are icteric, the use of IVF emulsions has been considered hazardous, if indeed, unbound or free bilirubin might potentially increase the risk of kernicterus. There have been several studies suggesting that the use of IVF emulsions may not be dangerous unless the amount of fatty acid liberated increases significantly, so that bilirubin-binding sites on the albumin molecule would be compromised (67). Andrew and co-workers recommended that a safe method to monitor and prevent such complications would be to maintain a free fatty acid to serum albumin molar ratio (FA/SA) at six or less (2). Using a simplified method to measure the FA/SA (5), Kerner and co-workers found that in preterm infants receiving 0.5 to 3.3 g/kg/day of continuous IVF infusions, the mean ratio was only 1.1 (39). If, on the other hand, bolus infusions are utilized, the FA/SA ratio might be altered, and the patient might be at risk.

In recent studies, Dr. Levine and co-workers have questioned the role of free or unbound bilirubin as a major factor in producing kernicterus (43). They have demonstrated, at least in laboratory animals made icteric, that alteration of the blood–brain barrier by rapid infusion of hypertonic solutions resulted in deposition of bilirubin into tissues of the central nervous system. Thus, we must be more concerned of the hazards of hypoxia, acidosis, and hyperosmolarity in damaging the blood–brain barrier, than of the potential of utilizing medications or nutriments that may displace bilirubin from the albumin molecule. While the IVF emulsions or free fatty acids themselves may not potentiate the risk of the infant developing kernicterus, it is possible that the rate of infusion of IVF might cause the infant to become hypoxic and acidotic and may increase the risk of the infant developing bilirubin encephalopathy.
No matter what the basic cause of kernicterus is, one must use IVF with caution in infants with indirect hyperbilirubinemia. Often the infusion of IVF will not be initiated until the infant's serum bilirubin has decreased to a level that is considered safe, and the infant is no longer at risk of developing bilirubin encephalopathy.

**Hypocarnitinemia**

In order for fatty acids to be metabolized completely, they must be acetylated and then transported across the mitochondrial membrane, where, through a process of $\beta$-oxidation, they are converted to water, $\text{CO}_2$, and energy (70). Carnitine is a naturally occurring trimethylamine which, in the form of one or several acylcarnitines, facilitates the transport of fatty acids into mitochondria (70). Carnitine can be synthesized from both lysine and methionine, but, in the newborn period, the synthetic pathway does not seem to be functioning appropriately. Carnitine is present in human milk and in Similac® (1 mg/dl), but it is absent in soybean formulas and in any of the currently available amino acid preparations (62).

Preterm and term infants receiving TPN with IVF have been found to have decreased concentrations of total carnitine, acylcarnitine, and free carnitine as compared to infants who have received enteral nutrition containing carnitine. In addition, following an infusion of IVF in preterm infants, concentrations of $\beta$-hydroxybuturate as well as free fatty acids and triglycerides rose rapidly in plasma (63).

Although there are reports that adding carnitine to the diet of infants potentiates growth and weight gain (8), there have not been any documented abnormalities encountered in preterm infants who have hypocarnitinemia. In addition, infants have a rapid decrease in urinary excretion of carnitine during TPN, indicating that they are capable of preserving whatever carnitine they possess (53).

Whether hypocarnitinemia is a chemical abnormality in search of a clinical syndrome is purely speculative. However, patients with defects of carnitine biosynthesis have been described who have either cardiomyopathy (73) or a form of lipid storage disease in which patients have episodes of lethargy, somnolence, hypoglycemia, hepatomegaly, and hyperammonemia (12). Families with cardiomyopathy have been described who have markedly decreased serum and tissue levels of carnitine, and those patients with this disorder have been shown to have a beneficial response to oral carnitine intake. Not only did the patients with cardiomyopathy have heart failure and what appeared to be endocardial fibroelastosis, but they also developed severe metabolic acidosis (73).

In newborn infants, especially infants who have abnormalities of the cardiopulmonary system, such as chronic lung or heart disease, the finding of hypocarnitinemia might be significant, and might indicate that these infants have poor myocardial function. Detection of abnormalities with X-rays, elec-
trocardiography, and echocardiography may be important, especially if the
dysfunction can be reversed with the addition of oral carnitine.

Thus, hypocarnitinemia is an enigma as far as our present understanding
of this biochemical finding is concerned, and a great many more studies have
to be accomplished before any definite recommendations regarding its routine
use in patients receiving TPN and IVF can be made.

Additional Actual and Theoretical Complications

Several other actual or theoretical complications associated with the use of
IVF emulsions are described:

1. Altered rates of synthesis of prostaglandins which might lead to abnor-
malities of platelet function and possibly abnormalities of pulmonary func-
tion (24).

2. Increased concentrations of IVF in plasma which might interfere with sev-
eral biochemical tests. The first is spurious hyperbilirubinemia, which is
encountered when certain spectrophotometric methods are utilized to mea-
sure bilirubin (61), and the second is spurious hyponatremia, which is
carried by the space-occupying effect of fat. This latter inaccuracy can be
corrected if the serum is ultracentrifuged prior to the determination.

3. Transient sinus bradycardia (68).

4. Arachidonic acid deficiency occurring in spite of the high linoleic acid
content of IVF (21).

5. Malassezia-Furfur-induced pulmonary vasculitis (56).

6. Decreased concentrations of ionized calcium in serum (77).

MONITORING

Although serum turbidity may reflect increased lipid levels in blood asso-
ciated with IVF infusion, the gross estimation of turbidity by looking at the
serum lactesence has been totally ineffective in evaluating the extent of the
increased concentration of lipid in plasma. The use of a micronephelometer
to measure the plasma light-scattering index (LSI) and, in turn, the IVF con-
centration, was thought to be a very sensitive method of monitoring fat levels,
especially if the IVF levels increased above 100 mg/dl (9). Schreiner and co-
workers adapted a simplified modification of the nephelometer using a fluo-
rometric technique (64). They were able to demonstrate that the in vitro flu-
orometric technique correlated well with the nephelometry measurements, but
that the correlations of LSI with free fatty acids, cholesterol, and triglycerides
in vivo were poor. In a study carried out in 23 infants, D'Harlingue and co-
workers noted a positive correlation between serum IVF levels as determined
by micronephelometry and triglycerides, but also that the IVF level did not
reliably detect elevated levels of triglycerides, cholesterol, or free fatty acid–
albumin molar ratios (16). Neonates receiving IVF, therefore, cannot be mon-
itored by nephelometry alone, and adequate monitoring requires the measurement of the specific fractions of lipid in serum. The data also indicate that if the serum triglyceride levels exceed 150 mg/dl, the rates of IVF must be decreased in preterm infants. In some infants, especially those with pulmonary insufficiency, the serum triglyceride concentrations in serum should be maintained at about 100 mg/dl.

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