Intravenous lipid (IL) emulsions are important constituents of total parenteral nutrition (TPN) because they provide essential fatty acids and allow an increase in energy intake without giving an excess of glucose, which may be associated with an increase in carbon dioxide production. In the very low-birthweight (VLBW) infants, who often cannot be fed enterally for days or weeks in the early neonatal period, IL emulsions are considered a major source of energy for adequate nutrition.

However, the utilization of IL emulsions during the very first days of life is still debated, especially during the early stage of respiratory distress, since unwanted effects have been described, including hypertriglyceridemia, possible impairment of the immune system, a negative effect on bilirubin albumin binding, impaired coagulation, and intolerance of the lipid during stress. Such unwanted side effects have often been described at doses or infusion rates that may not be appropriate for VLBW infants or extremely low-birthweight (ELBW) infants in clinical practice because of their metabolic immaturity.

It is well known and accepted that intravenous glucose or amino acids have to be given at a constant rate and in amounts that do not induce metabolic disturbances or exceed the metabolic capacity of the infant. It is obvious that a similar argument must be applied when intravenous lipids are infused.

Triglyceride clearance from the bloodstream is the first step in the metabolic utilization of IL emulsions and is dependent on lipoprotein lipase activity, which is the rate-limiting enzymatic step in the hydrolysis of circulating triglycerides. Free fatty acids (FFA) released by this hydrolysis recirculate bound to albumin, causing an increment in plasma FFA that can be used as a metabolic fuel in liver, heart, or skeletal muscle. In liver these FFA may also be converted to VLDL and enter the lipoprotein cycle. FFA may also enter adipose tissue, where they can be re-esterified to triglycerides and stored.

Plasma lipid clearance is less efficient in VLBW infants than in term infants, especially in those who are small for gestational age (SGA) (1,2). It is also variable from one infant to another and—for the same dosage regimen—is improved when IL emulsions are given as a continuous infusion over 24 hours (3). Clearance capacity...
is evaluated by measuring the serum triglyceride concentration, though the allowable upper limit of serum triglyceride has not yet been established. In infants fed pooled human milk, triglyceride concentrations of 100 to 200 mg/dl are usual. Because significant increases in plasma cholesterol, phospholipids, and very low-density lipoproteins have been described when plasma triglyceride values exceed 100 to 150 mg/dl in infants receiving intravenous lipids, it seems reasonable to take this as the upper limit for unstable VLBW infants.

The most important factor to consider is not the overall daily intake of intravenous lipid given to the infant but the infusion rate—that is, the amount given in unit of time (g/kg per minute or hour), so as not to exceed the plasma clearance capacity. This was well illustrated in a study by Kao et al. (3). Thus instead of saying that 1 or 2 g/kg·d of intravenous lipid may be given to a particular infant, it is preferable to say that a rate of 0.4 or 0.8 g/kg·h can be infused and to remember that increasing this infusion rate may be harmful, just as it is harmful to make a sudden increase in the infusion rate of glucose. The clearance capacity may also be modified by stress of any type (infection, inflammation, surgery, and so on) (4), and in these circumstances utilization of intravenous lipids must be restricted or even halted.

The use of 10% and 20% lipid emulsions has been investigated in recent studies. These have shown that excessive quantities of phospholipid liposomes contained in 10% lipid emulsions impede the removal of triglycerides from plasma and are associated with higher plasma triglyceride concentrations and raised cholesterol and phospholipid levels. It is now clear that 20% lipid emulsions should be used rather than 10% emulsions (5,6).

Oxidation of infused fat will depend on the total energy expenditure of the infant and on the concomitant carbohydrate intake. If the amount of energy given as carbohydrate is greatly above the level of energy expenditure, the amount of perfused lipid that will be oxidized will be low (7). Data show that above a glucose intake of 20 g/kg·d, most of the infused lipid may be stored and not oxidized. Thus utilization (oxidation) of IL emulsion as an energy source will depend on the total energy intake, on the total glucose intake, and on the level of energy expenditure.

It is not clear whether supplementation with carnitine can increase fat oxidation, and studies evaluating carnitine supplementation in VLBW infants have been controversial (8,9). However, as the need for added carnitine for better fat oxidation is still not established, it may be wise to try to keep tissue carnitine stores or plasma carnitine concentrations at the levels observed in human milk-fed VLBW infants.

EARLY INTRAVENOUS LIPID STILL DEBATED

Can we start intravenous lipid in the first 3 to 4 days of life, or do we have to wait until the end of the first week? Few studies have focused on this point. Hammerman and Aramburo (10) compared two groups of VLBW infants (less than 1,750 g at birth) randomly assigned to receive TPN with or without 10% lipid emulsion for 5 days. One group received 10% lipid emulsion after the third day of life, and the other received it only after the eighth day. Lipids were started at 0.5 g/kg·d and progressively
increased to 2.5 g/kg·d. All infants received 1 ml/d of a multivitamin preparation. Chronic lung disease appeared to be increased in duration and tended to be more severe after lipid intake, as the number of days of ventilation (37 ± 35 versus 21 ± 18 days) and of oxygen therapy (51 ± 39 versus 28 ± 23 days) was increased significantly in the lipid group. The vasoconstrictor metabolite thromboxane B2 was raised in the IL group in comparison with the group receiving no lipids.

Sosenko et al. (11) randomly assigned 133 infants to receive 20% Intralipid or not during the first week of life, separating the infants in two weight strata: 600 to 800 g (42 infants receiving IL versus 37 control), and 801 to 1,000 g (28 IL versus 26 control). The IL groups were given lipids at less than 12 hours of age, starting at 0.5 g/kg·d, increasing to 1.5 g/kg·d maintained through to day 7. Control groups received no Intralipid until after day 7. Both groups received the same amount of a multivitamin solution. The results showed that in the overall population there was no significant difference in mortality (32.9% versus 25.4%, IL versus control) but that the mortality was higher in the 600- to 800-g stratum in infants receiving IL (47.5% versus 24.3% in the control group). Though the clinical data were similar in the two groups, it may be important to observe that the numbers of infants whose mother received corticosteroids was significantly higher in the controls (30%) than in the IL group (7%), and this may have introduced bias (relating to the influence of antenatal corticosteroid administration on the survival of ELBW infants). It is also important to emphasize that in the 801- to 1,000-g group there were more than twice as many deaths in the controls (7/26) as in the IL group (3/28). In that stratum, maternal corticosteroid administration was 11% in the IL group versus 19% in the controls. No significant difference was observed for chronic lung disease, but there was a significant increase in pulmonary hemorrhage, and a larger number of infants required supplemental oxygen at day 7 in the lipid groups. However, it was shown that by day 28 the number of infants requiring supplemental oxygen was greater in the control groups for both weight strata, and the number of infants requiring oxygen at 60 days was more than twice as high in the control group as in the IL group.

Similarly, Gilbertson et al. (12) studied 29 VLBW infants of less than 1,500 g receiving isocaloric, isonitrogenous parenteral feeding from day 1 with either intravenous lipid given at 1 g/kg·d from day 1 increasing to 3 g/kg·d by day 4 (IL group, n = 16) or intravenous lipid given only after day 8 (control group, n = 13). Lipids were given over 20 hours. At the end of the trial, there was no difference between the two groups for chronic lung disease, jaundice, septicemia, periventricular hemorrhage, necrotizing enterocolitis, or any other selected variables. The authors concluded that when lipids are infused at rates not exceeding 0.15 g/kg·h (3 g/kg·d over 24 hours), with stepwise dose increases from the first day of life, they can be tolerated by sick VLBW infants without an increase in the incidence of adverse effects.

More recently, Fox et al. (13) undertook a meta-analysis of six randomized clinical trials designed to assess the effect of early (day 1 to 5) versus late (day 5 to 14) introduction of intravenous lipids. They found no significant trend or effect on the incidence of death or chronic lung disease (at 28 days or at 36 weeks).
INTRAVENOUS LIPIDS AND JAUNDICE

In jaundiced newborn infants caution has been advised over the use of lipid emulsions because the fatty acids released during hydrolysis can displace bilirubin from albumin binding sites, producing unbound bilirubin and increasing the risk of kernicterus.

*In vitro* studies have shown that at a molar ratio of free fatty acids to serum albumin (FFA/Alb) of 4, no free bilirubin is released (14). *In vivo*, no generation of unbound bilirubin is demonstrated if the FFA/Alb ratio is below 6 (1). There are even some data (15) showing that Intralipid binds bilirubin and may serve as a potential vehicle for serum transport of bilirubin. In the study by Sosenko *et al.* (11), jaundice was not an exclusion criterion. In the study by Hammerman and Aramburo (10) severe hyperbilirubinemia (not defined more precisely) was an exclusion criterion. However, in the patients studied there was no detectable difference in bilirubin levels between the lipid group and the control group on days 1, 3, or 5 (IL group *versus* control: day 3, 7.3 ± 3.9 *versus* 7.7 ± 2.8 mg/dl; day 5, 5.6 ± 2.6 *versus* 6.0 ± 2.9 mg/dl).

In the study by Gilbertson *et al.* (12) it was stated that the molar ratio of fatty acid to serum albumin remained below 3 in all cases. The incidence of significant jaundice—defined as serum bilirubin concentrations above 200 µmol/liter (11.7 mg/dl) and days of phototherapy (2.46 ± 0.40 days *versus* 2.23 ± 0.51 days, IL *versus* control)—was similar in the two groups.

Adamkin *et al.* (16) specifically studied the effect of administration of 10% lipid emulsion on triglycerides, free fatty acids, albumin, and unconjugated bilirubin in 26 VLBW infants weighing ≤ 1,500 g at birth, six being less than 750 g. Lipid emulsion was started on the fourth postnatal day at 0.5 g/kg·d. This was increased by 0.5 g/kg·d from postnatal day 7 in infants below 1,200 g. In infants above 1,200 g, lipid intake was advanced to 1 g/kg·d on postnatal day 5 and increased by 0.5 g/kg·d from postnatal day 7. A maximum lipid intake of 3.5 g/kg·d was achieved by postnatal day 10. The lipid infusion time was 18 hours in each 24-hour period. Data were provided for 8 days of TPN that included lipid administration. Five VLBW infants had a single serum triglyceride value above 200 mg/dl (defined as hypertriglyceridemia). All infants had FFA/Alb ratios below 3. A mean peak serum unconjugated bilirubin of 5.8 mg/dl occurred on postnatal day 3 (baseline) and was stable or fell during the next 10 days of lipid infusion.

Brans *et al.* (17) studied 38 neonates below 1,500 g on TPN, divided into three groups: group I received fat emulsion at a constant rate over 24 hours, starting at 1 g/kg·d and increasing by 1 g/kg·d to a maximum of 4 g/kg; group II received the same intake of fat emulsion but over 16 hours; group III received fat emulsion over 24 hours but starting at a dose of 4 g/kg·d. The study was stopped if a baby was unable to tolerate the fat emulsion (plasma frankly creamy). Blood samples were obtained every 24 hours (*i.e.*, 8 hours after the end of fat infusion in group II). One infant in group II and one in group III had severe hyperlipemia. In all groups the FFA increased significantly. Serum total bilirubin concentrations were not statistically different from preinfusion levels and were similar between groups for a given day.
Serum apparent unbound bilirubin ranged from 1 to 45 μmol/liter, and the authors found no correlation with the FFA concentrations.

Most of these studies show that IL emulsion can be given in jaundiced VLBW infants if the serum level of FFA stays within the permitted range. Once again, the infusion rate of the IL emulsion is the key issue.

**INTRAVENOUS LIPIDS, GAS EXCHANGE, AND PULMONARY VASCULAR RESISTANCE**

Numerous studies have addressed the issue of the potentially deleterious effect of fat emulsions on pulmonary function in VLBW infants. This deleterious effect may be the result of alteration in vascular tone leading to a state of pulmonary hypertension or of infiltration of pulmonary tissue by lipids. It is obvious that most cases of pulmonary side effects described have been associated with high rates of lipid infusion.

The study by Brans et al. (18), where VLBW infants (less than 1,500 g at birth) were given intravenous lipids according to the protocol described previously (17), showed that infants receiving 4 g/kg-d of IL over 16 hours had an increased pulmonary alveolar/arteriolar gradient of oxygen (A-aDO₂) when compared with infants receiving the same amount over 24 hours. Their data suggest that the continuous administration of fat emulsions at a constant rate over 24 hours was safer than intermittent infusion, thus showing yet again that infusion rate is more important than the total daily amount infused.

Shulman et al. (19) made a retrospective comparison of necropsy data on neonates (not all were VLBW) who received or did not receive lipid infusions. Lipids were infused continuously over 24 hours, and the rate of infusion was decreased when triglyceride levels were above 150 mg/dl. Fourteen of 26 infants in the lipid group and two of 13 in the nonlipid group were found to have pulmonary vascular lipid deposition. The fact that pulmonary vascular lipid deposits were present even in infants who had never received intravenous fat suggests the need for caution before drawing definite conclusions about a relation between intravenous fat infusions and lung lipid deposition. However, in their conclusion the authors pointed out that their results suggested that vascular deposits were at least partly determined by the amount and duration of intravenous fat administration.

Prasertsom et al. (20) used two-dimensional echocardiography to estimate pulmonary vascular resistance from the ratio of right ventricular pre-ejection period to ejection time (RVPEP/ET) in 11 preterm infants with respiratory distress syndrome receiving a 20% lipid emulsion. Intravenous lipid was started on the second postnatal day at a dose of 0.0625 g/kg-h (1.5 g/kg-d) for 24 hours and increased to 0.125 g/kg-h (3 g/kg-d) on the third day. Intravenous lipid was discontinued for 24 hours on the fourth day and then restarted for 24 hours on the sixth day at 0.0625 g/kg-h. The RVPEP/ET ratio increased by 20% after 24 hours of intravenous lipid at 1.5 g/kg-d, by 45% after 24 hours at 3 g/kg-d, and returned to baseline 24 hours after the lipid infusion had been discontinued. The increases in RVPEP/ET ratio were not observed immediately after starting or restarting intravenous lipids but after several
hours of infusion, and the authors discussed the role of changes in eicosanoid metabolism, suggesting that the dose-dependent increase in pulmonary arterial pressure was thromboxane mediated. None of their infants was said to be hyperlipemic (though serum triglyceride concentrations were not quoted).

Similar data were published by Lloyd and Boucek (21) from a study on six premature infants (birthweight between 1,500 and 2,500 g) receiving 0.1 to 0.45 g/kg-h of intravenous lipid (2.4 to 10.8 g/kg-d), but in that study the increase in RVPEP/ET ratio was observed within 2 hours of infusion onset, the faster response being assumed to be due to the high lipid infusion rate.

**INTRAVENOUS LIPID AND PEROXIDATION**

Unsaturated fatty acids are highly susceptible to peroxidation, and the products (hydroperoxides) can interfere with arachidonic acid metabolism or react to form organic free radicals, which can initiate peroxidative injury in tissues. Stimulation of cyclooxygenases may also result, causing increased production of prostaglandin H2, and then prostacyclin (PGI2) and thromboxane (Tx) A2, which are important vasoactive products.

Several studies have shown that lipid peroxidation occurs in intravenous lipid emulsions used in preterm infants (22–24). The concentration of lipid hydroperoxides is variable between bottles and is said to increase under light exposure, especially under phototherapy lights (23,25). Protecting the emulsions from light with aluminum foil or by adding antioxidant products such as ascorbic acid directly to the bottles eliminates the phototherapy effect (25).

However, other factors or nutrients may contribute to the *in vitro* generation of peroxides. Lavoie *et al.* (26) showed that multivitamin preparations (MVI) mixed in parenteral nutrition solutions were the major contributor to the generation of peroxides, with a 10-fold increase in fat-free TPN solutions but only a fourfold increase in lipid-containing TPN solutions. They showed a dose/response relation between the concentration of MVI and the peroxide level. The effect of light was the strongest in the presence of multivitamins. These investigators found that lipid emulsions had a significant but minor additive effect compared with multivitamin preparations. According to these data, it may be desirable to protect intravenous emulsions from light, particularly phototherapy light, until more data are available on the consequences of peroxide production in TPN preparations.

**CONCLUSION**

Intravenous lipid infusions are an important component of TPN during the early days of life in VLBW infants, at a time when enteral feeding is impossible or poorly tolerated, since they provide both essential fatty acids and high-density energy. Better current knowledge of the metabolic fate of the infused lipids permits their use during the first week of life if the infusion rate does not exceed the immature metabolic capacity of these infants. This may be difficult to assess, especially in very sick and un-
stable infants, and explains why we still have to be cautious. However, there is a further debate that still has not been entirely resolved by current published studies, and that is over the quality of lipid emulsions. There is reason to believe that the quality of the available emulsions needs to be improved to obtain a more suitable fatty acid composition and a lower phospholipid content; we also need a better understanding of how to prevent lipid peroxidation.

REFERENCES


**DISCUSSION**

*Prof. Koletzko:* I would like to stimulate you to comment a bit more on the question of the quality of lipids. You rightly emphasized your concern about peroxidation with soybean oil emulsion. Many of us have been concerned about exposing very small premature infants to these high concentrations of PUFA, and soybean oil emulsion does not contain much in the way of biologically active antioxidants. Also, the very marked disturbance of the fatty acid patterns of endogenous lipids, both in plasma and tissue, with soybean oil emulsion may well be directly related to the disturbances of thromboxane levels that you've shown. We have just completed a randomized trial comparing Intralipid with olive oil–based emulsion in small premature infants. I found the results very encouraging, because with the olive oil emulsion there is a much more physiological fatty acid pattern, a more physiological lipoprotein pattern, and maybe most important, a much improved vitamin E status with less peroxidative stress.

*Dr. Putet:* It's clear that there is too much polyunsaturated fatty acid in the available lipid infusion solutions, which increases the possibility of peroxidation. There are enough published data to show that peroxidation can occur in ambient light, and even more so under phototherapy. The peroxidation rate of TPN containing protein, multivitamins, and lipids may increase to such an extent that it could be harmful. For example, it could disturb arachidonic acid metabolism and interfere with prostaglandin and prostacyclin/thromboxane production. This would cause vasoconstriction in the pulmonary bed, as has been shown in almost every study that has investigated peroxidative phenomena. All the data suggest that we should try to improve lipid solutions by reducing their content of polyunsaturated fatty acids. You mentioned a new solution with oleic acid, but we already have a solution made from a 50:50 mix of medium-chain triglycerides and long-chain triglycerides. This solution has 50% less polyunsaturated fatty acid and consequently less peroxidation. We also know that the cholesterol level is reduced in infants who are infused for several days or a week with this solution, so this is obviously already one way toward an improved intravenous lipid solution.

*Prof. Koletzko:* Do you think we have enough information on the safety of MCT emulsion in premature infants? I'm concerned, in view of data of Deckelbaum and coworkers [1], that a very high proportion of MCT emulsion is apparently not split by lipoprotein lipase and is incorporated into cells intact, at least *in vitro*. Is that not a concern in relation to preterm infants?
Dr. Putet: There may be cause for concern if too much MCT is given. However, there is no evidence at present that a 50:50 solution MCT/LCT given at, say, 1.5 or 2 g/kg·d causes any problems. I would say that the advantages of this form of lipid infusion, in relation to reduced peroxidation, would outweigh any possible disadvantages.

Prof. Moro: Do you think that the levels of peroxidation described may be associated in vivo with liver damage, and so with TPN-associated cholestasis?

Dr. Putet: Maybe Prof. Chessex could answer that question. In any event, I think that if we can show that there is a substantial increase in peroxidation in either parenteral or enteral feeds, it may be harmful.

Dr. Chessex: We have been looking at animal models. We have shown a decrease in lung glutathione in such models perfused with either multivitamin solution or peroxides at the same concentration, and we have also shown a fall in the liver content of glutathione. We are currently looking at these livers, which show a relative increase in weight compared with the body weight of the animals. Thus we are looking at precisely the issue that Prof. Moro asked about: Could this be one of the factors explaining cholestasis? Then we have begun to look at what happens in children. We have been measuring urinary peroxide excretion in babies before and after giving a multivitamin solution, and there is a doubling of the urinary excretion of peroxides and other markers of peroxidation such as isoprostins. The next step was to look at the effect of light. When we protect the solution from light (i.e., just the tubing coming down from the bag; the bag is already covered), we have a 50% fall in urinary peroxide excretion. We are now trying to determine whether this may have any functional effect in the infants in the long term.

Prof. Berger: I'd also like to comment on peroxidation. I think it is important to investigate the possibility that parenteral feeding produces a decreased output of free radicals. As Prof. Heird emphasized, we know we have trouble giving enough cysteine, and we have problems with vitamin E. If there is not enough cysteine, we're probably not allowing these babies to make enough glutathione. In 1987, we postulated that cholestasis was the result of a free radical process. On looking at the literature, we were interested to find reports of the compound lipofuscin, which had been named intravenous fat pigment and was commonly found in biopsies from babies with cholestasis in the United States, where they had not been using Intralipid. We therefore suggested that lipofuscin was a clue that this cholestasis was in fact a peroxidation process. This emphasizes that the problem isn't related only to lipids but is related to many other factors—trace elements, amino acids, and other antioxidants that influence the output of free radicals. If we want to understand this process, it is important to look at the factors influencing the input, the output, and the target organ sensitivity.

Prof. Heird: As you know, MCT-containing emulsions are not available in the United States, but they would seem to have some advantages with respect to oxidation, and thus as an immediate energy source for babies whose total energy intake is decreased—for example, in the first few days of TPN. Is anything known about the effects of MCT versus LCT in promoting nitrogen retention or nitrogen utilization?

Dr. Putet: This is a controversial subject. We know that MCT are oxidized more readily than LCT. This has been shown in adults and even in infants, using labeled carbon. There may ultimately be little difference between these two forms of lipid with respect to the amount of energy actually utilized by the body, since there appears
to be some futile cycling with MCT, but the amounts involved are very small. I doubt whether, in a situation where not more than 20% of the energy will be given as fat, there will be much difference in utilization between LCT and MCT/LCT solutions.

**Dr. Rashwan:** When should you stop giving lipid infusions? Some say you should stop when 50% of the intake is enteral. Do you agree with this?

**Dr. Putet:** I think this is mainly a question of the total nonprotein energy intake. If you are giving enough enteral feeding to give, say, at least 70 to 80 kcal/kg-d, I think you can then stop parenteral nutrition. I think in terms of the total amount of lipid given either enterally or parenterally, and the total amount of glucose given either enterally or parenterally. When I give TPN along with some enteral nutrition, I calculate the overall lipid and glucose intake, and try not to include more than 30% to 40% of the energy as lipids. When the infant is weaned onto enteral nutrition, the proportion of lipid in the energy intake will be higher, around 40% to 50%. With TPN, I do not increase the lipid part of the total nonprotein energy intake above 20% to 25%.

**Dr. Filijo:** Do you think it is necessary to use intravenous L-carnitine to assist the metabolism of parenteral lipids at the mitochondrial level?

**Dr. Putet:** The carnitine question is still controversial. I think it reasonable to try to ensure that the carnitine level is at least at the lower end of the range found in babies fed with breast milk. I would be in favor of giving it because I see no reason for letting it be low, and we know that plasma carnitine becomes very low in infants on TPN for more than a week or so. However, we have no evidence that it increases the oxidation rate of the lipids given, though it has been shown that ketone bodies are increased, even in small infants. In all, I think there are more arguments in favor of giving it than against.

**Prof. Moro:** A very practical question: should Intralipid be given in a separate bag or in the same bag with other nutrients?

**Dr. Putet:** The problem of putting lipids, glucose, vitamins, proteins, calcium, and phosphorus in one solution is a galenic one. If the pharmacist is able to produce a stable solution, which is in fact feasible, then I think there is no problem in using this. We have done several studies to ensure that lipid solutions do not interfere with calcium, phosphorus, and other nutrients, and it is probably simpler to use a single solution than a Y connector. You do have to be careful about particles, however, when you put lipids in a solution. If the solution is unstable, you may get large particles in it, so it is best to use a filter.

**Dr. Schanler:** The problem of particulates arises if you try to increase the calcium and phosphorus content of IV solutions. At high concentrations of calcium and phosphorus, we occasionally do see precipitates, so I would be very cautious about that. On the other hand, you get better vitamin A and E levels in babies when you mix the vitamins with the intravenous lipid.

**Dr. Putet:** I agree. You really have to be sure that your pharmacist can produce a stable preparation.

**Prof. Lucas:** I am confused about oleic acid. When it was first shown that Intralipid could cause lung damage, there were many studies trying to get to the bottom of the problem. As you know, oleic acid is a major component of Intralipid. Studies by Grossman on experimental animals showed that infusion of oleic acid had very detrimental effects on a number of aspects of lung function. Now you are promoting it as an important lipid. Are you saying that these animal studies don’t apply to humans?
Dr. Putet: Most of these studies have relevance to humans, but I would emphasize again that what is important is the infusion rate—the amount given per unit of time. As with glucose, if you infuse too much too fast, you will get a lot of trouble.

Prof. Endres: There are several old reports of pulmonary intra-arterial thromboses after high-rate Intralipid infusions. Do you think this is linked to chronic lung disease in premature babies?

Dr. Putet: There may be lipid deposition in the lungs of individuals who have never received lipids. This has been shown in infants, in adults, and in animals, in vitro and in vivo. Where lipid infusions are given, if the infusion rate exceeds the clearance capacity of the plasma, lipid particles will be taken up by the reticuloendothelial system in the endothelium. So under those circumstances, when you exceed the metabolic capacity of the infant, you may get problems. That is my understanding, at least.

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