**Clinical Problem**

Particulate contamination occurs in parenteral nutrition

Particles in intravenous fluids can arise from various sources as:
- particulate contamination in the individual infusate components.
- particles shed from containers and infusion equipment during use.

In intensive care, patients very often receive not only parenteral nutrition but also numerous drugs. This may add to the problem of particulate contamination:
- particulate contamination in the individual infusate components.
- particles shed from containers and infusion equipment during use.

Several studies investigated the total particulate load in PN and found that patients receiving intensive IV therapy can receive more than two million particles a day.1,4

One group studying paediatric PN reported more than 37,000 particles of 2-100 µm in the daily feed for a 3 kg infant. This level of contamination has since been confirmed by other authors.3

**Enlarged lipid droplets can occur in admixtures**

The presence of a significant proportion of enlarged lipid droplets in admixtures may be undesirable, since lipid droplets over 5 µm can lodge in the pulmonary microvasculature and may contribute to lipid embolism. It is possible to reduce the number of enlarged lipid droplets without adversely affecting admixture stability.11

Patients receiving parenteral nutrition are at increased risk of fungaemia

Fungal infections are increasingly common, particularly amongst immunocompromised patients.12 Parenteral nutrition is an acknowledged risk factor for fungaemia, with Candida species being the most common organisms involved.13 Candida grows rapidly in lipid-containing admixtures.14 Whilst endogenous Candida commonly leads to disseminated disease, the exogenous nosocomial acquisition of Candida occurs in parenteral nutrition and has been seen to cause significant morbidity and mortality.11,14 Nosocomial transmission of Candida species may involve carriage on the hands of healthcare workers.12,13,16

**Retention of fungal contamination from lipid-containing preparations is possible**

Fungal contaminants commonly associated with infection in patients receiving PN can be retained by appropriate filters.17

**Air embolism is a risk with central venous catheters**

Patients with central lines are at risk from air embolism,19 due to disconnections, incomplete priming of the infusion system or degassing as solutions are warmed. The presence of lipid in an admixture can obscure this air.

**Precipitates can occur in admixtures and remain undetected**

Infusion of admixtures containing undetected gross particulate contamination in the form of calcium phosphate precipitate resulted in two patient deaths and several cases of serious respiratory distress. This has led some authorities to advise that filters should be used during administration of PN.20 Compounding guidelines for calcium and phosphate additions should prevent such gross precipitation, but interactions between components do occur and unfortunately the presence of lipid can obscure precipitation:

"the lipid emulsion concealed the precipitation as effectively as if the container were in a brown paper bag."17

**Particles have serious clinical consequences**

High levels of particles in infusions can exceed the clearance capacity of the reticuloendothelial system.2 Post mortem observations of granulomatous2,4 and microthrombi2,4 in the lung tissue of patients who had received IV therapy give some clue as to the potential pathogenic consequences of particle contamination in infusates; involvement in ARDS and MOF has been suggested. This is supported by the respiratory distress seen in the surviving patients involved in the aforementioned precipitation incident.5,6 Particles have also been implicated in the pathogenesis of thrombophlebitis in peripheral vein infusions; several controlled trials in which patients received filtered versus non-filtered, non-lipid IV therapy, have shown at least a 50% reduction in the incidence of phlebitis when filtration was used.5,10

"Although the precise toxic dose of enlarged fat globules from unstable TNAs is not known, the presence of droplets of 5 µm or more constituting ≥4.0% of the final fat concentration are unstable and pharmaceutically unfit for administration."11

"A filter should be used when administering either central or peripheral nutrition admixtures...standards of practice vary, but the following is suggested: a 1.2 micron air eliminating filter for lipid containing admixtures and 0.2 micron air elimination filter for nonlipid containing admixtures" US FDA.5

"Administering a TNA without an inline filter to a patient is like playing Russian roulette." LA Trissel7

"...total exposure to large LDs (lipid droplets) was significantly reduced suggesting that in-line TNA filtration should be a standard part of nutritional therapy." D.F. Driscoll 11

"Appropriate filters should be used during the administration of PN to patients who require intensive or prolonged parenteral therapy, the immunocompromised, neonates and children, and patients receiving home PN because of the large volume of potentially particulate-contaminated fluid administered and their increased susceptibility to the detrimental effects of particulate contamination." Bethune15

"Practice Guidelines: In-Line Filtration..." 1. A 0.2 µm filter should be used for 2-in-1 formulations. A 1.2 to 5um filter should be used for TNAs. Alternatively, a 1,2µm filter may be used for all PN formulations. 2. A filter that clogs during administration of PN is indicative of a problem and may be replaced but should never be removed entirely." ASPEN National Advisory Group on Standards and Practice Guidelines for Parenteral Nutrition 21

"...Each PPN admixture should be tested for stability before clinical use and infused into patients through an appropriate filter."21

**Patient Protection**

Filtration has been recommended for patient protection in parenteral nutrition.

Leading authorities in nutrition recommend filtration to protect patients receiving PN.5,7,11,12,20

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Summary

- Particulate contamination occurs in parenteral nutrition.
- Precipitates can occur in admixtures and remain undetected.
- Particles have serious clinical consequences.
- Oversize lipid droplets can occur in admixtures and have serious clinical consequences.
- Patients receiving parenteral nutrition are at increased risk of fungaemia.
- Retention of *Candida* from lipid-containing preparations is possible with an appropriate filter.
- Air embolism is a risk with central venous catheters.
- Filtration has been recommended for patient protection in parenteral nutrition.

References