



# Hôpitaux Universitaires de Genève

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Pharmacie des HUG

# LES PARTICULES DANS LES MELANGES PARENTÉRAUX: CONSEQUENCES CLINIQUES?

Journées francophones de Nutrition  
Bordeaux, 12.12.2013

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**UNIVERSITÉ  
DE GENÈVE**

FACULTÉ DES SCIENCES  
Section des sciences  
pharmaceutiques



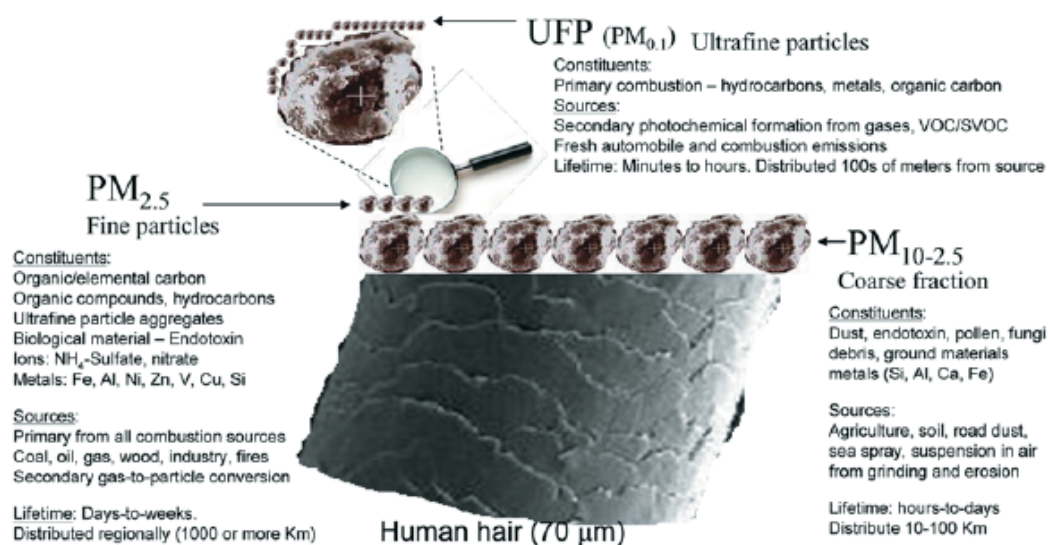
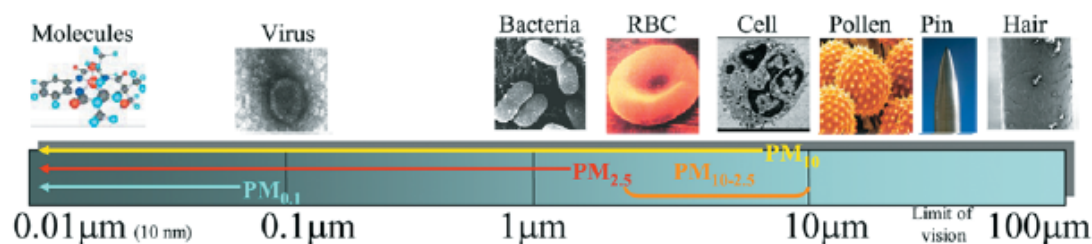
# CONFLITS D'INTÉRÊT

- Activités de conseil, fonctions de gouvernance, rédaction de rapport: **NON**
- Essais cliniques, autres travaux, communications de promotion: **NON**
- Intérêts financiers (actions, obligations) : **NON**
- Liens avec des personnes ayant des intérêts financiers ou impliquées dans la gouvernance: **NON**
- Réception de dons sur une association dont je suis responsable: **NON**
- Détention d'un brevet, rédaction d'un ouvrage utilisé par l'industrie: **NON**

# SOURCES A L'HOPITAL



# POLLUTION DE L'AIR



**Visible:**  
env . 50 μm

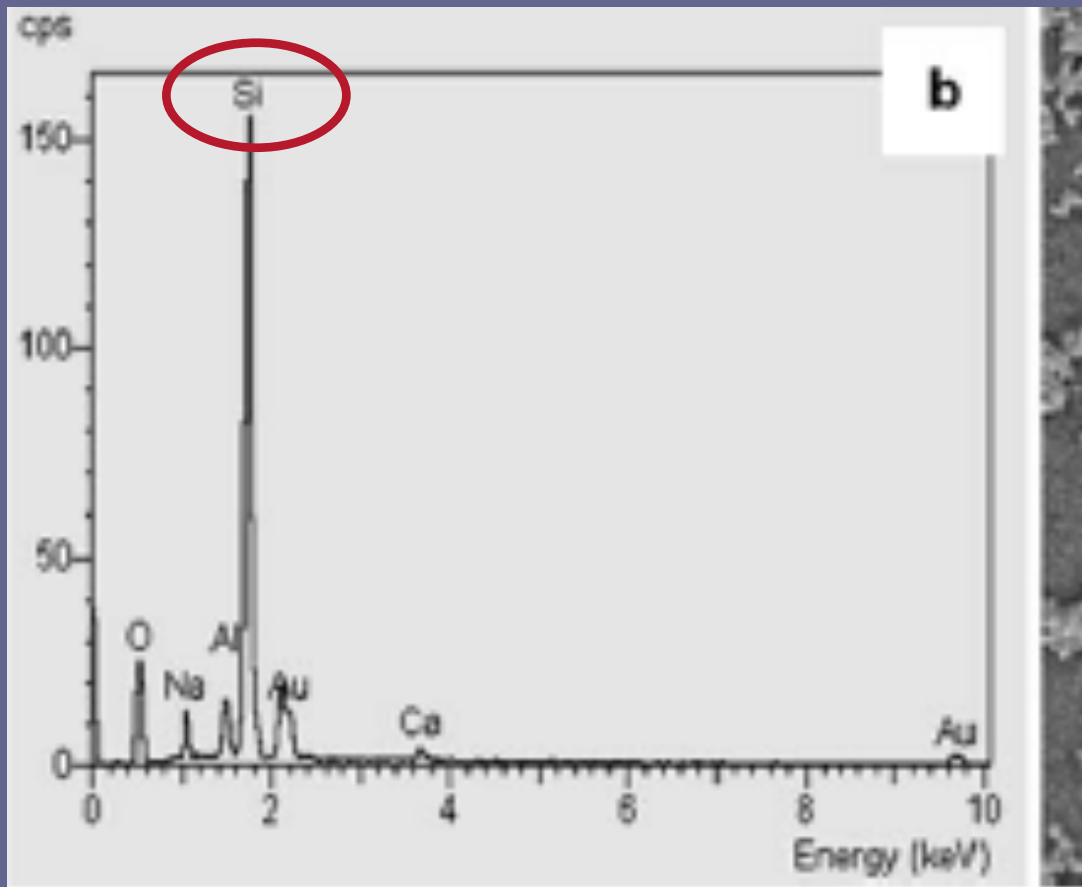
**Erythrocytes:**  
env. 7.5 μm

**Capillaires:**  
8-10 μm

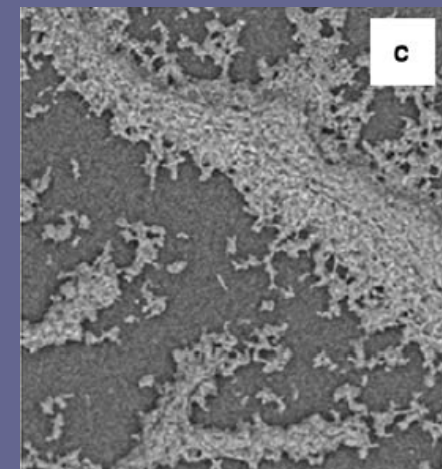
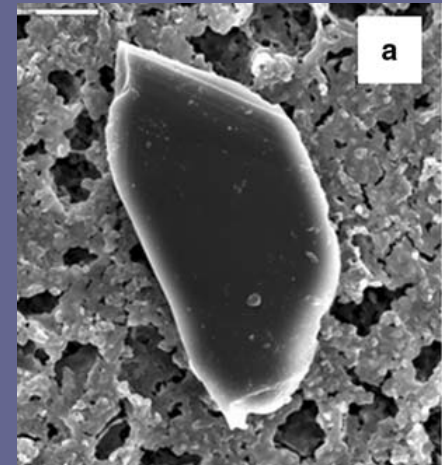
**Figure 1** Size, sources and composition of PM air pollution

RBC, red blood cell; SVOC, semi-volatile organic carbons; UFP, ultra-fine particles; VOC, volatile organic carbons.

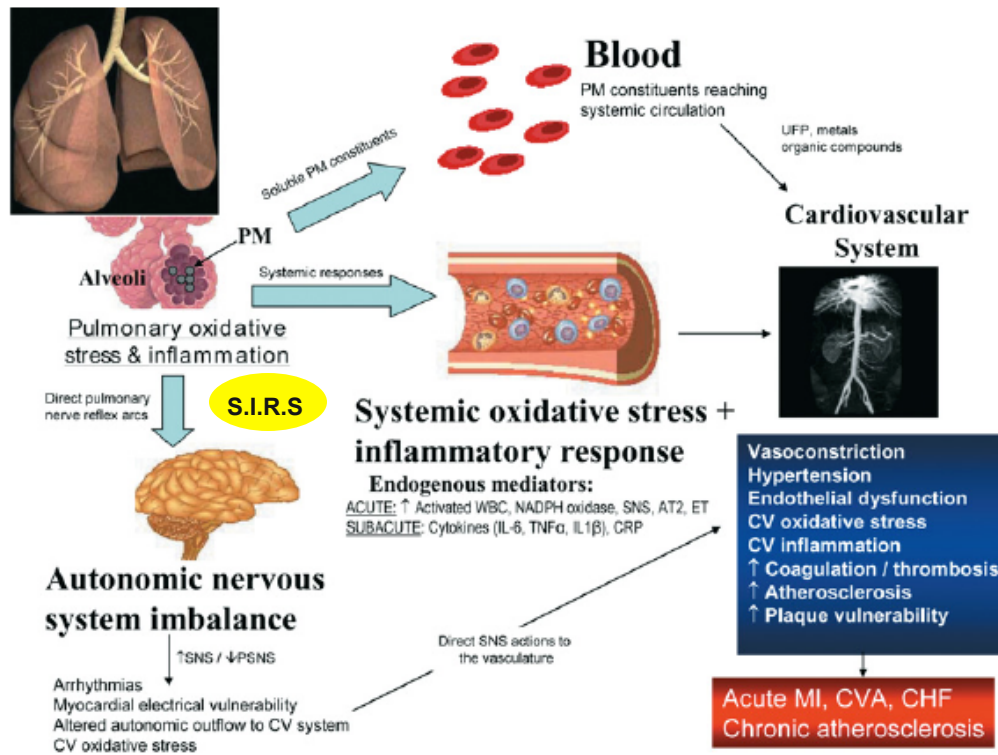
# COMPOSITION ET TAILLE



Jack T et al. Intensive Care Med 2010;36:707-711

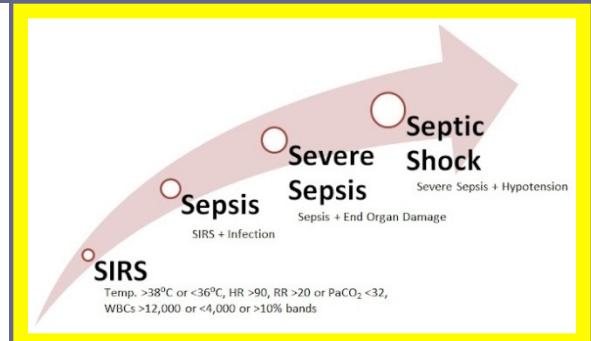


# CONSÉQUENCES CLINIQUES



**Figure 2** Broad biological pathways whereby PM may cause CV events

AT2, angiotensin II; CVA, cerebrovascular accident; CHF, congestive heart failure; ET, endothelins; MI, myocardial infarction; ROS, reactive oxygen species; UFP, ultra-fine particles; WBC, white blood cells.



- Agression mécanique
- Action inflammatoire et thrombotique

Brook RD. Clinical Science 2008;115:175-187

# CONSEQUENCES ECONOMIQUES

| Complications resulting from Particle Contamination  | Severity    | Clinical Treatment   | Length of Stay                | Additional Cost <sup>6</sup> |
|--|-------------|--|-------------------------------|------------------------------|
| <b>Atteinte organique</b><br>ARDS <sup>4</sup><br>Pulmonary Embolism <sup>4</sup><br>Major Organ Dysfunctions <sup>2</sup> | High        | Full ICU treatment (Treating/Monitoring/Feeding etc.)              | 4-30d ICU + 4-30d Normal Ward | 7,556 € - 56,670 €           |
| <b>Obstruction</b><br>Myocarditis <sup>5</sup><br>Local Embolus <sup>5</sup>   | Medium High | ICU/Intermediate care treatment (Observation/Monitoring/Treatment) | 1-7d RICU + 1-7d Normal Ward  | 1,136 € - 7,952 €            |
| <b>Microcirculation</b><br>Minor Organ Dysfunctions <sup>2</sup><br>Thrombosis <sup>3</sup>                                | Medium      | Extension of clinical treatment (Observation/Monitoring)           | 0d RICU + 1-3d Normal Ward    | 382 € - 1,146 €              |
| <b>Phlébite</b><br>Thrombo-phlebitis <sup>1</sup><br>Phlebitis <sup>1</sup>  | Medium Low  | Local treatment (No additional Monitoring)                         | 0d ICU + 0-1d Normal Ward     | 0 € - 382 €                  |
| Local Redness <sup>1</sup>   | Low         | No complication for patient  | 0d ICU<br>0d Normal Ward      | 0 €                          |

Particulate Contamination

References

- <sup>1</sup> Yorioka et al 2006, Grünewald et al 2004, Ellenbogen et al, 1975
- <sup>2</sup> Yorioka et al 2006, Lye 2003, Puntis et al 1992, Walpot et al 1989, Turco et al 1971
- <sup>3</sup> Lehr et al 2002, Panknin 2007, Walpot et al, 1989
- <sup>4</sup> Walpot et al, 1989, Garvan 1971, Gross et al 1966
- <sup>5</sup> Kossovsky et al, 1995, Lehr et al 2002, Douglas et al 2001
- <sup>6</sup> Gianino et al 2007, Bertolini et al, 2005

Bbraun. Particulate contamination, 03/2011

# PARTICULES ET TPN

## Hazards of parenteral treatment: do particles count?

J W L Puntis, K M Wilkins, P A Ball, D I Rushton, I W Booth

### Abstract

After prolonged parenteral nutrition a 12 month old infant died with pulmonary hypertension and granulomatous pulmonary arteritis. A review of necropsy findings in 41 infants who had been fed parenterally showed that two of these also had pulmonary artery granulomata, while none of 32 control patients who died from sudden infant death syndrome had similar findings. Particulate contaminants have been implicated in the pathogenesis of such lesions and these were quantified in amino acid/dextrose solutions and fat emulsions using automated particle counting and optical microscope counting respectively. Parenteral feed infusions compounded for a 5000 g infant according to standard nutritional regimens were found to include approximately 37 000 particles between 2 and 100  $\mu\text{m}$  in size in one day's feed, of which 80% were derived from the fat emulsion. In-line end filtration of intravenous infusions may reduce the risk of particle associated complications. A suitable particle filter is required for use with lipid.

nutrition, and to determine the number and size of particles in parenteral feeding solutions.

### Subjects and methods

#### NECROPSY STUDY

#### Subjects

Postmortem material from all parenterally fed infants from a regional neonatal intensive care unit who had died between 1980 and 1989 were reviewed. Forty one such patients were identified, with a median (range) gestational age of 28 weeks (25–40) and weight 880 g (450–2820). The most common indication for parenteral nutrition was prematurity and failure to tolerate enteral feeding in association with respiratory distress requiring ventilatory support ( $n=38$ ); indications in the three remaining patients were necrotising enterocolitis, ischaemic colitis, and ileal atresia. Parenteral nutrition was prescribed according to a standard protocol<sup>5</sup> with a fluid intake of 150 ml/kg. The median (range) duration of parenteral feeding was 14 days (1–46).

Puntis JWL et al. Arch Dis Child 1992;67;1475-77



# INCIDENTS CLINIQUES ET TPN

0148-6071/89/1302-0209\$02.00/0  
 JOURNAL OF PARENTERAL AND ENTERAL NUTRITION  
 Copyright © 1989 by the American Society for Parenteral and Enteral Nutrition

Vol. 13, No. 2  
 Printed in U.S.A.

## Pulmonary Deposition of Calcium Phosphate Crystals as a Complication of Home Total Parenteral Nutrition

JAROL B. KNOWLES, M.D., GIL CUSSON, B.S., R.PH., MARILYN SMITH, R.N., AND  
 MICHAEL D. SITRIN, M.D.

*From the Nutrition Support Service and Clinical Nutrition Research Unit, Department of Medicine, University of Chicago, Chicago, Illinois*

**ABSTRACT.** A patient on home total parenteral nutrition (TPN) developed a diffuse granulomatous interstitial pneumonitis secondary to calcium phosphate deposition. Calcium and phosphorus concentrations in the TPN formula were not unusually high, indicating that other factors contributed to

calcium phosphate crystallization. The effects of duration of storage of the TPN formulation, solution temperature, pH, and magnesium concentration on calcium phosphate precipitation are discussed. (*Journal of Parenteral and Enteral Nutrition* 13:209-213, 1989)

pp. 1352-1354 (© 2003)

### CASE REPORT

STEVEN E. HILL, MD†; LESLIE S. HELDMAN, MD‡; EDWIN D. H. GOO, PHARMD§; PAUL E. WHIPPO, DVM|| ;  
 AND JOSEPH C. PERKINSON, MD†

*From the Departments of †Surgery, ‡Pathology, §Pharmacy, and ||Clinical Investigation, Tripler Army Medical Center, Honolulu, Hawaii*

**ABSTRACT. Background:** Paroxysmal respiratory failure and death occurred in two young adult females with pelvic infections. Autopsy revealed an amorphous material containing calcium obstructing the pulmonary microvasculature of each patient. Both patients received an identical total nutrient admixture (TNA) solution before their deaths. **Methods:** Infusion of TNA into an animal model was undertaken in an effort to reproduce the clinical effect. Laboratory investigation was also performed to isolate a precipitate and identify the factors contributing to precipitation. **Results:** A nonvisible precipitate containing calcium, phosphorus, and organic material was isolated from the TNA so-

lution. Infusion of the formulation into healthy pigs resulted in sudden death within 4 hours. Alteration of the amino acid component, mix sequence, agitation technique, and mixing container influenced precipitate formation. **Conclusion:** Pulmonary embolization of a precipitate containing calcium phosphate resulted in the death of two patients. The pH of the amino acid component, transient elevation of calcium and phosphorus concentrations during mixing, and the lack of agitation during automated preparation of the formulation were identified as the etiologic factors producing the fatal precipitate. (*Journal of Parenteral and Enteral Nutrition* 20:81-87, 1996)

## Total Parenteral Nutrition Associated Crystalline Precipitates Resulting in Pulmonary Artery Occlusions and Alveolar Granulomas

TERRY McNEARNEY, MD,\*†‡ CHRISTOPHER BAJAJ, DO,\* MICHAEL BOYARS, MD,\*  
 JOHN COTTINGHAM, MS IV,§ and ABIDA HAQUE, MD§

**KEY WORDS:** parenteral nutrition; crystalline precipitates; pulmonary artery occlusion; alveolar granulomas.

Crystal precipitation from total parenteral nutrition (TPN) and systemic embolization has been described in patients on TPN, including in the lung (1-4). This is a rare and usually fatal complication of TPN (1,2). We report a case

sequence as recommended by American Society for Parenteral and Enteral Nutrition and American Journal of Health System Pharmacy guidelines was as follows: Automix: intralipid 20%, 177 ml; Travesol 10%, 815 ml; dextrose 70%, 457 ml.; sterile wa-

McNearney T et al. Dig Dis Sci 2003;48:1352-4

Knowles JB et al. JPEN 1989;13:209-13

Hill SE et al. JPEN 1996;20:81-87

# COMPLEXATION ET CALCIUM

## Intravenous Ceftriaxone and Calcium in the Neonate: Assessing the Risk for Cardiopulmonary Adverse Events

John S. Bradley, MD<sup>a</sup>, Ronald T. Wassel, PharmD<sup>b</sup>, Lucia Lee, MD<sup>c</sup>, Sumathi Nambiar, MD, MPH<sup>d</sup>

<sup>a</sup>Rady Children's Hospital San Diego, San Diego, California; <sup>b</sup>Office of Surveillance and Epidemiology and <sup>c</sup>Office of New Drugs, Office of Antimicrobial Products, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland; <sup>d</sup>Office of Vaccines Research and Review, Center for Biologics Evaluation and Research, US Food and Drug Administration, Rockville, Maryland

The authors have indicated they have no financial relationships relevant to this article to disclose.

### What's Known on This Subject

The package label for ceftriaxone was changed in August 2007 to contraindicate the co-administration of ceftriaxone with calcium-containing intravenous solution.

### What This Study Adds

The cases reported to the FDA and the FDA AERS database search are provided and discussed to provide clinicians the basis for these new precautions.

### ABSTRACT

**OBJECTIVES.** Unsolicited reports regarding potentially serious adverse drug reactions in neonates and young infants were reported to the Food and Drug Administration, leading to changes in the package label for ceftriaxone. This report describes and summarizes the reported cases that led to safety concerns regarding the concurrent administration of intravenous ceftriaxone and calcium in this age group.

**METHODS.** Nine reported cases were assessed. The Food and Drug Administration Adverse Event Reporting System database was searched for potential drug interactions in patients who were receiving concomitant ceftriaxone and calcium therapy.

**RESULTS.** Eight of the reported 9 cases (7 were  $\leq 2$  months of age) represented possible or probable adverse drug events. There were 7 deaths. None of the cases were reported from the United States. The dosage of ceftriaxone that was administered to 4 of 6 infants for whom this information was available was between 150 and 200 mg/kg per day. The rate of occurrence of these serious adverse drug reactions cannot be accurately determined from available data.

**CONCLUSIONS.** The concurrent use of intravenous ceftriaxone and calcium-containing solutions in the newborn and young infant may result in a life-threatening adverse drug reaction. Contributing factors for infants in this report may include the use of ceftriaxone at dosages higher than those approved by the Food and Drug Administration, intravenous "push" administration, and administration of the total daily dosage as a single infusion. *Pediatrics* 2009;123:e609–e613

[www.pediatrics.org/cgi/doi/10.1542/peds.2008-3080](http://www.pediatrics.org/cgi/doi/10.1542/peds.2008-3080)

doi:10.1542/peds.2008-3080

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Food and Drug Administration.

#### Key Words

ceftriaxone, calcium, newborn, drug therapy/adverse event, cardiopulmonary arrest

#### Abbreviations

FDA—Food and Drug Administration  
AERS—Adverse Event Reporting System

Accepted for publication Dec 17, 2008

Address correspondence to John S. Bradley, MD, 3020 Children's Way, Mail Code 5041, San Diego, CA 92123. E-mail: [jbradley@rhhad.org](mailto:jbradley@rhhad.org)

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2009 by the American Academy of Pediatrics

complexe insoluble calcium-ceftriaxone

Bradley JS et al. *Pediatrics* 2009;123:609-13

# CONSTAT

→ Réduire le nombre de particules!



C. Fonzo-Christe



# APT: RISQUE DE PARTICULES



- Procédure GMP pour la fabrication
- Flush des tubulures pour diminuer la charge en particules \*

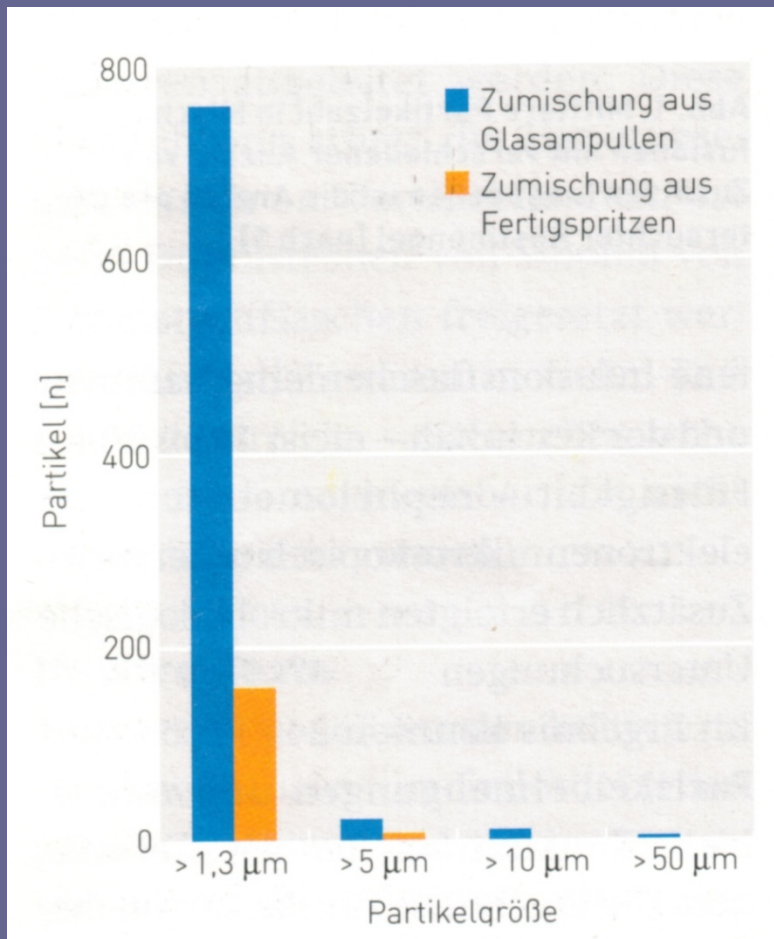


## FLUSHING VOLUME

| Analyzed elements | Number of units | Mean Number of particles $\geq 10\mu\text{m}$ | Mean Number of particles $\geq 25\mu\text{m}$ |
|-------------------|-----------------|---|---|
| Flushing volume   | 9               | 62  | 1   |

\* Stucki C et al. EAHP 2004. [http://pharmacie.hug-ge.ch/rd/posters/eahp04\\_hi\\_particules\\_baxa\\_cs.pdf](http://pharmacie.hug-ge.ch/rd/posters/eahp04_hi_particules_baxa_cs.pdf)

# CIVAS (PRÊT À L'EMPLOI)

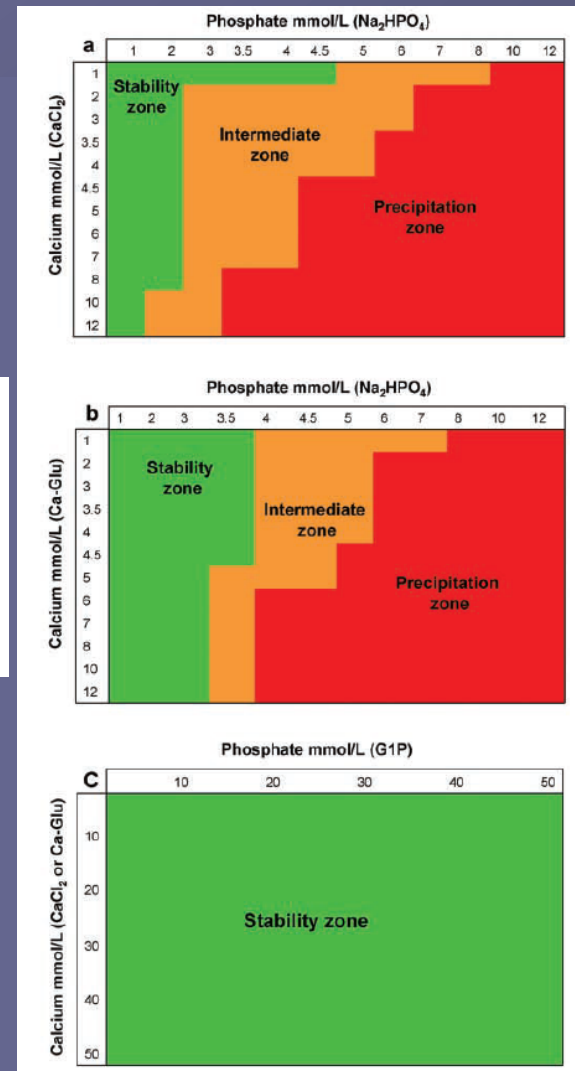


Panknin HT. Krankenhauspharmazie 2008;29:97-105

# TPN ET CALCIUM / PHOSPHATE

## Maximizing Calcium and Phosphate Content in Neonatal Parenteral Nutrition Solutions Using Organic Calcium and Phosphate Salts

Bouchoud L et al. JPEN J Parenter Enteral Nutr. 2010;4:542-5



# GESTION INCOMPATIBILITES

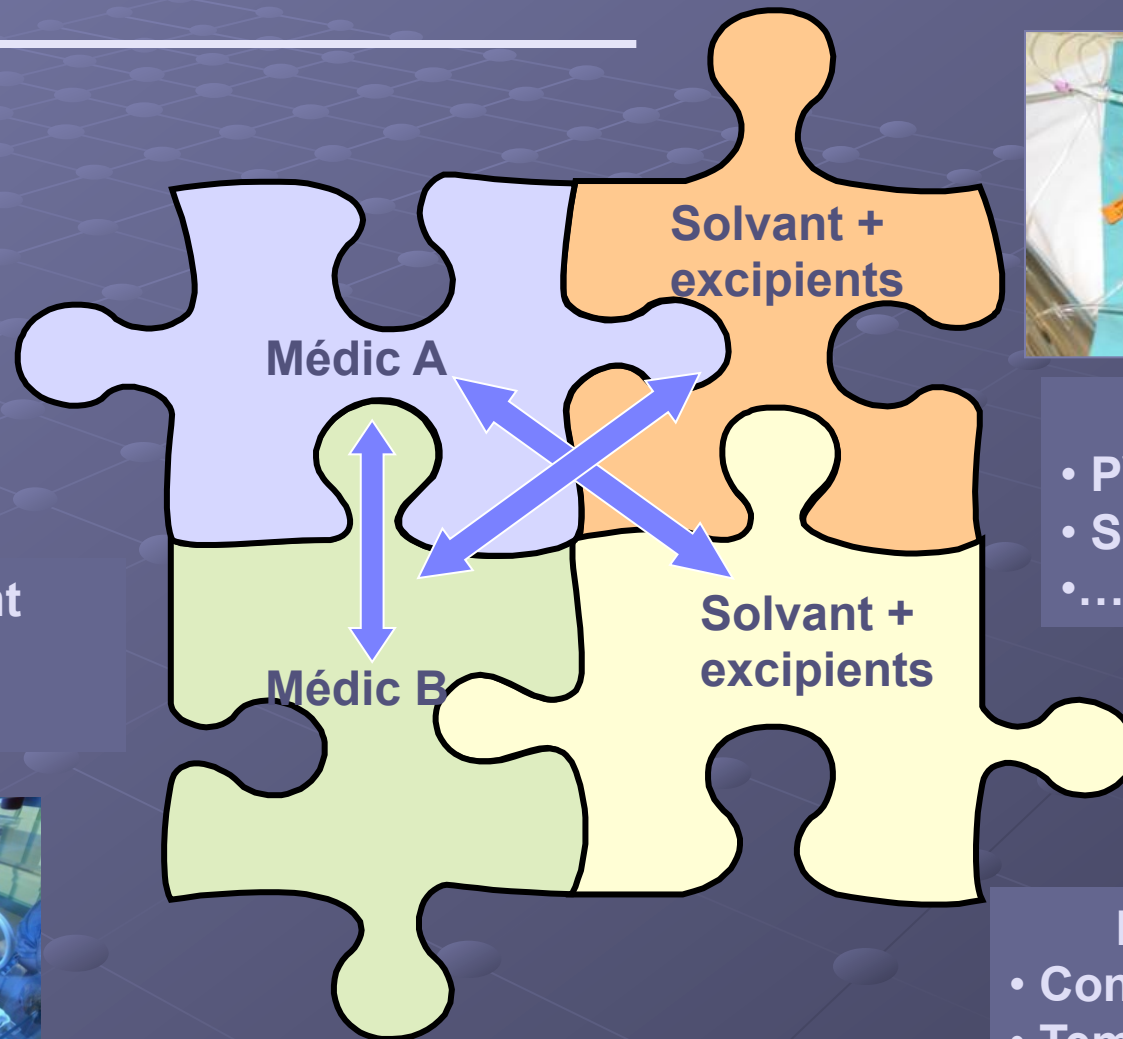


**Environnement**

- Température
- Lumière



C. Fonzo-Christe



**Matériel**

- PVC (DEHP)
- Silicone
- ...

**Facteurs**

- Concentration
- Temps de contact

# CROSS-TABLES

Site Web de la Pharmacie des HUG - <http://pharmacie.hug.ge.ch>  
Assistance pharmacotique No 16, Interne 31000

### COMPATIBILITES DES MEDICAMENTS INJECTABLES ADMINISTRES EN Y

RECOMMANDATIONS GENERALES:

- En l'absence de données, ne pas perfuser en Y les médicaments
- Connecter les perfusions en Y la plus proche possible du point de perfusion
- Perfuser le sang et les dérivés sanguins toujours tout seuls

Code couleur :

- C** = compatible (tests physiques ou physico-chimiques)
- CC** = compatible avec héparine diluée à 50 UI/ml, selon mode de dilution proposée sur la dilution de la solution concentrée à 420 UI/ml
- X** = incompatible
- Ø** = aucune donnée publiée (contacter l'assistante)
- ∅** = référence employée:
  - a) Trase LA, Venobox ou Vascular drug, 16th
  - b) King, G. et al., Guide to Parenteral Admixtures, 2e
  - c) Trase LA et al., Trase's table of compatibility
  - d) Compendium suisse des médicaments ou Intermed
  - e) Test au labo de Contrôle de Qualité de la Pharmacie
  - f) Test au labo de Contrôle de Qualité de la Pharmacie
  - g) Urocinject healthcare Dates, Thomson Health

Table grid showing compatibility between various injectable drugs. The grid is color-coded according to the legend.

[http://pharmacie.hug-ge.ch/infomedic/utilismedic/HUG\\_CompatAdm\\_DCI.pdf](http://pharmacie.hug-ge.ch/infomedic/utilismedic/HUG_CompatAdm_DCI.pdf)

**KING® GUIDE TO PARENTERAL ADMIXTURES** CRIT

HOW THIS CHART WAS PREPARED: For each drug combination that appears, the symbol indicated is based upon evaluating compatibility across the fluid specified. If the drug combination is compatible in all of these fluids, the symbol on the chart will indicate the combination may be compatible in fluid and in direct admixture. The first two columns, DSW (Dextrose 5%), and NS (Sodium Chloride Injection), indicate compatibility of a single drug in a fluid specified.

**KEY TO SYMBOLS**

- C** The combination may be compatible. Actual compatibility is determined by several variables, including drug concentration, pH, infusion fluid, temperature, type of container, order of mixing, specific brand of drug, and method of administration.
- X** The combination has been reported to be incompatible.
- Ø** Conflicting data have been reported in the literature, so the specific combination may be compatible or incompatible.
- ∅** No Data Available. Admixture not advised.

[www.kingguide.com](http://www.kingguide.com)

|                                    | DSW | NS | ABACAVIR SODIUM | ACICLOVIR SODIUM | ALBUMIN, SERUM HUMAN | ALTEPLASE | AMIKACIN SULFATE | AMINOPHYLLINE | AMIODARONE HYDROCHLORIDE | AMPHOTERICIN B | AMPHOTERICIN B CHOLESTERYL SULFATE | AMPICILLIN SODIUM | AMPCILLIN SODIUM - SULBACTAM | ARGATROBAN | ASCORBIC ACID | ATRACURIUM BESYLATE | AZTREONAM | BUMETANIDE | BUTORPHANOL TARTRATE | CALCIUM CHLORIDE | CALCIUM GLUCONATE | CASPOFUNGIN ACETATE | CEFAZOLIN SODIUM | CEFOTAXIME SODIUM | CEFTAZIDIME | CEFOXITAN DISODIUM | CEFOXITIN SODIUM | CEFOXITIN DISODIUM |
|------------------------------------|-----|----|-----------------|------------------|----------------------|-----------|------------------|---------------|--------------------------|----------------|------------------------------------|-------------------|------------------------------|------------|---------------|---------------------|-----------|------------|----------------------|------------------|-------------------|---------------------|------------------|-------------------|-------------|--------------------|------------------|--------------------|
| ABACAVIR SODIUM                    | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ACICLOVIR SODIUM                   | Ø   | Ø  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ALBUMIN, SERUM HUMAN               |     |    |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ALTEPLASE                          | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMIKACIN SULFATE                   | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMINOPHYLLINE                      | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMIODARONE HYDROCHLORIDE           | Ø   | Ø  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMPHOTERICIN B                     | Ø   | Ø  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMPHOTERICIN B CHOLESTERYL SULFATE | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMPICILLIN SODIUM                  | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AMPCILLIN SODIUM - SULBACTAM       | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ARGATROBAN                         | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ASCORBIC ACID                      | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| ATRACURIUM BESYLATE                | X   | Ø  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| AZTREONAM                          | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| BUMETANIDE                         | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| BUTORPHANOL TARTRATE               | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CALCIUM CHLORIDE                   | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CALCIUM GLUCONATE                  | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CASPOFUNGIN ACETATE                | X   | Ø  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFAZOLIN SODIUM                   | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFOTAXIME SODIUM                  | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFOXITAN DISODIUM                 | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFOXITIN SODIUM                   | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFOXITIN DISODIUM                 | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |
| CEFTAZIDIME                        | C   | C  |                 |                  |                      |           |                  |               |                          |                |                                    |                   |                              |            |               |                     |           |            |                      |                  |                   |                     |                  |                   |             |                    |                  |                    |

<https://www.kingguide.com/>



# TESTS IN VITRO

## Compatibility of Intravenous Medications With Parenteral Nutrition: In Vitro Evaluation

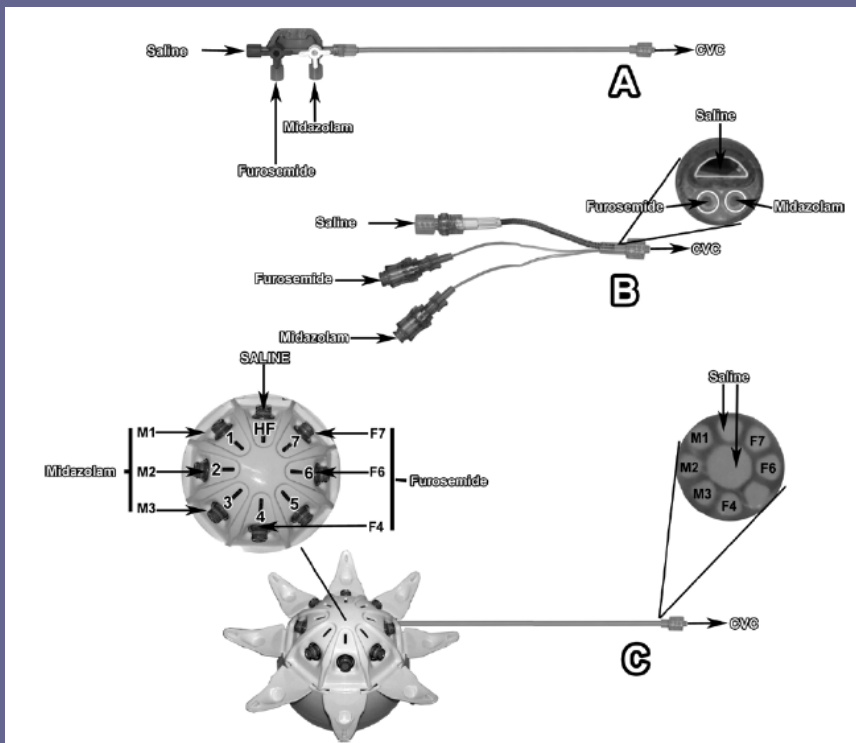
**Table 8.** Overall Physicochemical Compatibility Data of the 25 Tested Admixtures

| Medication            | Tested Concentrations  | Contact 1:1 Compatibility With PN After 1 h | Contact 1:1 Compatibility With PN After 4 h |
|-----------------------|------------------------|---|---|
| <b>Albumin</b>        | <b>200 mg/mL</b>       | <b>I</b>                                    | <b>I</b>                                    |
| Amoxicillin/Ac. clav. | 50 mg/mL (amoxicillin) | C   | I   |
|                       | 10 mg/mL (Ac. clav.)   |   |   |
| Calcium chloride      | 0.13 mmol/mL Ca        | C   | C   |
| Cefepime              | 100 mg/mL              | C   | I   |
| Cyclosporine          | 2.5 mg/mL              | C   | C   |
| <b>Esomeprazole</b>   | <b>0.8 mg/mL</b>       | <b>I</b>                                    | <b>I</b>                                    |
| Fentanyl              | 0.05 mg/mL             | C   | C   |
| <b>Fluorouracil</b>   | <b>25 and 50 mg/mL</b> | <b>I</b>                                    | <b>I</b>                                    |
| Fluorouracil          | ≤12.5 mg/mL            | C   | C   |

Bouchoud L et al. JPEN J Parenter Enter Nutr. 2013;37:416-24

# CHOIX MATERIEL DE PERFUSION

## The Impact of Multilumen Infusion Devices on the Occurrence of Known Physical Drug Incompatibility: A Controlled In Vitro Study



Foinard A et al. Anesth Analg 2013;116:101-6

# CONSTAT

→ Réduire le nombre de particules!

**Filtres en ligne**

PREPARATION



ADMINISTRATION



# EVIDENCE



## Intravenous in-line filters for preventing morbidity and mortality in neonates

**Pas d'évidence sur morbidité ni mortalité**

### Main results

There were four eligible studies that recruited a total of 704 neonates. This review found no significant effect of in-line filters in any of the reported outcomes of overall mortality, proven and suspect septicaemia, local phlebitis and thrombus, necrotizing enterocolitis, duration of cannula patency, length of stay in hospital, number of catheters inserted and financial costs.

### Authors' conclusions

There is insufficient evidence to recommend the use of intravenous in-line filters to prevent morbidity and mortality in neonates.

Foster JP et al. Cochrane Database of Systematic Reviews 2006 (review June 2011), Issue 2. Art. No.: CD005248. DOI: 10.1002/14651858.CD005248.pub2

# QUID?

## Intravenous in-line filters: filtering the evidence

Patrick A. Ball

### Purpose of review

The routine use of intravenous in-line filters on infusion lines has been controversial for many years, with strong advocates, detractors and many fence-sitting observers. The purpose of this review was to examine the literature for new developments and to cast the net a little wider than in previous reviews in an attempt to draw useful parallels.

### Introduction

It is generally held that the medical community was made aware of the issue of particulate contamination in the 1960s [1], yet the following quote suggests the problem has been known for much longer: 'Mackintosh described in great detail the saline injection procedure which he began to use in May of 1832...He warned of

Current Opinion in Clinical Nutrition and Metabolic Care 2003, 6:319–325

# TPN: RECOMMANDATION

1. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR)

## *Recommendations*

- Sodium chloride 0.9% should be used to flush the CVC between all therapies and heparin should be instilled at least weekly when the CVC is not in use. **GOR D**
- Terminal in-line filters should be used for all PN fluids. **GOR D**
- Occlusion of in-line filters should be investigated. **GOR D**



Koletzko B et al. JPGN 2005;41:S1-S4

# THROMBOPHLEBITES

Acta Pædiatr 93: 658–662. 2004

Taylor & Francis  
healthsciences

## The use of in-line intravenous filters in sick newborn infants

RA van Lingen<sup>1</sup>, W Baerts<sup>1</sup>, ACM Marquering<sup>1</sup> and GJHM Ruijs<sup>2</sup>

Department of Paediatrics Princess Amalia<sup>1</sup>, Division of Neonatology  
Diseases, Isala Clinics, Zwolle, The Netherlands

**Thrombophlébites  
Réduction coûts**

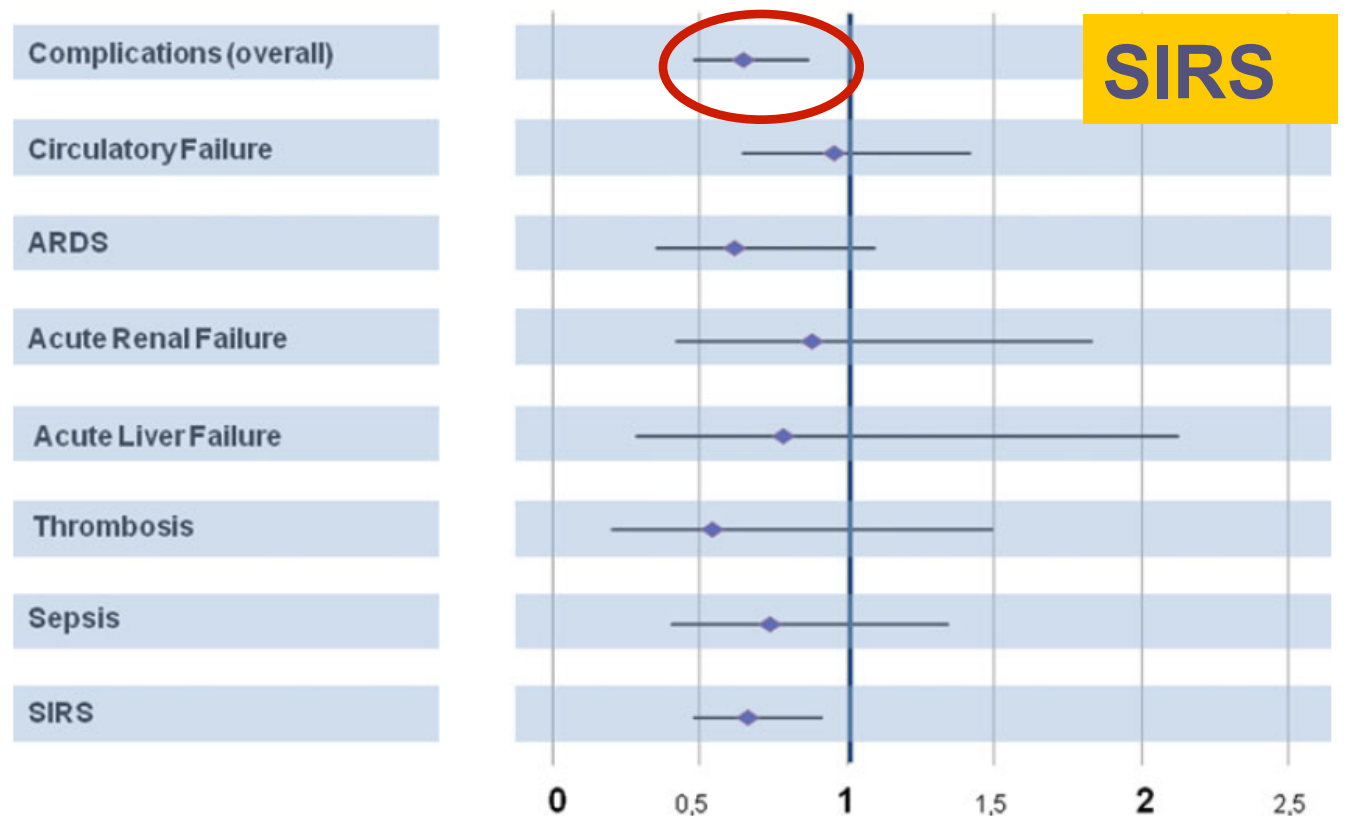
Van Lingen RA, Baerts W, Marquering ACM, Ruijs GJHM. The use of in-line intravenous filters in sick newborn infants. Acta Pædiatr 2004; 93: 658–662. Stockholm. ISSN 0803-5253

*Aim:* This study assesses the improvement in outcome for newborn infants by decreasing major complications associated with intravenous fluid therapy by using an in-line filter, and evaluates the economical impact this might have in relation to daily changing of i.v. lines. *Methods:* In a prospective controlled study, 88 infants were randomly assigned to receive either filtered (except for lipids, blood and blood products) or non-filtered infusions via a central catheter. Main outcome measures such as bacteraemia, phlebitis, extravasation, thrombosis, septicaemia and necrosis were all scored. The costs attributable to patients during a standard 8-day stay were also recorded. *Results:* Significant reductions were found in major complications such as thrombi and clinical sepsis (control group (21), filter group (8);  $p < 0.05$ ). Bacterial cultures of the filters showed a contamination rate on the upstream surface of 15/109 filters (14%). The mean costs of disposables were less in the filter group, showing a reduction from €31.17 to €23.79.

*Conclusions.* The use of this in-line filter leads to a significant decrease in major complications and substantial cost savings.

# SIRS

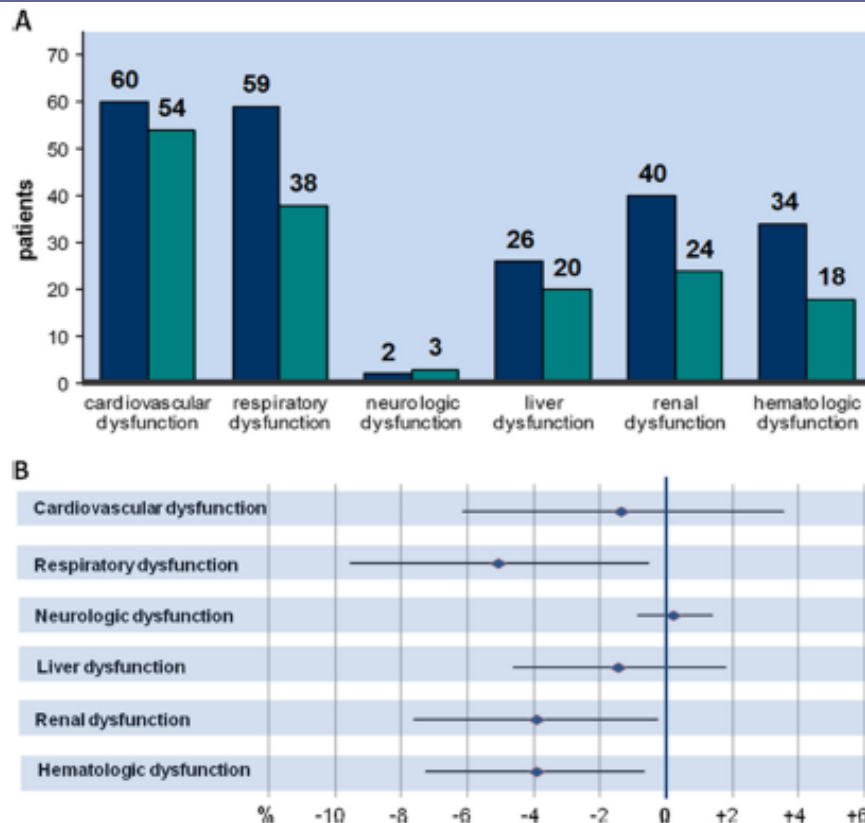
**Fig. 2** Hazard ratios of primary objectives for the treatment effect of in-line filtration. The incidence of overall complications and systemic inflammatory response syndrome (*SIRS*) were significantly reduced in the filter group. A trend towards a reduction in acute respiratory distress syndrome (*ARDS*) was evident for the filter group ( $P = 0.08$ ). No significant differences were found for the incidence of sepsis, circulatory failure, acute renal failure, acute liver failure and thrombosis. *Filled rhombi* Hazard ratios, *horizontal lines* 95 % confidence intervals



Jack T et al. Intensive Care Med 2012;38:1008-1016



# COMPLICATIONS



**Dysfonction  
respiratoire,  
rénale et  
hématologique**

**Figure 1** Incidence of organ dysfunction in control (blue columns) and filter group (grey columns) (A) and corresponding differences in incidence rates with 95% confidence intervals (B). Respiratory, renal and hematologic dysfunction were significantly reduced in the filter group (Panel A). Filled rhomb: differences in incidence rates; horizontal lines: 95% confidence intervals. (Panel B).

Boehne et al. BMC Pediatrics 2013;13:21

# COUTS

## Coûts

**Table 2** Morbidity outcomes

| Characteristics                                     | Control group<br>(n = 406) | Filter group<br>(n = 401) | P value <sup>a</sup> | 95 % Confidence interval |
|---|----------------------------|---------------------------|----------------------|--------------------------|
| Primary objectives (n)                              |                            |                           |                      |                          |
| Complications (overall)                             | 166                        | 124                       | 0.003                | 0.484–0.865              |
| Adjusted to PIM II                                  |                            |                           | 0.011                | 0.502–0.914              |
| SIRS  | 123                        | 90                        | 0.011                | 0.485–0.913              |
| Adjusted to PIM II                                  |                            |                           | 0.026                | 0.500–0.958              |
| Sepsis  | 27                         | 20                        | 0.313                | 0.406–1.337              |
| Circulatory failure                                 | 60                         | 57                        | 0.593                | 0.604–1.334              |
| ARDS  | 35                         | 22                        | 0.082                | 0.354–1.069              |
| Acute renal failure                                 | 16                         | 14                        | 0.736                | 0.425–1.831              |
| Acute liver failure                                 | 9                          | 7                         | 0.631                | 0.289–2.125              |
| Thrombosis  | 11                         | 6                         | 0.230                | 0.200–1.489              |
| Secondary objectives                                |                            |                           |                      |                          |
| Mortality (n)                                       | 27                         | 16                        | 0.093                | 0.309–1.100              |
| Length of stay (days) <sup>b</sup>                  | 3.89 (2.96–4.81)           | 2.98 (2.33–3.63)          | 0.025                |                          |
| Duration of mechanical ventilation (h) <sup>b</sup> | 14.0 (5.6–22.4)            | 11.0 (7.1–14.9)           | 0.028                |                          |

Comparison of primary and secondary outcomes between control and filter group

ARDS Acute respiratory distress syndrome, SIRS systemic inflammatory response syndrome

<sup>a</sup> P values were calculated using Pearson's Chi-Square test, Fisher's exact test or log-rank test as indicated

<sup>b</sup> Data are presented as the median with the range given in parenthesis

# CONCLUSION

---

- Particules: effets délétères!
- Réduction de la charge particulaire à tous les niveaux pour les patients les plus à risques
  - Utilisation adéquate du matériel
  - Préparation et filtration
  - Réduction du risque d'incompatibilités
  - Filtres en ligne

# PRÊTS À INVESTIR?

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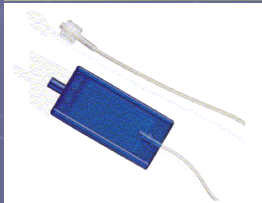


# FILTRES EN LIGNE: CHOIX





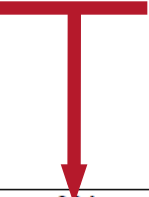
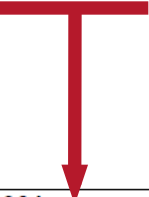

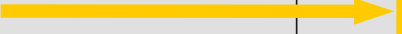
## Difficultés pour implémentation

- au moins deux types de filtres (0.2 et 1.2  $\mu\text{m}$ )
- aspects techniques (priming, flush)
- risques aseptiques
- pas de filtration de certains produits
- filtres bloqués: procédure

→ Enseignement, procédures détaillées, suivi essentiels



# USI-NEONATOLOGIE HUG

| TABLEAU RECAPITULATIF      |  |   |   |   |
|----------------------------|--|---|---|---|
| Photo Filtre               |   |   |    |  |
| Type filtre                | NEO96  | ELD96   | NLF2  | TNA1E   |
| Membrane                   | 0,2 µm   | 0,2 µm  | 1,2 µm  | 1,2 µm  |
| Volume                     | 0,4 ml   | 2ml   | 0,8 ml  | 2,3 ml  |
| Débits                     | inférieur ou égal à 75ml/h   | supérieur à 75ml/h  | débit maximum 75 ml/h   | débit supérieur à 75 ml/h   |
| Solution                   | solutions aqueuses   | solutions aqueuses  | émulsions lipidiques et autres  |   |
|                            |    |  | <ul style="list-style-type: none"> <li>- Lipides : Lipofundin MC<sup>®</sup>, Omegaven</li> <li>- Nutrition parentérale (APT), StractoKabiven<sup>®</sup>, Nutriflex Lipid spécial<sup>®</sup>, PeriOlimel<sup>®</sup></li> <li>- Propofol<sup>®</sup>, Disoprivan<sup>®</sup></li> <li>- Etomidate Lipuro<sup>®</sup></li> <li>- Vitalipid<sup>®</sup></li> <li>- Cernevit<sup>®</sup></li> </ul>  |   |
| Changement du filtre       | 96 heures  | 96 heures   | 24 heures   | 24 heures   |
| Médicaments non filtrables | <ul style="list-style-type: none"> <li>○ sang et dérivés sanguins (PFC,CE, thrombaphèrese)</li> <li>○ facteurs de coagulation : Novoseven<sup>®</sup>, Haemate P<sup>®</sup>, Kogenate SF<sup>®</sup>, Prothromplex NF<sup>®</sup>, Immunine STIM plus<sup>®</sup>, Fibrogammin P<sup>®</sup>, Advate<sup>®</sup>, Hélixate<sup>®</sup></li> <li>○ Albumine 20%</li> <li>○ Konakion MM<sup>®</sup> (phytoménadion, vitamine K)</li> <li>○ Ambisome<sup>®</sup> (amphotéricine B liposomale)</li> <li>○ Gardéнал<sup>®</sup> (phénobarbital)</li> <li>○ Privigen<sup>®</sup>, Kiovig<sup>®</sup></li> </ul>  |   |   |   |

# PATIENTS: TRANSFERT



**Soins intensifs**

Filtres (amines)



**Bloc opératoire**



**Chirurgie**

# ECOTOXICOLOGIE

Firefox Les nanoparticules de dioxyde de titane ...

www.notre-planete.info/actualites/actu\_2197\_nanoparticules\_dioxyde\_titane\_danger\_sante.php

notre-planete.info

Google Recherche personnalisée

Actualités Environnement La Terre Écologie Photos

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+ Recevoir une alerte mail à chaque nouvelle actualité + Les actualités sur votre smartphone + Flux RSS

**Les nanoparticules de dioxyde de titane sont-elles dangereuses pour l'homme ?**

01 décembre 2009, 14 h 10 13291 lectures / 4 commentaires

Qu'on le sache ou non, on retrouve les nanoparticules de dioxyde de titane (TiO2) dans la plupart des produits cosmétiques, dans les crèmes solaires, dans les colorants alimentaires et dans les compléments nutritionnels.

Bien que le TiO2 à l'état macroscopique et microscopique soit chimiquement inerte, il a déjà été montré qu'à l'échelle nanoscopique le TiO2 a un impact sur la santé : il existe une cancérogénèse pulmonaire chez le rat, (non

Observatoire Midi-Pyrénées

LES GRANDS SEMINAIRES DE L'OBSERVATOIRE MIDI-PYRENEES

14 avenue Edouard Belin - 31400 TOULOUSE

Salle Coriolis 11 heures

Mardi 19 Mai 2009

Francelyne Marano  
Ecotoxicologue à l'Université Paris-Diderot

Le développement rapide du marché des nanotechnologies va conduire dans un avenir proche à une exposition humaine accrue aux nanoparticules (particules dont au moins une des dimensions est inférieure à 100nm), par voie respiratoire ou cutanée, par ingestion voire par injection médicamenteuse. Les applications des nanotechnologies sont en effet à la fois diversifiées et nombreuses, par exemple la nanoelectronique, la purification de l'eau, la cosmétologie, les traitements de surface... La médecine développe leur utilisation pour l'imagerie et le diagnostic, et les recherches sur le ciblage des médicaments sont potentiellement très prometteuses, en particulier pour les médicaments anticancéreux. Enfin, de nouveaux matériaux nanostructurés sont à l'étude dans le domaine des prothèses. Certaines applications sont déjà commercialisées et largement diffusées, par exemple en cosmétologie.

L'exposition aux NP risque donc d'être à la fois professionnelle, environnementale et médicale et recouvre une grande variété de nanoparticules utilisées sous des formes et avec des conditionnements très nombreux. Cependant, l'évolution rapide de ces technologies, dont on dit qu'elles seront la révolution industrielle du 21ème siècle impose d'en évaluer en amont les dangers et les risques, à partir d'une meilleure connaissance de leurs effets biologiques. Les recherches récentes des toxicologues montrent des propriétés particulières des nanoparticules et ont conduit au développement de la nanotoxicologie qui devrait permettre une meilleure évaluation des risques des nanomatériaux pour l'homme et l'environnement.

Nanoparticules : les bienfaits et les risques