



self-care dialysis

symposium

Enigmatic Cyanosis in a chronic home hemodialysis patient

Dr Seront B
Dr Van Ende C
Pr Goffin E

Case presentation



I.M. 54 years old

Case presentation



Past Medical History :

✦ Kidney related:

- ✦ CIN secondary to vesicoureteral reflux
- ✦ Started on HD by december 1981
- ✦ 15/10/1983 : kidney transplantation with right nephrectomy
- ✦ 02/1998: severe proteinuria (2,6g/24h). Graft biopsy: chronic allograft nephropathy (sclerosis 4/6)
- ✦ 26/5/2006 : started on peritoneal dialysis
- ✦ 2/12/2010 : stop PD because of multiple episodes of peritonitis so started on Home hemodialysis

Case Presentation



Medical history :

- ✦ Subtotal Parathyroidectomy
- ✦ Multiple colonic polyps
- ✦ Lower limb arteriopathy :
 - ✦ 08/2010 :right popliteal artery et tibial posterior artery angioplasty
 - ✦ 07/2011 : right femoro-popliteal bypass
 - ✦ 02/2012 : left popliteal artery angioplasty
- ✦ Carotid atheromatosis :
 - ✦ External bilateral carotid stenosis (right: 50-60%, left: 60-70%)

Case Presentation



Current treatment:

- ✦ Cardioaspirine 100mg once per day
- ✦ Emconcor 2,5 mg DWD
- ✦ Zocor 20 mg once per day
- ✦ Kayexalate Na DWD
- ✦ Rocaltrol 0,25 µg once per day
- ✦ CaCO₃ 1g twice a day
- ✦ Dialysis :
 - ✦ Aranesp 100µg 3/w
 - ✦ Injectafer 300mg/6w

Case Presentation



Current problem :

✦ 04/08/2013 : walk in the Herve countryside, and chinese restaurant

✦ 05/08/2013 : home hemodialysis in the afternoon

- ✦ At the end of session: weakness, dizziness and nausea.
Her Husband noticed she had a red flushed face.
Her vital signs were stable.
- ✦ 10 pm: symptomatic treatment was prescribed by her family physician
- ✦ 04:00 am : no amelioration. Litalan was prescribed by her GP and blood sample was drawn.
- ✦ 06:00 am: call from the laboratory: Hemoglobin is 4,7 g/dL!!!

Case Presentation



× 06/08/2013: Emergency Department

✦ Nausea, dizziness, dyspnea .

✦ Physical Examination:

✦ BP 113/84mmHg, HR 120pm, RR 40/min, SaO2 : 94%

GCS 15/15, T° 36°C,

✦ Cardiopulmonary : (-)

✦ Abdomen (-)

✦ No ankle swelling

✦ Red-blue coloration of the skin!







Cyanosis

× Central Cyanosis

✦ Pulmonary origin :

- ✦ Pneumonia, PE, COPD, asthma, interstitial lung disease , PNO, pleural effusion, arterio venous fistula, central apnea

✦ Cardiac origin :

- ✦ Cardiac disease with shunt.

✦ Hemoglobic cyanosis :

- ✦ Methemoglobinaemia
- ✦ Sulfhemoglobinaemia

× Peripheral cyanosis

✦ Generalized :

- ✦ Heart Failure
- ✦ Hematologic: polycythemia vera (Vaquez) cryoglobulinaemia, agglutinin

✦ Local :

- ✦ Venous thrombosis
- ✦ Raynaud Phenomenon

✦ Cyanosis like

- ✦ Silver deposit
- ✦ Amiodarone

Case Presentation



Laboratory results:

✦ Blood sample:

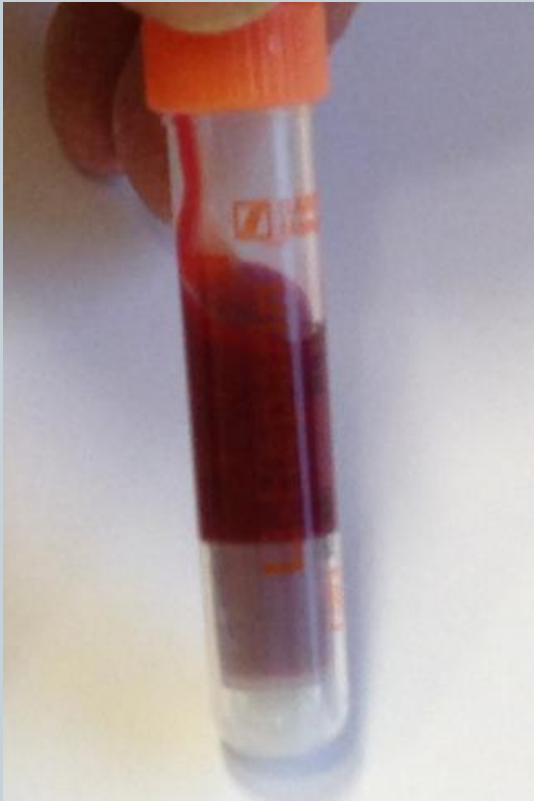
- ✦ Hb 4.7g/dl
- ✦ GB 17.170/ μ l
- ✦ Platelets 176.000/ μ l.
- ✦ Haptoglobin 18mg/dl
- ✦ LDH 3800UI/L
- ✦ Hemolysis

✦ ABG's :

- ✦ pH 7.43
- ✦ paO2 101mmHg
- ✦ pCO2 20mmHg
- ✦ HCO3 13.4mmol/L
- ✦ K+ 5.1mmol/L
- ✦ Lactate 11mmol/L

Methemoglobin
n 20.9 %

Case Presentation



BEFORE DIALYSIS

MetHb 6,5%

Hb 9,8 g/dl



AFTER DIALYSIS

MetHb 14,5%

Hb 4,3 g/dl

Diagnosis?



Methemoglobinaemia and massive hemolysis

- ④ Transfert to Intensive Care Unit
- ④ R/ Methylene Blue 2mg/kg IV

Case Presentation



In the ICU (06/08 – 19/08) :

- Hemolytic anemia => blood transfusion (5 units)
- Cyanosis persisting despite the use of Methylene Blue
 - Exsanguino transfusion
 - Storage of Methylene Blue (anuric patient)
- Very agitated state—> intubation.
- Severe hypotension requiring vasopressors:
 - Diffuse alteration of left ventricle function

Case Presentation



- × Progressive improvement over few days
- × Transfert to the nephrology unit 19/08
- × Learning NxStage

Methemoglobinemia



- × Definition : Oxydation of the iron present in the Heme
 - ✦ Fe⁺⁺ (ferrous) becomes Fe⁺⁺⁺ (ferric)
 - ✦ Unable to carry oxygen.

- × Pathophysiology :
 - ✦ Daily production: 3% of total Hb, which is constantly reduced by protective enzymatic or chemical systems.

- Ⓜ MetHb < 0.80% of total Hb

Methemoglobinaemia



× Pathophysiology :

✦ Reducing systems of Met Hb:

- ✦ NADH-cytochrom-b5-reductase
- ✦ NADPH-MetHb-reductase : use with Methylene Blue

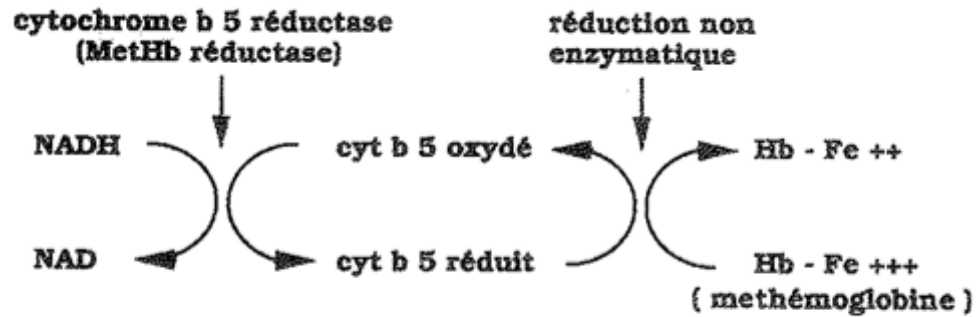
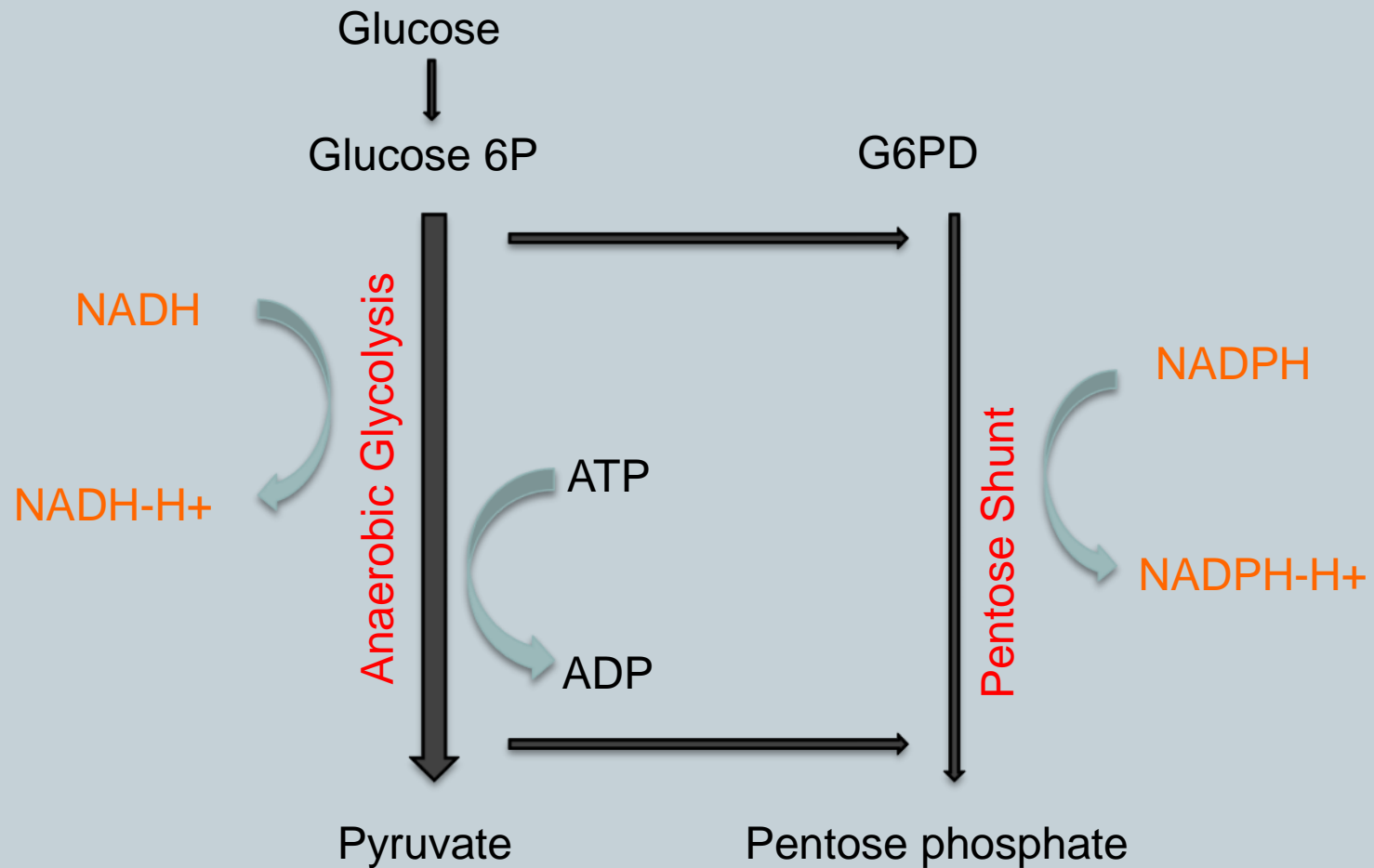


Fig. 3. Voie principale, NADH-dépendante.



Fig. 4. Voie accessoire, NADPH-dépendante.

Methemoglobinaemia



Methemoglobinemia



× Causes :

✦ Inherited :

- ✦ NADH-cytochrome b5 reductase Deficit (AR)
- ✦ Hemoglobin M Disease (AD)
- ✦ NADPH-MetHb-reductase deficit

✦ Acquired (Toxic)

Methemoglobinemia



| | |
|---|--|
| Inorganic Compounds | <ul style="list-style-type: none">- Nitrates- Nitrous gases- Chlorates |
| Organic Compounds (nitrate and chlorate base) | <ul style="list-style-type: none">- Sulfamides- Sulfones- Nitrobenzene and derivatives- Nitrotoluene and derivatives- Aminobenzene (aniline) and derivatives.- Phenylacetamide and derivatives (phenacetine,...)- Phenazopyridine- Metoclopramide (premature baby only)- Organic Nitrates- Nitroglycerine- Primaquine and pentaquine- Benzocaïne- Methylene Blue |
| Other Organic Compounds | <ul style="list-style-type: none">- Quinine- Resorcine |

Hemolysis also

Methemoglobinemia



| MetHb levels (% of Hemoglobin) | Symptoms |
|-----------------------------------|---|
| 0-15 | None |
| 15-20 | Cyanosis « Chocolate » blood |
| 20-45 | Dyspnea, fatigue, dizziness, headaches |
| 45-55 | Central nervous system suppression |
| 55-70 | Coma, seizures, arrhythmias |
| >70 | Death |

Methemoglobinemia



× Treatment :

✦ Symptomatic :

- ✦ O₂
- ✦ Basic life support
- ✦ Gastric lavage, active charcoal
- ✦ Cutaneous decontamination

✦ Specific Treatment

Methemoglobinemia



✗ Treatment :

✦ Specific:

✦ Methylene Blue 1%

✦ Indication : if MetHb >30% and/or hypoxia

✦ Dosage : 1-2mg/kg IV.

✦ Contre-Indications : Allergy, severe renal failure, G6PD deficiency, NADPH-réductase deficiency.

✦ Exsanguinotransfusion :

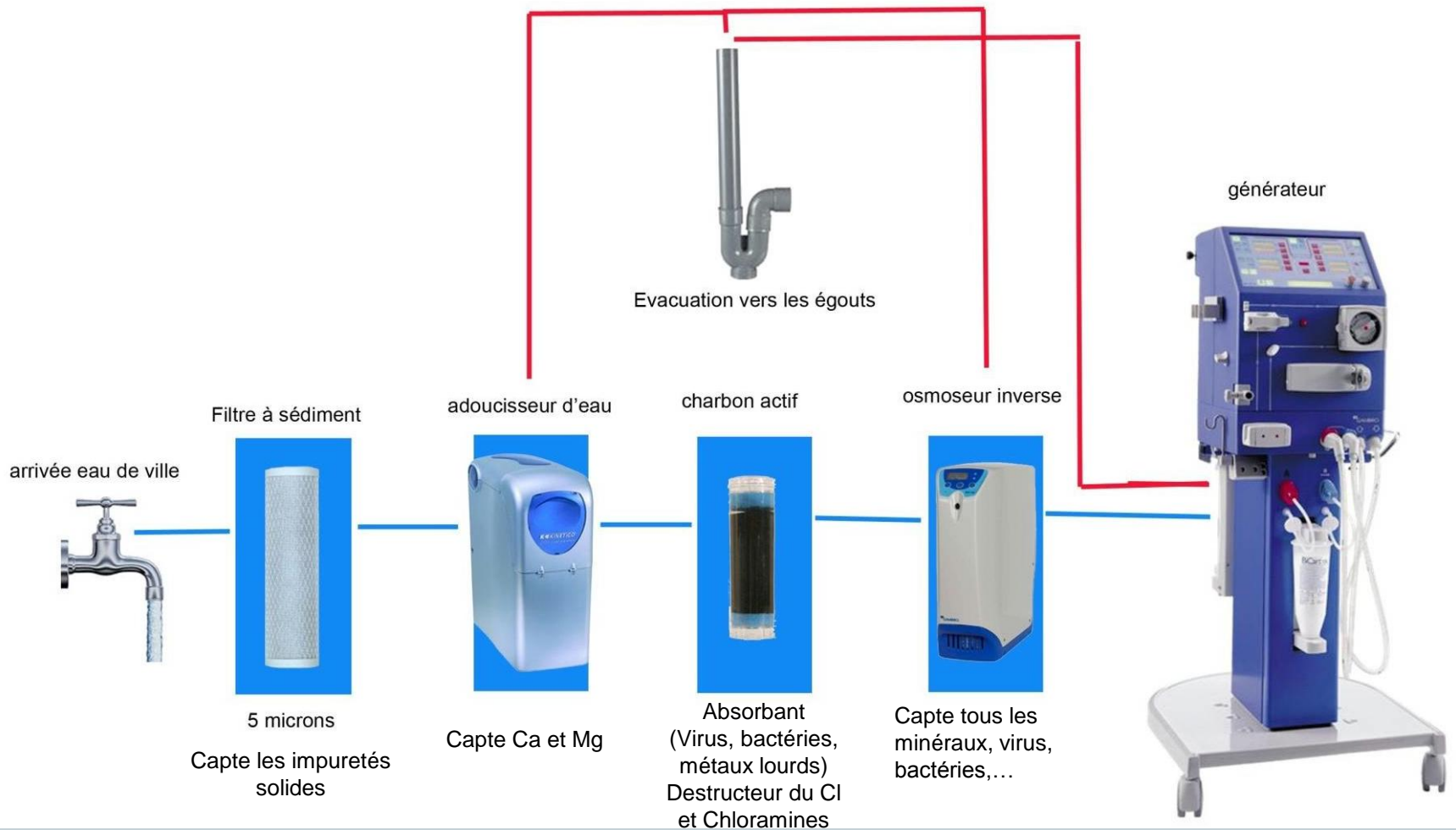
✦ Indication : MetHb > 60-70%, Hemolysis, SulfHb.

Methemoglobinemia and Hemodialysis



- × Chloramines
- × Nitrates
- × Hydrogen peroxyde
- × Copper
- × Dapsone

Coulliette AD. *Sem. Dial.*
Nessim SJ. *Kidney Int.* 2010
Davidovits M. *Nephrol Dial Transplant.* 2003

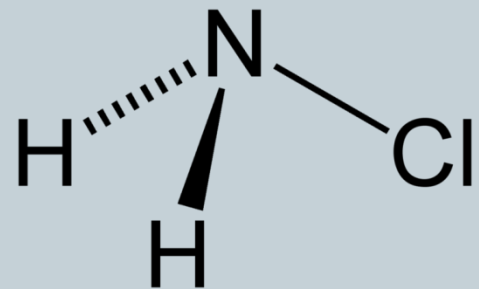


Methemoglobinemia et Hemodialysis.



× Chloramines

- ✦ Chlorine is added to municipal water supplies (disinfectant)
- ✦ Substitution of H⁺ of ammonia (NH₃) by Cl: Chlor-amine
- ✦ Public water contains chloramine in the range of 1-2,5 mg/L
- ✦ If bacterial contamination of the water increases, it's necessary to increase concentration of chloramines.



Methemoglobinemia et Hemodialysis.

29

× Chloramines

- ✦ Causes red-blood-cell oxidant damage

 - ✦ conversion of haemoglobin to methemoglobin

 - ✦ formation of Heinz bodies

- ✦ Removed by activated charcoal (depends on the time of contact)
and ascorbic acid (more expensive)

- ✦ In HD, recommendation : total chloride $< 0.1 \text{ mg/L}$

- ✦ If $0,2$ to $0,3 \text{ mg/L}$ → methemoglobinemia

- ✦ If $> 0,5 \text{ mg/L}$ → hemolysis



× Nitrates

- ✦ Metabolised to nitrites.
- ✦ Main source :
 - ✦ The fertilizers.
 - ✦ The Enterobacteriaceae.



So what is the origin of this hemolysis and this methemoglobinemia?

Back to the case



× Toxic origine :

- ✦ No new drugs taken.
- ✦ No evidence of infection (Negative hemocultures)
- ✦ Blood tests looking for metals or volatiles solvents: negative
- ✦ Home water analysis (by SWDE): nothing to mention (negative for chlorure, nitrates and nitrites).
- ✦ Dialysis fluid (rinsing machine) and dialysate analysis: negative

× Congenital origine :

- ✦ Normal Hb electrophoresis.
- ✦ No deficit in G6PD and pyruvate kinase.
- ✦ Cryohemolysis test $<0.5\%$ (nl : $< 6\%$)

Is it the only case?

33

Crit Care. 2009;13(5):R162. doi: 10.1186/cc8128. Epub 2009 Oct 12.

Methemoglobinemia in critically ill patients during extended hemodialysis and simultaneous disinfection of the hospital water supply.

[Bek MJ](#)¹, [Laule S](#), [Reichert-Jünger C](#), [Holtkamp R](#), [Wiesner M](#), [Keyl C](#).

Am J Kidney Dis. 2002 Jun;39(6):1307-9.

Hemodialysis-associated methemoglobinemia in acute renal failure.

[de Torres JP](#)¹, [Strom JA](#), [Jaber BL](#), [Hendra KP](#).

Nephrol Dial Transplant. 1999 Jul;14(7):1687-91.

Chloramine-induced haemolysis presenting as erythropoietin resistance.

[Fluck S](#)¹, [McKane W](#), [Cairns T](#), [Fairchild V](#), [Lawrence A](#), [Lee J](#), [Murray D](#), [Polpitiye M](#), [Palmer A](#), [Taube D](#).

Clin Nephrol. 1978 Sep;10(3):105-8.

Prevention of chloramine-induced hemolysis in dialyzed patients.

[Neilan BA](#), [Ehlers SM](#), [Kolpin CF](#), [Eaton JW](#).

Proc Eur Dial Transplant Assoc Eur Ren Assoc. 1985;21:321-5.

Nitrate induced anaemia in home dialysis patients.

[Salvadori M](#), [Martinelli F](#), [Comparini L](#), [Bandini S](#), [Sodi A](#).

Back to the case



- × Really bad weather a few days before
- × Saturation of charcoal filter?
 - ✦ Chloramine intoxication
 - ✦ Current analysis of the filter

What did we learn?



× Use of two charcoal filters

× Two water tests

✦ Water hardness

✦ Chlorine test



Thank you for your attention !



References



- × HahnJM., Médecine Interne Checklists de Médecine, Maloine 2005.
- × Danel V, Barriot P, Intoxications aiguës en réanimation 2ème édition, Arnette 1999, 39-48.
- × Coulliette AD., Arduino MJ, Hemodialysis and Water Quality. *Sem. Dial.*, 2013;26(4):427-38
- × Nessim SJ, Lipman ML. The case/ cyanosis in a hemodialysis patient. *Kidney Int.* 2010;78(3):327-8.
- × Davidovits M, et al. Methaemoglobinaemia and haemolysis associated with hydrogen peroxide in a paediatric haemodialysis centre: a warning note. *Nephrol Dial Transplant.* 2003;18(11):2354-8.
- × Allard B., Les Chloramines en hémodialyse. *Journal de l'Association des Techniciens de Dialyse.* Juin 2004