Excessive accumulation of aluminum (Al) in the bones of patients on long term parenteral nutrition (PN): post-mortem analysis

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Introduction to Aluminum (Al)

- Al comprises 8% of Earth's crust
  - contaminates food, water, and extracted minerals
- Healthy adults ingest ~3-5 mg Al/day, but only absorb ~15 µg/day (gastrointestinal barrier)
- A small amount reaches blood, is bound by proteins, and is eventually excreted through the kidneys

Introduction to Aluminum (Al)

- Al toxicity can occur if:
  - renal excretion is impaired (uremic, dialysis patients)
  - gastrointestinal barrier is bypassed (parenteral nutrition)
- Al toxicity can occur in:
  - bones (osteomalacia, fractures)
  - brain (premature dementia, seizures, death)

Aluminum in PN Patients

- Al toxicity associated with PN use well known since the early 1980's (adults and infants)
  - Al accumulation at mineralization front in bone
  - Impaired bone – mineral uptake (calcium)
  - Reduced bone formation
  - Bone pain (long bones, weight-bearing joints)
  - Osteomalacia

History of Aluminum Contamination in PN Solutions

- 1970's: Switch from casein/fibrin hydrolysates to crystalline amino acids
- 1986: FDA recommends elimination of Al from ingredients used in PN solutions
- 1991: "Safe" level of Al administration through PN is
  < 2 µg Al/kg body weight/day
- 2004: FDA regulations
  - LVPs contain < 25 µg/L
  - SVPs are labeled with maximum Al concentrations at expiration
  - 'Warnings' section for toxicity of Al > 5 µg/kg/day

Measuring Aluminum in Bone

- Vertebrae or long bone samples from 7 long term PN patients collected at autopsy
- Control samples (*n* = 18) obtained from hip or knee replacement patients

- At least 2 cm x 2 cm in size
- Placed in acid-washed/Al-free plastic containers
- Stored in a -70^{o}C freezer until analysis

- Clinical patient information also collected

Bone Preparation

Clean with H_2O_2
De-fat with diethyl ether

Freeze-dry

Section with Diamond Disc saw

Digest with HNO_3 in microwave

Bone Analysis

Graphite Furnace Atomic Absorption Spectrometry

light energy

ground state Al atom

excited state Al atom

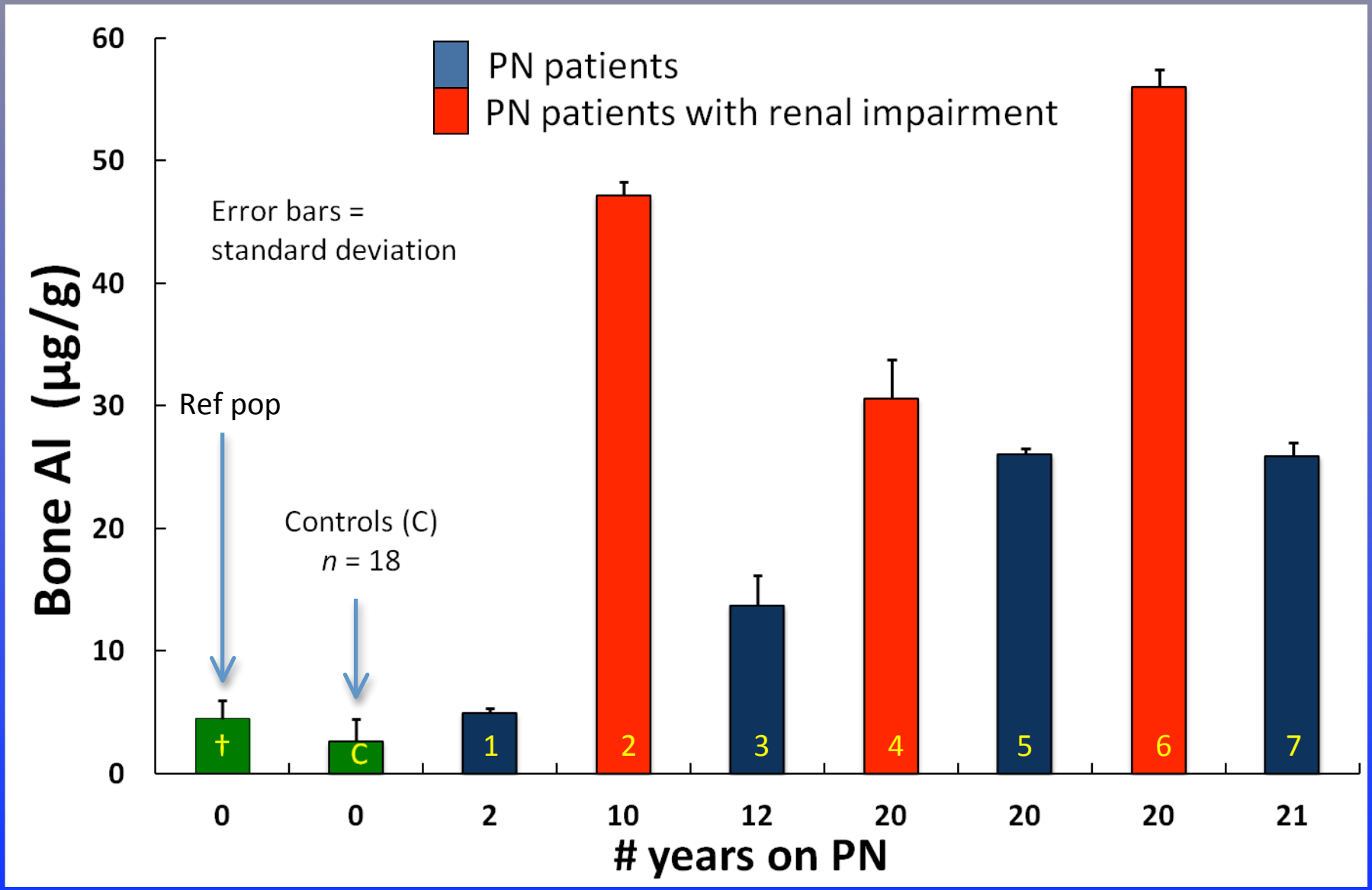
PN Patient Information

Patient #	1	2	3	4	5	6	7
Diagnosis leading to SBS	Bowel Ischemia	Bowel Ischemia	Bowel Ischemia	Bowel Ischemia	Crohn's Disease	Crohn's Disease	Crohn's Disease
Remaining bowel	duodenum + ½ colon	80 cm jejunum + ¾ colon	80 cm jejunum + ½ colon	55cm jejunum + ½ colon	110 cm jejunum, no colon	80 cm jejunum, no colon	80 cm jejunum, no colon
Years on PN	2	10	12	20	20	20	21
Other disorders		kidney failure, dialysis 18 mos.	recurrent catheter sepsis, osteomye-litis	chronic renal disease	HTN	kidney failure, dialysis 8 mos.	cirrhosis, HepC+

CHF = congestive heart failure; HepC+ = hepatitis C positive; HTN = hypertension

Howard et al., JPEN 2007; 31(5): 388-396

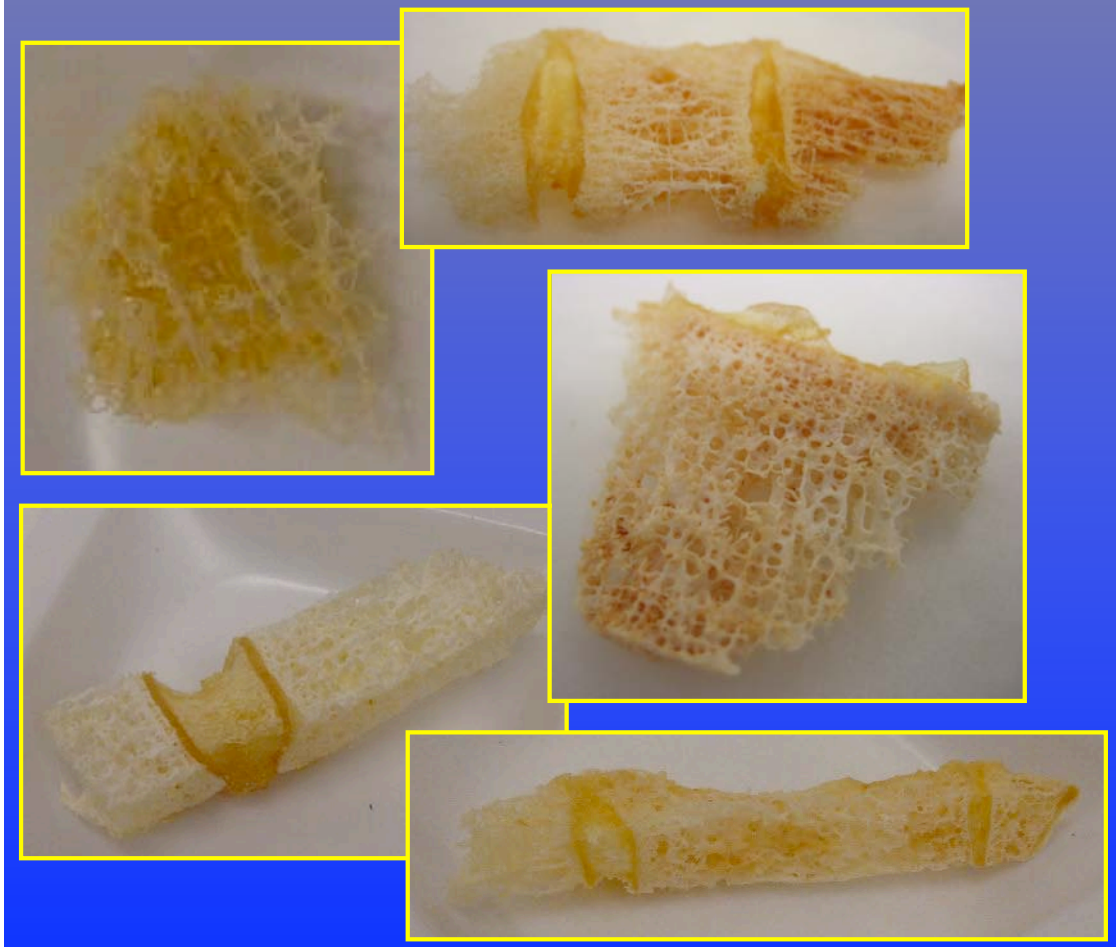
Bone Aluminum Results



†Reference population (Tang et al. 1999. Biol Trace Elem Res; 68, 267-279)

Bone Samples

PN patient samples



Control samples

Where do we go from here? Continuing Problems

- Where is Al still present?
  - PN additives: multivitamins, trace elements, Ca, Mg, and phosphate salts, heparin, albumin
    - contamination of PN solutions with Al is variable and unpredictable
  - other sources of Al?
- How can we reduce Al exposure?
  - use plastic containers for PN ingredients
  - replace Al-rich components ($C_{12}H_{22}CaO_{14}$ with $CaCl_2$ salts, K_3PO_4 with Na_3PO_4 salts)

Where do we go from here? Monitoring PN Patient Bone Health

- Predictors of excess bone Al accumulation?
  - urine, plasma, serum, blood Al content
  - serum Al – deferoxamine (Al chelator) infusion test
  - iron status – anemia may cause easier Al absorption
- *In vivo* neutron activation analysis in hand bone
- Other trace elements in bone

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