Controlling Magnesium in the OR, ICU, and Beyond

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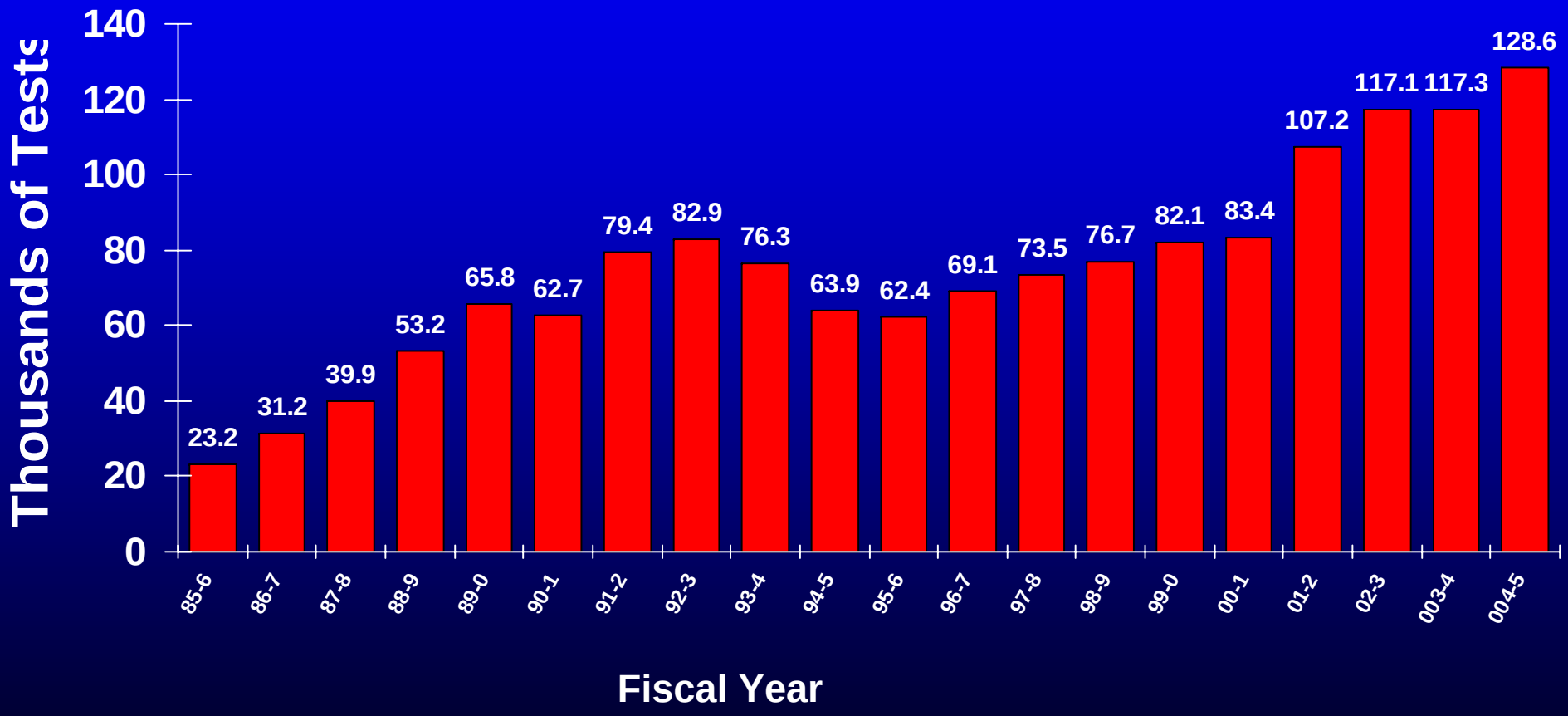
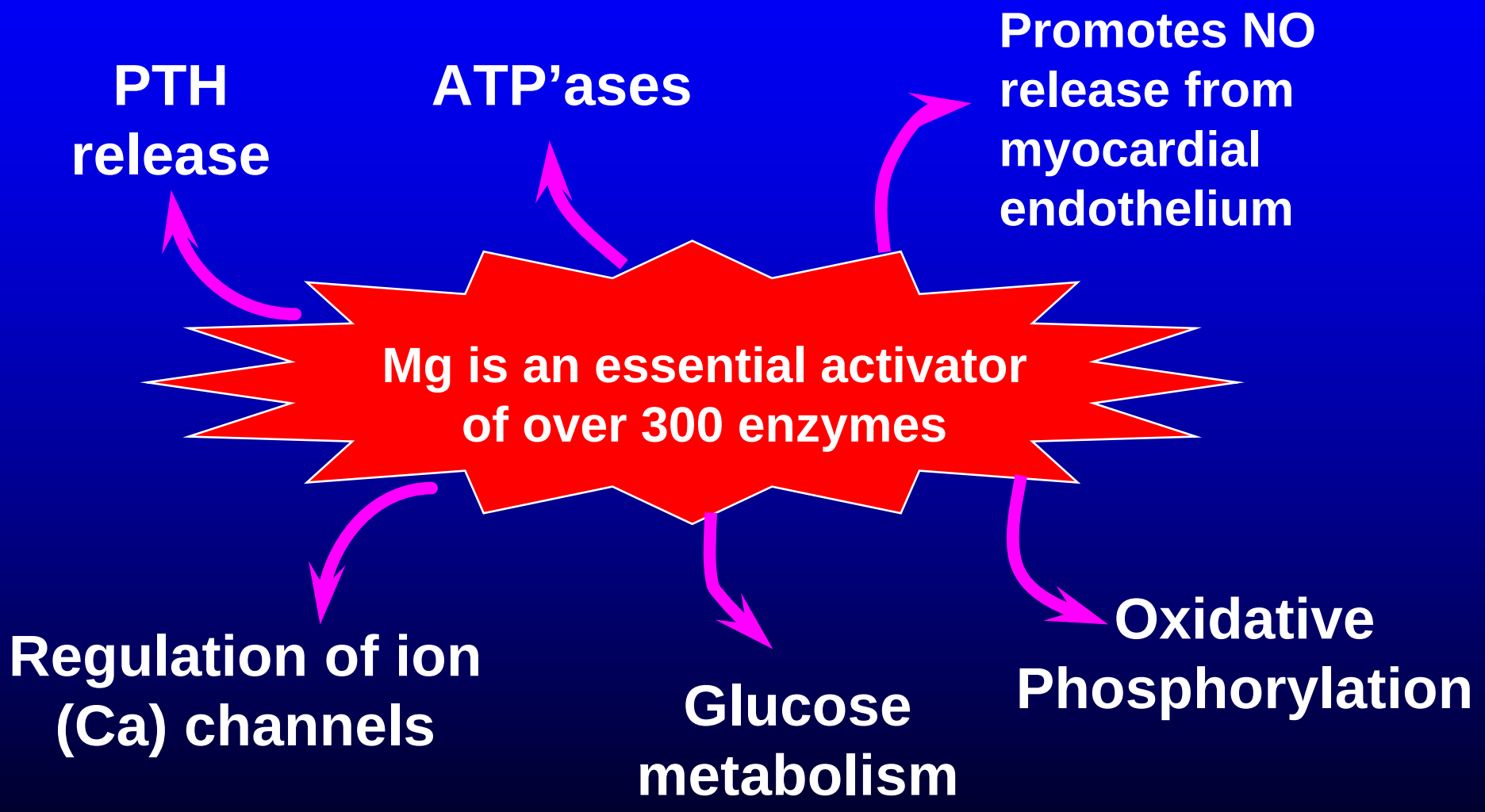
Magnesium Testing at Duke Medical Center



Mg Has Biochemistry on its Side

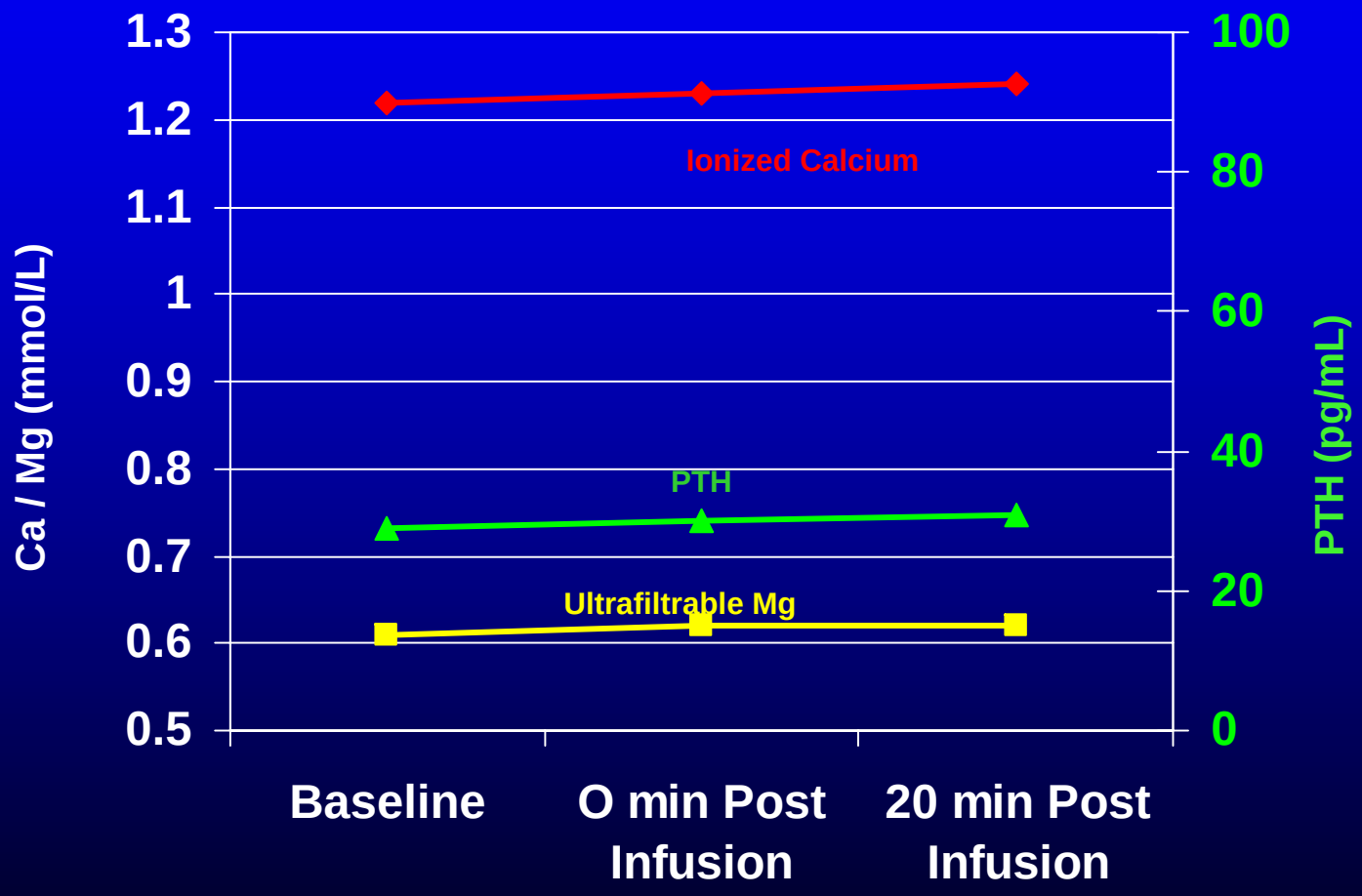


Which Hormones Might Play a Role in Mg Regulation?

- **PTH:**
  - **Increases renal Mg absorption in loop**
  - **Mobilizes Mg from bone.**
  - **PTH secretion inhibited by low Mg**
- **Calcitonin:**
  - **Acts opposite to PTH?**
- **Aldosterone, ADH, and glucagon:**
  - **Increases renal reabsorption of Mg.**
- **Insulin:**
  - **Low serum Mg associated with high insulin levels**
  - **Insulin action inhibited by low Mg**
  - **Affects Mg exchange between cells and ECF.**
- **Catecholamines:**
  - **Apparently cause hypo Mg**
  - **Affects Mg exchange between cells and ECF.**

Does the Parathyroid Gland Respond to a Decrease in Blood Magnesium?

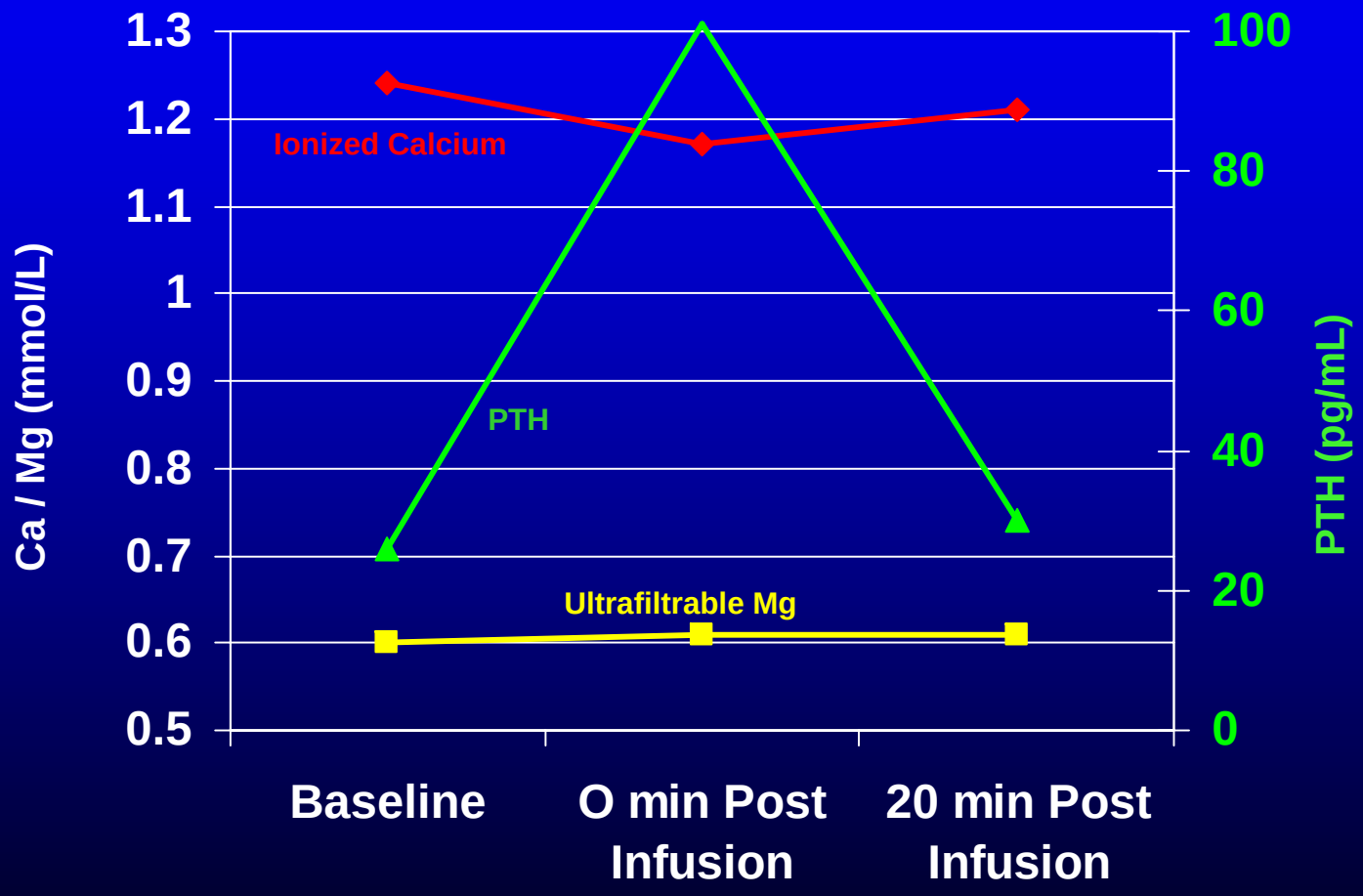
Changes in Ionized Ca, UF Mg, and PTH in Blood Donors Infused with Control Fluid



Control Fluid:
Ion Ca: 1.25 mmol/L
Tot Mg: 1.20 mmol/L
Albumin: 40 g/L
Na: 140 mmol/L
K: 5.0 mmol/L
Cl: 90 mmol/L
Gluconate: 23
Acetate: 27
pH: 7.40 @ 37C

Toffaletti JG, Cooper DL, Lobaugh B: Metabolism 1991; 40: 814-818.

Changes in Ionized Ca, UF Mg, and PTH in Blood Donors Infused with No-Calcium Fluid



No Calcium Fluid:
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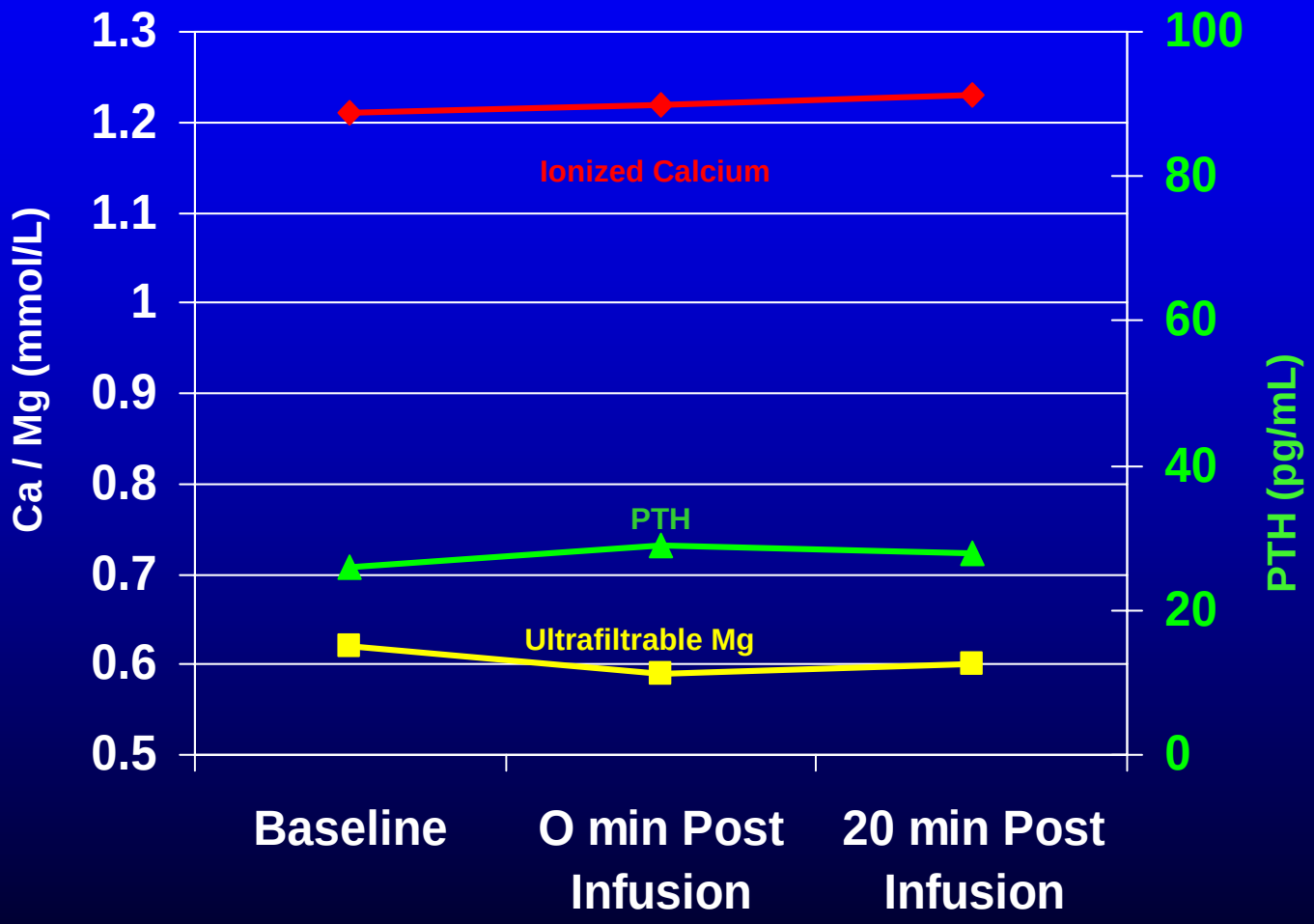
Changes in Ionized Ca, UF Mg, and PTH in Blood Donors Infused with No-Magnesium Fluid



No Magnesium Fluid:
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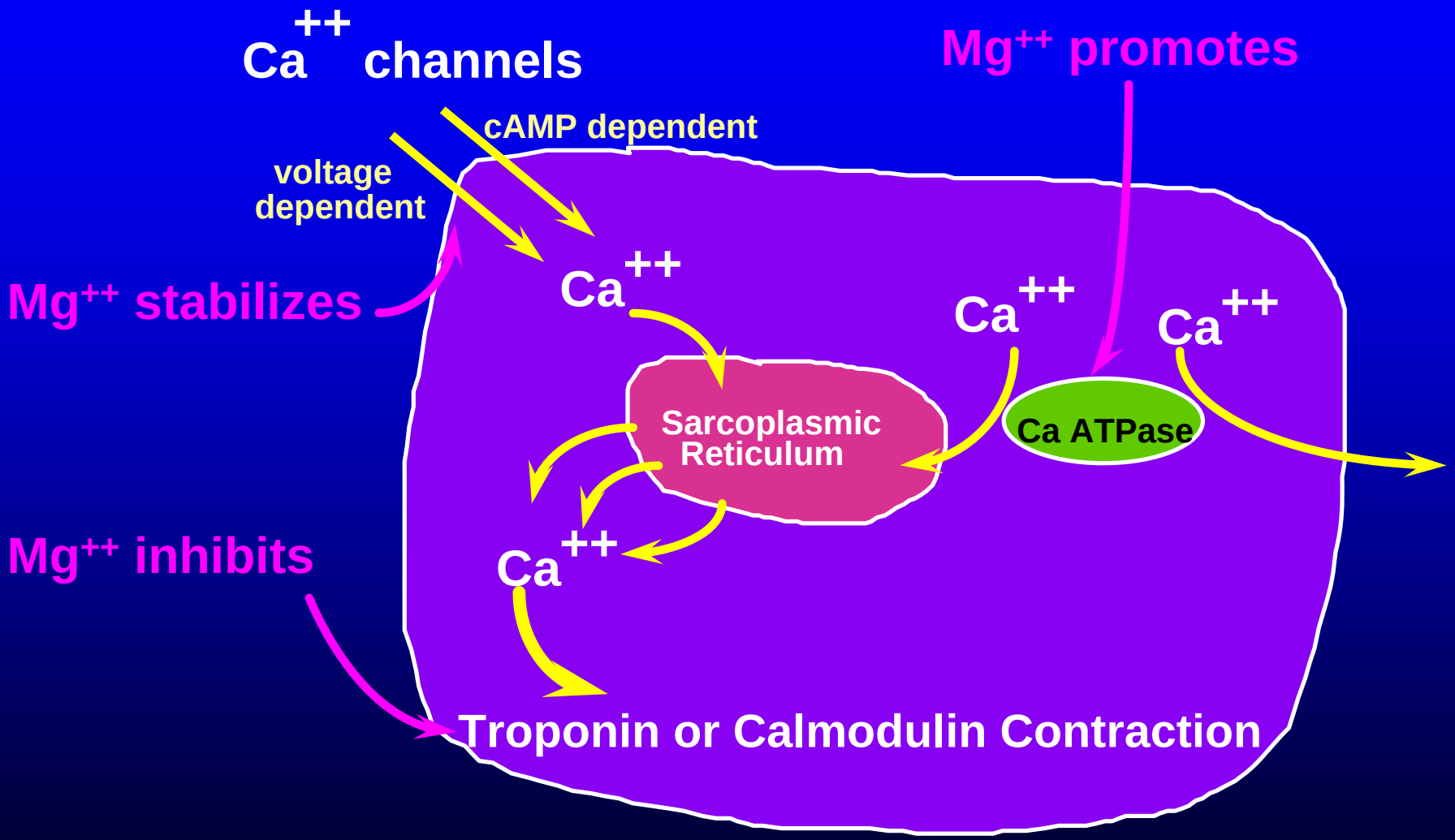
Conditions That May Lead To Magnesium Depletion

- **Drugs** (cyclosporine, etc
- **Diuretics** (esp loop agents)
- **GI loss** (diarrhea, etc)
- **Alcohol**
- **Diabetes**
- **Dietary**
- **Eclampsia**
- **PTH deficit** (sepsis, hypoPTH)
- **Metabolic "stress"**
  - surgery, sepsis, etc
  - catecholamines
  - ATP depletion

Some Clinical Manifestations of Magnesium Deficiency

- **Electrolyte abnormalities**
  - **Hypokalemia, hypocalcemia, and hypophosphatemia**
  - **All require Mg for correction.**
- **Cardiovascular complications**
  - **Arrhythmia, vasoconstriction, fibrillation, coronary thrombosis, low cardiac output.**
- **Endothelial cell dysfunction**
  - **Pro-inflammatory, pro-thrombotic, and pro-atherogenic.**
- **Diabetes**
  - **More severe insulin resistance.**

Mg Ions Stabilize Ca Channels and Oppose Contraction



Is Mg Supplementation Helpful in Myocardial Infarction?

- **Some studies found no benefit or harm:**
  - **MAGIC Trial of 6213 patients with ST elevation MI.** *(Lancet 2002; 360: 1189-96)*
  - **A smaller study with iv Mg given before, during, and after reperfusion.** *(Am Heart J 2000; 140: 891-7)*
- **Some studies found a benefit:**
  - **LIMIT-2 study of 2316 patients given Mg immediately and for 24 hours.** *(Lancet 1994; 343: 816)*
  - **Several smaller trials:**
    - *Am J Cardiol 1995; 75: 321-3*
    - *Int J Cardiol 1999; 71: 209-15*
    - *Am Heart J 2000; 139: 703*
    - *Coronary Artery Dis 1996; 7: 352*

Magnesium Has Protective Effects on the Heart

- **IV magnesium inhibits platelet adhesion in patients following CABG operations (Anesth Analg 1999; 88: 1213).**
- **A normal blood Mg promotes nitric oxide (NO) release from coronary endothelium (Ann Thorac Surg 1998; 65: 967-72).**
- **Mg ion stabilizes Ca channels in cells and can inhibit Ca flux during early ischemia or hypoxia.**

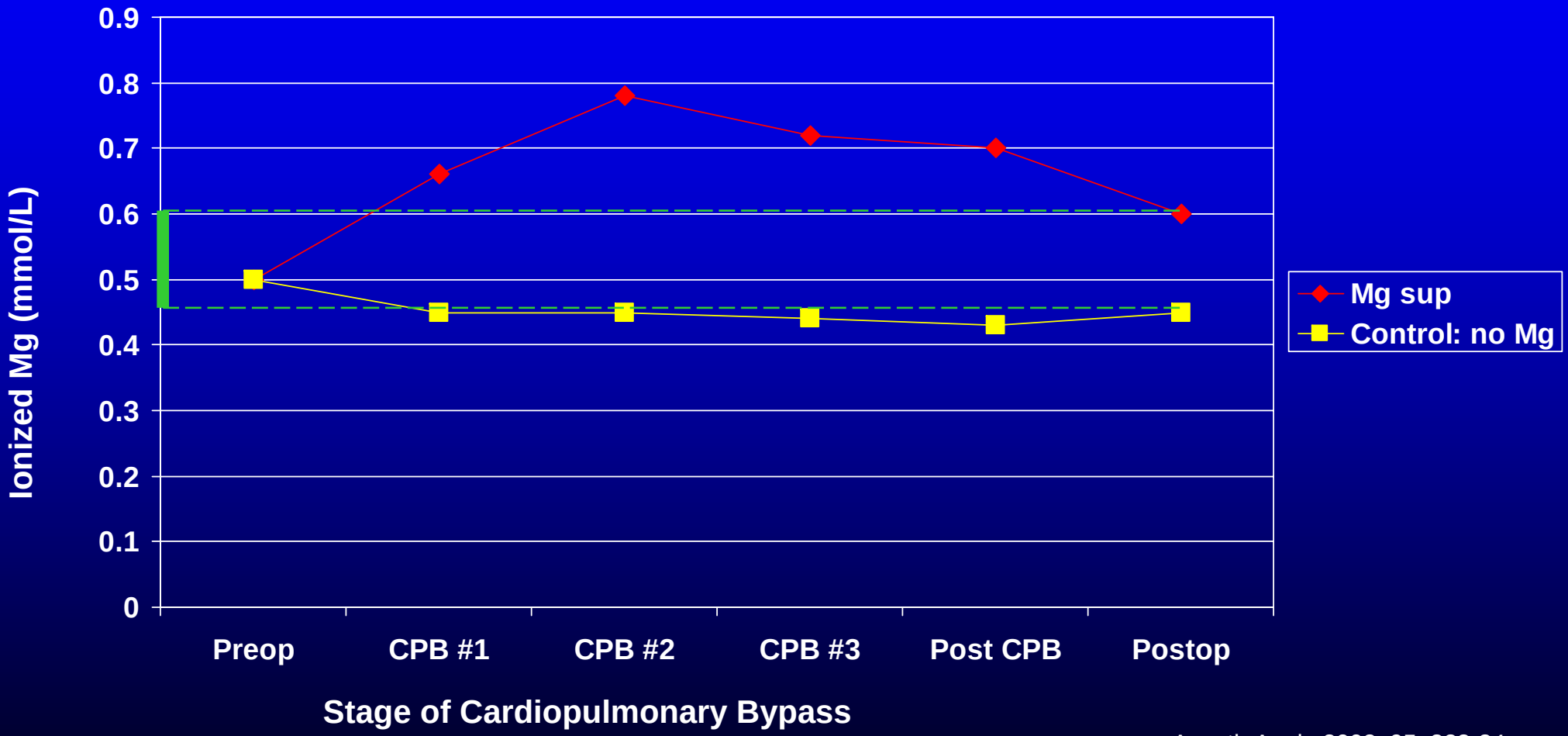
What Are Some Common Events After Cardiac Surgery with CPB?

- Hypomagnesemia
- Inflammatory response
- Cardiac complications
- Platelet inhibition and activation?
- Disordered coagulation
- Localized ischemia?
- Cognitive dysfunction / stroke

Adequate Magnesium Improves Outcomes in Cardiac Surgery

- **50 patients (vs 50 controls) given Mg postoperatively:**
  - **had fewer dysrythmias (16% vs 34% in controls).**
  - **had increased cardiac output.** *(JAMA 1992; 268: 2395)*
- **43 patients (vs 42 controls) who had ionized/total Mg corrected during surgery by Mg administration:**
  - **had 7% incidence of vent tachycardia vs 30% in control group.** *(Anesth Analg 2002; 95: 828-34)*
- **957 patients had serum total Mg measured daily for 8 days after surgery. In one-year followups:**
  - **12.3% of patients with low serum Mg had MI or died.**
  - **9.2% of patients with normal Mg had MI or died.** *(Am Heart J 2003; 145: 1108)*

Mean Plasma Ionized Mg Levels During Cardiopulmonary Bypass Surgery



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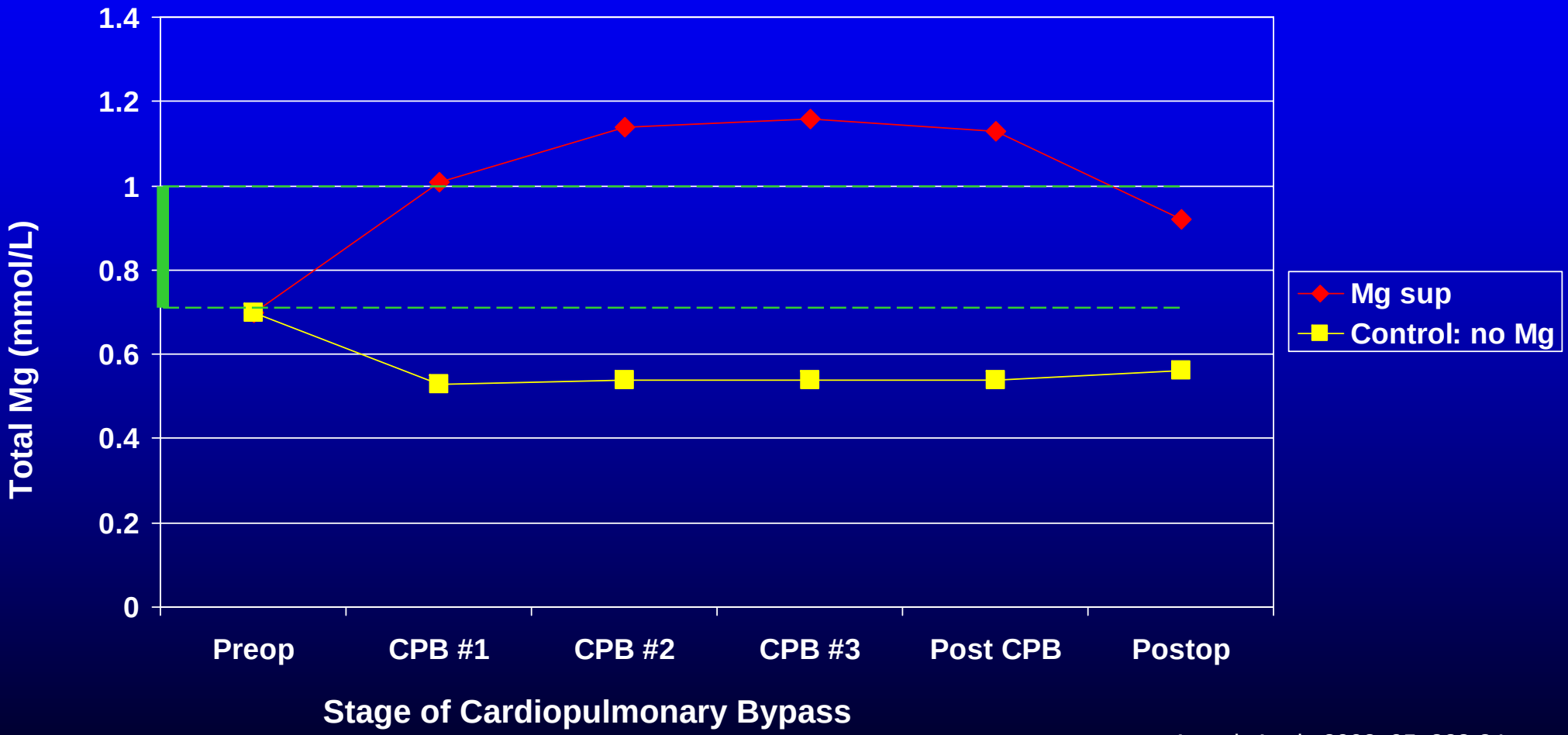

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Mg Supplementation Improves Outcome in Pediatric Cardiac Surgery

- **Adding Mg to the prime solution maintained normal ionized Mg levels that prevented K loss and arrhythmias (20 pediatric patients vs 20 controls).**

  (Anesth Analg 2003; 96: 1617)

- **Giving iv Mg immediately after CP bypass markedly reduced the incidence of tachycardia:**
  - **0 of 13 in Mg group developed tachycardia.**
  - **Control (saline) group remained hypomagnesemic for 20 h post surgery: 4 of 15 had ectopic tachycardia.**

    (Am Heart J 2000; 139: 522)

Recommended Approach to Preventing or Treating Magnesium Depletion

- **Oral supplement to correct Mg depletion:**
  - **At least 600 mg/day**
- **In acute situations:**
  - **Give 25 to 50 mmol of Mg iv over 12 hours.**
- **Assess renal function to avoid hypermagnesemia.**

Recommended Administration of Mg In Cardiopulmonary Bypass

- **In patients receiving Mg-free cardioplegia solution:**
  - **4 g $MgSO_4$ over 20 min just before bypass**
- **In patients receiving Mg supplemented cardioplegia solution:**
  - **a single 2 g bolus just before removal of aortic cross clamp**
- **In both cases, supplementation should be continued postoperatively:**
  - **12 g during first day; 3 g/day for 2-4 days**
  - **measure serum Mg and creatinine**

  (Anesthesiol 1998; 89: 222-240)

What Is The Best Way to Diagnose Altered Mg Homeostasis?

Total Mg
Ionized Mg
Cellular Mg
Mg Retention Test
Biomarker for Mg deficiency?

Studies With Both Ionized Mg and Total Mg Measured

n	Patient Group	Better Parameter?	What Happened to Each?	Reference
9	Liver Transplant [high citrate]	Ionized Mg	Ion Mg decreased Tot Mg stayed same	Liver Transplant Surg 1996; 2: 343-7
33	Malignancy: given Mg supplements	Either	Both decreased similarly: Tot Mg 15%; ion Mg 10%	J Crit Care 2000; 15: 36-40.
31	Abdominal Surgery	Either	Both decreased similarly: tot Mg 23%; ion Mg 15%	J Clin Anesthiol 2003; 15: 245-9.
42	Cardiac Surgery (Controls: No Mg)	Either	Preop: tot Mg 53%; ion Mg 13%. CPB: tot Mg 100%; ion Mg 75%.	Anesth Analg 2002; 95: 828-34.
34	ICU Patients	Either	Hypo total Mg 18% Hypo ion Mg 21%	J Crit Care 2002; 17: 203-5.
115	ICU Patients	Ionized Mg	Hypo total Mg 51% Hypo ion Mg 14% *Hypo RBC Mg 0%*	Am J Clin Pathol 2000; 114: 688-95.
144	ICU Patients	Ionized Mg	Hypo total Mg 53% Hypo ion Mg 14%	Int Care Med 2005; 31: 151-6.
69	Critically ill post-op	RBC Mg	Hypo total Mg 16% Hypo ion Mg 22% Hypo RBC Mg 37% (best)	Clin Chim Acta 2004; 349: 67-73.

Some Possible Biomarkers for Magnesium Deficiency

- **Energy-requiring pump activity:**
  - **Na/K ATPase**
- **Platelet activity:**
  - **Thromboxane**
- **Acute Phase Proteins:**
  - **C-reactive protein**
- **Endothelial damage:**
  - **Endothelin-1**

Franz KB. A functional biological marker is needed for diagnosing Mg deficiency.

J Amer Coll Nutr 2004; 23: 738S-741S.

Standard Reference Ranges for Total and Ionized Magnesium in Blood

- **Total Magnesium (adults): 0.65 - 1.05 mmol/L**
- **Ionized Magnesium: 0.40 - 0.65 mmol/L**
  - **About 70% of total Mg is ionized.**

What Should Be the Reference Range for Total Mg?
(Especially the Lower Limit)

Information Source	Reference Range (mmol/L)	Ref Range (mg/dL)	Rate of Missed HypoMg
Jacobs & Demott 5th Edition (2001)	0.62 – 0.95	1.5 – 2.3	Apparently High
Tietz Textbook 3rd Ed (1999)	0.66 – 1.07	1.6 – 2.6	Apparently High
Duke Med Center	0.66 – 0.91	1.6 – 2.2	Apparently High
J Am Coll Nutr 2004; 23: 730S	0.70 - XXX	1.7 - XXX	90%
"	0.75 - XXX	1.8 - XXX	50%
"	0.80 - XXX	1.9 - XXX	<10%

The "Beyond": Clinical Disorders Associated with Magnesium Deficiency

- Depression
- Diabetes
- Epilepsy
- Parkinsonism / tremor
- Arrythmias
- Stroke
- Atherosclerosis
- Cardiac infarction
- Hypertension
- Confusion
- Migraine / Cluster headache
- Cramps
- Neuro-vegetative disorders
- Abdominal pain
- Osteoporosis
- Asthma
- Stress-dependent disorders
- Tinnitus
- Ataxia
- Pre-eclampsia

Cited from: About the misdiagnosis of magnesium deficiency. J Am Coll Nutrition 2004; 23: 730S

Magnesium Research (1991) **4**, 3/4, 201–202

Magnesium and extinction of dinosaurs. Was magnesium deficit a major cause?

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Summary: Chinese researchers have recently demonstrated that, before the extinction of dinosaurs, there was an impressive lowering in the magnesium concentration of fossil dinosaur eggshell. The structural and functional importance of eggshell magnesium – mainly in the cone layer – for embryonic viability and hatchability of oviparous species supports the hypothesis that magnesium deficit may have had a direct role in dinosaur extinction. Conversely this low magnesium concentration seems a questionable marker of magnesium deficit. The natural forces involved in the extinction of dinosaurs are more likely to induce magnesium depletion than magnesium deficiency. These very interesting preliminary data call for further research.

Key words: Dinosaur, eggshell, embryo, hatchability, magnesium, porosity.

Introduction

A recent Chinese study from the Institute of Geochemistry, Academia Sinica (Guyang, Guizhou Province) presented a new hypothesis on the extinction of dinosaurs. Jian Jiuyu, Professor of Life Elements

species. Secondly they fail to explain how oth oviparous species persisted under the same unsa isfactory nutritional conditions.

Structural and functional importance of eggshell

Low Serum Mg Increases Risk of Neurological Events in Patients with Advanced Atherosclerosis

- Studied 323 patients with symptomatic peripheral artery disease and claudication.
- Patients were followed for 20 months:
  - Serum total Mg was measured.
  - Neurologic events (ischemic stroke and/or need for carotid stenting or endarterectomy) were noted.
- Neurologic events occurred in 35 patients (11%):
  - Serum Mg < 0.76 mmol/L associated with 3.3 fold increased risk.

Stroke 2004; 35: 22-27