Depot medroxyprogesterone acetate use and blood lead concentrations: Results from NHANES 2003-2012

Arianna V. E. Foster, Mandy S. Hall, Natalie P. Barstys, Kristen Upson

Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, Michigan, USA.
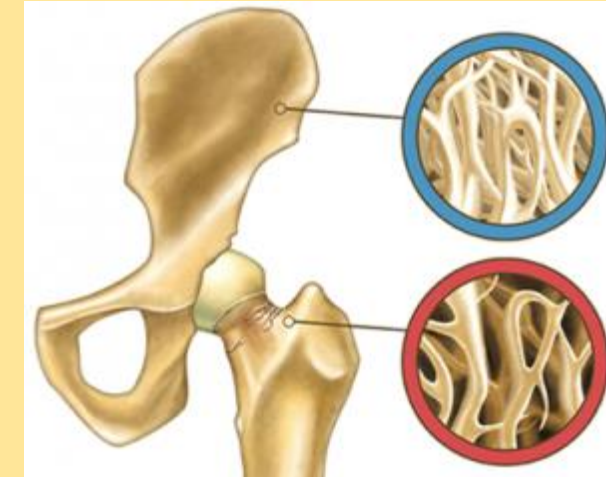
Background

Depot medroxyprogesterone acetate (DMPA)

- 3-month progestin-only injectable contraceptive
- FDA-approved in 1992
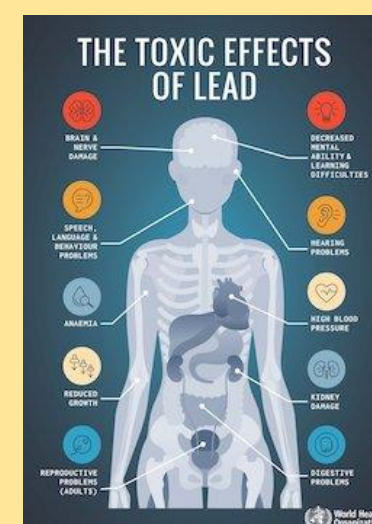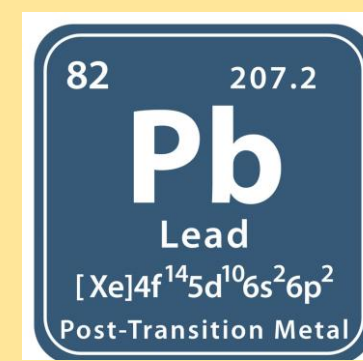- Used by 1 in 5 U.S. women
- Currently used by 1.5 million U.S. women

DMPA and bone mineral density (BMD)

- DMPA ↑ bone resorption, therefore…
  - ↓ bone mineral density
  - BMD returns to normal after DMPA discontinuation

Lead (Pb) stored in bone, released to blood

- Bone is primary storage site for lead (>90%)
- Pb can remain in bones for 1-2 decades
- ↑ skeletal mobilization of lead to blood with ↑ bone resorption
- No safe level of lead in the body
- Negative health consequences in everyone, including adults
- Affects almost every organ system

Objective

To investigate if current DMPA use is associated with ↑ blood lead concentrations in women ages 20-49 years

Methods

Data: National Health and Nutrition Examination Survey
- Cycles 2003-2012
- Representative sample of US population
- Cross-sectional analysis

Study sample (n=3,189, unweighted)
- Premenopausal females, ages 20-49 years

Exposure: Self-report of *current* DMPA use

Outcome: Whole blood lead (µg/dl)
- Division of Laboratory Sciences, National Center for Environmental Health
- ICP-MS

Analyses: Multivariable linear regression
- Percent difference in blood lead (95% CI)
- Adjusted for age, education, smoking, alcohol, birth in last year, cycle year, and conditions/medications associated with bone loss

Results

DMPA use and blood lead concentrations (µg/dl)

Current DMPA	n[a] (%)[b]	Blood lead (µg/dl) GM (95% CI)	Model 1 % Difference (95% CI)[c]	Model 2 % Difference (95% CI)[d]
No	3087 (97)	0.85 (0.83, 0.87)	(Reference)	(Reference)
Yes	102 (3)	0.93 (0.79, 1.09)	21% (6%, 38%)	18% (3%, 42%)

Abbreviations: GM, geometric mean; CI, confidence interval.
[a]Unweighted n.
[b]Weighted percent.
[c]Adjusted for age, education, smoking, alcohol consumption, birth in the past year, and cycle year.
[d]Adjusted for age, education, smoking, alcohol consumption, birth in the past year, hemoglobin, past DMPA use, 25(OH)D, total calcium intake, and conditions/medications associated with bone loss.

> **Current DMPA users had 18% higher blood lead concentrations than non-users**

Participant characteristics (n=3189, unweighted)

- Median age: 35 years
- 39% BMI ≥30 kg/m^2
- 25% lower education (< high school/GED)
- 25% higher poverty income ratio (>3.5)
- 25% current smokers
- 24% past DMPA users
- 17% birth in the last year
- 92% parous

Participant characteristics – DMPA Use & Blood Lead

DMPA use
- 3% current users

Current DMPA use characteristics
- ↓ Age
- ↓ Education
- ↓ Poverty income ratio
- ↑ BMI
- ↑ Current smokers
- ↑ No alcohol consumption

Blood lead GM

0.86 µg/dl (95% CI: 0.83, 0.87)

↑ Blood lead characteristics (among non-DMPA users)
- ↑ Age
- ↓ Education
- ↓ Poverty income ratio
- ↓ BMI
- ↑ Current smokers
- ↑ No alcohol consumption

SENSITIVITY ANALYSES

DMPA use and blood lead concentrations (µg/dl)

	Current DMPA	n[a](%)[b]	Blood lead (µg/dL) GM (95% CI)	Model 2 % Difference (95% CI)[c]
Restricted to never smokers	Yes	75 (3)	0.89 (0.80, 0.99)	21% (2%, 42%)
	No	2305 (97)	0.78 (0.76, 0.81)	
Excluding current hormonal medication users	Yes	99 (3)	0.93 (0.81, 1.06)	19% (4%, 37%)
	No	2698 (97)	0.87 (0.84, 0.90)	
Additional Hemoglobin adjustment	Yes	102 (3)	0.93 (0.79, 1.09)	21% (6%, 38%)
	No	3083 (97)	0.85 (0.83, 0.87)	
Past DMPA users as the comparison group	Yes	102 (3)	0.93 (0.79, 1.09)	21% (6%, 37%)
	No	3087 (97)	0.85 (0.83, 0.87)	

Abbreviations: GM, geometric mean; CI, confidence interval.
[a]Unweighted n
[b]Weighted percent.
[c]Adjusted for age, education, smoking, alcohol consumption, birth in the past year, hemoglobin, past DMPA use, 25(OH)D, total calcium intake, and conditions/medications associated with bone loss

> **Association persisted after accounting for other factors that may explain the observed result**

Limitations & Strengths

Limitations
- Cross-sectional design
- No information on DMPA duration
- Low prevalence of current DMPA use

Strengths
- Large sample size
- Population-based sampling
- Rich, widely variable data
- Robust, consistent results

Conclusion

- Current DMPA use and ↑ blood lead concentrations
  - Consistent with prior study that reported DMPA users had 18% higher blood lead levels (95% CI: 8, 29)
- Findings warrants further investigation
  - Prospective study to examine temporal relationship

Acknowledgements