

## Clinical application of biomarkers in lead poisoning

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### Case 1. A-50-year-old man

CC abdominal pain and hand weakness for 1 month

PI 1 month prior to admission, he developed acute and intermittent colicky pain of his abdomen.

He also experienced weakness of both hands.

## Case 1. A-50-year-old man

PE BP 140/90 mmHg, HR 100/min.  
Pale, not icteric  
Otherwise was unremarkable

## Case 1. A-50-year-old man



pure motor, extensors weaker than flexors

## Case 1. A-50-year-old man

### Laboratory tests

CBC: Hb 10.4 g/dl, Hct 30.6%

WBC 9,450 cell/mm<sup>3</sup> (N79% L20% Eo1%)

Platelet 320,000 /mm<sup>3</sup>

## Case 1. A 50-year-old man

What is the diagnosis?

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BLL 89 mcg/dl

## Case 1. A 50-year-old man

What is the diagnosis?

Lead poisoning?

Why?

## Case 2. A 24-year-old man

**Chief complaint:** having BLL of 70 mcg/dl

**Present illness:**

By annual routine check up, his BLL was 70 mcg/dl.

He was asymptomatic.

**Personal history:**

He has worked in the battery factory for 6 months.

Pre-employment BLL was 9 mcg/dl

**Physical Examination:**

BP 120/70 mmHg, HR 60/min.

Others: unremarkable

## Case 2. A 24-year-old man

What is the diagnosis?

Lead poisoning?

Why?

## Case 3. A-23-year-old man

CC abdominal pain for 3 days

PI 7 days PTA, he experienced abdominal discomfort and intermittent colicky pain. The symptoms lasted 3 days, then spontaneously subsided.

3 days PTA, intermittent colicky abdominal pain recurred at periumbilical area. The pain was increasing in intensity.

### Case 3. A-23-year-old man

PE: A young man, poor hygiene, looked distress due to pain

BT 36.8°C, BP 166/108 mmHg, PR 80/min, RR 18/ min

HEENT: not pale conjunctivae, anicteric sclera

Heart: normal S<sub>1</sub>S<sub>2</sub>, no murmur

Lungs: clear

### Case 3. A-23-year-old man

Abdomen: soft, not tender,  
impalpable liver and spleen,  
normal bowel sound

Extremities: no edema

Neurological: motor grade V/V all  
normal pinprick & proprioceptive sensation  
deep tendon reflex 2+all

### Case 3. A-23-year-old man

CBC: Hb 11.8 g/dl, Hct 36.3%  
WBC 8,360 cell/mm<sup>3</sup>(N76% L15% Eo7% B1%),  
Platelet 221,000 /mm<sup>3</sup>

Lipase 42 u/l, Amylase 65 u/l

BUN/Creatinine: 21/1.1 mg/dl

Electrolyte: Na 138, K 3.41, Cl 98, CO<sub>2</sub> 30.8 mmol/l

LFT:	AST/ALT	27/43 u/l
	ALP/GTG	89/86 u/l
	TB/DB	1.1/0.3 mg/dl

### Case 3. A-23-year-old man

What is the diagnosis?



### Case 3. A-23-year-old man

Blood Lead Level	65.5 mcg/dl
(Unexposed adult	< 25 mcg/dl
Exposed adult	< 40 mcg/dl)

### Case 3. A-23-year-old man

What is the diagnosis?

Lead poisoning?

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## Biomarkers

- Biomarkers of exposure
- Biomarkers of effect
- Biomarkers of susceptible

## Biomarkers of lead poisoning

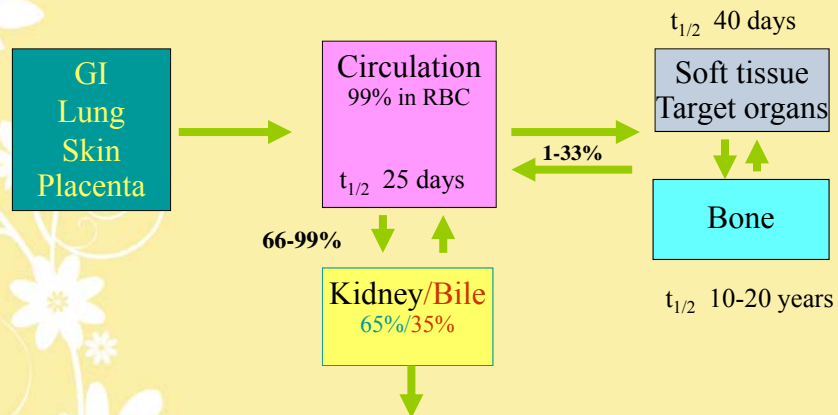
### Biomarkers of exposure

- Blood lead level (BLL)
- Urinary lead content
- K x-ray

### Biomarkers of effect

- Free (Zinc) erythrocyte protoporphyrin (FEP)
- Aminolevulinic acid dehydratase (ALA-D)
- Urine aminolevulinic acid (ALA)
- Urine coproporphyrinogen III (CP3)
- IQ test

## Lead kinetics



## Biomarkers of exposure

**Pros**

- Quantify the causative agent
- Most available test

## Correlation of BLL and its effects

Lead Concentration (µg/Pb/dl)	Effect	Function Change
150	Death	-
100	Encephalopathy	-
~90	Encephalopathy, Nephropathy, Frank anemia	-
~80	Colic	-
60	Decreased longevity	-
40	Hemoglobin synthesis (▼), Peripheral neuropathies, Infertility (Men), Nephropathy	Decreased
30	Systolic blood pressure (Men) (▲), Hearing Acuity (▼)	Increased/Decreased
20	Erythrocyte protoporphyrin (Men) (▲)	Increased
10	Erythrocyte protoporphyrin (Women) (▲), Hypertension (?) (▲)	Increased
0-10	Developmental toxicity (▼), IQ (▼), Hearing (▼), Growth (▼), Transplacental transfer	Decreased

Source: Am Family Physician. 1998

## Serum calcium & Total body calcium

- Hypercalcemia  $\neq$  high total body calcium
- In hyperparathyroid
  - High serum calcium
  - Low total body calcium

## Biomarkers of exposure

### Pros

- Quantify the causative agent
- Most available test

### Cons

- Correlation with effects by extrapolation
- Host susceptibility is not taken to account
- Multifactorial etiologies

## Biomarkers of lead poisoning

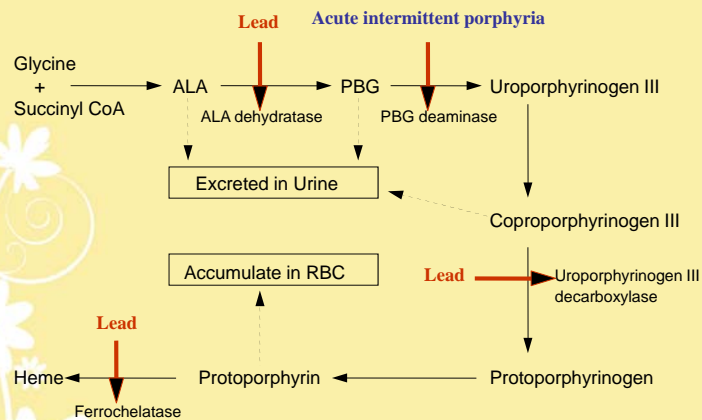
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## The heme biosynthetic pathway



## Biomarkers of effect

### Pro

- Demonstrate the effects or interference of the specific pathways
- Indicator of early abnormality or diseases

### Con

- May not be specific for a certain etiology

## Biomarker of susceptibility

### Pro

- Indicate an inherit or acquired susceptibility of a person to response to the exposed xenobiotic substance
- Applicable for early detection or identify the susceptible person

### Con

- Not indicate the existing of health status
- Multifactorial disease



## Biomarker of susceptibility

- Vitamin D receptor polymorphism
  - BsmI: BB genotype associates with low BLL
  - TaqII: tt genotype associate with low BLL
- ALAD polymorphism
  - ALAD1 homozygous associates more heme synthesis interference





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## Case 1. A 50-year-old man

What is the diagnosis? Lead poisoning

Evidence:

Clinical presentation: compatible with lead poisoning

BLL was high

How to treat the patient?

Parenteral chelating agent: CaNa<sub>2</sub> EDTA iv.

How many days for the chelating agent?

## Case 1. A 50-year-old man

### Laboratory findings

Blood Lead level	89 (0-40 mcg/dl)
24 hr urine lead (after CaNa <sub>2</sub> EDTA)	
Day 1	7,210 mcg/day
Day 2	3,480 mcg/day
Day 3	1,705 mcg/day

## Case 2. A 24-year-old man

**Chief complaint:** having BLL of 70 mcg/dl

**Present illness:**

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He was asymptomatic.

**Personal history:**


He has worked in the battery factory for 6 months.

Pre-employment BLL was 9 mcg/dl

**Physical Examination:**

BP 120/70 mmHg, HR 60/min.

Unremarkable




## Case 2. A 24-year-old man

What is the diagnosis?

Lead poisoning?

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## Case 2. A 24-year-old man

2.1	BLL	70 mcg/dl
	Free Erythrocyte Protoporphyrin (FEP)	456 mcg/l (17-77 mcg/dl RBC)

Diagnosis: Subclinical lead poisoning

## Case 2. A 24-year-old man

2.1 BLL 70 mcg/dl  
 Free Erythrocyte Protoporphyrin (FEP)  
 456 mcg/l (17-77 mcg/dl RBC)  
 Diagnosis: Subclinical lead poisoning

2.2 BLL 70 mcg/dl  
 Free Erythrocyte Protoporphyrin (FEP)  
 100 mcg/l (17-77 mcg/dl RBC)  
 Diagnosis: High blood lead level from recent exposure

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## Case 3. A-23-year-old man

What is the diagnosis?

Lead poisoning



## Case 3. A-23-year-old man

Blood Lead level	65.5 mcg/dl
FEP	517 mcg/dl RBC (17-77 ug/dl RBC)
ALA-D	90 U/ml RBC (108-299 U/ml RBC)
ALA in urine	29.67 mg/l (0-6 mg/l)



### Case 3. A-23-year-old man

What is the diagnosis?

Lead poisoning

Clinical presentation is compatible with lead poisoning

Evidences:

BLL indicates exposure to lead

FEP indicates lead effects on heme pathway

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Blood Lead level	65.5 mcg/dl
FEP	517 mcg/dl RBC (17-77 ug/dl RBC)
ALA-D	90 U/ml RBC (108-299 U/ml RBC)
ALA in urine	29.67 mg/l (0-6 mg/l)
Urine lead after chelation	
Urine 24 hr urine	
Day 1	2,626 mcg/day
Day 2	540 mcg/day
Day 3	389 mcg/day

## Conclusion

- BLL alone has its limitation for clinical application.
- Combined biomarkers (BLL and FEP) are helpful for increase the accuracy and details of the diagnosis.
- Urine lead content should be used for estimation of body burden chelatable lead.

谢谢大家的关注

*Thank you for your attention.*

ขอบคุณครับ

