MODELING BLOOD LEAD

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For all chemicals except lead, safe levels in soil or waste correspond to <u>doses</u> which are not harmful. Safe doses of chemicals usually account for just one route of exposure.

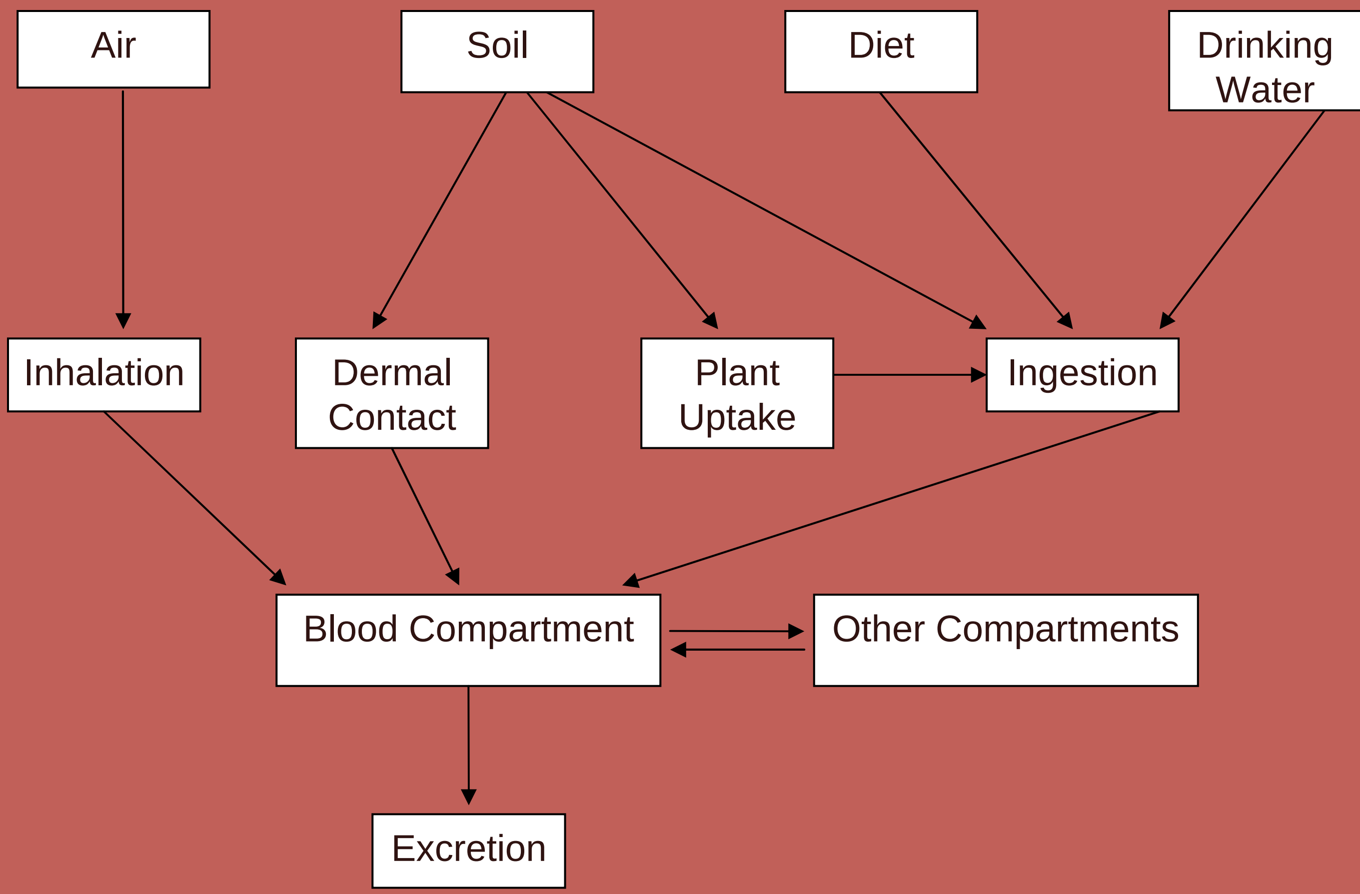
- *e.g.* oral RfD, inhalation RfC

Evaluating Lead Toxicity

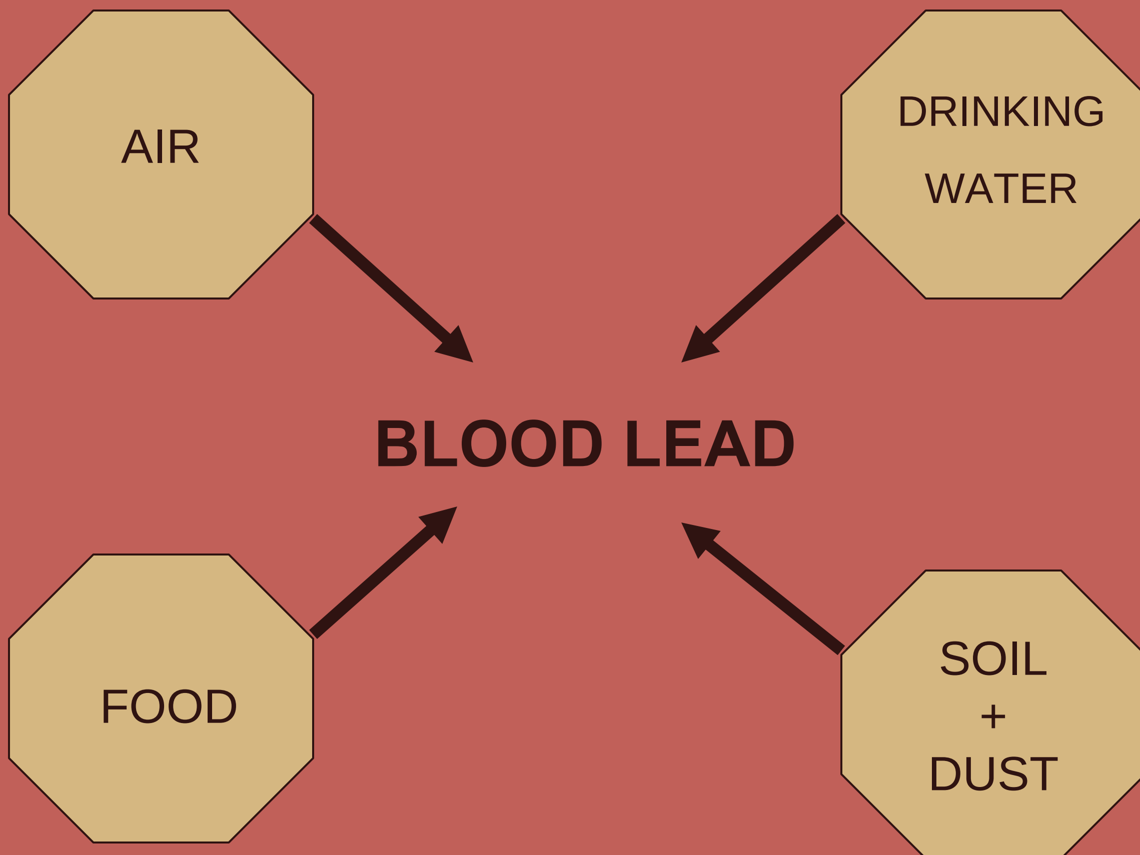
- There is a large database of information about toxicity of lead compared to blood lead level.
- Blood lead is a good indicator of recent lead exposure.
- Lead exposure/toxicity is evaluated by comparison to blood lead levels

For lead, we choose a level in soil which results in 99% of a population having blood lead levels not exceeding 10 µg/dL, including all routes of exposure.

Blood Lead Modeling



INPUTS TO BLOOD LEAD



Estimating Blood Lead

- Both USEPA and DTSC use “slope factors” to estimate blood lead from an environmental input.
- A slope factor is the change in blood lead for each µg/day of lead intake.

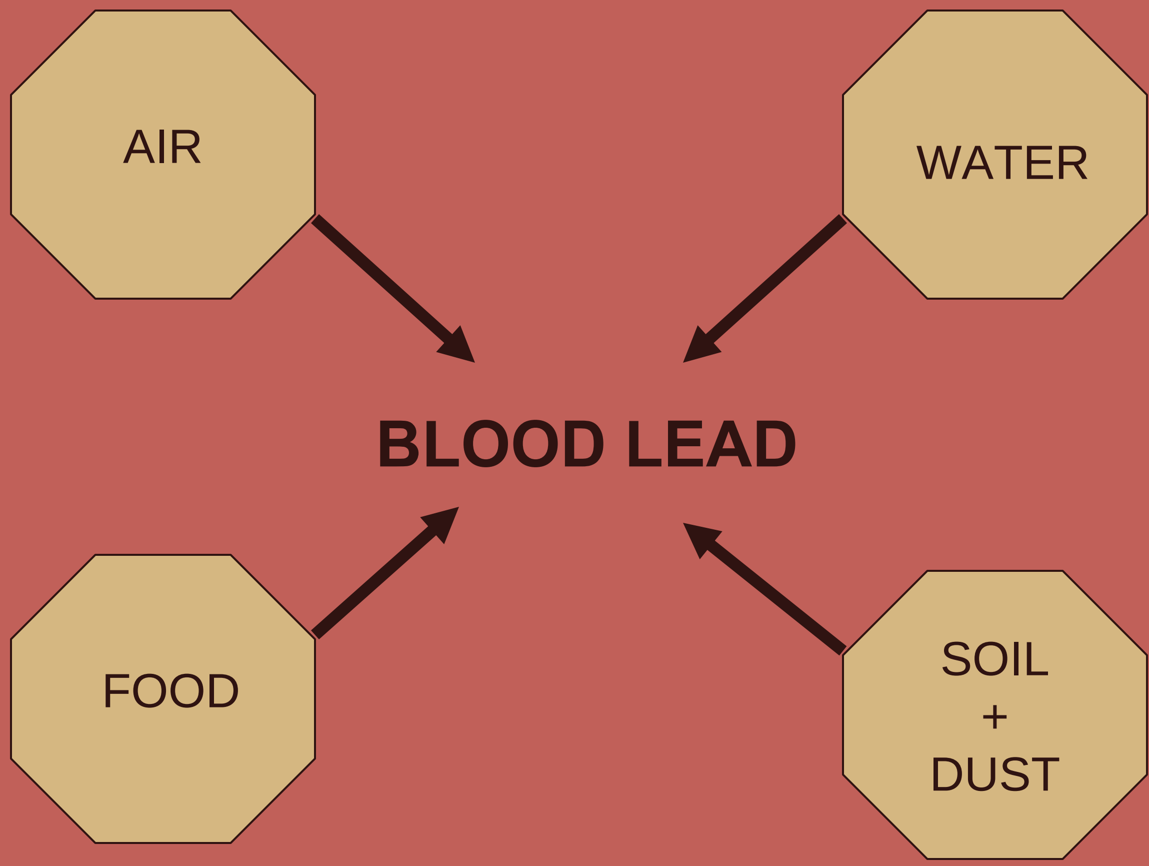
Example of a Slope Factor

- Pocock *et al.* (1983) showed a linear increase in blood lead in thousands of men in the U.K. exposed to various levels of lead in drinking water.
- Blood lead in adult males increased 0.622 µg/dL for each additional 1 µg lead/day taken in from drinking water.
- If drinking water contains 5 µg/L,then the contribution to blood lead from drinking water is 3.1 µg/dL.

LeadSpread

- **Calculates cleanup levels for lead in in soil, given inputs for lead in air, water, and food.**
- **Calculates for 2-3 year old child. The adult module of LeadSpread is being re-evaluated.**
- **Inputs are “central tendency” values, not worst cases.**

INPUTS TO BLOOD LEAD



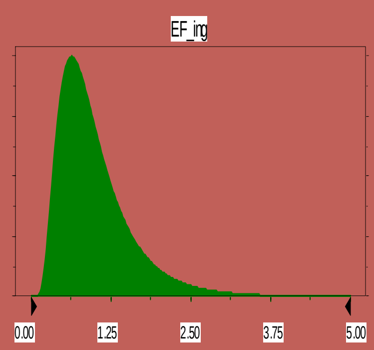
LeadSpread

The central tendency of blood lead is estimated:

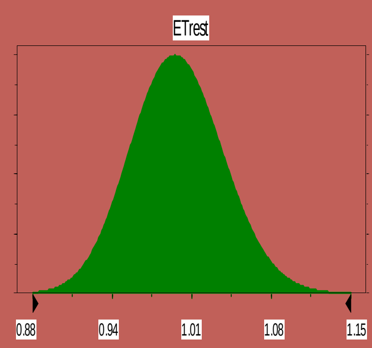
$$\Sigma\ [Pb_{AIR}*SF_{AIR} + Pb_{WATER}*SF_{WATER} + Pb_{FOOD}*SF_{FOOD} + Pb_{SOIL}*SF_{SOIL} + Pb_{DUST}*SF_{DUST}]$$

LeadSpread

- **Blood lead in human populations has been shown repeatedly to be lognormally distributed. Lognormal distributions are not symmetrical, but the logs of the individual values are normally distributed.**



Lognormal Distirubtion



Normal Distirubtion

LeadSpread

- **Using the geometric mean (mean of log-transformed blood lead values) and an assumed geometric standard deviation (s.d of logs), any percentile of the lognormal distribution can be estimated:**

$$95^{th}\ \%ile = 10^{[\log(GM)+1.65*\log(GSD)]}$$

$$99^{th}\ \%ile = 10^{[\log(GM)+2.33*\log(GSD)]}$$

LEAD RISK ASSESSMENT SPREADSHEET
CALIFORNIA DEPARTMENT OF TOXIC SUBSTANCES CONTROL

USER'S GUIDE to version 7

INPUT	
MEDIUM	LEVEL
Lead in Air (µg/m^3)	0.028
Lead in Soil/Dust (µg/g)	146.0
Lead in Water (µg/L)	15
% Home-grown Produce	7%
Respirable Dust (µg/m^3)	1.5

OUTPUT	Percentile Estimate of Blood Pb (µg/dL)					PRG-99	PRG-95
	50th	90th	95th	98th	99th	(µg/g)	(µg/g)
BLOOD Pb, ADULT	1.5	2.8	3.3	4.0	4.6	694	1,080
BLOOD Pb, CHILD	3.3	6.1	7.2	8.8	10.0	146	247
BLOOD Pb, PICA CHILD	4.4	8.0	9.5	11.5	13.1	94	159
BLOOD Pb, OCCUPATIONAl	1.1	2.1	2.5	3.0	3.4	3,565	5,554

EXPOSURE PARAMETERS	units	adults	children
Days per week	days/wk	7	
Days per week, occupational		5	
Geometric Standard Deviation		1.6	
Blood lead level of concern (µg/dL)		10	
Skin area, residential	cm^2	5,700	2,900
Skin area occupational	cm^2	2,900	
Soil adherence	µg/cm^2-day	70	200
Dermal uptake constant	(µg/dL)/(µg/day)	9.6 E-5	
Soil ingestion	mg/day	50	100
Soil ingestion, pica	mg/day		200
Ingestion constant	(µg/dL)/(µg/day)	0.04	0.16
Bioavailability	unitless	0.44	
Breathing rate	m^3/day	20	6.8
Inhalation constant	(µg/dL)/(µg/day)	0.08	0.192
Water ingestion	L/day	1.3	0.4
Food ingestion	kg food/day	1.9	1.1
Lead in market basket	µg Pb/kg food	3.1	
Lead in home-grown produce	µg Pb/kg food	65.7	

PATHWAYS

ADULTS	Residential			Occupational		
	Pathway Contribution			Pathway Contribution		
Pathway	PEF	µg/dL	Percent	PEF	µg/dL	Percent
Soil Contact	3.8E-5	0.01	0%	1.4E-5	0.00	0%
Soil Ingestion	8.8E-4	0.13	8%	6.3E-4	0.09	8%
Inhalation, bkgrnd		0.05	3%		0.03	3%
Inhalation	2.5E-6	0.00	0%	1.8E-6	0.00	0%
Water Ingestion		0.78	51%		0.78	68%
Food Ingestion, bkgrnd		0.22	14%		0.24	21%
Food Ingestion	2.4E-3	0.35	23%			0%

CHILDREN	Typical Child			Child with Pica		
	Pathway Contribution			Pathway Contribution		
Pathway	PEF	µg/dL	Percent	PEF	µg/dL	Percent
Soil Contact	5.6E-5	0.01	0%		0.01	0%
Soil Ingestion	7.0E-3	1.03	31%	1.4E-2	2.06	47%
Inhalation	2.0E-6	0.00	0%		0.00	0%
Inhalation, bkgrnd		0.04	1%		0.04	1%
Water Ingestion		0.96	29%		0.96	22%
Food Ingestion, bkgrnd		0.51	15%		0.51	12%
Food Ingestion	5.5E-3	0.81	24%		0.81	18%

Click here for REFERENCES

IEUBK

- **Models blood lead for children 6 months to 7 years old.**
- **IEUBK is an <u>uptake</u> model. It models blood lead from the <u>absorbed</u> dose.**
- **LeadSpread uses <u>applied</u> dose.**

IEUBK Similarities with LeadSpread

- **Both predict central tendency of blood lead, then generate a lognormal distribution using an assumed geometric standard deviation**
- **Both allow site-specific inputs.**

IEUBK Is More Detailed

- Corrects for maternal contribution to blood lead.
- Corrects for non-linearities in absorption, distribution, and excretion of lead. [Slope factors allow only linear response.]
- Corrects for changing diet and water consumption with age.

IEUBK Is More Detailed

- **Makes many pharmacokinetic corrections as children grow:**
  - increasing body size
  - decreasing G-I absorption of lead
  - storage of lead in bone
  - increasing bone mass
  - multiple types of bone
  - storage of lead in soft tissues

IEUBK Is More Detailed

- Distinguishes between exposures to outside soil and inside dust.
- Allows user to build an extra pathway for special exposures, such as paint, cosmetics, or cookware.
- Allows exposure at more than one site.

IEUBK Is More Detailed

- **Output includes the probability of a child exceeding a blood lead value of 10 µg/dL, given the specific inputs.**

Uncertainties

- **The largest uncertainty in either model is the assumed estimate of variance, the geometric standard deviation.**
- **The default value of 1.6 is actually a combination of variability in:**

  - concentration in soil

  - exposure parameters

  - pharmacokinetcs

Conclusions

- IEUBK provides the most detailed modeling available for blood lead in children.
- LeadSpread provides a first approximation of IEUBK results for the 2-3 year old child.

Uncertainties

- **We would like our estimate of variability to be confined to “inter-individual variability”, which does not include the variability in concentration in soil.**
- **Separating out the three types of variability is not a simple task.**
- **The default value of 1.6 errs on the high side, which is the health-protective direction.**