Perchlorate Drinking Water Regulations

James C. Lamb Ph.D., DABT, Fellow ATS

jlamb@exponent.com

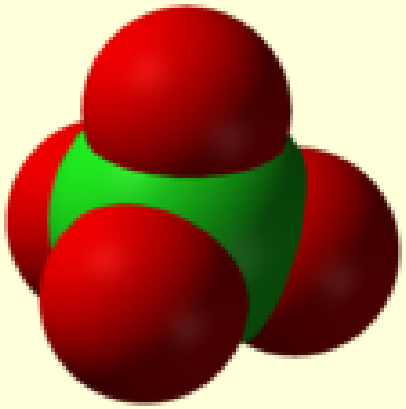
What will be discussed?

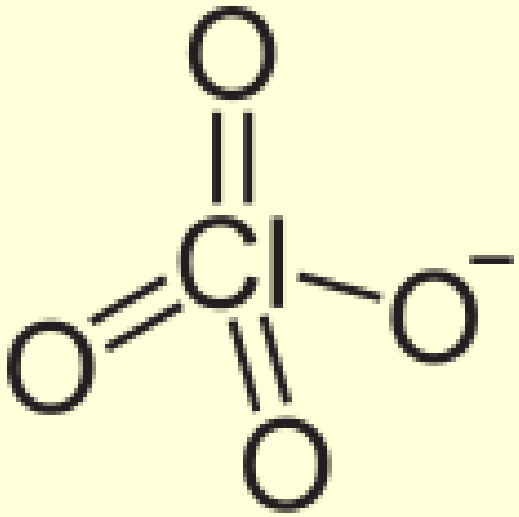
- Perchlorate in general
- NAS
- Exposure
- EPA today
- California today

Perchlorate

- Simple molecule
- Oxidizer
- Water soluble

- Natural
- Synthetic

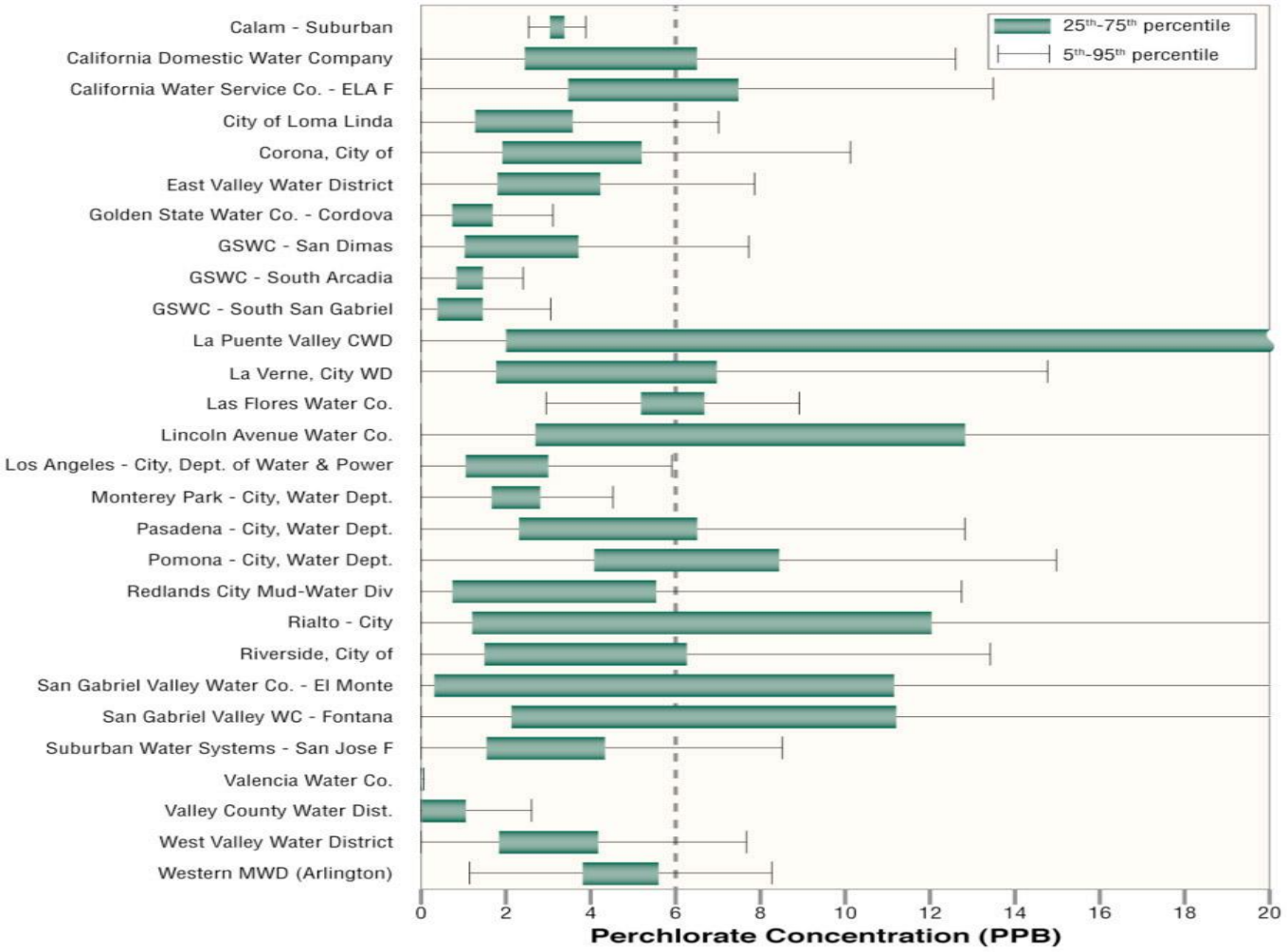




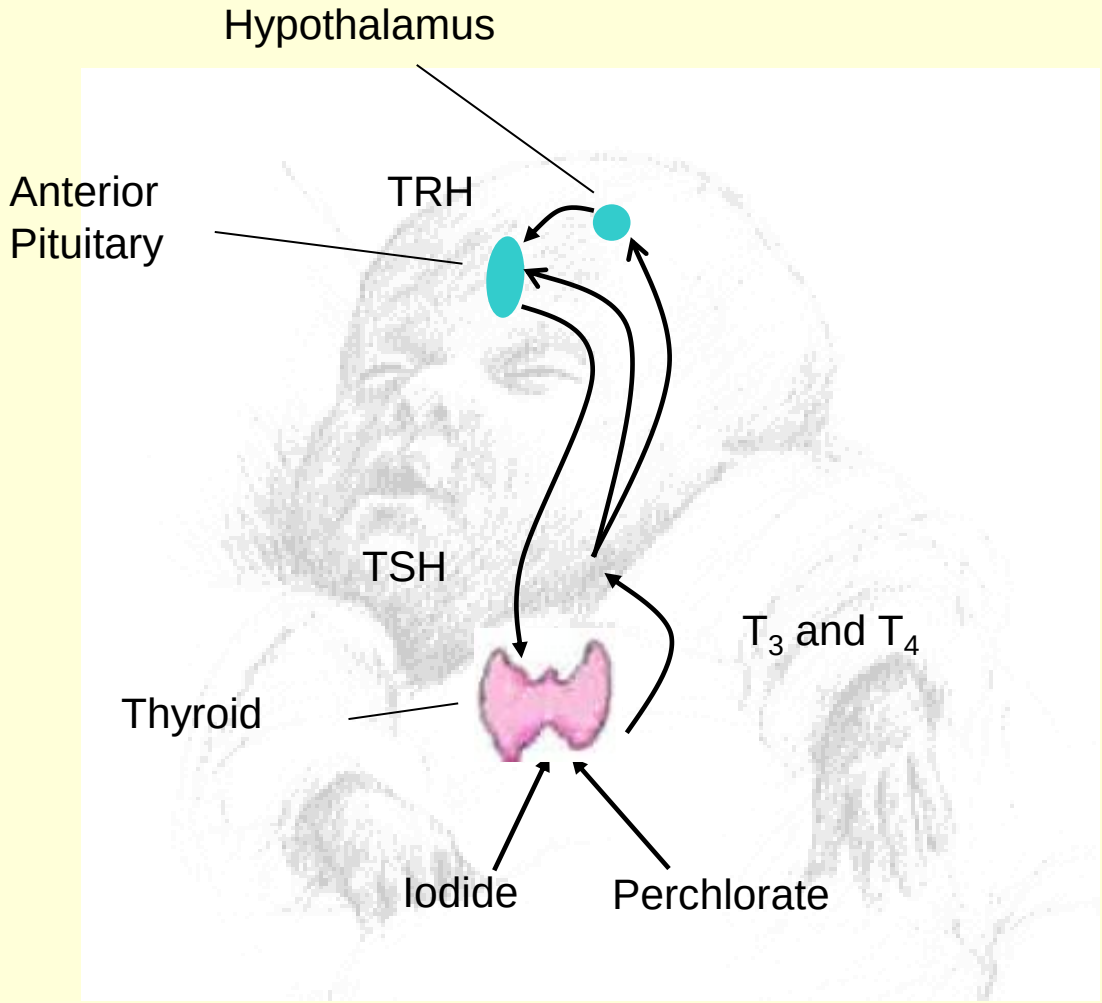
Where is it found or used?

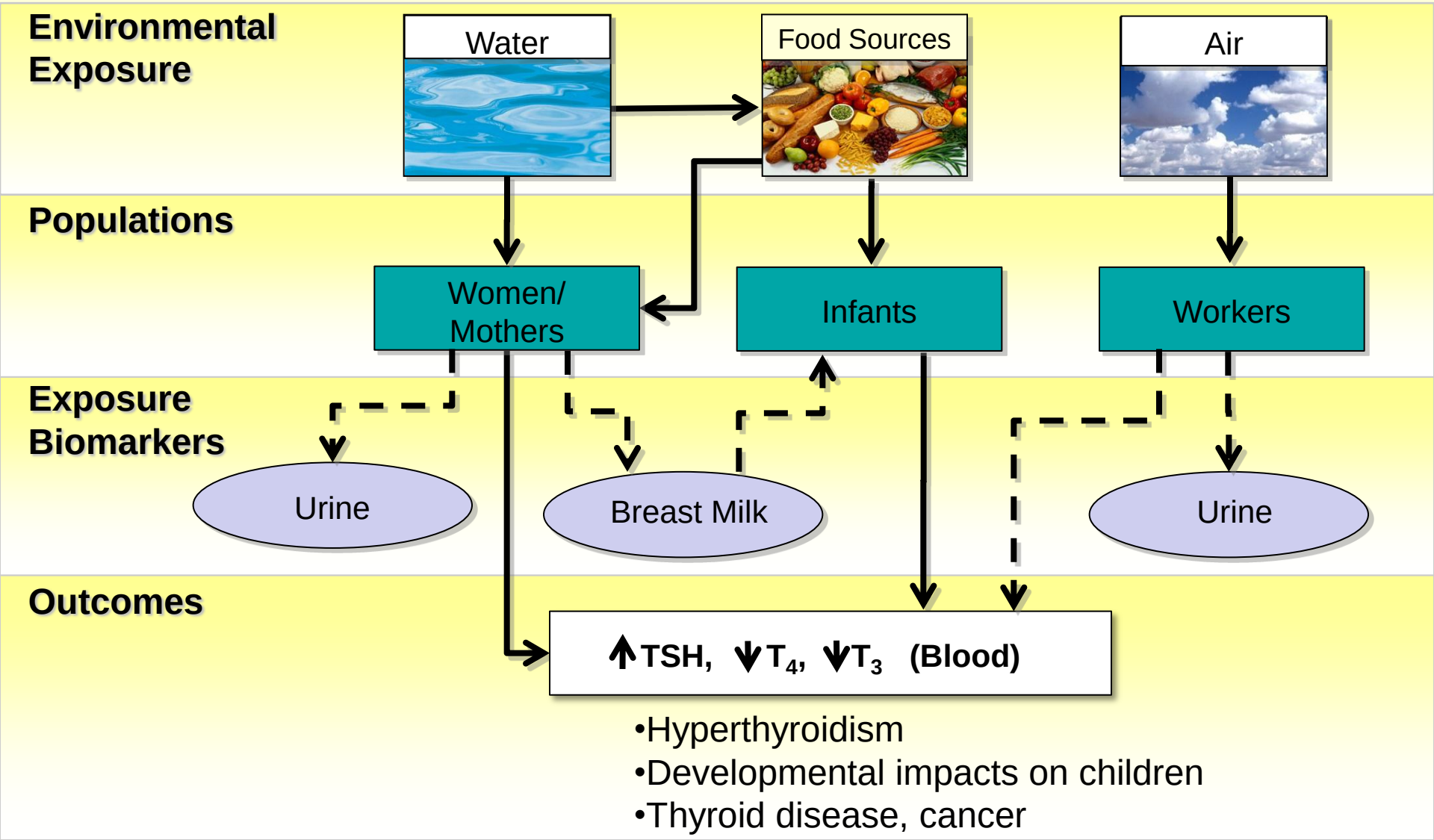
- **Drinking water and ground water**
  - No drinking water standard
  - 11 million people with at least 4 ppb or µg/L
- **Food**
- **Fertilizer mined from Chilean saltpeter**
- **Rocket fuel (tons per rocket)**
- **Automotive air bags**
- **Medical applications**
  - Graves disease, 40-120 mg/kg/d with normal T_3 and T_4

Perchlorate Monitoring for Selected Communities (DWP, 1997-2005)



Mechanism of Perchlorate Effect on Thyroid Function

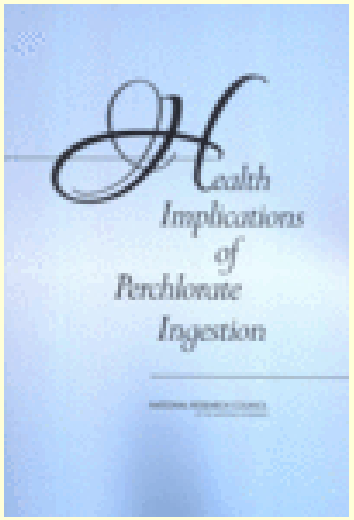




- Hyperthyroidism
- Developmental impacts on children
- Thyroid disease, cancer

NAS Report: Health Implications of Perchorate

- Reviewed current state of science (2005)
- EPA's draft risk assessment based on brain morphometry and thyroid hormones and histopathology
- Suggested major changes
  - Human data
  - Endpoints
  - Different uncertainty factors



EPA's Assessment

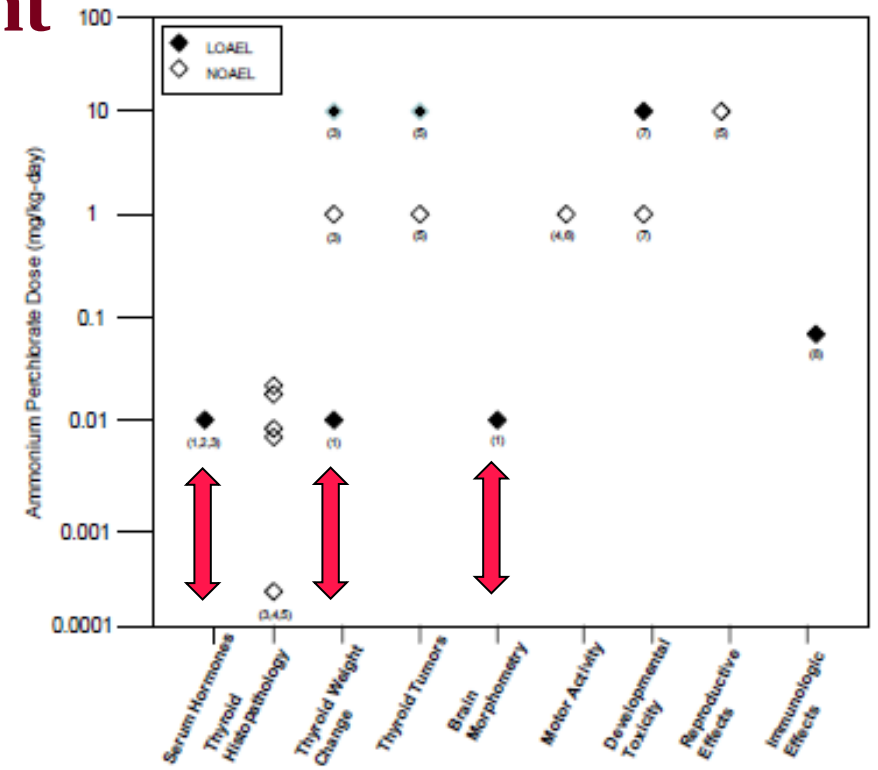


FIGURE 5-3 EPA's summary of NOAELs and LOAELs for various health effects in *rat* studies. Numbers indicate the following sources: 1, Argus Research Laboratories (2001), Consultants in Veterinary Pathology (2003); 2, Springborn Research Laboratories (1998); 3, Springborn Research Laboratories (1998); 4, Argus Research Laboratories (1998); 5, Argus Research Laboratories (1999); 6, Bekkedal et al. (2000); 7, Argus Research Laboratories (2000); 8, BRT-Burleson Research Technologies (2000a,b,c). Adapted from EPA 2003, p. 7-30.

EPA Point of Departure

TABLE 4-3 Summary of Morphometric Findings in Rat Pups Exposed to Perchlorate[a]

Neuroanatomic	Argus 1998		Argus 2001		EPA 2003
Region	Day 10-12	Day 82-85	Day 10	Day 22	Day 22
Frontal cortex	No change	Increase at high dose only in males	Increase at low or intermediate doses but not at high dose	Increase at high dose only in males	Not measured
Parietal cortex	No change	No change	Increase at low or intermediate doses but not at high dose	No change	Not measured
Striatum	Decrease at low or intermediate doses but not at high dose	Increase at high dose only in males	Increase at low or intermediate doses but not at high dose	Decrease at low or intermediate doses but not at high dose	All dose groups increased
Corpus callosum	Increase at high dose only	Increase at high dose only in males	Increase at low or intermediate doses but not at high dose in males; Decrease at low or intermediate doses but not at high dose in females	Increase at low or intermediate doses but not at high dose	Increase at low or intermediate doses but not at high dose
Hippocampus gyrus	Decrease at low or intermediate doses but not at high dose	No change	No change	No change	Not measured
Dentate gyrus	Not measured	Not measured	No change	No change	Not measured
CA1 portion	Not measured	Not measured	Decrease at low or intermediate doses but not at high dose in females; Increase at low or intermediate doses but not at high dose in males	No change	Not measured

Mode of Action and Point of Departure

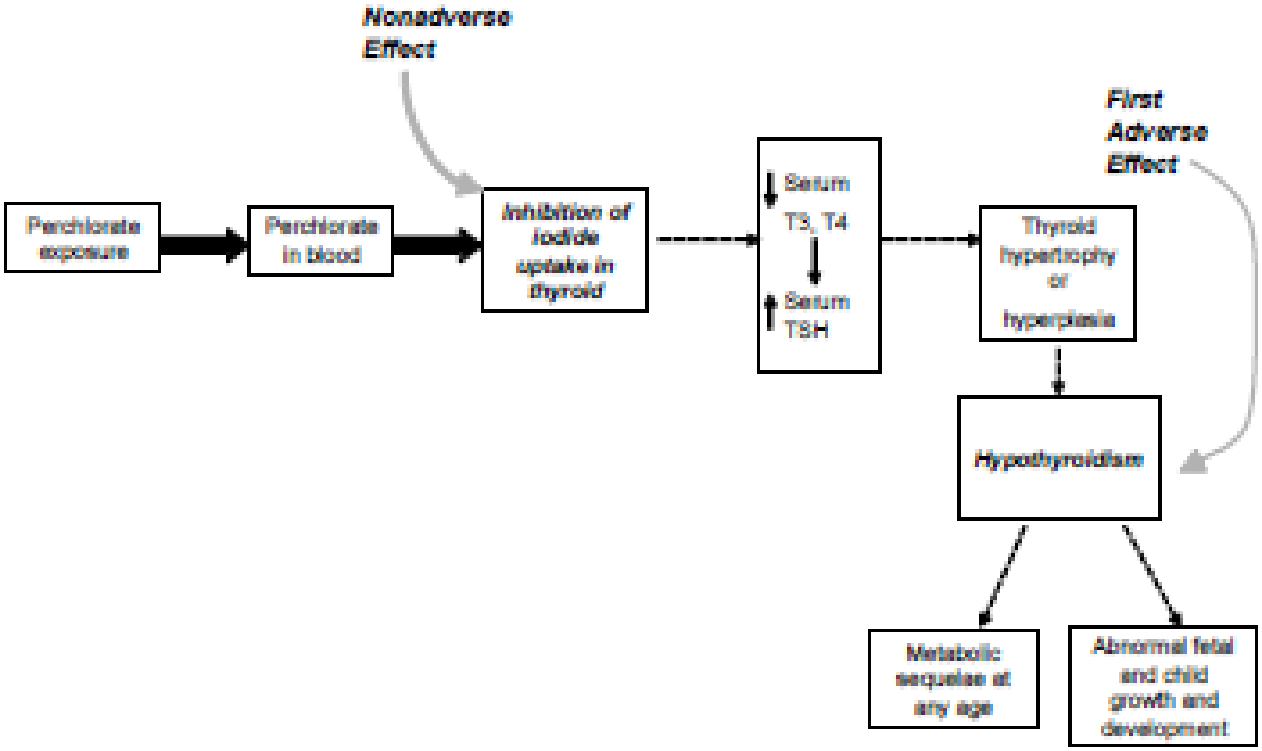


FIGURE 5-2 Committee's suggested mode-of-action model for perchlorate toxicity in humans indicating first adverse effect in the continuum.

NAS Conclusions

- Rat is not a good model, overly sensitive, endpoints poorly chosen
- Transient changes in thyroid hormones and TSH were not viewed as adverse
- Hypothyroidism is the first adverse effect
- Use key measured biochemical precursor events (inhibition of iodide uptake) for a protective risk assessment

NAS – Uncertainty Assessment

- Human data allowed the use of one 10X UF to protect fetuses of pregnant women
- 10x UF is conservative and protective from adult data

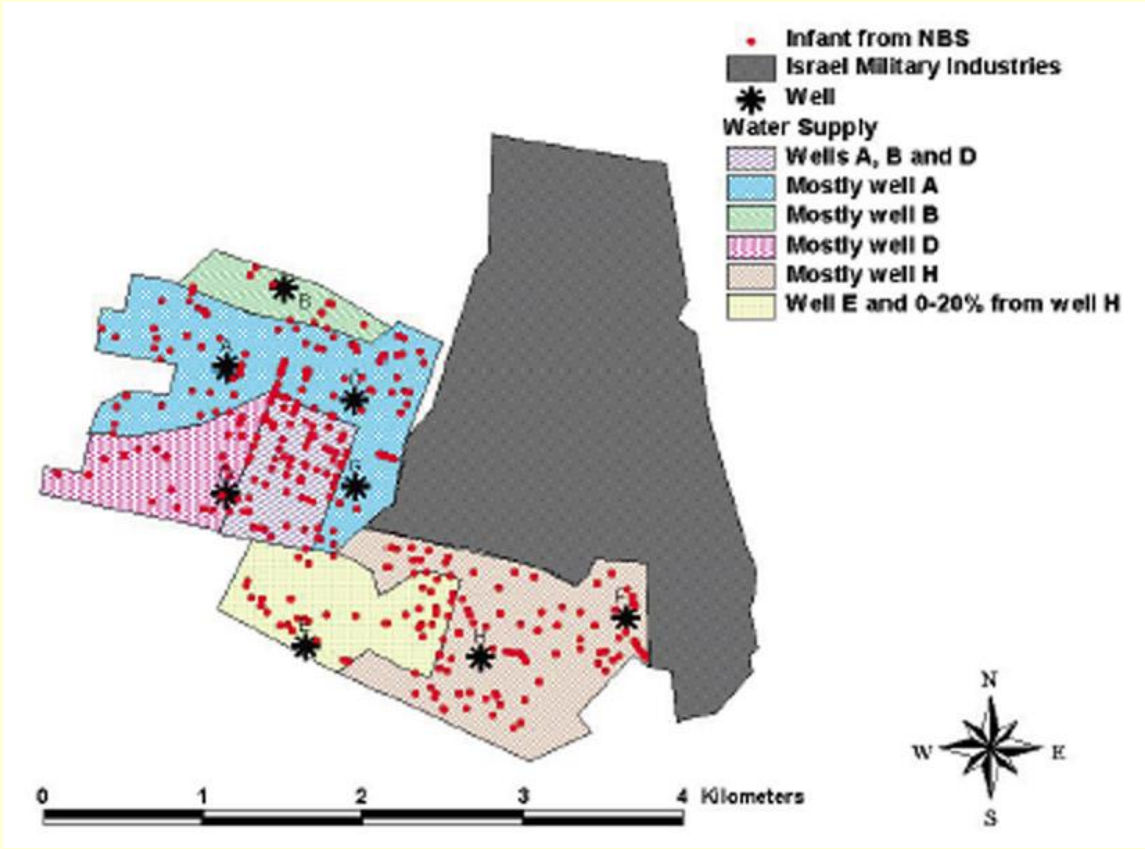
NOAEL 7 µg/kg/d

RfD 0.7 µg/kg/d

EPA translated to 15 µg/L (ppb)

Perchlorate Contamination in Ramat Hasharon, Israel

- **Source:**
  - Military industry
- **Water supply:**
  - Local wells
- **Perchlorate in DW:**
  - Regions A,B,C,D:
    - Wells: 42–94 ppb
    - Home: 42–80 ppb
  - Region H:
    - Well: 684 (1,100) ppb
    - Home: 340 ppb



Source: Amitai et al. (2008)

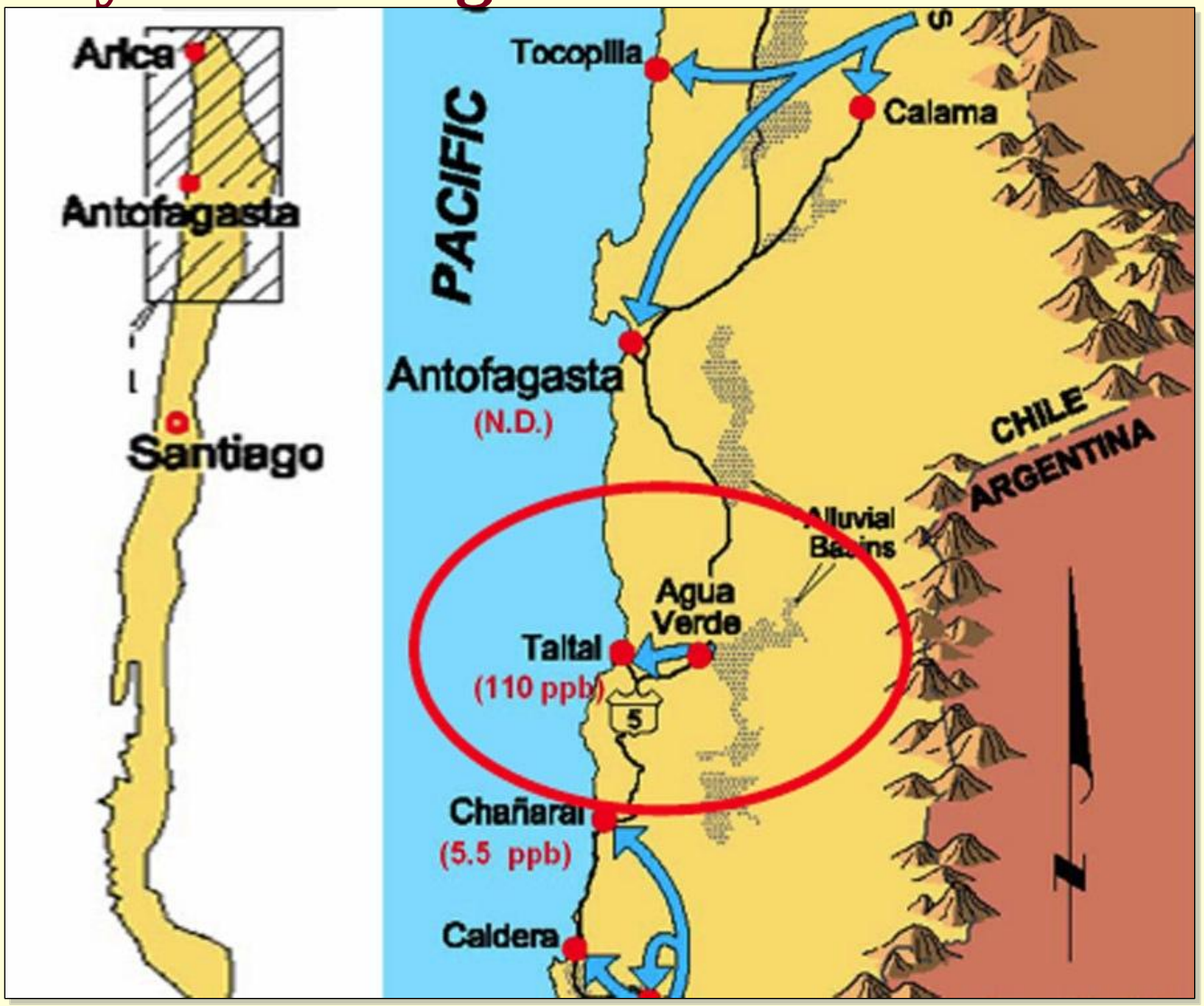
T_4 Levels in Newborns with Very High, High and Low Gestational Perchlorate Exposures

Region	Group (N)	Perchlorate in Drinking Water (PPB)	T_4 (µG/dL) (±S.D.)
Ramat Hasharon **(H)**	A (88)	≥ 340	14.1 (±3.7)
Ramat Hasharon **A–D**	B (209)	42–94	14.0 (±3.4)
Hertzilia **(control)**	C (805)	2.0–2.7	14. (±3.5)

Big Difference No Difference

Source: Amitai et al. (2008)

Naturally Occurring Perchlorate in Chile



Source: Gibbs (2008)

Chilean Study: Perchlorate Concentrations (Drinking Water)

	1999		2003	
	N	ppb	N	ppb
Antofagasta	25	< 4.0	63	0.5
Chañaral	25	5.5 ± 1.6	54	5.8 ± 0.6
Taltal	25	112 ± 6.7	60	113 ± 13

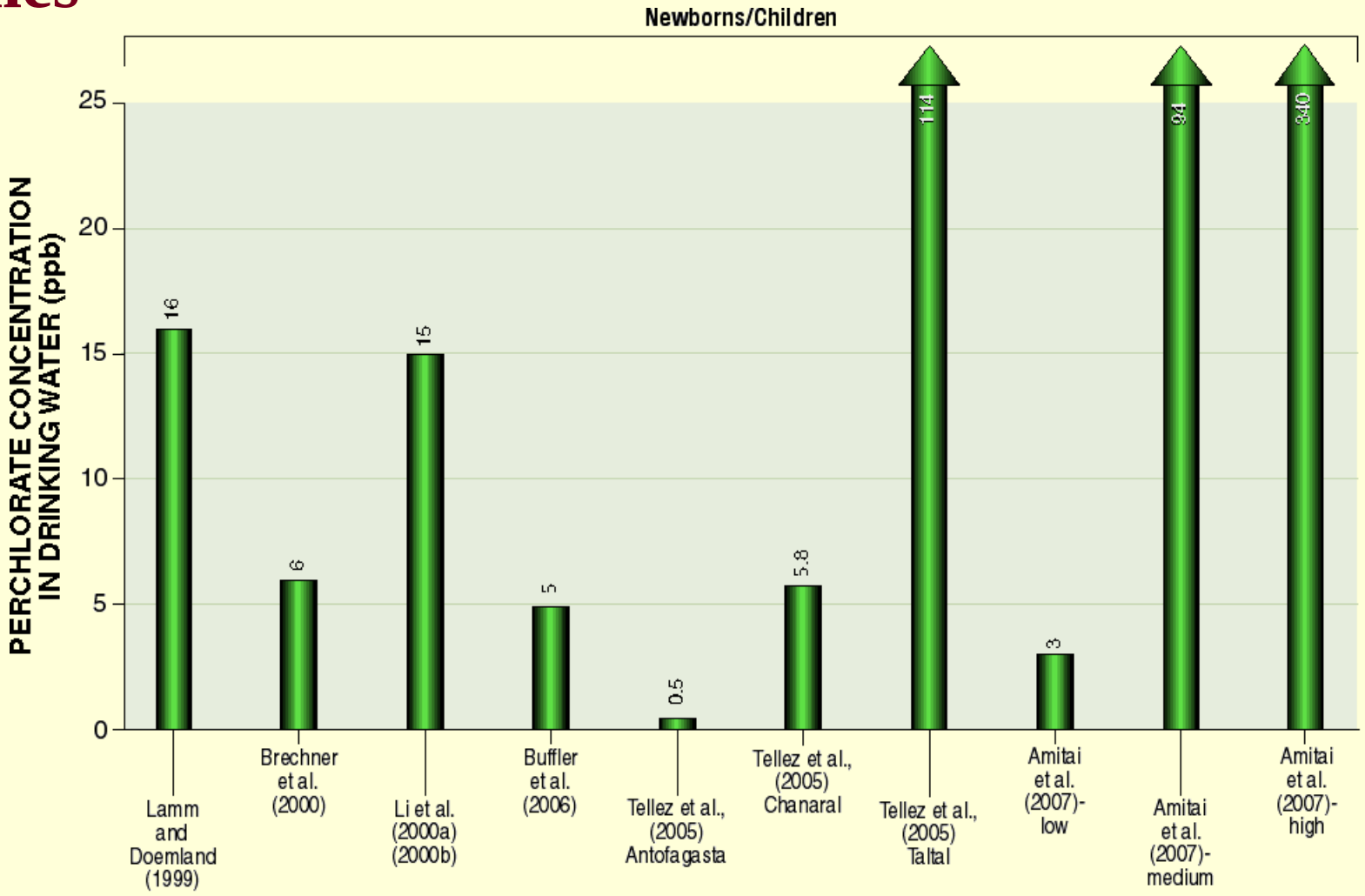
Source: Gibbs (2008)

Chilean Study: First Prenatal Visit

	Antofagasta		Chañaral		Taltal		
	N	Mean	N	Mean	N	Mean	P-value
Weeks gestation	46	16	46	17.1	64	15.3	0.05
T_3 (ng/dL)	64	183	52	207	64	189	<.01
Free T_4 (ng/dL)	64	0.95	52	0.95	64	0.99	0.25
TSH (µU/ml)	64	2.63	52	2.81	64	2.61	0.91
Thyroglobulin (ng/ml)	58	4.32	45	3.67	57	3.67	0.32
Iodine/g creatinine	61	391	38	355	57	322	0.06

Source: Gibbs (2008)

Estimated perchlorate concentrations in community studies



CDC-NHANES Analysis (Blount et al., 2006)

- **1/3 subsample of 2001-2002 NHANES survey**
  - 1,111 women,12 yrs or older with urinary perchlorate data and TSH/T4 serum measurements, no history of thyroid disease/meds
- **Controlled for numerous variables thought to affect thyroid:**
  - Age, race, pregnancy, menopause, BMI, cotinine, C-protein, medication use, dietary factors
- **Urinary perchlorate was a predictor of TSH and T4 in women – but not in men**

Study of Iodine Deficient Pregnant Women (Pearce et. al. 2010)

- **Study group:** **pregnant women in first trimester, iodine deficient (UK and Italy)**
- **Objective:** **To examine relationships between urinary perchlorate and thyroid hormones (T4, TSH)**

- **Results:**
  - All subjects had perchlorate detected in urine
  - No associations between urinary perchlorate and thyroid function

EPA – Recent Years

- **Oct 10, 2008 – EPA preliminary determination not to regulate perchlorate**
- **Dec 2008 – Interim Drinking Water Advisory for Perchlorate (15 µg/L based on NAS)**
- **August 2009 – EPA sought comments on regulating perchlorate**
  - "A key focus of the re-evaluation has been consideration of exposure of infants and young children to perchlorate, which can affect the thyroid gland."
- **April 19, 2010 – EPA OIG Report**

EPA OIG

- **Thoughtful review of the NAS proposal**
- **Raised significant issues**
  - Other iodide uptake inhibitors in the diet and environment
  - Cumulative risk assessment for iodide uptake inhibitors
    - Thiocyanate
    - Nitrate
    - **Iodine deficiency**
- **Perchlorate is a minor player and further reductions will not further protect human health**

California

- **Public Health Goal proposed Jan 2011 – 1 µg/L**
  - Followed NAS approach, in principle
    - Estimated ADD in µg/kg/d
  - Used 95% conf limit for infant water intake
  - BMDL for a 5% decrease in TIU (0.37 not 0.7 µg/kg/d), lowest effects in humans AND animals
  - Still used a 10x UF

- **Result is a 15-fold lower RfD or ADD and 1 ppb in drinking water is proposed**

Conclusions

- NAS rejected EPA's animal data in favor of human
- Used a measurable, but very health protective precursor endpoint, TUI
- First adverse effect is hypothyroidism
- Adult human study called for 10X UF to protect sensitive populations

Conclusions II

- Currently no EPA drinking water regulation exists, but they keep talking about it…
- EPA OIG correctly identified that a cumulative assessment is called for and addressing iodine deficiency, not perchlorate, is the better path
- California followed a very different path with multiple conservative assumptions

Acknowledgements

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All the opinions, however, are mine.