

Richard C. Pleus, Ph.D.

Intertox Inc., Seattle, WA

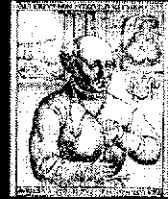
Department of Pharmacology
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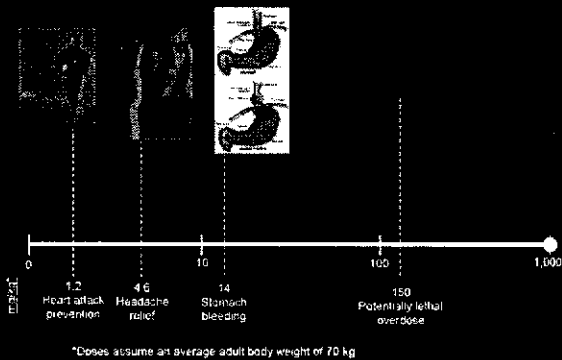
Important Starting Information

- ✓ Presence \neq Toxicity
- ✓ Dose-response relationship

*"All substances are poisons;
there is none which is not a
poison.
The right dose differentiates a
poison from a remedy."*
-Paracelsus (1493-1541)

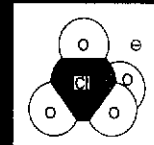
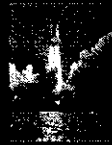


A Dose-Response Example: Aspirin



Perchlorate Background

- Used as an oxidizer in solid rocket fuel
- Found in fertilizer
- For 50 years, therapeutic agent for Graves' Disease
- Found naturally



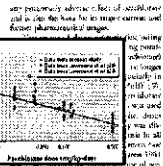
The Greer *et al.*, 2002 Clinical Trial

Health Effects Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition of Thyroidal Radiiodine Uptake in Humans

Monte A. Greer,¹ Gay Goodman,² Ronald C. Pleus,³ and Susan E. Greer¹

¹Duquesne University, Pittsburgh, PA; ²University of Maryland, Baltimore, MD; ³University of Maryland, Eastern Shore, Maryland, MD

Application of a sensitive and specific method for thyroidal radiiodine uptake (RAIU) to a population of humans exposed to perchlorate in drinking water... The study was designed to determine the dose response for inhibition of thyroidal radiiodine uptake in humans exposed to perchlorate in drinking water... The study was conducted in a controlled environment... The study was conducted in a controlled environment... The study was conducted in a controlled environment...



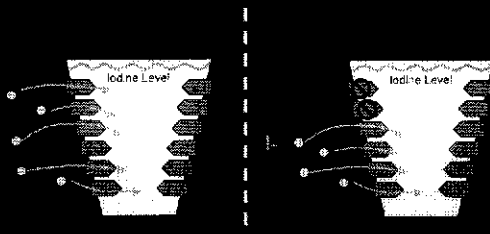
Collaborative work with Drs. Monte Greer, Gay Goodman, and Ms. Susan Greer

Environ Health Perspect 110:927-937 (2002)

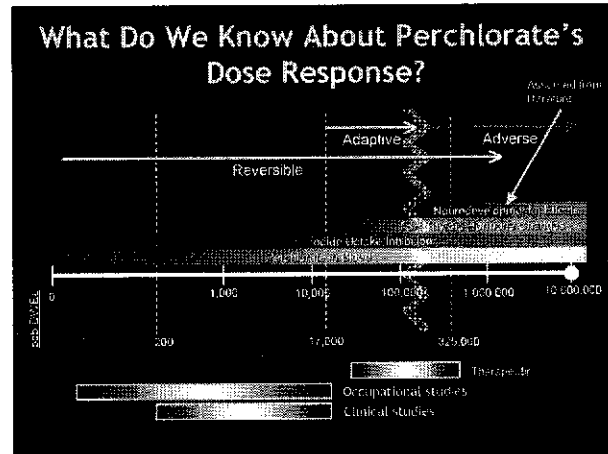
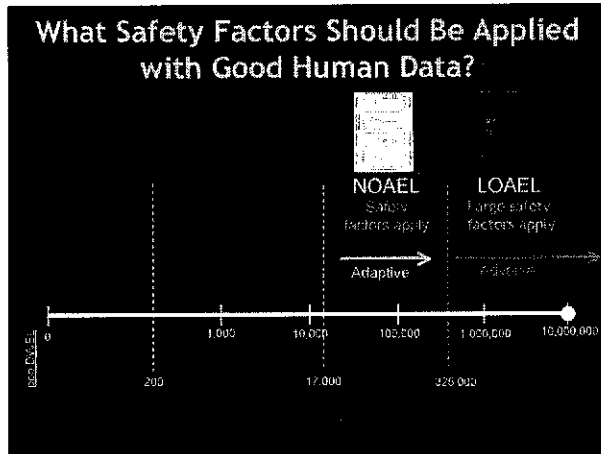
Perchlorate Toxicology

- Greer and Lamm studies show no effect on thyroid hormone levels at exposures up to an equivalent of 17,000 parts per billion in drinking water
- Perchlorate does not accumulate in the body
- Perchlorate is excreted from the body quickly

The Thyroid Iodide Pump



Show animation



Is Perchlorate the Only Chemical that Inhibits Iodine Uptake?

- **No**; other chemicals act through the same mechanism
- **Nitrate**
 - Commonly found in drinking water, meats, vegetables
- **Thiocyanate**
 - Found in milk, vegetables

Common Foods Containing Nitrate

✓ Milk	✓ Kimchi	✓ Carrots
✓ Bacon	✓ Garlic	✓ Onion
✓ Sausage	✓ Artichoke	✓ Green Beans
✓ Pepperoni	✓ Peas	✓ Melon
✓ Beef	✓ Corn	✓ Turnip
✓ Ham	✓ Sweet potatoes	✓ Sweet pepper
✓ Broccoli	✓ Lima Beans	✓ Squash
✓ Celery	✓ Cucumber	✓ Cabbage
✓ Lettuce	✓ Tomatoes	✓ Leek
✓ Radish	✓ Parsley	✓ Cauliflower
✓ Spinach	✓ Brussels sprouts	✓ Pumpkin
✓ Beets	✓ White potatoes	✓ Endive
✓ Rhubarb	✓ Eggplant	✓ Kale
		✓ Turnip Greens

Have Other Authoritative Organizations Reviewed Perchlorate?



UC Peer Reviews



- Greer Study most appropriate
- Perchlorate does not cause cancer
- NOT a consensus opinion; reviewers disagree

"No public health emergency is evident in California to drive the rush to regulate trace perchlorate ingestion in drinking water" - UC Peer Reviewer

UNMC Perchlorate State of the Science Symposium



- Existing animal studies are invalid
- Human studies offer greater insight
- Inhibition of iodide uptake is not adverse

Issues Under Study By the National Academy of Science Relevant to California



- What percent iodide uptake would be protective of individuals at various life stages and thyroid status?
- What information is needed to inform the selection of uncertainty factors?
- What levels of changes in thyroid hormones may lead to adverse effects in humans?