

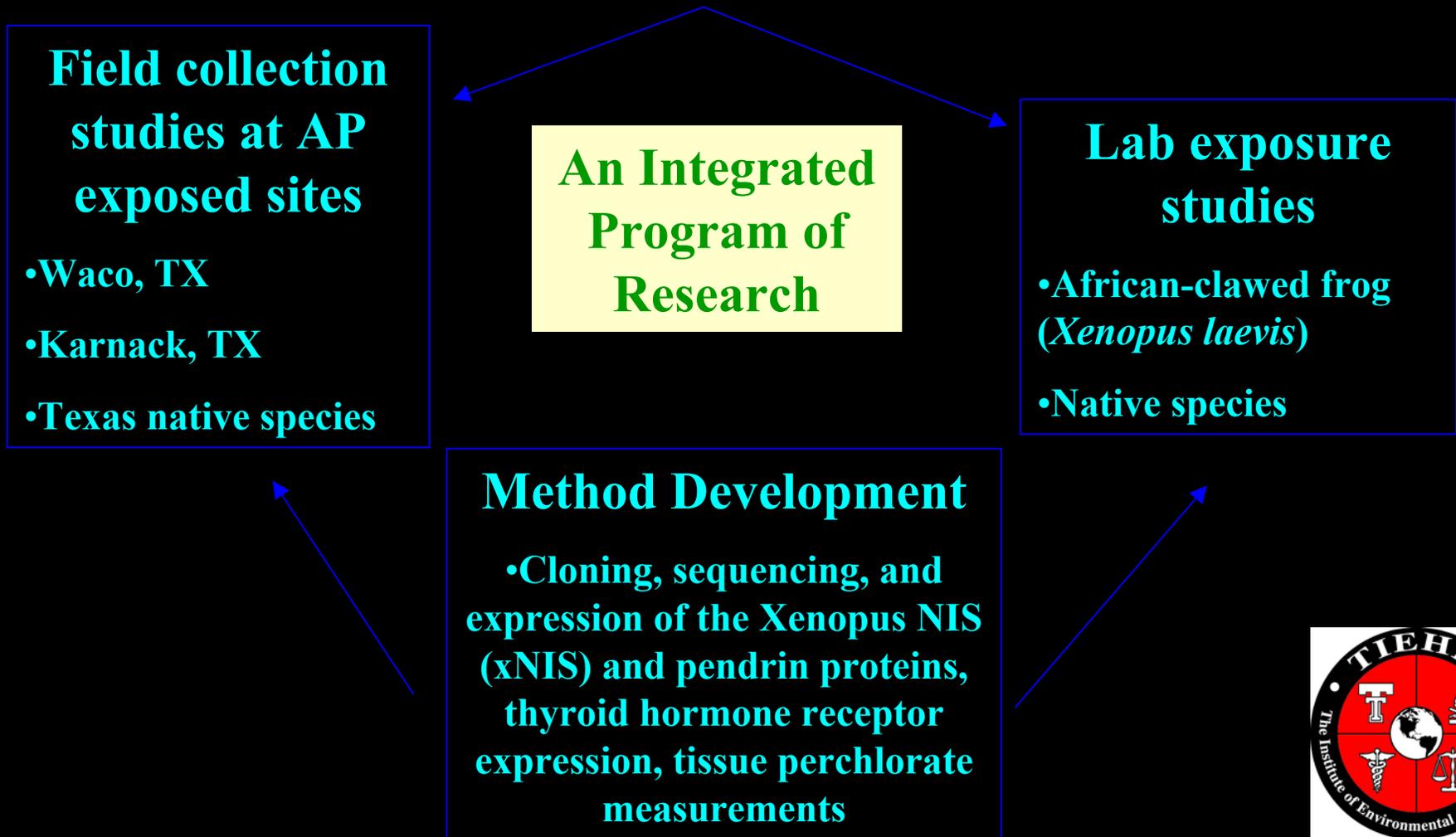
Ammonium Perchlorate Disruption of Thyroid Function in Natural Amphibian Populations: Assessment and Potential Impact

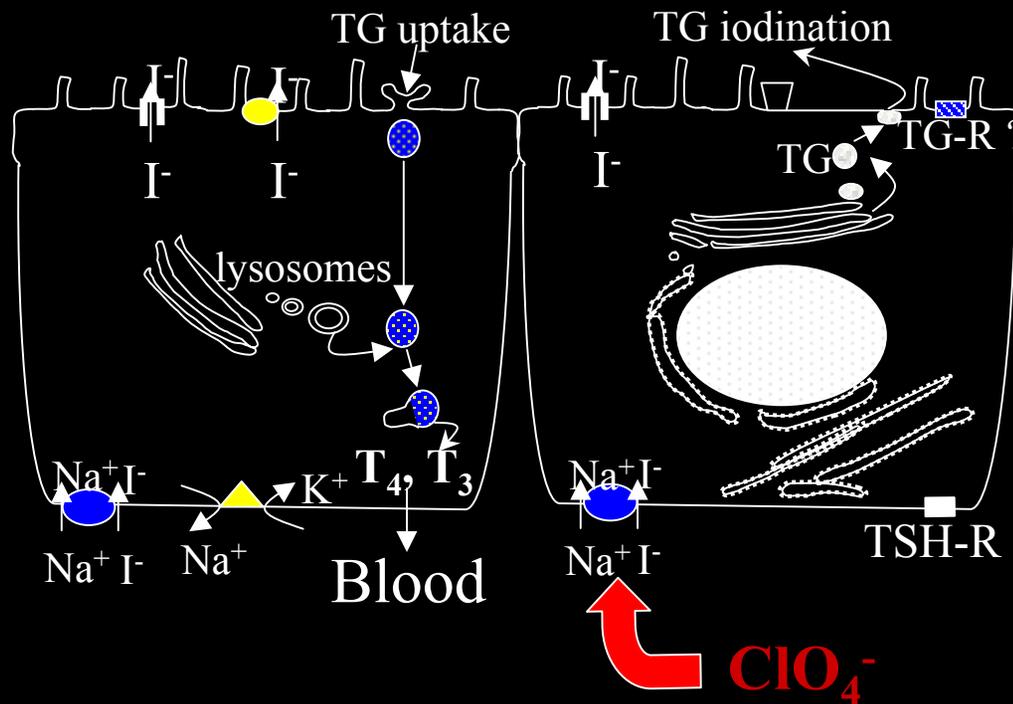
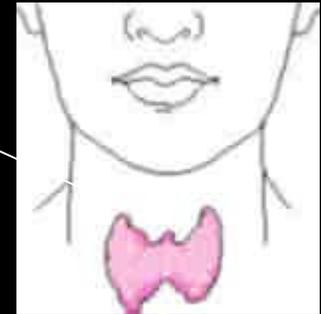
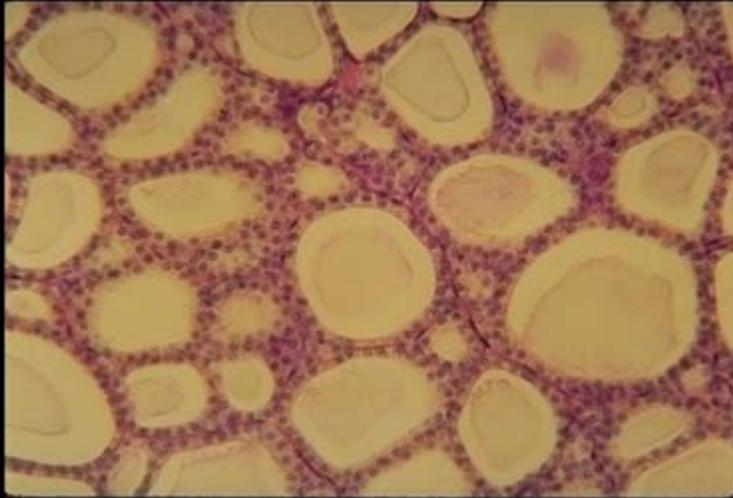
James A. Carr, Ph.D.

Department of Biological Sciences, Texas Tech University, Lubbock
The Institute of Environmental and Human Health Texas Tech University,
Lubbock



Overall Objective: To assess the effects of environmentally relevant levels of ammonium perchlorate on amphibian development



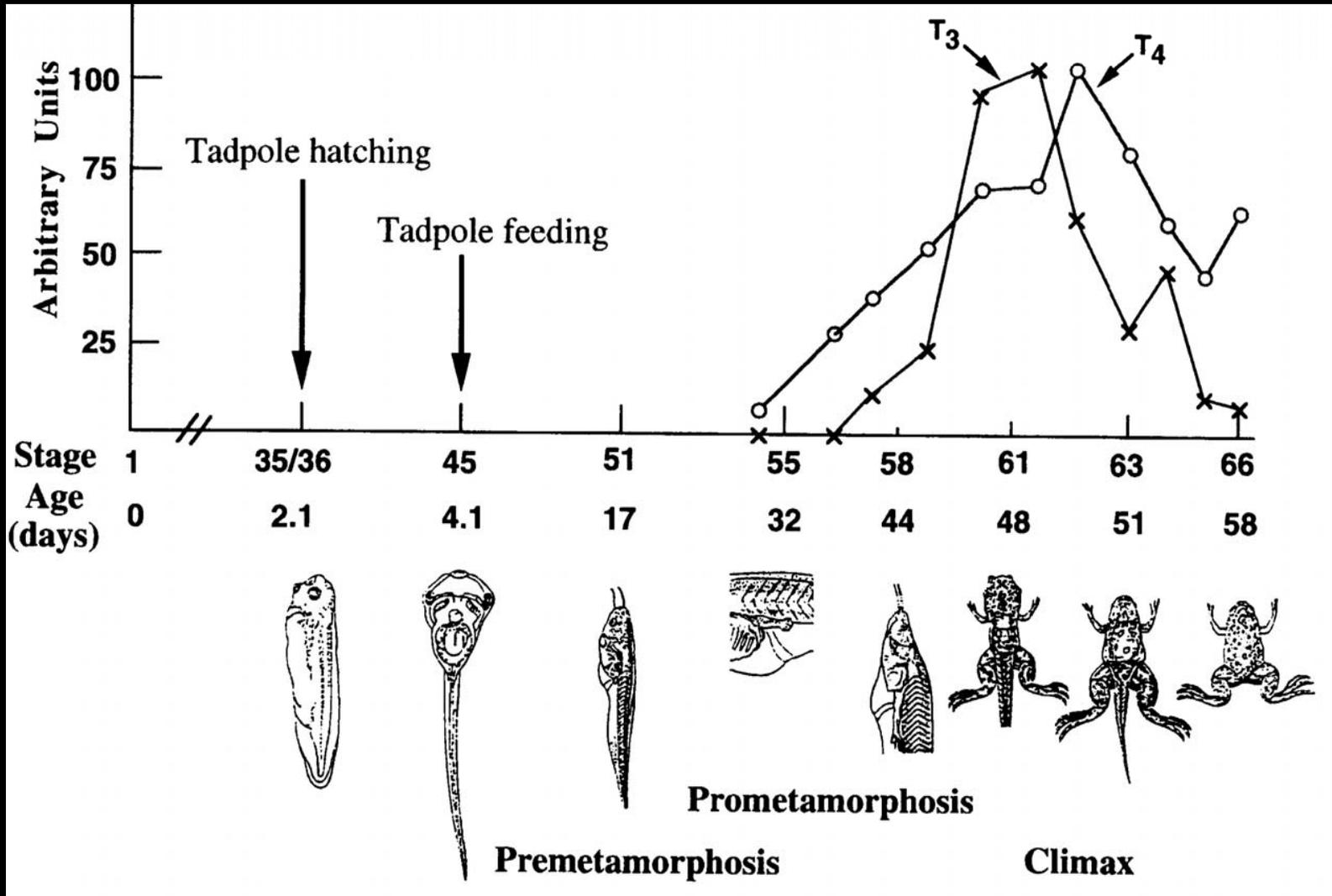


ClO_4^- :

- inhibits I^- uptake
- blocks T_4 , T_3 synthesis
- causes enlarged thyroid



Why Investigate the Response of Amphibians to Ammonium Perchlorate?



From Shi, 2000





Overview of Laboratory Studies

Goals:

- To determine the response of developing *X. laevis* and native species to environmentally-relevant concentrations of AP.
- To determine the mechanism of AP action.
- To determine the effects of AP on maternal thyroid hormone transfer to eggs.
- To determine AP uptake and elimination in amphibians.

Endpoints:

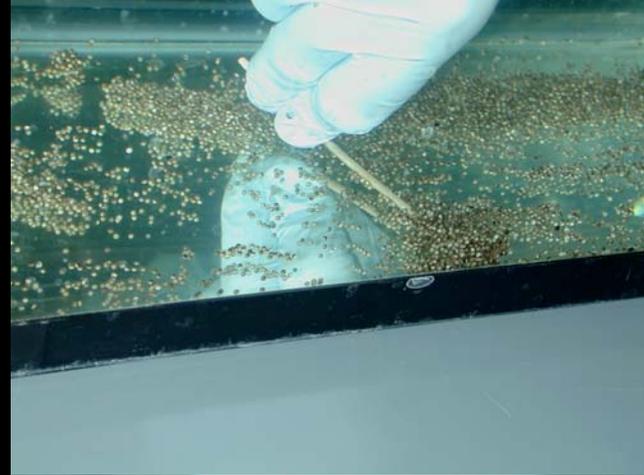
- Metamorphosis
- Thyroid function (hormone measurements, histopathology)
- Reproductive development
- Tissue perchlorate levels.
- NIS expression.



General Design

- **70-day larval exposure from <24 h after fertilization.**
- **All experiments performed in FETAX medium.**





Summary of Dose-response studies

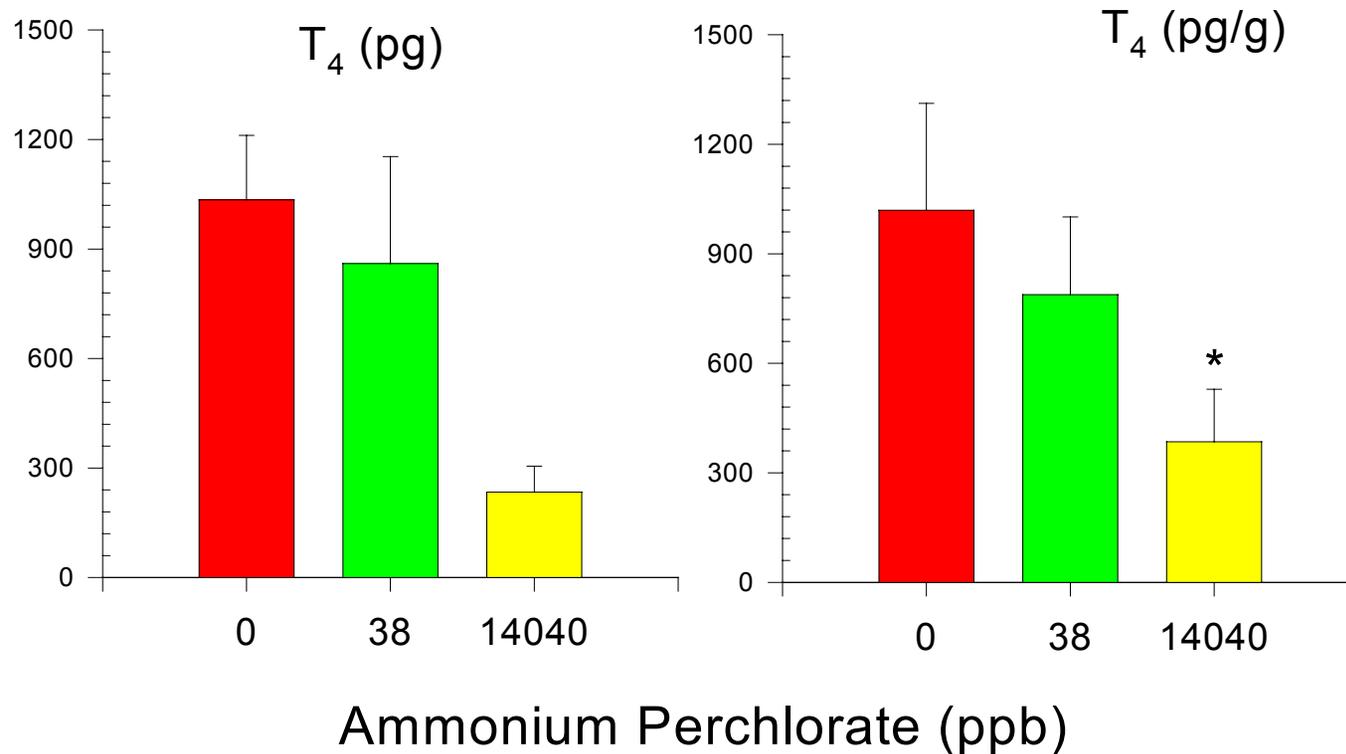
- AP is not especially lethal; 5- and 70-day LC₅₀s were 510 ± 36 ppm and 223 ± 13 ppm, respectively.
- ≥ 147 ppb perchlorate prevented forelimb emergence and tail resorption over 70-d exposure.

Goleman, W.L., Urquidi L.J., Anderson, T.A., Kendall, R.J., Smith, E.E., Carr, J.A. (2002). Environ. Toxicol. Chem. 21: 424-430.

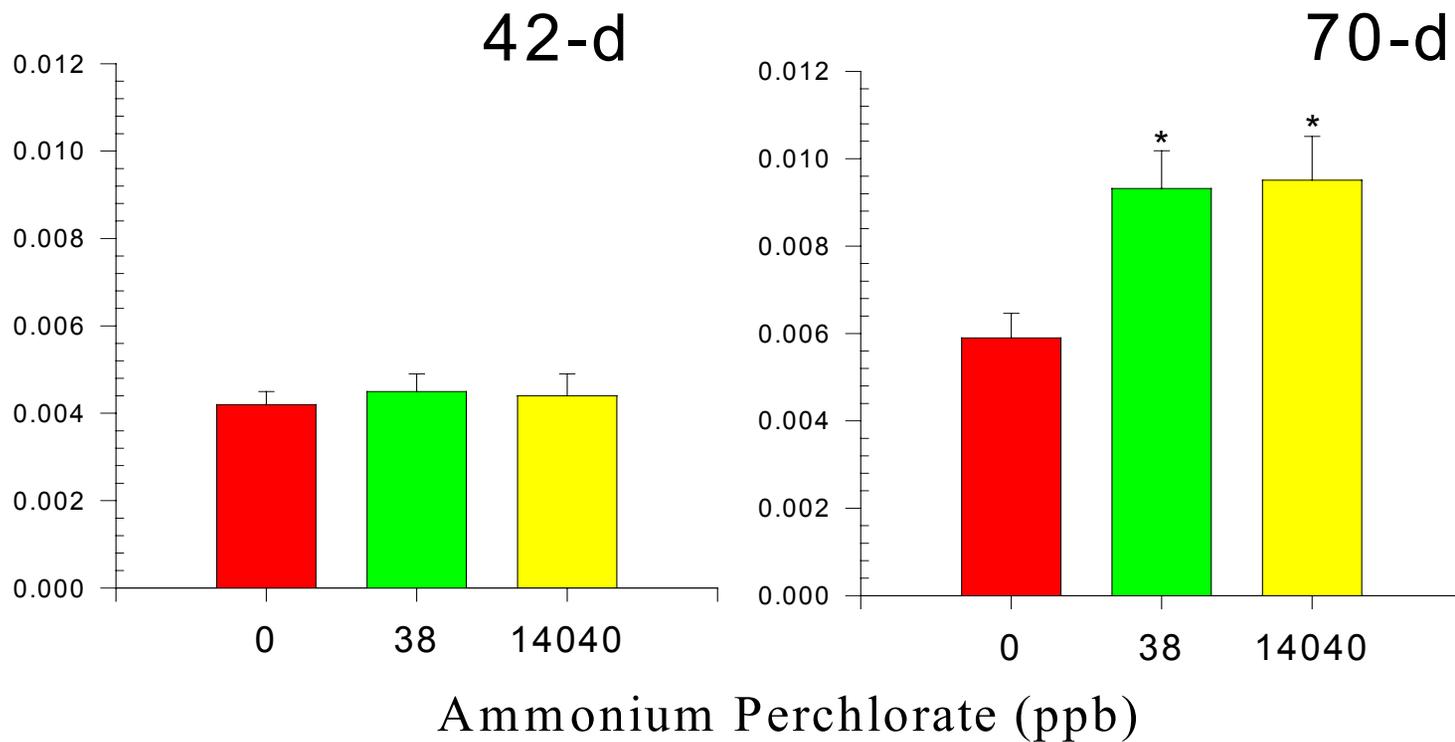


Whole Body T_4 Levels After 70 d AP Exposure

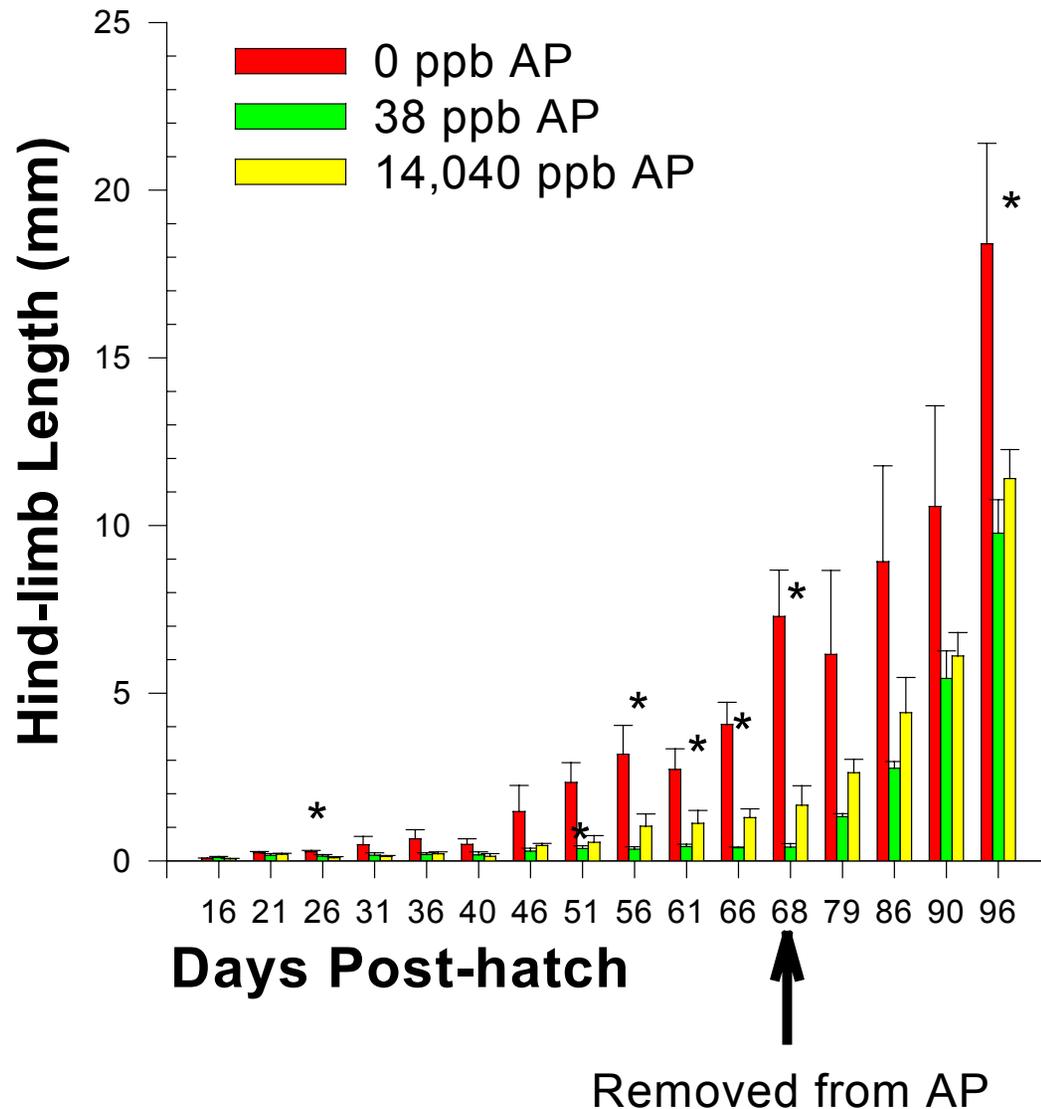
70-d AP exposure- T_4



Thyroid Follicle Cell Heights



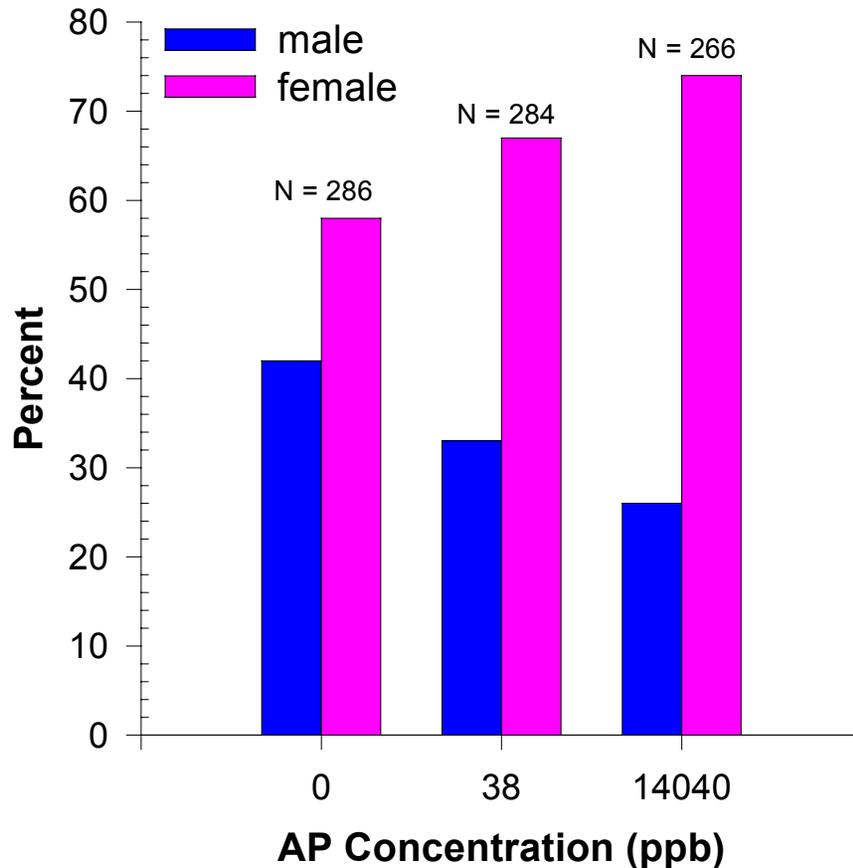
“Reversible” Effects of AP on Hindlimb Length



- Hindlimb measurements were recorded every 5 days.



AP Reduces the Percentage of Male Offspring



AP (ppb)	χ^2	p
0	3.41	= 0.06
38	16.7	< 0.0001
14040	31.7	< 0.0001

Thyroid hormones are required for the upregulation of androgen receptors. (Robertson and Kelley, 1996, Dev. Biol. 176: 108-123)

Goleman, W., Carr, J.A., and Anderson, T.A. (2002). Environ. Toxicol. Chem. 21:590-597.



Summary

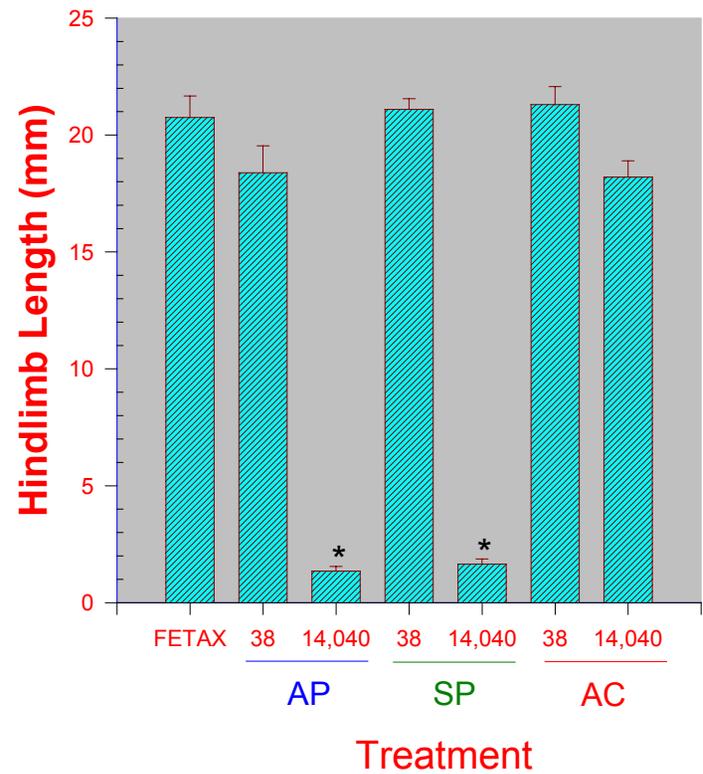
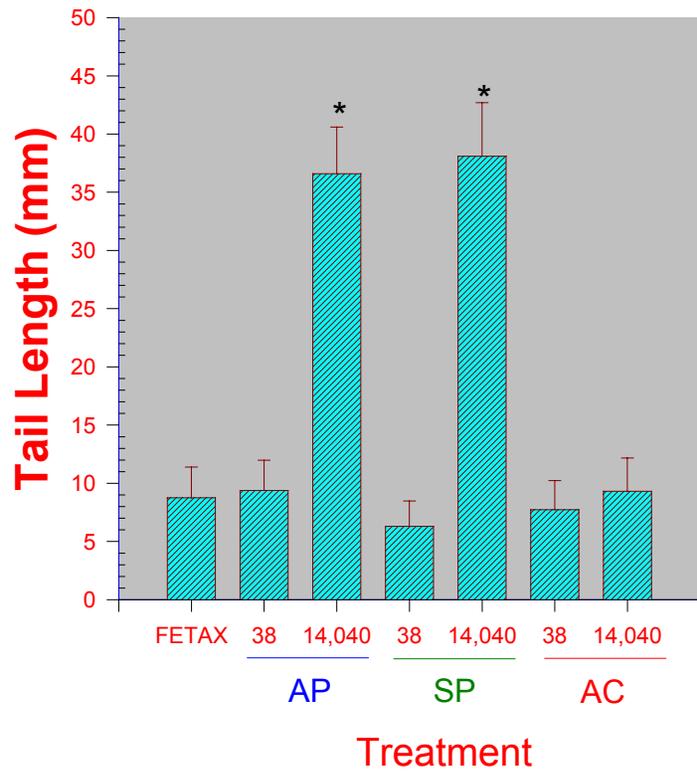
- **Inhibitory effects of AP on forelimb emergence, hindlimb growth, and tail resorption appear to be reversible.**
- **Follicle cell height is a more sensitive indicator of perchlorate exposure than T4 levels, with measurable effects on cell height at 38 ppb (nominal).**
- **Perchlorate reduces the percentage of males in a concentration-dependent manner. At present we do not know if the effects on gonadal differentiation are reversible.**



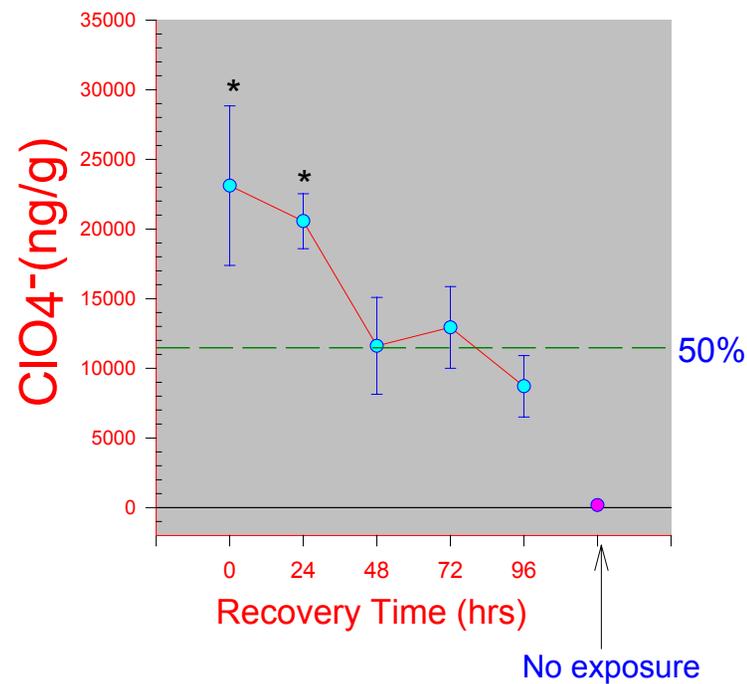
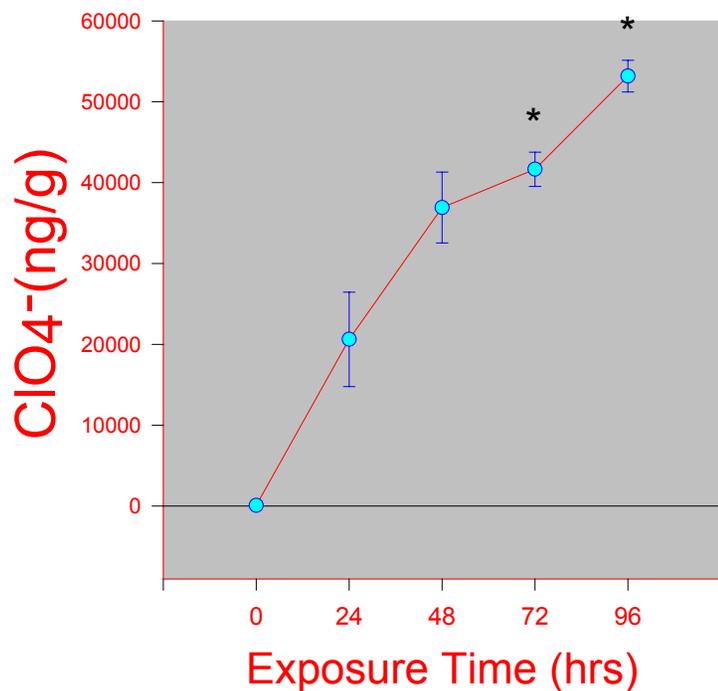
Ammonium Ions Contribute to the Lethality but not the Developmental Effects of Ammonium Perchlorate

Compound	LC ₅₀	Reference
AP	510 ppm	Goleman, Urquidi, Anderson, Kendall, Smith, Carr. 2002. Environ. Toxicol. Chem. 21: 424-430.
SP	>1,220 ppm	unpublished
AC	118 ppm	unpublished





Whole-body Perchlorate Uptake and Elimination in *Rana catesbeiana* tadpoles. t_{50} for whole body perchlorate elimination approx. 48 hr



Potential implications and uncertainties

Because

- the effects of perchlorate are reversible
 - this anion is eliminated relatively rapidly
 - exposure may vary month to month
- tadpoles with a long larval period (2-3 yrs, such as bullfrogs bullfrogs) may undergo non-exposure recovery periods.



Potential implications and uncertainties

- In contrast, perchlorate may pose a greater threat to tadpoles inhabiting temporary ponds, where exposure over a period of weeks may prevent complete metamorphosis before pond-drying occurs.
- How perchlorate interacts with environmental iodide is unknown, but the amount of dietary and environmental iodide available to the animal must certainly influence the potency of environmental perchlorate.

