

Neonatal Neurobehavioral Impacts of Iodine Insufficiency and Pesticide Exposures

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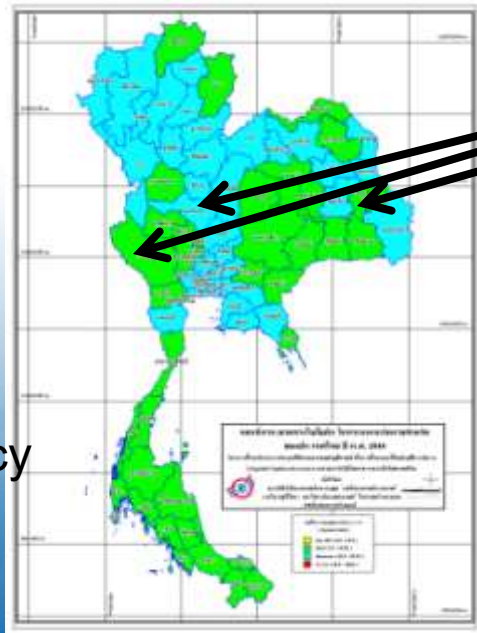


History of the project

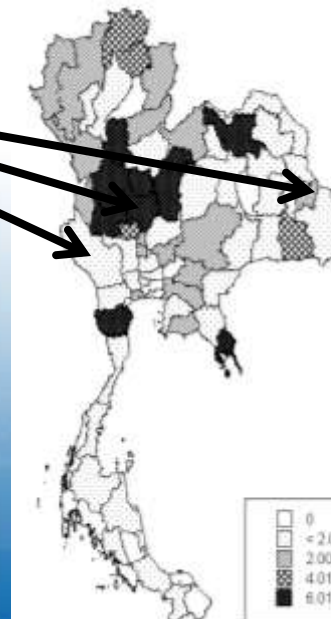
- 2010 NIH funded 2 year pilot project
- UMass Lowell partnered with Mahidol University Faculty of Public Health in Bangkok Thailand
- Hypothesis: low maternal iodine and pesticide exposure may act synergistically to alter thyroid hormone status resulting in deficiencies in child neurobehavioral development

Methods

- Recruit pregnant women from 3 provinces in Thailand representing a range of risks for pesticide exposure and iodine deficiency disorders.



Hospitals



of

Methods

- At recruitment (7 months)
 - Urine for iodine & pesticide metabolite (organophosphates (OP))
 - Extensive health history, exposure history, dietary questionnaire
- At birth
 - Urine for maternal iodine, pesticide metabolites (OP's)
 - Blood for maternal thyroid hormone & hemoglobin levels
 - Placental cord blood for thyroid hormone
 - APGAR and other birth data
 - Brazelton Newborn Behavioral Assessment Survey (BNBAS)



Newborn Behavioral Assessment Scale (NBAS)

- NBAS covers 28 behavioral items and 16 primitive reflexes.
- Cluster scored into 7 domains:
 - habituation,
 - orientation,
 - motor,
 - range of state,
 - regulation of state,
 - autonomic stability,
 - number & type of abnormal primitive reflexes
- Used Certified NBAS trainer to train Thai pediatricians
- Test in first 4 days of life
 - (avg 1.8 days; 91% < 3; max 4)



Further Data Collection

- **Age 2 months:** maternal urine & breast milk for pesticides and iodine & questionnaires
- **Age 5 months:** Neurobehavioral testing with observational Bayley Scales and physiological testing with EEG/ERP (Electroencephalogram/Event Related Potential) & questionnaires
- **Questionnaires:** infant health, behavior, food intake, mothers nutrition and exposure to pesticides

– EEG/ERP

- Infants view images of mother vs stranger (500ms each)
- EEG/ERP data is collected for 1500 ms after each picture appears on the screen
- ERP components relate to perceptual processing



– Bayley Scales

- Observational assessment of motor skills (fine & gross) and cognitive development (attention, memory, learning)
 - Mental Development Index
 - Psychomotor Development Index



Unforeseen Complications

- In Oct 2010 the MoPH began providing iodine supplement tablets to pregnant women.
- Major flooding Sept 2011-Jan 2012
 - 13.6 million people affected. 65/77 provinces were declared flood disaster zones, > 20,000 km² (7,700 mi²) land damaged, seven major industrial estates flooded to 3 m (10 ft)



Results

- Recruited 112 women at 7 months pregnancy
 - 27 agricultural workers
 - 30 live with agricultural workers or worked in fields less than 1 day per week for only 1 trimester.
 - 55 unexposed to agricultural pesticides
 - 30 (55%) reported applying insecticide in home during pregnancy
- NBAS data collection on 82 newborns
 - 27% loss to follow-up from recruitment due to cesarean section, prematurity (<37 weeks), delivered elsewhere (some due to flooding).

Pesticide Use



Pregnant agricultural workers report:

- 81% used insecticides on their farm
 - 41% used organophosphates
 - 4% report using pyrethroids
- 85% used herbicides on their farm
 - 41% used glyphosate
 - 59% used paraquat
 - 26% use 2,4-D

Pesticide Use

During pregnancy Agworkers reported:

- 19% used pesticides to treat seeds
- 59% mixed pesticides
- 63% applied pesticides to crops
- 37% applied pesticides to animals
- 63% entered fields sprayed with pesticides on the same day
- 74% washed clothes used to mix or apply pesticides (42% wash with regular clothes)
- 57% never use rubber gloves when mixing pesticides



Newborn Behavioral Assessment Scale (NBAS)

- 3/7 Thai test results significantly poorer than CHAMACOS longitudinal birth cohort in California (85% Mexican-American; 64% \leq poverty level; many agricultural workers)
- 2/7 Thai tests results better than CHAMACOS

Variable	Mean	Std Dev	Δ CHAMACOS – our data	t-test with CHAMACOS p-value
Habituation	7.3	1.2	-0.7	< 0.001
Orientation	6.1	1.5	1.4	<0.001
Motor	5.7	0.8	0.1	0.25
Range of State	3.9	0.5	-0.5	<0.001
Regulation of State	5.2	1.7	0.5	0.003
Autonomic Stability	6.1	1.1	0.9	<0.001
Abnormal Reflex	1.8	2.3	-0.1	0.08

NBAS

- Each NBAS cluster score examined for association with potential covariates in linear or poisson regression (reflex). Covariates included in final model if $p \leq 0.15$
 - Mother's age, income, education, parity, marital status, alcohol use, cough medicine use, caffeinated soda use, nonprescription medicine use, babies gender, NBAS tester
- Final models include **Agworker & Iodine (0/1) variables**
 - Agricultural worker (n=21): at least 2-3 days/month in field in any trimester for mother
 - Iodine tablet supplement (n=71): medical staff report of date tablets provided & subject reported receiving tablets during at least 1 trimester.

Final NBAS Model Estimates

	Orientation	Motor	Range of State	Regulation of State	Habituation	Autonomic Stability	Abnormal Reflexes Rel Risk
Maternal Agworker	-0.41 p=0.30	-0.22 p=0.24	0.27 p=0.04	-0.03 p=0.95	-0.45 p=0.10	-0.07 p=0.72	0.77 ChiSq=0.31
Iodine tablets provided	0.02 p=0.97	0.22 p=0.36	0.17 p=0.34	0.78 p=0.17	-0.24 p=0.55	-0.05 p=0.87	0.45 ChiSq=0.09

- Agworker parameter direction (N.S.) for 5/7 tests suggests being Agworker results in poorer newborn neurological function.
- Iodine parameter direction (N.S.) for 5/7 suggests tablets improve newborn neurological function

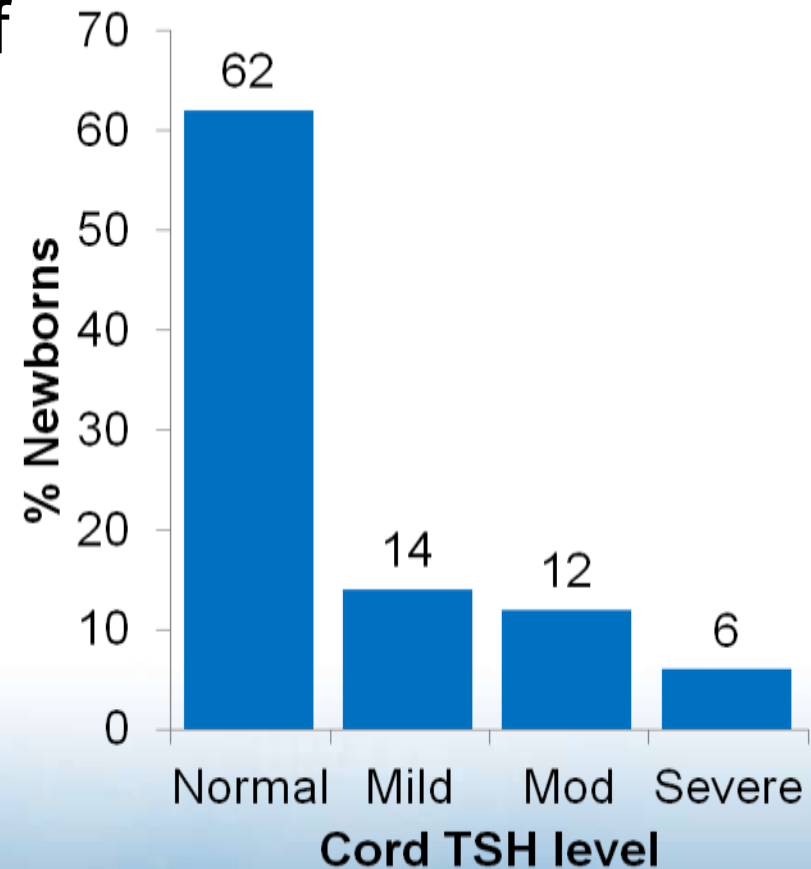
Newborn Demographics

- Birth data on 78 of 82 NBAS babies.
- Using linear and logistic regression with covariates: **Agworker or Iodine tablet supplements were not significant predictors of birth outcomes.**

Newborn	Mean	SD	% < norm
Weight (kg)	3.08	0.41	11
Height(cm)	51.6	2.3	9
Head circumference (cm)	22.3	1.4	9
Apgar 1 min	8.9	1.0	7
Apgar 5 min	9.7	0.5	5
Apgar 10 min	9.8	0.4	5

Cord Blood Thyroid Hormone

- 35% of newborns were out of normal TSH range.
 - 6.5% had severely high TSH levels
 - Compared to 4.6% of >5000 neonates at a Bangkok hospital in 2003
- 34% of newborns had low free T4 levels.
- 11.6% newborns clinically hypothyroid based on cord blood



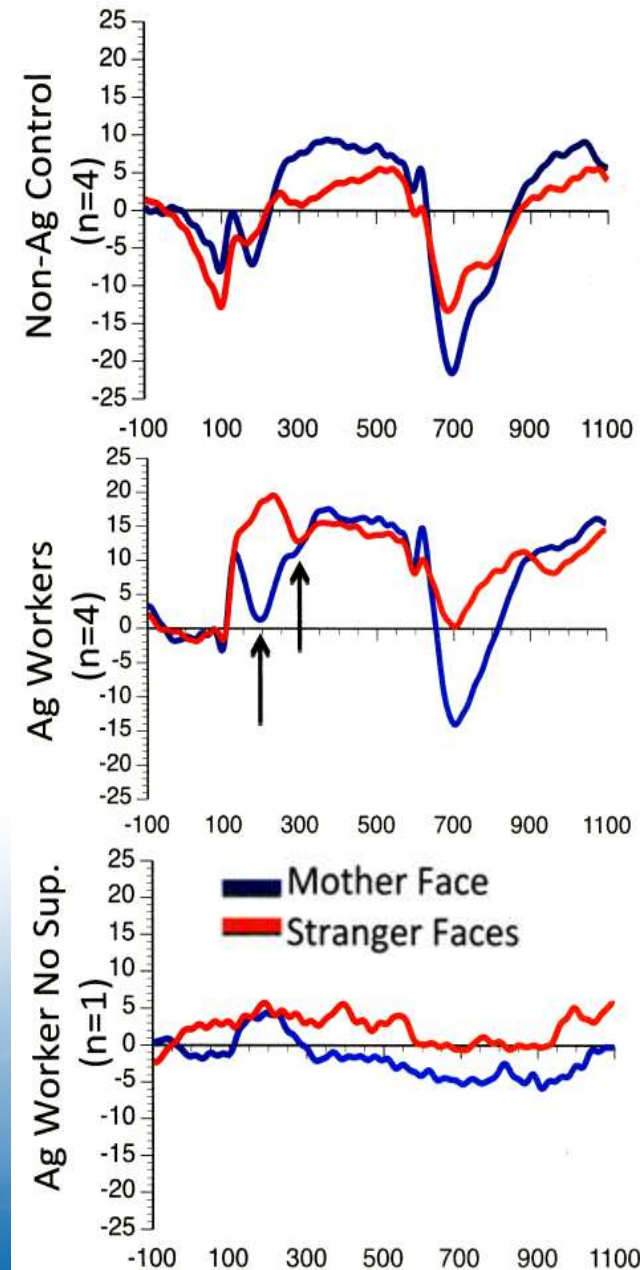
Thyroid Hormone, Iodine supplements & Agworker status

- Using linear and logistic regression with covariates: **Agworker or Iodine tablet supplements were not significant predictors of thyroid levels or hypothyroid status of either the mother or newborn cord blood.**



EEG/ERP

- The latency and amplitude differences for the ERPs suggest slower processing of novel stimuli (stranger's faces) from the infants of agricultural workers.
- Single child of an agricultural worker who did not receive iodine supplementation showed no discernible ERP components, suggesting very delayed development.



Future Directions

- For NBAS, Thyroid hormone, Birth data
 - Add organophosphate (OP) urinary metabolite levels at 7 months and birth to models
 - Add estimates of iodine uptake from food frequency questionnaire and tablet intake
- Complete collection/analysis of Bayley & EEG/ERP :
 - OP urine metabolite & breast milk levels
- Increase power by recruitment in follow-up study
- Follow subjects longitudinally
- Examine herbicide exposures

