occupational OP exposure and deficits on behavioural performance tests. We studied pesticide application teams in Egypt who are primarily exposed to one OP, chlorpyrifos (CPF), differing in exposure experience based on their job category.

Methods Trailmaking A and B were administered to 54 engineers (who typically watch the applications from beside the field), 59 technicians (who typically guide the applicators in the field), 31 applicators (using knapsack sprayers), and 150 controls (who did not work in the fields) at 2 different times during the OP application season and also immediately and 1.5 months after applications had ended.

Results A consistent dose-response relationship was seen in performance speed: Controls had the best performance through most of the application season on Trailmaking A ($p \leq 0.04$) and B ($p < 0.001$). Applicators had slower performance than engineers ($p = 0.015$) and technicians ($p = 0.032$). On the more complex Trailmaking B test, applicators and technicians had comparable performance that was significantly slower ($p = 0.003$ and $p = 0.012$ respectively) than performance of the engineers. Test performance at 1.5 months after applications ended and in the following year revealed that differences between the groups were persistent, and some differences were significant. 3,5,6-Trichloro-2-pyridinol (TCPy) levels in urine confirmed the pattern of higher to lower exposures across the job categories of the pesticide application teams, and these were all greater than exposures in controls. Increasing TCPy concentrations were significantly correlated with slower Trailmaking B performance at 1.5 months after the exposures had ceased, but not during or immediately after exposures.

Conclusion This study identifies a dose-response based on job category and establishes that the OP chlorpyrifos is neurotoxic.

1639d PRECLINICAL MODEL OF CHLORPYRIFOS EXPOSURES AND EFFECTS DOCUMENTED IN EGYPTIAN PESTICIDE APPLICATORS

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10.1136/oemed-2018-ICOHabstracts.822

Introduction Organophosphorus pesticide (OP)-induced neurotoxicity remains a significant occupational health concern, management of which is complicated by the lack of biomarkers that reliably identify at-risk individuals. To address this issue, we used a preclinical model of occupational OP exposure to evaluate the relationship between OP-induced cognitive deficits and expression of conventional and novel biomarkers of exposure and effect.

Methods Adult male Long Evans rats were exposed to CPF (3 or 10 mg/kg/d, s.c.) or an equal volume of vehicle for up to 21 days. Previous PBPK modelling studies confirmed that this exposure paradigm resulted in urinary TCPy levels and blood cholinesterase activity within the range of those observed in exposed Egyptian pesticide applicators. Learning and memory were assessed using appetitive Pavlovian discrimination between two tones and by Pavlovian fear conditioning. Tissues were collected for quantification of peripheral and central biomarkers of CPF exposure, inflammation and oxidative stress.

Results Subchronic CPF exposure for 21 d interfered with the maintenance and reversal of appetitive behaviour, but these effects were not reliable. In contrast, CPF caused robust and reproducible dose-dependent deficits in Pavlovian fear conditioning at 21 but not 4, 10 or 15 days of exposure. CPF also increased urinary TCPy levels, caused a delayed decrease in blood and brain cholinesterase activity, increased urinary and brain F2-isoprostanes and upregulated expression of multiple oxidative stress biomarkers in brain and in the periphery. Of these biomarkers, only oxidative stress biomarkers correlated with cognitive deficits. Moreover, CPF-induced cognitive deficits were prevented by co-administration of the antioxidant Trolox (1 mg/kg, i.p.).

Conclusion These findings demonstrate that subchronic exposures to CPF at levels that do not cause systemic cholinergic toxicity impair learning and memory via effects on the amygdala and hippocampus. Biomarker analyses suggest that oxidative stress, but not cholinesterase inhibition, contribute to CPF-induced cognitive deficits.

Funding: R01 ES016308

1639e EFFECTIVENESS OF EXPOSURE PREVENTION CLOTHING IN THE EGYPTIAN APPLICATORS THAT COULD BE IMPLEMENTED WITH MINIMAL COST

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10.1136/oemed-2018-ICOHabstracts.823

Introduction Chlopyrifos organophosphorous pesticides (OPs) are regularly applied for protection of the cotton crop in Egypt. OP absorption subsequent to dermal exposure has been estimated to be 94%–96% of the total dose. Legs and lower body parts are the most affected during cotton pesticide applications. Pesticides residues on the cotton plants also contaminate clothing and uncovered arms or legs of the applicators as they pass. Protective equipment is not readily available in Egypt. This pilot study was conducted to determine if wearing plastic coverings over pants or changing work practices could reduce pesticide exposure among Egyptian pesticide workers.

Methods A controlled intervention study included:

- protective clothing (plastic pants modelled by the workers and staff who participated in 4 educational focus groups);
- spray away (instructions were provided to spray away form the workers' path);
- control (followed routine work practices).

Exposure was assessed measuring pre- and post-application urinary TCPy levels (3,5,6-trichloro-2-pyridinol), the primary chlorpyrifos metabolite used as a biomarker of absorbed dose. Work activities were recorded throughout the three-day study period.

Results Twenty-four adult workers ($n = 8$ per group) participated in the study. Time spent applying (range 15–36 min) and mixing (range 10–12 min) pesticides varied between groups and job categories. Other than the pants group, none of the workers had protective clothing. Spraying away did not produce consistent results. Average TCPy levels of the protective clothing group were lower compared to the other two groups, though the differences were not statistically significant ($p > 0.05$).

Conclusion Work habits, time spent applying or mixing pesticides and environmental conditions (e.g., wind direction) are important exposure determinants of urinary TCPy levels. However, use of protective clothing covering legs and lower

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parts of the body would reduce skin contamination, a major route of pesticide exposure.

Work was supported by NIEHS grants ES017223 and ES016308.

1714 OCCUPATIONAL NEUROTOXICOLOGY – RECENT STUDIES

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10.1136/oemed-2018-ICOHabstracts.824

Aim of the special session International researchers summarise their studies on adverse nervous system effects of occupational exposure to neurotoxic compounds.

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1714a PARKINSONISM PREDICTIVE MODEL IN MN-EXPOSED WORKERS

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10.1136/oemed-2018-ICOHabstracts.825

Introduction Manganese (Mn) over-exposure in occupational settings is associated with basal ganglia toxicity and a movement disorder characterised by parkinsonism (i.e., the signs and symptoms of Parkinson disease). A simple test to help non-neurologists identify workers with clinical Mn neurotoxicity represents an unmet need.

Methods Using a cohort of 536 Mn-exposed workers, age ≤65 years, from welding worksites, with extensive clinical data, we developed a linear regression model to predict the Unified Parkinson Disease Rating Scale motor subsection part 3 (UPDRS3) score. We primarily considered factors easily obtained in a primary care or occupational medicine clinic, including timed motor task results and selected symptoms/conditions. Secondarily we considered other demographic variables and welding exposure. We selected the model based on simplicity for clinical application, biologic plausibility, and statistical significance and magnitude of regression coefficients.

Results The final model contained age, timed motor task scores for each hand, and indicators of action tremor, speech difficulty, anxiety, depression, loneliness, pain and current cigarette smoking. When we examined how well the model identified workers with clinically significant parkinsonism (UPDRS3 ≥15), the receiver operating characteristic area under the curve (AUC) was 0.72 (95% confidence interval [CI] 0.67, 0.77). With a cut point that provided 80% sensitivity, specificity was 52%, the positive predictive value in our cohort was 29%, and the negative predictive value was 92%. Using the same cut point for predicted UPDRS3, the AUC was nearly identical for UPDRS3 ≥10, and was 0.83 (95% CI: 0.76 to 0.90) for UPDRS3 ≥20.

Conclusion Since welding exposure data were not required after including its putative effects, this model may help identify workers with clinically significant Mn neurotoxicity in a variety of settings, as a first step in a tiered occupational screening program.

1714b EVALUATION OF PARKINSONISM AMONG MANGANESE EXPOSED WORKERS

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10.1136/oemed-2018-ICOHabstracts.826

Introduction Accumulation of manganese in the brain may result in a neurological condition with cognitive, psychiatric, and movement abnormalities. The clinical and toxicological literature demonstrates that manganese accumulates in the basal ganglia which may result in parkinsonism. There is little published about the prevalence of Parkinsonism among manganese exposed workers. We present a case series of 6 workers from a single factory and discuss methods of neurological assessment of the manganese exposed worker for the occupational health provider.

Methods IH sampling of a large tire factory employing 527 production workers was conducted for heavy metals. A walkthrough was performed assessing safety, hygiene, ventilation and use of personal protective equipment. Workers in the departments with manganese concentrations above NIOSH REL completed a symptoms survey and were assessed by occupational medicine physicians, with a specific focus on neurological assessments.

Results Environmental sampling of manganese concentration was above 1 mg/m^3 in three departments; highest measurement was 6.7 mg/m^3. Walkthrough survey revealed inadequate ventilation in all three departments and improper PPE use among 72% workers. 27 exposed workers were evaluated with symptom questionnaire and clinical exam focusing on neuropsychologic and neuropsychiatric findings; 4 of those workers had evidence of parkinsonism on exam and symptom survey. Those workers were immediately removed from the worksite. Biomarkers were sent for evaluation and the workers were sent for neurological referral.

Conclusion Manganese exposure at work is associated with increased risk of Parkinsonism. We identified a cluster of manganese exposed workers with Parkinsonism in a factory with inadequate ventilation and poor hygiene practice. Based on the findings from this case study we are able to develop a simple neurological assessment tool for the exposed worker.

1714c ASSOCIATION BETWEEN H3K4ME3/BDNF AND THE COGNITIVE FUNCTION OF WORKERS OCCUPATIONALLY EXPOSED TO ALUMINIUM

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10.1136/oemed-2018-ICOHabstracts.827

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