patient to refrain from an avoidance behaviour for the triggers, thus improving quality of life and social functioning.

1639 ORGANOPHOSPHORUS PESTICIDE-INDUCED NEUROTOXICITY IN HUMAN APPLICATORS AND ANIMALS WITH COMPARABLE EXPOSURES

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Aim of special session Preventable chlorpyrifos exposures produce durable behavioural deficits in humans and animals; animal studies suggest oxidative stress contributes to cognitive deficits.

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1639a BIOMARKERS OF CHLORPYRIFOS AND PROFENOFOS EXPOSURE AND EFFECT IN ADULT AND ADOLESCENT EGYPTIAN COTTON FIELD WORKERS

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Introduction Chlorpyrifos (CPF) and profenofos (PFF) are organophosphorus (OP) pesticides that are applied seasonally in Egypt to cotton fields. Urine trichloro-2-pyridinol (TCPy), a specific CPF metabolite, and 4-bromo-2-chlorophenol (BCP), a specific PFF metabolite, are biomarkers of exposure, while inhibition of blood butyrylcholinesterase (BChE) and acetylcholinesterase (AChE) activities are effect biomarkers which may be associated with neurotoxicity.
Methods Urine TCPy and BCP and blood BChE and AChE activities were measured in 37 adult Egyptian Ministry of Agriculture workers during and after 9–17 consecutive days of CPF application followed by PFF (8–10 days), and a second CPF application (5 days) in 2008. In a separate longitudinal study, 57 adolescent applicators and 38 age-matched non-applicators were studied over 10 months in 2010.
Results During the OP applications, mean TCPy and BCP levels were significantly higher than baseline levels and remained elevated following the application periods. Peak urinary BCP and peak TCPy levels for individuals (ranging from 13.4 to 8052 and 16.4 to 30,107 ug/g creatinine, respectively) were also highly correlated ($r=0.77$, $p<0.001$). In adults, a significant inverse correlation was observed between urinary TCPy and blood BChE and AChE activities. In the adolescent study, the mean peak TCPy levels were less than the adults, but the exposure-effect relationship for BuChE inhibition was similar to adults. Both adolescent groups had elevated TCPy and depressed BChE which persisted for 4–7 weeks after spraying ended.
Conclusion Biomarker data in the adolescent non-applicators, which mirrored that of the applicators, indicated that the non-applicators received environmental CPF exposures. The variability in environmental and occupational exposures suggest that job title and work location should not be used as the sole basis for categorising OP exposures. Together, these results can serve to guide future investigations in assessing health risks of OPs and guide efforts to reduce exposures.

1639b OCCUPATIONAL PESTICIDE EXPOSURE AMONG EGYPTIAN ADOLESCENTS: CHANGES OVER TIME

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Introduction While the impact of acute high exposures (i.e., poisoning) to organophosphorus insecticides is well understood, the impact of low level exposures, particularly on neurobehavioral functioning, is still under debate. Even less information is available regarding cumulative exposure, particularly among adolescents who may be working in agriculture. The goal was to examine the impact of chlorpyrifos exposure on biomarkers of exposure and neurobehavioral performance in adolescents across an application season.
Methods Male Egyptian adolescents (applicators and non-applicators) were assessed 35 times before, during and after the pesticide application season. At each session, participants ($n=89$) completed a neurobehavioral test battery and urine was collected for analysis of the chlorpyrifos metabolite 3,5,6-trichloro-2 pyridinol (TCPy) (biomarker of exposure). Cumulative urinary TCPy over the study period was used to classify participants into low (<median) and high (≥median) exposure groups.
Results Urinary TCPy increased during application with recovery following the end of application. High exposed participants had significantly elevated metabolite levels throughout the 10 month study period. Deficits in motor skills and slower reaction times, along with deficits in executive function and short-term memory were found between the high and low exposure groups. Changes in neurobehavioral performance across the application season indicate a pattern of impaired performance among the high exposed compared to the low exposed. Deficits increased during the application season and remained for months after application ended.
Conclusion The findings indicate that neurobehavioral deficits increase during the application season, as exposure also increases, and remain after the application ends, even when the biomarkers of exposure are reduced. This is particularly important when considering the developmental changes that occur during adolescence. An intervention to reduce pesticide exposure has been implemented in this population.

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1639c ORGANOPHOSPHORUS PESTICIDE NEUROTOXICITY IN EGYPTIAN APPLICATORS

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Introduction Chronic occupational exposure to organophosphorus pesticides (OPs) is consistently associated with deficits on neurobehavioral tests when compared to unexposed groups. However, a dose-response relationship has not been established, leading some to doubt an association between

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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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.

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

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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