A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP1677.

Respiratory, Dermal, and Eye Irritation Symptoms Associated with Corexit™ EC9527A/EC9500A following the *Deepwater Horizon* Oil Spill: Findings from the GuLF STUDY

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Background: The large quantities of chemical oil dispersants used in the oil spill response and cleanup (OSRC) work following the *Deepwater Horizon* disaster provide an opportunity to study associations between dispersant exposure (Corexit™ EC9500A or EC9527A) and human health.

Objectives: Our objectives were to examine associations between potential exposure to the dispersants and adverse respiratory, dermal, and eye irritation symptoms.

Methods: Using data from detailed Gulf Long-term Follow-up (GuLF) Study enrollment interviews, we determined potential exposure to either dispersant from participant-reported tasks during the OSRC work. Between 27,659 and 29,468 participants provided information on respiratory, dermal, and eye irritation health. We estimated prevalence ratios (PRs) to measure associations with symptoms reported during the OSRC work and at study enrollment, adjusting for potential confounders including airborne total hydrocarbons exposure, use of cleaning chemicals, and participant demographics.

Results: Potential exposure to either of the dispersants was significantly associated with all health outcomes at the time of the OSRC, with the strongest association for burning in the nose, throat, or lungs [adjusted PR (aPR) = 1.61 (95% CI: 1.42, 1.82)], tightness in chest [aPR = 1.58 (95% CI: 1.37, 1.81)], and burning eyes [aPR = 1.48 (95% CI: 1.35, 1.64). Weaker, but still significant, associations were found between dispersant exposure and symptoms present at enrollment.

Conclusions: Potential exposure to Corexit™ EC9527A or EC9500A was associated with a range of health symptoms at the time of the OSRC, as well as at the time of study enrollment, 1–3 y after the spill. https://doi.org/10.1289/EHP1677

Introduction

Background

Over 4.9 million barrels of crude oil was released into the Gulf of Mexico between the explosion of the *Deepwater Horizon* rig on 20 April 2010 and the top-capping of the wellhead on 15 July 2010 (United States Coast Guard 2011). As part of the oil spill response and cleanup (OSRC), approximately 1.8 million gallons (6.8 million liters) of oil dispersant was applied both to the sea surface [1.07 million gallons (4.05 million liters)] and directly into the stream of oil leaving the wellhead 5,000 feet (1.5 km) underwater [0.77 million gallons (2.9 million liters)] (United States Coast Guard 2011). Dispersants are typically used to reduce the interfacial tension between crude oil and water and facilitate the breakup of oil slicks into small droplets that are thought to be more easily dispersed by natural processes such as wind and wave action (Chapman et al. 2007). Two dispersants were used in the *Deepwater Horizon* spill response: Corexit™ EC9500A (9500A), which was applied at both the water surface and the subsurface wellhead, and Corexit™ EC9527A (9527A), which was applied only at the water surface (Kujawinski et al. 2011). Both dispersants are composed of propylene glycol and organic salts including dioctyl sodium sulfosuccinate (DOSS). Additionally, 9500A contains petroleum distillates, whereas 9527A does not contain petroleum distillates but does contain 2-butoxyethanol (Wise and Wise 2011).

Dispersants were applied to the surface either through aerial spraying or by vessels within 3 nautical miles (5.5 km) of the wellhead area. Aerial application consisted of both 9527A and 9500A from 22 April until 22 May, after which 9500A was used exclusively. Vessels in the wellhead area applied 9500A exclusively (BP Gulf Science Data 2016a). Subsurface application of 9500A was accomplished through a remotely operated underwater vehicle injecting dispersant directly into the stream of oil leaving the wellhead (BP Gulf Science Data 2016b). Based on these uses, the most likely avenues for human exposure among responders are from dermal exposure and from inhalation of dispersant aerosol droplets.

Previous epidemiologic studies have found adverse health effects associated with oil spill cleanup work (Aguilera et al. 2010; Laffon et al. 2016). Effects have included increased lumbar pain, migraine, dermatitis, eye and throat irritation, and respiratory symptoms. Most epidemiologic studies have focused on the acute effects of crude oil exposure during spill cleanup, although Zock et al. (2012) found an association between participating in cleanup work and self-reported respiratory symptoms 5 y after the spill response in workers who responded to the *Prestige* oil spill in 2002. Although dispersants were used in some of these previous OSRC operations, no studies looked at distinguishing effects of exposure to the dispersants.

In contrast, much of the research on dispersants has focused on their efficacy in dispersing oil (Prince et al. 2013) and on potential adverse impacts on the environment (Kleindienst et al.

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Supplemental Material is available online (https://doi.org/10.1289/EHP1677).
M.R.S. provided a deposition for the Celanese Chemical Company, which has no oil or gas holdings, in August 2016. During this deposition, M.R.S. served as a corporate representative and not an expert witness on Celanese's asbestos-related practices in the 1950s, 1960s, and 1970s. M.R.S. worked for Celanese Chemical Group from 1972 to 1992 as the Manager of Industrial Hygiene. All other authors declare they have no actual or potential competing financial interests.

Received 25 January 2017; Revised 20 June 2017; Accepted 26 June 2017; Published 15 September 2017.

2015). Wise and Wise (2011) published a review of studies examining the toxicity of various dispersants, including 9500A and 9527A, in certain model species, finding that both dispersants exhibited similar acute toxicity to crustaceans and mollusks and that oral exposure to 9527A adversely affected intestinal function in rat models.

In response to public concerns regarding the use of dispersants during the OSRC, the U.S. Environmental Protection Agency (EPA) commissioned a series of trials testing the acute toxicity of eight oil dispersants in representative Gulf species, classifying 9500A as either "slightly toxic" or "practically nontoxic" depending on the species (Hemmer et al. 2010a). Similarly, dispersant–oil mixtures were reported to be no more toxic to those Gulf species than crude oil alone (Hemmer et al. 2010b). However, the U.S. EPA did not investigate the effects of exposure to 9527A. Since the spill, additional research has shown that dermal exposure to 9500A resulted in dermal irritation and sensitization in mice (Anderson et al. 2011), although a 5-h inhalation exposure to 9500A did not appear to result in significant adverse pulmonary symptoms in rats (Roberts et al. 2011). However, these studies of mice and rats did not include a coexposure of crude oil or other petroleum by-products that would be expected to be present in the *Deepwater Horizon* oil spill environment.

Using *in vitro* cultures of human bronchial cells, Shi et al. (2013) showed that exposure to either 9500A or 9527A resulted in a significant loss of cell viability and that the loss of viability was dose-dependent. Similarly, Major et al. (2016) found that exposing human bronchial cells to individual mixtures of 9500A and 9527A with crude oil induced both cytotoxic and genotoxic effects. Although data on toxicity of dispersants are limited, there is some evidence of effects caused by the component ingredients of each dispersant. Human exposure studies have shown that propylene glycol is a mild irritant when applied dermally, and animal studies of respiratory effects due to inhalation exposure are inconclusive (ATSDR 1997). In contrast, 2-butoxyethanol is considerably more toxic, with acute respiratory effects and eye irritation observed in both human and animal studies, although minimal dermal effects have been observed in human studies (ATSDR 1998). The Material Safety Data Sheet (MSDS) for DOSS lists the chemical as irritating to the skin and eyes and as a possible respiratory irritant (Acros Organics 2013). We were unable to find any studies of direct effects of either 9500A or 9527A on human health.

Given the lack of epidemiologic research into the effects of dispersant exposure on human health, our study used data from a large cohort of workers participating in the *Deepwater Horizon* OSRC to assess two related objectives. The first objective was to quantify associations of potential exposure to dispersants with adverse respiratory, eye irritation, and dermal effects at the time of the OSRC; the second objective was to quantify associations of potential exposure to dispersants with adverse respiratory, eye irritation, and dermal effects in the 30 days before study enrollment, 1–3 years after the OSRC.

Methods

Study Design

Data were from the Gulf Long-term Follow-up Study (GuLF STUDY), a prospective cohort study of persons involved in the OSRC following the 2010 *Deepwater Horizon* oil spill (Kwok et al. 2017). Briefly, a total of 32,608 participants completed a telephone interview to enroll in the study between March 2011 and March 2013. This detailed interview collected information on particulars of the participant's OSRC work, if any, in addition to demographic factors, lifestyle information, and medical history/symptoms both at the time of the OSRC and at the time of the interview. The interview for Vietnamese-speaking participants was abbreviated and did not collect information that could be used to assess potential dispersant exposure; therefore, those participants ($n = 999$) were excluded from this analysis. Additionally, we excluded any remaining participants with missing data on the exposure of interest, on the outcomes of interest, or on covariates, leaving study populations of 28,636 for analyses of respiratory outcomes, 27,659 for dermal outcomes, and 29,468 for eye irritation outcomes. The study was approved by the Institutional Review Board of the National Institute of Environmental Health Sciences/National Institutes of Health. After receiving information about the study in the mail, participants provided verbal consent for the enrollment telephone interview.

Exposure Assessment

Participants were categorized as workers if they worked at least one day engaged in OSRC activities. Nonworkers received safety training but never worked on the response. For respiratory and eye irritation analyses, dispersant exposure for workers was classified as "ever/never" based on a positive response to any interview question asking about direct work with dispersants or work on a ship from which dispersants were applied (see Table S1). Additionally, participants were classified as exposed if they responded positively to working on any task that involved dispersant-related equipment, such as pumps, for more than half of the time. For dermal analyses, dermal dispersant exposure for workers was classified as "ever/never" based on self-reported skin or clothing contact with dispersants during the OSRC for breaking up the oil on or below the surface of the water. Although the questionnaire did not specifically refer to either Corexit™ 9527A or Corexit™ 9500A by name, these were the only oil dispersants used during the OSRC, and it is therefore reasonable to consider reported exposure to dispersants as reported exposure to either Corexit™ 9527A or Corexit™ 9500A. Office workers, workers who said no to all dispersant-related questions, and those who received safety training but did not work on the OSRC were assumed to be unexposed and were categorized as such for all analyses.

Using publicly available data on dates and locations of use of specific dispersants in the spill response (BP Gulf Science Data 2016a, 2016b), we categorized exposed participants as potentially exposed to 9500A only or as potentially additionally exposed to 9527A. Because 9527A was used in aerial applications only prior to 22 May 2010, we categorized participants who reported working on the relevant tasks during that period as potentially exposed to 9527A. Those who only worked on spraying dispersant from vessels or pumping dispersant to the wellhead and those who only reported working with dispersants after 22 May were classified as potentially exposed to 9500A only.

Additionally, among those classified as exposed in the respiratory and eye irritation analyses, participants were classified as directly working with dispersants if they had a positive response to any questionnaire item related to personally working with dispersants (see Table S1). Any participant who reported a positive response to a question about dispersant exposures but did not report this direct exposure was categorized as indirectly working with dispersants.

Outcome Assessment

Outcomes were based on participant responses to questions on the enrollment interview about the frequency of symptoms at the time of the OSRC or at the time of the enrollment interview.

Participants reported the frequency of symptoms on an ordinal scale: "never," "rarely," "sometimes," "most of the time," or "all of the time," and a symptom was considered present (yes vs. no) if the response was "most of the time" or "all of the time." Five distinct respiratory symptoms (cough, wheeze, tightness in chest, shortness of breath, burning in nose/throat/lungs), one dermal symptom ($\geq$2 d of eczema, dermatitis, other skin rashes, sores, or blisters), and two eye irritation symptoms (itchy eyes, burning eyes) were assessed.

Potential Confounders

We considered a variety of potential confounders. Demographic data including age, race, gender, and education level, as well as smoking status, employment status, financial worry, preexisting lung conditions, potential exposure to equipment decontamination chemicals and skin/clothing contact with oil or decontamination chemicals were assessed from responses on the enrollment interview. Residential proximity to the spill site was categorized based on the proximity of the county of residence to the Gulf [adjacent to the Gulf Coast, counties one county inland from the Gulf coast, other Gulf state (AL, FL, LA, MS, TX) counties, or non–Gulf state counties]. Approximate maximum daily time-weighted average airborne level of total hydrocarbons (THC) exposure over all OSRC tasks was estimated using an ordinal job exposure matrix (Kwok et al. 2017; Stewart et al. in press). Perceived stress was assessed using Cohen's Perceived Stress Scale (Cohen et al. 1983).

Statistical Analyses

Owing to the cross-sectional nature of the data and the moderately high prevalence of the outcomes of interest among the study population (Table 1), we calculated adjusted prevalence ratios (aPRs) as the measure of effect rather than odds ratios because of ease of interpretation (Thompson et al. 1998). We fit multivariable log-binomial regression models to directly estimate the PR for each outcome in the exposed group compared with the unexposed group. Models were adjusted for a variety of *a priori* potential confounders depending on the outcome of interest. All models were adjusted for age at enrollment (<30, 30–45, >45), race (white, black, or other), gender, and education level (>high school degree or not). Models of dermal symptoms were also adjusted for skin or clothing contact with oil or tar (yes/no) and skin or clothing contact with equipment decontamination chemicals (yes/no). Models of both eye irritation and respiratory symptoms were also adjusted for residential proximity to the spill site, smoking status (never smoker, former smoker, light current smoker, or heavy current smoker), potential exposure to equipment decontamination chemicals (yes/no), and the maximum estimated airborne level of THC exposure (<0.3 ppm, 0.3–0.99 ppm, 1.00–2.99 ppm, $\geq$3.00 ppm) across all OSRC work. Models for respiratory symptoms were further adjusted for the presence of self-reported preexisting lung conditions (yes/no). All models of symptoms at the time of enrollment were further adjusted for employment status (employed, unemployed, disabled, retired), financial worry (yes/no), and Cohen's Perceived Stress Scale (0–5, 6–10, $\geq$11) at enrollment.

Because nonconvergence can be an issue with log-binomial regression owing to the model's restricted parameter space, we used the weighted COPY method outlined by Deddens and Petersen (2008) to approximate the maximum likelihood estimates and related standard errors for any models that did not initially converge, using 1,000,000 virtual copies of the data set. All analyses were performed using SAS version 9.3 (SAS Institute Inc.). We used a significance level of $p < 0.05$ for all analyses.

Sensitivity/Secondary Analyses

Because these data are self-reported, there is a potential for recall and reporting bias to influence the participant's reporting of symptoms. We used self-reported excessive hair loss at the time of the OSRC or in the 30 d before enrollment to identify participants who may have over-reported their symptoms because there is no known biological mechanism that would relate dispersant exposure to excessive hair loss. All analyses were repeated after restricting the study populations to those without self-reported excessive hair loss at the time point of interest (i.e., symptoms during the spill or within 30 d of enrollment) to help assess any potential impact of reporting bias on the results.

Some nonworkers who completed safety training but were not hired to work on the OSRC may have had preexisting health conditions or other factors (such as obesity) that either prevented them from working or made them less attractive to contractors charged with staffing the cleanup effort. As such, having them as a part of the comparison group in the analyses could result in biased estimates in comparison with an analysis comparing exposed workers with unexposed workers. To help assess any impact of such a potential healthy-worker selection effect, we repeated all analyses with nonworkers excluded from the analysis.

Because some participants who worked on land reported working directly with dispersants, there was concern that participants may have confused dispersants with chemicals used to clean and decontaminate equipment because these chemicals were used to "disperse" the oil from the equipment. Therefore, we conducted a sensitivity analysis excluding any respondents whose only exposure was reported handling of dispersants on land who also reported active participation in equipment decontamination activities. We also conducted sensitivity analyses excluding exposed workers who reported being exposed outside the known dates of dispersant use; furthermore, we performed sensitivity analyses assessing potential confounding resulting from relevant personal protective equipment (PPE) use during the OSRC (i.e., respirators/facemasks for respiratory symptoms, rubber gloves or coveralls for dermal symptoms). We also assessed potential effect measure modification by PPE (i.e., respirator or face mask) use among respiratory outcomes. More than 97% of those reporting dermal exposure also reported the use of PPE (i.e., gloves, protective clothing); therefore, there was insufficient heterogeneity to investigate potential effect modification of dispersant contact by this variable (Table 1). In the questionnaire, we did not ascertain whether PPE was worn during specific tasks, so here, we used overall PPE use as a proxy.

Among OSRC workers, models of respiratory and eye irritation were stratified based on three mutually exclusive worker locations—ever worked on the water in the area of the wellhead, ever worked on the water but not near the wellhead, or worked only on land—to capture potential environmental differences between the locations. For example, workers near the wellhead area would likely have been exposed to increased particulate matter from the flaring of oil/gas by two vessels in the wellhead area. For models of symptoms within 30 d of enrollment, participants were also stratified by the reported presence/absence of the symptom of interest at the time of the spill in order to investigate persistence across time points.

Given that those exposed to dispersants largely worked in areas where they might have also had exposure to THC, we investigated potential effect modification of the dispersant by the estimated maximum airborne level of THC (<0.3 ppm, 0.3–0.99 ppm, 1.0–2.99 ppm, and $\geq$3.0 ppm) over all OSRC jobs. We also investigated potential effect modification by exposure to decontamination chemicals. Because 97% of those reporting skin/clothing

Table 1. Enrollment characteristics of each analysis population.

Characteristic	Respiratory analysis group[a] ($n=28,636$)		Eye irritation analysis group[a] ($n=29,468$)		Dermal analysis group[a] ($n=27,659$)	
	Dispersant exposure ($n=2,178$)	No dispersant exposure ($n=26,458$)	Dispersant exposure ($n=2,238$)	No dispersant exposure ($n=27,230$)	Dispersant exposure ($n=1,039$)	No dispersant exposure ($n=26,620$)
Age at enrollment, years						
<30	532 (24%)	5,182 (20%)	543 (24%)	5,285 (19%)	187 (18%)	5,241 (20%)
30–45 years	911 (42%)	9,861 (37%)	932 (42%)	10,130 (37%)	458 (44%)	9,882 (37%)
>45	735 (34%)	11,415 (43%)	763 (34%)	11,815 (43%)	394 (38%)	11,497 (43%)
Gender						
Male	1,961 (90%)	21,137 (80%)	2,014 (90%)	21,735 (80%)	962 (93%)	21,153 (79%)
Female	217 (10%)	5,321 (20%)	224 (10%)	5,495 (20%)	77 (7%)	5,467 (21%)
Race						
White	952 (44%)	18,105 (68%)	976 (44%)	18,501 (68%)	481 (46%)	17,861 (67%)
Black	986 (45%)	5,701 (22%)	1,011 (45%)	5,918 (22%)	411 (40%)	5,983 (22%)
Other	240 (11%)	2,652 (10%)	251 (11%)	2,811 (10%)	147 (14%)	2,776 (10%)
Education						
High school education or less	1,318 (61%)	11,741 (44%)	1,355 (61%)	12,195 (45%)	625 (60%)	11,946 (45%)
Greater than high school education	860 (39%)	14,717 (56%)	883 (39%)	15,035 (55%)	414 (40%)	14,674 (55%)
Maximum total hydrocarbon exposure, ppm						
<0.3	28 (1%)	5,040 (19%)	28 (1%)	5,136 (19%)	–	–
0.3–0.99	369 (17%)	6,857 (26%)	373 (17%)	7,050 (26%)	–	–
1.0–2.99	635 (29%)	5,966 (23%)	658 (29%)	6,147 (23%)	–	–
≥3.0	1,146 (53%)	1,949 (7%)	1,179 (53%)	2,002 (7%)	–	–
Exposed to decontamination chemicals						
Yes	1,612 (74%)	5,068 (19%)	1,656 (74%)	5,254 (19%)	–	–
No	566 (26%)	21,390 (81%)	582 (26%)	21,976 (81%)	–	–
Residential proximity to spill						
Directly affected county	1,301 (60%)	14,208 (54%)	1,338 (60%)	14,705 (54%)	–	–
Indirectly affected county	163 (7%)	1,717 (6%)	164 (7%)	1,778 (7%)	–	–
Other Gulf state county	465 (21%)	5,434 (21%)	483 (22%)	5,582 (20%)	–	–
Non–Gulf state residence	249 (11%)	5,099 (19%)	253 (11%)	5,165 (19%)	–	–
Smoking status						
≥1 pack per day	229 (11%)	2,687 (10%)	233 (10%)	2,768 (10%)	–	–
<1 pack per day	629 (29%)	4,888 (18%)	640 (29%)	5,057 (19%)	–	–
Former smoker	357 (16%)	5,865 (22%)	369 (16%)	6,022 (22%)	–	–
Never smoker	963 (44%)	13,018 (49%)	996 (45%)	13,383 (49%)	–	–
Preexisting lung condition						
Yes	263 (12%)	3,186 (12%)	–	–	–	–
No	1,915 (88%)	23,272 (88%)	–	–	–	–
Any relevant PPE use[b]						
Yes	777 (48%)	2,149 (21%)	–	–	1,012 (97%)	13,284 (89%)
No	839 (52%)	8,196 (79%)	–	–	27 (3%)	1,684 (11%)
Skin or clothing contact with oil/tar						
Yes	–	–	–	–	1,006 (97%)	8,306 (31%)
No	–	–	–	–	33 (3%)	18,314 (69%)
Skin or clothing contact with decontamination chemicals						
Yes	–	–	–	–	624 (60%)	1,434 (5%)
No	–	–	–	–	415 (40%)	25,186 (95%)

Note: PPE, personal protective equipment.
[a]Dashes (–) indicate variables that were not examined as covariates in that analysis population.
[b]$n=11,961$ for respiratory analysis population, $n=16,007$ for dermal analysis population.

contact with dispersants also reported skin/clothing contact with oil/tar (Table 1), there was insufficient heterogeneity to investigate whether oil/tar contact modified the effect of dispersant contact.

Results

Table 1 shows the baseline characteristics of participants in each analytic study population. Approximately 7.6% of participants included in the respiratory symptom and eye irritation analyses were considered exposed to dispersants. Among those included in the analysis of dermal symptoms, 3.8% had direct skin or clothing contact with dispersants.

The study population was overwhelmingly male; approximately 80% of the unexposed were men as were ~90% of the exposed. Those exposed to dispersants were more likely to be nonwhite, less likely to have any education beyond high school, and more likely to be <45 y old compared with those who were unexposed. For the respiratory and eye irritation analyses, those exposed were more likely to be current smokers (39% vs. 29% for the unexposed) and live in Gulf Coast counties. Given where dispersants were used during the OSRC, it is unsurprising that those exposed to dispersants were more likely to have also been exposed to levels of airborne THC >3.0 ppm (ppm) (53% vs. 7%) and to have worked with equipment decontamination chemicals (74% vs. 19%). Among those included in the respiratory analyses, there was no difference in the prevalence of preexisting lung conditions between the exposed and unexposed groups. For the dermal analyses, those exposed to dispersants were substantially more likely to have also come into contact with oil or tar (97% vs. 31% for the unexposed group) as well as more likely to have come into contact with equipment decontamination chemicals (60% vs. 5%).

Table 2 presents the prevalence of each symptom reported at the time of the OSRC along with aPRs. The prevalence of each

Table 2. Symptoms at spill response associated with dispersant exposure (GuLF STUDY, 2011–2013).

Symptom	Exposed [*n* (%)]	Unexposed [*n* (%)]	aPR (95% CI)[a]
Cough[b]	534 (25%)	2,642 (10%)	1.41 (1.28, 1.55)
Wheeze[b]	426 (20%)	2,050 (8%)	1.36 (1.23, 1.52)
Tightness in chest[b]	305 (14%)	1,248 (5%)	1.58 (1.38, 1.81)
Shortness of breath[b]	387 (18%)	1,827 (7%)	1.41 (1.26, 1.58)
Burning in nose, throat, lungs[b]	367 (17%)	1,325 (5%)	1.61 (1.42, 1.83)
Burning eyes[c]	512 (23%)	2,261 (8%)	1.49 (1.35, 1.64)
Itching eyes[c]	659 (29%)	3,362 (12%)	1.35 (1.24, 1.46)
Skin irritation[d]	548 (53%)	4,345 (16%)	1.34 (1.25, 1.43)

Note: aPR, adjusted prevalence ratio; CI, confidence interval.
[a]All models adjusted for gender, age, race, education. Skin irritation models further adjusted for contact with oil/tar, contact with cleaning chemicals, and dispersant/oil interaction. Respiratory and eye irritation models at spill further adjusted for smoking, residential proximity to oil spill, level of oil exposure (total hydrocarbons, THC), use of decontamination chemicals, and preexisting lung disease (respiratory models).
[b]$n = 28{,}636$ (2,178 exposed, 26,458 unexposed).
[c]$n = 29{,}468$ (2,238 exposed, 27,230 unexposed).
[d]$n = 27{,}659$ (1,039 exposed, 26,620 unexposed).

respiratory symptom reported at the time of the OSRC (cough, wheeze, shortness of breath, tightness in the chest, and burning in the nose, throat, or lungs) was significantly higher in the exposed group than in the unexposed group, with aPRs ranging from 1.36 [95% confidence interval (CI): 1.23, 1.52] for wheeze to 1.61 (95% CI: 1.42, 1.83) for burning in the nose, throat, or lungs. Similarly, the adjusted prevalences at the time of the OSRC for burning in the eyes and for itching in the eyes, as well as the adjusted prevalence for ≥2 d of itching or dermatitis, were significantly higher in the exposed group than in the unexposed group. Direct exposure to dispersants was more strongly associated with each respiratory and eye irritation outcome at the time of the OSRC than was indirect exposure, with nonoverlapping confidence intervals for shortness of breath (Table 3).

For most symptoms at the time of the OSRC, aPRs were higher for possible exposure to 9527A than for exposure to only 9500A, although the aPRs were not markedly different except for tightness in the chest [aPR = 1.79 (95% CI: 1.45, 2.21) vs. aPR = 1.33 (95% CI: 1.10, 1.63), respectively] and burning in the nose, throat, or lungs [aPR = 1.82 (95% CI: 1.52, 2.19) vs. aPR = 1.22 (95% CI: 1.01, 1.47) respectively], and only the latter symptom had nonoverlapping confidence intervals (see Table S2).

There was little difference in the associations between symptoms and dispersant use in analyses stratified by work location, and the confidence intervals overlapped, although aPRs tended to be higher among those who worked on the water away from the wellhead than among those who did not work on the water and those who worked near the wellhead (see Table S3). Exclusion of participants reporting hair loss ($n = 578$, $n = 612$, and $n = 617$ for respiratory, eye, and dermal symptoms, respectively) did not materially change any of the PR estimates or confidence intervals, although there was a nonsignificant positive association between self-reported hair loss and dispersant exposure [aPR = 1.24 (95% CI: 0.95, 1.61)]. Similarly, excluding participants whose only dispersant exposure was on land and who also worked with cleaning chemicals did not affect the results, indicating that any potential misclassification resulting from confusing cleaning chemicals with dispersants was minor. Exclusion of nonworkers and exclusion of participants with invalid self-reported dates of dispersant use also had negligible effects on the results.

Table 3. Respiratory and eye irritation symptoms at the time of spill response associated with dispersant exposure, differentiating exposure by direct or indirect exposure (GuLF STUDY 2011–2013).

Outcome	Direct work with dispersants PR[a] (95% CI)	Indirect work with dispersants PR[a] (95% CI)
Cough	1.47 (1.31, 1.63)	1.29 (1.13, 1.47)
Wheeze	1.45 (1.28, 1.63)	1.17 (1.01, 1.36)
Tightness in chest	1.74 (1.48, 2.04)	1.30 (1.07, 1.58)
Shortness of breath	1.63 (1.43, 1.85)	1.07 (0.90, 1.27)
Burning in nose/throat/lungs	1.75 (1.52, 2.02)	1.30 (1.09, 1.55)
Burning eyes	1.58 (1.41, 1.76)	1.28 (1.12, 1.47)
Itchy eyes	1.39 (1.27, 1.52)	1.17 (1.05, 1.31)

Note: CI, confidence interval; PR, prevalence ratio.
[a]Adjusted for gender, age, race, education, smoking, residential proximity to oil spill, level of oil exposure (total hydrocarbons, THC), use of decontamination chemicals, and preexisting lung disease (respiratory models).

Table 4. Symptoms within 30 days of study enrollment associated with dispersant exposure (GuLF STUDY, 2011–2013).

Symptom	Exposed [*n* (%)]	Unexposed [*n* (%)]	aPR (95% CI)[a]
Cough[a]	594 (27%)	3,896 (15%)	1.03 (0.96, 1.11)
Wheeze[a]	479 (22%)	2,400 (9%)	1.16 (1.06, 1.26)
Tightness in chest[a]	337 (16%)	1,455 (6%)	1.30 (1.16, 1.46)
Shortness of breath[a]	434 (20%)	2,129 (8%)	1.15 (1.06, 1.26)
Burning in nose, throat, lungs[a]	246 (11%)	1,005 (4%)	1.55 (1.34, 1.80)
Burning eyes[c]	363 (17%)	1,699 (6%)	1.44 (1.28, 1.61)
Itching eyes[c]	482 (22%)	2,758 (11%)	1.24 (1.12, 1.36)
Skin irritation[d]	207 (21%)	8,891 (35%)	0.84 (0.74, 0.95)

Note: aPR, adjusted prevalence ratio; CI, confidence interval.
[a]All models adjusted for gender, age, race, education, unemployment, disability, financial and perceived stress. Skin irritation models further adjusted for contact with oil/tar, contact with cleaning chemicals, and dispersant/oil interaction. Respiratory and eye irritation models at spill further adjusted for smoking, residential proximity to oil spill, level of oil exposure (total hydrocarbons, THC), use of decontamination chemicals, and preexisting lung disease (respiratory models).
[b]$n = 28{,}183$ (2,163 exposed, 26,020 unexposed).
[c]$n = 28{,}363$ (2,181 exposed, 26,182 unexposed).
[d]$n = 26{,}249$ (1,001 exposed, 25,248 unexposed).

Stratification by the estimated maximum level of THC exposure over all OSRC jobs did not reveal any meaningful differences in the associations between dispersant exposure and any of the respiratory and eye irritation symptoms at the time of the spill (see Table S4). Reported PPE use at any time during the OSRC did not confound the association between dispersant exposure and any of the respiratory or dermal symptoms at the time of the spill, and there was no significant evidence of effect measure modification among any of the respiratory symptoms.

For each symptom, the aPR was lower for symptoms present at the time of study enrollment than for symptoms present at the time of the OSRC (Table 4). However, dispersant exposure remained significantly associated with the prevalence of symptoms at the time of study enrollment, with the exception of cough and skin irritation.

Among participants who reported the presence of a given symptom at the time of the OSRC, dispersant use remained significantly associated only with burning eyes at the time of study enrollment. However, among those participants who did not report a given symptom at the time of the OSRC, dispersant use was significantly associated with all outcomes except cough and itching eyes at the time of study enrollment (see Table S5). Exposure to dispersants was associated with a decreased likelihood of reported skin irritation within 30 d of enrollment among those who did not report skin irritation at the time of the spill.

Discussion

This study is the first to evaluate associations between potential exposure to dispersants, specifically Corexit™ EC9527A or EC9500A, and respiratory, eye irritation, and dermal symptoms both during the OSRC and at study enrollment 1–3 y later. OSRC workers with potential exposure to either Corexit™ product were more likely to have reported adverse symptoms at the time of the spill. Previous studies have shown an association between exposure to crude oil and adverse effects among spill responders (Aguilera et al. 2010; Laffon et al. 2016), but no previous spill involved this level of dispersant use or resulted in an investigation of potential associations between dispersant use and adverse health effects. *In vitro* results suggested that 9527A and 9500A may have adverse effects on human lung tissue (Major et al. 2016; Shi et al. 2013). Our results provide epidemiological evidence to suggest that exposure to 9527A or 9500A may be associated with adverse health effects, even after taking into account exposure to the crude oil.

Based on the known irritant properties of chemicals in the dispersants, we hypothesized that there might be acute effects at the time of the cleanup, but we did not expect there to be longer-term effects at the time of enrollment. Although we observed associations between dispersant use and symptoms at both time points, among participants with a given symptom at the time of the OSRC, only increased prevalence of burning eyes at enrollment remained significantly associated with dispersant exposure, consistent with a lack of persistent effects of the dispersants. The significant associations between exposure and symptoms at the time of enrollment among those who did not have symptoms at the time of the OSRC were unexpected and are difficult to explain. Although it is possible that these associations are measuring some latent effect of exposure to the dispersants, another possibility is that some of these symptoms may have been present at the time of the OSRC but were not intense enough for the study participants to recall 1–3 y later. The inverse association between skin/clothing contact with dispersant during the OSRC and skin irritation reported at the time of enrollment was also unexpected and is difficult to explain. Many media reports at the time of the study linked skin lesions with work or recreational activities involving contact with water from the Gulf of Mexico (Marsa 2016; Landau 2010). We were unable to account for current recreational contact with the water in this analysis.

As would be expected, direct work with dispersants was more strongly associated with the respiratory and eye irritation outcomes than indirect exposure through working in an area where dispersants were used. Even so, for most symptoms, indirect exposure was significantly associated with the symptom, indicating that these likely lower exposures may also be important. Stratification by airborne level of THC exposure showed no evidence for effect modification by THC on the associations between dispersant exposure and either respiratory or eye irritation symptoms.

The exposure measures used in this analysis were based on self-reported responses to questions about work locations and dispersant-related tasks and do not allow exploration of exposure–response relationships. A quantitative job exposure matrix for Corexit™ exposure that takes into account the chemical and physical properties of the chemicals and external information on patterns of use may allow evaluation of exposure–response relationships in the future.

The GuLF STUDY is the largest prospective study of OSRC workers to date, and it provides an excellent opportunity to investigate less-common spill-related exposures and health outcomes (Kwok et al. 2017). The detailed questionnaire provided the opportunity to assess previously understudied health effects associated with dispersants while also taking into account a wide variety of potentially confounding factors.

However, our approach relied almost entirely on self-reported data, which provides several opportunities for bias. When possible, these potential sources of bias were investigated using a variety of sensitivity analyses. One potential concern is the over-reporting of symptoms. We addressed this concern by investigating the relationship between each exposure metric and self-reported unusual amount of hair loss at the time of the spill, which does not have any known biological relationship to exposure to either 9527A or 9500A. The positive association between dispersant exposure and self-reported excessive hair loss, although not statistically significant, suggests the possibility of bias due to over-reporting. However, excluding participants who reported excessive hair loss did not meaningfully change the results, suggesting that over-reporting does not explain our findings. Similarly, exclusion of nonworkers did not result in a meaningful difference in any of the results, indicating no appreciable effect on the overall associations resulting from nonworkers potentially having preexisting worse health than workers (i.e., a healthy worker selection effect). Associations between dispersant exposure and each outcome were somewhat stronger among workers who spent time on the water away from the wellhead than among workers who worked only on land or those workers who worked near the wellhead. However, associations at all work locations remained significant, providing evidence that the overall associations were not being driven by unmeasured characteristics of a particular work location.

Misclassification of exposure is another potential problem because of the reliance on self-reported information about the work performed. For example, there was some evidence in open-ended responses in the questionnaire that some participants were confused by the term "dispersant" when responding to questions about decontamination tasks. We attempted to address this issue by excluding participants who reported only a land-based exposure and also reported working on equipment decontamination. The results of that analysis are qualitatively similar to the overall results, indicating that this potential misclassification was unlikely to have played an appreciable role in our results.

It would be expected that the proper use of PPE would help reduce received exposure and any potential adverse effects of this exposure. The MSDSs for both dispersants recommend the use of gloves and standard protective clothing, as well as the use of respirators when concentrations exceed recommended limits (NALCO 2012a, 2012b). Measurements taken by BP and by the National Institute for Occupational Safety and Health (NIOSH) during the OSRC indicate that it is unlikely that airborne concentrations of either 2-butoxyethanol or propylene glycol exceeded recommended limits (BP Gulf Science Data 2016c; NIOSH 2010). No measurements were available for airborne concentrations of DOSS, nor were any dermal exposure measurements during the OSRC available. Although we had no way to ascertain if PPE was used specifically during dispersant-related tasks, a sensitivity analysis among participants who reported PPE use during the OSRC indicated no confounding of the main association by reported PPE use, nor any effect measure modification among respiratory outcomes.

Although our results suggest an association between exposure to 9527A, 9500A, or both and adverse acute symptoms, we were not able to completely distinguish these exposures. Participants who were potentially exposed to 9527A, as identified by date and method of use, reported slightly higher prevalence of most symptoms than those who would have been exposed to only 9500A. Although this outcome could have been caused by the presence of more acutely toxic agents in 9527A, a substantially larger quantity of dispersants was applied during the early period of the OSRC, when both dispersants were being used, than in the later stages of the OSRC, when only 9500A was used (BP Gulf Science Data 2016a, 2016b).

Conclusion

Our findings suggest associations between exposure to dispersants, specifically Corexit™ EC9527A or Corexit™ EC9500A, and adverse acute health effects at the time of the OSRC as well as with symptoms that were present at the time of study enrollment 1–3 y later.

Acknowledgements

The authors thank A. Hodges, J. McGrath, and the rest of the staff at Social and Scientific Systems for data collection and management. We also thank the GuLF STUDY cohort members.

This study was funded by the National Institutes of Health (NIH) Common Fund and the Intramural Program of the National Institute of Environmental Health Sciences/NIH (ZO1 ES 102945).

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