Mechanisms of petroleum hydrocarbon toxicity in fish at early life history stages

ABSTRACT: Intertidal and shallow subtidal zones are areas of high biological diversity and productivity that are particularly susceptible to impact by coastal oil spills. These coastal areas provide critical spawning and rearing habitat for many different marine fish species. For example, several of the major forage fish species (e.g. herring, smelts) in the northeastern Pacific deposit eggs on inter- or subtidal sediments or algal substrates, where they may be directly exposed to oil after a spill. The *Exxon Valdez* spill occurred during the spawning of Pacific herring in Prince William Sound, and subsequent field and laboratory studies documented a common syndrome of edema, craniofacial and body axis defects that occurred in fish larvae that were exposed as embryos to polycyclic aromatic hydrocarbons (PAHs) in weathered crude oil. Even in the absence of malformations, pink salmon exposed to PAHs during development showed a significantly lower rate of marine survival. The toxic mechanisms underlying these effects of PAHs are unknown. Follow-up studies to the 1989 *Exxon Valdez* spill in Alaska and the 1969 *Florida* spill in Massachusetts showed that petroleum hydrocarbons can persist in coastal sediments for decades. However, there is still considerable debate about the lingering effects of oil spills on fish and other wildlife in nearshore ecosystems. Early life history stages tend to be more sensitive to toxic contaminants than adult animals, and new data on the sublethal biological responses of embryonic and larval fish to PAHs are needed to resolve current debate. To understand the mechanisms of PAH toxicity in fish at early life history stages, we are using the zebrafish (*Danio rerio*), a major model for basic studies of vertebrate development and for which there is a broad array of tools for molecular, genetic, and cellular analyses. In preliminary studies, those 3-ring PAHs that are most abundant in weathered crude oil (e.g. phenanthrene) induced a suite of malformations in zebrafish identical to those described for herring and salmon exposed to weathered crude oil under natural post-spill conditions. Using genetic techniques unique to zebrafish, we found that characteristic PAH-induced malformations were secondary to cardiac dysfunction, while the primary mechanism underlying toxicity of 3-ring PAHs appeared to be inhibition of cardiac conduction. Because cardiac morphogenesis is intimately linked to cardiac function, and in fish continues well into the juvenile period, even transient cardiac dysfunction could have irreversible sequelae. Here we propose to extend these mechanistic studies to characterize potential defects in cardiac structure produced by sublethal exposure to model PAH compounds and weathered crude oil, and explore other potential molecular pathways of PAH toxicity in fish embryos and larvae.