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Contamination by oil crude extraction – Refinement and their effects on human health☆

Maria Isabel Ramirez*, Ana Paulina Arevalo, Santiago Sotomayor, Natalia Bailon-Moscoso

[a] Departamento de Ciencias de La Salud, Universidad Técnica Particular de Loja, San Cayetano Alto, Loja, 11-01-608, Ecuador

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ABSTRACT

The harmful effects of oil on various species of flora and fauna have been studied extensively; however, few studies have studied the effects of oil exposure on human health. The objective of this research was to collect information on the acute health effects and serious psychological symptoms of the possible consequences of such exposure to crude oil. Some studies focused on the composition of different chemicals used in the extraction process, and wastes generated proved to be highly harmful to human health. Thus, studies have shown that individuals who live near oil fields or wells – or who take part in activities of cleaning oil spills – have presented health conditions, such as irritation to the skin, eyes, mucous membranes, kidney damage, liver, reproductive, among others. In Ecuador, this reality is not different from other countries, and some studies have shown increased diseases related with oil crude and oil spills, like skin irritation, throat, liver, lung, infertility, and abortions, and it has been linked to childhood leukemia. Other studies suggest a direct relationship between DNA damage because of oil resulting in a genetic instability of the main enzymes of cellular metabolism as well as a relationship with some cancers, such as leukemia.

1. Introduction

The importance of oil began after WWII where large economic growth was seen worldwide (Guseo et al., 2007). With the use of these fossil fuels, new problems arose as evidence suggested that the processes of the extraction, refinement, storage, transportation and combustion of oil and its derivatives caused major global problems, such as the greenhouse effect, depletion of the ozone layer as well as acid rain and pollution. In addition to representing a problem to the environment, it ultimately poses a great danger to life on our planet due to the damage that it causes to the health of entire populations and ecosystems (Ogri, 2001; Veziroğlu & Şahin, 2008). For example, human health effects can result from consuming contaminated food or by bathing in polluted water mainly of rivers (Badawy et al., 1993).

This article briefly reviews the main compounds that are used or produced as waste in the process of oil extraction – as well as products exposed by spills – and their relationships with health problems, since for years, studies have reported health effects, ranging from skin irritation to cancer. Furthermore, we review research both globally and locally, including studies from Ecuador.

2. Study strategy

We performed a literature review using different databases and several key words, including 'health effects caused by oil', 'oil spill health effects', and 'effects of oil derivatives on health'. Our objective was to identify research results where they were assessed; we sought to identify both the physical and psychological health effects on people working in disaster areas associated with oil spills as well as the effects of different exposures (e.g., exposure to workers vs. People living near extraction sites). We organized globally reported data related to health problems and its direct connection with crude oil, oil spills, worker exposure, and, in some cases, the effects of derivatives of crude oil. We sought to better understand this connection since this compound directly affects the lives of people living near oil wells and refining factories or those who have been present at the time of spills either because they lived in the area or near clean-up activities.

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* Corresponding author.
E-mail addresses: miramirez@utpl.edu.ec (M.I. Ramirez), aparevalo1@utpl.edu.ec (A.P. Arevalo), sab_andre@hotmail.com (S. Sotomayor), ncbailon@utpl.edu.ec (N. Bailon-Moscoso).

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3. Contaminants associated with the extraction of crude oil

Oil exploitation involves operational steps including exploration, extraction, refinement, and transportation. Extraction is responsible for bringing natural hydrocarbons (e.g., crude oil) to the surface; for this activity, there are several methods (e.g., mechanical pumping, hydraulic pumping, use of acids). All of these processes produce serious environmental damage, including deforestation and pollution in the air, water, and soil.

The exploration phase, which determines the location and size of oil reserves, is the stage in which several extractions are performed daily in order to evaluate the product. The residuals are placed in pools and in other cases are burned; this generates a large part of the waste and increases the impact on nearby ecosystems and the health of surrounding populations (Bravo, 2007). Moreover, countries like Mexico, Taiwan, Finland, Austria, Spain, among others have expressed concern about the impact of crude oil on their ecosystems and inhabitants (Maldonado and Narváez, 2003; Shcroeder et al., 1999).

As mentioned above, some countries have already expressed concern about the presence of petroleum-derived pollutants, since oil is a complex mixture of several chemical compounds and contains a variety of agents of various toxicological power, including benzene, toluene, xylene, and polycyclic aromatic hydrocarbons, among others. Table 1 summarizes the main reported effects of the chemicals used in the oil extraction process as well as the harmful substances resulting from this process.

Exposure to compounds such as detailed in Table 1 are of concern, and most are ubiquitous in various environmental compartments. They can bioaccumulate in food chains where they disrupt the biochemical or physiological activities of many organisms, thus causing carcinogenesis of some organs, mutagenesis in genetic material, and impairment in reproductive capacity in exposed population (Onwurah et al., 2007).

These pollutants come in direct contact with nature in the form of large atmospheric emissions, waste generation, and effluents that pollute the air, water, and soil in addition to the biota associated with these means (Bravo, 2007; Rico et al., 2007).

For example, people that live in small communities scattered along rivers that receive oil industry waste use this water as a food source (e.g., fishing) as well as to facilitate the growth of crops, yet this water contains polynuclear aromatic hydrocarbons (PAH) at 10 to 10 000 times greater than the U.S. EPA guidelines (Hurtig and Sebastián, 2002).

Crude oil or its components can travel a number of routes to come into contact with the human body, including i) absorption through the skin; ii) ingestion of food and drink; and iii) inhalation through breathing. Oil exposure is not limited to the area close to the pollution. The heavier components tend to deposit sediment where they can contaminate water sources repeatedly or be consumed by organisms that can enter the human food chain. This article describes various pathologies related to exposure to oil, its derivatives, or its residues.

4. Findings and discussion

4.1. Human health impacts

As mentioned, phases of exploration and exploitation of oil produce environmental risks and often take months to produce a disease and in some cases can lead to death (Guilbert, 2003). Currently, there are multiple studies on crude oil spills in coastal areas (Campbell et al., 1993; Lyons et al., 1999), but in most of these studies, the post-impact assessments do not highlight the long-term human health effects on impacted communities (Ordinioha and Brisibe, 2013).

The majority of crude oil spills are technological disasters (Picou, 2011). Major oil spills have been reported in Mediterranean Europe, North Africa, and in North America. Considering the high population density of these geographical areas (Linet et al., 2015a; Tabacova and Balabaeva, 1993a; Torres-bustillos, 2006), they are of major interest from an epidemiological point of view (Aguilera et al., 2010; M. a. D'Andrea and Reddy, 2014a).

Adverse human health symptoms associated with crude oil usually include hematopoietic, hepatic, renal, and pulmonary abnormalities (M. a. D'Andrea and Reddy, 2014b), changes in mood and cognitive functions (Ismail and Lewis, 2006), psychological problems (Gill et al., 2012), damage to reproductive health (Tabacova and Balabaeva, 1993a), respiratory tract involvement (Campbell et al., 1993; Lyons et al., 1999; Ordinioha and Brisibe, 2013), cancer (Yang et al., 2000), and general health problems (Aguilera et al., 2010; M. a. D'Andrea and Reddy, 2013, 2014a).

Fig. 1 summarizes health disorders associated with exposure to crude oil. Moreover, some of the major health problems related to exposure to petroleum are detailed.

4.2. Psychological health

It is known that many people exposed to crude oil pollution due to accidents (oil spills) experience psychological health problems (M. a. D'Andrea and Reddy, 2014a; Jernelöv, 2010). In all cases where crude oil pollution affects a community, either directly or through other means, there can be negative psychological symptoms, such as stress, anxiety, and depression (Gay et al., 2010). Symptoms like anxiety were significantly associated with exposure and the known toxicological effect of oil, suggesting a direct health effect on the exposed population by extraction activity (Lyons et al., 1999).

An example of this is shown in crude oil spills like the Exxon-Valdez in March 1989 in Alaska. In this case, results suggest that the oil spill's impact on the psychosocial environment was as significant as its impact on the physical environment (L. A. Palinkas et al, 1992; L. a Palinkas et al., 1993). Studies regarding oil spills like the Exxon Valdez and the 2010 BP spill showed that the strongest stresses were from family health concerns, commercial ties to renewable resources, and concern about economic future, economic loss, and exposure to the oil. On the other hand, it is interesting to understand the effects that produced income loss after the spill may have a greater psychological health impact than the presence of oil on the immediately adjacent shoreline (Grattan et al., 2011; L. A. Palinkas et al., 1992; L. a Palinkas et al., 1993) (Fig. 1).

Moreover, several studies have observed that people living in areas where spills have been reported in some cases have witnessed changes in the behavior of children and increased economic instability. Also, a high percentage of people move away from the area and experience the stress associated with these situations (e.g., mood, anxiety) (Aguilera et al., 2010; David et al., 2010; Morris et al., 2013).

Although, in the case of oil spills, it is not clear whether the observed psychological effect is due to the emotional impact or chronic exposure to crude oil. Kilburn & Warshaw mention that those who have been exposed to hydrogen sulfide (H_2S) as a result of working at or living downwind from crude oil processing facilities have persistent neurobehavioral dysfunction including depression and personality changes (Kilburn and Warshaw, 1991).

4.3. Blood disorders

Human exposure to crude oil can cause deterioration effects on

Table 1
Main compounds used and discarded during oil extraction and their toxic health effects.

Extraction Phase	Chemical	Toxic Effects
Drilling sub-phas	Bentonite (Almeida & Maldonado, 2002; International programme on chemical safety, 2000).	Causes skin and eye irritation as well as coughing (International programme on chemical safety, 2000). *In vitro*, it has been shown to increase the cytotoxic and genotoxic damage on human lymphocytes and human lung fibroblasts (Huang et al., 2013; Smith & Oehme, 1991).
	Anionic polyacrylamide (Almeida & Maldonado, 2002; Lin et al., 2001).	Prolonged exposure can cause irritation, numbness of fingers, and peeling upper lung tissue. Ingestion of large amounts produces phosphate deficiency. It can cause bone thinning as well as eye, skin, and respiratory tract ulcerations (Smith & Oehme, 1991).
	Potassium hydroxide (Almeida & Maldonado, 2002; Lin et al., 2001)	Effects of short-term exposure: Skin contact: Sight disorders swallowed, irritations of the mucosae in the mouth, throat, esophagus, and intestinal tract. Effects of longterm or repeated exposure: Risk of perforation intestinal and esophagus (Center for disease cotrol and prevention, 2015b).
	Polypac / Cellulose (Almeida & Maldonado, 2002; Lin et al., 2001).	Particles can cause mechanical irritation of the eyes, nose, throat, and lungs. Inhaling particles can cause pulmonary fibrosis, chronic bronchitis, emphysema, and asthma. Dermatitis and asthma may result from short contact (Hoskin, 1999).
	Sodium carbonate (Almeida & Maldonado, 2002; Lin et al., 2001).	The substance enters the body by inhalation and Ingestion, and it irritates the skin and the respiratory tract. It is corrosive to the eyes. The intake of high doses can cause death (Center for disease cotrol and prevention, 2015c).
	Calcium oxide (Almeida & Maldonado, 2002; Lin et al., 2001).	The substance is corrosive to the eyes, skin, and respiratory tract. It is corrosive upon ingestion. Inhalation may cause lung edema. The effects may not form immediately. Prolonged or repeated contact with the skin can cause dermatitis, ulceration, and perforation nasal septum (Center for disease cotrol and prevention, 2015a).
	Uranium (Almeida & Maldonado, 2002; Lin et al., 2001).	Natural and depleted uranium produce the same effects in the body. Kidney damage has been observed in humans and animals that inhaled or ingested uranium compounds (Agency for toxic substances and disease registry, 2013). Other effects include respiratory disorders. In addition, uranium causes DNA damage, mutagenicity, cancer, and neurological defects (Agency for Toxic Substances and Disease Registry, 2012; Meinrath, Schneider, & Meinrath, 2003).
	Cadmium (Almeida & Maldonado, 2002; Lin et al., 2001).	Breathing air with lower levels cadmium for extended periods (over years) can cause a buildup in the kidneys, and, if it becomes high enough, it can cause kidney disease. Other possible effects of breathing cadmium are damages to the lungs and bone fragility (Agency for Toxic Substances and Disease Registry, 2012). According to the IARC, cadmium occurs in people with lung cancer, and it can possibly induce this or be related to prostate and liver cancer (Hengstler, 2003; IARC, 2012).
	Lead (Almeida & Maldonado, 2002; Lin et al., 2001)	Lead primarily affects the nervous system in both children and adults. Prolonged exposure to occupational lead has caused changes in some functions of the nervous system. It can also cause weakness in fingers, wrists, or ankles and can cause anemia. High exposure levels can seriously damage the brain and kidneys in adults or children and can cause death. In pregnant women, the levels of high exposure can cause abortions. In men, exposure to high levels of lead can alter sperm production (Agencia para sustancias toxicas y el registro de enfermedades, 2007b). This compound or derivatives probably induce stomach cancer in humans, though there is not sufficient evidence for this (International agency for reserch on cancer, 2015). Some *in vitro* studies showed increased genotoxic damage determined by comet assay in human leucocytes (Agencia para sustancias toxicas y el registro de enfermedades, 2007b; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2012) .
	Mercury (Almeida & Maldonado, 2002; Lin et al., 2001)	Mercury can affect different brain areas and functions that are associated with these areas, which manifests itself in a variety of symptoms. These include personality changes (irritability, shyness, nervousness), tremors, impaired vision (reduction of the field visual), deafness, muscle incoordination, loss of sensation, and memory difficulties (Lebel et al., 1996; Zahir, Rizwi, Haq, & Khan, 2005).
	Arsenic (Almeida & Maldonado, 2002; Lin et al., 2001)	Perhaps the most characteristic effect of exposure prolonged oral to inorganic arsenic is skin disorders. These include skin darkening and appearance of small corns or warts on the palms, the plant feet and torso, which are often associated with alterations in blood vessels in the skin. It can also develop skin cancer. Also, swallowing arsenic increases the risk of developing liver cancer and cancer of the bladder and lungs. The Department of Health and Human Services (DHHS) and the EPA have determined that inorganic arsenic is recognized as being a carcinogenic substance to humans. The IARC has determined that inorganic arsenic is carcinogenic to humans (Agencia para sustancias toxicas y el registro de enfermedades, 2007a). In some studies, this compound showed a direct relation with some types of cancer in human-like skin (other malignant melanoma), lung, urinary bladder. Though suspected, these compounds probably induced liver, prostate, kidney, liver and bile duct cancer (International agency for reserch on cancer, 2015). On the other hand, arsenic can induce vascular diseases, hypertension, and diabetes. It also seems to have a negative impact on reproductive processes (infant mortality and weight of newborn babies) (Hopenhayn, 2006; Tchounwou, Patlolla, & Centeno, 2003).
	Volatile organic compounds (Paz-y-Miño & López-Cortés, 2014).	**Benzene:** Studies focus on the route of exposure of benzene, including inhalation, oral, and dermal. It can cause death and produce systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects (Wilbur et al., 2008). Also, sufficient evidence showed that it could induce leukemia and/or lymphoma (International agency for reserch on cancer, 2015). Some studies showed that exposure to higher levels of benzene may contribute to oxidative DNA damage (Buthbumrung et al., 2008; Huff, 2013). On the other hand, a study showed that 250 workers exposed to benzene exhibited significantly lower white blood cell and platelet counts than in 140 controls, even for exposure below 1 ppm in air (Lan et al., 2004). **Toluene:** It has been determined that prolonged exposure to this compound causes damage to myelin of the central nervous system, resulting in neuropathological damage (Filley et al., 2004) **Xylene:** The effects of this compound depends largely on the exposure time and can range from mild symptoms such as headaches and nausea to long-term-exposure symptoms such as insomnia, agitation, extreme tiredness, tremors, deterioration of concentration, and short-term memory (Kandyala et al., 2010). **Ethylbenzene:** Exposures to high levels of ethylbenzene in the air cause eye and throat irritation in the short term. At higher levels, exposure causes breathing problems, muscle and dizziness. It is toxic to the CNS and an irritant to mucous membranes and eyes. The IARC determined that it is possibly carcinogenic to humans (IARC, 2012).
	Polycyclic aromatic hydrocarbons (Almeida & Maldonado, 2002)	The U.S. EPA has reported 16 compounds as polycyclic aromatic hydrocarbons, including naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benzo (a) anthracene, chrysene, benzo (b) fluoranthene, benzo (k) fluoranthene, Benzo (a) pyrene, dibenzo (a) anthracene, benzo (ghi) perylene, and indene (1,2,3-cd) pyrene. Most of these compounds are also classified as 2B by the IARC, and some of them have been attributed a genotoxic potential (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2012). The most toxic of this group is benzo (a) pyrene; it produces cancer of pharynx and larynx (Abbas et al., 2013).

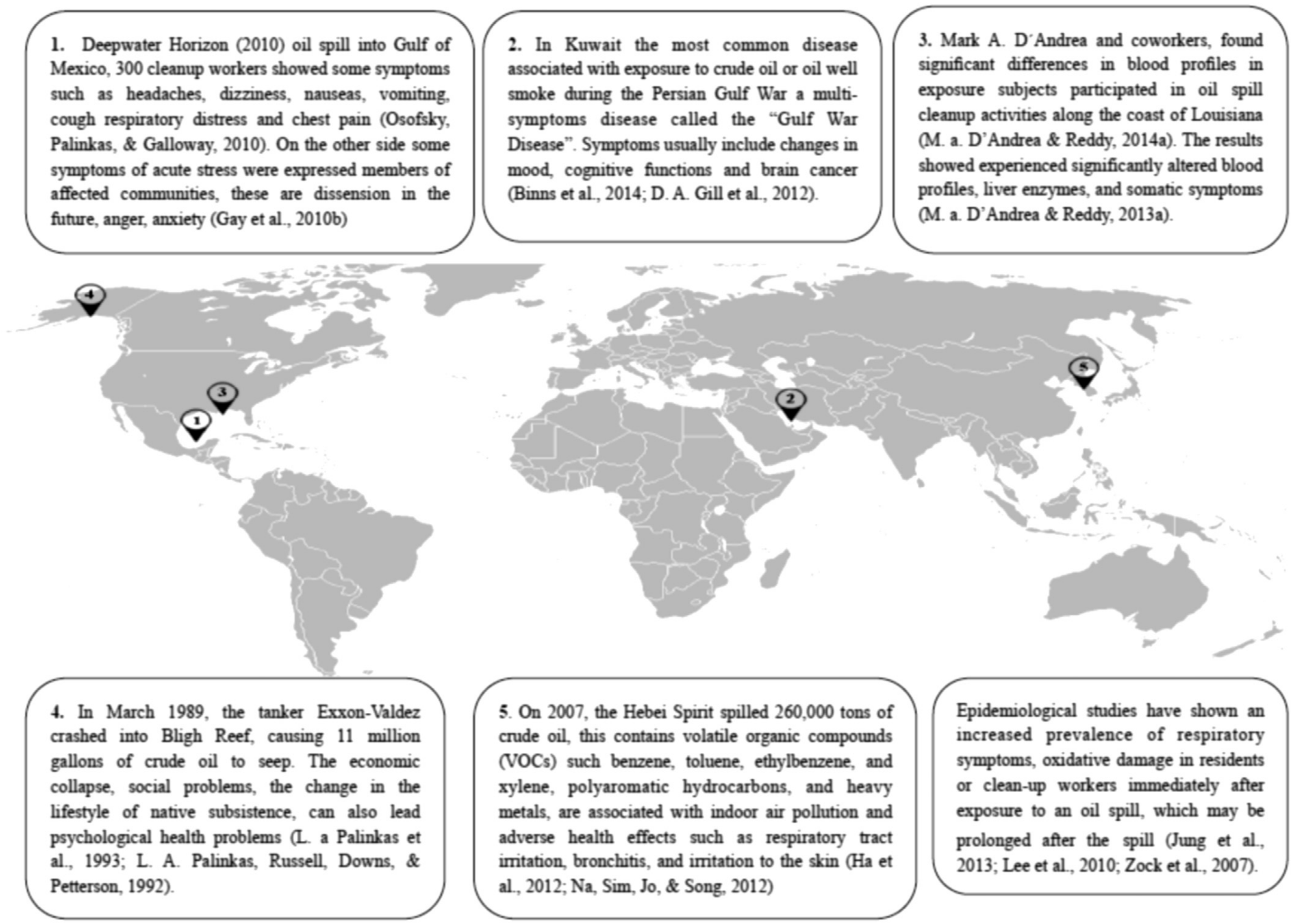

Fig. 1. Reports of multiple studies that show the negative effects in human health such as psychological problems, respiratory tract irritation, and disturbance of blood profile by exposure to crude oil spills.

many biological systems, including changes in the hematologic system. One of the hematological disorders that is evident in people exposed to hydrocarbons is leukemia, which in general terms is defined as a group of diseases in which the common manifestation is an unregulated and malignant proliferation of endogenous bone marrow cells. In China, after an investigation with surveys covering 46 investigating areas, the incidences of some types of leukemia like nonlymphocytic leukemia, acute lymphocytic leukemia, chronic myelocytic leukemia, and chronic lymphocytic leukemia in oil fields and polluted areas were significantly higher than those in other areas.

Others studies demonstrated different alterations in hematologic profiles associated with exposure people to crude oil spills. Mark A. D'Andrea and coworkers (2013–2014) found significant differences in blood profiles between exposed and unexposed subjects with respect to the Deepwater Horizon oil spill; participants in the oil spill clean-up operation presented changes in values of white blood cells and platelet counts, blood urea nitrogen, creatinine, hemoglobin, hematocrit, and urinary phenol levels (M. a. D'Andrea and Reddy, 2014; Jernelöv, 2010; Pérez-Cadahía et al., 2008a,b). When the oil tanker Prestige wreck and sank, it was a great concern for the health of people exposed to oil. In this case, studies evaluated the concentration of heavy metals in the blood of exposed humans, and their results showed aluminum and nickel, the two metals remained statistically significant (Pérez-Cadahía et al., 2008a,b) (Fig. 2).

4.4. Reproductive health and developmental toxicity

Only few epidemiologic studies have examined the association between exposures to oil pollutants and outcomes of pregnancy, particularly among women living close to petrochemical industries. Benzene, for example, crosses the placenta and may harm a developing fetus (Goldstein et al., 2011) (Fig. 2). Exposure to petroleum hydrocarbons or petrochemicals might induce chromosomal aberrations in humans (M. A. D'Andrea and Reddy, 2014; Pérez-Cadahía et al., 2008a,b). Fig. 2 shows some conditions that have been associated with exposure to oil, such as chromosomal aberrations (i.e., direct damage to DNA), among others (Marcon et al., 1999).

As for women, in all of the cases studied, increases were found in spontaneous abortion (SAB) due to exposure to contaminants from petrochemical industries (Merhi, 2010a). In Swedish women, pregnancies showed a significant increase in SAB ($P < 0.05$ between expected and observed number of SAB among 55 pregnancies), specifically in women engaged in laboratory work at a petrochemical plant (Merhi, 2010b) (Fig. 2). In addition, it is important to note that, in the case of China, where female workers are exposed to petrochemicals (benzene, gasoline, and hydrogen sulphide) at a plant, they were evaluated during the first trimester of their pregnancies. A significant increase in the risk of SAB in exposed women (8.8%) was found when compared with controls (2.2%) after adjusting for reproductive history, smoking habits, alcohol

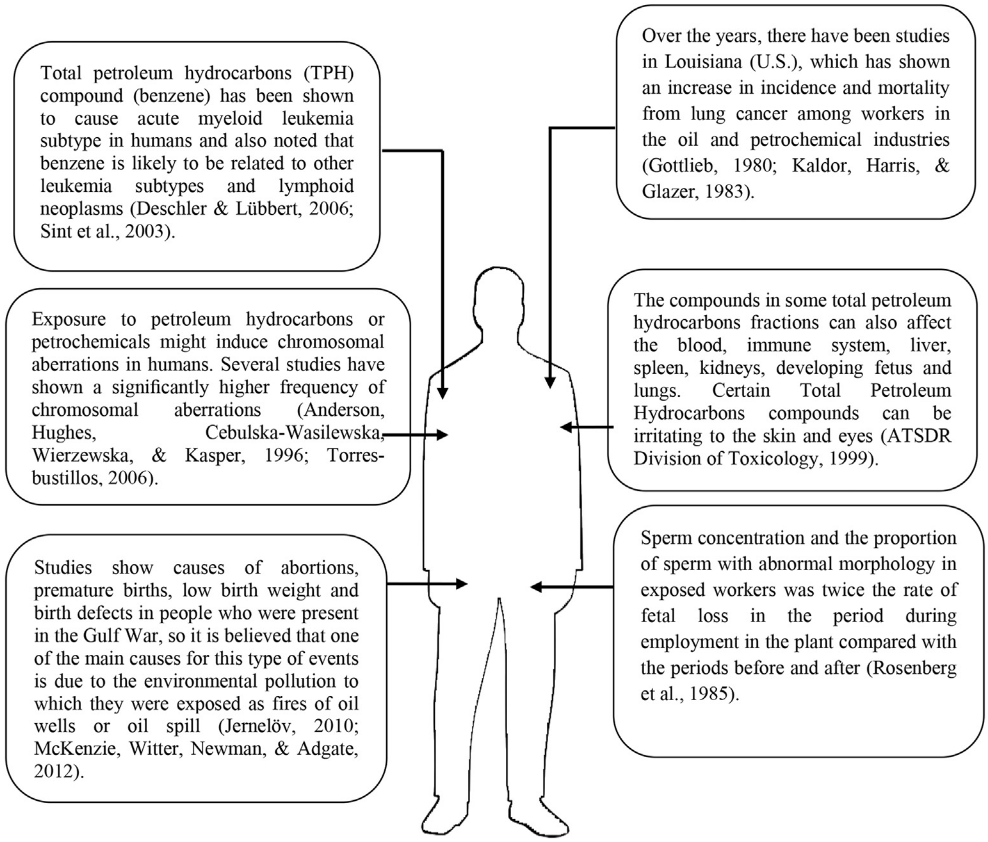

Fig. 2. Reports of multiple studies that show the negative health effects caused in humans, such as myeloid leukemia subtypes (Deschler and Lubbert, 2006; Sint et al., 2003), lung cancer (Gottlieb, 1980; Kaldor et al., 1983), chromosomal aberrations and deletions (Anderson et al., 1996; Torres-bustillos, 2006), increase of spontaneous abortion (Jernelöv, 2010; McKenzie et al., 2012) and decrease on sperm quality from exposure to oil derivatives and petrochemical industry pollutions (ATSDR Division of Toxicology, 1999; Rosenberg et al., 1985).

consumption, indoor air pollution, and demographic variables (Xu et al., 1998).

The same happened in towns near the petrochemical industry in Bulgaria, where significantly higher prevalence of toxemia, spontaneous abortion, and prematurity were found among populations living in areas polluted by petrochemical industries (Tabacova and Balabaeva, 1993b).

Other abnormal characteristics were found in the semen of exposed workers; those characteristics include alterations in viscosity, liquefaction capacity, sperm count, and sperm motility. The number of subjects with normozoospermia was greater in the unexposed workers than in the exposed group (De Celis et al., 2000). Additionally, some abnormal semen characteristics correlated with the number of years of hydrocarbon exposure (De Celis et al., 2000).

This deterioration in the quality of semen in paternal workers exposed to petrochemical pollution is associated with an increase in delayed conception and congenital malformation (A. A. Arif and Shah, 2007a).

4.5. Respiratory issues

Little is known about the effect of crude oil spills on the human respiratory system. A few epidemiological studies have shown an increased prevalence of respiratory symptoms in residents or clean-up workers immediately after exposure to an oil spill, which may be prolonged after the spill (Campbell et al., 1993; Lyons et al., 1999) (Fig. 2).

Crude oil spills release volatile organic compounds (VOCs) such as benzene, toluene, ethylbenzene or xylene, polyaromatic hydrocarbons (PAHs) as well as heavy metals. VOCs, which typically contain 1-18 carbon atoms, are associated with air pollution and adverse health effects, such as respiratory tract irritation, bronchitis, and irritation to the skin (A. A. Arif and Shah, 2007a) (Fig. 2).

PAHs, a group of small organic compounds containing three to five benzene rings, can induce oxidative stress in the respiratory tract and aggravate asthma symptoms (Miller et al., 2010). This was shown by a study of the oil spill from the Hebei Spirit that evaluated the respiratory effects on children who lived along the Yellow Coast of South Korea. All subjects completed a health examination, including a skin prick test, pulmonary function test, and methacholine bronchial provocation test (MBPT), and the results showed that exposure to a crude oil spill is a risk factor for asthma in children (Jung et al., 2013).

These VOCs can also trigger asthma in adults, according to a report by Ahmed A. Arif Shah and Syed M. They reported a cross-sectional study of a representative sample of the U.S. population and showed that environmental exposure to VOCs, especially aromatic compounds, were associated with adverse respiratory effects like asthma (A. Arif and Shah, 2007b).

Although a higher prevalence of asthma in children and adolescents living near petrochemical sites could not be demonstrated in Tarragona (Catalonia, Spain), respiratory hospitalizations and nocturnal cough could be related to short-term exposures to pollutants from petrochemical sites (Brand et al., 2016).

In addition, the consequences of exposure to the gases emitted by oil refineries have been evaluated. In Ecuador, a study was carried out with workers from the refinery industry and students from nearby schools where it was observed that one of the main pollutants is nickel; note that nickel has been shown to produce irritability at the skin level as well as cause respiratory tract lesions and is finally known to be a recognized human carcinogen (Harari et al., 2016). In an another study that analyzed the association between asbestos exposure and risk of mesothelioma to workers from two oil refineries located in the northern Italian cities of Genoa and La Spezia, the authors demonstrated that exposure to asbestos in oil refineries causes pleural mesotheliomas (Gennaro et al., 1994).

Subjects working in the petroleum refinery have significantly impaired lung functions. In the Middle East, a large number of petrochemical refineries are located mainly in the Gulf Cooperation Council (GCC) countries, including Saudi Arabia, UAE, Qatar, Kuwait, and Bahrain. Meo et al., 2015 described that workers in the petroleum refinery have significantly impaired lung functions, and the lung function impairment pattern provides evidence of an obstructive lung disease (Meo et al., 2015)

4.6. *Genotoxic damage and cancer issues induced by crude oil*

This section shows several studies that have found a relationship between exposure to oil compounds and DNA damage using classical tests of genotoxicity. One such work is done by Laffon; the study compares the results obtained by a comet and micronucleus assay from 35 people exposed to oil spills with 34 controls, noting that there is an increase in DNA damage in exposed people compared to controls. On the other hand, the study showed no clastogenic damage as determined by the micronucleus test (Laffon et al., 2006). Continuing with this line research, Perez-Cadahía in 2006 applied several tests for genotoxicity to test the sister chromatid exchange as well as a micronucleus test and comet assay in four groups of individuals that included (68 total exposed vs 42 controls) volunteers, hired manual workers, hired high-pressure cleaners, and controls. The first three groups were exposed to crude oil during the clean-up after a large oil spill. Oil exposure during the cleaning tasks caused an increase in the genotoxic damage in individuals, and the comet assay was the most sensitive detection biomarker (Pérez-Cadahía et al., 2006).

By taking into account exposure to genotoxic compounds that damage DNA, the number of cancer cases greatly increases. We have compiled information that highlights the relationship between cancer and exposure to crude oil. Although crude oil is not classifiable regarding its carcinogenicity to humans (Group 3) by the International Agency for Research on Cancer (IARC), it has been evaluated that employment in the oil refining industry is probably carcinogenic to humans (2A) (International agency for reserch on cancer, 2015; Schnatter et al., 2012). Table 2 shows some studies relating exposure to crude oil and the risk of various cancers. There is great controversy in the results, but when it is related to specific components in more controlled occupational exposure environments, studies have identified more effectively the type of cancer that is produced. Thus, benzene has been shown to cause acute myeloid leukemia subtype in humans and is likely to be related to other leukemia subtypes and lymphoid neoplasms (Agency for Toxic Substances and Disease Registry, 1999; Huff, 2013; Tchounwou et al., 2003). A systematic review of the relation between benzene exposure and leukemia subtypes concluded that there was consistent evidence that the risk of acute myeloid leukemia is related to benzene exposure with an indication of a dose-response pattern and a suggestion for chronic lymphoid leukemia, whereas the data for chronic myeloid leukemia and acute lymphocytic leukemia remain sparse (Schnatter et al., 2005). Polycyclic hydrocarbons are risk factors for the development of skin cancer (Danadevi et al., 2003; Tomatis, 2000) and liver cancer. Other types of cancers are related to exposure to petroleum products, such as lung, esophagus, rectum, kidney, and bladder cancer (Tomatis, 2000); furthermore, it is also related to the increase of cervical cancer in women (M San Sebastián et al., 2001).

The incidence of cancer can vary according to the genetic susceptibility of each individual.

Table 2
Studies in various regions of the world regarding cancer and occupational exposure to crude oil.

Country	Exposure	Type cancer	Risk	Reference
Finland	Hydrocarbons in the oil-refining activity	Kidney	(Odds ratio, 3.1; confidence interval, 1.1 to 8.9; 11 exposed cases).	(Anttila et al., 2015)
U.S and Puerto Rican	Gasoline or petroleum products	Breast	(HR: 2.3, 95%CI: 1.1–4.9) and invasive (HR: 2.5, 95%CI: 1.1–5.9)	(Ekenga et al., 2015)
Australia, Denmark, Germany, Sweden and the United States	Gasoline and other petroleum products	Kidney	(RR, 1.6; 95% CI = 1.2–2.0) (RR, 1.6; 95% CI = 1.3–2.1).	(Mandel et al., 1995)
Chinese	Benzene-exposed	All neoplasms Non-Hodgkin lymphomas Lymphoid leukemia	RR 5 1.1, 95% CI = 1.1–1.2) 3.9, 95% CI = 1.5, 13 5.4 95% CI= (1.0, 99)	(Linet et al., 2015b)
Norway		Hematologic neoplasms myelogenous leukemia multiple myeloma Non-Hodgkin lymphoma.	(RR) 1.90, 95% confidence interval (95% CI): 1.19–3.02) (RR 2.89, 95% CI: 1.25–6.67) (RR 2.49, 95% CI: 1.21–5.13) Non-significant associations	(Kirkeleit et al., 2008)
Taiwan	Work in the crude petroleum and natural gas extraction industry	Prostate cancer	Odds ratio 2·29; CL 1·03, 5·11).	(Mills et al., 1984)
Chinese	Petroleum refnery plant began	Lung cancer		(Yang et al., 2000)
UK	Oil refinery	Gall bladder pleura melanoma	(Observed, 24; expected, 14.0; SMR = 172) (observed, 38; expected, 15.0;SMR = 254) (observed, 36; expected, 22.2;SMR = 162).	(Sorahan et al., 2002)
Northeastern United States	Refinery	Prostate	Non significant associations	(Raabe et al., 1998)
US, Canada and Australia.	Refinery petrochemical plants	Non-Hodgkin lymphomas	Non significant associations	(Wong and Raabe, 1997)

4.6.1. Genetic susceptibility and carcinogens

The biotransformation of PAHs (i.e., the important constituents of oil crude) involves enzymes that catalyze reactions of oxidation, reduction, and hydrolysis (cytochrome P-450 CYP) and enzymes that catalyze conjugation reactions, among which is the family of Glutathione -S transferases (GST). These enzyme systems are distributed in all tissues of the body, although the liver is the most important organ involved in biotransformation of xenobiotics (López-Cima et al., 2012; Torres et al., 2008).

The enzymes from the CYP and GST families are responsible for the adaptive response to the aggression of environmental chemicals, and efficiency in detoxification of mutagens such as PAHs nitrosamines, phenol, chloroform, nitrocloroetileno, benzene, toluene, and others depends on the coordination of the expression of these two enzyme families (Torres et al., 2008).

Many toxic compounds implicated in carcinogenesis require both activation by metabolic enzymes classified as Phase I and detoxification by enzymes classified as Phase II. Genetic changes in genes that encode metabolic Phase I enzymes and detoxification Phase II enzymes are linked to increases in metabolic activation and decreases in metabolic detoxification of environmentally derived pro-carcinogens and may increase cancer susceptibility (López-Cima et al., 2012).

The CYP enzymes are responsible for most Phase I reactions and are responsible for the metabolism of numerous xenobiotic and endogenous compounds, including the metabolic activation of most environmental toxic chemicals and carcinogens, such as PAHs, nitroaromatics, and acrylamides. Genetic polymorphisms of CYP are related with human cancer risk and susceptibility to environmental hazards (Hong and Yang, 1997).

Polimorphisms in CYP have been reported to be associated with several cancers, such as in the lung, liver, colorectal, prostate, leukemia, brain, esophagus, stomach, pancreas, melanoma, ovarian, and kidney (Agundez, 2004).

Some studies suggest that CYP1A1 polymorphisms contribute to increased lung cancer susceptibility. The Ile462Val polymorphism was related with the increased risk for lung cancer and particularly for squamous-cell and small-cell lung carcinoma. Also, the Thr461Asn polymorphism was found to be associated with small-cell lung carcinoma in a Caucasian population (San Jose et al., 2010). The CYP1B1 Leu432Val polymorphism was significantly associated with lung cancer susceptibility in Caucasians as well. The combination of this polymorphism with Phase II enzyme polymorphism NQO1 C (609)T showed an association with the highest risk of lung cancer, increasing the risk of OR 2.87, 95% CI 1.63–5.07 to OR 4.14, 95% CI 1.60–10.74 (Wenzlaff et al., 2005).

Glutathione S-transferases (GSTs) are Phase II transformation enzymes involved in the detoxification of hazardous agents. The *GST* gene family encodes genes that are critical for certain life processes as well as for toxicity and detoxification mechanisms (Uddin et al., 2014).

The exposure to polycyclic aromatic hydrocarbons by itself increases the risk of lung cancer (Suárez et al 2014); however, the presence of polymorphisms in genes of the GST family can modify individual susceptibility to cancer. The Ile105Val polymorphism of the GSTP1 gene showed an association with lung cancer, and the presence of the G allele in heterozygous or homozygous form increases the cancer risk of 3–6 times with respect to the reference genotype AA, respectively (Uddin et al., 2014).

The Ile105Val variant has been associated with prostate cancer as well; men who carry the *Val a*lelle and are exposed to high levels of occupational PAH have increased risk for prostate cancer (Rybicki et al., 2006).

CYP1A1 Ile462Val and GSTM1-null polymorphisms were associated with susceptibility for the development of skin manifestations in people exposed to polychlorinated biphenyls and dibenzofurans (Tsai et al., 2006) and with genetic damage in oil workers (Ilyinskikh and Ilyinskikh, 2014).

Polymorphisms in *GSTM1*, *GSTT1*, and *GSTP1* genes constitute an important genetic risk factor for gastric cancer in the Chinese population (Setiawan et al., 2000), epithelia ovarian cancer in individuals from southeastern Brazil (Oliveira et al., 2012), and can play an important role in a respiratory diseases (Tamer et al., 2004).

Individual differences in susceptibility may be very important in determining the actual risk to human health from environmental toxicants. Individual susceptibility to cancer may be partly explained by genetic variability in metabolic activities related to phase I and phase II detoxification enzyme pathways. The studies of polymorphism hold great promise for identifying susceptible individuals from environmental toxicity (Garte, 1998; Hong and Yang, 1997).

5. Health effects caused by oil activity in Ecuador

This paper has reviewed the global health problems associated with oil. Thus, in this section, we highlight some research that has been done in Ecuador in populations living in the Amazon. Table 3 shows the results of several studies that demonstrate a direct relationship between oil production and health conditions; on the other hand, some studies indicate that there is a direct relationship in the deteriorating health of villages near oil wells.

6. Discussion

While oil is one of the main sources of non-renewable energy and an important contributor to the economy of certain sectors, at the same time, it has become a source of environmental pollution, since with each exploration well that is drilled, a large amount of waste is produced, which is detrimental to the environment (Jernelv, 2010; San Sebastián and Hurtig, 2005).

Oil exploitation usually occurs in areas where people have scarce economic resources (Engelder et al., 2011). These populations in these areas also typically lack knowledge regarding the importance of reducing chronic exposure to chemicals (Freije, 2015). In addition, these areas may be affected by the sum of other factors such as the lack of attention, which the makes studies in human health difficult by exposure to oil crude. However, the studies collected in this review have demonstrated a number of human health effects that result from exposure and contact to oil; these range from irritation of the skin, eyes, and throat to more serious illnesses, as psychological problems, symptoms at the reproductive level (increases in the number of spontaneous abortions). Overall, the most reported disorder is cancer—mainly leukemia but also liver, breast, prostate, and lung cancer. (Binns et al., 2014; Boers et al., 2005; M. a. D'Andrea and Reddy, 2014a; Deschler and Lübbert, 2006; Pérez-Cadahía et al., 2008a,b; Stenehjem et al., 2015).

The effects on human health observed in this article are supported by what is also observed separately from compounds present in other contaminating environments due to difficulties associated with monitoring. In general, the extraction of crude oil is carried out in places that are difficult to access and may be deficient systems without environmental controls; in the case of refinement and spills, the situation changes. It is clear that it is more accessible to measure the impact of obtaining crude oil in the environment than in humans, because it is possible to monitor various biological models in addition to having a larger number of samples (Bamberger and Oswald, 2012).

Also, the different forms of extraction as well as the different types of compounds and the variability in the concentration of

Table 3
Summary of different studies in the Amazon about the impact of oil activity on health.

Location	Population	Results	Year	Statistics	References
Orellana, Sucumbios	80 communities 1520 volunteers	87% of families live in permanent contact with pollution associated with oil and gas. The diseases attributed to pollution include skin conditions (96%); breathing problems (75%); and digestive problems (64%). The main causes of death are cancer or leukemia, followed by unknown causes associated with stomach aches, liver problems, headaches, body aches; next cardiovascular, respiratory, digestive, infectious diseases, among others. The incidence of cancer in areas affected by oil crude is three times higher than the average in the rest of the country.	2003	They calculated the mortality and used the overall mortality rate. (lapsica reference per 1000 population.	(Maldonado and Narváez, 2003)
Orellana and Sacha	260 women exposed the 9 communities and unexposed the 14 communities	It was observed that women living in exposed areas have suffered from several symptoms such as nose and throat irritation, headache, eye irritation, diarrhea, and gastritis. The results for the study on reproduction increased abortions on women living near oil wells in comparison the group of unexposed women was observed. Moreover no association was not observed between living or not near oil stations and the risk of stillbirth.	2004	To study the health and reproductive effects, logistic regression analysis was performed on prevalence ratios such disorders adjusted for potential confounders.	(Miguel San Sebastián et al., 2004)
Napo, Orellana, Sucumbios, and Pastaza	nd	Due to the lack of records in the Amazonian region of Ecuador and the methodology used, it was difficult to demonstrate an increased risk of cancer in these populations compared with the inhabitants of the province of Pichincha.	1990–2005	Age- and sex-adjusted mortality rate ratios (RR) and 95% confidence intervals (CI) were estimated to evaluate total and cause-specific mortality in the study regions.	(Kelsh et al., 2009)
Sucumbios, Orellana, Napo y Paztasa	985 cancer cases	For this study, data were recorded by the Nacionla cancer Tumor Registry between 1985 and 1998. The results found a cancer incidence of 39.99 per 100,000 men and 68.25 for women. The most common cancers in men were stomach cancer, skin, lymph nodes, hematopoietic system, and prostate cancer. Moreover, the results revealed that the most common cancer types for women were for cervical, stomach, breast, skin, and hematopoietic systems. A significantly greater relative risk was observed in cases of cancer reported by villagers in areas exposed. One example is greater incidence of children with leukemia in contaminated areas. In conclusion, more research is needed to determine whether the observed associations really reflect a relationship of chance.	2004	Incidence rates for all sites combined and for each specific cancer site calculated. Crude rates, age-specific rates, truncated rates, and standardized rates were also calculated. In the comparative study of the cantons, relative risks (RR) and confidence intervals of 95% (95% CI) for men and women were calculated as reasons for the incidence rates adjusted for age and risk groups.	(Hurtig and San Sebastia, 2004)
San Carlos	18 patients	This study showed that the water the people used for drinking, washing, and bathing had high levels of contaminated derivatives of oil activity. These results evidence the relation with contamination and some cases of cancer such as stomach, liver, and melanoma.	2001	In this report, the statistical analysis was based on the comparison of observed and expected numbers of cancer cases. Observed and expected values, observed/expected ratios, and their 95% confidence intervals based on the Poisson distribution exact method are reported.	(M San Sebastián et al., 2001)
Orellana; communities: Los vencedores, 15 de Abril, Asociacion Payamino and Flor de Maduro	25 women	Researchers suggest that there is an increased risk of cancer, congenital malformations, and abortions in areas closer to oil activity. The proximity to the contaminated zones favors the DNA mutation.	2010	The authors conducted a classification of damage in six categories depending on the level of DNA fragmentation present in the comet tail, ranging from the lowest—level A (without damage)—to the highest—level F (total damage).	(Paz-Miño et al., 2010)
Napo, Pastaza, Orellana and Sucumbios	For this study, the population represents cantons in the Amazonian provinces. In 1990, 2001, and 2010, data were obtained from the Ecuador National Census	This is an ecological study to incorporate quantitative measures of oil exploration and production. In this case, the studies compared oil-producing towns and towns that did not have oil production facilities. The total data of cancer mortality of males and females combined the RR and were compared between towns mentioned above with RR values greater than 0.8. The results showed no excess of mortality from acute non-lymphocytic, myeloid, or childhood leukemia. Standardized mortality ratios were consistent with RRs. In the Amazon towns, specific RRs showed no pattern in relation to oil-production volume or well years. On the other hand, they showed no association between the extent of these activities (oil exploration and production) and cancer mortality, including from cancers associated with benzene exposure.	2013	In this study, the researchers analyzed their data by comparing overall and site-specific cancer mortality between seven oil-producing cantons and thirteen non-oil-producing cantons. The analyses used both Poisson regression and indirect standardization following the age–cohort method proposed by Breslow and Day.	(Moolgavkar et al., 2014)

crude oil have been shown to contribute to the genetic variability of each affected individual. Since only a relatively small number of people have been exposed to these conditions, it is difficult to extrapolate the observed results. Therefore, it is important to take preventive measures such as implementing sustainable processes that allow the exploitation of this resource with a notable decrease in environmental impacts in order to protect the health of those who are engaged in this activity or those who live near oil areas.

7. Conclusion

After an exhaustive investigation and review of several authors quoted in our work, we conclude that there is sufficient scientific evidence to affirm that acute or chronic exposure to crude oil (or its derivatives) is responsible for several human health effects associated with those who inhabit the areas close to the oil fields as well as those who work for the oil industry.

7.1. Special recommendations

(1) Identify the main sources of exposure and contact with oil.
(2) Recognize the potential adverse human health effects that may result from exposure to crude oil.
(3) Raise awareness regarding the risks to people living or working in or near oil fields, and initiate preventive measures such as regulations or laws to protect human health and the environment.

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Conflict of interest

Authors declare no conflict of interest.

Author contribution

MIR: Worked on Bibliography and drafted the main effects of petroleum on human health; revised the manuscript.

APA: Wrote about genetic susceptibility, and revised the manuscript.

SS: Worked on Bibliography, and wrote about the different substances used in the oil exploitation phase and their implications for health.

NBM: Worked on Bibliography, wrote about genotoxic and cancer issues, and revised the manuscript.

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