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LITERATURE REVIEW OF STUDIES LINKING BENZENE AND LEUKEMIA

Kylene Owens

Montana Tech of the University of Montana

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**LITERATURE REVIEW OF STUDIES LINKING BENZENE AND
LEUKEMIA**

by

Kylene Owens

A report submitted in partial fulfillment of the
requirements for the degree of

Master of Science:

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I. Abstract

The purpose of this review was to discover how the by-products of oil production, such as benzene played a significant role in health issues, particularly leukemia. The objective is to evaluate the association of benzene exposure and leukemia through laboratory toxicity studies and public and occupational epidemiology studies.

Multiple articles were researched to find a link between benzene exposure and the development of leukemia. Several articles were viewed and some eliminated due to their irrelevant to this paper or their duplicated information with other articles. A total of six articles were selected for this paper. Research has shown that benzene is a carcinogen and exposure to it can lead to the development of leukemia after a latency period. Still unknown is the specific dose, exposure time, and if a certain cell type is specific to benzene exposure induced leukemia.

Keywords:

Benzene, oil production, leukemia

II. Dedication

I wish to thank my Mom and Dad for their support and love. A special thanks to my best friends Levi and Bobbie for the late night pep talks and shoulders to lean on. Last but not least to my dear friend Lori who has not only been there for the ups and downs over these past two years, but has also taken time to help me with my homework and proof read my papers. Finally my boss, Kirk, who has so graciously worked with my school schedule and has been understanding when it comes to meeting school deadlines.

III. Acknowledgements

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Glossary of Terms

Dyscrasias: a malfunction or abnormal condition, especially an imbalance of the constituents of the blood.

Hydroquinones: a white, crystalline compound, $C_6H_6O_2$, formed by the reduction of quinone : used chiefly in photography and to inhibit autoxidation reactions.

Leukemia: any of several cancers of the bone marrow that prevent the normal manufacture of red and white blood cells and platelets, resulting in anemia, increased susceptibility to infection, and impaired blood clotting.

Lymphohematopoietic: of, relating to, or involved in the production of lymphocytes and cells of blood, bone marrow, spleen, lymph nodes, and thymus.

Myelogenous: production in the bone marrow.

Myelotoxicity: bone marrow suppression.

Phenyl-mercapturic acid: is a condensation product formed from the coupling of cysteine with aromatic compounds.

Quinone: a quinone is a class of organic compounds formed by oxidizing aniline or hydroquinone.

Semiquinone radicals: any of the class of free radicals formed as intermediates in the oxidation of hydroquinone to a quinone.

1. Introduction

Oil Production

The oil industry began in the 19th Century. It experienced a massive growth after the Spindletop geyser was discovered in 1901. Over 1,500 oil companies had been chartered one year after this discovery (Wall, 2014).

What is known as Spindletop Hill was formed by an underground salt dome that continued to push the earth above it higher and higher. Geologist Patillo Higgins was the first to think oil could be underneath Spindletop (History.com Staff, 2010). In 1892 the company named Gladys City Oil, Gas, and manufacturing, Higgins organized this company, decided to look into Higgins speculations of oil being beneath Spindletop Hill. However drilling did not begin until 1900. In early January of 1901 drillers had reached a depth of 1,020 feet and then on January 10, 1901 oil began spilling from the drilling site. (History.com Staff, 2010).

The Gladys City Oil, Gas, and Manufacturing Company was the first company to drill on Spindletop. Three attempts were made by the company beginning in 1893. In 1899, Anthony F. Lucas joined the Gladys City Oil, Gas, and Manufacturing Company; using a heavier, more efficient rotary bit, Lucas and his team were able to drill through the difficult oil sands (Wooster & Sanders, 2003).

January 10, 1901 in Beaumont Texas at the drilling site on Spindletop Hill erupted, spilling oil onto the southeastern Texas soil (History.com Staff, 2010). The oil spilling from this geyser reached over 150 feet and produced approximately 100,000 barrels per day. From this geyser many oil companies in America grew, especially in the Gulf Coast. Some of these companies include Texaco and Exxon (History.com Staff, 2010).

In its first year Spindletop produced more than 3.5 million barrels of oil and in its second year it produced 17.4 million barrels. The discovery of Spindletop paved the way for a new era in Texas-based industry and oil production (History.com Staff, 2010).

Oil or petroleum has a long history dating back years before the Spindletop discovery; starting in 480 B.C. where it was used by the Persian military to soak their flaming arrows (EXTREME OIL, 2004) Fast forward to the end of the 19th Century and the beginning of the 20th Century, this is when the oil boom began and oil fueled boomtowns began to rise (Wall, 2014).

Benzene is emitted during oil and gas production. It is a natural component of oil and is added to gas for its anti-knock properties. It is also used as a solvent in the industry (Southwell, 2010). It can occur in crude petroleum at levels of 4g/L (World Health Organization, 2010).

Human exposure to benzene can happen during a variety of activities. Including the processing of petroleum products, coking of coal, and productions of toluene, xylene, and other aromatic compounds (World Health Organization, 2010). Benzene exposure can also occur during the production of consumer products; for example gasoline and heating oils. Other methods of exposure include off-gassing from building materials, landfill leakage and disposal of benzene waste (World Health Organization, 2010).

Development of Industrial Hygiene

When oil production began OSHA and other regulatory agencies, whose purpose is to protect workers, were not in existence. During oil production's early years exposures to potential chemical hazards were not given much consideration. Industrial hygiene did not really begin until Dr. Alice Hamilton, in 1910, began studying worker exposures to hazards such as lead and silica (DiNardi, 1997).

As time progressed, the industrial hygiene field advanced. During the 1970s the Division of Industrial Hygiene, what is now known as the National Institute for Occupational Safety and Health (NIOSH), started to perform walk through surveys on more than 5,000 workplaces. This helped to provide a comprehensive evaluation of workplace hazards. Also in 1970 the Occupational Safety and Health Act (OSHA) passed. From these steps, the practice of industrial hygiene grew and several organizations and policies were accepted and designed to protect the worker, and prevent injury or death. (DiNardi, 1997).

History of Benzene Exposure

Benzene is an organic chemical compound used in the production of many products; plastics, oil, and dyes are a few examples. Benzene was discovered by Michael Faraday in 1825. He was able to separate it from oil gas. Forest fires and volcanoes also produce benzene naturally. Benzene has a sweet smell and was used as aftershave in the 19th century because of its sweet odor. This was before people became aware of the serious health effects caused by benzene exposure (Wisegeek, 2014).

If a person is exposed to high levels of benzene they may experience difficulty breathing, dizziness, drowsiness, headaches, and nausea. Ingesting benzene can lead to death (Crystal, 2014). Several studies have shown a strong correlation to benzene exposure and the development of leukemia. The production of oil and its by-products expose workers to many hazardous chemicals and toxicants (Wisegeek, 2014).

One of the earliest documented cases of benzene exposure occurred in 1909 in Maryland. Three girls became ill after being exposed to benzene; at this time it was being used as a rubber solvent for sealing tin cans. They became ill one month after exposure and two of the girls died 4-5 months after exposure (U.S. Department of Health; National Institute for Occupational Safety and Health, 1974).

Other cases involving death after long-term exposure have been documented in England in 1926 and during World War I. In Great Britain, from 1941-1959, 13 fatal cases were reported from benzene exposure in enclosed spaces such as tanks containing benzene residue inside. Other effects noted from this type of exposure were convulsive movements, paralysis, and unconsciousness (U.S. Department of Health; National Institute for Occupational Safety and Health, 1974).

The purpose of this report was to research literature written about the association of benzene exposure and the development of leukemia. This paper was written by first researching benzene and leukemia to gain a better understanding how each works and affects the body. Then articles and case studies pertaining to studies on benzene exposure and the link between the development leukemia were researched. After sorting the articles and case studies, to determine which ones were fact based and pertained to this study. Then the selected articles and case studies were reviewed to determine an association between benzene and leukemia after exposure.

2. Methods

Search Criteria

A systematic review of literature was conducted by reviewing articles in several journals pertaining to benzene exposure and leukemia. The key searched words used were benzene and leukemia. The articles selected were risk assessments or reports on benzene exposure and the development of leukemia.

Data Collection

Each article was reviewed. Results were reviewed and re-assessed. Finally results from each case studied were summarized to form a final conclusion on the link between benzene and the development of leukemia. All sources were documented in the reference list.

Results

A total of six studies were selected to be reviewed. Each study was based on workplace exposures. The cases did provide information on the link between benzene exposure and the development of leukemia. However some studies were unable to provide information on the latency periods and the exact amount of benzene an individual would need to be exposed to, or if an accumulation of exposure was a contributing factor.

3. Leukemia

Background

Leukemia was first documented approximately 150 years ago. In the years since, several advances have been made in understanding the mechanisms of leukemia. Medical advances have developed better ways of diagnosing, treating, tracking cases, and classifying leukemia in recent years. However being able to link the development of this disease to environmental, developmental, and physical factors still remains largely a mystery (Lackritz, 2001).

Leukemia is a type of cancer involving the blood forming cells; mostly white blood cells. When a person has leukemia their white blood cells do not mature fully and their body rapidly produces immature white blood cells. These cells are different from normal cells and are unable to perform the functions mature cells do. Eventually these leukemic cells replace normal cells in the bone marrow of an individual. Often this uncontrolled proliferation can cause the leukemic cells to spill over into the blood stream and eventually enter vital organs. This decreases the amount of room available for normal/mature cells like red blood cells, nonmalignant white cells, and platelets. There are several types of leukemia. Each type affects a different type of white blood cell and involves a different level the white blood cells maturity (Lackritz, 2001).

Types of Leukemia

There are four types of leukemia: Acute myeloid leukemia (AML), Chronic myeloid leukemia (CML), Acute lymphocytic leukemia (ALL), and Chronic lymphocytic leukemia (CLL) (Cancer Treatment Centers of America, 2014).

Acute myeloid leukemia (AML) is type of cancer that is fast growing and found in the blood and bone marrow of an individual. AML is the most common type of leukemia. It develops from the body's bone marrow making blast cells that do not fully mature and then these immature cells develop into white blood cells. Due to these cells being immature they are unable to defend the body against infections. The bone marrow may also produce abnormal red blood cells and platelets. Theses abnormal cells will outnumber the normal cells in time due to their ability to rapidly produce (Cancer Treatment Centers, 2014).

Chronic myeloid leukemia (CML) is similar to AML. It starts in the bone marrow, where immature cells do not develop into mature cells and eventually outnumber the mature cells. CML can start out slow but its progression can become fast like that of AML and spread to any organ in the body. However it does have one main difference. It has been proven that CML is associated with chromosome Philadelphia (Ph chromosome). The Ph chromosome is made when a piece of chromosome 22 breaks off and attaches to chromosome 9; chromosome 9 will also have a piece detach and attach itself to the chromosome 22. This breaking and reattaching of the chromosomes creates certain genes that become known as the cancer gene when they combine (Cancer Treatment Centers, 2014).

Acute lymphocytic leukemia (ALL) develops after abnormal white blood cells accumulate in the bone marrow. ALL's progression is rapid. Healthy lymphocytes are replaced with immature cells that are unable to function. These immature cells eventually make their way to the blood stream where they are transported to other organs and tissues; including the brain, liver, lymph nodes. Once they reach other organs and tissues the cells continue to reproduce rapidly. ALL mainly affects the B and T cells; which play an active role in protecting the body from infection (Cancer Treatment Centers, 2014).

Chronic lymphocytic leukemia is very similar to ALL except it is slow in progression. Mature, healthy lymphocytes are overgrown and crowded by immature cells that are able to function properly. These immature cells are transported to other parts of the body, brain, liver, lymph nodes, via the bloodstream. Like ALL once these cell types have reach their destination they begin to reproduce, just slower (Cancer Treatment Centers, 2014).

Benzene

Scientists have found a link between certain occupations involving chemical exposures and the development of leukemia (Klaassen, 2008). There have been various studies that suggest exposure to benzene may lead to the development of leukemia. However the dose or concentration required to induce leukemia, as well as the latency period for development can vary depending on the study. Latency period can be 5-15 years according to National Institute of health (Triebig, , 2009) or one study found it could be 5-30 years (Rinsky, et al., 1987, p. 1046).

The first occupational cases to benzene exposure began to be documented in literature in the 1930's. Because of its seriousness, exposure investigations were directed at cause, recognition, and control. These reports eventually led to the use of other solvents (U.S. Department of Health; National Institute for Occupational Safety and Health, 1974).

Benzene is a colorless liquid with a sweet odor. It is also known as benzoyl (Public Health Statement for Benzene, 2011). Derived mainly from petroleum benzene is produced commercially in the United States. It is largely used as a product for the synthesis of other chemicals. Benzene's main route of exposure is inhalation in the industrial and everyday field (Klaassen, 2008). People can start to smell benzene at about 60 ppm, the odor threshold for benzene is 61 ppm, according the American Industrial Hygiene Association (EPA, 2013). A person can taste benzene in the water at 0.5-4.5 ppm (Public Health Statement for Benzene, 2011).

4. Benzene: Mechanism of toxicity

In order to understand the toxicity of benzene, its mechanism of metabolism must first be understood. The initial step involves the oxidation of benzene into an epoxide. The main catalyst for this is the hepatic CYP2E1.

Once oxidized, benzene becomes benzene oxide and it is further metabolized by three pathways. The first is joining with the growth stimulating hormone (GSH) to form a permercapturic acid. This acid is then converted into phenyl-mercapturic acid. Another method is the rearrangement of benzene without the help of enzymes to form phenol. The third method is by hydration. Benzene is hydrated by epoxide hydrolase form benzene dihydrodiol. Benzene dihydrodiol is then oxidized by dihydrodiol dehydrogenase to form catechol. Catechol can be converted to benzoquinones. Benzoquinones are believed to be the most toxic metabolite of benzene. (Klaassen, 2008) In Figure 1 the biotransformation of benzene is demonstrated.

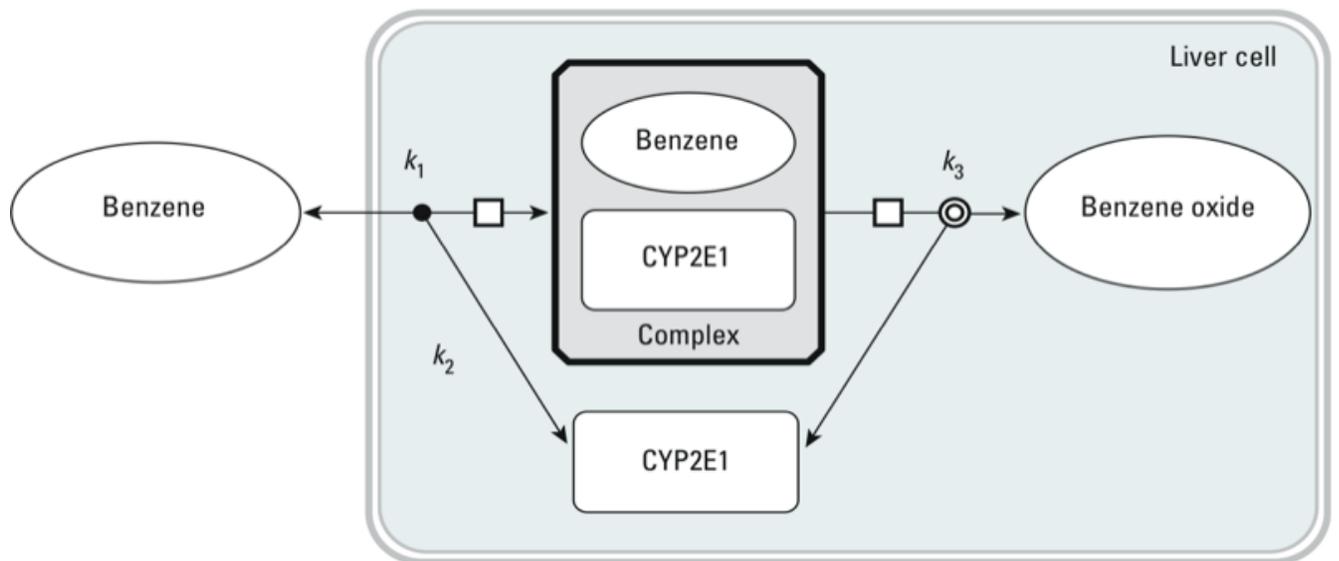


Figure 1: Biotransformation of benzene (ehp.niehs.nih.gov, n.d.)

The liver is the main organ that metabolizes benzene. Many authorities believe it is also metabolized in the bone marrow and this is why it plays a role in the development of leukemia. Through laboratory studies, it has been determined that DNA and protein adduct levels were higher in bone marrow than in the liver of benzene-dosed mice (Klaassen, 2008). It was thought and now accepted that phenolic conjugates that are produced in the liver are transported to the bone marrow via the blood. Once in the bone marrow they are hydrolyzed and oxidized to form benzoquinones (LaVelle, 1991).

Benzene metabolites can target a number of cells in the bone marrow. Exposure to benzene results in the inhibited growth and development of bone marrow pluripotent stem cells. Even more mature cells like stromal cells, and erythroid and myeloid colony forming cells can be affected by an exposure to benzene. Interleukin synthesis is prohibited by macrophage inducing hydroquinone; this results in altered differentiation of myeloid and lymphoid cells, which are normally active in the immune system (Klaassen, 2008).

Research has suggested killing of stromal macrophages and fibroblasts can result in a decrease in cytokines and growth factors. This reduction can lead to the death of immature or mature hematopoietic progenitors by apoptosis. Apoptosis occurs because of the changes made in the cells from stromal macrophage deaths and the decrease in cytokines. This programmed cell death is the body's mechanism for ensuring abnormal cell production does not increase. Note that the erythroid cell types are more susceptible than the myeloid cell types to benzene. Myeloid cells do have the ability to reproduce, unlike erythroid cells, if exposed to benzene. However the myeloid cells develop neoplastic characteristics and the end results is acute myelogenous leukemia (AML) (Klaassen, 2008).

Several investigations have discovered there are several mechanisms for benzene toxicity/leukemogenesis. Previously mentioned, benzene and its metabolite's actions are required together to cause myelotoxicity. It is now known that benzene metabolites have the ability to bind to GSH, proteins, DNA, and RNA. This binding results in the changing of the hematopoietic microenvironments and its functions. These changes occur because the necessary enzymes for normal cell function are inhibited, cell populations are destroyed, and cell growth is altered for certain cell types. When hydroquinones bind to the spindle fiber proteins of cells by covalent bonding, cell reproduction is stopped (Hedli & Snyder, 1996).

Through research it has been determined that there is a good possibility that oxidative stress contributes to benzene toxicity. Peroxidase activity is abundant in bone marrow; the phenolic metabolites of benzene are able to be activated in the bone marrow because of this process. Here they become quinone derivatives. Myeloperoxidase in murine and human progenitor cells can interact with hydroquinone to become p-benzoquinone. There is evidence to suggest that p-benzoquinone treated cells can form semiquinone radicals. Leading to the belief that reactive oxygen moieties are made from the formation of semiquinone radicals. These oxygenated radicals cause strands to break in the DNA, which causes cell mutation and apoptosis. It is thought that this apoptosis could lead to abnormal hematopoiesis and neoplastic progression (Klaassen, 2008). Figure 2 demonstrates the multiple pathways leading to toxicity benzene takes once it enters the body.

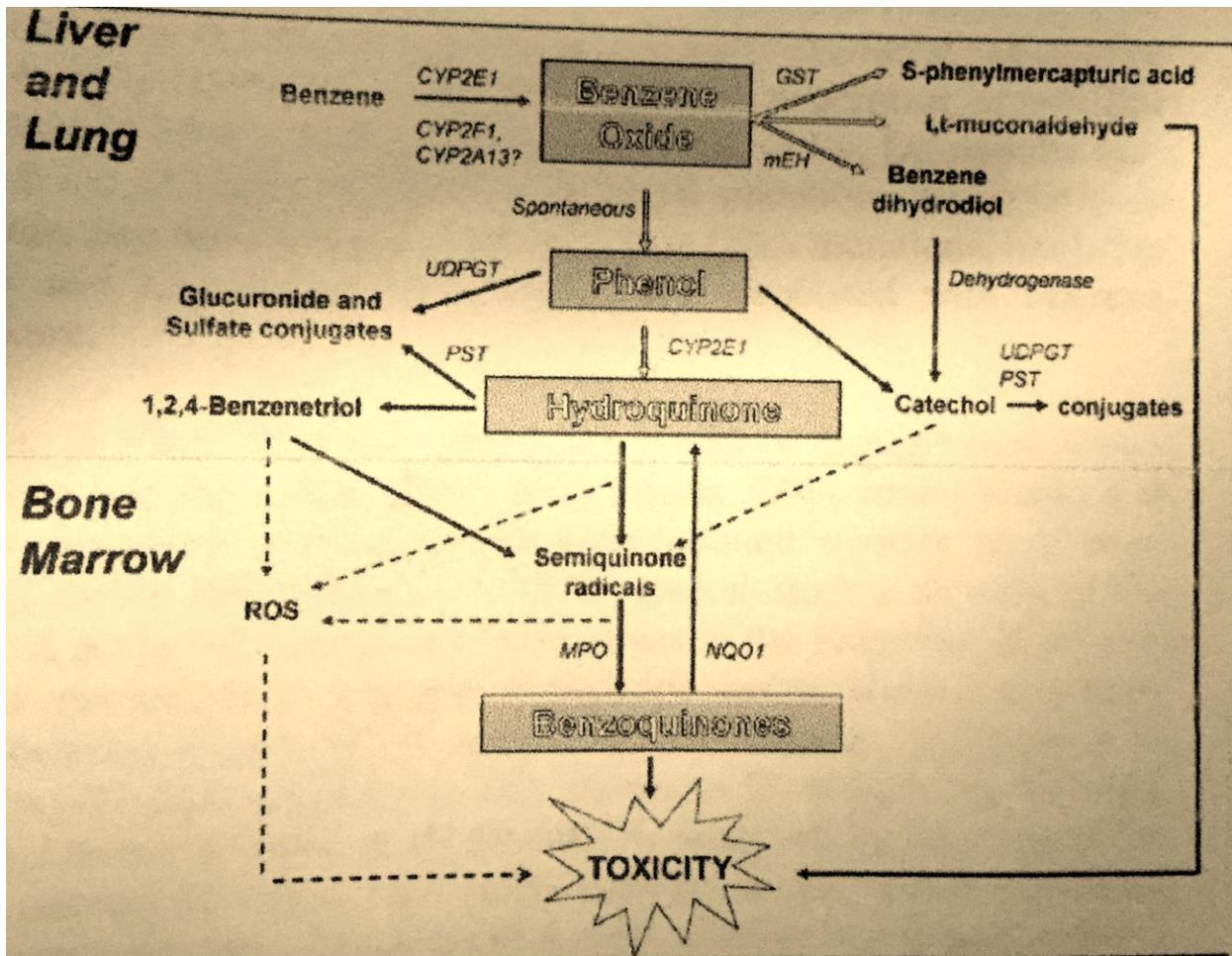


Figure 2: Description of benzene's mechanism of action (Hedli & Snyder, 1996)

Benzene Exposure: Occupations with potential exposure

If an individual works in an industry that uses and/or produces benzene then this individual may have a risk for exposure. Some of these industries include benzene production (petrochemicals, petroleum refining, coke and coal chemical manufacturing), rubber tire making, and storage and/or transport of benzene and petroleum products that contain benzene. Steel workers, rubber workers, shoe makers, laboratory technicians, firefighters, and gas station employees are other occupations that expose workers to benzene (Safety and Health Topics: Benzene, 2014).

Benzene has three routes of exposure: ingestion, inhalation, and absorption. The primary route of exposure is through inhalation. Once it enters the body it is absorbed in the blood stream. Once in the bloodstream, benzene travels throughout the body and can store in certain parts of the body; bone marrow and fat. However benzene can go through biotransformation in the body as previously discussed. This biotransformation occurs in the hepatic region and plays an important role in toxicity (Hedli & Snyder, 1996).

Exposure Limits

Since benzene is a known carcinogen, OSHA and NIOSH have set established exposure limits. OSHA has a permissible exposure limit (PEL) for a TWA (time weighted average) 1ppm and short-term limit exposure limit (STEL) of 5ppm. NIOSH's recommended exposure limit (REL) for a TWA is 0.1ppm and for a ST it is 1ppm (NIOSH Pocket Guide to Chemical Hazards-Benzene, 2012). Due to its carcinogenic effects on the body several organizations have placed exposure limits on benzene. Table 1 displays the exposure limits for benzene as determined by OSHA, NIOSH, and ACGIH.

Table 1

Exposure Limits	Limit Value
OSHA Permissible Exposure Limit (PEL) - General Industry	1 ppm TWA 5 ppm STEL
OSHA PEL - Sectors Excluded from General Industry Note: These values apply to the industry segments exempt from the 1 ppm 8-hour TWA and 5 ppm STEL of the benzene standard at 1910.1028	10 ppm TWA 25 ppm Ceiling 50 ppm Maximum peak above ceiling (10 minutes)
OSHA PEL - Construction Industry	1 ppm TWA 5 ppm STEL

(OSHA, 2014)

Recommendations for workplace safety

Skin and eye protection equipment is recommended for employees who have the potential to come in physical contact with benzene. Workers who have a potential for an exposure or a previous exposure should have medical monitoring: analyzing urine for total phenol levels, physical examinations, and monthly lab draws (U.S. Department of Health; National Institute for Occupational Safety and Health, 1974). This monitoring will help prevent workers from being over exposed.

If the urine phenol level is greater than $25\mu\text{/g}$ with a specific gravity of 1.024, then two follow up urine screens should be performed within a week (Adopted Biological Exposure Determinants). If the elevated findings are confirmed measures need to be taken to reduce the workers exposure. These steps include personal protective equipment (gloves, goggles, protective clothing, respirators, and etc.) and environmental controls (housekeeping, proper ventilation, proper disposal, and etc.), and finally all employees should be made aware they are working with hazardous materials and each employee should have medical records kept for further reference and monitor (U.S. Department of Health; National Institute for Occupational Safety and Health, 1974).

5. Epidemiology Literature Review

A literature search was conducted to assess the public and occupational exposure to benzene and the risk for disease, specifically leukemia. A summary of these studies and their relevance is presented below.

Search Criteria

A systematic review of literature was conducted by reviewing articles in several journals pertaining to benzene exposure and leukemia. The key searched words used were benzene and leukemia. The articles selected were risk assessments or reports on benzene exposure and the development of leukemia.

Data Collection

Each article was reviewed. Results were reviewed and re-assessed. Finally results from each case studied were summarized to form a final conclusion on the link between benzene and the development of leukemia. All sources were documented in the bibliography.

Results

A total of six studies were selected to be reviewed. Each study was based on workplace exposures. The cases did provide information on the link between benzene exposure and the development of leukemia. However some studies were unable to provide information on the latency periods and the exact amount of benzene an individual would need to be exposed to, or if an accumulation of exposure was a contributing factor.

The New England Journal of Medicine: Benzene and Leukemia – An Epidemiologic Risk Assessment.

The purpose of this analysis was to assess quantitatively the association between benzene exposure and leukemia. The researches followed 1165 workers from three rubber manufacturing plants in two locations from January 1, 1940 to December 31, 1965 (Rinsky, et al., 1987).

The study concluded that if a person's cumulative exposure to benzene decreased then a person's risk for death from leukemia would decrease. According to the statistical analysis of the data in the study a person with an average exposure level of 10 ppm for years would have an increased risk of death from leukemia of 154.5 (95% confidence interval). If this exposure level was dropped to 1 ppm the risk level would decrease to 1.7 (95% confidence interval). If the exposure amount could be lowered to 0.1 ppm then the risk would be equal to background (Rinsky, et al., 1987).

Environmental Health Perspectives: Consistencies and Inconsistencies Underlying the Quantitative Assessment of Leukemia Risk from Benzene Exposure

According to the authors the purpose of this analysis was to examine risk assessments for benzene and observe the inconsistencies within the study and consistencies between studies that could affect the quantitative determination of the risk from exposure to benzene and the development of AML, and its variants; ALL, CML, CLL (Lamm, Walters, Wilson, Byrd, & Grunwald, 1989).

The data collected strongly supported the idea of AML being caused by excessive benzene exposure (Lamm, Walters, Wilson, Byrd, & Grunwald, 1989). This corresponds with other recent studies. However information supporting the development of ALL, CML, and CLL were inconsistent to support this theory. This study did conclude that if data was to be used for a risk assessment the data should be limited to AML cases.

Leukemia Risk Associated With Low-level Benzene Exposure

Study focused on men who were part of an Australian petroleum industry cohort who had been found to have lymph-hematopoietic cancer. It was thought an occupational exposure to benzene was the cause of this (Glass, et al., 2003).

Results showed an exposure above 2 ppm/years with intensity at the highest of 0.8 ppm would increase the risk for leukemia. The study found risk for leukemia was an excess and it was associated with cumulative benzene exposures and at benzene exposure levels lower than reported in previous studies. (Glass, et al., 2003).

Lympho-haematopoietic Malignancies and quantitative estimates of exposure to benzene in Canadian petroleum distribution workers.

In this case study analysis was conducted to evaluate the relationship between mortality from lympho-haematopoietic cancer and long term low level benzene exposures in males working the petroleum distribution field (Schnatter, et al., 1996).

The study found risk for developing leukemia, non-Hodgins's lymphoma, and multiple myeloma was not associated with increasing cumulative exposures to benzene. It was determined that duration of the exposure to benzene was more closely associated with the risk for leukemia (Schnatter, et al., 1996)

Aplastic Anemia in Petrochemical Factory Workers.

Report was written based on analysis of exposures to low levels of benzene and the development of aplastic anemia in an exposed worker. In 1998 a former petrochemical worker developed aplastic anemia. He was non-smoker and did not drink alcohol (Baak, 1999, p. 851).

Between 1993-1998 industrial hygienists performed routine surveys of air quality at the plant. The amount of benzene in the air was approximately 0.28ppm. These findings led researches to conclude that low level exposure to benzene is toxic. The writers of this case study did state more research needed to be performed to establish the toxicity of exposure to low levels of benzene (Baak, 1999, p. 852).

Occupational Exposure to Benzene at the ExxonMobil refiner at Baton Rouge, Louisiana (1977-2005)

The authors of this study wanted to focus on the airborne concentrations of benzene at a specific refinery; no extensive study like this had been done before. Airborne concentrations at a refinery in Baton Rouge were evaluated over a period of time (Panko, et al., 2009). Data was collected for non-task and task specific samples.

Results showed the average benzene air concentration at the refinery for all non-task samples was 0.097 ppm and 43% of the workers sampled had air concentrations below detection (Panko, et al., 2009). The task specific sample showed air concentrations that were not detectable for the majority of the specified tasks (Panko, et al., 2009). The authors concluded the results from this study were consistent with results from other studies on occupational benzene exposures in the petroleum industry (Panko, et al., 2009).

6. Discussion:

Benzene is used in the production of many products and can be a by-product in the production of oil. For many years it has been known that exposure to benzene can cause severe health effects. Studies have found a link to benzene exposure and the development of leukemia.

Benzene has been classified as a carcinogen because of this association. OSHA and NIOSH have established permissible exposure limits. These limits are low because of the severe effects of exposure. Researchers believe a cumulative exposure over a period of time is how a worker develops leukemia. Many studies have examined the exposures of workers to benzene in the petroleum or industrial field. These studies found some workers had developed leukemia 20-30 years after first being exposed.

Researches are unclear of how much benzene or how long a person has to be exposed to it before their risk increase. Most researchers believe being exposed to 2 ppm-year could cause an increase in risk. A very few believe it would take an exposure of 220 ppm-year. However, most researchers agreed a cumulative exposure to benzene over a period of time was risk for the development of leukemia.

7. Conclusion

Benzene can have serious health effects on a person. It has been shown a person may develop leukemia after being exposed to benzene. What is still unknown is the amount of benzene and how long a person has to be exposed before they are at risk.

It is thought a person may develop leukemia or become at risk for developing leukemia after being cumulatively exposed over a long period of time to benzene. The amount of benzene is still not known. Some researchers believe a small amount over a period of time could be detrimental to a human health.

There is also speculation that benzene causes other types of cancer. The literature reviewed in this analysis concluded that there wasn't enough consistent data to support this and more studies would need to be conducted to determine if this theory was positive. The literature did conclude however that benzene could cause different types of leukemia based on cell type. It was found more research would be needed in order to determine which cell type leukemias were associated specifically with benzene exposure.

What is known is benzene is a carcinogen and exposure to it can lead to the development of leukemia later on in life. What is not known for sure is the amount of exposure, exposure time, and if a certain cell type is specific to benzene exposure induced leukemia.

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