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MODULE 13
OCCUPATIONAL LEAD EXPOSURE

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Disclosure: Capt. Fajardo does not have any financial arrangements or affiliations with any corporate organizations that might constitute a conflict of interest with regard to this continuing education activity.

Goals:

1. Learn the principles of Occupational Lead Exposure.
2. Know the effects of lead on organ system function.
3. Understand the basis of the clinical evaluation.
4. Learn the management of lead poisoning

As part of this lecture the reader should become familiar with the following reading material, included as part of this presentation:

Lead Toxicity- case studies in Environmental Medicine.

LEAD

Lead is a naturally occurring blue-gray metal, which commonly consists of lead sulfide, lead sulfate and lead carbonate. These lead ores are usually found in association with ores from other metals such as iron, zinc, copper, and silver. Lead is ubiquitous in our environment. Lead is an ancient metal that has been used since prehistoric times in the making of jewelry, statues and vases. The 20th Century saw a greater use of lead products than any previous time period. This heavy use reflects the industrial adaptation of this metal and its use as a transportation fuel additive. Unfortunately, the mining and use of lead has produced a sharp increase of lead concentration on the earth's surface. Lead from gasoline has been a particular offender, since virtually all the lead from gasoline emissions is deposited as a fine particulate causing widespread contamination of the air, water, and soil. Even though lead gasoline has been practically eliminated in the United States, it continues to be a problem in other parts of the world. In order to minimize and further reduce lead accumulation limitations and standards controlling the use of lead products and its manufacturing have been implemented. Industrial lead exposure in the U.S. is regulated by the 1978 OSHA lead standard. Exempt from this regulation are construction and agricultural workers. It is estimated that approximately 3 million workers are still potentially exposed to lead in their work environment.

Commercial lead is extracted from the mining and processing of lead ore, a primary source of occupational lead well documented throughout recorded history. The recycling of scrap metal, in particular lead recovered from lead-acid batteries, accounts for over 90% of the secondary sources of lead. Most lead exposures result from a variety of moderate to high-risk occupational settings involving inorganic lead. However, exposure to organic lead, in particular tetraethyl lead (TEL), also occurs in the manufacturing of this product. Occupations associated with exposure to inorganic lead include:

Battery makers	Brass makers
Cable makers	Chemical operators
Demolition workers	Firing range users/workers
Foundry workers	Glass polishers
Gun (barrel) makers	Jewelers
Lead burners	Metal grinders
Painters	Pigment makers
Pipe cutters	Ship burners
Solderers	Glassmakers (stain glass)
Welders	Printers

Of all the aforementioned occupations some are considered high-risk. These include operations where lead products are burned and lead fumes are generated, such as smelting, welding and cutting of lead or lead painted surfaces. Others in this category are spray painting, sanding and scraping of lead paints, automobile radiator repair operations, crystal glass mixing, and the production of plastics that include the mixing of lead salt stabilizers. Moderate risk occupations include solderers, plumbers, factory workers, automobile repair mechanics, lead founders and glass blowers, ship repair workers, stain glass and pottery glazers, cable makers and stereo typesetters.

Inhalation or ingestion are significant sources of inorganic lead exposure and accumulation in occupational settings. However, outside the workplace, in the overwhelming majority of adult poisonings and in children the primary source of exposure is lead paint. Soil is a secondary source of exposure and water is a third and less important source. Children are the group, within the general population, that is most susceptible to the toxic effects of lead. In the U.S. the mean blood lead level for children is $7\mu\text{g}/\text{dl}$, with levels of $10\mu\text{g}/\text{dl}$ or higher indicative of excessive exposure. According to CDC estimates over 10 million children in the U.S. have excessive blood lead levels with the proportion being particularly high among inner city preschoolers. The major high-dose concentrated source of lead among U.S children remains lead-based paint. Lead paint removal during housing renovations, paint chip ingestion, preparation of baby formula with lead contaminated water and exposure to contaminated parental work place clothing are noted as primary sources of contamination among children less than 1 year of age. Older homes tend to have higher lead levels than newer homes build after the lead paint prohibition of the late 1970's. However, even newer homes have been found to have significant amounts of lead paint. Solder used in water pipes is also a source of lead

contamination. Approximately 20% of lead contamination in adults and 50% of lead contamination in children results from gastrointestinal ingestion.

Measurements of blood and air lead levels are necessary in the evaluation of inorganic lead exposures. The measurement of lead in the air helps provide information on the source and level of the exposure. Blood levels identify those individuals with unusual high exposures not detected by air monitoring. OSHA lead standards mandate that any worker with lead levels at or above 50µg/dl must be removed from the work area and not allowed to return until levels have fallen below 40µg/dl.

The best method of assessing lead contamination in children is by determining blood lead levels. A variety of chemical and physical techniques are also available to determine lead levels in the general environment. For example, air samplings are performed in accordance with the Environmental Protection Agency's (EPA) *Air Lead Standard*, which in the U.S. are set at 1.5 µg/m³. Lead in water is also measured in accordance with EPA standards. The *Water Lead Standard* level is presently set at 50µg/L. Lead levels in paint products can be determined by using a portable hand held x-ray fluorescent (XRF) detector. Lead levels in soil and dust are determined by standard chemical techniques. Workers with a significant risk for lead exposure need to be placed in a monitoring program, such as OMSEP, in accordance with specific and explicit OSHA regulations. Medical surveillance is determined by a number of factors, including the working conditions, toxicity of the agent, and the level and degree of exposure. In general, conditions that result in exposure levels above the "action level" for that particular substance will require surveillance. The "action level" as per the OSHA standard is referred to one half of the "threshold limit value" (TLV) established by the American Conference of Governmental Industrial Hygienists (ACGIH) and followed by OSHA as the permissible exposure limit (PEL). In the OSHA *Lead Standard* the action level represents 60% of the upper exposure limit, which is 8 hours, time-weighted average. Detection of blood lead levels above 40µg/dl is indicative that a significant overexposure has occurred. Workers with levels above 60µg/dl on one test or with a six-month average above 50µg/dl must be removed from the worksite.

The manufacturing as well as the cleaning of tanks and pipes known to have contained, in particular, the fuel additive tetraethyl lead (TEL) are an important source of organic lead exposure. Intentional inhalation of gasoline vapors for recreational use is a common source of organic lead exposure. Elevated blood levels are noted soon after inhalation of these products.

LEAD POISONING

Concerns about lead overexposure are addressed through routine biological monitoring testing. In low risk children this is accomplished by scheduled blood lead level (BLL) testing at ages 1 and 2 and more frequently for high-risk children. Inhalation and ingestion of lead and lead products can result in accumulation in three primary body sites: blood, bone and soft tissue.

Neurological Effects:

Lead effects are most noticeable on nervous system function, primarily in children. Lead encephalopathy, manifested by apathy, seizures and coma, is typical in children while peripheral nervous system effects are more commonly noted in adults. Lead induces pathologic changes in the nerve fibers including segmental demyelination and axonal degeneration. Children who recover from acute lead encephalopathy are often left with neuropsychological deficits, including decreased intelligence and attention span, mood changes and irritability. The functions most affected are visual intelligence and visual motor coordination. These changes have been specially noted with lead blood levels of 70 μ g/dl or higher. Depression, fatigue and short-term memory loss are also found with increased prevalence along with senile dementia, motoneuron disease (amyotrophic lateral sclerosis)[ALS] and chronic psychiatric conditions. Children with chronic lead exposure have been found to have lower IQ scores when compared to unexposed children. Neonatal studies have also confirmed the negative effects on intelligence with blood lead core values as low as 15-20 μ g/dl. In the past blood lead toxicity was considered at a level of 25 μ g/dl. At present any children with blood lead levels of 10 μ g/dl are required to undergo medical evaluation and surveillance. It should be noted that acute and chronic neurological effects of lead have been attributed to an apparent displacement of calcium ions. The changes in intracellular calcium concentrations induced by lead have been shown to interfere with mechanisms involved in memory, learning, and neurodevelopment. Encephalopathy is the most serious complication of acute inorganic lead poisoning in children. Early recognition of lead exposure is essential in preventing permanent neurological sequelae.

Clinical Manifestations:

The clinical effects of lead can vary and produce three distinct toxic patterns: acute, subclinical and chronic.

Acute: An intense and brief exposure can lead to acute lead poisoning. Abdominal pain, constipation, irritability, vomiting, fatigue, central nervous system dysfunction, peripheral neuropathy and hemolytic anemia manifest this syndrome. This syndrome can progress to full encephalopathy manifested by coma, convulsions and papilledema. Personality changes, headaches and abnormalities of hepatic transaminases have also been reported in milder presentations along with arthritic symptoms, myalgias and arthralgias. Blood lead levels in this syndrome have been reported at 70 μ g/dl or higher.

Subclinical: Subclinical toxicity reflects the harmful effects of lead at levels previously thought to be safe. It usually denotes a low-level exposure that causes harmful effects in the absence of symptoms. Short-term verbal memory functions are consistently impaired as the levels rise above 40 μ g/dl, while changes in behavior and cognitive function are typical at BLL below 70 μ g/dl. Toxic signs can be identified through specialized testing while the patient remains asymptomatic.

Chronic: long term overexposure can lead to an insidious illness manifested by weakness, depression, headaches, arthralgias, impotence, loss of libido, abdominal colic and anemia. Laboratory abnormalities often reflect an elevated reticulocyte count, decreased thyroid and adrenal function and impaired renal function. The latter can progress to chronic renal failure in more advanced stages of the disease. Hypertension is a common finding and can contribute to the development of encephalopathy as the disease progresses. Sniffing of gasoline is a common etiology for this condition. Other symptoms noted with chronic lead intoxication include seizures due to current or past exposures. These are noted on the EEG as focal and/or paroxysmal abnormalities. The auditory system can also be affected with disruption of the auditory pathways, an effect that lasts long after the blood lead levels have been lowered. The chronic effects of lead on the peripheral nerves have already been noted. It should be pointed out that Nerve Conduction Studies (NCS) could be used to detect subclinical neuropathy and quantify the level of severity of this condition. This type of studies has shown that individuals involved in the cutting of lead-painted steel with acetylene torches reveal slower motor nerve conduction velocities than other lead exposed workers. Levels above 30 $\mu\text{g}/\text{dl}$ have been shown to have a more significant decrease on motor nerve conduction velocities. This dose-response relationship has also been noted in the peripheral nerve conduction velocities of children. NCS has also been utilized to document the subclinical effects in of low-level exposure from paint chip pica in children.

Renal Effects:

Lead nephropathy is an insidious process manifested by the destruction of tubular cells, primarily those lining the proximal tubules. The functional impairment with noted elevations of the BUN and serum creatinine do not become evident until 50-70% of the nephrons have been replaced by fibrosis. Atrophy and interstitial fibrosis with dilatation of the renal tubules is the hallmark of chronic lead nephropathy. These changes are indistinguishable from changes resulting from chronic hypertension that is often coexisting. Urine lead levels tend to fluctuate with changes in renal function and thus do not reflect current exposure, as is the case with blood lead levels (BLL). The ratio of urine lead levels to BLL is higher with organic lead level exposure than with inorganic lead products. This subtlety can be useful in determining the source of the exposure. In children acute lead poisoning is manifested by large quantities of glucose, phosphates and amino acids in the urine due to the injurious effects of lead on the proximal tubular cells and the development of acute Fanconi's Syndrome. This syndrome is usually reversible with no known predisposition for long-term sequelae. Other effects of lead on the renal system include inhibition of the metabolic hydroxylation of Vit D, formation of dense intranuclear inclusion bodies resulting from a lead-protein complex and increased reabsorption of uric acid by the tubular cells leading to hyperuricemic gout. Some of the inhibitory effects of lead on renal function occur at blood lead levels below 25 $\mu\text{g}/\text{dl}$, while the formation of lead-protein complexes occur at blood levels of 40-80 $\mu\text{g}/\text{dl}$.

Hypertension:

The association between lead toxicity and hypertension has been well documented in toxicological studies. Periodic blood pressure monitoring is essential in individuals with lead exposure since even low-level elevations have proven to be associated with increase mortality from heart disease and stroke. The principal neuropathological finding found in individuals with terminal lead encephalopathy is cerebral edema, which is associated with arterial hypertension. This is accompanied by purpuric hemorrhages, swollen brain tissue and changes in the white matter characterized by diffuse fragmentation of the myelin sheaths and reactive astrocytosis.

Reproductive Effects:

Lead toxicity can induce permanent developmental defects if left uncorrected. Lead passes freely across the placental barrier with the resultant effect being an irreversible neurological impairment on the fetus. Women with a BLL above 20 $\mu\text{g}/\text{dl}$ should cease further lead exposure and wait 1-2 years before becoming pregnant. If a woman with prior lead exposure wishes to become pregnant further examinations should be conducted to determine the body burden of lead or undergo a chelation mobilization challenge before conception. Adding to this problem is the mobilization of stored iron induced by the stressors of pregnancy, which enters the mother's blood and subsequently the child.

Studies have found that cord blood lead levels as low as 15 $\mu\text{g}/\text{dl}$ can negatively affect childhood intelligence. Experimental studies on the effects of lead toxicity have also demonstrated that both sexes suffer negative effects in fertility as a result of lead toxicity. Effects on sperm morphology and total sperm counts have been noted at lead levels below 50-60 $\mu\text{g}/\text{dl}$ although it has not been demonstrated that high exposure to lead on the father, before conception, results on fetal injury.

Clinical Evaluation:

Confirming excess lead absorption and resultant lead induced organ system impairment is essential in the diagnosis of inorganic lead intoxication. Approximately 1% of the body lead burden is in blood bound to red cells. Elevations of lead in the blood remain the best indicators of acute lead exposures. The level of lead in the blood rises rapidly after an acute exposure and can remain elevated for several weeks after the exposure. The half-life of lead in the blood is 36 days. The normal adult BLL is 10 $\mu\text{g}/\text{dl}$ and hypertension, which is usually the first manifestation of toxicity, is noted at levels between 10-20 $\mu\text{g}/\text{dl}$. Other clinical symptoms, such as irritability, abdominal colic, fatigue and others begin to manifest at levels of 30-40 $\mu\text{g}/\text{dl}$. The frequency and severity of symptoms increase as the lead levels rise. Under OSHA standards workers with BLL above 50 $\mu\text{g}/\text{dl}$ must be removed from lead exposure and cannot return to work until the levels have fallen below 40 $\mu\text{g}/\text{dl}$. Approximately 90% of absorbed lead is ultimately deposited in bone, where the half-life is estimated at 10,000 days. In individuals with long term chronic exposure the influence of lead from bone and soft tissue make the BLL a poor indicator of current exposure. Under these conditions the BLL primarily reflects the release of lead from

skeletal stores. The BLL may still serve to assess the long-term dose-response effects of lead exposure in the renal, vascular and central nervous systems.

Lead Analysis Procedures:

There are several procedures available to measure the lead body burden. Some of these procedures are based on old standards while others utilize new technology. X-ray fluorescence (XRF) analysis is one of the new technology procedures, which permits direct measurement of bone lead concentrations by taking advantage of the fact that lead is the principal depot for lead. This non-invasive technique provides an individualized assessment of the body's lead burden. Older known tests include the zinc protoporphyrin (ZPP) or free erythrocyte protoporphyrin (FEP) levels, which reflect the toxic effects of lead on erythrocytes. Unfortunately, FEP levels rise when the lead levels are above 30-40 μ g/dl and remain elevated for several months after the acute levels have fallen. This persistent elevation makes this test unreliable as a screening test for occupational lead exposure. The gold standard for determining body lead burden is the urinary lead excretion after the intramuscular administration of 1 G of Calcium EDTA. This procedure is better known as the chelation challenge. Its interpretation of lead toxicity is based on the urinary excretion of over 600 mg of lead in a 72-hour period following the injection. This finding is diagnostic of past excessive exposure and an elevated lead body burden. It is expected that the XRF will replace the chelation challenge test in the future as the gold standard for cumulative lead absorption.

Other tests that are still recommended during the initial evaluation of lead intoxication include a complete blood cell count, routine blood chemistries, creatinine clearance, BUN, thyroid function tests and blood pressure readings. These baseline tests should be performed on all asymptomatic workers exposed to lead. The finding of lead lines on the gums during the physical examination, clinical evident anemia, and basophilic stippling are unreliable, unpredictable and often late manifestations of lead toxicity.

Management of Lead Toxicity:

The primary treatment modality for acute inorganic lead exposure is removal from the exposure site in all cases of acute intoxication. This is followed by chelation therapy with calcium EDTA for 2-3 days. This involves the administration of 1 G calcium EDTA with a constant infusion of saline. Major complications include the development of hypokalemia, oliguria, or hematuria. Oral penicillamine at 2 g/d may be used subsequently to continue with the chelation therapy. Succimer (dimercaptosuccinic acid) is gradually supplanting EDTA as the chelating agent of choice. The threshold for chelation therapy in children and adults is cited, in most textbooks, as 45 μ g/100cc of whole blood. However, a growing number of clinicians are advocating treatment at levels as low as 25 μ g/100cc. Chronic lead intoxication is managed in a similar fashion although treatment efficacy has not been proven. Management of organic lead exposure (TEL) is primarily supportive. Chelation has not proven effective; Observation and sedation are often required for prolonged periods.

Proceed to:

Case Studies in Environmental Health- Lead Toxicity

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