Jurnal Teknokes
International: Rapid Review: Open Access Journal Vol. 16, No. 3, Sept. 2023, pp. 156–163 e-ISSN 2407-8964; p-ISSN 1907-7904

RESEARCH ARTICLE **OPEN ACCESS**

Manuscripts received July 18, 2023; revised August 10, 2023; accepted August 12, 2023; Publish date: 25 September 2023
Digital Object Identifier (**DOI**): https://doi.org/10.35882/teknokes.v16i3.617

How to cite: Michael J Bobzien, "A Systematic Review of Research to Determine Toxicity of Involuntary Tobacco Smoking as Compared to First Hand Smoking and if Chronic Involuntary Tobacco Smoking during Childhood Causes Skeletal Diseases Later in Life", Jurnal Teknokes, vol. 16, no. 3, pp. 156–163, September. 2023.

A Systematic Review of Research to Determine Toxicity of Involuntary Tobacco Smoking as Compared to First Hand Smoking and if Chronic Involuntary Tobacco Smoking during Childhood Causes Skeletal Diseases Later in Life

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ABSTRACT A healthy adult life depends on a healthy childhood. Toxic exposures during childhood impact human development and negatively impact adulthood. It is important to be aware of the impact of toxic exposures children may be exposed to. A child will breath up to 3 times the volume per body weight compared to an adult and take in the same ratio of airborne toxicants. A child's organs and immune system are not fully developed to offer protection from airborne and residual toxins compared to an adult. Children have limited options to escape toxins if they are in the home. Thus, children are the most susceptible to the effects of toxins in their environment and should be protected from such exposures. Comprehensive literature review utilizing google scholar searching the terms; secondhand smoke, tobacco smoke, passive smoking, cadmium, lead, mercury, polycyclic aromatic hydrocarbons, osteoporosis, osteoarthritis, and arthritis. Results: Tobacco Smoke exposure is the greatest toxic exposure risk a child faces in a home environment. Tobacco Smoke exposure starts in the womb when the embryo embeds in the mother's uterus and connects to their mother's blood flow. Tobacco smoke contains many osteotoxic, nephrotoxic, cytotoxic, and genotoxic chemicals that significantly alter genetic material in the developing fetus and child having long term consequences. Involuntary smoking is more of a health risk than active smoking. Children in the home environment are more vulnerable to the toxins produced by active smokers even if the smoking takes place when the child is not physically in the home. The child's toxic exposure has long-term health effects leading to poor bone health and skeletal diseases later in life. As parents and members of the general public we need to implement safeguards to protect children in the home from involuntary tobacco smoking..

INDEX TERMS Cadmium, Lead, Polycyclic Aromatic Hydrocarbons, Osteoarthritis, Osteopenia, Osteoporosis, Bone Disease, Passive Smoking

I. INTRODUCTION

After reviewing a 1981 experiment sponsored by Philip Morris at the Institut Fur Biologische Forschung (INBIFO), their secret German research facility with the stated objective: "in this 21-day inhalation study on rats {60 days old} the subacute toxicity of sidestream cigarette smoke has been compared to the subacute toxicity of mainstream smoke on the basis of equal TPM concentrations." The experiment had 5 randomized groups of 20 rats, one group of 20 rats kept in cages, one control of 20 put in the ventilation tubes, one mainstream smoke group of 20 exposed to mainstream cigarette smoke and two sidestream smoke groups of rats (40 in total) differentiated by exposure to puffed (20 rats) and non-puffed sidestream smoke (20 rats). In the summary of the experiment one rat in the mainstream group died and 20 rats in the sidestream groups died and 3 more in the sidestream groups were killed in a moribund state. Not counting these last three rats the sidestream smoke had a 50%

death rate whereas the mainstream smoke only had a 5% death rate. This experiment can be reviewed by searching the Philip Morris Public Document Site (pmdocs.com) using the Bates number 2029190417. This author wanted to know what the effect sidestream tobacco smoke had on children since by body weight they breathe up to 3 times the volume of air compared to adults. This means children inhale up to 3 times the volume of toxins as adults breathing the same air. Environmental toxins will be more impactful on children given the fact that their organs (kidneys and liver) are not fully developed, leaving them more vulnerable and less able to remove the environmental toxins from their bodies and there exists a dose dependency effect of tobacco smoke. Exposure of children to second-hand smoke has been linked to a variety of immediate health effects, including respiratory infections, middle ear disease, and development of asthma. [1] It is a known fact cigarette smoking is a confirmed risk factor for osteoporosis and fractures in adults but nothing is stated as to the impact of secondhand smoke and sidestream tobacco smoke exposure on children's skeletal development and their risk of osteoporosis in adulthood. This article uncovers pieces of research data available since the 1950s which cumulatively answers the question of the toxicity of secondhand smoke as compared to first hand smoking and what effect chronic involuntary smoking has on children's skeletal development..

II. METHOD

A literature review dating as far back as the 1950s was conducted to gather as much published information as possible comparing mainstream and sidestream smoke. Google scholar was searched using the keywords; "sidestream smoke, passive smoking, secondhand smoke, mainstream smoke and tobacco smoke". The references of the filtered studies were manually searched yielding 7000+ compounds in tobacco smoke which led to more literature review focused on the most toxic components of tobacco smoke; "cadmium, lead, mercury and polycyclic aromatic hydrocarbons" and their impact on "human development". .

III. RESULT

The Young Finn Study was the only in depth research that followed 1422 Finnish children aged 3-18 exposed to secondhand smoke in their homes beginning in 1980 for 28 years and establishes from a large human sample size; involuntary smoking during childhood has a negative impact on peak bone mass density achieved by end of puberty. In adulthood, peripheral bone traits were assessed with peripheral quantitative CT (pQCT) at the tibia and radius. [2] The calcaneal mineral density was estimated with quantitative ultrasound. [2] Exposure to passive smoking in childhood, determined by parental smoking and serum cotinine concentrations, was an important determinant of reduced bone mass, density and strength indices measured 28 years later in adulthood with two different methods. [2] The effect of passive smoking in childhood was not attenuated after adjustments for age and sex and possible intermediate or confounding factors, including BMI, active smoking, serum 25-OH vitamin D concentration, physical activity, parental school years, and birth weight. [2] Individuals with low cotinine levels had a low-energy fracture rate of 11.3%, and among those with elevated cotinine it was 14.3% (P = 0.15 in a logistic regression model adjusted for age, sex, and childhood factors). [2]

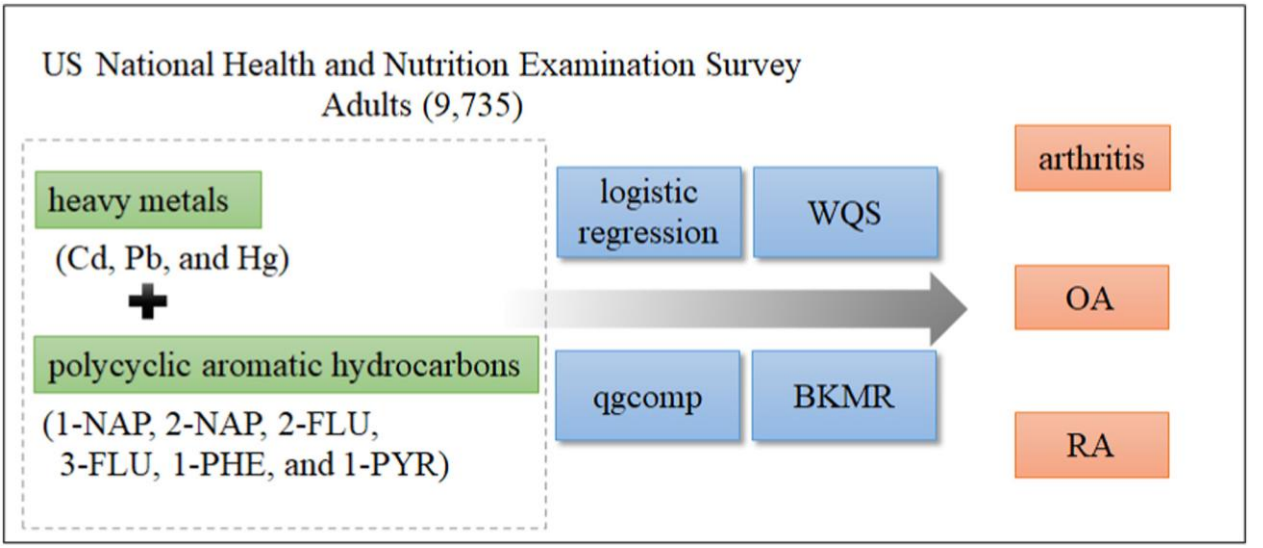

FIGURE 1. The levels of lead and cadmium in the maxillary bone corresponds to the environmental exposure to these heavy metals in the patient's place of residence [7].

Children with higher cotinine levels (a by-product of nicotine) had lower bone mineral density levels in adulthood, indicating a dose dependency effect. Children of parents who smoke have evidence of impaired bone health in adulthood. [2] The human body stops accumulating bone mass within months of attainment of adult height marking the end of puberty. Environmental and behavioural factors account for 20%–40% of PBM (peak bone mass) attainment, optimizing determinant factors associated with strengthening the bone structure and PBM is of great importance. [3] Peak bone mass (PBM) achieved at the end of the second decade of life is an important determinant of osteoporotic fractures occurring in adulthood. [3] Osteoarthritis of the hip and knee have lower bone mineral density than healthy individuals without Osteoarthritis. [4] Cartilage tissue forms from mesenchymal stem cells during development of the fetus. A 2016 Study exposed healthy mesenchymal stem cells from non-smoking donors found COL2AI expression lacking in cigarette smoke exposed (mesenchymal stem) cells indicates a softer cartilage that increases the risk of osteoarthrosis… there are lasting effects on mesenchymal stem cells for cellular signaling with impaired osteogenic and chondrogenic lineages. [5] A 2023 study provides novel evidence that co-exposure to heavy metals (cadmium, lead & mercury) and PAHs (polycyclic aromatic hydrocarbons) positively correlates with arthritis, especially OA (osteoarthritis). [6]

IV. DISCUSSION

Tobacco smoke contains the heavy metals Cadmium, Lead, Mercury and Polycyclic Aromatic Hydrocarbons. The average smoker in Finland consumed 18.1 cigarettes in 1980 and 16 cigarettes in 1996. [8] (pg 72 of supplement) The average smoker in the US consumed 31.9 in 1980 and 29.5 in 1996. [8] (pg 95 of supplement). US children's exposure to tobacco smoke was nearly double the exposure levels of Finnish children in the Young Finn Study, The Young Finn Study established tobacco smoke as dose dependent. A child in the US with smoking parents will have less bone mineral density in adulthood than a child growing up with non-smoking parents and on average will have less bone mineral density than a child in the Young Finn Study based on the fact the effects from tobacco smoke exposure are dose dependent and the average parent in the US smoked about twice what a Finnish parent smoked.

The US Agency for Toxic Substances and Disease Registry lists 30 chemicals of concern because of widely acknowledged reproductive and developmental consequences, 20 (emboldened) of the 30 are found in tobacco smoke. The 30 chemicals are alcohol, arsenic, cadmium, carbon disulfide, carbon monoxide, chlordecone, chloroprene, DDT, DBCP, DES, ethylene dibromide, EGEE, EGME, ethylene oxide, gossypol, hexachlorobenzene, lead, lithium, mercury, nicotine, PBBs, PCBs, 2,4,5-T, TCDD, tobacco smoke (PAH), toluene, vinyl chloride, vitamin A, and warfarin. [9] (pg 13)

Lead: (Pb) The lead content in tobacco smoke has been attributed to lead residues present in the soils of tobacco fields as a result of the former use of lead arsenate as an insecticide. [10] (section 3.3.6) The concentration of lead in two separate brands of cigarettes and in a composite sample of five brands; were 19, 80, and 39 mg/kg at 58%, relative humidity or 21, 84, and 41 µg per cigarette. [11](table lll) The highest transfer rate from tobacco to cigarette smoke was found for Cadmium (81–90%), followed by Lead (46–60%) and Arsenic (33–44%). [12] 2% of lead in a cigarette transfer to mainstream smoke [13] are fair estimates. [10](section 3.3.6) Secondhand Smoke (SHS) or Environmental Tobacco Smoke (ETS) consists of Sidestream Smoke (SS) plus 50% of the mainstream smoke (MS) inhaled and subsequently exhaled by a smoker. [14](pg 196) Using 84 µg lead per cigarette and a transfer rate of 60% less the 1% retained in the smoker's lungs leaves 59% of the lead toxin ending up in the Environmental Tobacco Smoke. This means one cigarette is toxifying the environment with 50 µg of lead. Half life of lead in the body is as long as 30 years with 94% stored in the bone, causing long-term internal exposure. [15](Chapter 11.3) & [16] Accumulation in bone remains as a continuous internal source of lead to the vascular endothelium and other tissues as it leaches out over decades of life.[17] Both lead and cadmium as environmentally acquired contaminants increase atherosclerotic cardiovascular risk in a dose-dependent manner. [17] Low-level environmental lead exposure, almost universally ignored by clinicians, constitutes an important cardiovascular and skeletal risk factor. [18] This is directly from the US National Kidney Foundation website "In children, however, even mild exposure over many years can lead to health effects later in life, including kidney damage. Children have a higher risk for health problems from lead exposure. Children aged six or under have the highest risk. Excess lead is stored in the bones. Pregnancy and nursing tends to release lead from the mother's bones back into circulation. Lead poisoning is a serious health problem. It can happen if lead builds up in your body, usually over many months or years. Lead poisoning can be harmful in adults, but is especially harmful in children because they have a small body size and are still growing. Children age six and under are at highest risk." [19] Blood Lead Level (BLL) is negatively correlated with Bone Mineral Density (BMD) at different sites of interest in children and adolescents aged 8-19 years. [20] Osteoporosis is a reduction in bone mass sufficient to increase the risk of fracture. [21] Lead exposure during childhood may be a risk factor for low bone mineral density (BMD). [21] A significant inverse association between lead exposure and BMD exists. [16] Lead exposure is associated with decreased total femur and spine BMD, and (increases) in FRAX (Fracture Risk Assessment) score in the general US population. [16] The accumulation of lead in the bone leads to the replacement of calcium ions by ions of the abiotic element and causes further changes in the bone structure:

TABLE 1
Trends in Tobacco Smoke Exposure and Blood Lead Levels Among Youths and Adults in the United States [26]

Demographic Characteristic	Overall Geometric Mean Level, µg/dL	Nonsmokers			Smokers	Nonsmokers and Smokers, *P* Values			Nonsmokers Only, *P* Values		
		Geometric Mean Level Without SHS Exposure, µg/dL	Geometric Mean Level With Lower SHS Exposure, µg/dL	Geometric Mean Level With Higher SHS Exposure, µg/dL	Geometric Mean Level, µg/dL	Overall	Quadratic Trend	Linear Trend	Overall	Quadratic Trend	Linear Trend
Age, y											
3–5	1.57 (1.48–1.66)	1.24 (1.15–1.34)[c]	1.55 (1.43–1.67)[c]	2.06 (1.88–2.23)[c]	NA			NA	<.001	.5195	<.001
6–11	1.18 (1.13–1.23)	0.98 (0.94–1.02)[c]	1.20 (1.14–1.26)[c]	1.53 (1.43–1.63)[c]	NA			NA	<.001	.4652	<.001
12–18	0.88 (0.85–0.91)	0.78 (0.75–0.81)[c]	0.92 (0.88–0.97)[d]	1.02 (0.97–1.07)	0.93 (0.87–0.99)[c]	<.001	<.001	<.001	<.001	.1465	<.001
19–34	1.07 (1.04–1.10)	0.87 (0.84–0.90)[c]	1.00 (0.94–1.06)	1.04 (0.99–1.09)[c]	1.42 (1.36–1.48)[c]	<.001	.001	<.001	<.001	.1303	<.001
35–49	1.42 (1.37–1.46)	1.15 (1.11–1.19)[c]	1.40 (1.31–1.48)	1.45 (1.33–1.57)[c]	1.97 (1.88–2.06)[c]	<.001	.036	<.001	<.001	.0146	<.001
50–64	1.84 (1.79–1.89)	1.60 (1.54–1.66)[c]	1.77 (1.70–1.85)	1.92 (1.75–2.09)[c]	2.50 (2.40–2.59)[c]	<.001	.002	<.001	<.001	.6853	<.001
≥65	2.08 (2.03–2.13)	1.97 (1.91–2.04)	2.08 (1.97–2.18)[e]	2.38 (2.21–2.54)	2.62 (2.45–2.78)[c]	<.001	.336	<.001	<.001	.2349	<.001

inhibition of growth processes, decreased density, the development of osteopenia and osteoporosis. [22] Clinical studies have shown that lead accumulated in the body has negative effects on bone, decreasing cortical width and bone density and increasing fracture risk. [23] Lead is cardiotoxic and reduces cardiac contractility, making the heart prone to arrhythmias (Afib). [24] Common ailments of lead and cadmium accumulation are often viewed as outcomes of aging. [25] Although the highest concentrations of Cd and Pb are found, respectively, in kidneys and bone, toxic effects of these metals are not confined to diseases of the kidney and skeleton. [25] Lead does not disappear once the Tobacco Smoke clears but settles on nearby surfaces. Secondhand smoke exposure contributes to blood lead levels above the level caused by smoking. [26]. Note in table 1 below, the blood levels of children aged 3 to 5 exposed to low and high levels of secondhand smoke have higher lead levels than do smokers in the 19 to 34 year age group as do the children in the 6 to 11 year age group also exposed to higher levels of secondhand smoke. Notice that children in the 12 to 18 year age group who do not smoke but are exposed to secondhand smoke have for practical purposes the same level of lead in their blood and more as do children of the same age who smoke. If measures were taken of children less than 3 years of age the blood lead levels would have been worse given the fact the youngest children filter a higher volume of air compared to older children based on body size. These figures in Table 1 come from the National Health and Nutrition Examination Surveys, 1999–2008 cited by Richter, P.A., Bishop, E.E., Wang, J., Kaufmann, R. in their research: Trends in Tobacco Smoke Exposure and Blood Lead Levels Among Youths and Adults in the United States [26] (Table 1).

Cadmium:(Cd) Cadmium is the 7th most toxic heavy metal. [27] Once this metal gets absorbed by humans, it will accumulate inside the body throughout life. [27], [28] The general population is exposed to cadmium from breathing cigarette smoke. [29] The human lung absorbs 40-60% of inhaled cadmium. [30] Breathing high levels of cadmium damages people's lungs and can cause death. [29] Exposure to low levels of cadmium in air, food, water, and particularly in tobacco smoke over time may build up cadmium in the kidneys and cause kidney disease and fragile bones. [29] Cadmium is considered a cancer-causing agent. [29] Cadmium is heavily concentrated in tobacco leaves and 50% of inhaled cadmium through smoking can be absorbed into the body, making it the highest toxic metal found in cigarette smoke. Tobacco smoking is the most important single source of Cd exposure in the general population. [31] With an exceptionally long biological half-life of 15-20 years, cadmium is considered a cumulative toxin and can pose great health risks including neurological disorder and reproductive system defects. [32] In 2004, cadmium was officially categorized as a Class I human lung carcinogen based on epidemiological studies. [32] Cadmium also plays an important role in prostate, renal, liver, bladder, and stomach cancers. [32] Mainstream smoke has 2% of total cadmium found in a cigarette. [33](pg 51) Sidestream Smoke has 88% of total cigarette cadmium and exhaled mainstream smoke by active smokers adds another 1% totaling 89% of the cadmium found in a cigarette. Secondhand Smoke has 89 times more cadmium than what a smoker absorbs. It (cadmium) is an odorless heavy metal which accumulates in the human body primarily in the kidney, liver and bones. [34] Small amounts of cadmium taken in over many years may cause kidney damage and fragile bones. [34] Due to slow excretion, cadmium accumulates in the body over a lifetime and its biological half life may be up to 38 years. [35](pg 21) The accumulation of cadmium, one of the world's most poisonous substances, can inhibit skeletal growth and bone

maturation, thus causing osteoporosis. [36] Cadmium directly induces mitochondrial dysfunction of human embryonic kidney cells. [37] Cadmium exposure can elicit measureable, harmful effects on biological health even at levels well below the current safety standards used by environmental and occupational agencies. [38] Participants in the highest quartile of blood cadmium concentration had, on average, 6% shorter LTLs (Leukocyte Telomere Lengths) than did those in the lowest quartile. [38] The difference between participants with low and high cadmium exposure of the same chronological age is equivalent to 11 years of calendar age. [38] Telomere shortening in children from prenatal tobacco exposure is shown to be dose dependent and can cause premature aging and increased health risks. [39] Children living in smoking households have 248% more body cadmium levels and 158% more body lead levels than children from non smoking households. [40] A consistent association exists between cadmium exposure and biomarkers of bone resorption and bone demineralization in 10-year old children. [41] Chronic Cadmium exposure can transform cells to become more resistant to oxidative stress; also, as an epigenetic mechanism cadmium acts indirectly on DNA repair mechanisms via alteration of reactions upstream. [42] Those transformed cells acquire resistance to apoptosis and deregulation of calcium homeostasis. [42] Leading to uncontrolled carcinogenic cell proliferation and inherent DNA lesions. [42] Cadmium exposure causes cancer in lungs and prostate. [43] A significant association exists between blood cadmium and involuntary smoke exposure in non-smokers. [44] The blood cadmium level by involuntary smoking of adolescents had higher effect values than that of adults in both genders. [43] There is no significant difference between Cd levels in the blood of active smokers and passive smokers with Type 2 diabetes. [45] The emerging epidemiological view that bone health, adjudged by mineral density, is extremely sensitive to even background levels of environmental Cadmium. [46] Importantly, data also suggest that Cadmium may play an even greater role in compromised bone health than prior indirect estimates of exposure could reveal. [46] Environmental Cadmium may play an even greater role in poor bone health than prior, insensitive proxies for exposure could reveal and, hence, this toxic element might be a substantial determining factor in osteoporosis. [46] Exposure to low levels of cadmium in air, food, water, and particularly in tobacco smoke over time may build up cadmium in the kidneys and cause kidney disease and fragile bones. [29] Cadmium is considered a cancer-causing agent. [29] A few studies in animals indicate that younger animals absorb more cadmium than adults. [47] Animal studies also indicate that the young are more susceptible than adults to a loss of bone and decreased bone strength from exposure to cadmium. [47] Cadmium is found in breast milk and a small amount will enter the infant's body through breastfeeding. [47] The amount of cadmium that can pass to the infant depends on how much exposure the mother may have had. [47] Studies in animals exposed to high enough levels of cadmium during pregnancy have resulted in harmful effects in the young. [47] The nervous system appears to be the most sensitive target. [47] Young animals exposed to cadmium before birth have shown effects on behavior and learning. [47] The general population is exposed from breathing cigarette smoke or eating cadmium contaminated foods. [48] Cadmium damages the kidneys, lungs, and bones. [48] Cadmium has been found in at least 1,014 of the 1,669 National Priorities List (NPL) sites identified by the Environmental Protection Agency (EPA). [48] There is also some information from animal studies that high enough exposures to cadmium before birth can reduce body weights and affect the skeleton in the developing young. [47] In vivo studies in experimental animals have shown that chronic exposure to Cd decreases mineralization of vertebral bodies, altering their biomechanical properties and rendering them more susceptible to deformity and fracture [49]. It is also well documented that Cd decreases expression of markers of osteoblastic differentiation (Runx2, osteocalcin), of extracellular bone matrix proteins (type I collagen), and of enzymes involved in the mineralization process (alkaline phosphatase-ALP), altering the bone formation and mineralization process. [49] Other studies provide evidence that chronic exposure to Cd decreases bone volume and increases the percentage of tartrate resistant acid phosphatase (TRAP) positive cells in subchondral tibial bone; the increase in TRAP activity would be an indication that osteopenia is induced by the increase in resorption. [49] The association between extremely low doses of cadmium and cardiovascular disease including endothelial dysfunction, promotion of atherosclerosis, impaired cardiac function and peripheral artery disease has been proved. [50] Doses of cadmium well below toxic concentrations may initiate pathological changes in blood vessel walls. [50] Cadmium like Lead is a heavy metal and settles on surfaces after the visible Tobacco Smoke clears. Tobacco smoke is a likely source of Pb and Cd that accumulates in settled house dust in multiunit housing, suggesting that Pb and Cd are constituents of thirdhand smoke that lingers long after smoking has ended. [51]

Polycyclic Aromatic Hydrocarbons(PAHs): Cigarette smoke has many PAHs. PAH content in sidestream smoke(SS), measured by collection of all the smoke produced by a lit cigarette in a glass chamber, was about tenfold higher compared with mainstream smoke(MS). [52] Sidestream Smoke has 91% and mainstream smoke has 9.1% of total PAHs (10:1) approximately. This means the smoker exhales half of the 9.1% PAHs inhaled from active smoking into Secondhand Smoke (SHS) also referred to as Environmental Tobacco Smoke (ETS). The SHS has 95.45% of total PAHs and the smoker retains the remaining 4.55%. This makes SHS PAH level 21 times more toxic compared to what a smoker absorbs by active smoking. People exposed to PAHs for a long time are at risk of bone metabolism diseases such as osteoporosis (bone loss),

arthritis and fracture. [53] Many studies have shown that PAH-derived compounds, such as BaP, BaA, and 3MC, activate the AhR pathway, resulting in an imbalance in bone homeostasis. [53] Blood Cd, Pb, and certain PAH metabolites significantly increased total arthritis, OA (Osteoarthritis), and RA (Rheumatoid Arthritis) risk. [6] Second, WQS, qgcomp, and BKMR analyses consistently demonstrated that co-exposure to high concentrations of heavy metals (Cd, Pb, Mercury) and PAHs could increase the risk of total arthritis, OA, and RA. [6] By burning, the unit length of a cigarette released about 5-7 ng of mercury into smoke. [54]

V. CONCLUSION

Tobacco Smoke is osteotoxic, causing loss of bone mass and lowering peak bone mass density in children which would otherwise have been attained by the age of puberty. As a consequence the exposed child enters adulthood with insufficient bone mass density to sustain them till the end of life. This environmental chronic exposure to tobacco smoke during the developmental years increases the risk of future fractures and early onset of arthritis due to softening joint cartilage reducing its compressive strength compared to normal healthy non-tobacco smoke-exposed cartilage cells. The malformed cartilage and below normal peak bone mass caused by environmental exposure to toxins from tobacco smoke during childhood will result in the onset of pain and loss of physical function from arthritic joints, degenerating vertebral discs, bone and vertebral fractures appearing earlier in life than otherwise would be considered normal. Common ailments of lead and cadmium accumulation from chronic tobacco smoke exposure are often viewed incorrectly as outcomes of aging. In summary, chronic smoke exposure during developmental years leads to early onset of osteoporosis, osteoarthritis, arthritis, rheumatoid arthritis, degenerative disc disease, vertebral compression fractures and other bone related maladies later in life.

DECLARATIONS

Ethics Approval and Consent to Participate - Not Applicable
Consent for Publication - Author consents
Availability of Data and Materials - Not Applicable
Competing Interests - Not Applicable
Funding - Not Applicable
Authors Contributions - Substantial contribution
Acknowledgements - Not Applicable

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