

Report

Tobacco and lead toxicity

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Lead plays a significant role in tobacco toxicity. It contributes to lung cancer through the release of radiation from Pb-210, with possible small impacts on some other cancer. It plays a direct role in cardiovascular problems associated with smoking cigarettes. The higher blood lead associated with smoking plays a role in neurological and behavioral problems associated with smoking. There is a consistent link between tobacco smoking and lead levels. Part of this is due to the lead content of the tobacco itself. However, there may be additional impact from increased bone resorption both directly from the impact of smoking, which is still poorly understood, and indirectly from falling estrogen levels associated with smoking, particularly in post-menopausal women. [Bone resorption is the release of minerals, including lead, from bone through dissolution of the bone.]



Kop van een skelet met brandende sigaret
[TRANSLATION: ***Skull of a Skeleton with Burning Cigarette***] 1886 [Oil on Canvas, 32 X 24.5 cm] by Vincent Van Gogh (1853-1890). Source: Van Gogh Museum, The Netherlands www.vangoghmuseum.nl
NB: Van Gogh's suicide may have been precipitated by plumbism (lead poisoning) caused by ingesting leaded oil paints and other lead sources. (Weissman, 2008)

Smoking also impacts on vitamin D levels, possibly increasing lead deposition during bone formation. Further, the toxic impact of lead may be exacerbated by the depletion of protective molecules by other toxins in tobacco smoke and the reduced availability of protective molecules, such as vitamin C and E, caused by the tobacco consumption itself.

Sources of the lead found in tobacco

Lead found in tobacco comes from two primary sources. Non-radioactive Pb-206 is largely derived from atmospheric pollution. Lead in the atmosphere is trapped on the surface of the leaf by trichomes (sticky hairs that trap particles and retain them after washing with water). The overall lead content of North American cigarettes may have as much as halved between 1988 and 1997, due to declining atmospheric lead as leaded petrol was phased out (Mannino 2005 p459-60) while similar reductions were obtained in Europe between 1987 and 1991 (Pesch 1992).

The amount of Pb-206 is measured in micrograms per gram. In Europe in 1991 the average for western cigarettes was 1.66 µg/g. In Australia in the mid 1990's, assuming cigarettes contained a little under a gram of tobacco, the equivalent figure would have been around 0.3 µg/g (Donovan 1996 p67) and the North American figure was around 0.7 µg/g (Mannino 2005 p459). Pb 206 (or Pb 210) is not volatilised at temperatures normally found in cigarettes (600-800°C), and tends to enter cigarette smoke as a particulate or solid particle (Khater 2004 p34).

Around 11% of the lead in cigarettes enters the smoke that is emitted from the cigarette (Mannino 2005 p459-60, Galazyn-Sidorczuk 2007). The bulk of the remaining lead goes into the ash, though small amounts contribute to environmental lead pollution, notably in the residences of smokers. Approximately 6% of the lead from a cigarette is believed to enter the lungs of a smoker, varying widely depending on factors such as smoking intensity and depth of inhalation.

Illegal tobacco may also have higher levels of heavy metals including lead (Pappas 2007). There is also a high risk of adulteration. Because lead is cheap and has significant weight, it has been used to increase the weight of tobacco, or more commonly marijuana, leading in one case in Germany to 95 out of 145 regular marijuana users screened having blood lead levels equal to or above 25 µg/dL (Busse 2008).

However, of more concern is radioactive lead (Pb-210). This is present in much lower quantities and is measured in nanograms per gram. Its progenitor is radon 226 (half life 4 days). The half life of a substance is the time it takes for half the amount of a radioactive substance to transform into the next substance on the decay path. During each transformation it releases potentially carcinogenic radiation, and the shorter the half-life the more radiation is emitted. Radon gas is produced as a natural radioactive decay product from igneous rocks. The use of phosphate fertilizers can increase radon gas levels in areas of low concentration. Radon decays through short-lived (total half life 50 minutes) daughter isotopes to become radioactive Pb (lead)-210 (half life 22 years), which then in turn decays through Bismuth 210 (half life 5 days) and polonium 210 (half life 138 days) to become the stable, non radioactive isotope Pb-206 (Field 1999). Pb-210 or its precursors can be caught by the surface of tobacco leaves by trichomes (Rego 2009 p466-67, Skwarzec 2001b). After smoking tobacco, Pb-210 and polonium are taken into the lungs. The insolubility of lead may result in small quantities of Pb-210 being retained in the lower bronchial lobes within the lungs, where it causes ongoing radiation damage, potentially increasing the risk of tumors, as it decays into Bismuth-210 and Polonium-210 (Rego 2009 p460).

An average smoker (1 pack a day) is exposed to 16-50mSv [Millisilverts] of radiation a year from smoking tobacco, the average being equivalent to over ten times the average US radiation exposure or over 300 chest X-rays, over one third of that from Pb-210 and most of the remainder from polonium (Skwarzec 2001a, Khater 2004, Kovaks 2007, Papastefanou 2009). By itself, this radiation exposure is inadequate to account for the increased risk of lung cancer experienced by smokers (Hecht 1999 p1196, Prueitt 2009 p158-159, NCRP Council 2010).

Possibly more important is that cigarette smoke can increase the susceptibility of lung tissue to radiation (Tokarskaya 2002, Darby 2004) and to other carcinogens (Tang 2010), probably partially due to the inactivation of the tumor suppressing gene p16 INK4a (Prueitt 2009).



Cancer Patients Aid Association (CPAA) anti-smoking ceiling posters made for smoking areas - showing mourners at a funeral. Ad by Everest Brand Solutions, Mumbai, India www.ineverest.com (Source: Advertising/Design Goodness Blog by Freddy Samuel, www.frederiksamuel.com/blog/images/cpas.jpg 21/06/06.)

Cigarettes contain over 4000 chemicals, twenty of which are likely carcinogens (Hecht 1999), while over sixty are mutagenic (capable of modifying DNA expression) and therefore potentially playing a role, directly or indirectly, in tumor development (Pleasant 2010). The expression of over 323 genes in the lymphocyte system alone (central of the immune and anti-tumor response) are modified by cigarette smoking (Charlesworth 2010). The exact weighting to give to each component of carcinogenesis is difficult to evaluate since most interactions between components have yet to be elucidated. There is some evidence that non-radioactive lead (Pb-206) might play a modest role in lung cancer development (Fu 1995, Steenland 2000), but latter studies have failed to confirm this (Jemal 2002, Rousseau 2007, Khalil 2009, Weisskopf 2009), and the presence of trace elements of Pb-210 in Pb-206 would make separating their effects difficult.

Risks of dying of lung cancer

Smokers of European descent have a 22.1% risk of dying of lung cancer before the age of 85 if male, and 11.9% if female, with the comparable rates for non smokers being 1.1% and 0.8% (Thun 2008 p1363). Only 6-7% of the over 157 thousand lung cancer deaths, representing 28% of all cancer deaths (ACS 2010 p15), each year in the U.S.A. occur among individuals who have never smoked (Thun 2006) although this percentage is significantly higher in East Asian countries (Marugame 2005, Kuang 2009). Women are more susceptible to the carcinogenic impacts of cigarette smoking, but their lung cancers are likely to have better outcomes if treated (Olak 2004). Women of East Asian descent (Epplein 2005, Thun 2008) and African Americans (Alberg 2007, Thun 2008) are more vulnerable to lung cancer though the extent to which this is genetic has yet to be determined.

Passive or 'second-hand' smoking

Environmental tobacco smoke (ETS), which consists of side stream and exhaled (second-hand) smoke, contains carcinogens, including Pb-210; increasing the risk of lung cancer deaths from living with a smoker by 15-31% (RR 1.5-3.1) (Hackshaw 1997, Taylor 2007) and from occupational exposure to side stream smoke by around 24% (RR 1.24) (Stayner 2007). [RR (Relative risk or Risk Ratio) : added risk to exposed individuals frequently translated into a percentage http://en.wikipedia.org/wiki/Relative_risk] It must be noted, however, that

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occupational exposure's contribution is difficult to estimate, since most lung cancers are multi-factorial and more than one carcinogenic source is likely to be present: e.g. waiting staff, generally listed as having had a high exposure to passive smoking, may also be exposed to the polycyclic aromatic hydrocarbons [PAH] from cooking oil. The raw statistic may also conceal the fact that ETS may have minimal impact on lung cancer mortality on never-smokers (OR 1.05) and a large impact for former smokers (OR 2.32) (Vineis 2005 table 3 p3). [OR (odds ratio): the probability of the event divided by the probability of an event *not* occurring – not the same as RR and the translation of this figure into percentage increase can be very misleading see http://stats.org/stories/2008/odds_ratios_april4_2008.html]. OR 1.05 is comparable to the increased risk of lung cancer if taking more than 50mg of vitamin E a day (OR1.03-1.1) (Slatorre 2008 p528). Those who were exposed to ETS as children may have their risk of lung cancer doubled (HR 2.00-3.63) (Vineis 2005 Table 4 p 4, Vineis 2007 table 2 p5). [HR (Hazard Ratio) – similar to RR see http://en.wikipedia.org/wiki/Hazard_ratio]

Risks from other air toxics by comparison

By comparison, living near a heavily trafficked road increases this risk to OR 1.47 (Vineis 2007 table 2 p5). Among Canadian non-smokers, occupational exposure to wood dust raised the risk of lung cancer to OR 1.8, solvents to OR 2.8, smoke (other than tobacco) or exhaust to OR 2.8 and welding equipment to OR 3.4 (Brenner 2010).

Nor is domestic exposure to ETS the overwhelming influence on cancer risk one might expect. Heavy exposure to wood or coal smoke through its use in both heating and cooking in European households increases the risk of contracting lung cancer to OR 1.24 (Lissowska 2005), a figure surprisingly close to that for ETS (adjusting for 84% mortality (ACS 2010) roughly 18-38% for household exposure (Hackshaw 1997, Taylor 2007)). Like ETS, wood smoke inactivates the p16 INK4A tumor suppressing gene (Delgado 2005). Intensive Chinese style fried cooking (over 4 dishes a day for 25 years, exposing an individual to PAH) increases lung cancer risks by from 3 to 8 times (Yu 2006). Exposure to ETS may be far from the unique risk factor for lung cancer many believe it to be, a fact that may limit the role that can be attributed to the radioactive element in tobacco smoke.

Not Tobacco alone

The multifactorial nature of lung cancer genesis and development is demonstrated by the fact that Japanese smokers are 60% less likely to develop lung cancer and 66% (RR 0.34) less likely to die of it as comparable smokers in the USA, but Japanese non-smokers are three times more likely to die of lung cancer as US non-smokers, if male, and twice as likely if female (Marugame 2005 p123, 121). Nor is such variability unique to Japan (Van Der Griendt 2009), nor limited to nationality (Thun 2006, Alberg 2007). It is clear that the impact of a particular air toxic, such as tobacco smoke or the Pb-210, can not be evaluated in isolation from other environmental contaminants, environmental conditions such as household ventilation, possible nutritional impacts or genetic modifications.

Other smoking related cancers & lead

But lung cancer is not the only cancer that has a higher prevalence among smokers. Of the cancers more common among cigarette smokers, stomach and bladder are possibly influenced by lead. There is strong evidence that tetra-ethyl lead, once used in petrol, and still used in aviation and specialty fuels, can triple the risk of stomach cancer, but the evidence for inorganic lead (Pb-206) neither definitively confirms or rules out a minor role (Rousseau 2007). Bladder cancer is one of the cancers most strongly associated with smoking, with half of male and a third of female individuals with bladder cancer having smoked at some time. Some studies have found a link between lead and bladder cancer (Fu 1995, Golabek 2009), but most have not (Steenland 2000, Jemal 2002, Rosseau 2007, Weisskopf 2009). Fu's analysis of other studies was of occupational exposure, meaning higher blood lead levels (average varied from 24µg/dL to 80µg/dL), and Golabek's failed to specify the smoking status of the individuals, which is a major flaw, given that smoking is linked both to higher lead levels and bladder cancer. While a role for lead in bladder cancer cannot be ruled out, the evidence is so far rather weak, especially at lower lead levels. In terms of the cancer risk from higher lead levels occasioned by cigarette

smoking, one of the strongest links is with a type of brain cancer (meningioma) (Bondy 2008 p9), predominantly in conjunction with the presence of a particular gene variant, ALAD2 (Rajaraman 2006), which, when combined with prolonged lead exposure can increase the risk by OR 2.4. It must be emphasized that meningioma is not a common cancer, occurring at an age-adjusted rate of 2.75 for males and 6.01 for females per 100,000 per year in the USA, with under 4% occurring before the age of 45 and malignancy rate of under 8% (Barnholtz-Sloan 2007).

Cardiovascular impacts

Smoking and lead levels also increase your risk of cardiovascular problems. Prior to the age of 65 male smokers in the USA are more likely to die of heart disease or stroke than of cancer; smoking more than doubles your risk (Woloshin 2008). Exposure to large amounts of ETS increases your risk of a cardiovascular disease by 25-30%, while a range of ETS exposure increases your short term risk of heart attack by 24-62% (IOM 2010 212-213). Cardiovascular problems are also strongly linked with higher lead levels, with comparatively modest levels making a significant difference; individuals with blood lead levels of 3.62 µg/dL - one third of the standard CDC [Centers for Disease Control, USA] definition of a high lead level for children – having more than half again the risk of cardiovascular mortality than individuals with a blood lead of less than 1.94 µg/dL (Menke 2006). A study of older women found that having a blood lead level of 8 µg/dL or more, still lower than the current CDC standard for children, tripled their risk of cardiovascular mortality (Khalil 2009). Smoking has been found in some studies to more than quadruple the risk of peripheral arterial disease, PAD (blocking of peripheral arteries), with almost a quarter of the increased risk being attributed to the impact of lead (Navas-Acien 2004). However, there is a clear threshold effect for PAD, with only individuals with the top 25% of cotinine levels impacted on PAD risks, and no impact from ETS or tobacco other than cigarettes (Agarwal 2009). Lead (Hu 1996) and smoking (Bowman 2007) have both been linked to hypertension (high blood pressure), though with pregnancy-induced hypertension, high blood lead increases (Yazbeck 2009) and smoking decreases the risk (Yang 2005). While some have linked cardiovascular problems to a lead-induced increase in blood pressure, the preponderance of evidence is that any increase in blood pressure is the result of lead's more complex impact on cardiovascular function (Nawrot 2006, Vaziri 2008). In contrast with cancer, lead content plays a clear and direct role in smoking's cardiovascular impact.

Cognitive and behavioural impacts

Smoking and lead levels can also impact on neurocognitive function. Both play a major prenatal role. Smoking (Kyrklund-Blomberg 2005)¹ and even moderate lead levels (Vigeh 2010) can increase the risks of pre-term labour with all the associated problems for the infant, including those of mental and behavioral development (Bhutta 2002). Gestational age and birth weight are a dominant factor for both IQ (Breslau 2005) and ADD/ADHD (Linnet 2006). Lead exposure during pregnancy has clear impacts on mental (Gomma 2002, Hu 2006) and behavioral development (Wright 2008, Patel 2006). There are more doubts about smoking and pregnancy (Breslau 2005). However, a recent study found a significant link between smoking during pregnancy and children's blood lead levels: children exposed to both to prenatal tobacco and in the top third of lead levels had an eight times higher risk of being diagnosed with ADHD while the risk if exposed to only one of these factors was only doubled (Froehlich 2009). Childhood exposure to tobacco, specifically the PAH found in tobacco, has been linked to both lower IQ and greater behavioral problems (Cho 2010, Edwards 2010). The same is true of lead (Lidsky 2003, Wright 2008). Both smoking, among women only, and lead level have been linked to the rare neurodegenerative disorder Amyotrophic Lateral Sclerosis [ATL or Lou Gehrig's disease] (Fang 2010). It is likely that lead plays a significant role in neurocognitive impacts of tobacco, though precise attributions are likely to remain elusive.

Tobacco Smoking and Adult Blood Lead Levels

Smoking has a direct impact on lead levels. Studies based on the U.S. National Health and Nutritional Survey (NHANES III – 1988-1994) found that female smokers were 4½ times more likely to be in the highest 10% of blood lead levels than non-smokers (Lee 2005 p4). Male smokers in America were almost six times more likely

to have blood lead levels of 5µg/dL or over in 1988-1994 (Mannino 2005 Table 4). While not directly comparable to these statistics, the risk of smokers having blood lead levels above 5µg/dL in 1998-2002 was less than 4 times (Muntner 2005 table 3 p2159) from a significantly lower base (Muntner 2005 Table 1 p2157), indicating a relative decline. This is likely to be an effect of declining atmospheric lead, affected by the phasing out of leaded gasoline, and decreasing contamination of tobacco (Mannino 2005 p459-60), though there could also be effects from a reduction of cigarette consumption among smokers by 15% over the same period (O'Conner 2006).

Passive Smoking & Children

Exposure to ETS or passive smoking is generally measured using cotinine levels, as cotinine is a breakdown product of nicotine. Passive smoking can increase the blood lead levels of children (Donovan 1996, Khaji 1997, Maninno 2003, Pino 2004). According to the largest study (Mannino 2003), children 4-16 with high cotinine levels had lead levels 38% higher than those with low cotinine levels and were four times more likely to have blood lead levels greater than 10 µg/dL. It must be emphasised that these statistics were based on data collected in 1988-1994. Maternal (or presumably caregiver) smoking habits have the greatest impacts (Khaji 1997, Freidman 2005); a fact generally consistent with the pattern of cotinine levels, where maternal smoking habits have more impact than paternal smoking habits, and far more than that of other household residents (Whitrow 2010 table 3 p6). Smoking also increases the contamination of the home environment, increasing lead levels in the air and house dust (Mannino 2005 p460, Willers 2005, Dixon 2009).

However, post natal exposure may have less impact than prenatal exposure: in Canada in 1990, every 10 cigarettes smoked per day by a pregnant woman increased the lead cord level by 15%, indicating a stronger pre-natal effect than that of the child's exposure to ETS from its parents after birth (Rhiands 1997). It is also worth noting that the exposure of children to passive smoke from parents can vary widely between ethnic groups (Mannino 2001, Whitrow 2010), and tends to be marginally higher in single parent families, particularly white families, at least in the UK (Whitrow 2010). Cotinine levels in the children of non-smokers living in the USA declined by 68% between 1988 -1991 and 1999 -2002, though the falls were much less for all children (including those of smokers) 4-11 than for other groups, with the fall from home exposure being 37.7% (Schober 2008). Still, this decline is likely to have played a role in the reduction of the rate of children having a blood lead of ≥ 10 µg/dL from 4.4% to 1.6% in the same period (CDC 2005).

Passive Smoking & Adults

Current indications are that passive smoking has a more muted impact on the blood lead levels of adults, with blood lead levels varying less than with children, and having a stronger impact for white individuals (Mannino 2003, Mannino 2005); particularly taking into account that equal weighting of cotinine levels overstate the exposure of African-Americans to cigarette smoke (Wilson 2007). Light or intermittent exposure to ETS [environmental tobacco smoke] had little or no impact on the odds of Americans of African descent having blood lead levels of 5 µg/dL (Mannino 2005 table 4 p563 adjusting for Wilson 2007), and only slightly more for individuals of Mexican descent (Mannino 2005 table 4 p563), though this may relate to these groups tending to have higher blood lead levels to begin with (Mannino 2005 table 2 p561). Mannino himself noted he had no explanation for the degree of the link between passive smoking and blood lead levels he had found (Mannino 2005 p562-563). A Polish study found that the blood lead levels of pregnant women rose in proportion to their exposure to ETS (Jedrychowski 2006). A major study using urine rather than blood levels found that high exposure to ETS had an higher impact than actual smoking on lead levels in the urine for individuals below the US poverty index, but this must be seen in the context of a study where social status had more of an impact than smoking and where smoking, active or passive, had less impact than in Mannino's previous studies (Richter 2009, Mannino 2003, Mannino 2005). Indeed, in Richter's study, exposure to low levels of ETS had no effect on the geometric mean of lead levels among those below the poverty index or among women and higher ETS exposure correlated in lower geometric means for lead levels in US whites and Mexican Americans. For

Mexican Americans with high ETS exposure, mean adjusted lead levels were no higher than for those with no significant ETS exposure (Richter 2009 table 4 p1936-1937).

Not all studies have found a significant impact of passive smoking on the blood lead levels of adults or older children (Khaji 1997, Neo 2000,) and it is curious that these studies are of non-Caucasian populations with very different degrees of exposure to lead and were based on data collected later than in with Maninno's study. Cotinine levels in adult non-smokers in the USA declined by almost 75% between 1988 -1991 and 1999 - 2002 (CDC 2005). Combined with the declining non-radioactive lead content it seems likely that lead exposure from ETS has declined by a factor of at least 8 for non smokers in the USA since 1988-1991, and is unlikely to be a major source (raising blood lead by an average of more than 0.09 µg/dL) of lead for most adult non-smokers in countries that have limited smoking in public areas. The decline in the USA was undoubtedly influenced by the reduction in smoking prevalence from 28% to 21% between 1988 and 2004 (Schober 2008) and the 15% decline in consumption among smokers (O'Conner 2006).

Smoking, the skeleton and lead impacts

Of the lead contained in the body 80-95% is stored in the bones where it replaces calcium and other minerals (Patrick 2006). Lead is released from the bones predominantly through resorption. Periods where resorption relative to bone formation is high will lead to larger releases of lead (raising blood lead levels and increasing lead impacts), lower bone mineral density [BMD] and a reduction of the bone mass within the body.

Smoking tobacco has generally been linked to lower BMD and bone mass, with strong indications that this is more due to increased resorption rather than reduced bone formation (Szulc 2002, Sampson 2003, Wong 2007). One of the strongest indicators of this is that bone mass in post menopausal women declines faster in smokers rather than non-smokers or ex-smokers (Oncken 2006, Compton 2007), though the increased metabolism (use and/or breakdown) of oestrogen [US spelling estrogen] and earlier menopause in smokers complicates the picture (Compton 2007, Wong 2007).

The exact mechanism by which tobacco impacts on bone resorption is not clear. Nicotine seems to play a marginal role, possibly impacting on vitamin D levels (Fung 1999) and increasing resorption rates of calcium phosphate (Henemyre 2003), but having little overall impact (Akhter 2003). There are indications that hydrocarbons found in tobacco products may have a larger impact but much more research is needed (Lee 2002). There may be ancillary impacts from life style factors associated with tobacco smoking, such as alcohol consumption, low body weight and lower amounts of exercise (Sampson 2003, Wong 2007). In spite of much greater knowledge of bone metabolism, little appears to have changed in pinning down the overall mechanisms of smoking's impact on bone: two groups of researchers a decade apart noting the failure to explain the fact that increased bone loss, itself only partially accounted for, accounts for under a quarter of increased fracture risk for smokers (Law 1997, Wong 2007).

It is worth noting that cortical rather than trabecular bone has a greater impact on fracture risks. Cortical or compact bone makes up 80% of bone and stores the bulk of the skeleton's lead for very long periods; trabecular (cancellous or spongy bone) makes up 20% of the bone mass, is shorter lived, porous, rich in blood vessels, and can release minerals through osmosis (exchange from the blood) (Wikipedia 2010). As a result trabecular bone has the greatest impact on blood levels in the years immediately following lead exposure, cortical bone provides a reserve of more highly leaded bone that can have large impacts on blood lead, and consequent lead toxicity, if released (Manton 2003, Patrick 2006 p4-5). The fact that smoking has poorly-understood impacts on cortical bone can only be a cause of concern.

Smoking decreases vitamin levels

Another problem is that smoking impacts on three key vitamins that reduce the impact of lead on various body systems. Smoking reduces levels of vitamin D in the body, not only increasing bone resorption but potentially increasing the amount of lead deposited in the bones (Supervia 2006, Taylor 2010). Of equal concern are the much lower levels of vitamin E and C in smokers (Bruno 2006a). Vitamin E and C work together to reduce the

impacts of lead induced oxidative damage (Taylor 2010). Increasing an individual's vitamin E intake through supplementation (as opposed to food consumption) has considerable risks including a greater risk of lung cancer, particularly among smokers (Byers 2008, Slatore 2008). Fortunately supplementing vitamin C intake by 1000 mg not only reduces vitamin E requirements by 25% but may reduce the blood lead levels of smokers as well as reducing some impacts of lead toxicity. (Bruno 2006b, Taylor 2010).

Summary

In summary tobacco smoking has clear impacts on cancer risk, cardiovascular problems and neurocognitive development. Lead plays a clear and major role in cardiovascular problems and less easy to quantify role in neurocognitive or behavioral problems, partially because these can cover such a wide range. It plays a definite though probably not decisive role in smoking-related carcinogenesis, predominantly through the radiation released by the radioactive lead in cigarettes (Pb-210) as it decays to Polonium within the lung. Tobacco smoking increases lead toxicity both by the absorption of lead through the lung and by accelerating the release of lead from the bones. It restricts the body's reaction to lead toxicity by restricting the availability of key vitamins. The overall effect of smoking is to increase both the body's lead burden and exacerbate lead's impact.

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