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Tobacco smoke iron: an initiator/promoter of multiple diseases

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Abstract Tobacco smoking enhances risk for a diversity of acute and chronic diseases. Iron is a constant prominent component of mainstream tobacco smoke. The manifold toxic activities of inhaled iron could be responsible for a notable portion of the spectrum of smoking-related diseases.

Keywords Impaired hearing · Infection · Iron · Neoplasm · Osteoporosis · Tobacco smoke · Vascular disease

Introduction

Tobacco smoking has long been known to increase risk of a considerable variety of disease conditions. Among these are impaired hearing; fungal, bacterial, and viral infections; neoplasms of respiratory and gastrointestinal tracts; osteoporosis; and, not least, such vascular disorders as coronary artery and cerebrovascular diseases (Table 1). In recent years, it has become apparent that these same illnesses are enhanced by excessive iron in specific tissue sites (Weinberg 2007).

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Toxic iron in tobacco smoke

That a portion of iron from tobacco leaf and cigarette paper is present in mainstream smoke is well established. The iron content of tobacco has been reported to be 440–1150 μg/g; of cigarette paper, 420 μg/g (Mussala-Rauhammae et al. 1986). Approximately 0.1% of the cigarette iron is present in mainstream smoke. Thus, a one pack/day smoker can inhale over 1 μg of iron per day (Thompson et al. 1991). Alveolar macrophages of smokers have up to six times as much iron as in macrophages of non-smokers (McGowan and Henley 1988; Mateos et al. 1998). Although about 75% of the intracellular metal is incorporated in insoluble hemosiderin, the remainder is found in ferritin and can be released by polyhydroxybenzenes in tobacco smoke (Wesselius et al. 1994; Lapenna et al. 1995).

Among the >4,000 compounds in tobacco smoke are numerous mutagens and carcinogens (Newcomb and Carbone 1992). The iron component, however, not only is mutagenic and carcinogenic but also uniquely possesses several additional toxic activities. As noted in Table 2, a salient role of iron is that of stimulating microbial and neoplasmic cell growth. The metal is essential for proteins required for DNA synthesis and energy production. In the replication of human immunodeficiency virus, five iron dependent and iron regulated steps have been described (Drakesmith and Prentice 2008).

Another critical attribute of iron is its catalytic production of dangerous amounts of hydroxyl (free)

Table 1 Examples of disease conditions enhanced by tobacco smoke

Disorder	Relative risk as compared with non-smokers		References
Impaired hearing	Current smokers	1.7	Cruickshanks et al. (1998)
	Passive smokers	1.9	
Infection			
Fungal (*Cryptococcus neoformans*)	Current smokers	2.0	Hajjeh et al. (1999)
Bacterial			
Legionella pneumophila	Current smokers	2–10	Edelstein (2008)
Mycobacterium tuberculosis	Ever smokers	4.2	Gajalakshmi et al. (2003)
Neisseria meningitidis	Smoking mothers who had ill children	3.5	Fischer et al. (1997)
Streptococcus pneumoniae	Current smokers	4.1	Nuorte et al. (2000)
	Passive smokers	2.5	
Viral (HIV)	Current smokers	4.5[a]	Abbud et al. (1995)
Neoplasms			
Lung cancer	Male smokers	22	Newcomb and Carbone (1992)
	Female smokers	12	
Oral cancer	Male smokers	27	Newcomb and Carbone (1992)
	Female smokers	6.0	
Hepatic cancer	Male smokers	1.5	Chen et al. (2003)
	Female smokers	1.45	
Hepatic cancer	>20 pack-years	4.9	Marrero et al. (2005)
Colonic adenoma	>40 pack-years	3.3	Kikendall et. al (1989)
Osteoporosis	Male smokers	2.3	Seeman et al. (1983)
Vascular disease			
Coronary artery	Male smokers	2.5	McBride (1992)
Cerebrovascular	Female smokers	3.0	McBride (1992)

[a] Fold increase in viral antigen load in alveolar macrophages

radicals. In aminoglycoside antibiotic ototoxicity, the 1:1 drug–iron complex is required for radical generation (Forge and Schacht 2000). Neoplasmic cell initiation, osteoblast suppression, and vascular cell toxicity likewise are attributed to iron-catalysed hydroxyl radical formation.

Perspectives

Excessive iron in specific tissue sites can be acquired by inhalation, ingestion or injection, or by destruction of such iron loaded cells as erythrocytes. Our ability to prevent accumulation of hazardous levels of unbound (free) iron can be offset by behavioral and environmental factors. Especially troublesome is inhalation of such iron contaminated vehicles as tobacco smoke, ferriferous industrial aerosols, coal dust, asbestos, and subway air particulates (Weinberg 1999).

In the association of smoking with enhanced respiratory tract infection and neoplasms, the role of inhaled iron is more prominent than that of ingested or injected iron. On the other hand, ingested and injected routes of iron entry can be more accountable than inhaled iron for the development of non-respiratory tract disorders. Nevertheless, patients at elevated risk for diseases of iron loading by either ingestion (e.g., hemochromatosis, African siderosis) or by erythrocyte injection (thalassemia, myelodysplasia) should be cautioned about inhaling materials laden with iron such as tobacco smoke.

Moreover, it is now becoming apparent that, for all individuals, prevention of excessive iron acquisition by each of the three routes, coupled with methods of

Table 2 Examples of diverse roles of iron in disease causation

Disorder	Role of iron	References
Impaired hearing	Activation of aminoglycoside toxicity	Forge and Schacht (2000)
Infection		
Fungal (*Cryptococcus neoformans*)	Nutrient essential for growth	Boelaert and Blasi (1999)
Bacterial		
Legionella pneumophila	Nutrient essential for growth	Viswanathan and Cianciotto (2001)
Mycobacterium tuberculosis	Nutrient essential for growth	Boelaert et al. (2003) and Basaraba et al. (2008)
Neisseria meningitidis	Nutrient essential for growth	Zarantonelli et al. (2007)
Streptococcus pneumoniae	Nutrient essential for growth	Lambert and Hunter (1990)
Viral (HIV)	Promotion of viral replication	Drakesmith and Prentice (2008)
Neoplasms	Initiation via OH radical formation to cause point mutations, DNA cross linking, and strand breaks	Weinberg (1996)
	Promotion via serving as a nutrient essential for growth	
Osteoporosis	Suppression of osteoblast activity	Weinberg (2006)
Vascular disease	Oxidation of low density lipoprotein to result in atheromatus foam cells	Yuan et al. (1996)
	Impairment of endothelium-dependent vasorelaxation	Day et al. (2003)

deironing, can promote an increase in overall health and longevity (Weinberg 2007).

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