amount of nicotine-containing aerosol use in recent years, the role of nicotine is a relevant public health concern. A number of recent studies and health education sites have focused on nicotine aerosol-induced adverse lung function, and neglected CV impairments and diseases. A critical review of the present scientific literature leads to the hypothesis that nicotine mediates the effects of cigarette smoke in the CV system by increasing MAPK signaling, inflammation, and oxidative stress through NADPH oxidase 1 (Nox1), to induce vascular smooth muscle cell (VSMC) senescence. The accumulation of senescent VSMCs in the lesion cap is detrimental as it increases the pathogenesis of atherosclerosis by promoting an unstable plaque phenotype.

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THE EFFECTS OF MEALS AND AGE ON NICOTINE METABOLISM

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Introduction. Nicotine underlies tobacco addiction, influences tobacco use patterns, and is used as a pharmacological aid to smoking cessation. The absorption, distribution and disposition characteristics of nicotine from tobacco and medicinal products are reviewed. Nicotine is metabolized primarily by the liver enzymes CYP2A6, UDP-glucuronosyltransfease (UGT), and flavin-containing monooxygenase (FMO). In addition to genetic factors, nicotine metabolism is influenced by diet and meals, age, sex, use of estrogen-containing hormone preparations, pregnancy and kidney disease, other medications, and smoking itself. Substantial racial/ethnic differences are observed in nicotine metabolism, which are likely influenced by both genetic and environmental factors.

Materials and methods. Analysis of scientific literature and results of clinical diagnostic parameters of medical organizations.

Results and discussion. An implication of the high degree of hepatic extraction is that clearance of nicotine should be dependent on liver blood flow. Thus, physiological events, such as meals, posture, exercise, or drugs perturbing hepatic blood flow, are predicted to affect the rate of nicotine metabolism. Meals consumed during a steady state

infusion of nicotine result in a consistent decline in nicotine concentrations, the maximal effect seen 30–60 min after the end of a meal. Hepatic blood flow increases about 30% and nicotine clearance increases about 40% after a meal.

Menthol is widely used as a flavorant in foods, mouthwash, toothpaste, and cigarettes. A moderate inhibition of CYP2A6-mediated nicotine metabolism in human liver microsomes by menthol and various related compounds has been reported. This is supported by a crossover study in people, showing that mentholated cigarette smoking significantly inhibits metabolism of nicotine to cotinine and nicotine glucuronidation when compared to smoking nonmentholated cigarettes [2].

Grapefruit juice inhibits CYP2A6, as evidenced by inhibition of coumarin metabolism in people. Grapefruit juice has been shown to inhibit the metabolism of nicotine to cotinine in nonsmokers who were given nicotine orally, with evidence of a greater effect with larger doses of grapefruit juice. Grapefruit juice also increased renal clearance of nicotine and cotinine by an unknown mechanism. Grapefruit juice had no significant effect on overall exposure to nicotine (area under the plasma concentration–time curve) because the effects of slowed metabolism were offset by the effects on increased renal clearance. Whether the effects of grapefruit juice on nicotine levels in users of tobacco are significant has not been investigated. Consumption of watercress enhances the formation of nicotine glucuronide, cotinine glucuronide, and 3′-hydroxycotinine glucuronide in smokers. Watercress has no effect on the excretion of nicotine, cotinine, and 3′-hydroxycotinine in smokers. Thus, watercress may induce some UGT enzymes involved in nicotine metabolism, but has no effect on CYP2A6-mediated nicotine metabolism [3].

Clearance of nicotine is decreased in the elderly (age >65) compared to adults. Total clearance was lower by 23%, and renal clearance lower by 49% in the elderly compared to young adults. Lower nicotine metabolism in the elderly may be contributed to by reduced liver blood flow, since no decrease in CYP2A6 protein levels or nicotine metabolism in liver microsomes due to age has been detected. No differences in steady-state nicotine plasma levels or estimated plasma clearance values were detected in three age groups (18–39, 40–59, and 60–69 years) using patches with the same nicotine content. The volume of distribution of nicotine is lower in older subjects due to a decrease in lean body mass.

Neonates have diminished nicotine metabolism, as demonstrated by a nicotine half-life of three to four times longer in newborns exposed to tobacco smoke than in adults. Cotinine half-life is reported to be similar in neonates, older children, and adults in two studies. Other studies found that the half-life of urine cotinine was about three times longer in children less than one year old than to the cotinine half-life in adults. Urine cotinine half-life can be influenced by variations in urine volume and excretion of creatinine. The study by Dempsey et al. was the only one in which the half-life of cotinine was calculated based on both the blood and urine cotinine concentrations. In that study, both the blood and urine half-lives were similar to adult values, supporting the notion that neonates have the same cotinine half-life as older children and adults [4].

Why nicotine has a much longer half-life in neonates than in adults, whereas the cotinine half-life is essentially the same in newborns and adults, might partially

be explained by differing sensitivities of nicotine and cotinine clearances to changes in hepatic blood flow. As a drug with a high extraction ratio, the clearance of nicotine is influenced by changes in hepatic blood flow, whereas clearance of cotinine with low extraction ratio is more dependent on changes in intrinsic clearance, i.e., amount and activity of metabolic enzymes. Studies in newborn animals, mainly sheep, have shown that hepatic blood flow is low immediately after delivery because of the loss of the umbilical venous blood supply and the patency of ductus venosus. Hepatic blood flow rises to adult levels within the first week, due to increased blood flow in the portal vein and gradual closure of ductus venosus, which is complete by the eighteenth day in human neonates. This would mean that nicotine clearance should rise and the nicotine half-life shorten within the first couple of weeks as hepatic blood flow increases. Another explanation could be that nicotine and cotinine are metabolized mainly by enzymes other than CYP2A6 in neonates. However, neonates have only slightly lower amounts of CYP2A6, CYP2D6, and CYP2E1 protein in liver microsomes, whereas the CYP2B6 amount is clearly diminished in neonates compared to adults and older children [5].

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BIOCHEMICAL SYNTHESIS OF COENZYME Q IN PLANTS

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Introduction. Coenzyme Q (CoQ), also known as ubiquinone, is an essential electron transporter in the oxidative respiratory chain that generates adenosine triphosphate (ATP). CoQ is synthesized by nearly all eukaryotes and some proteobacteria. Structurally, CoQ is composed of a benzoquinone head group attached to a polyisoprenoid tail whose number of isoprene units varies among species: 10 (CoQ10) in humans and some crops (such as tomato and soybean), CoQ9 in *Arabidopsis* thaliana and rice, CoQ8 in *Escherichia* coli, and CoQ6 in yeast (*Saccharomyces cerevisiae*). The quinone head group of CoQ can exist in three oxidation states: the fully oxidized form