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Third-hand smoke exposure and results

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Abstract:

Diseases and deaths due to smoking are still a major public health problem, which is still the leading cause of death in the world. Today, the harmful effects of active smoking and second hand cigarette smoke on health are clearly known. However, the concept of third-hand smoke (THS) exposure, a new concept, is a relatively new definition in the area of environmental and public health. The third-hand smoke (THS) consists of residual cigarette smoke gases and particles that settle on the surface. Studies evaluating the presence of tobacco specific nitrosamines (TSNA) in house dust samples have shown that THS is an important source of exposure to TSNA. Investigations on animals estimating human exposure, it has been found that THS contains tobacco smoke compounds, which can stay for months on internal surfaces and in dust for months, and that it is re-released into the air as gaseous. In addition, surface chemicals in the surroundings and in dust can produce additional toxins as a result of various chemical reactions. Although it is premature to estimate the health impacts of THS as a whole, the health effects of TSNAs have been previously reported in the literature. Future studies should be directed at investigating the biological effects and consequences of THS on humans. This article will address the implications of THS exposure and the results of current studies conducted in this area.

Keywords:

Second-hand smoke, smoking, third-hand smoke

Introduction

Smoking and related diseases and deaths are still a major public health problem in the world. About 22% of cancer-related deaths worldwide are associated with smoking.^[1] Active smoking is causally linked to many health problems such as cancer, stroke, coronary heart disease, respiratory diseases, diabetes mellitus, rheumatoid arthritis, and impaired immune system. The International Cancer Research Center reported that by the year 2020, there will be 10 million cigarettes-related deaths per year with 70% of them occurring in developing countries.^[2,3] Exposure to cigarette smoke causes serious consequences

for nonsmokers, especially children. According to a study, 6,600,000 premature deaths occurred as a result of cancer caused by second-hand smoke (SHS) exposure between 1965 and 2014 and this number has been shown to reach 20 million with deaths due to other causes.^[4] The negative effects of smoking on health are the most common causes of smoking cessation.^[5] However, the cessation of smoking is still not at the desired level, and the cessation rates decrease depending on time.^[6,7] In a worldwide evaluation conducted in 2004, data from 192 countries showed that 35% of the nonsmoker women, 33% of the nonsmoker males, and 40% of the children were exposed to cigarette smoke. The causes of death due to SHS exposure include ischemic heart disease, lower respiratory tract infections, asthma, and lung cancer.^[2,8]

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Today, the harmful effects of active smoking and SHS on health are clearly known. However, the concept of exposure to third-hand smoke (THS), a new concept, is a relatively new definition in the field of environment and public health.^[9,10] The third-hand smoke is composed of cigarette smoke, residues of cigarette smoke, and particles settled on the surface and dust. The effects of these products on health are still under investigation. However, these products are potentially carcinogenic substances. Therefore, it is considered that smoking environments can pose a health threat for children, spouses, and employees.^[10-13] The first research on THS was performed by Invernizzi *et al.* time of cleansing of the lungs from the last smoking of 10 cigarette smokers was evaluated. The particle concentration of 0.3–1.0- μm particles in exhaled air was monitored in real time. Average time of cleansing of the cigarette smoke from the lungs was 58.6 s (minimum-maximum: 18–90 s). These data indicate THS as a hidden source of pollution for closed areas.^[9] Research on THS is fairly young and there are currently only a limited number of animal studies investigating the effects of THS-specific components on health.^[14]

THS is closely related to SHS. Secondary cigarette smoke exposure is the passive inhalation of environmental fume from the combination of mainstream and sidestream smoke. The mainstream smoke spreads from exhalation of smokers, whereas the sidestream smoke emerges from cigarettes or cigars of smokers. SHS, over time, leads to harmful chemicals by settling on the surfaces, and the accumulated chemical residues form THS. THS is also known as leftover or residual tobacco. Matt *et al.* described the residues on the surface and dust after tobacco smoking as “tobacco smoke pollutants.”^[15] THS is found in indoor environments such as floors, benches, walls, and furniture and can stay for several months after smoking.^[15-17] In addition, THS products can be found in the hair, skin, and clothing of smokers.^[18] The presence of THS products on dust, air, and surfaces leads to multiple exposure routes. THS exposure can occur through dermal absorption, digestion, and inhalation. Especially, children and babies are under higher risk for THS exposure, because they are more likely to contact the floor surface at home.^[19] Dermal absorption can also be caused by the polluted environment such as nonsmokers’ homes which were previously used by smokers. Especially the formation of high levels of nicotine in the environment increases the likelihood of unwanted exposure.^[16]

THS reacts with various chemicals over time. It is reported that the residues of cigarette smoke on the surfaces (furniture, walls, skin, and clothing) and atmospheric origin oxidants (O_3 , HONO, NO_x) react and as a result of this reaction, toxic nitrosamines

tobacco-specific nitrosamines (TSNA) form, which is known to be toxic carcinogens. Nicotine, which is absorbed in the environment, reacts with nitrous acid to form TSNA (4-(methylnitroamino)-4-(3-pyridyl) butanal (NNA), and 4-(methylnitroamino)-1-(3-pyridyl)-1-butanone (NNK). In addition, a significant amount of TSNA levels were measured on surfaces in a smoking car.^[20] Furthermore, in addition to TSNA, hydrogen cyanide, butane, toluene, formaldehyde, radioactive polonium-210, and polycyclic aromatic hydrocarbons have been identified in THS content.^[21]

Sources of third-hand smoke

THS can be found in many indoor spaces. Even where smoking prohibitions are applied, including personal homes, public buildings, rental houses and apartments, rental cars and public transport, and nonsmoker individuals may be affected by THS. THS exposure is a major problem in multi-unit houses since cigarette smoke can pass through air ducts, walls, cracks in floors, and through electrical installation lines and contaminates other units. In this way, residents can be exposed to THS without smoking.^[16] In a study, carcinogenic N-nitrosamines and TSNA were measured in household dust samples using an extremely sensitive and selective analytical approach. The cancer risk estimated by applying the current toxicological information has been shown to increase in especially early life stage (1–6 years) who exposure to TSNA. Depending on exposure to all nitrosamines measured in a smoking house, the risk of cancer was found to be one in 1000 cases per person. This study has been shown that especially for child THS exposure could potentially have serious consequences in the long term.^[11]

A study was conducted to evaluate residual contamination due to cigarette smoking after smoking. Three types of fabric: wool, cotton, and polyester were used and to determine THS adsorbed to the clothing fibers was planned. A surface acoustic wave sensor consisting of oxidized hollow mesoporous carbon nanospheres was used to detect chemical compounds of THS, such as nicotine and 3-ethenylpyridine. In the evaluation, it has been shown that woolen fabric adsorbs THS at most and polyester absorbs at least. Desorption time of THS on polyester was found to be much shorter than natural fiber, wool, and cotton.^[22]

The effects of third-hand smoke on health

Nowadays, there is no study that shows the negative effects of THS in human health. However, THS components are estimated to have potentially harmful effects on human health including DNA damage, allergic symptoms, asthma, inflammation, and even brain and lung development in children.^[23] In a study conducted on mice under conditions that mimic THS exposure to

Table 1: Comparison of second- and third-hand smoke

	SHS	THS
Source	Mainstream smoke exhaled by active cigarette and sidestream current fume of tobacco product	Usually media surfaces, furniture surfaces, hair, skin and cigarette smoke residues
Basic compounds	Benzene, toluene, styrene, acetone, xylene, naphthalene, formaldehyde, polonium-210, phenol, PAHs, nicotine, 3-ethenylpyridine, carbon monoxide, and N-nitrosamine	Nicotine, 3-ethenylpyridine, phenol, cresol, formaldehyde, TSNA, naphthalene, xylene, styrene, benzene, toluene (concentrations lower)
Associated diseases	Lung cancer, oral cancer, asthma, COPD, coronary heart disease	Allergic symptoms, asthma, changes in brain and lung development in children

SHS: Second-hand smoke, COPD: Chronic obstructive pulmonary disease, TSNA: Tobacco specific nitrosamines, PAHs: Polycyclic aromatic hydrocarbons, THS: Third-hand smoke

human, the biological effects of THS exposure were investigated. In the study, mice cages were exposed to tobacco smoke by means of a device 6 h/day, 5 days a week, for 24–26 weeks. After exposure, it was observed that the tobacco-specific carcinogen (NNAL) levels increased in various organs and secretions of exposed mice. In mice exposed to THS, changes in many organs have been shown.^[14] In exposed mice, the urine levels of 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol, which is the main metabolite of NNK and is known as a tobacco-specific carcinogen biomarker, were found to be similar to those reported in infants and newborns aged between 2 and 4 years who were exposed to SHS and thus to THS.^[14,24] The sources, contents, and results of the second-hand smoke and THS are given in Table 1.^[17,22]

As a result of the study on mice, THS has been shown to result in increased lipid levels in the liver, nonalcoholic fatty liver disease, and cirrhosis, which lead to cancer and contribute to cardiovascular disease. Exposed mice had steatosis in hepatocytes, increased triglyceride levels, increased low-density lipoprotein levels, decreased high-density lipoprotein levels, and impaired blood sugar regulation. It has been suggested that their combination may increase the likelihood of cerebrovascular event and Type 2 diabetes mellitus. In animals exposed to THS, fasting glucose levels were elevated, and insulin use was impaired to control blood glucose levels. When the lungs of the exposed mice were examined, terminal bronchi and alveolar walls were found to be thicker than that of unexposed mice. It has also been shown to induce fibrosis, leading to excessive collagen production in the lungs and high levels of inflammatory cytokine release. This suggests that inflammation-induced diseases such as chronic obstructive pulmonary disease and asthma may be induced. In addition, the healing process of injured skin in THS exposed mice was similar to the poor healing of surgical incisions observed in smokers. Finally, behavioral tests have shown that mice exposed to THS become hyperactive.^[14] The data are consistent with the findings that children exposed to tobacco smoke are more hyperactive than nonexposed.^[14,25] These data suggest that, with prolonged exposure, even more severe neurological disorders may be experienced along with behavioral problems in children under SHS or THS

exposure. This study on rats constitutes the basis for studies on the toxic effects of THS in humans.^[14]

In a recent study, it has been reported that THS is genotoxic in human cells. In this study, the genotoxicity of THS in the human cell line was evaluated in two *in vitro* experiments. Acute and chronic exposure of THS was established in laboratory simulation systems, and analyzes were performed using liquid chromatography-tandem mass spectrometry. TSNAs and common tobacco alkaloids were analyzed in THS extracts absorbed into cellulose substrates. Exposure of human HepG2 cells to acute or chronic THS for 24 h has been shown to cause significant increases in DNA strand breaks. In the same experiment, DNA damage was significantly higher in cell cultures exposed to 4-(Methylnitrosamino)-4-(3-pyridyl) butanol, also known as “NNA” alone. NNA is the basic TSNA present in THS when the nicotine reacts with HONO shortly after smoking is not present in freshly spread second-hand smoke. NNA and 8 volatile N-nitrosamine and 5 tobacco-specific nitrosamine are cancer-causing compounds as a result of DNA damage.^[11,23] NNA can cause breakage or breakdown in the DNA chain. It may also cause oxidative damage in the hypoxanthine phosphoribosyltransferase 1 gene, which plays a critical role in nucleotide metabolism.^[26,27] The type of damage caused by NNA and NNK may lead to a base mutation in DNA that causes “uncontrolled cell growth and the formation of cancerous tumors”.^[28]

In a study evaluating whether the effect of THS exposure on health depends on time, an *in vivo* exposure system was established on mice that mimic exposure of humans to THS, and their effects on serum, liver, and biological markers in the brain were investigated. Mice were exposed to THS for 1, 2, 4, or 6 months, and brain, liver, and serum samples were obtained. Exposure to THS has been shown to increase circulating inflammatory cytokine levels and stress hormones within a short period of 1 month. This increase has been shown to be 2-fold in tumor necrosis factor, 1.5-fold in granulocyte macrophage colony-stimulating factor, 1.5-fold in epinephrine level, and 2.5-fold in aspartate aminotransferase in the liver damage. In addition, it has been shown that the increased exposure duration also increases the effects and mice

become hyperglycemic and hyperinsulinemic.^[12] This result suggested that prolonged THS exposure may cause insulin resistance.

The children and infants spend more time close to the ground in a closed environment. As a result, they further inhale dust particles contaminated with THS compounds. In addition, because this age group has more hand-mouth contact, gastrointestinal intake of THS compounds also increases. The rate of dust absorption in infants was found to be more than twice the rate in adults.^[29] Prolonged exposure to THS in infants and children may cause some cognitive, developmental, and neurological disorders and conditions such as attention deficit, decreased muscle, and bone growth. The degree of exposure depends on the degree of contamination and the duration of exposure of the medium with THS.^[30]

Winickoff *et al.* investigated the thoughts of adults about the health effects of THS exposure and whether these differed among smokers and nonsmokers. The data were obtained by telephone survey with 1510 people across the country in 2005. About 95.4% of nonsmokers and 84.1% of smokers thought that SHS is harmful to children's health. However, 65.2% of nonsmokers and 43.3% of smokers thought that SHS is harmful to children's health. In the study, nonsmokers were shown to better obey the rules that prohibit smoking at home (26.7% vs. 88.4%). It has been shown that there is no correlation between the number of people who think that SHS is harmful to children's health and the application of the rules that prohibit smoking at home and in the car. In other words, although smokers know that cigarettes are harmful to children, they do not obey the rules in their daily lives. Therefore, this study emphasized that SHS and thus, THS should be prevented from smoking at home and in the car to prevent the harm to child health.^[10] In another study evaluating the thoughts of THS among parents who smoke, it is reported that parents who smoke more than 10 cigarettes a day are less likely to believe THS is harmful.^[31]

In a study, information and attitudes about THS were evaluated in a low-income population. This study focuses on THS awareness, perceived harm, and motivations for making a nonsmoking home. For this purpose, 6 nonsmokers and 39 nonsmokers with six focal points were established. Most of the participants were African-American, women, and university graduates. First, the participants were asked whether they were informed about the THS and its harms. Most of the participants told they are not familiar with the expression "THS;" however, after the definition, some participants stated that they experienced the smell of cigarette smoke residues in their clothes and houses. Later, when asked about their thoughts on smoking in

their homes and being protected from THS, nonsmokers who live with smokers stated that they would be eager to prevent smoking in their homes to protect their homes from THS.^[32]

Approaches for Protection

Since the SHS is partly visible, a large number of comprehensive studies have been conducted to investigate adverse health outcomes. Most individuals in the community have been aware of SHS's negative health outcomes through public service announcements, smoking cessation programs, and other projects aimed at reducing involuntary tobacco exposure.^[33] However, there are no studies that have confirmed the harmful effects of THS on humans. Animal studies have been conducted to estimate the results of human exposure. It has been shown that THS can remain in the interior surfaces and dusts for a long time, and the compounds it contains react once again to the chemical reactions and spreads again into the air as a gas. For this reason, the most basic approach in protecting nonsmokers from THS should be the prevention of smoking in indoor environments. These indoor environments should include all closed spaces including homes, workplaces, public transports, restaurants, nursing homes, hospitals, cars, and shopping centers. First, it is necessary to separate smokers from nonsmokers and prevent smoking in multi-storey buildings and in indoor environments.

While reviewing policies and laws on cigarette smoke, the impact of THS should be taken into account. In Turkey, with Law no. 4207, which was put into practice in July 2009, smoking was prohibited in indoor areas. With this law, "tobacco products cannot be consumed in closed areas of buildings belonging to private persons with all kinds of education, health, production, trade, social, cultural, sports, entertainment, and similar purposes." With the implementation of the law, it has been shown that SHS exposure decreased in public areas.^[34] With the effective implementation of the law, both SHS and THS exposure will end. Informing the society about THS and raising awareness could particularly ensure the protection of small-age individuals who have high risk.

With the implementation of the law, the most effective method will be to ensure that people quit smoking. Encouraging people to quit smoking and supporting the ones who are trying so will provide a clean and smoke-free environment as well as health protection. Efforts to improve the nonsmoking environment in public spaces should continue. Studies indicate that tobacco toxins are still relatively high after smoking. It is difficult to remove THS by opening windows or by using fans, and THS exposure lasts more than 2 months.^[10] Ventilating the environment by opening

Argüder: Third-hand smoke

doors and windows in a smoking environment, using aspirators or air conditioners, building a separate room for smoking can reduce the exposure of SHS and THS for others. In addition, for the prenatal period where the risk is the highest, it will be protective to evaluate the smoking status of other people at home during the follow-up of pregnant women and to give education in this direction to the pregnant woman and her family. Evaluation of cotinine or nicotine levels to assess exposure in children will lead to more objective results.^[35] To clearly define the effects of THS, it would be ideal to assess the conditions, in which there is no active cigarette smoking and no SHS exposure. Future studies should determine how THS affects people biologically. Manufacturing a highly sensitive THS sensor can protect people from long-term tobacco hazards. In this way, in addition to preventing infants and children from breathing air contaminated with tobacco smoke, they can also be protected from daily physical contact with THS residues.

Finally, THS is the result of first-hand and second-hand smoke. The most effective policy to adopt should be focusing on, tobacco control and other factors relating to smoking. Nevertheless, approaches that focus on THS by increasing public health awareness will definitely bring positive results.

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Conflicts of interest

There are no conflicts of interest.

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Argüder: Third-hand smoke

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