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RESEARCH ARTICLE

Biological monitoring of wood-smoke exposure

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Abstract

It has been clearly established that exposure to wood smoke is associated with a variety of adverse health effects in humans. However, we still have much to learn about the relationship between wood-smoke exposure and disease, including determination of what should be considered a "safe" level of exposure, and whether wood smoke should be regulated separately from other sources of air pollution. To help answer these questions, improved measures of exposure in populations exposed to wood smoke are required. In this mini-review we discuss how biomarkers of exposure can be used to complement the current suite of methods used to assess wood-smoke exposures. We critically review the compounds that are currently being evaluated as biomarkers of exposure to wood smoke, and we identify the strengths and weaknesses of these compounds. We find that, in general, these compounds show promise in situations where wood-smoke exposures are high, but where exposures are low non-wood-smoke sources are likely to be the major determinants of biomarker levels. We also outline a research framework that will move this field forward and maximize the potential for wood-smoke biomarkers to add value to epidemiological studies of wood-smoke health effects.

Keywords: *Biological monitoring; exposure assessment; wood smoke*

Introduction

Wood smoke contains many toxic agents including several known carcinogens, and exposure to wood smoke is associated with a variety of adverse health effects (Naeher et al. 2006). Accurate and robust measures of personal exposure to wood smoke are required for use in epidemiological studies of the health impacts caused by wood-smoke exposures. However, due to the chemical complexity of wood smoke, and the spatial and temporal variability in ambient wood-smoke concentrations, traditional techniques for measuring airborne pollutant levels that rely on fixed-area monitors often fail to adequately represent personal exposure to wood smoke. Biological monitoring has been proposed as a potential tool to address these limitations and to obtain reliable individual-level estimates of personal exposure to wood smoke. In this mini-review we consider critical issues regarding biomonitoring of wood-smoke exposures. Material presented in this mini review was obtained from relevant articles in the peer-reviewed literature, and from the presentations and breakout group discussions at the International Biomass Smoke Health Effects Conference (IBSHE) held at the University of Montana in Missoula, MT, August 2007.

How can biomarkers help improve exposure assessment for wood smoke?

Obtaining accurate measures of personal exposure and, more importantly, of absorbed dose for particulate air pollution is inherently difficult. This is due to the substantial spatial and temporal variation in pollutant levels, coupled with the fact that people constantly move between different microenvironments. In the case of wildfire events, extreme, short-term exposures occur that may not be captured by a fixed site operating on a typical 1-day-in-6 monitoring schedule. Furthermore, the highest wood-smoke exposures frequently occur in isolated rural communities or outlying suburbs of urban centers where little or no air quality monitoring takes place. Thus, traditional fixed-site monitors fail

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to capture the full variability in exposures experienced by individuals. Although active personal monitors are effective in accurately monitoring personal exposures, it is impractical and expensive to implement active personal monitoring on a large scale.

An alternative approach to exposure assessment that addresses many of the limitations just noted is biomonitoring. Biological monitoring of exposure offers several potential advantages over other exposure assessment techniques such as questionnaires or environmental monitoring. Biomarker levels represent the absorbed dose of a chemical, integrated across all microenvironments and routes of exposure. Thus the biomarker levels account for factors that modify the relationship between environmental concentrations and dose, including interindividual differences in absorption, ventilation, and exertion, use of personal protective equipment, and personal behaviors that modify exposure such as staying indoors, using HEPA filters in the home or workplace, and reducing physical activity when smoke levels increase.

Furthermore, biological monitoring can potentially take place retrospectively; that is, the biological samples can be collected after the exposures have occurred. This is a particularly important consideration in the case of smoke exposures due to wildfires, where it is typically not possible to predict a priori where or when a wildfire event will occur.

What potential biomarkers are available for monitoring exposure to wood smoke?

An exposure biomarker should meet the criteria of sensitivity, specificity, and practicality (NRC 2006; Metcalf 2004). Several classes of chemicals have been proposed as biomarkers for smoke exposures: carboxyhemoglobin, polycyclic aromatic hydrocarbon (PAH) metabolites, levoglucosan, and methoxyphenols (Hinwood et al. 2008; Liou et al. 1989; Rothman et al. 1993; Feunekes et al. 1997; Burgess et al. 2001; Dills et al. 2001). Table 1 summarizes the studies in which these biomarkers have been evaluated as metrics of wood-smoke exposure.

Exposure to carbon monoxide (CO) present in wood smoke leads to formation of carboxyhemoglobin. Carboxyhemoglobin can be measured directly in venous blood (Burgess et al. 2001), or indirectly as CO in exhaled breath (Cone et al. 2005). Elevated carboxyhemoglobin levels have been measured in active and passive cigarette smokers (Istvan and Cunningham 1992), and in tunnel workers and loggers (references in Burgess et al. 2001). However, in a study of wildland firefighters, Dunn et al. reported that carboxyhemoglobin levels only showed an association with CO exposure when the workshift time-weighted average exposure to CO was greater than 5 ppm (Dunn et al. 2005). Thus, this marker exhibited poor sensitivity. Carboxyhemoglobin may be a useful biomarker of smoke exposure where wood smoke is the dominant source of CO, and where exposures are elevated. However in many situations this marker will be confounded by cigarette smoking and non-biomass combustion emissions.

The PAH compound pyrene is abundant in wood smoke. Upon uptake by humans, pyrene is extensively modified to 1-hydroxypyrene and excreted in the urine and faeces. Several studies have reported associations between smoke exposure and urinary 1-hydroxypyrene (Feunekes et al. 1997; Moen and Ovrebo 1997; Caux et al. 2002; Kato et al. 2004). Metabolism of many PAHs has been shown to generate reactive intermediates that can bind to cellular macromolecules, generating PAH adducts. Liou et al. found higher levels of PAH adducts in peripheral blood cells in wildland firefighters exposed to wood smoke as compared to nonexposed controls (Liou et al. 1989). In contrast, Rothman et al. reported no association between smoke exposures and PAH-DNA adducts in peripheral blood from wildland firefighters (Rothman et al. 1993). PAH–DNA adducts were, however, associated with charbroiled beef consumption. PAHs are by no means specific to wood smoke; they are a component of incomplete combustion and are present in a variety of PM sources including vehicle exhaust, gas and coal combustion, and cooking fumes. Therefore, PAH biomarkers in urine or blood are only likely

Table 1. Published studies where associations between exposure biomarkers and wood-smoke exposures have been investigated.

Biomarker	Population	Reference
Carboxyhemoglobin	Structural firefighters	Burgess et al. (2001)
Carboxyhemoglobin/exhaled CO	Structural firefighters	Cone et al. (2005)
Carboxyhemoglobin/exhaled CO	Wildland firefighters	Dunn et al. (2005)
Urinary PAH metabolites (1-hydroxypyrene)	Charcoal production workers	Kato et al. (2004)
Urinary PAH metabolites (1-hydroxypyrene)	Structural firefighters	Feunekes et al. (1997)
Urinary PAH metabolites (1-hydroxypyrene)	Structural firefighters	Moen and Ovrebo (1997)
Urinary PAH metabolites (1-hydroxypyrene)	Structural firefighters	Caux et al. (2002)
PAH–DNA adducts in peripheral blood lymphocytes	Structural firefighters	Liou et al. (1989)
PAH–DNA adducts in peripheral blood lymphocytes	Forest firefighters	Rothman et al. (1993)
Urinary methoxyphenols	Campfire exposure, 1 adult	Dills et al. (2001)
Urinary methoxyphenols	Campfire exposure, 9 adults	Dills et al. (2006)
Urinary methoxyphenols	Villagers, rural Guatemala,(20 adults)	Clarke et al. (2007)
Urinary methoxyphenols	Wildland firefighters, United States	Neitzel et al. (2008)
Urinary levoglucosan	Wildland firefighters, Australia	Hinwood et al. (2008)
Urinary levoglucosan	Community impacted by residential woodstove use, United States	Migliaccio et al. (2009)

to be significantly associated with wood-smoke exposures when the exposures are very high, such that inhalation of wood smoke is the dominant exposure pathway for PAHs.

Levoglucosan is formed from pyrolysis of cellulose. Since levoglucosan is one of the most abundant particle-phase organic compounds in wood smoke, this compound may be a viable biomarker of wood-smoke exposure. Recently, several groups have begun to evaluate the suitability of urinary levoglucosan as a biomarker for wood-smoke exposure (Needham 2007; Hinwood et al. 2008; Migliaccio et al. 2009). In an inhalational exposure study Migliaccio found that mice exposed to wood smoke had higher levels of levoglucosan in the urine, compared to control mice exposed to clean air. Furthermore, they reported a mean urinary levoglucosan concentration of 55 ng/mg creatinine in schoolchildren from Libby, MT. Libby is a community impacted by high wintertime levels of wood smoke due to residential wood combustion. Hinwood reported mean urinary levoglucosan concentrations of 5700 ng/mg creatinine in urine collected from emergency service personnel who participated in a 1-day controlled burn training session. However, urinary levoglucosan concentrations were not significantly different in postexposure samples compared to preexposure samples (Hinwood et al. 2008). The hundred-fold discrepancy between these two studies in reported urinary concentrations of levoglucosan indicates further study of this biomarker is necessary.

Methoxyphenols are formed from pyrolysis of the wood polymer lignin. Thus, their presence in air samples is unique to biomass combustion. Several studies have investigated the utility of these compounds as urinary biomarkers of wood-smoke exposure (Dills et al. 2001; Dills et al. 2006; Clarke et al. 2007; Neitzel et al. 2008). Multiple methoxyphenols are detectable in the urine of individuals with no known elevated exposure to wood smoke, and a substantial increase in urinary methoxyphenol excretion was reported subsequent to inhalation of wood smoke from a campfire (Dills et al. 2001; Dills et al. 2006). These studies found that biomarker levels were greatly affected by diuresis, and that creatinine correction dramatically improved the relationship between biomarker levels and wood-smoke exposure. Associations between urinary methoxyphenol biomarker levels and wood-smoke exposure were also reported for wildland firefighters (Neitzel et al. 2008), and for residents in rural Guatemala exposed to smoke from indoor cookstoves (Clarke et al. 2007). In all four studies, wood-smoke exposures were relatively high—in the range of 500–2000 $\mu g/m^3$ $PM_{2.5}$. The half-life for urinary excretion of the methoxyphenols was 2–6 h (Dills et al. 2006), which indicates that in the case of acute exposure events urine samples would need to be collected within 6–12 h postexposure.

What are some potential pitfalls and limitations for using biomarkers for wood-smoke exposure assessment?

While biomarkers offer great potential as a tool in exposure assessment, there are a number of factors that may limit their utility for measuring wood-smoke exposures. Wood smoke is an inherently complex and variable mixture of chemicals produced from different sources. The composition of smoke varies depending upon fire type (e.g., wildfire vs. residential wood stove), fuel source (hardwood, softwood, compressed logs), fuel moisture, and combustion conditions (e.g., smoldering vs. flaming combustion). Different relationships are likely to exist between bulk smoke constituents (particulate matter, CO, CO_2), exposure biomarker levels, and health endpoints for each of the different combustion scenarios just described. For example, Dills et al. reported that a combination of several methoxyphenols was a more robust biomarker of exposure than using a single compound (Dills et al. 2006). In their study, where the fuel included both hardwoods and softwoods, both syringyl- and guaiacyl-type methoxyphenols showed a positive association with the wood-smoke exposure. In contrast, Clarke et al. reported that only specific syringyl-type methoxyphenols were associated with wood smoke from cookstoves in rural Guatemala (Clarke et al. 2007), whereas Neitzel et al. found only specific guaiacyl-type methoxyphenols were elevated in wildland firefighters exposed to smoke from prescribed burn activities in South Carolina (Neitzel et al. 2008). It was hypothesized that differences in the fuels burned and hence the smoke composition were responsible for the different biomarker responses observed in these three studies.

Regrettably, the wood-smoke biomarkers evaluated thus far have all proved to be somewhat limited in regard to sensitivity and specificity. As noted earlier, the association between wood-smoke exposures and carboxyhemoglobin would be confounded by cigarette smoking and non-biomass combustion emissions, and carboxyhemoglobin has only shown an association with wood-smoke exposures when those exposures are relatively high (Dunn et al. 2005). Similarly, pyrene is abundant in many combustion sources, so urinary 1-hydroxypyrene measurements would also be confounded by cigarette smoking and non-biomass combustion emissions. Dietary sources of biomarker compounds can also obscure associations between wood-smoke exposure and biomarker response—especially for exposure at or near ambient concentrations. Previous studies estimated that for nonsmokers not occupationally exposed, the major portion of PAH dose is taken up through the diet (Chuang et al. 1999;). Similarly ingestion of food items containing wood-smoke flavoring (e.g., smoked salmon) caused a substantial increase in urinary methoxyphenol excretion (Dills et al. 2001; Dills et al. 2006). The possibility also exists for a large dietary contribution of levoglucosan from caramelized sugars (Ratsimba et al. 1999). The variation in biomarker levels from dietary sources has the effect of limiting the sensitivity of these biomarkers. The sensitivity of these biomarkers can be improved somewhat if the pre- and postexposure samples can be obtained, and a difference between pre and post exposure biomarker levels calculated.

What are the key research needs in order to further the use of biomarkers for assessment of wood-smoke exposures?

At the current time, most potential biomarkers for wood-smoke exposure have been incompletely validated. Controlled exposure studies, ideally conducted in exposure chambers, should be undertaken in which smoke chemistry and composition are measured in great detail, concurrently with measurement of multiple exposure and effect biomarkers. Such controlled exposure studies permit rigorous testing of variables such as fuel type and combustion conditions, and ensure that smoke exposures and dose can be well measured. The controlled exposure studies would also lead to a winnowing down of potential biomarkers, with only those that exhibited appropriate sensitivity, specificity, and reliability being selected for further study.

The second stage in wood-smoke biomarker evaluation is execution of field studies in populations exposed to high concentrations of wood smoke. Unfortunately, the highest community exposures to wood smoke are typically associated with wildfires, which occur randomly and with little to no warning. It is challenging to execute a successful exposure and health study in this setting, and often difficult or impossible to repeat the study (in order to validate initial findings), or to draw direct comparisons with other studies. A few successful field studies using biomarkers have been undertaken in highly exposed populations in the developing world (e.g., Kato et al. 2004; Clarke et al. 2007), and in occupationally exposed wildland firefighters in training or conducting prescribed burn activities (e.g., Hinwood et al. 2008; Dunn et al. 2005; Neitzel et al. 2008).

Much of the recent work in evaluation of wood-smoke biomarkers has used highly sensitive and specific analytical techniques combining chromatography and mass spectrometry. This approach is appropriate for biomarker development, but the expense of these assays will limit their application in large population studies. Development of inexpensive dipstick-style immunoassays or chemical sensors (similar to a home pregnancy test) would facilitate utilization of wood-smoke biomonitoring in large epidemiology studies. The same technology could be implemented in portable multi-analyte sensor arrays, enabling inexpensive determination of a suite of wood-smoke exposure and health effect biomarkers.

Conclusions

Obtaining reliable estimates of individual or community-level exposures to wood smoke using traditional methods such as questionnaires or environmental monitoring has proven to be challenging. As a consequence there is widespread interest in using a biomarker to obtain measurements of wood-smoke exposure for use in epidemiological studies. A significant amount of progress has been made in this direction, with several groups actively engaged in evaluating the suitability of a variety of putative biomarkers of wood-smoke exposure. A number of recent studies have successfully demonstrated strong associations between biomarker levels and wood-smoke exposure, albeit in circumstances where the wood-smoke exposures were relatively high. However, much work remains before these markers can be used routinely as an exposure assessment tool. Based on the evidence to date, none of the putatative biomarkers are uniquely associated with wood-smoke exposures. As a consequence, exposure from non-wood-smoke combustion sources and through the diet limits the sensitivity and specificity of these biomarkers. In the case of urinary methoxyphenols, PAH metabolites, and carboxyhemoglobin, the markers may well have a role in assessment of wood-smoke exposures in high-exposure situations (e.g., occupational or developing-world exposures), but it seems unlikely that these specific biomarkers will be useful for monitoring population exposures to wood-smoke levels below about 100 $\mu g/m^3$ $PM_{2.5}$.

It should also be emphasized that wood-smoke exposures are encountered in a variety of situations: occupational and environmental; acute and chronic; and industrialized nations and less developed countries. The wood-smoke composition and the presence of confounding sources for specific wood-smoke biomarkers will differ for each exposure scenario. A single biomarker is unlikely to be suitable for all situations, and we will likely find that different biomarkers or biomarker combinations are effective, dependent upon the exposure scenario.

In the end, biomonitoring of wood-smoke exposures should be viewed not as a panacea, but as simply another exposure assessment tool that is best used in combination with other exposure assessment methods such as questionnaires, environmental measurements, geographic information systems (GIS) models, and land-use regression models.

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References

Burgess, J. L., Nanson, C. J., Bolstad-Johnson, D. M., Gerkin, R., Hysong, T. A., Lantz, R. C., Sherrill, D. L., Crutchfield, C. D., Quan, S. F., Bernard, A. M., and Witten, M. L. 2001. Adverse respiratory effects following overhaul in firefighters. J. Occup. Environ. Med. 43(5):467–73.

Caux, C., O'Brien, C., and Viau, C. 2002. Determination of firefighter exposure to polycyclic aromatic hydrocarbons and benzene during fire fighting using measurement of biological indicators. Appl. Occup. Environ. Hyg. 17(5): 379–386.

Chuang, J. C., Callahan, P. J., Lyu, C. W., and Wilson, N. K. 1999. Polycyclic aromatic hydrocarbon exposures of children in low-income families. J. Expos. Anal. Environ. Epidemiol. 9(2): 85–98.

Clarke, M., Paulsen, M., Canuz, E., Smith, K. R., and Simpson, C. D. 2007. Urinary methoxyphenol biomarkers and woodsmoke exposure: Comparisons in rural Guatemala with personal CO and kitchen CO, levoglucosan, and $PM_{2.5}$. Environ. Sci. Technol. 41(10): 3481–3487.

Cone, D. C., MacMillan, D. S., Van Gelder, C., Brown, D. J., Weir, S. D., and Bogucki, S. 2005. Noninvasive fireground assessment of carboxyhemoglobin levels in firefighters. Prehospital Emergency Care 9: 8–13.

Dills, R. L., Paulsen, M., Ahmad, J., Kalman, D. A., Elias, F. N., and Simpson, C. D. 2006. Evaluation of urinary methoxyphenols as biomarkers of woodsmoke exposure. Environ. Sci. Technol. 40(7): 2163–2170.

Dills, R. L., Zhu, X., and Kalman, D. A. 2001. Measurement of urinary methoxyphenols and their use for biological monitoring of wood smoke exposure. Environ. Res. 85(2): 145–158.

Dunn, K. H., Devaux, I.,Stock, A.,Mott, J., and Naeher, L. P. 2005. Evaluation of exposure to carbon monoxide during prescribed forest burns. Presentation at the American Industrial Hygiene Conference and Exposition, Atlanta, GA. May, 2005.

Feunekes, F. D., Jongeneelen, F. J., van der Laan, H., and Schoonhof, F. H. 1997. Uptake of polycyclic aromatic hydrocarbons among trainers in a fire-fighting training facility. Am. Ind. Hyg. Assoc. J. 58(1): 23–28.

Hinwood, A., Trout, M., Meurby, J., Barton, C., and Symons, R. 2008. Assessing urinary levoglucosan and methoxyphenols as biomarkers for use in woodsmoke exposure studies. Sci. Total Environ. 402:139–146.

Istvan, J. A., and Cunningham, T. W. 1992. Smoking rate, carboxyhemoglobin and body mass in the second National Health and Nutritional Examination Survey (NHANES II). J. Behav. Med. 15(6): 559–572.

Kato, M., Loomis, D., Brooks, L. M., Gattas, G. F., Gomes, L., Carvalho, A. B., Rego, M. A., and DeMarini, D. M. 2004. Urinary biomarkers in charcoal workers exposed to wood smoke in Bahia State, Brazil. Cancer Epidemiol. Biomarkers Prev.13(6):1005–1012.

Liou, S. H., Jacobsen-Kram, D., Poirier, M. C., Nguyen, D., Strickland, P. T., and Tockman, M. S. 1989. Biological monitoring of fire fighters: Sister chromatid exchange and polycyclic aromatic hydrocarbon–DNA adducts in peripheral blood cells. Cancer Res. 49(17): 4929–4935.

Metcalf, S. W., and Orloff, K. G. 2004. Biomarkers of exposure in community settings. J. Toxicol. Environ. Health A 67(8–9):715–726

Migliaccio, C. T., Bergauff, M. A., Palmer, C. P., Jessop, F. Noonan, C. W.and Ward, T. 2009. Urinary levoglucosan as a biomarker of woodsmoke exposure: Observations in a mouse model and in children. Environ Health Perpect. 117(1):74–79.

Moen, B. E., and Ovrebo S. 1997. Assessment of exposure to polycyclic aromatic hydrocarbons during firefighting by measurement of urinary 1-hydroxypyrene. J. Occup. Environ. Med. 39(6): 515–519.

Naeher, L. P., Brauer, M., Lipsett, M., Zelikoff, J. T., Simpson, C.D., Koenig, J. Q., and Smith, K. R. 2006. Woodsmoke health effects: A review. Inhal. Toxicol. 19: 67–106.

Needham, L.L. 2007. Biomonitoring of Human Exposure to Biomass Burning. Presentation at the International Biomass Smoke Health Effects Conference, University of Montana, August 2007. http://www.umt.edu/cehs/ibshe_presentations.htm (accessed November 4, 2008).

Neitzel, R., Naeher, L. P., Paulsen, M., Dunn, K. H., Stock, A., and Simpson, C. D. 2009. Biological monitoring of smoke exposure among wildland firefighters: A pilot study comparing urinary methoxyphenols with personal exposures to carbon monoxide, particulate matter and levoglucosan. J. Expos. Sci. Environ. Epidemiol. 19:349–358. (Published online April 30).

National Research Council (NRC). 2006. Human Biomonitoring for Envionmental Chemicals. Washington, DC: National Acadamy Press

Ratsimba, V., Fernandez, J. M. G., Defaye, J., Nigay, H., and Voilley, A. 1999. Qualitative and quantitative evaluation of mono- and disaccharides in D-fructose, D-glucose and sucrose caramels by gas-liquid chromatography-mass spectrometry: Di-D-fructose dianhydrides as tracers of caramel authenticity. J. Chrom. B A 844(1–2): 283–293.

Rothman, N., Correa-Villasenor, A., Ford, D. P., Poirier, M. C., Haas, R., Hansen, J. A., O'Toole T., and Strickland, P. T. 1993. Contribution of occupation and diet to white blood cell polycyclic aromatic hydrocarbon–DNA adducts in wildland firefighters. Cancer Epidemiol. Biomarkers Prev. 2(4): 341–347.