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Human Placenta and Markers of Heavy Metals Exposure

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In their review, Esteban-Vasallo et al. (2012) discussed the use of human placenta to evaluate biomarkers of exposure to heavy metals. They correctly concluded that the use of placental tissue specimens to assess heavy metal exposure is actually underused. Surprisingly, they did not mention the well-documented relationship between mercury released from mercury-containing dental amalgam fillings and mercury disposition in placental tissues (Clarkson and Magos 2006; Gundacker and Hengstschläger 2012; Richardson et al. 2011).

Studies have suggested an association between mercury levels in placental tissues and the observed mercury dental amalgams in women (Ask et al. 2002; Palkovicova et al. 2008; Richardson et al. 2011). Elevated placental mercury levels have been reported in dental workers who, throughout pregnancy, were exposed to mercury vapor (Hg^0) released during preparation of mercury amalgam in dental offices (Guzzi and Pigatto 2007; Wannag and Skjaeråsen 1975). As noted by Drasch et al. (1994), the mother-to-fetus transfer of mercury Hg^0 from amalgams has been reported in human autopsy samples, and elevated levels of total mercury have been observed in the brain, liver, and kidney of human fetuses; these levels have been linked to the number of maternal amalgam-restored surfaces.

Transplacental exposure to heavy metals may affect child growth and cause neurodevelopmental delays. Thus, further efforts should be made to measure and quantify maternal exposure to heavy metals in placenta to estimate environmental prenatal exposure.

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REFERENCES

Ask K, Åkesson A, Berglund M, Vahter M. 2002. Inorganic mercury and methylmercury in placentas of Swedish women. Environ Health Perspect 110:523–526.
Clarkson TW, Magos L. 2006. The toxicology of mercury and its chemical compounds. Crit Rev Toxicol 36(8):609–662.
Drasch G, Schupp I, Höfl H, Reinke R, Roider G. 1994. Mercury burden of human fetal and infant tissues. Eur J Pediatr 153:607–610.
Esteban-Vasallo MD, Aragonés N, Pollan M, López-Abente G, Perez-Gomez B. 2012. Mercury, cadmium and lead levels in human placenta: a systematic review. Environ Health Perspect 120:1369–1377.
Gundacker C, Hengstschläger M. 2012. The role of the placenta in fetal exposure to heavy metals. Wien Med Wochenschr 162:201–206.
Guzzi G, Pigatto PD. 2007. Occupational exposure to mercury from amalgams during pregnancy. Occup Environ Med 64:715–716.
Palkovicova L, Ursinyova M, Masanova V, Yu Z, Hertz-Picciotto I. 2008. Maternal amalgam dental fillings as the source of mercury exposure in developing fetus and newborn. J Expo Sci Environ Epidemiol 18:326–331.
Richardson GM, Wilson R, Allard D, Purtill C, Douma S, Gravière J. 2011. Mercury exposure and risks from dental amalgam in the US population, post-2000. Sci Total Environ 409:4257–4268.
Wannag A, Skjaeråsen J. 1975. Mercury accumulation in placenta and foetal membranes. A study of dental workers and their babies. Environ Physiol Biochem 5:348–352.

Human Placenta and Markers of Heavy Metals Exposure: Esteban-Vasallo et al. Respond

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We appreciate the interest of Pigatto et al. in our review (Esteban-Vasallo et al. 2012). We understand their concern regarding mercury amalgams; however, the purpose of our review was to summarize the available information on total mercury, cadmium, and lead levels in human placental tissue, obtained from studies that reported original quantitative data. Published evidence suggests a possible association between mercury released from mercury-containing dental amalgam fillings and levels of this metal in diverse fetal tissues (kidney, brain, and cord blood) (Drasch et al. 1994). In contrast, studies focusing on human placenta and amalgams are scarce and their results inconsistent. The only two studies included in our review that assessed a possible relationship between dental fillings and total mercury—a small study in Taiwan (46 women) (Hsu et al. 2007) and another in Jamaica (52 women) (Grant et al. 2010)—found no association. Only Ask et al. (2002)

reported higher mercury levels in mothers with a higher number of fillings, but they studied inorganic mercury and not total mercury.

None of the studies mentioned by Pigatto et al. in their letter (Clarkson and Magos 2006; Gundacker and Hengstschlager 2012; Richardson et al. 2011) includes original data, although we did identify an additional reference from those articles that might provide more data on this issue, a symposium abstract by Ursinyova et al. (2006). In this abstract, the authors described a significant correlation between the number of amalgams and placental mercury levels in 409 women; however, these findings have not yet been published in a full report that would allow us to better evaluate the results. In addition, Wannag and Skjaeråsen (1975) seemed to provide original information, but we were unable to find this paper for our review. In this context, we have to disagree with Pigatto et al.; in our opinion, the association between mercury exposure from dental amalgam fillings and levels of this metal in human placenta cannot yet be considered as well-established.

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REFERENCES

Ask K, Åkesson A, Berglund M, Vahter M. 2002. Inorganic mercury and methylmercury in placentas of Swedish women. Environ Health Perspect 110:523–526.
Clarkson TW, Magos L. 2006. The toxicology of mercury and its chemical compounds. Crit Rev Toxicol 36(8):609–662.
Drasch G, Schupp I, Höfl H, Reinke R, Roider G. 1994. Mercury burden of human fetal and infant tissues. Eur J Pediatr 153:607–610.
Esteban-Vasallo MD, Aragonés N, Pollan M, López-Abente G, Perez-Gomez B. 2012. Mercury, cadmium and lead levels in human placenta: a systematic review. Environ Health Perspect 120:1369–1377.
Grant C, Lalor G, Fletcher H, Potter T, Vutchkov M, Reid M. 2010. Elements in human placentae in Jamaica. West Indian Med J 59:479–485.
Gundacker C, Hengstschläger M. 2012. The role of the placenta in fetal exposure to heavy metals. Wien Med Wochenschr 162:201–206.
Hsu CS, Liu PL, Chien LC, Chou SY, Han BC. 2007. Mercury concentration and fish consumption in Taiwanese pregnant women. BJOG 114:81–85.
Richardson GM, Wilson R, Allard D, Purtill C, Douma S, Graviere J. 2011. Mercury exposure and risks from dental amalgam in the US population, post-2000. Sci Total Environ 409:4257–4268.

Ursinyova M, Masanova V, Palkovicova L, Wsolova L. 2006. The influence of mother's dental amalgam fillings on prenatal and postnatal exposure of children to mercury [Abstract]. Epidemiology 17:S494–S495.

Wannag A, Skjaeråsen J. 1975. Mercury accumulation in placenta and foetal membranes. A study of dental workers and their babies. Environ Physiol Biochem 5:348–352.

Airborne Particulate Matter and Acute Lung Inflammation

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In their article, Strak et al. (2012) connected real-world exposure to markers of acute lung function and inflammation. However, some points in the paper require further explanation. Strak et al. used fractional exhaled nitric oxide (FE_{NO}) as a marker of lung inflammation. Exhaled NO is produced throughout the respiratory tract and shows significant variability in source strength across the respiratory tract (Barnes et al. 2010; Kharitonov and Barnes 2001). Factors such as particle size, hygroscopicity, composition, and concentration; lung function parameters; and environmental temperature and humidity (Varghese and Gangamma 2006, 2009), which vary across experimental locations and between participants, modify particle deposition sites in the lung. These changes in the deposition site may influence the amount of NO exhaled. In their paper, Strak et al. (2012) did not discuss how these parameters influenced their conclusions. Thus, how the linear regression model they used accounts for these influences needs to be explained.

Inflammation in the lung resulting from air pollution exposure involves various cell types, such as epithelial cells in upper airways and macrophages and recruited neutrophils in the lower respiratory tract. A significant source of exhaled NO is epithelial cells in the upper airways, which are associated with eosinophilic inflammation (Barnes et al. 2010; Kharitonov and Barnes 2001). Many components of particulate matter (PM), such as endotoxin or bacteria, induce neutrophil inflammation in the lung, but the effects of these components may not be reflected in the concentration of exhaled NO. Thus, FE_{NO} measurements as a marker of inflammation could easily be misinterpreted by attributing a particular part of the total inflammatory response within the lung to air pollution. Strak et al. (2012) did not discuss such possibilities.

In their article, Strak et al. (2012) did not provide sufficient details about the NIOX MINO monitor (Aerocrine 2010) they used to measure exhaled NO concentration. I assume that NO measurement involves flow measurement and diffusion of NO to a sensor. Temperature and humidity of exhaled air or body temperature of the subjects likely interfere with these operations. Strak et al. did not describe any of these parameters or how they may interfere with NO measurement. Moreover, the absolute values of FE_{NO} observed during the experiments are not readily available. However, in the "Discussion," Strak et al. indicated that the observed variations between FE_{NO} measurements that are associated with particle number concentration (PNC) were most likely within the range of 5–15%. The technical specification of the instrument used for NO measurement has precision values of 5 ppb or 10% for concentrations > 30 ppb (Aerocrine 2010). Strak et al. used the difference between two sets of readings (preexposure and postexposure) as the input data for regression calculations. Thus, measurement error associated with the calculations could be much higher than that for a single set of measurements. Therefore, many of the observed differences in NO values were likely to fall within the error range of the instrument. Strak et al. should have discussed the propagation of error in the measurements or provided sufficient experimental data on the precision of the measurements. They should also have explained how the regression analysis is not biased by such instrument errors.

Strak et al. (2012) reported measurement of PNC with a condensation particle counter (CPC model 3007; TSI 2007), but their Table S2 did not report the accuracy or limit of detection of this instrument. CPC measurement depends on parameters such as ion concentration and particle composition, but because the measurements in the paper were from different environments, it is likely that these parameters varied significantly across the sites. Moreover, the CPC has a low sampling flow rate, and it is not clear whether this sampling rate is suitable for ambient measurement (aspiration efficiency in case of fluctuations in ambient wind velocity).

Overall, the article is an excellent attempt by Strak et al. (2012) to use noninvasive methods to understand the acute response of the respiratory system in response to air pollution exposure. However, a careful explanation of theory behind the experiments, experimental design, and limitations of measurement methods (if any) should have been discussed in the article.

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REFERENCES

Aerocrine. 2010. NIOX-MINO Technical Specifications. Available: http://aerocrine.com/Global/pdf/NIOX_MINO/EMD-000380-04_NIOX_MINO_Technical_Specifications.pdf [accessed 4 August 2012].

Barnes PJ, Dweik RA, Gelb AF, Gibson PG, George SC, Grasemann H, et al. 2010. Exhaled nitric oxide in pulmonary diseases: a comprehensive review. Chest 138:682–692.

Kharitonov SA, Barnes PJ. 2001. Exhaled markers of pulmonary disease. Am J Respir Crit Care Med 163:1693–1722.

Strak M, Janssen NA, Godri KJ, Gosens I, Mudway IS, Cassee FR, et al. 2012. Respiratory health effects of airborne particulate matter: the role of particle size, composition, and oxidative potential—the RAPTES project. Environ Health Perspect 120:1183–1189.

TSI (Trust Science Innovation). 2007. Particle Instruments; Condensation Particle Counter 3007. Available: http://www.tsi.com/Condensation-Particle-Counter-3007/#Accessories [accessed 5 August 2012]

Varghese SK, Gangamma S. 2006. Particle deposition in human respiratory tract: effect of water-soluble fraction. Aerosol Air Qual Res 6:360–379.

Varghese SK, Gangamma S. 2009. Particle deposition in human respiratory system: deposition of concentrated hydroscopic aerosols. Inhal Toxicol 2:619–630.

Airborne Particulate Matter and Acute Lung Inflammation: Strak et al. Respond

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We thank Gangamma for a number of excellent observations and would like to respond to the issues raised.

Gangamma points out that the levels of fractional exhaled nitric oxide (FE_{NO}) may be influenced by the site of particle deposition in the lung and requests further explanation on how this could affect the analysis and conclusion of our study (Strak et al. 2012). In an observational study such as ours, it is not possible to assess precise locations of particle deposition in the respiratory tract. Although variations in location of particle deposition likely introduced some noise in the FE_{NO} readings, we could not take this into account in the regression model.

Gangamma notes that many components of particulate matter (PM) can induce neutrophil inflammation in the lung; thus, focusing only on FE_{NO} may not sufficiently reflect their effects. FE_{NO} is an indicator of airway inflammation that is used fairly often in observational and experimental studies. As we stated above, in a study such as ours (Strak et al. 2012), it would be very challenging to address many possible inflammation pathways. In addition, the focus of our study was more on the components and characteristics of air pollution and associated health effects. We included other inflammatory markers (e.g., interleukin-6, neutrophils) measured both in blood and nasal lavage in our health measurements, but those were outside of the scope of our paper.

The next issue raised by Gangamma deals with the suggestion that many of the measured FE_{NO} values could be within error range of the measurement instrument; therefore, data on the precision of the measurements should be provided and explanation should be given on how it could affect the regression analysis. Measurement error is an