

## Letter to the Editor

**Mercury in dental amalgams: A great concern for clinical toxicology in developing countries?**

Amalgam as a dental filling material contains approximately 50% mercury (Hg) by weight, as well as other metals, including silver (Ag), tin (Sn), copper (Cu), and zinc (Zn) [1]. In Norway and Sweden, this type of dental filling material is banned [2,3]. In many other European countries, the current use of dental amalgam is less than 5% of dental restorations [4]. From 1 July 2018, new rules from the European Union restrict the use of dental amalgam in children under 15, and in pregnant or breast-feeding women [5]. However, the international market for dental amalgam is "still going strong". By the end of 2023, this market is expected to reach USD 500 million dollars. During 2018–2023, the market for dental amalgam is estimated to grow at around 5% annually [6].

The potential adverse human health consequences of using dental amalgams appear to be a concern for human and environmental health, particularly in many developing countries [7–9]. Fig. 1 shows the distribution of dental amalgams in the world based on recent data. The American Dental Association (ADA) has opposed a complete ban on dental amalgams [10]. The US Food and Drug Administration (FDA) has also considered the question of banning the use of Hg-containing dental materials [11,12]. Despite this, many environmental toxicology researchers still question whether the adverse human health effects of dental amalgams have fully been considered and appropriately addressed by dentists, dental laboratories and government.

The global distribution reported in Fig. 1 concludes that many developing countries still use dental amalgam. From an epidemiological point of view, many developed countries such as Japan, the United States, and Scandinavia have vastly reduced human Hg exposure over the last several decades. Unfortunately, many people in developing nations continue to experience ongoing large-scale human exposure to Hg-containing products [13].

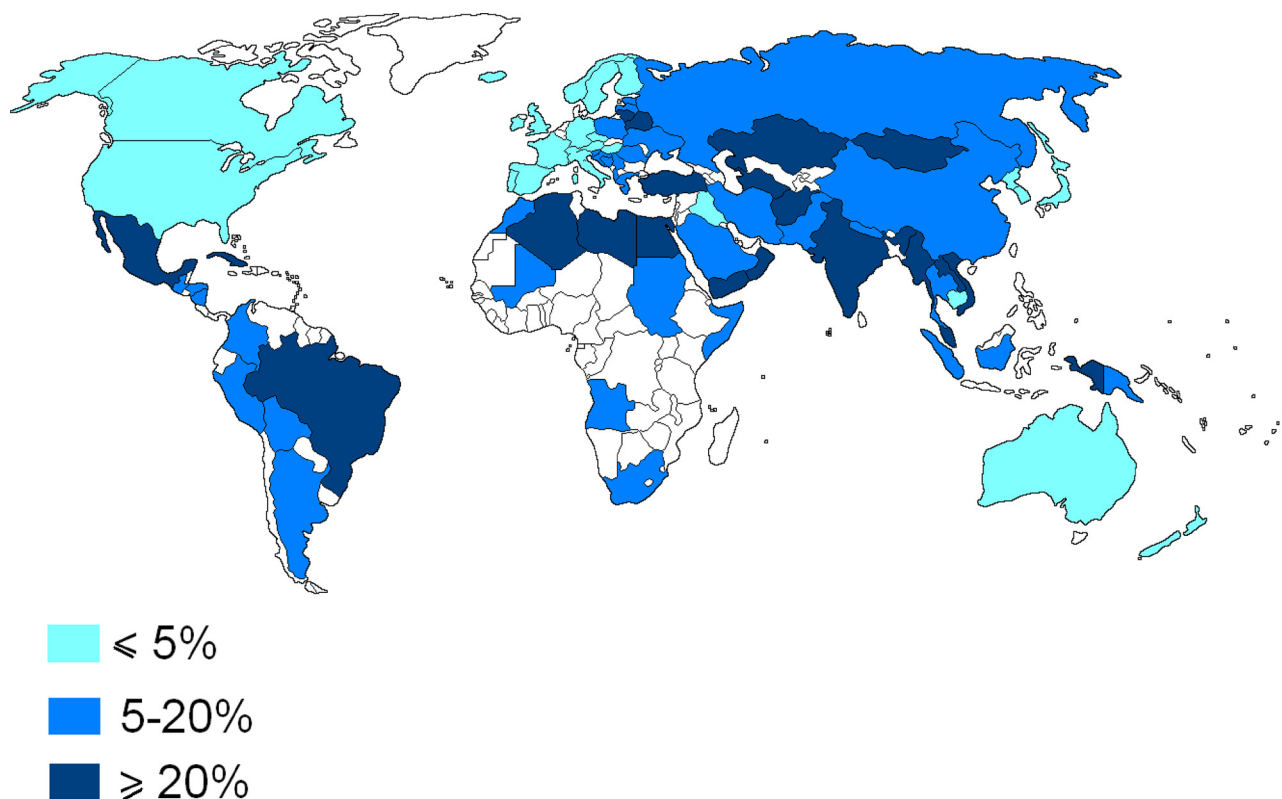
The adverse human impacts of Hg used in dental amalgams, vaccines, eye drops, traditional (folk) medicines, etc. may be difficult to assess because Hg toxicity usually arises many months or even years following low or moderate exposure because it is stored and accumulates in the body [14–16]. At present, research is being undertaken to evaluate the potential correlation between Hg release from dental

amalgams, and a number of chronic and degenerative human diseases [17,18]. Dental amalgam emits Hg vapor, which upon inhalation is rapidly absorbed into the blood, and a fraction of the absorbed Hg<sup>2+</sup> amount also penetrates into the brain [16,19]. Some investigators have failed to find a link between Hg exposure from dental amalgams and adverse human health consequences [20,21]. Indirect evidence for a link between Hg exposures from dental amalgams has been reported [22–24]. However new evidence has revealed significant increased Hg blood levels in patients receiving amalgam fillings [25]. A recent report from Turkey showing increased Hg release from dental amalgams after high-powered MRI [26]. From a biochemical point of view, Hg is known to significantly affect human biochemical processes by interfering with complex cellular redox machinery used by cells to regulate cell survival and mitochondrial function [27,28]. The production of superoxide anions in the mitochondrial matrix might promote demethylation of methyl-Hg, causing an increase of inorganic Hg inside the cells [29]. Cells with increased oxidative stress, for instance during an inflammatory immune reaction or upon toxic chemical challenge, may be more susceptible to Hg toxicity than in healthy highly controlled conditions.

As a consequence, individuals living in developing countries who have frequent chronic health conditions resulting from immune and toxic stressors may be much more susceptible to the adverse consequences of Hg exposure than those with similar health problems living in developed countries [30,31].

Oral hygiene may also exacerbate the adverse consequences of Hg exposure [32,33]. Therefore, Hg toxicology should be reviewed in countries where dental amalgam is more frequently used than in other parts of the world, and hygiene and environmental conditions should also be considered.

In conclusion, both epidemiological research and scientific reviews about the potential human adverse consequences of Hg exposure from dental amalgams should take into account socioeconomic and environmental conditions. We hope such efforts will help to reduce and prevent toxic Hg effects in human communities.



**Fig. 1.** Distribution of dental amalgams worldwide (sources Pubmed, FDI World Dental Federation, ADA documents, EC medical observational panel on Hg-pollution No 8765/R, 2016, surveys on years 2014, 2016 and 2017. (Data was unavailable for blank areas).

#### Conflict of interest

The authors declare no conflict of interest.

#### References

- [1] U.G. Bengtsson, L.D. Hylander, Increased mercury emissions from modern dental amalgams, *Biomaterials* 30 (2017) 277–283, <https://doi.org/10.1007/s10534-017-0004-3>.
- [2] Ministry of the Environment, Bans Mercury in Products, Press release, 21 December (2007) (Accessed 14 July 2018), <https://www.regjeringen.no/en/aktuelt/Bans-mercury-in-products/id495138>.
- [3] Swedish Chemicals Agency, The Swedish Chemicals Agency's Chemical Products and Biotechnological Organisms Regulations. KIFS 2008: 2 in English Consolidated Up to KIFS 2012: 3.
- [4] BIO Intelligence Service, Study on the potential for reducing mercury pollution from dental amalgam and batteries, Final Report. Directorate-General for Environment, European Commission, Brussels, 2012 (Accessed 14 July 2018), [http://ec.europa.eu/environment/chemicals/mercury/pdf/final\\_report\\_110712.pdf](http://ec.europa.eu/environment/chemicals/mercury/pdf/final_report_110712.pdf).
- [5] Regulation (EU), 2017/852 of the European Parliament and of the Council of 17 May 2017 on Mercury, and Repealing Regulation (EC) No 1102/2008, European Parliament, Brussels, 2017 (Accessed 14 July 2018), [http://www.europarl.europa.eu/meetdocs/2014\\_2019/plmrep/COMMITTEES/ENVI/DV/2017/01-12/MercuryConsolidated\\_EN.pdf](http://www.europarl.europa.eu/meetdocs/2014_2019/plmrep/COMMITTEES/ENVI/DV/2017/01-12/MercuryConsolidated_EN.pdf).
- [6] Market Research Future, Dental Amalgam Market Scope and Challenges 2018-2023 by Types and Applications with Worldwide Players as DMP Dental, Patterson Dental, DMP etc. Medgadget 16.05.2018. [www.medgadget.com/2018/05/dental-amalgam-market-scope-and-challenges-2018-2023-by-types-and-applications-with-worldwide-players-as-dmp-dental-patterson-dental-dmp-etc.html](http://www.medgadget.com/2018/05/dental-amalgam-market-scope-and-challenges-2018-2023-by-types-and-applications-with-worldwide-players-as-dmp-dental-patterson-dental-dmp-etc.html), 2018 (Accessed 14 July 2018).
- [7] B. Peretz, The Minamata convention on mercury and dental amalgam, *Refuat Hapeh Vehashinayim* 31 (2014) 60.
- [8] B.M. Faraj, H.M. Mohammad, K.M. Mohammad, The changes in dentists' perception and patient's acceptance on amalgam restoration in Kurdistan-Iraq: a questionnaire-based cross-sectional study, *J. Clin. Dent. Res.* 9 (2015) ZC22–ZC25, <https://doi.org/10.7860/JCDR/2015/13028.5790>.
- [9] M.A. Khwaja, S. Nawaz, S. Ali, Mercury exposure in the work place and human health: dental amalgam use in dentistry at dental teaching institutions and private dental clinics in selected cities of Pakistan, *Rev. Environ. Health* 31 (2016) 21–27, <https://doi.org/10.1515/reveh-2015-0058>.
- [10] D. Engel, The ADA opposes a worldwide ban on mercury products, *J. Mich. Dent. Assoc.* 93 (2011) 20.
- [11] Food and Drug Administration, HHS, Dental devices: classification of dental amalgam, reclassification of dental mercury, designation of special controls for dental amalgam, mercury, and amalgam alloy, Final rule, Fed. Regist. 74 (2009) 38685–38714.
- [12] Food and Drug Administration, HHS, Dental devices: classification of dental amalgam, reclassification of dental mercury, designation of special controls for dental amalgam, mercury, and amalgam alloy; technical amendment, Final Rule; Technical Amendment, Fed. Regist. Vol. 75 (2010), pp. 33169–33170.
- [13] K. Karita, M. Sakamoto, M. Yoshida, N. Tatsuta, K. Nakai, M. Iwai-Shimada, T. Iwata, E. Maeda, K. Yaginuma-Sakurai, H. Satoh, K. Murata, Recent epidemiological studies on methylmercury, mercury and selenium (in Japanese), *Nihon Eiseigaku Zasshi* 71 (2016) 236–251.
- [14] B.J. Ye, B.G. Kim, M.J. Jeon, S.Y. Kim, H.C. Kim, T.W. Jang, H.J. Chae, W.J. Choi, M.N. Ha, Y.S. Hong, Evaluation of mercury exposure level, clinical diagnosis and treatment for mercury intoxication, *Ann. Occup. Environ. Med.* 28 (5) (2016), <https://doi.org/10.1186/s40557-015-0086-8>.
- [15] F. Zhou, C. Feng, G. Fan, Combined exposure of low dose lead, cadmium, arsenic, and mercury in mice, *Chemosphere* 165 (2016) 564–565, <https://doi.org/10.1016/j.chemosphere.2016.08.132>.
- [16] J. Aaseth, B. Hilt, G. Bjørklund, Mercury exposure and health impacts in dental personnel, *Environ. Res.* 164 (2018) 65–69, <https://doi.org/10.1016/j.envres.2018.02.019>.
- [17] K.G. Homme, J.K. Kern, B.E. Haley, D.A. Geier, P.G. King, L.K. Sykes, M.R. Geier, New science challenges old notion that mercury dental amalgam is safe, *Biomaterials* 27 (2014) 19–24, <https://doi.org/10.1007/s10534-013-9700-9>.
- [18] J.K. Kern, D.A. Geier, G. Bjørklund, P.G. King, K.G. Homme, B.E. Haley, L.K. Sykes, M.R. Geier, Evidence supporting a link between dental amalgams and chronic illness, fatigue, depression, anxiety, and suicide, *Neuro Endocrinol. Lett.* 35 (2014) 537–552.
- [19] T.W. Clarkson, L. Magos, G.J. Myers, The toxicology of mercury—current exposures and clinical manifestations, *N. Engl. J. Med.* 349 (2003) 1731–1737, <https://doi.org/10.1056/NEJMra022471>.
- [20] D.C. Bellinger, F. Trachtenberg, L. Barregard, M. Tavares, E. Cernichiari, D. Daniel, S. McKinlay, Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial, *JAMA* 295 (2006) 1775–1783, <https://doi.org/10.1001/jama.295.15.1775>.
- [21] J.R. Mackert Jr., Randomized controlled trial demonstrates that exposure to mercury from dental amalgam does not adversely affect neurological development in children, *J. Evid. Dent. Pract.* 10 (2010) 25–29, <https://doi.org/10.1016/j.jebdp.2009.11.010>.
- [22] U. Lindh, R. Hudecek, A. Danersund, S. Eriksson, A. Lindvall, Removal of dental amalgam and other metal alloys supported by antioxidant therapy alleviates symptoms and improves quality of life in patients with amalgam-associated ill

- health, *Neuro Endocrinol. Lett.* 23 (2002) 459–482.
- [23] P. Frisk, A. Lindvall, R. Hudecek, U. Lindh, Decrease of trace elements in erythrocytes and plasma after removal of dental amalgam and other metal alloys, *Biol. Trace Elem. Res.* 113 (2006) 247–259, <https://doi.org/10.1385/BTER:113:3:247>.
- [24] P. Frisk, A. Danersund, R. Hudecek, U. Lindh, Changed clinical chemistry pattern in blood after removal of dental amalgam and other metal alloys supported by antioxidant therapy, *Biol. Trace Elem. Res.* 120 (2007) 163–170, <https://doi.org/10.1007/s12011-007-8026-2>.
- [25] L. Yin, K. Yu, S. Lin, X. Song, X. Yu, Associations of blood mercury, inorganic mercury, methyl mercury and bisphenol A with dental surface restorations in the U.S. Population, NHANES 2003–2004 and 2010–2012, *Ecotoxicol. Environ. Saf.* 134P1 (2016) 213–225, <https://doi.org/10.1016/j.ecoenv.2016.09.001>.
- [26] S. Yilmaz, M.Z. Adisen, Ex vivo mercury release from dental amalgam after 7.0-T and 1.5-T MRI, *Radiology* 288 (2018) 799–803, <https://doi.org/10.1148/radiol.2018172597>.
- [27] R.A. Bernhoft, Mercury toxicity and treatment: a review of the literature, *J. Environ. Public Health* 2012 (2012), <https://doi.org/10.1155/2012/460508>.
- [28] M. Farina, D.S. Avila, J.B. da Rocha, M. Aschner, Metals, oxidative stress and neurodegeneration: a focus on iron, manganese and mercury, *Neurochem. Int.* 62 (2013) 575–594, <https://doi.org/10.1016/j.neuint.2012.12.006>.
- [29] R.J. Mailloux, E. Yumvihoze, H.M. Chan, Superoxide produced in the matrix of mitochondria enhances methylmercury toxicity in human neuroblastoma cells, *Toxicol. Appl. Pharmacol.* 289 (2015) 371–380, <https://doi.org/10.1016/j.taap.2015.11.001>.
- [30] S.A. Farahat, L.A. Rashed, N.H. Zawilla, S.M. Farouk, Effect of occupational exposure to elemental mercury in the amalgam on thymulin hormone production among dental staff, *Toxicol. Ind. Health* 25 (2009) 159–167, <https://doi.org/10.1177/0748233709105270>.
- [31] A.M. Samir, W.M. Aref, Impact of occupational exposure to elemental mercury on some antioxidative enzymes among dental staff, *Toxicol. Ind. Health* 27 (2011) 779–786, <https://doi.org/10.1177/0748233710397420>.
- [32] M. Rathore, A. Singh, V.A. Pant, The dental amalgam toxicity fear: a myth or actuality, *Topical. Int.* 19 (2012) 81–88, <https://doi.org/10.4103/0971-6580.97191>.
- [33] H. Yilmaz, E. Tutkun, K.Ö. Demiralp, F.M. Yilmaz, V. Aliyev, T. Söylemezoğlu, Exposure to mercury among dental health workers in Turkey: correlation with amalgam work and own fillings, *Topical. Ind. Health* 31 (2015) 951–954, <https://doi.org/10.1177/0748233713484652>.

Geir Bjørklund\*

Council for Nutritional and Environmental Medicine, Mo i Rana, Norway

Ulf Lindh

Biology Education Centre, Uppsala University, Uppsala, Sweden

Jan Aaseth<sup>a,b</sup>

<sup>a</sup> Research Department, Innlandet Hospital Trust, Brumunddal, Norway

<sup>b</sup> Inland Norway University of Applied Sciences, Elverum, Norway

Joachim Mutter

Environmental Medicine, Konstanz, Germany and Paracelsus Clinica al Ronc, Castaneda, Switzerland

Salvatore Chirumbolo

Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

E-mail address: [geir.bjorklund@conem.org](mailto:geir.bjorklund@conem.org) (G. Bjørklund)

\* Corresponding author at: Council for Nutritional and Environmental Medicine, Toften 24, 8610 Mo i Rana, Norway.