



Opinion

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Children's Exposure to emerging Bisphenols other than Bisphenol A: It's time for more biomonitoring studies

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There is a great deal of evidence which has raised the need for various governmental organizations to regulate the use of bisphenol A (BPA) as plasticizer [1-4]. Indeed, BPA has shown endocrine disruptor effects, associated with a wide range of health outcomes [5,6]. Furthermore, biomonitoring investigations have frequently detected the presence of BPA in human urine, serum and breast milk; therefore, the exposure to this substance has been reported to be widespread [7-9].

Because of the endocrine disrupting potency, BPA exposure to young children is particularly harmful and for this reason the use of BPA in baby bottles and pacifiers has been banned in several countries such as United States, Canada, and Europe [10]. In addition, in 2017, BPA has been added to the list of substances of very high concern by the European Chemical Agency (ECHA) [11]. Following these actions, other bisphenols (BPs) have recently emerged as alternative to bisphenol A in the production of many consumer products. Many of these bisphenols have been identified in environmental studies, such as bisphenol AF (BPAF), bisphenol AP (BPAP), bisphenol B (BPB), bisphenol BP (BPBP), bisphenol C (BPC), bisphenol E (BPE), bisphenol F (BPF), bisphenol G (BPG), bisphenol M (BPM), bisphenol P (BPP), bisphenol PH (BPPH), bisphenol S (BPS), bisphenol TMC (BPTMC) and bisphenol Z (BPZ) [12]. Given the structural similarity between these BP analogues and bisphenol A, it is highly likely that these BPs have similar biological activity as bisphenol A also with regard to health effects [13,14]. Indeed, some toxicological studies on these BPs, such as bisphenol AF, bisphenol B, bisphenol C, bisphenol E, bisphenol

F, and bisphenol S, have shown endocrine disruption activities comparable or even greater than that of BPA [15-19]. Very few biomonitoring studies have investigated the human exposure to these bisphenol analogues [20]. In particular, considering urine samples as the best approach to monitor total BPs concentrations, only nine BPs (i.e. BPA, BPAF, BPAP, BPB, BPF, BPM, BPP, BPS, BPZ) between the most common bisphenols, have been researched in human urinary samples [12]. Among these studies, BPA, BPF and BPS resulted the most frequently detected in adults and children with BPA generally detected in 74-100% of the samples [21].

The simultaneous investigation of the most common BPs (i.e. the 14 BPs listed above) has been reported for the first time in a very recent study. This work has analyzed the presence of these BP analogues in the urine extracted from disposable diapers in young Swiss children aged between 6 and 36 months of life (n = 109) [22].

This study has shown a decrease in the detection frequency of urinary BPA compared to previous studies and an increased detection frequency of bisphenol M and bisphenol C. In particular, BPM and BPC were the most frequently detected BP analogues with a detection frequency of 25% and 23%, respectively. Meanwhile, BPA was detected only in 7% of the samples.

This change in detection frequency is probably since BPA is increasingly being replaced by its BP analogues. Indeed, more and more often different kinds of children's consumer products are claimed BPA free. On the other hand, there is no information concerning the extent to which the other BPs are actually used nor is there any legal obligation for producers of chemicals of release



this information. Furthermore, in the same study, significantly higher concentrations of BPM were detected in infants with respect to toddlers. Although biomonitoring studies suffer from the disadvantage of not being able to determine the routes of exposure, this result highlights different sources of exposure for infants and toddlers that should be further characterized.

All these findings highlight the need for extended biomonitoring studies on BP analogues exposure including larger population size. Biomonitoring is an essential tool to supervise human exposure to emerging chemical compounds [23], and the most at-risk classes such as children. Therefore, the still scarce investigations on these BP derivatives, should be enlarged to obtain statistically significant exposure data, useful as tools for the implementation of human health protection measures as has been done for bisphenol A in the past.

In conclusion, these studies should be taken as starting point for assessing human exposure to potentially harmful substances and more biomonitoring data should be carried out before embarking on new routes that could be even less safe than BPA.

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