Life and occupational environment, lifestyle and physio-pathological conditions of human populations. An epidemiological study of oxidative stress and health effects to design the best policies of primary prevention

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There is an increasing evidence that bisphenol A (BPA), widely used in the production of plastic products, might be harmful to human health due to its actions as an endocrine-disrupting chemical (EDC) and as inducer of oxidative stress (OS) . Researchers have raised concerns about the use of BPA; this has prompted industry to seek alternative chemicals or to remove BPA from their products; so there has been a gradual shift to using bisphenol analogs, like for example BPS. Bisphenols intake is estimated to be highest in newborns and children because they are thought to be sensitive and fragile to these contaminants. The PhD project deals to investigate the oxidative status in relation with several range of age and with the urinary BPA levels (STUDY 1), and at the same time, to clarify if neonatal exposure to BPA and BPS, during pregnancy and first day of breast-feeding may cause oxidative alterations (STUDY 2).

STUDY 1: 223 urine samples from a population of healthy students (7-19 years old), were analyzed for cotinine as a specific metabolite of nicotine, 15F2t-IsoP as a sensitive biomarker of systemic OS status, and BPA levels. Urinary cotinine was measured by GC/MS; $15F_{2t}$-IsoP was measured with a specific ELISA Kit; finally, BPA-glucuronides were identified by HPLC; while the quantitative analyses were carried out by tandem mass spectrometry with Ion Trap equipped with an Electrospray Ionization Source (ESI). The result of piecewise linear robust regression shows a break point at 1.79 (95%CI: 1.56 - 2.02; $p < 0.001$) of the effect of BPA on 15F2t –IsoP; thus, Isoprostane concentration increases exponentially (more than threefold each one log unit of BPA), when BPA concentration overcomes the break point. MLR analysis shows a positive effect of log-cotinine concentration on log 15F2t-IsoP. In particular, a 12% increment of 15F2t-IsoP is observed for each one-unit-increment of log-cotinine. Furthermore, the result of the relationship between log (ng15F2t - IsoP/mg CREA) and age shows a significant decrease (p=0.026) between infancy (7 -10 year old) and the beginning of adolescence (11 – 13) and then a new increase after 15 years of age.

STUDY 2: 170 urine and breast milk samples from phisyological and patological (diabetes, hypertension and thyroid disease) mothers hospitalized at the Universitary Unit of Neonatology of the Sant'Anna Hospital, and the corresponding 170 babies' urines were collected for the quantification of 15F2t –IsoP, Cotinine (but only on mother's samples), total (glucoronidate + free) BPA and BPS. $15F_{2t}$-IsoP was quantified by ELISA technique previously described; urinary cotinine was measured by ELISA Kit according to manufacturer's instructions.
Considered that the epidemiological sample is constituted also of newborns with lower concentrations of these contaminants than adults, the identification of urine and breast milk samples were carried out by using UPLC able to detect a very few amounts of bisphenols and equipped with a low-pH resistant reverse phase column. Finally, the quantitative analysis were carried out by tandem mass spectrometry analyzed with a Qtrap equipped with an Electrospray Ionization Source (ESI). At the moment, the setting up of the extraction/quantification method and the analysis are finished, while the statistical analysis are still under processing.

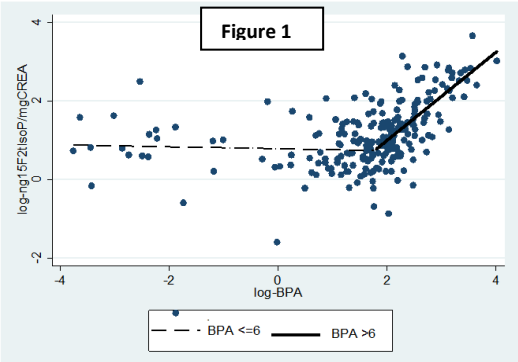

Figure 1. Piecewise linear robust or "hockey stick" regression shows a break point at 1.79 (95%CI: 1.56 - 2.02).

Figure 2. Plot of the relation between log 15F2t –IsoP and age.