

BPA and Prenatal Exposures

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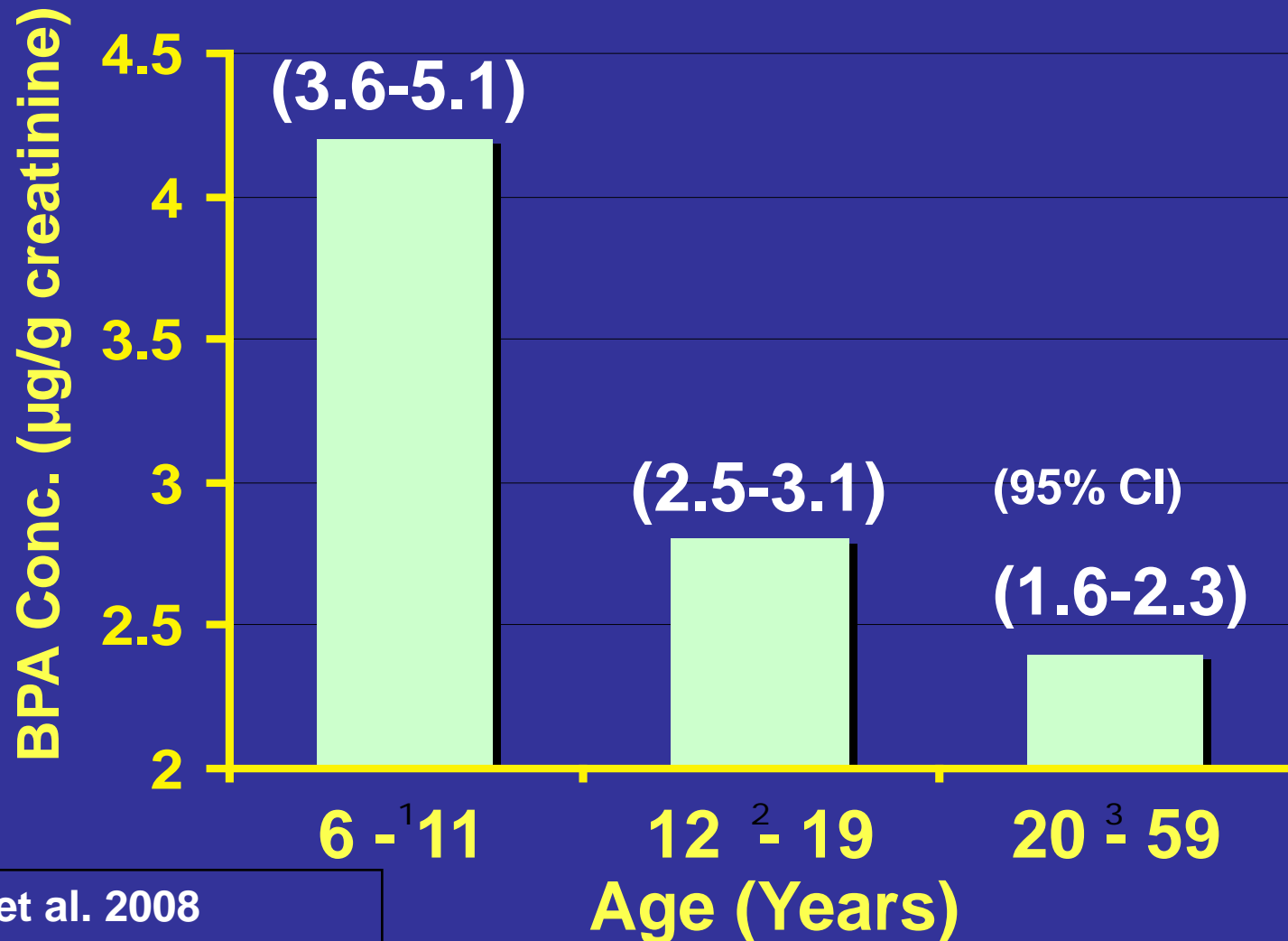
Key Points

- BPA levels in US population
- BPA metabolism and influence on toxicity
- Important determinants of fetal exposures
- BPA levels during pregnancy

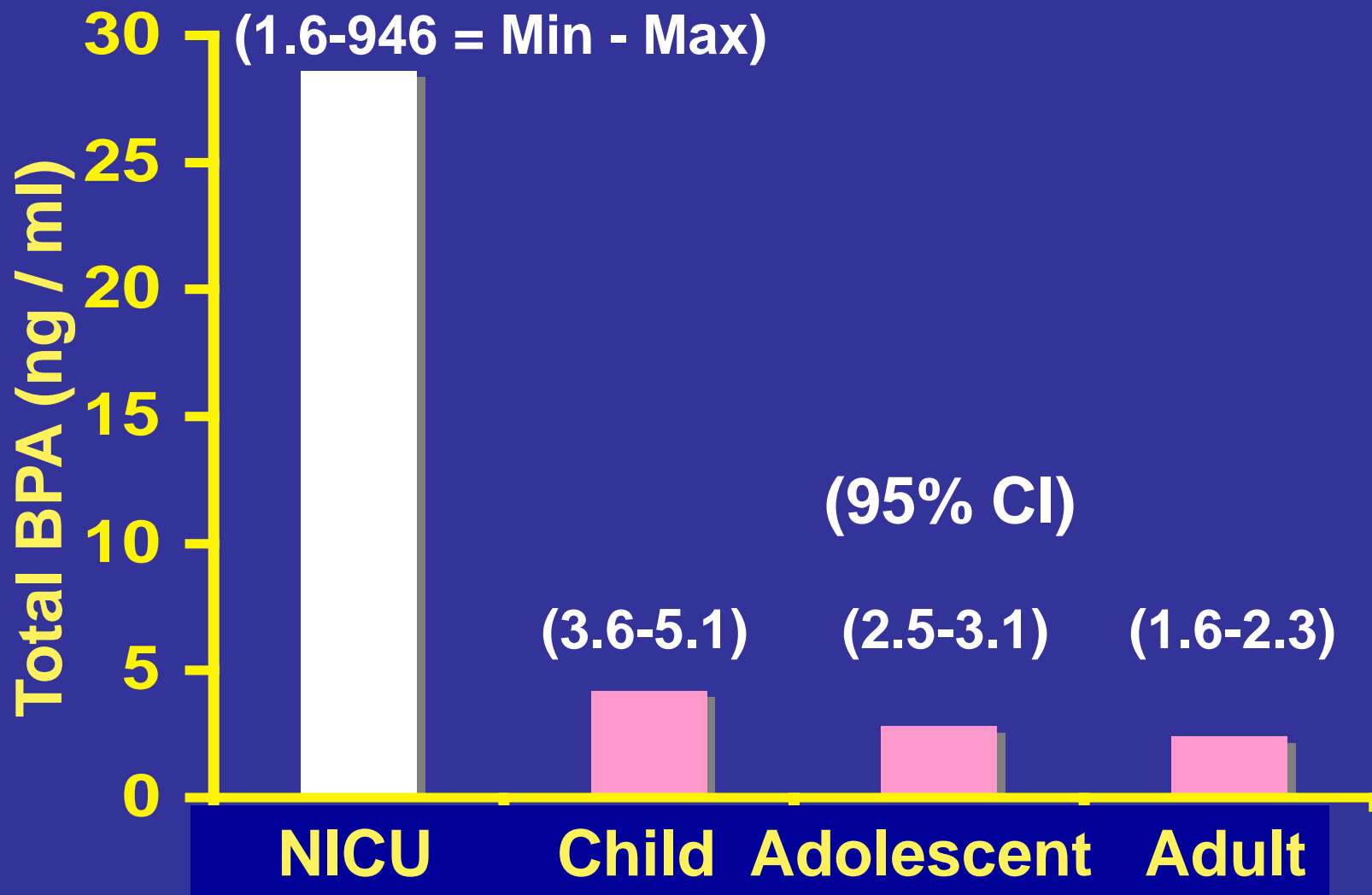
MEAN BPA CONCENTRATION IN URINE

From CDC NHANES 2003-2004

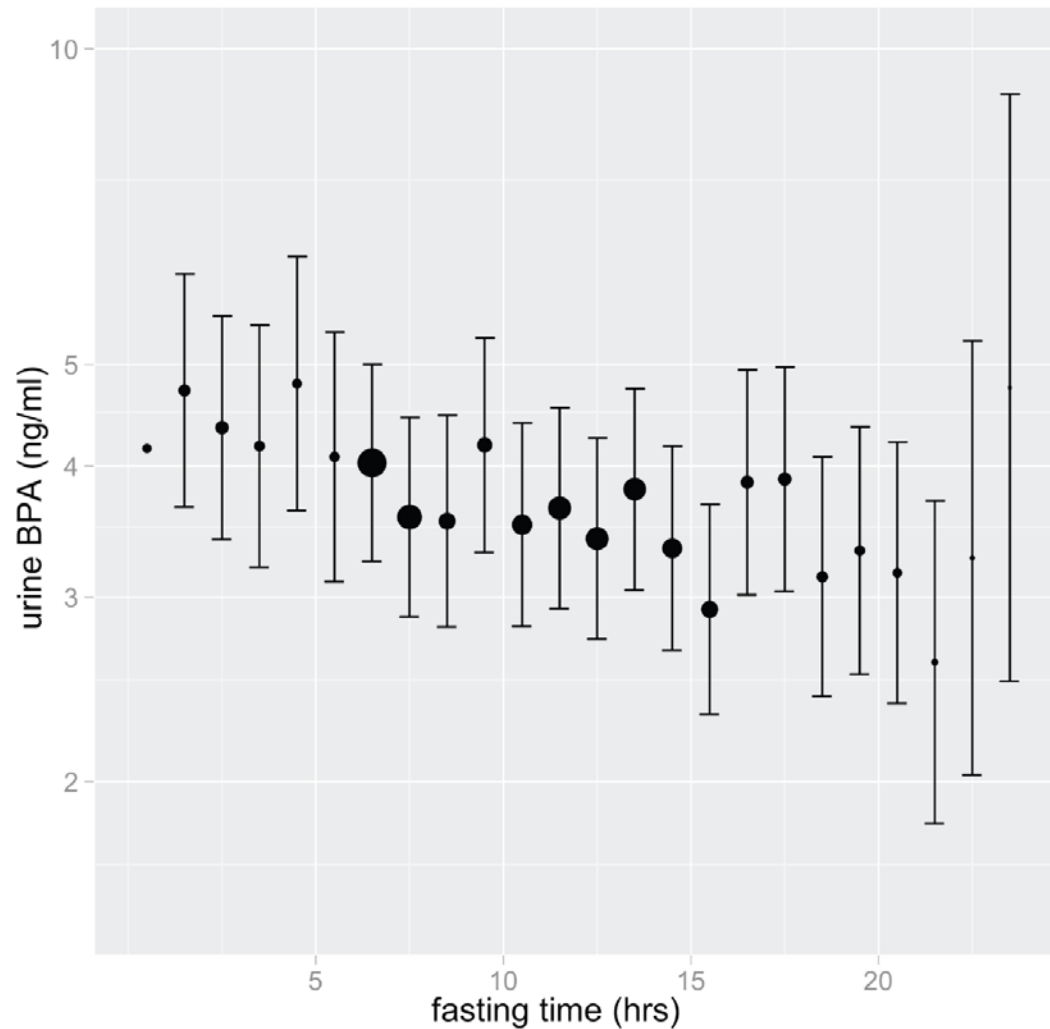
n=2,514, 93% of population with detectable BPA



BPA IN URINE OF PREMATURE INFANTS, CHILDREN, ADOLESCENTS AND ADULTS (CDC)



Adjusted urine BPA level vs. fasting time



Stahlhut
RW 2009
EHP

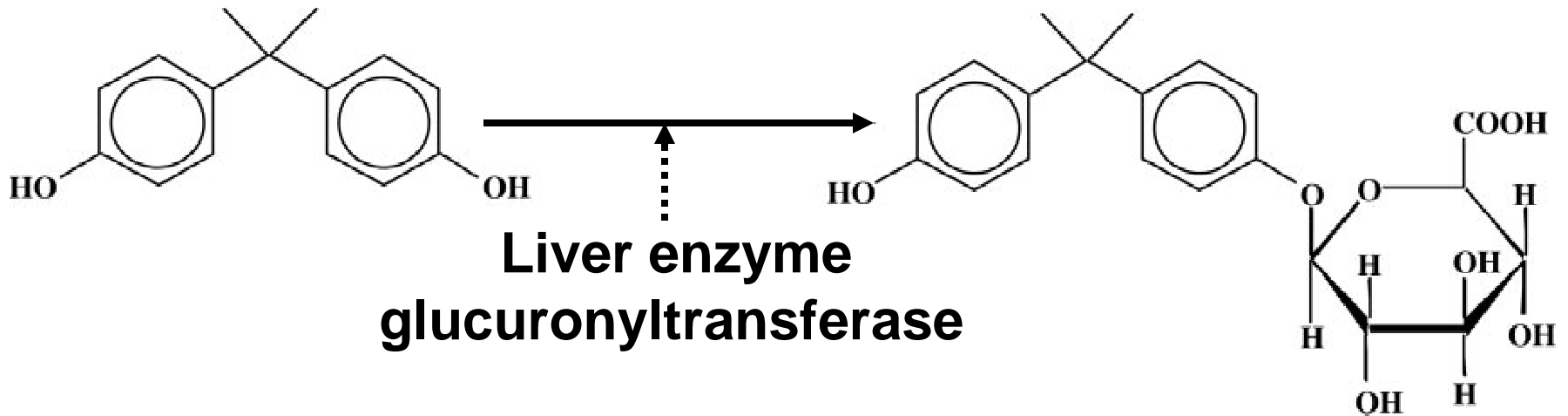
Important determinants of fetal exposure

- Placental transfer
 - Animal studies show BPA is rapidly transported through the placenta and accumulates in the placenta and the fetus, such that levels can surpass maternal levels shortly after dosage
 - Zalko, D., 2003; Welshons, W.V., 2006; *NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of Bisphenol A*. 2007.
- UGT capacity to conjugate BPA
 - Metabolic transformation of BPA via glucuronidation is anticipated to be substantially reduced in the undeveloped fetal liver due to limited or absent UGT activity (Ring, 1999)

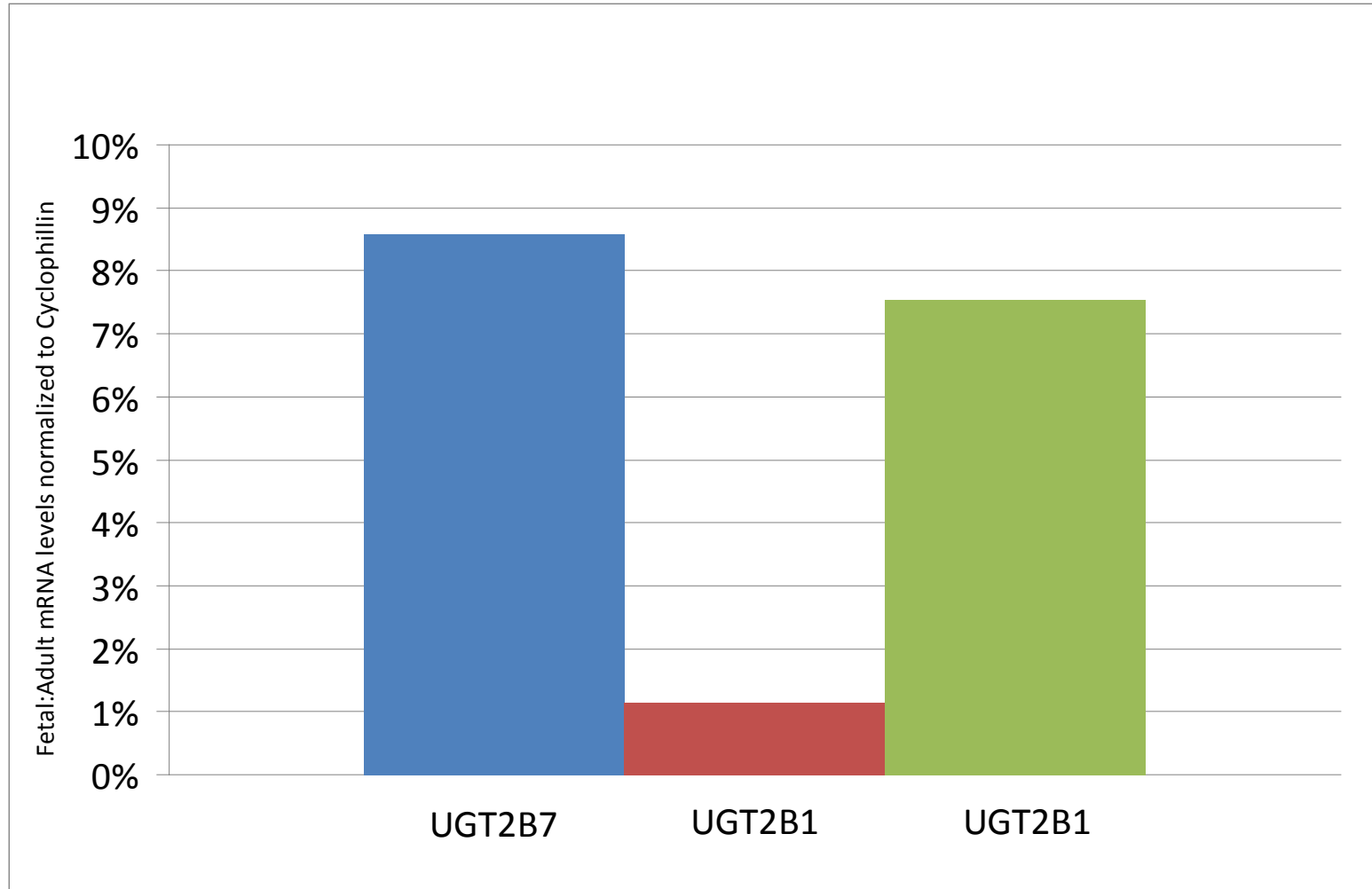
Metabolism in The Liver of Biologically Active Unconjugated BPA to Inactive Conjugated BPA (BPA Glucuronide)

Unconjugated BPA

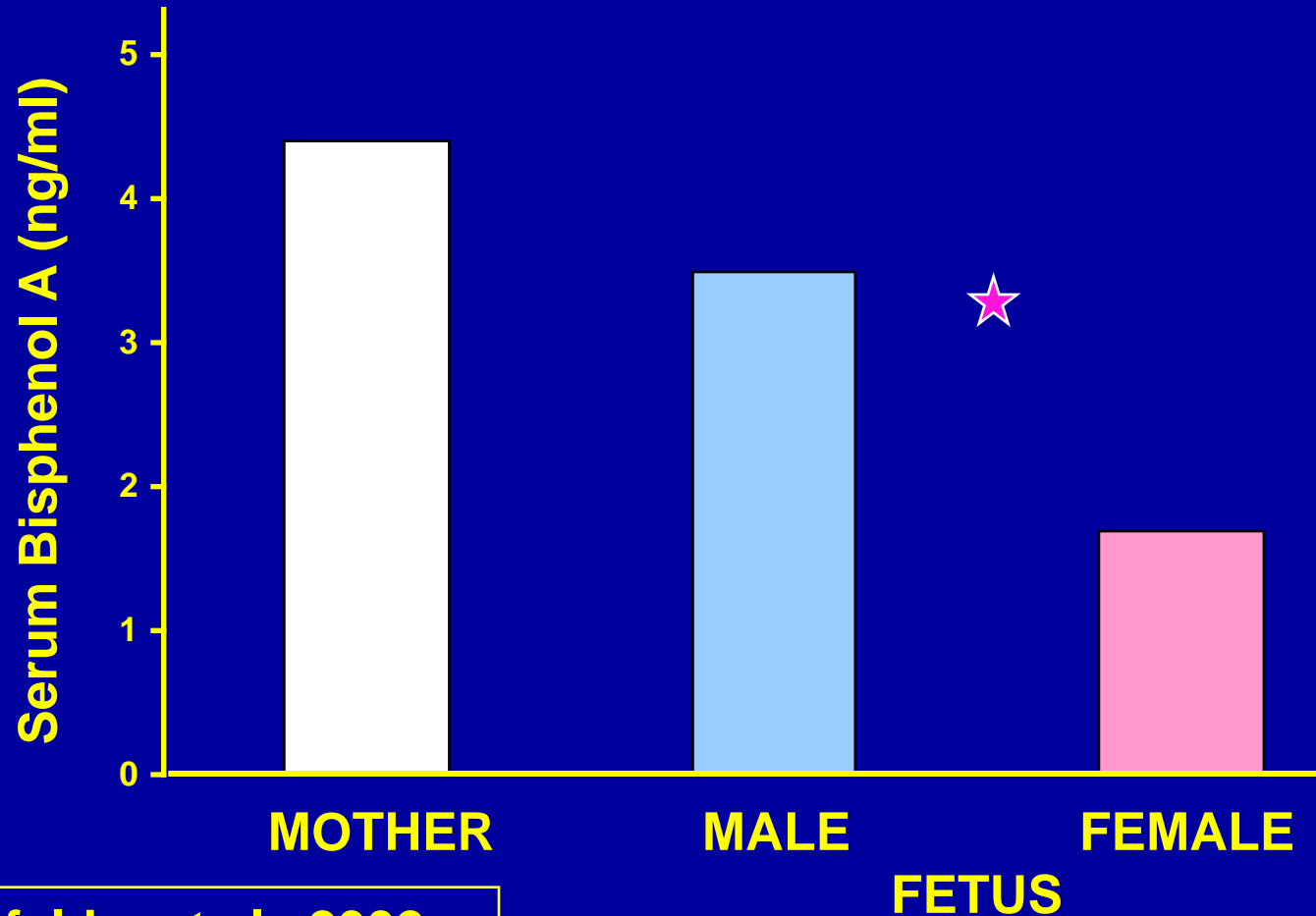
BPA Glucuronide



Ratio of Fetal to Adult levels of UDP-glucuronosyltransferase (UGT) 2B7, 2B17 and 2B15

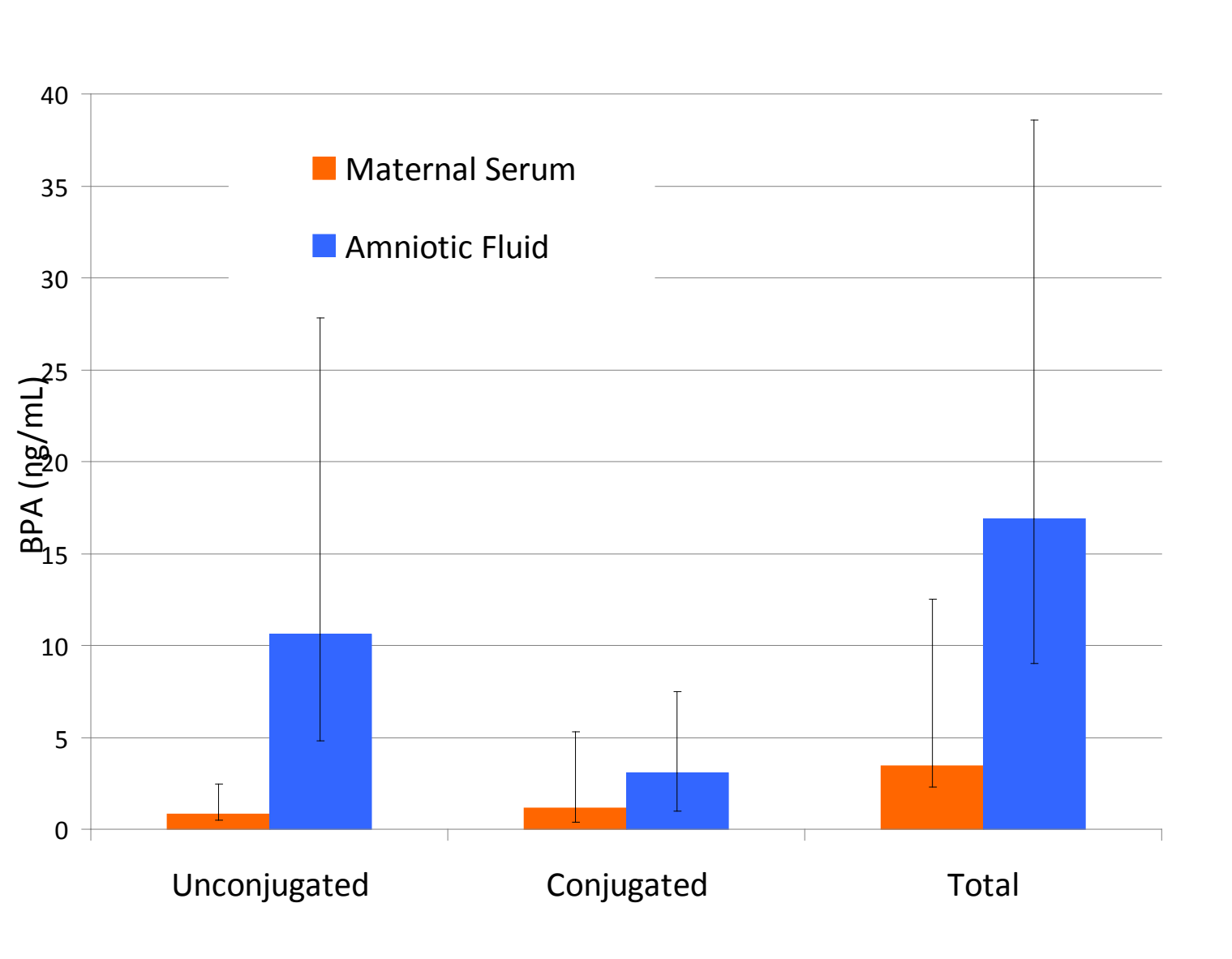


UNCONJUGATED SERUM BPA IN PREGNANT WOMEN AND FETUSES (Parts Per Billion; ppb)

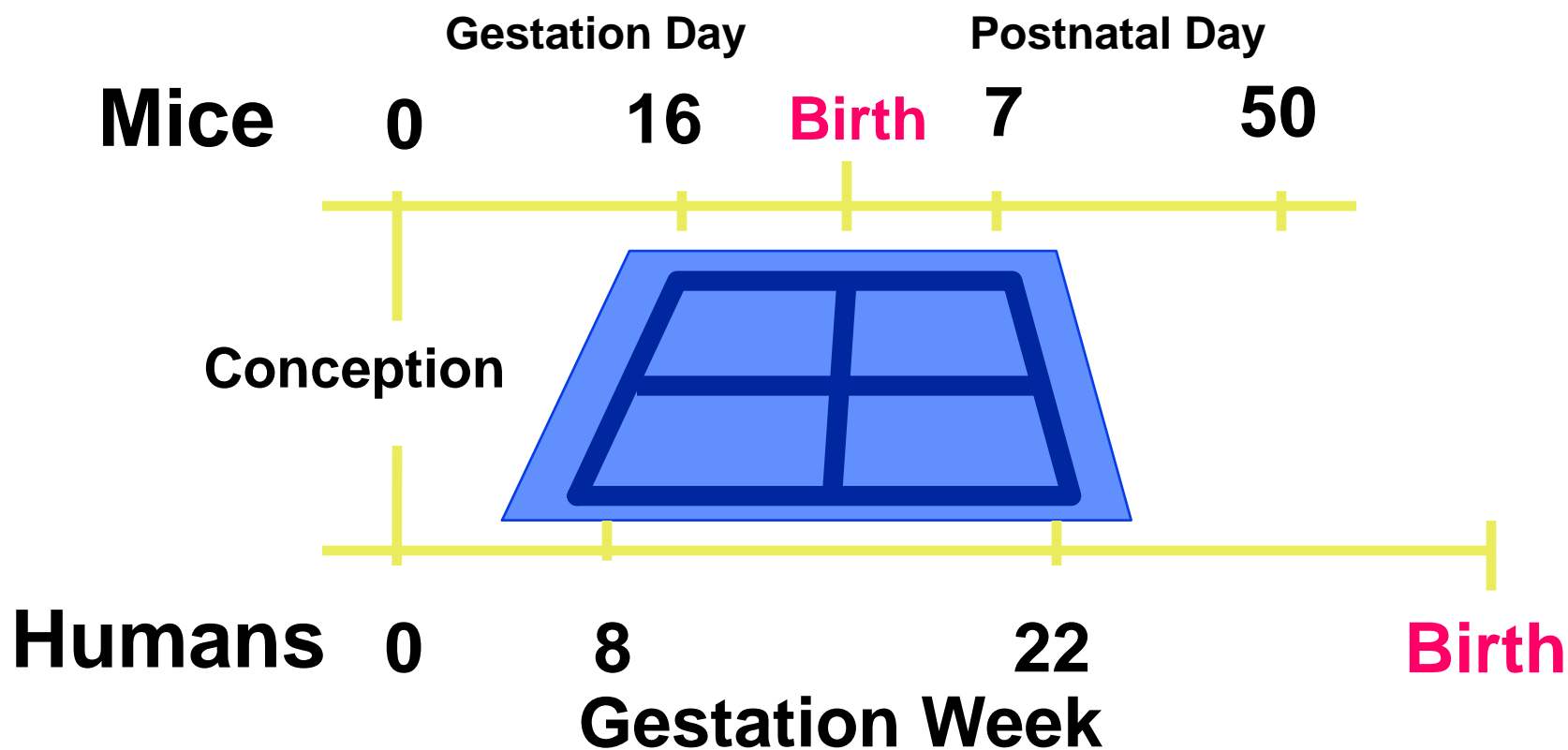


Schonfelder et al., 2002
Environ. Health Perspect.

Median (IQR) Unconjugated, Conjugated and Total BPA (ng/mL) in 9 Paired Maternal Serum and Amniotic Fluid Samples



Developmental Window of Vulnerability of Reproductive Organs to Estrogenic Chemicals in Humans and Mice



Conclusions

- BPA is present in almost everyone in the US
- BPA can cross the placenta
- The fetus has limited capacity to conjugate BPA
- The fetus is exposed to unconjugated BPA