highest exposure of the fetus to be determined. However, as PCB concentrations in the mother do not vary to a marked extent within a time frame of some months, this cannot be the reason for the increase. One should then assume either an increased penetration to the fetus during late pregnancy, or disappearance of the chemicals from meconium over time.

It is a pity that the authors[15] did not measure fat content of the meconium samples in order to be able to express the lipid soluble chemicals on a lipid basis. This would help the reader to compare the concentrations with previous studies on maternal concentrations of the same chemicals. In a very limited study, cord blood concentrations of dioxins were in the same range as those in meconium when both were expressed per lipid.[7] Current information on fetal or neonatal concentrations of persistent environmental chemicals is very patchy, because for ethical and technical reasons samples are not easy to obtain. Therefore all efforts to find novel tools for this research are valuable. After careful validation studies, meconium might be another tool to help environmental health researchers solve these overwhelmingly difficult issues on children's health and wellbeing.

Arch Dis Child 2006;**91**:627–628.
doi: 10.1136/adc.2006.095059

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Competing interests: none

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Environmental pollution

Meconium analysis to detect fetal exposure to neurotoxicants

E M Ostrea Jr, D M Bielawski, N C Posecion Jr

Second perspective on the paper by Ortega García *et al* (see page 642)

An accurate detection of fetal exposure to drugs and other compounds (xenobiotics) is essential for studying the true prevalence of antenatal exposure to these compounds and their possible adverse effects on the fetus and infant. The ideal matrix to analyse is one that can be obtained non-invasively and is representative of a wide period of exposure of the fetus throughout gestation. Meconium is formed by the fetus as early as the 12th week of gestation, accumulates throughout pregnancy, and is normally excreted after birth by the infant. Throughout gestation, xenobiotics and their metabolites are principally deposited in meconium either directly from bile secretion or from fetal swallowing of amniotic fluid which contains these compounds which are excreted via the fetal urine. Meconium is therefore a repository of many of the xenobiotics that the fetus is exposed to throughout pregnancy and its analysis has consequently been used for the detection of fetal exposure to illicit drugs. In addition, meconium has also been successfully analysed to detect fetal exposure to various licit drugs and over the counter medications as well as to cotinine and fatty acid ethyl esters which are indices of fetal exposure to tobacco and alcohol, respectively.[1]

Recently, meconium has also been analysed to detect fetal exposure to toxicants in the environment, specifically pesticides and heavy metals.[2] In the first published study, a cohort of newborn infants from Manila, Philippines showed the following pesticides in meconium: chlordane, chlorpyrifos, diazinon, DDT (dichlorodiphenyl trichloroethane), lindane, malathion, parathion, and pentachlorphenol. Of the heavy metals, lead, mercury, and cadmium were also detected in meconium. Other studies have subsequently reported on the presence of DDT and its metabolite, DDE (dichlorodiphenyl dichloroethylene) in meconium[3] as well as the metabolites of organophosphate.[4] Multiple classes of pesticides have also been analysed in meconium which will help in determining the interaction of these compounds in various clinical outcome studies.[5] In an article published in this issue,[6] organochlorine compounds were detected in meconium, specifically pentachlorobenzene, hexachlorobenzene, polychlorinated biphenyls, DDT, DDE, and hexachlorocyclohexane isomers. Concentrations of some of these compounds were also significantly and positively correlated with their concentrations in the infants' cord blood.

Compared to other matrices, meconium is a more sensitive matrix to analyse for neurotoxicants in the environment because of its wide window of exposure to these compounds. In an ongoing study we are conducting which compares the analysis of various matrices (maternal blood, maternal hair, infant hair, cord blood, and meconium) to detect exposure to various pesticides, preliminary results among 750 mother/infant dyads has shown a significantly higher percentage of exposure by meconium analysis.[7]

Meconium analysis has an added advantage in that exposure to the toxicants may occur only in small amounts but repeatedly over prolonged periods. Thus, the analysis of a cumulative, repository matrix (meconium) compared to an acute phase matrix (blood), may be more sensitive in detecting such types of exposure. Furthermore, meconium represents fetal tissue and is therefore a direct measure of fetal exposure to the toxicant compared to maternal blood or maternal hair. The latter are indirect measures of fetal exposure and can be influenced by the metabolism of the drug/compound by the mother as well as by factors that affect placental transfer of the compounds.

Different methods have been used to analyse neurotoxicants in meconium, although GC-MS (gas chromatography/mass spectrometry) provides the most sensitive and specific method of analysis.[5] However, strict criteria for the identity of compounds have to be used; otherwise the high specificity of the method will be compromised. Unless the molecular ions are detected in the mass spectrum, the presence of breakdown ion masses alone may not be sufficient for identity unless specific ratios of target ion to qualifiers are also required.

Whether meconium analysis can be used to determine the timing of xenobiotic exposure is a possibility that merits further investigation. Theoretically, since meconium is not normally excreted in utero, serial analysis of meconium may indicate periods of xenobiotic exposure during gestation. This concept has been explored with illicit drugs in animal and human studies. In a study of pregnant rats that were serially exposed to morphine or cocaine during gestation, the concentration of the drugs in the pups' meconium was significantly correlated to the timing, duration, and dose of cocaine or morphine that were administered to the dams.[8] Similar relationships have also been clinically reported in infants born to mothers who have used cocaine and heroin during pregnancy.[9 10] However, extrapolation of this observation to neurotoxicants, specifically for the pesticides, may be premature at the moment since the toxicants may undergo different patterns of metabolism and distribution compared to the drugs of abuse. What is therefore needed is an animal model or human circumstance that can study such a relationship.

A major limitation of meconium analysis is that meconium is a more complex and difficult matrix to analyse compared to blood or urine. Meconium analysis requires a thorough, preliminary clean up procedures (e.g. solid phase extraction) prior to any analytical assays. This is a critical step, especially in GC-MS assays, where sensitivity and specificity are greatly influenced by background noise (matrix effects). As previously mentioned, the use of GC-MS for the analysis and identification of compounds in meconium must employ strict criteria for identification since many materials in meconium may co-elute with the compounds of interest.

Overall, meconium analysis is a sensitive and powerful technique to detect fetal exposure to xenobiotics, including neurotoxicants. The latter is important because the fetal brain is most vulnerable to the adverse effects of these compound due to its rapid state of brain growth and development during gestation. Thus, the sensitive detection of exposure and the amount of exposure can be helpful in our understanding of the immediate and long term effects of these compounds on the newborn infant and developing child.

Arch Dis Child 2006;**91**:628–629.
doi: 10.1136/adc.2006.097956

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Competing interests: none declared

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Newborn screening

Newborn screening for congenital toxoplasmosis: feasible, but benefits are not established

R Gilbert, C Dezateux

Perspective on the paper by Schmidt *et al* (see page 661)

The report on the Danish newborn screening programme for congenital toxoplasmosis in this month's issue adds to evidence from similar programmes across the globe that newborn screening is feasible.[1–5] Screening for toxoplasma specific IgM antibodies in newborn dried blood spots was first offered in 1988 by the New England Neonatal Screening Program. Since then, newborn screening programmes for congenital toxoplasmosis have been established in Denmark (in 1992),[1] Poznan, Poland (in 1994),[4] Porto Alegre, Brazil (in 1995),[6] and Campos dos Goytazaces, Brazil (in 1999).[7] In addition, screening studies have been conducted for a limited period in southern Sweden (1997–98)[8] and Ireland (2005–07).[9] The estimated birth prevalence of congenital toxoplasmosis per 10 000 live births reported by these programmes ranges from 0.7 in Sweden[8] and 0.8 in Massachusetts,[3] to 7.1 in Poland,[4 10] and in Brazil, 5.4 in the