# Validation of a Screening Questionnaire for a Human Milk Bank to Determine the Presence of Illegal Drugs, Nicotine, and Caffeine

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**Objectives** To validate the health and lifestyle questionnaire answered by donors to a human milk bank with respect to the presence of illegal drugs, nicotine, and caffeine levels in donor milk.

**Study design** A total of 400 human milk samples from 63 donors were analyzed by liquid chromatography tandem mass spectrometry for the presence of 14 illegal drugs, nicotine, and caffeine. Demographics and clinical and lifestyle data (illegal drugs, tobacco, and caffeinated beverage use) were collected from the required screening questionnaire of a human milk bank. The relationship between the 2 evaluation techniques was determined.

**Results** Illegal drugs were not found in donor milk. Nicotine (46.1 ng/mL) and cotinine (138.6 ng/mL) were quantified in one milk sample from a donor who did not report tobacco use in the questionnaire (1.6% false negative). Caffeine was detected in 45.3% (181/400) of the total milk samples, with a mean concentration of 496 ± 778 ng/mL. The sensitivity and specificity of the questionnaire to detect caffeine in donor milk was 46% and 77%, respectively.

**Conclusions** The lifestyle questionnaire is reliable for the assessment of illicit drug use by donors to a human milk bank, but there are certain limitations regarding the identification of second-hand smoke exposure and the disclosure of consumption of caffeinated beverages. Data such as smoking habits of partners, type and volume of beverage or food containing caffeine, method of preparation, and time of day of consumption should be collected by the questionnaire. *(J Pediatr 2014;164:811-4)*.

Mother's own milk is the ideal choice for feeding infants during at least the first 6 months of life because of the health benefits it confers. When mother's milk is not available or is insufficient, milk from a human donor is recommended.[1] The selection of healthy and reliable donors is one of the most important aspects of human milk banks. Internationally, these centers have monitored the risk of transmission of infectious agents through donor milk by developing screening questionnaires, blood tests and, as an additional security measure, pasteurization of donor milk (62.5°C for 30 minutes) to kill viruses and potential pathogenic bacteria.[2,3]

There is less emphasis placed on determining the presence or absence of legal or illegal drugs in this biologic fluid. The only information available is provided by the donors themselves in the self-report required by the screening questionnaire that must be completed before the women are accepted as donors.

Psychoactive drugs and caffeine taken by the mother during breastfeeding are known to be secreted into breast milk.[4] The American Academy of Pediatrics recommends against breastfeeding in mothers with positive illegal drug screening and suggests avoiding the consumption of tobacco and alcohol.[1] By contrast, some experts believe that a maternal limit of 300 mg daily of caffeine might be a safe level of intake.[5] Risk assessment based on the subject's self-report by a questionnaire is widely used. However, there is no validation of the questionnaire. The objective of the present study was to validate the health and lifestyle questionnaire answered by donors with respect to the presence of illegal drugs, nicotine, and caffeine in the donor milk.

## Methods

This study was approved by the local Ethics Committee, with informed consent from all participants. The study was conducted at Human Milk Bank, Neonatology Unit, Hospital 12 de Octubre, Madrid, Spain, between February and July 2009.

Each donor who wished to participate in the study was provided with several glass containers for expressing human milk along with labels for her name and the expression date of the milk. A different container was used for each new expression. All containers were kept frozen in the donor's home and transported to the milk bank without the transporter breaking the cold chain. Subsequently,

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| LC–MS/MS | Liquid chromatography tandem mass spectrometry |

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to perform an adequate pasteurization, different containers of milk from the same donor were mixed into a pool (maximum 1 L). From each of these pools, an aliquot of 1.5 mL of human milk was stored frozen at −20°C until it was analyzed for illegal drugs, nicotine, and caffeine. The aliquots were collected in the chronological order in which they arrived at the milk bank. Consequently, each sample used in the study spans an average time period of 1 month from the beginning of the donation period. In total, 400 human milk samples were collected for analysis of illegal drugs, nicotine, and caffeine from 400 different pools.

### Health Questionnaire

A health and lifestyle questionnaire was completed by each donor participant on the first visit to the milk bank before any of her expressed milk was accepted. The following data were collected from the enrolled donors: demographic data (maternal age and birthplace), clinical data (gestational age, parity, medications or vitamin supplements) and lifestyle data (number of coffee, tea, and soft drinks per day; active smoker; illegal drug user).

Expression dates gathered from the labels of each milk container and data from the questionnaire permit classification of samples according to type: colostrum (milk from less than 7 days after delivery), intermediate milk (7-21 days after delivery), and mature milk (more than 21 days after delivery). The study included 63 donors who fulfilled the requirements of the Human Milk Bank. The exclusion criteria for rejecting a mother as donor included the use of illicit drugs, being an active smoker, and daily consumption of more than 2 caffeinated beverages per day (coffee, tea, or soft drinks).

### Biochemical Analyses

A validated, reversed-phase liquid chromatography tandem mass spectrometry (LC–MS/MS) test[6] was used to determine the concentration of illegal drugs, nicotine, and caffeine. The analysis was performed with an Alliance High Performance Liquid Chromatography system (Waters, Etten-Leur, The Netherlands) interfaced to a Micromass Quattro micro API triple quadrupole mass spectrometer (Waters Corporation, Milford, Massachusetts) equipped with an electrospray ion source.

Analytes were extracted from the human milk buffered at pH 5.5 with solid-phase extraction for substance recovery ranging from 71.1% to 86.5%. The intra- and interassay imprecision (measured as coefficient of variation) and inaccuracies (measured as % error) were always lower than 20%. The analytes and limits of detection in breast milk were as follows: 3 ng/mL for caffeine; 3 ng/mL for nicotine; 2 ng/mL for cotinine; 1.5 ng/mL for morphine; 1 ng/mL for 6-acetylmorphine and codeine; 2 ng/mL for amphetamine; 2.5 ng/mL for 3,4-methylenedioxy-methamphetamine; 1 ng/mL for methamphetamine; 1 ng/mL for benzoylecgonine and cocaine; 2 ng/mL for cocaethylene; 1 ng/mL for 1-*nor*-9-carboxy-delta-9-tetrahydrocannabinol; 1.5 ng/mL for 11-hydroxy-$\Delta^9$-tetrahydrocannabinol and delta-9-tetrahidrocarbocannabinol; 2 ng/mL for methadone; and 2.5 ng/mL for 2-ethylidene- 1,5-dimethyl-3,3-dphenylpyrrolidine. Alcohol was not analyzed.

Human milk testing has a detection window with a typical range from a few hours to 1 day after a single intake of substances such as nicotine, cotinine, caffeine, cocaine, heroin, and morphine. Others, such as cannabis or amphetamines, can be detected up to a few days or months later.[4]

### Statistical Analyses

Biochemical data were tested for normality of distribution by a Kolmogorov-Smirnov test. Caffeine concentration was expressed as the mean and 95% CI of the mean. The average number of samples per donor was expressed as the median and IQR because they were not normally distributed.

Agreement or disagreement between self-report use and LC-MS/MS results was determined by kappa coefficients.[7,8] Sensitivity and specificity values are reported with 95% CIs for illegal drugs, nicotine, and caffeine. The effect of collection date on caffeine concentration was determined by the Fisher test. Donors who delivered human milk samples for at least 2 months were included in this analysis. Caffeine levels were categorized into 4 classes: low (0 ng/mL), medium (1-165 ng/mL), high (166-625 ng/mL), and very high levels (>625 ng/mL). Differences were considered significant at $P < .05$. Statgraphics Centurion XVI version 16.1.15 (Statpoint Technologies Inc, Warrenton, Virginia) was used to perform these analyses.

## Results

The Human Milk Bank accepted milk from 64 donor mothers. Of these 64, 63 accepted to participate in the study with a mean age of 35.7 ± 4.75 years (range, 23-53). Among these donor mothers, 50 had a term delivery (after 37 weeks of gestation), and 39 were primigravida. A total of 85.7% (54/63) of the mothers were from Spain, 12.7% (8/63) were from Central and South America, and 1.6% (1/63) was from another European country. Of these donors, 52 gave samples of mature milk, 4 gave both intermediate and mature milk, 2 donors gave colostrum and intermediate milk, 4 donors gave only colostrums, and 1 donor gave colostrum, intermediate and mature milk.

The average number of samples per donor was 4 ± 13.4 (IQR, 2-6). In total, 400 milk specimens were used in the study: 16 colostrum, 19 intermediate milk, and 365 mature milk.

No illegal drugs were found, consistent with the answers given by the donors on the questionnaire because none reported taking these substances. Thus, the false-negative rates of the questionnaire for illicit drugs were 0% and the specificity of the questionnaire to detect illegal drugs was 100%.

Nicotine and its metabolite cotinine were found in one mature human milk sample. Nicotine levels were 46.1 ng/mL, and cotinine levels were 138.6 ng/mL. This positive sample belonged to a donor who had provided another 102 samples for the study which tested negative for legal and illegal drugs. No donor said she was an active smoker on the questionnaire (exclusion criteria).

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