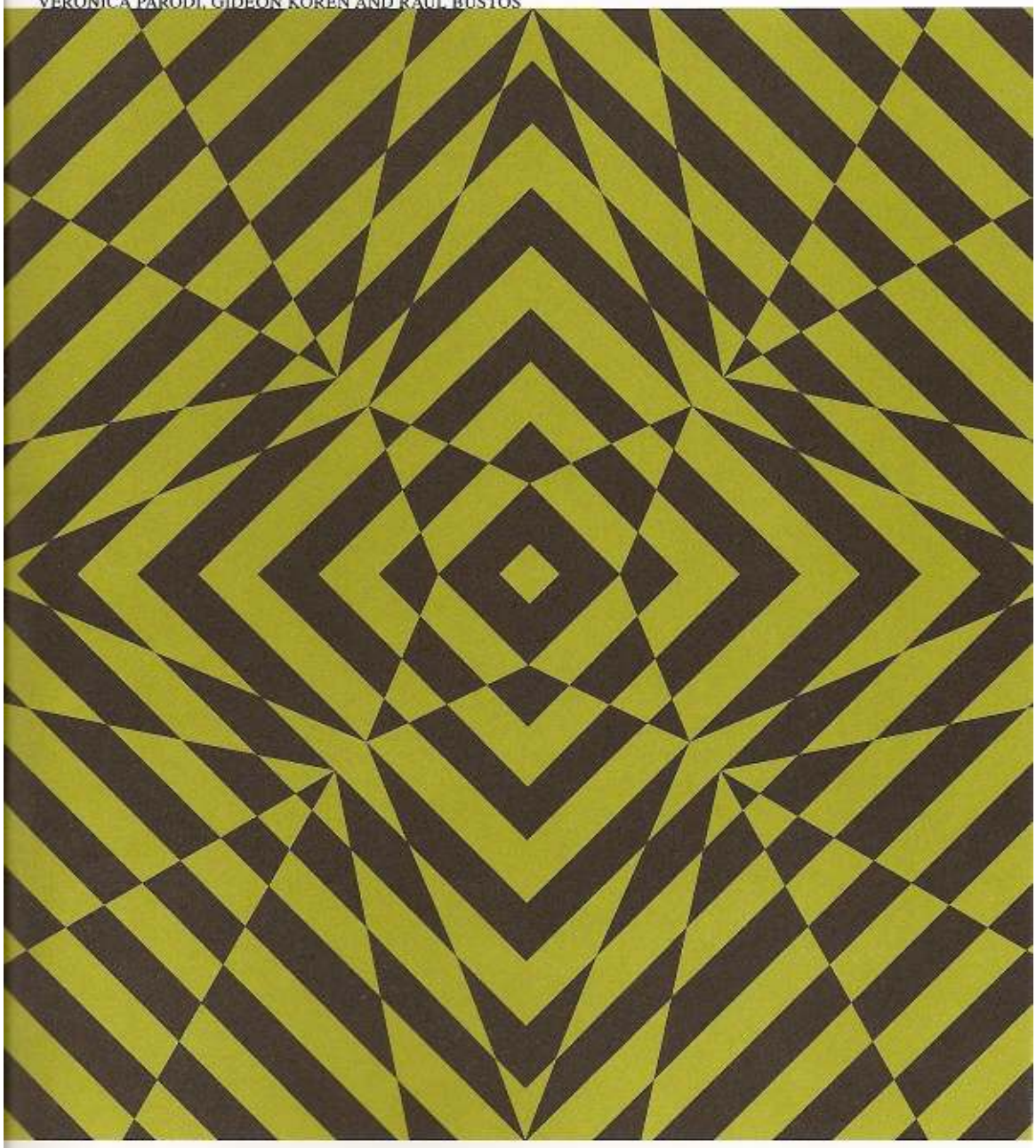
CONTEMPORARY DRUG PROBLEMS

Advances in the determination of alcohol and other drug consumption during pregnancy: A study of 900 births in Montevideo, Uruguay

BY RAQUEL MAGRI, JANINE HUTSON, HUGO MÍGUEZ, HÉCTOR SUAREZ, ADRIANA MENENDEZ, VERÓNICA PARODI, GIDEON KOREN AND RAUL BUSTOS

AN INTERDISCIPLINARY QUARTERLY



Advances in the determination of alcohol and other drug consumption during pregnancy: A study of 900 births in Montevideo, Uruguay

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A study was performed in Uruguay to estimate the prevalence of drug consumption during pregnancy. The study consisted of a survey and biological samples to validate the responses and investigate information concerning risks involved in drug consumption during pregnancy. The survey consisted of 900 face-to-face interviews performed within 48 hours after birth. Perinatal registries were taken from hospital archives. Nine hundred meconium samples were tested for alcohol, tobacco, illegal drugs, and tranquilizers. The results of the survey indicated consumption during pregnancy of the following: 41.3% tobacco, 36.8% alcohol, 16.3% tranquilizers, 68% caffeine (more than 400 mg/day), and 1.4% illegal drugs. In addition, 8.9% of the pregnancies were

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unplanned. Among the planned pregnancies, some physicians warned their patients about risks associated with tobacco (34%), alcohol (27%) and illegal drugs (7%). Meconium analysis revealed tobacco (cotinine), 51.8%; alcohol (fatty acid ethyl esters, or FAEES), 43.5%; and cocaine (base paste), 2.5%. Newborns whose mothers smoked tobacco presented statistically lower birth weights: 11% of all newborns at low birth weight, with health problems reported for 14.8%.

KEY WORDS: *Newborn, alcohol, drugs, caffeine, mate, pregnancy information.*

Background

For a long time numerous studies have shown that alcohol and other drug consumption during fetal gestation causes diverse health problems for the mother and child (American Academy of Pediatrics [AAP] Committee on Substance Abuse 1995; Centers for Disease Control [CDC] 1989; Cnattingius et al. 2000; Huestis & Choo 2002; Espinoza 1999; Kullander & Kallen 1971; Lacassie & Núñez 2000; Lemoine, Harouseau, Borteryu & Menuet 2003; Mann 2004; Sokol 1981). The effects are lifelong, not limited to the embryonic and fetal stages, and can also be observed in the placenta (Larsen & Graem 1999; Vander Veen & Fox 1982). One of the most common effects seen in newborn babies is low birth weight, which can result from preterm gestation (before 37 weeks) or restricted intrauterine growth.

According to the World Health Organization (WHO), a weight below 2,500 grams is considered to be low birth weight. Epidemiological studies show that newborn babies who weigh less than 2,500 grams at birth have 20 more chances of dying than those born weighing more. Low birth weight is also asso-

ciated with greater morbidity and less growth and development, as well as chronic diseases, as well as fetal, maternal and environmental diseases. It is related to the mother's body mass index (BMI); the altitude at which she resides; her age (very young mothers have smaller children); diseases such as acute diabetes, hypertension, syphilis, and other infectious diseases such as human immuno deficiency virus (HIV); the mother's diet and nutrition; poverty; extreme workloads; and tobacco, alcohol and caffeine, as well as other, illegal drugs. The sum of these factors can increase the negative effects on the fetus.

In its 2002 Action Plan, the United Nations (UN) established lowering the incidence of low weight in newborn babies as one of their goals in "A World for Children." This reduction is also part of the UN's Millennium Development Goals (MDG), with the aim of decreasing the number of infant deaths. Low birth weight is a major indicator for monitoring progress in achieving these objectives. More than 20 million children (15.5% of all births) are born with low birth weight, and 95.6% are in developing countries. Thus, 16% of newborns in these countries present low birth weight, whereas the figure for developed countries is less than half of this (7%).

In Uruguay, according to the most recent report of Sistema Informatico Pernatal (SIP) (Sistema Informatico Perinatal en el Uruguay 2001), the percentage of newborns presenting low birth weight is 10.1% in the public hospital sector and 6.4% in the private hospital sector, with an increase clearly evident in both. According to the Pan-American Health Organization (PAHO), one of the main ways of preventing low birth weight is basic prenatal assistance. An adolescent mother is expected to mature not only biologically and psychologically but also socially. The menarche, which in many cases now begins when a girl is 10 years old or younger, may lead to mothers who have matured but who are still physically small. This, combined with nutritional deficiencies that result in anemia, can also predispose their children to low birth weight. They

have not yet achieved maturity at a psychological and social level, and that can affect the newborn as much as the mother herself. The ideal reproductive age is considered to be between 20 and 34 years old; mothers younger than 20 years of age and those older than 34 incur social and reproductive risks.

When we want to determine the prevalence of some of the factors in low birth weight, such as drugs, surveys can be unreliable if they are based exclusively on self-declaration of consumption and if the respondent recognizes that certain responses may imply that they acted irresponsibly (Derauf, Katz & Easa 2003). Behavior concerning alcohol consumption is also linked to cultural guidelines. In the River Plate area in Uruguay and Argentina, up until 20 years ago alcohol was part of a family's diet because of a marked Mediterranean influence. However, this cultural pattern began to change into more "harmful, risky and dangerous" forms, according to Míguez (2004).

Psychoactive substance consumption as a risk factor

Alcohol consumption is the main problem, considering its popularity among Uruguay's adult population; almost 50% of the female population consumes alcohol (Junta Nacional de Drogas 2001), 32% tobacco and 5.3% illegal drugs. Fetal exposure to other substances, prescribed by medical doctors, also has its effects and must be taken into account when evaluating the results obtained. Effects vary according to maternal use, health and nutrition and the mother's socioeconomic situation.

As for the risks associated with alcohol consumption, we find that alcohol can be harmful to practically every organ and system in the body. It is psychoactive and can cause alterations in most, if not all, cerebral systems and structures. Alcohol consumption is also linked to a series of risky behaviors such as unsafe sexual relations and use of other psychoac-

tive substances. Therefore alcohol use shows a high level of co-morbidity with disorders connected with the use of other substances—nicotine dependence in particular—and with sexually transmitted diseases. Recent studies also imply that perhaps there is a link between disorders caused by alcohol and HIV/Acquired immune deficiency syndrome (AIDS).

Alcohol consumption in women during their fertile years can increase the risk of unplanned pregnancy or prenatal exposure of the fetus to alcohol and can contribute to congenital defects and growth anomalies, including fetal alcohol syndrome. There is still controversy about the levels of alcohol capable of producing fetal problems during pregnancy. However, the American Academy of Pediatrics suggests that "there is no safe figure until new studies are available to science" (AAP Committee on Substance Abuse and Committee on Children with Disabilities 2000). Alcohol has proven to be a neuroteratogen (Calvo Botella 2003; Guerri 1998c; Jones & Smith 1973a) to lower-than-needed thresholds, producing alterations in fetal growth and persistent inhibitory effects on deoxyeibonucleic acid (DNA) synthesis and irreversible neuronal loss.

Alcohol consumption among women

Alcohol and other drug consumption during gestation is also linked to the relationship between the mother and her health team and the information that is given to her. This implies an opportunity for the health team to provide accurate information. The World Health Organization has already encouraged all countries to "consider the harmful use of alcohol, particularly in youth and pregnant women" (WHO 2004).

Recent epidemiological data in Uruguay indicate a slow increase in female drug consumption and an increase in prevalence rates, and show that women start consuming drugs at younger ages than in previous years (Junta Nacional de Drogas 2001). The highest prevalence is found in the age

range that also has the higher pregnancy rate (Taylor et al. 2007)·.

The effects of alcohol on the fetus were first recognized in terms of the fetal alcohol syndrome, or FAS, a group of physical and behavioral anomalies that include prenatal and postnatal deficiencies. The syndrome is defined as including a delay in intrauterine growth (Jones et al. 1973b; Jouitteau, Massias & Sanyas 2000; Canada's Drug Strategy Division 2000), defects in the central nervous system that result in mental retardation (Guerri & Renau-Piqueras 1997), and facial defects characterized by microcephaly, a flat face, an indistinct philtrum, a thin upper lip and a short, snub nose, as well as small palpebral indentations (Gerberding, Cordero & Floyd 2005).

The FAS concept was later amplified, adding the term fetal alcohol effect (FAE) for cases in which only one of the characteristics found in FAS appeared or whenever there was a problem during pregnancy that could be related to alcohol. It is estimated that the incidence of FAE is double that of FAS. Major or minor problems such as low birth weight and mental and motor difficulties generally appear in a child that has FAE. In recent years many terms have been used to describe the effects of alcohol on the fetus, including FAE, alcohol-related birth defects (ABD) and alcohol-related development/neurological disorder (ARND).

Eventually a new term was introduced: fetal alcohol spectrum disorder (FASD). In April 2004 some United States (U.S.) organizations concerned with this topic—the Centers for Disease Control (CDC), National Institutes of Health (NIH), and Substance Abuse and Mental Health Services Administration (SAMHSA)—and a group of experts were mandated by the National Organization on Fetal Alcohol Syndrome (NOFAS) to develop a consensual definition: "FASD is a term that describes the range of effects that may occur in an individual whose mother drank alcohol during the pregnancy.

These effects may be physical, mental and/or inabilities in learning with possible life-long consequences. The term FASD has no use as a clinical diagnosis." It is clear that the term FASD is more adequate for relating the cause to the effect than FAS, at least within the context of the goals of this study.

The incidence of FASD varies from study to study, but we can confirm that in general we are facing rates from 0.08 to 5.2 per 1,000 newborns, according to a prevalence summary from different authors completed by May & Gossage (2001). According to the CDC, between 800 to 1,300 babies born each year in the U.S. present with fetal alcohol syndrome. Prenatal exposure to alcohol is an issue that brings up challenges not only in the U.S. but also in the rest of the world. An epidemiological study in a South African community (May, Brooke, Gossage et al. 2000) identified rates that were 18 to 141 times greater than those registered in the U.S. This study "confirmed that FAS is a serious public health problem." FAS rates were high in the four communities that were studied, but the rate varied from community to community. Investigators noted that the differences were probably due to "differences in the local alcoholism patterns, alcohol availability, poverty, unemployment, health problems and other risk factors."

According to other authors, this frequency oscillates between 1 to 3 per 1,000 live births and 1 in 300 in the case of the FASD. In the U.S., Barr & Streissguth (2001) suggested the importance of being able to rapidly detect a mother's consumption during pregnancy so as to limit neurological injury, as well as to rapidly detect it at birth in order to start treatment. According to other authors, such as Jouitteau in France, the frequency oscillates between 0.2 to 1 per 1,000 live births.

According to the U.S. Center for Chronic Disease Prevention, FAS prevalence rates vary greatly according to the population that is being studied and the methods used to investigate. According to Health Canada, at least one child presenting with FAS is born per day. This variation in incidence percentages is

due partly to the small proportions of the overall population studied, the variety of cases and differences in detection methods and classification. It is also important to understand that FAS can be overrepresented in studies that focus on the lower and middle-to-lower social classes, where it is commonly studied, and underrepresented in the higher social classes. FAS is also not easily detected at birth, but detection is feasible as differences in development are manifested during growth.

From another perspective it is known that approximately 30% to 50% of children are born to mothers who drink alcoholic beverages during gestation, and it has been found that in some populations 6% of gestating mothers are chronic alcoholics, which could elevate the percentage of affected newborns to 2.4%. The problem becomes even more serious if other factors are added to the equation, such as maternal dehydration, liver disease or the use of other toxic substances such as tobacco and other drugs. In Chile, Alvear, Andreani & Cortes (1988) found a 1.97% incidence in newborns, of which 70% were girls. The average age for the mothers was 33 +/–7 years, and they were usually at low socio-economic levels. Another risk factor is related to multiparous women who are more than 30 years old and present low weight gain during pregnancy. Smoking seems to increase the effects of alcohol on the fetus. Drugs can also alter the fetal response to alcohol, although interactions between alcohol and drugs during pregnancy have not been fully studied.

Currently the FAS issue garners its importance from the fact that it is the third most frequent cause of mental retardation in the world, behind trisomy and neural channel defects (if neonatal anoxia is not considered). FAS is also the only one of these three that is truly preventable and, therefore, avoidable. It is important to recognize that alcohol affects the fetus during the entire gestation period, not just in the first three months when fetal formation occurs (the embryonic phase), as was previously believed. During this first gestational phase some of the facial abnormalities associated with FAS occur. These include the characteristic long and flat philtrum, the

snub nose, the fine upper lip, the narrow palpebral indentations and the small cranial perimeter. However, neurons are affected during the entire period of gestation.

Even after birth the newborn is capable of recognizing some smells that are retained in its memory. If ethanol was present within the amniotic fluid in quantities from 50 ml (and being highly specific; Abate, Apear & Molina 2001), the newborn will remember it. During lactation a specific olfactory memory is also created, and this is affected if the mother drinks alcohol during the breastfeeding period.

Other Drugs

Tobacco There is cause for concern about smoking in pregnant Uruguayan women, as described in the SIPs during 1985–1999 (2001), with 22% of all smoking pregnant women living in the capital (compared to 14% in the rest of the country), and more commonly found in public rather than private hospitals.

Prenatal tobacco consumption is associated with low birth weight caused by nicotine's anorexigenic effect and its hypoxic effect on the placenta. It is a known risk factor for sudden death in nursing babies and respiratory diseases, as well as for second-hand smoke inhalation during the postnatal period. It is also known as a generator of neurological problems such as deficiencies in language and learning development, behavior problems, and attention deficit and hyperactivity. Tobacco consumption during pregnancy negatively affects pulmonary compliance and volume (Kullander & Kallen 1971) and is also a cause of asthma (Jaakkola & Gissler 2004). Teratogenic effects that derive from tobacco consumption include cleft palate, harelip, clubfoot, congenital heart diseases, gastroschisis, and anal imperforation.

If a mother smokes during pregnancy there is an elevated possibility that her child will be a regular smoker during youth or adulthood. If she smokes a pack a day, the risk of the child

turning into a smoker or a tobacco addict doubles (Mann 2004). The effect that tobacco may have on the genitourinary tract has been described, as well as the effects of tobacco and cocaine—chronic exposure causing laparoschisis or lateral hernia, missing sacs, craniostenosis, polymalformations, delays in growth and learning difficulties, plus all the usual effects of tobacco and alcohol.

Caffeine

Caffeine is yet another psychoactive substance that can affect the fetus. Studies show that dosages of more than 400 mg of caffeine per day can at least affect the newborn's weight (Cnattingius et al. 2000). Caffeine ingestion during pregnancy can also account for increased risk of spontaneous abortion in gestating mothers who are carrying fetuses with no anomalies in their karyotypes.

Caffeine is culturally established in our society, and this can clearly be seen when considering intake levels of coffee, tea, and soda drinks and, to a lesser degree, considering the socio-economic level of those who consume these energizing drinks. In Uruguayan culture specifically, the use of mate (a caffeine-based beverage) is widespread among the population, not only as a cultural element but also to mitigate hunger in some cases, particularly among those of a low or mid-to-low socio-economic level. For these reasons we decided to include in this study the hypothesis that caffeine consumption could lead towards at least low birth weight in newborns.

Cocaine paste and amphetamines

Cocaine, like other drugs, passes through the placenta and increases levels of dopamine and norepinephrine, causing a decrease in the blood flow to the fetus and peripheral vasoconstriction, which in turn cause hypoxia and therefore possible malformation of the organs, such as gastroschisis.

The most well-known risks associated with cocaine and cocaine-derivative consumption are premature birth, placenta detachment and fetal death. Placental and encephalic hypoxia in the fetus, maternal anorexia and vasoconstriction of the pla-

cental vessels all affect the fetus and its brain, making them a probable cause of the malformations—such as defects in the urinary and digestive tracts—that usually come with consumption of this substance. Cocaine consumption also increases the risk of gastroschisis, as well as microcephaly, by four times. Irritability, hyper-excitability and sleep alterations can also be found frequently in newborns whose mothers consume cocaine; another pattern shows that newborns become depressed (Calvo Bottella 2003).

Similar to cocaine and caffeine, amphetamines cause delays in growth, premature births and increased neonatal mortality and are associated with neurological alterations (CDC 1989; Chasnoff et al. 1985; Zuckerman et al. 1989).

Opiates

Opiates aren't frequently used in Uruguay at the present time, except in some cases where they are specifically related to medical treatment. Their use by gestating mothers is associated with spontaneous abortions, premature births and low birth weight, size and cranial perimeter for gestational age, as well as abstinence syndrome and posterior neurological alterations. Opiates have also been associated with malformations affecting the respiratory tract, but there are no conclusive studies to prove it (Rathmell, Viscomi & Ashburn 1997).

Cannabis

Cannabis consumption in gestating mothers has been associated with premature births as well as attention deficit disorders and neurological, sleep and appetite alterations in the newborn. However, it is not easy to study the effects of cannabis since it is usually consumed jointly with other drugs.

Benzodiazepines

Benzodiazepines are associated with teratogenic effects such as facial defects (cleft palate), duodenal atresia, spastic plegia with chlordiazepoxides, facial dysmorphia and defects in the central nervous system (caused by oxazepam), even though some people still debate its effects (Laegreid, Olegard, Wahlstrom & Conrad 1989; Rosenberg et al. 1983). It is also associated with abstinence syndrome in the newborn, espe-

cially when consumed during the first trimester, including hypotonic or "floppy infant" syndrome (Bergman, Rosa & Baum 1992).

Anti-depressants

The teratogenic effects of antidepressants have been described with regard to the fetus and newborn baby as pulmonary persistent hypertension as well as abstinence syndrome. Antidepressants are widely used by women in Uruguay, whether prescribed or not (Chambers et al. 2006).

Objectives

The general objective of this study was to determine the nature and magnitude of the consumption of different drugs during pregnancy, in order to contribute to prevention planning and to diminish drug effects on fetuses and newborns. The specific objectives were

- To learn about drug consumption patterns according to socio-economic context.
- To confirm consumption with biological markers in meconium samples.
- To determine the prevalence of fetal alcohol syndrome in the chosen population.
- To learn the level of information among mothers as to risks associated with drug consumption.

Methodology

Technical outline

All research involved a sample of puerperal mothers during their admittance to specific assistance centres. The admitted mother had to be in good post-birth health and could participate only upon providing signed consent to become part of this study. The study design included collection of information from three different sources: interviews, clinical records, and biological tests.

Interviews The interview consisted of a precoded survey lasting approximately 20 minutes. The subjects were women between 13 and 45 years old who had been admitted to various assistance centers. The main contact points were the assistance centers. The geographic context was Montevideo, the capital city of Uruguay. The fieldwork period was 45 days.

The first phase consisted of selection of the assistance centers (according to convenience and financial constraints), taking into account their proportional size. Two of the main assistance centers in the country's capital were selected: Pereyra Rossell Hospital, the main maternity center in the country, and the Clínicas Hospital, a university hospital. Together they account for 15% of all births in Uruguay and 33% of all in Montevideo. Since these hospitals account for 50% of births in the lower socio-economic sector, the study population overrepresents mothers belonging to low and mid-to-low socioeconomic levels, with lower than average educational levels and who lack private medical assistance services.

The second phase involved selecting individual cases within the specific time frame of this study, during which the total number of available cases was registered. Therefore, the study population consists of puerperal women admitted during a period of 45 days in the selected centers; that is, all the women admitted during that time who fulfilled the requirements previously noted in order to reach the predicted number of 900 cases. These cases are representative of the caseload during the study period, and considering the lack of seasonal variation found in a pilot study, it can be hypothesized that these cases correspond to the profile of the relevant population.

There were 1,115 cases registered—that is, births during the study period—and 900 of the mothers completed the survey. In addition, 215 cases were classified as "non-consigned"; that is, they were impossible to survey because of the mother's refusal to participate, lack of perinatal date, patient transfers, etc.

The questionnaire was created with the help of a neonatology physician as well as a doctor-psychologist with expertise in addiction cases.

Clinical records

Secondary data were obtained from SIP, the Uruguay perinatal information system. SIP is a permanent registry (SIP 2001) that includes every case that comes to the attention of the country's health system. It collects information concerning the perinatal care offered (prenatal control, growth-delay diagnosis, neonatal depression, breastfeeding, discharge), such as perinatal indicators, Apgar score, gestational age, birth weight, size, cranial perimeter, and any pathology present in the newborn.

The prenatal diagnosis included prenatal mortality, maternal mortality, and maternal pathologies. To facilitate better detection of fetal alcohol syndrome characteristics, the face of a child with FAS and a list of these characteristics were attached to the clinical history. The newborn's clinical examination was done by the residing pediatrician and was supervised by the neonatology service's second-rank pediatrician. In cases in which the newborn died after being admitted to an intensive care unit, a pathological study was undertaken on the body of the deceased and the placenta (if available) in order to better understand the situation. The director in charge of pathology services at the Pereyra Rossell Hospital supervised this study.

Biological tests

The main pathway for metabolism of ethanol in humans is oxidative metabolism. A minor pathway is non-oxidative esterification with fatty acids to fatty acid ethyl esters (FAEEs). Meconium testing for FAEEs serves as an objective biomarker of prenatal alcohol exposure and confirms the answers with a biological marker (Derauf et al. 2003). A novel biomarker for prenatal alcohol exposure is FAEEs in meconium (Bar-Oz et al. 2003; Chan, Caprara, Blenchette, Klein & Koren 2004; Moore, Jones, Lewis & Buchi 2003; Ostrea et al. 2006). FAEEs have been shown to be elevated in infants born to mothers who consume more than three drinks a month.

Also, low levels of FAEEs are found in the general population; thus a positive cut-off of 2 nmol/gram meconium is used with 100% sensitivity and 98.4% specificity. In this protocol, seven different fatty acid ethyl esters—ethyl palmitate, ethyl palmitoleate, ethyl stearate, ethyl oleate, ethyl linolate, ethyl linoleate, and ethyl arachidonate—were measured and the cumulative amount used as a biomarker of prenatal alcohol exposure during the later two-thirds of pregnancy. A positive test for FAEEs in meconium means that the mother consumed alcohol in the second and/or third trimester.

We do not know the exact amount of alcohol required to produce a positive result in a meconium sample because mothers do not tell the exact truth about how much alcohol they consumed. But we know that with fewer than three drinks a month (1–2 drinks/month) they do not have a positive test (i.e., the meconium is within the baseline for the population).

A detailed study of all possible matrixes was done and current drug detection and time-of-consumption detection technology was used so that one could differentiate between consumption during pregnancy and earlier consumption. This primary evaluation suggested that the mother's hair, fingernails and toenails, as well as the newborn's meconium, were the resources for detecting evidence of alcohol consumption in both time periods. Nails were not used because they can provide only short-term information (depending on the length of the nails); in addition they are altered by nail polish, polish remover, and other paints. Nails are useful only when considering people who do not paint them.

The mother's hair and the newborn's meconium were left to be considered as possible matrices in detecting consumption. Hair allows detection primarily of chronic drug consumption. Additionally, hair differs between blondes and brunettes, the latter being more useful for study because of better drug retention information in dark hair. Natural blondes retain only 10% to 20% of what a natural brunette retains. Dyed hair would not

be useful to this analysis, as the chemicals used for such processes modify and destroy the drug metabolites that we wish to detect.

A previous study determined that 40% of puerperal women at the Pereyra Rossell and Clínicas hospitals used dyes, henna or hair bleaches. In light of this information it was decided that the best solution was to study the newborn's meconium, since it concentrates all substances received from the mother during gestation. This makes it a good indicator for maternal drug consumption, both legal and illegal, particularly alcohol, since it attaches to the fecal matter as ethylic esters from fatty acids.

The meconium samples were collected and stored at the chemistry school of the Universidad de la Republica and then sent by courier to the Toronto Hospital for Sick Children, where Dr. Janine Hutson of the Motherisk Group performed the biological determinations. These are summarized as follows:

- 1 g meconium → liquid extraction (5:2 hexane:acetone) → solid phase extraction (amino columns)
- gas chromatography/mass spectrometry positive samples → gas chromatography/flame ionization detection.

ELISA (enzyme-linked immunosorbent assay) techniques were used to detect tobacco and other drugs. To check tobacco, one of its metabolites, cotinine, was used, as there is no nicotine present in the meconium of babies born to heavy smokers (Baranowski, Pochopien & Baranowski 1998). Cotinine is the major metabolite of nicotine in humans and can also be found in the meconium. Samples are hydrolyzed with a strong base, then cotinine forms reversible Schiff bases with amino acids; this reaction is used in ELISA analysis. The limit of quantitation is 40 ng/gram meconium. For the other drugs ELISA analysis was also used.

This study followed the international ethical guidelines that the WHO established for all epidemiological studies (CIOMS 1991). This included presenting all corresponding authoriza-

tions, ethics committee approval and the consent forms signed by the mothers.

Training

Those conducting the survey were appropriately trained by the technicians responsible for the study. Throughout the entire procedure the project team took responsibility for following all the fieldwork, submitting it to the corresponding supervisor in order to guarantee the quality of work.

Data collection

As indicated above, the survey was conducted in the selected hospitals between March 20, 2005 and June 5, 2005. Answers were obtained from 80% of the relevant population, that is, 900 interviews were obtained from 1,115 total cases. The team analyzed the patient data where interviews could not be obtained, in order to find possible differences in age and socioeconomic background and other variables between those surveyed and other eligible persons. There were no significant differences in the variables considered.

Coding and information analysis

The database was created by specialized personnel, who used the SPSS (data entry application) statistical package. The technicians associated with the project undertook the primary statistical analysis according to an analysis plan designed by the research team. The SPSS statistical package was also used for this purpose.

Analysis plan

The analysis plan was informed by the objectives of the study. It included provision of descriptive information pertaining to the study's population, testing of hypothesis using an indicator of discrimination relevance, preparation of a consumption profile of alcohol and tobacco, and use of univariable tables (frequency distribution, percentage, grouping, etc.) as well as preparation of contingency tables (variable cross-tabulations using associative statistics such as chi-squared, lambda, etc., depending on variable type).

We first developed a frequency list that was used to detect and correct possible errors, adjust bases and recode variables.

During a second stage a general exploration of the data was undertaken in which the main independent variables were crossed with the other questionnaire responses, which presented a sufficient number of cases for a bi-variable analysis.

Descriptive report

The results presented below illustrate a serious preventive health problem that requires urgent corrective measures. Even without the multivariable analysis of the risk factors examined and in the absence of an adequate predictive model, these results show a profile with high percentages of low-birth-weight infants and high prevalence of alcohol and tobacco use. Most important, health teams are not providing critical information to the population that is most in need of it.

Only one case of fetal alcohol syndrome was found. This figure is consistent with other world data, although that does not mean there are not other FASD cases that could be detected at this age.

Sample characteristics

Socio-demographic data

The analysis of principal socio-demographic characteristics of the sample indicated that they were similar to those found in the total population found in these health centers. The population is of a low to mid-to-low socio-economic level, with an educational level that is lower than for the general population in this age range: an average of seven years of formal education, just one year beyond primary education. Just 5.5% of the mothers have completed secondary school. Most are unemployed (only 11% employed; 25% unemployed, and 60% "housewife"), so that 93% are economically dependent on others. Most have an informal union with their spouse (18% married, 60% common-law union). About 19% are single; this is more common among mothers who are below the age of 21.

A low percentage of the population is currently in their first pregnancy. The mothers in the sample have an average of 2.6 previous pregnancies, a figure that is well over the popula-

tion's distribution. This fact corresponds to Uruguay's demographical dynamics, where demographic growth in general is almost below the replacement value and where families that are below the poverty line sustain this number.

The median age of the mothers is 24.0, and the average is slightly higher (25.35). There is a high percentage of young mothers—16% are 18 or younger. A young mother lacking medical assistance involves a substantial risk for a newborn, especially if the baby is born in Latin America.

Perinatal data

Fifty-three percent of the babies were male. C-Section was used in 26.2% of the births, and forceps in 3.5%. The average gestation was 38.33 weeks, the average weight at birth 3,089 grams, the average encephalic perimeter 34.14 cm, and the average length 48.17. A high percentage of newborns presented with low birth weight—11% of newborns weighed less than 2.5 kilos—and 15% of all newborns presenting health problems. As for perinatal medical appointments, almost 9% reported not ever having one, and 30% of the cases went to fewer than four appointments.

Psychoactive substance consumption

Table 1 shows the data obtained from the women's self-reports regarding psychoactive substance consumption before and during the gestation period. Caffeine consumption is high in Uruguayan mothers because of the consumption of mate, a herbal tea that is very popular and consumed daily by many members of the population. In our sample it was consumed by almost all, and for 68% of the mothers the calculated typical level was higher than 400 mg of caffeine. Mate is used to keep awake but also as a substitute for meals.

When it comes to legal drugs, tobacco presents the most frequent substance, with consumption prevalence during pregnancy of 42%. This rate does not differ significantly from the general population, which leads us to think that smoking is maintained during pregnancy in the majority of cases. There was also a higher percentage of smokers among single mothers.

TABLE 1 **Tobacco, alcohol, and other drug consumption (%) and age at first use (average)**

Substance	*Consumption at least once in lifetime*	*Age at first use*	*Consumption during pregnancy*
Alcohol	93.5	15.5	37.0
Tobacco	79.2	15.3	41.7
Tranquilizers	18.5	21.8	16.5
Marijuana	12.9	15.6	1.5
Hallucinogens	0.8	15.0	0.0
Methamphetamines	0.6	15.4	0.0
Cocaine	4.1	16.4	0.0
Stimulants	1.3	21.9	1.0
Cocaine paste	1.3	18.9	0.4
Inhalation drugs	1.0	14.7	0.0
Hashish	0.4	15.7	0.0
Opium/morphine	0.1	20.0	0.0

BASE: Total sample (n = 996), Hospital Pereyra Rossell and Hospital de Clínicas, 2005.
No use of heroin, crack, or ecstasy was reported.

As for alcohol, we observed that 37% of all women consumed alcohol during their pregnancy. Even though this percentage is lower than the proportion drinking in the same socio-economic and age segment of the general population, it is still considered to be high, especially considering the risks associated with alcohol consumption. In terms of consumption intensity, there is an important decline in the frequency of its use. In the vast majority of the cases alcohol consumption is occasional and mainly associated with festive events, according to the women's descriptions of their consumption patterns. Only 0.6% reported drinking three or more times a week, 2.5% once a week and 2.7% once every 15 days; 12.9% reported drinking once a month. About 18% reported drinking less often than once a month.

In contrast to what was found for tobacco, alcohol consumption is higher in the older age groups: the higher consumption levels

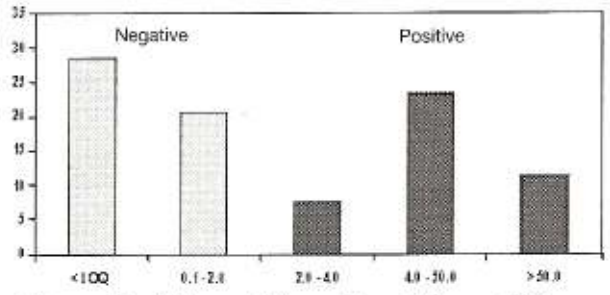
were found in mothers who are more than 30 years old. Finally, consumption of illegal drugs during pregnancy was not common, marijuana being the most prevalent. It should be noted that the reports of previous consumption are very high, surpassing regular population parameters. As with tobacco, the highest rates can be found with the youngest mothers. To summarize, the preliminary data indicate that 68% of the respondents reported consumption of some psychoactive substance during the gestation period (excluding caffeine, where the prevalence is almost 89% of the sample, with 68% over 400 mg).

Biological results

Seventy-one percent of the positive samples had a total FAEE concentration well above the positive cut-off (> 4 nmol/g) (Figures 1 and 2) and 39.9% of the samples tested positive. If we include the 8% error, assuming that the population distribution is similar to the rest of the sample, it would come to 43.5% (Table 2).

FIGURE 1

Meconium samples with cutoff of 2 nmol/g (% samples/ sum of 7 FAEEs; *n* = 817)



SOURCE: Hutson, Magri, Suarez, Míguez, Gareri & Koren, 2006

TABLE 2

FAEEs (fetal alcohol esters)

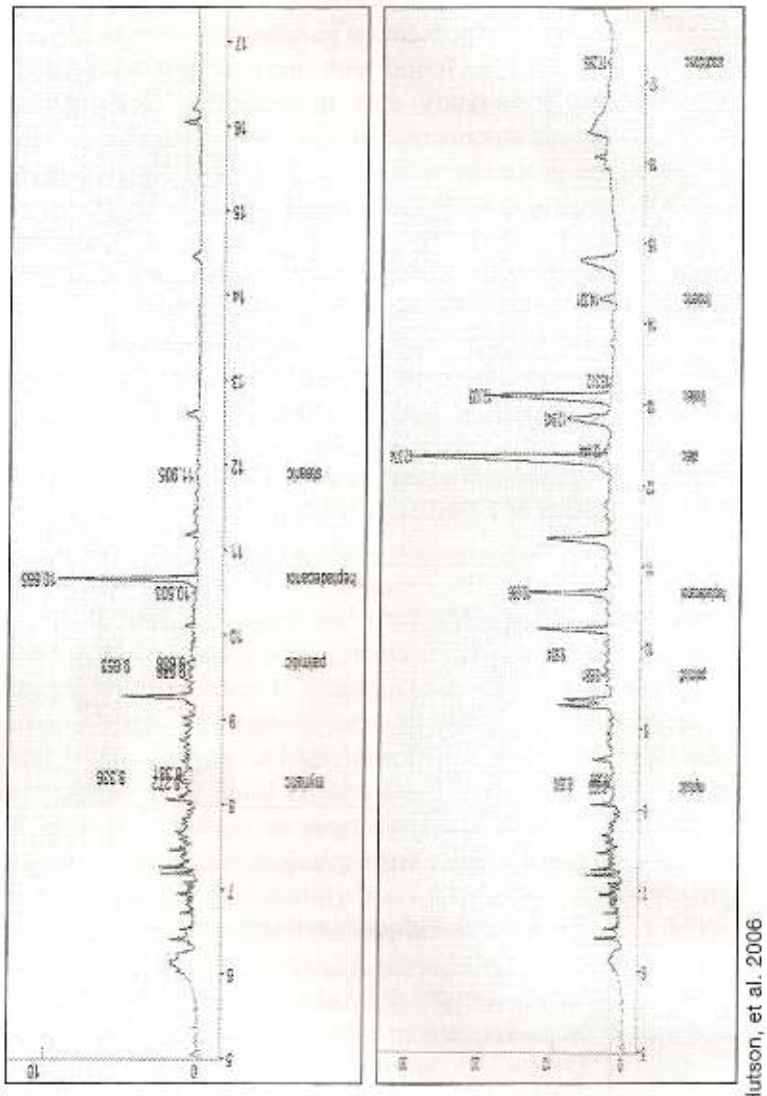
	Frequency	*Valid Percent*	*Cumulative Percent*
Valid positive	310	39.9	39.9
Negative	403	51.9	91.9
Error	63	8.1	
Total	776	99.9	100.0

MS: 224

SOURCE: Hospital Pereyra Rossell and Hospital de Clínicas, 2005

FIGURE 2

Representative GC-FID chromatograms from (A) a negative meconium sample for FAEEs; (B) a positive meconium sample containing 3 FAEEs that sum to > 2 nmol/g



SOURCE: Hutson, et al. 2006

Ethyl oleate (e18:1) was detected in all positive samples, and ethyl linoleate (e18:2), ethyl palmitate (e16) and ethyl arachidonate (e20:4) were each found in > 85% of the samples. Four or more individual FAEEs were detected in 86% of the positive samples. Low levels of FAEE were detected in 40% of the negative samples, with a mean of 0.99 nmol/g. Cotinine was very high at 51.8%, and higher than declared prevalence by respondents—41.7%. This difference could be due to underreporting or to second-hand smoke (Table 3).

With regard to other drugs, there were few positive findings for most. There were 4 positive findings for THC, 5 for cocaine and coca paste and 1 for opiates. The number of positive findings for amphetamine use was high—17 positive findings. It is possible that some positive findings here result from the use of other drugs, possibly antidepressants, so the samples will be rechecked with other techniques (see Table 4 for results for all drugs except alcohol and nicotine).

TABLE 3 **Cotinine: self-response vs. cotinine in meconium (*n* valid = 91)**

	Smoked during Pregnancy				
	Did Not Smoke	*Entire Pregnancy*	*First 3 Months*	*Last 6 Months*	*Total*
Cotinine					
Positive number	11	37	1	3	52
Negative number	34	1	4	0	39
Total number	45	38	5	3	91

Because of cost limitations, tests were done on a subsample selected by Motherisk.

TABLE 4 **All cases who consumed any drugs tested for except alcohol and cotinine**

	Frequency	*Valid Percent*	*Cumulative Percent*
Valid negative	178	87.3	87.3
positive	26	12.7	100.0
total	204	100.0	

SOURCE: Hospital Pereyra Rossell and Hospital de Clínicas, 2005. Because of cost limitations, tests were done on a subsample selected by Motherisk.

For marijuana, cocaine (or base paste), and opium derivates, there was actually a higher prevalence data from the biological analysis than from the mothers' self-reports. Only one case of FAS was found in the sample, similar to what is found in almost all other studies of FAS prevalence.

Psychoactive substance use during pregnancy and related damages

This preliminary examination of data generated some noteworthy findings with regard to alcohol consumption. Even though the general sample shows a smaller encephalic perimeter in newborns born to mothers who consumed alcohol, the differences are not statistically significant (Table 5). We also did not find significant differences with regard to length and weight of the babies when alcohol-consuming and abstaining mothers were compared. We did find, as expected, a smaller birth weight in neonates born of smoking mothers (Table 6). In cases in which the mother consumed both tobacco and alcohol during pregnancy, newborns show lower values with regard to birth weight, gestation weeks and encephalic perimeter when compared to newborns born to mothers who did not consume either substance.

TABLE 5 **Encephalic perimeter at birth and alcohol consumption in mothers during pregnancy**

	Average	*Standard Deviation*
Not consumed	34.19	2.05
Consumer	34.06	1.78
General	34.14	1.95

Base: Total sample

SOURCE: Hospital Pereyra Rossell and Hospital de Clínicas, 2005.

TABLE 6 **Birth weight and maternal smoking**

	Average	*Standard Deviation*
Non-smoking	3156.31	547.92
Smoking	3023.42	558.37
General	3101.06	555.82

Base: Total sample of mothers who used only tobacco

SOURCE: Hospital Pereyra Rossell and Hospital de Clínicas, 2005.

An interesting fact related to alcohol consumption during pregnancy is that finding of FAEEs in meconium was related to a longer gestation period in our group of mothers. Those with a positive finding averaged 38.55 weeks, and those with a negative finding averaged 38.18 weeks ($p = 0.021$). This could be related to the effect of alcohol as a tocolytic, used many years ago as a treatment for inhibiting premature labor (Fuchs, Fuchs, Poblete & Risk 2004).

According to the self-report data, 13 in every 100 women had some sort of problem or conflict regarding alcohol (Table 7). Using self-reports as an indicator, there is a higher percentage of positive answers when compared with the biological measures, although it might be noted that the self-reports are on a lifetime basis. About half of the women continued consuming alcohol during pregnancy, as is indicated by the data presented. The biggest problems with regard to alcohol can be seen in single or separated women between 19 and 25 years old who are unemployed and have a low educational level.

TABLE 7 **Dependency indicators and/or alcohol abuse**

Indicator as CAGE Item	*% over Sample Total*
Have you ever had the impression that you should drink less?	11.1
Have you ever felt annoyed over someone criticizing your drinking?	2.6
Have you ever felt guilty for your drinking habits?	3.8
Have you ever had a drink to ease your nerves first thing in the morning?	1.3
Positive answer to at least one indicator	13.5

BASE: Total sample, Hospital Pereyra Rossell and Hospital de Clínicas, 2005

Information received regarding drug consumption

This section presents data related to the information that the mothers received from their medical and health care workers regarding alcohol, tobacco and other drug consumption, as well as the risks associated with drug consumption. First, it

should be noted that almost one in every 10 pregnant women never received medical supervision during their pregnancies. From those who did, 31% did so through a midwife. When asked if their doctors had informed them or asked them about psychoactive substance consumption (legal and illegal), we found that only a low percentage of physicians warned them. For alcohol, 27.9% had been given information; 35% on smoking; and 7.8% concerning other drugs. The doctor had only asked about consumption, without advice, in 24.2% of cases for alcohol, and 27% for smoking and for drugs. Doctors were less likely to provide advice to older women. When asked about the type of information received regarding tobacco and alcohol, the mothers reported that some doctors told them they could continue their consumption as long as they reduced it.

Main emerging conclusions

From this descriptive report the following main findings may be noted. The studied population presents high percentages of low birth weight and newborn health deficits. This reflects a population with poor or no medical assistance, with a high proportion of teenage mothers who haven't reached their full physical, psychological and social potential. The findings from the study also suggest that attempts to make mothers aware of the risks of alcohol, tobacco, and other drug use during pregnancy have not succeeded. New, improved and more effective measures are needed by health teams and other sectors within the community in order to address this challenge.

Almost 7 of every 10 women declared that they consumed some sort of psychoactive substance during pregnancy. The main drugs were alcohol and tobacco. There is currently sufficient evidence to hypothesize that self-reports of consumption can be underestimated, in contrast to biological tests. This has implications for increasing awareness among mothers about the possible associations between consumption and the new-

born's health. According to self-reports, 37% of mothers indicated alcohol consumption during pregnancy, compared with 45.3% where a positive meconium alcohol test indicated alcohol consumption. This deserves further investigation. Biological test results, in our case meconium drug testing, are an important tool to validate mothers' responses.

Health teams need to receive more information on drug effects on the fetus, and this information should be an essential component of both degree and graduate curricula and prenatal medical doctor appointments, as well as being more widely disseminated to other sectors of the community. There should be an easily accessible network of rehabilitation treatments for pregnant mothers, whether ambulatory or with in-patient options. Those responsible for alcohol management and control and for alcohol sales and promotion are encouraged to compromise on trade and market agendas and also to inform the general population of the effects of alcohol on the fetus.

There are both positive and negative aspects to using a biological marker. The positive aspect is that it enhances the diagnosis and allows early treatment. It is also possible to contact the mother pre- or post-partum, initiating treatment to encourage abstinence from drugs and to provide the parents, biological or foster, with valuable information about the child. These markers also have drawbacks, as they could stigmatize the mother or the child, provoke legal problems or reduce adoptions, and there are high costs associated with follow-up for those whose health might be compromised.

There is a very low level of information and control among health personnel with regard to effects of drug use on the fetus. As noted above, most puerperal women admit to not having been informed of the risks associated with drug consumption. The study by Todd & Triunfo (2006) on risk factors and low birth weight shows that, given a range of 0 to 9 appointments, the newborn's birth weight varies by 451 grams. Our own data, which is consistent with this study, shows that new-

borns weighing less than 2,500 grams have mothers who went to an average of four prenatal appointments. This is a very significant fact and presents an important challenge when it comes to prevention efforts. Within the sample we studied, those of lower socio-economic and educational levels were particularly vulnerable. There are also high percentages of pregnancies among young, single women; in 68% of these cases pregnancy was not planned.

This challenges the utilization of available human capital in order to promote health and reduce mortality among women in this group and their babies. The findings of this study need to be taken into account in health promotion and prevention strategies and campaigns to generate policies that will reduce the use of alcohol and other drugs among women of childbearing age.

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