The International Medical e-Network devoted to
Fetal Alcohol Spectrum Disorders

NOFAS-UK
National Organisation for Fetal Alcohol Syndrome – UK
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INTRODUCTION

I have been living in the Fetal Alcohol World since I adopted my wonderful daughter in 1988.

How long have you been living in our Fetal Alcohol World? I imagine you too have seen FASD awareness increase along with FASD scepticism.

The 146 study abstracts in this issue continue to provide the evidence: Fetal Alcohol Spectrum Disorders are real, they are serious and FASD is widespread.

As the Publisher of the FETAL ALCOHOL FORUM, I have observed an increase in global FASD research. Since our first issue in 2009 we have published 996 abstracts from 29 countries. Once again, we are privileged to have original articles written for us by some of the world’s leading FASD experts.

Dr Forrester Cockburn, known to friends as ‘Coby’, has worked tirelessly to put FASD on the health agenda in Scotland. Though Dr Coburn has been trying to retire, we have persuaded him to postpone retirement for a little longer to write an article reflecting on his FASD experience in Scotland.

In this issue you will find new studies looking at FASD in correctional institutions and prison populations, new animal studies (from sheep to Japanese Rice Fish), new ‘low level’ studies and Zebra Fish with prenatally altered hearing and balance.

Fathers are finally brought into the FASD equation and further neuro-protective intervention and new DNA research is presented. Queens University continues its ground breaking eye movement work and new meconium studies look promising for early detection.

Susan Fleisher
Publisher
The table on the next page shows the FASD Studies done worldwide during the past 6 months.

NOTE: FASD studies worldwide during the past 6 months

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We always appreciate your comments and valuable feedback at info@nofas-uk.org. You can download issues of the FETAL ALCOHOL FORUM from our website: www.nofas-uk.org, or if you would like to be added to the FETAL ALCOHOL FORUM mailing list, please click here.

Susan Fleisher
Publisher

Beata Ewertowska
Editor

Vandana Alimchandani
Editor/ Technical Supervisor

Elizabeth Mitchell
Associate Editor
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I. FASD AND PROGRESS IN LAW ENFORCEMENT AND CORRECTIONAL SETTINGS

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The risk of conflict with the law is a major concern for people living with FASD. Parents, advocates and affected persons exchange stories, fears, and strategies to prevent or minimize correctional problems. At the same time, they hold little expectation that legal or correctional systems would be familiar with why FASD so often manifests in unlawful behaviors. When such cases occur, will the accused individual meet with appropriately balanced measures of justice? Thanks to recent progress in FASD-awareness in legal and correctional systems, we can now expect these systems to rise to better understand individuals with FASD.

Recently my 10-year old daughter, Lucia, faced a distressing accusation. She was in art class doing paper maché. According to her, a classmate had a cellphone out on a table against classroom rules, where it was getting splattered with the gluey mixture. Lucia also got a splatter on the phone (a small one, she says), and the classmate then accused Lucia of ruining her phone and insisted that she should buy her a new one. The accusation was frightening to my daughter and she worried about the ongoing blame on the following days at school. Nevertheless, Lucia was aware of some difficulties that her classmate lived with, and this understanding seemed to help her accept the classmate’s behavior. Fortunately, the girls have reconciled as time passed and are now friendly together.

Most of us have had an experience when we were blamed for something we did not do, or did unwittingly and without intention. These occurrences can be uncomfortable and distressing. ‘Why are you accusing me? Did I really do that? If I didn't mean to do it, why am I still in trouble?’ If a person doesn't understand why they are blamed in the first place, how are they to give a reasonable response, understandable to the accuser, who may also be angry or hurt?

Being asked to account for harm to others can be an opportunity for remorse, apology and corrective action. Yet when a person is falsely accused or could not reasonably envision or control the harm caused by their action, the harm can expand to engulf the accused person as well. For people living with FASD, this picture may be frequent and familiar – often finding themselves in trouble for something they don’t understand. And when someone with FASD faces law enforcement to account for an unlawful action, the process can involve disproportionate and devastating penalties unless there is recognition of the impact of their disability on their cognition, emotions and behavior.

In a good society, people should strive for justice, whether as the accused or in the role of judges. Our notion of justice is rooted in fairness, which in judicial processes includes treating all people equally while at the same time adapting for individual or circumstantial differences that can influence a person’s control over their action. Justice systems also seek to minimize future unlawful harms by using resources efficiently to reduce recidivism. Additionally, social justice includes supporting the needs of people in areas where they are too vulnerable to protect themselves. Pertinent to all of these facets of justice is the impaired brain functioning that is characteristic of FASD.

The brain injury that accompanies FASD can include difficulties with organized thinking, sensory
integration, mental health disorders and emotional self-regulation, and the affected individual typically lacks insight that their brain functions differently than most others. When adequate protective supports are lacking, individuals are vulnerable to feeling confused, overwhelmed, or unsafe, impairing their sense of control. While they can usually agree to or repeat a list of rules, their abilities to anticipate, plan and apply rules, and restrain impulses, can be compromised. In Streissguth and colleagues’ report of life history interviews with caretakers or informants, they found that among 253 people with Fetal Alcohol diagnoses aged 12 and above, an alarming 60% of these individuals had experienced problems with the law, and 35% had been incarcerated (1).

People with FASD can be easy targets for misplaced attributions of reasoning and intent. Stephen (last name withheld), who is the older brother of Michael who has an FASD, tells the story of when they were both involved in a traffic accident. No one was seriously hurt, but Michael continuously laughed at the scene and on the drive home. Stephen attests to feeling extremely annoyed -- until he had the insight that Michael's laughter was an expression of his own distress. I imagine how such unusual laughter could be misperceived by a police officer or in a courtroom, and how perceptions can change with better understanding.

For justice system workers, the relation between FASD and unlawful behaviors has risen to new attention. FASD is increasingly recognized by law enforcement, courts and diversion programs, jails and prisons. Though only a fraction of law and justice personnel are yet adequately FASD-aware, the trajectory is on an encouraging path. We have established a higher bar of expectations for all justice systems to rise to.

A fundamental challenge is to get a measure of the prevalence of FASD in justice systems to demonstrate the scope of the problem. In 2004, Burd and colleagues (2) published results from their survey of United States corrections facilities, investigating how many inmates were known to have FAS or alcohol-related neurodevelopmental disorder (ARND). To be sure, a majority of people affected by FASD do not receive an accurate identification that this is their primary disability. Most of them do not present “tell-tale” signals like the cluster of facial features that is present among individuals with an FAS diagnosis. Most often, they do not meet criteria for intellectual disability, and individuals are inclined to use their strengths and areas of high functioning to hide their deficits. In addition, suspicions about family circumstances or drug misuse can cloud others from recognizing the underlying brain injury to understand the person. In the Burd study, completed responses representing most of 3 million inmates revealed only one person known to have FAS. The authors demonstrate that even if the prevalence of fetal alcohol disorders were no higher in correctional settings than in the general population, the systems lack awareness of this disability among tens of thousands of affected inmates.

Yet growing research on FASD prevalence in corrections is helping to correct this lack of awareness. In 2011, Popova and colleagues (3) published an article reviewing international studies addressing FASD prevalence in corrections systems. Among the studies that directly assessed individuals or their charts in various correctional settings (all taking place in Canada), rates of FASD were reported ranging from approximately 10% (MacPherson and Chudley (4)) to 23% (Fast et al (5)). While the Popova review concludes that numbers of persons with unidentified FASD in corrections are high, they note that the studies’ modest sample sizes, and the variety of settings and methods to ascertain FASD rates, limit our ability to currently draw conclusions about general prevalence in corrections. These important studies have helped clear the path toward needed comprehensive research to better identify correctional prevalence rates.

Alongside recognition of the high frequency of people with FASD involved in justice systems, organizations within these systems are mounting successful initiatives to respond. In 2010, the Canadian Bar Association passed a resolution on FASD in the Criminal Justice System (6), the first national resolution of this magnitude. Among its resolutions is to “urge the federal government to amend criminal sentencing laws to accommodate the disability of those with FASD.” Following Canada’s progress, the American Bar Association passed an FASD resolution and report in 2012 (7), calling for effective responses to FASD in a breadth of human services and justice settings. In March of this year, the Australian NOFASARD drafted an inquiry report with recommendations in
response to a request by the Senate Standing Committee on Legal and Constitutional Affairs (8) to prevent adverse involvement in justice systems related to FASD. Nations are individually building momentum as well as looking to each other in recognizing FASD as a matter of justice.

Justice systems are increasingly welcoming to FASD education to better serve those who are affected. Advocates across the globe are involved in FASD training to impact law enforcement, courts, jails and prisons. In my own trainings, I find that correctional systems professionals readily connect FASD characteristics with individuals in the populations they serve, and are eager to learn strategies to help them. Resources specific to correctional applications are proliferating. At the University of Washington (United States), the Fetal Alcohol and Drug Unit (FADU) has long hosted legal resources expertise, accessible at http://depts.washington.edu/fadu/resources/fas-and-the-law. In 2013 prior to the International conference on FASD in Vancouver, Canada, Kathryn Kelly of the FADU, along with others, coordinated a gathering to engage in "FASD and the Law: A Conversation about Current Research and Practices" where people from four continents discussed concerns and strategies to move forward. A resource in the United States for attorneys, FASDExperts (at http://fasdéxperts.com) is an interdisciplinary forensic FASD diagnostic team, providing information and consultation to attorneys who seek an FASD evaluation and court testimony for clients with FASD who face criminal charges. The John Howard Society of Ontario, Canada has produced a 4-page fact sheet on FASD and the criminal justice system that clearly demonstrates the urgency of this topic and includes constructive strategies, available at http://fasdjustice.ca. Also of note are the excellent fact sheets for Juvenile and Criminal justice applications by the United States' Substance Abuse and Mental Health Services Administration at http://fasdcenter.samhsa.gov/grabGo/factSheets.aspx. Justice workers are proving to be a receptive match for dedicated FASD trainers, partnering to minimize the harms of FASD upon individuals who face so much misunderstanding.

To be sure, not everyone with FASD will face the law. We should take note that among those who do, many seek legal assistance for victimization by others who may take advantage of their disability (including their common eagerness to please others) by manipulation, theft, physical or sexual violation or other offenses. Also, justice systems can network with support and treatment services to offer intervention for women of childbearing potential with alcohol use disorders when they encounter law enforcement related to their misuse. People working in justice systems are called to respond to FASD from multiple angles.

Progress on FASD awareness in justice systems offers opportunity to celebrate and build on momentum that can influence all areas of FASD advocacy. For correctional systems, the stage is set to better determine FASD prevalence rates in legal proceedings, jails and prisons; to develop evidence-based practices for structuring effective diversion programs, appropriate correctional practices, and to prevent recidivism; and for educating correctional workers that people with FASD can have more lawful and better lives, when we adapt our expectations to match their abilities. As we all aim to live together in just societies, simple understanding of people living with FASD is a first step on the path to progress.

References

Scotland has the unenviable distinction of having one of the greatest rates of alcohol ingestion per head of population in Europe and the eighth *per capita* consumption of alcohol in the world. Nearly 50 million litres of pure alcohol was consumed in Scotland in 2007, equivalent to 11.8 litres each for every person aged over 16 years. England and Wales had an average consumption of 9.9 litres *per capita*¹. That the UK has one of the highest rates of underage drinking and teenage pregnancy in the industrialised world must give rise to concern that alcohol is damaging the health of our communities².

Ethyl alcohol or ethanol (commonly known as alcohol) is a fluid produced from sugars in industrial quantities throughout the world. Much of it is used for industrial purposes, such as a solvent, and in Brazil it is used for its combustive properties to power motor vehicles. In Scotland, our brewing and distilling companies dilute and process the alcohol which is then sold in industrial quantities to a willing public for its mind altering properties. The embryo, fetus, infant and child have no say as to whether they should be exposed to the mind altering properties of alcohol. The healthy mind and body of each child is the most precious resource of every family and community and should be safeguarded.

When asked by Susan Fleisher to comment on my experience of the adverse effects of alcohol on children in Scotland I thought that I would ask you to consider how a child’s mind develops and then to look at how alcohol disrupts these complex processes.

The brain, peripheral and sympathetic nervous and neuroendocrine systems sub-serve the functions of the mind. Everyone has an unique mind of his or her own which we identify as our “self”. The basis of our adult mindful thinking processes is largely established in our early formative years. Children of 5 years certainly have minds of their own and most mothers are aware that their infants (less than one year and not yet speaking) have minds of their own.

**Alcohol damage before birth**

Sullivan in 1899 examined the results of 600 pregnancies of 120 alcoholic women in a Liverpool
prison population and found that the infant mortality and stillbirth rate was two and a half times that of their non-alcoholic female relatives. He also showed that the forced abstinence of imprisonment improved the pregnancy outcome. There was parliamentary comment in the UK at the time but no action taken. Lemoine et al in 1969 described 127 children with characteristic facial abnormalities and poor growth. The same features were recognised in the USA and Canada in the 1970’s and since then many other countries including Scotland have identified the problems now known as the fetal alcohol spectrum disorder (FASD).

When women drink alcohol during the first eight weeks of pregnancy there is a significant risk that the developing organs of the embryo will be malformed and grow poorly. Some women and embryos with inherited defective enzyme systems for the removal of alcohol are more susceptible to damage than others. Mothers with nutritional deficits such as zinc, folic acid, docosahexaenoic acid (DHA) and vitamin D may also be more susceptible to fetal alcohol damage. At birth, the most severely affected infants will be small, have small heads and brains, typical abnormal facial features and a variety of congenital (present at birth) malformations of the brain, heart, kidneys, spine, limbs, palate and skin. These infants are said to have the fetal alcohol syndrome (FAS) and form part of the FASD. They will remain small, often requiring major surgery for their heart and other defects, and may present with a range of later difficulties such as poor coordination, learning and behavioural disorders including attention deficit/hyperactive disorder (ADHD), autistic spectrum disorder (ASD) and a range of life-long social and other problems.

After the eight week embryonic period, fetal development continues by a process largely of cell division so that by term (40 weeks gestation) the brain weighs 350g and is about 10% of the total body weight. In normal adults the brain weighs between 1250 to 1400g and is 2% of total body weight. Neurones and other brain cells are not only growing and dividing throughout fetal life, there are carefully timed and genetically determined organised migrations of cells within the brain and a complex system of interneuronal and other connections being developed. Visual, auditory, endocrine and other biochemical and sensory signals are already beginning to influence the developing brain cells and the developing mind of the child to be.

Alcohol can disrupt all of these processes and lead to a diminished brain size with cells missing, cells in the wrong positions and with abnormal function. Although mothers who only drink alcohol after the first eight weeks will probably not have infants with the obvious facial and other malformations seen with FAS, the damage to the developing nervous system can be severe.

Some women may drink during early pregnancy yet avoid causing the overt malformations of FAS but still damage the developing mind of the child. Others may drink throughout pregnancy, produce no overt malformations, yet have a child with severe behavioural and educational problems. Whereas it is relatively easy to diagnose FAS, it is more difficult to confirm the diagnosis of infants in the rest of the FASD group. There are many other inherited and acquired causes of the same clinical features found in FASD.

**Alcohol damage after birth**

Just as abuse of alcohol can adversely affect the structures and functions of the brain before birth, chaotic care in the first years after birth, in an environment “controlled” by alcohol abusing carers, can prove equally damaging. A combination of damage before and after birth can be devastating for the child.

Human infant attributes such as coordination of finger and facial movements, self awareness, memory, mimicry, thought processes, speech, language and socialisation are vulnerable to nutritional and emotional disorder in the two years after birth. During the first year after birth normal infant brain weight increases from about 350g to 1000g with most of this growth taking place in the first 6 months. At 2 years, the brain weighs~1200g. Over 60% of the energy intake of the infant in the first year is devoted to brain growth and function and used largely to construct the phospholipid membranes and myelin of neurones and glial cells of the brain. The nutrient materials needed to construct these phospholipids, many of which contain special long chain polyunsaturated fats...
(LCPUFA) including DHA, can best be provided by milk from a well nourished breast feeding mother. When the correct fats are not provided they are substituted with other fatty acids which make the nerve cell membranes more vulnerable to alcohol damage.

The developing infant brain requires tactile, visual, aural and emotional stimuli, as well as good nutrition to properly develop the brain and endocrine pathways which subserve and integrate normal brain and mind function. Sensory input to the infant is largely dependent on the mother’s physical, intellectual and emotional state and on the family and social support she receives. Interactions between mother or other primary care givers and the infant, particularly in response to stressful situations during the first two years, can determine the final adaptive brain structures of the infant, which in turn determine self regulation of emotional states and behaviour. Excessive maternal and infant stress potentiates the developmental psychopathology that underlies the various forms of the later behavioural and psychiatric disorders characteristic of FASD.

How common is FASD?

Assessments of the prevalence of FAS and FASD is not easy, partly because they are not recognised by paediatricians, nurses, psychiatrists, social workers, teachers and others and partly because women frequently underestimate or fail to recall or disclose their alcohol use in pregnancy. There are no such data yet available for Scotland or the UK. Studies from the USA and Canada suggest a minimum prevalence of FAS of 3.1 per 1000 and 9.5 per 1000 for FASD but report much higher rates (FASD >100 per 1000) in population sub-groups with high rates of alcohol consumption5,6.

Many individuals with FASD have relatively well preserved non-verbal skills without significant cognitive impairment but frequently demonstrate social adaptive, executive function, attention and functional memory deficits. These contribute to school failure, mental health problems, drug and alcohol abuse, inability to function independently in society, inappropriate aggression and violence, trouble with the law and imprisonment.

It was when I moved to Glasgow in 1977 that I first became acquainted with FAS and with paediatric colleagues identified and reported in the British Medical Journal of July, 1983, forty children with FAS, born in the West of Scotland between 1971 and 19817. In November 1986 Dr Ruth Day, a Consultant Paediatrician in Developmental Medicine and I reported in The British Journal for Nurses in Child Health some of our follow-up findings on these children8. In both publications we emphasised the need for further prospective research to define the origins and extent of FAS in the UK and for appropriate resource allocation for education, intervention and prevention. In the 30 years since our first report there has been a three fold increase in alcohol related deaths in Scotland and an alarming increase in binge drinking, particularly in women of child bearing age. The proportion of fifteen year old girls drinking alcohol regularly had increased to 40% in 2004; more than double the rate in 19809. There is no doubt that social marketing through the production of drinks attractive to young people, targeted advertising and the easy availability of relatively less expensive and stronger alcohol products are major factors in this move to increased alcohol consumption. Given the current high rates of teenage pregnancy in the UK it is unlikely that there has been a reduction in the prevalence of FASD in Scotland over the past 30 years.

Data from household surveys show that around 93,500 babies aged under one year in the UK live with a parent classified as a “problematic” drinker (“hazardous” or “harmful”), and around 31,000 babies in the UK live with a parent who is “dependent” on alcohol10.

FASD and Public Health

There had been very slow progress in public awareness of the adverse effects caused by intrauterine exposure of the developing baby to alcohol between Sullivan’s report from Liverpool at the end of the 19th century and our West of Scotland 20th century reports. However, during this first part of the 21st century there have been a series of events which are making the adverse influences of alcohol on the general health and well-being of our population more widely...
I have already indicated that some mothers and some fetuses have inherited genetic defects which prevent or diminish their ability to detoxify alcohol and are more prone to develop FASD. It is now known that there are also epigenetic factors at work. Epigenetics, is the study of the effects of environmental influence on the genetic code in our inherited DNA. Experimental animal studies have shown that diet during pregnancy, exposure to alcohol, nurturing behaviour by mothers and exposure to stress can alter the way an infant’s genes are modified\textsuperscript{11,12,13}. The embryo and fetus is very susceptible to epigenetic changes which alter the times at which genes are switched on and off. These switches are responsible for shaping the structures and functions of the face, heart and brains of the developing embryo and most importantly can be transmitted to the next generations through both males and females.

The Chief Medical Officer for Scotland, Sir Harry Burns, in his 2011 Annual Report emphasised the need for a concentrated effort across the whole of Scottish society to make the changes in life-style required to combat health inequalities. In chapter 2 of the report he examined the psychological, social and biological determinants of health and a number of studies including some on epigenetic factors currently underway\textsuperscript{14}. Improving the early years of a child’s life was identified as a good place to start reversing health inequalities. In England, the Children’s Commissioner September 2012 report “Silent Voices: Supporting children and young people affected by parental alcohol misuse” gives a large body of evidence and some guidance on how to combat the problem\textsuperscript{15}. Suggestions included increasing the price of alcohol and restricting advertising.

The Scottish Government has passed legislation to introduce minimum unit pricing of alcohol but is facing a legal challenge by the Scotch Whisky Association. More than 500 public health professionals and NGO representatives from 60 countries have on the 5th April, 2013, sent to the WHO Director General, Dr Margaret Chan, a joint Statement of Concern about the activities of the global alcohol producers. The Statement highlights how, despite claims to be supportive of reducing harms caused by alcohol, they actually cause a threat to effective health policies due to the inherent conflict of interest between profit and public health\textsuperscript{16}. Similar arguments apply to the alcohol marketing industry which aims to groom and increase the next generation’s drinking habits by spending £800m annually\textsuperscript{17,18}.

I am optimistic that increased knowledge and understanding of the insidious adverse effects caused to the unborn child by maternal alcohol ingestion will overcome the social and commercial pressures which combine to cause FASD.

NOFAS and other NGO and knowledgeable parent groups will be able to help create the necessary political pressures and significantly reduce the prevalence of this entirely preventable condition. We are, after all, a civilised society and healthy children are our most precious resource.

References:

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III. NEW ZEALAND'S CURRENT RISK PROFILE ON DRINKING ALCOHOL BEFORE AND DURING PREGNANCY

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"[Liquor] impoverishes us; our children are not born healthy because the parents drink to excess, and the child suffers. (Excerpt from Petition of Haimona Te Aoterangi and 167 others, to New Zealand House of Representative in 1874)"

As evidenced by the quote cited above from an 1874 petition, drinking during pregnancy has historical as well as modern significance in New Zealand. The link between maternal alcohol consumption and developmental deficits in their children has been recognised for decades, and research, such as that being discussed herein, continues to highlight the risk. Despite this, the harm emanating from risky maternal drinking has remained hidden and has been largely unaddressed in New Zealand. This may in part be because of a lack of any formal surveillance of the effects of maternal alcohol consumption on New Zealand children born exposed to this teratogen. Without evidence of the patterns, prevalence and severity of the harm that results from this risky behaviour, programmes and policies for prevention at the population and individual level...
cannot be developed effectively. In other words, it is difficult to prevent the invisible. These and other issues will be explored in this discussion, alongside findings from the most recent study of maternal drinking in New Zealand from Mallard and colleagues.

Aside from a brief flirtation with alcohol prohibition in the early part of the 20th century, like many developed countries, New Zealand has a long and robust alcohol trading history and a relatively light touch when it comes to harm reduction measures. Consequently, alcohol has retained a strong social and cultural underpinning that is accompanied by a sustained burden of disease and disability. Liquor control legislation was significantly deregulated 23 years ago in deference to freeing up the alcohol market and the night time economy, thereby dramatically increasing its availability.

A number of studies have helped to shed some light on the patterns of drinking and extent of harm for some population groups over that time. The most recent econometric study to examine the burden of harm from alcohol in New Zealand, measured it at 5 billion NZ$ per annum (Burl et al 2010). This figure however, does not account for the burden of harm that can result from drinking alcohol during pregnancy. As mentioned above, New Zealand has not yet measured the extent of the harm from prenatal alcohol exposure. However, international estimates suggest that the prevalence of Fetal Alcohol Spectrum Disorder (FASD) could lie between 2-5% of live births, which for New Zealand would equate to 1200 to 3000 children born affected each year (Sellman and Connor, 2009). The annual cost burden of this lifelong disability would be substantial (Popova et al, 2012). However, until this harm is measured, we are reliant on data from surveys of hazardous drinking during pregnancy and extrapolation of international FASD prevalence data. While this is far from ideal, these studies do nevertheless provide important information on maternal risk factors and a reasonable basis upon which to draw some conclusions about potential harm.

One such study was conducted recently by researchers from the University of Otago’s Departments of Human Nutrition and Preventive and Social Medicine (Mallard et al, 2013). The Vitamins and Minerals in Pregnancy Survey surveyed 723 women during their postpartum stay in hospitals and birthing centres across New Zealand in March and April 2011. Although the main focus of the survey was to collect data on supplement use before and during pregnancy, questions on alcohol consumption were also included due to the paucity of data currently available in New Zealand. Despite current New Zealand Ministry of Health guidelines recommending total abstinence from alcohol when pregnant, one-third (34%) of all women reported drinking during their pregnancy. This percentage is higher than that reported recently in Australia (29%) (Maloney et al, 2011), the US (14%) (Zhao et al, 2012) and Canada (11%) (Walker et al 2011), countries in which total abstinence during pregnancy is also officially recommended. Almost one-quarter (24%) of drinkers continued to drink following pregnancy recognition, and, the more frequently a woman drank before pregnancy, the more likely she was to continue to drink. This association has been noted in similar studies elsewhere (Skagerström et al, 2011) and indicates that the habit of frequent alcohol consumption—even at low levels—places fetuses at unnecessary risk. Binge drinking (> 4 standard drinks on one occasion) produces the high peak blood alcohol concentrations that are most detrimental to fetal development (Maier and West, 2001). The estimated percentage of pregnancies exposed to binge drinking in early gestation was 12%, with indigenous Māori women at almost five times higher risk and Pacific women at 3.4 times higher risk than New Zealand Europeans. Given that the study sample was restricted to mothers 18 years or over of full-term healthy infants, and that hospitals in the Northland region, where a higher proportion of people identifying themselves as Māori and Pacific reside, were not included, the prevalence of binge drinking in early pregnancy was likely underestimated. However, the information provided by the study is directly relevant to the development of future public health policies and indicates that Māori and Pacific communities may currently bear a disproportionate burden of alcohol-related harm in New Zealand.

Women have traditionally been viewed as a low risk drinking group compared to men (Rankin, 2012), however, that gap is closing. Data from the most recent national New Zealand Health Survey presented the expected dimorphic pattern, with men reporting far higher levels of hazardous drinking (26% of all past-year drinkers) than women (12%) (Ministry of Health, 2013).
In the period between the 2006/07 and 2011/12 New Zealand Health Surveys, hazardous drinking levels fell significantly for men (30% to 26%), whereas the level of hazardous drinking among female past-year drinkers remained stable. Furthermore, the longitudinal trend towards lower levels of hazardous drinking overall was reversed for women aged 25-36 years. In addition to an increase in hazardous drinking behaviour, a New Zealand study tracking alcohol consumption patterns from 1990 to 2000 identified that reproductive age women were also the only group drinking more frequently (Huckle et al, 2012). The authors suggested that the introduction of wine sales in supermarkets from 1990 had allowed women to feel more comfortable purchasing wine because it had become a grocery item.

Several aspects of the market-driven policy reforms of the sale and supply of alcohol have likely combined to amplify this shift in drinking patterns among young, reproductive age women. In addition to permitting the sale of wine in supermarkets in 1990, in 1999 the alcohol purchasing age was lowered from 20 to 18 years, ensuring an earlier onset of regular drinking among teens. This coincided with the development of sweetened, colourful spirit-based ready-to-drink beverages, perhaps more appropriately known as “alcopops” in the UK, marketed particularly at the young females. The push to market these as a positive and pleasurable pursuit for young people has intensified following the advent of social networking sites, which have been well utilised by the alcohol industry (McCreanor et al, 2013).

From this latest data on drinking before and during pregnancy in New Zealand, it is clear that the level of risky maternal drinking is considerable, and is likely having a negative impact on the next generation. At present, few policies and programmes are aimed at reducing drinking among pregnant women and women of reproductive age. Without any counter to the intense normalisation of frequent and risky drinking the increase in the number of women drinking hazardously is set to continue, along with its potential to damage the next generation. Formal surveillance of the prevalence and impact of FASD in New Zealand may be needed to convince policy makers of the magnitude of the current problem.

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Petition of Haimona Teatorangi and 167 others in Whanganui (1874). Appended to the Journals of the House of Representatives 1874 Session I. J-01. atojs.natlib.govt.nz

IV. NEONATOLOGISTS’ CONTRIBUTION TO ALCOHOL-RELATED DISORDERS IN ITALY: A LOT OF WORK HAS BEEN DONE BUT THERE’S A LONG WAY TO GO YET

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As a Paediatrician and a Neonatologist, I should admit that Italian Professionals in my category are not trained to diagnose maternal drug-abuse effects on newborn behaviour.

In 2006, I was working in the paediatric ward in Ravenna Hospital in Italy and I couldn’t identify the exact diagnosis in a newborn with hyperexcitability and persistent opisthotonus along with absence of cerebral damage on neuroimaging. An article by Simona Pichini on nicotine neonatal withdrawal syndrome enlightened me and we were able to confirm the diagnosis in my patient by a more exhaustive interview of the mother and chromatographic-spectrometric assay of nicotine and its principal metabolite cotinine in mother’s and baby’s hair.

Since that time, Simona became one of my very best friends and together with other passionate Colleagues, we started to go through the path of those newborns born from mothers who are prone to abuse psychotropic drugs during pregnancy and particularly alcohol.

In 2008 for the first time in Europe, the “Meconium Project” was initiated as a joint investigation between Spain and Italy in order to estimate the prevalence of drug abuse by pregnant women and the effects of chronic intrauterine exposure on fetus and infant. In this concern, to assess fetal exposure to ethanol, we validated a liquid chromatography-tandem mass spectrometry method to measure direct ethanol biomarkers, the fatty acid ethyl esters (FAEES) in meconium (first neonatal fæces) samples from newborns of two cohorts of infant-mother dyads from Reggio Emilia, Italy, and from Barcelona, Spain. Given total seven FAEES > 2 nmol/g as the cutoff, meconium analysis revealed a very different prevalence of in-utero alcohol exposure in Reggio Emilia samples compared to those from Barcelona (1.7% vs. 44.5%), being this last a cohort with lower socio-economical characteristics.

With the precious help of the forensic toxicologist, Luca Morini in Pavia, Italy, research went on and we were able to detect for the first time in meconium samples two other direct ethanol metabolite, ethyl glucuronide (EtG) and ethyl sulfate (EtS), these being potentially very good alternative biomarkers to FAEES.

At that time, my curiosity towards the burden of in utero alcohol-exposed newborns was growing...
along with awareness that this was surely an underestimated and not completely studied problem among Neonatologists. Simona Pichini and I decided then to build up a questionnaire in order to evaluate the experience, knowledge and confidence of Italian Neonatologists and Paediatricians with respect to the diagnosis of FAS and FASD, along with an evaluation of Professionals’ awareness of maternal drinking patterns during pregnancy\. With the help of Oscar Garcia-Algar, the same questionnaire was proposed to Spanish Professionals. The response rate from Italian Professionals was very low (16\%) since just a few Neonatologists among the ones contacted for the survey, completed the questionnaire. In spite of repeated contacts with non-responders to the first approach, probably this survey was not considered so important or Neonatologists did not feel comfortable in answering this questionnaire. Moreover, when asked about diagnosis of FASD, Neonatologists referred maternal interviews as a reliable help and only around 20\% knew about the possibility to diagnose in utero alcohol exposition by means of biomarkers.

These findings were the definite demonstration that there was a long way to go yet … even if our investigations had enlightened the unknown problem of prenatal exposure to maternal alcohol and fetal alcohol spectrum disorders.

In 2011, the first Italian multicentre study on the prevalence of in utero alcohol exposure, objectively measured by biomarkers analysis in meconium, disclosed an overall percentage of 7.9\% exposed newborns from 7 different neonatal wards along the peninsula, ranging from e.g. 0\% of Verona, 5\% in Naples and Florence, 10\% in Reggio Emilia and 29\% in Rome.

Our results showed that Neonatologists nowadays can face a diagnosis of in utero exposure to maternal alcohol that until a few years ago was an exclusive prerogative of few well-trained Paediatricians and/or Geneticists. Indeed, the chance to diagnose alcohol exposed newborn by meconium analysis can be of great interest, given that FAS and FASD have many overlapping signs with other genetic syndromes and non-genetic paediatric conditions. Moreover, in cases of alcohol abuse during pregnancy, maternal interviews are often unreliable, even when reservedly collected by experienced Professionals.

Measurement of ethanol biomarkers in neonatal meconium can disclose newborns who have been exposed to “alcohol abuse” during intrauterine life. As a consequence, these newborns can be included in an adequate and precocious multiprofessional targeted follow-up.

References:

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1. **ANTHOCYANINS PROTECT AGAINST ETHANOL-INDUCED NEURONAL APOPTOSIS VIA GABAB1 RECEPTORS INTRACELLULAR SIGNALING IN PRENATAL RAT HIPPOCAMPAL NEURONS**  
   Ali Shah S, Ullah I, Lee HY, Kim MO.  
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**ABSTRACT**

Here, we investigated the possible involvement of GABA-aminobutyric acid b1 receptor (GABAB1R) in mediating the protective effects of black soybean anthocyanins against ethanol-induced apoptosis in prenatal hippocampal neurons because GABARS are known to play an important role in the development of central nervous system. Treatments were performed on primary cultures of prenatal rat hippocampal neurons transfected with or without GABAB1R small interfering RNA (siRNA). The results showed that, when ethanol treatment was followed by anthocyanins treatment, cellular levels of proapoptotic proteins such as Bax, activated caspase-3, and cleaved poly (ADP-ribose) polymerase 1 (PARP-1) were decreased, and the cellular level of the antiapoptotic protein BCL-2 was increased compared to treatment with ethanol alone. Furthermore, the effects of ethanol on cellular levels of GABAB1R and its downstream signaling molecules such as protein kinase A, calcium/calmodulin-dependent protein kinase II (CAMKII), and phosphorylated cAMP response element binding protein were diminished or reversed by anthocyanins treatment. The ability of anthocyanins to reverse the effects of ethanol on cellular levels of Bax, BCL-2, active caspase-3, cleaved PARP-1, GABAB1R, and CAMKII were abrogated in cells transfected with GABAB1R siRNA. In a GABAB1R-dependent manner, anthocyanins also inhibited the ability of ethanol to elevate intracellular free Ca2+ level and increase the proportion of cells with low mitochondrial membrane potential in the population. Cell apoptosis assay and morphological studies also confirmed the neuroprotective effect of anthocyanins against ethanol via GABAB1R. Our data suggest that GABAB1R plays an important role in the neuroprotective effects of anthocyanins against ethanol.

Read Full Article,  
2. REHABILITATION TRAINING USING COMPLEX MOTOR LEARNING RESCUES DEFICITS IN EYEBLINK CLASSICAL CONDITIONING IN FEMALE RATS INDUCED BY BINGE-LIKE NEONATAL ALCOHOL EXPOSURE

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ABSTRACT
BACKGROUND: Effective treatments for the behavioral and cognitive deficits in children with fetal alcohol spectrum disorders (FASD) are lacking, and translational approaches using animal models can help develop rational interventions. One such model, binge-like alcohol exposure in neonatal rats during the period of brain development comparable with that of the human third trimester, causes structural and functional damage to the cerebellum and disrupts cerebellar-dependent eyeblink classical conditioning. The eyeblink conditioning deficits first demonstrated in this rat model predicted the similar deficits subsequently demonstrated in children with FASD.

METHODS: The current study extends this translational approach by testing the hypothesis that rehabilitation training involving 20 days of training on traversal of an obstacle course (complex motor learning) would ameliorate the deficits on classical conditioning of eyeblink responses produced by the neonatal alcohol exposure. We have previously shown that this training stimulates cerebellar synaptic plasticity and improves alcohol-induced deficits on motor coordination tasks.

Results: The current studies found that rehabilitation training significantly attenuated alcohol-induced deficits in acquisition of eyeblink conditioning in females but not in males. These results are consistent with normalization of cerebellar-dependent learning, at least in alcohol-exposed females.

Conclusions: These findings extend previous studies in this model suggesting that rehabilitation of adolescents with FASD using training with complex motor learning tasks could be effective in ameliorating functional impairments associated with cerebellar damage. Eyeblink classical conditioning deficits are now well documented in children with FASD and could serve as an evaluation measure to continue to develop therapeutic interventions such as complex motor learning.


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3. THE ROLE OF ACIDEMIA IN MATERNAL BINGE ALCOHOL-INDUCED ALTERATIONS IN FETAL BONE FUNCTIONAL PROPERTIES

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ABSTRACT
Background: Heavy alcohol consumption during pregnancy negatively impacts the physical growth of the fetus. Although the deleterious effects of alcohol exposure during late gestation on fetal brain development are well documented, little is known about the effect on fetal bone mechanical properties or the underlying mechanisms. The purpose of this study was to investigate the effects of late gestational chronic binge alcohol consumption and alcohol-
induced acidemia, a critical regulator of bone health, on functional properties of the fetal skeletal system.

**Methods:** Suffolk ewes were mated and received intravenous infusions of saline or alcohol (1.75 g/kg) over 1 hour on 3 consecutive days per week followed by 4 days without treatment beginning on gestational day (GD) 109 and concluding on GD 132 (term = 147 days). The acidemia group was exposed to increased inspired fractional concentrations of CO₂ to closely mimic the alcohol-induced decreases in maternal arterial pH seen in the alcohol group.

**Results:** Fetal femurs and tibias from the alcohol and acidemia groups were ~3 to 7% shorter in length compared with the control groups (p < 0.05). Three-point bending procedure demonstrated that fetal femoral ultimate strength (MPa) for the alcohol group was decreased (p < 0.05) by ~24 and 29%, while the acidemia group exhibited a similar decrease (p < 0.05) of ~32 and 37% compared with the normal control and saline control groups, respectively. Bone extrinsic and intrinsic mechanical properties including maximum breaking force (N) and normalized breaking force (N/kg) of fetal bones from the alcohol and acidemia groups were significantly decreased (p < 0.05) compared with both control groups.

**Conclusions:** We conclude that late gestational chronic binge alcohol exposure reduces growth and impairs functional properties of the fetal skeletal system and that the repeated episodes of alcohol-induced maternal acidemia may be at least partially responsible for these effects.


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4. **SULFORAPHANE PROTECTS AGAINST ETHANOL-INDUCED OXIDATIVE STRESS AND APOPTOSIS IN NEURAL CREST CELLS BY THE INDUCTION OF NRF2-MEDIATED ANTIOXIDANT RESPONSE**

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Department of Cancer Biology and Pharmacology, University of Illinois College of Medicine, Peoria, IL, USA.

**ABSTRACT**

**Background and Purpose:** Nuclear factor erythroid 2-related factor (Nrf2) is a transcription factor that up-regulates a diverse array of antioxidant genes and protects cells from oxidative damage. This study is designed to determine whether D-L-sulforaphane (SFN) can protect neural crest cells (NCCs), an ethanol-sensitive cell population implicated in fetal alcohol spectrum disorders, against ethanol-induced apoptosis and whether protective effects of SFN are mediated by the induction of Nrf2-mediated antioxidant response.

**Experimental Approach:** Control, SFN-treated or Nrf2-siRNA transfected NCCs were exposed to ethanol. Nrf2 activation, the expression and activities of Nrf2 downstream antioxidant proteins, reactive oxygen species generation and apoptosis were determined in control and ethanol-exposed NCCs.

**Key Results:** Exposure of NCCs to SFN alone significantly increased Nrf2 activation and the expression of Nrf2 downstream antioxidants as well as the activities of the antioxidant enzymes. Treatment of NCCs with SFN along with ethanol significantly decreased ethanol-induced oxidative stress and apoptosis. In contrast, knockdown of Nrf2 by siRNA significantly increased the sensitivity of NCCs to ethanol-induced oxidative stress and apoptosis.
Suppression of Nrf2 signalling in NCCs also significantly diminished SFN-mediated antioxidant response and abolished the protective effects of SFN on ethanol-induced oxidative stress and apoptosis.

**Conclusions and Implications:** These results demonstrated that Nrf2-mediated antioxidant response plays an important role in the susceptibility of NCCs to ethanol-induced oxidative stress and apoptosis and that the protection of SFN against ethanol-induced oxidative stress and apoptosis in NCCs is mediated by the induction of Nrf2 signalling.

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doi: 10.1097/OGX.0b013e31828736d5  
CME Articles: Reducing Fetal Alcohol Exposure

5. **REDUCING FETAL ALCOHOL EXPOSURE IN THE UNITED STATES**

Waterman, Emily H. MD, MPH; Pruett, Dawn MA; Caughey, Aaron B. MD, PhD  
USA

**ABSTRACT**

Fetal alcohol exposure is the leading preventable cause of birth and developmental defects in the United States. Despite a growing body of knowledge about the spectrum of disorders resulting from fetal alcohol exposure, 1 in 9 pregnant women continues to drink alcohol during pregnancy, and a small percentage of pregnant women continues to binge drink. Health care providers do not consistently screen pregnant women for alcohol use, nor do health professionals necessarily know how to counsel pregnant women effectively about the risks of fetal alcohol exposure. In this article, we review the epidemiology of fetal alcohol exposure and discuss current strategies for screening and prevention of fetal alcohol exposure. We also explore the multiple barriers that exist toward reducing alcohol-exposed pregnancies from the patient, provider, and systems perspectives. Finally, we make recommendations for improved clinical and public health strategies to eliminate fetal alcohol exposure in the United States.

**Target Audience:** Obstetricians and gynecologists, family physicians

**Learning Objectives:** After completing this CME activity, physicians should be better able to describe rates of fetal alcohol exposure in the United States, describe the demographic characteristics of women at highest risk for fetal alcohol exposure, counsel patients appropriately regarding the risk of poor fetal outcomes in association with fetal alcohol exposure, and understand the barriers to effective counseling about fetal alcohol exposure.

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http://journals.lww.com/obgynsurvey/Abstract/2013/05000/Reducing_Fetal_Alcohol_Exposu re_in_the_United.19.aspx

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6. MODERATE ALCOHOL USE AND HEALTH: A CONSENSUS PAPER


NFI (Nutrition Foundation of Italy), Viale Tunisia 38, 20124 Milan, Italy. Electronic address: poli@nutrition-foundation.it.

ABSTRACT

Aims: The aim of this consensus paper is to review the available evidence on the association between moderate alcohol use, health and disease and to provide a working document to the scientific and health professional communities.

Data Synthesis: In healthy adults and in the elderly, spontaneous consumption of alcoholic beverages within 30 g ethanol/d for men and 15 g/d for women is to be considered acceptable and do not deserve intervention by the primary care physician or the health professional in charge. Patients with increased risk for specific diseases, for example, women with familiar history of breast cancer, or subjects with familiar history of early cardiovascular disease, or cardiovascular patients should discuss with their physician their drinking habits. No abstainer should be advised to drink for health reasons. Alcohol use must be discouraged in specific physiological or personal situations or in selected age classes (children and adolescents, pregnant and lactating women and recovering alcoholics). Moreover, the possible interactions between alcohol and acute or chronic drug use must be discussed with the primary care physician.

Conclusions: The choice to consume alcohol should be based on individual considerations, taking into account the influence on health and diet, the risk of alcoholism and abuse, the effect on behaviour and other factors that may vary with age and lifestyle. Moderation in drinking and development of an associated lifestyle culture should be fostered.


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7. SCREENING FOR SUBSTANCE ABUSE IN WOMEN'S HEALTH: A PUBLIC HEALTH IMPERATIVE

Goodman DJ, Wolff KB.

2013 by the American College of Nurse-Midwives, USA

ABSTRACT

Alcohol and drug use is a significant public health problem with particular implications for the health and safety of women. Women who abuse these substances are more likely to have untreated depression and anxiety and are at higher risk for intimate partner violence, homelessness, incarceration, infectious disease, and unplanned pregnancy. Substance abuse during pregnancy places both mother and fetus at risk for adverse perinatal outcomes. Data regarding the prevalence of substance abuse in women are conflicting and difficult to interpret. On the clinical level, strong arguments exist against routine urine drug testing and in favor of the use of validated instruments to screen women for drug and alcohol use both in
primary women’s health care and during pregnancy. A number of sex-specific screening tools are available for clinicians, some of which have also been validated for use during pregnancy. Given the risks associated with untreated substance abuse and dependence in women, the integration of drug and alcohol screening into daily clinical practice is imperative. This article reviews screening tools available to providers in both the prenatal and primary women’s health care settings and addresses some of the challenges raised when women screen positive for drug and alcohol abuse.


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8. USE OF HEALTH, EDUCATION, AND SOCIAL SERVICES BY INDIVIDUALS WITH FETAL ALCOHOL SPECTRUM DISORDER
Marni D Brownell, Ana C de B. Hanlon Dearman, Leonard R MacWilliam, Albert E Chudley, Nora Lou P Roos, Lauren P Yallop, Sally E A Longstaffe

Department of Community Health Sciences (Manitoba Centre for Health Policy) Faculty of Medicine, University of Manitoba; Department of Pediatrics and Child Health, Faculty of Medicine, University of Manitoba; Department of Biochemistry and Medical Genetics, Faculty of Medicine, University of Manitoba; Department of Psychology, Faculty of Arts, University of Manitoba, Canada.

ABSTRACT
Background: Fetal Alcohol Spectrum Disorder (FASD) is the leading cause of intellectual disability in western society, presenting a significant burden on health, education and social services. Quantifying the burden of FASD is important for service planning and policy and program development.

Objective: To describe the health, education and social service use of individuals with FASD to provide an indication of the burden of service use of the disorder.

Methods: Using a matched-cohort design health, education and social service data were linked with clinical records on individuals 6+ years diagnosed with FASD between 1999/2000-2009/10 (N=717). Matching was 2:1 with a general population (gPop) and asthma group by age, sex and area-level income. Adjusted rates and relative risks were calculated using Generalized Linear Models.

Results: Hospitalizations were higher in the FASD compared to gPop (adjusted relative risk=3.44 (95% confidence interval=2.29, 5.17)) and asthma (2.87 (1.94, 4.25)) groups, whereas for physician visits and overall prescriptions, the FASD group differed from only the gPop group (1.58 (1.34, 1.84); 1.44 (1.22, 1.72), respectively). Antibiotics, pain killers and anti-psychotics were similar across groups whereas antidepressants and psychostimulants were higher in the FASD group (antidepressants: FASD vs. gPop 8.76 (2.82, 27.21); FASD vs. asthma 2.10 (1.15, 3.83); psychostimulants: FASD vs. gPop 5.78 (2.89, 11.57); FASD vs. asthma 2.47 (1.37, 4.47)). Attention-deficithyperactivity disorder was higher in the FASD than the gPop and asthma groups (6.41 (3.29, 12.49); 3.12 (1.97, 4.93), respectively). Education and social service use was higher for the FASD than either of the other groups for all measures (FASD vs. gPop and FASD vs. asthma, respectively for: grade repetition 3.06 (1.58, 5.94); 3.48 (1.79, 6.78); receipt of any special education funding 9.22 (6.23, 13.64); 6.10 (4.14, 8.99); family receipt of income assistance 1.74 (1.33, 2.27); 1.89 (1.45, 2.47); child in care 13.19 (5.84, 29.78); 10.70 (4.80, 23.88); and receipt of child welfare services 5.70 (4.21, 7.71); 4.94 (3.67, 6.66)).
Conclusion: The health, education and social service utilization burden of individuals with FASD is substantial, greater than that of individuals in the general population and with chronic illness (i.e., asthma). The findings highlight the need for multisystem supports for those with FASD, and comprehensive prevention programs.


9. COUNTING FETAL ALCOHOL SPECTRUM DISORDER IN AUSTRALIA: THE EVIDENCE AND THE CHALLENGES
Burns L, Breen C, Bower C, O’Leary C, Elliott EJ.
National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia.

ABSTRACT
Issues: Alcohol exposure in utero is associated with a range of adverse outcomes in pregnancy and can cause long-term disability. Fetal alcohol spectrum disorder (FASD) is an umbrella term to describe a range of effects from prenatal alcohol exposure including fetal alcohol syndrome (FAS). Determining the prevalence of FASD is challenging.

Approach: This narrative review collates information on the prevalence of FASD in Australia and documents the various methods used for attaining estimates and the limitations of the available data.

Key Findings: Birth prevalence of FASD is most commonly measured through clinic-based studies, passive surveillance systems and active case ascertainment. Alcohol use in pregnancy and FAS in Australia is predominantly monitored through passive surveillance systems and under-ascertainment of cases is likely. State- and territory-based studies have reported birth prevalence rates of FAS of between 0.01 and 0.68 per 1000 live births. Prevalence rates of FASD have not been estimated in Australia. As reflected in the international data, Australian studies have found higher rates of FAS among some Indigenous communities. This likely reflects patterns of alcohol use and other socioeconomic risk factors.

Implications: Under-recognition of FASD reflects incomplete and inconsistent data collections recording alcohol use in pregnancy, lack of awareness among health professionals and a lack of diagnostic and support services.

Conclusion: Accurate measurement of FASD prevalence is crucial to inform policy, resource and service development in the areas of health, education, justice and community. There is a need for consensus on the collection and best use of data. [Burns L, Breen C, Bower C, O’Leary C, Elliott EJ. Counting fetal alcohol spectrum disorders in Australia: the evidence and the challenges. Drug Alcohol Rev 2013].


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10. DEVELOPMENTAL IMMUNOTOXICITY IN MALE RATS AFTER JUVENILE EXPOSURE TO ETHANOL
Tonk EC, Verhoef A, Gremmer ER, van Loveren H, Piersma AH.
Department of Toxicogenomics, Maastricht University, Maastricht, The Netherlands; Laboratory for Health Protection Research, National Institute for Public Health and Environment (RIVM), Bilthoven, The Netherlands. Electronic address: ilse.tonk@rivm.nl.

ABSTRACT
The aim of the present study was to determine the sensitivity of the developing immune system to ethanol (EtOH) after exposure from postnatal day (PND) 10 onward. Adult Wistar dams and litters were exposed to EtOH via drinking water (0, 0.25, 1.5, 2.75, 4, 5.25, or 6.5% (w/v) EtOH ad libitum) and drinking water exposure of the F1 was continued from weaning until sacrifice. Immune assessments were performed at postnatal days (PNDs) 21, 42, and 70. Furthermore, Keyhole Limpet Hemocyanin (KLH) specific immune responses were evaluated following subcutaneous immunizations on PNDs 21 and 35. EtOH exposure affected innate immune responses, such as LPS-induced NO-production by adherent splenocytes, as well as adaptive immune responses as represented by KLH-specific parameters. The most sensitive developmental parameters included effects on maternal and pup bodyweight with calculated BMDs of 4.0% and 4.3% EtOH, respectively. The most sensitive immune parameters were affected at dose levels lower than those affecting developmental parameters and included KLH-specific immune responses, LPS-induced NO production by adherent splenocytes, and IL-10 production by ConA stimulated splenocytes. Calculated BMDs for these parameters were between 0.01% and 0.1% EtOH. A comparison of the results of this juvenile study with an extended one-generation reproductive toxicity study revealed that the juvenile study design may result in a higher sensitivity related to differences in the exposure design. These findings demonstrate the relative sensitivity of the developing immune system for EtOH exposure, the additional value of assessing functional immune parameters, and the importance of the juvenile window in developmental immunotoxicity testing.

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11. EXPERIMENTAL METHODS FOR TESTING THE EFFECTS OF NEUROTROPHIC PEPTIDE, ADNF-9, AGAINST ALCOHOL-INDUCED APOPTOSIS DURING PREGNANCY IN C57BL/6 MICE
Youssef Sari

Department of Pharmacology, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, USA.

ABSTRACT
Experimental designs for investigating the effects of prenatal alcohol exposure during early embryonic stages in fetal brain growth are challenging. This is mostly due to the difficulty of microdissection of fetal brains and their sectioning for determination of apoptotic cells caused by prenatal exposure to alcohol. The experiments described here provide visualized techniques from mice breeding to the identification of cell death in fetal brain tissue. This study used C57BL/6 mice as the animal model for studying fetal alcohol exposure and the role of trophic peptide against alcohol-induced apoptosis. The breeding consists of a 2-hr
matting window to determine the exact stage of embryonic age. An established fetal alcohol exposure model has been used in this study to determine the effects of prenatal alcohol exposure in fetal brains. This involves free access to alcohol or pair-fed liquid diets as the sole source of nutrients for the pregnant mice. The techniques involving dissection of fetuses and microdissection of fetal brains are described carefully, since the latter can be challenging. Microdissection requires a stereomicroscope and ultra-fine forceps. Step-by-step procedures for dissecting the fetal brains are provided visually. The fetal brains are dissected from the base of the primordium olfactory bulb to the base of the metencephalon. For investigating apoptosis, fetal brains are first embedded in gelatin using a peel-away mold to facilitate their sectioning with a vibratome apparatus. Fetal brains embedded and fixed in paraformaldehyde are easily sectioned, and the free floating sections can be mounted in superfrost plus slides for determination of apoptosis or cell death. TUNEL (TdT-mediated dUTP Nick End Labeling; TdT: terminal deoxynucleotidyl transferase) assay has been used to identify cell death or apoptotic cells. It is noteworthy that apoptosis and cell-mediated cytotoxicity are characterized by DNA fragmentation. Thus, the visualized TUNEL-positive cells are indicative of cell death or apoptotic cells. The experimental designs here provide information about the use of an established liquid diet for studying the effects of alcohol and the role of neurotrophic peptides during pregnancy in fetal brains. This involves breeding and feeding pregnant mice, microdissecting fetal brains, and determining apoptosis. Together, these visual and textual techniques might be a source for investigating prenatal exposure of harmful agents in fetal brains.

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12. TRANSCENDENTAL PHENOMENOLOGY AND CLASSIC GROUNDED THEORY AS MIXED DATA COLLECTION METHODS IN A STUDY EXPLORING FETAL ALCOHOL SPECTRUM DISORDER IN NEW ZEALAND
Jenny Salmon, Stephen Buetow

ABSTRACT
Background: Despite the risk of ‘method slurring’, researchers have triangulated within a single qualitative study methods that are philosophically incongruent or in a limited context, are congruent, as with hermeneutic phenomenology and constructivist grounded theory.

Methods/ Materials: We aimed to make the case that what works best can be to mix two qualitative methods that are philosophically congruent. Thus, we used transcendental phenomenology (TP) and classic grounded theory (CGT) in synergetic sequence to answer our research question. These methods have not previously been used together and one method would not have sufficed. Using the same participant sample, we sought to explore and understand the daily challenges of living with fetal alcohol spectrum disorder (FASD) since no study to date had addressed these issues within New Zealand. Our retrospective exploratory two-phase sequential design was framed by the meta-theory of pragmatism. It mixed qualitative strategies that are ontologically and epistemologically compatible (i.e. TP and CGT are ontologically realist, but epistemologically idealist). They are useful together for the aim of meaningfully studying the lived experiences of purposively selected participants. Empirical data, as secondary results, provide supportive evidence.

Conclusion: The first paper from this study was published in J Popul Ther Clin Pharmacol
Vol 19(1):e41-e50 when the main findings were reported. This second paper gives greater focus to the methodologies employed and data analysis from the second phase.

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European Journal of Paediatric Neurology
Received 21 March 2013; accepted 24 March 2013. published online 24 April 2013.

13. **DIAGNOSIS OF FETAL ALCOHOL SYNDROME (FAS): GERMAN GUIDELINE VERSION 2013**

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Affiliations
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German Society for Pediatrics, Deutsche Gesellschaft für Kinder- und Jugendmedizin, DGKJ, Berlin, Germany
Society for Neuropediatrics, Gesellschaft für Neuropädiatrie, GNP, Berlin, Germany

**ABSTRACT**

**Background:** Fetal alcohol syndrome (FAS) belongs to the umbrella of fetal alcohol spectrum disorders (FASD) and affects 0.02–0.8% of all annual births with a high number of undetected cases. FAS has severe and life determining consequences for the affected individual and his family.

**Aim:** The aim of the German guideline version 2013 is to provide objectively evaluated, evidence-based, clinically relevant and easily applicable diagnostic criteria for the full picture FAS.

**Methods:** A systematic literature review (2001–2011), analysis of international guidelines and focused hand search were performed. Based on the evidence-assessed literature the multidisciplinary guideline group (14 German Professional Societies, the patient support group “FASD Germany” and 15 additional experts) consented recommendations for the diagnosis of FAS.

**Results:** The following diagnostic criteria for FAS resulted: at least one deficit of growth, three defined facial characteristics and one functional or structural anomaly of the central nervous system. Confirmation of intrauterine alcohol exposure is not considered as a prerequisite for FAS diagnosis.

**Conclusion:** The German guideline presented here constitutes an unbiased evidence-based approach to the diagnosis of patients with fetal alcohol syndrome. It includes a practical pocket guide FAS for a quick overview of the diagnostic workup in everyday clinical work.

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Lee JY, Ko YJ, Park SM.
Department of Obstetrics and Gynaecology, Seoul National University College of Medicine, Seoul, Republic of Korea.

ABSTRACT

Objective: To identify factors associated with smoking and heavy alcohol consumption among women of reproductive age.

Study design: Cross-sectional study.

Methods: Data from 5031 women aged 20-49 years who participated in the Fourth Korean National Health and Nutrition Examination Survey 2007-2009 were analysed. Variables were classified as sociodemographic factors, psychological factors, gynaecological factors and chronic conditions. Factors that influence high-risk behaviours associated with adverse pregnancy outcomes were identified using multiple logistic regression analysis.

Results: Among women of reproductive age, prevalence rates of smoking, heavy alcohol consumption and both were 7.3%, 21.4% and 4.3%, respectively. Among the sociodemographic factors, young age, a lower level of education and unmarried status were more likely to be associated with high-risk behaviours such as smoking, heavy alcohol consumption and both. Psychological factors such as stress intensity and suicidal ideation were also significantly associated with all the above-mentioned high-risk behaviours. In addition, an association was found between high-risk behaviours and oral contraceptive use.

Conclusions: Identifying the factors associated with high-risk behaviours may help in the design of interventions to decrease the prevalence of smoking and heavy alcohol consumption. Population-level reduction of these high-risk behaviours among women of reproductive age may improve pregnancy outcomes and also decrease the prevalence of chronic diseases, including cancer, in the long term.


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15. ALCOHOL EXPOSURE DURING LATE OVINE GESTATION ALTERS FETAL LIVER IRON HOMEOSTASIS WITHOUT APPARENT DYSMORPHOLOGY

Sozo F, Dick AM, Bensley JG, Kenna K, Brien JF, Harding R, De Matteo R.
Monash University, South Africa.

ABSTRACT

High levels of alcohol (ethanol) exposure during fetal life can affect liver development and can increase susceptibility to infection after birth. Our aim was to determine the effects of a moderate level of ethanol exposure in late gestation on the morphology, iron status and inflammatory status of the ovine fetal liver. Pregnant ewes were chronically catheterized at 91 days of gestation (DG; term ~145DG) for daily I.V. infusion of ethanol (0.75g/kg maternal body weight, n=8) or saline (n=7) over 1h from 95-133DG. At necropsy (134DG), fetal livers...
were collected for analysis. Liver weight, general liver morphology, hepatic cell proliferation and apoptosis, perivascular collagen deposition, and interleukin (IL)-1β, IL-6 or IL-8 mRNA levels were not different between groups. However, ethanol exposure led to significant decreases in hepatic content of ferric iron and gene expression of the iron-regulating hormone hepcidin and tumor necrosis factor (TNF)-α (all P<0.05). In the placenta, there was no difference in transferrin receptor, divalent metal transporter 1 and ferritin mRNA levels; however, ferroportin mRNA levels were increased in ethanol-exposed animals (P<0.05) and ferroportin protein tended to be increased (P=0.054). Plasma iron concentration was not different between control and ethanol-exposed groups; control fetuses had significantly higher iron concentrations than their mothers, whereas maternal and fetal iron concentrations were similar in ethanol-exposed animals. We conclude that daily ethanol exposure during the third-trimester-equivalent in sheep does not alter fetal liver morphology; however, decreased fetal liver ferric iron content and altered hepcidin and ferroportin gene expression indicate that iron homeostasis is altered.


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16. PREVALENCE OF FETAL ALCOHOL SYNDROME AND MATERNAL CHARACTERISTICS IN A SAMPLE OF SCHOOLCHILDREN FROM A RURAL PROVINCE OF CROATIA
Petković G, Barišić I.
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ABSTRACT
Fetal alcohol syndrome (FAS) is a congenital syndrome caused by maternal alcohol consumption during pregnancy and is entirely preventable by abstinence from alcohol drinking during this time. Little is known about the prevalence of FAS and maternal alcohol consumption during pregnancy in Western countries. We present the results of FAS/partial fetal alcohol syndrome (PFAS) prevalence study and maternal characteristics in a sample of schoolchildren from a rural province of Croatia. This study involved seven elementary schools with 1,110 enrolled children attending 1st to 4th grade and their mothers. We used an active case ascertainment method with passive parental consent and Clarified IOM criteria. The investigation protocol involved maternal data collection and clinical examination of children. Out of 1,110 mothers, 917 (82.6%) answered the questionnaire. Alcohol exposure during pregnancy was admitted by 11.5%, regular drinking by 4.0% and binge drinking by 1.4% of questioned mothers. Clinical examination involved 824 (74.2%) schoolchildren and disclosed 14 (1.7%) with clinical signs of FAS and 41 (5.0%) of PFAS. The observed FAS prevalence, based on 74.2% participation rate, was 16.9, PFAS 49.7 and combined prevalence was 66.7/1,000 examined schoolchildren. This is the first FAS prevalence study based on active ascertainment among schoolchildren and pregnancy alcohol drinking analysis performed in a rural community of Croatia and Europe. High prevalence of FAS/PFAS and pregnancy alcohol consumption observed in this study revealed that FAS is serious health problem in rural regions as well as a need to develop future studies and preventive measures for pregnancy alcohol drinking and FASD.


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17. **BINGE ALCOHOL-INDUCED ALTERATIONS IN BDNF AND GDNF EXPRESSION IN CENTRAL EXTENDED AMYGDALA AND PYRIFORM CORTEX ON INFANT RATS**

Balaszczuk V, Bender C, Pereno G, Beltramino CA. Instituto de Investigación Médica Mercedes y Martín Ferreyra, Friuli 2434, 5016 Córdoba, Argentina; Departamento de Biología Evolutiva Humana, Facultad de Psicología, Universidad Nacional de Córdoba, 5000 Córdoba, Argentina. Electronic address: vbalaszczuk@psyche.unc.edu.ar.

**ABSTRACT**

Mothers who consume alcohol during pregnancy may cause a neurotoxic syndrome termed fetal alcohol spectrum disorder (FASD) in the offspring, which includes cognitive deficits and emotional/social disturbances. These alterations are thought to be caused, at least in part, by alcohol-induced imbalance in neurotrophic factor levels, which are critically involved in normal neurodevelopment. Our goal was to study whether brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) expression were affected by alcohol in central extended amygdala (CEXA) and pyriform cortex (Pyr), structures strongly involved in emotional/social behaviors. Further, we evaluated how these changes could be related to blood and brain alcohol concentrations. Postnatal day (PND) pups at 7, 15 and 20-days old were administered alcohol (2.5g/kg s.c. at 0 and 2h) or saline. Immunohistochemistry was used to detect the expression of BDNF and GDNF at 2, 12 and 24h after drug administration. Also, gas chromatography was bused to measure blood alcohol levels (BALs) and brain alcohol levels (BrALs) at each hour, from 2 to 8h after the second alcohol administration. Results showed: (1) alcohol-induced enhancement of BDNF positive cells on PND 7 and 20, a decrease on PND 15 in the CEXA, and no changes in the Pyr on PND 7 and 20, but a diminished on PND 15; (2) GDNF positive cells rise after alcohol administration for the three ages in the CEXA and Pyr except on PND 15, where there was a decline; and (3) pharmacokinetics analysis demonstrated age-related differences showing equal BALs on PND 7 and 20 but higher BALs on PND 15. In contrast, BrALs were higher on PND 7 than 15 and 20. Hence, BALs may not be predictive of BrALs in postnatal rats. Furthermore, we did not find a relationship between age in pharmacokinetic differences and neurotrophins response. In conclusion, the CEXA and Pyr are brain structures sensitive to alcohol-induced imbalance in neurotrophic factors expression; and BALs are not a mirror of BrALs.


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18. **ALTERED ACCURACY OF SACCADIC EYE MOVEMENTS IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER**

Angelina Paolozza, Rebecca Titman, Donald Brien, Douglas P. Munoz, James N. Reynolds* Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada

*James Reynolds, PhD, Botterell Hall, Queen's University, 18 Stuart Street, Kingston, ON, Canada K7L 3N6; Tel.: 613-533-6946; Fax: 613-533-6840; E-mail: jnr@queensu.ca

**ABSTRACT**

**Background:** Prenatal exposure to alcohol is a major, preventable cause of neurobehavioral dysfunction in children worldwide. The measurement and quantification of saccadic eye
movements is a powerful tool for assessing sensory, motor, and cognitive function. The quality of the motor process of an eye movement is known as saccade metrics. Saccade accuracy is 1 component of metrics, which to function optimally requires several cortical brain structures as well as an intact cerebellum and brain-stem. The cerebellum has frequently been reported to be damaged by prenatal alcohol exposure. This study, therefore, tested the hypothesis that children with fetal alcohol spectrum disorder (FASD) will exhibit deficits in the accuracy of saccades.

**Methods:** A group of children with FASD (n = 27) between the ages of 8 and 16 and typically developing control children (n = 27) matched for age and sex, completed 3 saccadic eye movement tasks of increasing difficulty. Eye movement performance during the tasks was captured using an infrared eye tracker. Saccade metrics (e.g., velocity, amplitude, accuracy) were quantified and compared between the 2 groups for the 3 different tasks.

**Results:** Children with FASD were more variable in saccade endpoint accuracy, which was reflected by statistically significant increases in the error of the initial saccade endpoint and the frequency of additional, corrective saccades required to achieve final fixation. This increased variability in accuracy was amplified when the cognitive demand of the tasks increased. Children with FASD also displayed a statistically significant increase in response inhibition errors.

**Conclusions:** These data suggest that children with FASD may have deficits in eye movement control and sensory-motor integration including cerebellar circuits, thereby impairing saccade accuracy.

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**19. LONG LASTING ALTERATIONS TO DNA METHYLATION AND NCRNAS MAY UNDERLIE THE EFFECTS OF FETAL ALCOHOL EXPOSURE**

**ABSTRACT**
Fetal Alcohol Spectrum Disorders (FASD) are characterized by life long changes in gene expression, neurodevelopment, and behavior. What mechanisms initiate and maintain these changes are not known, but current research suggests a role for alcohol induced epigenetic changes. In this report we assessed alterations to adult mouse brain tissue by assaying DNA cytosine methylation and small noncoding RNA (ncRNA) expression, specifically the microRNA (miRNA) and small nucleolar RNA (snoRNA) subtypes. We found long lasting alterations in DNA methylation as a result of fetal alcohol exposure, specifically in the imprinted regions of the genome harboring ncRNAs and sequences interacting with regulatory proteins. A large number of major nodes from the identified networks, such as Pten signaling, contained CTCF binding sites in their promoters, illustrating the functional consequences of alcohol induced changes to DNA methylation. Next, we assessed ncRNA expression using two independent array platforms and qPCR. The results identified 34 genes that are targeted by the deregulated miRNAs. Of these, four (Pten, Nmnat1, Slitrk2, and Otx2) were viewed critical in the context of FASD given their roles in the brain. Furthermore, ~20% of the altered ncRNAs mapped to three imprinted regions: Snrpn-Ube3a, Dlk1-Dio3, and Sfmbt2, which showed differential methylation and have been previously implicated in neurodevelopmental disorders. The findings of this report help to expand on the mechanisms behind the long lasting changes in the brain transcriptome of FASD individuals. The
observed changes may contribute to the initiation and maintenance of the long lasting effect of alcohol.

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20. ANANDAMIDE-CB1 RECEPTOR SIGNALING CONTRIBUTES TO POSTNATAL ETHANOL-INDUCED NEONATAL NEURODEGENERATION, ADULT SYNAPTIC, AND MEMORY DEFICITS
Subbanna S, Shivakumar M, Psychoyos D, Xie S, Basavarajappa BS.  
Division of Analytical Psychopharmacology, Nathan Kline Institute for Psychiatric Research, Orangeburg, New York 10962, Institute of Biosciences and Technology, Texas A & M University Health Science Center, Houston, Texas 77030, and New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA.

ABSTRACT
The transient exposure of immature rodents to ethanol during postnatal day 7 (P7), which is comparable with the third trimester in human pregnancy, induces synaptic dysfunctions. However, the molecular mechanisms underlying these dysfunctions are still poorly understood. Although the endocannabinoid system has been shown to be an important modulator of ethanol sensitivity in adult mice, its potential role in synaptic dysfunctions in mice exposed to ethanol during early brain development is not examined. In this study, we investigated the potential role of endocannabinoids and the cannabinoid receptor type 1 (CB1R) in neonatal neurodegeneration and adult synaptic dysfunctions in mice exposed to ethanol at P7. Ethanol treatment at P7, which induces neurodegeneration, increased anandamide (AEA) but not 2-arachidonylglycerol biosynthesis and CB1R protein expression in the hippocampus and cortex, two brain areas that are important for memory formation and storage, respectively. N-Arachidonoyl phosphatidylethanolamine-phospholipase D (NAPE-PLD), glycerophosphodiesterase (GDE1), and CB1R protein expression were enhanced by transcriptional activation of the genes encoding NAPE-PLD, GDE1, and CB1R proteins, respectively. In addition, ethanol inhibited ERK1/2 and AKT phosphorylation. The blockade of CB1Rs before ethanol treatment at P7 relieved ERK1/2 but not AKT phosphorylation and prevented neurodegeneration. CB1R knock-out mice exhibited no ethanol-induced neurodegeneration and inhibition of ERK1/2 phosphorylation. The protective effects of CB1R blockade through pharmacological or genetic deletion resulted in normal adult synaptic plasticity and novel object recognition memory in mice exposed to ethanol at P7. The AEA/CB1R/pERK1/2 signaling pathway may be directly responsible for the synaptic and memory deficits associated with fetal alcohol spectrum disorders.

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21. ETHANOL ALTERS THE BALANCE OF SOX2, OCT4, AND NANOG EXPRESSION IN DISTINCT SUBPOPULATIONS DURING DIFFERENTIATION OF EMBRYONIC STEM CELLS
Ogony JW, Malahias E, Vadigepalli R, Anni H.
Preliminary results from this work have been presented at the 35th Research Society on Alcoholism Annual Meeting, 2012, San Francisco, California, USA.

ABSTRACT
The transcription factors Sox2, Oct4, and Nanog regulate within a narrow dose-range embryonic stem (ES) cell pluripotency and cell lineage commitment. Excess of Oct4 relative to Sox2 guides cells to mesendoderm (ME), while abundance of Sox2 promotes neuroectoderm (NE) formation. Literature does not address whether ethanol interferes with these regulatory interactions during neural development. We hypothesized that ethanol exposure of ES cells in early differentiation causes an imbalance of Oct4 and Sox2 that diverts cells away from NE to ME lineage, consistent with the teratogenesis effects caused by prenatal alcohol exposure. Mouse ES cells were exposed to ethanol (0, 25, 50, and 100 mM) during retinoic acid (10 nM)-directed differentiation to NE for 0-6 days, and the expression of Sox2, Oct4, and Nanog was measured in single live cells by multiparametric flow cytometry, and the cellular phenotype was characterized by immunocytochemistry. Our data showed an ethanol dose- and time-dependent asymmetric modulation of Oct4 and Sox2 expression, as early as after 2 days of exposure. Single-cell analysis of the correlated expression of Sox2, Oct4, and Nanog revealed that ethanol promoted distinct subpopulations with a high Oct4/Sox2 ratio. Ethanol-exposed cells differentiated to fewer β-III tubulin-immunoreactive cells with an immature neuronal phenotype by 4 days. We interpret these data as suggesting that ethanol diverted cells in early differentiation from the NE fate toward the ME lineage. Our results provide a novel insight into the mode of ethanol action and opportunities for discovery of prenatal biomarkers at early stages.

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22. BASAL REGULATION OF HPA AND DOPAMINE SYSTEMS IS ALTERED DIFFERENTIALLY IN MALES AND FEMALES BY PRENATAL ALCOHOL EXPOSURE AND CHRONIC VARIABLE STRESS
Uban KA, Comeau WL, Ellis LA, Galea LA, Weinberg J.
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ABSTRACT
Effects of prenatal alcohol exposure (PAE) on central nervous system function include an increased prevalence of mental health problems, including substance use disorders (SUD). The hypothalamic-pituitary-adrenal (HPA) and dopamine (DA) systems have overlapping neurocircuitsries and are both implicated in SUD. PAE alters both HPA and dopaminergic activity and regulation, resulting in increased HPA tone and an overall reduction in tonic DA activity. However, effects of PAE on the interaction between HPA and DA systems have not been investigated. The present study examined PAE effects on basal regulation of central stress and DA systems in key brain regions where these systems intersect. Adult Sprague-Dawley male and female offspring from prenatal alcohol-exposed (PAE), pairfed (PF), and ad libitum-fed control (C) groups were subjected to chronic variable stress (CVS) or remained as
a no stress (non-CVS) control group. Corticotropin releasing hormone (CRH) mRNA, as well as glucocorticoid and DA receptor (DA-R) expression were measured under basal conditions 24h following the end of CVS. We show, for the first time, that regulation of basal HPA and DA systems, and likely, HPA-DA interactions, are altered differentially in males and females by PAE and CVS. PAE augmented the typical attenuation in weight gain during CVS in males and caused increased weight loss in females. Increased basal corticosterone levels in control, but not PAE, females suggest that PAE alters the profile of basal hormone secretion throughout CVS. CVS downregulated basal CRH mRNA in the prefrontal cortex and throughout the bed nucleus of the stria terminalis (BNST) in PAE females but only in the posterior BNST of control females. PAE males and females exposed to CVS exhibited more widespread upregulation of basal mineralocorticoid receptor mRNA throughout the hippocampus, and an attenuated decrease in DA-R expression throughout the nucleus accumbens and striatum compared to CVS-exposed control males and females. Overall, these findings enhance our understanding of PAE effects on the cross-talk between HPA and DA systems, and provide insight into possible mechanisms underlying mental health problems that are related to stress and DA signaling, including SUD, which have a high prevalence among individuals with FASD.


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23. COST OF FETAL ALCOHOL SPECTRUM DISORDER DIAGNOSIS IN CANADA
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ABSTRACT
Background: Fetal Alcohol Spectrum Disorder (FASD) is underdiagnosed in Canada. The diagnosis of FASD is not simple and currently, the recommendation is that a comprehensive, multidisciplinary assessment of the individual be done. The purpose of this study was to estimate the annual cost of FASD diagnosis on Canadian society.

Methods: The diagnostic process breakdown was based on recommendations from the Fetal Alcohol Spectrum Disorder Canadian Guidelines for Diagnosis. The per person cost of diagnosis was calculated based on the number of hours (estimated based on expert opinion) required by each specialist involved in the diagnostic process. The average rate per hour for each respective specialist was estimated based on hourly costs across Canada. Based on the existing clinical capacity of all FASD multidisciplinary clinics in Canada, obtained from the 2005 and 2011 surveys conducted by the Canada Northwest FASD Research Network, the number of FASD cases diagnosed per year in Canada was estimated. The per person cost of FASD diagnosis was then applied to the number of cases diagnosed per year in Canada in order to calculated the overall annual cost.

Results: Using the most conservative approach, it was estimated that an FASD evaluation requires 32 to 47 hours for one individual to be screened, referred, admitted, and diagnosed with an FASD diagnosis, which results in a total cost of $3,110 to $4,570 per person. The total cost of FASD diagnostic services in Canada ranges from $3.6 to $5.2 million (lower estimate), up to $5.0 to $7.3 million (upper estimate) per year.
**Discussion:** As a result of using the most conservative approach, the cost of FASD diagnostic services presented in the current study is most likely underestimated. The reasons for this likelihood and the limitations of the study are discussed.

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24. **MATURATION OF THE ADOLESCENT BRAIN**
Saint James School of Medicine, Kralendijk, Bonaire, The Netherlands.

**ABSTRACT**
Adolescence is the developmental epoch during which children become adults - intellectually, physically, hormonally, and socially. Adolescence is a tumultuous time, full of changes and transformations. The pubertal transition to adulthood involves both gonadal and behavioral maturation. Magnetic resonance imaging studies have discovered that myelogenesis, required for proper insulation and efficient neurocybernetics, continues from childhood and the brain's region-specific neurocircuitry remains structurally and functionally vulnerable to impulsive sex, food, and sleep habits. The maturation of the adolescent brain is also influenced by heredity, environment, and sex hormones (estrogen, progesterone, and testosterone), which play a crucial role in myelination. Furthermore, glutamatergic neurotransmission predominates, whereas gamma-aminobutyric acid neurotransmission remains under construction, and this might be responsible for immature and impulsive behavior and neurobehavioral excitement during adolescent life. The adolescent population is highly vulnerable to driving under the influence of alcohol and social maladjustments due to an immature limbic system and prefrontal cortex. Synaptic plasticity and the release of neurotransmitters may also be influenced by environmental neurotoxins and drugs of abuse including cigarettes, caffeine, and alcohol during adolescence. Adolescents may become involved with offensive crimes, irresponsible behavior, unprotected sex, juvenile courts, or even prison. According to a report by the Centers for Disease Control and Prevention, the major cause of death among the teenage population is due to injury and violence related to sex and substance abuse. Prenatal neglect, cigarette smoking, and alcohol consumption may also significantly impact maturation of the adolescent brain. Pharmacological interventions to regulate adolescent behavior have been attempted with limited success. Since several factors, including age, sex, disease, nutritional status, and substance abuse have a significant impact on the maturation of the adolescent brain, we have highlighted the influence of these clinically significant and socially important aspects in this report.

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COMMONALITY IN DOWN AND FETAL ALCOHOL SYNDROMES

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ABSTRACT

Background: Down syndrome (DS) and Fetal Alcohol Syndrome (FAS) are two leading causes of birth defects with phenotypes ranging from craniofacial abnormalities to cognitive impairment. Despite different origins, we report that in addition to sharing many phenotypes, DS and FAS may have common underlying mechanisms of development.

Methods: Literature was surveyed for DS and FAS as well as mouse models. Gene expression and apoptosis were compared in embryonic mouse models of DS and FAS by qPCR, immunohistochemical and immunofluorescence analyses. The craniometry was examined using MicroCT at postnatal day 21.

Results: A literature survey revealed over 20 comparable craniofacial and structural deficits in both humans with DS and FAS and corresponding mouse models. Similar phenotypes were experimentally found in pre- and postnatal craniofacial and neurological tissues of DS and FAS mice. Dysregulation of two genes, Dyrk1a and Rcan1, key to craniofacial and neurological precursors of DS, was shared in craniofacial precursors of DS and FAS embryos. Increased cleaved caspase 3 expression was also discovered in comparable regions of the craniofacial and brain precursors of DS and FAS embryos. Further mechanistic studies suggested overexpression of trisomic Ttc3 in DS embryos may influence nuclear pAkt localization and cell survival.

Conclusions: This first and initial study indicates that DS and FAS share common dysmorphologies in humans and animal models. This work also suggests common mechanisms at cellular and molecular levels that are disrupted by trisomy or alcohol consumption during pregnancy and lead to craniofacial and neurological phenotypes associated with DS or FAS. Birth Defects Research (Part A) 97:187–197, 2013


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26. AEROBIC EXERCISE MODERATES THE EFFECT OF HEAVY ALCOHOL CONSUMPTION ON WHITE MATTER DAMAGE

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ABSTRACT

Background: Chronic alcohol abuse is related to numerous deleterious neurobiological consequences, including loss of gray matter, damage to white matter (WM), and impairment of cognitive and motor functions. Aerobic exercise has been demonstrated to slow cognitive decline and decrease the negative neural changes resulting from normal aging and from several diseases. It is possible that exercise may also prevent or repair alcohol-related neurological damage. This study tested the hypothesis that aerobic exercise protects WM in anterior and dorsal areas of the brain from damage related to heavy alcohol use.

Methods: Sixty individuals underwent a diffusion tensor imaging session and completed measures of alcohol consumption, loss of control over drinking, and aerobic exercise participation. Analyses examined the relationship of exercise, alcohol, and their interaction to fractional anisotropy (FA) in the superior longitudinal fasciculus (SLF), external capsule (EC), superior and anterior corona radiata, and fornix. The relationship of aerobic exercise and alcohol consumption to self-reported loss of control over drinking were also examined.

Results: A significant interaction was observed between alcohol consumption and aerobic exercise participation on FA in the SLF and EC. In the models examining loss of control over drinking, a significant interaction between aerobic exercise and alcohol consumption was observed, such that alcohol consumption was associated with loss of control more strongly for low exercisers than high exercisers.

Conclusions: These results indicate that the association between heavy alcohol consumption and WM damage in the EC and SLF and the association between alcohol consumption and loss of control over drinking are greater among individuals who do not exercise regularly. These results are consistent with the notion that exercise may protect WM integrity from alcohol-related damage.


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27. **DIFFUSION TENSOR IMAGING CORRELATES OF SACCADIC REACTION TIME IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER**
Green CR, Lebel C, Rasmussen C, Beaulieu C, Reynolds JN.
The Centre for Neuroscience Studies, Queen’s University, Kingston, ON, Canada; Department of Biomedical and Molecular Sciences, Queen’s University, Kingston, ON, Canada.

**ABSTRACT**

**Background:** Eye movement tasks provide a simple method for inferring structural or functional brain deficits in neurodevelopmental disorders. Oculomotor control is impaired in children with fetal alcohol spectrum disorder (FASD), yet the neuroanatomical substrates underlying this are not known. Regions of white matter have been shown by diffusion tensor imaging (DTI) to be different in FASD and thus may play a role in the delayed saccadic eye movements. The objective of this study was to correlate oculomotor performance with regional measures of DTI-derived white matter anisotropy in children with FASD.

**Methods:** Fourteen children (8 to 13 years) with FASD were recruited for oculomotor assessment and DTI. Eye movement control was evaluated using the pro- and antisaccade tasks, in which subjects look at (prosaccade) or away from (antisaccade) a peripheral target. Saccadic reaction time (SRT; time for subjects to move their eyes after the target appears) and direction errors (saccades made in the incorrect direction relative to the instruction) were measured and correlated to fractional anisotropy (FA) on a voxel-by-voxel basis across the whole brain white matter.

**Results:** A significant positive correlation was observed between antisaccade SRT and FA in a large cluster containing anterior and posterior sections of the corpus callosum just to the right of the midline; prosaccade SRT and FA correlated positively in the genu of the corpus callosum and the right inferior longitudinal fasciculus (ILF), and correlated negatively in the left cerebellum.

**Conclusions:** The negative correlation for prosaccade SRT and cerebellum demonstrated that individuals with slower reaction times had lower FA values relative to their faster responding counterparts, a finding that implicates cerebellar dysfunction as a significant contributor to deficits in oculomotor control. The higher FA in the corpus callosum and ILF corresponding to longer reaction times for both pro- and antisaccade was opposite to what was expected, but nonetheless implies that altered brain structure in these regions underlies deficits in oculomotor control.


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28. **COMMENTS AND REFLECTIONS ON ETHICS IN SCREENING FOR BIOMARKERS OF PRENATAL ALCOHOL EXPOSURE**
Neuroethics Research Unit, Institut de recherches cliniques de Montréal, Montreal, Quebec, Canada.

**ABSTRACT**

Early identification of and intervention for fetal alcohol spectrum disorder (FASD) has been shown to optimize outcomes for affected individuals. Detecting biomarkers of prenatal
alcohol exposure (PAE) in neonates may assist in the identification of children at risk of FASD enabling targeted early interventions. Despite these potential benefits, complicated ethical issues arise in screening for biomarkers of PAE and these must be addressed prior to the implementation of screening programs. Here, we identify and comment, based on a North American perspective, on concerns raised in the current ethical, social, and legal literature related to meconium screening for PAE. Major ethical concerns revolve around the targeting of populations for PAE screening, consent and respect for persons, stigma and participation rates, the cost-benefit analysis of a screening program, consequences of false-positive and false-negative test results, confidentiality and appropriate follow-up to positive screen results, and the use of screen results for criminal prosecution. We identify gaps in the literature on screening for PAE, most notably related to a lack of stakeholder perspectives (e.g., parents, healthcare providers) about screening and the ethical challenges it presents.


29. GETTING IT RIGHT FROM BIRTH TO KINDERGARTEN: WHAT'S NEW IN THE ROURKE BABY RECORD?
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ABSTRACT
Objective: To provide an overview of the 2011 edition of the Rourke Baby Record (RBR), which includes developments on its website and new related initiatives that incorporate recent literature on preventive health care for children aged 0 to 5 years.

Quality of Evidence: As in past RBR editions, recommendations are identified as supported by good, fair, or consensus evidence, according to the classifications adopted by the Canadian Task Force on Preventive Health Care in 2011.

Main Message: New information and recommendations are given for growth monitoring, nutrition, physical examination maneuvers, and immunizations for varicella, pneumococcus, meningococcus, and rotavirus. There is now good evidence for converting to the World Health Organization growth charts adapted for Canada, universal newborn hearing screening, and use of immunization pain reduction strategies. Anticipatory guidance has been updated for safe sleeping, health supervision of foster children, fetal alcohol spectrum disorder, lead and anemia screening risk factors, and dental care and oral health. New RBR website items include a parent resources section, modifications for unique populations such as those living in Nunavut, a version of the RBR that highlights what has changed from the 2009 version for quick viewing, and an expansion of the "Explore the RBR" feature with associated links to relevant information. A one-visit-per-page format is now available. The 2011 RBR is endorsed by the College of Family Physicians of Canada and the Canadian Paediatric Society, and is available in English and French in national and Ontario versions.


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ABSTRACT

Summary: The aims of the research were to:

- assess justice professionals' awareness and knowledge of FASD;
- assess the perceived impact of FASD on practice within the justice system;
- and identify the information needs relating to FASD for the justice system in Western Australia.

Separate surveys were undertaken within four sectors of the WA justice system, this included: justice system; judicial, legal, corrections and police. Even though response rates to the survey were low (23 per cent), responses were relatively consistent across sectors. Over 90 per cent of judicial officers, lawyers and Department of Corrective Services (DCS) staff, and almost 75 per cent of police officers were aware of Fetal Alcohol Syndrome (FAS). Awareness of Fetal Alcohol Spectrum Disorders (FASD) was lower than for FAS across all sectors.

Each survey assessed:

- socio-demographic characteristics;
- knowledge of FASD;
- sources of information about FASD; and
- information and training needs.

Outcomes: More than 75 per cent of judicial officers, 85 per cent of lawyers and DCS staff, and almost 50 per cent of police officers perceived FASD as relevant to their work.

Knowledge about FASD was highest amongst DCS staff, who were more likely to report having a good understanding of how FASD affects children and adults (44 per cent) rather than participants from the other sectors.

Almost 80% of all participants agreed that FASD is a real condition. However when participants were asked to describe their understanding of FASD differences were found between the judicial, legal and corrections sectors in being able to identify key aspects of FASD. Across all four sectors of the justice system most participants reported only a basic understanding of FASD and how it affects individuals.

Participants across all sectors reported recognition of suspected FASD among individuals they dealt with, and raised concerns about the management of these individuals within the justice system.

Approximately 60 per cent of participants from the judicial and legal sectors, 67 per cent of staff from the corrections sector, and 43 per cent from the police sector reported ever dealing with a person who may have been affected by FASD.

Most participants (72 per cent) indicated a need for more information about FASD, including how to improve the identification of individuals in need of specialist assessment, and
guidelines on how to deal with people with FASD. The research also found strong support across all sectors for the development of appropriate alternative or diversionary sentencing options for people with FASD.

Critically the research highlights the importance of access to services and programs for the appropriate diagnosis and management of people with FASD both within the justice system and the wider community. There was widespread agreement (judicial officers 79 per cent and lawyers 92 per cent) that the assessment and diagnosis of FASD would improve the possibilities for people with FASD and would prevent their continued engagement with the justice system over time.

Overall the research found that the WA justice system is poorly prepared and resourced to consider the neurocognitive impairments associated with FASD and that training and resources for those working in the justice system are required.

**Recommendations:** The research makes the following recommendations for the effective management of individuals with FASD within the justice system including:

- training and education to improve awareness of the specific impairments associated with FASD that impact on the treatment of individuals with FASD across the justice system of WA;
- training and education to describe how individuals with FASD should be managed;
- improved methods for the identification of individuals with FASD and referral for specialist assessment;
- identified specialist diagnostic services for FASD;
- information to enable the appropriate recognition and management of an individual’s neurocognitive and behavioural impairments within the justice system;
- effective alternative sentencing options;
- programs and resources to provide appropriate treatment for the underlying fixed brain injury; and
- management and supportive environments specific to the needs of individuals with FASD.

Ultimately, the findings from this work emphasise the need for change within and outside of the justice system to prevent the continued engagement of people with FASD with the justice system. Participants recognised the importance of a co-ordinated cross-sector approach to the development of policies to improve both the recognition of, and response to, FASD.

**Further research:** The strong engagement established among project partners provides a valuable foundation for continued collaboration to facilitate the development of locally appropriate resources and interventions to enable the more effective identification and management of people with FASD in the WA justice system.

There is also a need to develop effective early intervention programs to prevent children and youth with FASD appearing, or reappearing, before the courts.

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**31. CYCLIC ADENOSINE MONOPHOSPHATE AND BRAIN-DERIVED NEUROTROPHIC FACTOR DECREASED OXIDATIVE STRESS AND APOPTOSIS IN DEVELOPING HYPOTHALAMIC NEURONAL CELLS: ROLE OF MICROGLIA**

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ABSTRACT

Background: We have previously shown that ethanol (EtOH) increases cellular apoptosis to developing neurons via the effects on oxidative stress of neurons directly and via increasing production of microglia-derived factors. To study further the mechanism of EtOH action on neuronal apoptosis, we determined the effects of 2 well-known PKA activators, dibutyryl cAMP (dbcAMP) and brain-derived neurotrophic factor (BDNF), on EtOH-activated oxidative stress and apoptotic processes in the hypothalamic neurons in the presence and absence of microglial cells' influence.

Methods: In enriched neuronal cells from fetal rat hypothalami treated with EtOH or with conditioned medium from EtOH-treated microglia, we measured cellular apoptosis by the free nucleosome assay and the levels of cAMP, BDNF, O2-, reactive oxygen species (ROS), nitrite, glutathione (GSH), and catalase following treatment with EtOH or EtOH-treated microglial culture conditioned medium. Additionally, we tested the effectiveness of dbcAMP and BDNF in preventing EtOH or EtOH-treated microglial conditioned medium on cellular apoptosis and oxidative stress in enriched hypothalamic neuronal cell in primary cultures.

Results: Neuronal cell cultures following treatment with EtOH or EtOH-activated microglial conditioned medium showed decreased production levels of cAMP and BDNF. EtOH also increased apoptotic death as well as oxidative status, as demonstrated by higher cellular levels of oxidants but lower levels of antioxidants, in neuronal cells. These effects of EtOH on oxidative stress and cell death were enhanced by the presence of microglia. Treatment with BDNF or dbcAMP decreased EtOH or EtOH-activated microglial conditioned medium-induced changes in the levels of intracellular free radicals, ROS and O2-, nitrite, GSH, and catalase.

Conclusions: These data support the possibility that EtOH by acting directly and via increasing the production of microglial-derived factors reduces cellular levels of cAMP and BDNF to increase cellular oxidative status and apoptosis in hypothalamic neuronal cells in primary cultures.


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mechanism is unclear. Alcohol exposure has been shown to alter the expression of genes that regulate the fate, survival, migration and differentiation of pyramidal and granule cells. Undermining this process might compromise hippocampal development underlying the learning and memory deficits known in Fetal Alcohol Spectrum Disorders (FASD). We have previously demonstrated that DNA methylation was programmed along with neural tube development. Here, we demonstrated that DNA methylation program (DMP) proceeded along with hippocampal neuronal differentiation and maturation, and how this DMP was affected by fetal alcohol exposure. C57BL/6 mice were treated with 4% v/v ethanol through a liquid diet along with pair-fed and chow-fed controls from gestation day (E) 7 to E16. We found that a characteristic DMP, including 5-methylcytidine (5mC), 5-hydroxymethylcytidine (5hmC) and their binding proteins, led the hippocampal neuronal differentiation and maturation spatiotemporally as indicated by their phenotypic marks in the CA and DG pre- and post-natally. Alcohol hindered the acquisition and progression of methylation marks, and altered the chromatin translocation of these marks in the nucleus, which was correlated with developmental retardation.

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http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0060503

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33. PRENATAL ETHANOL EXPOSURE CAUSES GLUCOSE INTOLERANCE WITH INCREASED HEPATIC GLUCONEOGENESIS AND HISTONE DEACETYLASES IN ADULT RAT OFFSPRING: REVERSAL BY TAUROUSODEOXYCHOLIC ACID
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Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada
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Department of Physiology, University of Manitoba, Winnipeg, Manitoba, Canada

ABSTRACT
Prenatal ethanol exposure results in increased glucose production in adult rat offspring and this may involve modulation of protein acetylation by cellular stress. We used adult male offspring of dams given ethanol during gestation days 1–7 (early), 8–14 (mid) and 15–21 (late) compared with those from control dams. A group of ethanol offspring was treated with tauroursodeoxycholic acid (TUDCA) for 3 weeks. We determined gluconeogenesis, phosphoenolpyruvate carboxykinase (PEPCK), glucose-6-phosphatase, hepatic free radicals, histone deacetylases (HDAC), acetylated foxo1, acetylated PEPCK, and C/EBP homologous protein as a marker of endoplasmic reticulum stress. Prenatal ethanol during either of the 3 weeks of pregnancy increased gluconeogenesis, gluconeogenic genes, oxidative and endoplasmic reticulum stresses, sirtuin-2 and HDAC3, 4, 5, and 7 in adult offspring. Conversely, prenatal ethanol reduced acetylation of foxo1 and PEPCK. Treatment of adult ethanol offspring with TUDCA reversed all these abnormalities. Thus, prenatal exposure of rats to ethanol results in long lasting oxidative and endoplasmic reticulum stresses explaining increased expression of gluconeogenic genes and HDAC proteins which, by deacetylating foxo1 and PEPCK, contribute to increased gluconeogenesis. These anomalies occurred regardless of the time of ethanol exposure during pregnancy, including early embryogenesis. As these anomalies were reversed by treatment of the adult offspring with TUDCA, this compound has therapeutic potentials in the treatment of glucose intolerance associated with prenatal ethanol exposure.
34. **ALCOHOL EXPOSURE DURING DEVELOPMENT: IMPACT ON THE EPIGENOME.**
Perkins A, Lehmann C, Lawrence RC, Kelly SJ.
Department of Psychology, University of South Carolina, Columbia, SC, 29208, United States. Electronic address: fincha@sc.edu.

**ABSTRACT**
Fetal alcohol spectrum disorders represent a wide range of symptoms associated with in utero alcohol exposure. Animal models of FASD have been useful in determining the specific neurological consequences of developmental alcohol exposure, but the mechanisms of those consequences are unclear. Long-lasting changes to the epigenome are proposed as a mechanism of alcohol-induced teratogenesis in the hippocampus. The current study utilized a three-trimester rodent model of FASD to examine changes to some of the enzymatic regulators of the epigenome in adolescence. Combined pre- and post-natal alcohol exposure resulted in a significant increase in DNA methyltransferase activity (DNMT), without affecting histone deacetylase activity (HDAC). Developmental alcohol exposure also caused a change in gene expression of regulators of the epigenome, in particular, DNMT1, DNMT3a, and methyl CpG binding protein 2 (MeCP2). The modifications of the activity and expression of epigenetic regulators in the hippocampus of rodents perinatally exposed to alcohol suggest that alcohol's impact on the epigenome and its regulators may be one of the underlying mechanisms of alcohol teratogenesis.


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35. **FOOD INSECURITY AND ALCOHOL USE AMONG PREGNANT WOMEN AT ALCOHOL-SERVING ESTABLISHMENTS IN SOUTH AFRICA**
Lisa A. Eaton, Eileen V. Pitpitan, Seth C. Kalichman, Kathleen J. Sikkema, Donald Skinner, Melissa H. Watt, Desiree Pieterse, Demetria N. Cain

**ABSTRACT**
South Africa has the highest rate of fetal alcohol syndrome (FAS) in the world. While efforts have been made to curb the high rate of FAS, little is known about situational factors that may contribute to alcohol use during pregnancy. In the current paper, we focus on the role of food insecurity and its relationship to alcohol use among pregnant women. Women completed computer-assisted interviews. Generalized linear modeling was used in all analyses. Women attending alcohol-serving establishments in a township in Cape Town, South Africa were recruited for the study. Five hundred sixty women were sampled and 95 women reported being pregnant. High levels of alcohol use were reported among pregnant women: 65 % of women consumed alcohol at least every month and 29 % consumed alcohol as often as two to three times per week. Thirty-four percent of the women reported having six or more drinks per occasion on at least a weekly basis. The majority (87 %) of pregnant women reported experiencing some form of food insecurity (e.g., food unavailable, eating less) in the past month. Alcohol use was significantly associated with food insecurity, even when controlling for relevant demographic variables. Intervention with pregnant women who...
consume alcohol is urgently needed. Future research should focus on understanding the intersection of food insecurity and alcohol, and how the experience of food insecurity may contribute to greater rates of alcohol use and abuse among pregnant women.

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36. IMPACT OF LOW DOSE PRENATAL ETHANOL EXPOSURE ON GLUCOSE HOMEOSTASIS IN SPRAGUE-DAWLEY RATS AGED UP TO EIGHT MONTHS
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ABSTRACT
Excessive exposure to alcohol prenatally has a myriad of detrimental effects on the health and well-being of the offspring. It is unknown whether chronic low-moderate exposure of alcohol prenatally has similar and lasting effects on the adult offspring’s health. Using our recently developed Sprague-Dawley rat model of 6% chronic prenatal ethanol exposure, this study aimed to determine if this modest level of exposure adversely affects glucose homeostasis in male and female offspring aged up to eight months. Plasma glucose concentrations were measured in late fetal and postnatal life. The pancreas of 30 day old offspring was analysed for β-cell mass. Glucose handling and insulin action was measured at four months using an intraperitoneal glucose tolerance test and insulin challenge, respectively. Body composition and metabolic gene expression were measured at eight months. Despite normoglycaemia in ethanol consuming dams, ethanol-exposed fetuses were hypoglycaemic at embryonic day 20. Ethanol-exposed offspring were normoglycaemic and normoinsulinaemic under basal fasting conditions and had normal pancreatic β-cell mass at postnatal day 30. However, during a glucose tolerance test, male ethanol-exposed offspring were hyperinsulinaemic with increased first phase insulin secretion. Female ethanol-exposed offspring displayed enhanced glucose clearance during an insulin challenge. Body composition and hepatic, muscle and adipose tissue metabolic gene expression levels at eight months were not altered by prenatal ethanol exposure. Low-moderate chronic prenatal ethanol exposure has subtle, sex specific effects on glucose homeostasis in the young adult rat. As aging is associated with glucose dysregulation, further studies will clarify the long lasting effects of prenatal ethanol exposure.

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MECONIUM FATTY ACID ETHYL ESTERS AS BIOMARKERS OF LATE GESTATIONAL ETHANOL EXPOSURE AND INDICATOR OF ETHANOL-INDUCED MULTI-ORGAN INJURY IN FETAL SHEEP

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ABSTRACT

Background: Meconium fatty acid ethyl esters (FAEE) constitute a biomarker of heavy fetal ethanol exposure. Our objective was to measure meconium FAEE in fetal sheep following daily, relatively moderate-dose ethanol exposure in late gestation, and to evaluate their utility in identifying fetal organ-system injury.

Methods: Pregnant ewes received ethanol (0.75 g/kg; n=14) or saline (n=8) via 1-h i.v. infusion daily during the third trimester equivalent, while additional pregnant sheep served as untreated controls (n=6). The daily ethanol regimen produced similar maximal maternal and fetal plasma ethanol concentrations of 0.11-0.12 g/dL. Ewes and fetuses were euthanized shortly before term, and meconium was collected and analyzed for FAEE (ethyl palmitate, stearate, linoleate, and oleate).

Results: Meconium total FAEE concentration was significantly higher in ethanol-exposed fetuses compared with controls, and a positive cut-off of 0.0285 nmol total FAEE/g meconium had 93.3% sensitivity and specificity for detecting fetal ethanol exposure. When the studied animals (ethanol-exposed and controls) were classified according to meconium FAEE concentration, FAEE-positive and FAEE-negative groups frequently differed with respect to previously examined pathological endpoints, including nephron endowment, lung collagen deposition, cardiomyocyte maturation, and tropoelastin gene expression in cerebral vessels. Furthermore, in all studied animals as a group (ethanol-exposed and controls combined), meconium FAEE concentration was correlated with many of these pathological endpoints in fetal organs.

Conclusions: We conclude that, in fetal sheep, meconium FAEE could serve as a biomarker of daily ethanol exposure in late gestation and could identify fetuses with subtle ethanol-induced toxic effects in various organs. This study illustrates the potential for using meconium FAEE to identify neonates at risk for dysfunction of major organs following in-utero ethanol exposure that does not result in overt physical signs of ethanol teratogenicity.

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ABSTRACT
Objective: To examine the effects of low to moderate maternal alcohol consumption and binge drinking in early pregnancy on behaviour in children at the age of 5 years.

Design: Prospective cohort study.


Population: A total of 1628 women and their children sampled from the Danish National Birth Cohort.

Methods: Participants were sampled based on maternal alcohol drinking patterns during early pregnancy. When the children were 5 years of age the parent and teacher versions of the Strengths and Difficulties Questionnaire (SDQ) were completed by the mothers and a preschool teacher, respectively. The full statistical model included the following potential confounding factors: maternal binge drinking or low to moderate alcohol consumption, respectively; parental education; maternal IQ; prenatal maternal smoking; the child's age at testing; the child's gender; maternal age; parity; maternal marital status; family home environment; postnatal parental smoking; prepregnancy maternal body mass index (BMI); and the child's health status.

Main outcome measure: Behaviour among children assessed by the SDQ parent and teacher forms.

Results: Adjusted for all potential confounding factors, no statistically significant associations were observed between maternal low to moderate average weekly alcohol consumption and SDQ behavioural scores (OR 1.1, 95% CI 0.5–2.3; OR 1.1, 95% CI 0.6–2.1 for the total difficulties scores) or between binge drinking and SDQ behavioural scores (OR 1.2, 95% CI 0.8–1.7; OR 0.8, 95% CI 0.6–1.2).

Conclusion: This study observed no consistent effects of low to moderate alcohol consumption or binge drinking in early pregnancy on offspring behaviour at the age of 5 years.


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THE EFFECT OF LOW-MODERATE DOSE ETHANOL CONSUMPTION ON RAT MAMMARY GLAND STRUCTURE AND FUNCTION, AND EARLY POSTNATAL GROWTH OF OFFSPRING

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ABSTRACT
High levels of alcohol consumption during pregnancy can lead to growth deficits in early postnatal life. However, the effects of low to moderate alcohol consumption during pregnancy are less clearly defined. The aim of this study was to determine if low-moderate ethanol (EtOH) consumption throughout pregnancy in the rat alters maternal mammary gland morphology and milk protein levels, thereby affecting lactation and the growth of pups after birth. Sprague-Dawley rats were fed an ad-libitum liquid diet ± 6% v/v EtOH throughout pregnancy. Mammary glands from dams were collected at embryonic day (E) 20 or postnatal day (PN) 1 and expression of milk proteins (α-lactalbumin, β-caesin and whey acidic protein) examined. In addition, relative amounts of alveoli, lactiferous ducts, adipose tissue and blood vessels were determined at PN1. A subset of rats littered down and offspring growth and milk intake recorded. Mammary gland weight was unaltered by EtOH and stereological analysis showed no differences in gland structure compared to Control. Although there were no significant changes in mammary gland gene expression at the RNA level, protein levels of α-lactalbumin were increased and whey acidic protein were decreased by EtOH. Offspring of EtOH-fed dams consumed less milk than controls in the lactational period however, this did not alter their early postnatal growth. Overall, it appears that low-moderate dose prenatal EtOH exposure does not significantly alter mammary gland development but may alter the composition of the various proteins found within the milk in a manner that maintains overall pup growth.

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DENTAL HOSPITAL ADMISSIONS IN THE CHILDREN OF MOTHERS WITH AN ALCOHOL-RELATED DIAGNOSIS: A POPULATION-BASED, DATA-LINKAGE STUDY

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ABSTRACT
Objective: To investigate the relationship between maternal alcohol-use disorder and dental hospital admissions in children up to 5 years of age.

Study Design: Mothers with an International Classification of Diseases, 9th revision/10th revision alcohol-related diagnosis, a proxy for alcohol-use disorder, were identified through
the Western Australian data-linkage system. Exposed mothers were frequency-matched by maternal age, Aboriginal status, and child's birth year to randomly selected comparison mothers without an alcohol diagnosis. Linkage with the Midwives Notification System (1983-2002) identified all births of these mothers; "exposed" (non-Aboriginal, n = 11,171; Aboriginal, n = 8,145) and comparison cohorts (non-Aboriginal, n = 32,508; Aboriginal, n = 16,719). Dental hospital admissions were identified through linkage with Hospital Morbidity Data (1983-2007) (3.2% exposed; 3.0% comparison) and cases of fetal alcohol syndrome (n = 84) through linkage with the Western Australian Register of Developmental Anomalies. ORs and 95% CIs for having a dental admission (International Classification of Diseases, 9th revision: 520-529; International Classification of Diseases, 10th revision: K0-K14.9) were generated by the use of generalized estimating equations, which we adjusted for potential confounding factors (aOR).

Results: Children of mothers with an alcohol-related diagnosis had increased adjusted odds of gingivitis and periodontal diseases (aOR 1.67; 95% CI 1.12-2.51) and "other" diseases of the lip and oral mucosa (aOR 1.56; 95% CI 1.21-2.01). Diseases of the salivary glands were increased only in Aboriginal children of mothers with an alcohol-related diagnosis (aOR 2.65; 95% CI 1.09-6.44). Children diagnosed with fetal alcohol syndrome had increased ORs of any dental admission (aOR 2.58; 95% CI 1.30-5.11).

Conclusions: Maternal alcohol-use disorder was associated with dental admissions related to disorders of the soft tissues, but questions remain regarding perinatal influences on dental admissions and disease.


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41. NEUROPROTECTIVE PROFILE OF PYRUVATE AGAINST ETHANOL-INDUCED NEURODEGENERATION IN DEVELOPING MICE BRAIN

Ullah N, Naseer MI, Ullah I, Kim TH, Lee HY, Kim MO.
Division of Life Science, College of Natural Sciences (RINS) and Applied Life Science, Gyeongsang National University, Chinju, 660-701, Republic of Korea.

ABSTRACT

Exposure to ethanol during developmental stages leads to several types of neurological disorders. Apoptotic neurodegeneration due to ethanol exposure is a main feature in alcoholism. Exposure of developing animals to alcohol induces apoptotic neuronal death and causes fetal alcohol syndrome. In the present study, we observed the possible protective effect of pyruvate against ethanol-induced neurodegeneration. Exposure of developing mice to ethanol (2.5 g/kg) induces apoptotic neurodegeneration and widespread neuronal cell death in the cortex and thalamus. Co-treatment of pyruvate (500 mg/kg) protects neuronal cell against ethanol by the reduced expression of caspase-3 in these brain regions. Immunohistochemical analysis and TUNNEL at 24 h showed that apoptotic cell death induced by ethanol in the cortex and thalamus is reduced by pyruvate. Histomorphological analysis at 24 h with cresyl violet staining also proved that pyruvate reduced the number of neuronal cell loss in the cortex and thalamus. The results showed that ethanol increased the expression of caspase-3 and thus induced apoptotic neurodegeneration in the developing mice cortex and thalamus, while co-treatment of pyruvate inhibits the induction of caspase-3 and reduced the cell death in these brain regions. These findings, therefore, showed that treatment of pyruvate inhibits ethanol-induced neuronal cell loss in the postnatal seven (P7) developing mice brain and may appear as a safe neuroprotectant for treating neurodegenerative disorders in newborns and infants.
42. NEURODEVELOPMENTAL ALCOHOL EXPOSURE ELICITS LONG-TERM CHANGES TO GENE EXPRESSION THAT ALTER DISTINCT MOLECULAR PATHWAYS DEPENDENT ON TIMING OF EXPOSURE

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ABSTRACT

Background: Maternal alcohol consumption is known to adversely affect fetal neurodevelopment. While it is known that alcohol dose and timing play a role in the cognitive and behavioral changes associated with prenatal alcohol exposure, it is unclear what developmental processes are disrupted that may lead to these phenotypes.

Methods: Mice (n=6 per treatment per developmental time) were exposed to two acute doses of alcohol (5 g/kg) at neurodevelopmental times representing the human first, second, or third trimester equivalent. Mice were reared to adulthood and changes to their adult brain transcriptome were assessed using expression arrays. These were then categorized based on Gene Ontology annotations, canonical pathway associations, and relationships to interacting molecules.

Results: The results suggest that ethanol disrupts biological processes that are actively occurring at the time of exposure. These include cell proliferation during trimester one, cell migration and differentiation during trimester two, and cellular communication and neurotransmission during trimester three. Further, although ethanol altered a distinct set of genes depending on developmental timing, many of these show interrelatedness and can be associated with one another via ‘hub’ molecules and pathways such as those related to huntingtin and brain-derived neurotrophic factor.

Conclusions: These changes to brain gene expression represent a ‘molecular footprint’ of neurodevelopmental alcohol exposure that is long-lasting and correlates with active processes disrupted at the time of exposure. This study provides further support that there is no neurodevelopmental time when alcohol cannot adversely affect the developing brain.
PERFORMANCE MEASUREMENT: A PROPOSAL TO INCREASE USE OF SBIRT AND DECREASE ALCOHOL CONSUMPTION DURING PREGNANCY

O’Brien PL.
The Heller School for Social Policy and Management, Brandeis University, Waltham, MA, USA, pegmlob@brandeis.edu.

ABSTRACT
Alcohol consumption during pregnancy has negative implications for maternal and child health. Appropriate early universal Screening, Brief Intervention and Referral to Treatment (SBIRT) for pregnant women is necessary to identify women at risk and reduce the likelihood of continued drinking. Because SBIRT is not consistently used, the development and use of performance measures to assure implementation of SBIRT are key steps towards intervention and reduction of alcohol consumption during pregnancy. Practice guidelines provide ample support for specific instruments designed for SBIRT in prenatal care. An examination of existing performance measures related to alcohol consumption during pregnancy, however, reveals no comprehensive published performance measure designed to quantify the use of SBIRT for alcohol use in prenatal care. Process performance measures were developed that can determine the proportion of pregnant women who are screened during the course of prenatal care and the proportion of women requiring either brief intervention or referral to substance use disorder treatment who received those interventions. The measures require use of screening instruments validated for use with pregnant women. The two proposed measures would represent a significant step in efforts to assure appropriate intervention for women who drink during pregnancy, hold accountable providers who do not employ SBIRT, and provide a basis from which necessary systemic changes might occur. Pregnancy is a time when many women are motivated to stop drinking. That opportunity should be seized, with timely intervention offering assistance for pregnant women who have not stopped drinking of their own accord.


ALCOHOL-INDUCED EPIGENETIC ALTERATIONS TO DEVELOPMENTALLY CRUCIAL GENES REGULATING NEURAL STEMNESS AND DIFFERENTIATION

Veazey KJ, Carnahan MN, Muller D, Miranda RC, Golding MC.
College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas, USA.

ABSTRACT
Background: From studies using a diverse range of model organisms, we now acknowledge that epigenetic changes to chromatin structure provide a plausible link between environmental teratogens and alterations in gene expression leading to disease. Observations from a number of independent laboratories indicate that ethanol (EtOH) has the capacity to act as a powerful epigenetic disruptor and potentially derail the coordinated processes of cellular differentiation. In this study, we sought to examine whether primary neurospheres cultured under conditions maintaining stemness were susceptible to alcohol-induced alterations in the histone code. We focused our studies on trimethylated histone 3 lysine 4 and trimethylated histone 3 lysine 27, as these are 2 of the most prominent posttranslational histone modifications regulating stem cell maintenance and neural differentiation.

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Methods: Primary neurosphere cultures were maintained under conditions promoting the stem cell state and treated with EtOH for 5 days. Control and EtOH-treated cellular extracts were examined using a combination of quantitative RT-PCR and chromatin immunoprecipitation techniques.

Results: We find that the regulatory regions of genes controlling both neural precursor cell identity and processes of differentiation exhibited significant declines in the enrichment of the chromatin marks examined. Despite these widespread changes in chromatin structure, only a small subset of genes including Dlx2, Fabp7, Nestin, Olig2, and Pax6 displayed EtOH-induced alterations in transcription. Unexpectedly, the majority of chromatin-modifying enzymes examined including members of the Polycomb Repressive Complex displayed minimal changes in expression and localization. Only transcripts encoding Dnmt1, Uhrf1, Ehmt1, Ash2 l, Wdr5, and Kdm1b exhibited significant differences.

Conclusions: Our results indicate that primary neurospheres maintained as stem cells in vitro are susceptible to alcohol-induced perturbation of the histone code and errors in the epigenetic program. These observations indicate that alterations to chromatin structure may represent a crucial component of alcohol teratogenesis and progress toward a better understanding of the developmental origins of fetal alcohol spectrum disorders.


45. PRENATAL ETHANOL EXPOSURE DELAYS THE ONSET OF SPERMATOGENESIS IN THE RAT
Lan N, Vogl AW, Weinberg J. Department of Cellular and Physiological Sciences, Faculty of Medicine, Life Sciences Institute, University of British Columbia, Vancouver, BC, Canada; Department of Anatomy, College of Basic Medical Sciences, China Medical University, Shenyang, China.

ABSTRACT

Background: During late prenatal and early postnatal life, the reproductive system in males undergoes an extensive series of physiological and morphological changes. Prenatal ethanol (EtOH) exposure has marked effects on the development of the reproductive system, with long-term effects on function in adulthood. The present study tested the hypothesis that prenatal EtOH exposure will delay the onset of spermatogenesis.

Methods: Development of the seminiferous tubules and the onset of spermatogenesis were examined utilizing a rat model of fetal alcohol spectrum disorder (FASD). Male offspring from ad libitum-fed control (C), pair-fed (PF), and EtOH-fed (prenatal alcohol exposure [PAE]) dams were terminated on postnatal (PN) days 5, 15, 18, 20, 25, 35, 45, and 55, to investigate morphological changes through morphometric analysis of the testes from early neonatal life through young adulthood.

Results: PAE males had lower relative (adjusted for body weight) testis weights compared with PF and/or C males from PN15 through puberty (PN45). In addition, fewer gonocytes (primordial germ cells) were located on the basal lamina on PN5, while more of those touching the basal lamina were dividing in PAE compared with PF and C males, suggesting delayed cell division and migration processes. As well, the percentage of tubules with open lumena was lower in PAE compared with PF and C males on PN18 and 20, and PAE males had fewer primary spermatocytes per tubule on PN18 and round spermatids per tubule on PN25 compared with C males. Finally, the percentage of tubules at stages VII and VIII, when...
mature spermatids move to the apex of the epithelium and are released, was lower in PAE compared with PF and/or C males in young adulthood (PN55).

**Conclusions:** Maternal EtOH consumption appears to delay both reproductive development and the onset of spermatogenesis in male offspring, with effects persisting at least until young adulthood.

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46. **MULTIPLE RISK FACTORS DURING PREGNANCY IN SOUTH AFRICA: THE NEED FOR A HORIZONTAL APPROACH TO PERINATAL CARE**
Department of Psychology, Stellenbosch University, Stellenbosch, South Africa, markt@sun.ac.za.

**ABSTRACT**
South African children's long-term health and well-being is jeopardized during their mothers' pregnancies by the intersecting epidemics of HIV, alcohol use, low birth weight (LBW; <2,500 g) related to poor nutrition, and depressed mood. This research examines these overlapping risk factors among 1,145 pregnant Xhosa women living in 24 township neighborhoods in Cape Town, South Africa. Results revealed that 66 % of pregnant women experienced at least one risk factor. In descending order of prevalence, 37 % reported depressed mood, 29 % were HIV+, 25 % used alcohol prior to knowing that they were pregnant, and 15 % had a previous childbirth with a LBW infant. Approximately 27 % of women had more than one risk factor: depressed mood was significantly associated with alcohol use and LBW, with a trend to significance with HIV+. In addition, alcohol use was significantly related to HIV+. These results suggest the importance of intervening across multiple risks to maternal and child health, and particularly with depression and alcohol use, to positively impact multiple maternal and infant outcomes.

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47. **DEVELOPMENT OF A RELIABLE QUESTIONNAIRE TO ASSIST IN THE DIAGNOSIS OF FETAL ALCOHOL SPECTRUM DISORDERS (FASD)**
James P Fitzpatrick, Jane Latimer, Manuela Ferreira, Alexandra LC Martiniuk, Elizabeth Peadon, Maureen Carter, June Oscar, Emily Carter, Meredith Kefford, Rhonda Shandley, Harry Yungabun and Elizabeth J Elliott
Australia

**ABSTRACT (provisional)**
Background: A battery of clinical assessments was used in the Liliawan* Project, Australia's first population-based Fetal Alcohol Spectrum Disorders (FASD) prevalence study, conducted in the remote Fitzroy Valley, Western Australia. One objective was to develop and
assess test-retest reliability of an acceptable questionnaire for collecting health information in remote Aboriginal communities feasible for use in the Lililwan Project.

**Methods:** A questionnaire was developed by paediatricians to assist in diagnosis of FASD. Content was based on a literature review of FASD diagnostic criteria, existing questionnaires and risk factors for FASD and birth defects. Aboriginal community members, including qualified Aboriginal language interpreters, adapted the questionnaire to ensure language and cultural components were appropriate for use in the Fitzroy Valley. Locally developed pictorial aids were used for gathering accurate information on alcohol use. Aboriginal ‘community navigators’ assisted researchers to translate the questions into Kimberley Kriol or local Aboriginal languages depending on participant preference.

A subset of 14 questions was assessed for test-retest reliability in 30 parents/carers of children in the Lililwan Project cohort, who were interviewed by one rater using the entire questionnaire, then by a second rater who repeated 14 critical questions at least 6 hours later.

**Results:** The full questionnaire contained 112 items and took 50 minutes to administer. For a subset of 14 items from the full questionnaire percent exact agreement between raters ranged from 55-90%, and was below 70% for only 2 questions. Test-retest reliability was excellent (Kappa 0.81-1.00) for 5 items, substantial (Kappa 0.61-0.80) for 5 items, and moderate, fair or slight (Kappa <=0.60) for the remaining 4 items tested. Test-retest reliability for questions relating to alcohol use in pregnancy was excellent. When questions had moderate, fair or slight agreement, information was obtained from alternate sources e.g. medical records. Qualitative feedback from parents/carers confirmed acceptability of the questionnaire.

**Conclusions:** This questionnaire had acceptable test-retest reliability and could be used to collect demographic, socio-cultural and biomedical information relevant to the diagnosis of FASD in Aboriginal communities throughout Australia and elsewhere. Community input is crucial when developing and administering questionnaires for use in cross-cultural contexts.

*Lililwan is a Kimberley Kriol word meaning ‘all the little ones’. Kimberley Kriol is the main language spoken by Aboriginal people in the Fitzroy Valley.

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http://www.biomedcentral.com/1471-2431/13/33/abstract

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48. **PRENATAL ETHANOL EXPOSURE DOES NOT CAUSE NEUROLOGICAL ALTERATIONS IN ADULT CD1 MICE**
Wei S, Xu Z, Gao J, Ding J, Xiao M.
Department of Anatomy, Wuxi Higher Health Vocational Technology School, Wuxi, Nanjing Medical University, Nanjing, Jiangsu, PR China.

**ABSTRACT**
Genetic factors are involved in variation in fetal alcohol spectrum disorders (FASD), which is also observed among various inbred mouse strains. The CD1 mouse strain is often used in toxicological and genetic experiments. However, there is little literature using this strain to study long-term neurologic abnormalities of FASD. In the present study, we addressed the effect of prenatal ethanol exposure on neurological alterations in adult CD1 mice. The female CD1 mice received exposure to ethanol solution (10 vol%) starting from 2 weeks before mating up to pups born (postnatal day 1). At 24 weeks after the birth, the prenatal ethanol-
exposed mice and control mice showed no difference in spatial learning and memory performance in a Morris water maze. Consistently, pathological changes, such as increased neuronal apoptosis, decreased synaptic protein synaptophysin expression, synaptic loss and reactive astrogliosis, were not observed in the hippocampus of mice prenatally exposed to ethanol. These results suggest that CD1 mice are highly resistant to prenatal alcohol exposure and may serve as genetic modification models of FASD.

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49. **ALCOHOL-INDUCED MORPHOLOGICAL DEFICITS IN THE DEVELOPMENT OF OCTAVOLATERAL ORGANS OF THE ZEBRAFISH (DANIO RERIO)**
Zamora LY, Lu Z.
1 Department of Biology, University of Miami, Coral Gables, Florida, USA.

**ABSTRACT**
Prenatal alcohol exposure is known to have many profound detrimental effects on human fetal development (fetal alcohol spectrum disorders), which may manifest as lifelong disabilities. However, how alcohol affects the auditory/vestibular system is still largely unknown. This is the first study to investigate morphological effects of alcohol on the developing octavolateral system (the inner ear and lateral line) using the zebrafish, Danio rerio. Zebrafish embryos of 2 hours post fertilization (hpf) were treated in 2% alcohol for 48 hours and screened at 72 hpf for morphological defects of the inner ear and lateral line. Octavolateral organs from both alcohol-treated and control zebrafish were examined using light, confocal, and scanning electron microscopy. We observed several otolith phenotypes for alcohol-treated zebrafish including zero, one, two abnormal, two normal, and multiple otoliths. Results of this study show that alcohol treatment during early development impairs the inner ear (smaller ear, abnormal otoliths, and fewer sensory hair cells) and the lateral line (smaller neuromasts, fewer neuromasts and hair cells per neuromast, and shorter kinocilia of hair cells). Early embryonic alcohol exposure may also result in defects in hearing, balance, and hydrodynamic function of zebrafish.

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50. **TOWARDS IDENTIFYING A CHARACTERISTIC NEUROPSYCHOLOGICAL PROFILE FOR FETAL ALCOHOL SPECTRUM DISORDER. ANALYSIS OF THE MOTHERISK FASD CLINIC**
Kelly Nash, Sara Stevens, Joanne Rovet, Ellen Fantus, Irena Nulman, Donna Sorbara, Gideon Koren
Canada

**ABSTRACT**
Objective: Children with FASD display a heterogeneous profile and may have deficits in physical, behavioural, emotional, and social functioning, as the result of prenatal alcohol exposure. The major objective of the current study was to identify if a specific pattern of neuropsychological functioning exists among children prenatally exposed to alcohol who
received a diagnosis, versus exposed children who did not. We compared groups on domains of intellectual functioning, memory, attention, executive functioning, motor functioning, language/communication and achievement.

**Methods:** One hundred and seventy children who were seen in the clinic between 2005 and 2009 were included in this study. Out of the total 170 children seen, 109 received an FASD diagnosis.

**Results:** We identified a specific neuropsychological profile that typifies children diagnosed with an FASD versus those exposed prenatally to alcohol, who did not receive a diagnosis. Diagnosed children displayed a neuropsychological profile characterized by weaknesses in the areas of verbal reasoning, memory, overall language functioning, math reasoning and calculation. Groups did not differ on measures of attention or executive functioning.

**Conclusion:** The information gained from these analyses, are essential for informing best practices for diagnosis and treatment.

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J Popul Ther Clin Pharmacol Vol 20 (1);e53-e62; March 4, 2013

51. **TOWARDS IDENTIFYING A CHARACTERISTIC NEUROPSYCHOLOGICAL PROFILE FOR FETAL ALCOHOL SPECTRUM DISORDERS. SPECIFIC CAREGIVER-AND TEACHER-RATING**

Sara A Stevens, Kelly Nash, Ellen Fantus, Irena Nulman, Joanne Rovet, Gideon Koren

Canada

**ABSTRACT**

**Objectives:** This study compares the behavioral profile of children with fetal alcohol spectrum disorder (FASD) who were diagnosed using the Canadian Guidelines with children with prenatal alcohol exposure who did not meet criteria for a FASD diagnosis.

**Methods and Procedures:** To accomplish this, we used caregiver and teacher questionnaires evaluating different aspects of behavior. Investigated were 170 children, 109 who received a diagnosis of FASD (Diagnosed Group) and 61 who did not (Non-Diagnosed Group). On the caregiver report, children in the Diagnosed Group had more internalizing and externalizing problems on the CBCL, more executive function difficulties on the BRIEF and more attention problems on the Conner's Rating Scale, compared to the Non-Diagnosed Group. On teacher report, children in the Diagnosed Group had more internalizing and externalizing problems on the TRF and more attention problems on the Conner's Rating Scale, compared to the Non-Diagnosed Group. For both informants, more children in the Diagnosed group had scores in the clinically elevated range.

**Conclusion:** Overall, the present results identify key caregiver- and teacher-rated profiles of children with FASD diagnoses. These profiles will aid in better understanding, diagnosing and providing focused treatment approaches for children with FASD.

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52. PERICONCEPTIONAL MATERNAL ALCOHOL CONSUMPTION AND NEURAL TUBE DEFECTS
Makelarski JA, Romitti PA, Sun L, Burns TL, Druschel CM, Suarez L, Olshan AF, Siega-Riz AM, Olney RS; National Birth Defects Prevention Study.
Department of Epidemiology, The University of Iowa, Iowa City, Iowa 52242, USA.

ABSTRACT
Background: Neural tube defects (NTDs), which occur when the neural tube fails to close during early gestation, are some of the most common birth defects worldwide. Alcohol is a known teratogen and has been shown to induce NTDs in animal studies, although most human studies have failed to corroborate these results. Using data from the National Birth Defects Prevention Study, associations between maternal reports of periconceptional (1 month prior through 2 months postconception) alcohol consumption and NTDs were examined.

Methods: NTD cases and unaffected live born control infants, delivered from 1997 through 2005, were included. Interview reports of alcohol consumption (quantity, frequency, variability, and type) were obtained from 1223 case mothers and 6807 control mothers. Adjusted odds ratios (aOR)s and 95% confidence intervals were estimated using multivariable logistic regression analysis.

Results: For all NTDs combined, most aORs for any alcohol consumption, one or more binge episodes, and different type(s) of alcohol consumed were near unity or modestly reduced (≥ 0.7 < aOR ≤ 1.1) and were not statistically significant. Findings were similar for individual NTD subtypes.

Conclusions: These findings suggest no elevated association between maternal periconceptional alcohol consumption and NTDs. Underreporting of alcohol consumption, due to negative social stigma associated with alcohol consumption during pregnancy, and limited reports for mothers with early pregnancy loss of a fetus with an NTD may have affected the estimated odds ratios. Future studies should aim to increase sample sizes for less prevalent subtypes, reduce exposure misclassification, and improve ascertainment of fetal deaths and elective terminations.

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53. FETAL ALCOHOL SPECTRUM DISORDER - POVERTY TRAP?
Commentary
NX Thanh, E Jonsson, J Moffatt, L Dennett
Canada

ABSTRACT
The disease or injury poverty trap refers to a relationship between ill-health and poverty in which poverty is a result of ill-health. At the household level, non-poor people may be pushed into poverty by their ill-health as a result of paying for health care in combination with productivity and income losses. The economic consequences of FASD and the poverty trap of intellectual disability suggest a possibility of the existence of an FASD-poverty trap – an area that needs further studies, probably longitudinal, to be determine and identify the
pathways leading people with FASD to poverty.

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54. THE IMPACT OF PREGNATAL ALCOHOL EXPOSURE ON ADDICTION TREATMENT
Grant TM, Brown NN, Dubovsky D, Sparrow J, Ries R.
Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle 98109, USA. granttm@u.washington.edu

ABSTRACT
Fetal alcohol spectrum disorders (FASDs) are conditions caused by prenatal alcohol exposure in amounts sufficient to cause permanent deficits in brain functioning. Extent of damage largely depends on timing, dose, frequency, and pattern of exposure. Timing is especially important because prenatal alcohol exposure during critical periods of gestation can affect brain development in ways that produce varying patterns of neurocognitive deficits and associated adaptive impairments. This article describes some of the more serious neurophysiological and neuropsychological sequelae of prenatal alcohol exposure that contribute to increased risk for substance abuse problems among people with an FASD. We discuss the unique interface between pharmacological treatment and FASD, noting that failure to consider the possibility of FASD in treatment planning may result in treatment failure and/or relapse. Finally, we present a clinical case example and recommend service accommodations to address some of the impairments in FASD that limit substance abuse treatment success.

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55. FETAL ALCOHOL SPECTRUM DISORDER AND THE LAW IN AUSTRALIA: THE NEED FOR AWARENESS AND CONCERN TO TRANSLATE INTO URGENT ACTION
Freckelton I.
Australia

ABSTRACT
Awareness of the social tragedies and legal difficulties caused by Fetal Alcohol Spectrum Disorder has been emerging since the 1960s. However, although a great deal is now known clinically about the disorder, its diagnosis and what needs to be done by way of prevention and management, a co-ordinated therapeutic and public health response in Australia has thus far been lacking. In turn, this is having a range of repercussions for the courts in evaluating accused persons' criminal responsibility and culpability. Two high-quality and extensive reports during 2012 from Western Australian and Commonwealth parliamentary committees have documented the problems and provided a blueprint for a collaborative and comprehensive intergovernmental response. The challenge for government is now to implement the proposals throughout Australia (and be guided by them in New Zealand) as a matter of urgency.
56. **ALCOHOL USE IN PREGNANCY: INSIGHTS IN SCREENING AND INTERVENTION FOR THE CLINICIAN**

Jones TB, Bailey BA, Sokol RJ.
Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Wayne State University School of Medicine, Detroit, MI, USA. thjones@med.wayne.edu

**ABSTRACT**
Alcohol consumption during pregnancy remains a common occurrence and is associated with a multitude of adverse birth and long-term outcomes. Binge drinking in particular is shown to be particularly harmful to the developing fetus. Effects include full fetal alcohol syndrome, with characteristic facial dysmorphology, growth restriction, and developmental delays. Exposed children may also have partial fetal alcohol syndrome, alcohol-related birth defects, and alcohol-related neurodevelopmental disorders. These effects are preventable, and efforts must begin with accurate identification of women who consume alcohol during pregnancy. Several screening tools have been developed and validated for use in prenatal care settings, and the most recently proposed brief and easy to use T-ACER3 has demonstrated high sensitivity and specificity in both identifying risk drinking during pregnancy and predicting long-term neurobehavioral outcomes in exposed children. Once identified, effective interventions are available for use with pregnant women consuming alcohol. Brief interventions, which can be delivered by a health professional and involve motivational interviewing, have been demonstrated to significantly reduce alcohol consumption during pregnancy. These approaches, recommended by American College of Obstetricians and Gynecologists (ACOG), help move patients toward increased readiness to positively change their drinking behavior. Ultimately, all prenatal care providers should routinely screen all patients for alcohol use using validated tools, and where appropriate, should offer intervention.


57. **INTERSECTING EPIDEMICS AMONG PREGNANT WOMEN: ALCOHOL USE, INTERPERSONAL VIOLENCE, AND HIV INFECTION IN SOUTH AFRICA**

Russell BS, Eaton LA, Petersen-Williams P.
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**ABSTRACT**
A critical factor for understanding negative health outcomes is acknowledging the synergistic quality that clusters of health problems create. An important step in addressing clusters of health problems involves gaining an awareness of the contextual factors that connect them. This paper considers the intersection of 3 mutually reinforcing health problems: alcohol use, interpersonal violence (IPV), and HIV infection among pregnant women residing in South Africa. We explore how SAVA (substance abuse, violence, and AIDS) - a syndemics related
theory - underscores the dire need to intervene in various areas of psycho-social health and general well-being. Based on World Health Organization data, we highlight the remarkably high rates of alcohol use, IPV, and HIV infection among South African women compared with women residing in other countries around the world. We conclude by highlighting the need for improved recognition of the intersection of these epidemics and for improved surveillance of the prevalence of alcohol use among pregnant women. Finally, based on the literature reviewed, we provide recommendations for future interventions.


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58. THE FREE RADICAL SPIN TRAPPING AGENT PHENYLBUTYNITRONE REDUCES FETAL BRAIN DNA OXIDATION AND POSTNATAL COGNITIVE DEFICITS CAUSED BY IN UTERO EXPOSURE TO A NON-STRUCTURALLY TERATOGENIC DOSE OF ETHANOL: A ROLE FOR OXIDATIVE STRESS
Miller L, Shapiro AM, Cheng J, Wells PG.
Department of Pharmacology and Toxicology, Faculty of Medicine, University of Toronto, Toronto, ON, Canada M5S 1A8.

ABSTRACT
Reactive oxygen species (ROS), although implicated in morphological birth defects caused by ethanol (EtOH) during pregnancy, have not been directly linked to its behavioral deficits. To determine this, a pathogenic oxidative DNA lesion was measured in fetal brain, and a passive avoidance learning test was assessed postnatally in the progeny of CD-1 mice treated once on gestational day 17 with 4g/kg EtOH or its saline vehicle, with or without pretreatment with the free radical spin trapping agent α-phenyl-N-tert-butylnitrone (PBN; 40mg/kg). EtOH-exposed CD-1 progeny, unlike C57BL/6 progeny, had no morphological birth defects, but exhibited a learning deficit at 12 weeks of age (p<0.001), which continued to 16 weeks in males (p<0.01). Peak blood EtOH concentrations were 2.5-fold higher in C57BL/6 mice compared to CD-1 mice given the same dose. PBN pretreatment of CD-1 dams blocked both EtOH-initiated DNA oxidation in fetal brain (p<0.05) and postnatal learning deficits (p<0.01), providing the first direct evidence for ROS in the mechanism of EtOH-initiated neurodevelopmental deficits.


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59. THE ASSOCIATION BETWEEN PRENATAL ALCOHOL EXPOSURE AND BEHAVIOR AT 22 YEARS OF AGE
Day NL, Helsel A, Sonon K, Goldschmidt L.
Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA.

ABSTRACT
Background: Prenatal alcohol exposure (PAE) affects central nervous system development, growth, and morphology at higher exposure levels. Little is known about the effects of PAE at
lower exposure levels or in young adults. Research on children with higher levels of PAE has shown that PAE predicts behavior problems. The question remains whether these effects are permanent or ameliorated by maturation into adulthood.

**Methods:** These data are from a longitudinal study of PAE. Mothers were recruited from a prenatal clinic and interviewed during their fourth prenatal month, seventh month, and delivery. In the postpartum, mothers and offspring were seen at 8 and 18 months, and 3, 6, 10, 14, 16, and 22 years.

**Results:** At 22 years, PAE significantly predicted behavior as measured with the adult self-report. These findings were significant controlling for covariates. Exposure at each trimester predicted increased behavior problems on the Total Score, Internalizing, Externalizing, Attention, and Critical Items scales. Use across pregnancy predicted a higher rate of behavior problems compared to no use and use in the first trimester only.

**Conclusions:** The effects were dose-response and significant at each trimester of pregnancy. However, duration across pregnancy was a better predictor than drinking during the first trimester only. Binge drinking was not a better predictor of outcome compared to average daily volume (ADV), and within categories of ADV, binge drinking did not predict more problems than nonbinge drinking. Thus, there is no safe level or safe time during pregnancy for women to drink. These data demonstrate that the effects of PAE, even at low to moderate levels, extend into young adulthood and are most likely permanent.


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**60. THE INFLUENCE OF FETAL ETHANOL EXPOSURE ON SUBSEQUENT DEVELOPMENT OF THE CEREBRAL CORTEX AS REVEALED BY MAGNETIC RESONANCE IMAGING**

Leigland LA, Ford MM, Lerch JP, Kroenke CD.

Advanced Imaging Research Center, Oregon Health & Science University, Portland, Oregon; Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, Oregon, USA.

**ABSTRACT**

**Background:** Fetal alcohol syndrome and related disorders (commonly referred to as fetal alcohol spectrum disorder, or FASD) cause significant hardships to the individuals affected. Previously, histological studies in animals have characterized developmental cerebral cortical abnormalities that result from prenatal ethanol (EtOH) exposure. Additionally, magnetic resonance imaging (MRI) studies have identified abnormalities associated with fetal EtOH exposure in the cerebral cortices of human children and adolescents. However, there is still a need to bridge the gap between human MRI studies and animal histological studies. The goal of the research presented here was to perform postmortem MRI experiments on rodents, during time periods relative to late human gestation through adulthood, to characterize anomalies associated with FASD throughout development. Additionally, by determining how histologically identified abnormalities are manifest in MRI measurements specifically during the critical early time points, neuroimaging-based biomarkers of FASD can potentially be identified at much earlier ages in humans, thus reducing the impact of these disorders.

**Methods:** Cerebral cortical volume, thickness, and surface area were characterized by ex vivo MRI in Long-Evans rat pups born from dams that were EtOH-treated, maltose/dextrin-
treated, or untreated throughout gestation at 6 developmental time points (postnatal day [P] 0, P3, P6, P11, P19, and P60).

**Results:** Brain volume, isocortical volume, isocortical thickness, and isocortical surface area were all demonstrated to be reduced following prenatal exposure to EtOH. Significant differences among the treatment groups were observed throughout the range of time points studied, allowing for a comprehensive view of FASD influenced MRI outcomes throughout development. Isocortical surface area and isocortical thickness results contributed independent information important to interpreting effects of prenatal EtOH exposure on cerebral cortical development. Additionally, regional patterns in cortical thickness differences suggested primary sensory areas were particularly vulnerable to gestational EtOH exposure.

**Conclusions:** Structural MRI measurements were in accordance with previous histological studies performed in animal models of FASD. In addition to establishing a summary of MRI outcomes throughout development in FASD, this research suggests that MRI techniques are sufficiently sensitive to detect neuroanatomical effects of fetal EtOH exposure on development of the cerebral cortex during the period of time corresponding to late gestation in humans. Importantly, this research provides a link between animal histological data and human MRI data.


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were allocated clinically to the FAS (n = 22), partial FAS (n = 26) or nonsyndromal HE (n = 75) categories. We used dense surface modeling and signature analyses of 3-dimensional facial photographs to determine agreement between clinical categorization and classifications induced from face shape alone, to visualize facial differences, and to consider predictive links between face shape and neurobehavior.

**Results:** Face classification achieved significant agreement with clinical categories for discrimination of nonexposed from FAS alone (face: 0.97–1.00; profile: 0.92) or with the addition of partial FAS (face: 0.90; profile: 0.92). Visualizations of face signatures delineated dysmorphism across the fetal alcohol spectrum and in half of the nonsyndromal HE category face signature graphs detected facial characteristics consistent with prenatal alcohol exposure. This subgroup performed less well on IQ and learning tests than did nonsyndromal subjects without classic facial characteristics.

**Conclusions:** Heat maps and morphing visualizations of face signatures may help clinicians detect facial dysmorphism across the fetal alcohol spectrum. Face signature graphs show potential for identifying nonsyndromal heavily exposed children who lack the classic facial phenotype but have cognitive impairment.

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### 62. MATERNAL ALCOHOL USE AND SUDDEN INFANT DEATH SYNDROME AND INFANT MORTALITY EXCLUDING SIDS

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**ABSTRACT**

**Background:** Improvements in the rate of infant mortality (death in first year of life) have not occurred in recent years. This study investigates the association between maternal alcohol-use disorder and sudden infant death syndrome (SIDS) and infant mortality not classified as SIDS using linked, population-based health and mortality data.

**Methods:** Exposed mothers were identified through the presence of an International Classification of Diseases 9/10 alcohol diagnosis, a proxy for alcohol-use disorder, recorded on health, mental health, and/or drug and alcohol datasets (1983-2005). Comparison mothers without an alcohol diagnosis were frequency matched to exposed mothers on maternal age within maternal race and year of birth of their children. All offspring with their birth recorded on the Midwives Notification System compose the exposed (n = 21,841) and comparison (n = 56,054) cohorts. Cases of SIDS (n = 303) and infant mortality excluding SIDS (n = 598) were identified through linkage with the Western Australian Mortality Register. Analyses were conducted by using Cox regression and results presented as adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs).

**Results:** The highest risk of SIDS occurred when a maternal alcohol diagnosis was recorded during pregnancy (aHR 6.92, 95% CI 4.02-11.90) or within 1 year postpregnancy (aHR 8.61, 95% CI 5.04-14.69). An alcohol diagnosis recorded during pregnancy more than doubled the risk of infant deaths (excluding SIDS) (aHR 2.35, 95% CI 1.45-3.83). Maternal alcohol-use disorder is attributable for at least 16.41% (95% CI 9.73%-23.69%) of SIDS and 3.40% (95%
CI 2.28%-4.67%) of infant deaths not classified as SIDS.

Conclusions: Maternal alcohol-use disorder is a significant risk factor for SIDS and infant mortality excluding SIDS.


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63. PRENATAL SUBSTANCE ABUSE: SHORT- AND LONG-TERM EFFECTS ON THE EXPOSED FETUS
Behnke M, Smith VC; Committee on Substance Abuse; Committee on Fetus and Newborn. Collaborators (30)

ABSTRACT
Prenatal substance abuse continues to be a significant problem in this country and poses important health risks for the developing fetus. The primary care pediatrician's role in addressing prenatal substance exposure includes prevention, identification of exposure, recognition of medical issues for the exposed newborn infant, protection of the infant, and follow-up of the exposed infant. This report will provide information for the most common drugs involved in prenatal exposure: nicotine, alcohol, marijuana, opiates, cocaine, and methamphetamine.


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64. PRETERM BIRTH AND SMALL FOR GESTATIONAL AGE IN RELATION TO ALCOHOL CONSUMPTION DURING PREGNANCY: STRONGER ASSOCIATIONS AMONG VULNERABLE WOMEN? RESULTS FROM TWO LARGE WESTERN-EUROPEAN STUDIES
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www.nofas-uk.org
ABSTRACT

Background: Inconsistent data on the association between prenatal alcohol exposure and a range of pregnancy outcomes, such as preterm birth (PTB) and small for gestational age (SGA) raise new questions. This study aimed to assess whether the association between low-moderate prenatal alcohol exposure and PTB and SGA differs according to maternal education, maternal mental distress or maternal smoking.

Methods: The Amsterdam Born Children and their Development (ABCD) Study (N = 5,238) and the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) (N = 16,301) are both large studies. Women provide information on alcohol intake in early pregnancy, 3 months postpartum and up to 17 years retrospectively. Multivariate logistic regression analyses and stratified regression analyses were performed to examine the association between prenatal alcohol exposure and PTB and SGA, respectively.

Results: No association was found between any level of prenatal alcohol exposure (non-daily, daily, non-abstaining) and SGA. The offspring of daily drinkers and non-abstainers had a lower risk of PTB [ABCD: odds ratio (OR) 0.31, 95% confidence interval (CI) 0.13, 0.77; KiGGS: OR 0.75, 95% CI 0.57, 0.99]. Interactions with maternal education, maternal distress or maternal smoking were not significant.

Conclusions: Although these results should be interpreted with caution, both studies showed no adverse effects of low-moderate prenatal alcohol exposure on PTB and SGA, not even in the offspring of women who were disadvantaged in terms of low education, high levels of distress, or smoking during pregnancy.

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Measurements and findings: study 1 showed that midwives intended to advise complete abstinence, although this advice was mostly given when women indicated to consume alcohol. Midwives reported to lack good screening skills and sufficient knowledge about the mechanisms and consequences of antenatal alcohol use and did not involve partners in their alcohol advice. In Study 2, the views of pregnant women and partners were congruent to the findings reported in Study 1. In addition, pregnant women and partners considered midwives as an important source of information on alcohol in pregnancy. Partners were interested in the subject, had a liberal view on antenatal alcohol use and felt ignored by midwives and websites. Pregnant women indicated to receive conflicting alcohol advice from their health professionals.

Key conclusions: midwives' alcohol advice requires improvement with regard to screening, knowledge about mechanisms and consequences of antenatal alcohol use and the involvement of the partners in alcohol advice during pregnancy.

Implications for practice: Training should be given to Dutch midwives to increase their screening skills and their alcohol related knowledge to pregnant women. Research is needed to determine how the midwife's alcohol advice to the partner should be framed in order to optimise the partner's involvement concerning alcohol abstinence in pregnancy. More attention to the topic at a national level, for example via mass media campaigns, should also be considered to change views about alcohol use during pregnancy in all stakeholders.


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66. MITOGEN-ACTIVATED PROTEIN KINASE MODULATES ETHANOL INHIBITION OF CELL ADHESION MEDIATED BY THE L1 NEURAL CELL ADHESION MOLECULE
Dou X, Wilkemeyer MF, Menkari CE, Parnell SE, Sulik KK, Charness ME. Veterans Affairs Boston Healthcare System, Department of Neurology, Harvard Medical School, West Roxbury, MA 02132, USA.

ABSTRACT
There is a genetic contribution to fetal alcohol spectrum disorders (FASD), but the identification of candidate genes has been elusive. Ethanol may cause FASD in part by decreasing the adhesion of the developmentally critical L1 cell adhesion molecule through interactions with an alcohol binding pocket on the extracellular domain. Pharmacologic inhibition or genetic knockdown of ERK2 did not alter L1 adhesion, but markedly decreased ethanol inhibition of L1 adhesion in NIH/3T3 cells and NG108-15 cells. Likewise, leucine replacement of S1248, an ERK2 substrate on the L1 cytoplasmic domain, did not decrease L1 adhesion, but abolished ethanol inhibition of L1 adhesion. Stable transfection of NIH/3T3 cells with human L1 resulted in clonal cell lines in which L1 adhesion was consistently sensitive or insensitive to ethanol for more than a decade. ERK2 activity and S1248 phosphorylation were greater in ethanol-sensitive NIH/3T3 cells and NG108-15 cells. Likewise, leucine replacement of S1248, an ERK2 substrate on the L1 cytoplasmic domain, did not decrease L1 adhesion, but abolished ethanol inhibition of L1 adhesion. Stable transfection of NIH/3T3 cells with human L1 resulted in clonal cell lines in which L1 adhesion was consistently sensitive or insensitive to ethanol for more than a decade. ERK2 activity and S1248 phosphorylation were greater in ethanol-sensitive NIH/3T3 cells and NG108-15 cells. Likewise, leucine replacement of S1248, an ERK2 substrate on the L1 cytoplasmic domain, did not decrease L1 adhesion, but abolished ethanol inhibition of L1 adhesion. Stable transfection of NIH/3T3 cells with human L1 resulted in clonal cell lines in which L1 adhesion was consistently sensitive or insensitive to ethanol for more than a decade. ERK2 activity and S1248 phosphorylation were greater in ethanol-sensitive NIH/3T3 cells and NG108-15 cells. Likewise, leucine replacement of S1248, an ERK2 substrate on the L1 cytoplasmic domain, did not decrease L1 adhesion, but abolish...
sensitivity, but not L1 function, might facilitate the rational design of drugs that block ethanol neurotoxicity.

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67. THE FEASIBILITY AND COST OF NEONATAL SCREENING FOR PRENATAL ALCOHOL EXPOSURE BY MEASURING PHOSPHATIDYLETHANOL IN DRIED BLOOD SPOTS

Ludmila N. Bakhireva1,2,*, Renate D. Savich3, Dennis W. Raisch1, Sandra Cano1, Robert D. Annett3, Lawrence Leeman2,4, Mahek Garg1, Chelsea Goff1, Daniel D. Savage3,5
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ABSTRACT

Background: Accurate confirmation of prenatal alcohol exposure (PAE) is required as a diagnostic criterion for the majority of children adversely affected by PAE who do not manifest the physical features associated with fetal alcohol syndrome. A number of ethanol biomarkers have been used to assess PAE, often with suboptimal results. The purpose of this study was to evaluate the feasibility and cost of PAE screening in newborns by measuring phosphatidylethanol (PEth) in dried blood spot (DBS) cards.

Methods: The feasibility of collecting an additional DBS card during routine newborn screening and the background prevalence of PAE were evaluated in a de-identified sample of newborn children delivered at the University of New Mexico Hospital. Electronic orders to collect DBS cards from newborns who continue to bleed after the routine newborn screen, glucose, or hematocrit testing were initiated for all infants delivered during a 4-week time frame. Specimens were sent to a contract laboratory for PEth analysis by liquid chromatography–tandem mass spectrometry. A cost analysis was conducted to compare the cost of PAE screening by PEth in DBS versus PEth in conventional blood specimens and by meconium fatty acid ethyl esters.

Results: From 230 collected cards, 201 (87.4%) had at least 1 full blood spot (amount sufficient for PEth analysis), and 6.5% had PEth >20 ng/ml indicative of potential PAE in late pregnancy. PAE screening by PEth in DBS is logistically simpler and less expensive compared with 2 other screening approaches.

Conclusions: These results indicate that screening for PAE in DBS cards is a feasible procedure and that a majority of infants have enough blood after the routine heel prick to fill an additional card. Moreover, screening by PEth analysis from DBS cards is cost-efficient.
The acceptability of such screening by parents and corresponding ethical issues remain to be investigated.

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68. ALCOHOL-USE DISORDERS DURING AND WITHIN ONE YEAR OF PREGNANCY: A POPULATION-BASED COHORT STUDY 1985-2006
O'Leary C, Halliday J, Bartu A, D'Antoine H, Bower C. Centre for Population Health Research, Curtin University, Perth, WA, Australia; Division of Population Sciences Telethon Institute for Child Health Research Centre for Child Health Research, University of Western Australia, Perth, WA, Australia.

ABSTRACT
Objectives: To examine alcohol-use disorders in pregnant women and the extent of under-reporting.


Setting: Western Australia.


Methods: Mothers with an International Classification of Diseases 9/10 alcohol-related diagnosis, indicating heavy alcohol consumption, recorded on population-based health datasets (non-Aboriginal n = 5839; Aboriginal n = 2583) were identified through the Western Australian data-linkage system. This 'exposed' cohort was frequency matched (on maternal age, year of birth of offspring, Aboriginal status) with comparison mothers without an alcohol-related diagnosis (non-Aboriginal n = 33 979; Aboriginal n = 8005).

Main outcome measures: Trends in maternal alcohol diagnoses in relation to pregnancy for non-Aboriginal and Aboriginal women. The proportion of children diagnosed with fetal alcohol syndrome (FAS) who had a mother with an alcohol diagnosis recorded during pregnancy.

Results: The proportion of Aboriginal mothers in Western Australia with an alcohol diagnosis (23.1%) is ten times greater than for non-Aboriginal mothers (2.3%). There has been a six-fold increase in the percentage of non-Aboriginal births with a maternal alcohol diagnosis recorded during pregnancy and a 100-fold increase for Aboriginal births. Around 70% of the mothers of children diagnosed with FAS did not have an alcohol diagnosis recorded during pregnancy and 18% of the mothers had no record of an alcohol diagnosis.

Conclusions: Maternal alcohol exposure during pregnancy is significantly under-ascertained. Given the severe risks to the fetus from heavy prenatal alcohol exposure, assessment and recording of alcohol use should be routinely undertaken in maternity and other health settings.

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69. DOES BINGE DRINKING DURING EARLY PREGNANCY INCREASE THE RISK OF PSYCHOMOTOR DEFICITS?
Kesmodel US, Bay B, Wimberley T, Eriksen HL, Mortensen EL.
Department of Obstetrics and Gynaecology (USK), Aarhus University Hospital, Aarhus, Denmark; Section of Epidemiology, Department of Public Health, Aarhus University, Aarhus, Denmark.

ABSTRACT
Background: The potential effects of binge drinking during pregnancy on child motor function have only been assessed in a few, small studies. We aimed to examine the effects of binge alcohol consumption during early pregnancy, including number of binge episodes and timing of binge drinking, on child motor function at age 5.

Methods: We performed a prospective follow-up study of 678 women and their children sampled from the Danish National Birth Cohort based on maternal alcohol consumption during pregnancy. At 5 years of age, the children were tested with the Movement Assessment Battery for Children. Parental education, maternal IQ, prenatal maternal smoking, the child’s age at testing, sex of child, and tester were considered core confounders, while the full model also controlled for prenatal maternal average alcohol intake, maternal age and prepregnancy body mass index, parity, home environment, postnatal parental smoking, health status, participation in organized sport, and indicators for hearing and vision impairment.

Results: There were no systematic or significant differences in motor function between children of mothers reporting isolated episodes of binge drinking and children of mothers with no binge episodes. No association was observed with respect to the number of binge episodes (maximum of 12) and timing of binge drinking.

Conclusions: In this study, we found no systematic association between isolated episodes of binge drinking during early pregnancy and child motor function at age 5.

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70. GESTATIONAL CHOLINE SUPPLEMENTATION NORMALIZED FETAL ALCOHOL-INDUCED ALTERATIONS IN HISTONE MODIFICATIONS, DNA METHYLATION, AND PROOPIOMELANOCORTIN (POMC) GENE EXPRESSION IN B-ENDORPHIN-PRODUCING POMC NEURONS OF THE HYPOTHALAMUS
Bekdash RA, Zhang C, Sarkar DK.
Endocrine Program, Rutgers, The State University of New Jersey, New Brunswick, New Jersey; Graduate Program of Neuroscience, Rutgers, The State University of New Jersey, New Brunswick, New Jersey, USA.

ABSTRACT
Background: Prenatal exposure to ethanol (EtOH) reduces the expression of hypothalamic proopiomelanocortin (POMC) gene, known to control various physiological functions including the organismal stress response. In this study, we determined whether the changes
in POMC neuronal functions are associated with altered expressions of histone-modifying and DNA-methylating enzymes in POMC-producing neurons, because these enzymes are known to be involved in regulation of gene expression. In addition, we tested whether gestational choline supplementation prevents the adverse effects of EtOH on these neurons.

**Methods:** Pregnant rat dams were fed with alcohol-containing liquid diet or control diet during gestational days 7 and 21 with or without choline, and their male offspring rats were used during the adult period. Using double-immunohistochemistry, real-time reverse transcription polymerase chain reaction (RT-PCR) and methylation-specific RT-PCR, we determined protein and mRNA levels of histone-modifying and DNA-methylating enzymes and the changes in POMC gene methylation and expression in the hypothalamus of adult male offspring rats. Additionally, we measured the basal- and lipopolysaccharide (LPS)-induced corticosterone levels in plasma by enzyme-linked immunosorbent assay.

**Results:** Prenatal EtOH treatment suppressed hypothalamic levels of protein and mRNA of histone activation marks (H3K4me3, Set7/9, acetylated H3K9, phosphorylated H3S10), and increased the repressive marks (H3K9me2, G9a, Setdb1), DNA-methylating enzyme (Dnmt1), and the methyl-CpG-binding protein (MeCP2). The treatment also elevated the level of POMC gene methylation, while it reduced levels of POMC mRNA and β-EP and elevated corticosterone response to LPS. Gestational choline normalized the EtOH-altered protein and the mRNA levels of H3K4me3, Set7/9, H3K9me2, G9a, Setdb1, Dnmt1, and MeCP2. It also normalizes the changes in POMC gene methylation and gene expression, β-EP production, and the corticosterone response to LPS.

**Conclusions:** These data suggest that prenatal EtOH modulates histone and DNA methylation in POMC neurons that may be resulting in hypermethylation of POMC gene and reduction in POMC gene expression. Gestational choline supplementation prevents the adverse effects of EtOH on these neurons.

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71. **ALCOHOL USE DURING PREGNANCY IN CANADA: HOW POLICY MOMENTS CAN CREATE OPPORTUNITIES FOR PROMOTING WOMEN'S HEALTH**

Poole N, Greaves L.
British Columbia Centre of Excellence for Women's Health, Canada. npoole@cw.bc.ca.

**ABSTRACT**

This article addresses the challenge of igniting action on health promotion for women in Canada with respect to alcohol use during pregnancy. We illustrate that accelerated action on health promotion for women that engages multiple levels of players, women-centred and harm-reduction frameworks and a gendered approach to understanding women's lives can be achieved when the right policy moment occurs. We illustrate this by describing the opportunity afforded by the Olympic Games in 2010, where the BC government used the Games to encourage action on women's health promotion and the prevention of alcohol use in pregnancy. We suggest that the 2011 announcement of new low-risk drinking guidelines that recommend lower intake of alcohol for women than for men offers another, to date unused, opportunity.
A RANDOMIZED CONTROLLED TRIAL OF MOTIVATIONAL INTERVIEWING TO PREVENT RISK FOR AN ALCOHOL-EXPOSED PREGNANCY IN THE WESTERN CAPE, SOUTH AFRICA

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ABSTRACT

Aim: To test the effectiveness of motivational interviewing (MI) to reduce the risk of an alcohol exposed pregnancy (AEP) in a high-risk population.

Design: Randomized controlled trial.

Setting: Rural population in the Western Cape, South Africa.

Participants: A total of 165 women aged 18–44 years at risk of AEP.

Intervention: Five-session MI intervention.

Measurements: Structured questionnaires were administered pre-intervention and at 3 and 12 months follow-up. The primary outcome measure was AEP at 12 months. Secondary outcomes were AEP at 3 months, and alcohol use and effective contraception at 3 and 12 months.

Findings: There was a significant difference in the decline in the proportion of women at risk for an AEP in the MI group at 3 months (50 versus 24.59%; \( P = 0.004 \)), maintained at 12 months (50.82 versus 28.12%; \( P = 0.009 \)). In an intention-to-treat analysis these differences were also significant (32.93 versus 18.07%; \( P = 0.029 \); and 37.80 versus 21.69%; \( P = 0.024 \), respectively). The odds ratio for no longer being at risk of an AEP (MI versus control) at 12 months was 2.64 [95% confidence interval (CI): 1.18–5.94]. In the intention-to-treat analysis this ratio was 2.19 (95% CI: 1.05–4.65).

Conclusions: A five-session motivational interviewing intervention was found to be effective with women at risk of an alcohol-exposed pregnancy, and could be implemented as part of routine primary care clinic services in similar populations. The message of ‘no alcohol in pregnancy’ should be adapted to include better family planning and early recognition of pregnancy.
73. **PROSPECTIVE CORRELATES OF DRINKING CESSATION: VARIATION ACROSS THE LIFE-COURSE**
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**ABSTRACT**

**Aims:** To assess age variation in correlates of drinking cessation.

**Design:** Prospective study of a US general population sample.

**Setting:** Face-to-face household interviews.

**Participants:** Past-year ≥ monthly drinkers interviewed at baseline and 3-year follow-up (n = 14 885).

**Measurements:** Baseline values and selected changes over follow-up in alcohol consumption, alcohol use disorder (AUD), socio-demographic and health characteristics, other substance use and psychiatric comorbidity were used to predict drinking cessation in three age groups.

**Findings:** Correlates of drinking cessation varied over the life-course, with pregnancy/presence of an infant, nicotine or drug use disorder, incident AUD, cluster A personality disorder, liver disease and incident retirement being important at younger ages and high-school graduation, family income ≥ $70 000, volume of ethanol intake, Asian race/ethnicity, mood disorder and incident cardiovascular disease being significant at older ages. Age-invariant correlates included smoking cessation over follow-up, odds ratio (OR) = 2.82 [95% confidence interval (CI): 1.62-4.92] to 3.45 (2.20-5.39); college education, OR = 0.42 (0.27-0.65) to 0.54 (0.36-0.83); black and Hispanic race/ethnicity, OR = 1.74 (1.18-2.29) to 1.88 (1.21-2.93) and 1.58 (1.11-1.25) to 1.73 (0.83-3.63), respectively, and months since last drink, OR = 1.24 (1.13-1.36) to 1.29 (1.19-1.39).

**Conclusions:** Factors associated with ceasing alcohol use in US adults appear to differ over the life-course, reflecting age variation in both their prevalence and impact and supporting the importance of role transitions and health problems (the ‘sick quitter’ effect). The most consistent correlates of drinking cessation included factors reflecting ability/inability to give up potentially addictive substances and factors associated with perceived acceptability of drinking and subgroup-specific drinking contexts that might facilitate/impede continued drinking.

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74. EFFECTS OF EARLY POSTNATAL ALCOHOL EXPOSURE ON THE DEVELOPING RETINOGENICULATE PROJECTIONS IN C57BL/6 MICE

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ABSTRACT

Previous studies on the adverse effects of perinatal exposure to ethanol (EtOH) on the developing visual system mainly focused on retinal and optic nerve morphology. The aim of the present study was to investigate whether earlier reported retinal and optic nerve changes are accompanied by anomalies in eye-specific fiber segregation in the dorsal lateral geniculate nucleus (dLGN). C57BL/6 mice pups were exposed to ethanol by intragastric intubation at either 3 or 4 g/kg from postnatal days (PD) 3–10, the third trimester equivalent to human gestation. Control (C) and intubation control (IC) groups not exposed to ethanol were included. On PD9, retinojeniculate projections were labeled by intraocular microinjections of cholera toxin-β (CTB) either conjugated to Alexa 488 (green) or 594 (red) administrated to the left and right eye, respectively. Pups were sacrificed 24 h after the last CTB injection. The results showed that ethanol exposure decreased the total number of dLGN neurons and significantly reduced the total dLGN projection as well as the contralateral and ipsilateral projection areas.


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75. MODULATION OF ETHANOL TOXICITY BY ASIAN GINSENG (PANAX GINSENG) IN JAPANESE RICEFISH (ORYZIAS LATIPES) EMBRYOGENESIS

Haron MH, Avula B, Khan IA, Mathur SK, Dasmahapatra AK.

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ABSTRACT

Alcohol consumption by women during pregnancy often induces fetal alcohol spectrum disorder (FASD) in children who have serious central nervous system (CNS), cardiovascular, and craniofacial defects. Prevention of FASD, other than women abstaining from alcohol drinking during pregnancy, is not known. A limitation of the use of synthetic anti-alcoholic drugs during pregnancy led us to investigate herbal products. In particular, many plants
including Asian ginseng (Panax ginseng) have therapeutic potential for the treatment of alcoholism. We used Japanese ricefish (medaka) (Oryzias latipes), an animal model of FASD, for identifying herbal medicines that can attenuate ethanol toxicity. Fertilized eggs in standard laboratory conditions were exposed to ginseng (PG) root extract (0-2 mg/mL) either 0-2 (group A) or 1-3 (group B) day post fertilization (dpf) followed by maintenance in a clean hatching solution. The calculated IC50 as determined 10 dpf in A and B groups were 355.3±1.12 and 679.7±1.6 μg/mL, respectively. Simultaneous exposure of embryos in sub-lethal concentrations of PG (50-200 μg/mL) and ethanol (300 mM) for 48 h disrupted vessel circulation and enhanced mortality. However, PG (100 μg/mL) may partially protect trabecular cartilage (TC) deformities in the neurocranium in B group embryos induced by ethanol (300 mM). To understand the mechanism, embryonic ethanol concentration was measured at 2 dpf and adh5, adh8, aldh2, aldh9a, catalase, GST, and GR mRNAs were analyzed at 6 dpf. It was observed that although ethanol is able to reduce adh8 and GST mRNA contents, the simultaneous addition of PG was unable to alter ethanol level as well as mRNA contents in these embryos. Therefore, antagonistic effects of PG on ethanol toxicity are mediated by a mechanism which is different from those regulating ethanol metabolism and oxidative stress.


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76. **G9A-MEDIATED HISTONE METHYLATION REGULATES ETHANOL-INDUCED NEURODEGENERATION IN THE NEONATAL MOUSE BRAIN**

Subbanna S, Shivakumar M, Umapathy NS, Saito M, Mohan PS, Kumar A, Nixon RA, Verin AD, Psychoyos D, Basavarajappa BS.

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**ABSTRACT**

Rodent exposure to binge-like ethanol during postnatal day 7 (P7), which is comparable to the third trimester of human pregnancy, induces neuronal cell loss. However, the molecular mechanisms underlying these neuronal losses are still poorly understood. Here, we tested the possibility of histone methylation mediated by G9a (lysine dimethyltransferase) in regulating neuronal apoptosis in P7 mice exposed to ethanol. G9a protein expression, which is higher during embryogenesis and synaptogenic period compared to adult brain, is entirely confined to the cell nuclei in the developing brain. We found that ethanol treatment at P7, which induces apoptotic neurodegeneration in neonatal mice, enhanced G9a activity followed by increased histone H3 lysine 9 (H3K9me2) and 27 (H3K27me2) dimethylation. In addition, it appears that increased dimethylation of H3K9 makes it susceptible to proteolytic degradation by caspase-3 in conditions in which ethanol induces neurodegeneration. Further, pharmacological inhibition of G9a activity prior to ethanol treatment at P7 normalized H3K9me2, H3K27me2 and total H3 proteins to basal levels and prevented neurodegeneration in neonatal mice. Together, these data demonstrate that G9a mediated histone H3K9 and K27 dimethylation critically regulates ethanol-induced neurodegeneration in the developing brain. Furthermore, these findings reveal a novel link between G9a and neurodegeneration in the developing brain exposed to postnatal ethanol and may have a role in fetal alcohol spectrum disorders.
77. THE MATERNAL DRINKING HISTORY GUIDE: DEVELOPMENT OF A NATIONAL EDUCATIONAL TOOL
Gideon Koren, Moumita Sarkar, Charlotte Rosenbaum, Elaine Orrbine
Canada

ABSTRACT
Background: The National Taskforce for the development of screening tools for FASD has identified maternal drinking as a critical area that should be screened. We describe the steps of development and implementation of a knowledge translation program for health care providers. The slide presentation is attached in English and French to allow its maximal use.

Methods: In 2010, the National Taskforce for the development of screening tools for FASD identified maternal drinking as a critical area that should be screened. The systematic review and associated recommendations have been published and were included in the toolkit developed by the Canadian Association of Paediatric Health Centres with funding support from the Public Health Agency of Canada. Effective inquiry of maternal drinking can be conducted at three levels: Primary level, as part of practice-based screening; Level 2 use of structured questionnaires; and Level 3 laboratory-based screening.

Conclusion: It was acknowledged that most physicians do not ask women of reproductive age questions regarding their drinking habits, and the Taskforce was seriously concerned that even an effective guide may not change practice at the primary level. To that end, the Taskforce developed a three phase Knowledge Translation plan, to ensure that the educational program developed will be optimally effective for Canadian healthcare providers.


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78. ALCOHOL MODULATES EXPRESSION OF DNA METHYLTRANSFERASES AND METHYL CPG-CPG DOMAIN-BINDING PROTEINS IN MURINE EMBRYONIC FIBROBLASTS
Mukhopadhyay P, Rezzoug F, Kaikaus J, Greene RM, Pisano MM.
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ABSTRACT
Fetal alcohol syndrome (FAS), presenting with a constellation of neuro-/psychological, craniofacial and cardiac abnormalities, occurs frequently in offspring of women who consume alcohol during pregnancy, with a prevalence of 1-3 per 1000 livebirths. The present study was designed to test the hypothesis that alcohol alters global DNA methylation, and modulates expression of the DNA methyltransferases (DNMTs) and various methyl CpG-
binding proteins. Murine embryonic fibroblasts (MEFs), utilized as an in vitro embryonic model system, demonstrated ~5% reduction in global DNA methylation following exposure to 200mM ethanol. In addition, ethanol induced degradation of DNA methyltransferases (DNMT-1, DNMT-3a, and DNMT-3b), as well as the methyl CpG-binding proteins (MeCP-2, MBD-2 and MBD-3), in MEF cells by the proteasomal pathway. Such degradation could be completely rescued by pretreatment of MEF cells with the proteasomal inhibitor, MG-132. These data support a potential epigenetic molecular mechanism underlying the pathogenesis of FAS during mammalian development.


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ABSTRACT

Aim: to identify alcohol use and the associated factors in pregnant adolescents of the municipality of Teresina-PI.

Method: this is cross-sectional study with 256 pregnant adolescents whose data were obtained through questionnaires covering socioeconomic, pregnancy and alcohol consumption characteristics and through the application of the Alcohol Use Disorders Identification Test, an instrument developed by the World Health Organization for screening for the excessive use of alcohol. Descriptive statistical analysis was performed using the chi-square test and odds ratio.

Results: the study indicates a prevalence of 32.4% for alcohol use during pregnancy in adolescents. Of these, 36.1% had scores consistent with risky use. The factors associated with an increased risk of alcohol use during pregnancy are: not having a partner, living on less than 1 minimum wage, not being religious, performing up to 3 prenatal consultations, having suffered violence and alcohol use in previous pregnancies.

Conclusion: a high prevalence of alcohol consumption by pregnant adolescents and various risk factors involved in this process were identified. These data reflect the need for the use, by nurses, of screening technologies for alcohol consumption during pregnancy and health promotion strategies among groups of adolescents.

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81. HEALTHY NUTRITION IN PREGNANCY

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ABSTRACT

The right choices in eating when pregnant may influence the health of mother and child in the short and long term. Recent recommendations emphasize the intake of folic acid and iodide. The reader also obtains advice about the extent of weight gain, avoidance of alcohol and tobacco smoke and how to prevent food-borne infections.

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82. EPIGENETIC MEDICINE AND FETAL ALCOHOL SPECTRUM DISORDERS

Resendiz M, Chen Y, Oztürk NC, Zhou FC.
Stark Neuroscience Research Institute, Indiana University School of Medicine, Indianapolis, IN 46202, USA.

ABSTRACT

Epigenetic medicine is still in its infancy. To date, only a handful of diseases have documented epigenetic correlates upstream of gene regulation including cancer,
developmental syndromes and late-onset diseases. The finding that epigenetic markers are dynamic and heterogeneous at tissue and cellular levels, combined with recent identification of a new form of functionally distinct DNA methylation has opened a wider window for investigators to pry into the epigenetic world. It is anticipated that many diseases will be elucidated through this epigenetic inquiry. In this review, we discuss the normal course of DNA methylation during development, taking alcohol as a demonstrator of the epigenetic impact of environmental factors in disease etiology, particularly the growth retardation and neurodevelopmental deficits of fetal alcohol spectrum disorders.


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83. COMPARATIVE ASSESSMENTS OF THE EFFECTS OF ALCOHOL EXPOSURE ON FETAL BRAIN DEVELOPMENT USING OPTICAL COHERENCE TOMOGRAPHY AND ULTRASOUND IMAGING
Sudheendran N, Bake S, Miranda RC, Larin KV.
Texas, USA

ABSTRACT
The developing fetal brain is vulnerable to a variety of environmental agents including maternal ethanol consumption. Preclinical studies on the development and amelioration of fetal teratology would be significantly facilitated by the application of high resolution imaging technologies like optical coherence tomography (OCT) and high-frequency ultrasound (US). This study investigates the ability of these imaging technologies to measure the effects of maternal ethanol exposure on brain development, ex vivo, in fetal mice. Pregnant mice at gestational day 12.5 were administered ethanol (3 g/Kg b.wt.) or water by intragastric gavage, twice daily for three consecutive days. On gestational day 14.5, fetuses were collected and imaged. Three-dimensional images of the mice fetus brains were obtained by OCT and high-resolution US, and the volumes of the left and right ventricles of the brain were measured. Ethanol-exposed fetuses exhibited a statistically significant, 2-fold increase in average left and right ventricular volumes compared with the ventricular volume of control fetuses, with OCT-derived measures of 0.38 and 0.18 mm3, respectively, whereas the boundaries of the fetal mouse lateral ventricles were not clearly definable with US imaging. Our results indicate that OCT is a useful technology for assessing ventriculomegaly accompanying alcohol-induced developmental delay. This study clearly demonstrated advantages of using OCT for quantitative assessment of embryonic development compared with US imaging.


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84. LIGHT DRINKING IN PREGNANCY AND MID-CHILDHOOD MENTAL HEALTH AND LEARNING OUTCOMES
Sayal K, Draper ES, Fraser R, Barrow M, Davey Smith G, Gray R.
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ABSTRACT

Objective: To investigate whether light drinking in pregnancy is associated with adverse child mental health and academic outcomes.

Design: Using data from the prospective, population-based Avon Longitudinal Study of Parents and Children (ALSPAC), we investigated the associations between light drinking in pregnancy (<1 glass per week in the first trimester) and child mental health (using both parent and teacher rated Strengths and Difficulties Questionnaires (SDQs)) and academic outcomes based on Key Stage 2 examination results at age 11 years.

Participants: 11-year-old children from ALSPAC with parent (n=6587) and teacher (n=6393) completed SDQs and data from Key Stage 2 examination results (n=10 558).

Results: 39% of women had consumed <1 glass per week and 16% ≥1 glass per week of alcohol during the first trimester (45% abstaining). After adjustment, relative to abstainers, there was no effect of light drinking on teacher-rated SDQ scores or examination results. In girls, although there was a suggestion of worse outcomes (adjusted regression coefficient=0.38; 95% CI 0.01 to 0.74) on the parent-rated total SDQ score in those exposed to light drinking compared to abstainers, no dose-response relationship was evident.

Conclusions: Although the pattern of findings involving parent ratings for girls exposed to light drinking is consistent with earlier findings from this cohort, the overall lack of any adverse effects of light drinking is similar to findings from other recent cohort studies. Light drinking in pregnancy does not appear to be associated with clinically important adverse effects for mental health and academic outcomes at the age of 11 years.


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85. THE TRANSFER OF ETHYL GLUCURONIDE ACROSS THE DUALLY PERFUSED HUMAN PLACENTA

Matlow JN, Lubetsky A, Aleksa K, Berger H, Koren G.
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ABSTRACT

Introduction: Alcohol consumption during pregnancy can lead to Fetal Alcohol Spectrum Disorder (FASD), and because maternal self-reports are often unreliable, biomarkers of alcohol use are sometimes necessary to accurately determine fetal risk. Ethyl glucuronide (EtG), a direct metabolite of ethanol, has been detected in the meconium of infants born to mothers who consumed excessive alcohol during pregnancy. It is still unknown whether EtG detected in meconium originated from maternal hepatic glucuronidation of ethanol followed by subsequent placental transfer. Therefore, the objective of this study was to determine if EtG crosses the human placenta.

Methods: The transfer of EtG was measured using the ex vivo dual perfusion of an isolated human placental lobule. EtG (1 μg/mL) was added to the maternal circulation and samples were taken throughout the 1 h pre-experimental and 3 h experimental phases for measurement of EtG and markers of placental viability.
Results: After 3 h, the fetal-to-maternal ratio was 0.29 ± 0.02 and net maternal-to-fetal transfer was still occurring. Triplicate averages of EtG concentrations in perfused placental lobules ranged from 140 to 414 ng/g tissue. Placental validation markers were within normal ranges for all perfusions.

Discussion: The data show that EtG crosses the human placenta and primarily represents maternal exposure to alcohol.

Conclusions: This information can help with the development of more thorough biomarker screens for alcohol use during pregnancy.


86. LOW DOSE PRENATAL ETHANOL EXPOSURE INDUCES ANXIETY-LIKE BEHAVIOUR AND ALTERS DENDRITIC MORPHOLOGY IN THE BASOLATERAL AMYGDALA OF RAT OFFSPRING

Cullen CL, Burne TH, Lavidis NA, Moritz KM.
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ABSTRACT

Prenatal exposure to high levels of alcohol is strongly associated with poor cognitive outcomes particularly in relation to learning and memory. It is also becoming more evident that anxiety disorders and anxiety-like behaviour can be associated with prenatal alcohol exposure. This study used a rat model to determine if prenatal exposure to a relatively small amount of alcohol would result in anxiety-like behaviour and to determine if this was associated with morphological changes in the basolateral amygdala. Pregnant Sprague Dawley rats were fed a liquid diet containing either no alcohol (Control) or 6% (vol/vol) ethanol (EtOH) throughout gestation. Male and Female offspring underwent behavioural testing at 8 months (Adult) or 15 months (Aged) of age. Rats were perfusion fixed and brains were collected at the end of behavioural testing for morphological analysis of pyramidal neuron number and dendritic morphology within the basolateral amygdala. EtOH exposed offspring displayed anxiety-like behaviour in the elevated plus maze, holeboard and emergence tests. Although sexually dimorphic behaviour was apparent, sex did not impact anxiety-like behaviour induced by prenatal alcohol exposure. This increase in anxiety-like behaviour could not be attributed to a change in pyramidal cell number within the BLA but rather was associated with an increase in dendritic spines along the apical dendrite which is indicative of an increase in synaptic connectivity and activity within these neurons. This study is the first to link increases in anxiety-like behaviour to structural changes within the basolateral amygdala in a model of prenatal ethanol exposure. In addition, this study has shown that exposure to even a relatively small amount of alcohol during development leads to long term alterations in anxiety-like behaviour.


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87. **CHANGES IN ALCOHOL USE AND RELATIONSHIP SATISFACTION IN NORWEGIAN COUPLES DURING PREGNANCY.**

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**ABSTRACT**

**Background:** Numerous studies have documented a profound reduction in alcohol use among pregnant women, whereas research on expectant fathers has been scarce. The aim of this study was to measure changes in alcohol consumption from before pregnancy to 17 weeks in gestation for mothers and fathers, differentiating between parents with and without any previous children, and to measure how level and change in alcohol consumption into early pregnancy was associated with relationship satisfaction.

**Methods:** The data collection was conducted as part of the Norwegian Mother and Child Cohort Study (MoBa) at the Norwegian Institute of Public Health. This cohort now includes 108,000 children, 90,700 mothers and 71,500 fathers recruited from 1999 to 2008. The present study comprises 82,362 couples. Alcohol consumption was assessed using a questionnaire including items about usual drinking frequency, quantities, and number of occasions with heavy episodic drinking (HED). Relationship satisfaction was measured by five items scored on a Likert agreement scale.

**Results:** The findings indicate that both mothers and fathers reduce their drinking significantly during pregnancy. Reduction was apparent for all three measures of alcohol consumption. First-time fathers reduced their alcohol consumption more than experienced fathers, from initially higher levels. The gap between the fathers and their pregnant partner was greater for first-time parents compared to parents with previous children. Drinking pre-pregnancy and relationship satisfaction during pregnancy were weakly related within each partner, whereas no association across partners was observed.

**Conclusions:** Both expectant mothers and fathers changed their alcohol consumption patterns when expecting a child. Almost all mothers stopped drinking, whereas fathers reduced their drinking to a considerable degree. Relationship satisfaction was only slightly related to their drinking patterns. The findings may have important policy implications, mainly with regard to developing alcohol preventive strategies.

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88. **ALCOHOL CONSUMPTION BY PARENTS OF PACIFIC FAMILIES RESIDING IN NEW ZEALAND: FINDINGS FROM THE PACIFIC ISLANDS FAMILIES STUDY**

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**ABSTRACT**

Harmful alcohol consumption amongst Pacific people (those of Polynesian descent) is
recognized as a public health priority in New Zealand, yet little epidemiological information exists on this pattern of drinking. Using a large birth cohort study, which includes the mother, father and child triad, this study aims to determine the prevalence and change in any harmful drinking levels prenatally, antenatally and in the postpartum period for mothers and fathers, and to measure the concordance of both partners' reports of that drinking in an ethnically representative sample of Pacific families within New Zealand. Participants were selected from births where at least one parent was identified as being of Pacific ethnicity and a New Zealand permanent resident (1376 mothers and 825 fathers at baseline); many of whom are young to middle aged adults. These participants have been prospectively followed-up multiple times since. The Alcohol Use Disorders Identification Test consumption questions (AUDIT-C) were used over successive measurement waves to define any and harmful drinking levels. Recommended screening thresholds were employed. Longitudinal analyses on complete cases and imputed data, accounting for differential attrition, were undertaken and reported. Clear temporal patterns of alcohol consumption emerged for both mothers and fathers, together with significant and important ethnic differences. Moreover, there was considerable movement in alcohol consumption categories between consecutive measurement waves for both mothers and fathers. Among couples, there was significant asymmetry in drinking patterns and poor statistical agreement. However, 9.1% (14.1% in imputed analyses) of Pacific children aged 2 years had both parents indicated for harmful drinking. The significant important heterogeneity and ethnic differences suggest that both ethnic-specific and pan-Pacific interventions and prevention strategies are likely needed for successful interventions. More emphasis should be placed on targeting and addressing parents' alcohol misuse, particularly in the antenatal or postnatal period.

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89. A MODIFIED DELPHI STUDY OF SCREENING FOR FETAL ALCOHOL SPECTRUM DISORDERS IN AUSTRALIA
Rochelle E Watkins1*, Elizabeth J Elliott2,3,4, Jane Halliday5,6, Colleen M O’Leary1,7, Heather D’Antoine8, Elizabeth Russell9, Lorian Hayes10, Elizabeth Peadon2,3, Amanda Wilkins1,11, Heather M Jones1, Anne McKenzie1, Sue Miers12, Lucinda Burns13, Raewyn C Mutch1,11, Janet M Payne1, James P Fitzpatrick2,4, Maureen Carter14, Jane Latimer4 and Carol Bower1 
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12 National Organisation for Fetal Alcohol Syndrome and Related Disorders, Adelaide, Australia

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ABSTRACT

Background: There is little reliable information on the prevalence of fetal alcohol spectrum disorders (FASD) in Australia and no coordinated national approach to facilitate case detection. The aim of this study was to identify health professionals' perceptions about screening for FASD in Australia.

Method: A modified Delphi process was used to assess perceptions of the need for, and the process of, screening for FASD in Australia. We recruited a panel of 130 Australian health professionals with experience or expertise in FASD screening or diagnosis. A systematic review of the literature was used to develop Likert statements on screening coverage, components and assessment methods which were administered using an online survey over two survey rounds.

Results: Of the panel members surveyed, 95 (73%) responded to the questions on screening in the first survey round and, of these, 81 (85%) responded to the second round. Following two rounds there was consensus agreement on the need for targeted screening at birth (76%) and in childhood (84%). Participants did not reach consensus agreement on the need for universal screening at birth (55%) or in childhood (40%). Support for targeted screening was linked to perceived constraints on service provision and the need to examine the performance, costs and benefits of screening.

For targeted screening of high risk groups, we found highest agreement for siblings of known cases of FASD (96%) and children of mothers attending alcohol treatment services (93%). Participants agreed that screening for FASD primarily requires assessment of prenatal alcohol exposure at birth (86%) and in childhood (88%), and that a checklist is needed to identify the components of screening and criteria for referral at birth (84%) and in childhood (90%).

Conclusions: There is an agreed need for targeted but not universal screening for FASD in Australia, and sufficient consensus among health professionals to warrant development and evaluation of standardised methods for targeted screening and referral in the Australian context. Participants emphasised the need for locally-appropriate, evidence-based approaches to facilitate case detection, and the importance of ensuring that screening and referral programs are supported by adequate diagnostic and management capacity.

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90. FETAL ALCOHOL SPECTRUM DISORDERS: KNOWLEDGE AND SCREENING PRACTICES OF UNIVERSITY HOSPITAL MEDICAL STUDENTS AND RESIDENTS
Kate Arnold, Megan Burke, Ashley Decker, Emily Herzberg, Michael Maher, Kevin Motz, Hari Nandu, Luke O'Donnel, Altaf Pirmohamed, Michael Ybarra
USA

ABSTRACT

Background: Fetal alcohol spectrum disorder (FASD) is the leading cause of preventable intellectual disabilities in the United States and a significant public health issue.
Objectives: The purpose of this study is to evaluate the knowledge and screening practices of pre-clinical medical students and clinical providers on FAS, FASD, and alcohol consumption.

Methods: A short survey sent to medical students and residents on the campus of a large medical school and university hospital.

Results: On the survey of clinical providers, 38% of respondents stated they always survey pregnant women about their alcohol consumption, 34% stated they always screen patients planning to get pregnant, and 9% screen women of childbearing age. There were a significant percentage of providers who never screen women. When questioned regarding safe amounts of alcohol consumption during pregnancy, 69% of pre-clinical medical students and 67% of clinical providers stated there is no safe amount of alcohol consumption. Clinical providers were much more likely to correctly select the facial features necessary for the diagnosis (p-value < 0.01).

Conclusions: Significant differences exist in the knowledge and screening practices of these different healthcare providers and trainees. Future interventions should seek to improve knowledge on FAS, FASD, and alcohol consumption, in order for practitioners to be more consistent with national guidelines and the Surgeon General recommendations.

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91. MODERATE PRENATAL ALCOHOL EXPOSURE REDUCES PLASTICITY AND ALTERS NMDA RECEPTOR SUBUNIT COMPOSITION IN THE DENTATE GYRUS
Brady ML, Diaz MR, Iuso A, Everett JC, Valenzuela CF, Caldwell KK.
Department of Neurosciences, School of Medicine, University of New Mexico Health Sciences Center, Albuquerque, New Mexico 87131, USA.

ABSTRACT
Although it is well documented that heavy consumption of alcohol during pregnancy impairs brain development, it remains controversial whether moderate consumption causes significant damage. Using a limited access, voluntary consumption paradigm, we recently demonstrated that moderate prenatal alcohol exposure (MPAE) is associated with dentate gyrus-dependent learning and memory deficits that are manifested in adulthood. Here, we identified a novel mechanism that may underlie this effect of MPAE. We found that MPAE mice exhibit deficits in NMDA receptor (NMDAR)-dependent long-term potentiation (LTP) in the dentate gyrus. Further, using semiquantitative immunoblotting techniques, we found that the levels of GluN2B subunits were decreased in the synaptic membrane, while levels of C2'-containing GluN1 and GluN3A subunits were increased, in the dentate gyrus of MPAE mice. These data suggest that MPAE alters the subunit composition of synaptic NMDARs, leading to impaired NMDAR-dependent LTP in the dentate gyrus.


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92. BEHAVIOURAL CHANGE IN RELATION TO ALCOHOL EXPOSURE IN EARLY PREGNANCY AND IMPACT ON PERINATAL OUTCOMES - A PROSPECTIVE COHORT STUDY

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4 Department of Public Health and Primary Care, Trinity College Dublin, Dublin, Republic of Ireland

ABSTRACT

Background: There has been limited research addressing whether behavioural change in relation to alcohol exposure in pregnancy results in better perinatal outcomes.

Methods: A cohort study of 6725 women who booked for antenatal care and delivered in a large urban teaching hospital in 2010–2011. A detailed history of alcohol consumption pre-pregnancy and during early pregnancy was recorded at the first antenatal visit with follow-up of the mother and infant until discharge following birth. Adverse perinatal outcomes were compared for ‘non-drinkers’, ‘ex-drinkers’ and ‘current drinkers’.

Results: Of the 6017 (90%) women who reported alcohol consumption prior to pregnancy 3325 (55%) engaged in binge drinking and 266 (4.4%) consumed more than 14 units on average per week. At the time of booking 5649 (94%) women were ex-drinkers and of the 368 women who continued to drink 338 (92%) had a low intake (0–5 units per week), 30 (8%) an excess intake (6–20+ units per week) and 93 (25%) reported at least one episode of binge drinking. Factors associated with continuing to drink in early pregnancy included older maternal age (30–39 years), (OR 1.6; 95% CI 1.3 to 1.8), Irish nationality (OR 3.1; 95% CI 2.2 to 4.3) and smoking (OR 2.6; 95% CI 1.9 to 3.5). Ex-drinkers had similar perinatal outcomes to non-drinkers. Compared to non-drinkers current drinking was associated with an increased risk of intrauterine growth restriction (IUGR) (13% versus 19%, crude OR 1.6; 95% CI 1.1 to 2.2, adjusted OR 1.2; 95% CI 0.8 to 1.8). The greatest risk of IUGR was among women who continued to both drink and smoke, (9% versus 32%, crude OR 4.8; 95% CI 3.3 to 7.0, adjusted OR 4.5; 95% CI 3.1 to 6.7).

Conclusions: Public Health campaigns need to emphasise the potential health gains of abstaining from both alcohol and smoking in pregnancy.

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Plos One
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93. NOVEL OXYTOCIN GENE EXPRESSION IN THE HINDBRAIN IS INDUCED BY ALCOHOL EXPOSURE: TRANSGENIC ZEBRAFISH ENABLE VISUALIZATION OF SENSITIVE NEURONS
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ABSTRACT
Background: Fetal Alcohol Spectrum Disorders (FASD) are a collection of disorders resulting from fetal ethanol exposure, which causes a wide range of physical, neurological and behavioral deficits including heightened susceptibility for alcoholism and addictive disorders. While a number of mechanisms have been proposed for how ethanol exposure disrupts brain development, with selective groups of neurons undergoing reduced proliferation, dysfunction and death, the induction of a new neurotransmitter phenotype by ethanol exposure has not yet been reported.

Principal Findings: The effects of embryonic and larval ethanol exposure on brain development were visually monitored using transgenic zebrafish expressing cell-specific green fluorescent protein (GFP) marker genes. Specific subsets of GFP-expressing neurons were highly sensitive to ethanol exposure, but only during defined developmental windows. In the med12 mutant, which affects the Mediator co-activator complex component Med12, exposure to lower concentrations of ethanol was sufficient to reduce GFP expression in transgenic embryos. In transgenic embryos and larva containing GFP driven by an oxytocin-like (oxtl) promoter, ethanol exposure dramatically up-regulated GFP expression in a small group of hindbrain neurons, while having no effect on expression in the neuroendocrine preoptic area.

Conclusions: Alcohol exposure during limited embryonic periods impedes the development of specific, identifiable groups of neurons, and the med12 mutation sensitizes these neurons to the deleterious effects of ethanol. In contrast, ethanol exposure induces oxtl expression in the hindbrain, a finding with profound implications for understanding alcoholism and other addictive disorders.

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http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0053991

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ACUTE ALCOHOL EXPOSURE, ACIDEMIA OR GLUTAMINE ADMINISTRATION IMPACTS AMINO ACID HOMEOSTASIS IN OVINE MATERNAL AND FETAL PLASMA

Washburn SE, Sawant OB, Lunde ER, Wu G, Cudd TA.
Department of Veterinary Physiology and Pharmacology and Michael E. DeBakey Institute, Texas A&M University, College Station, Texas, 77843, USA, swashburn@cvm.tamu.edu.

ABSTRACT
Fetal alcohol syndrome (FAS) is a significant problem in human reproductive medicine. Maternal alcohol administration alters maternal amino acid homeostasis and results in acidemia in both mother and fetus, causing fetal growth restriction. We hypothesized that administration of glutamine, which increases renal ammoniagenesis to regulate acid-base balance, may provide an intervention strategy. This hypothesis was tested using sheep as an animal model. On day 115 of gestation, ewes were anesthetized and aseptic surgery was performed to insert catheters into the fetal abdominal aorta as well as the maternal abdominal aorta and vena cava. On day 128 of gestation, ewes received intravenous administration of saline, alcohol [1.75 g/kg body weight (BW)/h], a bolus of 30 mg glutamine/kg BW, alcohol + a bolus of 30 mg glutamine/kg BW, a bolus of 100 mg glutamine/kg BW, alcohol + a bolus of 100 mg glutamine/kg BW, or received CO(2) administration to induce acidemia independent of alcohol. Blood samples were obtained simultaneously from the mother and the fetus at times 0 and 60 min (the time of peak blood alcohol concentration) of the study. Administration of alcohol to pregnant ewes led to a reduction in concentrations of glutamine and related amino acids in plasma by 21-30 %. An acute administration of glutamine to ewes, concurrent with alcohol administration, improved the profile of most amino acids (including citrulline and arginine) in maternal and fetal plasma. We suggest that glutamine may have a protective effect against alcohol-induced metabolic disorders and FAS in the ovine model.

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IDENTIFICATION OF CELL-SPECIFIC PATTERNS OF REFERENCE GENE STABILITY IN QUANTITATIVE REVERSE-TRANSCRIPTASE POLYMERASE CHAIN REACTION STUDIES OF EMBRYONIC, PLACENTAL AND NEURAL STEM MODELS OF PRENATAL ETHANOL EXPOSURE

Carnahan MN, Veazey KJ, Muller D, Tingling JD, Miranda RC, Golding MC.
College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843, USA.

ABSTRACT
Identification of the transcriptional networks disrupted by prenatal ethanol exposure remains a core requirement to better understanding the molecular mechanisms of alcohol-induced teratogenesis. In this regard, quantitative reverse-transcriptase polymerase chain reaction (qPCR) has emerged as an essential technique in our efforts to characterize alterations in gene expression brought on by exposure to alcohol. However, many publications continue to report the utilization of inappropriate methods of qPCR normalization, and for many in vitro models, no consistent set of empirically tested normalization controls have been identified. In the present study, we sought to identify a group of candidate reference genes for use within studies of alcohol exposed embryonic, placental, and neurosphere stem cells under both conditions maintaining stemness as well as throughout in vitro differentiation. To this end, we
surveyed the recent literature and compiled a short list of fourteen candidate genes commonly used as normalization controls in qPCR studies of gene expression. This list included: Actb, B2m, Gapdh, Gusb, H2afz, Hk2, Hmbs, Hprt, Mrpl1, Pgk1, Ppia, Sdha, Tbp, and Ywhaz. From these studies, we find no single candidate gene was consistently refractory to the influence of alcohol nor completely stable throughout in vitro differentiation. Accordingly, we propose normalizing qPCR measurements to the geometric mean C(T) values obtained for three independent reference mRNAs as a reliable method to accurately interpret qPCR data and assess alterations in gene expression within alcohol treated cultures. Highlighting the importance of careful and empirical reference gene selection, the commonly used reference gene Actb was often amongst the least stable candidate genes tested. In fact, it would not serve as a valid normalization control in many cases. Data presented here will aid in the design of future experiments using stem cells to study the transcriptional processes driving differentiation, and model the developmental impact of teratogens.

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96. MATERNAL FACTORS ASSOCIATED WITH HEAVY PERICONCEPTIONAL ALCOHOL INTAKE AND DRINKING FOLLOWING PREGNANCY RECOGNITION: A POST-PARTUM SURVEY OF NEW ZEALAND WOMEN  
Mallard SR, Connor JL, Houghton LA.  
Department of Human Nutrition, University of Otago, Dunedin, New Zealand.

ABSTRACT

Introduction and Aims: Alcohol consumption during pregnancy places the foetus at risk of Foetal Alcohol Spectrum Disorders. Little is known about the current prevalence and patterns of alcohol consumption before and following pregnancy recognition in New Zealand.

Design and Methods: A retrospective survey of 723 post-partum women resident in maternity wards located across New Zealand was conducted using a self-administered questionnaire. Maternal sociodemographic and obstetric characteristics and alcohol intake before and after pregnancy recognition were assessed.

Results: Of the 968 women invited to participate, 78% agreed. Eighty-two percent of women reported consuming alcohol prior to pregnancy and 20% reported typically consuming >4 New Zealand standard drinks per occasion. Overall, 34% of women reported drinking at some time during pregnancy. Twelve percent of pregnancies were at high risk of heavy alcohol exposure in early gestation. In fully adjusted analysis, pregnancies most at risk were those of indigenous Māori women, Pacific women, smokers and drug users. Almost one-quarter (24%) of drinkers continued to drink following pregnancy recognition, and in fully adjusted analysis, continuing to drink was positively associated with frequency of alcohol consumption before pregnancy (P < 0.001 for linear trend).

Discussion and Conclusions: To reduce the burden of alcohol-related harm to the foetus, these findings suggest that New Zealand alcohol policy should be focused not only on promoting total abstinence when planning a pregnancy and when pregnant, but also on reducing ‘binge drinking’ culture and the frequent consumption of lower levels of alcohol.

Link to the Article,  
http://www.ncbi.nlm.nih.gov/pubmed/23305204

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97. **DIAGNOSTIC OUTCOMES OF 27 CHILDREN REFERRED BY PEDIATRICIANS TO A GENETICS CLINIC IN THE NETHERLANDS WITH SUSPICION OF FETAL ALCOHOL SPECTRUM DISORDERS**

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**ABSTRACT**

The characteristics of fetal alcohol spectrum disorders (FASD) constitute a specific facial phenotype, growth failure and neurodevelopmental defects. Reported FASD prevalences vary widely from 0.08 per 1,000 up to 68.0–89.2 per 1,000. We aimed to evaluate to which extent children referred with a suspicion of FASD, indeed have FASD. We included all 27 children referred to our genetic department with a suspicion of FASD between 2005 and 2010. Nineteen children (70.3%) were of non-Dutch ancestry, and 24 (88.9%) had been adopted. We used both the 4-Digit Code and the Revised Institute of Medicine criteria. More than half of the children did not meet either criteria for the diagnosis of FASD. Of note, after evaluation 8/27 children appeared not to have confirmed prenatal alcohol exposure. Two children referred for suspicion of FASD (neither of which were exposed to alcohol or met the criteria for FASD) had a pathogenic microstructural chromosomal rearrangement (del16p11.2 of 542 KB and dup1q44 of 915 KB). In 22/24 children (91.7%) there were other factors that may have affected their intellectual abilities, such as familial intellectual disability and social deprivation. We recommend a critical approach towards the diagnosis FASD, and to investigate all patients suspected to have FASD for other causative factors including genetic abnormalities.

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98. **BRIEF FASD PREVENTION INTERVENTION: PHYSICIANS' SKILLS DEMONSTRATED IN A CLINICAL TRIAL IN RUSSIA**


Russia

**ABSTRACT**

Background: Alcohol consumption during pregnancy can result in a range of adverse pregnancy outcomes including Fetal Alcohol Spectrum Disorders (FASD). Risky drinking...
among Russian women constitutes a significant risk for alcohol-exposed pregnancies (AEP). Russian women report that obstetrics and gynecology (OB/GYN) physicians are the most important source of information about alcohol consumption during pregnancy and developing effective prevention interventions is indicated. This is the first study focused on implementation of an AEP prevention intervention at women's clinics in Russia.

Method: The paper describes the intervention protocol and addresses questions about the feasibility of a brief FASD prevention intervention delivered by OB/GYN at women's clinics in Russia. Brief physician intervention guidelines and two evidence-based FASD prevention interventions were utilized to design a brief dual-focused physician intervention (DFBPI) appropriate to Russian OB/GYN care. The questions answered were whether trained OB/GYN physicians could feasibly deliver DFBPI during women's routine clinic visits, whether they maintained skills over time in clinical settings, and which specific intervention components were better maintained. Data were collected as part of a larger study aimed at evaluating effectiveness of DFBPI in reducing AEP risk in non-pregnant women. Methods of monitoring the intervention delivery included fidelity check lists (FCL) with the key components of the intervention completed by physicians and patients and live and audio taped observations of intervention sessions. Physicians (N= 23) and women (N= 372) independently completed FCL, and 78 audiotapes were coded.

Results: The differences between women's and physicians' reports on individual items were not significant. Although the majority of physician and patient reports were consistent (N=305), a discrepancy existed between the reports in 57 cases. Women reported more intervention components missing compared to physicians (p<0.001). Discussing barriers was the most difficult component for physicians to implement, and OB/GYN demonstrated difficulties in discussing contraception methods.

Conclusions: The results supported the feasibility of the DFBPI in Russia. OB/GYN physicians trained in the DFBPI, monitored, and supported were able to implement and maintain skills during the study. In addition to the alcohol focus, DFBPI training needs to have a sufficient component to improve physicians' skills in discussing contraception use.


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Wiley Online Library - Child: Care, Health and Development
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99. DIAGNOSTIC NOMENCLATURE FOR FOETAL ALCOHOL SPECTRUM DISORDERS: THE CONTINUING CHALLENGE OF CAUSALITY
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1 Division of Developmental Pediatrics, Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada
2 Developmental Neurosciences & Child Health, Child & Family Research Institute, Vancouver, BC, Canada
3 Sunny Hill Health Centre for Children, Vancouver, BC, Canada
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Anton R. Miller, Department of Pediatrics, University of British Columbia, F515-4480 Oak Street, Vancouver, BC, Canada, E-mail: amiller@cw.bc.ca

ABSTRACT
Prenatal alcohol exposure is a risk factor for neurologically based cognitive and adaptive disability. Diagnostic nomenclature for prenatally exposed children with cognitive and
adaptive disability who lack features for foetal alcohol syndrome (FAS) or partial FAS includes the terms alcohol-related neurodevelopmental disorder (ARND) and foetal alcohol spectrum disorder(s) (FASD). Although these terms are now widely used, this paper argues that both are problematic. ARND is flawed by unjustifiably turning a risk factor into a causal factor and shrouding the result in terminological ambiguity, while FASD is not appropriate as a clinical label, and its use as a proxy for ARND deflects critical attention from the causal inferencing that is integral to diagnosing children with an alcohol-related teratogenic condition. Existing nomenclature is at odds with logical and evidence-based diagnosing and also has implications for interpretation of epidemiological data. Diagnostic nomenclature that is not tightly linked to causal inference is preferable at the present stage of this field's development.


100. DEVELOPMENTAL TOXICITY OF POLYETHYLENE GLYCOL-G-POLYVINYL ALCOHOL GRAFTED COPOLYMER IN RATS AND RABBITS
Heuschmid FF, Schneider S, Schuster P, Lauer B, Ravenzwaay BV. Product Safety Department BASF SE, Ludwigshafen, Germany.

ABSTRACT
Polyethylene glycol-g-polyvinyl alcohol (PEG-PVA) grafted copolymer was evaluated in developmental toxicity studies with Wistar rats and Himalayan rabbits. Pregnant Wistar rats were gavaged with 0 (vehicle control), 100, 300, or 1000mg PEG-PVA grafted copolymer/kg bw/day from gestation day (GD) 6-15. Pregnant Himalayan rabbits received the same treatment from GD 6 to 19. On GD 20 and 29 for rats and rabbits, respectively, the animals were euthanized and were examined grossly. For each dam, corpora lutea were counted and number and distribution of implantation sites were determined. The fetuses were removed, sexed, weighed, and evaluated for any external, soft tissue, and skeletal findings. No significant findings were found that could be attributed to administration of PEG-PVA grafted copolymer. Under the conditions of these studies, the no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity in both species was the highest dose tested of 1000mg/kg bw/day.


101. EFFECTS OF ETHANOL EXPOSURE DURING EARLY PREGNANCY IN HYPERACTIVE, INATTENTIVE AND IMPULSIVE BEHAVIORS AND MECP2 EXPRESSION IN RODENT OFFSPRING
ABSTRACT
Prenatal exposure to alcohol has consistently been associated with adverse effects on neurodevelopment, which is collectively called fetal alcohol spectrum disorder (FASD). Increasing evidence suggest that prenatal exposure to alcohol increases the risk of developing attention deficit/hyperactivity disorder-like behavior in human. In this study, we investigated the behavioral effects of prenatal exposure to EtOH in offspring mice and rats focusing on hyperactivity and impulsivity. We also examined changes in dopamine transporter and MeCP2 expression, which may underlie as a key neurobiological and epigenetic determinant in FASD and hyperactive, inattentive and impulsive behaviors. Mouse or rat offspring born from dam exposed to alcohol during pregnancy (EtOH group) showed hyper locomotive activity, attention deficit and impulsivity. EtOH group also showed increased dopamine transporter and norepinephrine transporter level compared to control group in the prefrontal cortex and striatum. Prenatal exposure to EtOH also significantly decreased the expression of MeCP2 in both prefrontal cortex and striatum. These results suggest that prenatal exposure to EtOH induces hyperactive, inattentive and impulsive behaviors in rodent offspring that might be related to global epigenetic changes as well as aberration in catecholamine neurotransmitter transporter system.

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102. ORAL AND DERMAL DEVELOPMENTAL TOXICITY STUDIES OF PHENYLETHYL ALCOHOL IN RATS.
Research Institute for Fragrance Materials, Inc, 50 Tice Boulevard, Woodcliff Lake, NJ 07677, USA.

ABSTRACT
Phenylethyl alcohol (PEA) was tested for developmental toxicity. Pregnant rats were fed 0, 83, 266, or 799 mg/kg/d PEA on gestation days (GDs) 6 to 15; only minimal, nonsignificant effects were observed. In dermal studies, PEA (neat) was applied to the skin on GDs 6 to 15 at dosages of 0, 140, 430, or 1400 mg/kg/d and at 0, 70, 140, 280, 430, or 700 mg/kg/d in a corroborative study. Observations included maternal and embryo-fetal toxicity/abnormalities at ≥1400 mg/kg/d, increased incidences of rudimentary cervical ribs at ≥430 mg/kg/d, and reduced fetal body weights at ≥140 mg/kg/d. Dermal maternal and developmental no-observed-adverse-effect levels are 70 mg/kg/d, based on dermal irritation and reductions (nonsignificant) in fetal body weights. Human exposure from fragrances is 0.02 mg/kg/d, resulting in a margin of safety >2600, when marked differences in dermal absorption between rats and humans are considered. Under normal fragrance use conditions, PEA is not a developmental toxicity hazard for humans.

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103. PREVENTION OF ALCOHOL-EXPOSED PREGNANCIES AMONG NONPREGNANT AMERICAN INDIAN WOMEN
Hanson JD, Miller AL, Winberg A, Elliott AJ.
Center for Health Outcomes and Prevention Research, Sanford Research, 2301 E. 60th St. N., Sioux Falls, SD 57104, USA. Jessica.D.Hanson@sanfordhealth.org

ABSTRACT
Purpose: The goal of this project was to evaluate an intervention on reducing alcohol-exposed pregnancies with nonpregnant American Indian women, with a focus on risky drinking and ineffective contraception use.

Design: This study had a descriptive longitudinal study design, with follow-up every 3 months for 1 year.

Setting: Three American Indian tribes in the Northern Plains.

Subjects: Participants were 231 nonpregnant American Indian women.

Intervention: Participants responded to drinking and contraception questions through the telephone and then received intervention materials via mail. Follow-up telephone surveys occurred at 3, 6, 9, and 12 months after the baseline call, and participants were again mailed intervention materials.

Measures: Alcohol consumption and birth control measurements were modified from the Project CHOICES program. The intervention was based on motivational interviewing constructs.

Analysis: Analysis techniques included covariate-adjusted generalized estimating equation methods and Bonferroni correction.

Results: All of the alcohol consumption amount responses had significant decreases with each follow-up intervention session; the average change for the range of questions was -26% to -17%. The proportion of those stating they did not use birth control decreased from 29% to 10% during the first 3 months.

Conclusions: The intervention was successful in modifying self-reported drinking and contraception behaviors. This project is the only one to date that has focused on preventing alcohol-exposed pregnancies in nonpregnant American Indian women.


104. BRIEF INTERVENTION FOR RISK-DRINKING WOMEN: A MIXED METHODS ANALYSIS OF CONTENT AND PROCESS
DeMarinis V, Caplan J, Chang G.
Uppsala University, Uppsala, Sweden.

ABSTRACT
Background and Objectives: Although brief interventions (BIs) are among the most highly
promoted treatments for alcohol problems, their effective components are unknown. This may be particularly important when considering women since some reviews have suggested that BIs are more efficacious among men. The purpose of this pilot study is to utilize a mixed methods and gender analysis approach to generate hypotheses about the effective components of BIs given to women with medical problems exacerbated by problem drinking.

**Methods:** Random sample of 20 BIs given to women with diabetes, hypertension, infertility, or osteoporosis. Quantitative and qualitative analytic methods were undertaken in a stepwise progression, followed by a gender analysis using the Worldview Assessment Framework.

**Results:** Main findings include that a worldview encompassing drinking as an entitlement may be a moderator limiting the effectiveness of a BI, that understanding the impact of alcohol on infertility problems as distinct from prenatal alcohol use may be a mediator for BI effectiveness, and that providing information about sensible drinking limits in the context of a specific medical problem was feasible.

**Conclusions and Significance:** Content and process areas are important to consider when offering BI for risk-drinking women with medical problems and may help to improve treatment efficacy in this group.

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105. **FETAL ALCOHOL EXPOSURE: CONSEQUENCES, DIAGNOSIS, AND TREATMENT.**  
Pruett D, Waterman EH, Caughey AB.  
School of Medicine, Department of Family Medicine, Oregon Health and Science University, Portland, OR 97239, USA. pothierd@ohsu.edu

**ABSTRACT**  
Maternal alcohol use during pregnancy is prevalent, with as many as 12% of pregnant women consuming alcohol. Alcohol intake may vary from an occasional drink, to weekly binge drinking, to chronic alcohol use throughout pregnancy. Whereas there are certain known consequences from fetal alcohol exposure, such as fetal alcohol syndrome, other effects are less well defined. Craniofacial dysmorphologies, abnormalities of organ systems, behavioral and intellectual deficits, and fetal death have all been attributed to maternal alcohol consumption. This review article considers the theoretical mechanisms of how alcohol affects the fetus, including the variable susceptibility to fetal alcohol exposure and the implications of ethanol dose and timing of exposure. Criteria for diagnosis of fetal alcohol syndrome are discussed, as well as new methods for early detection of maternal alcohol use and fetal alcohol exposure, such as the use of fatty acid ethyl esters. Finally, current and novel treatment strategies, both in utero and post utero, are reviewed.

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106. **THE ROLE OF NADPH OXIDASE ENZYMES IN FETAL ALCOHOL SYNDROME**
Alexandria Hill, Huazhi Yin, Ester Tamayo, Nathan Drever, George Saade, Egle Bytautiene
USA

No Abstract Available.

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107. **CREATING A CULTURALLY APPROPRIATE WEB-BASED BEHAVIORAL INTERVENTION FOR AMERICAN INDIAN/ALASKA NATIVE WOMEN IN SOUTHERN CALIFORNIA: THE HEALTHY WOMEN HEALTHY NATIVE NATION STUDY.**
Gorman JR, Clapp JD, Calac D, Kolander C, Nyquist C, Chambers CD.
Department of Pediatrics, University of California San Diego, La Jolla, CA 92093, USA.

**ABSTRACT**
Health disparities in fetal alcohol spectrum disorders (FASD) are of high importance to American Indian/Alaska Native (AI/AN) communities. We conducted focus groups and interviews with 21 AI/AN women and key informants in Southern California to modify a brief, Web-based program for screening and prevention of prenatal alcohol use. This process resulted in several important program modifications and was essential for fostering partnerships between researchers and the community, engaging community members in research, and identifying community priorities.

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108. **LETHALITY OF TAURINE AND ALCOHOL COADMINISTRATION IN MICE**
Taranukhin AG, Saransaari P, Oja SS.
University of Tampere Medical School, Tampere, Finland. andrey.taranukhin@uta.fi

**ABSTRACT**
Alcohol consumption by mothers during pregnancy causes a fetal alcohol syndrome associated with massive neuronal apoptosis. We have recently shown that taurine at a dose of 2 g/kg saves about 50% of dying cerebellar neurons from ethanol-induced apoptosis in 7-day-old mice. However, a further increase in the taurine dose to ethanol-treated mice had a toxic and in some cases lethal effect. In the present work we studied the toxic effects of taurine and ethanol coadministration in three age groups: 7-day-old, adult (5 to 6 months old), and old (12 to 13 months old) mice. Taurine and ethanol were injected in two half-doses: taurine at 0 and 4 h and ethanol at 1 and 3 h. The minimal 100% lethal doses in coadministration of taurine and ethanol were the following: 7-day-old mice-6 g/kg taurine + 5 g/kg ethanol, adult mice-10 g/kg of taurine + 8 g/kg of ethanol, and old mice-above 6 g/k of taurine + 6 g/kg of ethanol. All mice treated with taurine or ethanol alone survived. The adult
and old mice dying from the combined toxicity of taurine and ethanol showed a marked fall in blood glucose, which may be one reason for lethality. A comparison of the lethal doses of taurine and ethanol coadministration in different age groups allows us to conclude that the adverse effect of the combined toxicity of taurine and ethanol is age dependent.


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109. PRENATAL ALCOHOL EXPOSURE AFFECTS VASCULATURE DEVELOPMENT IN THE NEONATAL BRAIN
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Email: Bruno José Gonzalez PhD (bruno.gonzales@univ-rouen.fr)

ABSTRACT
Objective: In humans, antenatal alcohol exposure elicits various developmental disorders, in particular in the brain. Numerous studies focus on the deleterious effects of alcohol on neural cells. Although recent studies suggest that alcohol can affect angiogenesis in adults, the impact of prenatal alcohol exposure on brain microvasculature remains poorly understood.

Methods: We used a mouse model to investigate effects of prenatal alcohol exposure on the cortical microvascular network in vivo and ex vivo and the action of alcohol, glutamate, and vascular endothelial growth factor A (VEGF) on activity, plasticity, and survival of microvessels. We used quantitative reverse transcriptase polymerase chain reaction, Western blot, immunohistochemistry, calcimetry, and videomicroscopy. We characterized the effect of prenatal alcohol exposure on the cortical microvascular network in human controls and fetal alcohol syndrome (FAS)/partial FAS (pFAS) patients at different developmental stages.

Results: In mice, prenatal alcohol exposure induced a reduction of cortical vascular density, loss of the radial orientation of microvessels, and altered expression of VEGF receptors. Time-lapse experiments performed on brain slices revealed that ethanol inhibited glutamate-induced calcium mobilization in endothelial cells, affected plasticity, and promoted death of microvessels. These effects were prevented by VEGF. In humans, we evidenced a stage-dependent alteration of the vascular network in the cortices of fetuses with pFAS/FAS. Whereas no modification was observed from gestational week 20 (WG20) to WG22, the radial organization of cortical microvessels was clearly altered in pFAS/FAS patients from WG30 to WG38.

Interpretation: Prenatal alcohol exposure affects cortical angiogenesis both in mice and in

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110. VARIABILITY IN CLASSROOM SOCIAL COMMUNICATION: PERFORMANCE OF CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS AND TYPICALLY DEVELOPING PEERS
Kjellmer L, Olswang LB.
Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden.

ABSTRACT
Purpose: This research examined how variability in classroom social communication performance differed between children with fetal alcohol spectrum disorders (FASD) and pair-matched peers developing typically. Methods Twelve pairs of children were observed in their classrooms, 40 minutes a day (20 minutes per child) for four days across two weeks. Coders documented classroom social communication during situations of Cooperation and following School Rules by recording performance on handheld computers using the Social Communication Coding System (SCCS). The SCCS consists of six behavioral dimensions (prosocial/engaged, passive/disengaged, irrelevant, hostile/coercive, assertive, and adult seeking). The frequency of occurrence and duration of each dimension was recorded. These measures were then used to examine variability in performance within and across days (changeability and stability respectively). RESULTS: Children with FASD were more variable than their peers in terms of changing between behavioral dimensions more often (changeability) and varying their behavior more from day-to-day (stability) independent of classroom situation. Implications Documenting performance variability may provide a clearer understanding of the classroom social communication difficulties of the child with mild FASD.

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111. PRENATAL ETHANOL EXPOSURE INCREASES ETHANOL INTAKE AND REDUCES C-FOS EXPRESSION IN INFRALIMBIC CORTEX OF ADOLESCENT RATS
Fabio MC, March SM, Molina JC, Nizhnikov ME, Spear NE, Pautassi RM.
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ABSTRACT
Prenatal ethanol exposure significantly increases later predisposition for alcohol intake, but the mechanisms associated with this phenomenon remain hypothetical. This study analyzed (Experiment 1) ethanol intake in adolescent inbred WKAH/Hok Wistar rats prenatally exposed to ethanol (2.0g/kg) or vehicle, on gestational days 17-20. Subsequent Experiments (2, 3 and 4) tested several variables likely to underlie the effect of gestational ethanol on adolescent ethanol preference, including ethanol-induced locomotor activation (LMA), ethanol-induced emission of ultrasonic vocalizations (USVs) after exposure to a rough
exteroceptive stimulus, and induction of the immediate early gene C-fos in brain areas associated with processing of reward stimuli and with the retrieval and extinction of associative learning. Prenatal ethanol induced a two-fold increase in ethanol intake. Adolescents exhibited significant ethanol-induced LMA, emitted more aversive than appetitive USVs, and postnatal ethanol administration significantly exacerbated the emission of USVs. These effects, however, were not affected by prenatal ethanol. Adolescents prenatally exposed to ethanol as fetuses exhibited reduced neural activity in infralimbic cortex (but not in prelimbic cortex or nucleus accumbens core or shell), an area that has been implicated in the extinction of drug-mediated associative memories. Ethanol metabolism was not affected by prenatal ethanol. Late gestational exposure to ethanol significantly heightened drinking in the adolescent offspring of an inbred rat strain. Ethanol-induced LMA and USVs were not associated with differential ethanol intake due to prenatal ethanol exposure. Prenatal ethanol, however, altered basal neural activity in the infralimbic prefrontal cortex. Future studies should analyze the functionality of medial prefrontal cortex after prenatal ethanol and its potential association with predisposition for heightened ethanol intake.


112. RETROSPECTIVE ANALYSIS OF NEONATAL DATA IN A MONOCENTRIC COHORT OF 170 NEWBORNS OF POLYDRUG-USING MOTHERS, ILE-DE-FRANCE, 1999-2008
Lejeune C, Genest L, Miossec E, Simonpoli AM, Simmat-Durand L.
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ABSTRACT
Objectives: To analyze neonatal morbidity in a single-center retrospective cohort (1999-2008) according to the mothers' polydrug use and to the social and demographic context.

Material and Methods: One hundred and seventy newborns were identified whose mothers used two or more substances (such as heroin, cocaine, opioid maintenance treatment, tobacco, alcohol, hashish, amphetamines, benzodiazepines, or other psychotropics) at the beginning of their pregnancies. The database included 168 sociodemographic variables describing mothers' living conditions and their drug-abuse characteristics; perinatal variables such as gestational age, weight, neonatal abstinence syndrome, and modalities of discharge; and correlations with the main neonatal morbidities.

Results: The mothers' mean age at delivery was 31.6yrs. It was the first pregnancy for 35.2% of the mothers but the mean number of previous abortions was 1.14 and 16.3% already had previous children in foster care. At delivery only 8.2% used only one product, 52.9% 2 or 3 products, and 37.6% four or more substances. All sociodemographic variables, the deprivation score, the number of previous abortions and miscarriages, and poor prenatal monitoring were significantly different for the mothers using four products or more. The uses changed along the years of study: fewer mothers used heroin but more used hashish, combined with other substances. The medical care also changed: greater participation on the part of mothers in neonatal care, more frequent breastfeeding, less medication for neonatal abstinence syndrome with the same severity score: i.e., 45.5% of infants with a Lipsitz score between 8 and 12 received a morphine treatment in 1999-2000 versus only 5.5% in 2005-2006 and none in 2007-2008. The mean gestational age was 38.1weeks. Preterm births

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(22.2%) and intrauterine growth restriction (18% with birth weight <10th percentile) were mainly correlated with the number of substances at delivery (17.3% preterm if three substances or less and 31.3% if four substances or more; p<0.001), social deprivation, poor prenatal care, and mothers having gained less than 5kg in weight during pregnancy (57.1% of intrauterine growth restriction versus 14.5%). Birth weight, height, and head circumference were significantly different for mothers having drunken alcohol. Among the newborns, seven showed complete fetal alcohol syndrome. The neonatal abstinence syndrome severity (23% with a Lipsitz score>9, one-quarter of whom were medicated with morphine) was correlated with an in-utero exposure to opiates, mainly in combination with benzodiazepines, and with the use of four or more substances. The mean age of infants at discharge was 18.1 days (SD 3.39): 21.1% stayed 30 days or more in the hospital, mainly because of prematurity or intrauterine growth restriction, a high neonatal abstinence syndrome score, maternal polydrug use, psychosocial deprivation, or foster care placement decisions. Decisions for foster care placement (15%) applied to polydrug users, with social deprivation, undermonitored pregnancies, or bonding difficulties.

**Conclusion:** The main factors correlated with poor neonatal results were polydrug use, maternal psychiatric pathologies, and social deprivation. Overall, prenatal and postnatal care such as rooming-in improved the results.

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113. **INVESTIGATING THE INFLUENCE OF PRENATAL ANDROGEN EXPOSURE AND SIBLING EFFECTS ON ALCOHOL USE AND ALCOHOL USE DISORDER IN FEMALES FROM OPPOSITE-SEX TWIN PAIRS**

Ellingson JM, Slutske WS, Richmond-Rakerd LS, Martin NG. Department of Psychological Sciences, University of Missouri-Columbia, Columbia, Missouri, Australia; Midwest Alcohol Research Center, Columbia, Missouri, Australia.

**ABSTRACT**

**Background:** There are robust sex differences for alcohol phenotypes, with men reporting more drinking and alcohol use disorder (AUD) symptoms than women. However, the sources of these effects are not completely understood. Sex hormones, a substantial biological sex difference, exert neurobehavioral influences and are candidates for influencing sex differences in alcohol phenotypes. This study investigated the effects of prenatal androgens based on the hypothesis of prenatal hormone transfer, which posits that hormones from one twin influence the development of a cotwin.

**Methods:** This study compared female twins from opposite-sex (OSF) and same-sex (SSF) pairs to investigate associations between prenatal androgens and alcohol phenotypes. Additional analyses distinguished prenatal and postnatal effects by comparing OSFs and SSFs with a close-in-age older (CAO) brother.

**Results:** OSFs endorsed more lifetime AUD symptoms than SSFs (d = 0.14). Females with a CAO brother reported greater intoxication frequency (d = 0.35), hangover frequency (d = 0.24), typical drinking quantity (d = 0.33), and max drinks (i.e., the most drinks ever consumed in a 24-hour period; d = 0.29). Controlling for postnatal effects, OSFs still endorsed more lifetime AUD symptoms than SSFs with a CAO brother (d = 0.16).
Conclusions: Prenatal exposure to a male cotwin was associated with increases in AUD symptoms, above the effect of postnatal exposure to a male sibling. Prenatal exposure to a male cotwin was not associated with increases in other alcohol-related phenotypes, but postnatal exposure to older male siblings produced medium effect sizes for indicators of alcohol consumption. Sex differences in AUDs, but not alcohol use, may be partially due to the neurodevelopmental effects of prenatal androgens. However, sibling effects may be larger than any effect of prenatal androgen exposure.


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114. MATERNAL DRINKING BEHAVIOR AND FETAL ALCOHOL SPECTRUM DISORDERS IN ADOLESCENTS WITH CRIMINAL BEHAVIOR IN SOUTHERN BRAZIL
Momino W, Félix TM, Abeche AM, Zandoná DI, Scheibler GG, Chambers C, Jones KL, Flores RZ, Schüler-Faccini L.
Departamento de Genética, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil. Serviço de Genética Médica, Hospital de Clínicas de Porto Alegre, Porto Alegre, RS Brazil.

ABSTRACT
Prenatal alcohol exposure can have serious and permanent adverse effects. The developing brain is the most vulnerable organ to the insults of prenatal alcohol exposure. A behavioral phenotype of prenatal alcohol exposure including conduct disorders is also described. This study on a sample of Brazilian adolescents convicted for criminal behavior aimed to evaluate possible clinical features of Fetal Alcohol Syndrome (FAS). These were compared to a control group of school adolescents, as well as tested for other environmental risk factors for antisocial behavior. A sample of 262 institutionalized male adolescents due to criminal behavior and 154 male students aged between 13 and 21 years comprised the study population. Maternal use of alcohol was admitted by 48.8% of the mothers of institutionalized adolescents and by 39.9% of the school students. In this sample of adolescents we could not identify individual cases with a clear diagnosis of FAS, but signs suggestive of FASD were more common in the institutionalized adolescents. Social factors like domestic and family violence were frequent in the risk group, this also being associated to maternal drinking during pregnancy. The inference is that in our sample, criminal behavior is more related to complex interactions between environmental and social issues including prenatal alcohol exposure.


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115. PARENTAL ALCOHOL CONSUMPTION AND RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AND BRAIN TUMORS
Milne E, Greenop KR, Scott RJ, de Klerk NH, Bower C, Ashton LJ, Heath JA, Armstrong BK. Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, West Perth, WA, 6872, Australia. lizm@ichr.uwa.edu.au

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ABSTRACT

Purpose: Childhood acute lymphoblastic leukemia (ALL) is the most common childhood malignancy and brain tumors (CBTs) are the leading cause of cancer death in children. In our Australian case-control studies of these cancers, we investigated whether parental alcohol consumption before or during pregnancy was associated with risk.

Methods: Cases were identified through the ten Australian pediatric oncology centers, and controls were recruited through national random-digit dialling. Detailed information on alcohol consumption, including beverage type, amount, and timing, was collected from 690 case families (388 ALL and 302 CBT) and 1,396 control families. Data were analyzed using unconditional logistic regression.

Results: We found no evidence that maternal alcohol use before or during pregnancy was associated with an increased risk of either cancer; rather, there was evidence of inverse associations, particularly with wine. For both cancers, we observed U-shaped associations with paternal alcohol consumption in the year before the pregnancy, possibly driven by reduced risk at moderate levels of beer and wine intake and increased risk associated with high levels of beer intake. Moderate intake of spirits by fathers was associated with an increased risk of CBT but not ALL. These findings would be strengthened by corroboration in other studies. While the inverse associations with wine may be interesting mechanistically, the public health message remains that maternal alcohol use during pregnancy causes serious disorders in the offspring and should be avoided.

Conclusions: Our findings suggest that men, as well as women, should limit their alcohol intake when planning a pregnancy.


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116. CHRONIC PRENATAL ETHANOL EXPOSURE INCREASES ADIPOSITY AND DISRUPTS PANCREATIC MORPHOLOGY IN ADULT GUINEA PIG OFFSPRING

Dobson CC, Mongillo DL, Brien DC, Stepita R, Poklewska-Kozieł M, Winterborn A, Holloway AC, Brien JF, Reynolds JN.

Department of Biomedical and Molecular Sciences, Pharmacology and Toxicology Graduate Program, Queen's University, Kingston, Ontario, Canada.

ABSTRACT

Background: Ethanol consumption during pregnancy can lead to a range of adverse developmental outcomes in children, termed fetal alcohol spectrum disorder (FASD). Central nervous system injury is a debilitating and widely studied manifestation of chronic prenatal ethanol exposure (CPEE). However, CPEE can also cause structural and functional deficits in metabolic pathways in offspring.

Objectives and Methods: This study tested the hypothesis that CPEE increases whole-body adiposity and disrupts pancreatic structure in guinea pig offspring. Pregnant guinea pigs received ethanol (4 g kg(-1) maternal body weight per day) or isocaloric-sucrose/pair-feeding (control) for 5 days per week throughout gestation.

Results: Male and female CPEE offspring demonstrated growth restriction at birth, followed by a rapid period of catch-up growth before weaning (postnatal day (PD) 1-7). Whole-body magnetic resonance imaging (MRI) in young adult offspring (PD100-140) revealed increased visceral and subcutaneous adiposity produced by CPEE. At the time of killing (PD150-200),
CPEE offspring also had increased pancreatic adipocyte area and decreased β-cell insulin-like immunopositive area, suggesting reduced insulin production and/or secretion from pancreatic islets.

**Conclusion:** CPEE causes increased adiposity and pancreatic dysmorphology in offspring, which may signify increased risk for the development of metabolic syndrome and type 2 diabetes mellitus.

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**117. APPROACHING THE PREVALENCE OF THE FULL SPECTRUM OF FETAL ALCOHOL SPECTRUM DISORDERS IN A SOUTH AFRICAN POPULATION-BASED STUDY**

Philip A. May¹,² *, Jason Blankenship², Anna-Susan Marais³, J. Phillip Gossage², Wendy O. Kalberg², Ronel Barnard³, Marlene De Vries³, Luther K. Robinson⁴, Colleen M. Adnams⁵, David Buckley², Melanie Manning⁶, Kenneth L. Jones⁷, Charles Parry³ ⁸, H. Eugene Hoyme⁹, Soraya Seedat³

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**ABSTRACT**

**Background:** The prevalence and characteristics of fetal alcohol spectrum disorders (FASD) were determined in this fourth study of first-grade children in a South African community.

**Methods:** Active case ascertainment methods were employed among 747 first-grade pupils. The detailed characteristics of children within the continuum of FASD are contrasted with randomly selected, normal controls on (i) physical growth and dysmorphology; (ii) cognitive/behavioral characteristics; and (iii) maternal risk factors.

**Results:** The rates of specific diagnoses within the FASD spectrum continue to be among the highest reported in any community in the world. The prevalence (per 1,000) is as follows:
fetal alcohol syndrome (FAS)—59.3 to 91.0; partial fetal alcohol syndrome (PFAS)—45.3 to 69.6; and alcohol-related neurodevelopmental disorder (ARND)—30.5 to 46.8. The overall rate of FASD is therefore 135.1 to 207.5 per 1,000 (or 13.6 to 20.9%). Clinical profiles of the physical and cognitive/behavioral traits of children with a specific FASD diagnosis and controls are provided for understanding the full spectrum of FASD in a community. The spectral effect is evident in the characteristics of the diagnostic groups and summarized by the total (mean) dysmorphology scores of the children: FAS = 18.9; PFAS = 14.3; ARND = 12.2; and normal controls, alcohol exposed = 8.2 and unexposed = 7.1. Documented drinking during pregnancy is significantly correlated with verbal (r = −0.253) and nonverbal ability (r = −0.265), negative behaviors (r = 0.203), and total dysmorphology score (r = 0.431). Other measures of drinking during pregnancy are significantly associated with FASD, including binge drinking as low as 3 drinks per episode on 2 days of the week.

**Conclusions:** High rates of specific diagnoses within FASD were well documented in this new cohort of children. FASD persists in this community. The data reflect an increased ability to provide accurate and discriminating diagnoses throughout the continuum of FASD.

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respectively. One-third (32%) of children diagnosed with fetal alcohol syndrome had intellectual disability.

**Interpretation:** Maternal alcohol use disorder is the leading known risk factor for intellectual disability with no identified genetic origin.

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119. **GLOBAL FUNCTIONAL CONNECTIVITY ABNORMALITIES IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS**
Wozniak JR, Mueller BA, Bell CJ, Muetzel RL, Hoecker HL, Boys CJ, Lim KO.
Department of Psychiatry, University of Minnesota, Minneapolis, Minnesota, USA.

**ABSTRACT**

**Background:** Previous studies, including those employing diffusion tensor imaging (DTI), have revealed significant disturbances in the white matter of individuals with fetal alcohol spectrum disorders (FASD). Both macrostructural and microstructural abnormalities have been observed across levels of FASD severity. Emerging evidence suggests that these white matter abnormalities are associated with functional deficits. This study used resting-state functional MRI (fMRI) to evaluate the status of network functional connectivity in children with FASD compared with control subjects.

**Methods:** Participants included 24 children with FASD, ages 10 to 17, and 31 matched controls. Neurocognitive tests were administered including Wechsler Intelligence Scales, California Verbal Learning Test (CVLT), and Behavior Rating Inventory of Executive Functioning. High-resolution anatomical MRI data and 6-minute resting-state fMRI data were collected. The resting-state fMRI data were subjected to a graph theory analysis, and 4 global measures of cortical network connectivity were computed: characteristic path length, mean clustering coefficient, local efficiency, and global efficiency.

**Results:** Results revealed significantly altered network connectivity in those with FASD. The characteristic path length was 3.1% higher (p = 0.04, Cohen's d = 0.47), and global efficiency was 1.9% lower (p = 0.04, d = 0.63) in children with FASD compared with controls, suggesting decreased network capacity that may have implications for integrative cognitive functioning. Global efficiency was significantly positively correlated with cortical thickness in frontal (r = 0.38, p = 0.005), temporal (r = 0.28, p = 0.043), and parietal (r = 0.36, p = 0.008) regions. No relationship between facial dysmorphism and functional connectivity was observed. Exploratory correlations suggested that global efficiency and characteristic path length are associated with capacity for immediate verbal memory on the CVLT (r = 0.41, p = 0.05 and r = 0.41, p = 0.01, respectively) among those with FASD.

**Conclusions:** Resting-state functional connectivity measures provide new insight into the integrity of brain networks in clinical populations such as FASD. Results demonstrate that children with FASD have alterations in core components of network function and that these aspects of brain integrity are related to measures of structure and cognitive functioning.

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120. IMBALANCED SYNAPTIC PLASTICITY INDUCED SPATIAL COGNITION IMPAIRMENT IN MALE OFFSPRING RATS TREATED WITH CHRONIC PRENATAL ETHANOL EXPOSURE
An L, Yang Z, Zhang T.
College of Life Sciences, Nankai University, Tianjin, China.

ABSTRACT
Background: As chronic prenatal ethanol (EtOH) exposure (CPEE) may cause deficiencies in a variety of behavioral and cognitive functions, the aim of present study is to investigate the effects of CPEE on spatial learning and memory and examine the action of CPEE on synaptic plasticity balance in the hippocampus of adolescent male rats.

Methods: The animal model was produced by EtOH exposure throughout gestational period with 4 g/kg bodyweight, while the male offspring rats were used in the study. Morris water maze (MWM) test was performed, and then, long-term potentiation (LTP) and depotentiation were recorded from Schaffer collaterals to CA1 region in the hippocampus.

Results: It was shown that escape latencies in learning period and re-acquisition period were prolonged in CPEE-treated group compared with that in control group. Furthermore, LTP was drastically inhibited, and depotentiation was distinctly enhanced in CPEE-treated group compared with that in control group.

Conclusions: It is suggested that the balance between cognitive stability and flexibility was broken by the bidirectional effects of long-term synaptic plasticity. In addition, the spatial cognition was attenuated by the alteration of synaptic plasticity balance in CPEE-treated male adolescent rats.


121. CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE HAVE DIFFERENT FREQUENCY DOMAIN SIGNAL CHARACTERISTICS WHEN PRODUCING ISOMETRIC FORCE.
Nguyen TT, Ashrafi A, Thomas JD, Riley EP, Simmons RW.
Center for Behavioral Teratology, Department of Psychology, San Diego State University, San Diego, CA 92120, USA.

ABSTRACT
To extend our current understanding of the teratogenic effects of prenatal alcohol exposure on the control of isometric force, the present study investigated the signal characteristics of power spectral density functions resulting from sustained control of isometric force by children with and without heavy prenatal exposure to alcohol. It was predicted that the functions associated with the force signals would be fundamentally different for the two groups. Twenty-five children aged between 7 and 17 years with heavy prenatal alcohol exposure and 21 non-alcohol exposed control children attempted to duplicate a visually represented target force by pressing on a load cell. The level of target force (5 and 20% of...
maximum voluntary force) and the time interval between visual feedback (20 ms, 320 ms and 740 ms) were manipulated. A multivariate spectral estimation method with sinusoidal windows was applied to individual isometric force-time signals. Analysis of the resulting power spectral density functions revealed that the alcohol-exposed children had a lower mean frequency, less spectral variability, greater peak power and a lower frequency at which peak power occurred. Furthermore, mean frequency and spectral variability produced by the alcohol-exposed group remained constant across target load and visual feedback interval, suggesting that these children were limited to making long-time scale corrections to the force signal. In contrast, the control group produced decreased mean frequency and spectral variability as target force and the interval between visual feedback increased, indicating that when feedback was frequently presented these children used the information to make short-time scale adjustments to the ongoing force signal. Knowledge of these differences could facilitate the design of motor rehabilitation exercises that specifically target isometric force control deficits in alcohol-exposed children.


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122. "THEY SILENTLY LIVE IN TERROR..." WHY SLEEP PROBLEMS AND NIGHT-TIME RELATED QUALITY-OF-LIFE ARE MISSED IN CHILDREN WITH A FETAL ALCOHOL SPECTRUM DISORDER

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ABSTRACT

Children and adolescents with a Fetal Alcohol Spectrum Disorder (FASD) are at high-risk for developing sleep problems (SPs) triggering daytime behavioral co-morbidities such as inattention, hyperactivity, and cognitive and emotional impairments. However, symptoms of sleep deprivation are solely associated with typical daytime diagnosis, such as attention deficit hyperactivity disorder (ADHD) and treated with psychotropic medications. To understand how and why SPs are missed, we conducted qualitative interviews (QIs) with six parents and seven health care professionals (HCPs), and performed comprehensive clinical sleep assessments (CCSAs) in 27 patients together with their caregivers referred to our clinic for unresolved SPs. We used narrative schema and therapeutic emplotment in conjunction with analyzes of medical records to appropriately diagnose SPs and develop treatment strategies. The research was conducted at British Columbia Children's Hospital in Vancouver (Canada) between 2008 and 2011. In the QIs, parents and HCPs exhibited awareness of the significance of SPs and the effects of an SP on the daytime behaviors of the child and the associated burdens on the parents. HCPs' systemic inattention to the sequelae of SPs and the affected family's wellbeing appears due to an insufficient understanding of the various factors that contribute to nighttime SPs and their daytime sequelae. In the CCSAs, we found that the diagnostic recognition of chronic SPs in children and adolescents was impaired by the exclusive focus on daytime presentations. Daytime behavioral and emotional problems were targets of pharmacological treatment rather than the underlying SP. Consequently, SPs were also targeted with medications, without investigating the underlying problem. Our study highlights deficits in the diagnostic recognition of chronic SPs among children with chronic neurodevelopmental disorders/disabilities and proposes a clinical practice strategy, based on therapeutic emplotment that incorporates patients and parents' contributions in recognizing SPs and related sequelae in designing appropriate treatment and care.
123. **FETAL ALCOHOL SPECTRUM DISORDER: CAN DIMINISHED RESPONSIBILITY DIMINISH CRIMINAL BEHAVIOUR?**

Mela M, Luther G.
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**ABSTRACT**
This text examines how current scientific knowledge has the potential of fulfilling one of the major functions of the criminal justice system. Scientific knowledge should be used to ensure that the criminal justice system's functioning results in maximizing societal protection and crime reduction. Abnormal states of the mind contribute to criminal behaviour and are considered in exculpatory defences. The failure of the long standing insanity defence and its utility among cognitively impaired offenders, provided impetus to this work. In estimating the success rates (or lack thereof) of raised defences for the cases of the 'invisible disorder', fetal alcohol spectrum disorder (FASD), coming before the Canadian Courts, we sought to expound on the reasons, from knowledge and pragmatic perspectives. We propose that a diminished responsibility defence and verdict that recognizes the 'grey zone' between 'knowing' and 'not knowing' based on neurocognitive disparities in FASD serves the individual, legal system and the society better than the current practice.
ABSTRACT
Ethanol exposure during pregnancy can cause structural and functional changes in the brain that can impair cognitive capacity. The hippocampal formation, an area of the brain strongly linked with learning and memory, is particularly vulnerable to the teratogenic effects of ethanol. In the present experiments we sought to determine if the functional effects of developmental ethanol exposure could be linked to ethanol exposure during any single trimester-equivalent. Ethanol exposure during the 1st or 3rd trimester-equivalent produced only minor changes in synaptic plasticity in adult offspring. In contrast, ethanol exposure during the 2nd trimester equivalent resulted in a pronounced decrease in long-term potentiation, indicating that the timing of exposure influences the severity of the deficit. Together, the results from these experiments demonstrate long-lasting alterations in synaptic plasticity as the result of developmental ethanol exposure and dependent on the timing of exposure. Furthermore, these results allude to neural circuit malfunction within the hippocampal formation, perhaps relating to the learning and memory deficits observed in individuals with fetal alcohol spectrum disorders.


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125. THE ROLE OF CORTISOL IN CHRONIC BINGE ALCOHOL-INDUCED CEREBELLAR INJURY: OVINE MODEL
Washburn SE, Tress U, Lunde ER, Chen WJ, Cudd TA.
Department of Veterinary Physiology and Pharmacology and Michael E. DeBakey Institute, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843, USA. swashburn@cvm.tamu.edu

ABSTRACT
Women who drink alcohol during pregnancy are at high risk of giving birth to children with neurodevelopmental disorders. Previous reports from our laboratory have shown that third trimester equivalent binge alcohol exposure at a dose of 1.75 g/kg/day results in significant fetal cerebellar Purkinje cell loss in fetal sheep and that both maternal and fetal adrenocorticotropin (ACTH) and cortisol levels are elevated in response to alcohol treatment. In this study, we hypothesized that repeated elevations in cortisol from chronic binge alcohol are responsible at least in part for fetal neuronal deficits. Animals were divided into four treatment groups: normal control, pair-fed saline control, alcohol and cortisol. The magnitude of elevation in cortisol in response to alcohol was mimicked in the cortisol group by infusing pregnant ewes with hydrocortisone for 6 h on each day of the experiment, and administering saline during the first hour in lieu of alcohol. The experiment was conducted on three consecutive days followed by four days without treatment beginning on gestational day (GD) 109 until GD 132. Peak maternal blood alcohol concentration in the alcohol group was 239 ± 7 mg/dl. The fetal brains were collected and processed for stereological cell counting on GD 133. The estimated total number of fetal cerebellar Purkinje cells, the reference volume and the Purkinje cell density were not altered in response to glucocorticoid infusion in the absence of alcohol. These results suggest that glucocorticoids independently during the third trimester equivalent may not produce fetal cerebellar Purkinje cell loss. However, the elevations in cortisol along with other changes induced by alcohol could together lead to brain injury seen in the fetal alcohol spectrum disorders.
126. ALCOHOL-INDUCED OXIDATIVE/NITROSATIVE STRESS ALTERS BRAIN MITOCHONDRIAL MEMBRANE PROPERTIES
Department of Biochemistry, Sri Krishnadevaraya University, Anantapur 515 055, AP, India.

ABSTRACT
Chronic alcohol consumption causes numerous biochemical and biophysical changes in the central nervous system, in which mitochondria is the primary organelle affected. In the present study, we hypothesized that alcohol alters the mitochondrial membrane properties and leads to mitochondrial dysfunction via mitochondrial reactive oxygen species (mROS) and reactive nitrogen species (RNS). Alcohol-induced hypoxia further enhances these effects. Administration of alcohol to rats significantly increased the mitochondrial lipid peroxidation and protein oxidation with decreased SOD2 mRNA and protein expression was decreased, while nitric oxide (NO) levels and expression of iNOS and nNOS in brain cortex were increased. In addition, alcohol augmented HIF-1α mRNA and protein expression in the brain cortex. Results from this study showed that alcohol administration to rats decreased mitochondrial complex I, III, IV activities, Na(+)/K(+) -ATPase activity and cardiolipin content with increased anisotropic value. Cardiolipin regulates numerous enzyme activities, especially those related to oxidative phosphorylation and coupled respiration. In the present study, decreased cardiolipin could be ascribed to ROS/RNS-induced damage. In conclusion, alcohol-induced ROS/RNS is responsible for the altered mitochondrial membrane properties, and alcohol-induced hypoxia further enhance these alterations, which ultimately leads to mitochondrial dysfunction.

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Epub 2012 Dec 1.

127. BLOOD LEVELS OF PHOSPHATIDYLETHANOL IN PREGNANT WOMEN REPORTING POSITIVE ALCOHOL INGESTION, MEASURED BY AN IMPROVED LC-MS/MS ANALYTICAL METHOD
Department of Laboratory Medicine, Cheil General Hospital and Women's Healthcare Centre, Kwandong University School of Medicine, Seoul, Republic of Korea.

ABSTRACT
Objective: A reliable biomarker of low alcohol exposure during pregnancy is needed to clarify the controversy on the teratogenicity of low-to-moderate alcohol levels.

Methods: Blood samples were obtained from 13 pregnant women who self-reported alcohol ingestion between 2.5 and 20 drinks/week, and from 26 controls. Total lipids were extracted, and phosphatidylethanol (PhE) species 16:0/16:0, 16:0/18:1, and 16:0/18:1 were separated by high-performance liquid chromatography (HPLC) on a reverse-phase phenyl column.
These PEth species were quantified by MS/MS using phosphatidylpropanol as internal standard, with electrospray ionization and MRM.

**Results:** PEth species were not detected in women who abstained from alcohol ingestion during pregnancy, whereas PEth-16:0/18:1 was > 5 nmol/L in those with positive alcohol ingestion. PEth species were detected for up to 4 weeks after cessation of exposure.

**Conclusions:** PEth-16:0/18:1 was detected in pregnant women at 4-6 weeks after their last low-to-moderate alcohol ingestion, and therefore appears to be a reliable biomarker of prenatal alcohol exposure to study the teratogenicity of alcohol at these exposure levels.


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**128. PRECONCEPTIONAL MOTIVATIONAL INTERVIEWING INTERVENTIONS TO REDUCE ALCOHOL-EXPOSED PREGNANCY RISK**
Karen S. Ingersoll, Ph.D., Sherry D. Ceperich, Ph.D., Jennifer E. Hettema, Ph.D., Leah Farrell-Carnahan, Ph.D., J. Kim Penberthy
University of Virginia Department of Psychiatry and Neurobehavioral Sciences, Center for Addiction Research and Education, 1670 Discovery Drive Suite 110, Charlottesville VA 22911, USA. kareningersoll@virginia.edu

**ABSTRACT**
Alcohol exposed pregnancy (AEP) is a leading cause of preventable birth defects. While randomized controlled trials (RCTs) have shown that multi-session motivational interviewing-based interventions reduce AEP risk, a one-session intervention could facilitate broader implementation. The purposes of this study were to: (1) test a one-session motivational AEP prevention intervention for community women and (2) compare outcomes to previous RCTs. Participants at risk for AEP (N=217) were randomized to motivational interviewing+assessment feedback (EARLY), informational video, or informational brochure conditions. Outcomes were drinks per drinking day (DDD), ineffective contraception rate, and AEP risk at 3 and 6months. All interventions were associated with decreased DDD, ineffective contraception rate, and AEP risk. Participants who received EARLY had larger absolute risk reductions in ineffective contraception and AEP risk, but not DDD. Effect sizes were compared to previous RCTs. The one-session EARLY intervention had less powerful effects than multi-session AEP prevention interventions among community women, but may provide a new option in a continuum of preventive care.


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129. INCREASED LEVELS OF MONOAMINE-DERIVED POTENTIAL NEUROTOXINS IN FETAL RAT BRAIN EXPOSED TO ETHANOL.
School of Life Science, Beijing Institute of Technology, 5 South Zhongguancun Street, Haidian District, Beijing 100081, People's Republic of China.

ABSTRACT
Pregnant SD rats were exposed to ethanol (25 % (v/v) ethanol at 1.0, 2.0 or 4.0 g/kg body weight from GD8 to GD20) to assess whether ethanol-derived acetaldehyde could interact with endogenous monoamine to generate tetrahydroisoquinoline or tetrahydro-beta-carboline in the fetuses. The fetal brain concentration of acetaldehyde increased remarkably after ethanol administration (2.6 times, 5.3 times and 7.8 times as compared to saline control in 1.0, 2.0 and 4.0 g/kg ethanol-treated groups, respectively) detected by HPLC with 2,4-dinitrophenylhydrazine derivatization. Compared to control, ethanol exposure induced the formation of 1-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline (salsolinol, Sal), N-methyl-salsolinol (NMSal) and 1-methyl-6-hydroxy-1,2,3,4-tetrahydro-beta-carboline (6-OH-MTHBC) in fetal rat brains. Determined by HPLC with electrochemical detector, the levels of dopamine and 5-hydroxytryptamine in whole fetal brain were not remarkably altered by ethanol treatment, while the levels of homovanillic acid and 5-hydroxyindole acetic acid in high dose (4.0 g/kg) of ethanol-treated rats were significantly decreased compared to that in the control animals. 4.0 g/kg ethanol administration inhibited the activity of mitochondrial monoamine oxidase (51.3 % as compared to control) and reduced the activity of respiratory chain complex I (61.2 % as compared to control). These results suggested that ethanol-induced alteration of monoamine metabolism and the accumulation of dopamine-derived catechol isoquinolines and 5-hydroxytryptamine-derived tetrahydro-beta-carbolines may play roles in the developmental dysfunction of monoaminergic neuronal systems.


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130. PILOT EVALUATION OF THE TEXT4BABY MOBILE HEALTH PROGRAM.
Evans WD, Wallace JL, Snider J.
School of Public Health and Health Services, the George Washington University, Washington, DC 20037, USA. wdevans@gwu.edu

ABSTRACT
Background: Mobile phone technologies for health promotion and disease prevention have evolved rapidly, but few studies have tested the efficacy of mobile health in full-fledged programs. Text4baby is an example of mobile health based on behavioral theory, and it delivers text messages to traditionally underserved pregnant women and new mothers to change their health, health care beliefs, practices, and behaviors in order to improve clinical outcomes. The purpose of this pilot evaluation study is to assess the efficacy of this text messaging campaign.

Methods: We conducted a randomized pilot evaluation study. All participants were pregnant women first presenting for care at the Fairfax County, Virginia Health Department. We randomized participants to enroll in text4baby and receive usual health care (intervention), or continue simply to receive usual care (control). We then conducted a 24-item survey by telephone of attitudes and behaviors related to text4baby. We surveyed participants at...
baseline, before text4baby was delivered to the intervention group, and at follow-up at approximately 28 weeks of baby's gestational age.

Results: We completed 123 baseline interviews in English and in Spanish. Overall, the sample was predominantly of Hispanic origin (79.7%) with an average age of 27.6 years. We completed 90 follow-up interviews, and achieved a 73% retention rate. We used a logistic generalized estimating equation model to evaluate intervention effects on measured outcomes. We found a significant effect of text4baby intervention exposure on increased agreement with the attitude statement "I am prepared to be a new mother" (OR = 2.73, CI = 1.04, 7.18, p = 0.042) between baseline and follow-up. For those who had attained a high school education or greater, we observed a significantly higher overall agreement to attitudes against alcohol consumption during pregnancy (OR = 2.80, CI = 1.13, 6.90, p = 0.026). We also observed a significant improvement of attitudes toward alcohol consumption from baseline to follow-up (OR = 3.57, CI = 1.13 - 11.24, p = 0.029).

Conclusions: This pilot study is the first randomized evaluation of text4baby. It is a promising program in that exposure to the text messages was associated with changes in specific beliefs targeted by the messages.

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131. LOW-LEVEL ALCOHOL CONSUMPTION IN EARLY PREGNANCY MAY NOT AFFECT CHILD INTELLIGENCE, ATTENTION OR EXECUTIVE FUNCTION AT 5 YEARS OF AGE.  
Jacobson JL, Jacobson SW.  
Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan 48207, USA. joseph.jacobson@wayne.edu

Comment on  
The effect of different alcohol drinking patterns in early to mid pregnancy on the child's intelligence, attention, and executive function. [BJOG: 2012]

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132. NEUROTROPHIC PEPTIDES, ADNF-9 AND NAP, PREVENT ALCOHOL-INDUCED APOPTOSIS AT MIDGESTATION IN FETAL BRAINS OF C57BL/6 MOUSE  
Sari Y, Weedman JM, Nkrumah-Abrokwa M.  
Department of Pharmacology, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, 3000 Arlington Avenue, Toledo, OH 43614, USA. youssef.sari@utoledo.edu

ABSTRACT  
Prenatal alcohol exposure is known to induce fetal brain growth deficits at different embryonic stages. We focused this study on investigating the neuroprotective effects against
alcohol-induced apoptosis at midgestation using activity-dependent neurotrophic factor (ADNF)-9, a peptide (SALLRSIPA) derived from activity-dependent neurotrophic factor, and NAP, a peptide (NAPVSIQP) derived from activity-dependent neuroprotective protein. We used an established fetal alcohol exposure mouse model. On embryonic day 7 (E7), weight-matched pregnant females were assigned to the following groups: (1) ethanol liquid diet (ALC) group with 25 % (4.49 %, v/v) ethanol-derived calories, (2) pair-fed (PF) control group, (3) ALC combined with i.p. injections (1.5 mg/kg) of ADNF-9 (ALC/ADNF-9) group, (4) ALC combined with i.p. injections (1.5 mg/kg) of NAP (ALC/NAP) group, (5) PF liquid diet combined with i.p. injections of ADNF-9 (PF/ADNF-9) group, and (6) PF liquid diet combined with i.p. injections of NAP (PF/NAP) group. On day 15 (E15), fetal brains were collected, weighed, and assayed for TdT-mediated dUTP nick end labeling (TUNEL) staining. ADNF-9 or NAP was administered daily from E7 to E15 alongside PF or ALC liquid diet exposure. Our results show that NAP and ADNF-9 significantly prevented alcohol-induced weight reduction of fetal brains. Apoptosis was determined by TUNEL staining; NAP or ADNF-9 administration alongside alcohol exposure significantly prevented alcohol-induced increase in TUNEL-positive cells in primordium of the cingulate cortex and ganglionic eminence. These findings may pave the path toward potential therapeutics against alcohol intoxication during pregnancy stages.


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133. COCAETHYLENE AS A HAIR BIOMARKER TO PREDICT HEAVY ALCOHOL EXPOSURE AMONG COCAINE USERS
Aniket Natekar, Ilan Motok, Paula Walasek, Chitra Rao, Georgina Clare-Fasullo, Gideon Koren
Canada

ABSTRACT

Background: Cocaethylene (CE) is a cocaine metabolite formed during alcohol and cocaine co-consumption. There are no previous studies to assess the effectiveness of hair CE as a biomarker indicating chronic alcohol consumption among individuals who have consumed cocaine.

Objectives: To establish the ability of CE to predict chronic alcohol use among individuals testing positive for cocaine.

Methods: We studied all cases referred to our laboratory where both chronic cocaine and alcohol consumption were sought, and values of hair cocaine, benzoylegconine (BE), CE, and FAEEs (as marker of chronic alcohol consumption) were available. Cocaine, BE and CE were screened by ELISA and confirmed using headspace-solid phase microextraction (HS-SPME) and GC-MS. FAEE were analyzed using HS-SPME and GC-MS/EI. Sensitivity, specificity, and predictive values of CE as a marker of alcohol consumption among cocaine users were calculated using different FAEE cutoffs.

Results: Cocaine (P<0.001) and BE (P<0.001) concentrations were associated with increased FAEE. The positive predictive value of CE to identify alcohol consumption was 0.66 for excessive drinking and 0.76 for chronic drinking among positive cocaine users. Negative CE ruled out almost completely excessive alcohol consumption.

Conclusion: Positive hair CE results had high specificity for chronic excessive alcohol consumption among cocaine users. With no established safe level of alcohol in pregnancy,
identification of CE in hair of pregnant women who have used cocaine can serve as a biomarker for fetal alcohol spectrum disorder.

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134. SELF-MEDICATION: POTENTIAL RISKS AND HAZARDS AMONG PREGNANT WOMEN IN UYO, NIGERIA.
Abasiubong F, Bassey EA, Udobang JA, Akinbami OS, Udoh SB, Idung AU.
Department of Psychiatry, Faculty of Clinical Sciences, College of Health Sciences, University of Uyo, Akwa Ibom State, Nigeria.

ABSTRACT
Introduction:
There is increasing evidence that self-medications among pregnant women are common in many developing countries. Despite the adverse impact on pregnancy, there are few programs available for their control. The objective of this study was to assess the level of self-medication amongst Nigerian pregnant women in order to determine possible harmful effects on fetus.

Methods: Five hundred and eighteen 518 pregnant women, aged between 18 and 40 years, drawn from three General hospitals in Akwa Ibom State were assessed for self-medication and substance abuse using an instrument, adapted from a modified form of 117-item self-report questionnaire based on the WHO guidelines for students' substance use survey.

Results: Of the 518 pregnant women assessed, 375 (72.4%) indulged in one form of self-medication or the other; 143 (27.6%) used only drugs prescribed from the antenatal clinic. A total of 157 (41.9%) pregnant women self-medicate fever/pain relievers; 47 (9.1%) mixture of herbs and other drugs; 15 (4.0%) sedatives; 13 (3.5%) alcohol; while 5 (1.3%) used kolanuts. Reasons for using these substances range from protection from witches and witchcrafts, preventing pregnancy from coming out, for blood; poor sleep, fever and vomiting and infections. There was a significant difference in the rate of using analgesics (X2=9.43, p=0.001); and antibiotic (X2=4.43, p=0.001) among pregnant women who were highly educated compared to those with little or no education. However, the level of education has no impact in the usage of native herbs.

Conclusion: This study shows that self-medication is common among pregnant women in our environment. There is need for adequate education of pregnant women during antenatal clinics on the potential danger of self-medication so as to prevent child and maternal morbidity and mortality.


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135. [ALCOHOL--WOMAN, PREGNANCY AND A NEWBORN CHILD].
Jagielska I, Kazdepka-Ziemińska A, Stankiewicz M, Kaźmierczak J.
Katedra i Klinika Położnictwa, Chorób Kobiecych i Ginekologii Onkologicznej Uniwersytetu Mikołaja Kopernika w Toruniu, Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy.
Poland

ABSTRACT
According to the World Health Organization, alcohol is the third most dangerous factor following smoking of tobacco and hypertension of risks impacting health of the population. 50 % of men and 10 % of women suffer from diseases caused by alcohol drinking. Chronic consumption of alcohol damages the nervous system, causes adverse changes in the circulatory system and intestine, increases the risk of cancers. Comparing the impact of alcohol on the health of women and men, in case of women, even similar levels of consumption cause stronger action. Alcohol is the cause of endocrine diseases and among others- reduces fertility. It is the risk factor of premature deliveries, abortions, and placenta-associated pathologies. Disorders of children with prenatal exposure to alcohol are described as fetal alcohol syndrome, alcohol related neurodevelopmental disorders and alcohol related birth defects. It is recommended to impose a total ban on alcohol consumption by pregnant women. Moreover one should emphasize that the minimum safe dose of alcohol for the foetus cannot be specified. In order to resolve alcohol drinking problems a cooperation of representatives of many professions such as: doctors, psychologists, educators and employees of care facilities is necessary. It is also obligatory to obtain support and assistance from the nearest surroundings of the patient.

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136. ALCOHOL-INDUCED CHANGES IN THE DEVELOPING CEREBELLM. ULTRASTRUCTURAL AND QUANTITATIVE ANALYSIS OF NEURONS IN THE CEREBELLAR CORTEX
Lewandowska E, Stępień T, Wierzb-Bobrowicz T, Felczak P, Szpak GM, Pasennik E.
Department of Neuropathology, Institute of Psychiatry and Neurology, Warsaw, Poland.
lewandow@ipin.edu.pl

ABSTRACT
Maternal ethanol consumption during pregnancy may cause foetal alcohol syndrome (FAS). Our experiments of ethanol-treated female rats were based on the FAS model in humans; therefore, the results obtained may help explain the clinical mechanism of the disease development. The ultrastructural examination of the cerebellar cortex of ten-day-old rat pups of ethanol-treated dams during pregnancy (group IA), pregnancy and lactation (group IIA), and lactation (group IIIA) revealed that alcohol administration leads to a delayed maturation of Purkinje cells. This was most strongly manifested in the pups of dams treated with ethanol during pregnancy and lactation. Moreover, this study showed degenerative changes in Purkinje cells as well as in granular layer cells in all experimental groups. There was a difference in the ultrastructural picture of both types of dying cells, which might result from different time frame of their sensitivity to ethanol administration. The quantitative analysis showed the most pronounced decrease in the density of Purkinje cells in the posterior superior fissure of cerebellar cortex in the pups of dams treated with ethanol during pregnancy.
137. **AUTISM SPECTRUM DISORDER AND FETAL ALCOHOL SPECTRUM DISORDER. PART II: A QUALITATIVE COMPARISON OF PARENTING STRESS.**

Watson SL, Hayes SA, Coons KD, Radford-Paz E.
Laurentian University, Ontario, Canada.

**ABSTRACT**

Background: Researchers investigating the impact of parenting children with disabilities suggest that regardless of the specific diagnosis, parents experience increased levels of stress. However, particular disabilities may be associated with distinct stressors and strains.

Method: Parents of children with autism spectrum disorder (ASD) and parents of children with fetal alcohol spectrum disorder (FASD) participated in in-depth qualitative interviews employing a basic interpretative approach.

Results: Both groups described some similar stressors, such as multi-tasking, the diagnostic process, and dealing with behavioural issues, but there are distinct differences between families of children with FASD and families of children with ASD. Whereas parents of children with FASD focused on their children's illegal behaviours, parents of children with ASD struggled with their children's tantrums and anxieties.

Conclusions: Supports must be tailored to meet the specific needs of parents of children with different types of disabilities.


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138. **AUTISM SPECTRUM DISORDER AND FETAL ALCOHOL SPECTRUM DISORDER. PART I: A COMPARISON OF PARENTING STRESS**

Watson SL, Coons KD, Hayes SA.
Laurentian University, Ontario, Canada.

**ABSTRACT**

Background: There is a long history of research on parents of children with disabilities, but to the authors' knowledge, no study has compared the stress of parents of children with fetal alcohol spectrum disorder (FASD) to parents of children with autism spectrum disorder (ASD).

Method: Twenty-five parents of children with ASD and 25 parents of children with FASD completed the Parenting Stress Index - Short Form (PSI-SF) and the Questionnaire on Resources and Stress - Friedrich's Version (QRS-F).
Results: Although both parent groups reported elevated stress, PSI-SF results indicated that parents of children with FASD were experiencing significantly more stress compared to parents of children with ASD. No significant differences were found between groups on the total QRS-F, but parents of children with FASD had higher scores on the Pessimism subscale.

Conclusions: The authors call for measures grounded in theory as well as mixed methods research that includes the subjective experience of parents' stress.


139. MATERNAL HAIR ANALYSIS FOR THE DETECTION OF ILICIT DRUGS, MEDICINES, AND ALCOHOL EXPOSURE DURING PREGNANCY
Lendoiro E, González-Colmenero E, Concheiro-Guisán A, de Castro A, Cruz A, López-Rivadulla M, Concheiro M.
Sección de Toxicología, Instituto de Ciencias Forenses, Universidad de Santiago de Compostela, Santiago de Compostela; Sección de Neonatología, Complejo Hospitalario Universitario de Vigo, Vigo; Departamento de Desarrollo y Validación de Métodos Cromatográficos, Cienytech S.L., Santiago de Compostela, Spain; and Chemistry and Drug Metabolism Section, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, Maryland, USA.

ABSTRACT
Background/Objectives: Drug of abuse consumption throughout pregnancy is a serious public health problem and an important economic cost to the health system. The aim of this work was to compare maternal interview and hair analysis to determine drug consumption throughout pregnancy and to study relations among maternal interview, hair results, and neonatal outcomes.

Methods: Two hundred nine mothers agreed to participate. After delivery, they were interviewed and a hair sample collected. Hair samples were segmented in trimesters and analyzed for 35 drugs [opioids, cocaine, amphetamines, Δ-tetrahydrocannabinol (THC), ketamine, methadone, antidepressants, benzodiazepines, and hypnotics; limits of quantification 5-100 pg/mg] and for ethyl glucuronide (limit of quantification 10 pg/mg) by liquid chromatography-tandem mass spectrometry. Statistical analysis was performed with χ test and t test.

Results: In the interview, 4.3% mothers declared using illicit drugs during pregnancy (cocaine 1.4%, THC 2.9%, and opiates 1%), 3.3% medicines (methadone 1.9%, benzodiazepines 1.9%, and antidepressants 0.5%), 21.5% tobacco, and 13.7% alcohol. Hair analysis showed 15.4% prevalence in illicit drugs (cocaine 12.4%, THC 3.8%, opiates 1%, and ketamine 1%), 22.5% in medicines (methadone 3.3%, benzodiazepines 11%, antidepressants 9.1%, zopiclone 1%, and fentanyl 1.4%), and 3.9% in alcohol. Neonatal abstinence syndrome was developed in 8.1% newborns, all of them from mothers with high methadone-positive hair results (>926.2 pg/mg). Statistically significant lower newborn weight and length were found in neonates from declared smokers compared with nonsmokers (P < 0.05).

Conclusions: Maternal hair analysis showed to be more sensitive than maternal interview to detect drug use during pregnancy, except for alcohol. In this preliminary study, no statistically significant differences were found between exposed and nonexposed newborns to drugs, except for tobacco consumption.

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ABSTRACT

Background: The deleterious effects exerted by prenatal ethanol exposure include physical, mental, behavioral, and/or learning disabilities that are included in the term fetal alcohol spectrum disorder. The measurement of ethylglucuronide (EtG) in alternative biological matrices, including neonatal and maternal hair, neonatal meconium, and maternal nails, is receiving increasing interest for the accurate evaluation of the in utero exposure to alcohol.

Objective: To evaluate the correlation between EtG in maternal hair and nails with EtG in neonatal meconium to further explore the suitability of these biomarkers in disclosing prenatal exposure to ethanol.

Methods: A total of 151 maternal hair strands (0-6 cm), nail clips (2-6 mm), and corresponding neonatal meconium and nails samples were obtained from neonatal wards of 4 Mediterranean public hospitals: Rome, Florence, and Belluno in Italy and Barcelona in Spain. Hair, nails, and meconium were analyzed for the presence of EtG by validated liquid chromatography mass spectrometry assay. Meconium was also analyzed for the presence of fatty acid ethyl esters (FAEEs) as a complementary biomarker of potential in utero exposure to alcohol.

Results: Eighteen newborns resulted in utero exposed to maternal alcohol consumption by FAEE testing in meconium with EtG values between 0.5 and 1.5 nmol/g. Unfortunately, none of these cases were confirmed by the presence of EtG in maternal hair and nails samples, which resulted all negative to this biomarker.

Discussion and conclusions: The results confirm that FAEEs and EtG in meconium are the best biomarkers to assess in utero exposure to maternal alcohol. EtG in hair and nails are not good biomarkers to disclose alcohol consumption lower than on daily basis and lower than 1-2 alcoholic units per day.
141. **FOSTERING ITSELF INCREASES NICOTINE SELF-ADMINISTRATION IN YOUNG ADULT MALE RATS**
Roguski EE, Chen H, Sharp BM, Matta SG.
Department of Pharmacology, University of Tennessee Health Science Center, 115 Crowe Research Building, 874 Union Ave., Memphis, TN, 38163, USA. erguski@uthsc.edu.

**ABSTRACT**

**Rationale:** In gestational exposure studies, a fostered group is frequently used to control for drug-induced maternal effects. However, fostering itself has varying effects depending on the parameters under investigation. OBJECTIVES: This study was designed to assess whether maternal behavior contributed to enhanced acquisition (higher number of bar presses compared to controls) of nicotine self-administration (SA) displayed by offspring with gestational nicotine and ethanol (Nic+EtOH) exposure.

**Methods:** Offspring were exposed to Nic+EtOH throughout full gestation, that is, gestational days (GD) GD2-20 and during postnatal days 2-12 (PN2-12), the rodent third trimester equivalent of human gestation during which rapid brain growth and synaptogenesis occur. Young adult (PN60) male offspring acquired operant nicotine SA, using a model of unlimited (i.e., 23 h) access to nicotine.

**Results:** Gestational drug treatments did not alter litter parameters (body weight, volume distribution, crown-rump length, and brain weight) or postnatal growth of the offspring. Fostering increased locomotor activity to a novel environment on PN45 regardless of gestational treatment group. Surprisingly, fostering per se significantly increased the SA behavior of drug-naive pair-fed controls, so that their drug-taking behavior resembled the enhanced nicotine SA observed in non-fostered offspring exposed to Nic+EtOH during gestation. In contrast, fostering did not change the SA behavior of the Nic+EtOH group.

**Conclusions:** Fostering is shown to be its own experimental variable, ultimately increasing the acquisition of nicotine SA in control, drug-naive offspring. As such, the current dogma that fostering is required for our gestationally drug-exposed offspring is contraindicated.

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142. **ALCOHOL USE IN PREGNANCY: PREVALENCE AND PREDICTORS IN THE LONGITUDINAL STUDY OF AUSTRALIAN CHILDREN**
Hutchinson D, Moore EA, Breen C, Burns L, Mattick RP.
National Drug and Alcohol Research Centre, Faculty of Medicine, University of New South Wales, Sydney, Australia.

**ABSTRACT**

**Introduction and Aims:** This study aimed to estimate the prevalence and describe the patterns of alcohol use during pregnancy among Australian mothers. The study also aimed to examine the characteristics associated with alcohol use in pregnancy.

**Design and Methods:** Data comprised two representative samples of families (infant cohort = 5107 parents of 0- to 1-year-olds; child cohort = 4983 parents of 4- to 5-year-olds) from the 2005 Longitudinal Study of Australian Children.
Results: Alcohol use in pregnancy was reported by 37.6% of mothers of infants aged 0-1 years and 27.6% of mothers of children aged 4-5 years. The majority of women reported low level/occasional use of alcohol but, when extrapolated to population level, this equates to 131,250 children in these two age groups exposed to alcohol in utero, with over 1000 children exposed to alcohol most days and an estimated 671 infants exposed to three or more drinks per occasion. Among mothers of infants, alcohol use in pregnancy was associated with increasing maternal age, higher education, greater economic advantage and fewer physical health problems in pregnancy. Among mothers of children, maternal drinking in pregnancy was associated with increasing maternal age and smoking in pregnancy.

Discussion and Conclusions: Alcohol use during pregnancy is common with around one-third of all mothers reporting use. Most women reported only occasional use, and among those who were asked, consumed one standard drink on average per occasion. Significant numbers were exposed to three or more drinks on one occasion or to alcohol most days while in utero. National guidelines recommend abstinence as no ‘safe’ threshold has been determined. Public health campaigns are needed to educate pregnant women regarding national guidelines.

Conclusions: 23.3% of women attending prenatal care in Brazzaville reported alcohol use during pregnancy and 83% of them continued to drink after recognition of pregnancy. Prenatal alcohol exposure should be the focus of efforts to improve identification of alcohol use prior to and during pregnancy to improve maternal and child health.


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144. A COMPARISON OF THE SENSORY PROFILE AND SENSORY PROCESSING MEASURE HOME FORM FOR CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS
Kathleen Deirdre Hansen¹ & Tracy Jirikowic²
1 Kathleen Hansen, OTD, LLC, Juneau, USA
2 Department of Occupational Therapy, University of Washington, Seattle, USA
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ABSTRACT
This exploratory study compared the performance of children with fetal alcohol spectrum disorders (FASD; n = 11) and children with typical development (TD) without alcohol exposure (n = 12) on the Short Sensory Profile (SSP) and Sensory Processing Measure (SPM) Home Form. The child's primary caregiver completed both measures. For children with FASD, 90.9% had probable or definite differences on the SSP and 81.8% had some problems or definite dysfunction on the SPM Home Form. All children with TD (100%) scored in the typical range on total scores for both measures. For the children with FASD, the percent agreement between the two measures was 36.6% for the three classification categories (typical, probable/some, and definite) and 81.8% when classification was collapsed into two categories (typical and probable/definite difference). Both measures detected sensory processing differences for children with FASD, however, categorization of clinical severity varied based on the cutoffs used.


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145. OPHTHALMOLOGIC FINDINGS IN RUSSIAN CHILDREN WITH FETAL ALCOHOL SYNDROME.
Gummel K, Ygge J.
Karolinska Institutet, Stockholm - Sweden and St. Petersburg State Pediatric Medical Academy, St. Petersburg - Russia

ABSTRACT
Purpose: To study functional and anatomic characteristics of eyes of Russian children with fetal alcohol syndrome (FAS).
**Methods:** One hundred children aged 10-16 years from Russian orphanages (St. Petersburg) were examined: 50 with verified diagnosis of FAS and 50 healthy children. All children were tested for distance visual acuity (VA) with subjective optimal correction (Sivtsev chart), skiascopy, visual inspection for FAS external ocular features, biomicroscopy, eye alignment using cover test, and indirect ophthalmoscopy.

**Results:** All analyzed parameters were worse in children with FAS compared with controls. Children with FAS showed a higher incidence of amblyopia, hyperopia, astigmatism, and anisometropia. In children with FAS, the incidence of blepharophimosis was 34% (8% in controls), epicanthus 14% (2% in controls), telecanthus 32% (compared to 4% in controls), eyelid ptosis 9% (none in controls), and strabismus 26% (10% in controls). Ophthalmoscopy revealed a tilted optic disc in 5 children with FAS (7%) compared with none in controls.

**Conclusion:** Russian children with FAS have a higher incidence of vision problems and eye pathology that needs to be taken into account and requires ophthalmologist monitoring.

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The pace of research on Autism Spectrum Disorders (ASD) can only be described as extraordinary as this volume shows. It is extremely difficult for any single professional to keep abreast of all the developments in this area. This volume gathers together leading researchers and expert clinicians from many different parts of the world to produce this "up-to-the-minute" volume. It gives an in depth view of many areas of research which may be unfamiliar to the clinician and indeed researcher focused on their own area of interest. The volume gives an in depth overview of the field of Autism Spectrum Disorders.

Chapter 20 - Clinical Implications of a Link Between Fetal Alcohol Spectrum Disorders (FASD) and Autism or Asperger's Disorder – A Neurodevelopmental Frame for Helping Understanding and Management
By Kieran D. O'Malley

ALCOHOL IN THE EUROPEAN UNION. CONSUMPTION, HARM AND POLICY APPROACHES
World Health Organization
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This new report uses information gathered in 2011 to update key indicators on alcohol consumption, health outcomes and action to reduce harm across the European Union (EU). It gives an overview of the latest research on effective alcohol policies, and includes data from the EU, Norway and Switzerland on alcohol consumption, harm and policy approaches. The data were collected from a 2011 survey, carried out as part of a project of the European Commission and the WHO Regional Office for Europe. The report updates the evidence base for some important areas of alcohol policy, and provides policy-makers and other stakeholders in reducing the harm done to health and society by excessive drinking with useful information to guide future action.

Alcohol is one of the world’s top three priority areas in public health. Even though only half the global population drinks alcohol, it is the world’s third leading cause of ill health and premature death, after low birth weight and unsafe sex. In Europe, alcohol is the third leading risk factor for disease and death after tobacco and high blood pressure.
A. HEALTH NOTES: NORTHLAND EFFORT TO CURB FETAL-ALCOHOL SYNDROME DRAWS NATIONAL SPOTLIGHT

A St. Louis County program aimed at reducing the number of babies born with fetal-alcohol syndrome has earned national notice.

Superior Babies has earned the 2013 Emerging Practices Award from the Association of Maternal and Child Health Programs, a St. Louis County news release said.

The program, which began in 1998, is carried out by the county’s Public Health and Human Services Department in collaboration with Arrowhead Center Inc. Its goal is to identify and serve pregnant women who were suspected or known to use or abuse alcohol and other drugs and work with them to increase positive birth outcomes.

The free and voluntary program provides scheduled home visits by both a public-health nurse and a licensed alcohol and drug counselor.

In 2010, 31 babies were born to mothers in the program, and 96 percent of them were normal in birth weight and other measures, the news release said.

Superior Babies provides services for pregnant women in northern St. Louis County. For more information, call (218) 749-0600 or visit stlouiscountymn.gov.

Link to the Article, http://www.duluthnewstribune.com/event/article/id/260009/

B. NIH STUDY FINDS MISSED OPPORTUNITIES FOR UNDERAGE ALCOHOL SCREENING

Physicians often fail to ask high school-aged patients about alcohol use and to advise young people to reduce or stop drinking, according to a study led by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health.

In a random survey of more than 2,500 10th grade students with an average age of 16 years, researchers from NIAAA and the Eunice Kennedy Shriver National Institute of Child Health and Human Development found that 34 percent reported drinking alcohol in the past month. Twenty-six percent said they had binged, defined as five or more drinks per occasion for males, and four or more for females.

“While more than 80 percent of 10th graders said they had seen a doctor in the past year, just 54 percent of that group were asked about drinking, and 40 percent were advised about alcohol harms,” says lead author Ralph W. Hingson, Sc.D., M.P.H., director of NIAAA’s division of epidemiology and prevention research. He adds that, among students who had been seen by a
doctor in the past year and who reported drinking in the past month, only 23 percent said they were advised to reduce or stop drinking. The findings are now online in the February issue of Pediatrics.

The researchers also reported that students who said that they had been asked about their drinking were more likely to be advised about alcohol. Nevertheless, among the 43 students who said that they were drunk six times or more in the past month and who said they had been asked about their drinking by a doctor, about 30 percent were not advised about drinking risks, and two-thirds were not advised to reduce or stop drinking.

The researchers caution that in the survey students were asked about past-month drinking, not what they may have told their physicians about their drinking.

Studies have shown that screening and brief interventions by health care providers — asking patients about alcohol use and advising them to reduce risky drinking — can promote significant, lasting reductions in drinking levels and alcohol-related problems among adults. Accumulating evidence supports the use of alcohol screening among adolescents.

In 2011, NIAAA and the American Academy of Pediatrics released a two-question screening tool designed to help clinicians overcome time constraints and other common barriers to youth alcohol screening. Examples of these questions, which vary slightly for elementary, middle, and high school ages, include:

- “Do you have any friends who drank beer, wine, or any drink containing alcohol in the past year?”
- “How about you — in the past year, on how many days have you had more than a few sips of beer, wine, or any drink containing alcohol?”
- “Alcohol is by far the drug of choice among youth,” says NIAAA acting director Kenneth R. Warren, Ph.D. “The findings reported by Dr. Hingson and his colleagues indicate that we must redouble our efforts to help clinicians make alcohol screening a routine part of patient care for young people in the United States.”

The National Institute on Alcohol Abuse and Alcoholism, part of the National Institutes of Health, is the primary U.S. agency for conducting and supporting research on the causes, consequences, prevention, and treatment of alcohol abuse, alcoholism, and alcohol problems. NIAAA also disseminates research findings to general, professional, and academic audiences. Additional alcohol research information and publications are available at [http://www.niaaa.nih.gov](http://www.niaaa.nih.gov).

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Alcohol intake during pregnancy puts the fetus at risk for cognitive and neuropsychological impairment and physical abnormalities, including dysmorphic facial features (such as micrognathia), restricted prenatal growth, cardiac defects, and eye and ear abnormalities. There is no threshold dose of alcohol that is safe during pregnancy, according to the American College of Obstetricians and Gynecologists.
Alcohol: An unfortunate teratogen

Fetal alcohol syndrome is entirely preventable. We need to remind ourselves and our patients of this fact.

Erin E. Tracy, MD, MPH

Medical students learn early in their education that alcohol is a teratogen. Despite this widespread knowledge, many obstetricians counsel patients about the safety of low doses of alcohol in pregnancy.1 Indeed, the Royal College of Obstetricians and Gynaecologists’ position on this is, “while the safest approach may be to avoid any alcohol during pregnancy, it remains the case that there is no evidence of harm from low levels of alcohol consumption, defined as no more than one or two units of alcohol once or twice a week.”2

Like many providers, I was aware of this controversy, but it became truly personal when a beloved family member was diagnosed with fetal alcohol syndrome (FAS). In this paper, I will review some of the controversy regarding alcohol in pregnancy, highlight findings from the literature, provide tools for prevention, and identify new developments regarding this devastating, preventable condition.

Charlie
To know my nephew Charlie is to fall in love with my nephew Charlie. One of the happiest moments of my life was when I learned my brother and sister-in-law had adopted twins from Kazakhstan. When my little niece and nephew started their new life in the United States, certain medical issues seemed to merit additional attention. Although both were very small for their age and required significant nutritional support, Charlie seemed to be a bit more rambunctious and required additional supervision.

The children were fortunate enough to have incredibly loving, dedicated parents, who have access to exceptional medical care as residents of Philadelphia, Pennsylvania. After extensive testing, it became clear what was causing Charlie’s developmental delay; his pediatric team made the diagnosis of FAS. My brother and sister-in-law became incredibly well-read about this challenging disorder, and threw themselves into national advocacy work to help prevent this unnecessary tragedy.

Recent data point to teratogenicity, but media confuse the issue

Some recent media coverage3 of celebrities who apparently drank while pregnant was in response to an article in the Journal of Epidemiology and Community Health.4 The authors of this study concluded that, “at age 5 years, cohort members born to mothers who drank up to one to two drinks per week or per occasion during pregnancy were not at increased risk of clinically relevant behavioral difficulties or cognitive deficits, compared...
The US Surgeon General stated in 1996 that no safe level of alcohol intake had been identified with children of mothers in the not-in-pregnancy group."

This is certainly not the first occasion the popular press has covered a published study that seems to indicate no ill effects of alcohol use in pregnancy. A 2008 report by Kelly and colleagues, and its subsequent media coverage, prompted the Fetal Alcohol Spectrum Disorders Study Group to state that the panel of experts was “alarmed” by recent newspaper reports suggesting that light drinking during pregnancy may be beneficial for an unborn child. They noted misleading and irresponsible media reports of the findings, which suggested that 3-year-old children whose mothers drank “lightly” during pregnancy were not at risk for certain behavioral problems.

What the study authors proceeded to note, however (that the media did not mention), was that the light drinkers in their study had socioeconomic advantages, compared with nondrinkers. (Advantaged economic status is established to be beneficial for childhood development.) They also noted that the study involved preschool-aged children, stating “Generally the adverse effects of light drinking during pregnancy are subtle and may go undetected in young children. However, other group studies of more moderate or ‘social’ drinking levels during pregnancy have shown an adverse impact on multiple aspects of development through adolescence and young adulthood, even when important environmental factors are taken into account.” A sentence I thought was most compelling in their statement was, “It is an inconvenient fact of life that alcohol is a teratogen.” Now, this fact is well supported in the literature.

There are animal studies regarding the use of “low-dose” or “moderate” alcohol in pregnancy that demonstrate adverse behavioral outcomes with exposure to even small doses of alcohol. It is an American tragedy that, according to the Centers for Disease Control and Prevention (CDC), rates of FAS in this country range from 0.2 to 2.0 cases per 1,000 live births. Indeed, the rates of fetal alcohol spectrum disorders (FASD) might be at least three times this rate. As is the case with other disorders, there are health disparities regarding the prevalence of this condition as well.

**FAS: A long history of preventable disease**

1973: *Identified.* FAS was first described in a 1973 *Lancet* report, “Pattern of malformation in offspring of chronic alcoholic mothers.”

1996: **Call for prevention.** In 1995, the US Surgeon General issued a statement regarding alcohol use in pregnancy, noting, “We do not know what, if any, amount of alcohol is safe.” In 1996, the Institute of Medicine released a paper calling FAS and FASD “completely preventable birth defects and neurodevelopmental abnormalities.”

2000: **The troubling effects gathered.** The American Academy of Pediatrics (AAP) published a monograph on FAS in 2000, defining it as a constellation of physical, behavioral, and cognitive abnormalities.

These features classically define FAS:
- dysmorphic facial features
- prenatal and postnatal growth abnormalities
- mental retardation.

Approximately 80% of children with this condition have:
- microcephaly
- behavioral abnormalities.

As many as 50% of affected children also exhibit:
- poor coordination
- hypotonia
- attention-deficit hyperactivity disorder
- decreased adipose tissue
- identifiable facial anomalies (such as maxillary hypoplasia, cleft palate, and micrognathia).

Also common:
- cardiac defects
- hemangiomas
- eye or ear abnormalities.

The AAP further noted that data current to the time (and still true today) did not support the concept of a safe level of alcohol consumption by pregnant women below which no damage to a fetus will occur.

CONTINUED ON PAGE 40
Surveys reveal that few women’s health providers advise patients that zero alcohol is the safest level of consumption in pregnancy, although ACOG guidelines clearly recommend this counseling.

**Despite the knowledge we’ve gained, FAS persists**

According to a 2006–2010 CDC analysis involving more than 345,000 women of reproductive age from all 50 states, 7.6% of pregnant women reported alcohol use and 1.4% (or 1 in 71) reported binge drinking (defined, respectively, as at least one alcoholic drink and four or more alcoholic drinks on one occasion in the past 30 days). The highest prevalence of obstetric alcohol consumption occurs in women who are:
- aged 35 to 44 years
- white
- college graduates
- employed.

**The problem may be bigger than reported.** The incidences of alcohol and binge drinking found in the CDC report include women’s self-report—but women drink alcohol without knowing they’re pregnant. Only 40% of women realize they’re pregnant at 4 weeks of gestation, a critical time for organogenesis, and approximately half of all births are unplanned.

When my brother and sister-in-law adopted my beautiful niece and nephew, they were very aware of the risk for conditions like FAS. In an evaluation of 71 children adopted from Eastern Europe at 5 years of age, FAS was diagnosed in 30% of children and "partial FAS" in another 9%. Birth defects attributed to alcohol were present in 11% of the children.

**Are women’s health providers up to date on FAS education?**

In recognition of alcohol’s potentially life-altering consequences for the developing fetus, the American College of Obstetricians and Gynecologists (ACOG) produced an FASD prevention tool kit in 2006 and published a 2011 committee opinion on at-risk drinking and alcohol dependence and their implications for obstetrics and gynecology. Both guidelines direct clinicians to advise patients to abstain from alcohol during pregnancy.

Results from a 2010 survey of 800 ACOG fellows revealed that only 78% of obstetricians advised abstinence from alcohol during pregnancy. Fifty-eight percent of respondents did not use a validated screening tool for alcohol use in their pregnant patients, and only 72% felt prepared to screen for risky or hazardous drinking. (Most were unaware of the ACOG tool kit, which had been published several years earlier.)

In a survey of pediatricians, obstetricians, and family physicians, clinicians said that about 67% of their patients asked about alcohol use in pregnancy, with about 2% of those patients specifically mentioning FAS. About 41% of these same physicians erroneously placed the threshold for FAS at one to three drinks per day, when in fact there is no threshold of drinking that has been proven to be safe.

A survey of 1,000 actively practicing ACOG fellows revealed that, while 97% of obstetricians routinely asked their patients about alcohol use, only 20% of providers reported to their patients that abstinence was safest, and 4% of providers didn’t believe that consumption of eight or more drinks weekly posed fetal risk.

**How can we educate our patients about the dangers of alcohol in pregnancy?**

**Fetal death.** A recent Danish study of 79,216 pregnant women revealed that 45% had consumed some alcohol during pregnancy. Two percent reported at least four drinks per week, and 25% admitted to binge drinking during pregnancy. Term infants born to women in the latter two groups had increased neonatal mortality, with hazard ratios of 3.56 (95% confidence interval [CI], 1.15–8.43) and 2.69 (95% CI, 1.27–5.69), respectively.

**Decreased cognitive status.** A study by Willford and colleagues evaluated the relationship between prenatal alcohol exposure and cognitive status of 1,360 10-year-old children. The authors utilized the Stanford-Binet Intelligence Test, including the composite scores and verbal, abstract/visual, quantitative, and short-term memory scores. After controlling for other variables, among
A prospective 2012 study indicated no threshold dose of causation for the physical abnormalities present in FAS, and FAS effects were dose-related.

African American offspring they found that, for each additional drink, the average composite score decreased by 1.9 points. This difference was more striking for second-trimester use, and was significant even for one drink daily versus abstention from alcohol.

Impaired neuropsychological development. Another study evaluating light to moderate amounts of prenatal alcohol exposure in 10- and 11-year-old children found significantly worse scores regarding a number of neuropsychological developmental assessments.

No threshold dose of causation. Results of a 2012 prospective study in California, with data collected on 992 subjects from 1978 until 2005, revealed that many physical FAS features, including microcephaly, smooth philtrum, and thin vermillion border; reduced birth length; and reduced birth weight, were associated with alcohol exposure at specific gestational ages, and were dose-related. This paper didn’t reveal any evidence of a threshold dose of causation.

Neurobehavioral outcomes of FAS are not always considered

Another recent study that the media recently highlighted as finding “no association between low or moderate prenatal alcohol exposure and birth defects” was by O’Leary and colleagues. Like other similarly limited studies, this one involved only children younger than 6 years and didn’t assess any of the important neurobehavioral outcomes of FAS.

FAS encompasses much more than visible birth defects. As the aforementioned ACOG tool kit stated, “For every child born with FAS, many more children are born with neurobehavioral deficits caused by alcohol exposure but without the physical characteristics of FAS.”

The costs of FAS are felt with dollars, too

The financial cost to our nation is extraordinary. In 1991, Abel and Sokol estimated the incremental annual cost of treating FAS at nearly $75 million, with about three-quarters of that cost associated with FAS cases involving mental retardation.

A 2002 assessment estimated the lifetime cost for each individual with FAS (adjusting for the change in the cost of medical care services, lost productivity, and inflation) at $2 million. This figure consists of $1.6 million for medical treatment, special education, and residential care for persons with mental retardation, and $0.4 million for productivity losses.

Where human studies fall short, animal studies can help elucidate causation

Unquestionably, there are flaws in the existing literature on the causation of FAS. Many studies rely on self-reporting by pregnant women, and underreporting in these cases is a real concern. There often are other confounders potentially negatively affecting fetal development, making it difficult to differentiate causation. The animal studies that don’t share these limitations do suggest a causal relationship between antenatal alcohol exposure and poor obstetric outcomes, however. These studies suggest mechanisms such as altered gene expression, oxidative stress, and apoptosis (programmed cell death).

Warren, Hewitt, and Thomas describe how intrauterine alcohol exposure interferes with the function of L1CAM, the L1 cell-adhesion molecule. They noted that just one drink could interfere with the ability of L1CAM to mediate cell adhesion and axonal growth. Prenatal alcohol exposure is also thought to contribute to interference in neurotransmitter and N-methyl-D-aspartate receptor coupling, which may have potential therapeutic implications.

Considerations in FAS identification and treatment

There is a potential to identify alcohol exposure in the womb. The majority of ingested alcohol is eventually converted to carbon dioxide and water in both maternal
The odds of escaping the troubling outcomes that face patients with FAS, such as confinement in jail or an inpatient setting, are increased fourfold with early diagnosis and stable environment.

Research shows potential therapeutic approaches during pregnancy. While the use of biomarkers has the potential to assist with the identification of at-risk newborns, it merely identifies past alcohol use; it doesn’t necessarily permit identification and prevention of the known negative pediatric sequelae. Preliminary animal studies reveal the potential benefit of neuroprotective peptides to prevent brain damage in alcohol-exposed mice. Further research is ongoing.

Prevent FAS: Provide contraception, screen for alcohol use, intervene

While ObGyns aren’t likely to diagnose many children with FAS, we are in an excellent position to try to prevent this tragedy through our counseling of reproductive-aged women. I suspect that most obstetricians spend a considerable amount of time discussing much less frequent obstetric sequelae, such as listeriosis, in the prenatal care setting. Validated alcohol screening tools take moments to administer, and once patients who might have alcohol problems are identified, either a serious discussion about contraception or an honest discussion of FAS may be appropriate. There have been a number of screening tools developed.

The CAGE screen is frequently taught in medical schools, but it isn’t as sensitive for women or minorities. The T-ACE (Tolerance, Annoyed, Cut Down, Eye-opener) tool involves four questions that take less than 1 minute to administer (FIGURE 1, page 43). TWEAK is another potential tool identified by Russell and colleagues (Tolerance, Worry, Eye opener, Amnesia, and Cut down in drinking). Other methods utilized include an AUDIT screen and a CRAFFT screen. Regardless of which tool is utilized, screening is not time-consuming and is better than merely inquiring about alcohol consumption in general.
When alcohol use is found, intervene

Once patients with at-risk behavior are identified, obstetric staff should offer brief interventions to influence problem drinking. Miller and Sanchez summarized the key elements that were most successful in these programs with the acronym FRAMES: Feedback, Responsibility, Advice, Menu, Empathy, Self-efficacy (FIGURE 2). This approach has been formally evaluated in the CDC’s multisite pilot study entitled Project CHOICES.

In this motivational intervention, sexually active, fertile women of reproductive age underwent up to four motivational counseling sessions and one visit to a provider. At 6 months, 69% of women reduced their risk for an alcohol-exposed pregnancy—although the women who drank the least amount had the greatest benefit, primarily by choosing effective contraception, but also by reducing alcohol intake.

A single, brief intervention is effective in already-pregnant women. Chang and colleagues conducted a randomized trial of a single-session brief intervention given to pregnant women with positive T-ACE screens and their partners (FIGURE 3, page 44). Either the study nurse or physician participated in the intervention, and each single session took 25 minutes on average. The pregnant women with the highest level of alcohol use reduced their drinking the most, and this effect was even larger when their partners participated. Other studies of brief interventions showed similar benefits.

Another study evaluating a brief intervention involving training of health-care providers to improve screening rates revealed...

### FIGURE 1  T-ACE validated alcohol screening tool

<table>
<thead>
<tr>
<th>TOLERANCE:</th>
<th>How many drinks does it take to make you feel high?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(&gt;2 DRINKS = 2 POINTS)</td>
</tr>
<tr>
<td>ANNOYED:</td>
<td>Have you been annoyed when others criticize your drinking?</td>
</tr>
<tr>
<td></td>
<td>(YES = 1 POINT)</td>
</tr>
<tr>
<td>CUT DOWN:</td>
<td>Have you ever felt you should cut down on your drinking?</td>
</tr>
<tr>
<td></td>
<td>(YES = 1 POINT)</td>
</tr>
<tr>
<td>EYE OPENER:</td>
<td>Have you ever had a drink first thing in the morning to either steady your nerves or get rid of a hangover?</td>
</tr>
<tr>
<td></td>
<td>(YES = 1 POINT)</td>
</tr>
</tbody>
</table>

2 POINTS = POSITIVE SCREEN


### FIGURE 2  FRAMES model to deliver brief interventions

<table>
<thead>
<tr>
<th>FEEDBACK:</th>
<th>Compare the patient’s level of drinking with drinking patterns that are not risky. She may not be aware that what she considers normal is actually risky.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESPONSIBILITY:</td>
<td>Stress that it is her responsibility to make a change</td>
</tr>
<tr>
<td>ADVICE:</td>
<td>Give direct advice (not insistence) to change her drinking behavior</td>
</tr>
<tr>
<td>MENU:</td>
<td>Identify risky drinking situations and offer options for coping</td>
</tr>
<tr>
<td>EMPATHY:</td>
<td>Use a style of interaction that is understanding and involved</td>
</tr>
<tr>
<td>SELF-EFFICACY:</td>
<td>Elicit and reinforce self-motivating statements such as, “I am confident that I can stop drinking.” Encourage the patient to develop strategies, implement them, and commit to change.</td>
</tr>
</tbody>
</table>


Among women who were already pregnant, a single 25-minute intervention was effective at reducing alcohol intake among the heaviest drinkers.
Alcohol: An unfortunate teratogen

improved detection and therapy among at-risk patients.46

FAS prevention begins with routine counseling and contraception

Although FAS is often thought of in relation to obstetric populations, appointments for preconception counseling or routine health maintenance among women of reproductive age are an essential tool in FAS prevention. As previously mentioned, since approximately half of all pregnancies in this country are unplanned, long-acting reversible contraception is widely available to facilitate improved family planning.

Other contraceptive options also should be discussed. ACOG has teamed up with the CDC to develop a phone app for providers to use at the patient’s bedside to assist with identification and treatment of women at risk for alcohol use during pregnancy.47

The stakes are high; it’s time to step up

As obstetricians, we are powerless to prevent many conditions—such as vasa previa, acute fatty liver of pregnancy, and amniotic band syndrome. FAS is 100% preventable.

There aren’t that many proven teratogens in our profession, and there are none that involve behavior that is more socially acceptable than alcohol consumption. It is time for our profession to encourage women to appreciate how small a percentage of one’s life is spent pregnant, how many more years there are to enjoy an occasional cocktail, and how very high the stakes are during this important period of their lives. Oh, how I wish someone had been able to communicate all of this to sweet Charlie’s biologic mother. I am so grateful he’s getting the exceptional care he’s getting and very optimistic regarding his future. I only hope others in his situation are given the same opportunities.

References

10. Centers for Disease Control and Prevention. Fetal alcohol...
ABSTRACT

Background
Despite the risk of ‘method slurring’, researchers have triangulated within a single qualitative study methods that are philosophically incongruent or in a limited context, are congruent, as with hermeneutic phenomenology and constructivist grounded theory.

Methods/ Materials
We aimed to make the case that what works best can be to mix two qualitative methods that are philosophically congruent. Thus, we used transcendental phenomenology (TP) and classic grounded theory (CGT) in synergetic sequence to answer our research question. These methods have not previously been used together and one method would not have sufficed. Using the same participant sample, we sought to explore and understand the daily challenges of living with fetal alcohol spectrum disorder (FASD) since no study to date had addressed these issues within New Zealand. Our retrospective exploratory two-phase sequential design was framed by the meta-theory of pragmatism. It mixed qualitative strategies that are ontologically and epistemologically compatible (i.e. TP and CGT are ontologically realist, but epistemologically idealist). They are useful together for the aim of meaningfully studying the lived experiences of purposively selected participants. Empirical data, as secondary results, provide supportive evidence.

Conclusion
The first paper from this study was published in J Popul Ther Clin Pharmacol Vol 19(1):e41-e50 when the main findings were reported. This second paper gives greater focus to the methodologies employed and data analysis from the second phase.

Key Words: Classic grounded theory, fetal alcohol spectrum disorder, mixed methods, pragmatism, qualitative approaches, transcendental phenomenology, triangulation

The mixed methods (MM) approach has emerged as a ‘third wave’ (circa 1990s) for social and health sciences research. It is formally defined as the class of research that mixes or combines quantitative and qualitative research techniques into a single study. MM inquiry has been described as a new research paradigm which determines inter-related design criteria, i.e. identifying the reasons for mixing research methods in a given study, the implementation of sequence (concurrent or sequential) and the phase of research in which the integration or relationship between mixed data collection and analysis takes place. It is stated that sequential studies (two-phase studies) are when the researcher first conducts a qualitative phase of a study and then a quantitative phase or vice-versa. The two phases are separate, yielding two separate data sets. In our innovative single qualitative study we used TP as the first phase and CGT as the second phase. This paper predominantly highlights the data set of the second phase.
Other researchers\(^5\) believe that a MM design is stronger than one that uses a single method because the supplemental component enhances the validity of the project \textit{per se} by enriching or expanding understanding or by verifying results from another perspective. Although the dominant component dictates the theoretical drive of a MM study, there must be adherence to the methodological rules and assumptions inherent in each method which is related to the sample selection, method purpose and the contribution of the results to the overall research plan. More latterly MM has been defined as the incorporation of one or more methodological strategies drawn from a second method into a single research study\(^6\) as with our own project. Methods are mixed to access some part of the phenomena of interest that cannot be accessed through the use of the first method alone. MM research therefore, is a systematic way of using two or more research methods to answer a single research question with one set of findings validating the other.

Moreover, the methods that nurse researchers tend to mix are commonly qualitative, naturalistic in design and from within the same methodological tradition.\(^7\) That is to say some investigators have combined elements of grounded theory and phenomenology in one qualitative study without acknowledging the assumptions that underpin their use of these different methods\(^7,8\) (i.e. ‘method slurring’). They may be unaware of these assumptions or take the pragmatic position that the assumptions are unimportant on the basis that what matters most is the usefulness of combining the methods. Indeed, it is stated that while methods are often presented and discussed in detail in relation to the empirical findings, questions concerning methodological differences are placed on a highly abstract level with little obvious connection to the findings.\(^9\)

However, our position is first, that researchers should be aware of and accept the assumptions underlying different methods\(^10\) and then make those assumptions transparent. This will minimize the risk of ‘method slurring’ and produce research that has rigour. Second, the different qualitative methods that are useful and meta-theoretically congruent can then be most easily mixed. In other words, pragmatism is not necessarily an alternative to purism. It is noted that pragmatists “eschew methodological orthodoxy in favour of methodological appropriateness”.\(^11\) However, the pragmatist approach does not ignore the relevance of epistemology and other concepts from the philosophy of knowledge. In fact, the great strength of the pragmatic approach to health research methodology is its emphasis on the connection between epistemological concerns about the nature of the knowledge that we produce and technical concerns about the methods that we use to generate that knowledge.\(^12\) Furthermore, pragmatism is viewed as “offering an attractive philosophical partner to MM research, providing a framework for designing and conducting MM research”.\(^13\)

Perhaps what may work best in a given situation is to mix the methods that are the simplest to mix. These methods have philosophical premises that are commensurable with each other\(^14\) and with pragmatism. Patton\(^11\) wants to “leave the world of theory and enter the world of practice and pragmatism. Not all questions are theory based", but we contend that theory is always at least implicitly present. In its empirical emphasis on practical consequences, pragmatism is “deeply concerned with the union of theory and practice”.\(^15\) It draws on theory to inform decisions regarding which methods to mix in order to facilitate dialogue and practical action. Pragmatism and theoreticism ‘it seems’, are interwoven.

Consequently, our: (1) pragmatically purist approach used (2) Glaserian classic grounded theory (CGT)\(^16-20\) and (3) transcendental (pure) phenomenology (TP).\(^21\) Each angle of this triangle reflects realist ontology and an objectivist epistemology\(^8\) that assumes a correspondence theory of knowledge.\(^22\) More simply, we used TP and CGT in a single pragmatic study because their like qualities usefully complement each other on the basis of similar assumptions about the nature of reality and knowledge. Furthermore, their exact methods have not been previously mixed. Our pragmatic approach enabled us to oscillate between our data sets through an inductive process of inquiry\(^12\) maximizing strengths and
minimizing weaknesses (or deficiencies) of each one. At the same time it offered intersubjective-transferable aspects of our research through the connection of theory and data. Thus, new ways to think about classic methodological issues in health and nursing research were created.

**DESIGN**

Based on the novel approach as described above, presented below is a case example of the principles discussed. Rather than use the new term ‘core’, we will continue to use the term ‘dominant’ for the theoretically driven component of our inquiry of individuals with a neurodevelopmental disability and the level of our research programme. We believe that the term ‘dominant’ gives greater meaning to a data component rather than the term ‘core’.

Consequently, the lead author developed and applied a sequential design that mixed two different qualitative collection and analysis phases (see Figure 1) in order to produce dual data. The design incorporated McMillan and Schumacher’s sequential forms whilst acknowledging Morse’s simultaneous qualitative MM designs. The sequential design was particularly useful in serving the MM purposes of development (e.g. using the analysed results from the first method to inform the development of the second method) and elaboration (e.g. using the results from one method to enhance the results from the other method). A sequential data collection design was also used because of a time order issue with CGT (QUAL) being the dominant component. In Denscombe’s terms, “methods were mixed to produce a more complete picture, to avoid the biases intrinsic to the use of mono-method design and as a way of building on and developing initial findings”.

**FIG. 1**

Sequential Data Collection Strategy

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>qual (TP)</td>
<td>QUAL (CGT)</td>
</tr>
<tr>
<td>Unstructured</td>
<td>Unstructured</td>
</tr>
</tbody>
</table>

Interface \ Interpretation of two separate data sets

*Note:* “qual” stands for supplemental component; “QUAL” stands for dominant component; \( \Rightarrow \) stands for sequential. The two methods meet at the point of interface and were conducted separately in between.

Innovatively-since no study previously undertaken has used our design (Morse, 2010)-strategies from TP (qual) comprised the supplemental component and were applied first. This approach reverses the order advocated by Morse and Niehaus. Therefore, the saturated data collected from Phase 1 interviews were analyzed before applying constant comparative data analysis principles in the CGT (QUAL) data collection for the Phase 2 interviews. The data were interpreted using a two-phased analytic process whereby data from each phase were analyzed independently and inferences were made at the point of interface. Inherent to our pragmatic approach was the use of abduction (backward exploration of the data to infer its most likely
meanings)\textsuperscript{28} to examine pieces of the mixed data sets which we would otherwise not have seen or so validly used. Together, the inferences drawn from each component addressed our single area of inquiry that the dominant or supplemental component could not tackle alone. The latter component generated the major results that carry the greater weight of the two methods\textsuperscript{29,30}.

However, TP and CGT worked harmoniously in combination, being ontologically and epistemologically congruent and complementing each other in a pragmatic sense. In summary, working within a post-positivist frame, we embraced a pragmatist perspective that used a sequential MM method design to address our inductive theory-driven research question. Presented below is our experience of systematically using this approach.

METHODS

Qualitative methodology was chosen for our study since it seeks to understand the experienced phenomenon through narrative rather than statistics. Because some individuals with FASD have great difficulty in reading and understanding the written word, verbal communication within the setting is desirable and sometimes essential.

Unlike Annells\textsuperscript{8} who used a different sample for each approach, we used purposive sampling sequentially for both approaches borne out of the difficulty encountered in recruiting participants. The sample was identified through three Fetal Alcohol Spectrum Disorder (FASD) agencies throughout New Zealand. Eligible participants were aged 14 and over, had been diagnosed with FASD and were able to converse verbally. Recruited participants were interviewed once. Face-to-face in-depth questioning was used to elicit individual participants’ narratives that responded flexibly to their cognitive needs, avoiding complex questioning that could increase suggestibility, confabulation and acquiescence.

Rather than adopting Annells\textsuperscript{8}’s recommendation to engage grounded theory as the first of the two approaches, our first phase used phenomenology to gather descriptive accounts of 14 people with FASD. Initial questions asked participants to describe their experiences of living with FASD. We felt that individuals with this neurodevelopmental disability would initially be better able to describe their experiences rather than interpret them. CGT was used to understand the meanings grounded in the experiences of their condition, as described in Phase 1. Questions posed in Phase 2 emerged from Phase 1. Following the gaining of written assent and consent (using the process of both affirmations for each participant), the interviews were audio-recorded (in opposition to Glaser’s [1978] recommendations)\textsuperscript{17} to give an accurate account of each participant’s testimony. NP here Although Morse\textsuperscript{26} appears to have mixed simultaneous (+) and sequential QUAL +/- qual mixed method designs in her paper, she recommends that the data for the dominant component be collected and group analyzed. In our study, adoption of this suggestion would have contravened the constant comparative method of analysis intrinsic to CGT. However, group analysis did not prove an issue with the analytical structure of TP which used Moustakas’s (1994) modification of the Stevick-Colaizzi-Keen (1971, 1973, 1975) method of analysis.\textsuperscript{21} It uses Husserlian major concepts\textsuperscript{31} which suspend researchers’ perspectives to focus on those of the participants and identify themes from non-repetitive and non-overlapping significant statements in their narratives. The analysis synthesised these themes into descriptions of what the participants experienced and how they experienced it. This was followed by a composite description of the meanings and essences of the experiences of the group. To interpret the disability experiences of these individuals, Glaser and Strauss’s (1967) CGT was used.\textsuperscript{16} Its constant comparative method of analysis fractured the data into concepts, categories and themes. Emergent theoretical propositions were used to generate substantive theory contextually-grounded in the social processes of reality. That is to say, “grounded theory is not findings, but is rather an integrated set of conceptual hypotheses…”\textsuperscript{19}

Through different handling, separate data sets were produced from the same interviews through two phases whose methods were congruent. Although Thorne\textsuperscript{32} states that one can use the same interviews to generate data for each
component, we collected some data specifically for the second component. This approach was adopted because the descriptive data collected through the first method were insufficient to address dominant questions using the second one. Moreover, we applied CGT to the TP data to add voice to the participants’ perceptions and perspectives of their disabling condition. This also enabled us to gather up pertinent rich textural data that might otherwise have been omitted by TP and incorporate issues and themes which emerged from the supplemental component.

In contrast to Morse, we found that by applying a different analytical structure, including different sets of questions, each component was methodologically complete and constituted a separate, valid and credible project, albeit one made possible and informed by the other. We further suggest that our mixing of two methods, which we believe to be publishable as two separate reports (supported by Onwuegbuzie and Leech), does not constitute multiple methods as claimed by Morse.

Hence, this purist but pragmatic mixing of methods enabled us to address our study by triangulating different types of qualitative data and then analysing them at different levels to enrich our ability to tender warranted assertions. Through different forms and levels of analysis, the components - being different methodologically-contributed different valuable information about our context-bound, single area of inquiry.

RESULTS

In Phase 1, the disability revealed itself through invariant characteristics that constitute a thematic continuum of life events. Related concepts and relationships from Phase 2 data analysis were drawn upon in order to reveal the emerging theory which sought to explain and help resolve the main descriptive challenges as well as revealing the perspectives of the participants in Phase 1.

Of the 31 sub-themes emerging from TP analysis, six were categorized as essential themes.

These were:
1) Daily challenges in the classroom;
2) Daily challenges in the workplace;
3) Coping with mental health issues;
4) Memory issues;
5) Socialization issues;
6) Involvement with the law and authority.

Of the 10 categories that emerged from the CGT analysis (all being related to some degree), three were core categories.

These were:
1) People with FASD are under-supported by the social and health systems;
2) People with FASD are seen to have criminal behaviours;
3) People with FASD grow up and look back.

These results are fully reported in the first paper on this study, but a few of the more prominent findings from Phase 2 analysis are now highlighted.

People with FASD feel under-supported in the social and health systems

Receiving a professional diagnosis of FASD appeared difficult. “It is of no help” was the reason that one participant believed he was not initially diagnosed. Many participants had been diagnosed as having ADHD rather than FASD for which they had been prescribed Ritalin. This drug made the condition of many of the participants’ worse, so they refused to take it. Incorrect medication and lack of knowledge by doctors, as perceived by the participants, further eroded their trust.

People with FASD are seen to have criminal behaviours

All participants in the middle and older age groups reported mental health behaviours from the use of alcohol and recreational drugs. Pain and anxiety relief, boredom, addiction and impulsivity were major reasons. For five individuals (all males) marijuana calmed them down.

A few older participants became involved with the justice and/or legal system, e.g. through sentencing, assessment of fitness to stand trial and dealing with people working within the justice system. They reported that the police were
uninterested in them having FASD. Because one male individual did not know the difference between ‘yes’ and ‘no’, the courts had to examine him to establish whether he was fit to stand trial. These individuals appear to others to understand more than they do. For them to receive fair treatment and appropriate support, their disabilities need to be accommodated within the criminal justice system.

People with FASD grow up and look back
Some older and middle-age participants acknowledged their FASD and its impact on their families and themselves by identifying with its signs and symptoms. Their own knowledge of signs and symptoms can act as a support strategy as it helps them to understand themselves and be understood by others.

They reported that their quality of life and coping skills would be improved with the supply of an FASD-trained support worker in the home and workplace. As such, they would not have to rely on other people to help them with their numerous issues. Group homes were also mentioned whereby they could live independent lives.

Some older participants stated that the loss or weakening of relationships, friendships, self-esteem and identity during their lives were major issues. They have heard parents and teachers describe them as ‘stubborn’, ‘deviant’, ‘not motivated’, whereas in fact, they are overwhelmed with the sights, sounds, smells, textures and information bombarding them.

These findings pertain to our sample in which only four participants were reared or still nurtured by their biological mothers. Seven were reared by foster parents, one by biological grandparents, one by non-biological family members and one by guardians. In support of Streissguth’s findings, 10 participants had been in trouble with the law with 12 dropping out of or being expelled from school, which contributed to their entanglement in the criminal justice system.

DISCUSSION AND INTERPRETATION OF RESULTS

The results, being linked to the methodological thesis, indicate that what worked most easily was to mix two realist approaches. Annells believed that Wilson and Hutchinson’s discussion of grounded theory reflected the positivist philosophy of Glaserian CGT based on realist ontology with a received view of knowledge. She therefore, warned that unless the two approaches used share the same ontological foundation, the study will lose integrity from lack of harmony. Greene disagreed in explaining how there can be value in dialectically comparing and contrasting inferences from multiple worldviews and perspectives when they are conceived merely as conversational partners.

Strauss and Corbin subsequently predicted that adaptation of the grounded theory approach “will include combining it with other methods (hermeneutical, phenomenological, for instance)”. However, it is unclear if they meant some kind of fusion or instead two entirely separate phases, as proposed by Wilson and Hutchinson who were nevertheless, silent on the matter of sequential and concurrent data collection methods.

Through TP, we learnt from participants’ descriptions of their lived experience what daily life had been and still was like for them. This process helped us to understand the same types of issues that the participants subsequently raised in relation to the CGT questioning. However, the latter approach also required them to interpret their experiences by unveiling their perceptions and perspectives on their disability.

Although the theoretical level of analysis of the dominant component yielded richer data than did analysis of the supplemental component, the results from the two separate data sets were consistent with each other with some slight data overlap. Therefore, through verification and incorporation into the results narrative, this exploratory qualitative MM study demonstrated itself able to produce rich, thick descriptive and interpretive narratives through the pragmatic use of TP and CGT.

CONCLUSION

This paper has shown how it was useful in practice to triangulate congruent MM within a post-positivist frame. Ockham’s Razor emphasizes the methodological principle of taking the simplest
Transcendental phenomenology and classic grounded theory as mixed data collection methods in a study exploring fetal alcohol spectrum disorder in New Zealand

approach first. Our study has indicated that the qualitative methods that are the easiest to mix in a useful manner are those that are meta-theoretically congruent. Hence, pragmatism is able to complement purism. This conclusion builds on earlier writing, for example by Wilson and Hutchinson who had noted that when using grounded theory (the positivist classic mode of the approach), a second phase should use a form of phenomenology which is ontologically realist or critical realist and have an objectivist or modified objectivist epistemology. The second phase should also adopt a suitable methodology, such as Husserlian phenomenology (as adopted in our study) or phenomenology from the perspective of Merleau-Ponty or van Manen. The views that pragmatism most easily compares nevertheless are ontologically and epistemologically compatible. Our use of TP and CGT met this standard because both methods are meta-theoretically post-positivist which supported their integrity and harmony when used in sequence.

The study was based on a small sample. We cannot claim that the empirical findings it offers in support of our thesis are transferable beyond the individuals studied, although it is claimed that pragmatism can increase the generalization of the results. The principle of pragmatic complementarity (use of both methods) has also been novel and advantageous in enriching and illuminating the research, with CGT enabling identification of what society should seek to address to improve the quality of life of disabled people. The use of TP and CGT in sequence revealed increased complexity and depth of understanding of the study phenomena.

The employment of mixed methods has been extremely useful for researching our population and would indeed, be useful for engaging and researching other individuals with neurodevelopmental disabilities. Through methodological triangulation, the accountability, validity and credibility of the findings were enhanced when compared with the only other similar study. This work used single methodology and was undertaken in Canada in 2011. Our findings corroborate, add to and build on existing methodological knowledge and to understanding of how prenatal alcohol exposure can impact development across the life-course and suggest new paths to managing FASD. Although our combination of TP and CGT may fall under Denzin’s rubric ‘interpretive interactionism’, each method possesses its own integrity and yielded useful outcomes. Methodological purism and pragmatism can be used together to overcome the incompatibility thesis and move qualitative inquiry forwards.

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Declaration of Conflicting Interests
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Ethical Approval
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TOWARDS IDENTIFYING A CHARACTERISTIC NEUROPSYCHOLOGICAL PROFILE FOR FETAL ALCOHOL SPECTRUM DISORDERS

1. ANALYSIS OF THE MOTHERISK FASD CLINIC

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ABSTRACT

Objective
Children with FASD display a heterogeneous profile and may have deficits in physical, behavioural, emotional, and social functioning, as the result of prenatal alcohol exposure. The major objective of the current study was to identify if a specific pattern of neuropsychological functioning exists among children prenatally exposed to alcohol who received a diagnosis, versus exposed children who did not. We compared groups on domains of intellectual functioning, memory, attention, executive functioning, motor functioning, language/communication and achievement.

Methods
One hundred and seventy children who were seen in the clinic between 2005 and 2009 were included in this study. Out of the total 170 children seen, 109 received an FASD diagnosis.

Results
We identified a specific neuropsychological profile that typifies children diagnosed with an FASD versus those exposed prenatally to alcohol, who did not receive a diagnosis. Diagnosed children displayed a neuropsychological profile characterized by weaknesses in the areas of verbal reasoning, memory, overall language functioning, math reasoning and calculation. Groups did not differ on measures of attention or executive functioning.

Conclusion
The information gained from these analyses, are essential for informing best practices for diagnosis and treatment.

Key Words: Fetal Alcohol Spectrum Disorder, neuropsychological profile, diagnosis

Fetal Alcohol Spectrum Disorders (FASD) refers to the range of conditions arising from prenatal exposure to alcohol and encompasses a range of diagnoses including Alcohol Related Neurodevelopmental Disorder (ARND), Partial Fetal Alcohol Syndrome (P/FAS), Alcohol Related Birth Defects (ARBD), as well as the most severe diagnosis on the spectrum, Fetal Alcohol Syndrome (FAS). Despite the recent consensus on the terminology used to describe children with FASD, diagnosis is not simple and clinicians are required to consider several biopsychosocial factors in the diagnostic formulation. Moreover, since the condition was first identified in the literature a significant amount of research has aimed to address the elusive FASD behavioural phenotype, often raising more questions than answers. Despite the research attention given to FASD, prevalence rates and societal costs continue to remain high.

In the US, prevalence estimates of FASD range from 0.5-2 per 1000 births for FAS and 10 per 1000 births for ARND. In Canada, estimates are comparable ranging from 1 to 6 per 1000 live births, although variations do exist within and between the two countries. In some Canadian populations, the incidence may be as high as 10-20%. Unfortunately, to date, these rates have remained unchanged. Because a large proportion of individuals with FASD require extensive mental health services throughout their lifetime, the costs associated with FASD are staggering.
Towards identifying a characteristic neuropsychological profile for fetal alcohol spectrum disorders. Analysis of the Motherisk FASD clinic

Indeed, it is estimated that in Canada $344 million are spent annually on affected youth. Since incarceration and difficult-to-measure costs such as lost productivity, alcoholism, and poor quality of life, are excluded from these estimates, the actual cost of FASD is likely much higher.

Children with FASD display a heterogeneous profile and may have deficits in physical, behavioural, emotional, and social functioning, as the result of prenatal alcohol exposure. Neuropsychological deficits may include intelligence, achievement, executive functioning, memory, attention, visual spatial, language and processing speed weaknesses. Secondary disabilities are also often documented and include mental health problems, trouble with the law, confinement, alcohol and drug abuse and less likely to complete school.

According to a landmark report on the long-term outcomes of individuals with fetal alcohol exposure, early diagnosis and presumably early treatment are predictive in mitigating later secondary disabilities. Nevertheless a unifying diagnostic profile has not been firmly established, making it an extremely difficult condition to assess and diagnosis clinically, although several groups are currently working towards this goal. In order to better understand the FASD profile it is therefore important to identify if a specific pattern of strengths and weaknesses exists for children who have been exposed prenatally to alcohol and who meet criteria for FASD, compared to children exposed prenatally to alcohol who do not meet criteria for an FASD.

For nearly 20 years the Motherisk Clinic at the Hospital for Sick Children in Toronto, Ontario, Canada, has been assessing children with prenatal alcohol and drug exposures. The majority of the children are brought to this clinic by foster or adoptive parents who are concerned that their child’s learning and/or behavioural problems may be caused by prenatal alcohol exposure. Since the clinic began, diagnostic procedures have evolved from the use of the Institute of Medicine Criteria, our own profile of strengths and weaknesses, to our current utilization of the Canadian diagnostic guidelines. It was not until recently that a set of criteria existed that pertained specifically to a Canadian demographic and where the Motherisk clinic had enough children diagnosed using this methodology to fulfill the large sample size needed for scientific rigour.

In the current study, psychological assessment results were analyzed using the domains outlined by the Canadian Guidelines and diagnostic information will be conveyed, as per the guidelines using the Washington 4-Digit code. The major objective of the current study was to identify if a specific pattern of neuropsychological functioning exists among children prenatally exposed to alcohol who received a diagnosis, versus exposed children who did not. We compared groups on domains of intellectual functioning, memory, attention, executive functioning, motor functioning, language/communication and achievement. The information gained from these analyses is critical in enhancing best practices for diagnosis and treatment. Findings from this study have the potential to further refine the assessment process by identifying the key characteristics of those children receiving a diagnosis. The current study additionally adds to a similar attempt by including a group of children seen in the FASD clinic because of prenatal exposure to alcohol, but ultimately not meeting diagnostic criteria, as well as using a larger sample size.

METHODS

Participants
One hundred and seventy children who were seen in the clinic between 2005 and 2009 were included in this study. Demographic characteristics of the sample are presented in Table 1. Out of the total 170 children seen, 109 received an FASD diagnosis (Dx group, mean age = 10.33, SD = 3.57, 55% male) and 61 did not receive an FASD diagnosis (Non-Dx group, mean age = 8.94, SD = 3.41, 66% male).

Materials and Procedures
The diagnostic assessments were conducted by a multidisciplinary team consisting of a psychologist, psychometrist, and neurologist, who used a combination of standardized and nonstandardized measures, rating scales, interviews, clinical observations, and developmental history. Diagnoses were made using the Canadian Guidelines and children were classified using the 4-Digit Coding system developed at the University of Washington. Diagnostic expression is classified
Towards identifying a characteristic neuropsychological profile for fetal alcohol spectrum disorders. Analysis of the Motherisk FASD clinic

using a 4-point likert scale with 1 representing no evidence of the FASD profile and 4 reflecting the “classic” FAS profile. All participants in our clinic were required to have a confirmed history of prenatal exposure to alcohol either via Children's Aid's records, reported alcohol withdrawal at birth, or report from the biological mother.

With regards to the “brain” rankings used in diagnosis, Brain 1 refers to no evidence of brain damage caused by prenatal exposure to alcohol as evidenced on psychometric measures, Brain 2 refers to suspected damage, Brain 3 refers to probable brain dysfunction evidenced by psychometric measures, and Brain 4 is evidenced by damage confirmed by physical characteristics through medical examination. Children categorized by Brain 3 were required to show impairment (as classified by the Canadian Guidelines) in three or more of the following domains: sensory/motor, communication, attention, intellectual functioning, executive functioning, memory, and academic achievement. It is important to note that a Brain 4 ranking only occurs when there are “hard” medical criteria met, such as microcephly, structural abnormalities, and/or other hard neurological signs.

For the purposes of data analysis, children in the Brain 3 and 4 groups were considered diagnosed and those who received a brain score of 1 and 2 comprised the non-diagnosed group. As is importantly highlighted in the literature\(^2\), several diagnostic centres use different nomenclature to refer to different diagnostic categories on the FASD spectrum. Therefore for clarification, a ‘brain’ score of 3 is similar to either an ARND or p/FAS diagnosis, while a ‘brain’ score of 4 similar to an FAS diagnosis. ‘Brain’ scores of 1 and 2 are indicative of PAE, without meeting diagnostic criteria based on the Canadian guidelines. Table 2 indicates the breakdown by brain classification and diagnosis for the sample.

All children were administered a consistent series of neuropsychological measures, however due to the wide age range and children's ability to manage and cope with psychometric testing, sample sizes vary and are indicated as they pertain to each measure.

### TABLE 1 Demographic Information

<table>
<thead>
<tr>
<th></th>
<th>FASD Diagnosed Mean (SD)</th>
<th>FASD Non-Diagnosed Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>10.3 (3.6)</td>
<td>8.9 (3.4)</td>
<td>p&lt;.01</td>
</tr>
<tr>
<td>Number of placements</td>
<td>3.1 (1.9)</td>
<td>2.7 (1.5)</td>
<td>ns</td>
</tr>
<tr>
<td>SES</td>
<td>3.0 (1.2)</td>
<td>3.1 (1.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Brain 1 (%)</td>
<td>0</td>
<td>34.0</td>
<td>n/a</td>
</tr>
<tr>
<td>Brain 2 (%)</td>
<td>0</td>
<td>66.0</td>
<td>n/a</td>
</tr>
<tr>
<td>Brain 3 (%)</td>
<td>92.9</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>Brain 4 (%)</td>
<td>7.1</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>Female</td>
<td>n=60</td>
<td>n=40</td>
<td>ns</td>
</tr>
<tr>
<td>Male</td>
<td>n=21</td>
<td>n=49</td>
<td>ns</td>
</tr>
<tr>
<td>Cigarette Exposure</td>
<td>88(%)</td>
<td>87(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Cocaine Exposure</td>
<td>29(%)</td>
<td>22(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Marijuana Exposure</td>
<td>40(%)</td>
<td>27(%)</td>
<td>ns</td>
</tr>
<tr>
<td>ADHD Diagnosis</td>
<td>61(%)</td>
<td>40(%)</td>
<td>p&lt;.00</td>
</tr>
<tr>
<td>ODD Diagnosis</td>
<td>8(%)</td>
<td>2(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Special Education Placement</td>
<td>64(%)</td>
<td>42(%)</td>
<td>p&lt;.00</td>
</tr>
<tr>
<td>Maternal Mental Health Concerns</td>
<td>32(%)</td>
<td>18(%)</td>
<td>p&lt;.04</td>
</tr>
<tr>
<td>Maternal Learning Disorder</td>
<td>23(%)</td>
<td>18(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Paternal Substance Abuse</td>
<td>54(%)</td>
<td>56(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Paternal Learning Disorder</td>
<td>19(%)</td>
<td>15(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Paternal Mental Health Concerns</td>
<td>15(%)</td>
<td>4(%)</td>
<td>p&lt;.03</td>
</tr>
<tr>
<td><strong>Medication Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidol</td>
<td>12(%)</td>
<td>9(%)</td>
<td>ns</td>
</tr>
<tr>
<td>Zoloft</td>
<td>2(%)</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Dexedrine</td>
<td>4(%)</td>
<td>0</td>
<td>ns</td>
</tr>
</tbody>
</table>
Towards identifying a characteristic neuropsychological profile for fetal alcohol spectrum disorders. Analysis of the Motherisk FASD clinic

TABLE 2  Neuropsychological Profile by Domains

<table>
<thead>
<tr>
<th>Neuropsychological Domain</th>
<th>FASD Diagnosed Mean (SD)</th>
<th>FASD Non-Diagnosed Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intelligence (WISC-IV)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>86.9 (11.5)</td>
<td>92.4 (13.8)</td>
<td>p&lt; .01</td>
</tr>
<tr>
<td>VIQ</td>
<td>98.6 (8.4)</td>
<td>95.5 (14.1)</td>
<td>ns</td>
</tr>
<tr>
<td>PIQ</td>
<td>97.2 (8.7)</td>
<td>92.4 (16.4)</td>
<td>ns</td>
</tr>
<tr>
<td>WMI</td>
<td>86.2 (14.3)</td>
<td>87.3 (13.0)</td>
<td>ns</td>
</tr>
<tr>
<td>PSI</td>
<td>89.0 (15.2)</td>
<td>92.1 (18.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Similarities</td>
<td>9.2 (2.7)</td>
<td>10.1 (2.5)</td>
<td>p&lt; .05</td>
</tr>
<tr>
<td>Vocabulary</td>
<td>8.4 (2.4)</td>
<td>9.4 (2.6)</td>
<td>p&lt; .01</td>
</tr>
<tr>
<td>Comprehension</td>
<td>8.3 (2.4)</td>
<td>9.1 (2.4)</td>
<td>p&lt; .04</td>
</tr>
<tr>
<td>Information</td>
<td>7.7 (2.5)</td>
<td>8.9 (2.3)</td>
<td>p&lt; .05</td>
</tr>
<tr>
<td>Block Design</td>
<td>8.3 (3.4)</td>
<td>8.9 (3.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Picture Concepts</td>
<td>9.4 (2.9)</td>
<td>9.7 (2.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Matrix Reasoning</td>
<td>8.1 (3.2)</td>
<td>8.7 (2.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Picture Completion</td>
<td>9.4 (2.9)</td>
<td>9.7 (2.4)</td>
<td>ns</td>
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<tr>
<td>Digit Span</td>
<td>7.6 (2.9)</td>
<td>8.1 (2.6)</td>
<td>ns</td>
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<tr>
<td>Letter Number Sequencing</td>
<td>7.3 (3.1)</td>
<td>7.7 (2.5)</td>
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<tr>
<td>Arithmetic</td>
<td>6.9 (2.4)</td>
<td>8.5 (2.5)</td>
<td>p&lt; .00</td>
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<tr>
<td>Coding</td>
<td>7.9 (2.8)</td>
<td>8.5 (2.5)</td>
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<td>Symbol Search</td>
<td>8.5 (3.0)</td>
<td>9.1 (2.0)</td>
<td>ns</td>
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<tr>
<td>Cancellation</td>
<td>10.5 (2.5)</td>
<td>10.7 (2.7)</td>
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<tr>
<td><strong>Memory (CMS)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dot Locations Learning</td>
<td>8.97 (3.53)</td>
<td>10.0 (3.21)</td>
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<td>Dot Locations Total</td>
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<tr>
<td>Dot Locations Long Delay</td>
<td>9.26 (3.24)</td>
<td>10.3 (2.76)</td>
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<tr>
<td>Story Immediate</td>
<td>8.99 (5.81)</td>
<td>9.73 (2.91)</td>
<td>ns</td>
</tr>
<tr>
<td>Story Long Delay</td>
<td>9.09 (5.99)</td>
<td>9.56 (2.92)</td>
<td>ns</td>
</tr>
<tr>
<td>Story Recognition</td>
<td>8.77 (3.76)</td>
<td>9.62 (3.67)</td>
<td>ns</td>
</tr>
<tr>
<td>Faces Immediate</td>
<td>9.52 (3.71)</td>
<td>9.64 (3.27)</td>
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<tr>
<td>Faces Long Delay</td>
<td>9.37 (3.44)</td>
<td>9.29 (3.34)</td>
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<td>Word Pairs Learning</td>
<td>7.71 (3.40)</td>
<td>7.44 (2.89)</td>
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<td>Word Pairs Total</td>
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<td>Word Pairs Long Delay</td>
<td>7.67 (3.33)</td>
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<td>Word Pairs Recognition</td>
<td>8.38 (4.66)</td>
<td>8.87 (3.36)</td>
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<tr>
<td>Numbers</td>
<td>7.82 (7.71)</td>
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<td>Sequences</td>
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<table>
<thead>
<tr>
<th>Function</th>
<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Visual Immediate</td>
<td>95.4 (15.2)</td>
<td>99.9 (15.0)</td>
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<tr>
<td>Visual Delay</td>
<td>95.1 (14.9)</td>
<td>98.0 (18.7)</td>
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<tr>
<td>Verbal Immediate</td>
<td>87.8 (16.4)</td>
<td>91.4 (17.2)</td>
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<tr>
<td>Verbal Delay</td>
<td>88.3 (16.9)</td>
<td>93.4 (18.5)</td>
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<tr>
<td>General Memory</td>
<td>88.6 (16.8)</td>
<td>94.8 (19.5)</td>
<td>p&lt; .04</td>
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<tr>
<td>Attention/Concentration</td>
<td>83.1 (22.9)</td>
<td>83.8 (27.1)</td>
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</tr>
<tr>
<td>Learning</td>
<td>89.1 (15.9)</td>
<td>91.3 (18.2)</td>
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**Delayed Recognition**

**Language**

<table>
<thead>
<tr>
<th>Test</th>
<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
</tr>
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<tbody>
<tr>
<td>PPVT</td>
<td>94.1 (12.8)</td>
<td>97.4 (13.9)</td>
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<tr>
<td>EOWPVT</td>
<td>93.8 (12.4)</td>
<td>97.3 (14.2)</td>
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<tr>
<td>NEPSY Language Composite</td>
<td>89.4 (14.6)</td>
<td>96.8 (13.7)</td>
<td>p&lt;.04</td>
</tr>
<tr>
<td>NEPSY Phonological Processing</td>
<td>8.0 (3.0)</td>
<td>9.0 (2.5)</td>
<td>ns</td>
</tr>
<tr>
<td>NEPSY Speeded Naming</td>
<td>8.2 (3.1)</td>
<td>9.3 (3.0)</td>
<td>ns</td>
</tr>
<tr>
<td>NEPSY Comprehension of Instructions</td>
<td>8.6 (3.2)</td>
<td>9.6 (2.8)</td>
<td>ns</td>
</tr>
<tr>
<td>NEPSY Verbal Fluency</td>
<td>9.2 (3.0)</td>
<td>10.4 (3.1)</td>
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**Motor**

<table>
<thead>
<tr>
<th>Test</th>
<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>VMI</td>
<td>91.9 (13.1)</td>
<td>96.0 (13.6)</td>
<td>p&lt;.06</td>
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<tr>
<td>WRAVMA Pegs Right Hand</td>
<td>93.5 (17.4)</td>
<td>98.6 (16.8)</td>
<td>p&lt;.08</td>
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<tr>
<td>WRAVMA Pegs Left Hand</td>
<td>95.2 (15.3)</td>
<td>100.0 (16.1)</td>
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**Attention**

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<tr>
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<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
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<tr>
<td>Commission</td>
<td>51.0 (10.0)</td>
<td>51.5 (9.6)</td>
<td>ns</td>
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<tr>
<td>Reaction Time</td>
<td>53.3 (12.9)</td>
<td>53.0 (11.5)</td>
<td>ns</td>
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<tr>
<td>Attention</td>
<td>51.6 (9.92)</td>
<td>53.6 (8.65)</td>
<td>ns</td>
</tr>
<tr>
<td>Risk Taking</td>
<td>51.8 (10.3)</td>
<td>53.8 (12.3)</td>
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**Executive Functioning**

<table>
<thead>
<tr>
<th>Test</th>
<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trails A (z-score)</td>
<td>0.16 (1.32)</td>
<td>0.51 (1.71)</td>
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</tr>
<tr>
<td>Trails B (z-score)</td>
<td>0.35 (1.38)</td>
<td>0.82 (1.73)</td>
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**Achievement (WIAT)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Control Mean (SD)</th>
<th>FASD Mean (SD)</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Word Reading</td>
<td>84.0 (18.8)</td>
<td>90.0 (20.9)</td>
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</tr>
<tr>
<td>Reading Comprehension</td>
<td>88.2 (16.7)</td>
<td>89.7 (20.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Numerical Operations</td>
<td>77.2 (14.7)</td>
<td>86.0 (17.3)</td>
<td>p&lt;.02</td>
</tr>
<tr>
<td>Math Reasoning</td>
<td>76.9 (17.7)</td>
<td>86.4 (18.3)</td>
<td>p&lt;.03</td>
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<tr>
<td>Spelling</td>
<td>83.0 (22.1)</td>
<td>91.9 (17.6)</td>
<td>p&lt;.06</td>
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<tr>
<td>Math Composite</td>
<td>89.0 (35.5)</td>
<td>89.0 (24.1)</td>
<td>ns</td>
</tr>
</tbody>
</table>
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Intelligence
Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) The WISC-IV was administered to 152 children to assess general intelligence, using Canadian norms. The composite scales have a mean of 100 and standard deviation of 15 and subtests and mean of 10 and standard deviation of 3. Standard scores ranging from 90-110 are considered to be Average, scores from 80-89 are considered Low Average and from 70-79 to be in the Borderline range.

Memory
Children's Memory Scale (CMS) The CMS was administered to 158 children to assess memory functioning across various domains. The CMS yields six index scores: visual immediate, visual delayed, verbal immediate, verbal delayed, attention/concentration, and learning. Each index score has a mean of 100 and standard deviation of 15.

Language
The Peabody Picture Vocabulary Test (PPVT-III) The PPVT-III was administered to 136 children to assess receptive word naming abilities by requiring child to select from a set of four pictures, the one best depicting a word said by the examiner. This test has a mean of 100 and standard deviation of 15.

The Expressive One Word Picture Vocabulary Test (EOWVT) The EOWPVT was administered to 151 children to assess expressive word naming abilities by requiring the child to name objects or actions depicted in a series of increasingly more complex pictures.

The NEPSY Subtests from the NEPSY were used to assess speeded naming (n=100), comprehension of instructions (n= 116), verbal fluency (n = 87), as well as overall language functioning (n= 73). This test has a mean of 100 and a standard deviation of 15.

Executive Functioning
Trails A & B Executive functioning was measured using the Trails A and B subtests on 137 children. Scores from this test are presented in z-scores and have a mean of 0 and standard deviation of 0.10.

Attention
K-CPT In addition to the parent and teacher reported measures of attention in our companion paper, 137 children were also administered a computerized measure of attention using a child friendly version of the Continuous Performance Test. The K-CPT provides scores for: commission errors, reaction time, overall attention score, and risk taking score.

Motor
VMI The VMI was administered to 168 children to assess general visual motor precision. This test has a mean of 100 and standard deviation of 15.

WRAVMA The WRAVMA is a test that examines fine motor functioning in children’s right (n=157) and left (n=138) hands using a wooden pegboard. This test has a mean of 100 and a standard deviation of 15.

Achievement
Wechsler Individual Achievement Test (WIAT) Academic functioning was assessed using select subtests from the WIAT: word reading (n=85), reading comprehension (n= 111), numerical operations (n=82), math reasoning (n=81), spelling (n= 82), and the math composite (n= 72). This test has a mean of 100 and standard deviation of 15.

Data Analysis
Across each neuropsychological domain performance on each composite scale, as well as subtests, were examined to determine if a unique profile emerged for children who received a diagnosis on the FASD spectrum compared to those who did not. Additionally, for tests where differences emerged between groups, odds ratios were calculated to validate the clinical significance of the findings. Odds ratios and 95 percent confidence intervals are also presented for critical background variables associated with the sample.

RESULTS

Demographics
Odds ratio analyses, based on the variables
presented in Table 1, indicate that compared to undiagnosed children, children diagnosed with an FASD were two times more likely to have a previous ADHD diagnosis \( p < 0.01; \) odds ratio, 2.32; 95% confidence interval, 1.21 to 4.43, three times more likely to be in a special education placement \( p < 0.05; \) odds ratio, 2.48; 95% confidence interval, 1.30 to 4.73, two times more likely to have a biological mother with a mental health issue \( p < 0.05; \) odds ratio, 2.21; 95% confidence interval, 0.99 to 4.94, and four times more likely to have a biological father diagnosed with a mental health disorder \( p < 0.03; \) odds ratio, 4.68; 95% confidence interval, 1.02 to 21.4.

**Intellectual Functioning**
Children diagnosed with an FASD scored significantly lower on the Similarities \( F(1, 162) = 3.80, p < .05 \), Vocabulary \( F(1, 164) = 6.54, p < .01 \), Comprehension \( F(1, 162) = 4.37, p < .04 \), Information \( F(1, 71) = 4.16, p < .05 \), and Arithmetic subtests \( F(1, 120) = 10.89, p < 0.00 \) compared to exposed children who did not meet criteria for diagnosis. Furthermore, diagnosed children were significantly 2 times more likely than undiagnosed children to have a score in the clinical range (scaled score < 7) on the Similarities \( p < 0.05; \) odds ratio, 2.724; 95% confidence interval, 0.93 to 5.56, and three times more likely to have an Arithmetic score in the clinical range \( p < 0.01; \) odds ratio, 2.84; 95% confidence interval, 1.16 to 6.91 (Table 2).

**Memory Functioning**
Children diagnosed with FASD scored significantly lower on the Dot Locations long delay \( F(1, 156) = 4.43, p < .05 \) and General Memory Index \( F(1, 156) = 4.36, p < .05 \) of the CMS, compared to undiagnosed children. Furthermore, compared to undiagnosed children, those diagnosed with an FASD were found to be two times more likely to have a General Memory Index score in the clinical range (score < 85) \( p < 0.01; \) odds ratio, 2.43; 95% confidence interval, 1.15 to 5.14 (Table 2).

**Language**
Children diagnosed with an FASD scored significantly lower on the Language Composite of the NEPSY \( F(1, 71) = 4.55, p < .04 \), however group differences were not observed on the PPVT or EVT. Furthermore, compared to undiagnosed children, children with FASD are three times more likely to have a NEPSY Language Composite in the clinical range \( p < 0.05; \) odds ratio, 3.07; 95% confidence interval, 0.90 to 10.14 (Table 2).

**Executive Functioning**
No group differences were observed on the TRAILS A \( F(1, 129) = 0.535, p = ns \), or B \( F(1, 127) = 0.521, p = ns \).

**Attention**
Table 2 indicates results from the K-CPT. No group differences were found between diagnosed and undiagnosed children.

**Motor**
Table 2 indicated the results from the WRAVMA and VMI. No group differences emerged between diagnosed and undiagnosed children.

**Achievement**
Children diagnosed with an FASD scores significantly lower on the numerical operations \( F(1, 80) = 5.94, p < .02 \) and math reasoning \( F(1, 79) = 5.17, p < .03 \) compared to undiagnosed children. Furthermore, compared to undiagnosed children, children with FASD are three times more likely to have a Numerical Operations score in the clinical range \( p < 0.02; \) odds ratio, 3.26; 95% confidence interval, 1.15 to 8.68 and Math Reasoning score in the clinical range \( p < 0.05; \) odds ratio, 2.56; 95% confidence interval, 0.96 to 6.88. No other significant differences emerged (Table 2).

**DISCUSSION**
The present study identified a specific neuropsychological profile that typifies children diagnosed with an FASD versus those exposed prenatally to alcohol, who did not receive a diagnosis. Diagnosed children displayed a neuropsychological profile characterized by weaknesses in the areas of verbal reasoning, memory, overall language functioning, math reasoning and calculation. Groups did not differ on measures of attention or executive functioning. Present findings corroborate previous findings that children with FASD display a characteristic profile of deficits in the areas of language, memory and mathematical
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Interestingly, our findings did not support a specific profile of weakness in the areas of attention and executive functioning suggested by previous studies comparing children with FASD to typically developing children.\(^3,19,21\)

This discrepancy may occur for several reasons. First, our clinic battery of attention and executive functioning measures may not be as in depth as those administered as part of research protocols. Second, most children were taking medications for attention problems at the time of testing, which may have washed out differences that would be more apparent without medication. Thirdly, it may be that when compared to unexposed typically developing children, children with FASD display a profile characterized by weaknesses in EF and attention, but when compared to a more “clinical” comparison groups these weaknesses no longer typify the FASD profile. Lastly, as is often reported anecdotally, EF deficits may be more apparent in a “real world” context, rather than laboratory setting. It will be important for future studies to compare children with FASD to children with other behavioural diagnoses, as well as using ecologically valid measure of EF, in order to elucidate the specificity of the FASD profile.

Our findings have important implications regarding diagnostic process for FASD. In our clinic, this process is quite lengthy, often involving 4 days of assessment. One solution to reducing the assessment process would be to streamline the assessment battery for children with FASD, using an evidence-based approach, which would include only those tests found to differentiate diagnosed from undiagnosed children. Our findings suggest that important areas of inquiry might be language functioning and verbal reasoning, mathematics, and overall memory functioning, which is consistent with previous findings.\(^15\)

Reducing the time spent at the assessment stage, may lead to more efficiency at this stage and thus reduce wait-times.

This study was an attempt to better understand the neuropsychological profiles of Canadian children and adolescents with FASD, however this study is not without its limitations. Limitations include disproportionate sample sizes between diagnosed and undiagnosed children, not all children being administered every measure, and a sample based on children referred due to suspected problems. However, due to difficulties obtaining an appropriate sample, clinic referred samples are relatively common in the research on FASD.

In summary, the present study serves to identify a set of neuropsychological characteristics that typify children prenatally exposed to alcohol who received a diagnosis from alcohol exposed children who did not receive this diagnosis. While results identified language, memory, verbal reasoning and mathematics achievement as areas of concern, groups did not differ in attention and executive functioning domains. The information gained from these analyses, are essential for informing best practices for diagnosis and treatment.

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**REFERENCES**

Towards identifying a characteristic neuropsychological profile for fetal alcohol spectrum disorders. Analysis of the Motherisk FASD clinic


