The Consequences of Marijuana Use During Pregnancy: A Review of the Human Literature

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SUMMARY. In spite of marijuana being the most widely used illegal drug among women of reproductive age there is a relative paucity of literature dealing with this topic. Of the data available, particularly in offspring beyond three years of age, most is generated by two ongoing cohort studies with very different populations. Both have reported similar findings. Up to approximately 3 years of age there appears to be very little impact upon the offspring. Beyond that age, *in utero* cannabis exposure does not impact upon standardized derived IQ scores but is negatively associated with attentional behavior and visual analysis/hypothesis testing. These findings are hypothesized as prenatal marijuana exposure having a negative influence on aspects of executive function–a "top-down," multifaceted cognitive construct involved in organizing and integrating specific cognitive and output processes over a interval of time. The results and their interpretation are examined in terms of behavioral teratogenic effects (or lack of effects) during the various developmental stages of the offspring, the non-unitary

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nature of executive function, cannabis receptors, and the consequences of chronic marijuana use in the non-pregnant population.

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In the ongoing debate about the role of cannabis and health as well as the increased interest in amending laws pertaining to the legal status of marijuana there is one area that appears noteworthy for its lack of inclusion: the possible short- and long-term consequences on the offspring of women who use marijuana during pregnancy. Particularly as applied to the long-term cognitive and behavioral outcomes, the absence of this issue reflects, at least in part, the relatively sparse body of information available on this topic. Contributing to this paucity are a myriad of complex pragmatic, logistic and interpretative difficulties that are part and parcel of the longitudinal behavioral teratological research that is required to examine this question. These design issues have been the subject of a recent review (Fried 2002) and will not be reiterated in the present paper. In spite of the difficulties involved in the gathering of information, the indisputable fact that marijuana is the most commonly used illicit drug among women of reproductive age (Johnston et al. 1994; 1996) emphasizes the need for the gathering and dissemination of data from well controlled studies.

In NIDA's most recently completed National Pregnancy and Health Survey (1996), self-reported marijuana use during pregnancy was 2.9 percent which, incidentally, is approximately three times the frequency of cocaine/crack usage. Among high school seniors (those entering reproductive years), a December 2000 Monitoring the Future press release (*http://www.monitoringthefuture.org/data/00data/pr00t2.pdf*) reported that marijuana had been used by 22% of grade 12 students in the past 30 days. In our own work (the Ottawa Prenatal Prospective Study–OPPS), which will be described briefly later in this paper, among 120 predominantly middle-class 18-20 years olds, the rate of smoking a minimum of one joint in the past week, determined by self-report coupled with a urine analysis, was 34% and smoking at least that amount on a regular basis at some time during the past five years was 45% (unpublished data). In addition to the relatively extensive use of marijuana by both women who are pregnant and women of child-bearing age, among both heavy (e.g., Hurt et al. 1995) and social (e.g., Graham et al. 1992) maternal cocaine users, marijuana is frequently smoked. This adds additional importance to the determination of marijuana's possible pre-

natal impact for, in order to disentangle cocaine's potential effects, marijuana's role must be understood.

The purpose of the present paper, portions of which have recently appeared elsewhere (Fried 2001; Fried and Smith 2001; Fried 2002), is to objectively summarize the present state of knowledge pertaining to marijuana and pregnancy, an issue highly pertinent to the theme of this edition of the Journal.

Only two longitudinal cohort studies with very different sample characteristics have focused upon the possible consequences of prenatal marijuana in offspring beyond early school age. In our own work, the OPPS, the objective has been to examine the association between marijuana (and other socially used drugs) consumed during pregnancy and effects upon offspring in the areas of growth, cognitive development and behavior. This longitudinal work has been underway since 1978 with the sample consisting of low-risk, white, predominantly middle-class families. Details of the recruitment procedures, interview protocol and drug use ascertainment have been described elsewhere (Fried et al. 1980). In essence subjects within the sample, representative of the English-speaking Ottawa population, were interviewed once during each of the trimesters remaining in their pregnancy. Birth data have been collected from 682 women in the Ottawa area but, for pragmatic reasons, approximately 180 offspring were chosen to be followed beyond the neonatal period.

During each of the pregnancy interviews, information was collected concerning socio-demographic status, mother's health (both current and prior to the pregnancy), father's health history, previous obstetrical history, a 24-hour dietary recall, and past and present drug use with particular emphasis upon marijuana, cigarettes and alcohol. For the drug histories, information was gathered pertaining to the year before pregnancy and each trimester of pregnancy. During the pregnancy, neonatal, childhood and adolescent time frames for which data have been published, the OPPS has collected over 4000 variables. Further details describing the assessment procedures at various ages are presented throughout this paper.

The second longitudinal study that has reported on a number of outcomes of prenatal exposure to marijuana in children ranging in ages from infancy to early adolescence is the Maternal Health Practices and Child Development Study (MHPCD) based in Pittsburgh (Goldschmidt et al. 2000). This study was initiated in 1982 and has focused upon the consequences of prenatal use of marijuana, alcohol and cocaine. The subjects in this high-risk cohort are of low socioeconomic status and just over half are African-American. Growth, cognitive development, temperament and behavioral characteristics have been reported in offspring up to the age of 10 and the marijuana findings reported are those noted after controlling for other drug use.

In the discussion of the OPPS and MHPCD findings as well as other studies, unless otherwise stated, the results described have been reported in the original

articles as being statistically significant after controlling for potential confounding, mediating or moderating variables. In the present review, the use of the term significant refers to probability levels reported as > .05 whereas the term highly significant refers to probability levels of .01 or greater.

COURSE OF PREGNANCY

Over the centuries, in many parts of the world, marijuana has been anecdotally reported to hasten childbirth, with the drug increasing the frequency and intensity of contractions (Abel 1980). Contemporarily, Fried, Watkinson and Willan (1984) found a statistically significant reduction of approximately one week in the gestational age of infants born to mothers who used marijuana six or more times per week. A report (Greenland et al. 1982) that precipitate labor was significantly more frequent among women who reported using marijuana is consistent with the folk medicine and may be related to the shortened gestation noted in the OPPS sample. The approximate one week reduction in gestation length observed is of questionable clinical significance in and of itself. However, as the effect was dose related, the shortened gestation length may take on clinical significance if large amounts of the drug is consumed, if the Δ9-tetrahydrocannabinol levels are higher than those used in the early eighties, and/or if life-style habits include other risk factors such as alcohol. Some (Gibson et al. 1983; Hatch and Bracken 1986) but not all researchers (Tennes et al. 1985; Day et al. 1991) have reported an association between marijuana use during pregnancy and preterm delivery.

In the OPPS, no association with marijuana use and subjects' miscarriage rates, types of presentation at birth, Apgar status, and the frequency of neonatal complications or major physical abnormalities (Fried 1982; Fried et al. 1983) were found. No patterns of minor physical anomalies were noted among the offspring of marijuana users although two anomalies, true ocular hypertelorism and severe epicanthus, were observed only among children of heavy users of cannabis (O'Connell and Fried 1984). In general, researchers have not reported an association between prenatal marijuana use and morphologic abnormalities in offspring (e.g., Day et al. 1991) and, as reviewed elsewhere (Dalterio and Fried 1992; O'Connell and Fried 1984), the few reports of increased physical abnormalities may reflect a lack of control for confounding factors (e.g., prenatal exposure to alcohol) and/or the relative risk status of the women in the study.

The life-style and concomitant risk status are factors that appear to interplay with prenatal marijuana outcomes. For example, in the low-risk sample of the OPPS, no evidence of increased meconium staining was noted among the newborns of the heavy marijuana users (Fried et al. 1983). This observation contrasts with the first but not second of two reports by Greenland and associates (1982; 1983). One of the primary differences between the two Greenland studies was the

generally higher standard of living and health among the sample in the later (1983) report with these subjects being quite similar, demographically, to the OPPS sample. A study that manipulated non-marijuana factors and that utilized pregnant rats (Charlebois and Fried 1980) indirectly supports the critical role that life-style factors may have in interacting with the teratogenic effects of the drug. Briefly, different groups of pregnant rats were exposed to marijuana smoke while receiving diets varying in protein content. Compromised pregnancies were markedly potentiated when marijuana smoke was combined with a low-protein diet but, conversely, if marijuana smoke was coupled with a high-protein diet some risks associated with the cannabis exposure were attenuated.

GROWTH

The role of life-style interacting with marijuana's prenatal effect can be observed upon fetal growth (Fried et al. 1999). Most studies have not found marijuana to have a negative impact in this domain but, in some samples drawn from high-risk environments, a small but significant negative relationship between first trimester marijuana use and birth length (Day et al. 1991; Tennes et al. 1985) or birth weight and length (Zuckerman et al. 1989) have been reported. Intriguingly, in both the MHPCD and OPPS cohorts, prenatal marijuana use was associated with an increased weight: Day et al. (1994) found this association at birth between heavy third trimester use and birth weight in a minority, high risk sample, although it was not found with a combined marijuana and alcohol cohort (Day et al. 1994a) and Fried and O'Connell (1987) reported a positive relationship between marijuana use during each trimester and weight at 24 months in the low-risk, middle-class OPPS sample.

Of the few studies that have examined offspring beyond the newborn stage, no significant negative association with growth parameters was noted at 8 months (Day et al. 1992), 1 year (Fried et al. 1999; Tennes et al. 1985), 2 and 3 years (Fried and O'Connell 1987; Fried et al. 1999), 4 years (Fried et al. 1999), and 6 years (Day et al. 1994a; Fried et al. 1999). One growth parameter in the OPPS sample, a smaller head circumference, observed as a trend in all ages (birth, 1, 2, 3, 4 and 6 years) reached statistical significance among early adolescents (Fried et al. 1999) born to daily marijuana users but was not significant during mid-adolescence (Fried, James and Watkinson 2001). Maternal marijuana use was not associated with the timing of pubertal milestones in either adolescent males or females (Fried, James and Watkinson 2001).

NEUROBEHAVIORAL/COGNITIVE OUTCOMES IN NEWBORNS

The literature describing the neurobehavioral effects of prenatal marijuana use on the newborn, although provocative, is far from definitive. In the Ottawa sample, using the Brazelton Neonatal Assessment Scale (Brazelton, 1973), at less than one week of age, marijuana was associated with increased fine tremors typically accompanied by exaggerated and prolonged startles, both spontaneous and in response to mild stimuli (Fried et al. 1980; Fried 1982; Fried and Makin 1987). In the same sample, maternal marijuana use was associated with relatively similar observations in 9 and 30 day old infants (Fried et al. 1987). At 9 days, hand-to-mouth behaviour was associated with marijuana use during pregnancy. Many of the behaviours seen both in the newborn and at 9 and 30 days are consistent with, but milder in degree, than found among infants undergoing opioid withdrawal. Although these particular indicants of impairments in nervous system state regulation were not detected by some researchers (Richardson et al. 1995; Tennes et al. 1985), reports of altered autonomic arousal in other outcome measures have been reported. Neonates of maternal cannabis users have been noted as having an increased likelihood of exhibiting a high-pitched cry (Lester and Dreher 1989) and to spend less time in quiet sleep (Scher et al. 1988).

Habituation, which in infants is an indicator of nervous system functioning and integrity, was associated, in some studies, with prenatal marijuana exposure. In the OPPS sample, newborns of less than a week born to marijuana users have poorer habituation to visual, but not auditory, stimuli (Fried, 1982; Fried and Makin 1987). It is noteworthy that in a primate study (Golub et al. 1981), behaviour distinguishing marijuana offspring from controls was the failure to habituate to novel visual stimuli. At 9 and 30 days of age, no association in the OPPS sample was apparent between maternal marijuana use and visual outcome measures such as pupil dilation and nystagmus. Compared to the remainder of the sample, more marijuana babies demonstrated a lack of visual habituation but the increased incidence did not reach statistical significance (Fried et al. 1987). No negative relationship between infant behaviour and maternal marijuana use was found in three reports describing a Jamaican cohort (Hayes et al. 1988; Dreher, Nugent and Hudgins 1994; Dreher 1997), nor in two different American studies (Tennes et al. 1985; Richardson et al. 1989). However, the possible vulnerability of aspects of visual system functioning in the neonate is a theme that recurs both in the longer term evaluation of offspring of maternal marijuana users in the OPPS and MHPCD cohorts as well as in a polydrug study (Griffith et al. 1994). This recurrent pattern will be discussed later in this paper.

NEUROBEHAVIORAL/COGNITIVE OUTCOMES IN LATE INFANCY AND PRESCHOOLERS

Findings pertaining to the impact of prenatal marijuana exposure on offspring between the ages of 1 and 4 are quite limited but, in what is available, there is a degree of consistency that is intriguing. In the OPPS (Fried and Watkinson 1988), using the Bayley Scales of Infant Development (Bayley 1969), no association between marijuana use during pregnancy and infant mental or motor development was observed at 1 year of age. No relationship between Bayley outcomes and prenatal marijuana exposure has been reported by other workers (Astley and Little 1990; Tennes et al. 1985). In the high-risk MHPCD cohort, the use of 1 or more joints per day during the third trimester was associated with lowered mental scores on the Bayley at 9 months of age but no longer at 18 months (Richardson et al. 1995).

The failure to find an association between prenatal marijuana exposure and a variety of cognitive outcomes persisted in the OPPS sample until the offspring were 4 years of age. At 2, although there was a negative association with language comprehension, this relationship did not retain significance when the home environment was statistically controlled (Fried and Watkinson 1988). At 3 years of age, after controlling for confounding factors, prenatal marijuana exposure was not associated with language expression and comprehension or decreased cognitive scores (Fried and Watkinson 1990).

However, one year later, an association with prenatal marijuana exposure that remained significant after controlling for confounding factors, was observed. These four year old children in the OPPS, born to women who had used marijuana on a regular basis during pregnancy (more than 5 joints a week), scored significantly lower than the remainder of the sample on a number of verbal and memory outcome measures (Fried and Watkinson 1990) derived primarily from the McCarthy Scales of Children's Abilities (McCarthy 1972). These findings were similar to results from the MHPCD cohort when the children were 3 years of age (Day et al. 1994b) in that, among the offspring of women who had used marijuana on a daily basis, an impairment on the short-term memory, verbal and abstract/visual reasoning subscales of the Stanford-Binet Intelligence Test (Thorndike et al. 1986) was noted. In a study investigating the interaction between prenatal cocaine use and a number of drugs including marijuana in 3 year old offspring, maternal marijuana use of an unspecified amount was related to poorer performance on the abstract/visual reasoning subscale of the Stanford-Binet test (Griffith et al. 1994). In all three studies with these preschoolers there was no marijuana effect on the composite, intelligence scores. As will be emphasized below, this has important interpretative and theoretical consequences in evaluating the findings in school aged children prenatally exposed to marijuana.

Reports focusing upon the behavioral and cognitive outcomes in offspring beyond 36 months of age exposed prenatally to marijuana are limited to that of the OPPS and MHPCD. Within these two cohorts, as there was at younger ages, there is a considerable degree of concordance in the findings in the children beyond 3 years of age. Furthermore, in these longitudinal studies, as the offspring get older, the observations are consistent with and logically extend, in a number of ways, the outcomes reported at earlier stages of development. One sphere of functioning, which may be impacted by prenatal marijuana in the school-aged children, is within the behavioral/cognitive construct of executive function (EF). The hypothesis of a negative association between *in utero* marijuana exposure and facets of EF in older offspring has been developed elsewhere in detail (Fried 1998) and will be described briefly in the following sections of this paper.

EXECUTIVE FUNCTION (EF)

The nature of EF involves the interplay of subordinate cognitive operations and thus may be viewed as an overarching, "top-down" cognitive domain. EF involves the ability to organize and integrate specific cognitive and output processes over an interval of time (Denckla 1993). The mental control processes involved in carrying out such future oriented behaviors include cognitive flexibility in problem solving, sustained, focused attention, inhibition of prepotent responses, monitoring, evaluating and adjusting self-directed responses and working memory (the temporary storage of information while processing incoming data). EF therefore describes a multiple, non-unitary set of functions needed to successfully carry out effortful, non-routine, goal-oriented tasks (Fried 1998). In evaluating the adequacy of this higher-order, integrative mental control process in the offspring of marijuana users, competency in the underlying specific domains that are to be mentally manipulated and integrated must be ascertained (Fried and Smith 2001).

From both clinical and empirical research (e.g., Fuster 1989; Lezak 1995), EF has been shown to be primarily subserved by the prefrontal region of the brain although other structures such as the hippocampus and cerebellum are involved (e.g., Diamond 2000; Lezak 1995). Reflecting the prolonged developmental course of the prefrontal lobes, most EF behaviors are not apparent until the children approach or reach school age (Fried 1998; Levin et al. 1991; Welsh et al. 1991). It may be noteworthy that upon examining the distribution and concentration of cannabinoid receptors in the fetal, neonatal and adult human brain using autoradiographic procedures (Glass et al. 1997), binding sites were identified throughout the regions of the adult neocortex with the greatest density being in the middle gyrus of the frontal lobe, cingulate gyrus and temporal lobe. Although frontal cortex from either fetal or neonatal tissue was not available for analysis,

based on the material that was examined, the authors found that the receptor distribution was similar in the fetal and neonatal brain to the adult human brain except that the density of receptor binding was markedly higher in the developing brain. The conclusion reached by the authors was that one of the major cannabinoid receptor sites in the human brain is in that part of the forebrain associated with higher cognitive functions.

The role of the prefrontal lobes in human intelligence is complex. One must distinguish between intelligence as a capacity to engage in adaptive, goal directed behavior and intelligence as defined by performance on standard psychometric instruments (Fried 1998). Data derived from clinical studies in which injury to the prefrontal area has occurred (e.g., Damasio and Anderson 1993; Fuster 1989; Stuss 1992) suggest that the former but not the latter type of intelligence is vulnerable to prefrontal dysfunction. Underlying this disassociation, at least in part, is that traditional intelligence tests set up specific tasks and goals thus obscuring the assessment of such key aspects of EF as integration of domains of functioning, goal setting, planning and self-monitoring.

From the maturational perspective, the observations, summarized earlier, that no effects of the drug were observed in offspring beyond the neonatal period until the children were 3 (Day et al. 1994; Griffith 1994) or 4 years of age (Fried and Watkinson 1990) is consistent with the developmental course of executive functioning. Further, from a functional perspective in these studies of the preschoolers, the combination of an absence of a lowering of global IQ scores but a negative association with such subtests that assess memory and abstract/visual reasoning is also consistent with the hypothesis that *in utero* marijuana exposure impacts negatively on particular facets of EF.

NEUROBEHAVIORAL/COGNITIVE OUTCOMES IN SCHOOL-AGED CHILDREN

The data available on school-aged offspring born to women who used marijuana during pregnancy suggests an interesting, but certainly incomplete emerging picture. It is important to note that as of this writing, in neither the OPPS nor the MHCPD longitudinal studies has an analysis been completed to determine whether the children that were impacted at one stage of development were those that continued to be impacted at a later age.

At 5 and 6 years of age, no differences were noted in the prenatally marijuana exposed and non-exposed children in the OPPS when assessed with global tests of cognition and language (Fried et al. 1992). As mentioned above with respect to EF and intelligence, it is possible that the instruments used in this work (Fried et al. 1992) provide a general and broad description of cognitive abilities and may not be capable of identifying nuances in neurobehavior that discriminate between marijuana-exposed and non-marijuana-exposed children. In order to determine

whether this absence of an association was due to the limited assessment in the standardized intelligence test of such key aspects of EF as integration of domains of functioning, goal setting, planning and self-monitoring, two studies were undertaken to examine specific cognitive characteristics and strategies.

Both of these investigations involved the OPPS cohort when the subjects were between 9 and 12 years of age. In the first (Fried et al. 1998), a neuropsychological battery was administered that included tests that assessed various aspects of EF as well as tests designed to assess global intelligence. The second was a direct investigation of the possible influence of prenatal marijuana exposure on "top-down" visuoperception (Fried and Watkinson 2000).

In the report evaluating aspects of cognition (Fried et al. 1998) the assessment battery utilized included the Wechsler Intelligence Scale for Children-III (WISC-III) (Wechsler 1991) with its 13 subtests and 6 additional tests designed to evaluate aspects of EF. Included among the latter were tests of sustained attention and inhibition of prepotent responses (Gordon and McClure 1984), a problem solving task that required visually deducing abstract categories while adjusting responses on the basis of negative and positive feedback (Reitan and Davison 1974), a timed, difficult tactile, self-monitoring task (Reitan and Davison 1974), a measure of oral fluency (Spreen and Strauss 1991), and a working memory task (Siegel and Ryan 1989).

The results of the WISC-III were intriguing. As with the data collected from the OPPS sample at earlier ages, there was no association between the Full Scale IQ and *in utero* marijuana exposure. Among the 13 WISC-III subtests only 2, the Block Design and Picture Completion subtests, significantly differentiated among levels of prenatal marijuana exposure suggesting that *in utero* marijuana affects particular rather than global aspects of intelligence.

In the Block Design subtest, the children are directed to assemble blocks to form a design identical to one presented in a picture. This non-verbal, concept formation task requires the ability of perceptual organization, spatial visualization and abstract conceptualization (Wechsler 1991). The Picture Completion subtest requires the subject to identify a missing portion of an incompletely drawn picture and tests the ability to differentiate essential from nonessential details (Wechsler 1991).

These two subtests of the WISC are multifaceted, involving basic visuo-spatial and visuo-motor abilities as well as higher order cognitive processes. The latter likely include planning, impulse control, visuo-construction and visuo-analysis. Importantly, the marijuana findings on the two WISC subtests persisted after statistically controlling for basic spatial and motor abilities thus supporting the interpretation that the impact of prenatal marijuana exposure on these WISC subtests is upon "higher-order" or "top-down" cognitive processes. Although not the subject of this paper, it deserves mentioning that these findings are in considerable contrast to those found among the offspring of cigarette

smokers. Both the IQ scores and virtually all of the WISC subtests (particularly those with a verbal aspect) served to discriminate across levels of prenatal cigarette exposure (Fried et al. 1998). This disassociation between the prenatal consequences of marijuana and cigarettes suggests quite strongly that the findings pertaining to marijuana are not some sort of artifact within the OPPS sample that, in a generic sense, would be found as a consequence to *in utero* exposure to any drug.

The finding that prenatal marijuana exposure impacted upon two subtests of the WISC-III that required complex visual analysis is consistent with observations noted in the two other reports mentioned earlier that focused upon prenatal marijuana exposure (Day et al. 1994; Griffith et al. 1994). At 3 years of age in both of those cohorts, the children of marijuana users were reported to have poorer abstract/visual reasoning skills based on the pre-schooler having to complete a formboard and replicate different block designs. This consistency of findings among different cohorts persisted at 10 years of age in the MHCPD cohort where prenatal marijuana use continued to be negatively associated with abstract/visual reasoning (Richardson and Day, 1997). At that age, this cognitive domain was assessed by performance on a block design task, a progressive matrices task and the ability to copy geometric shapes. As described in the "Neurobehavioral/Cognitive Outcomes in Newborns" portion earlier in this paper, it may be noteworthy, from a longitudinal perspective, that when the children in the OPPS were less than a week old, prenatal marijuana exposure was associated with poorer visual habituation (Fried 1982; Fried and Makin 1987).

Among the 9 to 12 year olds in the OPPS cohort (Fried et al. 1998), the results of the non-WISC outcome measures, which assessed aspects of EF, were consistent with and extend the observations for the marijuana groups gleaned from the WISC tasks. Of the two non-WISC-III tests that maximally discriminated among the marijuana groups was one that required the application of visual deduction to a problem solving task and the other was an assessment of impulsivity. Thus, of the six tests thought to assess aspects of EF, the two that were found to be associated with marijuana involve impulse control, visual analysis and hypothesis testing. This is consistent with the WISC results as the two subtests in that battery associated with prenatal marijuana use–Block Design and Picture Completion–require visual analysis and hypothesis testing.

This combination of visual analysis and impulsivity, but not other aspects of EF being vulnerable to prenatal marijuana, has been interpreted (Fried 1998, Fried and Smith 2001) as being consistent with conceptualizing EF as a non-unitary process. Developmental research not involving prenatal exposure to drugs and utilizing a factor analytic approach examining EF in children at different ages (Welsh et al. 1991) provides an important avenue of support for the marijuana findings from two perspectives. It both reinforces the general notion that successful executive functioning is a multifaceted process and also yielded find-

ings that are consistent with the specific facets of EF that appear impacted by prenatal marijuana exposure (visual analysis/hypothesis testing and impulsivity). Welsh et al. (1991), using an extensive battery of tests with a normative sample, identified three independent factors in the developmental course of EF reflecting planning, verbal fluency, and hypothesis testing while controlling prepotent responding. The latter was derived from a convergence of cognitive processes based on visual hypothesis testing and impulse control. These components contributing to this factor labeled "Hypothesis Testing and Impulse Control" are strikingly similar to those neurobehavioral outcomes negatively associated with prenatal marijuana exposure in the 9 to 12 year old OPPS subjects (Fried et al. 1988). On the other hand, the other two factors which Welsh et al. (1991) labeled as a "Fluid and Speeded Response" (including a verbal fluency and a tactile performance task) and "Planning" (including a working memory and a tactile task) were not found to be associated with maternal marijuana use.

In terms of the developmental time course of the "Hypothesis Testing and Impulse Control" factor, competence is achieved at around 10 years of age (Welsh et al. 1991). This is consistent with the observation that marijuana's negative effect in this dimension of EF manifested itself in the 9-12 year olds.

In another report based on the 9-12-year-old OPPS subjects, persuasive evidence was obtained for the notion that prenatal marijuana may impact upon "top-down" neurocognitive functioning (Fried and Watkinson 2000), a major interpretative cornerstone of EF. In this study, visuoperceptual tasks ranging from those that required basic capabilities to those that required considerable integration and cognitive manipulation were utilized. Further, in order to ascertain whether any change in visuoperceptual functioning may in fact be due to demands upon nonvisual facets such as attentional, memory and/or motor components, tasks were included to assess and control for these underlying behaviors.

The consequences of prenatal marijuana use on the performance of visuoperceptual tasks varied, depending upon the nature of the demands of the tests (Fried and Watkinson 2000). No association was noted between maternal marijuana use and those tasks that required basic, fixed, functional visuoperceptual abilities with little or no analytical or integrative skills. Where *in utero* marijuana exposure did have a negative impact was on tasks that required the application of these basic visuoperceptual skills to problems involving planning, integration, analysis and synthesis. This negative association remained after statistically taking into consideration prenatal confounds plus both basic visuoperceptual abilities and the non-perceptual variables described above. Interestingly, once again the findings pertaining to prenatal marijuana exposure were disassociated from maternal use of cigarettes during pregnancy. In contrast to the marijuana findings, prenatal cigarette smoking was negatively associated with both the fundamental capabilities and the application of those basic "building blocks" to the resolution of complex, visual tests–a "bottom-up" impact.

The results of this study, linking *in utero* marijuana exposure to a poorer performance on complex visuoperceptual tasks were interpreted as being consistent with earlier theorizing that prenatal marijuana exposure impacts negatively upon certain facets of EF and by association reflecting aspects of altered prefrontal activity (Fried and Watkinson 2000). The clinical literature describing individuals with damage to this neuroanatomical region is consistent with the proposed marijuana hypothesis linking prenatal exposure with an impact upon the prefrontal area. Patients with injury to this area of the brain are not impaired on basic visuoperceptual tasks but are markedly impacted on tests requiring visuoperceptual planning and integration (Luria 1973; Stuss 1992).

A further line of evidence suggesting a link between prenatal marijuana exposure and aspects of EF can be derived from studies that have focused upon attention–a complex, multidimensional behavior (Denckla 1996; Barkely 1996; Mirskey 1996) with attributes that have considerable commonality with aspects of EF (Barkely 1997). This overlap includes the ability to withhold prepotent but unsuited response tendencies, the capacity to screen out distracting or irrelevant stimuli while focusing on the task at hand, and the faculty of both flexibility and sustainability of focus when appropriate.

The OPPS and MHCPD cohorts have been used at various ages with a number of outcome measures to investigate this domain of functioning. Although different aspects of attention appeared to be impacted, prenatal marijuana use was associated with a negative effect upon attentional processes in both cohorts. Children in the two studies were given a Continuous Performance Task (CPT) (Greenberg and Kindschi 1996).

Both the OPPS (Fried et al. 1992) and MHCPD (Leech et al. 1999) offspring were assessed in this domain at age 6. In the OPPS offspring, prenatal marijuana use was significantly predictive, in a dose response fashion, of increased inattentiveness. In the children born to women who had used more than 5 joints of marijuana per week during pregnancy, inattentiveness increased as the CPT progressed, suggesting that among these more heavily exposed children sustained attention may be particularly vulnerable.

Among the 6 year olds in the MHPCD cohort (Leech et al. 1999), prenatal marijuana exposure was also found to impact upon attentional processes in terms of increased impulsivity. The authors speculated that prenatal marijuana exposure may slow processing speed and that the deficit would become more pronounced over a longer task and if time pressure demands were increased. The CPT results were interpreted by Leech et al. (1999) to be consistent with Fried's (Fried 1996; Fried et al. 1998) speculation that prenatal marijuana exposure impacts upon aspects of EF.

Facets of attention have been the focus of a recent report of the 13 to 16 year olds participating in the OPPS (Fried and Watkinson 2001). The assessment battery that was used in this study permitted the investigation of a number of compo-

nents of attention which were similar to those described in a multifactorial model of attention developed by Mirsky (1996). Five different elements of attention were identified by factor analytical procedures in Mirsky's model. These included the ability to focus, shift, and maintain attention, consistency of attentional effort over time ("stability") and a process that is conceptually very similar to working memory (Halperin 1996). Among the adolescents in the OPPS study, prenatal marijuana exposure was significantly related with that element of attention described as "stability." Subjects who had been exposed more than 5 times per week *in utero* manifested CPT reaction times that became less consistent as the test proceeded.

The negative impact of prenatal marijuana exposure upon attention noted in the adolescents (Fried and Watkinson 2001) is similar to the findings in the same cohort on a CPT at 6 years of age (Fried et al. 1992). The wide range of ages over which this relationship has been found is consistent with the developmental course of sustained attention which, unlike some other elements of attention, continues to develop throughout childhood and adolescence (McKay et al. 1994).

In the OPPS work when the children were 6 years of age (Fried et al. 1992), in addition to the CPT assessment, the mothers were asked to rate their offspring using a behavioral symptom checklist (Conners 1989). Consistent with the findings on the experimental task, the children exposed prenatally to marijuana were rated by the parent as more impulsive and hyperactive. Paralleling the OPPS observations, a recent report of the MHPCD cohort at 10 years of age (Goldschmidt et al. 2000) noted an association between prenatal marijuana exposure in the first and third trimester and increased parental reports of hyperactivity, inattention and impulsivity.

In this MHPCD study, based on both maternal ratings of child behavior and teachers' reports, an association between increased levels of delinquency and externalizing behavior associated with prenatal marijuana exposure was observed. Using a path analysis, poor attentional skills were interpreted as mediating the association between the mothers' report of delinquency and prenatal marijuana use. This relationship between prenatal marijuana exposure and the behavioral problems in the offspring is similar to an earlier trend noted in the OPPS cohort when the children were between 9 and 12 years of age (O'Connell and Fried 1991). Mothers who had used marijuana regularly during pregnancy rated their children as having a higher rate of conduct disorders but this difference did not retain significance after extraneous variables were controlled.

OVERALL CONCLUSIONS

Although predicated upon a limited body of literature, a suggestive, relatively consistent albeit nascent theoretical picture may be derived. The apparent effects

of prenatal marijuana exposure upon offspring are subtle. The emergent picture is that such exposure *in utero* may impact upon particular aspects of a complex higher-order cognitive process termed executive function. Although it is not possible to control all of the host of complex factors that possibly influence the outcomes of interest (Fried and Smith 2000; Fried 2002), the major studies cited have considered and have attempted to take into statistical account such potential confounders and moderating variables as other drug use, parenting socioeconomic status and the home environment. In the longitudinal OPPS and MHPCD studies, in spite of the marked difference in their racial and socioeconomic backgrounds, a considerable degree of similarity in findings is evident lending both validity and reliability to the findings.

The observations and interpretations of the data reviewed in this paper can be synthesized and summarized as follows. After the moderating effects of other risk factors are taken into account, the course of pregnancy, fetal and postnatal growth, and behavior during the neonatal and toddler stages appears relatively unaffected by prenatal marijuana exposure. However, starting at approximately 3 years of age, there are converging findings from a number of researchers implicating that such exposure negatively affect facets of EF, a multifaceted, higher-order cognitive process mediated primarily by the prefrontal cortex. In particular, aspects of EF which appear impacted in the older offspring by maternal marijuana use are in two domains: (1) problem solving tasks that require complex visuoperceptual integration and (2) attention/impulsivity. Consistent with this proposed association is the developmental literature which has identified, via factor analysis, that these two cognitive processes follow a single maturational course.

Although there is a degree of consistency in the extant literature relating prenatal marijuana exposure and the consequences in offspring, the paucity of studies from which the data have been derived (particularly in children older than 3) coupled with the issues raised in the opening paragraphs combine to emphasize the continued need for well-controlled investigations in this topic.

REFERENCES

Abel, E.L. 1980. *Marihuana: The First Twelve Thousand Years*. New York: Plenum Press.

Astley, S., and R. Little. 1990. Maternal marijuana use during lactation and infant development at one year. *Neurotoxicol Teratol* 12:161-168.

Bayley, N. 1989. *Bayley Scales of Infant Development*. New York: Psychological Corporation.

Barkley, R.A. 1996. Critical issues in research on attention. In *Attention, Memory, and Executive Function*. Edited by G.R. Lyon, and N.A. Krasnegor. Baltimore: Paul H. Brookes.

Barkley, R.A. 1997. Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychol Bull* 121:65-94.

Brazelton, T.B. 1973. *Neonatal Behavioral Assessment Scale*. London: William Heinemann and Sons.

Charlebois, A.T., and P.A. Fried. 1980. The interactive effects of nutrition and cannabis upon rat perinatal development. *Dev Psychobiol* 13:591-605.

Conners, C. 1989. *Manual for Conners Rating Scales*. Toronto: MultiHealth Systems.

Dalterio, S.L., and P.A. Fried. 1992. The effects of marijuana use on offspring. In *Perinatal Substance Abuse*. Edited by T.B. Sonderegger. Baltimore: Johns Hopkins University Press.

Damasio, A.R., and S.W. Anderson. 1993. The frontal lobes. In *Clinical Neuropsychology, 3rd ed.* Edited by K.M. Heilman and E. Valenstein. New York: Oxford University Press.

Day, N., M. Cornelius, L. Goldschmidt, G. Richardson, N. Robles, and P. Taylor. 1992. The effects of prenatal tobacco and marijuana use on offspring growth from birth through 3 years of age. *Neurotoxicol Teratol* 14:407-414.

Day, N.L., G.A. Richardson, D. Geva, and N. Robles. 1994a. Alcohol, marijuana, and tobacco: Effects of prenatal exposure on offspring growth and morphology at age six. *Alcohol Clin Exper Res* 18:786-794.

Day, N.L., G.A. Richardson, L. Goldschmidt, N. Robles, P. Taylor, D.S. Stofer, M.D. Cornelius, and D. Geva. 1994b. Effect of prenatal marijuana exposure on the cognitive development of offspring at age three. *Neurotoxicol Teratol* 16:169-175.

Day N., U. Sambamoorthi, P. Taylor, G. Richardson, N. Robles, Y. John, M. Scher, D. Stoffer, M. Cornelius, and D. Jasperse. 1991. Prenatal marijuana use and neonatal outcomes. *Neurotoxicol Teratol* 13:329-334.

Denckla, M.B. 1993. Measurement of executive function. In *Frames of Reference for the Assessment of Learning Disabilities: New Views on Measurement Issues*. Edited by G.R. Lyon. Baltimore: Paul H. Brookes.

Denckla, M.B. 1996. A theory and model of executive function. In *Attention, Memory, and Executive Function*. Edited by G.R. Lyon and N.A. Krasnegor. Baltimore: Paul H. Brookes.

Diamond, A. 2000. Close interrelation of motor development and cognitive development of the cerebellum and prefrontal cortex. *Child Develop* 71:44-56.

Dreher, M. 1997. Cannabis and pregnancy. In *Cannabis in Medical Practice: A Legal, Historical and Pharmacological Overview of the Therapeutic Use of Marijuana*. Edited by M.L. Mathre. Jefferson, NC: McFarland.

Dreher, M.C., Nugent, K. and R. Hudgins. 1994. Prenatal marijuana exposure and neonatal outcomes in Jamaica: An ethnographic study. *Pediatrics* 93:254-260.

Fried, P.A. 1982. Marihuana use by pregnant women and effects on offspring: An update. *Neurotoxicol Teratol* 4:451-454.

Fried, P.A. 1996. Behavioral outcomes in preschool and school-age children exposed prenatally to marijuana: A review and speculative interpretation. In *Behavioral Studies of Drug-Exposed Offspring: Methodological Issues in Human and Animal Research*. Edited by C.L. Wetherington, V.L. Smeriglio, and L.P. Finnegan. National Institute on Drug Abuse Research Monograph 164. Washington: U.S. Government Printing Office.

Fried, P.A. 1998. Behavioral evaluation of the older infant and child. In *Handbook of Developmental Neurotoxicology*. Edited by W. Slikker Jr. and C.W. Chang. San Diego: Academic Press.

Fried, P.A. 2002. Conceptual issues in behavioral teratology and their application in determining long-term sequelae of prenatal marihuana exposure. *J Child Psychol Psychiat* 43:81-102.

Fried, P.A. 2001 Schwangerschaft. In *Cannabis und Cannabinoide. Pharmakologie, Toxikologie und therapeutisches Potenzial*. Edited by F. Grotenhermen. Bern, Switzerland: Verlag Hans Huber.

Fried, P.A., M. Buckingham, and P. Von Kulmiz. 1983. Marijuana use during pregnancy and perinatal risk factors. *Amer J Obstet Gynecol* 144:922-924.

Fried, P.A., and C.M. O'Connell. 1987. A comparison of the effects of prenatal exposure to tobacco, alcohol, cannabis and caffeine on birth size and subsequent growth. *Neurotoxicol Teratol* 9:79-85.

Fried, P.A., D.S. James, and B. Watkinson. 2001. Growth and pubertal milestones during adolescence in offspring prenatally exposed up to cigarettes and marihuana. *Neurotoxicol Teratol* 23:431-436.

Fried, P.A., and J.E. Makin. 1987. Neonatal behavioural correlates of prenatal exposure to marihuana, cigarettes and alcohol in a low risk population. *Neurotoxicol Teratol* 9:1-7.

Fried, P.A., C.M. O'Connell, and B. Watkinson. 1992. 60-and 72-month follow-up of children prenatally exposed to marijuana, cigarettes and alcohol: Cognitive and language assessment. *J Dev Behav Pediatr* 13:383-391.

Fried, P.A., and A. Smith. 2001. A literature review of the consequences of prenatal marihuana exposure. An emerging theme of a deficiency in aspects of executive function. *Neurotoxicol Teratol* 23:1-11.

Fried, P.A., and B. Watkinson. 1988. 12-and 24-month neurobehavioural follow-up of children prenatally exposed to marihuana, cigarettes and alcohol. *Neurotoxicol Teratol* 10:305-313.

Fried, P.A., and B. Watkinson. 1990. 36-and 48-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes and alcohol. *J Dev Behav Pediatr* 11:49-58.

Fried, P.A., and B. Watkinson. 2000. Visuoperceptual functioning differs in 9-to 12-year olds prenatally exposed to cigarettes and marihuana. *Neurotoxicol Teratol* 22:11-20.

Fried, P.A., and B. Watkinson. 2001. Differential effects on facets of attention in adolescents prenatally exposed to cigarettes and marihuana. *Neurotoxicol Teratol* 23:421-430.

Fried, P.A., B. Watkinson, R.F. Dillon, and C.S. Dulberg. 1987. Neonatal neurological status in a low-risk population after prenatal exposure to cigarettes, marijuana and alcohol. *J Dev Behav Ped* 8:318-326.

Fried, P.A., B. Watkinson, A. Grant, and R.K. Knights. 1980. Changing patterns of soft drug use prior to and during pregnancy: A prospective study. *Drug Alcohol Depend* 6:323-343.

Fried, P.A., B. Watkinson, and R. Gray. 1992. A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes and alcohol. *Neurotoxicol Teratol* 14:299-311.

Fried, P.A., B. Watkinson, and R. Gray. 1998. Differential effects on cognitive functioning in 9-to 12-year olds prenatally exposed to cigarettes and marihuana. *Neurotoxicol Teratol* 20:293-306.

Fried, P.A., B. Watkinson, and R. Gray. 1999. Growth from birth to early adolescence in offspring prenatally exposed to cigarettes and marihuana. *Neurotoxicol Teratol* 21:513-525.

Fried, P.A., B. Watkinson. and A. Willan. 1984. Marijuana use during pregnancy and decreased length of gestation. *Am J Obstet Gynecol* 150:23-27.

Fuster, J.M. 1989. *The Prefrontal Cortex: Anatomy, Physiology, and Neuropsychology of the Frontal Lobe, 2nd ed*. New York: Raven Press.

Gibson, G.T., P.A. Bayhurst, and G.P. Colley. 1983. Maternal alcohol, tobacco and cannabis consumption and the outcome of pregnancy. *Aust N Z J Obstet Gynaec* 23:15-19.

Glass, M., M. Dragunow, and R.L.M. Faull. 1997. Cannabinoid receptors in the human brain: A detailed anatomical and quantitative autoradiographic study in the fetal, neonatal and adult human brain. *Neuroscience* 77:299-318.

Goldschmidt, L., N.L. Day, and G.A. Richardson. 2000. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicol Teratol* 22:325-336.

Golub M.S., E.N. Sassenrath, and C.F. Chapman. 1987. Regulation of visual attention in offspring of female monkeys treated chronically with delta-9-tetrahydrocannabinol. *Dev Psychobiol* 14:507-512.

Gordon, M., and D.F. McClure. 1984. *Gordon Diagnostic System: Interpretative Supplement*. Golden, CO: Clinical Diagnostics.

Graham, K., A. Feigenbaum, A. Pastuszak, I. Nulman, R. Weksberg, T. Einarson, S. Goldberg, S. Ashby, and G. Koren. 1992. Pregnancy outcome and infant development following gestational cocaine use by social cocaine users in Toronto, Canada. *Clin Investigative Med* 15:384-394.

Greenberg, L.M., and C.L. Kindschi. 1996. *T.O.V.A.® Clinical Guide*. Los Alamitos: Universal Attention Disorders.

Greenland, S., G.A. Richwald, and G.D. Honda. 1983.The effects of marijuana use during pregnancy. II. A study in a low risk home-delivery population. *Drug Alcohol Depend* 11:359-366.

Greenland, S., K.J. Staisch, N. Brown, and S.J. Gross. 1982. The effects of marijuana use during pregnancy. I. A preliminary epidemiologic study. *Amer J Obstet Gynecol* 143:408-413.

Griffith, D.R., S.D. Azuma, and I.J. Chasnoff. 1994. Three-year outcome of children exposed prenatally to drugs. *J Amer Acad Child Adolesc Psychiat* 33:20-27.

Halperin, J.M. 1996. Conceptualizing, describing, and measuring components of attention. A summary. In *Attention, Memory, and Executive Function*. Edited by G.R. Lyon and N.A. Krasnegor. Baltimore: Paul H. Brookes.

Hatch, E.E., and M.R. Bracken. 1986. Effects of marijuana use in pregnancy on fetal growth. *Amer J Epidemiol* 124:986-993.

Hayes, J., M. Dreher, and K. Nugent. 1988. Newborn outcomes with maternal use in Jamaican women. *Pediatr Nurs* 14:107-110.

Hurt, H., N.L. Brodsky, L. Betancourt, L.E. Braitman, E. Malmud, and J. Giannetta. 1995. Cocaine-exposed children: Follow-up through 30 months. *Dev Behav Ped* 16:29-35.

Johnston, L., P. O'Malley, and J. Bachman. 1994. *National survey results on drug use from Monitoring the Future study, 1975-1993, vol. 2 College Students and Young Adults*. NIDA, Rockville, MD, NIH Publication Number 94-3809.

Johnston, L., P. O'Malley, and J. Bachman. 1996. *National survey results on drug use from the Monitoring the Future study, 1975-1994, vol. 2 College Students and Young Adults*. NIDA, Rockville, MD, NIH Publication Number 96-4027.

Leech, S.L., G. Richardson, L. Goldschmidt, and N.L. Day. 1999. Prenatal substance exposure: Effects on attention and impulsivity of 6-year-olds. *Neurotoxicol Teratol* 21:109-118.

Lester, B., and B.M. Dreher. 1989. Effects of marihuana use during pregnancy on newborn cry. *Child Dev* 60:765-771.

Levin, H.S., K.A. Culhane, J. Hartman, K. Evankovich, A.J. Mattson, H. Harward, G. Ringholtz, L. Ewing-Cobbs, and J.M. Fletcher. 1991. Developmental changes in performance on tests of purported frontal lobe functioning. *Develop. Neuropsychol* 7: 377-395.

Lezak, M.D. 1995. *Neuropsychological Assessment*, *3rd ed.* New York: Oxford University Press.

Luria, A.R. 1973. *The Working Brain. An Introduction to Neuropsychology*. London: Penguin Press.

McKay, K.E., J.M. Halperin, S.T. Schwartz, and V. Sharma. 1994. Developmental analysis of three aspects of information processing: Sustained attention, selective attention, and response organization. *Dev Neuropsychol* 10:121-132.

McCarthy, P. 1972. *McCarthy Scales of Children's Abilities*. New York: The Psychological Corporation.

Mirsky, A.F. 1996. Disorders of attention. A neuropsychological perspective. In *Attention, Memory, and Executive Function*. Edited by G.R. Lyon and N.A. Krasnegor. Baltimore: Paul H. Brookes.

National Pregnancy and Health Survey. 1996. *Drug use among women delivering live births*, *1992*. NIDA, Rockville, MD, NIH Publication Number 96-3819.

O'Connell, C.M., and P.A. Fried. 1984. An investigation of prenatal Cannabis exposure and minor physical anomalies in a low risk population. *Neurotoxicol Teratol* 6:345-350.

O'Connell, C.M., and P.A. Fried. 1991. Prenatal exposure to cannabis: A preliminary report of postnatal consequences in school-age children. *Neurotoxicol Teratol*, 13:631-639.

Reitan, R., and L. Davison. 1974. *Clinical Neuropsychology*. New York: John Wiley and Sons.

Richardson, G.A., and N.L. Day. 1997. A comparison of the effect of prenatal marijuana, alcohol, and cocaine use on 10-year child outcome. *Neurotoxicol Teratol* 19:256.

Richardson, G., N. Day, and P. Taylor. 1989. The effect of prenatal alcohol, marijuana, and tobacco exposure on neonatal behavior. *Infant Behav Dev* 12:199-209.

Richardson, G.A., N.L. Day, and L. Goldschmidt. 1995. Prenatal alcohol, marijuana, and tobacco use: Infant mental and motor development. *Neurotoxicol Teratol* 17:479-487.

Scher, M., G. Richardson, P. Coble, N. Day, and D. Stoffer. 1988. The effects of prenatal alcohol and marijuana exposure: Disturbances in neonatal sleep cycling and arousal. *Pediatr Res* 24:101-105.

Siegel, L.S., and E.B. Ryan. 1989. The development of working memory in normally achieving and subtypes of learning disabled children. *Child Dev* 60:973-980.

Spreen, O., and Strauss, E. 1991. *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary*. London: Oxford University Press.

Stuss, D.T. 1992. Biological and psychological development of executive functions. *Brain Cognit* 20:8-23.

Tennes, K., N. Avitable, C. Blackard, C. Boyles, B. Hassoun, L. Holmes, and M. Kreye. 1985. Marijuana: Prenatal and postnatal exposure in the human. In *Current Research on the Consequences of Maternal Drug Abuse*. Edited by T.M. Pinkert. NIDA Research Monograph No. 59. Rockville: U.S. Department of Human Health and Services.

Thorndike, R.L., E. Hagan, and J. Sattler. 1986. *The Stanford-Binet Intelligence Scale: 4th ed.* Chicago: Riverside Publishing.

Welsh, M.C., B.F. Pennington, and D.B. Groisser. 1991. A normative-developmental study of executive function: A window on prefrontal function in children. *Develop Neuropsychol* 7:131-149.

Wechsler, D. 1991. *Wechsler Intelligence Scale for Children 3rd ed.* New York: The Psychological Corporation.

Zuckerman, B., D. Frank, R. Hingson, H. Amaro, S. Levenson, H. Kayne, S. Parker, R. Vinci, K. Aboagye, L. Fried, H. Cabral, R. Timperi, and H. Bauchner. 1989. Effects of maternal marijuana and cocaine use on fetal growth. *N Eng J Med* 320:762-768.