Recent Changes in the Etiology of Hearing Disorders: Perinatal Drug Exposure

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Abstract

In recent years, we have observed causes of congenital or early onset hearing disorders that had not been recognized or known to exist before. These include drugs passed to an as-yet unborn child. Principal among them is alcohol, but others, such as cocaine, are now also occupying our attention. This article reviews the effects of such exposure on the communication skills of children who had been exposed. It is not yet clear whether there are specifically auditory effects, nor is it clear whether the communicative effects are long lasting.

Key Words: Alcohol, cocaine, drugs, hearing impairment

Exposure to drugs, illicit or otherwise, during gestation places the developing embryo and fetus at risk for developmental delays and disorders in postnatal life. In 1976, Schardein estimated that up to 5 percent of human congenital defects are drug related. That rate has probably increased since then. The range of disabilities incurred by this exposure, however, has yet to be described fully. Information from developmental and behavioral profiles of infants and toddlers exposed to drugs in utero is just now forthcoming. In this paper, we consider the knowledge that we do have on each of several drugs. It should be pointed out that users of drugs tend to use more than one; they are called “polydrug” users. Young (1987) reminded us that drug-using mothers not only use more than one illicit drug, they also drink alcohol, smoke, eat poor diets, usually live in poverty, and receive poor medical care.

ALCOHOL

We have greater familiarity, because of longer experience, with the effects of prenatal alcohol exposure than with the effects of other drugs. Alcohol is the most widely used drug. In the United States, in 1990, the per capita rate of alcohol consumption among persons over 14 years of age was 61.5 US gallons (over 23 dekaliters) per year (ARIS, 1992a). This is in spite of a marked decline in the number of consumers since 1980. In other words, fewer people are consuming more alcohol. One-third of these Americans account for 92 percent of the consumption, and therefore are considered to be heavy consumers of alcohol. In 1990, 57 percent of American adults identified themselves as drinkers; in 1992, that proportion had increased to 64 percent (ARIS, 1992b). The rate of alcohol dependence has been reported to be 2.5 per 1000 in the total population of the United States (Last and Wallace, 1992).

Sokol et al (1980) had reported alcohol-related complications of pregnancy in 1.7 percent of births in their hospital. Nearly a decade later, Charness et al (1989) reported fetal alcohol syndrome (FAS) to appear in 0.1 to 0.3 percent of births and about 6 percent of children born to alcoholic mothers. This is similar to the figure of about 2 of every 1000 births reported by Abel and Sokol (1986) and again by Abel (1990). Chasnoff (1992) reported FAS in 1.9 per 1000 live births. It has also been claimed that FAS occurs in 1 of every 650 births in the United States and Europe combined (Gerber, 1990).

The characteristics of FAS are prenatal and postnatal growth retardation, developmental delay with microcephaly (i.e., head size below the 3rd percentile), neurologic abnormalities, facial dysmorphology, and occasional other anomalies.
By 1991, FAS had become at least equal with Down syndrome as the most common cause of mental retardation, with the mean IQ being around 67 (Iosub et al., 1981; Streissguth et al., 1991).

The now classic papers on the subject are those of Kenneth L. Jones and his colleagues and date from the early 1970s (e.g., Jones et al., 1973, 1974). Those papers describe a syndrome of an alteration of morphogenesis involving craniofacial, cardiovascular (up to 40% of the babies), and limb defects, plus prenatal (and postnatal) growth deficiency and developmental delay. Similarly, Randall and Taylor (1979) observed anomalies of the cardiovascular, urogenital, nervous, and skeletal systems in ethanol-exposed mice. Specifically, the growth delay results in size under the 10th percentile; 66 percent of children with FAS are characterized as presenting with low birth weight, that is, less than 2500 grams (Abel, 1984). Incidence of small size for gestational age is increased twofold in this population (Olegard et al., 1979). Furthermore, this delay persists.

FAS results in facial anomalies including thin upper lip, underdeveloped filtrum, microphthalmia, and maxillary hypoplasia. Palatal clefts (but not clefts of the lip) are quite common: Majewski and Goecke (1982) found cleft palates in 7 percent of babies with FAS, and Young (1987) reported as many as one in eight (i.e., 12.5%). Hanson et al. (1976) and Clarren and Smith (1978) noted anomalies of the ear to be a common feature of FAS. Abel (1990) made the same observation. Young’s (1987) review revealed that one-third of babies with FAS were hearing impaired. Pettigrew and Hutchinson (1984) reported that four of the six children with FAS whom they had examined had abnormal auditory brainstem responses (ABRs). Church and Gerken (1988), in their group of 14 children, found that hearing impairment (due to bilateral recurrent bilateral serous otitis) appeared in 93 percent; 29 percent also had sensorineural impairments. They observed that the prevalence of serous otitis media in the FAS population exceeds even that in the Down syndrome population. Church, in an earlier paper (1987), reported that 33 percent of the children with FAS whom he had examined had sensorineural hearing losses (as compared to the 10–15% who fail school hearing screenings [Northern and Downs, 1991]), and that 92 percent of the group had conductive hearing impairments (vs 30% of all children with OME) secondary to recurrent otitis media. Children with FAS are properly described as otitis prone.

How can we know that it is alcohol, per se, that is the etiologic factor? It is important to separate alcohol exposure from its possible interactions with other substances, other prenatal environmental exposures, and endogenous factors. This can be done by studying animals in whom alcohol was the only potentially significant event. Church (1987) analyzed ABRs in rats exposed prenatally to alcohol. He found that 19 percent of these animals had sensorineural hearing impairments with recruitment. Prolonged auditory transmission times persisted to maturity, although there was a trend toward more nearly normal values. Moreover, as part of the study of cortical potentials, he found that the mice also had what he interpreted to be auditory processing dysfunction. Church and Gerken (1988) posited that alcohol exposure induces a "neuroectoderm syndrome" and that alcohol toxicity is a possible etiology of FAS. Abel (1984) suggested that prenatal alcohol exposure results in cellular hypoplasia, that is, a reduction of cell number. It has been observed that ethanol is clearly teratogenic in mice (Randall et al., 1977), but it has also been observed that there was no alcohol teratogenicity in mice, rats, or rabbits (Schwetz et al., 1978).

What, then, do we know about auditory or communicative teratogenicity of alcohol? First, this is not a new question. In 1912, William Wade claimed to have done some surveys in France and the United States that revealed no data supporting a claim that schools for the deaf were filled with the children of moderate drinkers. Mr. Wade’s finding is undoubtedly still true. The most pervasive finding is that prenatal alcohol exposure often leads to physical and mental developmental delay. Tennes and Blackard (1980) claimed to find no effect of maternal alcohol consumption on birth weight or increased incidence of minor physical anomalies. They did not screen for hearing impairment, but children with FAS are clearly otitis prone and present with sensorineural hearing impairments far more often than nonexposed children.

Are alcohol-exposed children without FAS hearing impaired? We don’t know, although we do know that they often have some traits similar to those who do have FAS. A diagnosis of FAS depends on three things: a characteristic face, developmental delay, and small stature. Some children who had been exposed do not exhibit all three of these characteristics. Nevertheless, they are said to have alcohol-related birth defects...
(ARBD). The variability of phenotype probably results from the amount of alcohol consumed and when in gestation it was consumed. Perhaps children who express ARBD could also present with hearing impairments in greater incidence than other children.

It seems, then, that FAS perhaps should be added to our high-risk registers for congenital or early-onset hearing loss. We must be clear, furthermore, that there is a dose-related effect. This means that it is not necessary for a gravida to be alcoholic to produce an alcohol-affected child; the effects may simply be attenuated in magnitude. Moreover, Chasnoff (1992) reported that children of alcoholic fathers have birth weights about 200 grams below the norm. The effects of exposure are multifactorial, that is, the drug interacts with other drugs and with endogenous factors. For example, the incidence of FAS is five times greater in children of native Americans than in other populations (Bean, 1992). Furthermore, 25 percent of mothers of children who have FAS will deliver a second or even a third child with FAS (Bean, 1992). There is no known safe amount of alcohol that may be consumed during pregnancy. Consequently, this is a matter that must be pursued with all our patients.

**COCaine**

In the United States, in 1990, 158,000 children were born who were known to have been prenatally exposed to cocaine; of course, this figure excludes those in whom the exposure is unknown. Using a combination of self-reporting and urine toxicology screens, the incidence of such prenatal exposure has been reported to range from 11 percent of births (Chasnoff and Griffith, 1989; McCalla et al, 1991) to about 14 percent (Phibbs et al, 1991). However, in a recent multicenter study, intraterine cocaine exposure was positively identified (by urine screen) in only 1.8 percent of all births (Corwin et al, 1992).

Exposure may have been more pervasive, but undetected in some studies, because most cocaine effects do not occur if use stops by about midterm (Chasnoff, 1992), or because the effects are not always evident in the newborn nursery. Nevertheless, cocaine accounts for more than 60 percent of drug-affected babies, excluding the 40 percent who aborted spontaneously (Chasnoff et al, 1987). Cocaine is a drug extracted from the leaves of erythroxylon coca, the coca plant of South America. It appears in the form often inhaled by users, cocaine hydrochloride. So-called “crack” is in a form that allows it to be smoked or even injected. Crack is made by dissolving cocaine hydrochloride in a volatile solvent such as ether. Therefore, crack cocaine may be still more dangerous because these other substances could be toxic themselves. Risks are increased by smoking crack because of the shorter time required for the drug to reach the brain. In addition, cocaine bought in the street frequently contains contaminants added to increase its bulk, making it more saleable. Some of the contaminants are themselves illicit drugs.

Cocaine crosses the placental barrier and blocks the uptake of catecholamines in the pregnant uterus. Pregnant women metabolize cocaine slower than other people, making them more sensitive to small amounts of the drug. Moreover, perhaps because of this slow uptake, metabolites of cocaine (i.e., benzoylecgonine) have been found in the urine of exposed infants for up to 4 days (Chasnoff et al, 1986) and even as long as 10 days (Dixon and Bejar, 1989) after birth. This may also be because cocaine’s greatest effect is in the third trimester. Hadeed and Siegel (1989), in a controlled prospective study, determined that “cocaine use during pregnancy can cause newborn infant growth retardation and microcephaly” (p. 209). As an aside, one should note that the impact of prenatal tobacco exposure has triple the effect of cocaine on birth weight.

Gravidae’s cocaine abuse causes vasoconstriction of blood vessels delivering nutrients and oxygen to a fetus. Peters and Theorell (1991) described the ensuing events as a corresponding lowering of oxygen in the blood being delivered to the fetus. This, they hypothesized, releases catecholamines, leading to increased oxygen demand and a cycle of hypoxia in the fetus. Moreover, diffusion of cocaine directly to the fetus leads to an increase of norepinephrine and (hence) vasoconstriction, hypoxemia, and exaggerated fetal cardiovascular response. Cocaine, like heroin, can lead to cerebral infarct (Healy, 1992).

Exposure to cocaine during gestation affects neurobehavioral development and predisposes an infant to disordered communication. Developmental dyspraxia has been reported to be the most common sequela (Healy, 1992). Infants born with intraterine exposure to cocaine present with a variety of disordered neurobehaviors, many of which are not evident in the early neonatal period. These may include abnormal sleep patterns, tremors, poor feeding, hypertonia, frantic fist sucking, hyperreflexia, and
gaze aversion (Ewing, 1991). Eisen et al (1991) observed that children prenatally exposed to cocaine present with several behavioral and psychological differences from nonexposed infants, such as abnormal reflex behavior including an abnormal Moro reflex, autonomic instability, excessive high-pitched crying, excessive mouthing, gastrointestinal signs including vomiting and diarrhea, hypertonia, irritability, restlessness, tachypnea, and tremors. Many of these disordered behaviors are frequently associated with recognized, high-risk factors.

Fetal hypoxia is a rather frequent cause of congenital deafness and neuromotor disability. Indeed, it is on the high-risk register of the U.S. Joint Committee on Infant Hearing. In a 1988 paper, Mencher and Mencher identified seven factors commonly associated with birth asphyxia that appeared in their population of hearing-impaired babies. Five of those factors — abnormal fetal signs, seizures, intrauterine growth retardation, hypoxic ischemic encephalopathy, and damage to other organs — have been mentioned in the literature associated with cocaine use. Although we can't always identify the cause of hypoxia, its presence is sufficient reason for a neonate to be considered at risk and to be screened for hearing impairment. Perhaps more of these cases than we previously thought may be attributed to unknown prenatal exposure to cocaine.

Testing for hearing impairment in the cocaine-exposed population presents us with another problem. Cocaine acts upon neurotransmitters that connect brainstem structures with the frontal lobe, and we assume that it is the frontal lobe that allows us to utilize communicative behaviors. Hence, infants exposed to cocaine during gestation have been described as "difficult to handle, care for, and soothe even by experienced professionals in the best of situations" (Rist, 1990, p. 3). Rist said that these babies are hypersensitive, so that even picking up such a child may elicit tremors and crying. The babies have difficulty with state control so that they have short durations of quiet, alert states and, therefore, have difficulty orienting to visible or audible stimuli.

In general, cocaine acts upon the central and the peripheral nervous systems. It inhibits nerve conduction by blocking reabsorption of the neurotransmitters norepinephrine and dopamine at the nerve's presynaptic site (Bresnahan et al, 1991). In the central nervous system, cocaine affects the dopaminergic system such that it creates a sense of euphoria and hence psychological addiction. But it may deplete the supply of dopamine, and this could lead to depression. Norepinephrine is the main neurotransmitter in locus coeruleus, said to be the center of arousal. If cocaine intensifies the responses in the norepinephrine system, it may cause affected infants to be hyper-responsive during screening procedures.

Shih et al (1988) investigated the ABR of 18 neonates born to women who had abused cocaine. These women all admitted cocaine use during pregnancy and tested positive on a urine toxicology screen for cocaine, and all the babies tested positive for cocaine on a urine toxicology screen. These infants were compared to 18 from the normal newborn nursery. The cocaine-exposed infants all had prolonged ABR interpeak latencies as compared to controls. Such prolongations are believed to "reflect abnormalities in brainstem conduction time rather than a deficit in the auditory periphery" (p. 250) and have been reported as well in infants with other nervous system insults. Moreover, 5 of the 18 infants had ABR thresholds poorer than 20 dB, suggesting the possibility of moderate hearing impairment. Salamy et al (1990) also showed that brain transmission times are abnormal in cocaine-exposed babies. These findings may reflect toxicity of the drug, placental vasoconstriction, which can result in disruption of formation of embryologic structures by cutting off blood supply, or intrauterine growth retardation. However, Tyrala et al (1992) found no significant difference between ABR hearing screening failure rates of cocaine-exposed infants and infants not exposed.

Although we must evaluate our test results on these neonates with caution, it appears that cocaine's effects on the developing brain stem will result in unfavorable neurobehavioral consequences and, perhaps, specifically auditory consequences as well. If we observe an infant who has these characteristics, it should be worthwhile to assess the possibility of intrauterine cocaine exposure in an attempt to uncover other potential neurodevelopmental difficulties.

**OTHER DRUGS**

The effects of LSD (lysergic acid diethylamide) are similar to those of PCP. PCP (phenylcyclidine), known as "angel dust," and LSD can cross the placental barrier to reach a fetus. Mothers who use PCP during pregnancy often deliver babies who have visual, auditory, and motor disturbances. These babies may also
have sudden outbursts of agitation and other rapid changes in awareness similar to responses in adults intoxicated with PCP. It is possible, then, that changes in the state of awareness may make such infants difficult to evaluate. Melnick and Myrianthropoulos (1979) reported infants born to mothers who used PCP in early pregnancy to display retarded cranial growth, hypertelorism, and micrognathia.

Mothers who are addicted to heroin or methadone have babies addicted to heroin or methadone. Hence, these babies show signs of narcotic withdrawal, and withdrawal from methadone seems to be more difficult than withdrawal from heroin. The children are hyperirritable for several months and may continue to be hyperactive. On the other hand, it appears that the effects of these narcotics are not permanent.

There are more than 400 substances identified as constituent to marijuana, but it is tetrahydrocannabinol that has the most active effect (Elage et al., 1991). Cannabis (marijuana) leads to withdrawal and behavioral effects similar to those of heroin, plus a high risk of embryonic death. Studies on animals have shown marijuana to be potentially damaging to the nervous system, the liver, and the limbs. It has been suggested that the effects of prenatal marijuana are similar to the effects of prenatal alcohol. Marijuana has the greatest effect on neonates' state regulation, more than cocaine, PCP, or alcohol. Unlike the effects of heroin, but like the effects of alcohol, the effects of marijuana do not disappear.

There are few, if any, reports of the specifically auditory effects of these drugs. However, as they do have overt communicative consequences, they must be or become apparent in our clinical efforts.

**POSTNATAL EFFECTS**

Cocaine, alcohol, and marijuana all can pass via breast milk, and there was a report of an infant cocaine affected in this way (Chasnoff et al., 1987). A study in Brazil (Elage et al., 1991) evaluated children between the ages of 10 and 17 years who were what we would call “glue sniffers.” There were three groups of subjects: one group not exposed, one exposed to inhaled toluene, and one using toluene and marijuana. All three groups underwent electronystagmography and brainstem audiometry. These authors concluded that “among the Toluene inhalers there was statistically significant damage in the brainstem auditory pathways” (p. 45) and that there were vestibular system abnormalities in the majority of toluene users.

In addition to these biologic effects, there are also social consequences. Some recent United States statistics show that three-quarters of crimes (including murder, rape, and child molestation) are done by persons influenced by alcohol and/or other drugs. Ninety percent of the homeless population abuse these substances. At least half of all hospital beds contain patients whose illnesses can be attributed to the use of alcohol, other drugs, and/or smoking. This is an expensive matter, expensive of funds and expensive of human welfare.

**SUMMARY**

With the exception of tobacco, alcohol, and cocaine are now the drugs most commonly ingested during pregnancy. Both are known to have permanent neurobehavioral effects, both are known to be teratogenic, and both have been shown to have developmental and communicative consequences. We propose, then, that our high-risk registers and screening programs include drug exposure.

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