POLICY FORUM: DRUG ABUSE

Cocaine Exposure and Children: The Meaning of Subtle Effects

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Early reports led to the fear that exposure to cocaine during prenatal life caused brain damage and intellectual and social impairment (*1*). But more recent evidence has presented a different picture, in which the effects of cocaine are more subtle (*2*). This view should not inspire complacency. From a public health perspective, these subtle effects can have profound consequences for the success of these children in school and for the cost of special education services.

To investigate the magnitude of these effects, we examined the studies in our Robert Wood Johnson database (*3*), a collection of the published literature on prenatal cocaine exposure and child outcome. Of the published studies, 101 met methodological inclusion criteria (original research, published in an English-language refereed journal, human subjects with prenatal cocaine exposure, neurobehavioral outcome measures, and inclusion of a control or comparison group with statistical analysis). Only eight of these studies were completed with school-age children (*4–11*); most were studies of infants and preschoolers. Intelligence quotient (IQ) was measured in five studies, receptive language in four, and expressive language in five, making it possible to get our first systematic glimpse of the long-term effects of prenatal cocaine exposure.

We quantified these cocaine effects using meta-analysis, a statistical procedure in which effects from different studies are pooled to provide a better estimate of the effect size, in this case prenatal cocaine exposure, than can be determined from a single study (*12*). A list of the 101 studies in the database and key details from each of the eight studies used in the meta-analysis can be found at *Science* Online at www.sciencemag.org.

In our meta-analysis, for each study a Z value was computed directly from the t statistic derived from mean differences between cocaine-exposed and control cases. These Z values were then weighted by the size of the cocaine-exposed group. Only the exposed group was used in weighting, because one study used a large normative sample as its control group, which would have unduly skewed the meta-analysis results toward that single study. The standard test for the pooled weighted Z's provided the significance criterion for the combined effect size. Effect sizes for each study were computed by taking the difference between the means of the exposed and control groups, divided by the pooled standard deviation. Finally, standard "file drawer" estimates were conducted to identify the number of studies with no difference between groups that was necessary to reduce the meta-analysis findings to nonsignificance. As shown in the table, the difference in IQ between cocaine-exposed and control groups in the studies examined is 3.26 IQ points. This difference, although small, is statistically significant and can have a substantial impact on society.

Early intervention and special education services are typically provided for children who score less than 2 standard deviations (SD) (or in some cases less than 1.5 SD) below the mean on standardized tests. This would correspond to IQ scores of <70 or <78). In a normal distribution (a good model for IQ scores), 2.28% of children will score <70 (2 SD) and 6.68% of children will score <78 (1.5 SD). When the IQ distribution is shifted downward by 3.26 IQ points, the number of children at the low end of the distribution will increase (see the table) to 3.75%. This results in a 1.6-fold increase in the number of children with IQs <70 and to a 10.03% or a 1.5-fold increase in the number of children with IQs <78. These distributional changes then allow estimation of some of the costs to society that are associated with prenatal cocaine exposure.

The National Pregnancy and Health Study (NPHS), which is based on maternal self-reporting, estimates that 45,000 cocaine-exposed children are born each year (*13*). The U.S. General Accounting Office reviewed hospital records and concluded that upwards of 375,000 cocaine-exposed children are born each year (*14*). These figures predict that the number of children affected by this 3.26-point difference in IQ is estimated to be between 1688 and 14,062 at <2 SD and between 4514 and 37,612 at <1.5 SD. According to the U.S. National Center for Education Statistics (*15*), special education services (additional services for special education) cost $6335 per child per year. The added costs of these special educational services for the number of cocaine-exposed children with IQs <70, based on a 3.26-point IQ difference, is $4 million to $35 million per year and $10 million to $80 million per year for children with an IQ of <78.

These IQ differences may also be thought of as an effect size in which the cocaine effect is expressed in SD units (*16*). For example, the standardized IQ score has a mean of 100 and a SD of 15. A difference of 7.5 IQ points would represent an effect size of 0.50. Effect size is a

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Measure	Effect (SEM)	Percent <2 SD (normal = 2.28%)	Increase	Additional affected children/year (no.)	Additional cost for services (millions)	Percent <1.5 SD (normal 6.68%)	Increase	Additional affected children/year (no.)	Addional cost for services (millions)
IQ difference (n = 5)	3.26 (2.01) IQ points	3.75	1.6×	1,688–14,062	$4–35	10.03	1.5×	4,514–37,612	$10–80
IQ effect size (n = 5)	0.33 (0.13) SD units	4.75	2.0×	2,138–17,812	$7–59	12.10	1.8×	5,445–45,375	$15–129
Receptive language effect size (n = 4)	0.71 (0.26) SD units	9.85	4.3×	4,432–36,938	$22–180	21.48	3.2×	9,666–80,550	$42–352
Expressive language effect size (n = 5)	0.60 (0.29) SD units	8.08	3.5×	3,636–30,300	$17–138	18.14	2.7×	8,163–68,025	$33–272

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useful construct because all measures are expressed in the same units (SD units); therefore, effects on different tests can be compared even if they use different scales of measurement. Effect sizes are graded as small (<0.5 SD), medium (0.5 to 0.75 SD), and large (>0.75 SD). The table shows the mean effect sizes weighted for the number of children in the exposed groups and standard errors for the IQ studies, as well as the studies of receptive and expressive language (receptive language refers to understanding or comprehension; expressive language refers to competence in language production or competence in spoken language). The analyses of effect sizes showed that cocaine-exposed children had significantly lower scores on tests of IQ ($Z = 2.61$, $P < 0.01$), receptive language ($Z = 4.44$, $P < 0.001$), and expressive language ($Z = 3.99$, $P < 0.001$). The language studies showed a medium effect size as compared with the small effect size shown in the IQ studies. The effect size for receptive language was more than twice the effect size for IQ, and expressive language showed an effect size 1.8 times greater than IQ. The table also shows the follow-up calculations for the percent of children newly affected at <2 SD and <1.5 SD, the number of children newly affected each year, and the cost of added special education services for these children annually. These estimates are higher for the IQ effect size than for the IQ difference score, because the variance for the effect size calculation is based on the children in the published studies rather than the IQ distribution in the general population. The moderate effect sizes in language result in a 2.7- to 4.3-fold increase in children who will be affected at clinically significant levels. For expressive language, this translates to between 3636 and 68,025 children newly diagnosed annually who will need special education services, resulting in additional costs of $17 million to $272 million per year. As these estimates are for additional costs due to cases newly diagnosed annually, the costs are underestimates because the costs and burden would be accrued, with the annual addition of children with the specific deficits identified.

It is also likely that these findings are underestimates for three other reasons. First, the NPHS found significant underreporting of cocaine use when maternal self-reporting (the method used to generate the lower value for this analysis) was compared with urine toxicology results. Second, the IQ distribution used in our estimates is based on that of the general population, but inner-city children fall disproportionately in the lower end of the distribution, especially as they grow older (*17*). This is a case of "double jeopardy": The additional burden of cocaine is placed on children who are already destined by social-economic and environmental factors to cross the boundary into the range where special education services are typically provided. Third, intervention services for language disabilities may be different from those required for low IQ. Thus, services may be additive, and other services not yet identified may be needed to address attentional, behavioral, and emotional problems.

These meta-analyses and follow-up cost estimates are based on a relatively small number of studies. Therefore, it is possible that with additional studies, the results could change. We can, however, estimate the number of studies with a null effect size (studies finding zero difference between exposed and control children), which if added to the meta-analysis would result in a nonsignificant difference across the aggregate of studies. These analyses show that it would take 15 additional zero-effect studies to negate the 0.33 IQ effect size, 18 zero-effect studies to negate the 0.71 effect size for receptive language, and 23 zero-effect studies to negate the 0.60 effect size for expressive language. We also conducted a test of heterogeneity for each of the cocaine effects. We found no significant heterogeneity of effect size, which indicates that there is no evidence for differences between the studies that need to be accounted for in the analysis.

Finally, we know that cocaine use often occurs in the context of poverty and other known risks to young children, including cigarette smoking and other drug use (*3*); thus, one might interpret the observed effects as resulting from these other factors. Two factors mitigate against such an explanation. First, studies were considered in our analysis only if they controlled for factors such as poverty. Second, control for the use of drugs other than cocaine was attempted either by exclusion or by including other drugs in both the cocaine and comparison groups. In the meta-analysis, findings were aggregated across studies; therefore, unless all studies had similar confounding variables (which they did not), we can conclude that these are reliable cocaine effects.

In summary, the published follow-up studies of cocaine-exposed children show that cocaine is associated with reliable decrements in cognitive development that are subtle in two ways. First, the effects are subtle in that they are of small magnitude as shown by the IQ findings. The small magnitude of the effects is in sharp contrast to the sensationalistic reports in popular media on the effects of prenatal cocaine exposure (*1*). Second, the effects are subtle in that we found larger effect sizes on more subtle domains of function, that is, specific language abilities than on global IQ. The public health consequences of both of these kinds of subtle effects are substantial, indicating that we should not equate small magnitude with lack of importance. Prenatal cocaine exposure may not cause devastating brain damage, but it may result in anatomical and molecular subtle brain damage, which are the basis for the cognitive and language deficits that we have described. Nevertheless, prenatal cocaine exposure will significantly increase the number of children who will fail in school and need special education services, at an estimated additional cost of up to $352 million per year. The "good news" is that these children are not hopelessly damaged and destined to become a burden to society. Instead, we can view them as children who can be helped to become productive members of society. Meanwhile, prevention efforts need to be directed toward ridding society of the cocaine problem and toward treatment programs for drug-using pregnant women in order to prevent the harm caused by cocaine use.

References and Notes

1. L. C. Mayes, R. H. Granger, M. H. Bornstein, B. Zuckerman, *J. Am. Med. Assoc.* **267**, 406 (1992).
2. B. M. Lester, *Ann. N.Y. Acad. Sci.* **846**, 295 (1998).
3. B. M. Lester, L. LaGasse, S. Brunner, *J. Drug Issues* **27**, 487 (1997).
4. S. D. Azuma and I. J. Chasnoff, *Pediatrics* **92**, 396 (1993).
5. S. L. Bender *et al.*, *Dev. Behav. Pediatr.* **16**, 418 (1995).
6. A. van Baar and B. M. T. de Graaff, *Dev. Med. Child Neurol.* **36**, 1063 (1994).
7. T. L. Hawley, T. G. Halle, R. E. Drasin, N. G. Thomas, *Am. J. Orthopsychiatr.* **63**, 364 (1995).
8. D. A. Rotholz, P. Snyder, G. Peters, *Educ. Treatment Children* **18**, 1 (1995).
9. G. A. Richardson, M. L. Conroy, N. L. Day, *Neurotoxicol. Teratol.* **18**, 627 (1996).
10. M. E. Malakoff, L. C. Mayes, R. S. Schottenfeld, *Clin. Res. Rep.* **3**, 346 (1994).
11. I. Nulman *et al.*, *Can. Med. Assoc. J.* **151**, 1591 (1994).
12. R. L. Rosenthal and R. L. Rosnow, *Essentials of Behavioral Research: Methods and Data Analysis* (McGraw-Hill, New York, ed. 2, 1991).
13. National Institute on Drug Abuse (NIDA), *National Pregnancy and Health Survey: Drug Use Among Women Delivering Livebirths: 1992* (National Institutes of Health, Publication No. 96-3819, NIH, Rockville, MD, 1996).
14. U. S. General Accounting Office (GAO), Report to the Chairman, Committee on Finance, U.S. Senate, *Drug Exposed Infants, A Generation at Risk* (U.S. GAO, Washington, DC, 1990).
15. U.S. National Center for Education Statistics, *Digest of Education Statistics* (1996), based on M. T. Moore, E. W. Strang, M. Schwartz, M. Braddock, *Patterns in Special Education Service Delivery and Cost* (Decision Resources, Washington, DC, 1988).
16. J. Cohen, *Statistical Power Analysis for the Social Sciences* (Lawrence Erlbaum, Hillsdale, NJ, ed. 2, 1988).
17. A. R. Jensen, *Bias in Mental Testing* (Free Press, New York, 1980).