

Metabolism of Catechol Estrogens by Erythrocyte

Catechol-O Methyltransferase

Fishman and Tulchinsky (1) present evidence that the catechol estrogen 2-hydroxyestrone suppresses serum prolactin in normal ovulatory young women. However, in 3 of the 12 subjects studied the authors were unable to suppress serum prolactin and suggested that prolactin response to 2-hydroxyestrone is subject- and not time-dependent.

In a study designed to evaluate the kinetics of catechol estrogen formation from plasma estrone *in vivo*, Bates *et al.* (2) were unable to compute the transfer constant of conversion of estrone to 2-hydroxyestrone because of intravascular metabolism of 2-hydroxyestrone by erythrocytes. During the infusion, the radioactively labeled 2-hydroxyestrone was metabolized to its methyl ether, 2-methoxyestrone, by erythrocyte catechol-O-methyltransferase (COMT). This finding led to the development of a radioenzymatic assay for quantifying COMT in erythrocytes with the use of radioactively labeled 2-hydroxyestrone as the substrate (3).

Weinshilboum *et al.* (4) have demonstrated a bimodal distribution of COMT activity in erythrocytes from 373 randomly selected young men and women. We have not identified a bimodal distribution of COMT activity in our investigations, but we have found increased

COMT activity in erythrocytes of pregnant women (5), in women with pregnancy-induced hypertension, and in fetal blood (6).

We suggest that the three subjects studied by Fishman and Tulchinsky who failed to have prolactin suppression may have increased erythrocyte COMT activity. This could result in intravascular metabolism of 2-hydroxyestrone before the infused material reached its site of action. We further suggest that measurement of erythrocyte COMT activity should be part of the investigation of catechol estrogen infusion studies.

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References and Notes

1. J. Fishman and D. Tulchinsky, *Science* **210**, 73 (1980).
2. G. W. Bates, C. D. Edman, J. C. Porter, P. C. MacDonald, *J. Clin. Endocrinol. Metab.* **45**, 1120 (1979).
3. G. W. Bates, C. D. Edman, J. C. Porter, J. M. Johnston, P. C. MacDonald, *Clin. Chim. Acta* **94**, 63 (1979).
4. R. M. Weinshilboum, F. A. Raymond, L. R. Elveback, W. H. Weidman, *Nature (London)* **252**, 49 (1974).
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6. G. W. Bates and E. Jackson, unpublished data.

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Duration of Preschool Effects on Later School Competence

Darlington and colleagues (1) report that children who had attended infant and preschool programs had significantly higher rates of meeting school requirements (defined as not being held back a grade or placed in special education) than did controls. They also report that IQ measures taken on the same subjects

showed large initial gains that had vanished 5 years after the completion of preschool. They made no attempt, however, to see whether preschool effects on school performance also diminished over time. Consequently, readers are left with the impression that, unlike the results for IQ, preschool effects on measures

of school performance were permanent.

Separating the studies analyzed by Darlington *et al.* into two groups according to grade at follow-up (Table 1) reveals that there is no significant effect of early enrichment beyond elementary school. The pooled z (2) for the four studies where follow-up took place in junior or senior high school is only 1.62 (pooled $P > .1$), whereas for the three studies with follow-up in elementary grades it is 3.6 (pooled $P < .001$). Darlington's test for the robustness of any finding was to delete the strongest result from a group of studies. When this test is applied to the follow-up of older children, the small preschool effect almost vanishes (pooled $z = .29$, pooled $P > .75$). Thus the beneficial effects of preschool on school performance (as defined by Darlington *et al.*) were no more durable than the preschool effects on IQ.

Concerning the effect on elementary school children, there is a possible source of confounding: teacher's knowledge of preschool attendance. The decision to retain a child in a grade or send him or her to special education might have been influenced by knowledge that the child had or had not already been given special training. If information about preschool attendance was part of the child's elementary school record, this effect might have been substantial, in which case what was measured by the variables chosen was not necessarily differences in school competence.

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References and Notes

1. R. B. Darlington, J. M. Royce, A. S. Snipper, H. W. Murray, I. Lazar, *Science* **208**, 202 (1980).
2. The method specified by Darlington *et al.* in their reference 10 (1) was used for these calculations.

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Table 1. Comparison of treatment and control groups on failure to meet school requirements. [Data from table 2 in (1)]

Grade	Project	N	Failed to meet requirements (%)		P (two-tailed)
			Treatment	Control	
Follow-up in junior or senior high school					
12	Gray	55	52.8	68.4	.263
12	Beller	69	45.9	50.0	.737
7	Palmer	221	24.1	44.7	.006
7	Miller	125	20.6	11.1	.346
Follow-up in elementary grades					
5	Gordon	82	39.1	61.5	.134
4	Weikart	123	17.2	38.5	.009
3	Levenstein	127	22.1	43.5	.035

Our report (1) presented data from a continuing study by the Consortium for Longitudinal Studies. The consortium members have since provided us with data past elementary school for all seven projects in Horn's table 1 (although the dependent variable for the Weikart project is placement in special education classes rather than a more general measure of failure to meet school requirements). These newer data yield a highly significant result (pooled $z = 3.55$, $P = .0004$) which is robust after deletion of the most significant single result (pooled $z = 2.68$, $P = .0074$). Thus there is no indication that effects last only through elementary school.