

Heavy Metal Pollution and Race as Factors in Hypertension and Heart Disease

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Jonathan Kahn's report on FDA approval of BiDil, a drug targeted to hypertension in blacks (*Scientific American*, Aug. 2007, pp. 40-45), fails to consider abundant evidence linking both toxic chemicals and race to hypertension and heart disease. Recent studies of environmental factors that contribute to higher rates of heart conditions indicates the following factors could influence the effectiveness of BiDil:

- **TOXINS:** Geographic differences in rates of cancer (Figure 1) reveal the importance of considering the possibility that pollution with lead or manganese can contribute to hypertension or heart disease. Lead has long been identified as a source of hypertension along with other health and behavioral problems.¹ Rates of heart disease in counties reporting pollution with either lead or manganese show these toxins both have a significant association with heart disease (Table 1a), whereas the only association found between the two toxins and hypertension is an interaction effect (Table 1b).²
- **RACE AND POVERTY:** Race plays an important role because blacks tend to absorb more lead than whites exposed to pollution in the same community (Figure 2). Moreover, lead absorption is increased where compounds called silicofluorides (H_2SiF_6 or Na_2SiF_6) are added to U.S. public water supplies -- and this increase in harm from pollution is more pronounced among blacks than whites.³ It should therefore not be surprising that county level data suggest there may be racial differences in vulnerability to hypertension and to other forms of heart disease:

¹ Needleman, H. (1992), *Human Lead Exposure* (Boca Raton: CRC Press).

² Masters, R, Hone, B, and Doshi, A. (1998). "Environmental Pollution, Neurotoxicity, and Criminal Violence," in J. Rose, ed., *Environmental Toxicology: Current Developments* (London: Gordon and Breach, 1998), pp. 13-48.

³ Masters, R. and Coplan, M. (1999a), "Water Treatment with Silicofluorides and Lead Toxicity," *International Journal of Environmental Studies*, 56: 435-49 [on children's blood lead in Mass.]; Masters, R. and Coplan, M. (1999b) "A Dynamic, Multifactorial Model of Alcohol, Drug Abuse, and Crime: Linking Neuroscience and Behavior to Toxicology," *Social Science Information*, 38:591-624 [data from children in NHANES III]; Masters, R.D., Coplan, M. J., Hone, B.T., and Dykes, J.E. (2000). "Association of Silicofluoride Treated Water with Elevated Blood Lead," *Neurotoxicology* 21: 101-1100 [analyzing venous blood lead samples of 131,422 children in New York state]; Masters, R.D. (2002). "MacLean's Evolutionary Neuroethology: Environmental Pollution, Brain Chemistry, and Violent Crime," Gerald A. Corey Jr. & Russell Gardner Jr., eds. *The Evolutionary Neuroethology of Paul MacLean* (Westport: Praeger), pp. 275-296 (Ch. 15) [data from children in NHANES III].

whereas rates of hypertension are higher in counties with above average blacks in the population (>.0857%), this effect is reversed for rates of heart disease (Table 2). Because a multiple regression analyses indicate that, controlling for 12 variables, both race and poverty can have significant effects on rates of heart disease (Table 3), new studies are needed to reconsider both racial and socio-economic differences in vulnerability to toxins.

The data just summarized include what appears to be contradictory evidence on cardiac illness among American blacks. In 2004, as Kahn reports, the national average rate for “heart deaths” was higher among blacks (280.6 per 100,000) than whites (213.3 per 100,000). Similarly, earlier CDC reports for rates of hypertension were *higher* in counties with over 8.57% blacks (16 per 100,000) compared to counties with fewer blacks where the rate was lower (12 per 100,000). In contrast, CDC rates of all “heart disease” were *lower* in counties with over 8.57% blacks (637 per 100,000) than in counties with fewer blacks (1255 per 100,000).

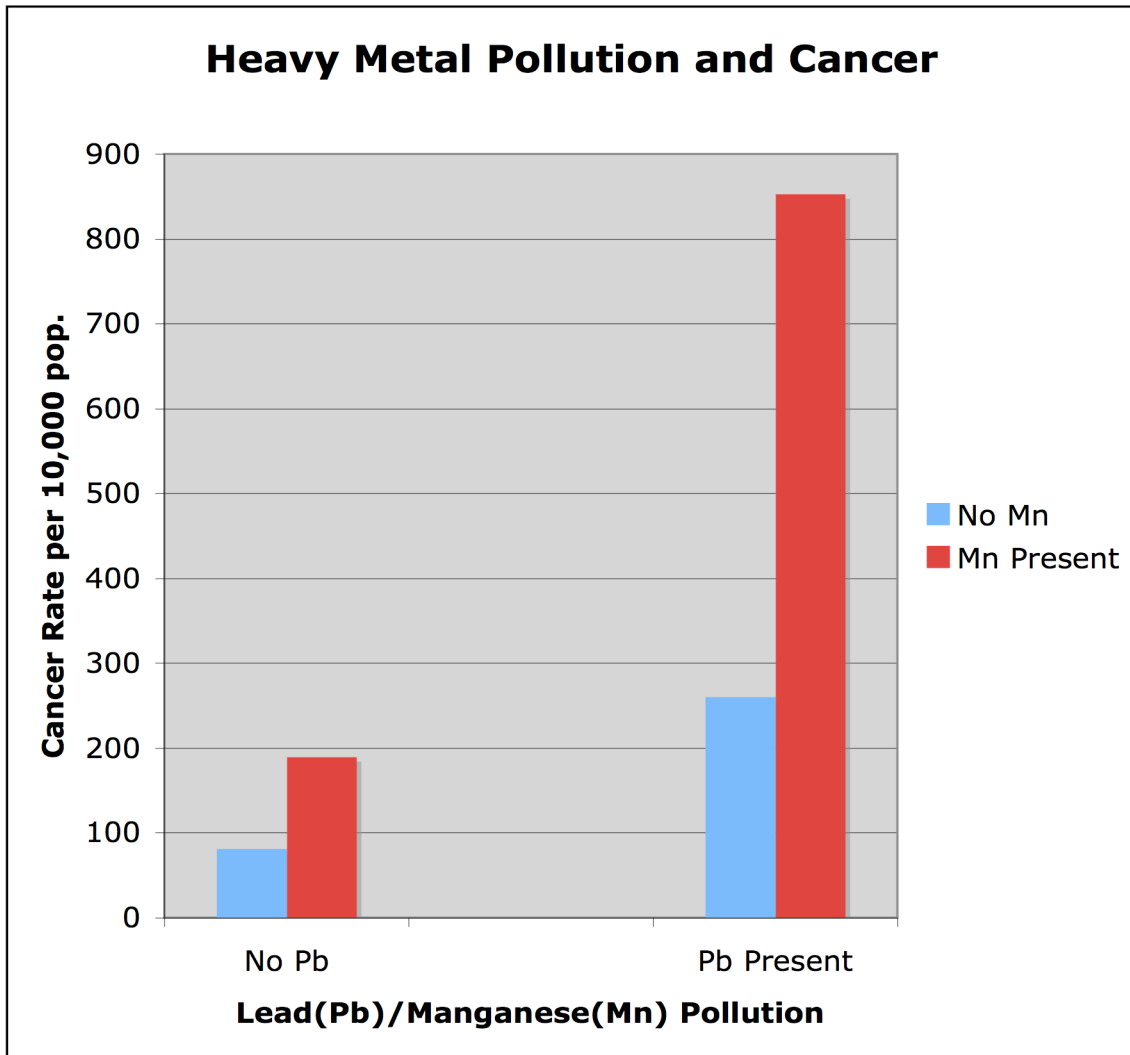
When data in Tables 1a-b are reconsidered with care, the difference between hypertension and heart disease is striking. Presence of pollution with either lead alone or manganese alone is linked to higher heart disease – and their combination is significantly worse than either alone (Table 1a). In contrast, rates of hyperactivity are actually lower in counties with industrial lead pollution alone or manganese pollution alone, and unchanged by the combination. These differences are especially clear when the effects of industrial lead pollution are compared for counties with higher or lower proportions of blacks in the population (Table 4).

Two results follow. First, because county level data concern overall population and blacks are usually a minority, individual case-control studies in different counties are essential when considering the impact of race or environmental pollution on hypertension and heart failure. Second, because environmental factors influencing hypertension seem to differ from those related to overall heart disease, a medications aimed at cardiac deficiencies need to consider the specific stages of disease as well as the populations affected.

The reasons cited by Jonathan Kahn for ignoring race in the study of BiDiI therefore ignore important recent scientific research. Approval of BiDiI needs to be revisited because blacks and whites differ in vulnerability to lead absorption (probably due to differing rates of lactose intolerance and poor diet). Given the well-established connection of lead to hypertension, any drug intended to treat it needs to measure individual blood lead levels – and for this purpose, control for race is necessary. Moreover, since environmental pollution can expose children to lead in soil, air, or water as well as from chips in lead paint or from lead solder in old houses, tests in a single location could easily miss environmental factors that influence BiDiI’s effectiveness. Finally, since a multiple regression analysis with 12 environmental factors shows % blacks is among five factors significantly associated with county level rates of heart disease, there is little reason to attribute race to spurious correlation.

In short, the evidence flatly contradicts Kahn's statement that considering racial differences in heart disease or hypertension implies "that African –Americans are somehow less fully representative of humanity than whites are" (p. 44). Indeed, since the multiple regression results in Table 3 show Blacks are *less* likely than whites to have heart disease, ignoring factors that have differential effects on the health of whites or blacks is both unscientific and medically unjustified. While more study of how environmental factors influence hypertension and heart disease is needed, overall data support the FDA's action to consider race when assessing the effectiveness of BiDil separately.

Figure 1

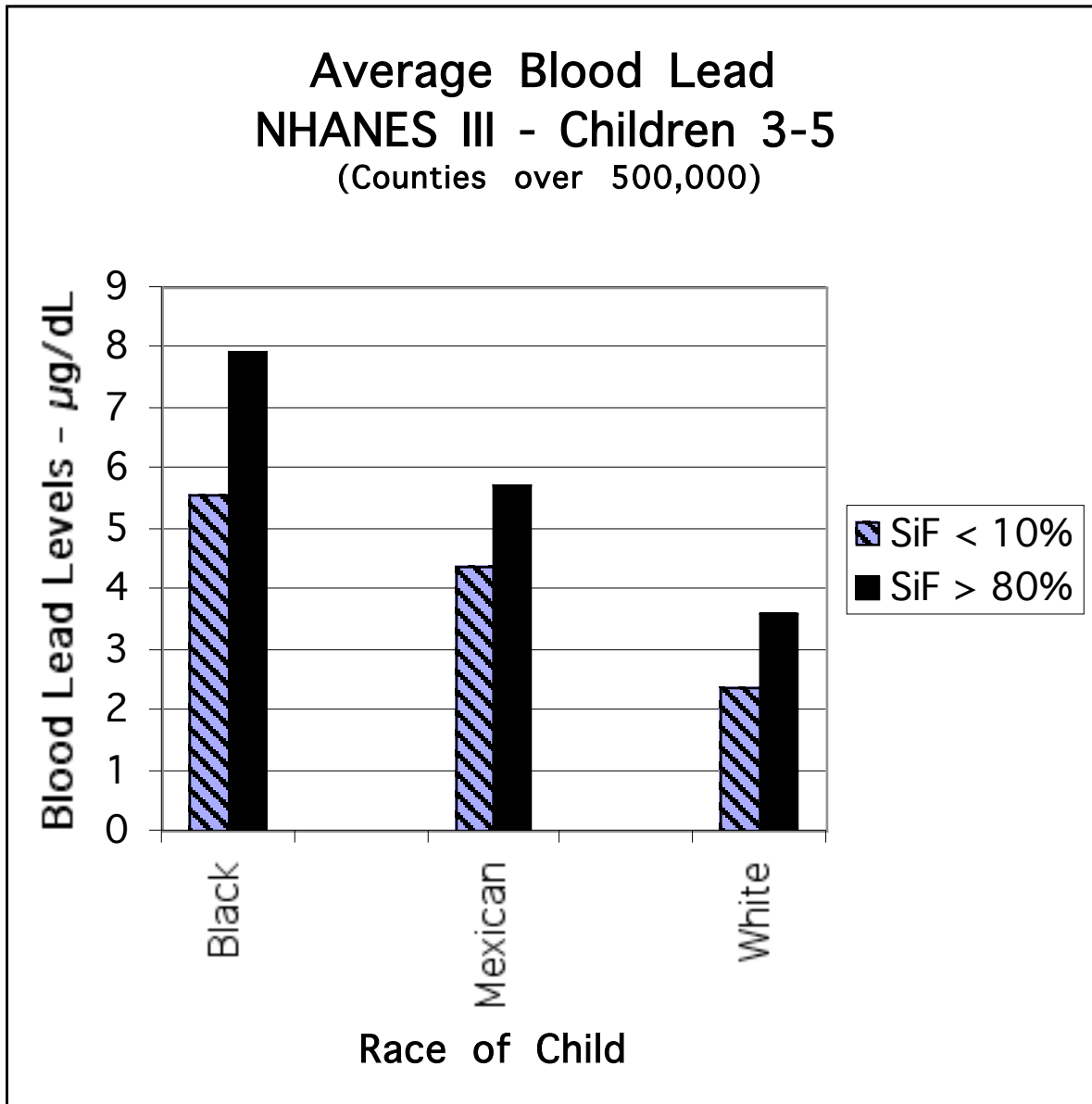


Rate of All Forms of Cancer per 10,000 population			
	<u>No Manganese TRI</u>	<u>Manganese TRI</u>	<u>Total</u>
<u>No Lead TRI</u>	81.4 (2356)	189.43 (305)	93.8 (2661)
<u>Lead TRI</u>	260.5 (204)	853.1 (246)	584.5 (450)
<u>Total</u>	100.7 (2560)	453.0 (551)	108.6 (3111)

Parentheses: number of counties. Probabilities:

Lead: p = .029 (F=4.75); Manganese: p= .0001 (F=14.83); Lead&Manganese: p=.035 (F=4.43).

FIGURE 2



For NHANES III Children 3-5, mean blood lead is significantly associated with silicofluoride use (DF 3, F 17.14, $p < .0001$) and race (DF 2, F 19.35, $p < .0001$). Interaction effect between race and fluoridation status: DF 6, F 3.333, $p < .0029$. Not shown here are effects of local poverty income ratio (DF 1, F 66.55, $p < .0001$), probably a factor in lead absorption due to calcium deficiencies associated with inadequate diet. Source: reanalysis of data from Masters, "MacLean's Evolutionary Neuroethology: Environmental Pollution, Brain Chemistry, and Violent Crime," p. 286.

Table 1a
Heart disease and Lead or Manganese Pollution
(Disease Rates per 100.000 in 3111 U.S. Counties)

Lead TRI	Manganese TRI		Totals:
	None	Present	
None	.01006 2356	.01219 305	.01031 2661
Present	.01015 204	.01742 246	.01413 450
Totals:	.01007 2560	.01453 551	.01086 3111

Source: Sum of Squares:			ANOVA		
			Mean Square:	F-test:	P value:
DichPb (A)	1	.00224	.00224	4.75206	.0293
DichMn (B)	1	.00698	.00698	14.83206	.0001
AB	1	.00208	.00208	4.43108	.0354
Error	3107	1.46134	.00047		

Table 1b
Hypertension and Lead or Manganese Pollution
(Disease Rates per 100.000 in 3111 U.S. Counties)

Lead TRI	Manganese TRI		Totals:
	<u>None</u>	<u>Present</u>	
None	.00013 2356	.00010 305	.00013 2661
Present	.00010 204	.00013 246	.00011 450
Totals:	.00013 2560	.00011 551	.00013 3111

Source:		Sum of Squares:	Mean Square:	F-test:	P value:
DichPb (A)	1	1.23701E-8	1.23701E-8	15816	.6909
DichMn (B)	1	2.34657E-10	2.34657E-10	.003	.9563
AB	1	3.20400E-7	3.20400E-7	4.09643	.0431
Error	3107	.00024	7.82144E-8		

Note: no main effect; interaction effect ($p < .05$) apparently occurs because, when only one of two toxins is present, rates are LOWER than no pollution; where both are present, rates are the same as where neither is present – and equal the national average. The contradiction between the relationship between toxins and hypertension or heart disease calls for further study, especially given earlier data linking lead with hypertension. Adding counties with above average blacks (which have lower hypertension) increases the puzzle (which may be due to reporting rather than actual effects).

Table 2

Racial Differences by Type of Cardiac Disease

Average Rates per 100,000 for U.S. counties with above and below average % Blacks

	%Blacks <.0857< (n = 2262)	>.0857 (n = 844)
Hypertension	12	16
Standard Deviation	(27)	(28)
Heart Disease	1255	637
	(2436)	(1137)

While overall rates of heart disease are roughly twice as high in counties with less than the median % of blacks in the population, rates of hypertension are 1/3 higher in the 844 counties with above 8.6% Blacks. If nothing else, these data indicate the need for careful restudy of race, geography, and other socio-economic factors influencing hypertension and other heart diseases.

**Table 3: Association of Environment and Race with Heart Disease & Hypertension
Multiple Regression – 12 Independent Variables in all U.S. Counties**

Coefficient Table (BOLD = statistically significance < .10)

Variable:	HEART DISEASE		HYPERTENSION	
	Standardized Coefficient	Probability	Standardized Coefficient	Probability
% BLACK	-.084	.0001	.146	.0001
% HISPANIC	-.017	n.s.	.042	.0279
% HS GRAD	.058	.0292	-.208	n.s.
POPULATION	.018	n.s.	-.031	n.s.
PC INCOME**	-.087	.0013	.081	.0025
PC INC BLACK	.013	n.s.	.012	n.s.
PC INC HISPANIC	-.023	n.s.	.033	.083
%UNEMPLOYED	-.015	n.s.	-.007	n.s.
LEAD POLLUTION*	.015	n.s.	.002	n.s.
Manganese POLLUTION*	.043	.0181	.003	n.s.
POP. DENSITY	.028	n.s.	.022	n.s.
%Age>65	.103	.0001	.146	.0001

Equation – Heart Disease

Count: 3111 R: .17723 R-squared: .03141 Adj. R-squared: .02766 RMS Residual: .02147

Analysis of Variance Table

Source	DF	Sum Squares	Mean Square	F-test
REGRESSION 12	.0463	.00386		8.37231
RESIDUAL	3098	1.42777	.00046	p = .0001
TOTAL	3110	1.47408		

Equation - Hypertension

Count: 3111 R: .18789 R-squared: .0353 Adj. R-squared: .03156 RMS Residual: .00028

Analysis of Variance Table

Source	DF	Sum Squares	Mean Square	F-test
REGRESSION 12	.00001	7.16389E-7	9.44702	
RESIDUAL	3098	.00023	7.58323E-8	p = .0001
TOTAL	3110	.00024		

*POLLUTION: measured by pounds per year of lead or manganese recorded in Toxic Release Inventory. (Unlikes Table 1 and 4, which are based on the *existence* of reported lead pollution). The differences in results suggest that proximity to industrial pollution is more likely to be a source of heart disease or hypertension than the amount of lead released in the county as a whole.
**PER CAPITA INCOME: note reversal of sign of the significant correlation with hypertension (positive = higher average wealth linked to higher rates) and heart disease generally (negative = poverty linked to higher rates). These statistics reveal need for further study.

Table 4a
Race and Heart Disease per Capita
(Rates per 100,000 by County, U.S.)*

	%Blacks in County:		<u>Totals:</u>
	<u><.0857</u>	<u>≥.0857</u>	
Lead Pollution			
<u>None</u>	1182 1972	598 685	1031 2657
<u>Present</u>	1749 290	806 159	1415 449

<u>Totals:</u>	1255 2262	637 844	1087 3106

ANOVA					
	Source:	Sum of Squares:	Mean Square:	F-test:	P value:
DichPb (A)	1	.00513	.00513	11.03658	.0009
Dich%Black (B)	1	.01994	.01994	42.91016	.0001
AB	1	.0011	.0011	2.36907	.1239
Error	3102	1.44172	.00046		

Table 4b
Hypertensive Heart Disease per Capita
(Rates per 100,000 by County, U.S.)*

	%Blacks in County		<u>Totals:</u>
	<u><.0857</u>	<u>≥.0857</u>	
Lead Pollution			
<u>None</u>	12 1972	16 685	.00013 2657
<u>Present</u>	9 290	16 159	.00011 449

<u>Totals:</u>	12 2262	16 844	.00013 3106

ANOVA					
	Source:	Sum of Squares:	Mean Square:	F-test:	P value:
DichPb (A)	1	1.11199E-7	1.11199E-7	1.42608	.2325
Dich%Black (B)	1	1.11764E-6	1.11764E-6	14.33321	.0002
AB	1	5.55636E-8	5.55636E-8	.71258	.3987
Error	3102	.00024	7.79753E-8		

*Note: data for all 3141 U.S. counties: only 3106 have all needed data.

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