UNIVERSITY OF WISCONSIN – MADISON

CENTER FOR ENVIRONMENTAL TOXICOLOGY

School of Medicine

101 Agricultural Hall
School of Natural Resources
College of Agricultural and Life Sciences
Madison, Wisconsin, 53706

School of Pharmacy

December 12, 1972

Dr. Alex Azar
Haskell Laboratory
Newark, Delaware 19711

Dear Alex,

Thanks for the copy of Pallies remarks on the Angle paper on lead in black school children. I have had a reply to my letter to Dr. Angle and I am enclosing copies for your file. I haven't yet digested her reply, so I'm not sure she answered all my questions.

Maybe see you soon. If not, Merry Christmas.

Sincerely,

J. Wesley Clayton, Jr.
Director

JWC:js

Enclosures

N40765

THE UNIVERSITY OF NEBRASKA MEDICAL CENTER
42ND AND DEWEY AVENUE
OMAHA, NEBRASKA 68105

December 7, 1972

J. Wesley Clayton, Jr., Director
Center for Environmental Toxicology
101 Agricultural Hall
School of Natural Resources
College of Agricultural & Life Sciences
Madison, Wisconsin 53706

Dear Doctor Clayton:

I wouldn't have been so slow in answering if you hadn't asked such tough questions, but, in reply:

1. Regarding standardization to the mean hematocrit of 38%; this was done in an attempt to eliminate any concommittant effect of anemia, and the data outlined in Table 1, with detailed hematologic data in Table 2.

   The question here is what is the effect of the non-significant difference in hematocrit? An even more basic question is the effect of iron deficiency on lead absorption and membrane permeability, i.e., the increased peroxide hemolysis of iron deficiency producing a decrease in reductive capacity just as does G-6-PD deficiency.

2. As noted on the enclosed Table 3 listing the hemoglobin and
3. hct at each school, school 6 is geographically in the middle distance group although NNE. The general health status of the G-6-PD deficient was not noticably altered (although we subsequently admitted one girl with acute renal failure, enclosure 4). Socioeconomic conditions, housing and general health are worst at schools 7-8 and best at school 6, and are reflected in the hemoglobin values. Schools 1,2, and 6 are all in relatively good neighborhoods of single dwelling houses in good repair. Housing deteriorates from school 3 to 4 to 7 and 8.

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4. Regarding Table I, 57.0 vs 48.8 is not significant, as stated in the paper; the other 3 t values were all double checked. It would take an afternoon to repeat them - please let us know if you strongly suspect an error.

5. Since we don't even know which type G-6-PD deficiency these children had we can only guess that the severity of the defect associated with the different variants may be the critical factor. Ganzoni and Rhomberg (Acta Haemat 34: 338) reported the case of an Italian worker (presumbably with the Mediterranean variant since he had no increase in enzyme activity with reticulocytosis) with acute hemolysis associated with a blood lead of 65 ug%. Shafer & Tague reported 2 blacks, each with moonshine nephropathy and hemolysis at blood leads of 70-100. Additional information might be available by calling Dr. Shafer at the University of Oklahoma (405) 336-1366 or the Oklahoma V.A.: 235-9421. The same phenomenon occurs in thalassemia. The Swiss and French write very indignant reports of immigrant workers with thalassemia trait who develop obvious hemolysis at blood leads well below 80.

6-10. The garbagemen are young, strong looking blacks of transient residence and undocumented health. The lead workers, particularly those with red cell leads above 130 (which corresponds to a blood lead of 70-80), had frequent complaints of fatigue, insomnia, colic, and "ulcer pain". The only specific studies we did in these were of platelet agglutination (grossly impaired) and electron microscopy of the platelets. After interviewing these men we were convinced that their complaints were valid and their health less satisfactory than comparable blue collar workers. Workers at Plant A rarely had red cell leads above 100 and were in general good health. Air leads at Plants B & C were investigated by OSHA office and found to exceed 20 mg/M^3 L resulting in multiple OSHA citations and fines and a definite cooling in our relations with industry. Alice Hamilton lives!

7. The data on ALA-D as given on Table 6 is insufficient for discrimination of enzyme deficient and non-deficient. Please note, however, that ALA-D correlates extremely well with red cell lead - data is in progress to see if the correlation is better than with Pb-B.

8-9. Detailed studies are now in progress of air, soil, water, milk, house dust, house paint, hair, teeth and dead cats of schools 1 and 9, and 2 control suburban schools (also preschool sibs at school 1). If you know of any way to measure ingested lead without doing balance studies please let us know instantly and save us from all this nonsense.

Your questions are all highly pertinent and provacative. After looking at our data of the effect of iron deficiency on red cell partition and blood lead I wonder if it wouldn't be worth while to study the effect of lead on glutathione peroxidase and peroxidase hemolysis in the neonate.

An other related phenomenon would be the possibility of increased placental transfer of lead from the mother with fewer red cells to bind lead. Our own data shows that 90-95% of lead is found in the red cell fraction in most normal adults, but that the fraction falls off to as low as 50% with anemia, high lead and with causes unknown - See Table 7.

Enough of these tables. We look forward to hearing of your own studies. As associate editor of CLINICAL TOXICOLOGY, I am always most interested in clinical studies that you might have in preparation that should reach clinical toxicologists as contrasted to epidemiologists or experimental pharmacologists. If so, please submit to:

Richard T. Rappolt, Sr., M.D.
Editor, CLINICAL TOXICOLOGY
4141 Geary, Suite 403
San Francisco, California 94118

With best regards,

Carol Angle
Carol R. Angle, M.D.
Professor of Pediatrics

CRA:mls
enclosures

BLOOD AND RBC LEAD AS RELATED TO LOCATION AND G-6-PD ACTIVITY

Blood Lead (May) µg%	Schools 1 & 2	3 - 9	Total	t for Location (1-2 vs 3-9)
G-6-PD 0- 4	34.2 ± 9.5 (20)	27.2 ± 7.1 (53)	29.1 ± 8.4 (73)	3.260 p < 0.005
4.1-15	34.2 ± 8.8 (11)	25.3 ± 4.1 (18)	28.6 ± 7.6 (29)	3.572 p < 0.005
> 15	32.8 ± 10.8 (13)	29.8 ± 7.9 (51)	27.3 ± 9.0 (64)	2.196 p < 0.05
Total	34.1 ± 9.7 (44)	26.3 ± 7.1 (122)	28.4 ± 9.0 (166)	4.808 p < 0.001
t for enzyme (0-4 vs >15)	n.s.	n.s.	n.s.	

Blood Lead µg% x $\frac{38\%}{\text{Hmt\%}}$	Schools 1 & 2	3 - 9	Total	t for Location (1-2 vs 3-9)
G-6-PD 0- 4	38.2 ± 12.8 (9)	30.9 ± 7.1 (23)	32.9 ± 9.7 (32)	p < 0.1
4.1-15	38.3 ± 10.4 (7)	27.2 ± 8.3 (11)	31.5 ± 10.7 (18)	p < 0.05
>15	27.0 ± 11.2 (5)	25.4 ± 8.2 (24)	25.7 ± 8.8 (29)	N.S.
Total	35.6 ± 12.6 (21)	27.9 ± 8.2 (58)	29.9 ± 10.2 (79)	p < 0.025
t for enzyme	N.S.	p < 0.025	p < 0.005	

(Mean & S.D.)

Rbc Lead µg%	Schools 1 & 2	3 - 9	Total	t for Location (1-2 vs 3-9
G-6-PD 0- 4	57.0 ± 15.5 (16)	42.4 ± 11.5 (32)	47.3 ± 14.7 (48)	p < 0.001
4.1-15	52.0 ± 16.4 (17)	36.1 ± 13.13 (15)	33.1 ± 11.6 (32)	p < 0.05
>15	48.8 ± 25.5 (6)	33.1 ± 11.6 (32)	35.6 ± 15.8 (38)	p < 0.025
Total	54.1 ± 18.5 (29)	37.4 ± 12.6 (79)	41.9 ± 16.2 (108)	p < 0.001
t for enzyme	N.S.	p < 0.005	p < 0.001	

(Mean & S.D.)

HEMATOLOGIC DATA

	G-6-PD 0-4	G-6-PD >15	t - test
Hct %	37.4 ± 3.6 (39)	38.1 ± 4.6 (34)	n.s.
Hb gm%	12.7 ± 1.0 (40)	13.3 ± 1.4 (34)	$p < .10$
RBC x 10^6/mm^3	4.38 ± 0.37 (40)	4.52 ± 0.64 (34)	n.s.
MCV μ^3	84.2 ± 5.2 (40)	83.6 ± 5.0 (34)	n.s.
MCH ٢٢	29.2 ± 2.3 (40)	29.8 ± 2.3 (34)	n.s.
Reticulocytes	1.2 ± 0.6 (40)	1.05 ± 0.6 (34)	n.s.
Haptoglobin mg% (all ages)	53.4 ± 36.4 (40)	74.5 ± 40.0 (30)	$p < .05$*

* n.s., corrected for age

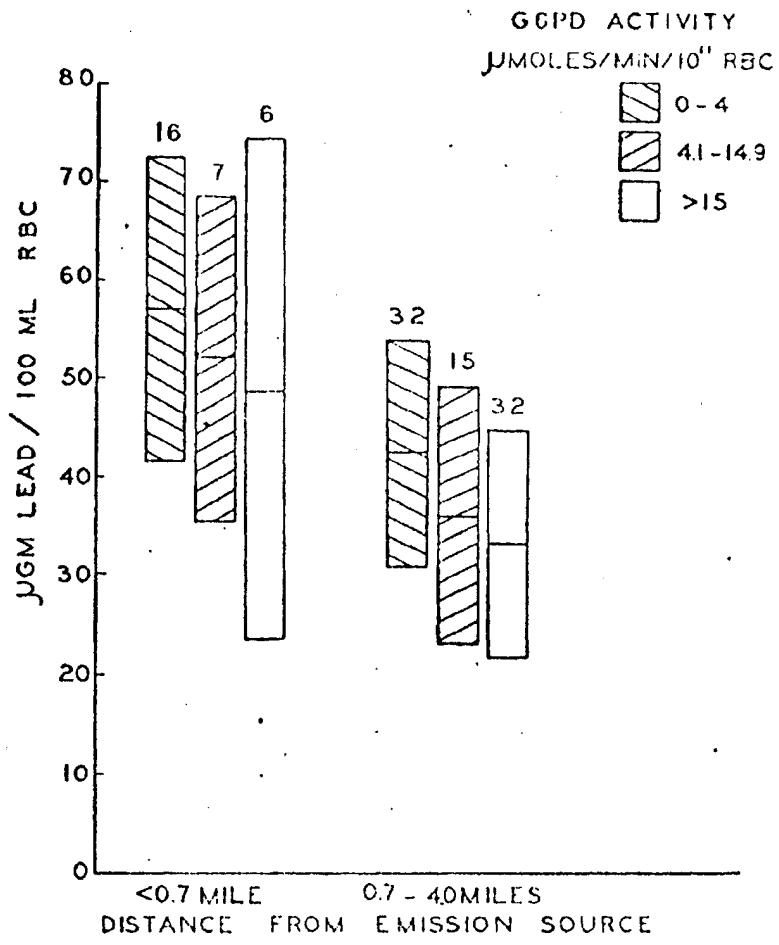
(3)

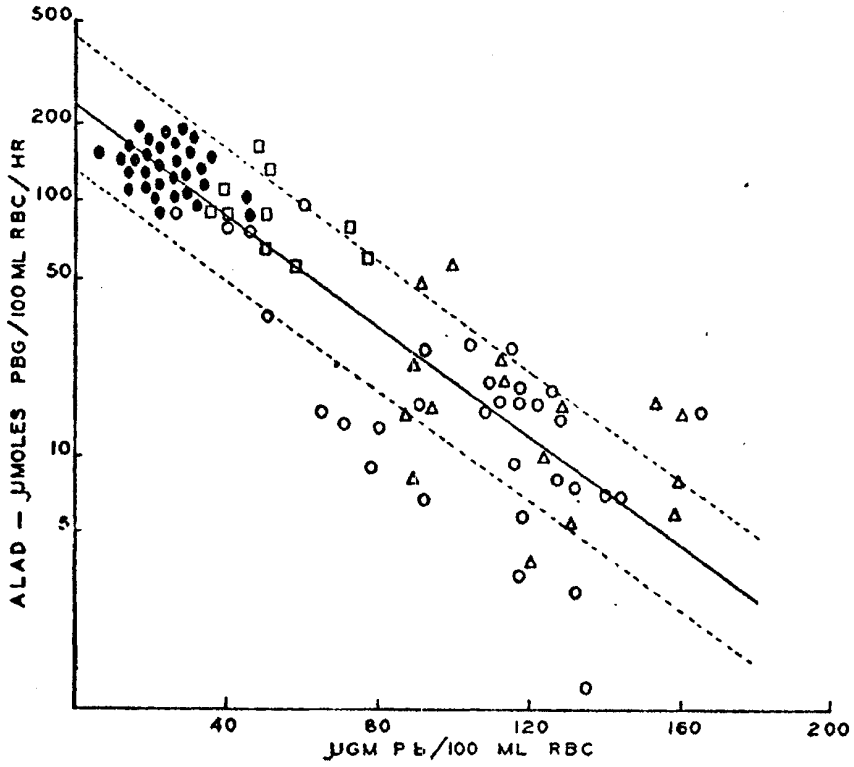
AGE, SEX, HEMATOCRIT AND BLOOD LEAD

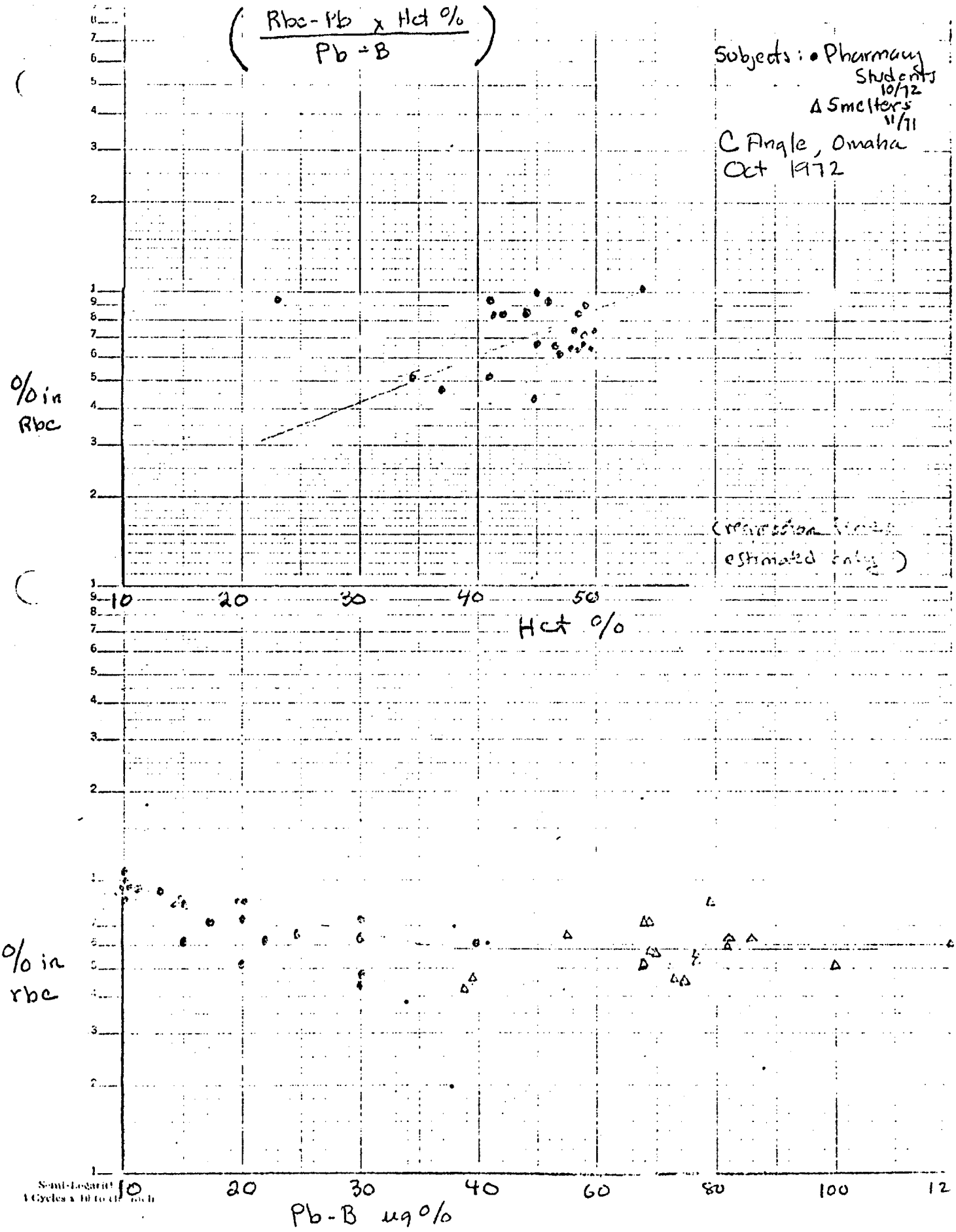
School	No. Students May	No. Students June	Age Mean	% Male	Hgb	Hct	Pb-B (May)	Pb-B (Nov)
1	22	16	8.2 ± 2.1	70	12.4 ± 0.8*	38.0 ± 2.4	34.6 ± 9.3**	57.6
2	19	14	9.7 ± 1.7	63	12.3 ± 1.0*	34.8 ± 2.8*	33.6 ± 10.0**	51.6
3	23	17	9.2 ± 1.6	57	12.2 ± 1.5*	34.8 ± 5.1*	27.9 ± 5.8	38.8
4	11	10	9.8 ± 1.7	73	13.3 ± 1.7	37.7 ± 5.8	25.2 ± 4.2	38.2
5	30	14	13.2 ± 1.9	71	13.1 ± 0.9	39.2 ± 2.8	25.1 ± 6.2	36.1
6	13	10	9.0 ± 0.5	54	13.2 ± 0.9	39.4 ± 3.0	23.2 ± 4.7	38.2
7	9	5	10.4 ± 1.2	44	13.5 ± 1.2	38.9 ± 4.2	30.4 ± 9.0	35.2
8	8	6	7.6 ± 1.1	88	12.3 ± 1.1*	36.5 ± 4.7	31.3 ± 5.4	43.7
9	28	13	14.6 ± 2.4	67	13.0 ± 1.2	38.7 ± 3.3	25.8 ± 9.0	29.3
Total			10.6 ± 2.9	66	12.89 ± 1.29 (13.9 ± 1.3) N = 93	37.41 4.28 37.4 ± 4.3 (N = 93)	28.4 ± 9.0 (N = 166)	

to compare with mean of total,
* $p < .05$; ** $p < .005$ that

* Hct at Schools 2 & 3, significantly lower ($p < .05$) than the mean
** Pb-B at Schools 1 & 2, significantly higher ($p < .005$) than the mean







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Legend

Figure 1: Correlation of red cell lead with red cell ALAD activity in 90 subjects, $y = 2.3713 - .01 \times r = 0.888$ •-medical and nursing students, □-urban school children, Δ- battery workers, ○- lead workers.