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CC: W.H. Walsh-ESD
IC 13/AH&HE

ENGINEERING DEPARTMENT

May 16, 1985

D. R. DIGGS-CHEMICALS & PIGMENTS DEPT-BRANDYWINE 16204
W. E. SMITH, IV-CHEMICALS & PIGMENTS DEPT-PET LAB-CHAMBERS WORKS
C. G. PFEIFER-ESD-LOUVIERS 5185

CASAC LEAD MEETING

Attached are copies of

1. The CASAC Lead Subcommittee membership list. Member attendance at the May 13-15 meeting on the Criteria Document and Staff Paper is shown by my handwritten notes.

2. The Agenda of the May 13-15 meeting. The only significant departure from the Agenda was that Mort Lippmann summarized the Criteria Document review after completion of the discussion early Tuesday afternoon. In essence, CASAC provisionally closed on the Criteria Document contingent on some corrections and revisions. Of key interest to us is that EPA committed to issuance of an Addendum revising the treatment of the BPb-BP relationship and risk assessment issues introduced in the Corrigenda. Du Pont's input at the CASAC meeting was decisive in forestalling CASAC acceptance of the Corrigenda. In accordance with the Notice and Comment rulemaking procedure, EPA will offer the Addendum for public comment before the fall CASAC meeting, which will be held sometime after October 1, 1985.

3. The charts/handout used by Joel Schwartz for his presentation on "Evidence for a Blood Lead - Blood Pressure Relationship."

ENGINEERING SERVICE DIVISION
Air, Hazards and Health Engineering

JM Pierrard

J. M. Pierrard
Senior Consultant

JMP:dll
JMP1:30

Atchs

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May 1985

U.S. ENVIRONMENTAL PROTECTION AGENCY
CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE
SCIENCE ADVISORY BOARD

Subcommittee on Lead

Chairman

* Dr. Morton Lippmann MON AM-PM WED TUE AM-PM
Institute of Environmental Medicine
Lanza Laboratory
Long Meadow Road
New York University
Tuxedo, New York 10987

Executive Secretary

Mr. Robert Flaak MON AM-PM WED TUE AM-PM
Science Advisory Board (A-101F)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Members/Consultants

Dr. Carol R. Angle TUE AM-PM
Department of Pediatrics
University of Nebraska Medical Center
42nd and Dewey Avenue
Omaha, Nebraska 68105

* Dr. Robert Frank MON AM-PM WED TUE AM-PM
Department of Environmental and Health Sciences
Johns Hopkins School of Hygiene and Public Health
615 North Wolfe Street
Baltimore, Maryland 21205

Dr. Julian Chisolm, Jr. MON AM-PM TUE AM-PM WED
Senior Staff Pediatrician
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Dr. Robert Goyer MON AM-PM TUE AM-PM
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Dr. Anita S. Curran TUE AM-PM WED
Commissioner
Department of Public Health
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Dr. Paul B. Hammond MON AM-PM WED TUE AM-PM
Professor of Environmental Health
Department of Environmental Health
University of Cincinnati
Cincinnati, Ohio 45267

Dr. Ben B. Ewing MON AM-PM WED TUE AM PM
Professor of Environmental Engineering
Institute for Environmental Studies
University of Illinois
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Dr. Lloyd Humphreys MON AM-PM WED TUE AM-PM
Department of Psychology and Educational Psychology
University of Illinois
Champaign, Illinois 61820

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U.S. Environmental Protection Agency
Science Advisory Board
Clean Air Scientific Advisory Committee (CASAC)

Subcommittee on Lead

Rosslyn Westpark Hotel
1900 North Fort Myer Drive
Rossyln, Virginia
Open Meeting - May 13-15, 1985

AGENDA

Monday - May 13

9:00 a.m.	Welcome and Opening Remarks	Dr. Lippmann
9:15	Introduction and Overview of the Air Quality Criteria Document for Lead	Dr. Grant Dr. Weil
9:30	CASAC Review of Volume II of the Criteria Document (Chapters 2-8)	

- Chapter 2 - Introduction
- Chapter 3 - Chemical and Physical Properties
- Chapter 4 - Sampling and Analytical Methods for Environmental Lead
- Chapter 5 - Sources and Emissions
- Chapter 6 - Transport and Transformation
- Chapter 7 - Environmental Concentrations and Potential Pathways to Human Exposure
- Chapter 8 - Effects of Lead on Ecosystems

10:45	Break
11:00	CASAC Review of Volume III of the Criteria Document (Chapters 9-11)

- Chapter 9 - Quantitative Evaluation of Lead and Biochemical Indices of Lead Exposure in Physiological Media
- Chapter 10 - Metabolism of Lead

- Chapter 11 - Assessment of Lead Exposures and Absorption in Human Population

12:15 p.m.	Lunch	
1:15	Evidence for a Blood Lead - Blood Pressure Relationship	Dr. Schwartz Dr. Landis
1:40	Blood Lead and Stature	Dr. Schwartz
2:00	Statements from the Public	

4 • Dr. John Pierrard - du Pont Corporation

2 • Dr. Jerome Cole - International Lead Zinc Research Organization (ILZRO)

3 • Dr. Robert Putnam - ILZRO

1 • Dr. Peter Gartside - University of Cincinnati Medical Center

• ~~Dr. Edward McCabe - University of Wisconsin Medical School~~

2:45	Break
3:00	CASAC Review of Volume IV of the Criteria Document

- Chapter 12 - Biological Effects of Lead Exposure

5:30 Recess

Tuesday - May 14

8:30 a.m. CASAC Review of Volume IV of the Criteria Document

- Chapter 13 - Evaluation of Human Health Risk Associated with Exposure to Lead and its Compounds

10:00	Break
10:15	CASAC Review of Volume IV of the Criteria Document (Chapter 13) - Continued

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11:15	CASAC Review of <u>Volume I</u> of the Criteria Document • Chapter 1 - Executive Summary and Conclusions	
12:00 p.m.	Lunch	
1:00	Wrap-up of the Criteria Document	
1:45	Lead in the Drinking Water Program	Dr. Cotruvo
2:00	Introduction and Overview of the Staff Paper for Lead	Mr. Jordan Mr. Cohen Mr. Haines
2:45	Break	
3:00	Modeling the Tail of the Blood Lead Distribution	Dr. Schwartz
3:15	CASAC Review of the Staff Paper for Lead	
5:15	Recess	
7:00	CASAC Dinner - Location to be Announced	

<u>Wednesday - May 16</u>

8:30 a.m.	CASAC Review of the Staff Paper - Continued	
9:30	Wrap-up of the Staff Paper	
10:00	Break	
10:15	Results of Expert Elicitation Project on the Effects of Lead Exposure on Hemoglobin Levels	Dr. Whitfield Dr. Wallsten
11:15	Chairman's Summary of the CASAC Review of the Air Quality Criteria Document for Lead and the Staff Paper for Lead	Dr. Lippmann
12:00 p.m.	Adjourn	

CHARTS / HANDOUT USED BY
J. SCHWARTZ, CASAC LEAD
COMMITTEE MEETING, ARLINGTON, VA.
5/13/85

EVIDENCE FOR A BLOOD LEAD BLOOD PRESSURE RELATIONSHIP

I. EXPERIMENTAL EVIDENCE

IN VIVO

VICTERY ET AL.	LEAD CAUSES BLOOD PRESSURE INCREASES IN RATS
IANNACONE ET AL.	LEAD CAUSES BLOOD PRESSURE INCREASES IN RATS, INCREASED REACTIVITY TO ALPHA ADRENERGIC STIMULATION
CARMIGNANI ET AL.	LEAD CAUSES BLOOD PRESSURE INCREASES IN RATS, INCREASED REACTIVITY TO ALPAH ADRENERGIC STIMULATION
PERRY AND ERLANGER	LEAD CAUSES BLOOD PRESSURE INCREASES IN RATS
KOPP	LEAD CAUSES BLOOD PRESSURE INCREASES IN RATS
REVIS ET AL.	LEAD CAUSES BLOOD PRESSURE INCREASES IN PIGEONS

IN VITRO

WEBB ET AL.	HELICAL STRIPS OF LEAD EXPOSED TAIL ARTERIES HAVE INCREASED REACTIVITY TO ALPHA ADRENERGIC STIMULATION IN VITRO
PICCININI ET AL.	LEAD ADDED TO MEDIA CAUSES CONSTRICTION OF WHOLE ARTERIES FROM UNEXPOSED RATS
FAVALLI ET AL.	INCREASED INTRACELLULAR CALCIUM STORES AND INCREASED SENSITIVITY TO EXTRACELLULAR CALCIUM
FILO ET AL.	SMOOTH MUSCLE TONE IS A FUNCTION OF INTRACELLULAR CALCIUM
POUNDS ROSEN GOLDSTEIN	LEAD ALSO INCREASES INTRACELLULAR CALCIUM IN HEPATOCYTES, OSTEOCLASTS AND NEURONS

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EPIDEMIOLOGICAL EVIDENCE

NON-OCCUPATIONAL STUDIES

BEEVERS ET AL.
MOREAU ET AL.
KROMHOUT ET AL.
BATUMAN ET AL.
KHERA ET AL.
POCOCK ET AL.
HARLAN ET AL.
PIRKLE ET AL.

ALL REPORT A STATISTICALLY SIGNIFICANT ASSOCIATION

OCCUPATIONAL STUDIES

SPLIT ABOUT EVENLY, BUT ARE CONFOUNDED BY METHODOLOGICAL PROBLEMS

- IGNORE HEALTHY WORKER EFFECT (E.G. COOPER)
- INADAQUATE EXPOSURE MEASURE (E.G. CRAMER AND DAHLBERG)
- INADAQUATE STATISTICS (E.G. RAMIREZ-CERVANTES)

ANALYSIS OF NHANES

WE FIRST LOOKED AT ALL MALES
(HARLAN ET AL.)

THEN EXAMINED THE AGE GROUP THAT MINIMIZED COLLINEARITY WITH AGE

WE WILL FIRST PRESENT MODELS FOR ALL ADULT MEN, THEN DISCUSS SUBGROUPS

METHODOLOGY WAS TO CONSIDER MANY POSSIBLE CONFOUNDING VARIABLES

FIND THE MODEL WHICH MAXIMIZES R-SQUARE FOR ANY MODEL SIZE

PICK LARGEST SIGNIFICANT MODEL
ALMOST EQUIVALENT TO ALL POSSIBLE REGRESSIONS

TEH 0350112

Table I

VARIABLES INCLUDED IN THE STEPWISE REGRESSION ANALYSIS

I. DIETARY VARIABLES

Dietary Sodium *	Salt shaker sodium
Dietary sodium*salt shaker sodium	dietary potassium*
dietary sodium-potassium ratio	dietary calcium*
dietary phosphorus*	dietary protein*
dietary fat*	dietary carbohydrates*
dietary cholesterol*	saturated fatty acids*
dietary oleic acid*	dietary linoleic acid*
dietary iron*	dietary vitamin A*
dietary vitamin C*	dietary thiamine*
dietary riboflavin*	dietary riboflavin*
dietary niacin*	total dietary grams*
total dietary calories*	

II. SERUM BIOCHEMISTRIES

serum vitamin c*	serum iron*
serum transferrin saturation	serum zinc*
serum copper*	serum albumin*
hemoglobin*	red cell count
serum creatinine*	

III. PERSONAL HISTORY VARIABLES

ethanol consumption/week*	cigarettes smoked/day
cigar or pipe smoking	tricep skinfold
subscapular skinfold	recreational exercise

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work-related exercise

recent weight loss

family history of hypertension

kidney disease

body mass index

age

age squared

IV. DEMOGRAPHIC VARIABLES

family income

poverty index

region of the country

season of the year

degree of urbanization

residence inside central city

educational level

* log and square transform also included

TABLE II

SYSTOLIC BLOOD PRESSURE
ALL MEN OVER 20

EFFECT	F VALUE	P VALUE
AGEYRS	12.58	0.0012
AGESQUARED	32.77	0.0000
BODY MASS INDEX	275.77	0.0000
LOGZINC	7.42	0.0104
ALBUMIN SQUARED	45.55	0.0000
CALCIUM	6.76	0.0140
FAMILY HISTORY	30.73	0.0000
LOG(FAT)	4.73	0.0361
LOG(BLOOD LEAD)	10.16	0.0031

DIASTOLIC BLOOD PRESSURE

ALL MEN OVER 20

AGE	94.76	0.0000
AGE SQUARED	63.67	0.0000
BODY MASS INDEX	68.94	0.0000
LOG(ZINC)	17.50	0.0002
LOG(VITAMIN C)	15.48	0.0004
ALBUMIN SQUARED	44.21	0.0000
CIGARETTES	6.89	0.0132
CALCIUM	4.76	0.0365
DIET VITAMIN C	10.49	0.0028
ZINC	12.78	0.0011
HEMOGLOBIN	19.17	0.0001
SUBSCAPULAR SKINFOLD	7.65	0.0094
FAMILY HISTORY	12.28	0.0014
RACE	12.28	0.0014
LOG(BLOOD LEAD)	7.92	0.0083

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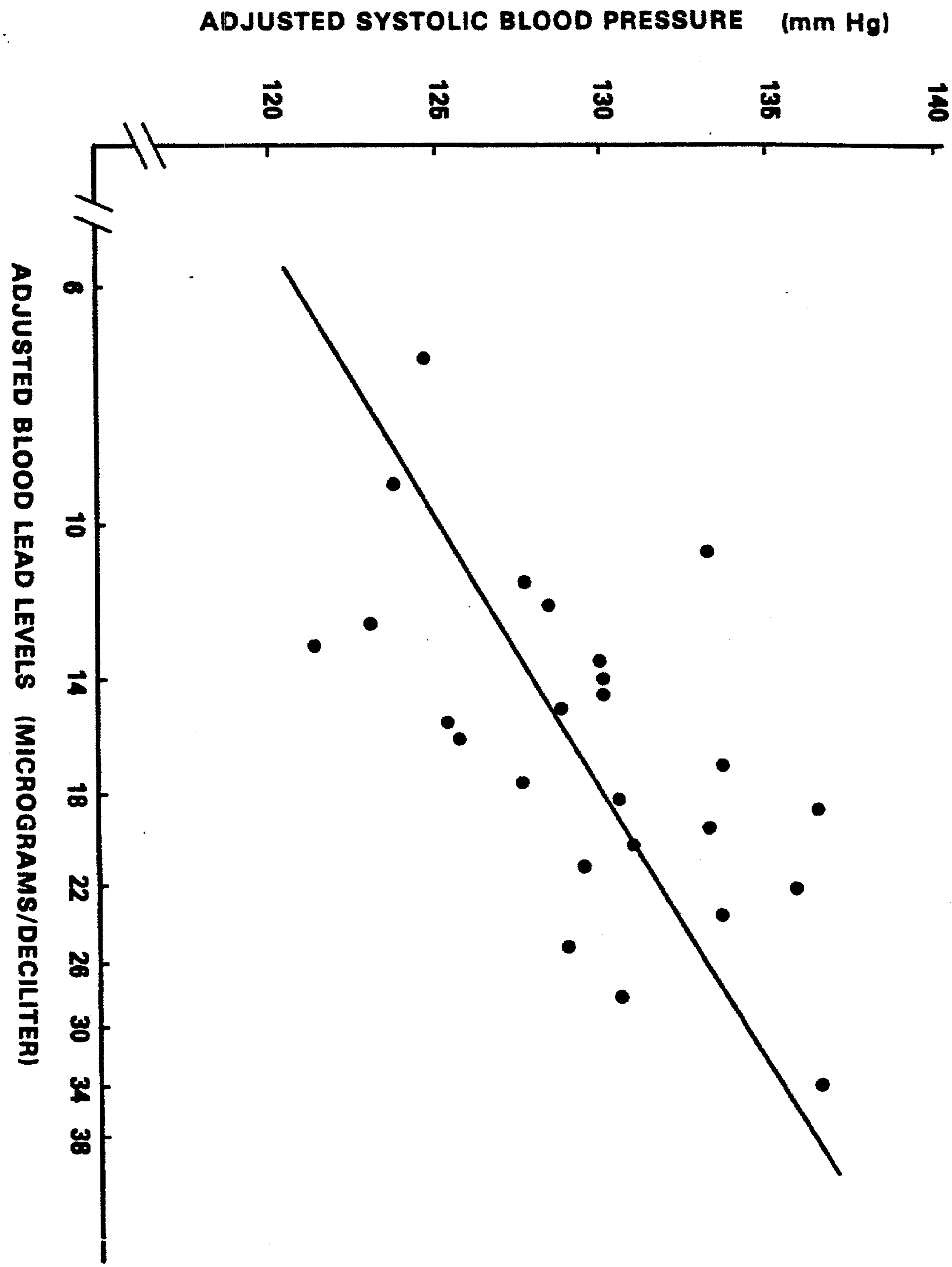
ADJUSTED SYSTOLIC BLOOD PRESSURE (mm Hg)
120
125
130
135
140
ADJUSTED BLOOD LEAD LEVELS (MICROGRAMS/DECILITER)
6
10
14
18
22
26
30
34
38

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TABLE III

Regression Results: Including Height and Coffee as Variables

SYSTOLIC BLOOD PRESSURE
ALL MEN OVER 20

EFFECT	F VALUE	P VALUE
AGE	8.11	0.0076
AGE SQUARED	26.51	0.0000
BODY MASS INDEX	273.09	0.0000
LOG(ZINC)	9.55	0.0041
ALBUMIN SQUARED	42.38	0.0000
CALCIUM	5.52	0.0251
FAMILY HISTORY	37.47	0.0000
COFFEE	11.59	0.0018
HEIGHT	9.51	0.0042
LOG(BLOOD LEAD)	11.22	0.0021

DIASTOLIC BLOOD PRESSURE
ALL MEN OVER 20

AGE	58.68	0.0000
AGE SQUARED	42.15	0.0000
BODY MASS INDEX	76.42	0.0000
LOG(ZINC)	15.88	0.0004
LOG(SERUM VIT C)	8.51	0.0064
ALBUMIN SQUARED	34.70	0.0000
LOG(SERUM CHOLESTEROL)	5.12	0.0305
CIGARETTES	5.52	0.0252
CALCIUM	5.58	0.0244
DIET VITAMIN C	6.61	0.0150
ZINC	11.61	0.0018
HEMOGLOBIM	19.32	0.0001
TRICEP SKINFOLD	4.80	0.0359
FAMILY HISTORY	36.71	0.0000
COFFEE	5.32	0.0277
HEIGHT	22.26	0.0000
RACE	11.60	0.0018
LOG(BLOOD LEAD)	7.96	0.0081

TEH 0350117

TABLE IV

Regression results: Including Height, Coffee, and Hypertensive Medication as Variables.

SYSTOLIC BLOOD PRESSURE
ALL MEN OVER 20

EFFECT	F VALUE	P VALUE
AGE	8.11	0.0076
AGE SQUARED	26.55	0.0000
BODY MASS INDEX	303.14	0.0000
LOG(ZINC)	10.39	0.0029
ALBUMIN SQUARED	39.13	0.0000
CALCIUM	5.22	0.0291
FAMILY HISTORY	26.25	0.0000
COFFEE	15.05	0.0005
HEIGHT	8.49	0.0065
HYPERTENSIVE MEDICATION	42.29	0.0000
LOG(BLOOD LEAD)	13.86	0.0008

DIASTOLIC BLOOD PRESSURE
ALL MEN OVER 20

AGE	82.28	0.0000
AGE SQUARED	59.53	0.0000
BODY MASS INDEX	74.84	0.0000
LOG(ZINC)	17.49	0.0002
ALBUMIN	40.38	0.0000
DIET VITAMIN C	9.83	0.0037
CIGARETTES	4.96	0.0331
CALCIUM	4.91	0.0339
ZINC	12.28	0.0014
HEMOGLOBIN	19.72	0.0001
TRICEP SKINFOLD	4.99	0.0326
FAMILY HISTORY	29.28	0.0000
COFFEE	6.57	0.0153
HEIGHT	16.92	0.0003
HYPERTENSIVE MEDICATION	41.45	0.0000
RACE	9.45	0.0043
LOG(SERUM VIT C)	13.65	0.0008
LOG(BLOOD LEAD)	9.69	0.0039

TEH 0350118

TABLE V

Regression Results Excluding Men on Hypertensive Medication

SYSTOLIC BLOOD PRESSURE
ALL MEN OVER 20

EFFECT	F VALUE	P VALUE
AGE	6.56	0.0153
AGE SQUARED	23.92	0.0000
BODY MASS INDEX	255.30	0.0000
LOG(ZINC)	13.16	0.0010
ALBUMIN SQUARED	43.98	0.0000
CALCIUM	5.79	0.0221
FAMILY HISTORY	29.20	0.0000
COFFEE	15.01	0.0005
HEIGHT	8.43	0.0066
LOG(BLOOD LEAD)	12.05	0.0015

DIASTOLIC BLOOD PRESSURE
ALL MEN OVER 20

AGE	47.17	0.0000
AGE SQUARED	32.27	0.0000
BODY MASS INDEX	265.06	0.0000
LOG(ZINC)	9.91	0.0036
LOG(SERUM VIT C)	9.30	0.0046
ALBUMIN SQUARED	28.36	0.0000
LOG(SERUM CHOLESTEROL)	7.28	0.0110
CIGARETTES	5.56	0.0247
DIET VITAMIN C	6.41	0.0165
ZINC	6.48	0.0160
HEMOGLOBIN	15.15	0.0005
FAMILY HISTORY	24.64	0.0000
COFFEE	7.14	0.0118
HEIGHT	22.34	0.0000
LOG(BLOOD LEAD)	11.53	0.0018

TEH 0350119

BECAUSE LEAD LEVELS FELL OVER THE FOUR YEARS WE TOOK STEPS TO ASSURE LEAD WAS NOT PICKING UP THE EFFECT OF ANOTHER VARIABLE BY

1. INCLUDING A LARGE SET OF VARIABLES INCLUDING ALL MAJOR PREDICTORS OF BLOOD PRESSURE SO THE CHANGE CAN BE PROPERLY ATTRIBUTED.

2. RUNNING THE STEPWISE REGRESSIONS WITH EVERY VARIABLE EXCEPT LEAD, FINDING THE BEST MODEL, AND REINSERTING LEAD. LEAD WAS STILL SIGNIFICANT ($P < 0.01$).

3. TESTING AN INTERACTION TERM BETWEEN LEAD AND THE FIRST TWO YEARS OF THE SURVEY. SINCE LEAD LEVELS FELL MUCH FASTER IN THE SECOND TWO YEARS BECAUSE OF THE CHANGE IN EPA'S GASOLINE LEAD RULE, IF LEAD WAS ONLY PICKING UP THE EFFECT OF ANOTHER VARIABLE THEIR CORRELATION SHOULD HAVE BEEN DIFFERENT IN THE TWO INTERVALS.

   THE INTERACTION TERMS WERE INSIGNIFICANT

   $P = .75$ SYSTOLIC

   $P = .79$ DIASTOLIC

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AGE SUBGROUPS

BECAUSE BOTH LEAD AND BLOOD PRESSURE ARE NOISY MEASURES, STATISTICAL POWER IS AN IMPORTANT CONCERN.

PIRKLE ET AL. LOOKED AT THE AGE SUBGROUP THAT MINIMIZED THE COLLINEARITY BETWEEN AGE AND LEAD. lEAD WAS HIGHLY SIGNIFICANT IN THE 40-59 YEAR AGEGROUP.

WE USED INTERACTION TERMS BETWEEN LEAD AND AGE TO TEST WHETHER THE RELATIONSHIP WAS DIFFERENT FOR 20-45 YEAR OLD MEN THAN FOR 46-74 YEAR OLD MEN AND THEY WERE INSIGNIFICANT.

WE ALSO RERAN OUR STEPWISE REGRESSION FOR BOTH AGE GROUPS, AND LEAD WAS STATISTICALLY SIGNIFICANT IN BOTH OF THEM.

TEH 0350121

TABLE 6

Regression Results: by age group

DIASTOLIC BLOOD PRESSURE
MEN 20-45

EFFECT	F VALUE	P VALUE
AGE	2.16	0.1517
AGE SQUARED	0.90	0.3510
BODY MASS INDEX	137.32	0.0000
CALCIUM SQUARED	5.74	0.0226
SERUM CHOLESTEROL SQUARED	6.90	0.0131
ALBUMIN SQUARED	15.42	0.0004
LOG(ZINC)	5.42	0.0264
FAMILY HISTORY	12.59	0.0012
LOG(SERUM VIT C)	13.78	0.0008
DIET VIT C	9.30	0.0046
CIGARETTES	7.15	0.0117
HEMOGLOBIN	5.61	0.0240
TRANSFERRIN SATURATION	4.59	0.0396
HEIGHT	18.33	0.0002
LOG(BLOOD LEAD)	11.32	0.0020

AGE 46-74

EFFECT	F VALUE	P VALUE
AGE	3.92	0.0564
AGE SQUARED	4.60	0.0396
BODY MASS INDEX	31.54	0.0000
CIGARETTES	4.77	0.0364
ALBUMIN	5.95	0.0205
HEMOGLOBIN	5.46	0.0259
TRICEP SKINFOLD	6.04	0.0196
FAMILY HISTORY	9.52	0.0042
COFFEE	8.29	0.0070
LOG(BLOOD LEAD)	5.72	0.0228

TEH 0350122

DR GARTSIDE'S COMMENTS FOR THE ETHYL CORPORATION

DID NOT USE BLOOD PRESSURE AS THE DEPENDENT VARIABLE

DID NOT DROP VARIABLES ONE AT A TIME IN BACKWARDS ELIMINATION

USED DATE OF EXAMINATION AS A VARIABLE

SINCE WE INCLUDED VARIABLES FOR ALL OF THE KNOWN CORRELATES OF BLOOD PRESSURE IN OUR MODEL DATE OF EXAMINATION IS NOT NEEDED TO PICK UP THE EFFECT OF AN OMMITTED VARIABLE, BUT IS HIGHLY CORRELATED WITH BLOOD LEAD, ARTIFICIALLY REDUCING ITS SIGNIFICANCE. not true

BUT WHEN GARTSIDE'S MODEL IS RE-ESTIMATED USING BLOOD PRESSURE AS THE DEPENDENT VARIABLE,

LEAD IS SIGNIFICANT

DATE IS INSIGNIFICANT

LEAD ALSO MAINTAINS ITS SIGNIFICANCE WHEN DATE IS ADDED TO OUR MODELS

TEH 0350123

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TABLE VII

regression with Gartside variables

DIASTOLIC BLOOD PRESSURE
WITH ALL GARTSIDE VARIABLES

EFFECT	F VALUE	P VALUE
AGE	10.43	0.0029
RACE	2.54	0.1211
POVERTY INDEX	0.02	0.8977
DEGREE OF URBAN.	0.19	0.6642
REGION OF COUNTRY	0.32	0.5780
DATE	2.66	0.1129
RECREATIONAL EXERCISE	4.98	0.0328
SODIUM	0.20	0.6594
HEIGHT	6.54	0.0155
BODY MASS INDEX	201.74	0.0000
LOG(BLOOD LEAD)	7.50	0.0100

AFTER STEPWISE BACKWARDS ELIMINATION

AGE	8.52	0.0064
RECREATIONAL EXERCISE	6.02	0.0197
HEIGHT	7.73	0.0090
BODY MASS INDEX	187.11	0.0000
LOG(BLOOD LEAD)	11.85	0.0016

TEH 0350124

TABLE VIII

REGRESSION RESULTS WITH DATE INCLUDED

SYSTOLIC BLOOD PRESSURE
ALL MEN OVER 20

EFFECT	F VALUE	P VALUE
AGE	12.20	0.0014
AGE SQUARED	32.29	0.0000
BODY MASS INDEX	280.83	0.0000
LOG(ZINC)	8.80	0.0056
ALBUMIN SQUARED	51.39	0.0000
LOG(FAT)	4.32	0.0458
CALCIUM	6.75	0.0140
FAMILY HISTORY	33.33	0.0000
DATE	5.48	0.0257
LOG(BLOOD LEAD)	6.88	0.0133

DIASTOLIC BLOOD PRESSURE

AGE	99.29	0.0000
AGE SQUARED	65.39	0.0000
BODY MASS INDEX	74.81	0.0000
LOG(ZINC)	17.15	0.0002
LOG(SERUM VIT C)	13.93	0.0007
ALBUMIN SQUARED	48.14	0.0000
CIGARETTES	6.31	0.0172
CALCIUM	4.88	0.0345
DIET VIT C	10.24	0.0031
ZINC	12.01	0.0015
HEMOGLOBIN	16.95	0.0003
SUBSCAPULAR SKINFOLD	11.11	0.0022
FAMILY HISTORY	39.44	0.0000
RACE	11.20	0.0021
DATE	6.04	0.0196
LOG(BLOOD LEAD)	4.35	0.0451

TEH 0350125

DR. GARTSIDE'S LETTER TO THE AMERICAN JOURNAL OF EPIDEMIOLOGY

- NEW MODEL
- RESTRICTED TO 21-65 YEAR AGE GROUP
- RESTRICTED TO WHITES

CLAIMED THAT LEAD WAS NOT SIGNIFICANT

BUT OVER THE FULL 21-65 YEAR AGEGROUP USING GARTSIDE'S MODEL

- LEAD IS SIGNIFICANT FOR BOTH SYSTOLIC AND DIASTOLIC BLOOD PRESSURE WITHOUT DATE IN THE MODEL
- LEAD IS SIGNIFICANT FOR BOTH SYSTOLIC AND DIASTOLIC BLOOD PRESURE EVEN WHEN DATE IS IN THE MODEL

DR GARTSIDE CAN ONLY MAKE LEAD INSIGNIFICANT BY SUBDIVIDING HIS AGE GROUP AND INCLUDING DATE

WE TESTED WHETHER LEAD HAD A DIFFERENT RELATIONSHIP TO BLOOD PRESSURE IN HIS TWO AGE GROUPS BY USING AN INTERACTION TERM. IT WAS HIGHLY INSIGNIFICANT

$P = .85$ SYSTOLIC
$P = .58$ DIASTOLIC

INDICATING THE SIGNIFICANT RELATIONSHIP IN HIS MODEL DID NOT DIFFER BY AGE GROUP

TEH 0350126

TABLE IX

REGRESSION ON AGES 21-65 WITH GARTSIDE VARIABLES

DIASTOLIC BLOOD PRESSURE

EFFECT	P VALUE
AGE	0.0001
BODY MASS INDEX	0.0001
HYPERTENSIVE MED.	0.0001
HEIGHT	0.0031
COFFEE	0.1515
LOG(BLOOD LEAD)	0.0004

SYSTOLIC BLOOD PRESSURE

AGE	0.0001
BODY MASS INDEX	0.0001
HYPERTENS. MED.	0.0001
HEIGHT	0.0076
COFFEE	0.0001
LOG(BLOOD LEAD)	0.0123

TABLE X

REGRESSION WITH GARTSIDE VARIABLES INCLUDING DATE 21-65

DIASTOLIC BLOOD PRESSURE

AGE	0.0000
BODY MASS INDEX	0.0000
HYPERTEN. MED.	0.0000
HEIGHT	0.0046
COFFEE	0.1504
DATE	0.0204
LOG(BLOOD LEAD)	0.0025

SYSTOLIC BLOOD PRESSURE

AGE	0.0000
BODY MASS INDEX	0.0000
HYPERTEN. MED.	0.0000
HEIGHT	0.0095
COFFEE	0.0001
DATE	0.0836
LOG(BLOOD LEAD)	0.0307

TEH 0350127

DR GARTSIDE'S LATEST ANALYSIS

- USES 20 YEAR AGE GROUPS, LIMITING SAMPLE SIZE
- STILL USES DATE OF EXAMINATION
- CREATES 25 AGE SUBGROUPS, 21-40, 22-41, ETC. SPANNING 21-65
- USES A FEW NEW VARIABLES
- FINDS LEAD IS NOT SIGNIFICANT

TO DEMONSTRATE THAT THIS IS MERELY AN ARTIFACT OF HIS SIMULTANEOUSLY REDUCING SAMPLE SIZE BY LOOKING AT SMALL AGE SUBGROUPS AND INCLUDING A HIGHLY COLLINEAR VARIABLE, WE HAVE DONE THREE ANALYSES

WE RERAN HIS MODEL FOR THE FULL AGE RANGE 21-65 AND LEAD WAS SIGNIFICANT

WE RERAN HIS MODEL USING HIS ENTIRE 21-65 AGE GROUP AND INCLUDED INTERACTION TERMS FOR EACH OF HIS 25 AGE SUBGROUPS TO SEE IF LEAD HAD A DIFFERENT RELATIONSHIP TO BLOOD PRESSURE IN ANY ONE. **NOT ONE INTERACTION TERM WAS SIGNIFICANT EITHER WITH OR WITHOUT DATE IN THE MODEL.**

WE REPEATED HIS ANALYSIS USING 25 AGE SUBGROUPS OF 30 YEARS EACH. THIS STILL TESTES WHETHER LEAD IS SIGNIFICANT IN YOUNGER OR OLDER SUBGROUPS, BUT ALLOWS A LARGE ENOUGH SAMPLE SIZE TO HAVE STATISTICAL POWER.

WHEN DATE WAS NOT IN THE MODEL LEAD WAS SIGNIFICANT IN EVERY AGE GROUP

WHEN DATE WAS IN THE MODEL, DATE WAS INSIGNIFICANT IN EVERY SUBGROUP, AND LEAD WAS SIGNIFICANT IN 22 OUT OF THE 25 SUBGROUPS. ELIMINATING THE INSIGNIFICANT DATE VARIABLE RETURNS LEAD TO SIGNIFICANCE IN EVERY AGE GROUP.

TEH 0350128

LEAD INTERACTION TERMS FOR DR GARTSIDE'S 25 AGE SUBGROUPS

AGE GROUP	P VALUE WITHOUT DATE	P VALUE WITH DATE
21-40	.6374	.6015
22-41	.6989	.6705
23-42	.7925	.7857
24-43	.8082	.8231
25-44	.7010	.7351
26-45	.8873	.8741
27-46	.4899	.4775
28-47	.3146	.2828
29-48	.3187	.3044
30-49	.4360	.4101
31-50	.4863	.4053
32-51	.8148	.7611
33-52	.9875	.9549
34-53	.6829	.6841
35-54	.1832	.1845
36-55	.0888	.1011
37-56	.0978	.1023
38-57	.1933	.1841
39-58	.4755	.4260
40-59	.4582	.4507
41-60	.6837	.6683
42-61	.9446	.9249
43-62	.9827	.9572
44-63	.9805	.9677

TEH 0350129

GARTSIDE MODEL WITH 30 YEAR AGE INTERVALS
P VALUE FOR LEAD (WITHOUT DATE)

	BEFORE BACKWARDS ELIMINATION	AFTER ELIMINATION
21-50	0.0134	0.0083
22-51	0.0284	0.0159
23-52	0.0353	0.0177
24-53	0.0277	0.0126
25-54	0.0236	0.0096
26-55	0.0107	0.0050
27-56	0.0084	0.0035
28-57	0.0063	0.0015
29-58	0.0070	0.0013
30-59	0.0096	0.0017
31-60	0.0206	0.0053
32-61	0.0438	0.0132
33-62	0.0334	0.0092
34-63	0.0236	0.0061
35-64	0.0124	0.0026
36-65	0.0107	0.0024
37-66	0.0084	0.0012
38-67	0.0106	0.0032
39-68	0.0169	0.0032
40-69	0.0135	0.0032
41-70	0.0156	0.0148
42-71	0.0469	0.0151
43-72	0.0533	0.0184
44-73	0.0653	0.0229
45-74	0.0533	0.0184

TEH 0350130

GARTSIDE MODEL WITH 30 YEAR AGE INTERVALS
P VALUE FOR LEAD AND DATE

AGE	LEAD	DATE
21-50	0.0459	0.0769
22-51	0.0826	0.0647
23-52	0.0779	0.0678
24-53	0.0643	0.0762
25-54	0.0467	0.0759
26-55	0.0185	0.0752
27-56	0.0116	0.0809
28-57	0.0037	0.0995
29-58	0.0020	0.2289
30-59	0.0049	0.1464
31-60	0.0131	0.1486
32-61	0.0300	0.1601
33-62	0.0247	0.2053
34-63	0.0158	0.1991
35-64	0.0095	0.1967
36-65	0.0064	0.2631
37-66	0.0090	0.1268
38-67	0.0045	0.1718
39-68	0.0118	0.1113
40-69	0.0134	0.1162
41-70	0.0113	0.1523
42-71	0.0394	0.1655
43-72	0.0474	0.1925
44-73	0.0413	0.2240
45-74	0.0306	0.2038

TEH 0350131

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OMODEL NUMBER 1
O 32 DENOMINATOR DEGREES OF FREEDOM

ODEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2DIA			
TEST FOR OVERALL MODEL	35.46	7	0.0000
OINDEPENDENT EFFECTS			
AGEYRS	0.55	1	0.4640
BMI	116.25	1	0.0000
HEIGHT	3.07	1	0.0896
HYPERMED	54.47	1	0.0000
COFFEE	6.28	1	0.0175
DATE	1.30	1	0.2631
LL16	8.51	1	0.0064

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OHYPOTHESIS TESTING RESULTS
OMODEL NUMBER 2
O 32 DENOMINATOR DEGREES OF FREEDOM

ODEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2DIA			
TEST FOR OVERALL MODEL	35.24	6	0.0000
OINDEPENDENT EFFECTS			
AGEYRS	0.66	1	0.4241
BMI	120.60	1	0.0000
HYPERMED	58.79	1	0.0000
COFFEE	5.80	1	0.0220
DATE	2.46	1	0.1268
LL17	7.73	1	0.0090

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OHYPOTHESIS TESTING RESULTS
OMODEL NUMBER 3
O 32 DENOMINATOR DEGREES OF FREEDOM

ODEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2DIA			
TEST FOR OVERALL MODEL	37.51	7	0.0000
OINDEPENDENT EFFECTS			
AGEYRS	0.02	1	0.8765
BMI	134.63	1	0.0000
HEIGHT	2.55	1	0.1202
HYPERMED	62.96	1	0.0000
COFFEE	5.86	1	0 0213
DATE	1.95	1	0.1718
LL18	9.34	1	0.0045

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OHYPOTHESIS TESTING RESULTS
OMODEL NUMBER 4
O 32 DENOMINATOR DEGREES OF FREEDOM

ODEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2DIA			
TEST FOR OVERALL MODEL	37.76	7	0.0000

TEH 0350132

DUPONT ANALYSIS

DUPONT HAS SUBMITTED A NEW ANALYSIS IN WHICH THEY USE A DUMMY VARIABLE FOR ALL 64 SITES OF THE NHANES II SURVEY

THIS APPROACH TO KEEPING BLOOD LEAD FROM CORRELATING WITH ANYTHING WAS REJECTED EARLIER IN THE DEBATE OVER THE GASOLINE LEAD - BLOOD LEAD RELATIONSHIP

THE POSSIBILITY OF OTHER VARIABLES SUCH AS OBESITY, EXERCISE, DEMOGRAPHIC FACTORS ETC CHANGING AS SAMPLING SITES CHANGED HAS ALREADY BEEN CONSIDERED BY INCLUSION OF THOSE VARIABLES IN THE MODEL, AND IN PARTICULAR BY LETTING THE STEPWISE REGRESSION SELECT VARIABLES WITHOUT COMPETITION FROM LEAD, AND THEN TESTING LEAD IN THOSE MODELS.

SINCE THESE OTHER FACTORS ARE WELL CONTROLLED FOR, AND DID NOT IN FACT VARY MUCH FROM SITE TO SITE, THE SITE VARIABLES ARE ESSENTIALLY DUMMY VARIABLES FOR LEAD EXPOSURE. no

WITH 65 LEAD EXPOSURE VARIABLES IN A MODEL IT IS DIFFICULT FOR ALL OF THEM TO MAINTAIN SIGNIFICANCE. not true

TO DEMONSTRATE THAT INSIGNIFICANT DEMOGRAPHIC FACTORS ARE NOT RESPONSIBLE FOR LEAD'S SIGNIFICANT RELATIONSHIP, WE PUT THEM BACK INTO OUR MODEL. LEAD IS SIGNIFICANT AFTER INCLUDING DEGREE OF URBANIZATION, REGIONS OF THE COUNTRY, EXERCISE, AND RESIDENCE IN OR OUT OF A CENTRAL CITY. not [illegible]

WHEN THE MEAN VALUES OF LEAD, BODY MASS INDEX, AND HEIGHT ARE COMPUTED FOR THE 64 SITES, WE SEE:

MEAN BLOOD LEAD LEVELS VARY FROM 11.7 TO 22.3

MEAN BMI ONLY VARIES FROM 23.4 TO 26.9

MEAN HEIGHT ONLY VARIES FROM 1.71M TO 1.79M

THEREFORE THE SITE DUMMIES ARE INDEED MAINLY REFLECTIONS OF BLOOD LEAD DIFFERENCES no

TEH 0350133

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0DEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2DIA			
TEST FOR OVERALL MODEL	50.85	24	0.0000
0INDEPENDENT EFFECTS			
AGEYRS	85.79	1	0.0000
AGESQ	60.99	1	0.0000
BMI	91.59	1	0.0000
LOGZINC	17.82	1	0.0002
ALBUMIN	49.19	1	0.0000
DIETVITC	8.97	1	0.0053
SMOKNUM	4.34	1	0.0454
CALCIUM	5.30	1	0.0279
ZINC	13.06	1	0.0010
HEMOGLOB	18.38	1	0.0002
TRICEPR	4.88	1	0.0344
FAMHYPER	28.13	1	0.0000
COFFEE	7.25	1	0.0112
HEIGHT	16.16	1	0.0003
HYPERMED	41.98	1	0.0000
RACE	9.72	1	0.0038
LOGVITC	12.97	1	0.0011
LL	13.26	1	0.0009
SIZE	0.26	1	0.6122
R1	0.31	1	0.5791
R2	0.09	1	0.7706
R3	0.02	1	0.8767
INCC	1.27	1	0.2685
RECEX	1.29	1	0.2638

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POTHESIS TESTING RESULTS
DEL NUMBER 2
32 DENOMINATOR DEGREES OF FREEDOM

0DEPENDENT EFFECT	F VALUE	DEGREES OF FREEDOM	PROBABILITY
BP2SYS			
TEST FOR OVERALL MODEL	79.38	17	0.0000
0INDEPENDENT EFFECTS			
AGEYRS	6.40	1	0.0165
AGESQ	22.99	1	0.0000
BMI	312.57	1	0.0000
LOGZINC	13.17	1	0.0010
ALBSQ	57.05	1	0.0000
CALCIUM	5.04	1	0.0318
FAMHYPER	27.61	1	0.0000
COFFEE	20.24	1	0.0001
HEIGHT	7.78	1	0.0088
HYPERMED	43.39	1	0.0000
LL	19.05	1	0.0001
SIZE	1.33	1	0.2568
R1	0.70	1	0.4096
R2	3.37	1	0.0758
R3	0.02	1	0.8925
INCC	0.45	1	0.5066
RECEX	2.22	1	0.1461

0NOTE- THE PROCEDURE CALCULATED THAT 63K WAS NEEDED FOR ARRAY STORAGE
? ***
JOB 5668 XPOSASPR ENDED AT NIHCU
? ***

TEH 0350134