OBSERVATION AND CONCLUSIONS BASED ON A STUDY ON THE HEALTH OF CAPACITOR WORKERS WITH HIGH PRIOR EXPOSURE TO PCBs

PRESENTATION AND DISCUSSION BY:

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THE HEALTH OF CAPACITOR WORKERS WITH HIGH PRIOR EXPOSURE TO PCB's: A CLINICAL CROSS-SECTIONAL STUDY

GENERAL ELECTRIC COMPANY
CORPORATE ENVIRONMENTAL PROGRAM

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OBJECTIVES OF STUDY

1. CHARACTERIZE HEALTH STATUS OF EXPOSED POPULATION
   - OVERALL ASSESSMENT (HISTORY, PHYSICAL)
   - 75 QUANTITATIVE PARAMETERS

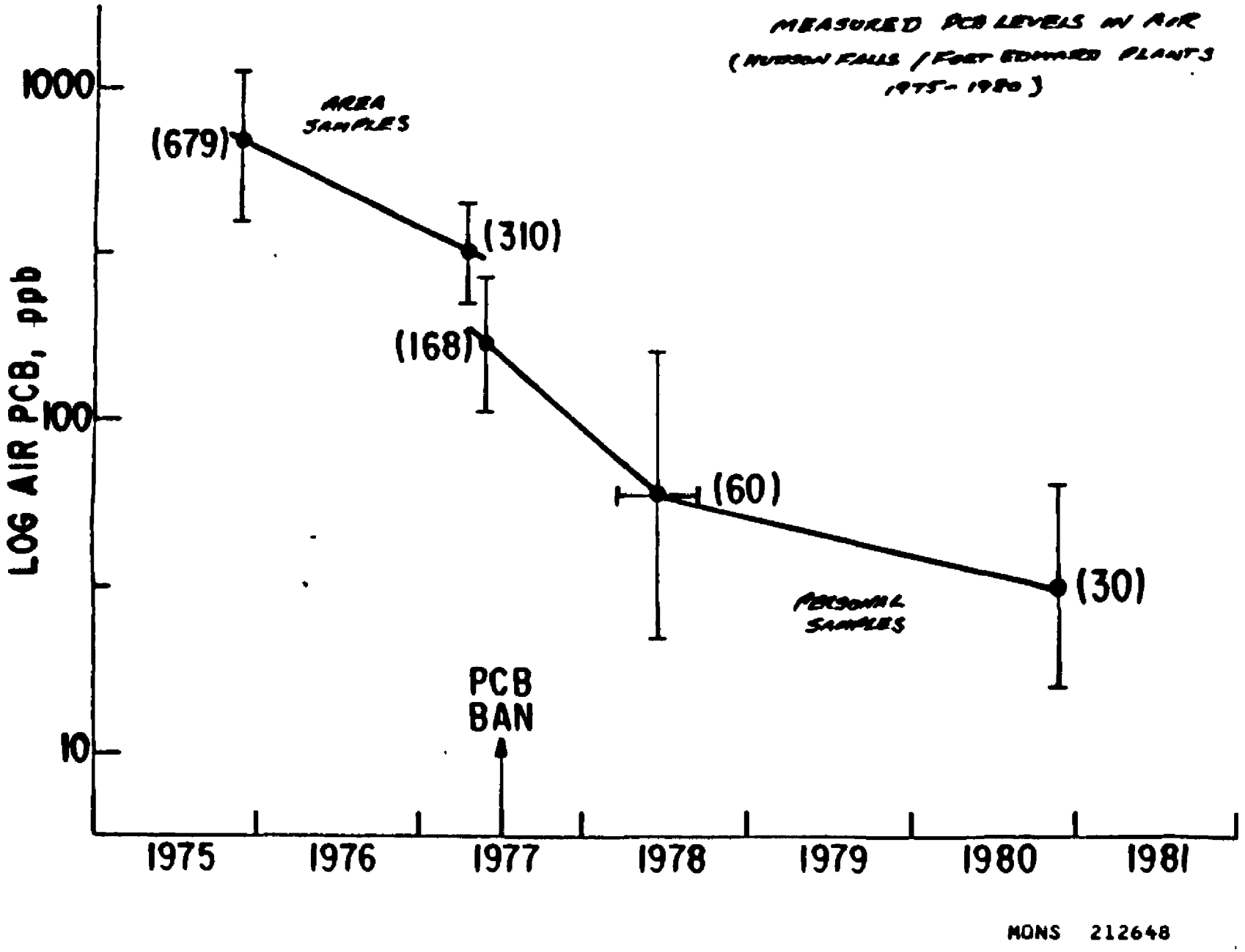
2. CHARACTERIZE EXPOSURE LEVELS
   - JOB ANALYSIS AND CATEGORIZATION
   - PCB AIR LEVELS
   - SERUM PCB MEASUREMENTS
     - ACTIVITY INDICATORS
     - PCB BODY BURDEN

3. ASSESS HEALTH EFFECT - EXPOSURE CORRELATION
   - CHECK REPORTED CORRELATIONS
   - LOOK FOR NEW ASSOCIATIONS AMONG VARIABLES

SIGNIFICANT BACKGROUND FACTORS

(GE HUDSON FALLS / FORT EDWARD PCB EXPOSURES)

- LARGEST U.S. PCB USER
  (15% OF TOTAL PCB CONSUMPTION (1966-1974)
- COMPOSITION OF PCB'S USED
  - 95% OF PRODUCTION
    AROCLOR 1254: 1946-1952
    AROCLOR 1242: 1952-1971
    AROCLOR 1016: 1971-1977
- DEFINEABLE EXPOSED POPULATION
  - LONG CONTINUOUS SERVICE
  - MANY WITH HEAVY EXPOSURE
- BEST OPPORTUNITY TO DEFINE ACTUAL EFFECTS OF PCB EXPOSURE IN HUMAN


MEASURED PCB LEVELS IN AIR
(HUDSON FALLS / FORT EDWARD PLANTS
1975- 1980)
1000
100
10
LOG AIR PCB, ppb
(679)
AREA SAMPLES
(310)
(168)
(60)
(30)
PERSONAL SAMPLES
PCB BAN
1975
1976
1977
1978
1979
1980
1981
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MULTIPLE PRIOR INVESTIGATIONS

- Fischbein, Selikoff et al
- Warshaw, Selikoff et al — Mt. Sinai
- Wolff, Selikoff et al
- Brown et al : NIOSH, Cincinnati, Ohio
- Taylor: NYSDH, Harvard School Public Health

Brown, D.P. and M. Jones. Mortality and industrial hygiene study of workers exposed to polychlorinated biphenyls. Arch. Environ. Health 36: 120-129, 1981.

Fischbein, A., Wolff, M.S., Lilis, R., Thornton, J., and I.J. Selikoff. Clinical findings among PCB-exposed capacitor workers. Ann. N.Y. Acad. Sci. 320: 703-715, 1979.

Warshaw, R., Fischbein, A., Thornton, J., Miller, A. and I.J. Selikoff. Decreased vital capacity in PCB-exposed workers in a capacitor manufacturing facility. Ann. N.Y. Acad. Sci. 320: 277-284, 1979.

Wolff, M.S., Fischbein, A., Thornton, J., Rue, C., Lilis, R. and I.J. Selikoff. Body burden of polychlorinated biphenyls among persons employed in capacitor manufacturing. Int. Arch. Environ. Health 49: 199-208, 1982.

Wolff, M.S.m Thornton, J., Fischbein, A., Lilis, R. and I.J. Selikoff. Disposition of polychlorinated biphenyl congeners in occupationally exposed persons. Toxicol. Appl. Pharmacol. 62:294-306, 1982.

HEALTH STATUS ANALYSIS

- Study population and selection
- Clinical measurements
- Medical findings

DESCRIPTION OF GE STUDY POPULATIONS

1976:	DIRECTLY EXPOSED CAPACITOR WORKERS (~ 10% OF WORKFORCE)	194
1979:	REPEAT STUDY	174
1981:	SMALL GROUP STUDIES	
	• HIGH EXPOSURE	12
	• CLERICAL AND ADMIN.	18
	• NEW EMPLOYEES SINCE 1977 (HIGH EXPOSURE ZONE)	16

Population Selection (194)

	No.
• Based on current exposure (1976)	
• continuous in high exposure zone	55
• continuous in periphery • intermittent high exposure	139

Plant PCB Use and Employment Date

• 1946-1954: Aroclor 1254	51
• 1954-1971: Aroclor 1242	93
• 1971-1977: Aroclor 1016	50

Mt. Sinai School of Medicine Study

(Fischbein et al)

1976 : volunteers	326
1979 : repeat study	
• workers in common	33
• adipose tissue biopsy	61

Population and Exposure (16)

- Sex
- Age
- Service
- Job Code
- Job Status
- Plant
- Ex/non-E
- Disease Status

- Blood PCB
  - 1242
  - 1254
  - 1260
- DDE
- Exp. Cat.
- Air PCB
- Mt. Sinai
- Past/non-Past (1976)

Metabolic Responses (10)

- Height
- Frame
- Pre-Empl. Wt.
- Body Wt.(76 & 79)
- Max. Ref. Wt.
- Body Wt/Height²

- Triglycerides
- Cholesterol
- Blood Sugar
- Uric Acid

Cardiovascular (3)

- ECG
- Blood Pressure
  - Systolic
  - Diastolic

Hepatic Responses (12)

- Total Bilirubin
- Direct Bilirubin
- SGOT
- SGPT
- GGTP
- Alkaline Phosph.
- LDH
- Total Protein
- Albumin
- Globulin
- A/G Ratio
- Amylase

Renal Responses (18)

- Bun
- Creatinine
- Bun/Creat. Ratio
- Na^{+}
- K^{+}
- Cl^{-}
- Ca^{++}
- Pb^{-}
- Mg^{++}

- Urinalysis
  - Appearance
  - pH

  - Sp. Gr.
  - Acetone
  - Albumin
  - Glucose
  - RBC
  - WBC
  - Casts

Hematology (13)

- Iron
- RBC
- HGB
- HCT
- MCV
- MCH
- MCHC
- WBC
- Differential
  - Polys
  - Lymphs
  - Monos
  - Eosins
  - Baso.

Pulmonary Function (4)

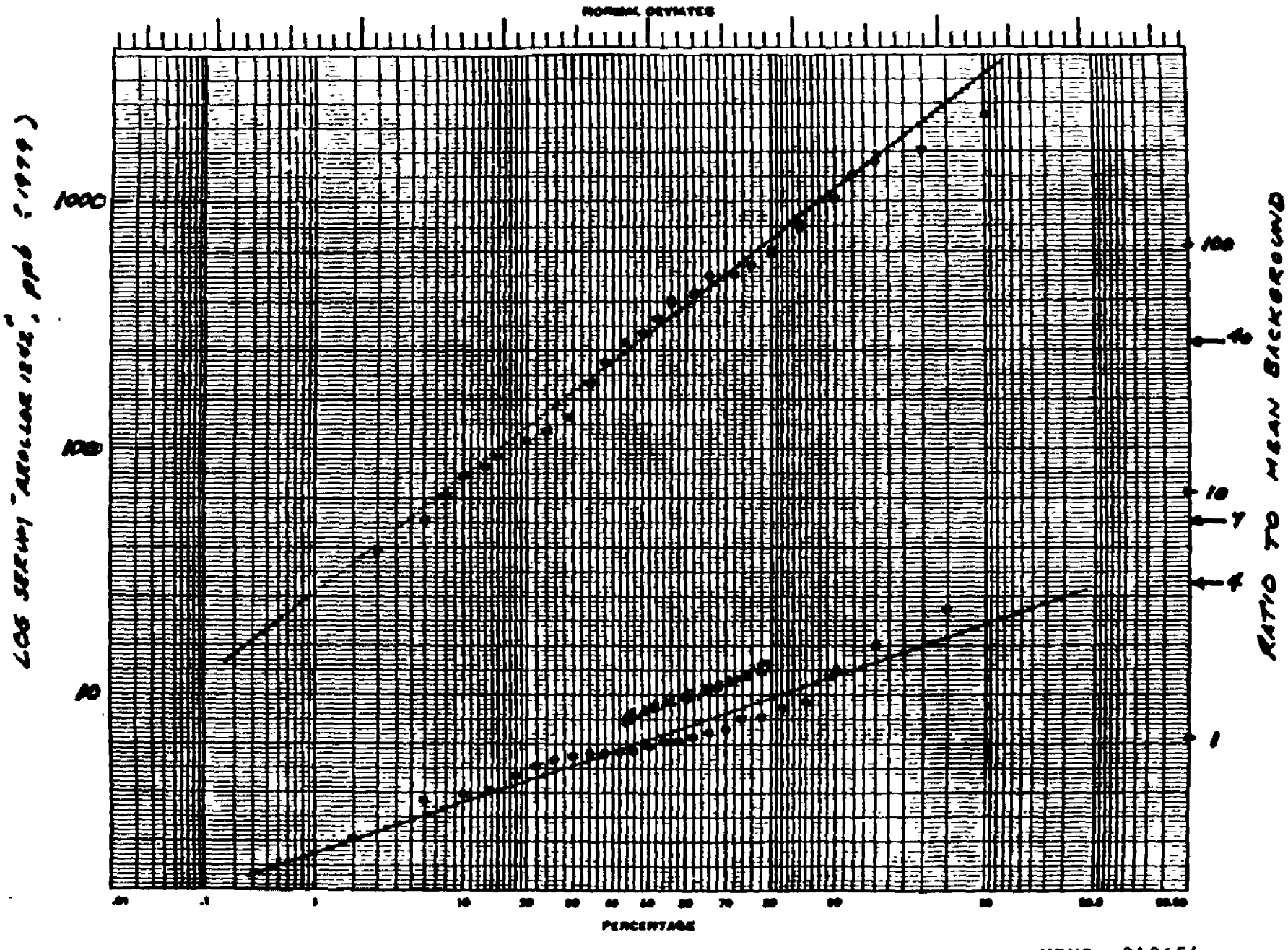
- FVC
- FEV_1
- FEV_1/FVC
- Chest x-ray

History (5)

- Smoking
- Alcohol use
- Drug use
- Diagnosis
- Surgery

Symptomatology (6)

- Dermatological
- Neurological
- Cardiovascular
- Respiratory
- Gastrointestinal
- Musculo Skeletal


NORMAL DEVIATES
LOG SERUM "AROLLOR 1242", ppb (1979)
1000
100
10
RATIO TO MEAN BACKGROUND
100
40
10
7
4
1
BACKGROUND
PERCENTAGE

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Clinical Findings in PCB-Exposed Capacitor Workers

1. Dermatological Findings

Medical record review (1970-1975) 1500-1800

	No.	
Non-Exposed Employees		
Skin irritations or dermatitis	70	(4.2%)
Occupationally related	16	(23%)
Non-occupational	54	

Medical record review (1960-1975)

PCB-Exposed Employees	
Contact dermatitis to dielectric fluid	49
Nausea, dizziness, eye and nasal irritation, etc. on short initial exposure	16

Medical History of Study Population

Rash	45
PCB-related 1	
Seborrhea	12
Infections	19
Eye complaints	7
Old acne	4
Other	13

Chloracne not observed

Plant Physician

CLINICAL FINDINGS IN PCB-EXPOSED CAPACITOR WORKERS (CONT.)

2. CHRONIC OBSTRUCTIVE LUNG DISEASE

- RESTRICTIVE PATTERNS (3) 1.8%
  OBSTRUCTIVE PATTERNS (26) 15.3%
  MIXED PATTERNS (3) 1.8%
- 65% OF POPULATION SMOKERS OR X-SMOKERS

3. OBESITY

- 50% OF POPULATION OVERWEIGHT
- MANY OBESE BY ANY STANDARD

4. HYPERTENSION

- HISTORY OF HYPERTENSION 22.7%
- DIASTOLIC BP ≥ 90 14.7 - 19.6% SINCE EMPLOY

5. GLUCOSE INTOLERANCE

- 45 CASES (20%): 5 DIABETICS, 10 OTHERS
  30 NORMAL POST PRANDIAL

6. ELEVATED CHOLESTEROL LEVELS

- 1976 - 41%; 1979 - 29% USING LRCP AGE ADJUSTED PERCENTILES
- INCIDENCE OF GALLSTONES, FATTY FOOD INTOLERANCE, ETC. 10%
- TRIGLYCERIDES 1976-9% : 1979-18%

7. OTHER BIOCHEMICAL VARIABLES
   IN NORMAL RANGES EXCEPT SGPT

3. Statistical Association Between Health Status Indicators and Measures of PCB Exposure

- Statistical procedures used
- Correlations observed
- Comparison of findings with others
- Conclusions

STATISTICAL PROCEDURE:

MULTIPLE LINEAR REGRESSION

- EXAMINE VARIABLE DISTRIBUTIONS
  - LOG TRANSFORMATION AS REQUIRED
  - W-TEST OF DISTRIBUTIONAL ASSUMPTIONS
- SELECT CONFOUNDERS
  - ~~% BODY FAT~~ urinary specific Gravity, SEX, SERVICE TIME
- TEST EACH VARIABLE FOR DEPENDENCE ON PCB'S AND CONFOUNDERS:

  (VAR1) = A + B(VAR2) + C(VAR3)+ .....

  DEPENDENT VARIABLE — INDEPENDENT VARIABLES
- STATISTICAL CRITERIA

  MODEL : F > 3.84; DF = 140-170

  COEFFICIENTS: 95% CONFIDENCE INTERVAL ≠ 0

TWO MEASURES OF PCB LEVELS USED

1. GROSS PCB CONCENTRATION IN SERUM
   - (WEIGHT PCB) / (WEIGHT SERUM)

2. CHEMICAL ACTIVITY OF PCB'S (a)
   - (WEIGHT TISSUE PCB) / (WEIGHT TISSUE LIPID)
   - AT EQUILIBRIUM, A TOXICANT MUST REACH SAME CHEMICAL ACTIVITY (a) IN ALL TISSUES OF THE BODY, INCLUDING ANY SITES OF PHARMACOLOGICAL ACTION. THIS ACTIVITY FUNCTION CORRELATES WITH TOXIC EFFECT.

FERGUSON, 1939

PCB EQUILIBRIUM IN BODY

- No evidence of active transport
- Equilibrium established within days
- PCB carriers in serum have been identified:
  - primarily, neutral lipid (NL) microphases of serum lipoproteins
  - secondarily, albumin (Alb)
- Equilibrium between adipose tissue (A) and serum (S) phases defined by chemical activity a:

$$a = \frac{[PCB]_A}{[NL]_A} = \frac{[PCB]_S}{b[NL]_S + K[Alb]_S} \approx \frac{[PCB]_S}{b'[NL]_S}$$

- Literature data indicate mean values of b' close to 1.0, if $[NL]_S$ be expressed as sum of serum triglycerides plus cholesterol, or as extractable lipids.

Results of Linear Regression Analysis

- Significant associations among observed clinical findings
  - obesity, hyperlipidemia, hypertension, etc.
  - smoking and pulmonary function
- Only three clinical measurements correlated with gross serum PCB concentrations
  - serum triglycerides
  - serum total cholesterol
  - serum γ-glutamyl transpeptidase
- Similar correlations reported previously

Association of Clinical Indicators with Serum Level and Pharmacological Availability of Lipophilic Agents

Measure of Lipophilic Agent	N	Clinical Measurement*		
		Triglyc.	Chol.	GGTP
Gross conc. in serum				
Aroclor 1242	156	+	+	+
Aroclor 1260	126	+	+	N.S.
DDE	156	+	+	N.S.
Chemical Activity				
Aroclor 1242	156	N.S.	N.S.	N.S.
Aroclor 1260	126	N.S.	N.S.	N.S.
DDE	156	N.S.	-	N.S.

* controlled for sex, service, sp. gr. (urine)

Clinical Parameters Significantly Associated with Gross Serum PCB Concentrations in PCB-Exposed Populations

Author (PCB)	Clinical Measurement					
	Tri	Chol	GGTP	SGOT	SGPT	HDLC
Present study	+	+	+	N.S.	N.S.	
Chase et al (1254)	+	N.S.	N.S.	+	N.S.	N.S.
Smith et al						
L-PCB	+	N.S.	+	+		N.S. (-)
H-PCB	+	+	+	+		-
Baker et al (1254)	+	+ (drinkers)	+ (drinkers)	N.S.	N.S.	N.S. (-)
Kreiss et al (1260)	N.S.	+	+		N.S.	N.S.

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SUMMARY

- RESONABLY LARGE POPULATION WITH HIGH PRIOR OCCUPATIONAL EXPOSURE TO PCB's
- HEALTH PROBLEMS OF THE POPULATION ARE THOSE OF THE MODERN AFFLUENT AMERICAN WORKER; E.G., OBESITY, HYPERLIPIDEMIA, HYPERTENSION, SMOKING
- THE STATISTICAL ASSOCIATIONS BETWEEN GROSS SERUM PCB CONCENTRATION AND SERUM LIPIDS AND LIVER ENZYMES FOUND TO BE THE CONSEQUENCE OF PCB EQUILIBRATION BETWEEN SERUM LIPOPROTEIN AND ADIPOSE TISSUE RESERVOIRS OF NEUTRAL LIPIDS

$$\frac{[PCB]_A}{[NL]_A} = \frac{[PCB]_S}{b'[NL]_S}$$

DESCRIPTION AND COMPARISON OF PCB EXPOSURE LEVELS

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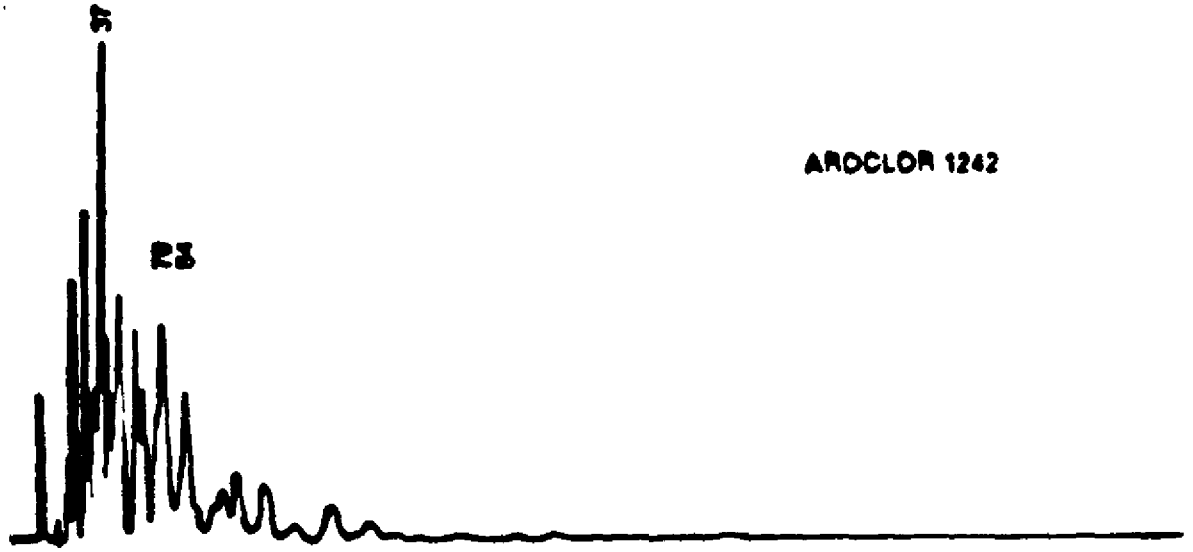
TOPICS TO BE DISCUSSED

1. Reporting of PCB analytical data
2. Estimation of cumulative uptake and clearance
3. Calculation of body burdens
4. Human vs. animal uptake comparisons
5. Capacitor vs. other occupational exposure
6. Ambient PCB levels in capacitor manufacturing vs. current environments



AROCLOR 1242



AROCLOR 1254



AROCLOR 1260



CAPE FEAR WORKERS' SERUM

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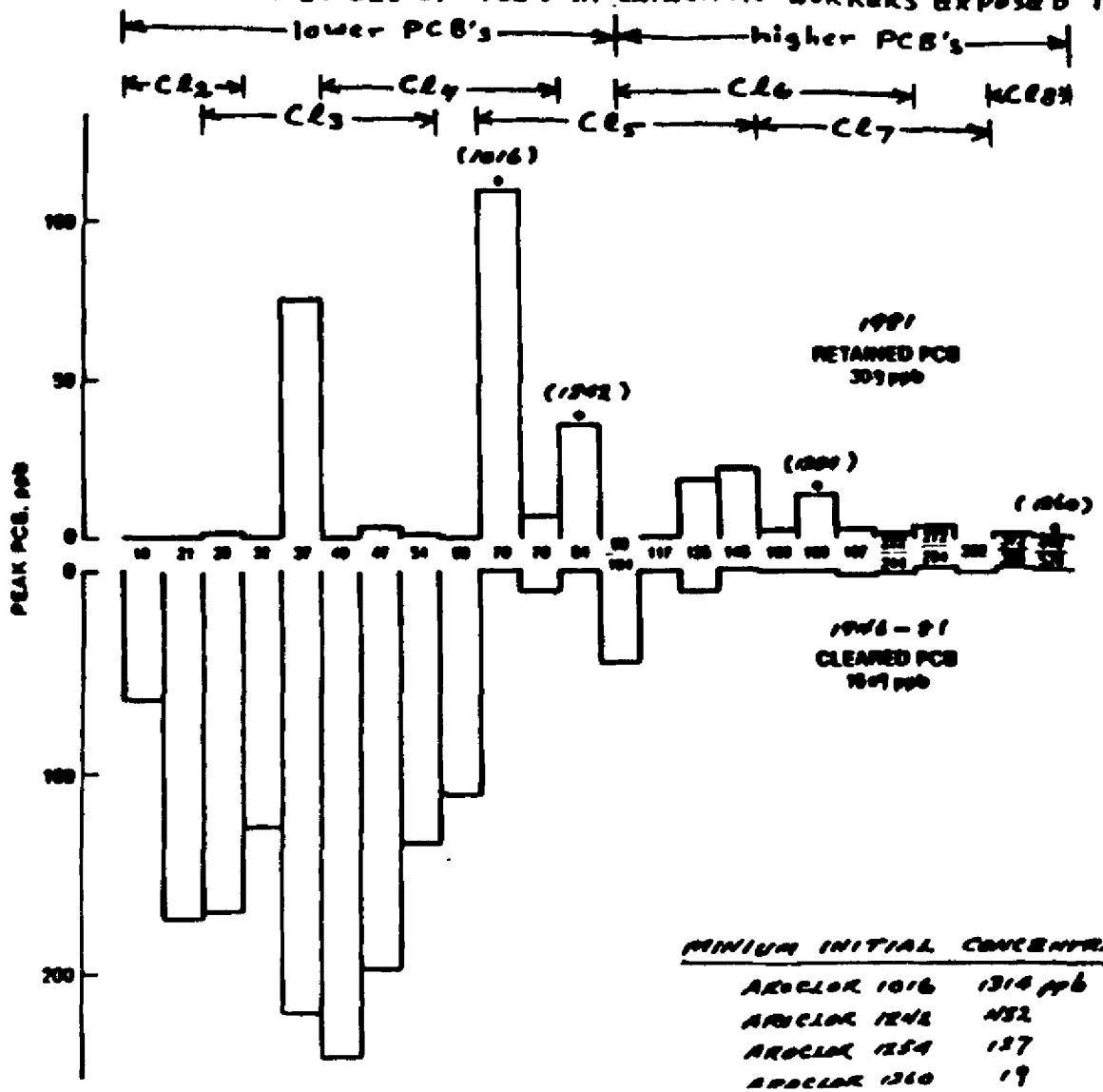
OBSERVED (1981) LEVELS OF PCB's IN CAPACITOR WORKERS EXPOSED 1955-77



MINIUM INITIAL CONCENTRATION	
AROCLOR 1016	1314 ppb
AROCLOR 1242	452
AROCLOR 1254	137
AROCLOR 1260	19

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TABLE II. Alternative Ways of Reporting Same Analytical Date on PCB Levels in Capacitor Worker's Sera

Reportable PCB Aggregate		Reportable Parameter (ppb)		
Description	Peak Numbers	Actual PCB's present	Analytical "Aroclor"	Minimum Initial conc.
∿2-4 Cl-BP	11-70	195	-	1739
∿5-6 Cl-BP	78-197	101	-	166
∿7-8 Cl-BP	222-528	7	-	7
Total	11-528	303		1912
LPCB's	11-98	237	-	1807
HPCB's	104-528	66	-	105
Total	11-528	303		1912
Aroclor 1016	11-70	-	-	1314
Aroclor 1242	11-146	-	1000	452
Aroclor 1254	47-244	-	150	127
Aroclor 1260	70-528	-	93	19
Total	11-528	303	1093[a]	1912

a. Sum of values for "Aroclor 1242" and "Aroclor 1260"

PCB EQUILIBRIUM IN BODY

- No evidence of active transport
- Equilibrium established within days
- PCB carriers in serum have been identified:
  - primarily, neutral lipid (NL) microphases of serum lipoproteins
  - secondarily, albumin (Alb)
- Equilibrium between adipose tissue (A) and serum (S) phases defined by chemical activity a:

$$a = \frac{[PCB]_A}{[NL]_A} = \frac{[PCB]_S}{b[NL]_S + K[Alb]_S} \approx \frac{[PCB]_S}{b'[NL]_S}$$

- Literature data indicate mean values of b' close to 1.0, if $[NL]_S$ be expressed as sum of serum triglycerides plus cholesterol, or as extractable lipids.

PCB Levels in Workers Directly Exposed (1946-1977)
(N = 12)

PCB's Present (1981)	Mean	Range
Serum	303 ppb	150-450
Tissue (est.)	44.9 ppm	23-67
Body Burden (22 kg fat)	1.0 gram	0.5-1.5

Minimum Initial Concentrations and Uptake		
Serum	1912 ppb	925-2775
Tissue (est.)	277 ppm	136-402
Uptake	6.1 grams	3.0-8.8

Minimal Clearance	84%

Comparisons Between PCB Uptakes in Directly Exposed Capacitor Workers and Animals Used in Chronic Toxicity Testing

Lower PCB's (Aroclors 1016, 1242)

Minimal toxic dose in rats [a]	> 4.	G/KG
Minimum uptake in directly-exposed capacitor workers	0.1	G/KG

Higher PCB's (Aroclor 1260)

Producing hepatocarcinoma in rats [b]	1.6	G/KG
Uptake in directly-exposed capacitor workers	0.003	G/KG

a. Burse, Kimbrough et al., 1974; Goldstein, 1975

b. Kimbrough et al. 1975

REPORTED ABSENCE OF CONSISTENT HEALTH EFFECTS IN INDIVIDUALS OCCUPATIONALLY EXPOSED TO PCB's USED AT MODERATE TEMPERATURES

AUSTRALIA

OUW ET AL, 1976

FINLAND

KARPPANEN AND KOLHO, 1972

ITALY

MARONI ET AL, 1981

JAPAN

HASEGAWA ET AL, 1972
HARA ET AL, 1974
KITAMURA ET AL, 1973

US

FISCHBEIN ET AL, 1979
BROWN AND JONES, 1981
SMITH ET AL, 1982
WARSHAW ET AL, 1979
CHASE ET AL, 1982
LAWTON ET AL, THIS STUDY

OBSERVATIONS OF HEAVY PCB EXPOSURE IN CAPACITOR WORKERS

AMBIENT PCB OR "AROCLOR" LEVELS 100-1000 $\mu G/M^3$

SERUM PCB OR "AROCLOR" LEVELS 100-1000 PPB

HASEGAWA ET AL, 1972
KITAMURA ET AL, 1973
FISCHBEIN ET AL, 1979
SMITH ET AL, 1982
KARPPANEN AND KOLHO, 1972
OUW ET AL, 1976
MARONI ET AL, 1981
LAWTON ET AL, THIS STUDY

US PCB USAGE AND OCCUPATIONAL EXPOSURE 1930-75

Applications		Est. No. Individuals Exposed	
Low Temperature Uses	(MM lbs)	Peripherally	Directly
Capacitors	630	32,000	1600
Transformers	335	-	-
Miscellaneous	163	-	-
Total	1228	~65,000	~9000
High Temperature Uses			
Heat Exchangers	20	-	-
Miscellaneous	5	-	-
	25	~1300	~200

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CONCLUSION 1

1930-1977 OCCUPATIONAL EXPOSURES TO PCB'S WERE WIDESPREAD

- CAPACITOR MANUFACTURING
- TRANSFORMER MANUFACTURING AND SERVICE
- PLASTICIZER AND PRINTING INK USERS
- MANY THOUSANDS DIRECTLY EXPOSED

CONCLUSION 2

1930-1977 OCCUPATIONAL EXPOSURES TO PCB'S WERE HIGH

- AMBIENT AIR LEVELS
- UPTAKE RATES
- RETAINED PCB'S

PAST AND PRESENT ENVIRONMENTAL PCB LEVELS

	NG/M^3
CAPACITOR MANUFACTURING (1955-77)	~1,000,000
CAPACITOR MANUFACTURING (1979)	30,000
BINGHAMTON OFFICE BLDG, AFTER DISRUPTION OF PCB TRANSFORMER (1983)	800 TO 1,600
VAULT CONTAINING PCB TRANSFORMERS (1982)	700 TO 900
AIR NEAR PAPER RECYCLING MILL (1977)	6 TO 120
AIR IN PCB-USING LABORATORY (1977)	40 TO 50
AIR IN OFFICE USING DATASCREEN TERMINALS (1982)	56 TO 81
OUTDOOR AIR, NORWAY, 1982	0.5 TO 1

CONCLUSION 3

IN VIEW OF PAST PCB EXPOSURE LEVELS AND UPTAKES IN CAPACITOR WORKER POPULATIONS, PRESENT ENVIRONMENTAL LEVELS PRESENT LITTLE CAUSE FOR CONCERN.

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PROPOSITION:

YUSHO INCIDENTS DON'T PREDICT HEALTH EFFECTS RESULTING FROM ORDINARY, LOW TEMPERATURE PCB USAGE

- DIFFERENT CHEMICAL COMPOSITION
- DIFFERENT IDENTIFIED TOXICANT
- HEALTH EFFECTS NOT SEEN IN OTHER EXPOSED POPULATIONS

COMPOSITIONS OF PCB MIXTURES PRESENTED TO HUMAN STUDY POPULATIONS

US Capacitor Workers

Mainly lower PCB's (Aroclors 1016, 1242)
Some higher PCB's (Aroclor 1254)
PCDF/PCB 0-2 ppm

US Transformer Workers

Mainly higher PCB's (Aroclors 1254, 1260)
Some lower PCB's (Aroclor 1242)
PCDF/PCB 0-5 ppm

Japanese Yusho Victims

Pyrolysed lower PCB (Kanechlor 400)
~50% PCQ, PCBP, PCDF, etc.
PCDF/PCB 2250 ppm

US PCB USAGE AND OCCUPATIONAL EXPOSURE 1930-75

Applications		Est. No. Individuals Exposed	
Low Temperature Uses	(MM lbs)	Peripherally	Directly
Capacitors	630	32,000	4600
Transformers	335	-	-
Miscellaneous	163	-	-
Total	1228	~65,000	~9000
High Temperature Uses			
Heat Exchangers	20	-	-
Miscellaneous	5	-	-
	25	~1300	~200

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REPORTED OBSERVATIONS OF CHLORACNEGENIC DISEASE IN INDIVIDUALS EXPOSED TO PCB's USED AT HIGH TEMPERATURES

Occupational Chloracne (appearing in high proportion of exposed workers)	Puccinelli, 1954 Meigs et al, 1954 Hofman et al, 1962 Birmingham, 1964
Yusho Disease •	~40 Japanese papers, 1969- ~10 Taiwanese papers, 1980-
• Primary toxicant identified as 2,3,4,7,8-pentachloro-dibenzofuran	Masuda et al, 1982

COMPARISONS BETWEEN YUSHO VICTIMS AND CAPACITOR WORKERS
IN PCB AND PCDF UPTAKE

	Yusho Victims		Directly Exposed Capacitor Workers
	Mean Dose	Minimum Toxic Dose	
Total Accumulation			
PCB's (g.)	0.63	0.11	>6
PCDF's (mg)	3.4	0.6	<0.01 (a)

a. Assuming <2 ppm PCDF in PCB absorbed

COMPARISONS BETWEEN YUSHO VICTIMS AND RATS IN PCB AND PCDF UPTAKE

Substance	Minimum Toxic Dose	
	Yusho Victims	Rats
Lower PCB's (g./kg)	0.002	> 4 (a)
Mixed PCDF's (ug/kg)	11	~10 (b)

a. Goldstein, 1975

b. Oishi, 1978

PROPOSITION:

YUSHO INCIDENTS DON'T PREDICT HEALTH EFFECTS RESULTING FROM ORDINARY, LOW TEMPERATURE PCB USAGE

- DIFFERENT CHEMICAL COMPOSITION
- DIFFERENT IDENTIFIED TOXICANT
- HEALTH EFFECTS NOT SEEN IN OTHER EXPOSED POPULATIONS