
Item ID Number 01656

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Report/Article Title Typescript: Dioxin Discussion Meeting - Veterans Administration, September 1, 1983

Journal/Book Title

Year 0000

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Color

Number of Images 15

Description Notes Includes meeting agenda, list of participants and a photocopy of Michele Flicker's handwritten notes from the meeting.

DIOXIN DISCUSSION MEETING - VETERANS ADMINISTRATION
Import-Export Building - Room 443
811 Vermont
Washington, D.C.

September 1, 1983

AGENDA

- 9:30 AM - J. S. Stanley - Opening Remarks, "Status of Adipose Tissue Analysis Programs"
- 9:45 - A. L. Young, "Status of VA/EPA Efforts in Adipose Tissue Programs"
- 10:00 - D. Stalling, "Applications of Pattern Recognition for Classification of PCDD/PCDF Data"
- 10:30 - J. McKinney, "Approaches to Bioincurred TCDD Studies"
- 11:00 - T. Tiernan, M. Taylor, "Interferences Encountered in the Analysis of Human Adipose Tissues"
- 11:30 - D. Cox, "Status of Survey Design Using NHMP Adipose Samples"
- 12:00 PM - Open Discussion

ADIPOSE MEETING

September 1, 1983

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REMARKS

Here is a summary of the meeting in note form which I presented to the VA advisory committee on health related effects

(I apologize for the handwriting - I had tried to type this but my memories of the salient points of the meeting.)

Questions? Before 9/22: FTS 754-1674
After 9/22: (816) 741-5647

FROM

Michelle

DATE

9/19/83

TEL. EXT.

I'm working on a typed version but am sending this to expedite available info.

Who I am -

VA/EPA coordinated program for the analysis of Dioxin in
human adipose tissue. purposes -

- ① Analytical method
- ② Detectable in human
- ③ Higher levels in war veterans
- ④ ~~correlation~~ correlation & health effects

I. PATTERN RECOGNITION

Highlights

A. - Data are now available → ^{Sources:} Canada

^{Sources:} Sweden

Dioxins, Furans - ^{agents, women do exist}
in the adipose tissue of ordinary citizens

That means we are not merely seeing the Dioxin
we know to have been present in Agent Orange,
^{related chemicals} but, from other sources -

such as fly ash

B. - Data also exist which imply a synergism ^{among} ~~toward~~
the chemicals ^{WRT health effects} ^(with respect to) Toxicity very much a function of co - Toxic ~~and~~

Toxic effects of ^{TDB} (e.g. Teratogenicity)
cleft palate

are magnified many-fold by, for example,
the presence of the furans

C. Find higher Dioxin + furans in accidental & occupational exposures

- Consensus ∴ reached in the panel that our
analytic method should be broad enough to
be able to detect several of these relatives
because such pattern recognition - i.e.
analyzing ^{WRT} ^{with respect to} relative proportions
of these related compounds (next sheet)

- will enable us to:
- ① get a handle on the origins - dietary fish vs A.O.
 - ② run a stricter quality control program

II. Bioinured

Also - because of the global distribution of these chemicals
 As part of developing our analytic method, it is also agreed that we should develop -

Bioinured standards

animals fed radioactively labelled representatives of these chemicals so that we can accurately test our methods + calculate yields - not confused by dioxins already "naturally present"

How much is due to exposure vs how much already there

9 Kg of FAT collected
 In Σ :

- Dioxin, Furans everywhere
 - Analytic Methods will be broader
 - Pattern recognition is a valid + necessary tool
- Have started

EPA has begun to identify the adipose tissue in its archives for Vietnam veterans

Calculations have been completed. Showing the study is feasible but has many complications/features



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REMARKS

Here are my reworked notes from the Dixon session.

I hope they are helpful.

Please call me should there be any questions - I have the original copy.

FTS til 9/22 - 754-1674 ← at work 10/6

Home 9/22 - 10/5 816-741-5647

FROM

M. Miller

DATE

9/20/83

TEL. EXT.

674

9/1/83

Discin Meeting
Washington, D.C.

- Search for methodology
baseline

Stanley - Standards

9 kg Adipose so far

No data on delay in Adipose tissue

Stalling - Pattern recognition - can be done & very useful for quality assurance

Dunn -> plot one of axes on 3 axes & get pt of 1.0
line (1 factor variable), plane - 2 factor variable

as well as regression +
verification of source

Rappe - Numer -

Blood -

SC_{1,2} - 2398

TCDD ->

Ironer

Yusho

> 12

B

Taiwan

2,37, P Tet CDF

< 3

< 3

< 30

< 30

Dairy Rates

My note

[This is probably from fat or blood]

(I was uncertain
which tissue
source Rappe
was describing)

occasionally exposed
in Scandinavia
75-85% reduction
octa, & hepta in 1 year

Yusho - PCB + PCDF

Three variables

-> 15% reduction

20% reduction

in 1 year (one)

PCP houses

160:1

165:1

octa

7 ppt

14

15

hept

5 ppt

hept CDD

dimer / adipose

CDF'S ~ 2/1

Andy Frankenberg

Baby

Isomer

Adipose tissue muscle? Omentum Diaphragm?

2,3,7,8

17

60

PBS

ny/s

3,6

27

38

64

48

Different target org ans diff isomers

Suedia, PCDD

P8/S

intense

Mengen Pesticide

2,4-D

2,4,5-T

milk

kidney

2,3,7,8

2 (1)

15 (1)

Octa-CDD

350 (4)

18 (4)

Hepta

STRIK, Netherlands

Adipose

tissue

Blood

2,3,7,8 -

5 PPT

ND

ND

Penta, Hexa, Hepta

Octa

Tetra CDF

was unable to copy part because

very little

E. Nordell

2,3,7,8 TCDF

PCDF hexa CDF

Hexa CDF PPT

hepta CDF

Octa CDF

12

9

6

30

150

56-81

(90-414)

2, 3, 7, 8 - 1.5 PPT

Penta 12 PPT

hexa CDD 19

Baltic - Herring, Fish-Eating Bird -

Tetra

Penta 1, 2, 3, 7, 8

Hexa 1, 2, 3, 4, 7, 8

Furans

Yusko liver -> 2, 3, 7, 8 - remainder of 64 congeners (Fur, lipid, dioxin = 70)

General exposure

tetra ≈ penta

Source of ^{1, 2, 3, 7, 8} penta CDD = Fly Ash?

Source of 2, 3, 7, 8 ≠ 2, 4, 5 T
2, 4, 5 TP
hexa chlorophen

∴ Pattern recognition is crucial

Bayhamton -

1,500

liver -> octa CDD

Hepta CDF

350 (8)

Highest liver

may be ≠ distribution

Σ Rappe - There is a background but it is complex

McKimm

Bioaccumulation → dioxin extraction, how much is 2^o exposure + how much originally there?

Toxicity → AH receptor (polarizability) ← electron
steric - how close the bonds are to
molecular active site
May want to pattern recognize the toxic compounds
vs the source point of dioxin

Toxicity is very much a function of the co-toxins
(TCDD reinforced by PCBs) PCBs >> Dioxin
e.g. incidence of left palate

Clair
Lippes
D. Stalling
- Tetrach 1, 3, 7, 8 CDD
hexachloro phenolphthalein ester } Agent Orange
very few furans - D F
- 107#

Phenols + phenoxyl phenols are not likely to be stored in adipose because they are readily conjugated + excreted

don Shroff → To generate the pattern → feed AD to animals
more feeding studies in cattle. 2, 3, 7, 8 →
Saponification will destroy the higher chlorinated dioxins

Furans - confirms simplifications of Dioxins + Furans in biological tissue

Mike Taylor

Schechter - Belgium - LLD ~ 10-20 PPT 2^o to interference.

Binghamton study:

Found higher dioxin + furan; exposed people may have had higher levels than control.
Dichloroethers are not the major interference.

Flowers "needs"
QA are \rightarrow spiked & desired + interferences

Schetter - Dilated ER + microsomal damage in liver ^{with} (biopsy) + LFT's elevated liver function tests
Jake Ryan - Tandem MS & Flash
variations in MS/MS (8, 10, 6) range of values on 1 sample

Advantages

Setup time

Sensitivity

Specificity

Disadvantages

isomer resolution (moderate)

expensive

FAT

Tetra

Penta

Hexa

Octa

2378 F

10.6 / 2.6

D.F

13.1 / 18.4

D.F

76 / 15.4

D.F

133 / 35

D.F

6 / 9 MD

6

1980

1978

ΣD

851

743

ΣE

71

(MS)² very good
levels up to PPB.

Joe Carra

Dave Cox - NHMP (National Human Monitoring)

Patricia Columbus (TAC)

Information retrieval - Toxic + Analysis Sample
retrieval samples come from Vietnam vets
need to go back to the institutions that the
samples were collected to get the ID.

TAC inventory 8,000 papers

EPA NHATS file 13,000 records, TAC information

Birth date / sex / No SS# (social security number)

Approach - Match letters 1937 + 52

MATCH TAC INVC EPA NHATS file

Contact institutions to get SS#

Check VA records

So far 544 potential vietnam vets - Approx 60 actual vietnam veterans

11% samples

92 institutions involved; 22 contacted with 122 records

50 SS#

Study Design: - Age, sex, + possible pair - get each veteran + a control

- Marine Division levels vet + control

- Assess statistical significance

Factors affecting detectable ratio

(See next page for definition of "detectable ratio")

1) Sample time

2) FP + FN rates

to falsely conclude vets he

3) Variable ages of the specimens + minor levels

no one known effect of storage over time

4) Combined variability - Analytic measurement prob

- Random variation in dioxin levels.

- Correlation betw dioxin levels of vets + control

Detectable ratio = (ie. ratio of elevated Dioxin levels in vets to controls in order to be detectable & statistically significant)

4.5 -> 1.5 Ratio of Dioxin levels detectable
Nud. Size of 100 to get a 2% (detectable ratio)

If variability is low, even a sample size of 30 can give useful results

Overall, variability is slightly more imp. than sample size in determining the detectability ratio

Question raised over

Subplot objectives -> differences in manufacture & sterilization procedures (Sander Strassman Study aware of this as a possible variable)

- Also can ↑ # of controls to improve the ratio
Eventually will or may model an region

Eventually may want to do a ~~total~~ profile
Conc. may indeed change in time in the fat samples
Many pit falls - body weight, height

May need a prospective study

Fish eater marker for example
Total body burden important ← already have this

Q: Does veteran veteran have Dioxin?
Does the Dioxin cause a document in health?

Someday we may tap into
Karlband

352-3584

Sander Strassman Study's phone #

Shadoff - look for a unique property in AD - such as carbon dating
Ape - e. ore phenylene

Barnes

- National Ocean Study