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Subgroup/Office of Origin: National AIDS Policy Office
Series/Staff Member: Kristine Gebbie
Subseries:

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August Chron Files 1993 [10]

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. report	[Personally Identifiable Information] [partial] (1 page)	00/00/1993	b(6)

COLLECTION:

Clinton Presidential Records
National AIDS Policy Office
Kristine Gebbie
OA/Box Number: 3766

FOLDER TITLE:

August Chron Files 1993 [10]

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RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

- P1 National Security Classified Information [(a)(1) of the PRA]
- P2 Relating to the appointment to Federal office [(a)(2) of the PRA]
- P3 Release would violate a Federal statute [(a)(3) of the PRA]
- P4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
- P5 Release would disclose confidential advice between the President and his advisors, or between such advisors [(a)(5) of the PRA]
- P6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Personal record misfile defined in accordance with 44 U.S.C. 2201(3).

RR. Document will be reviewed upon request.

Freedom of Information Act - [5 U.S.C. 552(b)]

- b(1) National security classified information [(b)(1) of the FOIA]
- b(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
- b(3) Release would violate a Federal statute [(b)(3) of the FOIA]
- b(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
- b(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
- b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
- b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
- b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

FEBRUARY 18, 1993

JOHN P. BADER, Ph.D.
CHIEF, ANTIVIRAL EVALUATIONS BRANCH
DEVELOPMENTAL THERAPEUTICS PROGRAM
DIVISION OF CANCER TREATMENT
NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTES OF HEALTH
ROCKVILLE PIKE
BETHESDA, MD 20892

DEAR DR. BADER,

ATTACHED ARE A COPY OF YOUR LETTER TO ME DATED JANUARY 26, 1993
AND A COPY OF PAGE 39 TAKEN FROM DRUGS, A TIME INC. PUBLICATION, COPYRIGHT
DATE 1967.

A BASIC QUESTION NEEDS TO BE ANSWERED - DOES ACETALDEHYDE DESTROY
THE AIDS VIRUS? FOR INSTANCE, IF A DROP OF ACETALDEHYDE WERE PLACED
IN A TEST TUBE CONTAINING THE BLOOD OF A VICTIM WHO HAD THE HIV VIRUS,
WOULD THAT VIRUS BE DESTROYED?

IF THE ANSWER TO THIS QUESTION IS "NO", YOU MAY AS WELL SKIP THE REST
OF THIS LETTER BECAUSE I'LL ONLY BE WASTING YOUR TIME.

HOWEVER, MY HUNCH IS THAT ACETALDEHYDE WILL DESTROY THE VIRUS,
AND I HAVE THE FOLLOWING OBSERVATIONS TO MAKE -

ON FEBRUARY 11 I BECAME AWARE OF PAGE 39 FROM DRUGS. AFTER READING
THIS PAGE I KNEW THAT I HAD FOUND THE POSSIBILITY OF A CURE FOR AIDS.
OF COURSE, I WAS EXTREMELY CURIOUS TO SEE IF ANYONE ELSE HAD EVER
THOUGHT OF IT BEFORE.

ON SATURDAY, FEBRUARY 13 I WENT TO THE CAMPUS LIBRARY OF INDIANA
UNIVERSITY NORTHWEST AND LOOKED AT THE ENTRIES HAVING TO DO WITH
"DISULFIRAM" IN THE CUMULATED INDEX MEDICUS. I STARTED WITH THE YEAR 1983
BECAUSE THAT IS WHEN THE FIRST MENTION OF "ACQUIRED IMMUNODEFICIENCY SYNDROME"
IS MADE IN THIS INDEX.

IN THE APRIL, 1992 ISSUE OF THIS INDEX AN ARTICLE WAS CITED -

ANTABUSE (DISULFIRAM) AND AIDS

AND IT APPEARED IN THE OCTOBER, 1991 ISSUE OF THE JOURNAL, "ALCOHOLISM,
CLINICAL AND EXPERIMENTAL RESEARCH".

ON MONDAY, FEBRUARY 15 THE SYSTEM SERVICES DIVISION OF THIS LIBRARY
OBTAINED FOR ME A FAX COPY OF THE ARTICLE FROM THE INDIANA UNIVERSITY
SCHOOL OF MEDICINE LIBRARY IN INDIANAPOLIS.

THE ARTICLE CITES FOUR ADDITIONAL REFERENCES. ONE REFERENCE WAS
FROM THE "JOURNAL OF EXPERIMENTAL MEDICINE", TWO WERE FROM "LANCET",
AND ONE WAS FROM "JAMA" (JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION).

ALL FOUR OF THESE REFERENCES WERE READILY AVAILABLE AT THE NORTHWEST
LIBRARY AND AT THE MEDICAL LIBRARY IN THE BUILDING JUST NEXT DOOR.

FROM WHAT I COULD UNDERSTAND FROM THESE ARTICLES, THERE SEEMS TO BE A DAWNING REALIZATION THAT SOMETHING VERY BENEFICIAL MIGHT BE AT HAND WITH THE UTILIZATION OF A METABOLITE OF DISULFIRAM. THIS METABOLITE HAS SEVERAL NAMES WITH THE SIMPLEST ONE BEING DITIOCARB OR DTC.

TO QUOTE FROM THE ARTICLE ITSELF - (IN A FEW PLACES I HAVE SUPPLIED THE PARENTHESIS AND THE UNDERLINES) -

"WHILE FOUR PATIENTS IN THE PLACEBO GROUP DEVELOPED CDC-DEFINED AIDS (CENTER FOR DISEASE CONTROL), NONE DID SO IN THE DTC GROUP. IN ADDITION, THE DTC GROUP SHOWED A DECREASE IN SPLENOMEGALY AND LYMPHADENOPATHY AND AN INCREASE IN CD4+ CELL COUNT AND SKIN TEST REACTIVITY."

"IT IS INTERESTING THAT MANY OF US IN THE FIELD OF ALCOHOLISM HAVE FOR DECADES BEEN ADMINISTERING A COMPOUND, DISULFIRAM, WHOSE METABOLITE DTC APPEARS TO BE BOTH SAFE AND EFFECTIVE FOR THOSE PATIENTS WITH SYMPTOMATIC HIV AND AIDS."

AND TO QUOTE FROM ONE OF THIS ARTICLE'S REFERENCES, "JAMA, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION", 265:1538-1544, MARCH 27, 1991, P.1543:

"IN SUMMARY, DITIOCARB IN THIS STUDY WAS BOTH SAFE AND EFFECTIVE THERAPY FOR THE PREVENTION OF DISEASE PROGRESSION TO NEW OIs (OPPORTUNISTIC INFECTIONS) IN PATIENTS WITH HIV INFECTION."

"DITIOCARB (IMUTHIOL) HAS BEEN GRANTED ORPHAN DRUG STATUS BY THE FOOD AND DRUG ADMINISTRATION FOR THE TREATMENT OF PATIENTS WITH AIDS."

IN NONE OF THE FIVE ARTICLES IS THERE ANY MENTION OF THE WORD, "ACETALDEHYDE".

DR. BADER, IN YOUR LETTER TO ME YOU STATED:

"THE MOLECULES YOU SUGGEST ARE NORMAL METABOLITES FORMED DURING NORMAL BODY FUNCTIONING, AND WOULD HAVE NO EFFECT ON HIV OR AIDS."

HOWEVER, CONSIDERING WHAT I BECAME AWARE OF ON FEBRUARY 11, WOULDN'T A NEW LIGHT BE THROWN UPON THE SITUATION, WOULDN'T IT REALLY BE "A TOTALLY NEW BALL GAME"?

THIS, OF COURSE, IS WHAT I BECAME AWARE OF ON FEBRUARY 11 - IF A PERSON HAS IN THEIR LIVER THE SUBSTANCE CALLED DISULFIRAM AND TAKES THE SLIGHTEST DRINK OF ALCOHOL, ACETALDEHYDE WILL FLOOD THROUGHOUT THAT PERSON'S BODY AS A DEADLY POISON.

MENTIONED THROUGHOUT THE CUMULATED INDEX MEDICUS ARE VARIOUS ARTICLES DEALING WITH THE ADVERSE EFFECTS OF ADMINISTERING DISULFIRAM; SOME OF THE TOPICS ARE - FULMINATING HEPATITIS, ARTHRITIS, LIVER DAMAGE, PSYCHOSES, TOXIC COMA, BRAIN DAMAGE, AND EVEN DEATH.

NO CELL IN THE BODY WOULD BE SAFE FROM FEELING THE EFFECTS OF THIS POISON.

OF COURSE, IF IT DESTROYS THE AIDS VIRUS AT THE SAME TIME, WHAT BETTER WAY COULD EVER BE FOUND TO CLEANSE THE BODY OF THIS DREADFUL ILLNESS?

CAREFUL, MEDICAL SUPERVISION OF THE PROCEDURE IS THE KEY; THE PROCEDURE COULD SIMPLY BE CALLED "THE DISULFIRAM/ALCOHOL PROCEDURE" FOR DESTROYING THE HIV VIRUS.

THE METHOD AND THE EFFECTS OF THE PROCEDURE WOULD BE AS FOLLOWS:

"PHYSIOLOGICAL THERAPIES. CHEMICAL FENCES. ONE OF THE POPULAR MODERN DRUG TREATMENTS OF ALCOHOLISM, INITIATED IN 1948 BY ERIC JACOBSEN OF DENMARK, USES DISULFIRAM (TETRAETHYLTHIURAM DISULFIDE). THE USUAL TECHNIQUE IS TO ADMINISTER HALF A GRAM IN TABLET FORM DAILY FOR A FEW DAYS; THEN, UNDER CAREFULLY CONTROLLED CONDITIONS AND WITH MEDICAL SUPERVISION, THE PATIENT IS GIVEN A SMALL TEST DRINK OF AN ALCOHOLIC BEVERAGE. THE PRESENCE OF DISULFIRAM IN THE DRINKER'S BODY CAUSES A REACTION OF HOT FLUSHING, NAUSEA, VOMITING, A SUDDEN SHARP DROP OF BLOOD PRESSURE, POUNDING OF THE HEART, AND EVEN A FEELING OF IMPENDING DEATH. THESE SYMPTOMS RESULT FROM AN ACCUMULATION OF THE HIGHLY TOXIC FIRST PRODUCT OF ALCOHOL METABOLISM - ACETALDEHYDE. NORMALLY, AS ALCOHOL IS CONVERTED TO ACETALDEHYDE, THE LATTER IS RAPIDLY CONVERTED, IN TURN, TO OTHER HARMLESS METABOLITES, BUT IN THE PRESENCE OF DISULFIRAM - ITSELF HARMLESS - THE METABOLISM OF ACETALDEHYDE IS BLOCKED, WITH THE RESULTING TOXIC SYMPTOMS."

ENCYCLOPAEDIA BRITANNICA, MACROPAEDIA, VOLUME 1, PAGE 447, 1974 EDITION

".....A PATIENT MUST BE WARNED BEFORE USE OF THE POSSIBLE REACTIONS FROM THE MIXTURE OF THE DRUG AND EVEN VERY SMALL AMOUNTS OF ALCOHOL. REACTIONS INCLUDE HEADACHE, THROBBING IN THE NECK, NAUSEA AND VOMITING, SWEATING, THIRST, AND BLURRED VISION. THEY VARY IN INTENSITY, GENERALLY IN PROPORTION TO THE AMOUNTS OF DRUG AND ALCOHOL INGESTED, AND LAST FROM 30 MINUTES TO SEVERAL HOURS."

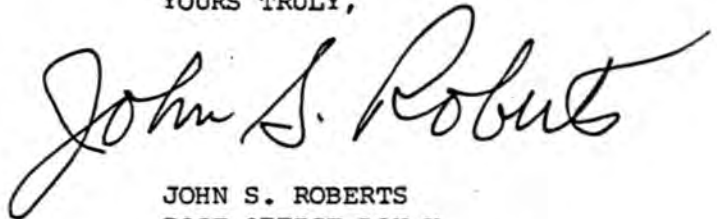
ACADEMIC AMERICAN ENCYCLOPEDIA, VOLUME 6, PAGE 202, 1985 EDITION

"ADMINISTRATION OF ANTABUSE, OR DISULFIRAM, AND TEMPOSIL, CITRATED CALCIUM CARBIMIDE, CAN HELP THE PATIENT CONTINUE IN THE PATH OF SOBRIETY. THESE DRUGS INCREASE THE CONCENTRATION OF ACETALDEHYDE IN THE BODY WHENEVER ALCOHOL IS CONSUMED, FOR THEY RETARD THE OXIDATION OF THAT SUBSTANCE TO ACETIC ACID. THE ACCUMULATION OF ACETALDEHYDE IN THE BODY PRODUCES A SERIES OF CHANGES WHICH RESEMBLE THOSE OF ACUTE HANGOVER. IN FACT, THE PATIENT FEELS SO UNCOMFORTABLE THAT FEAR OF THE RESULTS CAN STRENGTHEN ANY FALTERING DETERMINATION TO ABSTAIN FROM ALCOHOL. AFTER DISULFIRAM HAS BEEN TAKEN, EVEN THE SMALLEST AMOUNT OF AN ALCOHOLIC BEVERAGE CAN INITIATE ALMOST UNBEARABLE EFFECTS. THE DRINKER FIRST HAS A FEELING OF WARMTH IN HIS FACE; THE FACE, NECK AND CHEST ARE SUFFUSED WITH SCARLET AND THE EYES BECOME BLOODSHOT. AT THE SAME TIME HE IS AWARE OF PALPITATION OF THE HEART AND FEELS CHOKED FOR WANT OF AIR. NAUSEA AND VOMITING FOLLOW, AND THE INTENSE FLUSHING IS REPLACED BY PALLOR AS BLOOD PRESSURE FALLS."

ENCYCLOPAEDIA BRITANNICA, VOLUME 1, PAGE 550-551, 1971 EDITION

DR. BADER, IF HIV IS INDEED DESTROYED IN THE LABORATORY BY ACETALDEHYDE -
FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO -
RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.
COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR
NOT THE "DISULFIRAM/ALCOHOL PROCEDURE" IS EFFECTIVE IN CURING AIDS VICTIMS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO CONGRESSMAN PETER J. VISCLOSKY, DR. LUC MONTAGNIER, RANDY SHILTS
AND JIM GORDON

P.S. - FEBRUARY 19

LAST NIGHT, AFTER I HAD TYPED THIS LETTER, I WENT AGAIN TO THE LIBRARY
OF INDIANA UNIVERSITY NORTHWEST TO PICK UP THE FAX COPY OF ANOTHER ARTICLE
WHICH I HAD REQUESTED TO SEE.

IT COMES FROM THE "JOURNAL OF APPLIED TOXICOLOGY", OCTOBER, 1991, PAGES
373-6 AND THE TITLE OF THE ARTICLE IS 'ACETALDEHYDE'.

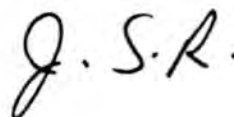
I DON'T KNOW WHETHER THIS PART OF THE ARTICLE HAS ANY PARTICULAR RELEVANCE
BECAUSE IT CONCERNS EXPERIMENTS ON RATS. HOWEVER, IT SAYS,

"IN CONTRAST, THE ACETALDEHYDE LEVELS IN THE LIVER FOLLOWING ETHANOL
ADMINISTRATION IS CONSIDERABLY HIGHER THAN THE OTHER TISSUES.

THE AUTHORS CONCLUDE THAT EITHER THE LIVER DOES NOT TAKE UP
ACETALDEHYDE FROM THE BLOOD OR ITS METABOLISM IS SO RAPID THAT IT
DOES NOT ACCUMULATE IN THE HEPATOCYTES. THE HALF-LIFE OF ACETALDHYE (sp.)
IN THE BLOOD WAS ESTIMATED AS 3.1 MIN." PAGE 374

AT SOME TIME DURING THE PAST MONTH I READ THAT ALL OF THE BLOOD IN THE
HUMAN BODY CIRCULATES THROUGH THE LIVER IN FOUR MINUTES TIME.

WITH "THE DISULFIRAM/ALCOHOL PROCEDURE" HOW LONG WOULD ACETALDEHYDE STAY
ACTIVE AS A POISON IN THE BODY? - - ONE/HALF HOUR?, ONE HOUR?, TWO HOURS?,
OR EVEN LONGER?





DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

January 26, 1993

Mr. John S. Roberts
P. O. Box H
Hobart, Indiana 46342

Dear Mr. Roberts:

The National Institutes of Health appreciates your concern about AIDS and your offer of a possibility for curing this dreaded disease. You are not alone either in your concern, or in offering suggestions for a cure. Nonetheless, serious qualified scientists with many years of experience in virology, biochemistry, molecular biology, and drug development related to AIDS research are devoted to this problem, and what may seem new and innovative to you has already been considered and/or tested by such scientists. The molecules you suggest are normal metabolites formed during normal body functioning, and would have no effect on HIV or AIDS. It is unfortunate that you have been encouraged to persist with your efforts to project what you think may be a cure for AIDS. With no hesitation, I can guarantee you that what you suggest would not be useful.

Sincerely yours,

A handwritten signature in black ink, which appears to read "John P. Bader".

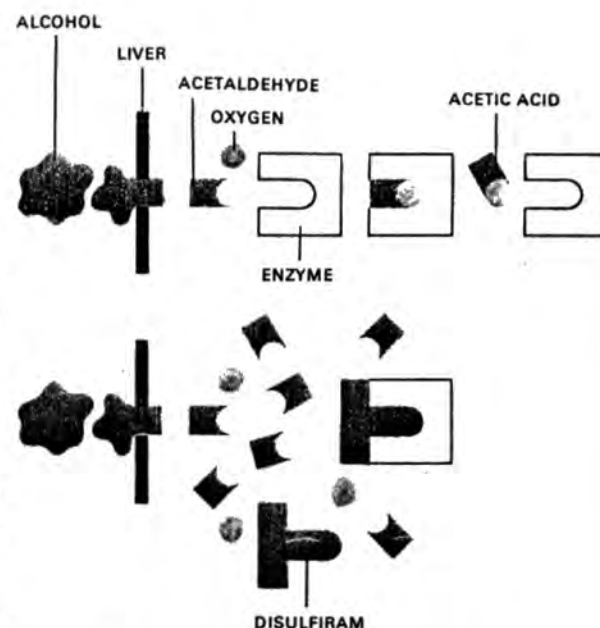
John P. Bader, Ph.D.
Chief, Antiviral Evaluations Branch
Developmental Therapeutics Program
Division of Cancer Treatment

JPBader:crj

Oddly enough, the interaction of alcohol with another chemical has been used to treat the most serious problem associated with the drug. Some 20 years ago, two Danish physicians were studying the compound disulfiram as a possible cure for intestinal worms. As part of their testing program, they dosed themselves with small quantities of the compound. Attending a cocktail party soon after, they suddenly found themselves flushed, dizzy and violently nauseated, with splitting headaches. On recovery, they suspected and soon confirmed that disulfiram was to blame. This substance, it turns out, inhibits the liver's transformation of alcohol. It blocks the second step in the process, in which acetaldehyde is transformed into acetic acid, thereby quickly producing a toxic pile-up of acetaldehyde in the body.

Anyone who has taken disulfiram (known commercially as Antabuse) cannot drink even a single glass without becoming violently ill. Unfortunately, as a treatment for alcoholism, disulfiram is seldom successful; the alcoholic usually finds he can give up disulfiram more easily than alcohol.

The limited usefulness of disulfiram indicates the frustrations the pharmacologist faces in trying to deal with the widespread disease of alcoholism. It cannot be explained, or even defined, in pharmacological terms alone. There is no known pharmacological reason why some people destroy their lives by drinking; neither dosage nor physical effects offer an infallible guide. A man who drinks heavily five nights out of seven may on occasion get drunk, but he is not necessarily an alcoholic. Some alcoholics, by contrast, may stay sober for days or even weeks at a time. But once they start drinking, they cannot stop short of abysmal intoxication. They are addicts, "hooked" on the drug alcohol. And addiction to alcohol, like addiction to any other drug, is essentially a psychological compulsion—and therefore the problems it raises are far more psychological, medical and social than pharmacological.



THE ACTION OF DISULFIRAM, a drug intended to discourage alcoholism, disrupts liver functioning so that an imbibor gets sick after drinking. The upper diagram shows how the liver normally handles alcohol. Entering the liver from left, alcohol is first converted into acetaldehyde, a poisonous substance, but this chemical and oxygen are quickly fitted together by an enzyme, forming harmless acetic acid. When disulfiram is taken (*lower diagram*), alcohol is converted into acetaldehyde, but disulfiram joins with the enzyme and prevents acetaldehyde from linking with oxygen to form acetic acid. As a result, toxic acetaldehyde collects, and the drinker becomes nauseated.

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

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PORTAGE, IN 46368
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February 11, 1993

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

Thank you for writing to update me on your research on the AIDS virus. I appreciate hearing from you.

In your letter, you asked if a pilot program can be established at two Chicago, Illinois hospitals to test whether or not acetaldehyde is effective in destroying the AIDS virus. Traditionally, the National Institutes of Health (NIH) is the principal biomedical research agency of the Federal Government. Therefore, I have taken the liberty of forwarding your letter to Dr. Bernadine Healy, Director of the National Institutes of Health, and have asked her to respond to your letter directly. Enclosed is a copy of my letter.

Should you have further questions regarding the development and implementation of AIDS research projects, I urge you to contact NIH. You may write to Dr. Bernadine Healy, Director, at the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, 20892.

Thank you again for sharing your thoughts with me. Should you have questions about federal legislation, please do not hesitate to let me know.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 19, 1993

THE HONORABLE PETER J. VISCLOSKY
UNITED STATES HOUSE OF REPRESENTATIVES
330 CANNON BUILDING
WASHINGTON, D.C. - 20515

DEAR CONGRESSMAN VISCLOSKY,

ATTACHED IS A COPY OF YOUR MAY 27, 1992 LETTER TO ME. THANK YOU VERY MUCH FOR THE HELP THAT YOU AFFORDED ME LAST YEAR.

I THINK THAT I HAVE DISCOVERED THE CURE FOR AIDS.

THROUGHOUT THE PAST THIRTEEN MONTHS THE IDEA HAS BEEN KICKING AROUND IN MY BRAIN THAT I MIGHT BE GENERATING IN MY BODY SOME SORT OF AN ACID THAT COULD BE EFFECTIVE IN DESTROYING THE AIDS VIRUS. AS I STUDIED A LITTLE BIT MORE ABOUT THE WAY ALCOHOL IS METABOLIZED IN THE BODY, I HAVE JUST ABOUT COME TO THE CONCLUSION THAT THAT ACID IS ACETIC.

NOW, WHETHER ACETIC ACID CAN OR CANNOT DESTROY THE AIDS VIRUS - I DON'T KNOW. HOWEVER, I HAVE BECOME AWARE OF SOMETHING MORE IMPORTANT.

I BELIEVE THAT IT WAS ON NEW YEAR'S DAY THAT MY WIFE SHOWED ME THE ATTACHED ARTICLE ABOUT A "HANGOVER CURE".

I READ THIS ARTICLE A COUPLE OF TIMES. AT SOME TIME DURING THE FIRST WEEK OF THIS MONTH THIS IDEA HIT ME LIKE A TON OF BRICKS -

THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

AS I REFLECT UPON THE PAST THIRTEEN MONTHS AND THE POINT I WAS TRYING TO MAKE ABOUT ACID IN MY BODY, I FEEL AS IF I HAD BEEN PLAYING WITH A FIRECRACKER AND HAVE ALL OF A SUDDEN BEEN HANDED A STICK OF DYNAMITE AND THAT DYNAMITE IS CALLED ACETALDEHYDE.

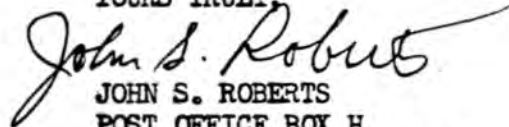
ON JANUARY 11 I MAILED THE ATTACHED LETTER TO DR. LUC MONTAGNIER WITH COPIES TO DR. JOHN BADER AND RANDY SHILTS.

IT IS MY HYPOTHESIS THAT WHILE ACETALDEHYDE IS POISONING THE BODY,
IT WILL AT THE SAME TIME DESTROY THE AIDS VIRUS.

FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO - RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.

COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR NOT ACETALDEHYDE IS EFFECTIVE IN DESTROYING THE AIDS VIRUS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO DR. LUC MONTAGNIER, DR. JOHN BADER AND RANDY SHILTS

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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May 27, 1992

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

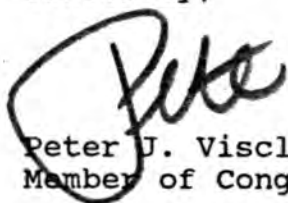
Thank you for sending me a copy of your letter to Dr. Luc Montagnier of the Institut Pasteur in Paris, France. I appreciate hearing from you.

I share your concern that a cure must be found for the devastating illness, Acquired Immunodeficiency Syndrome (AIDS). The illness is caused by the Human Immunodeficiency Virus (HIV) which causes an impairment of the immune systems and leaves its victims susceptible to certain types of cancer and a number of opportunistic diseases. Although drugs such as AZT have been developed to prolong the life of AIDS patients, there is currently no cure.

As you know, on January 31, 1992, I contacted the National Institutes of Health (NIH), on your behalf, regarding NIH's policy for donating blood samples for AIDS research. As a result of this action, on March 12, the NIH responded to your letter directly, and informed you to contact Dr. John P. Bader, who is responsible for the National Cancer Institute Preclinical AIDS Drug Screening Program, regarding the feasibility of analyzing your blood sample. Enclosed is a copy of NIH's letter. Should you have any questions regarding AIDS research-related federal legislation or have problems in contacting NIH, please do not hesitate to let me know.

Thank you again for sharing your thoughts with me.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 11, 1993

DR. LUC MONTAGNIER
25 RUE DU DOCTEUR ROUX
INSTITUT PASTEUR
PARIS, FRANCE 75015

DEAR DR. MONTAGNIER,

LAST YEAR I WROTE TO YOU A LETTER IN WHICH I ASKED IF YOU WOULD BE
INTERESTED IN TESTING MY BLOOD TO SEE WHETHER THERE POSSIBLY COULD BE
SOMETHING IN IT THAT WOULD DESTROY THE AIDS VIRUS.

IN THAT LETTER I ALSO SAID,

"YEARS AGO I SAW A TELEVISION PROGRAM IN WHICH SOMEONE SAID
THAT PERSONS WHO DRANK BRANDY DID NOT CATCH INFLUENZA
DURING THE HORRENDOUS EPIDEMIC OF 1918-1919."

ATTACHED IS A COPY OF A NEWSPAPER ARTICLE WHICH I RECENTLY READ.

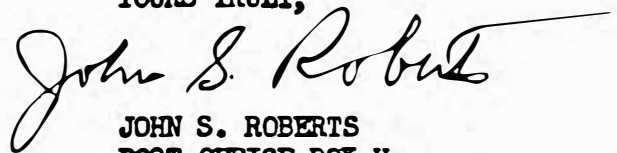
THIS ARTICLE CAUGHT MY ATTENTION BECAUSE I DO DRINK SOME ALCOHOL
EVERY NIGHT.

HAS ANY RESEARCH EVER BEEN CONDUCTED TO SEE WHETHER ACETALDEHYDE
MIGHT BE EFFECTIVE IN DESTROYING THE AIDS VIRUS?

COULD ACETALDEHYDE BE INJECTED INTO A PERSON WITH NO ILL EFFECTS
OTHER THAN TO MAKE THAT PERSON EXTREMELY SICK FOR A DAY?

BEING TOXIC, PERHAPS ACETALDEHYDE WAS THE SUBSTANCE THAT DESTROYED
THE INFLUENZA VIRUS. IN THE SAME MANNER, COULD IT ALSO POSSIBLY DESTROY
THE AIDS VIRUS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
UNITED STATES OF AMERICA

COPIES TO: DR. JOHN P. BADER
NATIONAL INSTITUTES OF HEALTH
ANTIVIRAL EVALUATIONS BRANCH
BETHESDA, MARYLAND

RANDY SHILTS
SAN FRANCISCO CHRONICLE
SAN FRANCISCO, CALIFORNIA

ORANGE BOWL

Nebraska vs. Florida St.
(Ch. 5, 16)

7:30 p.m.

SUGAR BOWL

Alabama vs. Miami (Ch. 7, 28)

side of the bowl.
"Flash Gordon" and
Cruise, "Close Encounte.
Kind" and "Blade Runner." at

WPWR (Ch. 50) counters with
starting at 9 a.m. with "The Shaggy Dog,"
"Son of Flubber" "That Darn Cat," "Alice in
Wonderland" "Return to Oz" and "Return
from Witch Mountain."

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Hangover cure? Nope

The Associated Press

► HEALTH

Even if you're in no condition to read this, you probably know that aspirin won't cure it and water won't prevent it.

It's the hangover, and it's inevitable if you drink too much alcohol.

The headache, upset stomach and bad aftertaste that accompany a hangover come from the toxic by-product of alcohol, a chemical called acetaldehyde, said Russell Mankes, associate professor of toxicology and pharmacology at the Albany Medical College.

Some typical folk remedies — eating cold pizza, taking aspirin before bed or drinking another cocktail — may do more harm than good.

Aspirin and ibuprofen are bad for the stomach lining and popping one when the stomach is already irritated from drinking dramatically increases the risk of an ulcer, Mankes said.

Tylenol won't harm the stomach, but it can strain the liver, which is already being damaged by the alcohol, Mankes said.

Drinking water while still intoxicated won't help either. Because alcohol induces urination, all the water that comes in, goes out, taking with it minerals and salts.

Don't even think about drinking another alcoholic beverage to reduce hangover symptoms.

"The 'hair of the dog' is the first step on the road to alcoholism," he said.

Coffee won't make a drinker sober. "All you end up with is a wide-awake drunk," he said.

So what's the cure?

"Avoid getting one in the first place," Mankes said. "That does not mean avoiding alcohol. One can drink responsibly."

AUGUST 31, 1993

TO: Ms. Kristine Gebbie
ATTENTION: Aids Policy Coordinator

FROM DECEMBER, 1985 TO JUNE, 1986 AN AMAZING THING HAPPENED IN FRANCE -

THE MEDICAL CONDITION OF SOME AIDS PATIENTS IMPROVED, AND THEY WERE NOT TAKING AZT.

THE FACTS ARE RELATED IN ONE OF THE MOST PRESTIGIOUS MEDICAL JOURNALS PUBLISHED IN THE WORLD - "THE LANCET", SEPTEMBER 24, 1988 ISSUE.

AS THE STUDY (ENCLOSED) STATES ON PAGE 704:

"WHEN CHANGE IN CLINICAL STATUS WAS SCORED AS IMPROVED, STABLE, OR WORSE BY THE PHYSICIANS AFTER 16 WEEKS, 42% OF THE DITIOCARB RECIPIENTS HAD IMPROVED COMPARED WITH ONLY 5% IN THE PLACEBO GROUP ($p < 0.01$)."

WHY THE IMPROVEMENT?

BY READING MY PROPOSAL YOU CAN SEE WHAT I THINK THE ANSWER TO BE.

I AM NOT A PHYSICIAN; CONSEQUENTLY, I CANNOT CONDUCT CLINICAL TRIALS.

MY HOPE IS THAT WHOEVER READS THIS HAS THE INTEREST AND WHEREWITHAL TO CONDUCT CLINICAL TRIALS TO TEST THE VALIDITY AND THE EFFECTIVENESS OF THE "DISULFIRAM/ALCOHOL PROCEDURE".

John S. Roberts

JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

P.S. TO CONGRESSMAN VISCLOSKY: COULD YOU DO ONE MORE THING FOR ME? IN MY PROPOSAL I NOTED THE FACT THAT DR. PETER S. ARNO STATED IN HIS BOOK, AGAINST THE ODDS - THE STORY OF AIDS DRUG DEVELOPMENT, POLITICS & PROFITS: "BETWEEN 1987 AND 1991 THE NATIONAL CANCER INSTITUTE TESTED 40,000 CHEMICAL COMPOUNDS AT FACILITIES IN FREDERICK, MARYLAND, AND BIRMINGHAM, ALABAMA, TO SEE IF ANY COULD DISABLE THE AIDS VIRUS." WOULD YOU PLEASE FIND OUT FROM THE NATIONAL CANCER INSTITUTE IF ACETALDEHYDE WAS ON THAT LIST OF 40,000. THANKS AGAIN FOR ALL YOUR HELP. *J.S.R.*

ENCLOSED: COPIES OF MY PROPOSAL, MY JUNE 26 LETTER TO CONGRESSMAN VISCLOSKY (INCLUDES "THE LANCET" STUDY), DR. HEALY'S LETTER TO CONGRESSMAN VISCLOSKY, CONGRESSMAN VISCLOSKY'S LETTERS TO DR. KIPSCHSTEIN AND MS. GEBBIE AND MY LETTER TO DR. CARAUX



National Institutes of Health
Bethesda, Maryland 20892

Building: 1
Room: 126
(301) 496-2433

JUN 25 1993

The Honorable Peter J. Visclosky
House of Representatives
Washington, DC 20515-1401

Dear Mr. Visclosky:

This is in response to your May 26 letter regarding additional correspondence from one of your constituents, Mr. John S. Roberts, who has written regarding AIDS research. Mr. Roberts has suggested that a researcher at the Thomas Jefferson University in Philadelphia evaluate an agent that Mr. Roberts proposes has anti-HIV properties. We understand from previous correspondence directed to the National Institutes of Health (NIH) that Mr. Roberts believes that, by meditating on his pineal gland and drinking alcohol, he can generate an acid, acetaldehyde, that may cure his myopia and cure AIDS.

Mr. Roberts' initial inquiry in January was forwarded to Dr. John Bader, Chief of the Antiviral Evaluation Branch at the National Cancer Institute (NCI). Dr. Bader oversees the drug screening program that evaluates the anti-HIV properties of natural product extracts and synthesized drugs. After review of Mr. Roberts' letter, Dr. Bader informed him that the molecules he suggested for evaluation "are normal metabolites formed during normal body functioning, and would have no effect on HIV or AIDS."

In response to an additional inquiry from Mr. Roberts that suggested a therapeutic role for alcohol in HIV-infected individuals, Dr. Jack Whitescarver, Deputy Director of the NIH Office of AIDS Research, informed him of research sponsored by the National Institute of Alcohol Abuse and Alcoholism that showed alcohol consumption suppresses the human immune system and may accelerate complications associated with HIV infection.

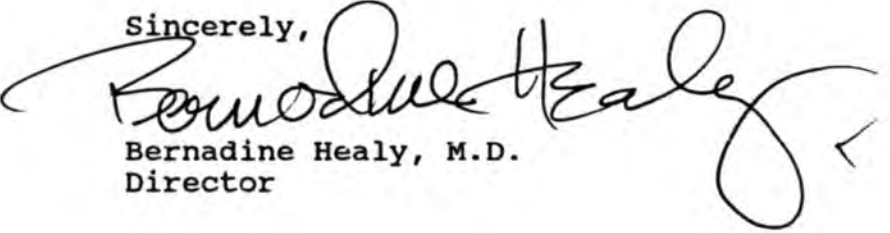
Mr. Roberts subsequently learned that a drug known as Ditiocarb (DTC), which happens to disrupt the metabolism of alcohol and increase blood concentrations of acetaldehyde, is being investigated as a possible anti-HIV agent. This led him to the incorrect conclusion that his theory regarding acetaldehyde was viable. The fact that DTC increases acetaldehyde concentrations, however, is unrelated to the proposed action of DTC. It is thought that DTC may induce the liver to produce hepatosin, which

Page 2 - The Honorable Peter J. Visclosky

in turn may stimulate the immune system. Acetaldehyde, however, only has been associated with some of the side effects of DTC, e.g., fatigue and nausea.

As there is currently no scientific basis to believe that acetaldehyde has any anti-HIV activity, the NIH is not pursuing the development or preclinical evaluation of this agent. I hope you will find this information useful in addressing Mr. Roberts request for assistance.

Sincerely,

A handwritten signature in cursive script, reading "Bernadine Healy". The signature is written in dark ink and is positioned to the right of the typed name and title.

Bernadine Healy, M.D.
Director

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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July 23, 1993

Dr. Ruth Kirschstein
Acting Director
National Institutes of Health
Bethesda, Maryland 20892

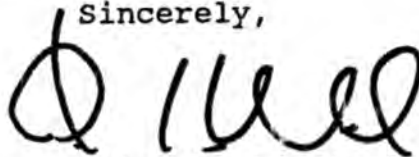
Dear Dr. Kirchstein:

I write on behalf of Mr. John Roberts, a resident of Indiana's First Congressional District.

Mr. Roberts has asked that I forward to you the enclosed packet of information regarding a possible treatment for those infected with the AIDS virus.

Thank you in advance for your serious consideration of this matter. Do not hesitate to let me know if you have any questions or need additional information.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV/sjg
Enclosure

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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Ms. Kristine Gebbie
Director of AIDS Policy
The White House
1600 Pennsylvania Avenue
Washington, D.C. 20500

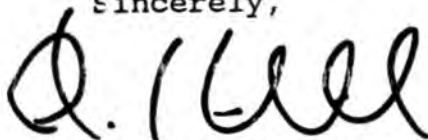
Dear Ms. Gebbie:

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Mr. Roberts has asked that I forward to you the enclosed packet of information regarding a possible treatment for those infected with the AIDS virus.

Thank you in advance for your serious consideration of this matter. Do not hesitate to let me know if you have any questions or need additional information.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV/sjg
Enclosure

JULY 19, 1993

DR. JEAN CARAUX
DEPARTMENT OF IMMUNOLOGY
INSTITUT MERIEUX
BP 7046
69348 LYON CEDEX 7
FRANCE

DEAR DR. CARAUX,

PLEASE EXCUSE ME, BUT I HAVE TO WRITE TO YOU IN ENGLISH. I NEVER LEARNED FRENCH. I HOPE THAT THIS DOES NOT CONSTITUTE A PROBLEM.

LAST MONTH I SENT TO YOU A COPY OF MY RESEARCH ENTITLED:

"A PROPOSAL FOR A PROCEDURE WHICH MIGHT PROVE TO BE EFFECTIVE IN DESTROYING THE HIV VIRUS."

I HAVE A QUESTION TO ASK YOU CONCERNING THE RESEARCH WHICH YOU AND YOUR COLLEAGUES CONDUCTED BETWEEN DECEMBER, 1985 AND JUNE, 1986 AND WAS PUBLISHED BY "THE LANCET" IN SEPTEMBER 24, 1988; THE RESEARCH IS ENTITLED:

"RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION".

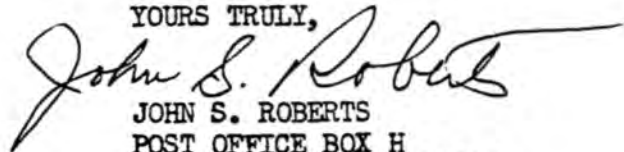
THE QUESTION IS -

DID YOU OR YOUR COLLEAGUES HAPPEN TO NOTICE OR ASK IF THE DITIOCARB PATIENTS WERE DRINKING WINE WITH THEIR MEALS?

IN MY OWN RESEARCH I ASSUMED THAT THEY WERE DRINKING WINE WITH THEIR MEALS BECAUSE IT IS THE CUSTOM IN FRANCE TO DO SO. OF COURSE, I COULD BE WRONG.

DR. CARAUX, I REALLY WOULD LIKE TO HEAR FROM YOU. THANK YOU FOR GIVING THIS MATTER YOUR TIME AND CONSIDERATION.

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
UNITED STATES OF AMERICA

COPIES TO: CONGRESSMAN PETER J. VISCLOSKY
PROFESSOR RUSSELL F. MANKES
DR. RUTH KIRSCHSTEIN, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
KRISTINE GEBBIE, AIDS POLICY COORDINATOR
INDIANA UNIVERSITY SCHOOL OF MEDICINE, DR. SUBBIAH SIVAM

JUNE 26, 1993

THE HONORABLE PETER J. VISCLOSKY
PUBLIC FORUM
PORTAGE PUBLIC LIBRARY
PORTAGE, INDIANA

DEAR CONGRESSMAN VISCLOSKY,

IT IS A PLEASURE TO MEET YOU IN PERSON.

WOULD YOU PLEASE OBTAIN FROM DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, THE ANSWER TO THIS QUESTION -

IS THE HIV VIRUS DESTROYED IN THE TEST TUBE BY ACETALDEHYDE?

IF THE ANSWER IS "YES", I THINK THAT THE LANG STUDY (COPY ATTACHED) SHOULD BE GIVEN CLOSE SCRUTINY.

IT IS MY FIRM CONVICTION THAT TWO BASIC FACTORS WERE NOT TAKEN INTO CONSIDERATION DURING THE COURSE OF THIS STUDY -

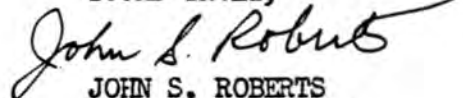
1. THE AMOUNT OF ALCOHOL THAT THE FRENCH DITIOCARB PATIENTS WERE DRINKING ON A DAILY BASIS.
- AND
2. THE CONSEQUENT AMOUNT OF UNMETABOLIZED ACETALDEHYDE THAT WAS BEING GENERATED WITHIN THEIR BODIES.

IT IS MY HYPOTHESIS THAT IT WAS THIS UNMETABOLIZED ACETALDEHYDE THAT WAS DESTROYING THE HIV VIRUS ITSELF - THUS CAUSING THE FRENCH DITIOCARB PATIENTS TO SHOW IMPROVEMENT IN THEIR CONDITIONS.

IF THE AUTHORS OF THIS STUDY (LANG, TREPO, KIRSTETTER ET AL) DO CONFIRM MY ASSUMPTION THAT THE FRENCH DITIOCARB PATIENTS WERE INDEED DRINKING ALCOHOL - NAMELY, WINE (SEE ATTACHMENTS) - ON A DAILY BASIS, I THINK THAT GOVERNMENTAL AUTHORITIES AND AGENCIES SHOULD ALERT THE PUBLIC THAT A VIABLE TECHNIQUE IS EXTANT WHEREBY IMMEDIATE THERAPY CAN BE RENDERED TO VICTIMS OF HIV AND AIDS - I SHALL SIMPLY CALL IT THE "DISULFIRAM/ALCOHOL PROCEDURE". THOSE KNOWING HOW TO ADMINISTER IT ARE PHYSICIANS SPECIALIZING IN THE "ANTABUSE" TREATMENT FOR ALCOHOLISM.

CONGRESSMAN VISCLOSKY, THANK YOU AND DR. HEALY FOR GIVING THIS MATTER YOUR TIME AND CONSIDERATION.

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342

COPIES WITH ATTACHMENTS TO:

DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
PROFESSOR RUSSELL F. MANKES, DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY,
THE ALBANY MEDICAL COLLEGE
INDIANA UNIVERSITY SCHOOL OF MEDICINE, NORTHWEST CAMPUS, GARY, INDIANA

possibility that naloxone may have had a positive inotropic effect as well.

Even in animal models, the mechanism of action of naloxone in reversing the haemodynamic changes of shock remains controversial. Holaday and Faden² suggested that central endorphin receptor blockade increases adrenal catecholamine release, basing this on the observation that naloxone was associated with a rise in serum adrenaline levels. However, Lechner et al¹⁰ suggested that naloxone potentiated the effects of circulating catecholamines on the myocardium resulting in improved contractility. Evidence for this suggestion was derived from an adrenalectomised dog with haemorrhagic shock in which serum catecholamines were kept constant. Recently Gurll et al¹¹ demonstrated improved left ventricular contractility after intravenous naloxone in a primate septic shock model despite observed three to five fold rises in plasma beta-endorphin and beta-lipotropin concentrations. Sagy et al¹² have shown a positive inotropic effect on isolated rat myocardium with D-naloxone—a non-opioid-blocking isomer. This effect was not prevented by pretreatment with propranolol, phentolamine, or morphine suggesting a primary cardiac site of activity unrelated to adrenergic or opioid receptors.

Because of the small population we studied, and the limited duration of naloxone infusion, we are not able to comment on its longer-term effects on haemodynamics or ultimate survival. Nevertheless, five patients from the naloxone group were discharged from hospital compared with only one in the placebo group, so we have no reason to suspect any lasting adverse effects of the infusion.

More extensive trials will be required to assess whether naloxone is a useful addition to current vasopressor/inotrope therapy and whether there is a positive effect on longer-term outcome. In addition, the unexpected finding of positive haemodynamic effects occurring only more than 4 h after the initial bolus of naloxone is not consistent with many of the currently proposed pharmacological actions of naloxone. Our results may stimulate new interest in this controversy.

We thank the nursing staff of the medical and surgical intensive care units at the Health Sciences Centre for their help in carrying out this trial. The study drug was provided by Du Pont Canada, Inc.

Correspondence should be addressed to D. E. R., Medical Intensive Care Unit, Health Sciences Centre, 820 Sherbrook Street, Winnipeg, Manitoba, R3A 1R9, Canada.

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RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION

JEAN-MARIE LANG¹ JEAN-LOUIS TOURAINE²
CHRISTIAN TREPO³ PATRICK CHOUTET⁴
MYRIAM KIRSTETTER⁵ ANNIE FALKENRODT¹
LAURENCE HERVIOU⁴ JEAN-MICHEL LIVROZET²
GENEVIEVE RETORNAZ³ FRANÇOISE TOURAINE²
GÉRARD RENOUX⁴ MICHELINE RENOUX⁴
MIRCEA MUSSET⁶ JEAN CARAUX⁶
AND THE AIDS-IMUTHIOL FRENCH STUDY GROUP*

Hôpital Hautepierre, Strasbourg;¹ Hôpital Edouard Herriot, Lyon;²
Hôtel Dieu, Lyon;³ Hôpital Bretonneau, Tours;⁴
Hôpital Saint Vincent de Paul, Paris;⁵
Department of Immunology, Institut Mérieux, Lyon;⁶ France

Summary 83 patients with human immunodeficiency virus (HIV) infection (CDC groups II, III, or IV-A) were randomised in a crossover trial of sodium-diethyldithiocarbamate (ditiocarb sodium, 'Imuthiol') (10 mg/kg body weight given orally once a week) against placebo. Each arm of the trial lasted 16 weeks. The disease did not progress to CDC-defined acquired immunodeficiency syndrome in the ditiocarb group but did so in 4 patients in the placebo group (3 between week 0 and 16, 1 between week 17 and 32). Ditiocarb was also associated to a significantly greater extent than placebo with relief of constitutional symptoms, improvement in clinical status (including shrinkage of enlarged spleen and lymph nodes), and improvement in immune function (as measured by CD4+ cell count and skin test reactivity). When placebo was replaced by ditiocarb, similar improvements were observed, whereas symptoms slowly reappeared and CD4+ cell levels progressively declined when ditiocarb treatment was replaced by placebo.

Introduction

SODIUM diethyldithiocarbamate (INN-ditiocarb sodium, 'Imuthiol') has potent immunorestorative, notably thymomimetic, properties.^{1,2} Ditiocarb, which is not mitogenic per se, induces the differentiation of T-cell precursors into mature and competent effectors, even in the absence of functional thymic epithelium.¹ It has been effective against the murine AIDS model (LP-BM5) of retroviral infection.³⁻⁴ It prevented disease and prolonged survival as long as treatment was maintained. The precise means by which ditiocarb exerts its effects has not been elucidated. However, it is well known that ditiocarb can influence several intracellular reactions. As a chelator of heavy metals ditiocarb is a potential antiviral agent,⁵⁻⁶ inhibiting a number of Cu-dependent enzymes;⁷⁻⁸ this property might affect the metal-dependent Tat gene product of HIV.⁹ By scavenging free-oxygen radicals, and by interfering with the metabolism of glutathione, it exerts anti-oxidant cytoprotective effects.^{10,11}

A previous clinical trial of ditiocarb in cancer patients in relapse¹⁴ has shown that ditiocarb can induce dose-

*The following persons are members of the AIDS-Imuthiol French Study Group: Macha Bachelet, André Burkel, Claude Charbonnier, Hervé Caspard, Michel Defayolle, Marie-Christine Delsaux, Jean-Marie Dupuy, Sonia Escaich, Alain Goudeau, Jean Paul Heyraud, Daniel Pialot, Corinne Platel, Marie-Paule Richard, Louise Telvi.

dependent restoration of delayed-type hypersensitivity. Since ditiocarb inhibited HIV infection in vitro,¹⁵ a pilot group of HIV-infected patients was given ditiocarb, with restoration of delayed-type hypersensitivity and a rise in CD4+ cell counts.^{16,17} A second pilot study comparing intravenously administered ditiocarb against no treatment showed that it produced improvement in symptoms of AIDS-related complex (ARC) and hampered progression to AIDS.¹⁸

On the basis of these findings, we conducted a randomised, double-blind, placebo-controlled trial to evaluate the clinical and immunological impact of ditiocarb in patients infected with HIV, before the occurrence of AIDS. We report here clinical and immunological data supporting the efficacy of ditiocarb in this group of HIV-infected patients.

Patients and Methods

Patients

All patients admitted to the study had serum antibodies to HIV by the Western blot technique. Patients were eligible if they belonged to groups II, III, or IV-A of the CDC classification¹⁹ and had a CD4 positive helper-inducer lymphocyte count of less than 600/ μ l. Patients were excluded if they had already presented with a single episode of any of the disorders included in the case definition of AIDS—opportunistic infections, neuropathy, or neoplasia, or if they were pregnant or lactating. Participants were recruited from five medical centres. The study was approved by the ethics committee at each participating centre, and patients gave their informed consent.

Study Design, Drug Regimens, and Monitoring of Patients

Patients were randomly assigned to treatment with either ditiocarb or placebo. Ditiocarb was given orally once a week in a dose of 10 mg/kg body weight (enterocoated capsules, 125 mg ditiocarb per capsule). After 16 weeks patients were crossed over to the alternative treatment for another 16 weeks. The crossover design was chosen for ethical reasons, to give every patient a chance to benefit from a possible favourable clinical effect of ditiocarb. Furthermore, at the end of the 3 months' double-blind follow up, all patients were offered the opportunity to receive ditiocarb in an open manner.

Every 8 weeks patients were examined and the following laboratory investigations were performed: blood counts, T-lymphocyte phenotyping by indirect immunofluorescence or flow cytometry with monoclonal antibodies and Ficoll-Hypaque-separated peripheral blood mononuclear cells, quantitative immunoglobulin determination, and serological tests for hepatitis B, cytomegalovirus, and Epstein-Barr virus. Every 16 weeks, delayed type hypersensitivity reactions were evaluated by means of a 'Multitest' apparatus (Institut Mérieux, Lyon) with seven antigens—tetanus toxoid, diphtheria toxoid, *Streptococcus* group C, tuberculin, candida, *Trichophyton mentagrophytes*, *Proteus mirabilis*—and a glycerin control. Lymphadenopathy was scored as follows: lymph node size < 1 cm, score 2; 1–2 cm, score 4; > 2 cm, score 8; the overall score was the mean score of left and right axillary and cervical nodes. Peripheral blood lymphocytes and serum samples from some patients were frozen and examined later for HIV load in culture (reverse transcriptase assay) or presence of viral antigen p24 (Abbot diagnostics).

Criteria for Clinical Response

Clinical evaluation was based on (i) progression to AIDS, (ii) clinical status (number and severity of symptoms in group IV-A patients), and (iii) influence on lymphadenopathy and splenomegaly. Serious events were not taken into account when they occurred less than 4 weeks after onset of treatment. All clinical data were carefully cross-checked by a panel of investigators to classify patient's clinical status according to the CDC classification.¹⁹

TABLE 1—DEMOGRAPHIC, CLINICAL, AND BIOLOGICAL FEATURES OF PATIENTS AT ENTRY

	Ditiocarb (n = 42)	Placebo (n = 41)
Mean age (yr)	32.6 (SD 7.0)	32.7 (SD 7.5)
Number of females	6	5
Risk groups		
Number homosexuals	30	32
Number i/v drug abusers	3	4
Number others	9	5
CDC group		
Number in group II	5	6
Number in group III	26	29
Number in group IV-A	11	6
Mean weight (kg)	65.6	62.8
Number with splenomegaly	7	8
Mean CD4+ count (/ μ l)	405 (SD 111)	389 (SD 131)
Mean IgG (g/l)	21.8	21.2
Mean IgA (g/l)	2.56	2.79
Proportion anergic	6/35	6/39

Data Handling and Statistical Analysis

The comparison of ditiocarb vs placebo was based on data from the first 16 weeks; data obtained after crossover were used only to assess the effect of ditiocarb interruption in the first group, or the effect of replacing placebo by ditiocarb in the second. Data were analysed with the Statistical Analysis System (SAS) version 6.02—procedure FREQ for comparison of qualitative data (χ^2 test, Fisher's exact test) and TTEST (Student's *t* test) for comparison of quantitative data. Fisher's exact test was used when theoretical frequencies were smaller than 5.

Results

Subject Groups

94 patients were considered for the study but 11 were excluded for the following reasons: CD4+ cell counts > 600/ μ l at entry (7), refusal to participate (2), serum antibodies to HIV not confirmed by Western blot (1), and detection of a Kaposi sarcoma at start of treatment (1). Thus 83 were randomised in the study between December, 1985, and June, 1986. The treatment and placebo groups were similar in all respects (table 1). During the first 4 months, 2 patients died: 1 died 10 days after enrolment from narcotic drug overdose, and the other after progression to AIDS. During these 16 weeks 6 patients withdrew for the following reasons: lost to follow up (4), intolerance (1), patient's choice (1). Thus 77 patients were evaluable after 4 months, and 75 entered the second phase. During the second 4 months, 1 patient died after AIDS developed, and 14 patients withdrew: lost to follow up or poor compliance (10), intolerance (1), patient's choice (3). Thus, 61 patients were evaluable after 8 months. No patient received zidovudine during the trial since it was not readily available in France then.

Clinical Effects

No patients in the ditiocarb group went on to have AIDS while 3 in the placebo group did so during the first 16 weeks of treatment (table 1). After 8 weeks 1 patient in the placebo group had *Pneumocystis carinii* pneumonia (PCP), bronchial candidosis, and HIV-associated neuropathy, and died 20 weeks later. Kaposi's sarcoma developed in another patient in the 8th week. Another patient died with *Mycobacterium avium-intracellulare* infection and cerebral candidosis in the 3rd month.

A definite improvement in clinical status of ditiocarb recipients was noted after 16 weeks when compared with

TABLE II—CLINICAL OUTCOME OF HIV INFECTION IN FIRST ARM OF TRIAL

	Active	Placebo	p†
Progression to AIDS	0/38	3/39 (PCP, <i>Mycobacterium avium</i> , and Kaposi's sarcoma)	...
Disappearance of constitutional symptoms* (IV-A patients)	8/11	0/5	<0.001
Lymphadenopathy score	-0.43† (SD 1.94)	+0.43† (SD 1.26)	<0.05
Disappearance of splenomegaly	4/7	0/8§	<0.05

*Persistent diarrhoea, weight loss, persistent fever.

†Fisher's exact test.

‡Change from baseline.

§No spleen became palpable; two additional spleen enlargements were noted.

placebo. Constitutional symptoms disappeared in 8 out of 11 group IV-A patients who received ditiocarb, but did not improve in any of the 6 group IV-A placebo-treated patients ($p < 0.001$). When change in clinical status was scored as improved, stable, or worse by the physicians after 16 weeks, 42% of ditiocarb recipients had improved compared with only 5% in the placebo group ($p < 0.01$). The clinical status of most placebo recipients (87%) remained unchanged during the 16 weeks. All the 9 patients in the ditiocarb group with a history of weight loss at entry regained normal weight after 16 weeks' treatment. The spleen became palpable in 4 of the 7 ditiocarb recipients, but in none of 8 placebo recipients, with splenomegaly at entry. Spleen enlargements were detected in 2 other placebo-treated patients at week 16 ($p < 0.05$). Lymphadenopathy diminished significantly in the ditiocarb group compared with the placebo group ($p < 0.05$). This diminution was not associated with clinical deterioration as seen at some late stages of HIV infection.

Immunological Effects

After 16 weeks ditiocarb patients had higher CD4+ cells cell count than did as the placebo group ($p < 0.05$) although absolute values were scattered (table III). 13 out of 36 (36%) evaluable ditiocarb recipients (see accompanying figure) and 5 out of 38 (13%) placebo recipients ($p < 0.05$) showed a striking and sustained increase of more than 200 CD4+ cells, which suggests some patients were more responsive to ditiocarb than others.

3 patients out of 29 evaluable subjects (10%) remained anergic to 7 recall antigens (Multitest apparatus) in the ditiocarb group, compared with 9 out of 32 (28%) in the placebo group ($p < 0.10$).

Virological Effects

Peripheral blood lymphocytes from 10 patients (5 ditiocarb, 5 placebo) chosen at random from one centre were sampled at weeks 0, 8, 16, 24, and 32, and frozen. These

TABLE III—CD4 CELL COUNT DURING THE FIRST ARM OF TRIAL

	Active		Placebo		p*
	Patients tested	Median (mean, SD) count	Patients tested	Median (mean, SD) count	
Baseline	42	415 (405, 111)	41	380 (389, 132)	NS
Week 8	36	479 (517, 172)	39	420 (461, 226)	NS
Week 16	36	522 (542, 215)	38	420 (447, 181)	<0.05

*Student's *t* test.

TABLE IV—SIDE-EFFECTS

Adverse reaction	Percentage of patients with adverse reactions	
	Active (n = 83)	Placebo (n = 79)
Unpleasant taste	41/32	4/3
Abdominal discomfort	33/26	8/6
Nausea	19/15	3/2
Sensation of malaise	10/8	1/1
Anorexia	9/7	1/1
Excitement	6/5	3/2
Somnolence	5/4	1/1
Vomiting	2/2	1/1
Rash	0/0	0/0

Number of patients in parentheses. No patient in either group had >25% drop in haemoglobin concentrations, red or white cell count, or platelet count.

samples were later thawed and reverse transcriptase activity was assayed in culture supernatants up to 28 days of culture. No significant change in HIV transcription rate was observed during ditiocarb administration, as evaluable by the day of peak reverse transcriptase activity in lymphocyte cultures. Similarly HIV p24 antigenaemia was not affected.

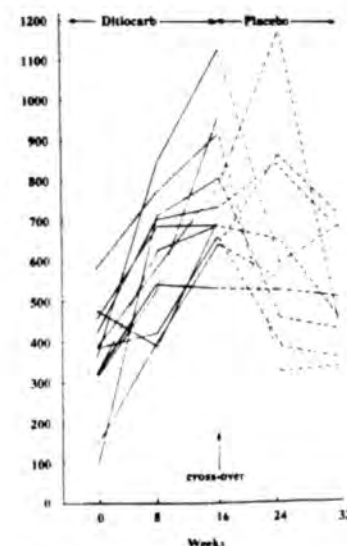
Effects of Replacing Placebo by Ditiocarb

When ditiocarb was given to patients previously treated by placebo, no patient progressed to AIDS. Clinical status improved in 26% of patients (9/35), whereas only 5% (2/39) improved while the group was on placebo. The number of constitutional symptoms diminished in 47% (16/34) of the patients now given ditiocarb. In 5 patients the absolute increase in CD4+ rose to beyond 200/ μ l.

Effects of Interrupting Ditiocarb Therapy

Clinical benefits obtained with ditiocarb were progressively lost when the drug was replaced by placebo. 1 patient progressed to AIDS (extrapulmonary *M. tuberculosis*) 3 months after the crossover. Although the

CD4+ Cell Counts



CD4+ cell counts in 13 patients responsive to ditiocarb, and effect of withdrawal of the drug.

Solid line, effect during ditiocarb therapy. Broken line, effect when ditiocarb replaced by placebo.

clinical status of 42% of the patients from this group had improved during ditiocarb administration, it deteriorated between week 16 and 32 in 36% of the group. Some constitutional symptoms reappeared. Although splenomegaly had disappeared in 4 out of 7 patients during ditiocarb therapy, the organ remained enlarged in the other 3 while they were on placebo, and splenomegaly developed in 2 additional patients.

CD4+ cell count had increased significantly during the first 16 weeks, but they declined from a mean of 554 CD4+ cells/ μ l (week 16) to 449 CD4+ cells/ μ l (week 32) in the 25 evaluable patients who had crossed over to placebo ($p < 0.05$). No patient who switched to placebo had an absolute increase in CD4+ cell counts of more than 200/ μ l. In those patients whose CD4+ count rose, nearly baseline values were attained (see accompanying figure).

Side Effects and Adverse Reactions

Ditiocarb did not induce more major adverse clinical or biological reactions than placebo (table IV), although it was associated more frequently with minor side-effects—unpleasant taste, abdominal discomfort, nausea, or malaise. Some patients reported fatigue and inability to concentrate on the day following ditiocarb ingestion. Ditiocarb had no adverse effect on blood counts. 2 patients had platelet counts of under 150 000/ μ l throughout the study. Platelet counts were not adversely affected by either ditiocarb or placebo.

Discussion

Oral administration of ditiocarb ('Imuthiol') to HIV-infected patients for 16 weeks produced more clinical and immunological benefits than did placebo. Ditiocarb forestalled progression of disease for at least the duration of therapy, this effect and the absence of deaths in the group being striking differences between the two treatment groups. Two other controlled studies, independent from the present one, have already observed the same trend towards impaired progression with ditiocarb: a randomised controlled study in Houston¹⁸ showed that AIDS developed in 5/16 untreated ARC patients, compared with 1/16 on ditiocarb. Similar findings have now been obtained in a matched-pairs, placebo-controlled study in Hamburg²⁰—the disease progressed to AIDS in 6 of 28 placebo-treated patients but in none of 28 on ditiocarb. Our ditiocarb-treated patients improved in at least two measures of immune function—CD4+ cell count and skin-test reactivity—which may have contributed to the clinical benefits. The changes in immune function can be attributed to ditiocarb since they persisted for the duration of treatment but were progressively lost when ditiocarb was discontinued.

The use of a T-cell recruiting agent to treat HIV-infected subjects carried a theoretical risk of stimulating an increase in the number of those very cells that harbour the retrovirus and thus producing clinical deterioration. This risk explains the cautiousness in our preliminary studies.^{21,22} The present findings, and those accompanying long-term administration of ditiocarb^{21,22} (3 years), clearly show that the CD4+ cell-defect is not aggravated. In fact, the reverse occurred, with ditiocarb producing an increase in CD4+ cells and improvement in constitutional symptoms of AIDS-related complex. Furthermore, preliminary data in a small number of patients indicate that ditiocarb does not enhance HIV replication in vitro or in vivo.

One possible means by which ditiocarb interferes with HIV infection is by producing the same "immunoanaleptic" effects as those produced in immunodeficient nude mice.¹ Although ditiocarb is not mitogenic per se, it can aid T-cell maturation and differentiation by increasing the number of T-cell precursors responsive to T-cell differentiation signals. A second possible means would be via its pharmacological properties. As a chelator of divalent cations,⁵ ditiocarb inhibits several Cu or Zn dependent enzymes.⁷⁻⁸ It might act in this way on enzymatic pathways that are required for HIV infection, such as those that involve the metal-linked Tat gene product of HIV.⁹ A third possibility is by its ability to influence intracellular scavenging of cell-toxic free-oxygen radicals.¹⁰⁻¹³ Ditiocarb can produce glutathione-SH peroxidase-like activity and, since it is itself a substrate for oxidation by H_2O_2 , it may exert some of its anti-oxidant protection by directly detoxifying peroxides. Its oxygen-radical scavenging activities might account for the anti-inflammatory effects, such as shrinkage of spleen or lymph node enlargements. The therapeutic effects of ditiocarb on HIV infection probably involve several of the above mechanisms. However, more knowledge is needed on the intracellular mechanisms of HIV cytopathic infection and the precise cascade of events leading to immunodeficiency before the mechanism of action of ditiocarb can be fully assessed.

An important question is whether ditiocarb therapy can be tolerated and can be prolonged for extended periods of time. Ditiocarb can be given orally and is well tolerated except for minor adverse reactions. Unlike antiretroviral agents, it does not impair haemopoiesis. It has now been given for up to 3 years to HIV patients and up to 5 years to cancer patients without untoward effects.^{21,22}

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CORRELATION OF PLASMA INTERLEUKIN 1 LEVELS WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Summary The mean plasma level of interleukin 1 beta (IL-1 beta), measured by immunoassay, was significantly higher in 51 patients with rheumatoid arthritis (RA) than in 21 healthy controls of similar age. Further, in the RA group, plasma IL-1 beta correlated positively with Ritchie joint index, pain score, and erythrocyte sedimentation rate and correlated negatively with haemoglobin concentration. In individual patients with active disease who had serial measurements, plasma IL-1 beta also correlated with clinical disease activity. These results support the idea that IL-1 beta has a central role in the pathogenesis of RA.

Introduction

IL-1 molecules are polypeptides with many biological activities related to host defence and tissue remodelling,¹ and interest has arisen in the pathogenic potential of IL-1 in inflammatory and immune diseases.² Two forms of human IL-1 (alpha and beta) are encoded by separate genes with inducible expression in macrophages, lymphocytes, endothelial cells, and other cell types. The initial product of each is a propeptide of 31 kD from which mature peptide of 17 kD is processed.³⁻⁵ IL-1 alpha and beta have only 26% amino acid homology but compete equally for receptors on target cells and have similar biological activities.⁶ In human monocytes IL-1 mRNA is inducible but after cellular activation it accumulates rapidly and IL-1 beta is usually the predominant form.^{3,5}

Many activities of IL-1 are relevant to rheumatoid arthritis (RA).⁷ IL-1 increases the release from synovial cells of vasoactive agents and mediators of tissue damage (eg, prostaglandins, proteinolytic enzymes, and reactive oxygen molecules)^{8,9} and is a powerful stimulus of bone¹⁰ and cartilage^{11,12} resorption. It also induces the acute-phase response¹⁰ and fever^{13,14} and may potentiate chronic inflammation by induction of lymphocyte growth factors such as interleukin 2 and its receptor.¹²

Much evidence¹⁵ has implicated IL-1 in the pathogenesis of RA: high levels are found in synovial exudates;^{14,16} RA synovial cells spontaneously produce biologically active IL-1 *in vitro*;¹⁷ *in-situ* hybridisation of mRNA shows that IL-1 gene expression is activated *in vivo* in RA synovial cells;¹⁶ and in laboratory animals a single intra-articular

INTERLEUKIN-1 BETA IN EXTRACTED PLASMA

	Plasma IL-1 beta (pg/ml)	
	Control	RA
n	21	51
Range	20-78	20-230
Median	50	90
Mean	44.7	98.2*
SEM	4.4	7.9

*Controls vs RA: $t = 4.28$; $p < 0.0001$

injection of IL-1 produced synovial fluid leucocytosis and increased proteoglycan breakdown.¹⁸

Despite the weight of circumstantial evidence for IL-1 as a pathogenic mediator in RA, it has not previously been possible to correlate IL-1 levels *in vivo* with clinical disease activity in patients because IL-1 measurement in blood and other biological fluids has been complicated by interfering factors.^{14,15} By means of a sensitive immunoassay combined with a single plasma extraction procedure we have now been able to measure circulating levels of immunoreactive IL-1 beta in patients with RA.

Methods

Patients with definite or classical rheumatoid arthritis¹⁹ attending a rheumatology outpatient department or admitted to a rheumatology ward were graded for disease activity by Ritchie joint index,²⁰ duration of early morning stiffness, and visual analogue pain score. At the same time, blood was taken for haemoglobin concentration, white cell count, platelet count, erythrocyte sedimentation rate (ESR), and rheumatoid factor titre as part of the normal management. Blood samples for plasma preparation were taken into EDTA (5×10^{-3} mol/l) tubes (Labco) containing aprotinin (bovine lung 15-30 U/mg; Sigma) at 0.67 U/ml. Plasma was separated from cells and platelets immediately by centrifugation at 400 g and then at 10 000 g and stored in 500 µl samples at -20°C until tested for IL-1 beta content. All patients received non-steroidal anti-inflammatory drugs (NSAID), and some received second-line antirheumatic drugs, including intra-articular steroids.

IL-1 beta Measurement

Before IL-1 measurement, samples were treated according to the method of Cannon et al.²¹ Plasma samples were thawed and extracted twice with chloroform (BDH, Paisley) by addition of 2 volumes of chloroform to 1 of plasma, mixing for 5 minutes, and then centrifugation at 10 000 g and removal of the aqueous phase for IL-1 beta testing in an enzyme-linked immunosorbent assay (IL-1 beta ELISA; Cistron Biotechnology Laboratory Impex). In our laboratory,²² this assay is sensitive to 20 pg/ml IL-1 beta, and has parallel dilution characteristics, less than 12% interassay variation, and detection recovery of added IL-1 beta in RA plasma of 82% after extraction ($n = 10$; mean 82.2 SEM 2.7%; difference from recovery in extracted normal plasma not significant). There is no cross-reactivity with IL-1 alpha. The ELISA test is

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wine. Mailmen, salesmen, truck drivers, and other itinerant workers typically spend a large portion of their day drinking in cafés and restaurants as they make their daily rounds.

The use of alcohol to complement food has been developed to a fine art by the French. Indeed, the words *connoisseur*, *savoir faire*, and *savoir-vivre*, all connoting an appreciation for good living, are closely connected with the art of matching food and wine most harmoniously. To do this properly, one must follow a prescribed ritual, which dictates the appropriate alcoholic beverage to accompany each part of the meal. To open the meal and stimulate the appetite, one first takes an *apéritif* such as vermouth, Pernod, or anise. During the meal one chooses a red, white, or rosé dinner wine to complement the main course. Another wine may be called for when the cheese arrives, and champagne or sparkling burgundy may be ordered as a dessert wine. Following the meal, a "digestif" of liqueur or brandy is usually taken to facilitate digestion.



A repair shop at the French wine market is available to take care of damaged barrels. Here, expert cask makers still employ the old methods taught at a coopers' school within the Halle aux Vins.

Although the term "alcoholic Republic" was first used to describe American drinking patterns following the American Revolutionary War, the term applies equally well to contemporary France. Of all the nations of the world, France has undisputed leadership in practically all things alcoholic. Not only do the French drink more per capita, they also lead the world in the production of alcohol and alcoholics.

Since the Middle Ages wine has been the national beverage and one of the major agricultural products of France. Although a significant proportion of France's fine *bordeaux*, *burgundies*, and *champagnes* are exported to all parts of the world, the less expensive wines are consumed domestically. In fact, there is hardly a province in France without its local brandy or wine. In Normandy, hard cider and Calvados, a brandy distilled from cider, are the traditional beverages. In Bordeaux, cognac and armagnac are distilled from the local



An Italian barrel maker works on a large wine cask, climbing inside to smooth the wooden staves. Constructed just outside Rome, the cask will later be filled with wine from the famous town of Frascati.

APPENDIX 1

APPENDIX 1: CONSUMPTION OF WINE, BEER, AND SPIRITS

Average Yearly Consumption of Wine, Beer, and Spirits
Per Person in 62 Countries

AREA	COUNTRY	INTER- NATIONAL RANK	LITERS OF ABSOLUTE ALCOHOL			TOTAL
			WINE	BEER	SPIRITS	
EUROPE	France	1	11.6	2.9	2.3	16.8
	Italy	2	11.1	.6	1.9	13.6
	Austria	3	4.1	6.0	2.3	12.4
	Portugal	4	9.9	.8	1.0	11.7
	Luxembourg	5	5.0	3.7	2.8	11.5
	Spain	6	7.1	1.4	2.9	11.4
	West Germany	7	2.3	5.8	2.9	11.0
	Switzerland	8	5.0	3.8	2.1	10.8
	Hungary	10	4.4	2.0	3.1	9.5
	Belgium	11	1.9	5.8	1.6	9.3
	Czechoslovakia	12	1.1	4.5	2.4	8.6
	Denmark	15	.9	5.3	1.5	7.7
	Yugoslavia	16	3.2	1.7	2.8	7.7
	Great Britain	18	.5	5.3	1.1	6.9
	East Germany	20	.7	3.2	2.9	6.8
	Netherlands	21	.8	3.3	2.3	6.4
	Soviet Union	23	2.0	.9	3.4	6.3
	Bulgaria	24	2.4	1.9	1.8	6.1
	Poland	25	.8	1.3	3.9	6.0
	Ireland	26	.5	3.8	1.7	6.0
	Sweden	27	1.0	2.1	2.7	5.8
	Greece	29	4.8	.5	.1	5.4
	Finland	30	.6	2.2	2.3	5.1
	Norway	34	.4	1.8	1.6	3.8
	Roumania	35	2.6		1.2	3.8
	Iceland	39	.2	.2	2.4	2.8
UNITED STATES & OTHER ENGLISH-SPEAKING COUNTRIES	Australia	13	1.1	6.3	1.1	8.5
	New Zealand	14	.9	6.1	1.2	8.2
	Canada	17	.9	4.1	2.6	7.6
	United States	19	.8	3.0	3.0	6.8
ASIA	Japan	28	2.8	1.6	1.1	5.5
	South Korea	32		.7	3.5	4.2
	Cyprus	33	1.2	.9	1.8	3.9
	Hong Kong	46		.6	1.2	1.8
LATIN AMERICA	Argentina	9	9.5	.7		10.2
	Chile	22	5.3	1.1		6.4
	Uruguay	31	3.1	1.5		4.6
	Surinam	36		1.1	2.5	3.6
	Panama	38		1.3	1.6	2.9
	Peru	40	.2	1.0	1.4	2.6
	Mexico	41		1.4	1.1	2.5
	Cuba	42	.2	1.0	1.3	2.5
	Bolivia	43		.4	1.7	2.1
	Venezuela	44		2.1		2.1
	Brazil	52	.1	.5	.2	.7
	Paraguay	54	.2	.3		.5

Average Yearly Consumption of Wine, Beer, and Spirits
Per Person in 62 Countries

AREA	COUNTRY	INTER- NATIONAL RANK	LITERS OF ABSOLUTE ALCOHOL		
			WINE	BEER	SPIRITS
AFRICA	South Africa	37	1.2	.7	1.0
	Cameroon	48		.9	
	Namibia	49		.9	
	Congo	50		.7	
	Kenya	56		.4	
	Senegal	57	.1	.2	
	Gambia	60	.1	.1	
MIDDLE EAST & MOSLEM COUNTRIES	Bahrain	45	.1	.7	1.3
	Israel	47	.5	.5	.7
	Tunisia	51	.4	.3	
	Turkey	53	.1		.4
	Lebanon	55	.4		
	Algeria	58	.1	.2	
	Morocco	59	.2	.1	
	Egypt	61			.1
	Syria	62			.1

SOURCE: 1972 survey by the Finnish Foundation of Alcohol Studies and World Health Organization.

To your health!

Salud!

Prosit!

A votre santé!

Kan pei!

Skål!

Terveysto!

Stin ygja sou!

Slaithis is saol agat!

L'chaim!

Alla tua salute!

Kwa afya yako!

Op je gezondheid!

Na zdrowie!

Za vashe z-dorovye!

Viva!

Ziveli!

Iechyd da i chivri!

I sveikata!

Egeszsegedre!



The drinking of "beals"
is one of the oldest and
most universal drinking
customs, as reflected in
the many languages in
which this toast appears.

A PROPOSAL FOR A PROCEDURE
WHICH MIGHT PROVE TO BE
EFFECTIVE IN DESTROYING
THE HIV VIRUS.

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CONSIDERING THE MULTITUDINOUS ARRAY OF SUBSTANCES THAT ARE FOUND IN THE CHEMICAL REALM, WHAT IS THE ONE AND ONLY DRUG THAT A PERSON COULD TAKE WHICH MIGHT INADVERTENTLY INCREASE THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN THAT PERSON'S BLOOD?

- DISULFIRAM (ANTABUSE) OR ITS METABOLITE DITIOCARB (DTC) -

I WANT TO EXAMINE IN GREATER DETAIL THESE THREE STUDIES -

JEAN-MARIE LANG, CHRISTIAN TREPO, MYRIAM KIRSTETTER, ET AL:
'RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF
DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY
VIRUS INFECTION', "THE LANCET", SEPTEMBER 24, 1988,
PAGES 702 - 706.

EMIL C. REISINGER, PETER KERN, MARTIN ERNST, ET AL: 'INHIBITION
OF HIV PROGRESSION BY DITHIOCARB', "THE LANCET", MARCH 24, 1990,
PAGES 680 - 682.

EVAN M. HERSH, M.D.; GARY BREWTON, M.D.; DONALD ABRAMS, M.D.;
JOHN BARTLETT, M.D. ET AL: 'DITIOCARB SODIUM (DIETHYLDITHIOCARBAMATE)
THERAPY IN PATIENTS WITH SYMPTOMATIC HIV INFECTION AND AIDS',
"JAMA - THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION",
MARCH 27, 1991, PAGES 1538 - 1544.

HEREINAFTER, I WILL REFER TO THESE STUDIES AS SIMPLY "LANG", "REISINGER"
AND "HERSH".

IN ALL THREE OF THESE STUDIES THERE WAS A VARIABLE THAT WAS NOT TAKEN
INTO ACCOUNT AND THEREFORE NOT MEASURED -

- THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN THE BLOOD OF THOSE
PATIENTS TO WHOM DITIOCARB HAD BEEN GIVEN -

FIRST, I WANT TO CLARIFY THE TERMS "METABOLIZED" AND "UNMETABOLIZED"
AS I THINK OF THEM.

TO ME, "METABOLIZED" SIMPLY MEANS:

- TO BE CHANGED INTO SOMETHING DIFFERENT -

WHEREAS "UNMETABOLIZED" SIMPLY MEANS:

- TO REMAIN THE SAME -

YOU WILL SEE HOW I ARRIVED AT THESE FIGURES LATER, BUT FOR NOW - WHEN THE HIGHLY TOXIC, POISONOUS SUBSTANCE KNOWN AS ACETALDEHYDE IS PROCESSED BY THE LIVER, 98.43% OF IT IS METABOLIZED (OR CHANGED) INTO HARMLESS ACETIC ACID WITHIN 18.6 MINUTES.

WHAT IF 98.43% OF IT COULD NOT BE CHANGED WITHIN 18.6 MINUTES? LET'S SAY, FOR SOME REASON, THE LIVER NOW TOOK 2 HOURS TO DO WHAT IT NORMALLY ACCOMPLISHED IN 18.6 MINUTES.

ISN'T IT TRUE THEN THAT FOR MORE THAN AN ADDITIONAL 1½ HOURS POISONOUS, UNMETABOLIZED (UNCHANGED) ACETALDEHYDE WOULD BE FLOWING THROUGHOUT THE BODY?

THIS THEN IS HOW I WILL BE THINKING OF THE TERMS "METABOLIZED" AND "UNMETABOLIZED" THROUGHOUT THE REST OF THIS FILE.

THE FIRST FEW PAGES OF THIS FILE ARE PRIMARILY A COMPARISON AND CONTRAST OF THE THREE AFOREMENTIONED STUDIES.

THE STUDIES TOOK PLACE IN FRANCE, GERMANY AND THE UNITED STATES.

THE FRENCH STUDY (LANG) TOOK PLACE FROM DECEMBER, 1985 TO JUNE, 1986. THE GERMAN STUDY (REISINGER) TOOK PLACE AT SOME TIME BETWEEN MAY, 1986 AND NOVEMBER, 1987. THE UNITED STATES STUDY (HERSH) TOOK PLACE AT SOME TIME BETWEEN JANUARY, 1987 AND APRIL, 1989.

NUMBER OF PATIENTS - LANG (83), REISINGER (60) AND HERSH (389).

CONDITION OF THE PATIENTS - IN THE LANG AND REISINGER STUDIES THE PATIENTS WERE AT THE SAME STAGE OF THE INFECTION; THEY HAD NOT YET DEVELOPED AIDS SYMPTOMS. IN THE HERSH STUDY THE AIDS SYMPTOMS HAD TO BE MORE IN EVIDENCE:

LANG (P. 703) - "ALL PATIENTS ADMITTED TO THE STUDY HAD SERUM ANTIBODIES TO HIV BY THE WESTERN BLOT TECHNIQUE. PATIENTS WERE ELIGIBLE IF THEY BELONGED TO GROUPS II, III, OR IV-A OF THE CDC CLASSIFICATION AND HAD A CD4 POSITIVE HELPER-INDUCER LYMPHOCYTE COUNT OF LESS THAN 600/uL."

REISINGER (P. 680) - "INCLUSION CRITERIA WERE MALE SEX, 18-55 YEARS, SERUM ANTIBODIES AGAINST HIV-1, WALTER REED STAGE 2-4, NORMAL BLOOD COUNTS, AND NORMAL SERUM CREATININE AND LIVER ENZYME LEVELS."

HERSH (P. 1539) - "PATIENTS WERE REQUIRED TO HAVE THREE OR MORE OF THE FOLLOWING: LYMPHADENOPATHY, FEVER, NIGHT SWEATS, WEIGHT LOSS, DIARRHEA, FATIGUE, THRUSH, HAIRY LEUKOPLAKIA"

LENGTH OF THE STUDIES - LANG (32 WEEKS), REISINGER (24 WEEKS) AND HERSH (24 WEEKS).

IN ALL THREE OF THE STUDIES ½ OF THE PATIENTS WERE GIVEN DITIOCARB AND ½ WERE GIVEN PLACEBO. THE PATIENTS WHO WERE GIVEN DITIOCARB WERE GIVEN IT ONCE A WEEK IN THE FOLLOWING AMOUNTS AND MANNER:

LANG: 10mg/kg BODY WEIGHT - ORALLY
REISINGER: 5mg/kg BODY WEIGHT - INTRAVENOUSLY OR
10mg/kg BODY WEIGHT - ORALLY
HERSH: 400mg/m2 OF BODY SURFACE AREA - ORALLY

NO, I DO NOT KNOW HOW TO CORRELATE THESE MEASUREMENTS - mg/kg BODY WEIGHT
VERSUS mg/m2 OF BODY SURFACE AREA, BUT BEAR WITH ME.
ZIDOVUDINE USE:

LANG (P.703) - "NO PATIENT RECEIVED ZIDOVUDINE DURING THE TRIAL
SINCE IT WAS NOT READILY AVAILABLE IN FRANCE THEN."
REISINGER - ZIDOVUDINE IS NOT MENTIONED. I ASSUME THAT IT WAS NOT
AVAILABLE IN GERMANY EITHER.
HERSH - (P. 1540) - YES/NO - DITIOCARB (35/18), Placebo (37/19)
SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB - REISINGER (P.679) STATES:

"A DOSE RESPONSE STUDY IN PATIENTS WITH AIDS-RELATED COMPLEX (ARC)
OR AIDS SHOWED THAT DOSES UP TO 400mg/m2 ADMINISTERED ONCE WEEKLY
WERE NOT TOXIC WHEREAS 800 mg/m2 EITHER ONCE OR TWICE A WEEK
HAD SIDE-EFFECTS."

I HAVE BEEN TRYING TO OBTAIN A COPY OF THE ARTICLE THAT ARRIVED
AT THESE CONCLUSIONS BUT HAVE THUS FAR BEEN UNSUCCESSFUL. IT IS -

REISINGER E., KERN P., DIETRICH M. 'CLINICAL TRIALS WITH
DIETHYLDITHIOCARBAMATE IN HIV-INFECTIONS'. "MITT ÖSTERR GES
TROPENMED PARASITOL" 1988; 10:287-92.

SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB:

LANG - I'LL TALK ABOUT THIS LATER.

REISINGER (P.681) - "NAUSEA AND FATIGUE WERE INFREQUENT IN BOTH
DTC GROUPS." (P.682) - "NO SEVERE SIDE-EFFECTS
WERE OBSERVED."

HERSH (P.1538) - "THE ADMINISTRATION OF DITIOCARB DID NOT INDUCE
ANY MAJOR ADVERSE CLINICAL OR BIOLOGICAL REACTIONS."
(P. 1542) - "THERE WERE ACTUALLY FEWER ADVERSE
REACTIONS ATTRIBUTED TO DITIOCARB THAN TO PLACEBO."

CONSEQUENTLY, I AM GOING TO MAKE THE ASSUMPTION THAT THE AMOUNT OF
DITIOCARB ADMINISTERED PER PATIENT IN THE REISINGER STUDY WAS JUST ABOUT
EQUAL TO THAT OF THE HERSH STUDY BECAUSE NO SIGNIFICANT SIDE EFFECTS
WERE NOTED IN EITHER STUDY.

THE DRINKING OF ALCOHOL

LANG - I'LL TALK ABOUT THIS LATER.

REISINGER (P.681) - "BECAUSE OF THE DISULFIRAM-LIKE EFFECT OF DTC, INTOLERANCE TO ALCOHOL (PALPITATION, RASH, DIZZINESS, NAUSEA, HEADACHE) WAS SEEN IN 4 PATIENTS (15%) WHO REPORTED ALCOHOL CONSUMPTION WITHIN 2 DAYS OF DTC ADMINISTRATION. HOWEVER, 11% OF PLACEBO-TREATED PATIENTS REPORTED SIMILARLY....."

HERSH (P.1539) - "BECAUSE DITHIOCARB IS A DITHIOCARBAMATE AND HAS DISULFIRAM (ANTABUSE)-LIKE EFFECTS, PATIENTS WERE ADVISED NOT TO CONSUME ALCOHOL FROM 12 HOURS BEFORE TO 48 HOURS AFTER TREATMENT."

CONSEQUENTLY, I ASSUME THAT THE DRINKING OF ALCOHOL WAS NOT A FACTOR IN EITHER THE REISINGER OR HERSH STUDIES, BECAUSE IF IT HAD BEEN, A LOT MORE SIDE-EFFECTS AND ADVERSE REACTIONS WOULD HAVE BEEN REPORTED IN BOTH OF THEM.
CONCLUSIONS OF THE REISINGER AND HERSH STUDIES -

REISINGER (P.682): "INTRAVENOUS DTC WAS SUPERIOR TO ORAL DTC AND TO PLACEBO IN HIV-1 INFECTION."

" "ORALLY DTC TENDED TO DECREASE HIV-RELATED DISEASES, BUT THE DIFFERENCE FROM THE ORAL PLACEBO GROUP WAS NOT SIGNIFICANT."

" "INTRAVENOUS ADMINISTRATION OF DTC IS MORE EFFECTIVE THAN ORAL ADMINISTRATION IN DELAYING THE PROGRESSION OF HIV-INFECTION IN THE EARLY SYMPTOMATIC STAGES."

(P.679): "55 PATIENTS WERE EVALUABLE AT THE END OF THE STUDY: NO PATIENT WHO HAD RECEIVED DTC BUT 6 PLACEBO PATIENTS HAD AIDS, A SIGNIFICANT DIFFERENCE. SIGNIFICANTLY DELAYED DISEASE PROGRESSION WAS OBSERVED IN THE INTRAVENOUS DTC GROUP COMPARED WITH ITS MATCHING PLACEBO. THE BENEFIT IN THE ORAL DTC GROUP WAS NOT STATISTICALLY SIGNIFICANT. DURING AN 18-MONTH FOLLOW-UP 3 DEATHS OCCURRED IN THE ORIGINAL PLACEBO GROUPS, WHEREAS NO PATIENT WHO HAD INITIALLY RECEIVED DTC DIED. A SIGNIFICANT DELAY IN PROGRESSION TO AIDS WAS OBSERVED IN THE DTC GROUPS."

HERSH (P.1538): "TEN NEW ACQUIRED IMMUNODEFICIENCY SYNDROM (AIDS)-
DEFINING OPPORTUNISTIC INFECTIONS OCCURRED IN THE
TREATED PATIENTS AND 21 IN THE CONTROLS. REDUCTION OF
NEW OPPORTUNISTIC INFECTIONS IN THE DITIOCARB GROUP
WAS SIGNIFICANT IN ALL PATIENTS (RELATIVE RISK [RR] 0.44)
AND IN PATIENTS WITH AIDS (CDC GROUPS 1V-C1
AND 1V-D) (RR, 0.12)."

(P.1542): "THE STATISTICALLY SIGNIFICANT BENEFIT OF DITIOCARB
WAS SEEN IN ALL PATIENTS, AND SEPARATELY IN THE
SUBGROUPS OF AIDS PATIENTS."

(P.1539): "PATIENTS FROM EIGHT MEDICAL CENTERS....."

(P.1541): "FINALLY, THE REDUCTION IN OIs IN THE DITIOCARB GROUP
WAS SEEN IN ALL STUDY CENTERS."

(P.1538): "WE CONCLUDE THAT, IN THIS STUDY, DITIOCARB WAS SAFE
AND REDUCED THE INCIDENCE OF OPPORTUNISTIC INFECTIONS
IN PATIENTS WITH SYMPTOMATIC HIV INFECTION."

EXPLANATION - VARIOUS EXPLANATIONS ARE ADVANCED, BUT NEITHER REISINGER
OR HERSH HAVE YET FOUND OUT THE DEFINITIVE REASON FOR DITIOCARB'S EFFECTIVENESS.
AS HERSH STATES (P.1543):

"THE PRECISE CASCADE OF EVENTS BY WHICH DITIOCARB EXERTS ITS ACTIVITY
IS NOT FULLY ELUCIDATED."

I THINK ANOTHER FACTOR HAS TO BE CONSIDERED - THE AMOUNT OF UNMETABOLIZED
ACETALDEHYDE THAT WAS FLOWING IN THE BLOOD OF THOSE PATIENTS TO WHOM DITIOCARB
HAD BEEN GIVEN. THE AMOUNT MUST HAVE BEEN VERY SMALL, ELSEWISE THE PATIENTS
WOULD HAVE BEEN DISPLAYING ALOT MORE ADVERSE REACTIONS.

YOU MIGHT ASK - IF THE DRINKING OF ALCOHOL WAS NOT A SIGNIFICANT FACTOR
IN THE REISINGER OR HERSH STUDIES, HOW COULD ACETALDEHYDE HAVE GOTTEN
INTO THE BLOOD OF THOSE PATIENTS TO WHOM DITIOCARB HAD BEEN GIVEN?

LET ME DIGRESS FOR A MOMENT -

WHAT DOES DITIOCARB (DISULFIRAM, ANTABUSE, DTC) DO WHEN IT ENTERS
THE BODY OF A PERSON?

- IT "PLUGS UP" THE LIVER AS FAR AS THE METABOLIZATION OF
ACETALDEHYDE IS CONCERNED -

IF YOU TAKE DITIOCARB TODAY YOU WON'T GET RID OF IT BY TOMORROW.
IT WILL STAY WITH YOU FOR DAYS.

REISINGER (P.679):

"DESPITE THE SHORT SERUM HALF-LIFE OF DTC SOME EFFECTS OF THIS DRUG
LAST UP TO 7 DAYS, INDICATING RAPID INTRACELLULAR PENETRATION."

ENCYCLOPEDIA AMERICANA, 1991 EDITION, VOLUME 1, PAGE 518:

"IN GENERAL, DISULFIRAM MAKES ALCOHOL SYMBOLICALLY UNAVAILABLE TO THE ALCOHOLIC AND THEREBY REDUCES THE DESIRE TO DRINK. ITS SLOW RATE OF METABOLISM IN THE BODY GIVES THE INDIVIDUAL PAUSE BEFORE IMPULSIVE RELAPSE."

REMEMBER - IN ALL THREE OF THESE STUDIES THE PATIENTS WERE GIVEN DITIOCARB ONCE A WEEK.

IN OTHER WORDS, THERE WASN'T A TIME DURING THE ENTIRE COURSE OF ALL THREE STUDIES THAT DITIOCARB WAS NOT PRESENT IN THE LIVERS OF THE DITIOCARB PATIENTS.

ACETALDEHYDE IS A HIGHLY TOXIC POISON. NORMALLY, HOW IS IT METABOLIZED BY THE LIVER?

THE "JOURNAL OF APPLIED TOXICOLOGY", OCTOBER, 1991 ISSUE STATES (P.374) THAT THE HALF-LIFE OF ACETALDEHYDE IN THE BLOOD OF RATS IS 3.1 MINUTES. I SHALL ASSUME THAT THIS RATE COULD BE APPLIED TO HUMAN BEINGS. MAYBE IT'S MORE, MAYBE IT'S LESS.

THIS FIGURES OUT THUSLY - 98.43% OF THE ACETALDEHYDE THAT IS IN THE BODY OF A HUMAN BEING WILL BE METABOLIZED IN 18.6 MINUTES BY THE LIVER IF IT IS FUNCTIONING NORMALLY (SEE CHART, PAGE 13). IN OTHER WORDS, JUST ABOUT ALL OF A HIGHLY TOXIC POISON WILL BE RENDERED HARMLESS BY THE LIVER IN LESS THAN 20 MINUTES.

IF THE LIVER IS "PLUGGED UP" IN ANY DEGREE WHATSOEVER WITH DITIOCARB THE ACETALDEHYDE CANNOT BE PROPERLY METABOLIZED. IF IT IS "PLUGGED UP" JUST A LITTLE BIT - SAY WITH THE RESIDUE THAT REMAINS 7 DAYS AFTER INITIAL ADMINISTRATION - PERHAPS THE ACETALDEHYDE WILL REMAIN TOXIC FOR ONLY A FEW EXTRA MINUTES. HOWEVER, WHAT IF IT IS NEWLY "PLUGGED UP" WITH THE ONCE A WEEK SERVING? COULD THE ACETALDEHYDE REMAIN POISONOUS FOR MAYBE AN HOUR OR LONGER? SINCE SIDE-EFFECTS AND ADVERSE REACTIONS WERE NOT A FACTOR IN EITHER THE PEISINGER OR HERSH STUDIES, THE AMOUNT OF ACETALDEHYDE MUST HAVE BEEN VERY SMALL INDEED.

INDEED, HOW MIGHT IT HAVE GOTTEN INTO THE PATIENTS' SYSTEMS IF THE DRINKING OF ALCOHOL WAS NOT A FACTOR?

THE SAME ISSUE OF THE "JOURNAL OF APPLIED TOXICOLOGY" STATES (P.374):

"ACETALDEHYDE HAS BEEN IDENTIFIED IN OAK LEAVES, TOBACCO, APPLES, BROCCOLI, COFFEE, GRAPES, GRAPEFRUIT, ORANGES, LEMONS, ONIONS, PEACHES, PEARS, PINEAPPLES, RASPBERRIES, STRAWBERRIES AND MANY SPICES. EUROPEAN BEERS HAVE BEEN FOUND TO CONTAIN AS MUCH AS 13.5mg l⁻¹. THE ACCEPTABLE DAILY INTAKE RECOMMENDED BY FAO/WHO IS 0.0-2.5mg kg⁻¹ BODY WEIGHT."

"ANOTHER SIGNIFICANT CONTRIBUTION IS MADE BY COFFEE ROASTING AND MOTOR VEHICLE EXHAUSTS."

"AMBIENT AIR LEVELS OF ACETALDEHYDE RANGE FROM NON-DETECTABLE TO 123 ug m⁻³ IN MAJOR U.S. CITIES."

ENCYCLOPEDIA AMERICANA, 1991 EDITION, VOLUME 1, PAGE 518:

"UNFORTUNATELY, HOWEVER, THE DISULFIRAM/ALCOHOL REACTION CAN BE SET OFF BY ALCOHOL USED IN FOOD PREPARATIONS OR BY INHALED FUMES (AS FROM AFTER-SHAVE LOTION)."

IN OTHER WORDS, A PATIENT WHO HAD DITIOCARB IN HIS LIVER COULD GET UP IN THE MORNING, HAVE A GLASS OF ORANGE JUICE, HAVE A CUP OR TWO OF COFFEE, SMOKE A CIGARETTE, SHAVE AND APPLY AFTER-SHAVE TO HIS FACE AND AUTOMATICALLY THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN HIS BLOOD WOULD HAVE BEEN INCREASED.

THROUGHOUT THE DAY IF HE ATE SOME FRUIT OR SIMPLY SMELLED AUTO EXHAUST FUMES HIS LEVEL OF UNMETABOLIZED ACETALDEHYDE WOULD BE INCREASED.

IF THE PATIENT TOOK HIS DITIOCARB CAPSULE ON SUNDAY EVENING AND SIX DAYS LATER ATE AN APPLE ON SATURDAY AFTERNOON, THERE WOULD STILL BE ENOUGH OF A DITIOCARB RESIDUE IN THAT PATIENT'S LIVER TO PREVENT NORMAL METABOLIZATION OF ACETALDEHYDE; 98.43% OF IT WOULD NOT BE METABOLIZED IN 18.6 MINUTES; PERHAPS 19.6 MINUTES WOULD BE REQUIRED TO DO THE JOB; THIS MEANS THAT ON THIS PARTICULAR SATURDAY AFTERNOON A TOXIC POISON WOULD BE FLOWING FREE THROUGH THE BLOOD OF THIS PATIENT FOR AN EXTRA MINUTE.

IN OTHER WORDS, THROUGHOUT THE ENTIRE COURSE OF THE WEEK VARYING AMOUNTS OF UNMETABOLIZED ACETALDEHYDE COULD BE IN THE BLOOD OF THOSE PATIENTS WHO TOOK DITIOCARB IF THOSE PATIENTS WERE INDEED EXPOSED TO THE FACTORS WHICH ARE LISTED ON PAGE 374 OF THE "JOURNAL OF APPLIED TOXICOLOGY" AND ON PAGE 518, VOLUME 1 OF THE ENCYCLOPEDIA AMERICANA.

GRANTED, IT MIGHT BE A MINUTE AMOUNT, NOT ENOUGH TO MAKE THE PATIENT NAUSEOUS, BUT THE FACT IS INDISPUTABLE - ACETALDEHYDE, IN ANY AMOUNT, CANNOT BE PROPERLY METABOLIZED BY THE LIVER IN A NORMAL MANNER IF DITIOCARB IS PRESENT IN ANY AMOUNT.

I THINK IT WAS THIS UNMETABOLIZED ACETALDEHYDE THAT WAS AT WORK IN THE REISINGER AND HERSH STUDIES: IT IS MY HYPOTHESIS THAT THE HIV VIRUS ITSELF WAS BEING DESTROYED BY THIS HIGHLY TOXIC POISON.

THE SAME CAN BE SAID FOR THE LANG STUDY; HOWEVER, I THINK THAT THE QUANTITY OF UNMETABOLIZED ACETALDEHYDE BEING GENERATED IN THESE FRENCH PATIENTS WAS GREATER AND THEREFORE MORE EFFECTIVE. HOW COULD THIS HAVE COME ABOUT?

BUT FIRST -

IN THE REISINGER STUDY 15 PATIENTS RECEIVED 5mg OF DITIOCARB (DTC) INTRAVENOUSLY ONCE A WEEK AND 15 PATIENTS RECEIVED 10mg OF DITIOCARB (DTC) ORALLY ONCE A WEEK. IN THE LANG STUDY ALL 83 PATIENTS RECEIVED 10mg OF DITIOCARB(DTC) ORALLY ONCE A WEEK.

NOW WE HAVE SOMETHING TO COMPARE.

WHAT DOES REISINGER HAVE TO SAY ABOUT THOSE PATIENTS WHO RECEIVED 10mg OF DITIOCARB (DTC) ONCE A WEEK? (P.682)

"ORALLY DTC TENDED TO DECREASE HIV-RELATED DISEASES, BUT THE DIFFERENCE FROM THE ORAL PLACEBO GROUP WAS NOT SIGNIFICANT."

NOW, LET US LOOK AT SOME OF THE OBSERVATIONS WHICH LANG MAKES ABOUT HIS PATIENTS; REMEMBER, THEY TOO RECEIVED 10mg OF DITIOCARB (DTC) ORALLY ONCE A WEEK:

- (P.702) - "THE DISEASE DID NOT PROGRESS TO CDC-DEFINED ACQUIRED IMMUNODEFICIENCY SYNDROME IN THE DITIOCARB GROUP BUT DID SO IN 4 PATIENTS IN THE PLACEBO GROUP (3 BETWEEN WEEK 0 AND 16, 1 BETWEEN WEEK 17 AND 32). DITIOCARB WAS ALSO ASSOCIATED TO A SIGNIFICANTLY GREATER EXTENT THAN PLACEBO WITH RELIEF OF CONSTITUTIONAL SYMPTOMS, IMPROVEMENT IN CLINICAL STATUS (INCLUDING SHRINKAGE OF ENLARGED SPLEEN AND LYMPH NODES), AND IMPROVEMENT IN IMMUNE FUNCTION (AS MEASURED BY CD4+ CELL COUNT AND SKIN TEST REACTIVITY). WHEN PLACEBO WAS REPLACED BY DITIOCARB, SIMILAR IMPROVEMENTS WERE OBSERVED, WHEREAS SYMPTOMS SLOWLY REAPPEARED AND CD4+ CELL LEVELS PROGRESSIVELY DECLINED WHEN DITIOCARB TREATMENT WAS REPLACED BY PLACEBO."
- (P.704) - "ALL THE 9 PATIENTS IN THE DITIOCARB GROUP WITH A HISTORY OF WEIGHT LOSS AT ENTRY REGAINED NORMAL WEIGHT AFTER 16 WEEKS' TREATMENT. THE SPLEEN BECAME IMPALPABLE IN 4 OF THE 7 DITIOCARB RECIPIENTS, BUT IN NONE OF 8 PLACEBO RECEPIENTS, WITH SPLENOMEGALY AT ENTRY."
- (P.704) - "WHEN CHANGE IN CLINICAL STATUS WAS SCORED AS IMPROVED, STABLE, OR WORSE BY THE PHYSICIANS AFTER 16 WEEKS, 42% OF DITIOCARB RECIPIENTS HAD IMPROVED COMPARED WITH ONLY 5% IN THE PLACEBO GROUP ($p < 0.01$)."
- (P.704) - LANG TABLE II (SEE MY PAGE 13) HIGHLIGHTS THE "DISAPPEARANCE OF CONSTITUTIONAL SYMPTOMS" AND THEY ARE "PERSISTENT DIARRHOEA, WEIGHT LOSS, PERSISTENT FEVER". ALSO NOTE "DISAPPEARANCE OF SPLENOMEGALY".

AND TO TOP IF OFF, THE LANG STUDY SHOWED AN INCREASE IN THE CD4-POSITIVE LYMPHOCYTES (T-HELPER CELLS) - SEE LANG TABLE III (MY PAGE 13) AND STATES (P.705):

"THE PRESENT FINDINGS, AND THOSE ACCOMPANYING LONG-TERM ADMINISTRATION OF DITIOCARB (3 YEARS), CLEARLY SHOW THAT THE CD4+ CELL-DEFECT IS NOT AGGRAVATED. IN FACT, THE REVERSE OCCURRED, WITH DITIOCARB PRODUCING AN INCREASE IN CD4+ CELLS AND IMPROVEMENT IN CONSTITUTIONAL SYMPTOMS OF AIDS-RELATED COMPLEX. FURTHERMORE, PRELIMINARY DATA IN A SMALL NUMBER OF PATIENTS INDICATE THAT DITIOCARB DOES NOT ENHANCE HIV REPLICATION IN VITRO OR IN VIVO."

WHEREAS WITH REISINGER (P.681) THESE CELLS "..... DECREASED IN PERIPHERAL BLOOD IN ALL TREATMENT GROUPS DURING THE STUDY."

SEE ALSO REISINGER TABLE II (MY PAGE 13).

WHAT IN THE WORLD COULD HAVE ACCOUNTED FOR THIS DRAMATIC DIFFERENCE IN RESULTS?

IN BOTH THE REISINGER AND HERSH STUDIES THE SUBJECT OF ALCOHOL IS MENTIONED ALMOST AS AN ASIDE.

IN THE LANG STUDY IT IS NOT MENTIONED AT ALL.

LATE FRIDAY AFTERNOON, MAY 14, THIS THOUGHT OCCURRED TO ME WHILE I WAS REVIEWING THE LANG STUDY:

- MOST FRENCHMEN DRINK WINE WITH THEIR MEALS. -

DOMINIQUE NORBROOK, PASSPORT TO FRANCE, PAGE 20:

"ALTHOUGH MEALS IN FRENCH RESTAURANTS MAY NEED A LOT OF ELABORATE PREPARATION, EVERYDAY COOKING AT HOME IS QUICK, SIMPLE AND TASTY. A MEAL MAY CONSIST OF SEVERAL COURSES, EATEN WITH SLICES OF FRESH, CRUSTY BREAD AND ACCOMPANIED BY WINE."

SUNDAY AFTERNOON, MAY 16, AS I COMPARED AND CONTRASTED THESE THREE STUDIES FOR THE UMPTEENTH TIME IT DAWNED UPON ME - IT DAWNED UPON ME WITH CRYSTAL CLARITY -

IF YOU TAKE A MINUTE AND STEP BACK AND LOOK AT IT FROM A CERTAIN PERSPECTIVE YOU CAN SEE WHAT THE LANG STUDY COULD BE INTERPRETED AS REPRESENTING (ASSUMING, OF COURSE, THAT THE FRENCH DITIOCARB PATIENTS WERE DRINKING WINE WITH THEIR MEALS) -

- THE LANG STUDY REPRESENTS THE SUCCESS OF THE "DISULFIRAM/ALCOHOL PROCEDURE".

1. P.702 - "THE DISEASE DID NOT PROGRESS....."
2. P.704 - "ALL THE 9 PATIENTS IN THE DITIOCARB GROUP....."
3. P.704 - "WHEN CHANGE IN CLINICAL STATUS WAS SCORED....."
4. P.704 - LANG TABLE II
5. P.705 - ".....WITH DITIOCARB PRODUCING AN INCREASE IN CD4+ CELLS....."

WINE DRINKING WITH MEALS IS SO MUCH A PART OF THEIR CULTURE THAT I THINK THE FRENCH RESEARCHERS SIMPLY OVERLOOKED ALCOHOL AS A FACTOR AND DID NOT REALIZE THAT AN EXCESS AMOUNT OF UNMETABOLIZED ACETALDEHYDE WAS BEING GENERATED WHENEVER THE DITIOCARB PATIENTS DRANK WINE WITH THEIR MEALS.

OTHER THAN INTERVIEWING THE PATIENTS THEMSELVES, WHAT CLUES DO WE HAVE THAT THIS MIGHT HAVE BEEN THE CASE?

SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB

SIDE EFFECTS AND ADVERSE REACTIONS WERE NOT FACTORS IN THE REISINGER AND HERSH STUDIES. I STILL CONCLUDED, HOWEVER, THAT THERE MUST HAVE BEEN A SMALL OR MINUTE AMOUNT OF UNMETABOLIZED ACETALDEHYDE AT WORK DESTROYING THE HIV VIRUS ITSELF.

LANG STATES (P.705):

"DITIOCARB DID NOT INDUCE MORE MAJOR ADVERSE CLINICAL OR BIOLOGICAL REACTIONS THAN PLACEBO (TABLE IV), ALTHOUGH IT WAS ASSOCIATED MORE FREQUENTLY WITH MINOR SIDE-EFFECTS — UNPLEASANT TASTE, ABDOMINAL DISCOMFORT, NAUSEA, OR MALAISE."

NOW LET'S LOOK AT LANG TABLE IV (SEE MY PAGE 13).

THERE IS ONE SIDE-EFFECT THAT I WANT TO FOCUS UPON - "NAUSEA". YOU WILL NOTE THAT 19% OF THE DITIOCARB PATIENTS SUFFERED NAUSEA WHEREAS THE REISINGER STUDY NOTED (P.681) THAT:

"NAUSEA AND FATIGUE WERE INFREQUENT IN BOTH DTC GROUPS."

REMEMBER - THE REISINGER "ORAL" GROUP GOT THE SAME DOSAGE AS DID ALL OF THE LANG "ORAL" GROUP - 10mg/kg PER PATIENT.

IF YOU LOOK BACK IN THIS FILE TO THE FEBRUARY 18 LETTER THAT I WROTE TO DR. BADER YOU WILL SEE A PAGE WHERE I LISTED THREE DIFFERENT DESCRIPTIONS WHICH I TOOK FROM THREE DIFFERENT ENCYCLOPEDIAS TO DESCRIBE THE "DISULFIRAM/ALCOHOL PROCEDURE".

IN ALL THREE DESCRIPTIONS IS FOUND THE WORD - "NAUSEA".

IT IS ON THIS BASIS AND LOOKING AT THE OTHER SIDE-EFFECTS LISTED IN LANG TABLE IV THAT I CONCLUDE THAT THE FRENCH DITIOCARB PATIENTS WERE EXPERIENCING "DISULFIRAM/ALCOHOL" REACTIONS.

LET'S SAY I AM CORRECT. LET'S SAY THAT THE "DISULFIRAM/ALCOHOL PROCEDURE" IS THE KEY TO THE ATTACK ON THE HIV VIRUS. HOW THEN SHOULD THE PROCEDURE BE IMPLEMENTED?

ON PAGE 22 OF HIS BOOK 100 QUESTIONS AND ANSWERS ABOUT AIDS - A GUIDE FOR YOUNG PEOPLE, MICHAEL THOMAS FORD STATES:

"TO MAKE THINGS WORSE, THE AIDS VIRUS MAY ENTER A CELL AND BECOME DORMANT, WAITING INSIDE THE CELL TO BE USED AT A LATER TIME. IT CAN STAY THERE AS LONG AS SIX MONTHS WITHOUT THE BODY RECOGNIZING ITS PRESENCE. HIV IS ALSO ABLE TO MUTATE, OR CHANGE ITS FORM, VERY EASILY. THIS MAKES IT VERY DIFFICULT FOR THE IMMUNE SYSTEM TO DESIGN AN EFFECTIVE PLAN OF ATTACK. THE IMMUNE SYSTEM FORMS DEFENSES BASED ON THE INVADING SUBSTANCE'S STRUCTURE. WHEN THAT STRUCTURE CHANGES, WHATEVER DEFENSES HAVE BEEN DESIGNED BECOME USELESS. WHEN HIV MUTATES, THE LYMPHOCYTES THAT HAVE BEEN PROGRAMMED TO ATTACK AND KILL IT NO LONGER RECOGNIZE IT, AND THE AIDS VIRUS CAN MOVE FREELY THROUGHOUT THE BODY UNTIL NEW DEFENSES ARE CREATED."

AND ON PAGE 28 HE STATES:

"SOME PEOPLE DEVELOP AN ACUTE FLULIKE SYNDROME, SIMILAR TO MONONUCLEOSIS, WITHIN TWO TO THREE WEEKS OF BECOMING INFECTED WITH HIV. THIS IS THEN FOLLOWED BY A LONG PERIOD DURING WHICH THE PERSON IS ASYMPTOMATIC, OR HAS NO SYMPTOMS AT ALL. THIS PERIOD CAN LAST FOR MANY YEARS. THIS IS DANGEROUS BECAUSE DURING THIS TIME AN INFECTED PERSON MAY UNKNOWINGLY PASS THE VIRUS ON TO OTHER PEOPLE. DURING THIS ASYMPTOMATIC PERIOD, THE VIRUS WILL CONTINUE TO MULTIPLY. FINALLY, MAYBE AS LONG AS EIGHT TO TEN YEARS AFTER THE INITIAL INFECTION, THE PERSON WILL ONCE AGAIN DEVELOP SYMPTOMS OF HIV INFECTION."

OF COURSE, TO KNOW ALL OF THIS IS VERY, VERY DISTRESSING AND DISCONCERTING. HOWEVER, WITH THE "DISULFIRAM/ALCOHOL PROCEDURE" PERHAPS ENOUGH OF THE HIV VIRUSES THEMSELVES CAN BE DESTROYED PERIODICALLY BY ACETALDEHYDE SO THAT THE CD-4 POSITIVE LYMPHOCYTES (T-HELPER CELLS) COUNT CAN BE INCREASED THUS VOIDING THE CHANCE FOR O.I.s (OPPORTUNISTIC INFECTIONS) TO DEVELOP IN THE BODY.

I DON'T KNOW IF THE HIV VIRUS CAN EVER BE TOTALLY "FLUSHED OUT" OF THE BODY, BUT, FOR STARTERS, THIS IS THE BEST WAY TO GO ABOUT IT THAT I CAN THINK OF -

ADMINISTER THE "DISULFIRAM/ALCOHOL PROCEDURE" ONCE EVERY TWO WEEKS FOR A YEAR - 26 SESSIONS ALL TOLD.

THE ADMINISTRATION WILL REQUIRE THE EXPERT SKILL OF A PHYSICIAN WHO IS WELL EXPERIENCED IN EMPLOYING THE "ANTABUSE" TECHNIQUE OF AVOIDANCE THERAPY TO CONTROL ALCOHOLISM.

THIS IS A VERY PERILOUS PROCEDURE. AS THE ENCYCLOPEDIA AMERICANA, VOLUME 1, PAGE 518, 1991 EDITION STATES:

"BECAUSE OF THE DANGER OF DEATH FROM HEART FAILURE OR RESPIRATORY FAILURE DURING AN ALCOHOL-DISULFIRAM REACTION, THE DRUG SHOULD BE ADMINISTERED ONLY UNDER CAREFULLY CONTROLLED CONDITIONS."

ALSO IN ATTENDANCE SHOULD BE A PHYSICIAN WHO IS A SPECIALIST IN AIDS. HIS JUDGEMENT OF THE PATIENT'S CONDITION WILL BE SOUGHT AND RELIED UPON TO DETERMINE "HOW MUCH" OF THE PROCEDURE SHOULD BE EXPERIENCED AT A TIME.

IN ADDITION, IT MIGHT BE ADVISABLE TO GIVE THE PATIENT ZINC SUPPLEMENTS FOR AS THE ENCYCLOPAEDIA BRITANNICA, MACROPAEDIA, VOLUME 1, PAGE 438, 1974 EDITION STATES:

"AS ABSORBED ALCOHOL IS PASSED THROUGH THE LIVER BY THE CIRCULATING BLOOD, IT IS ACTED UPON BY ADH (ALCOHOL DEHYDROGENASE), A ZINC-CONTAINING ENZYME FOUND CHIEFLY IN THE LIVER CELLS."

WITH THE DANGER OF DEATH ALWAYS AT HAND, THE APPLICATION OF THE PROCEDURE COULD NEVER BE "ROBUST".

I WOULD RANK IT IN TERMS OF "FROM VERY, VERY CONSERVATIVE TO CONSERVATIVE".

IN MY FEBRUARY 18 LETTER TO DR. BADER I USED THIS QUOTE FROM THE ACADEMIC AMERICAN ENCYCLOPEDIA:

".....A PATIENT MUST BE WARNED BEFORE USE OF THE POSSIBLE REACTIONS FROM THE MIXTURE OF THE DRUG AND EVEN VERY SMALL AMOUNTS OF ALCOHOL. REACTIONS INCLUDE HEADACHE, THROBBING IN THE NECK, NAUSEA AND VOMITING, SWEATING, THIRST, AND BLURRED VISION. THEY VARY IN INTENSITY, GENERALLY IN PROPORTION TO THE AMOUNTS OF DRUG AND ALCOHOL INGESTED, AND LAST FROM 30 MINUTES TO SEVERAL HOURS."

"VERY, VERY CONSERVATIVE" I WOULD CALL 30 MINUTES AND "CONSERVATIVE" I WOULD CALL 4 HOURS.

I THINK THAT PATIENTS WITH "FULL BLOWN" AIDS MIGHT CHANCE 30 MINUTES OF TREATMENT, AND PATIENTS WHO HAD RECENTLY BEEN EXPOSED TO AIDS AND HAD JUST BEEN DIAGNOSED AS BEING HIV-POSITIVE MIGHT CHANCE 4 HOURS.

WHEN I WAS 18 I GOT VERY, VERY DRUNK AND WAS SEVERELY HUNG-OVER THE NEXT DAY. IN MY EARLY TWENTIES I GOT VERY, VERY DRUNK THREE OR FOUR TIMES AND WAS SEVERELY HUNG-OVER THE NEXT DAY.

FROM ABOUT 7A.M. UNTIL ABOUT 7P.M. I FELT NAUSEOUS, VOMITED AND HAD A SPLITTING HEADACHE. AT TIMES DURING THIS APPROXIMATE 12 HOUR PERIOD I WAS FEELING SO MISERABLE THAT I WISHED THAT I WERE INDEED DEAD.

APPLICATION OF AND REACTION TO THIS SORT OF ACETALDEHYDE CONCENTRATION I WOULD CATEGORIZE AS BEING "ROBUST".

AFTER A YEAR'S TREATMENT OF THIS NATURE ($\frac{1}{2}$ TO 4 HOURS) THE SPECIALIST IN AIDS MIGHT BE ABLE TO DETERMINE WHETHER THE TREATMENT COULD BE SPACED OUT TO ONCE A MONTH. THEN, IF HE SEES FURTHER IMPROVEMENT, MAYBE A $\frac{1}{2}$ YEAR OF YEARLY "BOOSTER" OF THE "DISULFIRAM/ALCOHOL PROCEDURE" MIGHT BE ALL THAT WOULD BE NEEDED TO KEEP THE HIV VIRUSES FROM INORDINATELY MULTIPLYING.

WHO KNOWS, MAYBE ALL OF THEM COULD EVENTUALLY BE CLEANSED OUT OF THE BODY.

I WANT TO CONCLUDE BY REITERATING A STATEMENT WHICH I INITIALLY MADE IN MY JANUARY 19 LETTER TO CONGRESSMAN VISCLOSKY:

THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

IN TERMS OF METABOLISM, ACETALDEHYDE IS REALLY QUITE A UNIQUE SUBSTANCE AS FAR AS THE BODY IS CONCERNED, IS IT NOT?

THE CLOSEST "CHEMICAL COUSIN" TO ACETALDEHYDE IS THE GAS, FORMALDEHYDE. FORMALIN, A 37% SOLUTION OF CASEOUS FORMALDEHYDE, IS AN IMPORTANT INGREDIENT OF EMBALMING FLUID. WHAT MIGHT HAPPEN IF A LITTLE BIT OF FORMALIN WERE INJECTED INTO A PERSON? WOULD DEATH OR BLINDNESS BE THE RESULT?

ACETALDEHYDE IS ALSO CLOSELY RELATED TO THE GAS THAT IS USED IN COMBINATION WITH OXYGEN TO PRODUCE THE HOTTEST FLAME KNOWN TO MAN, THE FLAME THAT CUTS THROUGH STEEL - ACETYLENE ("ACETALDEHYDE IS MADE COMMERCIALY BY THE ADDITION OF WATER TO ACETYLENE IN THE PRESENCE OF SULFURIC ACID AND MERCURIC SULFATE." - THE NEW COLUMBIA ENCYCLOPEDIA, 1975 EDITION, P.11).

SYMBOLICALLY, PERHAPS ACETALDEHYDE WILL PROVE TO BE THE "INNER FLAME" BY WHICH THE HIV VIRUS CAN BE VANQUISHED FROM THE BODY.

I HOPE SO.

John S. Robert

LANG

704

TABLE II—CLINICAL OUTCOME OF HIV INFECTION IN FIRST ARM OF TRIAL

	Active	Placebo	p†
Progression to AIDS	0/38	3/39 (PCP, <i>Mycobacterium</i> , and Kaposi sarcoma)	..
Disappearance of constitutional symptoms* (IV-A patients)	8/11	0/5	<0.001
Lymphadenopathy score	-0.43† (SD 1.94)	+0.43† (SD 1.26)	<0.05
Disappearance of splenomegaly	4/7	0/8§	<0.05

*Persistent diarrhoea, weight loss, persistent fever.

†Fisher's exact test.

‡Change from baseline.

§No spleen became palpable; two additional spleen enlargements were noted.

LANG

TABLE III—CD4 CELL COUNT DURING THE FIRST ARM OF TRIAL

	Active		Placebo		p*
	Patients tested	Median (mean, SD) count	Patients tested	Median (mean, SD) count	
Baseline	42	415 (405, 111)	41	380 (389, 132)	NS
Week 8	36	479 (517, 172)	39	420 (461, 226)	NS
Week 16	36	522 (542, 215)	38	420 (447, 181)	<0.05

*Student's *t* test.

LANG

THE LANCET, SEPTEMBER 24, 1988

TABLE IV—SIDE-EFFECTS

Adverse reaction	Percentage of patients with adverse reactions	
	Active (n = 83)	Placebo (n = 79)
Unpleasant taste	41 (32)	4 (3)
Abdominal discomfort	33 (26)	8 (6)
Nausea	19 (15)	3 (2)
Sensation of malaise	10 (8)	1 (1)
Anorexia	9 (7)	1 (1)
Excitement	6 (5)	3 (2)
Somnolence	5 (4)	1 (1)
Vomiting	2 (2)	1 (1)
Rash	0 (0)	0 (0)

Number of patients in parentheses. No patient in either group had >25% drop in haemoglobin concentrations, red or white cell count, or platelet count.

REISINGER

TABLE II—T-HELPER CELL COUNTS PER μ l BLOOD IN PATIENTS WITH INITIAL COUNT BELOW 814/ μ l

Route	Time (mo)	Placebo	DTC
Oral	0	467 (193)	493 (204)
	6	442 (327)	428 (167)
	% loss	5.9 (53.5)	5.4 (37.7)
Intravenous	0	422 (283)	388 (225)
	6	250 (263)	352 (345)
	% loss	51.4 (35.6)	20.8 (30.4)

HALF-LIFE OF ACETALDEHYDE

$$10 \rightarrow 5 \text{ (3.1 min.)}$$

$$5 \rightarrow 2.5 \text{ (3.1 min.)}$$

$$2.5 \rightarrow 1.25 \text{ (3.1 min.)}$$

$$1.25 \rightarrow 0.625 \text{ (3.1 min.)}$$

$$\textcircled{6} \quad 0.625 \rightarrow 0.313 \text{ (3.1 min.)}$$

$$0.313 \rightarrow 0.157 \text{ (3.1 min.)}$$

$$0.157 \rightarrow 0.079 \text{ (3.1 min.)}$$

$$0.079 \rightarrow 0.040 \text{ (3.1 min.)}$$

$$0.040 \rightarrow 0.020 \text{ (3.1 min.)}$$

$$0.020 \rightarrow 0.010 \text{ (3.1 min.)}$$

$$0.010 \rightarrow 0.005 \text{ (3.1 min.)}$$

$$0.005 \rightarrow 0.0025 \text{ (3.1 min.)}$$

$$0.0025 \rightarrow 0.0013 \text{ (3.1 min.)}$$

$$6 \times 3.1 = 18.6 \text{ MINUTES}$$

$$\begin{array}{r} 98.43 \\ 1.57 \\ \hline 100.00 \end{array}$$

98.43%

METABOLIZED
AT THIS
POINT

P.S. TO CONGRESSMAN VISCLOSKY:

COULD CLINICAL TRIALS OF THE "DISULFIRAM/ALCOHOL PROCEDURE" BEGIN IMMEDIATELY AT ONE OF OUR LOCAL HOSPITALS IN LAKE OR PORTER COUNTY. I DO NOT THINK THAT ALOT OF FUNDING WOULD BE REQUIRED. ALL THAT IS NEEDED IS A HOSPITAL ROOM, THE SERVICES OF A PHYSICIAN SPECIALIZING IN THE "ANTABUSE" TREATMENT FOR ALCOHOLISM, THE SERVICES OF A PHYSICIAN SPECIALIZING IN THE TREATMENT OF AIDS AND THE EXPERTISE OF A LABORATORY TECHNICIAN.

RESPECTFULLY,

J.S.R.

COPIES TO:

CONGRESSMAN PETER J. VISCLOSKY
 PROFESSOR RUSSELL F. MANKES, DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY,
 THE ALBANY MEDICAL COLLEGE
 DONALD M. GALLANT, M.D., TULANE UNIVERSITY SCHOOL OF MEDICINE
 JEAN CARAUX, INSTITUT MERIEUX, LYON, FRANCE (LANG ET AL)
 PROFESSOR M. DIETRICH, BERNHARD NOCHT INSTITUTE FOR TROPICAL MEDICINE,
 HAMBURG, WEST GERMANY (REISINGER ET AL)
 EVAN M. HERSH, M.D., ARIZONA CANCER CENTER (HERSH ET AL)
 DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
 WYNDHAM H. WILSON, M.D., Ph.D., SPECIAL ASSISTANT TO THE DIRECTOR,
 NATIONAL INSTITUTES OF HEALTH
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 RANDY SHILTS, SAN FRANCISCO CHRONICLE
 JIM GORDON, GARY POST-TRIBUNE
 PETER S. ARNO, Ph.D., MONTEFIORE MEDICAL CENTER
 DR. MARTIN S. HIRSCH, DIRECTOR OF AIDS RESEARCH, MASSACHUSETTS GENERAL HOSPITAL
 "U.S.A. TODAY"
 "THE LANCET"
 "JAMA - THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION"
 "JOURNAL OF APPLIED TOXICOLOGY"
 OMAR BAGASRA, M.D., Ph.D., THOMAS JEFFERSON UNIVERSITY
 WILLIAM A. HASELTINE, CHIEF, LABORATORY OF BIOCHEMICAL PHARMACOLOGY,
 DANA-FARBER CANCER INSTITUTE, BOSTON; PROFESSOR, DEPARTMENT OF
 PATHOLOGY, HARVARD MEDICAL SCHOOL

MAY 3, 1993

DR. OMAR BAGASRA
JEFFERSON ALUMNI HALL
ROOM 328A
THOMAS JEFFERSON UNIVERSITY
1020 LOCUST STREET
PHILADELPHIA, PENNSYLVANIA 19107

DEAR DR. BAGASRA,
I HAVE NOT YET RECEIVED FROM YOU A REPLY TO MY LETTER OF APRIL 9.
JUST IN CASE YOU DID NOT RECEIVE IT, I AM SUBMITTING IT TO YOU AGAIN.
DR. BAGASRA, BEFORE THIS MONTH IS OVER, COULD YOU POSSIBLY ANSWER
THIS QUESTION FOR ME -

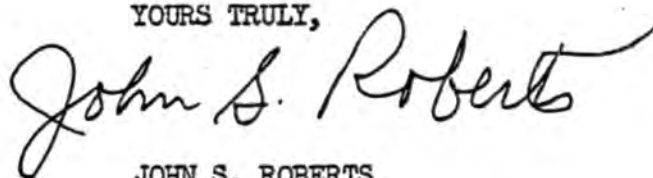
IS THE HIV VIRUS DESTROYED IN VITRO BY THE ADDITION OF ACETALDEHYDE?

BY THE FIRST OF JUNE, AT THE LATEST, I WANT TO "GO PUBLIC" WITH THIS
FILE BY MAKING ITS AVAILABILITY KNOWN THROUGH MEDIA ADVERTISEMENTS.

IN LIGHT OF PROFESSOR MANKES' APRIL 16 LETTER, ATTACHED, I HAVE DONE
SOME MORE RESEARCH AND WILL HAVE A FEW MORE PAGES TO ADD TO THIS FILE.

DR. BAGASRA, I REALLY WOULD APPRECIATE HEARING FROM YOU, AND I WANT
TO THANK YOU FOR GIVING THIS MATTER YOUR TIME AND CONSIDERATION.

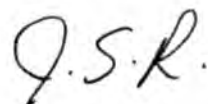
YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO: CONGRESSMAN PETER J. VISCLOSKY (WASHINGTON AND GARY OFFICES)
PROFESSOR RUSSEL F. MANKES, THE ALBANY MEDICAL COLLEGE

P.S. ON JUNE 1 I CALLED DR. BAGASRA AND WAS TOLD THAT HE HAD JUST LEFT
THE COUNTRY TO ATTEND A TWO WEEK CONFERENCE IN PARIS. WHEN I OBTAIN
AN ANSWER FROM HIM I WILL BE MORE THAN HAPPY TO INCLUDE IT IN THIS FILE.





The Albany Medical College

Albany, New York 12208

DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY
THE NEIL HELLMAN MEDICAL RESEARCH BUILDING, A-136
(518) 445-5303
FAX (518) 445-5799

Mr. John S. Roberts
POB H
Hobart, IN 46342

16 April, 1993

Dear Mr. Roberts,

I received a package of correspondence from and to you relative to acetaldehyde and HIV today. I am really not sure why it was sent to me as I am not an AIDS researcher, my area of expertise lies in Toxicology, specifically alcohol. From your correspondence it appears that you have developed the hypothesis that acetaldehyde may be a useful adjunct to therapy for HIV infected individuals. It appears that this hypothesis has generally been dismissed by the NIH, specifically by Dr. John Bader.

From my perspective I would like to add a degree of caution to your continued efforts. Acetaldehyde, a highly toxic intermediate of alcohol metabolism, could in fact cause damage to viruses. However, the danger lies in the specificity of the toxicity. The therapeutic drugs which are being developed (such as AZT, DDC, etc.) rely on the principal of selective (or specific) toxicity, they cause death or damage to the infectious agent or diseased cell at doses which do not significantly affect normal function. A chemical that kills the patient while it kills the virus or cancer is not a useful drug. In the case of acetaldehyde, as you so rightly pointed out, it is toxic (and severely so) to a wide variety of human organ systems at exceedingly low dose levels. We believe it may also target the T-cells of the immune system and produce a lessening of their function, something which would be very dangerous in an HIV infected human. I do not dismiss your hypothesis, only add a note of caution to your quest.

It is important to remember that the more we learn about the basic biology of a disease process, the more likely we are to find a cure. I would urge you to continue your efforts, particularly with members of congress, to increase funding for medical research generally since, as amply illustrated by your letters, we cannot determine from where the next advance will come (perhaps the cure for AIDS will be found by research on the genetics of the fruit fly!!).

If I may be of any assistance to you please do not hesitate to write.

Sincerely,

Russell F. Mankes, Ph.D.
Associate Professor

APRIL 9, 1993

DR. OMAR BAGASRA
JEFFERSON ALUMNI HALL
ROOM 328A
THOMAS JEFFERSON UNIVERSITY
1020 LOCUST STREET
PHILADELPHIA, PENNSYLVANIA 19107

DEAR DR. BAGASRA,

I RECENTLY READ ABOUT YOUR RESEARCH IN THE MARCH 22, 1993 ISSUE OF "USA TODAY".

WOULD YOU PLEASE GIVE SOME CONSIDERATION TO THE ATTACHED FILE.

WOULD YOU THINK OF DOING YOUR EXPERIMENT AGAIN, BUT THIS TIME ADD ONE ADDITIONAL INGREDIENT TO THE TEST TUBE - A DROP OR TWO OF ACETALDEHYDE.

SINCE ACETALDEHYDE IS A HIGHLY TOXIC POISON, IS THERE THE REMOTEST POSSIBILITY IN THE WORLD THAT IT COULD DESTROY THE HIV VIRUS?

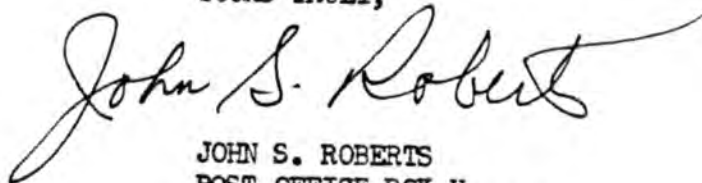
I THINK THAT THE EFFECTS OF THE "DISULFIRAM/ALCOHOL PROCEDURE" COULD LAST AS LONG AS 12 HOURS.

IN NORMAL CONDITIONS (WITHOUT DISULFIRAM IN THE BODY) I BELIEVE THAT ACETALDEHYDE IS METABOLIZED IN JUST A FEW MINUTES BY THE LIVER.

WHAT EFFECT WOULD "UNMETABOLIZED" ACETALDEHYDE HAVE UPON THE HIV VIRUS?

IN OTHER WORDS, AFTER 12 HOURS WOULD THE HIV VIRUS STILL BE ALIVE IN THE TEST TUBE AFTER A DROP OR TWO OF ACETALDEHYDE HAD BEEN ADDED TO IT?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO: CONGRESSMAN PETER J. VISCLOSKEY, BERNADINE HEALY, M.D.;
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DR. LUC MONTAGNIER, RANDY SHILTS, JIM GORDON, PETER S. ARNO, Ph.D;
DONALD M. GALLANT, M.D.; EVAN M. HERSH, M.D.; DR. MARTIN S. HIRSCH AND
YUNG-KANG CHOW, "USA TODAY"

British Academy of Film and Television Awards, seen as early pointers to the Oscars, presented Sunday. Robert Downey Jr. won the best actor award for his role in *Chaplin*, and the Alexander Korda Award for Best British Film went to *The Crying Game*. All three winners are nominated for Oscars to be awarded March 29.

MS DRUG APPROVED: The first drug designed to combat the crippling effects of multiple sclerosis was endorsed Friday by an advisory committee of the Food and Drug Administration. The panel heard evidence that MS patients treated with beta interferon suffer fewer and less severe attacks of the crippling disease that afflicts about 350,000 Americans.

AIDS AND ALCOHOL: A few drinks of alcohol may raise a healthy person's chances of becoming infected with the AIDS virus or speed up the disease in those already infected, a new study says. Researchers at Thomas Jefferson University in Philadelphia put the AIDS virus in a test tube along with white blood cells of 60 healthy people who had had several drinks over a weekend. They found that HIV, the virus that causes AIDS, quickly replicated. "Even casual consumption of alcohol stimulates replication of the AIDS virus in cell cultures," said Omar Bagasra, author of the study in the *Journal of Infectious Diseases*.

MOO HOO HOO: Former University of Maine student Andrea Pizzo, 23, is suing the school for not protecting her from a cow with a "dangerous disposition." Pizzo says officials in the school's livestock management department should have known that the Jersey heifer that attacked her in the spring of 1991 had a personality problem. The lawsuit seeks unspecified damages for knee and wrist injuries Pizzo claims she suffered when the 400-pound bovine head-butted her into the wall of its pen. Charles Wallace, Pizzo's instructor, says he has worked around cattle for more than a decade and was surprised by the lawsuit: "Cows are usually pretty docile. But that is the chance you take working around large animals."

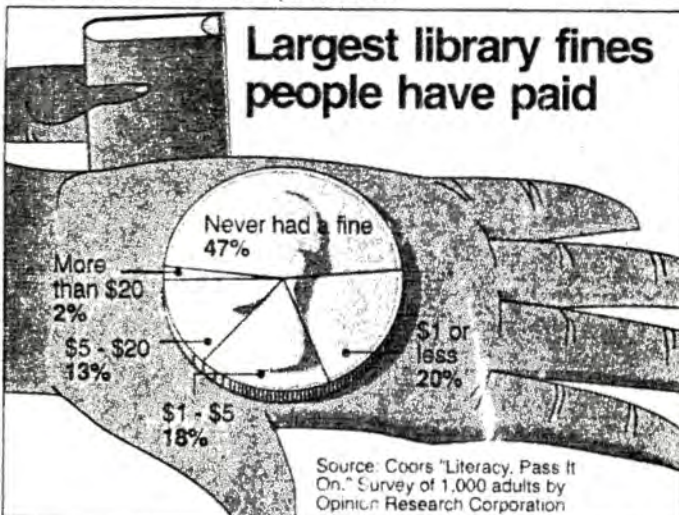
By Arlene Vigoda

Inside LIFE

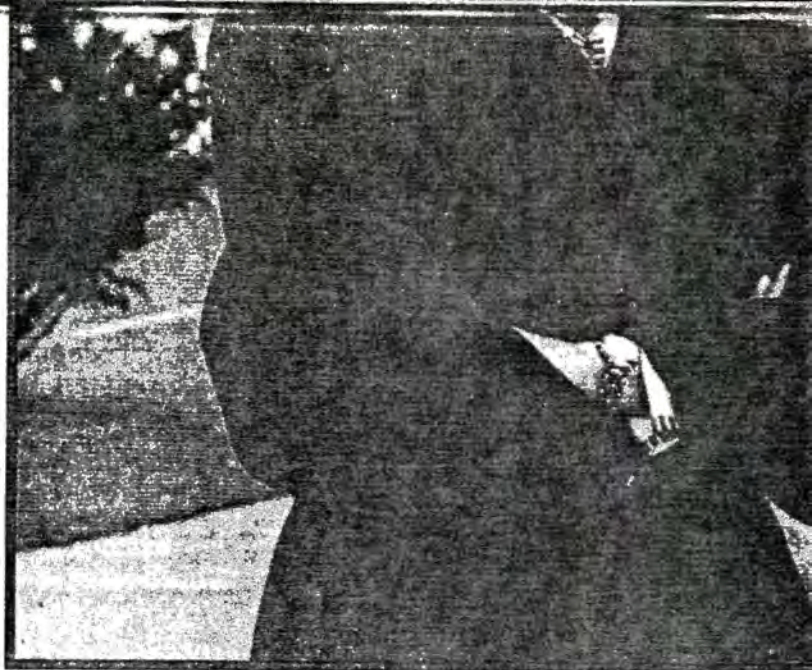
Crossword	5D	Show	4D
Larry King's People	2D	Television	3D
People	2D	TV Listings	6D

USA SNAPSHOTS®

A look at statistics that shape our lives.



By Elys A. McLean, USA TODAY



NO PUSHOVER: NBC correspondent Andrea Mitchell doesn't mind ruffling. 'My value to NBC is my ability to reach judgments about what decisions Clinton

COVER STORY

Clinton cadre has Andrea to answer to

For NBC journalist Mitchell, 'The whole point is to provoke a response.'

By Peter Johnson
USA TODAY

WASHINGTON — NBC's Andrea Mitchell is tenacious. Like a pit bull. With a bone.

That's why during a recent trip by President Clinton to Franklin Roosevelt's home in Hyde Park, N.Y., Mitchell — after a sound bite — had Air National Guardsmen chasing her across the tarmac wielding their M-16s,

handcuffs ready, as fellow White House reporters, sequestered in a bus, shouted "Go Andrea!"

Secret Service agents, who know Mitchell, got the soldiers to back off. The kicker: Mitchell got the one sound bite that colleagues needed: Clinton explaining an earlier remark about the possibility of a new tax.

"It was wonderful," says ABC's Brit Hume, savoring the image of Mitchell — assigned to the press pool that day — getting sprayed with jet wash from Air Force One and nearly getting arrested. "You don't want to be the one denying her entry unless you're heavily armed."

Is she the new Sam Donaldson of la Casa Blanca?

"I WOULDN'T HANG THAT MONIKER ON HER!" booms The Voice, ABC's Donaldson, who competed with

Please see COVER STORY next page ▶

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Maybe have been developm of late 'in maybe it's pah involu pan's Akin

MOVIE

SUSAN V

the greater time, for sewer-soak

But in Nina Tur nardo, Do gelo and R into creatu erate, like learned th their beds. half shell "cowabunga barely eve

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POINTE-AUX-TREMBLES [pwæ't o trā'bl], a town on Montreal Island, Quebec, Canada, situated on the St. Lawrence River about 10 mi. north of downtown Montreal and adjoining the industrial town of Montreal East. It is on Provincial Highway 2, and the Canadian Pacific Railway serves the town. It was founded as a parish in 1674 and as a town in 1912. Pop. 1951, 8,241. D.F.P.

POINTE-CLAIRE [pwæ't kle'r], a town on Montreal Island, Quebec, Canada, situated on the north shore of Lake Saint Louis, about 15 mi. southwest of downtown Montreal. It is on Provincial Highway 2 and is served by the Canadian National and Canadian Pacific railways. Founded as a parish in 1717, the community was incorporated as a village in 1854 and as a town in 1911. It is a residential and resort suburb of Montreal. Pop. 1951, 8,753. D.F.P.

POINTER. See DOG.

POISON ASH. See POISON IVY.

POISON GAS. See WARFARE (Chemical Warfare).

POISONING, TREATMENT OF. See FIRST AID.

POISON IVY, the name commonly given to a group of poisonous plants, considered by most botanists to be sumacs, *Rhus*. Other botanists have placed the group in a separate genus, *Toxicodendron*.

The common poison ivy, *R. radicans*, most widely distributed of the species, grows from Nova Scotia to British Columbia, south to Mexico, Florida, and Bermuda. Nevada is the only state from which it has not been reported. In many parts of its range, it is a low straggling shrub, but it frequently develops into a stout, woody vine climbing high trees. Similar is the southern poison oak, *R. toxicodendron*, a low shrub found in dry woodlands from New Jersey to Georgia and Texas. The western poison oak, *R. diversiloba*, is found from Washington south throughout California to Mexico. It is an erect, sometimes climbing shrub 4 to 8 ft. high. In California poison oak is more widely diffused than any other shrub. These three plants have leaves divided into three ovate leaflets, the margins variously toothed and lobed, but sometimes having little or no lobation. The flowers are inconspicuous greenish-white, appearing in clusters, and the small greyish-white waxy fruits, resembling those of the bayberry, *Myrica pensylvanica*, contain a small, bony stone. These three species, all known popularly as poison ivy, poison oak, and poison sumac, may eventually come to be considered as one variable species. The true poison sumac, *R. vernix*, also called poison elder, poison ash, and poison dogwood, is a large shrub growing sometimes as high as 25 ft. It has ash-like leaves of 7 to 13 entire leaflets, greenish flowers, and whitish fruit in long pendent clusters. It grows in swamps from Quebec and Minnesota, south to Florida and Texas. Poisoning is caused by a nonvolatile oil present in the sap.

Aside from the hazardous method of digging, plants may be eradicated by ammonium sulfamate, or 2, 4-D, (2, 4-dichlorophenoxyacetic acid) applied to the foliage according to directions. Also, 1 lb. of dry borax per square rod applied to the soil will kill poison ivy and numerous other plants. See also IVY POISONING. G. Gr.

POISON OAK. See POISON IVY.

POISONS, chemical agents which, when present in sufficient amounts, may injure or kill a living organism. They may be swallowed, inhaled, or absorbed or injected through the skin.

Classification. One method by which poisons may be classified is according to their chemical and physical types, e.g., acids, alkaloids, industrial solvents, inorganic chemicals, organic chemicals, poisonous gases, and poisonous foods. Another classification of poisons would be according to their physiological action. Some chemicals are local poisons; these are (1) the corrosive poisons, which destroy tissue by direct contact, e.g., the mineral acids, caustic alkalies, and phenol; and (2) the irritant compounds of arsenic, lead, mercury, zinc, and so on. Other chemicals are systemic poisons; these are absorbed into the blood stream, whence they are carried to, and act upon, the heart, kidneys, nervous system, and other vital organs. This type includes cyanide, hypnotics, opium derivatives, and strychnine.

Common Types of Poison. Some poisonous chemicals frequently found about the home, and therefore suspect if illness occurs, include the following:

Cleaners: ammonia, lye (sodium hydroxide), phenol (carbolic acid), phosphates, washing soda (sodium carbonate).

Insecticides: compounds containing arsenic, thallium, fluorine, lead, copper, and phosphorus: D.D.T., pyrethrum, orthodichlorobenzene.

Laxatives: calomel, phenolphthalein.

Liniments and Ointments: camphor, chloroform, oil of wintergreen.

Moth Repellent: camphor, naphthalene, paradichlorobenzene, arsenicals.

Soothing Sirup and Sedatives: opium derivatives, chloroform, bromides, acetanilide, barbiturates (Veronal).

Reports made by the city of New York give an interesting appraisal of the frequency of certain types of poisonings. In 1941 there were 500 suicidal and 676 accidental poisonings. Of the 500 suicides, the poisons employed were as follows: illuminating gas (carbon monoxide), 387; barbiturates, 33; phenol, 20; cyanide, 15; sodium fluoride, 10; and arsenicals, 7. Of the 676 accidental poisonings, the poisons used were as follows: alcohol, 424; anesthetics, 147; barbiturates, 17; narcotics, 16; wood alcohol, 7; arsenic or other heavy metals, 8.

Industrial solvents and hazardous chemicals deserve special mention. Besides the acute poisoning which may result from swallowing them, there is a hazard from continued exposure to vapors or liquid sprays. Such exposure results in chronic poisoning if the chemical accumulates in the body faster than it can be eliminated. Lead poisoning is an example. The following expression first observed by Fritz Haber in connection with war gas effects can be generally applied:

$$\text{Extent of poisoning} = \frac{\text{exposure}}{\text{time}} \times \text{concentration of the poison}$$

Thus, approximately the same body damage is caused by exposure to 50 parts per million (p.p.m.) for two hours as by 100 p.p.m. for one hour. Hydrogen cyanide gas is an exception to this rule.

Other poisons not previously mentioned include: acetaldehyde; acetanilide; acetone; acetylene and acetylene compounds; acids (glacial acetic, boric, hydrochloric, hydrofluoric, nitric, oxalic, phosphoric, sulphuric); alkaloids (aconite, apomorphine, atropine, caffeine, cocaine, codeine, digitalis, ergot, heroin, morphine, nicotine, strychnine); amyl acetate; aniline; antimony compounds; arnica; arsine; barium compounds; belladonna; benzene; benzine; bismuth compounds; bromine; cadmium compounds; calcium oxide; cantharides; carbon dioxide; carbon disulphide; carbon tetrachloride; chloral hydrate; chlorine; chloropicrin; croton oil; curare; di-



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

Building 31, Room 3A44
(301) 496-6404

March 24, 1993

Mr. John S. Roberts
P.O. Box H
Hobart, IN 46342

Dear Mr. Roberts:

Your letter to Dr. Bernadine Healy was referred to my office for reply. We, like you, are dedicated to finding a cure for HIV. However, acetaldehyde is a normal metabolite of the human body and will have no effect on HIV infection.

Dr. John Bader, Chief, Antiviral Evaluation Branch, has also reviewed your idea and has sent you a letter. I appreciate your interest.

Sincerely,

Wyndham H. Wilson, M.D., Ph.D.
Special Assistant to the Director
Division of Cancer Treatment

FEBRUARY 26, 1993

DR. BERNADINE HEALY
DIRECTOR
NATIONAL INSTITUTES OF HEALTH
BUILDING 1, ROOM 126
9000 ROCKVILLE PIKE
BETHESDA, MARYLAND 20892-0001

DEAR DR. HEALY,

ATTACHED ARE THE COPIES OF MY FEBRUARY 18 LETTER TO DR. BADER AND CONGRESSMAN VISCLOSKY'S LETTER OF FEBRUARY 11 TO ME (IN RESPONSE TO A PREVIOUS LETTER OF MINE) WHICH I DID NOT BECOME AWARE OF UNTIL AFTER I HAD MAILED THE FEBRUARY 18 LETTER.

IT IS TOO EARLY FOR ME TO HAVE RECEIVED A REPLY FROM DR. BADER; HOWEVER, I JUST THOUGHT I WOULD GO AHEAD AND WRITE TO YOU SINCE THIS LETTER WILL REFLECT MY MOST CURRENT IDEAS.

FIRST OF ALL - ABOUT THE POSSIBLE BENEFICIAL EFFECTS OF THE METABOLITE OF DISULFIRAM (ANTABUSE) KNOWN AS "DITIOCARB" OR "DTC" - DOES EVERYBODY KNOW ABOUT IT? THE "JAMA" ARTICLE WAS PUBLISHED MARCH 27, 1991, AND THE ONLY ENTRY IN THE CUMULATED INDEX MEDICUS HAVING TO DO WITH DISULFIRAM AND AIDS HAS TO DO WITH DR. GALLANT'S ARTICLE.

IN HIS ARTICLE, "ANTABUSE (DISULFIRAM) AND AIDS", DR. GALLANT STATES,

'A SIGNIFICANT PERCENTAGE OF ORAL DISULFIRAM IS RAPIDLY REDUCED IN THE BODY TO DTC.'

WOULD ALL AIDS PATIENTS BE IMMEDIATELY BENEFITTING THEMSELVES BY SIMPLY HAVING THEIR DOCTORS PRESCRIBE ANTABUSE TABLETS FOR THEM?; HOWEVER, KNOWING FULL WELL THAT THEY CANNOT DARE TO TAKE A SIP OF ALCOHOL WHILE DISULFIRAM IS IN THEIR BODY.

LET US SUPPOSE THAT A PILOT PROGRAM IS SET UP TO TEST THE EFFECTIVENESS OF "THE DISULFIRAM/ALCOHOL PROCEDURE", AND IT PROVES TO BE A FAILURE. THIS WOULD NOT NECESSARILY ABNEGATE THE POTENTIAL USEFULNESS OF ACETALDEHYDE.

ACETALDEHYDE COULD STILL BE LOOKED UPON AS PART OF THE ARSENAL IN THE QUEST TO DISCOVER THE "MAGIC BULLET" TO DESTROY THE HIV VIRUS.

ON PAGE 17 OF AGAINST THE ODDS - THE STORY OF AIDS DRUG DEVELOPMENT, POLITICS & PROFITS, DR. PETER S. ARNO STATES,

"BETWEEN 1987 AND 1991 THE NATIONAL CANCER INSTITUTE TESTED 40,000 CHEMICAL COMPOUNDS AT FACILITIES IN FREDERICK, MARYLAND, AND BIRMINGHAM, ALABAMA, TO SEE IF ANY COULD DISABLE THE AIDS VIRUS."

IN MACBETH, ACT IV, SCENE 1, LINES 10-21, SHAKESPEARE SAYS,

"ALL. DOUBLE, DOUBLE TOIL AND TROUBLE,
FIRE BURN AND CALDRON BUBBLE.
2. WITCH. FILLET OF A FENNY SNAKE,
IN THE CALDRON BOIL AND BAKE.
EYE OF NEWT AND TOE OF FROG,
WOOL OF BAT AND TONGUE OF DOG,
ADDER'S FORK AND BLINDWORM'S STING,
LIZARD'S LEG AND HOWLET'S WING,
FOR A CHARM OF POWERFUL TROUBLE,
LIKE A HELL BROTH BOIL AND BUBBLE.
ALL. DOUBLE, DOUBLE TOIL AND TROUBLE,
FIRE BURN AND CALDRON BUBBLE."

IF "THE DISULFIRAM/ALCOHOL PROCEDURE" DOES NOT WORK, I THINK EACH ONE OF THE 40,000 TESTS SHOULD BE REPEATED WITH ACETALDEHYDE BEING MIXED IN WITH EACH TEST. WHO KNOWS, IT MIGHT PROVE TO BE SOME SORT OF CATALYST BY WHICH THE DESTROYER OF THE HIV VIRUS IS DISCOVERED.

"DOUBLE, DOUBLE TOIL AND TROUBLE"

I HAVE HIGHLIGHTED AN INDISPUTABLE FACT OF NATURE -

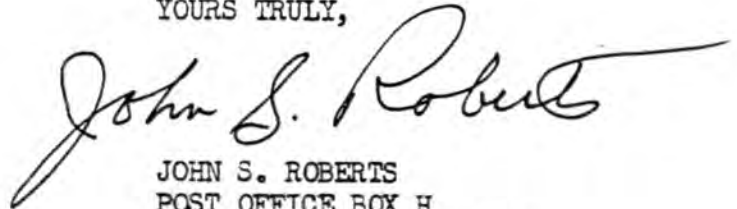
THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

IF A MEDICINE WERE INJECTED INTO A BODY WHILE THAT BODY WAS BEING POISONED WITH ACETALDEHYDE, THE RESULTS MIGHT BE FAR DIFFERENT THAN THEY WOULD NORMALLY BE, MIGHT THEY NOT?

WELL, THIS IS ABOUT ALL I HAVE TO SAY FOR NOW, DR. HEALY. AS A FIRST STEP, I HOPE THAT SOME OF THE CLINICAL TRIALS THAT ARE PRESENTLY BEING CONDUCTED IN CHICAGO WILL START TO EMPLOY "THE DISULFIRAM/ALCOHOL PROCEDURE".

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO CONGRESSMAN PETER J. VISCLOSKY, JOHN P. BADER, Ph.D, DR. LUC MONTAGNIER,
RANDY SHILTS, JIM GORDON, PETER S. ARNO, Ph.D., AND DR. DONALD M. GALLANT
AND DR. EVAN M. HERSH, PRIMARY AUTHOR OF THE "JAMA" ARTICLE

FEBRUARY 18, 1993

JOHN P. BADER, Ph.D.
CHIEF, ANTIVIRAL EVALUATIONS BRANCH
DEVELOPMENTAL THERAPEUTICS PROGRAM
DIVISION OF CANCER TREATMENT
NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTES OF HEALTH
ROCKVILLE PIKE
BETHESDA, MD 20892

DEAR DR. BADER,

ATTACHED ARE A COPY OF YOUR LETTER TO ME DATED JANUARY 26, 1993
AND A COPY OF PAGE 39 TAKEN FROM DRUGS, A TIME INC. PUBLICATION, COPYRIGHT
DATE 1967.

A BASIC QUESTION NEEDS TO BE ANSWERED - DOES ACETALDEHYDE DESTROY
THE AIDS VIRUS? FOR INSTANCE, IF A DROP OF ACETALDEHYDE WERE PLACED
IN A TEST TUBE CONTAINING THE BLOOD OF A VICTIM WHO HAD THE HIV VIRUS,
WOULD THAT VIRUS BE DESTROYED?

IF THE ANSWER TO THIS QUESTION IS "NO", YOU MAY AS WELL SKIP THE REST
OF THIS LETTER BECAUSE I'LL ONLY BE WASTING YOUR TIME.

HOWEVER, MY HUNCH IS THAT ACETALDEHYDE WILL DESTROY THE VIRUS,
AND I HAVE THE FOLLOWING OBSERVATIONS TO MAKE -

ON FEBRUARY 11 I BECAME AWARE OF PAGE 39 FROM DRUGS. AFTER READING
THIS PAGE I KNEW THAT I HAD FOUND THE POSSIBILITY OF A CURE FOR AIDS.
OF COURSE, I WAS EXTREMELY CURIOUS TO SEE IF ANYONE ELSE HAD EVER
THOUGHT OF IT BEFORE.

ON SATURDAY, FEBRUARY 13 I WENT TO THE CAMPUS LIBRARY OF INDIANA
UNIVERSITY NORTHWEST AND LOOKED AT THE ENTRIES HAVING TO DO WITH
"DISULFIRAM" IN THE CUMULATED INDEX MEDICUS. I STARTED WITH THE YEAR 1983
BECAUSE THAT IS WHEN THE FIRST MENTION OF "ACQUIRED IMMUNODEFICIENCY SYNDROME"
IS MADE IN THIS INDEX.

IN THE APRIL, 1992 ISSUE OF THIS INDEX AN ARTICLE WAS CITED -

ANTABUSE (DISULFIRAM) AND AIDS

AND IT APPEARED IN THE OCTOBER, 1991 ISSUE OF THE JOURNAL, "ALCOHOLISM,
CLINICAL AND EXPERIMENTAL RESEARCH".

ON MONDAY, FEBRUARY 15 THE SYSTEM SERVICES DIVISION OF THIS LIBRARY
OBTAINED FOR ME A FAX COPY OF THE ARTICLE FROM THE INDIANA UNIVERSITY
SCHOOL OF MEDICINE LIBRARY IN INDIANAPOLIS.

THE ARTICLE CITES FOUR ADDITIONAL REFERENCES. ONE REFERENCE WAS
FROM THE "JOURNAL OF EXPERIMENTAL MEDICINE", TWO WERE FROM "LANCET",
AND ONE WAS FROM "JAMA" (JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION).

ALL FOUR OF THESE REFERENCES WERE READILY AVAILABLE AT THE NORTHWEST
LIBRARY AND AT THE MEDICAL LIBRARY IN THE BUILDING JUST NEXT DOOR.

FROM WHAT I COULD UNDERSTAND FROM THESE ARTICLES, THERE SEEMS TO BE A DAWNING REALIZATION THAT SOMETHING VERY BENEFICIAL MIGHT BE AT HAND WITH THE UTILIZATION OF A METABOLITE OF DISULFIRAM. THIS METABOLITE HAS SEVERAL NAMES WITH THE SIMPLEST ONE BEING DITIOCARB OR DTC.

TO QUOTE FROM THE ARTICLE ITSELF - (IN A FEW PLACES I HAVE SUPPLIED THE PARENTHESIS AND THE UNDERLINES) -

"WHILE FOUR PATIENTS IN THE PLACEBO GROUP DEVELOPED CDC-DEFINED AIDS (CENTER FOR DISEASE CONTROL), NONE DID SO IN THE DTC GROUP. IN ADDITION, THE DTC GROUP SHOWED A DECREASE IN SPLENOMEGALY AND LYMPHADENOPATHY AND AN INCREASE IN CD4+ CELL COUNT AND SKIN TEST REACTIVITY."

"IT IS INTERESTING THAT MANY OF US IN THE FIELD OF ALCOHOLISM HAVE FOR DECADES BEEN ADMINISTERING A COMPOUND, DISULFIRAM, WHOSE METABOLITE DTC APPEARS TO BE BOTH SAFE AND EFFECTIVE FOR THOSE PATIENTS WITH SYMPTOMATIC HIV AND AIDS."

AND TO QUOTE FROM ONE OF THIS ARTICLE'S REFERENCES, "JAMA, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION", 265:1538-1544, MARCH 27, 1991, P.1543:

"IN SUMMARY, DITIOCARB IN THIS STUDY WAS BOTH SAFE AND EFFECTIVE THERAPY FOR THE PREVENTION OF DISEASE PROGRESSION TO NEW OIs (OPPORTUNISTIC INFECTIONS) IN PATIENTS WITH HIV INFECTION."

"DITIOCARB (IMUTHIOL) HAS BEEN GRANTED ORPHAN DRUG STATUS BY THE FOOD AND DRUG ADMINISTRATION FOR THE TREATMENT OF PATIENTS WITH AIDS."

IN NONE OF THE FIVE ARTICLES IS THERE ANY MENTION OF THE WORD, "ACETALDEHYDE".

DR. BADER, IN YOUR LETTER TO ME YOU STATED:

"THE MOLECULES YOU SUGGEST ARE NORMAL METABOLITES FORMED DURING NORMAL BODY FUNCTIONING, AND WOULD HAVE NO EFFECT ON HIV OR AIDS."

HOWEVER, CONSIDERING WHAT I BECAME AWARE OF ON FEBRUARY 11, WOULDN'T A NEW LIGHT BE THROWN UPON THE SITUATION, WOULDN'T IT REALLY BE "A TOTALLY NEW BALL GAME"?

THIS, OF COURSE, IS WHAT I BECAME AWARE OF ON FEBRUARY 11 - IF A PERSON HAS IN THEIR LIVER THE SUBSTANCE CALLED DISULFIRAM AND TAKES THE SLIGHTEST DRINK OF ALCOHOL, ACETALDEHYDE WILL FLOOD THROUGHOUT THAT PERSON'S BODY AS A DEADLY POISON.

MENTIONED THROUGHOUT THE CUMULATED INDEX MEDICUS ARE VARIOUS ARTICLES DEALING WITH THE ADVERSE EFFECTS OF ADMINISTERING DISULFIRAM; SOME OF THE TOPICS ARE - FULMINATING HEPATITIS, ARTHRITIS, LIVER DAMAGE, PSYCHOSES, TOXIC COMA, BRAIN DAMAGE, AND EVEN DEATH.

NO CELL IN THE BODY WOULD BE SAFE FROM FEELING THE EFFECTS OF THIS POISON.

OF COURSE, IF IT DESTROYS THE AIDS VIRUS AT THE SAME TIME, WHAT BETTER WAY COULD EVER BE FOUND TO CLEANSE THE BODY OF THIS DREADFUL ILLNESS?

CAREFUL, MEDICAL SUPERVISION OF THE PROCEDURE IS THE KEY; THE PROCEDURE COULD SIMPLY BE CALLED "THE DISULFIRAM/ALCOHOL PROCEDURE" FOR DESTROYING THE HIV VIRUS.

THE METHOD AND THE EFFECTS OF THE PROCEDURE WOULD BE AS FOLLOWS:

"PHYSIOLOGICAL THERAPIES. CHEMICAL FENCES. ONE OF THE POPULAR MODERN DRUG TREATMENTS OF ALCOHOLISM, INITIATED IN 1948 BY ERIC JACOBSEN OF DENMARK, USES DISULFIRAM (TETRAETHYLTHIURAM DISULFIDE). THE USUAL TECHNIQUE IS TO ADMINISTER HALF A GRAM IN TABLET FORM DAILY FOR A FEW DAYS; THEN, UNDER CAREFULLY CONTROLLED CONDITIONS AND WITH MEDICAL SUPERVISION, THE PATIENT IS GIVEN A SMALL TEST DRINK OF AN ALCOHOLIC BEVERAGE. THE PRESENCE OF DISULFIRAM IN THE DRINKER'S BODY CAUSES A REACTION OF HOT FLUSHING, NAUSEA, VOMITING, A SUDDEN SHARP DROP OF BLOOD PRESSURE, POUNDING OF THE HEART, AND EVEN A FEELING OF IMPENDING DEATH. THESE SYMPTOMS RESULT FROM AN ACCUMULATION OF THE HIGHLY TOXIC FIRST PRODUCT OF ALCOHOL METABOLISM - ACETALDEHYDE. NORMALLY, AS ALCOHOL IS CONVERTED TO ACETALDEHYDE, THE LATTER IS RAPIDLY CONVERTED, IN TURN, TO OTHER HARMLESS METABOLITES, BUT IN THE PRESENCE OF DISULFIRAM - ITSELF HARMLESS - THE METABOLISM OF ACETALDEHYDE IS BLOCKED, WITH THE RESULTING TOXIC SYMPTOMS."

ENCYCLOPAEDIA BRITANNICA, MACROPAEDIA, VOLUME 1. PAGE 447, 1974 EDITION

".....A PATIENT MUST BE WARNED BEFORE USE OF THE POSSIBLE REACTIONS FROM THE MIXTURE OF THE DRUG AND EVEN VERY SMALL AMOUNTS OF ALCOHOL. REACTIONS INCLUDE HEADACHE, THROBBING IN THE NECK, NAUSEA AND VOMITING, SWEATING, THIRST, AND BLURRED VISION. THEY VARY IN INTENSITY, GENERALLY IN PROPORTION TO THE AMOUNTS OF DRUG AND ALCOHOL INGESTED, AND LAST FROM 30 MINUTES TO SEVERAL HOURS."

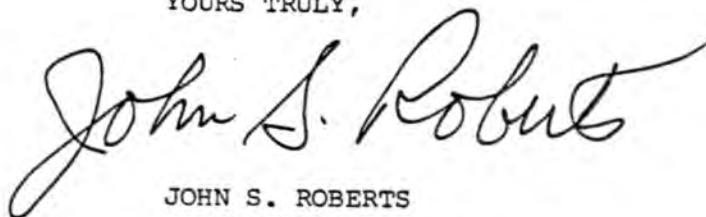
ACADEMIC AMERICAN ENCYCLOPEDIA, VOLUME 6, PAGE 202, 1985 EDITION

"ADMINISTRATION OF ANTABUSE, OR DISULFIRAM, AND TEMPOSIL, CITRATED CALCIUM CARBIMIDE, CAN HELP THE PATIENT CONTINUE IN THE PATH OF SOBRIETY. THESE DRUGS INCREASE THE CONCENTRATION OF ACETALDEHYDE IN THE BODY WHENEVER ALCOHOL IS CONSUMED, FOR THEY RETARD THE OXIDATION OF THAT SUBSTANCE TO ACETIC ACID. THE ACCUMULATION OF ACETALDEHYDE IN THE BODY PRODUCES A SERIES OF CHANGES WHICH RESEMBLE THOSE OF ACUTE HANGOVER. IN FACT, THE PATIENT FEELS SO UNCOMFORTABLE THAT FEAR OF THE RESULTS CAN STRENGTHEN ANY FALTERING DETERMINATION TO ABSTAIN FROM ALCOHOL. AFTER DISULFIRAM HAS BEEN TAKEN, EVEN THE SMALLEST AMOUNT OF AN ALCOHOLIC BEVERAGE CAN INITIATE ALMOST UNBEARABLE EFFECTS. THE DRINKER FIRST HAS A FEELING OF WARMTH IN HIS FACE; THE FACE, NECK AND CHEST ARE SUFFUSED WITH SCARLET AND THE EYES BECOME BLOODSHOT. AT THE SAME TIME HE IS AWARE OF PALPITATION OF THE HEART AND FEELS CHOKED FOR WANT OF AIR. NAUSEA AND VOMITING FOLLOW, AND THE INTENSE FLUSHING IS REPLACED BY PALLOR AS BLOOD PRESSURE FALLS."

ENCYCLOPAEDIA BRITANNICA, VOLUME 1, PAGE 550-551, 1971 EDITION

DR. BADER, IF HIV IS INDEED DESTROYED IN THE LABORATORY BY ACETALDEHYDE -
FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO -
RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.
COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR
NOT THE "DISULFIRAM/ALCOHOL PROCEDURE" IS EFFECTIVE IN CURING AIDS VICTIMS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO CONGRESSMAN PETER J. VISCLOSKY, DR. LUC MONTAGNIER, RANDY SHILTS
AND JIM GORDON

P.S. - FEBRUARY 19

LAST NIGHT, AFTER I HAD TYPED THIS LETTER, I WENT AGAIN TO THE LIBRARY
OF INDIANA UNIVERSITY NORTHWEST TO PICK UP THE FAX COPY OF ANOTHER ARTICLE
WHICH I HAD REQUESTED TO SEE.

IT COMES FROM THE "JOURNAL OF APPLIED TOXICOLOGY", OCTOBER, 1991, PAGES
373-6 AND THE TITLE OF THE ARTICLE IS 'ACETALDEHYDE'.

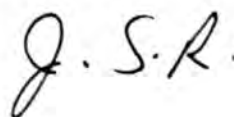
I DON'T KNOW WHETHER THIS PART OF THE ARTICLE HAS ANY PARTICULAR RELEVANCE
BECAUSE IT CONCERNS EXPERIMENTS ON RATS. HOWEVER, IT SAYS,

"IN CONTRAST, THE ACETALDEHYDE LEVELS IN THE LIVER FOLLOWING ETHANOL
ADMINISTRATION IS CONSIDERABLY HIGHER THAN THE OTHER TISSUES.

THE AUTHORS CONCLUDE THAT EITHER THE LIVER DOES NOT TAKE UP
ACETALDEHYDE FROM THE BLOOD OR ITS METABOLISM IS SO RAPID THAT IT
DOES NOT ACCUMULATE IN THE HEPATOCYTES. THE HALF-LIFE OF ACETALDHYE (sp.)
IN THE BLOOD WAS ESTIMATED AS 3.1 MIN." PAGE 374

AT SOME TIME DURING THE PAST MONTH I READ THAT ALL OF THE BLOOD IN THE
HUMAN BODY CIRCULATES THROUGH THE LIVER IN FOUR MINUTES TIME.

WITH "THE DISULFIRAM/ALCOHOL PROCEDURE" HOW LONG WOULD ACETALDEHYDE STAY
ACTIVE AS A POISON IN THE BODY? - - ONE/HALF HOUR?, ONE HOUR?, TWO HOURS?,
OR EVEN LONGER?





DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

January 26, 1993

Mr. John S. Roberts
P. O. Box H
Hobart, Indiana 46342

Dear Mr. Roberts:

The National Institutes of Health appreciates your concern about AIDS and your offer of a possibility for curing this dreaded disease. You are not alone either in your concern, or in offering suggestions for a cure. Nonetheless, serious qualified scientists with many years of experience in virology, biochemistry, molecular biology, and drug development related to AIDS research are devoted to this problem, and what may seem new and innovative to you has already been considered and/or tested by such scientists. The molecules you suggest are normal metabolites formed during normal body functioning, and would have no effect on HIV or AIDS. It is unfortunate that you have been encouraged to persist with your efforts to project what you think may be a cure for AIDS. With no hesitation, I can guarantee you that what you suggest would not be useful.

Sincerely yours,

A handwritten signature in black ink, which appears to read "John P. Bader".

John P. Bader, Ph.D.
Chief, Antiviral Evaluations Branch
Developmental Therapeutics Program
Division of Cancer Treatment

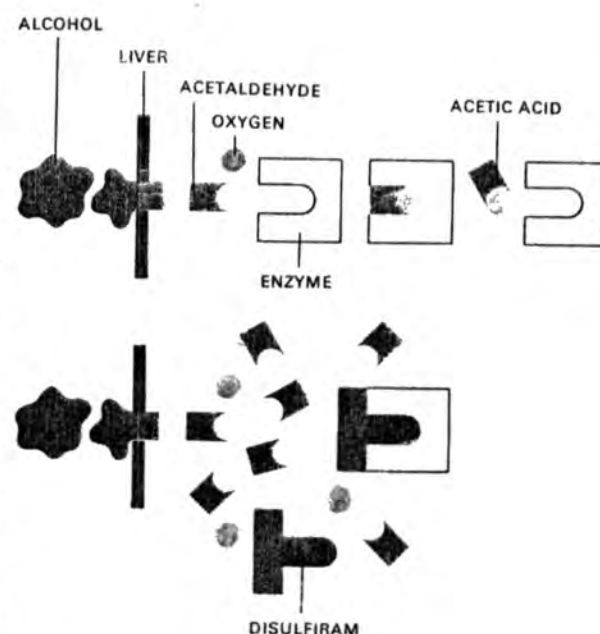
JPBader:crj

When liquor is poison

Oddly enough, the interaction of alcohol with another chemical has been used to treat the most serious problem associated with the drug. Some 20 years ago, two Danish physicians were studying the compound disulfiram as a possible cure for intestinal worms. As part of their testing program, they dosed themselves with small quantities of the compound. Attending a cocktail party soon after, they suddenly found themselves flushed, dizzy and violently nauseated, with splitting headaches. On recovery, they suspected and soon confirmed that disulfiram was to blame. This substance, it turns out, inhibits the liver's transformation of alcohol. It blocks the second step in the process, in which acetaldehyde is transformed into acetic acid, thereby quickly producing a toxic pile-up of acetaldehyde in the body.

Anyone who has taken disulfiram (known commercially as Antabuse) cannot drink even a single glass without becoming violently ill. Unfortunately, as a treatment for alcoholism, disulfiram is seldom successful; the alcoholic usually finds he can give up disulfiram more easily than alcohol.

The limited usefulness of disulfiram indicates the frustrations the pharmacologist faces in trying to deal with the widespread disease of alcoholism. It cannot be explained, or even defined, in pharmacological terms alone. There is no known pharmacological reason why some people destroy their lives by drinking; neither dosage nor physical effects offer an infallible guide. A man who drinks heavily five nights out of seven may on occasion get drunk, but he is not necessarily an alcoholic. Some alcoholics, by contrast, may stay sober for days or even weeks at a time. But once they start drinking, they cannot stop short of abysmal intoxication. They are addicts, "hooked" on the drug alcohol. And addiction to alcohol, like addiction to any other drug, is essentially a psychological compulsion—and therefore the problems it raises are far more psychological, medical and social than pharmacological.



THE ACTION OF DISULFIRAM, a drug intended to discourage alcoholism, disrupts liver functioning so that an imbiber gets sick after drinking. The upper diagram shows how the liver normally handles alcohol. Entering the liver from left, alcohol is first converted into acetaldehyde, a poisonous substance, but this chemical and oxygen are quickly fitted together by an enzyme, forming harmless acetic acid. When disulfiram is taken (*lower diagram*), alcohol is converted into acetaldehyde, but disulfiram joins with the enzyme and prevents acetaldehyde from linking with oxygen to form acetic acid. As a result, toxic acetaldehyde collects, and the drinker becomes nauseated.

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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PORTAGE, IN 46368
(219) 763-2904

Congress of the United States
House of Representatives
Washington, DC 20515-1401

February 11, 1993

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

Thank you for writing to update me on your research on the AIDS virus. I appreciate hearing from you.

In your letter, you asked if a pilot program can be established at two Chicago, Illinois hospitals to test whether or not acetaldehyde is effective in destroying the AIDS virus. Traditionally, the National Institutes of Health (NIH) is the principal biomedical research agency of the Federal Government. Therefore, I have taken the liberty of forwarding your letter to Dr. Bernadine Healy, Director of the National Institutes of Health, and have asked her to respond to your letter directly. Enclosed is a copy of my letter.

Should you have further questions regarding the development and implementation of AIDS research projects, I urge you to contact NIH. You may write to Dr. Bernadine Healy, Director, at the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, 20892.

Thank you again for sharing your thoughts with me. Should you have questions about federal legislation, please do not hesitate to let me know.

Sincerely,

Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 19, 1993

THE HONORABLE PETER J. VISCLOSKY
UNITED STATES HOUSE OF REPRESENTATIVES
330 CANNON BUILDING
WASHINGTON, D.C. 20515

DEAR CONGRESSMAN VISCLOSKY,

ATTACHED IS A COPY OF YOUR MAY 27, 1992 LETTER TO ME. THANK YOU VERY MUCH FOR THE HELP THAT YOU AFFORDED ME LAST YEAR.

I THINK THAT I HAVE DISCOVERED THE CURE FOR AIDS.

THROUGHOUT THE PAST THIRTEEN MONTHS THE IDEA HAS BEEN KICKING AROUND IN MY BRAIN THAT I MIGHT BE GENERATING IN MY BODY SOME SORT OF AN ACID THAT COULD BE EFFECTIVE IN DESTROYING THE AIDS VIRUS. AS I STUDIED A LITTLE BIT MORE ABOUT THE WAY ALCOHOL IS METABOLIZED IN THE BODY, I HAVE JUST ABOUT COME TO THE CONCLUSION THAT THAT ACID IS ACETIC.

NOW, WHETHER ACETIC ACID CAN OR CANNOT DESTROY THE AIDS VIRUS - I DON'T KNOW. HOWEVER, I HAVE BECOME AWARE OF SOMETHING MORE IMPORTANT.

I BELIEVE THAT IT WAS ON NEW YEAR'S DAY THAT MY WIFE SHOWED ME THE ATTACHED ARTICLE ABOUT A "HANGOVER CURE".

I READ THIS ARTICLE A COUPLE OF TIMES. AT SOME TIME DURING THE FIRST WEEK OF THIS MONTH THIS IDEA HIT ME LIKE A TON OF BRICKS -

THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

AS I REFLECT UPON THE PAST THIRTEEN MONTHS AND THE POINT I WAS TRYING TO MAKE ABOUT ACID IN MY BODY, I FEEL AS IF I HAD BEEN PLAYING WITH A FIRECRACKER AND HAVE ALL OF A SUDDEN BEEN HANDED A STICK OF DYNAMITE AND THAT DYNAMITE IS CALLED ACETALDEHYDE.

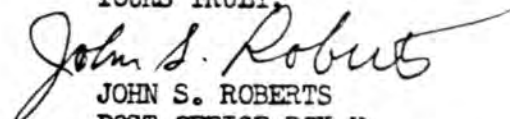
ON JANUARY 11 I MAILED THE ATTACHED LETTER TO DR. LUC MONTAGNIER WITH COPIES TO DR. JOHN BADER AND RANDY SHILTS.

IT IS MY HYPOTHESIS THAT WHILE ACETALDEHYDE IS POISONING THE BODY,
IT WILL AT THE SAME TIME DESTROY THE AIDS VIRUS.

FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO - RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.

COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR NOT ACETALDEHYDE IS EFFECTIVE IN DESTROYING THE AIDS VIRUS?

YOURS TRULY


JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO DR. LUC MONTAGNIER, DR. JOHN BADER AND RANDY SHILTS

PETER J. VISCLOSKY
1ST DISTRICT INDIANA

COMMITTEE ON APPROPRIATIONS
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May 27, 1992

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

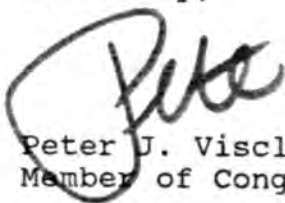
Thank you for sending me a copy of your letter to Dr. Luc Montagnier of the Institut Pasteur in Paris, France. I appreciate hearing from you.

I share your concern that a cure must be found for the devastating illness, Acquired Immunodeficiency Syndrome (AIDS). The illness is caused by the Human Immunodeficiency Virus (HIV) which causes an impairment of the immune systems and leaves its victims susceptible to certain types of cancer and a number of opportunistic diseases. Although drugs such as AZT have been developed to prolong the life of AIDS patients, there is currently no cure.

As you know, on January 31, 1992, I contacted the National Institutes of Health (NIH), on your behalf, regarding NIH's policy for donating blood samples for AIDS research. As a result of this action, on March 12, the NIH responded to your letter directly, and informed you to contact Dr. John P. Bader, who is responsible for the National Cancer Institute Preclinical AIDS Drug Screening Program, regarding the feasibility of analyzing your blood sample. Enclosed is a copy of NIH's letter. Should you have any questions regarding AIDS research-related federal legislation or have problems in contacting NIH, please do not hesitate to let me know.

Thank you again for sharing your thoughts with me.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 11, 1993

DR. LUC MONTAGNIER
25 RUE DU DOCTEUR ROUX
INSTITUT PASTEUR
PARIS, FRANCE 75015

DEAR DR. MONTAGNIER,

LAST YEAR I WROTE TO YOU A LETTER IN WHICH I ASKED IF YOU WOULD BE INTERESTED IN TESTING MY BLOOD TO SEE WHETHER THERE POSSIBLY COULD BE SOMETHING IN IT THAT WOULD DESTROY THE AIDS VIRUS.

IN THAT LETTER I ALSO SAID,

"YEARS AGO I SAW A TELEVISION PROGRAM IN WHICH SOMEONE SAID THAT PERSONS WHO DRANK BRANDY DID NOT CATCH INFLUENZA DURING THE HORRENDOUS EPIDEMIC OF 1918-1919."

ATTACHED IS A COPY OF A NEWSPAPER ARTICLE WHICH I RECENTLY READ.

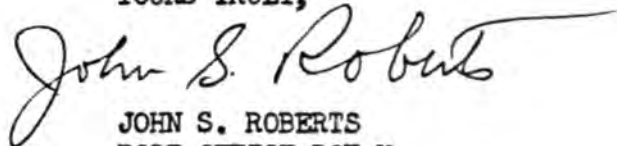
THIS ARTICLE CAUGHT MY ATTENTION BECAUSE I DO DRINK SOME ALCOHOL EVERY NIGHT.

HAS ANY RESEARCH EVER BEEN CONDUCTED TO SEE WHETHER ACETALDEHYDE MIGHT BE EFFECTIVE IN DESTROYING THE AIDS VIRUS?

COULD ACETALDEHYDE BE INJECTED INTO A PERSON WITH NO ILL EFFECTS OTHER THAN TO MAKE THAT PERSON EXTREMELY SICK FOR A DAY?

BEING TOXIC, PERHAPS ACETALDEHYDE WAS THE SUBSTANCE THAT DESTROYED THE INFLUENZA VIRUS. IN THE SAME MANNER, COULD IT ALSO POSSIBLY DESTROY THE AIDS VIRUS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
UNITED STATES OF AMERICA

COPIES TO: DR. JOHN P. BADER
NATIONAL INSTITUTES OF HEALTH
ANTIVIRAL EVALUATIONS BRANCH
BETHESDA, MARYLAND

RANDY SHILTS
SAN FRANCISCO CHRONICLE
SAN FRANCISCO, CALIFORNIA

ORANGE BOWL

Nebraska vs. Florida St.
(Ch. 5, 16)

7:30 p.m.

SUGAR BOWL

Alabama vs. Miami (Ch. 7, 28)

son of the dog,
"Flash Gordon" and
Cruise, "Close Encounte-
Kind" and "Blade Runner." at

WPWR (Ch. 50) counters with
starting at 9 a.m. with "The Shaggy Dog,"
"Son of Flubber" "That Darn Cat," "Alice in
Wonderland" "Return to Oz" and "Return
from Witch Mountain."

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Hangover cure? Nope

The Associated Press

► HEALTH

Even if you're in no condition to read this, you probably know that aspirin won't cure it and water won't prevent it.

It's the hangover, and it's inevitable if you drink too much alcohol.

The headache, upset stomach and bad aftertaste that accompany a hangover come from the toxic by-product of alcohol, a chemical called acetaldehyde, said Russell Mankes, associate professor of toxicology and pharmacology at the Albany Medical College.

Some typical folk remedies — eating cold pizza, taking aspirin before bed or drinking another cocktail — may do more harm than good.

Aspirin and ibuprofen are bad for the stomach lining and popping one when the stomach is already irritated from drinking dramatically increases the risk of an ulcer, Mankes said.

Tylenol won't harm the stomach, but it can strain the liver, which is already being damaged by the alcohol, Mankes said.

Drinking water while still intoxicated won't help either. Because alcohol induces urination, all the water that comes in, goes out, taking with it minerals and salts.

Don't even think about drinking another alcoholic beverage to reduce hangover symptoms.

"The 'hair of the dog' is the first step on the road to alcoholism," he said.

Coffee won't make a drinker sober. "All you end up with is a wide-awake drunk," he said.

So what's the cure?

"Avoid getting one in the first place," Mankes said. "That does not mean avoiding alcohol. One can drink responsibly."

*Terry
draft reply,
please -*

SEPTEMBER 17, 1993

MS. KRISTINE M. GEBBIE, RN, MN
NATIONAL AIDS POLICY COORDINATOR
THE WHITE HOUSE
WASHINGTON

DEAR MS. GEBBIE,

ATTACHED TO THIS LETTER IS A COPY OF THE REISINGER STUDY -

"INHIBITION OF HIV PROGRESSION BY DITHIOCARB".

ATTACHED TO MY JUNE 26, 1993 LETTER TO CONGRESSMAN VISCLOSKY IS A
COPY OF THE LANG STUDY -

"RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF DITHIOCARB
SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION".

WHETHER OR NOT I AM RIGHT OR WRONG ABOUT THE "DISULFIRAM/ALCOHOL PROCEDURE",
I THINK A FUNDAMENTAL QUESTION NEEDS TO BE ADDRESSED AT THIS TIME -

WHAT ACCOUNTED FOR THE DRAMATIC DIFFERENCE IN RESULTS
OBTAINED BY THESE TWO STUDIES?

LET'S LOOK AGAIN AT WHAT REISINGER AND LANG HAD TO SAY ABOUT THEIR
RESPECTIVE AIDS PATIENTS WHO EACH RECEIVED 10mg OF DITHIOCARB (DTC) ORALLY
ONCE A WEEK:
/K6

REISINGER - "ORALLY DTC TENDED TO DECREASE HIV-RELATED DISEASES,
BUT THE DIFFERENCE FROM THE ORAL PLACEBO GROUP
WAS NOT SIGNIFICANT." (P.682)

LANG - "THE DISEASE DID NOT PROGRESS TO CDC-DEFINED ACQUIRED
IMMUNODEFICIENCY SYNDROME IN THE DITHIOCARB GROUP
BUT DID SO IN 4 PATIENTS IN THE PLACEBO GROUP (3 BETWEEN
WEEK 0 AND 16, 1 BETWEEN WEEK 17 AND 32). DITHIOCARB
WAS ALSO ASSOCIATED TO A SIGNIFICANTLY GREATER EXTENT
THAN PLACEBO WITH RELIEF OF CONSTITUTIONAL SYMPTOMS,
IMPROVEMENT IN CLINICAL STATUS (INCLUDING SHRINKAGE
OF ENLARGED SPLEEN AND LYMPH NODES), AND IMPROVEMENT
IN IMMUNE FUNCTION (AS MEASURED BY CD4+ CELL COUNT
AND SKIN TEST REACTIVITY). WHEN PLACEBO WAS REPLACED
BY DITHIOCARB, SIMILAR IMPROVEMENTS WERE OBSERVED,
WHEREAS SYMPTOMS SLOWLY REAPPEARED AND CD4+ CELL LEVELS
PROGRESSIVELY DECLINED WHEN DITHIOCARB TREATMENT
WAS REPLACED BY PLACEBO." (P.702)

- LANG - "ALL THE 9 PATIENTS IN THE DITIOCARB GROUP WITH A HISTORY OF WEIGHT LOSS AT ENTRY REGAINED NORMAL WEIGHT AFTER 16 WEEKS' TREATMENT. THE SPLEEN BECAME IMPALPABLE IN 4 OF THE 7 DITIOCARB RECIPIENTS, BUT IN NONE OF 8 PLACEBO RECIPIENTS, WITH SPLENOMEGALY AT ENTRY." (P.704)
- LANG - "WHEN CHANGE IN CLINICAL STATUS WAS SCORED AS IMPROVED, STABLE, OR WORSE BY THE PHYSICIANS AFTER 16 WEEKS, 42% OF DITIOCARB RECIPIENTS HAD IMPROVED COMPARED WITH ONLY 5% IN THE PLACEBO GROUP ($p < 0.01$). " (P.704)
- LANG - TABLE II (P.704) HIGHLIGHTS THE "DISAPPEARANCE OF CONSTITUTIONAL SYMPTOMS" AND THEY ARE "PERSISTENT DIARRHOEA, WEIGHT LOSS, PERSISTENT FEVER". THIS TABLE ALSO HIGHLIGHTS THE "DISAPPEARANCE OF SPLENOMEGALY".

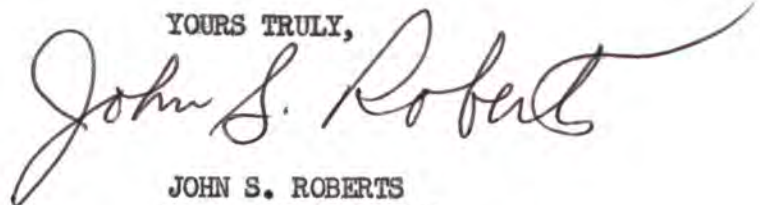
AND TO TOP IT OFF, THE LANG STUDY SHOWED AN INCREASE IN THE CD4-POSITIVE LYMPHOCYTES (T-HELPER CELLS) -TABLE III, P.704- AND STATES (P.705):

"THE PRESENT FINDINGS, AND THOSE ACCOMPANYING LONG-TERM ADMINISTRATION OF DITIOCARB (3 YEARS), CLEARLY SHOW THAT THE CD4+ CELL-DEFECT IS NOT AGGRAVATED. IN FACT, THE REVERSE OCCURRED, WITH DITIOCARB PRODUCING AN INCREASE IN CD4+ CELLS AND IMPROVEMENT IN CONSTITUTIONAL SYMPTOMS OF AIDS-RELATED COMPLEX. FURTHERMORE, PRELIMINARY DATA IN A SMALL NUMBER OF PATIENTS INDICATE THAT DITIOCARB DOES NOT ENHANCE HIV REPLICATION IN VITRO OR IN VIVO."

WHEREAS WITH REISINGER (P.681) THESE CELLS ".....DECREASED IN PERIPHERAL BLOOD IN ALL TREATMENT GROUPS DURING THE STUDY."

AGAIN, WHAT ACCOUNTED FOR THIS DRAMATIC DIFFERENCE IN RESULTS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342

COPIES WITH ENCLOSURES TO: CONGRESSMAN PETER J. VISCLOSKY
PROFESSOR RUSSELL F. MANKES, THE ALBANY MEDICAL COLLEGE
DR. RUTH KIRSCHSTEIN, ACTING DIRECTOR,
NATIONAL INSTITUTES OF HEALTH
INDIANA UNIVERSITY SCHOOL OF MEDICINE, NORTHWEST CAMPUS,
ATTENTION DR. SUBBIAH SIVAM

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Inhibition of HIV progression by dithiocarb

EMIL C. REISINGER PETER KERN MARTIN ERNST
PAUL BOCK HANS D. FLAD MANFRED DIETRICH
AND GERMAN DTC STUDY GROUP*

60 patients with HIV-1 infection in Walter Reed stages 2-4 were randomised to treatment with intravenous or oral dithiocarb (diethyldithiocarbamate, DTC) or placebo for 24 weeks in a paired double-blind design. 55 patients were evaluable at the end of the study: no patient who had received DTC but 6 placebo patients had AIDS, a significant difference. Significantly delayed disease progression was observed in the intravenous DTC group compared with its matching placebo. The benefit in the oral DTC group was not statistically significant. During an 18-month follow-up 3 deaths occurred in the original placebo groups, whereas no patient who had initially received DTC died. A significant delay in progression to AIDS was observed in the DTC groups.

Lancet 1990; 335: 679-82.

Introduction

Dithiocarb (diethyldithiocarbamate, DTC) inhibits HIV-1 expression and reverse transcriptase activity in peripheral blood lymphocytes from patients with HIV-1.¹ DTC may

restore immune function by modulating T-cell differentiation in vitro, in immunodepressed BALB/c mice, and in man.^{2,4} In phase I studies DTC was well tolerated by HIV-1 infected patients with persistent generalised lymphadenopathy; clinical and immunological variables improved.^{5,7} A dose response study in patients with AIDS-related complex (ARC) or AIDS showed that doses up to 400 mg/m² administered once weekly were not toxic whereas 800 mg/m² either once or twice a week had side-effects.^{8,9} Despite the short serum half-life of DTC some effects of this drug last up to 7 days, indicating rapid intracellular penetration.^{9,10} Lang et al.¹¹ demonstrated clinical and immunological benefit with oral DTC in HIV-1 infected patients. We have compared the intravenous or oral route for DTC with placebo.

Patients and methods

Patients

Patients were recruited in Hamburg and the surrounding region. The study accorded with ethical committee standards. All patients

*Members of the group: Ali Dorlemann, Stephan Schwander, Dirk Berzow, Herbert Schmitz, Paul Racz (Bernhard Nocht Institute for Tropical Medicine), Arndt Gottesleben (General Hospital Ochsenzoll), and Andreas Pettenberg, Wilhelm Meigel (General Hospital St Georg, Hamburg).

ADDRESSES Clinical Department, Bernhard Nocht Institute for Tropical Medicine, Hamburg (E C Reisinger MD, P Kern MD, Prof M Dietrich, MD); Department of Immunology and Cell Biology, Forschungsinstitut Borstel (M Ernst MD, Prof H D Flad MD); and Institut Mérieux (P Bock MD), Leimen, West Germany. Correspondence to Prof M Dietrich, Bernhard Nocht Institute for Tropical Medicine, Bernhard-Nocht-Str 74, 2000 Hamburg 36, West Germany.

TABLE I—DETAILS OF PATIENTS (n = 15 PER GROUP)

	Intravenous route		Oral route	
	DTC	Placebo	DTC	Placebo
Drop-outs	2	1	2	1
Homosexual	13	13	14	15
Drug abuser	0	0	1	0
Transfusion	1	0	0	0
Heterosexual	1	2	0	0
Age (yr)	37 (8)*	39 (9)	33 (7)	34 (9)
Weight (kg)	70 (11)	75 (8)	72 (8)	74 (9)

*Mean (SD).

were informed about DTC, including possible side-effects, and the study design. All gave written consent. Inclusion criteria were male sex, 18–55 years, serum antibodies against HIV-1, Walter Reed stage 2–4, normal blood counts, and normal serum creatinine and liver enzyme levels.

113 patients were evaluated as candidates for the study between May, 1986, and November, 1987. 11 patients did not fulfil the inclusion criteria. 60 were matched randomly into pairs (table 1). Matching was for: age (difference ± 10 years); T-helper cells ($\geq$ or $< 400/\mu\text{l}$); T-helper/T-suppressor ratio (maximum difference ± 0.30); CD3 positive lymphocytes ($\geq$ or $< 1000/\text{l}$); delayed skin reactivity ('Multitest Merieux' $\geq$ or < 10 mm total diameter of all positive reactions); and HBsAg (positive or negative) and positive or negative antibody status to HBsAg, cytomegalovirus, Epstein-Barr virus, and Epstein-Barr nuclear antigen. All patients were offered care by staff psychologists during and after the study.

42 patients could not be matched. Of these, 14 could not be followed-up; AIDS developed in 11 (*Pneumocystis carinii* pneumonia [PCP] 4, Kaposi sarcoma 4, candida oesophagitis 1, lymphoma 2) and 17 did not have AIDS within a mean observation period of 17 (SD 6) months.

Study design and treatment

15 matched pairs of patients were designated for an intravenous study, the other 15 pairs for an oral study. For each route 15 patients received DTC, their corresponding partner received placebo. Randomisation was done by computerised numbering of envelopes. The envelopes were allocated to the patients in numerical order. After matching, treatment was started immediately.

DTC or placebo were administered once weekly for 24 weeks at a dose of 5 mg/kg intravenously or 10 mg/kg orally. The treatment period was followed by a 3-month observation period without drug administration. Subsequently all patients were offered DTC intravenously or orally, according to their wishes, once a week for at least 6 months. Where possible, patients were followed up for an extra 6 months (total 18 months).

6 of the matched patients discontinued treatment and were not entered into data analysis. The withdrawals were not because of side-effects or disease progression.

Clinical and laboratory investigations

A 3-day hospital stay for staging purposes was required before and after the treatment period. All other examinations were performed on an outpatient basis. Clinical, dermatological, and overall assessment were done every 6 weeks; virological and immunological data were obtained every 12 weeks. All patients were

TABLE II—T-HELPER CELL COUNTS PER μl BLOOD IN PATIENTS WITH INITIAL COUNT BELOW $814/\mu\text{l}$

Route	Time (mo)	Placebo	DTC
Oral	0	467 (193)	493 (204)
	6	442 (327)	428 (167)
	% loss	5.9 (53.5)	5.4 (37.7)
Intravenous	0	422 (283)	388 (225)
	6	250 (263)	352 (34)
	% loss	51.4 (35.6)	20.8 (30.4)

examined at the clinical department of the Bernhard-Nocht-Institute; all the laboratory analyses were done in one laboratory and all the immunological investigations in another.

Clinical progression of disease was assessed with the 1986 Centers for Disease Control (CDC) classification.¹² AIDS was diagnosed according to the 1987 CDC surveillance case definition.¹³

Statistics

Sequential analysis was used to compare the outcome of every matched pair and to discontinue the study if one of the regimens was found to be superior. Numbers of subjects with disease progression were compared with the Kaplan-Meier plot and log-rank test. Laboratory values were compared by the Wilcoxon paired test, analysis of variance, or by the paired *t* test when the Kolmogorov-Smirnov test showed a normal distribution.

Results

Development of AIDS

Intravenous route. 4 patients in the placebo group but none in the DTC group had opportunistic infections or Kaposi sarcoma (table 11). Of the 4 patients in whom AIDS developed: 1 had PCP, candida pneumonia and cerebral toxoplasmosis; 2 had PCP alone; and 1 had Kaposi sarcoma in a lymph node. No death occurred during the 6 months. However, 3 of the 4 patients with AIDS died 8, 15, and 18 months after diagnosis of Kaposi sarcoma or PCP.

Oral route. 2 patients in the placebo group but none in the DTC group had opportunistic infections (table 11). There was recurrent salmonella septicaemia in 1 subject and candida oesophagitis in another. No deaths occurred during the 6 months, but 1 of the patients died of salmonella septicaemia 12 months after diagnosis.

Clinical progression

Intravenous route. 26 patients were available for evaluation as matched pairs. During the treatment period 7 placebo patients were progressively worse than their matched partners ($p < 0.02$) (fig 1). In 2 pairs both partners progressed and in 4 pairs all patients remained the same. Disregarding the matched pairs, 2 of 13 patients who received DTC worsened while 9 of 14 patients receiving placebo worsened ($p < 0.01$).

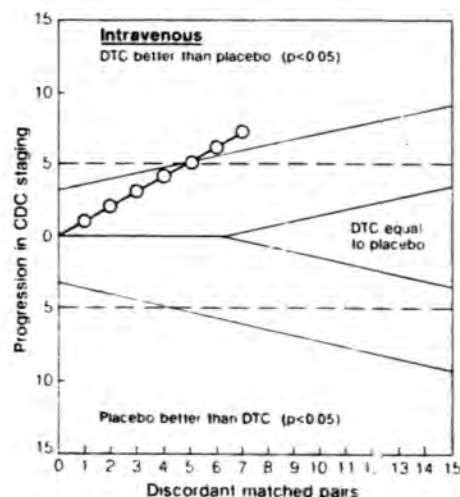


Fig 1—Sequential analysis of intravenously treated matched pairs for CDC class progression.

= DTC placebo benefit.

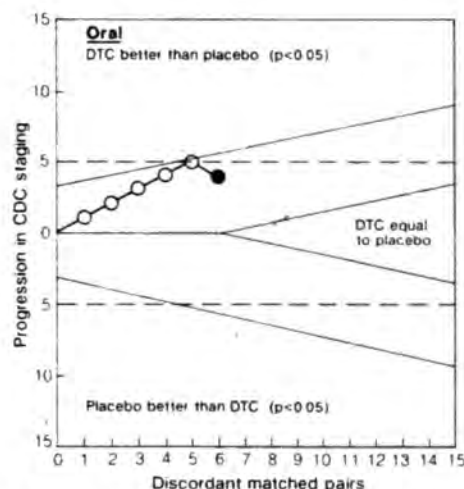


Fig 2—Sequential analysis of orally treated matched pairs for CDC class progression.

○ = DTC and ● = placebo benefit.

Oral route. 6 of 12 evaluable matched pairs had discordant courses of HIV infection during treatment. In 5 of these pairs the placebo-treated partners worsened and in 1 pair the DTC-treated partner worsened (not significant) (fig 2). In 1 pair both partners were worse and 5 pairs remained the same. Disregarding the matched pairs, 3 of 13 patients on DTC and 6 (a seventh discontinued after 3 months) of 13 on placebo worsened (not significant).

Immunological response

CD4-positive lymphocytes (T-helper cells) decreased in peripheral blood in all treatment groups during the study. In both groups of orally treated patients the decrease in T-helper cells was not significant. However, after 6 months of intravenous treatment, the T-helper cell count dropped significantly in the placebo group ($p < 0.03$) but not in the DTC group. Comparisons of the T-helper cell counts of matched partners did not show significant differences in either group. However, in patients with T-helper cell counts below 814/ μ l (the 67th percentile) before treatment, the proportion of T-helper cells lost during 6 months' treatment was significantly higher in the patients receiving intravenous placebo (51 [36%]) than in their DTC-treated partners (21 [30%], $p < 0.02$; table 11). We also found a significantly higher proportion of interleukin-2 (IL-2) receptor-positive monocytes in patients receiving intravenous DTC than in their matched partners ($p < 0.05$) after 6 months' treatment. No other significant differences were detected in sixteen further phenotype markers on peripheral blood lymphocytes.

Neurological findings

Severe neurological diseases appeared in the intravenous placebo group (cerebral toxoplasmosis, 1; multisegmental herpes zoster, 1) but not in the other groups. Mild neurological (memory loss, concentration loss), psychiatric (anxiety, intermittent signs of depression), and electroencephalographic (brain stem impairment, irregular foci, variation of vigilance, photosensitivity, subcortical instability) findings occurred in all groups before and after medication.

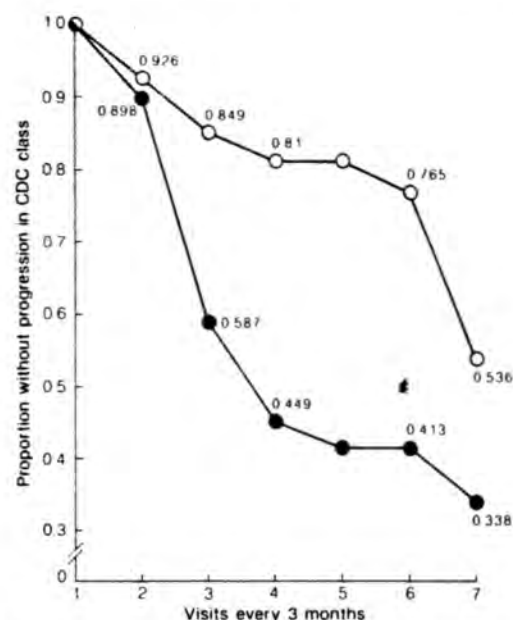


Fig 3—18-month follow-up for CDC-class progression.

Kaplan-Meier plots. Logrank = 4.195, $p < 0.05$. ○ = DTC and ● = placebo.

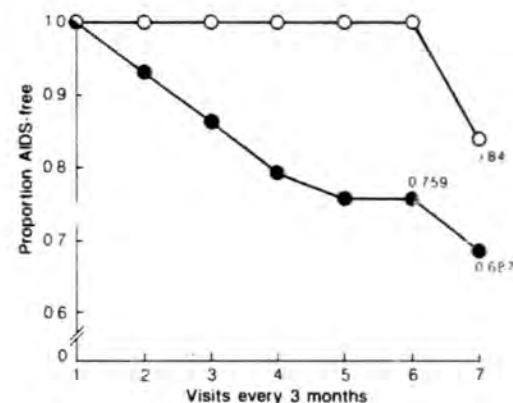


Fig 4—18-month follow-up for progression to AIDS.

Logrank = 3.866, $p < 0.05$. ○ = DTC and ● = placebo.

Side-effects

A metallic taste was reported by 77% of the patients in the oral and intravenous DTC groups compared with 25% of patients in the placebo groups. This effect lasted a few hours after intravenous administration and for up to a day after oral treatment. Abdominal discomfort (gastric complaints, flatulence, diarrhoea) occurred in 42% of the patients receiving DTC and in 24% of the placebo patients. Nausea and fatigue were infrequent in both DTC groups. Superficial gastritis was diagnosed by endoscopy in 1 patient after 24 weeks of oral DTC. Because of the disulfiram-like effect of DTC, intolerance to alcohol (palpitation, rash, dizziness, nausea, headache) was seen in 4 patients (15%) who reported alcohol consumption within 2 days of DTC administration. However, 11% of placebo-treated patients reported similarly. No allergic/toxic reactions, neurological, or haematopoietic side-effects were observed.

Follow-up

21 patients of the original DTC groups and 26 of the original placebo groups were available for follow-up 12 months after completion of randomised treatment. Within 18 months from the start of the study, 3 patients from the original placebo groups died, 8 patients had AIDS, and 18 progressed in CDC staging. In the original DTC groups no patient died, 2 had AIDS, and 9 progressed in CDC staging (figs 3 and 4). The differences in progression to AIDS and in CDC progression were both significant between the original DTC and placebo groups ($p < 0.05$).

Discussion

- ✓ Intravenous DTC was superior to oral DTC and to placebo in HIV-1 infection. Because of the multifactorial causes of disease progression in HIV infection, we used matched pairs with stringent criteria for admission and matching.
- ✓ Intravenous DTC significantly decreased the frequency of HIV-related diseases and symptoms as defined by CDC stage IV. Orally DTC tended to decrease HIV-related diseases, but the difference from the oral placebo group was not significant. Follow-up over 18 months showed a significantly delayed progression to AIDS and a significantly decreased frequency of HIV-related diseases and symptoms in the original DTC groups compared with the original placebo groups. No death occurred in the original DTC groups while 3 patients died in the original placebo groups. The immunological findings suggested that DTC was immunoprotective by stabilising the number of T-helper lymphocytes in peripheral blood when the number was lower before treatment. The number of T-helper lymphocytes in placebo-treated patients decreased significantly. This effect was not seen in the group of patients with counts over $814/\mu\text{l}$, which indicates a mechanism of action on impaired immune function.

DTC administration was followed by significantly enhanced IL-2 receptor expression on monocytes.¹⁴ This may be related to in-vivo preactivation of monocytes or to enhanced monocyte/lymphocyte interaction mediated by IL-2.¹⁵ We have found that membrane fluidity of peripheral blood lymphocytes from patients treated longterm was significantly decreased compared with that of untreated HIV-positive patients and non-infected subjects. Decreased membrane fluidity of lymphoid cells has been associated with increased capacity for antigen binding and increased lectin-induced mitogenicity,¹⁶ which was ascribed to an unmasking of membrane antigens and receptors. We suggested that decreased plasma membrane fluidity and thereby enhanced receptor availability and function may account for the beneficial effects of DTC on immune function.¹⁷

DTC has been reported to have antiretroviral efficacy.¹ However, the virological data from peripheral blood in our study did not show a difference in the virus load of the patients in the different groups before and after treatment. There is no evidence of direct antiretroviral efficacy in vivo, but also no evidence for increased virus load after treatment. Studies on lymph nodes did not show changes in structure or immunohistochemical properties, as has been described in mice.¹⁸

DTC is fungicidal and insecticidal.¹⁹ Our data support the concept of direct antimicrobial activity of DTC against typical secondary pathogens in HIV-infections.²⁰ **DTC seems to delay progression of HIV infection by acting at different sites against the underlying disease and secondary**

pathogens. No severe side-effects were observed. Intravenous administration of DTC is more effective than oral administration in delaying the progression of HIV-infection in the early symptomatic stages.

We thank Ms D. Malinski and Ms M. Hermes for attending to the patients; Mrs R. Bergmann, Mrs A. van Lunteren, and Mrs J. Schenck for technical assistance; and Mrs T. Thiede for typing the manuscript. We thank Prof G. J. Krejs and Dr K. Tamussino, Graz, for discussing the manuscript. DTC was provided by Institute Merieux, Lyon, France. This study was supported by grant FKZ II-003-86 from Bundesministerium für Forschung und Technologie and by Bundesministerium für Familien, Frauen, Jugend und Gesundheit, Bonn, West Germany.

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THE WHITE HOUSE

WASHINGTON

August 26, 1993

Mr. John S. Roberts
P.O. Box H
Hobart, Indiana 46342

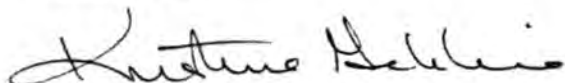
Dear Mr. Roberts:

I was recently contacted by Representative Peter J. Visclosky who forwarded your packet of information regarding a possible treatment for those infected with HIV.

As the AIDS Policy Coordinator, I will advocate public health policy that has a sound scientific basis. You can be assured that I will support the use of any treatment that has been shown to be safe and effective in finding a cure for this disease.

Best of luck with your efforts.

Sincerely,



Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

CC: Representative Peter J. Visclosky

THE "DISULFIRAM/ALCOHOL PROCEDURE" IS AN ESTABLISHED MEDICAL PROCEDURE
RELATIVE TO THE TREATMENT OF ALCOHOLISM.

I FEEL IT MIGHT HAVE SOME INTRINSIC MERIT RELATIVE TO THE TREATMENT
OF AIDS BECAUSE OF THE TOXICITY OF ACETALDEHYDE.

I THINK THAT AIDS PATIENTS SHOULD BE MADE AWARE OF THIS PROCEDURE.

THEY SHOULD AT LEAST BE AFFORDED THE PRIVILEGE OF A CHOICE OF
POSSIBLE EFFECTIVE TREATMENTS.

John S. Robert

AUGUST 31, 1993

TO: Ms. Kristine M. Gebbie, RN, MN
ATTENTION: National Aids Policy Coordinator

FROM DECEMBER, 1985 TO JUNE, 1986 AN AMAZING THING HAPPENED IN FRANCE -

THE MEDICAL CONDITION OF SOME AIDS PATIENTS IMPROVED, AND THEY WERE NOT TAKING AZT.

THE FACTS ARE RELATED IN ONE OF THE MOST PRESTIGIOUS MEDICAL JOURNALS PUBLISHED IN THE WORLD - "THE LANCET", SEPTEMBER 24, 1988 ISSUE.

AS THE STUDY (ENCLOSED) STATES ON PAGE 704:

"WHEN CHANGE IN CLINICAL STATUS WAS SCORED AS IMPROVED, STABLE, OR WORSE BY THE PHYSICIANS AFTER 16 WEEKS, 42% OF THE DITIOCARB RECIPIENTS HAD IMPROVED COMPARED WITH ONLY 5% IN THE PLACEBO GROUP ($p < 0.01$)."

WHY THE IMPROVEMENT?

BY READING MY PROPOSAL YOU CAN SEE WHAT I THINK THE ANSWER TO BE.

I AM NOT A PHYSICIAN; CONSEQUENTLY, I CANNOT CONDUCT CLINICAL TRIALS.

MY HOPE IS THAT WHOEVER READS THIS HAS THE INTEREST AND WHEREWITHAL TO CONDUCT CLINICAL TRIALS TO TEST THE VALIDITY AND THE EFFECTIVENESS OF THE "DISULFIRAM/ALCOHOL PROCEDURE".

John S. Roberts

JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

P.S. TO CONGRESSMAN VISCLOSKY: COULD YOU DO ONE MORE THING FOR ME? IN MY PROPOSAL I NOTED THE FACT THAT DR. PETER S. ARNO STATED IN HIS BOOK, AGAINST THE ODDS - THE STORY OF AIDS DRUG DEVELOPMENT, POLITICS & PROFITS: "BETWEEN 1987 AND 1991 THE NATIONAL CANCER INSTITUTE TESTED 40,000 CHEMICAL COMPOUNDS AT FACILITIES IN FREDERICK, MARYLAND, AND BIRMINGHAM, ALABAMA, TO SEE IF ANY COULD DISABLE THE AIDS VIRUS." WOULD YOU PLEASE FIND OUT FROM THE NATIONAL CANCER INSTITUTE IF ACETALDEHYDE WAS ON THAT LIST OF 40,000. THANKS AGAIN FOR ALL YOUR HELP. *J.S.R.*

ENCLOSED: COPIES OF MY PROPOSAL, MY JUNE 26 LETTER TO CONGRESSMAN VISCLOSKY (INCLUDES "THE LANCET" STUDY), DR. HEALY'S LETTER TO CONGRESSMAN VISCLOSKY, CONGRESSMAN VISCLOSKY'S LETTERS TO DR. KIRSCHSTEIN AND MS. GEBBIE AND MY LETTER TO DR. CARAUX



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Building: 1
Room: 126
(301) 496-2433

JUN 25 1993

The Honorable Peter J. Visclosky
House of Representatives
Washington, DC 20515-1401

Dear Mr. Visclosky:

This is in response to your May 26 letter regarding additional correspondence from one of your constituents, Mr. John S. Roberts, who has written regarding AIDS research. Mr. Roberts has suggested that a researcher at the Thomas Jefferson University in Philadelphia evaluate an agent that Mr. Roberts proposes has anti-HIV properties. We understand from previous correspondence directed to the National Institutes of Health (NIH) that Mr. Roberts believes that, by meditating on his pineal gland and drinking alcohol, he can generate an acid, acetaldehyde, that may cure his myopia and cure AIDS.

Mr. Roberts' initial inquiry in January was forwarded to Dr. John Bader, Chief of the Antiviral Evaluation Branch at the National Cancer Institute (NCI). Dr. Bader oversees the drug screening program that evaluates the anti-HIV properties of natural product extracts and synthesized drugs. After review of Mr. Roberts' letter, Dr. Bader informed him that the molecules he suggested for evaluation "are normal metabolites formed during normal body functioning, and would have no effect on HIV or AIDS."

In response to an additional inquiry from Mr. Roberts that suggested a therapeutic role for alcohol in HIV-infected individuals, Dr. Jack Whitescarver, Deputy Director of the NIH Office of AIDS Research, informed him of research sponsored by the National Institute of Alcohol Abuse and Alcoholism that showed alcohol consumption suppresses the human immune system and may accelerate complications associated with HIV infection.

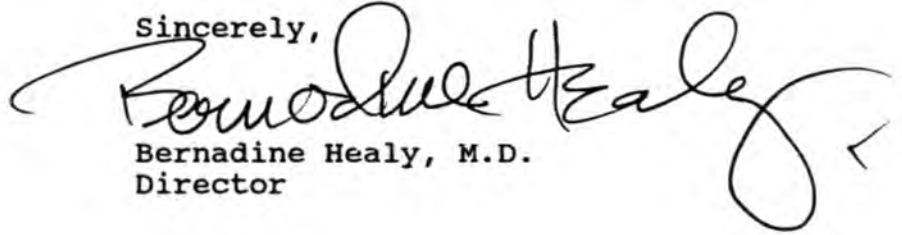
Mr. Roberts subsequently learned that a drug known as Ditiocarb (DTC), which happens to disrupt the metabolism of alcohol and increase blood concentrations of acetaldehyde, is being investigated as a possible anti-HIV agent. This led him to the incorrect conclusion that his theory regarding acetaldehyde was viable. The fact that DTC increases acetaldehyde concentrations, however, is unrelated to the proposed action of DTC. It is thought that DTC may induce the liver to produce hepatosin, which

Page 2 - The Honorable Peter J. Visclosky

in turn may stimulate the immune system. Acetaldehyde, however, only has been associated with some of the side effects of DTC, e.g., fatigue and nausea.

As there is currently no scientific basis to believe that acetaldehyde has any anti-HIV activity, the NIH is not pursuing the development or preclinical evaluation of this agent. I hope you will find this information useful in addressing Mr. Roberts request for assistance.

Sincerely,

A handwritten signature in cursive script, reading "Bernadine Healy". The signature is written in dark ink and is positioned to the right of the typed name and title.

Bernadine Healy, M.D.
Director

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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July 23, 1993

Dr. Ruth Kirschstein
Acting Director
National Institutes of Health
Bethesda, Maryland 20892

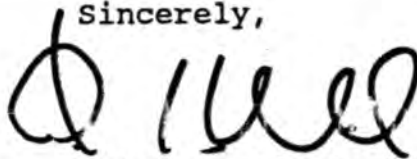
Dear Dr. Kirchstein:

I write on behalf of Mr. John Roberts, a resident of Indiana's First Congressional District.

Mr. Roberts has asked that I forward to you the enclosed packet of information regarding a possible treatment for those infected with the AIDS virus.

Thank you in advance for your serious consideration of this matter. Do not hesitate to let me know if you have any questions or need additional information.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV/sjg
Enclosure

PETER J. VISCLOSKY
1ST DISTRICT, INDIANA

COMMITTEE ON APPROPRIATIONS
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Ms. Kristine Gebbie
Director of AIDS Policy
The White House
1600 Pennsylvania Avenue
Washington, D.C. 20500

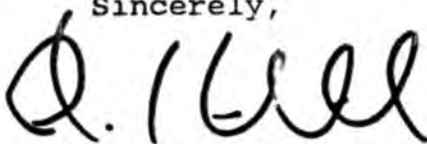
Dear Ms. Gebbie:

I write on behalf of Mr. John Roberts, a resident of Indiana's First Congressional District.

Mr. Roberts has asked that I forward to you the enclosed packet of information regarding a possible treatment for those infected with the AIDS virus.

Thank you in advance for your serious consideration of this matter. Do not hesitate to let me know if you have any questions or need additional information.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV/sjg
Enclosure

JULY 19, 1993

DR. JEAN CARAUX
DEPARTMENT OF IMMUNOLOGY
INSTITUT MERIEUX
BP 7046
69348 LYON CEDEX 7
FRANCE

DEAR DR. CARAUX,

PLEASE EXCUSE ME, BUT I HAVE TO WRITE TO YOU IN ENGLISH. I NEVER
LEARNED FRENCH. I HOPE THAT THIS DOES NOT CONSTITUTE A PROBLEM.
LAST MONTH I SENT TO YOU A COPY OF MY RESEARCH ENTITLED:

"A PROPOSAL FOR A PROCEDURE WHICH MIGHT PROVE TO BE
EFFECTIVE IN DESTROYING THE HIV VIRUS."

I HAVE A QUESTION TO ASK YOU CONCERNING THE RESEARCH WHICH YOU AND
YOUR COLLEAGUES CONDUCTED BETWEEN DECEMBER, 1985 AND JUNE, 1986 AND WAS
PUBLISHED BY "THE LANCET" IN SEPTEMBER 24, 1988; THE RESEARCH IS ENTITLED:

"RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF
DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY
VIRUS INFECTION".

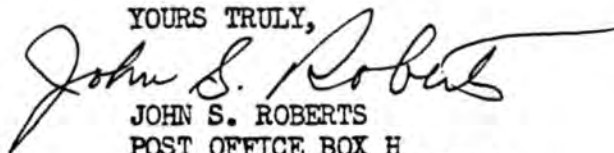
THE QUESTION IS -

DID YOU OR YOUR COLLEAGUES HAPPEN TO NOTICE OR ASK IF THE
DITIOCARB PATIENTS WERE DRINKING WINE WITH THEIR MEALS?

IN MY OWN RESEARCH I ASSUMED THAT THEY WERE DRINKING WINE WITH THEIR MEALS
BECAUSE IT IS THE CUSTOM IN FRANCE TO DO SO. OF COURSE, I COULD BE WRONG.

DR. CARAUX, I REALLY WOULD LIKE TO HEAR FROM YOU. THANK YOU FOR GIVING
THIS MATTER YOUR TIME AND CONSIDERATION.

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
UNITED STATES OF AMERICA

COPIES TO: CONGRESSMAN PETER J. VISCLOSKY
PROFESSOR RUSSELL F. MANKES
DR. RUTH KIRSCHSTEIN, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
KRISTINE GEBBIE, AIDS POLICY COORDINATOR
INDIANA UNIVERSITY SCHOOL OF MEDICINE, DR. SUBBLIAH SIVAM

JUNE 26, 1993

THE HONORABLE PETER J. VISCLOSKY
PUBLIC FORUM
PORTAGE PUBLIC LIBRARY
PORTAGE, INDIANA

DEAR CONGRESSMAN VISCLOSKY,

IT IS A PLEASURE TO MEET YOU IN PERSON.

WOULD YOU PLEASE OBTAIN FROM DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, THE ANSWER TO THIS QUESTION -

IS THE HIV VIRUS DESTROYED IN THE TEST TUBE BY ACETALDEHYDE?

IF THE ANSWER IS "YES", I THINK THAT THE LANG STUDY (COPY ATTACHED) SHOULD BE GIVEN CLOSE SCRUTINY.

IT IS MY FIRM CONVICTION THAT TWO BASIC FACTORS WERE NOT TAKEN INTO CONSIDERATION DURING THE COURSE OF THIS STUDY -

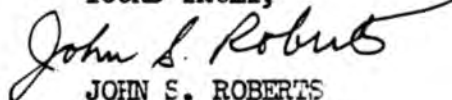
1. THE AMOUNT OF ALCOHOL THAT THE FRENCH DITIOCARB PATIENTS WERE DRINKING ON A DAILY BASIS.
- AND
2. THE CONSEQUENT AMOUNT OF UNMETABOLIZED ACETALDEHYDE THAT WAS BEING GENERATED WITHIN THEIR BODIES.

IT IS MY HYPOTHESIS THAT IT WAS THIS UNMETABOLIZED ACETALDEHYDE THAT WAS DESTROYING THE HIV VIRUS ITSELF - THUS CAUSING THE FRENCH DITIOCARB PATIENTS TO SHOW IMPROVEMENT IN THEIR CONDITIONS.

IF THE AUTHORS OF THIS STUDY (LANG, TREPO, KIRSTETTER ET AL) DO CONFIRM MY ASSUMPTION THAT THE FRENCH DITIOCARB PATIENTS WERE INDEED DRINKING ALCOHOL - NAMELY, WINE (SEE ATTACHMENTS) - ON A DAILY BASIS, I THINK THAT GOVERNMENTAL AUTHORITIES AND AGENCIES SHOULD ALERT THE PUBLIC THAT A VIABLE TECHNIQUE IS EXTANT WHEREBY IMMEDIATE THERAPY CAN BE RENDERED TO VICTIMS OF HIV AND AIDS - I SHALL SIMPLY CALL IT THE "DISULFIRAM/ALCOHOL PROCEDURE". THOSE KNOWING HOW TO ADMINISTER IT ARE PHYSICIANS SPECIALIZING IN THE "ANTABUSE" TREATMENT FOR ALCOHOLISM.

CONGRESSMAN VISCLOSKY, THANK YOU AND DR. HEALY FOR GIVING THIS MATTER YOUR TIME AND CONSIDERATION.

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342

COPIES WITH ATTACHMENTS TO:

DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
PROFESSOR RUSSELL F. MANKES, DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY,
THE ALBANY MEDICAL COLLEGE
INDIANA UNIVERSITY SCHOOL OF MEDICINE, NORTHWEST CAMPUS, GARY, INDIANA

possibility that naloxone may have had a positive inotropic effect as well.

Even in animal models, the mechanism of action of naloxone in reversing the haemodynamic changes of shock remains controversial. Holaday and Faden² suggested that central endorphin receptor blockade increases adrenal catecholamine release, basing this on the observation that naloxone was associated with a rise in serum adrenaline levels. However, Lechner et al¹⁰ suggested that naloxone potentiated the effects of circulating catecholamines on the myocardium resulting in improved contractility. Evidence for this suggestion was derived from an adrenalectomised dog with haemorrhagic shock in which serum catecholamines were kept constant. Recently Gurli et al¹¹ demonstrated improved left ventricular contractility after intravenous naloxone in a primate septic shock model despite observed three to five fold rises in plasma beta-endorphin and beta-lipotropin concentrations. Sagy et al¹² have shown a positive inotropic effect on isolated rat myocardium with D-naloxone—a non-opioid-blocking isomer. This effect was not prevented by pretreatment with propranolol, phentolamine, or morphine suggesting a primary cardiac site of activity unrelated to adrenergic or opioid receptors.

Because of the small population we studied, and the limited duration of naloxone infusion, we are not able to comment on its longer-term effects on haemodynamics or ultimate survival. Nevertheless, five patients from the naloxone group were discharged from hospital compared with only one in the placebo group, so we have no reason to suspect any lasting adverse effects of the infusion.

More extensive trials will be required to assess whether naloxone is a useful addition to current vasopressor/inotrope therapy and whether there is a positive effect on longer-term outcome. In addition, the unexpected finding of positive haemodynamic effects occurring only more than 4 h after the initial bolus of naloxone is not consistent with many of the currently proposed pharmacological actions of naloxone. Our results may stimulate new interest in this controversy.

We thank the nursing staff of the medical and surgical intensive care units at the Health Sciences Centre for their help in carrying out this trial. The study drug was provided by Du Pont Canada, Inc.

Correspondence should be addressed to D. E. R., Medical Intensive Care Unit, Health Sciences Centre, 820 Sherbrook Street, Winnipeg, Manitoba, R3A 1R9, Canada.

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- Lechner RB, Gurli NJ, Reynolds DG. Naloxone potentiates the cardiovascular effects of catecholamines in canine hemorrhagic shock. *Crit Shock* 1985; 16: 347-61.
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- Sagy M, Shavit G, Oron Y, Vidne BA, Gitter S, Sime Y. Nonopioid effect of naloxone on cardiac muscle contractility. *J Cardiovasc Pharmacol* 1987; 9: 682-85.

RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION

JEAN-MARIE LANG¹ CHRISTIAN TREPO² MYRIAM KIRSTETTER⁵ LAURENCE HERVIOL⁴ GENEVIEVE RETORNAZ³ GERARD RENOUX⁴ MIRCEA MUSSET⁶ JEAN-LOUIS TOURAINE² PATRICK CHOUTET⁴ ANNIE FALKENRODT¹ JEAN-MICHEL LIVROZET² FRANÇOISE TOURAINE² MICHELINE RENOUX⁴ JEAN CARAUX⁶
AND THE AIDS-IMUTHIOL FRENCH STUDY GROUP*

Hôpital Hautepierre, Strasbourg;¹ Hôpital Edouard Herriot, Lyon;² Hôtel Dieu, Lyon;³ Hôpital Bretonneau, Tours;⁴ Hôpital Saint Vincent de Paul, Paris;⁵

Department of Immunology, Institut Mérieux, Lyon;⁶ France

Summary 83 patients with human immunodeficiency virus (HIV) infection (CDC groups II, III, or IV-A) were randomised in a crossover trial of sodium-diethyldithiocarbamate (dithiocarb sodium, 'Imuthiol') (10 mg/kg body weight given orally once a week) against placebo. Each arm of the trial lasted 16 weeks. The disease did not progress to CDC-defined acquired immunodeficiency syndrome in the dithiocarb group but did so in 4 patients in the placebo group (3 between week 0 and 16, 1 between week 17 and 32). Dithiocarb was also associated to a significantly greater extent than placebo with relief of constitutional symptoms, improvement in clinical status (including shrinkage of enlarged spleen and lymph nodes), and improvement in immune function (as measured by CD4+ cell count and skin test reactivity). When placebo was replaced by dithiocarb, similar improvements were observed, whereas symptoms slowly reappeared and CD4+ cell levels progressively declined when dithiocarb treatment was replaced by placebo.

Introduction

SODIUM diethyldithiocarbamate (INN-dithiocarb sodium, 'Imuthiol') has potent immunorestorative, notably thymomimetic, properties.^{1,2} Dithiocarb, which is not mitogenic per se, induces the differentiation of T-cell precursors into mature and competent effectors, even in the absence of functional thymic epithelium.¹ It has been effective against the murine AIDS model (LP-BM5) of retroviral infection.^{3,4} It prevented disease and prolonged survival as long as treatment was maintained. The precise means by which dithiocarb exerts its effects has not been elucidated. However, it is well known that dithiocarb can influence several intracellular reactions. As a chelator of heavy metals dithiocarb is a potential antiviral agent,^{5,6} inhibiting a number of Cu-dependent enzymes;⁷⁻⁹ this property might affect the metal-dependent Tat gene product of HIV.⁹ By scavenging free-oxygen radicals, and by interfering with the metabolism of glutathione, it exerts anti-oxidant cytoprotective effects.^{10,13}

A previous clinical trial of dithiocarb in cancer patients in relapse¹⁴ has shown that dithiocarb can induce dose-

*The following persons are members of the AIDS-Imuthiol French Study Group: Macha Bachelet, Andre Burkelt, Claude Charbonnier, Hervé Caspard, Michel Defayolle, Marie-Christine Delsaux, Jean-Marie Dupuy, Sonia Escaich, Alain Goudeau, Jean Paul Heyraud, Daniel Pailot, Corinne Platel, Marie-Paule Richard, Louise Telvi.

dependent restoration of delayed-type hypersensitivity. Since ditiocarb inhibited HIV infection in vitro,¹⁵ a pilot group of HIV-infected patients was given ditiocarb, with restoration of delayed-type hypersensitivity and a rise in CD4+ cell counts.^{16,17} A second pilot study comparing intravenously administered ditiocarb against no treatment showed that it produced improvement in symptoms of AIDS-related complex (ARC) and hampered progression to AIDS.¹⁸

On the basis of these findings, we conducted a randomised, double-blind, placebo-controlled trial to evaluate the clinical and immunological impact of ditiocarb in patients infected with HIV, before the occurrence of AIDS. We report here clinical and immunological data supporting the efficacy of ditiocarb in this group of HIV-infected patients.

Patients and Methods

Patients

All patients admitted to the study had serum antibodies to HIV by the Western blot technique. Patients were eligible if they belonged to groups II, III, or IV-A of the CDC classification¹⁹ and had a CD4 positive helper-inducer lymphocyte count of less than 600/ μ l. Patients were excluded if they had already presented with a single episode of any of the disorders included in the case definition of AIDS—opportunistic infections, neuropathy, or neoplasia, or if they were pregnant or lactating. Participants were recruited from five medical centres. The study was approved by the ethics committee at each participating centre, and patients gave their informed consent.

Study Design, Drug Regimens, and Monitoring of Patients

Patients were randomly assigned to treatment with either ditiocarb or placebo. Ditiocarb was given orally once a week in a dose of 10 mg/kg body weight (enterocoated capsules, 125 mg ditiocarb per capsule). After 16 weeks patients were crossed over to the alternative treatment for another 16 weeks. The crossover design was chosen for ethical reasons, to give every patient a chance to benefit from a possible favourable clinical effect of ditiocarb. Furthermore, at the end of the 8 months' double-blind follow up, all patients were offered the opportunity to receive ditiocarb in an open manner.

Every 8 weeks patients were examined and the following laboratory investigations were performed: blood counts, T-lymphocyte phenotyping by indirect immunofluorescence or flow cytometry with monoclonal antibodies and Ficoll-Hypaque-separated peripheral blood mononuclear cells, quantitative immunoglobulin determination, and serological tests for hepatitis B, cytomegalovirus, and Epstein-Barr virus. Every 16 weeks, delayed type hypersensitivity reactions were evaluated by means of a 'Multitest' apparatus (Institut Mérieux, Lyon) with seven antigens—tetanus toxoid, diphtheria toxoid, *Streptococcus* group C, tuberculin, candida, *Trychophyton mentagrophytes*, *Proteus mirabilis*—and a glycerin control. Lymphadenopathy was scored as follows: lymph node size < 1 cm, score 2; 1–2 cm, score 4; > 2 cm, score 8; the overall score was the mean score of left and right axillary and cervical nodes. Peripheral blood lymphocytes and serum samples from some patients were frozen and examined later for HIV load in culture (reverse transcriptase assay) or presence of viral antigen p24 (Abbot diagnostics).

Criteria for Clinical Response

Clinical evaluation was based on (i) progression to AIDS, (ii) clinical status (number and severity of symptoms in group IV-A patients), and (iii) influence on lymphadenopathy and splenomegaly. Serious events were not taken into account when they occurred less than 4 weeks after onset of treatment. All clinical data were carefully cross-checked by a panel of investigators to classify patient's clinical status according to the CDC classification.¹⁹

TABLE 1—DEMOGRAPHIC, CLINICAL, AND BIOLOGICAL FEATURES OF PATIENTS AT ENTRY

	Ditiocarb (n = 42)	Placebo (n = 41)
Mean age (yr)	32.6 (SD 7.0)	32.7 (SD 7.5)
Number of females	6	5
Risk groups		
Number homosexuals	30	32
Number i/v drug abusers	3	4
Number others	9	5
CDC group		
Number in group II	5	6
Number in group III	26	29
Number in group IV-A	11	6
Mean weight (kg)	65.6	62.8
Number with splenomegaly	7	8
Mean CD4+ count (/ μ l)	405 (SD 111)	389 (SD 131)
Mean IgG (g/l)	21.8	21.2
Mean IgA (g/l)	2.56	2.79
Proportion anergic	6/35	6/39

Data Handling and Statistical Analysis

The comparison of ditiocarb vs placebo was based on data from the first 16 weeks; data obtained after crossover were used only to assess the effect of ditiocarb interruption in the first group, or the effect of replacing placebo by ditiocarb in the second. Data were analysed with the Statistical Analysis System (SAS) version 6.02—procedure FREQ for comparison of qualitative data (χ^2 test, Fisher's exact test) and TTEST (Student's *t* test) for comparison of quantitative data. Fisher's exact test was used when theoretical frequencies were smaller than 5.

Results

Subject Groups

94 patients were considered for the study but 11 were excluded for the following reasons: CD4+ cell counts > 600/ μ l at entry (7), refusal to participate (2), serum antibodies to HIV not confirmed by Western blot (1), and detection of a Kaposi sarcoma at start of treatment (1). Thus 83 were randomised in the study between December, 1985, and June, 1986. The treatment and placebo groups were similar in all respects (table 1). During the first 4 months, 2 patients died: 1 died 10 days after enrolment from narcotic drug overdosage, and the other after progression to AIDS. During these 16 weeks 6 patients withdrew for the following reasons: lost to follow up (4), intolerance (1), patient's choice (1). Thus 77 patients were evaluable after 4 months, and 75 entered the second phase. During the second 4 months, 1 patient died after AIDS developed, and 14 patients withdrew: lost to follow up or poor compliance (10), intolerance (1), patient's choice (3). Thus, 61 patients were evaluable after 8 months. No patient received zidovudine during the trial since it was not readily available in France then.

Clinical Effects

No patients in the ditiocarb group went on to have AIDS while 3 in the placebo group did so during the first 16 weeks of treatment (table II). After 8 weeks 1 patient in the placebo group had *Pneumocystis carinii* pneumonia (PCP), bronchial candidosis, and HIV-associated neuropathy, and died 20 weeks later. Kaposi's sarcoma developed in another patient in the 8th week. Another patient died with *Mycobacterium avium-intracellulare* infection and cerebral candidosis in the 3rd month.

A definite improvement in clinical status of ditiocarb recipients was noted after 16 weeks when compared with

TABLE II—CLINICAL OUTCOME OF HIV INFECTION IN FIRST ARM OF TRIAL

	Active	Placebo	p†
Progression to AIDS	0/38	3/39 (PCP, <i>Mycobacterium</i> , and Kaposi sarcoma)	...
Disappearance of constitutional symptoms* (IV-A patients)	8/11	0/5	<0.001
Lymphadenopathy score	-0.43† (SD 1.94)	+0.43‡ (SD 1.26)	<0.05
Disappearance of splenomegaly	4/7	0/8§	<0.05

*Persistent diarrhoea, weight loss, persistent fever.

†Fisher's exact test.

‡Change from baseline.

§No spleen became palpable; two additional spleen enlargements were noted.

placebo. Constitutional symptoms disappeared in 8 out of 11 group IV-A patients who received ditiocarb, but did not improve in any of the 6 group IV-A placebo-treated patients ($p < 0.001$). When change in clinical status was scored as improved, stable, or worse by the physicians after 16 weeks, 42% of ditiocarb recipients had improved compared with only 5% in the placebo group ($p < 0.01$). The clinical status of most placebo recipients (87%) remained unchanged during the 16 weeks. All the 9 patients in the ditiocarb group with a history of weight loss at entry regained normal weight after 16 weeks' treatment. The spleen became palpable in 4 of the 7 ditiocarb recipients, but in none of 8 placebo recipients, with splenomegaly at entry. Spleen enlargements were detected in 2 other placebo-treated patients at week 16 ($p < 0.05$). Lymphadenopathy diminished significantly in the ditiocarb group compared with the placebo group ($p < 0.05$). This diminution was not associated with clinical deterioration as seen at some late stages of HIV infection.

Immunological Effects

After 16 weeks ditiocarb patients had higher CD4+ cells cell count than did as the placebo group ($p < 0.05$) although absolute values were scattered (table III). 13 out of 36 (36%) evaluable ditiocarb recipients (see accompanying figure) and 5 out of 38 (13%) placebo recipients ($p < 0.05$) showed a striking and sustained increase of more than 200 CD4+ cells, which suggests some patients were more responsive to ditiocarb than others.

3 patients out of 29 evaluable subjects (10%) remained anergic to 7 recall antigens (Multitest apparatus) in the ditiocarb group, compared with 9 out of 32 (28%) in the placebo group ($p < 0.10$).

Virological Effects

Peripheral blood lymphocytes from 10 patients (5 ditiocarb, 5 placebo) chosen at random from one centre were sampled at weeks 0, 8, 16, 24, and 32, and frozen. These

TABLE III—CD4 CELL COUNT DURING THE FIRST ARM OF TRIAL

	Active		Placebo		p*
	Patients tested	Median (mean, SD) count	Patients tested	Median (mean, SD) count	
Baseline	42	415 (405, 111)	41	380 (389, 132)	NS
Week 8	36	479 (517, 172)	39	420 (461, 226)	NS
Week 16	36	522 (542, 215)	38	420 (447, 181)	<0.05

*Student's *t* test.

TABLE IV—SIDE-EFFECTS

Adverse reaction	Percentage of patients with adverse reactions	
	Active (n = 83)	Placebo (n = 79)
Unpleasant taste	41/32	4/3
Abdominal discomfort	33/26	8/6
Nausea	19/15	3/2
Sensation of malaise	10/8	1/1
Anorexia	9/7	1/1
Excitement	6/5	3/2
Somnolence	5/4	1/1
Vomiting	2/2	1/1
Rash	0/0	0/0

Number of patients in parentheses. No patient in either group had >25% drop in haemoglobin concentrations, red or white cell count, or platelet count.

samples were later thawed and reverse transcriptase activity was assayed in culture supernatants up to 28 days of culture. No significant change in HIV transcription rate was observed during ditiocarb administration, as evaluable by the day of peak reverse transcriptase activity in lymphocyte cultures. Similarly HIV p24 antigenaemia was not affected.

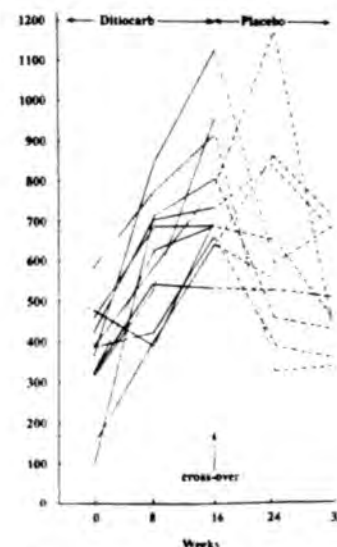
Effects of Replacing Placebo by Ditiocarb

When ditiocarb was given to patients previously treated by placebo, no patient progressed to AIDS. Clinical status improved in 26% of patients (9/35), whereas only 5% (2/39) improved while the group was on placebo. The number of constitutional symptoms diminished in 47% (16/34) of the patients now given ditiocarb. In 5 patients the absolute increase in CD4+ rose to beyond 200/ μ l.

Effects of Interrupting Ditiocarb Therapy

Clinical benefits obtained with ditiocarb were progressively lost when the drug was replaced by placebo: 1 patient progressed to AIDS (extrapulmonary *M. tuberculosis*) 3 months after the crossover. Although the

CD4+ Cell Counts



CD4+ cell counts in 13 patients responsive to ditiocarb, and effect of withdrawal of the drug.

Solid line: effect during ditiocarb therapy. Broken line: effect when ditiocarb replaced by placebo.

clinical status of 42% of the patients from this group had improved during ditiocarb administration, it deteriorated between week 16 and 32 in 36% of the group. Some constitutional symptoms reappeared. Although splenomegaly had disappeared in 4 out of 7 patients during ditiocarb therapy, the organ remained enlarged in the other 3 while they were on placebo, and splenomegaly developed in 2 additional patients.

CD4⁺ cell count had increased significantly during the first 16 weeks, but they declined from a mean of 554 CD4⁺ cells/ μ l (week 16) to 449 CD4⁺ cells/ μ l (week 32) in the 25 evaluable patients who had crossed over to placebo ($p < 0.05$). No patient who switched to placebo had an absolute increase in CD4⁺ cell counts of more than 200/ μ l. In those patients whose CD4⁺ count rose, nearly baseline values were attained (see accompanying figure).

Side Effects and Adverse Reactions

Ditiocarb did not induce more major adverse clinical or biological reactions than placebo (table IV), although it was associated more frequently with minor side-effects—unpleasant taste, abdominal discomfort, nausea, or malaise. Some patients reported fatigue and inability to concentrate on the day following ditiocarb ingestion. Ditiocarb had no adverse effect on blood counts. 2 patients had platelet counts of under 150 000/ μ l throughout the study. Platelet counts were not adversely affected by either ditiocarb or placebo.

Discussion

Oral administration of ditiocarb ('Imuthiol') to HIV-infected patients for 16 weeks produced more clinical and immunological benefits than did placebo. Ditiocarb forestalled progression of disease for at least the duration of therapy, this effect and the absence of deaths in the group being striking differences between the two treatment groups. Two other controlled studies, independent from the present one, have already observed the same trend to various impaired progression with ditiocarb: a randomised controlled study in Houston¹⁸ showed that AIDS developed in 5/16 untreated ARC patients, compared with 1/16 on ditiocarb. Similar findings have now been obtained in a matched-pairs, placebo-controlled study in Hamburg²⁰—the disease progressed to AIDS in 6 of 28 placebo-treated patients but in none of 28 on ditiocarb. Our ditiocarb-treated patients improved in at least two measures of immune function—CD4⁺ cell count and skin-test reactivity—which may have contributed to the clinical benefits. The changes in immune function can be attributed to ditiocarb since they persisted for the duration of treatment but were progressively lost when ditiocarb was discontinued.

The use of a T-cell recruiting agent to treat HIV-infected subjects carried a theoretical risk of stimulating an increase in the number of those very cells that harbour the retrovirus and thus producing clinical deterioration. This risk explains the cautiousness in our preliminary studies.^{21,22} The present findings, and those accompanying long-term administration of ditiocarb^{21,22} (3 years), clearly show that the CD4⁺ cell-defect is not aggravated. In fact, the reverse occurred, with ditiocarb producing an increase in CD4⁺ cells and improvement in constitutional symptoms of AIDS-related complex. Furthermore, preliminary data in a small number of patients indicate that ditiocarb does not enhance HIV replication in vitro or in vivo.

One possible means by which ditiocarb interferes with HIV infection is by producing the same "immunoanaleptic" effects as those produced in immunodeficient nude mice.¹ Although ditiocarb is not mitogenic per se, it can aid T-cell maturation and differentiation by increasing the number of T-cell precursors responsive to T-cell differentiation signals. A second possible means would be via its pharmacological properties. As a chelator of divalent cations,⁵ ditiocarb inhibits several Cu or Zn dependent enzymes.^{7,8} It might act in this way on enzymatic pathways that are required for HIV infection, such as those that involve the metal-linked Tat gene product of HIV.⁹ A third possibility is by its ability to influence intracellular scavenging of cell-toxic free-oxygen radicals.^{10,11} Ditiocarb can produce glutathione-SH peroxidase-like activity and, since it is itself a substrate for oxidation by H₂O₂, it may exert some of its anti-oxidant protection by directly detoxifying peroxides. Its oxygen-radical scavenging activities might account for the anti-inflammatory effects, such as shrinkage of spleen or lymph node enlargements. The therapeutic effects of ditiocarb on HIV infection probably involve several of the above mechanisms. However, more knowledge is needed on the intracellular mechanisms of HIV cytopathic infection and the precise cascade of events leading to immunodeficiency before the mechanism of action of ditiocarb can be fully assessed.

An important question is whether ditiocarb therapy can be tolerated and can be prolonged for extended periods of time. Ditiocarb can be given orally and is well tolerated except for minor adverse reactions. Unlike antiretroviral agents, it does not impair haemopoiesis. It has now been given for up to 3 years to HIV patients and up to 5 years to cancer patients without untoward effects.^{21,22}

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CORRELATION OF PLASMA INTERLEUKIN 1 LEVELS WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Summary The mean plasma level of interleukin 1 beta (IL-1 beta), measured by immunoassay, was significantly higher in 51 patients with rheumatoid arthritis (RA) than in 21 healthy controls of similar age. Further, in the RA group, plasma IL-1 beta correlated positively with Ritchie joint index, pain score, and erythrocyte sedimentation rate and correlated negatively with haemoglobin concentration. In individual patients with active disease who had serial measurements, plasma IL-1 beta also correlated with clinical disease activity. These results support the idea that IL-1 beta has a central role in the pathogenesis of RA.

Introduction

IL-1 molecules are polypeptides with many biological activities related to host defence and tissue remodelling,¹ and interest has arisen in the pathogenic potential of IL-1 in inflammatory and immune diseases.² Two forms of human IL-1 (alpha and beta) are encoded by separate genes with inducible expression in macrophages, lymphocytes, endothelial cells, and other cell types. The initial product of each is a propeptide of 31 kD from which mature peptide of 17 kD is processed.^{3,5} IL-1 alpha and beta have only 26% amino acid homology but compete equally for receptors on target cells⁶ and have similar biological activities. In human blood monocytes IL-1 mRNA is undetectable but after cellular activation it accumulates rapidly and IL-1 beta is usually the predominant form.^{3,5}

Many activities of IL-1 are relevant to rheumatoid arthritis (RA).⁷ IL-1 increases the release from synovial cells of vasoactive agents and mediators of tissue damage (eg, prostaglandins, proteinolytic enzymes, and reactive oxygen molecules)^{8,9} and is a powerful stimulus of bone¹⁰ and cartilage^{11,12} resorption. It also induces the acute-phase response¹³ and fever^{14,15} and may potentiate chronic inflammation by induction of lymphocyte growth factors such as interleukin 2 and its receptor.¹²

Much evidence¹⁶ has implicated IL-1 in the pathogenesis of RA: high levels are found in synovial exudates;^{14,16} RA synovial cells spontaneously produce biologically active IL-1 in vitro;¹⁷ in-situ hybridisation of mRNA shows that IL-1 gene expression is activated in vivo in RA synovial cells;¹⁶ and in laboratory animals a single intra-articular

INTERLEUKIN-1 BETA IN EXTRACTED PLASMA

	Plasma IL-1 beta (pg/ml)	
	Control	RA
n	21	51
Range	20-78	20-230
Median	50	90
Mean	44.7	98.2*
SEM	4.4	7.9

*Controls vs RA: $t = 4.28$; $p < 0.0001$

injection of IL-1 produced synovial fluid leucocytosis and increased proteoglycan breakdown.¹⁸

Despite the weight of circumstantial evidence for IL-1 as a pathogenic mediator in RA, it has not previously been possible to correlate IL-1 levels in vivo with clinical disease activity in patients because IL-1 measurement in blood and other biological fluids has been complicated by interfering factors.^{14,15} By means of a sensitive immunoassay combined with a single plasma extraction procedure we have now been able to measure circulating levels of immunoreactive IL-1 beta in patients with RA.

Methods

Patients with definite or classical rheumatoid arthritis¹⁹ attending a rheumatology outpatient department or admitted to a rheumatology ward were graded for disease activity by Ritchie joint index,²⁰ duration of early morning stiffness, and visual analogue pain score. At the same time, blood was taken for haemoglobin concentration, white cell count, platelet count, erythrocyte sedimentation rate (ESR), and rheumatoid factor titre as part of the normal management. Blood samples for plasma preparation were taken into EDTA (5×10^{-3} mol/l) tubes (Labco containing aprotinin (bovine lung 15-30 U/ml; Sigma) at 0.67 U/ml. Plasma was separated from cells and platelets immediately by centrifugation at 400 g and then at 10 000 g and stored in 500 μ l samples at -20°C until tested for IL-1 beta content. All patients received non-steroidal anti-inflammatory drugs (NSAIDs), and some received second-line antirheumatic drugs, including intra-articular steroids.

IL-1 beta Measurement

Before IL-1 measurement, samples were treated according to the method of Cannon et al.²¹ Plasma samples were thawed and extracted twice with chloroform (BDH, Paisley) by addition of 2 volumes of chloroform to 1 of plasma, mixing for 5 minutes, and then centrifugation at 10 000 g and removal of the aqueous phase for IL-1 beta testing in an enzyme-linked immunosorbent assay (IL-1 beta ELISA; Cistron Biotechnology Laboratory Impec). In our laboratory,²² this assay is sensitive to 20 pg/ml IL-1 beta, and has parallel dilution characteristics, less than 12% interassay variation, and detection recovery of added IL-1 beta in RA plasma of 92% after extraction ($n = 10$; mean 82.2 SEM 2.7%; difference from recovery in extracted normal plasma not significant). There is no cross-reactivity with IL-1 alpha. The ELISA test is

J. M. LANG AND OTHERS: REFERENCES—continued

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wine. Mailmen, salesmen, truck drivers, and other itinerant workers typically spend a large portion of their day drinking in cafés and restaurants as they make their daily rounds.

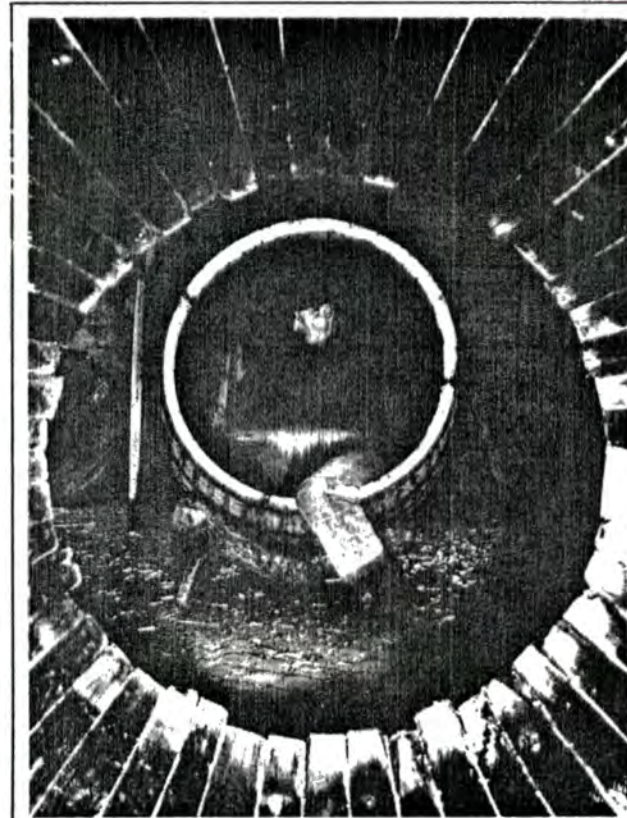
The use of alcohol to complement food has been developed to a fine art by the French. Indeed, the words *connoisseur*, *savoir faire*, and *savoir-vivre*, all connoting an appreciation for good living, are closely connected with the art of matching food and wine most harmoniously. To do this properly, one must follow a prescribed ritual, which dictates the appropriate alcoholic beverage to accompany each part of the meal. To open the meal and stimulate the appetite, one first takes an *apéritif* such as vermouth, Pernod, or anise. During the meal one chooses a red, white, or rosé dinner wine to complement the main course. Another wine may be called for when the cheese arrives, and champagne or sparkling burgundy may be ordered as a dessert wine. Following the meal, a "digestif" of liqueur or brandy is usually taken to facilitate digestion.



A repair shop at the French wine market is available to take care of damaged barrels. Here, expert cask makers still employ the old methods taught at a coopers' school within the Halle aux Vins.

Although the term "alcoholic Republic" was first used to describe American drinking patterns following the American Revolutionary War, the term applies equally well to contemporary France. Of all the nations of the world, France has undisputed leadership in practically all things alcoholic. Not only do the French drink more per capita, they also lead the world in the production of alcohol and alcoholics.

Since the Middle Ages wine has been the national beverage and one of the major agricultural products of France. Although a significant proportion of France's fine *bordeaux*, *burgundies*, and *champagnes* are exported to all parts of the world, the less expensive wines are consumed domestically. In fact, there is hardly a province in France without its local brandy or wine. In Normandy, hard cider and *Calvados*, a brandy distilled from cider, are the traditional beverages. In *Bordeaux*, *cognac* and *armagnac* are distilled from the local



An Italian barrel maker works on a large wine cask, climbing inside to smooth the wooden staves. Constructed just outside Rome, the cask will later be filled with wine from the famous town of Frascati.

APPENDIX 1

APPENDIX 1: CONSUMPTION OF WINE, BEER, AND SPIRITS

Average Yearly Consumption of Wine, Beer, and Spirits
Per Person in 62 Countries

AREA	COUNTRY	INTER- NATIONAL RANK	LITERS OF ABSOLUTE ALCOHOL			TOTAL
			WINE	BEER	SPIRITS	
EUROPE	France	1	11.6	2.9	2.3	16.8
	Italy	2	11.1	.6	1.9	13.6
	Austria	3	4.1	6.0	2.3	12.4
	Portugal	4	9.9	.8	1.0	11.7
	Luxembourg	5	5.0	3.7	2.8	11.5
	Spain	6	7.1	1.4	2.9	11.4
	West Germany	7	2.3	5.8	2.9	11.0
	Switzerland	8	5.0	3.8	2.1	10.8
	Hungary	10	4.4	2.0	3.1	9.5
	Belgium	11	1.9	5.8	1.6	9.3
	Czechoslovakia	12	1.1	4.5	2.4	8.6
	Denmark	15	.9	5.3	1.5	7.7
	Yugoslavia	16	3.2	1.7	2.8	7.7
	Great Britain	18	.5	5.3	1.1	6.9
	East Germany	20	.7	3.2	2.9	6.8
	Netherlands	21	.8	3.3	2.3	6.4
	Soviet Union	23	2.0	.9	3.4	6.3
	Bulgaria	24	2.4	1.9	1.8	6.1
	Poland	25	.8	1.3	3.9	6.0
	Ireland	26	.5	3.8	1.7	6.0
	Sweden	27	1.0	2.1	2.7	5.8
	Greece	29	4.8	.5	.1	5.4
	Finland	30	.6	2.2	2.3	5.1
	Norway	34	.4	1.8	1.6	3.8
	Roumania	35	2.6		1.2	3.8
	Iceland	39	.2	.2	2.4	2.8
UNITED STATES & OTHER ENGLISH-SPEAKING COUNTRIES	Australia	13	1.1	6.3	1.1	8.5
	New Zealand	14	.9	6.1	1.2	8.2
	Canada	17	.9	4.1	2.6	7.6
	United States	19	.8	3.0	3.0	6.8
ASIA	Japan	28	2.8	1.6	1.1	5.5
	South Korea	32		.7	3.5	4.2
	Cyprus	33	1.2	.9	1.8	3.9
	Hong Kong	46		.6	1.2	1.8
LATIN AMERICA	Argentina	9	9.5	.7		10.2
	Chile	22	5.3	1.1		6.4
	Uruguay	31	3.1	1.5		4.6
	Surinam	36		1.1	2.5	3.6
	Panama	38		1.3	1.6	2.9
	Peru	40	.2	1.0	1.4	2.6
	Mexico	41		1.4	1.1	2.5
	Cuba	42	.2	1.0	1.3	2.5
	Bolivia	43		.4	1.7	2.1
	Venezuela	44		2.1		2.1
	Brazil	52	.1	.5	.2	.7
	Paraguay	54	.2	.3		.5

Average Yearly Consumption of Wine, Beer, and Spirits
Per Person in 62 Countries

AREA	COUNTRY	INTER- NATIONAL RANK	LITERS OF ABSOLUTE ALCOHOL		
			WINE	BEER	SPIRITS
AFRICA	South Africa	37	1.2	.7	1.0
	Cameroon	48		.9	
	Namibia	49		.9	
	Congo	50		.7	
	Kenya	56		.4	
	Senegal	57	.1	.2	
	Gambia	60	.1	.1	
MIDDLE EAST & MOSLEM COUNTRIES	Bahrain	45	.1	.7	1.3
	Israel	47	.5	.5	.7
	Tunisia	51	.4	.3	
	Turkey	53	.1		.4
	Lebanon	55	.4		
	Algeria	58	.1	.2	
	Morocco	59	.2	.1	
	Egypt	61			.1
	Syria	62			.1

SOURCE: 1972 survey by the Finnish Foundation of Alcohol Studies and World Health Organization.

To your health!

Salud!

Prosit!

A votre santé!

Kan pei!

Skål!

Terveysteksi!

Stin ygia sou!

Slainthe is saol agat!

L'chaim!

Alla tua salute!

Kwa afya yako!

Op je gezonheid!

Na zdrowie!

Za vashe z-dorovyel!

Viva!

Ziveli!

Iechyd da i chivri!

I sveikata!

Egeszsegedre!



The drinking of "beals"
is one of the oldest and
most universal drinking
customs, as reflected in
the many languages in
which this toast appears.

A PROPOSAL FOR A PROCEDURE
WHICH MIGHT PROVE TO BE
EFFECTIVE IN DESTROYING
THE HIV VIRUS.

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BY

JOHN S. ROBERTS

JUNE 6, 1993
(D-DAY)

TO WHOM IT MAY CONCERN -

YOU HAVE RESPONDED TO THIS ADVERTISEMENT:

- AIDS -

DO YOU KNOW SOMEONE WHO HAS
TESTED HIV-POSITIVE? THE DRUG,
DISULFIRAM AND THE CHEMICAL,
ACETALDEHYDE MIGHT BE OF
SOME HELP. TO OBTAIN A 35 PAGE
FILE, SEND \$4.00 TO JOHN S. ROBERTS,
P.O. BOX H, HOBART, IND. 46342

IF YOU THINK THAT THERE MIGHT BE SOME MERIT TO THE
"DISULFIRAM/ALCOHOL PROCEDURE" YOU SHOULD IMMEDIATELY
SHOW THIS FILE TO YOUR PHYSICIAN. HE MAY REFER YOU TO
A PHYSICIAN WHO IS EXPERIENCED IN ADMINISTERING
THE "ANTABUSE" TREATMENT.

YOU MIGHT ALSO WISH TO WRITE TO YOUR CONGRESSMAN TO SEE
IF "CLINICAL TRIALS" COULD BE FUNDED IN THE CITY OR
TOWN IN WHICH YOU LIVE.

ANY AGENCY OF LOCAL, STATE OR FEDERAL GOVERNMENT WHICH
WISHES TO MAKE MULTIPLE COPIES OF THIS FILE TO DISTRIBUTE
TO WHOMEVER MAY ASK, HAS MY PERMISSION TO DO SO.

John S. Roberts

CONSIDERING THE MULTITUDINOUS ARRAY OF SUBSTANCES THAT ARE FOUND IN THE CHEMICAL REALM, WHAT IS THE ONE AND ONLY DRUG THAT A PERSON COULD TAKE WHICH MIGHT INADVERTENTLY INCREASE THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN THAT PERSON'S BLOOD?

- DISULFIRAM (ANTABUSE) OR ITS METABOLITE DITIOCARB (DTC) -

I WANT TO EXAMINE IN GREATER DETAIL THESE THREE STUDIES -

JEAN-MARIE LANG, CHRISTIAN TREPO, MYRIAM KIRSTETTER, ET AL:
'RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF
DITIOCARB SODIUM ('IMUTHIOL') IN HUMAN IMMUNODEFICIENCY
VIRUS INFECTION', "THE LANCET", SEPTEMBER 24, 1988,
PAGES 702 - 706.

EMIL C. REISINGER, PETER KERN, MARTIN ERNST, ET AL: 'INHIBITION
OF HIV PROGRESSION BY DITHIOCARB', "THE LANCET", MARCH 24, 1990,
PAGES 680 - 682.

EVAN M. HERSH, M.D.; GARY BREWTON, M.D.; DONALD ABRAMS, M.D.;
JOHN BARTLETT, M.D. ET AL: 'DITIOCARB SODIUM (DIETHYLDITHIOCARBAMATE)
THERAPY IN PATIENTS WITH SYMPTOMATIC HIV INFECTION AND AIDS',
"JAMA - THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION",
MARCH 27, 1991, PAGES 1538 - 1544.

HEREINAFTER, I WILL REFER TO THESE STUDIES AS SIMPLY "LANG", "REISINGER"
AND "HERSH".

IN ALL THREE OF THESE STUDIES THERE WAS A VARIABLE THAT WAS NOT TAKEN
INTO ACCOUNT AND THEREFORE NOT MEASURED -

- THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN THE BLOOD OF THOSE
PATIENTS TO WHOM DITIOCARB HAD BEEN GIVEN -

FIRST, I WANT TO CLARIFY THE TERMS "METABOLIZED" AND "UNMETABOLIZED"
AS I THINK OF THEM.

TO ME, "METABOLIZED" SIMPLY MEANS:

- TO BE CHANGED INTO SOMETHING DIFFERENT -

WHEREAS "UNMETABOLIZED" SIMPLY MEANS:

- TO REMAIN THE SAME -

YOU WILL SEE HOW I ARRIVED AT THESE FIGURES LATER, BUT FOR NOW - WHEN THE HIGHLY TOXIC, POISONOUS SUBSTANCE KNOWN AS ACETALDEHYDE IS PROCESSED BY THE LIVER, 98.43% OF IT IS METABOLIZED (OR CHANGED) INTO HARMLESS ACETIC ACID WITHIN 18.6 MINUTES.

WHAT IF 98.43% OF IT COULD NOT BE CHANGED WITHIN 18.6 MINUTES? LET'S SAY, FOR SOME REASON, THE LIVER NOW TOOK 2 HOURS TO DO WHAT IT NORMALLY ACCOMPLISHED IN 18.6 MINUTES.

ISN'T IT TRUE THEN THAT FOR MORE THAN AN ADDITIONAL 1½ HOURS POISONOUS, UNMETABOLIZED (UNCHANGED) ACETALDEHYDE WOULD BE FLOWING THROUGHOUT THE BODY?

THIS THEN IS HOW I WILL BE THINKING OF THE TERMS "METABOLIZED" AND "UNMETABOLIZED" THROUGHOUT THE REST OF THIS FILE.

THE FIRST FEW PAGES OF THIS FILE ARE PRIMARILY A COMPARISON AND CONTRAST OF THE THREE AFOREMENTIONED STUDIES.

THE STUDIES TOOK PLACE IN FRANCE, GERMANY AND THE UNITED STATES.

THE FRENCH STUDY (LANG) TOOK PLACE FROM DECEMBER, 1985 TO JUNE, 1986. THE GERMAN STUDY (REISINGER) TOOK PLACE AT SOME TIME BETWEEN MAY, 1986 AND NOVEMBER, 1987. THE UNITED STATES STUDY (HERSH) TOOK PLACE AT SOME TIME BETWEEN JANUARY, 1987 AND APRIL, 1989.

NUMBER OF PATIENTS - LANG (83), REISINGER (60) AND HERSH (389).

CONDITION OF THE PATIENTS - IN THE LANG AND REISINGER STUDIES THE PATIENTS WERE AT THE SAME STAGE OF THE INFECTION; THEY HAD NOT YET DEVELOPED AIDS SYMPTOMS. IN THE HERSH STUDY THE AIDS SYMPTOMS HAD TO BE MORE IN EVIDENCE:

LANG (P. 703) - "ALL PATIENTS ADMITTED TO THE STUDY HAD SERUM ANTIBODIES TO HIV BY THE WESTERN BLOT TECHNIQUE. PATIENTS WERE ELIGIBLE IF THEY BELONGED TO GROUP II, III, OR IV-A OF THE CDC CLASSIFICATION AND HAD A CD4 POSITIVE HELPER-INDUCER LYMPHOCYTE COUNT OF LESS THAN 600/ul."

REISINGER (P.680) - "INCLUSION CRITERIA WERE MALE SEX, 18-55 YEARS, SERUM ANTIBODIES AGAINST HIV-1, WALTER REED STAGE 2-4, NORMAL BLOOD COUNTS, AND NORMAL SERUM CREATININE AND LIVER ENZYME LEVELS."

HERSH (P. 1539) - "PATIENTS WERE REQUIRED TO HAVE THREE OR MORE OF THE FOLLOWING: LYMPHADENOPATHY, FEVER, NIGHT SWEATS, WEIGHT LOSS, DIARRHEA, FATIGUE, THRUSH, HAIRY LEUKOPLAKIA"

LENGTH OF THE STUDIES - LANG (32 WEEKS), REISINGER (24 WEEKS) AND HERSH (24 WEEKS).

IN ALL THREE OF THE STUDIES ½ OF THE PATIENTS WERE GIVEN DITIOCARB AND ½ WERE GIVEN PLACEBO. THE PATIENTS WHO WERE GIVEN DITIOCARB WERE GIVEN IT ONCE A WEEK IN THE FOLLOWING AMOUNTS AND MANNER:

LANG: 10mg/kg BODY WEIGHT - ORALLY
REISINGER: 5mg/kg BODY WEIGHT - INTRAVENOUSLY OR
10mg/kg BODY WEIGHT - ORALLY
HERSH: 400mg/m² OF BODY SURFACE AREA - ORALLY

NO, I DO NOT KNOW HOW TO CORRELATE THESE MEASUREMENTS - mg/kg BODY WEIGHT
VERSUS mg/m² OF BODY SURFACE AREA, BUT BEAR WITH ME.

ZIDOVUDINE USE:

LANG (P.703) - "NO PATIENT RECEIVED ZIDOVUDINE DURING THE TRIAL
SINCE IT WAS NOT READILY AVAILABLE IN FRANCE THEN."
REISINGER - ZIDOVUDINE IS NOT MENTIONED. I ASSUME THAT IT WAS NOT
AVAILABLE IN GERMANY EITHER.

HERSH - (P. 1540) - YES/NO - DITIOCARB (35/18), Placebo (37/19)
SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB - REISINGER (P.679) STATES:

"A DOSE RESPONSE STUDY IN PATIENTS WITH AIDS-RELATED COMPLEX (ARC)
OR AIDS SHOWED THAT DOSES UP TO 400mg/m² ADMINISTERED ONCE WEEKLY
WERE NOT TOXIC WHEREAS 800 mg/m² EITHER ONCE OR TWICE A WEEK
HAD SIDE-EFFECTS."

I HAVE BEEN TRYING TO OBTAIN A COPY OF THE ARTICLE THAT ARRIVED
AT THESE CONCLUSIONS BUT HAVE THUS FAR BEEN UNSUCCESSFUL. IT IS -

REISINGER E., KERN P., DIETRICH M. 'CLINICAL TRIALS WITH
DIETHYLDITHIOCARBAMATE IN HIV-INFECTIONS'. "MITT. ÖSTERR. GES.
TROPENMED. PARASITOL." 1988; 10:287-92.

SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB:

LANG - I'LL TALK ABOUT THIS LATER.

REISINGER (P.681) - "NAUSEA AND FATIGUE WERE INFREQUENT IN BOTH
DTC GROUPS." (P.682) - "NO SEVERE SIDE-EFFECTS
WERE OBSERVED."

HERSH (P.1538) - "THE ADMINISTRATION OF DITIOCARB DID NOT INDUCE
ANY MAJOR ADVERSE CLINICAL OR BIOLOGICAL REACTIONS."
(P. 1542) - "THERE WERE ACTUALLY FEWER ADVERSE
REACTIONS ATTRIBUTED TO DITIOCARB THAN TO PLACEBO."

CONSEQUENTLY, I AM GOING TO MAKE THE ASSUMPTION THAT THE AMOUNT OF
DITIOCARB ADMINISTERED PER PATIENT IN THE REISINGER STUDY WAS JUST ABOUT
EQUAL TO THAT OF THE HERSH STUDY BECAUSE NO SIGNIFICANT SIDE EFFECTS
WERE NOTED IN EITHER STUDY.

THE DRINKING OF ALCOHOL

LANG - I'LL TALK ABOUT THIS LATER.

REISINGER (P.681) - "BECAUSE OF THE DISULFIRAM-LIKE EFFECT OF DTC, INTOLERANCE TO ALCOHOL (PALPITATION, RASH, DIZZINESS, NAUSEA, HEADACHE) WAS SEEN IN 4 PATIENTS (15%) WHO REPORTED ALCOHOL CONSUMPTION WITHIN 2 DAYS OF DTC ADMINISTRATION. HOWEVER, 11% OF PLACEBO-TREATED PATIENTS REPORTED SIMILARLY....."

HERSH (P.1539) - "BECAUSE DITHIOCARB IS A DITHIOCARBAMATE AND HAS DISULFIRAM (ANTABUSE)-LIKE EFFECTS, PATIENTS WERE ADVISED NOT TO CONSUME ALCOHOL FROM 12 HOURS BEFORE TO 48 HOURS AFTER TREATMENT."

CONSEQUENTLY, I ASSUME THAT THE DRINKING OF ALCOHOL WAS NOT A FACTOR IN EITHER THE REISINGER OR HERSH STUDIES, BECAUSE IF IT HAD BEEN, A LOT MORE SIDE-EFFECTS AND ADVERSE REACTIONS WOULD HAVE BEEN REPORTED IN BOTH OF THEM.
CONCLUSIONS OF THE REISINGER AND HERSH STUDIES -

REISINGER (P.682): "INTRAVENOUS DTC WAS SUPERIOR TO ORAL DTC AND TO PLACEBO IN HIV-1 INFECTION."

"ORALLY DTC TENDED TO DECREASE HIV-RELATED DISEASES, BUT THE DIFFERENCE FROM THE ORAL PLACEBO GROUP WAS NOT SIGNIFICANT."

"INTRAVENOUS ADMINISTRATION OF DTC IS MORE EFFECTIVE THAN ORAL ADMINISTRATION IN DELAYING THE PROGRESSION OF HIV-INFECTION IN THE EARLY SYMPTOMATIC STAGES."

(P.679): "55 PATIENTS WERE EVALUABLE AT THE END OF THE STUDY: NO PATIENT WHO HAD RECEIVED DTC BUT 6 PLACEBO PATIENTS HAD AIDS, A SIGNIFICANT DIFFERENCE. SIGNIFICANTLY DELAYED DISEASE PROGRESSION WAS OBSERVED IN THE INTRAVENOUS DTC GROUP COMPARED WITH ITS MATCHING PLACEBO. THE BENEFIT IN THE ORAL DTC GROUP WAS NOT STATISTICALLY SIGNIFICANT. DURING AN 18-MONTH FOLLOW-UP 3 DEATHS OCCURRED IN THE ORIGINAL PLACEBO GROUPS, WHEREAS NO PATIENT WHO HAD INITIALLY RECEIVED DTC DIED. A SIGNIFICANT DELAY IN PROGRESSION TO AIDS WAS OBSERVED IN THE DTC GROUPS."

HERSH (P.1538): "TEN NEW ACQUIRED IMMUNODEFICIENCY SYNDROM (AIDS)-
DEFINING OPPORTUNISTIC INFECTIONS OCCURRED IN THE
TREATED PATIENTS AND 21 IN THE CONTROLS. REDUCTION OF
NEW OPPORTUNISTIC INFECTIONS IN THE DITIOCARB GROUP
WAS SIGNIFICANT IN ALL PATIENTS (RELATIVE RISK [RR] 0.44)
AND IN PATIENTS WITH AIDS (CDC GROUPS 1V-C1
AND 1V-D) (RR, 0.12)."

(P.1542): "THE STATISTICALLY SIGNIFICANT BENEFIT OF DITIOCARB
WAS SEEN IN ALL PATIENTS, AND SEPARATELY IN THE
SUBGROUPS OF AIDS PATIENTS."

(P.1539): "PATIENTS FROM EIGHT MEDICAL CENTERS....."

(P.1541): "FINALLY, THE REDUCTION IN OIs IN THE DITIOCARB GROUP
WAS SEEN IN ALL STUDY CENTERS."

(P.1538): "WE CONCLUDE THAT, IN THIS STUDY, DITIOCARB WAS SAFE
AND REDUCED THE INCIDENCE OF OPPORTUNISTIC INFECTIONS
IN PATIENTS WITH SYMPTOMATIC HIV INFECTION."

EXPLANATION - VARIOUS EXPLANATIONS ARE ADVANCED, BUT NEITHER REISINGER
OR HERSH HAVE YET FOUND OUT THE DEFINITIVE REASON FOR DITIOCARB'S EFFECTIVENESS.
AS HERSH STATES (P.1543):

"THE PRECISE CASCADE OF EVENTS BY WHICH DITIOCARB EXERTS ITS ACTIVITY
IS NOT FULLY ELUCIDATED."

I THINK ANOTHER FACTOR HAS TO BE CONSIDERED - THE AMOUNT OF UNMETABOLIZED
ACETALDEHYDE THAT WAS FLOWING IN THE BLOOD OF THOSE PATIENTS TO WHOM DITIOCARB
HAD BEEN GIVEN. THE AMOUNT MUST HAVE BEEN VERY SMALL, ELSEWISE THE PATIENTS
WOULD HAVE BEEN DISPLAYING ALOT MORE ADVERSE REACTIONS.

YOU MIGHT ASK - IF THE DRINKING OF ALCOHOL WAS NOT A SIGNIFICANT FACTOR
IN THE REISINGER OR HERSH STUDIES, HOW COULD ACETALDEHYDE HAVE GOTTEN
INTO THE BLOOD OF THOSE PATIENTS TO WHOM DITIOCARB HAD BEEN GIVEN?

LET ME DIGRESS FOR A MOMENT -

WHAT DOES DITIOCARB (DISULFIRAM, ANTABUSE, DTC) DO WHEN IT ENTERS
THE BODY OF A PERSON?

- IT "PLUGS UP" THE LIVER AS FAR AS THE METABOLIZATION OF
ACETALDEHYDE IS CONCERNED -

IF YOU TAKE DITIOCARB TODAY YOU WON'T GET RID OF IT BY TOMORROW.
IT WILL STAY WITH YOU FOR DAYS.

REISINGER (P.679):

"DESPITE THE SHORT SERUM HALF-LIFE OF DTC SOME EFFECTS OF THIS DRUG
LAST UP TO 7 DAYS, INDICATING RAPID INTRACELLULAR PENETRATION."

ENCYCLOPEDIA AMERICANA, 1991 EDITION, VOLUME 1, PAGE 518:

"IN GENERAL, DISULFIRAM MAKES ALCOHOL SYMBOLICALLY UNAVAILABLE TO THE ALCOHOLIC AND THEREBY REDUCES THE DESIRE TO DRINK. ITS SLOW RATE OF METABOLISM IN THE BODY GIVES THE INDIVIDUAL PAUSE BEFORE IMPULSIVE RELAPSE."

REMEMBER - IN ALL THREE OF THESE STUDIES THE PATIENTS WERE GIVEN DITIOCARB ONCE A WEEK.

IN OTHER WORDS, THERE WASN'T A TIME DURING THE ENTIRE COURSE OF ALL THREE STUDIES THAT DITIOCARB WAS NOT PRESENT IN THE LIVERS OF THE DITIOCARB PATIENTS.

ACETALDEHYDE IS A HIGHLY TOXIC POISON. NORMALLY, HOW IS IT METABOLIZED BY THE LIVER?

THE "JOURNAL OF APPLIED TOXICOLOGY", OCTOBER, 1991 ISSUE STATES (P.374) THAT THE HALF-LIFE OF ACETALDEHYDE IN THE BLOOD OF RATS IS 3.1 MINUTES. I SHALL ASSUME THAT THIS RATE COULD BE APPLIED TO HUMAN BEINGS. MAYBE IT'S MORE, MAYBE IT'S LESS.

THIS FIGURES OUT THUSLY - 98.43% OF THE ACETALDEHYDE THAT IS IN THE BODY OF A HUMAN BEING WILL BE METABOLIZED IN 18.6 MINUTES BY THE LIVER IF IT IS FUNCTIONING NORMALLY (SEE CHART, PAGE 13). IN OTHER WORDS, JUST ABOUT ALL OF A HIGHLY TOXIC POISON WILL BE RENDERED HARMLESS BY THE LIVER IN LESS THAN 20 MINUTES.

IF THE LIVER IS "PLUGGED UP" IN ANY DEGREE WHATSOEVER WITH DITIOCARB THE ACETALDEHYDE CANNOT BE PROPERLY METABOLIZED. IF IT IS "PLUGGED UP" JUST A LITTLE BIT - SAY WITH THE RESIDUE THAT REMAINS 7 DAYS AFTER INITIAL ADMINISTRATION - PERHAPS THE ACETALDEHYDE WILL REMAIN TOXIC FOR ONLY A FEW EXTRA MINUTES. HOWEVER, WHAT IF IT IS NEWLY "PLUGGED UP" WITH THE ONCE A WEEK SERVING? COULD THE ACETALDEHYDE REMAIN POISONOUS FOR MAYBE AN HOUR OR LONGER? SINCE SIDE-EFFECTS AND ADVERSE REACTIONS WERE NOT A FACTOR IN EITHER THE REISINGER OR HERSH STUDIES, THE AMOUNT OF ACETALDEHYDE MUST HAVE BEEN VERY SMALL INDEED.

INDEED, HOW MIGHT IT HAVE GOTTEN INTO THE PATIENTS' SYSTEMS IF THE DRINKING OF ALCOHOL WAS NOT A FACTOR?

THE SAME ISSUE OF THE "JOURNAL OF APPLIED TOXICOLOGY" STATES (P.374):

"ACETALDEHYDE HAS BEEN IDENTIFIED IN OAK LEAVES, TOBACCO, APPLES, BROCCOLI, COFFEE, GRAPES, GRAPEFRUIT, ORANGES, LEMONS, ONIONS, PEACHES, PEARS, PINEAPPLES, RASPBERRIES, STRAWBERRIES AND MANY SPICES. EUROPEAN BEERS HAVE BEEN FOUND TO CONTAIN AS MUCH AS 13.5mg/l. THE ACCEPTABLE DAILY INTAKE RECOMMENDED BY FAO/WHO IS 0.0-2.5mg kg-1 BODY WEIGHT."

"ANOTHER SIGNIFICANT CONTRIBUTION IS MADE BY COFFEE ROASTING AND MOTOR VEHICLE EXHAUSTS."

"AMBIENT AIR LEVELS OF ACETALDEHYDE RANGE FROM NON-DETECTABLE TO 123 ug m-3 IN MAJOR U.S. CITIES."

ENCYCLOPEDIA AMERICANA, 1991 EDITION, VOLUME 1, PAGE 518:

"UNFORTUNATELY, HOWEVER, THE DISULFIRAM/ALCOHOL REACTION CAN BE SET OFF BY ALCOHOL USED IN FOOD PREPARATIONS OR BY INHALED FUMES (AS FROM AFTER-SHAVE LOTION)."

IN OTHER WORDS, A PATIENT WHO HAD DITIOCARB IN HIS LIVER COULD GET UP IN THE MORNING, HAVE A GLASS OF ORANGE JUICE, HAVE A CUP OR TWO OF COFFEE, SMOKE A CIGARETTE, SHAVE AND APPLY AFTER-SHAVE TO HIS FACE AND AUTOMATICALLY THE LEVEL OF UNMETABOLIZED ACETALDEHYDE IN HIS BLOOD WOULD HAVE BEEN INCREASED.

THROUGHOUT THE DAY IF HE ATE SOME FRUIT OR SIMPLY SMELLED AUTO EXHAUST FUMES HIS LEVEL OF UNMETABOLIZED ACETALDEHYDE WOULD BE INCREASED.

IF THE PATIENT TOOK HIS DITIOCARB CAPSULE ON SUNDAY EVENING AND SIX DAYS LATER ATE AN APPLE ON SATURDAY AFTERNOON, THERE WOULD STILL BE ENOUGH OF A DITIOCARB RESIDUE IN THAT PATIENT'S LIVER TO PREVENT NORMAL METABOLIZATION OF ACETALDEHYDE; 98.43% OF IT WOULD NOT BE METABOLIZED IN 18.6 MINUTES; PERHAPS 19.6 MINUTES WOULD BE REQUIRED TO DO THE JOB; THIS MEANS THAT ON THIS PARTICULAR SATURDAY AFTERNOON A TOXIC POISON WOULD BE FLOWING FREE THROUGH THE BLOOD OF THIS PATIENT FOR AN EXTRA MINUTE.

IN OTHER WORDS, THROUGHOUT THE ENTIRE COURSE OF THE WEEK VARYING AMOUNTS OF UNMETABOLIZED ACETALDEHYDE COULD BE IN THE BLOOD OF THOSE PATIENTS WHO TOOK DITIOCARB IF THOSE PATIENTS WERE INDEED EXPOSED TO THE FACTORS WHICH ARE LISTED ON PAGE 374 OF THE "JOURNAL OF APPLIED TOXICOLOGY" AND ON PAGE 518, VOLUME 1 OF THE ENCYCLOPEDIA AMERICANA.

GRANTED, IT MIGHT BE A MINUTE AMOUNT, NOT ENOUGH TO MAKE THE PATIENT NAUSEOUS, BUT THE FACT IS INDISPUTABLE - ACETALDEHYDE, IN ANY AMOUNT, CANNOT BE PROPERLY METABOLIZED BY THE LIVER IN A NORMAL MANNER IF DITIOCARB IS PRESENT IN ANY AMOUNT.

I THINK IT WAS THIS UNMETABOLIZED ACETALDEHYDE THAT WAS AT WORK IN THE REISINGER AND HERSH STUDIES: IT IS MY HYPOTHESIS THAT THE HIV VIRUS ITSELF WAS BEING DESTROYED BY THIS HIGHLY TOXIC POISON.

THE SAME CAN BE SAID FOR THE LANG STUDY; HOWEVER, I THINK THAT THE QUANTITY OF UNMETABOLIZED ACETALDEHYDE BEING GENERATED IN THESE FRENCH PATIENTS WAS GREATER AND THEREFORE MORE EFFECTIVE. HOW COULD THIS HAVE COME ABOUT?

BUT FIRST -

IN THE REISINGER STUDY 15 PATIENTS RECEIVED 5mg OF DITIOCARB (DTC) INTRAVENOUSLY ONCE A WEEK AND 15 PATIENTS RECEIVED 10mg OF DITIOCARB (DTC) ORALLY ONCE A WEEK. IN THE LANG STUDY ALL 83 PATIENTS RECEIVED 10mg OF DITIOCARB(DTC) ORALLY ONCE A WEEK.

NOW WE HAVE SOMETHING TO COMPARE.

WHAT DOES REISINGER HAVE TO SAY ABOUT THOSE PATIENTS WHO RECEIVED 10mg OF DITIOCARB (DTC) ONCE A WEEK? (P.682)

"ORALLY DTC TENDED TO DECREASE HIV-RELATED DISEASES, BUT THE DIFFERENCE FROM THE ORAL PLACEBO GROUP WAS NOT SIGNIFICANT."

NOW, LET US LOOK AT SOME OF THE OBSERVATIONS WHICH LANG MAKES ABOUT HIS PATIENTS; REMEMBER, THEY TOO RECEIVED 10mg OF DITIOCARB (DTC) ORALLY ONCE A WEEK:

- (P.702) - "THE DISEASE DID NOT PROGRESS TO CDC-DEFINED ACQUIRED IMMUNODEFICIENCY SYNDROME IN THE DITIOCARB GROUP BUT DID SO IN 4 PATIENTS IN THE PLACEBO GROUP (3 BETWEEN WEEK 0 AND 16, 1 BETWEEN WEEK 17 AND 32). DITIOCARB WAS ALSO ASSOCIATED TO A SIGNIFICANTLY GREATER EXTENT THAN PLACEBO WITH RELIEF OF CONSTITUTIONAL SYMPTOMS, IMPROVEMENT IN CLINICAL STATUS (INCLUDING SHRINKAGE OF ENLARGED SPLEEN AND LYMPH NODES), AND IMPROVEMENT IN IMMUNE FUNCTION (AS MEASURED BY CD4+ CELL COUNT AND SKIN TEST REACTIVITY). WHEN PLACEBO WAS REPLACED BY DITIOCARB, SIMILAR IMPROVEMENTS WERE OBSERVED, WHEREAS SYMPTOMS SLOWLY REAPPEARED AND CD4+ CELL LEVELS PROGRESSIVELY DECLINED WHEN DITIOCARB TREATMENT WAS REPLACED BY PLACEBO."
- (P.704) - "ALL THE 9 PATIENTS IN THE DITIOCARB GROUP WITH A HISTORY OF WEIGHT LOSS AT ENTRY REGAINED NORMAL WEIGHT AFTER 16 WEEKS' TREATMENT. THE SPLEEN BECAME IMPALPABLE IN 4 OF THE 7 DITIOCARB RECIPIENTS, BUT IN NONE OF 8 PLACEBO RECIPIENTS, WITH SPLENOMEGALY AT ENTRY."
- (P.704) - "WHEN CHANGE IN CLINICAL STATUS WAS SCORED AS IMPROVED, STABLE, OR WORSE BY THE PHYSICIANS AFTER 16 WEEKS, 42% OF DITIOCARB RECIPIENTS HAD IMPROVED COMPARED WITH ONLY 5% IN THE PLACEBO GROUP ($p < 0.01$)."
- (P.704) - LANG TABLE II (SEE MY PAGE 13) HIGHLIGHTS THE "DISAPPEARANCE OF CONSTITUTIONAL SYMPTOMS" AND THEY ARE "PERSISTENT DIARRHOEA, WEIGHT LOSS, PERSISTENT FEVER". ALSO NOTE "DISAPPEARANCE OF SPLENOMEGALY".

AND TO TOP IT OFF, THE LANG STUDY SHOWED AN INCREASE IN THE CD4-POSITIVE LYMPHOCYTES (T-HELPER CELLS) - SEE LANG TABLE III (MY PAGE 13) AND STATES (P.705):

"THE PRESENT FINDINGS, AND THOSE ACCOMPANYING LONG-TERM ADMINISTRATION OF DITIOCARB (3 YEARS), CLEARLY SHOW THAT THE CD4+ CELL-DEFECT IS NOT AGGRAVATED. IN FACT, THE REVERSE OCCURRED, WITH DITIOCARB PRODUCING AN INCREASE IN CD4+ CELLS AND IMPROVEMENT IN CONSTITUTIONAL SYMPTOMS OF AIDS-RELATED COMPLEX. FURTHERMORE, PRELIMINARY DATA IN A SMALL NUMBER OF PATIENTS INDICATE THAT DITIOCARB DOES NOT ENHANCE HIV REPLICATION IN VITRO OR IN VIVO."

WHEREAS WITH REISINGER (P.681) THESE CELLS "..... DECREASED IN PERIPHERAL BLOOD IN ALL TREATMENT GROUPS DURING THE STUDY."

SEE ALSO REISINGER TABLE II (MY PAGE 13).

WHAT IN THE WORLD COULD HAVE ACCOUNTED FOR THIS DRAMATIC DIFFERENCE IN RESULTS?

IN BOTH THE REISINGER AND HERSH STUDIES THE SUBJECT OF ALCOHOL IS MENTIONED ALMOST AS AN ASIDE.

IN THE LANG STUDY IT IS NOT MENTIONED AT ALL.

LATE FRIDAY AFTERNOON, MAY 14, THIS THOUGHT OCCURRED TO ME WHILE I WAS REVIEWING THE LANG STUDY:

- MOST FRENCHMEN DRINK WINE WITH THEIR MEALS. -

DOMINIQUE NORBROOK, PASSPORT TO FRANCE, PAGE 20:

"ALTHOUGH MEALS IN FRENCH RESTAURANTS MAY NEED A LOT OF ELABORATE PREPARATION, EVERYDAY COOKING AT HOME IS QUICK, SIMPLE AND TASTY. A MEAL MAY CONSIST OF SEVERAL COURSES, EATEN WITH SLICES OF FRESH, CRUSTY BREAD AND ACCOMPANIED BY WINE."

SUNDAY AFTERNOON, MAY 16, AS I COMPARED AND CONTRASTED THESE THREE STUDIES FOR THE UMPTENTH TIME IT DAWNED UPON ME - IT DAWNED UPON ME WITH CRYSTAL CLARITY -

IF YOU TAKE A MINUTE AND STEP BACK AND LOOK AT IT FROM A CERTAIN PERSPECTIVE YOU CAN SEE WHAT THE LANG STUDY COULD BE INTERPRETED AS REPRESENTING (ASSUMING, OF COURSE, THAT THE FRENCH DITIOCARB PATIENTS WERE DRINKING WINE WITH THEIR MEALS) -

- THE LANG STUDY REPRESENTS THE SUCCESS OF THE "DISULFIRAM/ALCOHOL PROCEDURE".

1. P.702 - "THE DISEASE DID NOT PROGRESS....."
2. P.704 - "ALL THE 9 PATIENTS IN THE DITIOCARB GROUP....."
3. P.704 - "WHEN CHANGE IN CLINICAL STATUS WAS SCORED....."
4. P.704 - LANG TABLE II
5. P.705 - ".....WITH DITIOCARB PRODUCING AN INCREASE IN CD4+ CELLS....."

WINE DRINKING WITH MEALS IS SO MUCH A PART OF THEIR CULTURE THAT I THINK THE FRENCH RESEARCHERS SIMPLY OVERLOOKED ALCOHOL AS A FACTOR AND DID NOT REALIZE THAT AN EXCESS AMOUNT OF UNMETABOLIZED ACETALDEHYDE WAS BEING GENERATED WHENEVER THE DITIOCARB PATIENTS DRANK WINE WITH THEIR MEALS.

OTHER THAN INTERVIEWING THE PATIENTS THEMSELVES, WHAT CLUES DO WE HAVE THAT THIS MIGHT HAVE BEEN THE CASE?

SIDE EFFECTS AND ADVERSE REACTIONS TO DITIOCARB

SIDE EFFECTS AND ADVERSE REACTIONS WERE NOT FACTORS IN THE REISINGER AND HERSH STUDIES. I STILL CONCLUDED, HOWEVER, THAT THERE MUST HAVE BEEN A SMALL OR MINUTE AMOUNT OF UNMETABOLIZED ACETALDEHYDE AT WORK DESTROYING THE HIV VIRUS ITSELF.

LANG STATES (P.705):

"DITIOCARB DID NOT INDUCE MORE MAJOR ADVERSE CLINICAL OR BIOLOGICAL REACTIONS THAN PLACEBO (TABLE IV), ALTHOUGH IT WAS ASSOCIATED MORE FREQUENTLY WITH MINOR SIDE-EFFECTS — UNPLEASANT TASTE, ABDOMINAL DISCOMFORT, NAUSEA, OR MALAISE."

NOW LET'S LOOK AT LANG TABLE IV (SEE MY PAGE 13).

THERE IS ONE SIDE-EFFECT THAT I WANT TO FOCUS UPON - "NAUSEA". YOU WILL NOTE THAT 19% OF THE DITIOCARB PATIENTS SUFFERED NAUSEA WHEREAS THE REISINGER STUDY NOTED (P.681) THAT:

"NAUSEA AND FATIGUE WERE INFREQUENT IN BOTH DTC GROUPS."

REMEMBER - THE REISINGER "ORAL" GROUP GOT THE SAME DOSAGE AS DID ALL OF THE LANG "ORAL" GROUP - 10mg/kg PER PATIENT.

IF YOU LOOK BACK IN THIS FILE TO THE FEBRUARY 18 LETTER THAT I WROTE TO DR. BADER YOU WILL SEE A PAGE WHERE I LISTED THREE DIFFERENT DESCRIPTIONS WHICH I TOOK FROM THREE DIFFERENT ENCYCLOPEDIAS TO DESCRIBE THE "DISULFIRAM/ALCOHOL PROCEDURE".

IN ALL THREE DESCRIPTIONS IS FOUND THE WORD - "NAUSEA".

IT IS ON THIS BASIS AND LOOKING AT THE OTHER SIDE-EFFECTS LISTED IN LANG TABLE IV THAT I CONCLUDE THAT THE FRENCH DITIOCARB PATIENTS WERE EXPERIENCING "DISULFIRAM/ALCOHOL" REACTIONS.

LET'S SAY I AM CORRECT. LET'S SAY THAT THE "DISULFIRAM/ALCOHOL PROCEDURE" IS THE KEY TO THE ATTACK ON THE HIV VIRUS. HOW THEN SHOULD THE PROCEDURE BE IMPLEMENTED?

ON PAGE 22 OF HIS BOOK 100 QUESTIONS AND ANSWERS ABOUT AIDS - A GUIDE FOR YOUNG PEOPLE, MICHAEL THOMAS FORD STATES:

"TO MAKE THINGS WORSE, THE AIDS VIRUS MAY ENTER A CELL AND BECOME DORMANT, WAITING INSIDE THE CELL TO BE USED AT A LATER TIME. IT CAN STAY THERE AS LONG AS SIX MONTHS WITHOUT THE BODY RECOGNIZING ITS PRESENCE. HIV IS ALSO ABLE TO MUTATE, OR CHANGE ITS FORM, VERY EASILY. THIS MAKES IT VERY DIFFICULT FOR THE IMMUNE SYSTEM TO DESIGN AN EFFECTIVE PLAN OF ATTACK. THE IMMUNE SYSTEM FORMS DEFENSES BASED ON THE INVADING SUBSTANCE'S STRUCTURE. WHEN THAT STRUCTURE CHANGES, WHATEVER DEFENSES HAVE BEEN DESIGNED BECOME USELESS. WHEN HIV MUTATES, THE LYMPHOCYTES THAT HAVE BEEN PROGRAMMED TO ATTACK AND KILL IT NO LONGER RECOGNIZE IT, AND THE AIDS VIRUS CAN MOVE FREELY THROUGHOUT THE BODY UNTIL NEW DEFENSES ARE CREATED."

AND ON PAGE 28 HE STATES:

"SOME PEOPLE DEVELOP AN ACUTE FLULIKE SYNDROME, SIMILAR TO MONONUCLEOSIS, WITHIN TWO TO THREE WEEKS OF BECOMING INFECTED WITH HIV. THIS IS THEN FOLLOWED BY A LONG PERIOD DURING WHICH THE PERSON IS ASYMPTOMATIC, OR HAS NO SYMPTOMS AT ALL. THIS PERIOD CAN LAST FOR MANY YEARS. THIS IS DANGEROUS BECAUSE DURING THIS TIME AN INFECTED PERSON MAY UNKNOWINGLY PASS THE VIRUS ON TO OTHER PEOPLE. DURING THIS ASYMPTOMATIC PERIOD, THE VIRUS WILL CONTINUE TO MULTIPLY. FINALLY, MAYBE AS LONG AS EIGHT TO TEN YEARS AFTER THE INITIAL INFECTION, THE PERSON WILL ONCE AGAIN DEVELOP SYMPTOMS OF HIV INFECTION."

OF COURSE, TO KNOW ALL OF THIS IS VERY, VERY DISTRESSING AND DISCONCERTING. HOWEVER, WITH THE "DISULFIRAM/ALCOHOL PROCEDURE" PERHAPS ENOUGH OF THE HIV VIRUSES THEMSELVES CAN BE DESTROYED PERIODICALLY BY ACETALDEHYDE SO THAT THE CD-4 POSITIVE LYMPHOCYTES (T-HELPER CELLS) COUNT CAN BE INCREASED THUS VOIDING THE CHANCE FOR O.I.s (OPPORTUNISTIC INFECTIONS) TO DEVELOP IN THE BODY.

I DON'T KNOW IF THE HIV VIRUS CAN EVER BE TOTALLY "FLUSHED OUT" OF THE BODY, BUT, FOR STARTERS, THIS IS THE BEST WAY TO GO ABOUT IT THAT I CAN THINK OF -

ADMINISTER THE "DISULFIRAM/ALCOHOL PROCEDURE" ONCE EVERY TWO WEEKS FOR A YEAR - 26 SESSIONS ALL TOLD.

THE ADMINISTRATION WILL REQUIRE THE EXPERT SKILL OF A PHYSICIAN WHO IS WELL EXPERIENCED IN EMPLOYING THE "ANTABUSE" TECHNIQUE OF AVOIDANCE THERAPY TO CONTROL ALCOHOLISM.

THIS IS A VERY PERILOUS PROCEDURE. AS THE ENCYCLOPEDIA AMERICANA, VOLUME 1, PAGE 518, 1991 EDITION STATES:

"BECAUSE OF THE DANGER OF DEATH FROM HEART FAILURE OR RESPIRATORY FAILURE DURING AN ALCOHOL-DISULFIRAM REACTION, THE DRUG SHOULD BE ADMINISTERED ONLY UNDER CAREFULLY CONTROLLED CONDITIONS."

ALSO IN ATTENDANCE SHOULD BE A PHYSICIAN WHO IS A SPECIALIST IN AIDS. HIS JUDGEMENT OF THE PATIENT'S CONDITION WILL BE SOUGHT AND RELIED UPON TO DETERMINE "HOW MUCH" OF THE PROCEDURE SHOULD BE EXPERIENCED AT A TIME.

IN ADDITION, IT MIGHT BE ADVISABLE TO GIVE THE PATIENT ZINC SUPPLEMENTS FOR AS THE ENCYCLOPAEDIA BRITANNICA, MACROPAEDIA, VOLUME 1, PAGE 438, 1974 EDITION STATES:

"AS ABSORBED ALCOHOL IS PASSED THROUGH THE LIVER BY THE CIRCULATING BLOOD, IT IS ACTED UPON BY ADH(ALCOHOL DEHYDROGENASE), A ZINC-CONTAINING ENZYME FOUND CHIEFLY IN THE LIVER CELLS."

WITH THE DANGER OF DEATH ALWAYS AT HAND, THE APPLICATION OF THE PROCEDURE COULD NEVER BE "ROBUST".

I WOULD RANK IT IN TERMS OF "FROM VERY, VERY CONSERVATIVE TO CONSERVATIVE".

IN MY FEBRUARY 18 LETTER TO DR. BADER I USED THIS QUOTE FROM THE ACADEMIC AMERICAN ENCYCLOPEDIA:

".....A PATIENT MUST BE WARNED BEFORE USE OF THE POSSIBLE REACTIONS FROM THE MIXTURE OF THE DRUG AND EVEN VERY SMALL AMOUNTS OF ALCOHOL. REACTIONS INCLUDE HEADACHE, THROBBING IN THE NECK, NAUSEA AND VOMITING, SWEATING, THIRST, AND BLURRED VISION. THEY VARY IN INTENSITY, GENERALLY IN PROPORTION TO THE AMOUNTS OF DRUG AND ALCOHOL INGESTED, AND LAST FROM 30 MINUTES TO SEVERAL HOURS."

"VERY, VERY CONSERVATIVE" I WOULD CALL 30 MINUTES AND "CONSERVATIVE" I WOULD CALL 4 HOURS.

I THINK THAT PATIENTS WITH "FULL BLOWN" AIDS MIGHT CHANCE 30 MINUTES OF TREATMENT, AND PATIENTS WHO HAD RECENTLY BEEN EXPOSED TO AIDS AND HAD JUST BEEN DIAGNOSED AS BEING HIV-POSITIVE MIGHT CHANCE 4 HOURS.

WHEN I WAS 18 I GOT VERY, VERY DRUNK AND WAS SEVERELY HUNG-OVER THE NEXT DAY. IN MY EARLY TWENTIES I GOT VERY, VERY DRUNK THREE OR FOUR TIMES AND WAS SEVERELY HUNG-OVER THE NEXT DAY.

FROM ABOUT 7A.M. UNTIL ABOUT 7P.M. I FELT NAUSEOUS, VOMITED AND HAD A SPLITTING HEADACHE. AT TIMES DURING THIS APPROXIMATE 12 HOUR PERIOD I WAS FEELING SO MISERABLE THAT I WISHED THAT I WERE INDEED DEAD.

APPLICATION OF AND REACTION TO THIS SORT OF ACETALDEHYDE CONCENTRATION I WOULD CATEGORIZE AS BEING "ROBUST".

AFTER A YEAR'S TREATMENT OF THIS NATURE ($\frac{1}{2}$ TO 4 HOURS) THE SPECIALIST IN AIDS MIGHT BE ABLE TO DETERMINE WHETHER THE TREATMENT COULD BE SPACED OUT TO ONCE A MONTH. THEN, IF HE SEES FURTHER IMPROVEMENT, MAYBE A $\frac{1}{2}$ YEAR OF YEARLY "BOOSTER" OF THE "DISULFIRAM/ALCOHOL PROCEDURE" MIGHT BE ALL THAT WOULD BE NEEDED TO KEEP THE HIV VIRUSES FROM INORDINATELY MULTIPLYING.

WHO KNOWS, MAYBE ALL OF THEM COULD EVENTUALLY BE CLEANSED OUT OF THE BODY.

I WANT TO CONCLUDE BY REITERATING A STATEMENT WHICH I INITIALLY MADE IN MY JANUARY 19 LETTER TO CONGRESSMAN VISCLOSKEY:

THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

IN TERMS OF METABOLISM, ACETALDEHYDE IS REALLY QUITE A UNIQUE SUBSTANCE AS FAR AS THE BODY IS CONCERNED, IS IT NOT?

THE CLOSEST "CHEMICAL COUSIN" TO ACETALDEHYDE IS THE GAS, FORMALDEHYDE. FORMALIN, A 37% SOLUTION OF GASEOUS FORMALDEHYDE, IS AN IMPORTANT INGREDIENT OF EMBALMING FLUID. WHAT MIGHT HAPPEN IF A LITTLE BIT OF FORMALIN WERE INJECTED INTO A PERSON? WOULD DEATH OR BLINDNESS BE THE RESULT?

ACETALDEHYDE IS ALSO CLOSELY RELATED TO THE GAS THAT IS USED IN COMBINATION WITH OXYGEN TO PRODUCE THE HOTTEST FLAME KNOWN TO MAN, THE FLAME THAT CUTS THROUGH STEEL - ACETYLENE ("ACETALDEHYDE IS MADE COMMERCIALY BY THE ADDITION OF WATER TO ACETYLENE IN THE PRESENCE OF SULFURIC ACID AND MERCURIC SULFATE." - THE NEW COLUMBIA ENCYCLOPEDIA, 1975 EDITION, P.11).

SYMBOLICALLY, PERHAPS ACETALDEHYDE WILL PROVE TO BE THE "INNER FLAME" BY WHICH THE HIV VIRUS CAN BE VANQUISHED FROM THE BODY.

I HOPE SO.

John S. Robert

LANG

704

TABLE II—CLINICAL OUTCOME OF HIV INFECTION IN FIRST ARM OF TRIAL

	Active	Placebo	p†
Progression to AIDS	0/38	3/39 (PCP, <i>Mycobacterium</i> , and Kaposi sarcoma)	..
Disappearance of constitutional symptoms* (IV-A patients)	8/11	0/5	<0.001
Lymphadenopathy score	-0.43‡ (SD 1.94)	+0.43‡ (SD 1.26)	<0.05
Disappearance of splenomegaly	4/7	0/8§	<0.05

*Persistent diarrhoea, weight loss, persistent fever.

†Fisher's exact test.

‡Change from baseline.

§No spleen became palpable; two additional spleen enlargements were noted.

LANG

TABLE III—CD4 CELL COUNT DURING THE FIRST ARM OF TRIAL

	Active		Placebo		p*
	Patients tested	Median (mean, SD) count	Patients tested	Median (mean, SD) count	
Baseline	42	415 (405, 111)	41	380 (380, 132)	NS
Week 8	36	479 (517, 172)	39	420 (461, 226)	NS
Week 16	36	522 (542, 215)	38	420 (447, 181)	<0.05

*Student's *t* test.

LANG

THE LANCET, SEPTEMBER 24, 1988

TABLE IV—SIDE-EFFECTS

Adverse reaction	Percentage of patients with adverse reactions	
	Active (n = 83)	Placebo (n = 79)
Unpleasant taste	41 (32)	4 (3)
Abdominal discomfort	33 (26)	8 (6)
Nausea	19 (15)	3 (2)
Sensation of malaise	10 (8)	1 (1)
Anorexia	9 (7)	1 (1)
Excitement	6 (5)	3 (2)
Somnolence	5 (4)	1 (1)
Vomiting	2 (2)	1 (1)
Rash	0 (0)	0 (0)

Number of patients in parentheses. No patient in either group had >25% drop in haemoglobin concentrations, red or white cell count, or platelet count.

REISINGER

TABLE II—T-HELPER CELL COUNTS PER μ l BLOOD IN PATIENTS WITH INITIAL COUNT BELOW 814/ μ l

Route	Time (mo)	Placebo	DTC
Oral	0	467 (193)	493 (204)
	6	442 (327)	428 (167)
	% loss	5.9 (53.5)	5.4 (37.7)
Intravenous	0	422 (283)	388 (225)
	6	250 (263)	352 (345)
	% loss	51.4 (35.6)	20.8 (30.4)

HALF-LIFE OF ACETALDEHYDE

10
3.1 min → 5

$$6 \times 3.1 = 18.6 \text{ MINUTES}$$

3.1 min → 2.5

3.1 min → 1.25

3.1 min → 0.625

⑥ 3.1 min → 0.313 98.43% METABOLIZED AT THIS POINT

3.1 min → 0.157

3.1 min → 0.079

3.1 min → 0.040

3.1 min → 0.020

3.1 min → 0.010

3.1 min → 0.005

3.1 min → 0.0025

3.1 min → 0.0013

P.S. TO CONGRESSMAN VISCLOSKY:

COULD CLINICAL TRIALS OF THE "DISULFIRAM/ALCOHOL PROCEDURE" BEGIN IMMEDIATELY AT ONE OF OUR LOCAL HOSPITALS IN LAKE OR PORTER COUNTY. I DO NOT THINK THAT ALOT OF FUNDING WOULD BE REQUIRED. ALL THAT IS NEEDED IS A HOSPITAL ROOM, THE SERVICES OF A PHYSICIAN SPECIALIZING IN THE "ANTABUSE" TREATMENT FOR ALCOHOLISM, THE SERVICES OF A PHYSICIAN SPECIALIZING IN THE TREATMENT OF AIDS AND THE EXPERTISE OF A LABORATORY TECHNICIAN.

RESPECTFULLY,

J.S.R.

COPIES TO:

CONGRESSMAN PETER J. VISCLOSKY
 PROFESSOR RUSSELL F. MANKES, DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY,
 THE ALBANY MEDICAL COLLEGE
 DONALD M. GALLANT, M.D., TULANE UNIVERSITY SCHOOL OF MEDICINE
 JEAN CARAUX, INSTITUT MERIEUX, LYON, FRANCE (LANG ET AL)
 PROFESSOR M. DIETRICH, BERNHARD NOCHT INSTITUTE FOR TROPICAL MEDICINE,
 HAMBURG, WEST GERMANY (REISINGER ET AL)
 EVAN M. HERSH, M.D., ARIZONA CANCER CENTER (HERSH ET AL)
 DR. BERNADINE HEALY, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
 WYNDHAM H. WILSON, M.D., Ph.D., SPECIAL ASSISTANT TO THE DIRECTOR,
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 JOHN P. BADER, Ph.D., CHIEF, ANTIVIRAL EVALUATIONS BRANCH,
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 RANDY SHILTS, SAN FRANCISCO CHRONICLE
 JIM GORDON, GARY POST-TRIBUNE
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 DR. MARTIN S. HIRSCH, DIRECTOR OF AIDS RESEARCH, MASSACHUSETTS GENERAL HOSPITAL
 "U.S.A. TODAY"
 "THE LANCET"
 "JAMA - THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION"
 "JOURNAL OF APPLIED TOXICOLOGY"
 OMAR BAGASRA, M.D., Ph.D., THOMAS JEFFERSON UNIVERSITY
 WILLIAM A. HASELTINE, CHIEF, LABORATORY OF BIOCHEMICAL PHARMACOLOGY,
 DANA-FARBER CANCER INSTITUTE, BOSTON; PROFESSOR, DEPARTMENT OF
 PATHOLOGY, HARVARD MEDICAL SCHOOL

MAY 3, 1993

DR. OMAR BAGASRA
JEFFERSON ALUMNI HALL
ROOM 328A
THOMAS JEFFERSON UNIVERSITY
1020 LOCUST STREET
PHILADELPHIA, PENNSYLVANIA 19107

DEAR DR. BAGASRA,
I HAVE NOT YET RECEIVED FROM YOU A REPLY TO MY LETTER OF APRIL 9.
JUST IN CASE YOU DID NOT RECEIVE IT, I AM SUBMITTING IT TO YOU AGAIN.
DR. BAGASRA, BEFORE THIS MONTH IS OVER, COULD YOU POSSIBLY ANSWER
THIS QUESTION FOR ME -

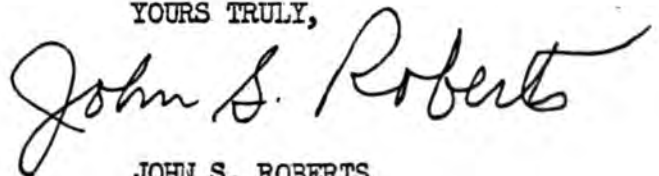
IS THE HIV VIRUS DESTROYED IN VITRO BY THE ADDITION OF ACETALDEHYDE?

BY THE FIRST OF JUNE, AT THE LATEST, I WANT TO "GO PUBLIC" WITH THIS
FILE BY MAKING ITS AVAILABILITY KNOWN THROUGH MEDIA ADVERTISEMENTS.

IN LIGHT OF PROFESSOR MANKES' APRIL 16 LETTER, ATTACHED, I HAVE DONE
SOME MORE RESEARCH AND WILL HAVE A FEW MORE PAGES TO ADD TO THIS FILE.

DR. BAGASRA, I REALLY WOULD APPRECIATE HEARING FROM YOU, AND I WANT
TO THANK YOU FOR GIVING THIS MATTER YOUR TIME AND CONSIDERATION.

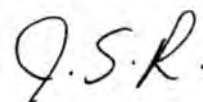
YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO: CONGRESSMAN PETER J. VISCLOSKY (WASHINGTON AND GARY OFFICES)
PROFESSOR RUSSEL F. MANKES, THE ALBANY MEDICAL COLLEGE

P.S. ON JUNE 1 I CALLED DR. BAGASRA AND WAS TOLD THAT HE HAD JUST LEFT
THE COUNTRY TO ATTEND A TWO WEEK CONFERENCE IN PARIS. WHEN I OBTAIN
AN ANSWER FROM HIM I WILL BE MORE THAN HAPPY TO INCLUDE IT IN THIS FILE.





The Albany Medical College

Albany, New York 12208

DEPARTMENT OF PHARMACOLOGY & TOXICOLOGY
THE NEIL HELLMAN MEDICAL RESEARCH BUILDING, A 136
(518) 445-5303
FAX (518) 445-5799

Mr. John S. Roberts
POB H
Hobart, IN 46342

16 April, 1993

Dear Mr. Roberts,

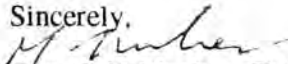
I received a package of correspondence from and to you relative to acetaldehyde and HIV today. I am really not sure why it was sent to me as I am not an AIDS researcher, my area of expertise lies in Toxicology, specifically alcohol. From your correspondence it appears that you have developed the hypothesis that acetaldehyde may be a useful adjunct to therapy for HIV infected individuals. It appears that this hypothesis has generally been dismissed by the NIH, specifically by Dr. John Bader.

From my perspective I would like to add a degree of caution to your continued efforts. Acetaldehyde, a highly toxic intermediate of alcohol metabolism, could in fact cause damage to viruses. However, the danger lies in the specificity of the toxicity. The therapeutic drugs which are being developed (such as AZT, DDC, etc.) rely on the principle of selective (or specific) toxicity, they cause death or damage to the infectious agent or diseased cell at doses which do not significantly affect normal function. A chemical that kills the patient while it kills the virus or cancer is not a useful drug. In the case of acetaldehyde, as you so rightly pointed out, it is toxic (and severely so) to a wide variety of human organ systems at exceedingly low dose levels. We believe it may also target the T-cells of the immune system and produce a lessening of their function, something which would be very dangerous in an HIV infected human. I do not dismiss your hypothesis, only add a note of caution to your quest.

It is important to remember that the more we learn about the basic biology of a disease process, the more likely we are to find a cure. I would urge you to continue your efforts, particularly with members of congress, to increase funding for medical research generally since, as amply illustrated by your letters, we cannot determine from where the next advance will come (perhaps the cure for AIDS will be found by research on the genetics of the fruit fly!!).

If I may be of any assistance to you please do not hesitate to write.

Sincerely,


Russell F. Mankes, Ph.D.
Associate Professor



An Institution of the Albany Medical Center

APRIL 9, 1993

DR. OMAR BAGASRA
JEFFERSON ALUMNI HALL
ROOM 328A
THOMAS JEFFERSON UNIVERSITY
1020 LOCUST STREET
PHILADELPHIA, PENNSYLVANIA 19107

DEAR DR. BAGASRA,

I RECENTLY READ ABOUT YOUR RESEARCH IN THE MARCH 22, 1993 ISSUE OF "USA TODAY".

WOULD YOU PLEASE GIVE SOME CONSIDERATION TO THE ATTACHED FILE.

WOULD YOU THINK OF DOING YOUR EXPERIMENT AGAIN, BUT THIS TIME ADD ONE ADDITIONAL INGREDIENT TO THE TEST TUBE - A DROP OR TWO OF ACETALDEHYDE.

SINCE ACETALDEHYDE IS A HIGHLY TOXIC POISON, IS THERE THE REMOTEST POSSIBILITY IN THE WORLD THAT IT COULD DESTROY THE HIV VIRUS?

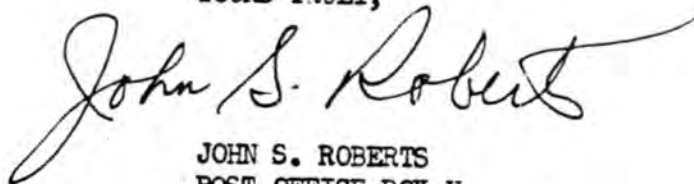
I THINK THAT THE EFFECTS OF THE "DISULFIRAM/ALCOHOL PROCEDURE" COULD LAST AS LONG AS 12 HOURS.

IN NORMAL CONDITIONS (WITHOUT DISULFIRAM IN THE BODY) I BELIEVE THAT ACETALDEHYDE IS METABOLIZED IN JUST A FEW MINUTES BY THE LIVER.

WHAT EFFECT WOULD "UNMETABOLIZED" ACETALDEHYDE HAVE UPON THE HIV VIRUS?

IN OTHER WORDS, AFTER 12 HOURS WOULD THE HIV VIRUS STILL BE ALIVE IN THE TEST TUBE AFTER A DROP OR TWO OF ACETALDEHYDE HAD BEEN ADDED TO IT?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO: CONGRESSMAN PETER J. VISCLOSKEY, BERNADINE HEALY, M.D.;
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DR. LUC MONTAGNIER, RANDY SHILTS, JIM GORDON, PETER S. ARNO, Ph.D.;
DONALD M. GALLANT, M.D.; EVAN M. HERSH, M.D.; DR. MARTIN S. HIRSCH AND
YUNG-KANG CHOW, "USA TODAY"

British Academy of Film and Television Awards, seen as early pointers to the Oscars, presented Sunday. Robert Downey Jr. won the best actor award for his role in *Chaplin*, and the Alexander Korda Award for Best British Film went to *The Crying Game*. All three winners are nominated for Oscars to be awarded March 29.

MS DRUG APPROVED: The first drug designed to combat the crippling effects of multiple sclerosis was endorsed Friday by an advisory committee of the Food and Drug Administration. The panel heard evidence that MS patients treated with beta interferon suffer fewer and less severe attacks of the crippling disease that afflicts about 350,000 Americans.

AIDS AND ALCOHOL: A few drinks of alcohol may raise a healthy person's chances of becoming infected with the AIDS virus or speed up the disease in those already infected, a new study says. Researchers at Thomas Jefferson University in Philadelphia put the AIDS virus in a test tube along with white blood cells of 60 healthy people who had had several drinks over a weekend. They found that HIV, the virus that causes AIDS, quickly replicated. "Even casual consumption of alcohol stimulates replication of the AIDS virus in cell cultures," said Omar Bagasra, author of the study in the *Journal of Infectious Diseases*.

MOO HOO HOO: Former University of Maine student Andrea Pizzo, 23, is suing the school for not protecting her from a cow with a "dangerous disposition." Pizzo says officials in the school's livestock management department should have known that the Jersey heifer that attacked her in the spring of 1991 had a personality problem. The lawsuit seeks unspecified damages for knee and wrist injuries Pizzo claims she suffered when the 400-pound bovine head-butted her into the wall of its pen. Charles Wallace, Pizzo's instructor, says he has worked around cattle for more than a decade and was surprised by the lawsuit. "Cows are usually pretty docile. But that is the chance you take working around large animals."

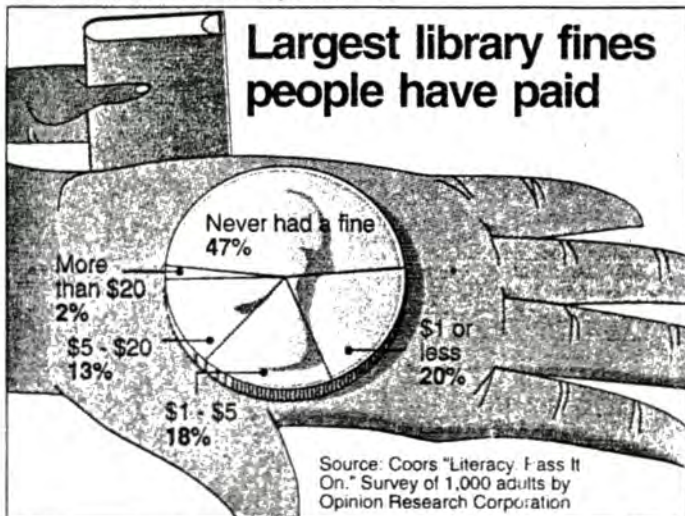
By Arlene Vigoda

Inside LIFE

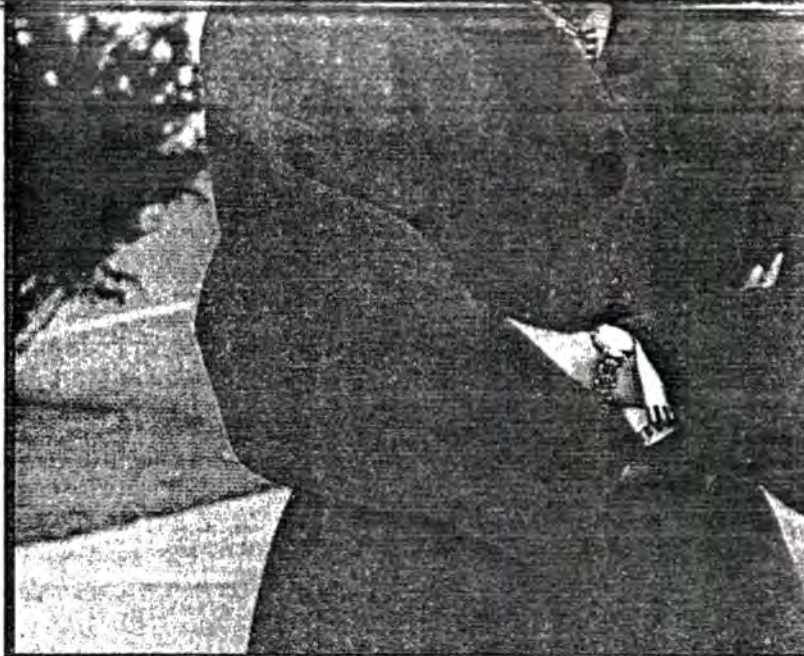
Crossword	5D	Show	4D
Larry King's People	2D	Television	3D
People	2D	TV Listings	6D

USA SNAPSHOTS®

A look at statistics that shape our lives



By Elys A. McLean, US/ TODAY



NO PUSHOVER: NBC correspondent Andrea Mitchell doesn't mind ruffling. 'My value to NBC is my ability to reach judgments about what decisions Clinton

COVER STORY

Clinton cadre has Andrea to answer to

For NBC journalist Mitchell, 'The whole point is to provoke a response.'

By Peter Johnson
USA TODAY

WASHINGTON — NBC's Andrea Mitchell is tenacious. Like a pit bull. With a bone.

That's why during a recent trip by President Clinton to Franklin Roosevelt's home in Hyde Park, N.Y., Mitchell — after a sound bite — had Air National Guardsmen chasing her across the tarmac wielding their M-16s,

handcuffs ready, as fellow White House reporters, sequestered in a bus, shouted "Go Andrea!"

Secret Service agents, who know Mitchell, got the soldiers to back off. The kicker: Mitchell got the one sound bite that colleagues needed: Clinton explaining an earlier remark about the possibility of a new tax.

"It was wonderful," says ABC's Brit Hume, savoring the image of Mitchell — assigned to the press pool that day — getting sprayed with jet wash from Air Force One and nearly getting arrested. "You don't want to be the one denying her entry unless you're heavily armed."

Is she the new Sam Donaldson of la Casa Blanca?

"I WOULDN'T HANG THAT MONIKER ON HER!" booms The Voice, ABC's Donaldson, who competed with

Please see COVER STORY next page ►

By H

Sti

Maybe have been developm of late (in maybe it's pah involu pan's Akin

MOVIE SUSAN

the great time, for sewer-soa

But in *Ninja Tur nardo*, D gelo and F into creat erate, like learned t their beds half shell "cowabun barely eve

Oh, they give "we soaked fir crack w s moment hothead takes a cl about the Like total

The sto *Samurai* grown up, quality as

POINTE-AUX-TREMBLES [pwă't o trĕ'bl], a town on Montreal Island, Quebec, Canada, situated on the St. Lawrence River about 10 mi. north of downtown Montreal and adjoining the industrial town of Montreal East. It is on Provincial Highway 2, and the Canadian Pacific Railway serves the town. It was founded as a parish in 1674 and as a town in 1912. Pop. 1951, 8,241.

D.F.P.

POINTE-CLAIRE [pwă't kle'r], a town on Montreal Island, Quebec, Canada, situated on the north shore of Lake Saint Louis, about 15 mi. southwest of downtown Montreal. It is on Provincial Highway 2 and is served by the Canadian National and Canadian Pacific railways. Founded as a parish in 1717, the community was incorporated as a village in 1854 and as a town in 1911. It is a residential and resort suburb of Montreal. Pop. 1951, 8,753.

D.F.P.

POINTER. See DOG.

POISON ASH. See POISON IVY.

POISON GAS. See WARFARE (Chemical Warfare).

POISONING, TREATMENT OF. See FIRST AID.

POISON IVY, the name commonly given to a group of poisonous plants, considered by most botanists to be sumacs, *Rhus*. Other botanists have placed the group in a separate genus, *Toxicodendron*.

The common poison ivy, *R. radicans*, most widely distributed of the species, grows from Nova Scotia to British Columbia, south to Mexico, Florida, and Bermuda. Nevada is the only state from which it has not been reported. In many parts of its range, it is a low straggling shrub, but it frequently develops into a stout, woody vine climbing high trees. Similar is the southern poison oak, *R. toxicodendron*, a low shrub found in dry woodlands from New Jersey to Georgia and Texas. The western poison oak, *R. diversiloba*, is found from Washington south throughout California to Mexico. It is an erect, sometimes climbing shrub 4 to 8 ft. high. In California, poison oak is more widely diffused than any other shrub. These three plants have leaves divided into three ovate leaflets, the margins variously toothed and lobed, but sometimes having little or no lobation. The flowers are inconspicuous greenish-white, appearing in clusters, and the small greyish-white waxy fruits, resembling those of the bayberry, *Myrica pensylvanica*, contain a small, bony stone. These three species, all known popularly as poison ivy, poison oak, and poison sumac, may eventually come to be considered as one variable species. The true poison sumac, *R. vernix*, also called poison elder, poison ash, and poison dogwood, is a large shrub growing sometimes as high as 25 ft. It has ash-like leaves of 7 to 13 entire leaflets, greenish flowers, and whitish fruit in long pendent clusters. It grows in swamps from Quebec and Minnesota, south to Florida and Texas. Poisoning is caused by a nonvolatile oil present in the sap.

Aside from the hazardous method of digging, plants may be eradicated by ammonium sulfamate, or 2, 4-D, (2, 4-dichlorophenoxyacetic acid) applied to the foliage according to directions. Also, 10 lb. of dry borax per square rod applied to the soil will kill poison ivy and numerous other plants. See also IVY POISONING.

G.Gr.

POISON OAK. See POISON IVY.

POISONS, chemical agents which, when present in sufficient amounts, may injure or kill a living organism. They may be swallowed, inhaled, or absorbed or injected through the skin.

Classification. One method by which poisons may be classified is according to their chemical and physical types, e.g., acids, alkaloids, industrial solvents, inorganic chemicals, organic chemicals, poisonous gases, and poisonous foods. Another classification of poisons would be according to their physiological action. Some chemicals are local poisons: these are (1) the corrosive poisons, which destroy tissue by direct contact, e.g., the mineral acids, caustic alkalies, and phenol; and (2) the irritant compounds of arsenic, lead, mercury, zinc, and so on. Other chemicals are systemic poisons; these are absorbed into the blood stream, whence they are carried to, and act upon, the heart, kidneys, nervous system, and other vital organs. This type includes cyanide, hypnotics, opium derivatives, and strychnine.

Common Types of Poison. Some poisonous chemicals frequently found about the home, and therefore suspect if illness occurs, include the following:

Cleaners: ammonia, lye (sodium hydroxide), phenol (carbolic acid), phosphates, washing soda (sodium carbonate).

Insecticides: compounds containing arsenic, thallium, fluorine, lead, copper, and phosphorus: D.D.T., pyrethrum, orthodichlorobenzene.

Laxatives: calomel, phenolphthalein.

Liniments and Ointments: camphor, chloroform, oil of wintergreen.

Moth Repellents: camphor, naphthalene, paradichlorobenzene, arsenicals.

Soothing Syrups and Sedatives: opium derivatives, chloroform, bromides, acetanilide, barbiturates (Veronal).

Reports made by the city of New York give an interesting appraisal of the frequency of certain types of poisonings. In 1941 there were 500 suicidal and 676 accidental poisonings. Of the 500 suicides, the poisons employed were as follows: illuminating gas (carbon monoxide), 337; barbiturates, 33; phenol, 20; cyanide, 15; sodium fluoride, 10; and arsenicals, 7. Of the 676 accidental poisonings, the poisons used were as follows: alcohol, 424; anesthetics, 147; barbiturates, 17; narcotics, 16; wood alcohol, 7; arsenic or other heavy metals, 8.

Industrial solvents and hazardous chemicals deserve special mention. Besides the acute poisoning which may result from swallowing them, there is a hazard from continued exposure to vapors or liquid sprays. Such exposure results in chronic poisoning if the chemical accumulates in the body faster than it can be eliminated. Lead poisoning is an example. The following expression first observed by Fritz Haber in connection with war gas effects can be generally applied:

$$\text{Extent of poisoning} = \text{exposure time} \times \text{concentration of the poison}$$

Thus, approximately the same body damage is caused by exposure to 50 parts per million (p.p.m.) for two hours as by 100 p.p.m. for one hour. Hydrogen cyanide gas is an exception to this rule.

Other poisons not previously mentioned include: acetaldehyde; acetanilide; acetone; acetylene and acetylene compounds; acids (glacial acetic, boric, hydrochloric, hydrofluoric, nitric, oxalic, phosphoric, sulphuric); alkaloids (aconite, apomorphine, atropine, caffeine, cocaine, codeine, digitalis, ergot, heroin, morphine, nicotine, strychnine); amyl acetate; aniline; antimony compounds; arnica; arsine; barium compounds; belladonna; benzene; benzine; bismuth compounds; bromine; cadmium compounds; calcium oxide; cantharides; carbon dioxide; carbon disulphide; carbon tetrachloride; chloral hydrate; chlorine; chloropicrin; croton oil; curare; di-



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

Building 31, Room 3A44
(301) 496-6404

March 24, 1993

Mr. John S. Roberts
P.O. Box H
Hobart, IN 46342

Dear Mr. Roberts:

Your letter to Dr. Bernadine Healy was referred to my office for reply. We, like you, are dedicated to finding a cure for HIV. However, acetaldehyde is a normal metabolite of the human body and will have no effect on HIV infection.

Dr. John Bader, Chief, Antiviral Evaluation Branch, has also reviewed your idea and has sent you a letter. I appreciate your interest.

Sincerely,

Wyndham H. Wilson, M.D., Ph.D.
Special Assistant to the Director
Division of Cancer Treatment

FEBRUARY 26, 1993

DR. BERNADINE HEALY
DIRECTOR
NATIONAL INSTITUTES OF HEALTH
BUILDING 1, ROOM 126
9000 ROCKVILLE PIKE
BETHESDA, MARYLAND 20892-0001

DEAR DR. HEALY,

ATTACHED ARE THE COPIES OF MY FEBRUARY 18 LETTER TO DR. BADER AND CONGRESSMAN VISCLOSKY'S LETTER OF FEBRUARY 11 TO ME (IN RESPONSE TO A PREVIOUS LETTER OF MINE) WHICH I DID NOT BECOME AWARE OF UNTIL AFTER I HAD MAILED THE FEBRUARY 18 LETTER.

IT IS TOO EARLY FOR ME TO HAVE RECEIVED A REPLY FROM DR. BADER; HOWEVER, I JUST THOUGHT I WOULD GO AHEAD AND WRITE TO YOU SINCE THIS LETTER WILL REFLECT MY MOST CURRENT IDEAS.

FIRST OF ALL - ABOUT THE POSSIBLE BENEFICIAL EFFECTS OF THE METABOLITE OF DISULFIRAM (ANTABUSE) KNOWN AS "DITIOCARB" OR "DTC" - DOES EVERYBODY KNOW ABOUT IT? THE "JAMA" ARTICLE WAS PUBLISHED MARCH 27, 1991, AND THE ONLY ENTRY IN THE CUMULATED INDEX MEDICUS HAVING TO DO WITH DISULFIRAM AND AIDS HAS TO DO WITH DR. GALLANT'S ARTICLE.

IN HIS ARTICLE, "ANTABUSE (DISULFIRAM) AND AIDS", DR. GALLANT STATES,

'A SIGNIFICANT PERCENTAGE OF ORAL DISULFIRAM IS RAPIDLY REDUCED IN THE BODY TO DTC.'

WOULD ALL AIDS PATIENTS BE IMMEDIATELY BENEFITTING THEMSELVES BY SIMPLY HAVING THEIR DOCTORS PRESCRIBE ANTABUSE TABLETS FOR THEM?; HOWEVER, KNOWING FULL WELL THAT THEY CANNOT DARE TO TAKE A SIP OF ALCOHOL WHILE DISULFIRAM IS IN THEIR BODY.

LET US SUPPOSE THAT A PILOT PROGRAM IS SET UP TO TEST THE EFFECTIVENESS OF "THE DISULFIRAM/ALCOHOL PROCEDURE", AND IT PROVES TO BE A FAILURE. THIS WOULD NOT NECESSARILY ABNEGATE THE POTENTIAL USEFULNESS OF ACETALDEHYDE.

ACETALDEHYDE COULD STILL BE LOOKED UPON AS PART OF THE ARSENAL IN THE QUEST TO DISCOVER THE "MAGIC BULLET" TO DESTROY THE HIV VIRUS.

ON PAGE 17 OF AGAINST THE ODDS - THE STORY OF AIDS DRUG DEVELOPMENT, POLITICS & PROFITS, DR. PETER S. ARNO STATES,

"BETWEEN 1987 AND 1991 THE NATIONAL CANCER INSTITUTE TESTED 40,000 CHEMICAL COMPOUNDS AT FACILITIES IN FREDERICK, MARYLAND, AND BIRMINGHAM, ALABAMA, TO SEE IF ANY COULD DISABLE THE AIDS VIRUS."

IN MACBETH, ACT IV, SCENE 1, LINES 10-21, SHAKESPEARE SAYS,

"ALL. DOUBLE, DOUBLE TOIL AND TROUBLE,
FIRE BURN AND CALDRON BUBBLE.

2. WITCH. FILLET OF A FENNY SNAKE,
IN THE CALDRON BOIL AND BAKE.
EYE OF NEWT AND TOE OF FROG,
WOOL OF BAT AND TONGUE OF DOG,
ADDER'S FORK AND BLINDWORM'S STING,
LIZARD'S LEG AND HOWLET'S WING,
FOR A CHARM OF POWERFUL TROUBLE,
LIKE A HELL BROTH BOIL AND BUBBLE.

ALL. DOUBLE, DOUBLE TOIL AND TROUBLE,
FIRE BURN AND CALDRON BUBBLE."

IF "THE DISULFIRAM/ALCOHOL PROCEDURE" DOES NOT WORK, I THINK EACH ONE OF THE 40,000 TESTS SHOULD BE REPEATED WITH ACETALDEHYDE BEING MIXED IN WITH EACH TEST. WHO KNOWS, IT MIGHT PROVE TO BE SOME SORT OF CATALYST BY WHICH THE DESTROYER OF THE HIV VIRUS IS DISCOVERED.

"DOUBLE, DOUBLE TOIL AND TROUBLE"

I HAVE HIGHLIGHTED AN INDISPUTABLE FACT OF NATURE -

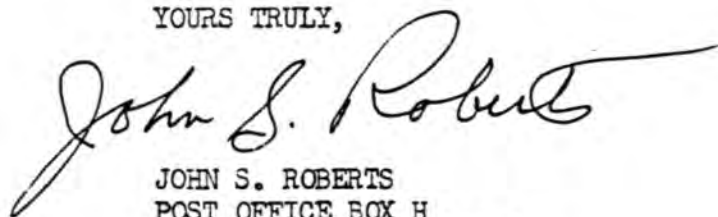
THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

IF A MEDICINE WERE INJECTED INTO A BODY WHILE THAT BODY WAS BEING POISONED WITH ACETALDEHYDE, THE RESULTS MIGHT BE FAR DIFFERENT THAN THEY WOULD NORMALLY BE, MIGHT THEY NOT?

WELL, THIS IS ABOUT ALL I HAVE TO SAY FOR NOW, DR. HEALY. AS A FIRST STEP, I HOPE THAT SOME OF THE CLINICAL TRIALS THAT ARE PRESENTLY BEING CONDUCTED IN CHICAGO WILL START TO EMPLOY "THE DISULFIRAM/ALCOHOL PROCEDURE".

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO CONGRESSMAN PETER J. VISCLOSKEY, JOHN P. BADER, Ph.D, DR. LUC MONTAGNIER,
RANDY SHILTS, JIM GORDON, PETER S. ARNO, Ph.D., AND DR. DONALD M. GALLANT
AND DR. EVAN M. HERSH, PRIMARY AUTHOR OF THE "JAMA" ARTICLE

FEBRUARY 18, 1993

JOHN P. BADER, Ph.D.
CHIEF, ANTIVIRAL EVALUATIONS BRANCH
DEVELOPMENTAL THERAPEUTICS PROGRAM
DIVISION OF CANCER TREATMENT
NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTES OF HEALTH
ROCKVILLE PIKE
BETHESDA, MD 20892

DEAR DR. BADER,

ATTACHED ARE A COPY OF YOUR LETTER TO ME DATED JANUARY 26, 1993
AND A COPY OF PAGE 39 TAKEN FROM DRUGS, A TIME INC. PUBLICATION, COPYRIGHT
DATE 1967.

A BASIC QUESTION NEEDS TO BE ANSWERED - DOES ACETALDEHYDE DESTROY
THE AIDS VIRUS? FOR INSTANCE, IF A DROP OF ACETALDEHYDE WERE PLACED
IN A TEST TUBE CONTAINING THE BLOOD OF A VICTIM WHO HAD THE HIV VIRUS,
WOULD THAT VIRUS BE DESTROYED?

IF THE ANSWER TO THIS QUESTION IS "NO", YOU MAY AS WELL SKIP THE REST
OF THIS LETTER BECAUSE I'LL ONLY BE WASTING YOUR TIME.

HOWEVER, MY HUNCH IS THAT ACETALDEHYDE WILL DESTROY THE VIRUS,
AND I HAVE THE FOLLOWING OBSERVATIONS TO MAKE -

ON FEBRUARY 11 I BECAME AWARE OF PAGE 39 FROM DRUGS. AFTER READING
THIS PAGE I KNEW THAT I HAD FOUND THE POSSIBILITY OF A CURE FOR AIDS.
OF COURSE, I WAS EXTREMELY CURIOUS TO SEE IF ANYONE ELSE HAD EVER
THOUGHT OF IT BEFORE.

ON SATURDAY, FEBRUARY 13 I WENT TO THE CAMPUS LIBRARY OF INDIANA
UNIVERSITY NORTHWEST AND LOOKED AT THE ENTRIES HAVING TO DO WITH
"DISULFIRAM" IN THE CUMULATED INDEX MEDICUS. I STARTED WITH THE YEAR 1983
BECAUSE THAT IS WHEN THE FIRST MENTION OF "ACQUIRED IMMUNODEFICIENCY SYNDROME"
IS MADE IN THIS INDEX.

IN THE APRIL, 1992 ISSUE OF THIS INDEX AN ARTICLE WAS CITED -

ANTABUSE (DISULFIRAM) AND AIDS

AND IT APPEARED IN THE OCTOBER, 1991 ISSUE OF THE JOURNAL, "ALCOHOLISM,
CLINICAL AND EXPERIMENTAL RESEARCH".

ON MONDAY, FEBRUARY 15 THE SYSTEM SERVICES DIVISION OF THIS LIBRARY
OBTAINED FOR ME A FAX COPY OF THE ARTICLE FROM THE INDIANA UNIVERSITY
SCHOOL OF MEDICINE LIBRARY IN INDIANAPOLIS.

THE ARTICLE CITES FOUR ADDITIONAL REFERENCES. ONE REFERENCE WAS
FROM THE "JOURNAL OF EXPERIMENTAL MEDICINE", TWO WERE FROM "LANCET",
AND ONE WAS FROM "JAMA" (JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION).

ALL FOUR OF THESE REFERENCES WERE READILY AVAILABLE AT THE NORTHWEST
LIBRARY AND AT THE MEDICAL LIBRARY IN THE BUILDING JUST NEXT DOOR.

FROM WHAT I COULD UNDERSTAND FROM THESE ARTICLES, THERE SEEMS TO BE A DAWNING REALIZATION THAT SOMETHING VERY BENEFICIAL MIGHT BE AT HAND WITH THE UTILIZATION OF A METABOLITE OF DISULFIRAM. THIS METABOLITE HAS SEVERAL NAMES WITH THE SIMPLEST ONE BEING DITIOCARE OR DTC.

TO QUOTE FROM THE ARTICLE ITSELF - (IN A FEW PLACES I HAVE SUPPLIED THE PARENTHESIS AND THE UNDERLINES) -

"WHILE FOUR PATIENTS IN THE PLACEBO GROUP DEVELOPED CDC-DEFINED AIDS (CENTER FOR DISEASE CONTROL), NONE DID SO IN THE DTC GROUP. IN ADDITION, THE DTC GROUP SHOWED A DECREASE IN SPLENOMEGALY AND LYMPHADENOPATHY AND AN INCREASE IN CD4+ CELL COUNT AND SKIN TEST REACTIVITY."

"IT IS INTERESTING THAT MANY OF US IN THE FIELD OF ALCOHOLISM HAVE FOR DECADES BEEN ADMINISTERING A COMPOUND, DISULFIRAM, WHOSE METABOLITE DTC APPEARS TO BE BOTH SAFE AND EFFECTIVE FOR THOSE PATIENTS WITH SYMPTOMATIC HIV AND AIDS."

AND TO QUOTE FROM ONE OF THIS ARTICLE'S REFERENCES, "JAMA, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION", 265:1538-1544, MARCH 27, 1991, P.1543:

"IN SUMMARY, DITIOCARE IN THIS STUDY WAS BOTH SAFE AND EFFECTIVE THERAPY FOR THE PREVENTION OF DISEASE PROGRESSION TO NEW OIs (OPPORTUNISTIC INFECTIONS) IN PATIENTS WITH HIV INFECTION."

"DITIOCARE (IMUTHIOL) HAS BEEN GRANTED ORPHAN DRUG STATUS BY THE FOOD AND DRUG ADMINISTRATION FOR THE TREATMENT OF PATIENTS WITH AIDS."

IN NONE OF THE FIVE ARTICLES IS THERE ANY MENTION OF THE WORD, "ACETALDEHYDE".

DR. BADER, IN YOUR LETTER TO ME YOU STATED:

"THE MOLECULES YOU SUGGEST ARE NORMAL METABOLITES FORMED DURING NORMAL BODY FUNCTIONING, AND WOULD HAVE NO EFFECT ON HIV OR AIDS."

HOWEVER, CONSIDERING WHAT I BECAME AWARE OF ON FEBRUARY 11, WOULDN'T A NEW LIGHT BE THROWN UPON THE SITUATION, WOULDN'T IT REALLY BE "A TOTALLY NEW BALL GAME"?

THIS, OF COURSE, IS WHAT I BECAME AWARE OF ON FEBRUARY 11 - IF A PERSON HAS IN THEIR LIVER THE SUBSTANCE CALLED DISULFIRAM AND TAKES THE SLIGHTEST DRINK OF ALCOHOL, ACETALDEHYDE WILL FLOOD THROUGHOUT THAT PERSON'S BODY AS A DEADLY POISON.

MENTIONED THROUGHOUT THE CUMULATED INDEX MEDICUS ARE VARIOUS ARTICLES DEALING WITH THE ADVERSE EFFECTS OF ADMINISTERING DISULFIRAM; SOME OF THE TOPICS ARE - FULMINATING HEPATITIS, ARTHRITIS, LIVER DAMAGE, PSYCHOSES, TOXIC COMA, BRAIN DAMAGE, AND EVEN DEATH.

NO CELL IN THE BODY WOULD BE SAFE FROM FEELING THE EFFECTS OF THIS POISON.

OF COURSE, IF IT DESTROYS THE AIDS VIRUS AT THE SAME TIME, WHAT BETTER WAY COULD EVER BE FOUND TO CLEANSE THE BODY OF THIS DREADFUL ILLNESS?

CAREFUL, MEDICAL SUPERVISION OF THE PROCEDURE IS THE KEY; THE PROCEDURE COULD SIMPLY BE CALLED "THE DISULFIRAM/ALCOHOL PROCEDURE" FOR DESTROYING THE HIV VIRUS.

THE METHOD AND THE EFFECTS OF THE PROCEDURE WOULD BE AS FOLLOWS:

"PHYSIOLOGICAL THERAPIES. CHEMICAL FENCES. ONE OF THE POPULAR MODERN DRUG TREATMENTS OF ALCOHOLISM, INITIATED IN 1948 BY ERIC JACOBSEN OF DENMARK, USES DISULFIRAM (TETRAETHYLTHIURAM DISULFIDE). THE USUAL TECHNIQUE IS TO ADMINISTER HALF A GRAM IN TABLET FORM DAILY FOR A FEW DAYS; THEN, UNDER CAREFULLY CONTROLLED CONDITIONS AND WITH MEDICAL SUPERVISION, THE PATIENT IS GIVEN A SMALL TEST DRINK OF AN ALCOHOLIC BEVERAGE. THE PRESENCE OF DISULFIRAM IN THE DRINKER'S BODY CAUSES A REACTION OF HOT FLUSHING, NAUSEA, VOMITING, A SUDDEN SHARP DROP OF BLOOD PRESSURE, POUNDING OF THE HEART, AND EVEN A FEELING OF IMPENDING DEATH. THESE SYMPTOMS RESULT FROM AN ACCUMULATION OF THE HIGHLY TOXIC FIRST PRODUCT OF ALCOHOL METABOLISM - ACETALDEHYDE. NORMALLY, AS ALCOHOL IS CONVERTED TO ACETALDEHYDE, THE LATTER IS RAPIDLY CONVERTED, IN TURN, TO OTHER HARMLESS METABOLITES, BUT IN THE PRESENCE OF DISULFIRAM - ITSELF HARMLESS - THE METABOLISM OF ACETALDEHYDE IS BLOCKED, WITH THE RESULTING TOXIC SYMPTOMS."

ENCYCLOPAEDIA BRITANNICA, MACROPAEDIA, VOLUME 1, PAGE 447, 1974 EDITION

".....A PATIENT MUST BE WARNED BEFORE USE OF THE POSSIBLE REACTIONS FROM THE MIXTURE OF THE DRUG AND EVEN VERY SMALL AMOUNTS OF ALCOHOL. REACTIONS INCLUDE HEADACHE, THROBBING IN THE NECK; NAUSEA AND VOMITING, SWEATING, THIRST, AND BLURRED VISION. THEY VARY IN INTENSITY, GENERALLY IN PROPORTION TO THE AMOUNTS OF DRUG AND ALCOHOL INGESTED, AND LAST FROM 30 MINUTES TO SEVERAL HOURS."

ACADEMIC AMERICAN ENCYCLOPEDIA, VOLUME 6, PAGE 202, 1985 EDITION

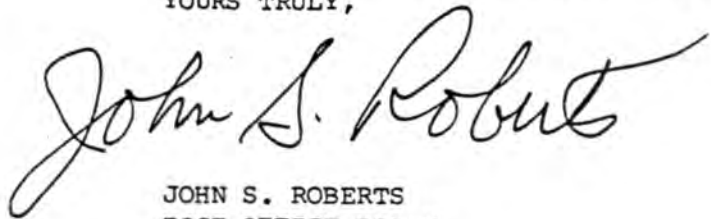
"ADMINISTRATION OF ANTABUSE, OR DISULFIRAM, AND TEMPOSIL, CITRATED CALCIUM CARBIMIDE, CAN HELP THE PATIENT CONTINUE IN THE PATH OF SOBRIETY. THESE DRUGS INCREASE THE CONCENTRATION OF ACETALDEHYDE IN THE BODY WHENEVER ALCOHOL IS CONSUMED, FOR THEY RETARD THE OXIDATION OF THAT SUBSTANCE TO ACETIC ACID. THE ACCUMULATION OF ACETALDEHYDE IN THE BODY PRODUCES A SERIES OF CHANGES WHICH RESEMBLE THOSE OF ACUTE HANGOVER. IN FACT, THE PATIENT FEELS SO UNCOMFORTABLE THAT FEAR OF THE RESULTS CAN STRENGTHEN ANY FALTERING DETERMINATION TO ABSTAIN FROM ALCOHOL. AFTER DISULFIRAM HAS BEEN TAKEN, EVEN THE SMALLEST AMOUNT OF AN ALCOHOLIC BEVERAGE CAN INITIATE ALMOST UNBEARABLE EFFECTS. THE DRINKER FIRST HAS A FEELING OF WARMTH IN HIS FACE; THE FACE, NECK AND CHEST ARE SUFFUSED WITH SCARLET AND THE EYES BECOME BLOODSHOT. AT THE SAME TIME HE IS AWARE OF PALPITATION OF THE HEART AND FEELS CHOKED FOR WANT OF AIR. NAUSEA AND VOMITING FOLLOW, AND THE INTENSE FLUSHING IS REPLACED BY PALLOR AS BLOOD PRESSURE FALLS."

ENCYCLOPAEDIA BRITANNICA, VOLUME 1, PAGE 550-551, 1971 EDITION

DR. BADER, IF HIV IS INDEED DESTROYED IN THE LABORATORY BY ACETALDEHYDE -

FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO -
RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.
COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR
NOT THE "DISULFIRAM/ALCOHOL PROCEDURE" IS EFFECTIVE IN CURING AIDS VICTIMS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO CONGRESSMAN PETER J. VISCLOSKEY, DR. LUC MONTAGNIER, RANDY SHILTS
AND JIM GORDON

P.S. - FEBRUARY 19

LAST NIGHT, AFTER I HAD TYPED THIS LETTER, I WENT AGAIN TO THE LIBRARY
OF INDIANA UNIVERSITY NORTHWEST TO PICK UP THE FAX COPY OF ANOTHER ARTICLE
WHICH I HAD REQUESTED TO SEE.

IT COMES FROM THE "JOURNAL OF APPLIED TOXICOLOGY", OCTOBER, 1991, PAGES
373-6 AND THE TITLE OF THE ARTICLE IS 'ACETALDEHYDE'.

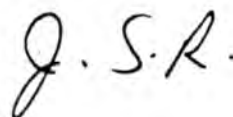
I DON'T KNOW WHETHER THIS PART OF THE ARTICLE HAS ANY PARTICULAR RELEVANCE
BECAUSE IT CONCERNS EXPERIMENTS ON RATS. HOWEVER, IT SAYS,

"IN CONTRAST, THE ACETALDEHYDE LEVELS IN THE LIVER FOLLOWING ETHANOL
ADMINISTRATION IS CONSIDERABLY HIGHER THAN THE OTHER TISSUES.

THE AUTHORS CONCLUDE THAT EITHER THE LIVER DOES NOT TAKE UP
ACETALDEHYDE FROM THE BLOOD OR ITS METABOLISM IS SO RAPID THAT IT
DOES NOT ACCUMULATE IN THE HEPATOCYTES. THE HALF-LIFE OF ACETALDHYE (sp.)
IN THE BLOOD WAS ESTIMATED AS 3.1 MIN." PAGE 374

AT SOME TIME DURING THE PAST MONTH I READ THAT ALL OF THE BLOOD IN THE
HUMAN BODY CIRCULATES THROUGH THE LIVER IN FOUR MINUTES TIME.

WITH "THE DISULFIRAM/ALCOHOL PROCEDURE" HOW LONG WOULD ACETALDEHYDE STAY
ACTIVE AS A POISON IN THE BODY? - - ONE/HALF HOUR?, ONE HOUR?, TWO HOURS?,
OR EVEN LONGER?





DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

January 26, 1993

Mr. John S. Roberts
P. O. Box H
Hobart, Indiana 46342

Dear Mr. Roberts:

The National Institutes of Health appreciates your concern about AIDS and your offer of a possibility for curing this dreaded disease. You are not alone either in your concern, or in offering suggestions for a cure. Nonetheless, serious qualified scientists with many years of experience in virology, biochemistry, molecular biology, and drug development related to AIDS research are devoted to this problem, and what may seem new and innovative to you has already been considered and/or tested by such scientists. The molecules you suggest are normal metabolites formed during normal body functioning, and would have no effect on HIV or AIDS. It is unfortunate that you have been encouraged to persist with your efforts to project what you think may be a cure for AIDS. With no hesitation, I can guarantee you that what you suggest would not be useful.

Sincerely yours,

John P. Bader, Ph.D.
Chief, Antiviral Evaluations Branch
Developmental Therapeutics Program
Division of Cancer Treatment

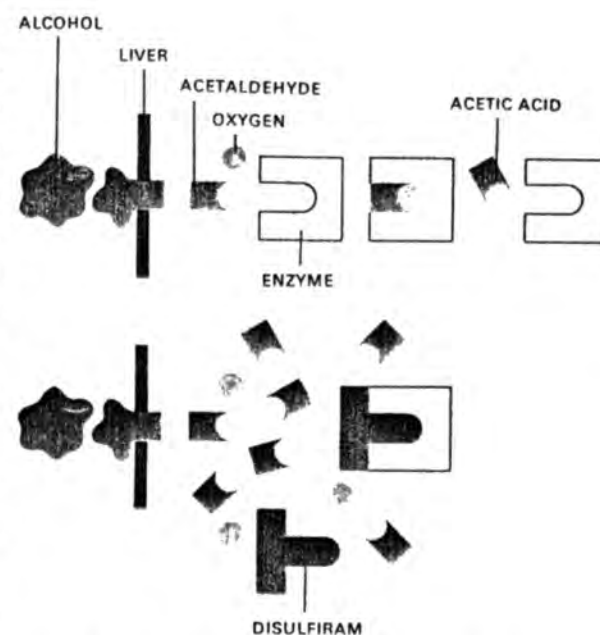
JPBader:crj

When liquor is poison

Oddly enough, the interaction of alcohol with another chemical has been used to treat the most serious problem associated with the drug. Some 20 years ago, two Danish physicians were studying the compound disulfiram as a possible cure for intestinal worms. As part of their testing program, they dosed themselves with small quantities of the compound. Attending a cocktail party soon after, they suddenly found themselves flushed, dizzy and violently nauseated, with splitting headaches. On recovery, they suspected and soon confirmed that disulfiram was to blame. This substance, it turns out, inhibits the liver's transformation of alcohol. It blocks the second step in the process, in which acetaldehyde is transformed into acetic acid, thereby quickly producing a toxic pile-up of acetaldehyde in the body.

Anyone who has taken disulfiram (known commercially as Antabuse) cannot drink even a single glass without becoming violently ill. Unfortunately, as a treatment for alcoholism, disulfiram is seldom successful; the alcoholic usually finds he can give up disulfiram more easily than alcohol.

The limited usefulness of disulfiram indicates the frustrations the pharmacologist faces in trying to deal with the widespread disease of alcoholism. It cannot be explained, or even defined, in pharmacological terms alone. There is no known pharmacological reason why some people destroy their lives by drinking; neither dosage nor physical effects offer an infallible guide. A man who drinks heavily five nights out of seven may on occasion get drunk, but he is not necessarily an alcoholic. Some alcoholics, by contrast, may stay sober for days or even weeks at a time. But once they start drinking, they cannot stop short of abysmal intoxication. They are addicts, "hooked" on the drug alcohol. And addiction to alcohol, like addiction to any other drug, is essentially a psychological compulsion—and therefore the problems it raises are far more psychological, medical and social than pharmacological.



THE ACTION OF DISULFIRAM, a drug intended to discourage alcoholism, disrupts liver functioning so that an imbibor gets sick after drinking. The upper diagram shows how the liver normally handles alcohol. Entering the liver from left, alcohol is first converted into acetaldehyde, a poisonous substance, but this chemical and oxygen are quickly fitted together by an enzyme, forming harmless acetic acid. When disulfiram is taken (*lower diagram*), alcohol is converted into acetaldehyde, but disulfiram joins with the enzyme and prevents acetaldehyde from linking with oxygen and forming acetic acid. As a result, toxic acetaldehyde collects, and the drinker becomes nauseated.

PETER J. VISCLOSKY
1ST DISTRICT INDIANA

COMMITTEE ON APPROPRIATIONS
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PORTAGE, IN 46368
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February 11, 1993

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

Thank you for writing to update me on your research on the AIDS virus. I appreciate hearing from you.

In your letter, you asked if a pilot program can be established at two Chicago, Illinois hospitals to test whether or not acetaldehyde is effective in destroying the AIDS virus. Traditionally, the National Institutes of Health (NIH) is the principal biomedical research agency of the Federal Government. Therefore, I have taken the liberty of forwarding your letter to Dr. Bernadine Healy, Director of the National Institutes of Health, and have asked her to respond to your letter directly. Enclosed is a copy of my letter.

Should you have further questions regarding the development and implementation of AIDS research projects, I urge you to contact NIH. You may write to Dr. Bernadine Healy, Director, at the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, 20892.

Thank you again for sharing your thoughts with me. Should you have questions about federal legislation, please do not hesitate to let me know.

Sincerely,

Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 19, 1993

THE HONORABLE PETER J. VISCLOSKY
UNITED STATES HOUSE OF REPRESENTATIVES
330 CANNON BUILDING
WASHINGTON, D.C. 20515

DEAR CONGRESSMAN VISCLOSKY,

ATTACHED IS A COPY OF YOUR MAY 27, 1992 LETTER TO ME. THANK YOU VERY MUCH FOR THE HELP THAT YOU AFFORDED ME LAST YEAR.

I THINK THAT I HAVE DISCOVERED THE CURE FOR AIDS.

THROUGHOUT THE PAST THIRTEEN MONTHS THE IDEA HAS BEEN KICKING AROUND IN MY BRAIN THAT I MIGHT BE GENERATING IN MY BODY SOME SORT OF AN ACID THAT COULD BE EFFECTIVE IN DESTROYING THE AIDS VIRUS. AS I STUDIED A LITTLE BIT MORE ABOUT THE WAY ALCOHOL IS METABOLIZED IN THE BODY, I HAVE JUST ABOUT COME TO THE CONCLUSION THAT THAT ACID IS ACETIC.

NOW, WHETHER ACETIC ACID CAN OR CANNOT DESTROY THE AIDS VIRUS - I DON'T KNOW. HOWEVER, I HAVE BECOME AWARE OF SOMETHING MORE IMPORTANT.

I BELIEVE THAT IT WAS ON NEW YEAR'S DAY THAT MY WIFE SHOWED ME THE ATTACHED ARTICLE ABOUT A "HANGOVER CURE".

I READ THIS ARTICLE A COUPLE OF TIMES. AT SOME TIME DURING THE FIRST WEEK OF THIS MONTH THIS IDEA HIT ME LIKE A TON OF BRICKS -

THE HUMAN BODY CAN BE POISONED WITH A HIGHLY TOXIC SUBSTANCE
AND STILL SURVIVE

AND THE NAME OF THAT SUBSTANCE IS ACETALDEHYDE.

AS I REFLECT UPON THE PAST THIRTEEN MONTHS AND THE POINT I WAS TRYING TO MAKE ABOUT ACID IN MY BODY, I FEEL AS IF I HAD BEEN PLAYING WITH A FIRECRACKER AND HAVE ALL OF A SUDDEN BEEN HANDED A STICK OF DYNAMITE AND THAT DYNAMITE IS CALLED ACETALDEHYDE.

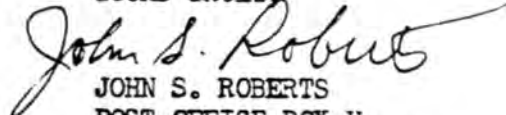
ON JANUARY 11 I MAILED THE ATTACHED LETTER TO DR. LUC MONTAGNIER WITH COPIES TO DR. JOHN BADER AND RANDY SHILTS.

IT IS MY HYPOTHESIS THAT WHILE ACETALDEHYDE IS POISONING THE BODY,
IT WILL AT THE SAME TIME DESTROY THE AIDS VIRUS.

FACILITIES ARE PRESENTLY ESTABLISHED AT TWO HOSPITALS IN CHICAGO - RUSH PRESBYTERIAN AND NORTHWESTERN - TO DO CLINICAL TRIALS OF AIDS PATIENTS.

COULD A PILOT PROGRAM BE SET UP AT EITHER ONE OF THEM TO TEST WHETHER OR NOT ACETALDEHYDE IS EFFECTIVE IN DESTROYING THE AIDS VIRUS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
219-763-1933

COPIES TO DR. LUC MONTAGNIER, DR. JOHN BADER AND RANDY SHILTS

PETER J. VISCLOSKY
DISTRICT INDIANA

COMMITTEE ON APPROPRIATIONS
CONGRESSIONAL STEEL CAUCUS
EXECUTIVE COMMITTEE
WHIP AT-LARGE

Congress of the United States
House of Representatives
Washington, DC 20515-1401

20515-1401
WASHINGTON, DC 20515-1401
(202) 225-2411

215 WEST 35TH AVENUE
GARY, IN 46408
TTY: TDD SERVICE AVAILABLE
(219) 884-1177

PORTAGE CITY HALL
6070 CENTRAL AVENUE
PORTAGE, IN 46368
(219) 763-2908

May 27, 1992

Mr. John Roberts
Post Office Box H
Hobart, Indiana 46324-0739

Dear John:

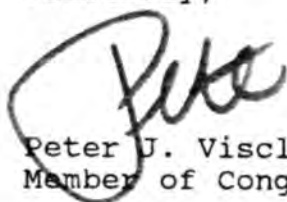
Thank you for sending me a copy of your letter to Dr. Luc Montagnier of the Institut Pasteur in Paris, France. I appreciate hearing from you.

I share your concern that a cure must be found for the devastating illness, Acquired Immunodeficiency Syndrome (AIDS). The illness is caused by the Human Immunodeficiency Virus (HIV) which causes an impairment of the immune systems and leaves its victims susceptible to certain types of cancer and a number of opportunistic diseases. Although drugs such as AZT have been developed to prolong the life of AIDS patients, there is currently no cure.

As you know, on January 31, 1992, I contacted the National Institutes of Health (NIH), on your behalf, regarding NIH's policy for donating blood samples for AIDS research. As a result of this action, on March 12, the NIH responded to your letter directly, and informed you to contact Dr. John P. Bader, who is responsible for the National Cancer Institute Preclinical AIDS Drug Screening Program, regarding the feasibility of analyzing your blood sample. Enclosed is a copy of NIH's letter. Should you have any questions regarding AIDS research-related federal legislation or have problems in contacting NIH, please do not hesitate to let me know.

Thank you again for sharing your thoughts with me.

Sincerely,



Peter J. Visclosky
Member of Congress

PJV:pn
Enclosure

JANUARY 11, 1993

DR. LUC MONTAGNIER
25 RUE DU DOCTEUR ROUX
INSTITUT PASTEUR
PARIS, FRANCE 75015

DEAR DR. MONTAGNIER,

LAST YEAR I WROTE TO YOU A LETTER IN WHICH I ASKED IF YOU WOULD BE INTERESTED IN TESTING MY BLOOD TO SEE WHETHER THERE POSSIBLY COULD BE SOMETHING IN IT THAT WOULD DESTROY THE AIDS VIRUS.

IN THAT LETTER I ALSO SAID,

"YEARS AGO I SAW A TELEVISION PROGRAM IN WHICH SOMEONE SAID THAT PERSONS WHO DRANK BRANDY DID NOT CATCH INFLUENZA DURING THE HORRENDOUS EPIDEMIC OF 1918-1919."

ATTACHED IS A COPY OF A NEWSPAPER ARTICLE WHICH I RECENTLY READ.

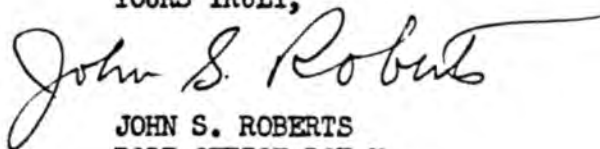
THIS ARTICLE CAUGHT MY ATTENTION BECAUSE I DO DRINK SOME ALCOHOL EVERY NIGHT.

HAS ANY RESEARCH EVER BEEN CONDUCTED TO SEE WHETHER ACETALDEHYDE MIGHT BE EFFECTIVE IN DESTROYING THE AIDS VIRUS?

COULD ACETALDEHYDE BE INJECTED INTO A PERSON WITH NO ILL EFFECTS OTHER THAN TO MAKE THAT PERSON EXTREMELY SICK FOR A DAY?

BEING TOXIC, PERHAPS ACETALDEHYDE WAS THE SUBSTANCE THAT DESTROYED THE INFLUENZA VIRUS. IN THE SAME MANNER, COULD IT ALSO POSSIBLY DESTROY THE AIDS VIRUS?

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342
UNITED STATES OF AMERICA

COPIES TO: DR. JOHN P. BADER
NATIONAL INSTITUTES OF HEALTH
ANTIVIRAL EVALUATIONS BRANCH
BETHESDA, MARYLAND

RANDY SHILTS
SAN FRANCISCO CHRONICLE
SAN FRANCISCO, CALIFORNIA

CHANGE BOWL

Nebraska vs. Florida St.
(Ch. 5, 16)

7:30 p.m.

SUGAR BOWL

Alabama vs. Miami (Ch. 7, 28)

son of the dog,
"Flash Gordon" and
Cruise, "Close Encounte-
Kind" and "Blade Runner." at

WPWR (Ch. 50) counters with
starting at 9 a.m. with "The Shaggy Dog,"
"Son of Flubber" "That Darn Cat," "Alice in
Wonderland" "Return to Oz" and "Return
from Witch Mountain."

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Hangover cure? Nope

The Associated Press

► HEALTH

Even if you're in no condition to read this, you probably know that aspirin won't cure it and water won't prevent it.

It's the hangover, and it's inevitable if you drink too much alcohol.

The headache, upset stomach and bad aftertaste that accompany a hangover come from the toxic by-product of alcohol, a chemical called acetaldehyde, said Russell Mankes, associate professor of toxicology and pharmacology at the Albany Medical College.

Some typical folk remedies — eating cold pizza, taking aspirin before bed or drinking another cocktail — may do more harm than good.

Aspirin and ibuprofen are bad for the stomach lining and popping one when the stomach is already irritated from drinking dramatically increases the risk of an ulcer, Mankes said.

Tylenol won't harm the stomach, but it can strain the liver, which is already being damaged by the alcohol, Mankes said.

Drinking water while still intoxicated won't help either. Because alcohol induces urination, all the water that comes in, goes out, taking with it minerals and salts.

Don't even think about drinking another alcoholic beverage to reduce hangover symptoms.

"The 'hair of the dog' is the first step on the road to alcoholism," he said.

Coffee won't make a drinker sober. "All you end up with is a wide-awake drunk," he said.

So what's the cure?

"Avoid getting one in the first place," Mankes said. "That does not mean avoiding alcohol. One can drink responsibly."

OCT 19 1993

OCTOBER 6, 1993

Please add this to the
packet of my Research which
I mailed to you last month.

John S. Roberts
219-763-1933

Copy to Ms. Gebbie

OCTOBER 6, 1993

JACK WHITESCARVER, Ph.D.
DEPUTY DIRECTOR
OFFICE OF AIDS RESEARCH
NATIONAL INSTITUTES OF HEALTH
BUILDING: 1
ROOM: 201
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20892

DEAR DR. WHITESCARVER,

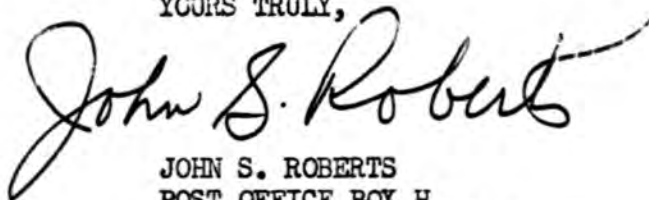
ATTACHED IS A COPY OF YOUR SEPTEMBER 22 LETTER.

CAN THE NIH OFFER AN EXPLANATION OF THE DIFFERENCE IN RESULTS OBTAINED BY THE REISINGER AND LANG STUDIES?

IN MY OPINION, THE LANG STUDY COULD BE VIEWED AS A REPRESENTATION OF THE EFFECTIVENESS IN VIVO WHICH UNMETABOLIZED ACETALDEHYDE HAS IN DESTROYING HIV.

AS YOU SUGGESTED, I AM RE-EXAMINING THE LITERATURE, BUT I HAVE NOT YET COME ACROSS A STUDY WHICH WOULD ABNEGATE MY HYPOTHESIS.

YOURS TRULY,



JOHN S. ROBERTS
POST OFFICE BOX H
HOBART, INDIANA 46342

COPIES TO CONGRESSMAN PETER J. VISCLOSKEY

PROFESSOR RUSSELL F. MANKES, THE ALBANY MEDICAL COLLEGE
MS. KRISTINE M. GEBBIE, RN, MN, NATIONAL AIDS POLICY COORDINATOR
INDIANA UNIVERSITY SCHOOL OF MEDICINE, NORTHWEST CAMPUS, DR. SUBBIAH SIVAM
AND OTHERS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Building: 1
Room: 201
(301) 496-0357

SEP 22 1993

Roberts
H
46342

Mr. John S. Roberts
Post Office Box H
Hobart, Indiana 46342

Dear Mr. Roberts:

Your memo to the Acting Director of the National Institutes of Health (NIH), Dr. Ruth L. Kirschstein, has been forwarded to the Office of AIDS Research.

In regard to your inquiry about the HIV/AIDS drug screening program conducted by the National Cancer Institute (NCI), we can tell you that acetaldehyde has not and will not be evaluated for anti-HIV properties. The reason why acetaldehyde is not considered a viable candidate for evaluation has been explained in a letter to you by Dr. John P. Bader, head of this program at the NCI. Acetaldehyde is a normal metabolite of the human body that would not significantly hinder HIV infection.

For an understanding of the pharmacological properties of Ditiocarb in relation to HIV infection, we suggest you consult your local librarian. Over 25 articles on this agent have been published since 1989 and none of them support the notion that acetaldehyde has a significant role in altering the course of HIV infection.

Sincerely,

Jack Whitescarver, Ph.D.
Deputy Director
Office of AIDS Research

THE WHITE HOUSE
WASHINGTON

August 26, 1993

Greg Hacke, D.C.
946C Marshall Avenue
Webster Groves, Missouri 63119

Dear Dr. Hacke:

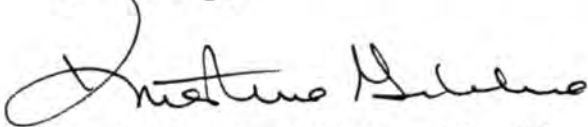
Thank you for writing and sharing your information regarding Topotecan and other alternative therapy options.

There are a number of essential steps in bringing any therapeutic product to market. For information about these measures, please contact:

Office of AIDS Coordination
Food and Drug Administration
Parklawn Building, Room 12A40 HF-12
5600 Fishers Lane
Rockville, Maryland 20857

As the AIDS Policy Coordinator, I will advocate public health policy that has a sound scientific basis. You can be assured that I will support the use of therapeutic agents that have been shown to be safe and effective.

Sincerely,

A handwritten signature in dark ink, appearing to read "Kristine Gebbie", with a stylized, flowing script.

Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

THE WHITE HOUSE
WASHINGTON

August 26, 1993

Dr. Greg Hacke
946C Marshall Ave.
Webster Groves, MO 63119

Dear Dr. Hacke:

Thank you for writing and sharing your information regarding Topotecan and other alternative therapy options.

There are a number of essential steps in bringing any therapeutic product to market. For information about these measures please contact:

Office of AIDS Coordination
Food and Drug Administration
Parklawn Building, Room 12A40 HF-12
5600 Fishers Lane
Rockville, Maryland 20857

As the AIDS Policy Coordinator I will advocate public health policy that has a sound scientific basis. . You can be assured that I will support the use of therapeutic agents that have been shown to be safe and effective.

Sincerely,

Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

Prepared by: APO: TFox: 8/24/93:202-690-5560:b:\foxltrs.gbe\hacke.gbe

[illegible]

**FILE
COPY**

Kristine Gebbie
Presidential AIDS Advisor
Executive Office of the President
Washington, D.C. 20500

8/2/93

Draft reply

Dear Ms. Gebbie:

Enclosed is a letter sent to the president of SmithKline Beecham urging him to quickly follow up on an *in vitro* study showing anti HIV activity for the drug Topotecan which his company is already testing in cancer patients. The study was published in March and now four months later as far as I know there is still no effort to organize human trials to test this drug against HIV. Unfortunately, this is not an uncommon situation. There are literally dozens of compounds that have shown clear *in vitro* or even *in vivo* activity against HIV and yet years are passing before any clinical trials are undertaken.

As the enclosed report shows, there were two other compounds besides Topotecan that were active against HIV. One of these compounds is Curcumin, found in the common herb Tumeric. Because this is a common food and not subject to patent by a drug company, this promising lead may suffer the neglect of similar *in vitro* active compounds that have languished for years in this AIDS epidemic waiting for someone to test them in humans. As the President's "AIDS Czar" what can you do to find government funding to test all of these neglected possible AIDS treatments? Any of the AIDS groups such as Project Inform could give you a list as long as your arm of candidates for testing. Some of these candidates are already existing prescription drugs such as Trental or Tagamet that could quickly move to Phase II studies since the safety data already exists.

In the case of Trental and Tagamet, small human trials ended late last year and yet here we are nine months later and no results have been released yet. The Phase II trials of Compound Q ended this past April and we are told that results will not be released until September at the earliest. Does it really take 6-9 months to compile the results of a study of a few hundred people?

As the Editor in Chief of a medical publishing house, I am not totally unfamiliar with what it takes to write a report, and in this age of computers I can not understand these delays other than in the light of reluctance on the part of drug companies to release early information that might adversely affect their marketing strategies. As the "AIDS Czar" what can you do to speed up the release of this information, perhaps addressing the marketing concerns of the drug companies if that is where the problem lies.

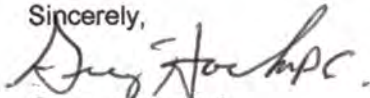
Still another area where you might take action involves the rapid screening of off-the-shelf drugs for possible *in vitro* activity. There have been several rapid screening tests developed by researchers, but they do not have the funds to screen the thousands of possibilities that they are capable of doing. A good example of this is the study that produced the information on the SmithKline Beecham drug Topotecan. The Harvard researchers that developed the new screening test were only able to test 15 compounds because of a lack of funds. They found three out of 15 that were active against HIV. How many more would they have found if they had been given the money to screen 1,500 compounds instead of just 15? Why isn't the federal research effort plugging these holes in the system? If federal funding is not a possibility, perhaps you

could coordinate with some of the private AIDS groups, since the screening efforts do not require the large sums that clinical trials do.

I and thousands of other patients are already taking drugs such as Trental, Tagamet, Compound Q and Curcumin in a desperate gamble that the early scientific evidence of their efficacy will later be confirmed, but we haven't got the luxury of waiting two to three years until someone in the AIDS bureaucracy decides to move.

As the long-awaited "AIDS Czar", Ms. Gebbie, tens of thousands are placing their hopes in you. This country put a man on the moon in ten years; we built the atomic bomb in four. What have we got to show for 12 years of AIDS funding? People are still dying.

Sincerely,



Greg Hacke, D.C.

AIDS TREATMENT NEWS

Issue Number 174
May 7, 1993

Published twice monthly by
John S. James
P.O. Box 411256
San Francisco, CA 94141
415/ 255-0588

Contents

New Kind of HIV Antiviral: Food Spice, Cancer Drug Show Activity	1
Urgent, Federal AIDS Funding: Kentucky, California, Connecticut, Florida, Illinois, Iowa, Maryland, New York, Ohio, Texas, and Wisconsin	3
Tat Drug: Parallel Track Negotiations Status	4
Alternative Medicine Grant Program Not Easily Accessible	5
Announcements:	
Children: NIH Begins First Pediatric Trial of Therapeutic Vaccine	7
KS: DaunoXome Study Recruiting, Compassionate Use Also Available	7
AIDS Health Fraud Congressional Hearings Set Quietly — Postponed to May?	7
San Francisco: ACT UP/Golden Gate Treatment Issues Committee Benefit, May 11	8
Alternative Medicine and Health-Care Reform Conference, Washington, May 20-23	8

New Kind of HIV Antiviral: Food Spice, Cancer Drug Show Activity

by John S. James

Researchers at Harvard Medical School, using laboratory tests, have developed a new class of anti-HIV compounds — substances which inhibit the LTR (long terminal repeat) sequence of HIV. Three substances which might have potential were reported in the March 1993 *Proceedings of the National Academy of Sciences, USA*. One, curcumin, is the main active ingredient in turmeric, a spice used in curry and other foods; another, topotecan, is being tested in humans as a possible cancer treatment; the third, beta-lapachone, has not been tested in humans, but laboratory and animal data suggest that it might be possible to find a useful dose.

HIV is often inactive, even after it has entered a cell and has become integrated in that cell's genetic machinery. (This does not contradict the recent report that HIV is active even early in the disease while there are no symptoms; the virus is active in some cells but not in others. For background information, see "AIDS Pathogenesis" in *AIDS Treatment News* #172, April 2, 1993.) The LTR of HIV appears to be critically important in "turning on" the virus (causing it to produce the proteins which are assembled into new viruses, and which cause other harmful

effects). The LTR also maintains viral activity after it has started, suggesting that inhibiting the LTR could slow or stop virus which has already been activated. Normally, many substances in the cells seem to be affecting the LTR — either to inhibit it and keep the virus inactive, or to activate the LTR and promote HIV growth and activity. Much is unknown about how this process works and what substances may affect it. But a drug which effectively inhibited the LTR might keep the virus inactive indefinitely — not only in acutely infected cells, but also in chronically infected cells, where AZT, ddI, etc. are largely ineffective.

Certain experimental treatments already in use in the community — pentoxifylline, NAC, and antioxidant nutrients such as beta carotene, vitamin C or vitamin E — may already be having some inhibitory effect on the HIV LTR. The Harvard work is new in that it demonstrates a way to systematically search for potential drugs which work through this particular viral target.

The Laboratory Experiments

The recent report described two kinds of experiments. One did not use any HIV or other virus; instead it used a genetically engineered human cell, which included a copy of the HIV LTR and also a "reporter" gene, controlled by that LTR, which creates an enzyme which could easily be detected in the laboratory. Scientists can grow this cell, and then add certain chemicals known to activate the LTR, and verify that the enzyme was indeed produced, as expected. Then they can add potential

drugs, in various concentrations; if one of the drugs stops the enzyme from being produced, that drug is probably inhibiting the LTR. [Incidentally, the cells for this experiment were developed in the laboratory of Leonard Herzenberg, Ph.D., a Stanford researcher studying NAC, whose group uses the cells in their studies of HIV activation and repression.]

The other experiments used cells infected with HIV, to verify that the substances which showed anti-LTR activity did indeed show anti-HIV activity in the laboratory. Both acutely infected and chronically infected cells were used.

Results

The most powerful of the three substances found may be topotecan, which was active against HIV in very small concentrations, and is reasonably well tolerated in cancer patients, according to published research. These patients tolerated 200 times the blood level of topotecan required to reduce p24 antigen production (a measure of HIV activity) by 80 percent in chronically infected cells.

Curcumin, found in the spice turmeric, was less active than topotecan. But it may be particularly important because, as one of the study's authors, Bruce J. Dezube, M.D., points out, "it is a food additive, readily available, non-toxic, and a potential benefit for developing countries." The paper notes that curcumin has been eaten for thousands of years [it is used especially in India, where turmeric is a major ingredient of curry]. It has also been tested for potential pharmaceutical uses, and it has been used for various purposes in traditional Indian, Chinese, and Western herbal medicine.

The third substance, beta-lapachone, had no human toxicity data available, but is well tolerated in mice. It was tested 20 years ago for other purposes, and abandoned. Its patent has now expired, so it may be hard to find a pharmaceutical company to develop it.

The research which found these three potential treatments is also important because it demonstrated a method which could be used to screen thousands of potential drugs to look for LTR inhibitors. Because of limited resources, this project did not screen many candidates; instead, the researchers were selective, trying to pick substances they considered likely to work. About fifteen potential compounds were tested to find the three listed above.

The Next Step

The next step in the development of this approach is unclear, because these three potential treatments have reached the point at which new AIDS drugs usually stop. Potential treatments developed in laboratories by well-respected scientists usually do get into scientific journals, but in most cases nothing further happens, because usually there is no drug company which has or can acquire the rights, and also has an interest in the drug, and the money and other resources available to develop it. (The government does little drug-development work, and most of that is on drugs which companies are already testing.) Even those drugs which are ultimately successful often float around at this stage

for several years, with progress largely stopped, before enough momentum develops to take them further. Of the three LTR inhibitors described above, two may be unpatentable, and the third is being developed by a company which, as far as we know, is not testing drugs for AIDS. We cannot rely on business as usual to get these substances tested. *SmithKline*

The problem is that there is still no institution to examine potential treatments which have reached this stage, select which ones are promising enough to begin human testing, and then quickly get that testing to happen. When an "AIDS czar" is appointed, that office may be a place to go to get this long-standing omission addressed. But this official will have a small staff and will probably focus mainly on non-technical issues; in addition, it will be hard to start anything new because of budget constraints.

Community-based research groups might be able to help. Topotecan has already been tested in people as a cancer treatment, so basic dosage and safety information is known. Various permissions would be required to test it for HIV; these permissions might or might not be an obstacle. The company developing topotecan, SmithKline Beecham, is testing it for cancer but not for AIDS.

Curcumin, at least in turmeric, would certainly be accessible. However, one German paper reported that it was poorly absorbed when given orally to animals, and more active when given by intraperitoneal injection. But a study in India found protection against cancer-causing chemicals in cigarette smoke when turmeric was given orally to people. (Most of the traditional uses have been topical; one study in India, for example, reported a 97 percent cure rate for scabies with a preparation of turmeric mixed with another herb.) A community-based research organization could relatively easily review the available literature, review traditional medicinal uses, and test turmeric or curcumin in a few patients to see if it reduced viral activity. The inexpensive, commercially available acid-dissociated p24 antigen test could be used to look for an antiviral effect. Or it might be possible to use more sophisticated virological tests, through collaboration with the researchers who are developing them. If little or no effect is found, then it might be worth investigating whether curcumin could be prepared in an injectable form.

In past years, the only way the AIDS community could move a drug forward in the face of institutional neglect was to develop it as an "alternative" treatment — i.e., let it go into widespread use — in the hope that if there were any substantial value it would be noticed, and if not, the substance would be retired through the usual "drug of the month" process. Maybe we can do better today.

References

Li CJ, Zhang LJ, Dezube BJ, Crumpacker CS, and Pardee AB. Three inhibitors of type 1 human immunodeficiency virus long terminal repeat-directed gene expression and virus replication. *Proceedings of the National Academy of Sciences, USA*. March 1993; volume 90, pages 1839-1842.

AIDS TREATMENT NEWS

Issue Number 178
July 9, 1993

Published twice monthly by
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P.O. Box 411256
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415/ 255-0588

Contents

Berlin Treatment Leads: Topotecan; Hydroxyurea	1
Berlin: Long-Term Survival Studies Suggest New Treatment Strategies.....	3
Amino Acids, Herbs, Other Supplements: FDA Proposes New Regulations, Public Comment Until August 17	7
Peptide T Unavailable in Buyers' Clubs	7
Political Funeral in Washington, D.C., Disrupted by Police	8
AIDS: An Expanding Tragedy — National Commission On AIDS Final Report	8

Berlin Treatment Leads

by John S. James

The following are two of a number of treatment leads presented at the IX International Conference on AIDS, held in Berlin on June 6-11, 1993.

Topotecan

Topotecan is a chemical now being tested in patients by SmithKline Beecham as a potential cancer treatment. Its possible use against AIDS was first proposed by researchers at Harvard Medical School, in a paper published in the March, 1993, *Proceedings of the National Academy of Sciences, USA*. This paper reported laboratory studies showing that topotecan inhibits HIV in chronically as well as acutely infected cells (which AZT, ddI, etc. do not do), and that it is effective at a concentration 200 times lower than that which has been tolerated by cancer patients — suggesting that as an AIDS treatment the drug may have a large therapeutic range (between effective and toxic doses).

The anti-HIV activity of topotecan was found by a screening test which looked for inhibitors of the "long terminal repeat" (LTR) of HIV, which is important in activation of the virus. The same test also found that curcumin, the ingredient which gives curry its yellow color, has the same kind of anti-HIV activity (see *AIDS Treatment News* #176, June 4, 1993, for background on curcumin, which also is effective against HIV in chronically as well as acutely infected cells). The laboratory tests found that topotecan is more powerful than curcumin as an inhibitor of HIV. But topotecan also has a disadvantage in that so far it is only available in an intravenous form (although an oral form may be

developed). And there is no way to obtain topotecan at this time, whereas curcumin is readily available. This is why there has been more public interest in curcumin than in topotecan.

The Berlin talk, by Boston AIDS researcher Clyde Crumpacker, M.D., who is one of the authors of the PNAS report, gave additional details that were not in the paper. In laboratory studies with cells acutely infected by HIV, topotecan worked about as well as AZT, and better than ddI. But it also worked well in chronically infected cells, where very little effect was found with AZT, and none with ddI. And topotecan was also effective against an HIV isolate highly resistant to AZT (with three different mutations for AZT resistance), giving 50 percent inhibition at about 0.08 micromolar concentration.

The research team is now trying to develop topotecan-resistant virus, in order to learn more about the mechanism of action of topotecan, which is largely unknown. But so far they have not identified any significant resistance.

The Berlin talk, on June 8, was to a large and attentive audience. Since then there has been considerable professional interest in getting topotecan tested as an HIV treatment (it has not yet been tested in people with HIV). We will follow this effort as it develops.

[Incidentally, during the question period Dr. Crumpacker was asked if he and his colleagues would continue looking at curcumin. He answered that, "Curcumin is not as active as topotecan on a microgram per microgram basis, but it is found as a normal food product, and many parts of the world consume this. We are pursuing curcumin, but how it would be developed in a clinical trial is unclear yet." The problem, apparently, is the old one of natural treatments not being tested because they are low cost and no company has a monopoly on them.]

AIDS TREATMENT NEWS

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Contents

Curcumin Update: Could Food Spice Be Low-Cost Antiviral?	1
The FDA and Buyers' Clubs	3
Fusion Toxin, New Kind of Potential AIDS Treatment, in Early Clinical Trial	7
Action Alert: San Francisco AIDS Care in Jeopardy	8

Curcumin Update: Could Food Spice Be Low-Cost Antiviral?

by John S. James

In March 1993, researchers at Harvard Medical School published results of laboratory tests of a new method of screening for potential AIDS drugs.¹ They used genetically engineered cells to test for inhibitors of the "LTR" (long terminal repeat) sequence in HIV; the LTR is important for viral activation. The new test found three inhibitors; one of them is curcumin, a chemical found in the food spice turmeric. Curcumin is the ingredient which gives curry its yellow color. It was effective against HIV in both acutely and chronically infected cells.

On May 7, 1993, *AIDS Treatment News* published a short review of the Harvard article. Since then, our readers have brought new information about curcumin to our attention:

- In Trinidad, about 40 percent of the population is of Indian descent, and uses curry extensively in their diet. Another 40 percent of the population is of African descent, and seldom uses curry. Several years ago, studies of AIDS in Trinidad found that persons of African descent were more than 10 times as likely to have the disease as persons of Indian descent.² (We do not have recent data; however, a new report on AIDS epidemiology in Trinidad, by F. Cleghorn, W. Blattner, and others, is expected at the Berlin conference.)

- One reader of *AIDS Treatment News* started using a turmeric extract with a very high concentration of curcumin

— about 100 times the concentration in ordinary turmeric — which he obtained from a San Francisco health-food store. He started using it on May 7, 1993. A week later his regularly scheduled blood tests showed a substantial drop in p24 antigen (a measure of viral activity). This unexpected change impressed his physician, a leading AIDS specialist in San Francisco.

The product he used was supplied in capsules, each containing "300 mg. turmeric extract concentrated and standardized for a minimum of preferred 95% curcumin" in a base of whole turmeric, according to the label on the bottle. He took three capsules three times a day — about 2.5 grams of curcumin per day, for a person who weighs about 100 kg. This dose was chosen arbitrarily; it is considerably greater than the amount of curcumin one would ordinarily get by eating curry, and we do not know whether or not it is safe. Even for this large dose the cost was low, about \$2 per day retail in the U.S.

We mention this single case because it may be the first time that anyone has taken curcumin as a potential treatment for HIV, and compared viral-activity measurements before and after starting.

Pharmacology

Curcumin is not soluble in water,³ and animal tests have found very little of it in the bloodstream after it is eaten.⁴ Therefore, it would seem that this chemical could not work as an oral drug. But other researchers have reported much higher absorption — as much as 60 percent or more.^{5,6} And in laboratory studies curcumin is often given to animals in the diet, and various effects are noted.

This apparent contradiction is resolved by results of animal tests, some with radioactive curcumin. Much of the

radioactivity does reach the blood and organs, even though the curcumin doesn't — meaning that the curcumin must have been changed into something else and absorbed in a different form. The same team had earlier reported that about 60 percent of the curcumin was absorbed, since only about 40 percent of the quantity administered was found remaining in the gut — although only traces were found in the blood.⁵ Another paper by the same group concluded that "curcumin undergoes transformation during absorption from the intestine," and noted an unidentified compound that it was changed into.⁶ So the fact that chemists do not find curcumin in the blood when they look for it does not rule out the possibility that oral use could have biological effects.

Curcumin is being studied as an anti-inflammatory,⁷ as a possible cancer inhibitor,⁸ and for other potential medical uses. It is a strong anti-oxidant. A recent search of the Excerpta Medica database found citations to 149 papers, abstracts, etc. which mention curcumin; the word "curcumin" appears in the title of 74 of these. A review of some possible medicinal uses of curcumin⁹ was published in 1991.

Turmeric is a mild spice. When curry is hot, that is due to other spices.

A recent paper listed the curcumin content of turmeric powder as about 0.6 percent.¹⁰

Safety

Curcumin and turmeric have long been in daily human use, and are believed to have little toxicity in moderate doses.¹ However, one group found that large doses caused stomach ulcers in rats.¹¹ A thorough literature review is needed before large doses are used.

What Does This Mean?

The information above is only suggestive, and does not show that curcumin will have any use in treating AIDS. Most new drug or treatment ideas fail, after later information shows that they are not useful. For curcumin as for any new treatment, the odds are that it, too, will be one of the failures.

But the possibility that curcumin or turmeric *might* be useful in treating HIV or AIDS is so important that it must be studied further without delay. Curcumin is known to be safe, at least in low and moderate doses, and could be available to everyone. Also, in the laboratory tests it was active against HIV not only in acutely infected but also in chronically infected cells — where the currently approved drugs such as AZT are ineffective.

The next step in research should be to give a high but safe dose to 10 to 20 people for several weeks, and measure

changes in viral activity, either with the readily available p24 test, or with sophisticated research tests such as quantitative PCR, or the branched DNA assay. Both natural turmeric and concentrated curcumin should be tested. If there is a dramatic decrease in viral activity in people (like that seen in the single case so far), then this potential treatment will receive plenty of attention. If there is little or no decrease, then we can forget about curcumin (except as a possible lead compound for drug development) and move on.

We do not know of anybody anywhere in the world doing such a study, or making plans to do so, or otherwise following up on curcumin as a possible AIDS treatment. This is not unusual; there has never been a serious institutional effort to test such treatment leads in early human trials. Medical research is expensive, and requires considerable effort and resources to make anything happen. Those with the resources — mainly large pharmaceutical companies — have little commercial or professional incentive to test low-cost, non-proprietary treatments. And government and non-profit research organizations have usually failed to focus on the critical need for getting safe, inexpensive treatment possibilities into small but credible tests for biological activity in humans.

We hope this article will help bring this treatment possibility to wider attention, so that the appropriate research can be organized.

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3. *The Merck Index*, 1989.
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7. Sato: anti-inflammatory) in *pa Clin. Phar* 12, pages

8. Nag: Inhibitor (*Nutrition*.

9. Amn *Curcuma* 57, pages

10. Muk PK. Anti-inflammatory analogues 12, number

11. Gur Prasad DN in rats. *Ina* pages 806-

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THE WHITE HOUSE
WASHINGTON

August 26, 1993

Mr. Thomas S. Vickery
Founder
Rainbow Bridge Organization
5400 N. Astor Lane #204
Rolling Meadows, Illinois 60008

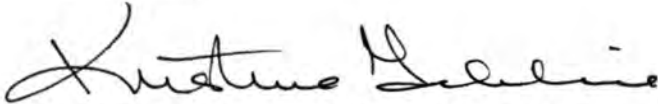
Dear Mr. Vickery:

I was pleased you took the time to write to me, and thank you very much for the information about the Rainbow Bridge Organization. You are to be applauded for your efforts to dispel misconceptions about persons with disabilities who are gay, lesbian, or bisexual.

I share your concern about discrimination against people living with HIV and AIDS. We must all work together to fight discrimination against people suffering from HIV disease and help to ensure that the provisions of Public Law 101-596, the Americans with Disabilities Act, are implemented.

Best wishes in your efforts.

Sincerely,

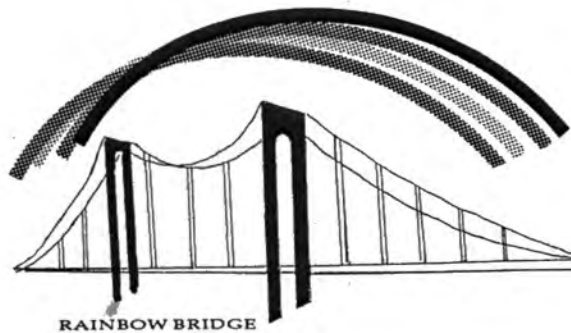


Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

August 24, 1993

[illegible]

August 10, 1993



Ms. Kristine Gebbie
AIDS Coordinator
The White House
1600 Pennsylvania Avenue
Washington, D.C. 20500

Dear Ms. Gebbie,

In a recent article of the San Francisco Chronicle you requested that AIDS and gay activist write and tell you of their concerns, expectations and suspicions. Therefore, I am accepting your invitation.

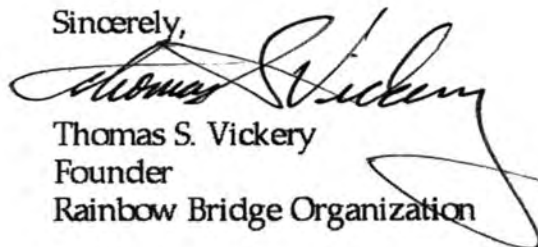
As you are undoubtedly aware, many provisions of the Americans with Disabilities Act (ADA), signed by President Bush in 1990, took effect this past year. Consequently, I feel that this is an appropriate time to educate the public on another important issue. That is that topic of homosexuality and the disabled.

Enclosed please find information which will provide you with a comprehensive understanding of the goals, purpose and history of the Rainbow Bridge Organization which I, a gay disabled man, founded in 1992. Upon receiving this information, I hope that you will contact me so that we can further discuss two topics that are currently receiving a lot of media attention: disabilities and homosexuality. You may contact me at:

5400 N. Astor Lane #204
Rolling Meadows, IL 60008
(708) 253-5164

Your time regarding this matter is certainly appreciated. Thank you!

Sincerely,


Thomas S. Vickery
Founder
Rainbow Bridge Organization



RAINBOW BRIDGE
P.O. BOX 42
ITASCA, IL 60143-0042

THE STORY BEHIND THE RAINBOW BRIDGE ORGANIZATION

Ellen met Sam at a social function at her school nearly forty-five years ago. No big deal since that is where most people meet the love of their life. The difference here however, is that Ellen has polio, and the school was designed for teaching the disabled. Ellen had to wear braces on her legs, her gait was not attractive. Sam looked beyond the obvious. Two years later they were married. A happy ending? Definitely. Ellen found a man that would love her and see to her needs and Sam found a woman that had courage and devotion beyond what is termed "normal."

What if you were disabled and also realized that you were lesbian, gay or bisexual? Where could you go to meet that one person who will "look beyond the obvious?" There are several groups throughout the country that recognize disabled lesbian, gay or bisexual individuals, but they also discriminate towards a particular disability, just as Ellen's school was for persons with polio.

Tom Vickery of Itasca, Illinois who is disabled and gay visualized a place where a lesbian, gay or bisexual person with any disability could go to meet, socialize and discuss their various interests and concerns. His vision became reality in June of 1992 when he founded the Rainbow Bridge Organization, the only organization outside of EDGE (Education in a Disabled Gay Environment) located in New York City, that does not discriminate against a particular disability. The name of Rainbow Bridge was chosen for two reasons: Rainbow to represent the gay flag which is rainbow colored and Bridge to represent disabled and non-disabled lesbian, gay or bisexual individuals coming together to become united to form one large community.

Tom is not alone with seeing the need of Rainbow Bridge as very important. Currently there are more than 70 people from across the country on this organizations roster. In addition, Rainbow Bridge has received endorsement letters from such notables as U.S. Senator Carol Moseley Braun, U. S. Senator Paul Simon and Illinois Governor Jim Edgar. Furthermore, articles regarding this organization have appeared in the Chicago Sun-Times, the Chicago Tribune and the Daily Herald. In addition, articles have also appeared in local as well as national gay publications and newsletters along with being in publications that pertain to persons with disabilities. Tom Vickery also had the distinct pleasure of being interviewed on Studs Terkel's radio talk show. One of the major goals of Rainbow Bridge is to eliminate the misconceptions and stereotypes that the general public have regarding two distinct minorities: persons with disabilities and persons who are lesbian, gay or bisexual. Therefore, members of Rainbow Bridge look forward to the opportunity of receiving more local and national press as well as being invited to speak at many conferences that pertain to these issues.

Tom's interest in assisting other persons with disabilities goes beyond his local area. Recently he had the distinction of serving as the national constituent representative for persons with disabilities for the 1993 March on Washington. The purpose of this march was for lesbian, gay and bi equal rights with the primary focus being placed on issues regarding healthcare and human rights. This important historical event which was held on April 25 in our nations capitol was attended by over 1,000,000 lesbian, gay and bisexual individuals and their supporters. Approximately 10,000 of these individuals were persons with disabilities.

To be gay and disabled can make for a very lonely life, and everyone needs more than the love and support of family members. For the lesbian, gay or bisexual community, many do not even have their families to lean on. This is why Rainbow Bridge does not limit membership to only the disabled. Just as Ellen and Sam found happiness, Rainbow Bridge offers the same future for those who are looking for that special person. No one deserves to be lonely.

Rainbow Bridge has both business meetings and an active social calendar every month. If persons feel that they could benefit from this organization or would like additional information, they could write to the Rainbow Bridge Organization at P.O. Box 42, Itasca, IL 60143-0042.

ANNIVERSARY NEWSLETTER OF THE RAINBOW BRIDGE ORGANIZATION

It has been one year since the Rainbow Bridge Organization was started in Chicago, Illinois. This organization started as an idea of Thomas S. Vickery's. The idea became a reality when an article written by Eric Zorn regarding the concept appeared in the June 18, 1992 issue of the Chicago Tribune. The conception was to have a place where persons with disabilities, as well as non-disabled individuals, who are members or supporters of the lesbian, gay or bisexual community could feel accepted and loved by others similar to themselves.

The first meeting of Rainbow Bridge was held on July 22, 1992, and by first meeting standards was a huge success. Our next two meetings were at the Gay and Lesbian Rodde Center, which proved to be a difficult location for people to get to. Fortunately, a more convenient and accessible location for future meetings was found. The location found, Progress Center for Independent Living, is in Oak Park, Illinois (a western suburb of Chicago).

A goal of Rainbow Bridge is to eliminate misconceptions, myths and stereotypes regarding two distinct minorities: those who are disabled and those who are of the lesbian, gay or bisexual community. One of the myths which this organization has successfully put to rest is that persons with disabilities are unable to socialize together with non-disabled individuals of the gay community. Proof of this myth no longer existing becomes apparent when one looks at the diverse group of people who have participated in our various social events. For instance, in December, members of Rainbow Bridge attended a performance of the play ROCK written by writer/actor Michael Kearns. This was followed in February by attending a Valentine's Dance in Villa Park, Illinois which was hosted by Holy Covenant MCC church. Then in March we saw the play Other People's Money which starred one of our own members.

On April 3, 1993 Rainbow Bridge hosted the First Kickoff Party for the March on Washington. This event was held at Chicago's own, Ann Sathers Restaurant, and was attended by 50 people, including various dignitaries. The March on Washington, held on April 25, in our nation's capitol was very important to Rainbow Bridge having had representation on both the local and national level. Our representative, Tom Vickery, served as Coordinator of Transportation for the Illinois Committee along with being the National Constituent Representative for Persons with Disabilities. In addition to attending this historical event, the Rainbow Bridge banner was also carried in the March. Another parade which Rainbow Bridge participated in was the Chicago Gay and Lesbian Pride Parade held on June 27, 1993.

The next major hurdle facing Rainbow Bridge is to further develop a strong membership base. Since the organization was formed, publicity has been a major goal and has been met with success by having articles published in many different local and national publications. Endorsements regarding Rainbow Bridge have also been procured from U. S. Senator Carol Moseley Braun, U.S. Senator Paul Simon and Illinois Governor Jim Edgar. In addition, Rainbow Bridge has been represented on a U.S. cable talk show and Stud Terkel's radio talk show. A telephone interview resulting in another article by disabled gay writer/poet Kenny Fries also took place. Kenny was a guest speaker at one of our monthly meetings.

The success of Rainbow Bridge is dependent on the total support of all its members. Consequently, members of the lesbian, gay or bisexual community who are disabled as well as those who are not disabled must become unified in order to put an end to the discrimination and oppression felt by all of us. With this goal in mind, wouldn't you like to become a member of Rainbow Bridge, if you haven't already joined?

For further information, or if anyone wishes to submit an article, comment, or letter, please write to:

Rainbow Bridge Organization
P.O. Box 42
Itasca, IL 60143-0042



RAINBOW BRIDGE ORGANIZATION

The goals and purpose of the Rainbow Bridge Organization is to:

1. Provide a safe and comfortable place for people to share and discuss interests and concerns that affect persons with disabilities who are lesbian, gay or bisexual.
2. In providing this first goal, it is hoped that other individuals who are or have an interest in persons with disabilities who are part of the lesbian or gay community will also find that this organization is accepting to not only their individual disability but also their lifestyle.
3. Provide a safe and acceptable environment where various forms of entertainment can be shared by many people. Some examples of this type of entertainment could include attending a variety of sporting events, concerts and plays, as well as having discussion groups, and game nights.
4. As more people (persons with disabilities as well as those who are not disabled) learn about Rainbow Bridge and its purpose it is hoped that society will become educated to the fact that the disabled population also has a significant part in the lesbian and gay community. As a result of this, it is hoped that the disabled and nondisabled that have been separated from each other for too long will unite together to form the lesbian and gay community rather than the current situation which is disabled lesbians, gays and bisexuals on one side, and nondisabled lesbians, gays and bisexuals on the other.

If you are interested in receiving more information regarding this organization, please write to us at:

Rainbow Bridge Organization
P.O. Box 42
Itasca, Illinois 60143-0042

THE WHITE HOUSE

WASHINGTON

August 26, 1993

Michael J. Swiller, D.C., M.S., C.C.N.
120 Whitney Street
Hartford, Connecticut 06105

Dear Dr. Swiller:

Thank you for writing to share your article on AIDS and immunity.

Both the National Institutes of Health and the Centers for Disease Control and Prevention are conducting research on HIV and AIDS. If you would like more information on HIV/AIDS related research, please write to these agencies at the following addresses:

Executive Secretariat
National Institutes of Health
Building 1, B-156
9000 Rockville Pike
Bethesda, Maryland 20892
ATTN: Sue Seigal

and

Office of AIDS Coordination
Centers for Disease Control and Prevention
Executive Park Building
1600 Clifton Road, N.E.
Mail Stop - D21
Atlanta, Georgia 30333
ATTN: Mary Jane Herwick

I also encourage you to work with universities in your area to initiate a study or design a clinical trial.

Again, thank you for sharing your thoughts.

Sincerely,



Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

THE WHITE HOUSE

WASHINGTON

August 26, 1993

Michael J. Swiller, D.C., M.S., C.C.N.
120 Whitney Street
Hartford, Connecticut 06105

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Again, thank you for sharing your thoughts.

Sincerely,

Kristine M. Gebbie, RN, MN
National AIDS Policy Coordinator

Prepared by: APO: KMGebbie: gw: 8/20/93: 632-1090: b:\swiller

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A Wide Variety of Conditions Respond to Chiropractic Care

MICHAEL J. SWILLER B.A., M.S., D.C.

Chiropractic Physician

120 Whitney Street • Hartford, CT 06105 • (203) 232-5500

*Manipulative Therapy
Nutritional Therapy
Sacro-Occipital Technique
Cranial-Sutural (T.M.J.)
Techniques*

11 August 1993

Kristine Gebbie, PhD.
AIDS Policy Coordinator
Dept. of Health & Human Services
200 Indiana Avenue S.W.
Washington, DC 20201

Dear Dr. Gebbie:

As a concerned human being, a doctor, a licensed chiropractor with a masters degree in biology / clinical nutrition and further certified by the International and American Association's of Clinical Nutritionists, as a Certified Clinical Nutritionist, I have taken a keen interest in the issue of AIDS.

In the following article I have combined numerous elements of current and not so current research on AIDS and immunity.

The article says that there may be an approach to AIDS, in all of it's stages, that has been suggested by academic researchers but then ignored by all of the "hands on" therapies.

I would like to request that you:

1. Read this article.
2. Give me any feedback you can, as to the approach suggested.
3. Suggest any way in which I might participate or initiate a study which investigates this approach.
4. Suggest how I would go about designing trials, in this area of therapy, which can qualify for federal grants.

Any help you can give me will be appreciated.

Thank you,

Michael J. Swiller D.C.
Michael J. Swiller, D.C., M.S., C.C.N.

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Michael Swiller, M.S., D.C., C.C.N.

120 Whitney Street
Hartford, CT 06105-2542
203-232-5500

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1600 Words

Center For Applied Nutritional Therapy

© Michael Swiller, M.S., D.C., C.C.N.

AIDS TREATMENT:

1. AFTER EXPOSURE BUT BEFORE SEROCONVERSION.
2. IN THE HIV-1 PATIENT WITHOUT AIDS.
3. IN THE HIV-1 PATIENT WITH AIDS.

A ROLE FOR NUTRITIONAL THERAPY.

Michael J. Swiller, B.A., M.S., D.C., C.C.N.

Summary

Current research suggests that a broad body of knowledge exists on the seroconversion mechanism as well as a profound understanding of biochemical developments progressing to AIDS.

Much of the research indicates that natural ingredients of the diet might be capable of preventing HIV-1 conversion and may account for the failure of AIDS to develop in 60% of the HIV-1+ population. The purpose of this paper is to examine the known factors which appear to play key roles in the apparent immunity of this 60% HIV-1+ population.

Introduction

The present therapy for AIDS exposed persons has been the use of Zidovudine. In spite of initiating this drug therapy within hours of exposure, these patient's still seroconvert to HIV-1+¹.

The biochemical defects associated with AIDS are: 1. The seroconversion from HIV-1- to HIV-1+, a process that seems to take from 60 to 90 days after exposure; 2. a drop in the body's production of T-Lymphocytes and the CD4+ lymphocytes²; and 3. a long prodromal variable period before the development of AIDS. It is reported that up to 60% of HIV-1+ persons never develop AIDS.

I have examined the actions of vitamin C, cysteine, thiamin, methionine, interferon, vitamin A, beta-carotene, zinc, lysine, vitamin B-6, glutathione, selenium, eicosapentaenoic acid and gamma linolenic acid, and present the role they seem to play in this immunity.

Research to date

Research just published in *Science*³ indicates that stimulation of the body's production of a specific type of T-Lymphocyte, The T-1 Helper cell, may enhance the immune system to such an extent that the body may be able to defend itself against AIDS.

The body's natural Lymphocyte population can be turned into T-Lymphocytes. These T-Lymphocytes are then transformed into CD4+ cells and these can be converted to T-1 helper cells. T-1 helper cells seem to do their work through the production of a chemical called Interferon. While interferon has antiviral activity itself, this chemical seems to stimulate the production of an antiviral protein substance. The raw materials necessary for the production of interferon include a number of sulfur containing agents⁴ such as: cysteine, thiamin and methionine. These

¹ Anonymous. *Lancet*. 24 April 93. Pg. 1077.

² Mosier, D., Gulizia, R. et al. Dept. of Immunology, Scripps Research Institute. "Rapid Loss of CD4+ T Cells in Human-PBL-SCID Mice by Noncytopathic HIV Isolates". *Science*. 260, 30 April 93. Pg. 689.

³ Scott, Philip. "IL-12: Initiation Cytokine for Cell Mediated Immunity". *Science*. 23 April 1993; 496-497.

compounds are well known natural immune system enhancers. Blood levels of each can be measured easily and all can be purchased at most health food stores.

Vitamin C, in doses of 5 gm's (5,000 mg) per day, has been shown to greatly stimulate the production of new lymphocytes⁵. When these lymphocytes pass through a normal Thymus gland, they become converted to T-Lymphocytes.

Many viruses have the ability to cause Thymus gland involution (atrophy). Vitamin A has the ability to prevent thymic gland involution and to return the thymus gland to normal function⁶. These agents usually insure adequate levels of Lymphocytes and T-Lymphocytes.

The CD4+ population is critical to the HIV-1 patient. Falling CD4+ levels are an indication of impending AIDS symptoms, the AIDS Related Complex. The Facts about CD4+ cells are: 1. CD4+ levels fall in vitamin A deficient patients. CD4+ levels can be brought back up by using Beta-carotene⁷ or vitamin A and; 2. CD4+ has a weak spot; The CD4+ coat is built in a folded form and the strands of the third section are held together by a disulfide bridge. When this disulfide, cysteine⁸, is replaced by another chemical, the molecule is weakened and may be destroyed. Cysteine levels can be maintained by way of supplements.

⁴ Bellanti, J., M.D. *Immunology III*. W.B. Saunders Co., Philadelphia, PA.; 1985 Pg. 291

⁵ Cameron, E. & Pauling, L. Ph.D. *Cancer & Vitamin C*. The Linus Pauling Institute of Science & Medicine; Menlo Park, CA.; 1979. Pg. 110

⁶ Passwater, Richard. M.D. *Cancer and its Nutritional Therapies*. Keats Publishing, Inc. New Cannan, CT. 1978. Pg. 187

⁷ Semba, R., Griffin, D. et al. Johns Hopkins School of Medicine. "Vitamin A Deficiency and Lymphocyte Subsets". *Lancet*. 341 10 April 93. Pg. 971

⁸ Brady, R., Dodson, E., et al. Dept. of Chemistry, University of York, York, United Kingdom. "Crystal Structure of Domains 3 and 4 of Rat CD4: Relation to the NH₂-Terminal Domains". *Science*. 260 14 May 93. Pg. 979-83.

The changing of CD4+ T-Lymphocytes into T-1 helper cells (T-1_h), and not T-2 helper cells (T-2_h), is essential to the life of the HIV-1 patient. If the HIV-1 infected body produces an overload of T-2_h cells, the patient dies. Interleukin 12 (IL-12), formerly called, "natural killer cell stimulatory factor", will cause the CD4+ cells to convert to T-1_h cells and will stimulate the production of interferon. Until this paper, it was known that large doses of vitamin C were able to stimulate interferon production but, there was no known association between vitamin C and the T-1_h cells. Vitamin C appears to mimic or accelerate IL-12 production. In order: vitamin C stimulates lymphocyte production, more lymphocytes will pass through the bone marrow where they become B-Lymphocytes, these cells produce the IL-12 which directs the conversion of CD4+ to T-1_h. Logic then precludes that with vitamin C there will be enhanced T-1_h cell biosynthesis and the patient will live.

The twists in the story are that vitamin A, after being absorbed from the intestines tends to become trapped in the liver and then cannot get to the thymus gland. Taking the mineral zinc, prevents the liver from trapping vitamin A. This means that zinc, too, is responsible for thymic health⁹. In order for zinc to be metabolized correctly, the use of vitamin B-6 is essential. In a manner similar to that of vitamin A, Dr. Kronhausen¹⁰ reports that, vitamin B-6 is "crucial" for proper thymus gland function.

The sulfur compound cysteine, which was referred to in connection with CD4+ survival, has also been reported in another form which has anti HIV activity. This report¹¹ also states that

⁹ Ibid. Passwater, Richard. Pg. 187

¹⁰ Kronhausen, E. Ed.D., Kronhausen, P., Ed.D. & Demopoulos, H., M.D. *Formula For Life*. William Morrow & Co.; New York, NY. 1989. Pg. 257.

¹¹ Marshall, W. & Caruthers, M. Dept. of Chemistry and Biochemistry, University of Colorado. "Phosphorodithioate DNA as a Potential Therapeutic Drug". *Science*. 259 12 March 1993. Pg. 1564-69.

lysine, an amino acid long known for its anti Herpes action¹², is an extremely potent HIV-1 inhibitor. Lysine, too, is a readily available nutrient.

In order for the AIDS virus to grow, it must go through a stage called reverse transcription (RT). The drug AZT does it's work by preventing the RT stage. Unfortunately, AZT has numerous side effects, works for about a year and then becomes ineffective. In looking for other agents to prevent RT, researchers have discovered that another compound manufactured by the body can stop the RT stage. This compound is glutathione¹³. Biochemists have been studying glutathione for years. It is known that cysteine¹⁴ determines how much glutathione is produced by the body. Adding selenium to the diet allows the body to produce glutathione peroxidase, a compound known to be highly protective and perhaps even act as an anticancer agent. Many AIDS victims develop a form of cancer called Kaposi's sarcoma. Could a lack of glutathione peroxidase allow this tumor to develop?

When investigating how HIV destroys the T-lymphocytes and CD4+, researchers have found that HIV causes a clumping (synctia) of these cells which is followed by cell death¹⁵.

T-lymphocytes are large cells, much larger than platelets. In many pathological conditions, platelets are also known to clump. High levels of a fatty acid called arachidonic acid (AA) is known to cause this clumping. During some inflammatory reactions the body responds with an arachidonic acid cascade.

¹² Braverman, E. M.D. & Pfeiffer, C. M.D., Ph.D. *The Healing Nutrients Within*. Keats Publishing, Inc.; New Canaan, CT. 1987. Pg. 294.

¹³ Johnston, M. & Hoth, D.; Basic Research & Development Program, Division of AIDS, National Institute of Health. "Present Status and Future Prospects for HIV Therapies". *Science*. 28 May 1993. Pg. 1286-93.

¹⁴ Ibid. Braverman & Pfeiffer. Pg. 91.

¹⁵ Weiss, Robin; Chester Beatty Laboratories, Institute of Cancer Research, London. "How Does HIV Cause AIDS". *Science*: 28 May 1993. Pg. 1273-78.

This is followed by excessive platelet aggregation. The clumping of platelets sounds very similar to the synctia of AIDS. The natural antidotes to arachidonic acid are the omega-3 fatty acids¹⁶, the fish oils, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Might arachidonic acid, itself, contribute to AIDS? At this moment, Dr. Donald Kotler of St. Luke's Roosevelt Hospital believes this is the case. He reports that arachidonic acid enhances the replication of the HIV virus¹⁷ and is trying to counter the prostaglandin effect with the use of aspirin.

Another fatty acid, gamma-linolenic acid (GLA), gives rise to dihomo-gamma-linolenic acid (DGLA) and this allows the formation of prostaglandin E-1 (PGE-1). PGE-1 is known for its ability to reduce inflammation, enhance T-lymphocyte function, prevent AA release¹⁸ and reduce platelet clumping. Blood levels of AA, EPA, DHA, GLA and DGLA are easily determined. EPA, DHA and GLA can be purchased at many health food stores.

Conclusions

We already have a lot of information on combating AIDS. HIV-1+ patients must be routinely checked for vitamin A, vitamin C, zinc, vitamin B-6, cysteine, thiamin, lysine, methionine, EPA, DHA, GLA or DGLA deficiencies. Double blind studies would seem to be irresponsible in this disease. There are enough HIV-1+ patients to serve as controls. A comparative study with 600 patients, in each progressive stage of HIV-1 infection, should be monitored for the chemicals mentioned in this report. Then each patient should be treated to bring his/her levels up to:

¹⁶ Fast, Julius. *The Omega-3 Breakthrough*. The Body Press; Tucson, AZ. 1987. Pg. 53.

¹⁷ Kotler, Donald; Community Research Initiative on AIDS, St. Lukes Roosevelt Hospital Center, New York. *New AIDS Drug Leaps Over the Counter Science*; 23 July 1993. Pg. 422.

¹⁸ Erasmus, Udo. Ph.D. *Fats and Oils*. Alive Books; Vancouver, Canada. 1986. Pg. 256-8.

1. Normal standards (200 patients).
2. 1 1/2 times above normal standards (200 patients).
3. Twice the normal standard level (200 patients).

These study groups could easily be compared to 200 patients receiving standard medical care. This trial should run for a minimum of 120 days. All patients demonstrating rising T-lymphocytes and CD4+ levels should be maintained on the program till all of the signs of the AIDS related complex are cleared. What this program intends to accomplish is to bring each patient's immune system up to a level capable of dealing with any genetic mutations the HIV virus might attempt.

Risk possibilities

Some patients might suffer from the effects of a vitamin A overload. These effects are no worse than patients receiving radiation therapy and are reversible on vitamin reduction. A mineral imbalance may develop as zinc counters copper and calcium metabolism. An amino acid imbalance may develop secondary to a cysteine overload. It is not anticipated that any patient will die as a result of this program and it is unlikely that any patient would have fared better on any other program.

Benefit possibilities

For many patients the AIDS related complex will be reversed. These patient's will remain HIV-1+ for life and may be at risk of developing AIDS at any time. If this therapy can be resumed at any time, at little cost, then we can consider the AIDS pandemic to be under control, in the industrialized world at least.

Final observation

For those patient's too ill to respond to this program, they have lost nothing. There is no other successful regimen for this

disease. The program outlined here is relatively inexpensive to monitor and administer. Nutritional therapists, most likely chiropractors with advanced degrees / certification in the field of nutrition, should be members of the research team.

Dr. Michael J. Swiller is a practicing Chiropractic physician. He has been utilizing nutritional therapy in his practice for 20 years. His B.A. is in Pre-medicine from New York University. His D.C. is from The Chiropractic Institute of New York. His M.S. is in Biology and Clinical Nutrition from the University of Bridgeport, Bridgeport, CT. He is board certified as a Clinical Nutritionist by the International and American Associations of Clinical Nutritionists. He is a member of the American Chiropractic Association, the A.C.A. Council on Nutrition and the American Association for the Advancement of Science. He is the Director of Research for the Center For Applied Nutritional Therapy at 120 Whitney Street, Hartford, Connecticut.

The End

BERNARD N. MERRILL, ATTORNEY AT LAW

ROGER GRAY, OF COUNSEL

August 26, 1993

Christine Gebbie
AIDS Policy Coordinator
Executive Office of the President
750 17th Street N.W., Suite 1020
Washington, DC 20500

RE: Misc.

Dear Chris:

Just a few things:

1. Senator Harkin of Iowa, a Senate ally, lost his 34 year old aide on Saturday in a traffic accident. His name was James M. Sweeney. I don't know if you know the senator, but if you do, you may want to send a note. You may be looking at Richard Socharetes (sp?) from the Senator's staff in the future and a note may make an early impression.
2. I have been contacted by Charlie VanderHorst M.D. (a friend) of the University of North Carolina who has one of the largest NIH grants and is one of the major players in the ACTG's. He has faxed me a private, working paper which will be discussed within the Advisory Group opposing some proposed steps by NIH with regard to breaking up the ACTG's to smaller groups. This position paper is being supported by community groups. Without committing to a position, yet, you may want to review it since I think a storm is coming with regard to the ACTG's. Patsy Fleming, also without taking a position, is prepared to brief you as to NIH's position.
3. I have asked Alvin Novick at Yale to send me a copy of his critique of some of the controlled trials which he presented at AAPHR.
4. Ben Schatz is willing to fly from San Francisco to Seattle to have breakfast with you on September 8th if you can give him an hour breakfast before you start your Seattle meetings. If you cannot, he is willing to be put on hold and come east. If its too much of a stretch, don't worry. He was very grateful that I

Letter to Christine Gebbie
Page 2
August 26, 1993

mentioned him to you and that I'm trying to get the two of you together sometime. I think that just the effort and to let him know that you're willing to talk with him meant a lot. He doesn't want to fly to Seattle that morning just for 15 minutes because he has to be in San Diego that early afternoon. Let me know if you want to see him the evening of September 7th or the morning of September 8th and I'll set it up.

5. I spoke with Art Leonard in New York today. He is an old friend and helped me a great deal with Lavender Law III programing. He is willing to open a very private back door with Larry Kramer and I am willing to sit and listen to Kramer yell. I think Kramer has the biggest ego in the universe but I have a suspicion that if he thought that he had a channel, he might modify his position or at least give you a chance. Kramer dealt very kindly with Leonard in Kramer's book and the two have a healthy respect for one another. Let me know if you want this to happen. I can make it happen.
6. I have begun to assemble a core group of names (no contacts yet) of a religious group. People such as Charles Carnahan (HIV Coordinator for United Methodist Church) and Rev Kenneth T. South, Executive Director of the AIDS National Interfaith Network. Other people, without "institutions" such as Bishop Fritz Mutti in Kansas (he and his wife Etta May have lost two sons to AIDS) who are will to talk to anyone about HIV/AIDS. I am sure that you have your own ideas about this but I know that I can pull together some very good people. And, an old friend, Larry Gherety, former president of Atlantic Union College has just been named president of La Sierra College and could get some very good people in the Adventist church. I think the way to crack all of the religious resistance is to focus them on "care" rather than "prevention" in order to keep them away from the "condom craze."

Finally, Ratina is a joy. She's off tomorrow, Friday, placing a few bets in Atlantic City. But she promised not to go over her budget!

I am working with personnel people at 5:30 AM PST tomorrow to clear up any ethical questions concerning my retaining an open office in Portland and working for you. Right now I'll make that September 1st deadline one way or another.

*Welcome
home from
Hawaii!
Bon*

THE WHITE HOUSE

WASHINGTON

August 26, 1993

NOTE TO: Dr. Anthony Fauci
Dr. David Kessler
Ms. Patsy Fleming

On August 6, I met with Mr. Jackson Stephens, and Mr. Gary Faulkner of ExOxEmis Inc. and Dr. Nancy Alexander of NICHD. Mr. Stephens and Mr. Faulkner have met before with NIH and FDA officials about their potential product, which would be a female-controlled spermicide/viricide. Dr. Alexander is currently doing some preliminary testing of the product through her research program.

There is some question of the process of moving the product along in the process. I indicated that I was available to answer questions or assist them if they hit snags, but that the ordinary process of product review should be workable for them.

I also indicated, since they seemed inclined to think of lobbying, that they might align themselves with groups lobbying for women's health research and research on women and AIDS.

I am attaching a copy of their letter to me for your information. Please call if you have questions.



Kristine Gebbie, RN, MN
National AIDS Policy Coordinator

Attachment

cc: Dr. Brian Biles

THE WHITE HOUSE

WASHINGTON

August 26, 1993

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Kristine Gebbie, RN, MN
National AIDS Policy Coordinator

Attachment

cc: Dr. Brian Biles

Prepared by: APO: KMGebbie: gw: 8/24/93: 632-1090: b:\fauciet.al

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OFFICE SURNAME	DATE	OFFICE SURNAME	DATE	OFFICE SURNAME	DATE