Weather Advisory: 40's & 50's, rain probable

WEDNESDAY, MARCH 4, 1987

8:30 AM  Dr. Baltimore DEPARTS Boston Logan Airport, United Airlines #95 en route San Francisco

9:00 AM  Dr. Koop & Dr. Samuels DEPART Dulles Airport, Washington DC United Airlines #21 en route San Francisco

11:32 AM  Dr. Koop & Dr. Samuels ARRIVE S.F. International Airport
  Met by Assemblyman Art Agnos

Advance:
Decker
Bush
Proceed to United Airlines Red Carpet Club - Conference Room 1, Phone # 876-5095
(Staff Time Apprx 25 Minutes)

11:47 AM  Dr. Baltimore ARRIVES San Francisco International Airport
  Met by Assemblyman Art Agnos

(Proceed to United Airlines Red Carpet Room for Staff Time Apprx. 5 Minutes)

12:00  Motorcade DEPARTS SFO en route San Francisco Examiner
  (Drive Time Apprx. 20 Minutes)

  Car #1
  Driver: Atkinson
  Bush
  Samuels
  Robin Henig

  Car #2
  Driver: Decker
  Agnos
  Koop
  Baltimore

  Car #3
  Driver: Park

12:20 PM  Motorcade ARRIVES San Francisco Examiner, 110 5th Street, (415)777-7923

Advance:
Shafer
Met by: Tom Dearmore, Editorial Director
Proceed to 3rd Floor Conference Room
12:30 PM  Meet with San Francisco Examiner Editorial Board  
(Approx. time 45 Minutes)

1:15 PM  DEPART 3rd Floor Conference Room en route Motorcade

1:20 PM  Motorcade DEPARTS San Francisco Examiner en route  
Coming Home Hospice  
(Drive time Approx 15 Minutes)

   Car #1  
   Driver:  Atkinson  
           Agnos  
           Bush

   Car #2  
   Driver:  Decker  
           Koop  
           Baltimore

   Car #3  
   Driver:  Park  
           Samuels  
           Ms. Robin Henig

1:35 PM  ARRIVE Coming Home Hospice, 115 Diamond Street  
(415-861-1110)

Advance:  Met by Assemblyman Art Agnos  
          Libby Denebeim, Co-Chair, Development Committee  
          David Werdegar, M.D., Director, Public Health,  
          City & County of San Francisco

Open Press Coverage (Approx time 10 Minutes)  
(Assemblyman Agnos welcomes Dr.'s Koop/Baltimore  
to San Francisco & both acknowledge - respond to  
brief questions)

1:45 PM  Begin Private Tour of Hospice Facility  
(Appprox 15 min) Conducted by:  Agnos  
          Denenbein  
          Werdegar

2:00 PM  Meet with Volunteers in Hospice Living Room  
Open Press Coverage - (Approximately 15 minutes)  
(Seated: Agnos, Dr. Koop, Dr. Baltimore & Dr. Werdegar  
talk informally about their reaction to tour.  
Glenn Jordon acknowledges on behalf of patients and  
volunteers)

2:15 PM  DEPART Living Room en route Motorcade
Visit by C. Everett Koop, M.D.
Page Three
WEDNESDAY, MARCH 4, 1987

2:25 PM  Motorcade DEPARTS Coming Home Hospice en route
San Francisco Chronicle
(Drive time Apprx 15 min)

  Car #1  
  Driver:  Atkinson
            Bush
            Samuels
            Randy Shilts

  Car #2  
  Driver:  Decker
            Koop
            Baltimore
            Agnos

  Car #3  
  Driver:  Park
            Housh
            Ms. Robin Henig  
            (Note: proceed to Hotel)

2:40 PM  ARRIVE San Francisco Chronicle, 901 Mission Street,  
          (415) 777-7181
Advance:  Met by:  Jerry Burns, Editor & Director
           Proceed to 3rd Floor Conference Room
2:45 PM  Meet with San Francisco Chronicle Editorial Board  
          (Apprx. Time 60 Minutes)
2:45 PM  DEPART Conference Room en route Motorcade
3:45 PM  DEPART San Francisco Chronicle en route Union  
          Square Holiday Inn, 430 Sutter Street, (415) 398-8900
Advance:  
           Housh

  Car #1  
  Driver:  Atkinson  (Note: proceed to Agnos home)
            Agnos
            Bush

  Car #2  
  Driver:  Decker
            Koop
            Baltimore
            Samuels
ARRIVE Holiday Inn Union Square, 480 Sutter Street, (415)398-8900
6th Floor Garage Level

Decker/Staff Office 606
Dr. Koop 616
Dr. Baltimore 618
Dr. Samuels 615
Ms. Robin Henig 614

(Staff Time 1 Hour, 40 Minutes)

DEPART Union Square Holiday Inn en route Dinner Celadon Restaurant
(Drive Time 5 Minutes)

Car #1
Driver: Decker
Koop
Baltimore

Car #2
Driver: Park
Samuels
Ms. Robin Henig

ARRIVE Celadon Restaurant for Dinner, 881 Clay Street, (415) 982-1168
(Apprx. Attendance 25)
Met by Assemblyman Art Agnos

Dinner is Served

Werdegar makes Remarks and Introduces Art
Toast by Agnos
Brief Baltimore & Koop Remarks

DEPART Celadon Restaurant en route Union Square Holiday Inn
(Drive time 5 Minutes)
Visit by C. Everett Koop, M.D.
Page Five  
WEDNESDAY, MARCH 4, 1987

Car #1
Driver: Atkinson
Bush
Samuels
Shilts

Car #2
Driver: Decker
Agnos
Koop
Baltimore

Car #3
Driver: Park
Foster
Pitman Lindeman
Henig

7:30 PM  ARRIVE  Holiday Inn Union Square for Medical Community Reception - Proceed to Savoy Room, 30th Floor
Advance:
Shafer
Housh

Met by:
Fred Armstrong, M.D., CMA
Helen Miramontes, R.N., C.N.A.
David Townsend, M.D., GSMA
Will Warner, M.D., BAPHR

Open Press Coverage (Mingle/Photo Opportunity)

8:30 PM  DEPART 30th Floor for 6th Floor
(Dr. Koop to meet privately with Dr. & Mr. Deutch)

Remain overnight - Holiday Inn, Union Square
(415)398-3900

9:00 PM  (Note: Car #3 to Sacramento with Bush)
Agnos in his car to Sacramento with Housh
Visit by C. Everett Koop, M.D.
Page Six
THURSDAY, MARCH 5, 1987

THURSDAY, MARCH 5, 1987

5:00 AM    WAKE-UP CALLS

5:30 AM    Motorcade DEPARTS Holiday Inn Union Square en route
Sacramento (Approx. Drive Time 2 Hours)

Car #1
Driver:    Atkinson
           Samuels
           Henig
           Shilts

Car #2
Driver:    Decker
           Koop
           Baltimore
           (Henig)

(Note: Baltimore Luggage and Koop change of
clothes - Car #2)

7:30 AM    Motorcade ARRIVE at Sacramento Bee, 21st & Q Streets,
            (916)321-1020
Advance:
            Met by Assemblyman Art Agnos & Mark Paul
Shaf er
            Proceed to Second Floor Conference Room for breakfast

7:35 AM    Meet with Sacramento Bee Editorial Board
            (Approx. 45 Minutes)

8:20 AM    DEPART Second Floor Conference Room en route
Motorcade

8:25 AM    Motorcade DEPARTS Sacramento Bee en route
State Capitol
            (Drive Time Approx. 10 Minutes)

Car #1
Driver:    Atkinson
           Bush
           Samuels
           Henig
           Shilts

Car #2
Driver:    Decker
           Agnos
           Koop
           Baltimore
Visit by C. Everett Koop, M.D.
Page Seven
THURSDAY, MARCH 5, 1987

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:35 AM</td>
<td>Motorcade ARRIVES State Capitol, Basement Entrance Proceed to Agnos' Office, Room 3151</td>
</tr>
<tr>
<td>Advance:</td>
<td>Housh</td>
</tr>
<tr>
<td>9:15 AM</td>
<td>Senator Hart to 3151 for private meeting. (Apprx. Time 15 Minutes)</td>
</tr>
<tr>
<td>9:30 AM</td>
<td>Meet with Assembly and Senate Leadership for Coffee and Photos - Speakers Conference Room</td>
</tr>
<tr>
<td>Advance:</td>
<td>Bush</td>
</tr>
<tr>
<td>10:00 AM</td>
<td>Assemblyman Agnos escorts Dr. Koop and Dr. Baltimore into Assembly Chamber - Joint Session of California State Senate and Assembly called to order. Open Press Coverage/Prepared Remarks</td>
</tr>
<tr>
<td>Advance:</td>
<td>Housh</td>
</tr>
<tr>
<td></td>
<td>Bush</td>
</tr>
<tr>
<td>10:55 AM</td>
<td>DEPART Assembly Chamber en route Governor's Office (First Floor)</td>
</tr>
<tr>
<td>11:00 AM</td>
<td>ARRIVE Governor's Office where Dr. Koop meets privately with Governor Deukmejian (15 Minutes)</td>
</tr>
<tr>
<td>Advance:</td>
<td>Decker</td>
</tr>
<tr>
<td>11:15 AM</td>
<td>Dr. Koop DEPARTS Governors Office en route Press Conference Room #1190</td>
</tr>
<tr>
<td>Advance:</td>
<td>Shafer</td>
</tr>
<tr>
<td>11:55 AM</td>
<td>DEPART Room #1190 en route Motorcade</td>
</tr>
</tbody>
</table>
Visit by C. Everett Koop, M.D.
Page Eight
THURSDAY, MARCH 5, 1987

12:00 Motorcade DEPARTS State Capitol en route Sacramento Athletic Club for Luncheon
(Drive Time Approx. 5 Minutes)

Car #1
Driver: Atkinson
        Bush
        Shilts

Car #2
Driver: Decker
        Koop
        Baltimore
        Agnos

Car #3
Driver: Park
        Samuels
        Henig

12:05 Motorcade ARRIVES Sacramento Athletic Club for Luncheon
808 "O" Street, (916)442-3663
Advance: Met by: Duane Dauner, President
Housh California Association of Hospitals and Health Systems, (916)443-7401

Proceed to Dining Room for Luncheon (Brief Stop to Change)
(Attendance Approx. 20)

1:15 PM DEPART Club Dining Room en route Motorcade

1:20 PM Motorcade DEPARTS Sacramento Athletic Club en route
Los Angeles Times Bureau.
(Drive Time Approx. 5 Minutes)

Alternate Car #1
Driver: Parker
        Samuels
        Baltimore
        Bush

Alternate Car #2
Driver: Cervantes
        Koop
        Roberti
        Agnos

1:20 PM Motorcade DEPARTS Sacramento Athletic Club en route
San Francisco International Airport
(Drive Time Apprx. 2 Hours)
Visit by C. Everett Koop, M.D.
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THURSDAY, MARCH 5, 1987

Car #1
Driver: Atkinson

Car #2
Driver: Decker
Henig

Car #3
Driver: Park

1:25 PM
Motorcade ARRIVES Los Angeles Times Bureau,
1121 "L" Street, (916)445-8860.
Advance: Shafer
Met by: Carl Ingram
Proceed to Second Floor

1:30 PM
ARRIVE on Second Floor for Interview
(Apprx. Time 45 Minutes)

2:15 PM
DEPART Second Floor Conference Room

2:20 PM
Motorcade DEPARTS Los Angeles Times en route
Sacramento Executive Airport, 6151 Freeport Blvd.
(Apprx. Drive Time 10 Minutes)

Car #2
Driver: Parker
Koop
Agnos
Baltimore

Car #3
Driver: Cervantes
Bush
Samuels

2:30 PM
Board King Aire #120JJ, Pilot: David Bell,
DEPART en route San Francisco International Airport/
Butler Aviation
(Flight Time 40 Minutes)

Manifest: Agnos
Koop
Baltimore
Samuels
Roberti
Bush
3:10 PM  ARRIVE Butler Aviation, San Francisco International Airport

3:15 PM  Motorcade DEPARTS Butler Aviation enroute Bay Guardian
          (Apprx. Drive Time 30 Minutes)

          Car #1
          Driver:  Atkinson
                     Bush
                     Henig

          Car #2
          Driver:  Decker
                     Agnos
                     Koop
                     Baltimore

          Car #3
          Driver:  Park
                     Samuels

3:45 PM  ARRIVE Bay Guardian for Meeting with Editorial Board
          2700 - 19th Street, (415)824-7660
          Advance:  Shafer
          (Apprx. Time 45 Minutes)

4:30 PM  DEPART Conference Room

4:35 PM  Motorcade DEPARTS en route Holiday Inn Union Square
          (Apprx. Time 15 Minutes)

          Car #1
          Driver:  Atkinson
                     Bush
                     Henig

          Car #2
          Driver:  Decker
                     Agnos
                     Koop
                     Baltimore

          Car #3
          Driver:  Park
                     Samuels

4:50    ARRIVE Holiday Inn Union Square
          (1 Hour, 30 Minutes Staff Time)

          Advance:  Housh
Visit by C. Everett Koop, M.D.
Page Eleven
THURSDAY, MARCH 5, 1987

6:20 PM  Motorcade DEPARTS Holiday Inn en route
          Castagnola Restaurant for Dinner, 286 Jefferson
          Street, (415)776-5015
          (Drive Time Apprx. 10 Minutes)

           Car #1                     (DEPART 6:00 PM)
           Driver:                    Atkinson
                                 Bush
                                 Agnos

           Car #2
           Driver:                    Decker
                                 Koop
                                 Agnos
                                 Baltimore

           Car #3
           Driver:                    Park
                                 Samuels
                                 Henig

6:30 PM  Motorcade ARRIVES Castangola Restaurant, (415)776-5015
          Proceed to Second Floor for private Dinner
          (Apprx. Attendance 50)

6:45 PM  Dinner is served

7:30 PM  Agnos Toast. Koop and Baltimore Respond.

7:50 PM  DEPART Second Floor en route Motorcade

7:55 PM  Motorcade DEPARTS en route KGO TV STUDIO,
          885 Battery Street, (415)954-7777
          (Apprx Drive Time 5 Minutes)

           Car #1
           Driver:                    Atkinson
                                 Bush

           Car #2
           Driver:                    Decker
                                 Koop
                                 Baltimore
                                 Agnos

           Car #3
           Driver:                    Park
                                 Henig
                                 Samuels

8:00 PM  ARRIVE KGO TV STUDIO to Second Floor for
          Filming of NightLine
8:05 PM  ARRIVE Studio for Filming of NightLine
          (Estimated time 55 Minutes)

9:00 PM  DEPART KGO TV en route Holiday Inn Union Square
          (Drive Time Apprx 10 Minutes)
          
          Car #1
          Driver:  Park
                   Agnos
                   Baltimore (To Airport)
                   (Drive Time Apprx 15 Minutes)
          
          Car #2
          Driver:  Decker
                   Samuels
                   Koop
                   Henig
          
          Car #3
          Driver:  Atkinson
                   Bush
          
9:10 PM  Motorcade ARRIVES Holiday Inn Union Square
          (Remain Overnight)

9:15 PM  Dr. Baltimore ARRIVES SF International for
          TWA Flight #44 en route Boston
FRIDAY, MARCH 6, 1987

7:00 AM Baggage Call

7:00 AM KQED Interview, Room #606
(Apprx. Time 10 Minutes)

7:20 AM DEPART 6th Floor en route Ballroom for Breakfast

7:25 AM ARRIVE Ballroom for Community Organization Breakfast
Met by: Assembly Speaker Willie Brown
Assemblyman Art Agnos

Advance:
Rector
Housh

Open Press Coverage
(Estimated attendance 250)

7:30 Dr. Koop Enters, Introduced and seated at the Head Table
Breakfast is Served (Dr. Koop Escorted by Mr. Agnos, mingles)

8:00 Assemblyman Agnos makes remarks about Dr. Koop's historic
visit and introduces Dr. Koop.
(Apprx. Time 5 Minutes)

8:10 Dr. Koop makes Remarks
(Apprx. Time 10 Minutes)

8:25 Dr. Koop is presented with Plaque at conclusion of
his Remarks by Tim Wolfred, San Francisco AIDS Foundation.
(Apprx. Time 10 Minutes)

8:35 Program Concludes - DEPART Ballroom en route Motorcade

8:45 Motorcade DEPARTS Holiday Inn Union Square en route
San Francisco Progress, 851 Howard Street,
(415)982-8022
(Apprx. Drive Time 10 Minutes)

Car #1
Driver: Atkinson
Bush
Henig

Car #2
Driver: Decker
Agnos
Samuels
Koop

8:50 AM Motorcade ARRIVES San Francisco Progress
(415)982-8022
Met by: Lynette Evans
9:00 AM Proceed to Editorial Board Meeting.  
(Apprx. Time 45 Minutes)

9:45 AM DEPART Conference Room en route Motorcade

9:50 AM Motorcade DEPARTS San Francisco Progress en route  
San Francisco Department Health  
(Drive Time Apprx. 10 Minutes)

Car #1  
Driver: Atkinson  
Bush  
Henig

Car #2  
Driver: Decker  
Agnos  
Samuels  
Koop

10:00 AM Motorcade ARRIVES San Francisco Department of Public  
Health, 101 Grove Street for Bay Area Researchers  
Conference on Women, Children and AIDS.  
Met by: Dr. Tim Wolfred, President,  
AIDS Foundation  
Proceed to Room 302 for AIDS Interdepartmental  
Meeting

Proceed to Room 300 For Conference

10:45 AM DEPART Room 300 en route Motorcade

10:50 AM Motorcade Departs San Francisco Department  
Public Health en route San Francisco General Hospital  
(Apprx. Drive Time 10 Minutes)

Car #1  
Driver: Atkinson  
Bush  
Henig  
Shilts

Car #2  
Decker  
Agnos  
Samuels  
Koop
Motorcade ARRIVES San Francisco General Hospital for Tour, 995 Potrero Avenue at 22nd Street
Contact: Roberta Wilson, (415)821-3038
Met by: Mayor Dianne Feinstein
Merle Sande, M.D.
Paul Volberding, M.D.
David Werdegar, M.D.

Motorcade DEPARTS San Francisco General Hospital en route San Francisco Airport
(Drive Time Apprx. 15 Minutes)

Motorcade ARRIVES San Francisco International Airport to United Airlines Red Carpet Club for Staff Time
(Apprx. Time 15 Minutes)

Proceed to Gate for United Airline Flight 70

Flight 70 DEPARTS en route Washington, D.C.
ADDRESS

BY
C. EVERETT KOOP, MD, ScD
SURGEON GENERAL
OF THE
U. S. PUBLIC HEALTH SERVICE
AND
DEPUTY ASSISTANT SECRETARY OF HEALTH
U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

PRESENTED TO THE JOINT SESSION ON AIDS
OF THE
CALIFORNIA LEGISLATURE
SACRAMENTO, CALIFORNIA
MARCH 6, 1987
MR. PRESIDENT, MR. SPEAKER... TO HOSTS, GUESTS, FRIENDS, ETC.)

IT IS AN HONOR AND A GREAT PRIVILEGE FOR ME TO ADDRESS THIS JOINT SESSION OF THE CALIFORNIA LEGISLATURE. AND WHILE YOUR INVITATION WAS ADDRESSED TO ME AND I WAS PLEASED TO ACCEPT IT-- I AM HERE TODAY -- REPRESENTING NOT JUST MYSELF BUT ALSO THE PERSONNEL OF THE U.S. PUBLIC HEALTH SERVICE. I WANT VERY MUCH TO SHARE THE HONOR OF THIS MOMENT WITH THEM, BECAUSE SO MUCH OF WHAT I HAVE TO SAY IS THE PRODUCT OF THEIR HARD WORK.

ALSO, THE RELATIONSHIP BETWEEN LOCAL AND STATE PUBLIC HEALTH OFFICERS IN CALIFORNIA AND MY COLLEAGUES IN P.H.S. IS EXCELLENT. IT HAS BEEN OVER THE YEARS AND I'M SURE IT WILL CONTINUE TO BE.

THAT'S GOOD FOR CALIFORNIA...AND IT'S GOOD FOR THE COUNTRY.
THIS IS AN UNUSUAL EVENT...AN HISTORIC EVENT...AND I AM MOVED BY THAT CONSIDERATION, ALSO. HOWEVER, AS I STAND IN THIS CHAMBER, I AM MOST MINDFUL OF THE FOLLOWING...SINGLE...OVERWHELMING AND PROFOUNDLY TRAGIC FACT:

THAT CALIFORNIANS WERE THE FIRST OF OUR CITIZENS, BACK IN JUNE OF 1981, TO BE IDENTIFIED AS BEING THE VICTIMS OF AIDS...THEY WERE AMONG THE FIRST TO DIE OF THE DISEASE...AND BEFORE THE REST OF OUR COUNTRY KNEW ABOUT -- OR TRULY UNDERSTOOD THE NATURE OF -- THIS CATASTROPHE, THE PEOPLE OF CALIFORNIA WERE ALREADY BEGINNING TO BURY THEIR DEAD.

I AM DEEPLY, DEEPLY SORRY THAT ANYONE -- HERE OR ANYWHERE IN THE WORLD -- HAS HAD TO DIE OF THIS DISEASE. AND I AM ESPECIALLY SORRY THAT THE PEOPLE OF THIS STATE HAVE HAD TO LIVE WITH THIS GRIEF THE LONGEST.
IT HASN’T BEEN 6 YEARS...YET, IT SEEMS LIKE AN ETERNITY...SINCE THOSE FIRST REPORTS CAME IN TO OUR CENTERS FOR DISEASE CONTROL IN ATLANTA. DURING THAT TIME...

WE’VE SEEN THE OFFENDING VIRUS AND WE’VE NAMED AND RENAMED IT...

WE’VE DEVELOPED A TEST TO DETERMINE IF THE VIRUS IS PRESENT IN SOMEONE’S BLOOD...

WE’VE BEEN ABLE TO GALVANIZE A LARGE, INTERNATIONAL ARMY OF BIOMEDICAL RESEARCHERS, AMONG WHOM, I MIGHT ADD, ARE MANY MEN AND WOMEN OF GENIUS WHO ARE WORKING ON THE PROBLEM IN LABORATORIES RIGHT HERE IN CALIFORNIA...

AND FINALLY, OVER THE PAST 6 YEARS, WE’VE DEVELOPED A WAY OF MONITORING THE SPREAD OF THE DISEASE SO AS TO HAVE SOME REASONABLE -- ALTHOUGH BY NO MEANS PERFECT -- BASIS UPON WHICH TO PLAN THE USE OF OUR RESOURCES TOMORROW AND FOR SOME YEARS IN THE FUTURE.
That last point is a difficult one...especially for the elected representatives of a free people. But we know that the disease of AIDS -- as it continues to spread throughout our population -- will be drawing ever more heavily upon our social and political capital, as well as our medical and financial capital.

It's a difficult challenge for Americans. But we are a good people. Through 200 years of often stormy and tumultuous history, the people of the United States have clung to this society's fundamental values of personal freedom, mutual assistance, and national unity.

Those values have withstood every test, and they are being tested again...right now...by the infiltration of this lethal disease.

But I firmly believe that those values will once more be our guides for collective action and once more we shall survive a grave threat to our health and well-being.
AND RIGHT HERE I MUST RECOGNIZE THE LEADERSHIP ALREADY DEMONSTRATED BY THE LEGISLATURE OF THE STATE OF CALIFORNIA, BY ITS GOVERNOR, GEORGE DEUKMEJIAN, AND BY THE RANK-AND-FILE PUBLIC HEALTH, MEDICAL, AND NURSING PERSONNEL THROUGHOUT THIS STATE. LIKE THE REST OF US, YOU’VE ONLY BEGUN WHAT APPEARS TO BE A LONG AND FEARFUL JOURNEY. BUT YOU’VE MADE A VERY COMMENDABLE START.

I’M THINKING IN PARTICULAR OF YOUR EARLY MOVES TO ESTABLISH MANDATORY REPORTING OF THE DISEASE AND A STATEWIDE REGISTRY OF CASES.

WITHIN A WEEK OF THE APPROVAL OF THE BLOOD TEST FOR AIDS, CALIFORNIA HAD ITS OWN EMERGENCY REGULATIONS IN PLACE TO PROTECT THE BLOOD SUPPLY. AND YOUR NETWORK OF ALTERNATIVE TEST SITES OUGHT TO BE A MODEL FOR EVERY OTHER STATE TO FOLLOW.

AND THROUGHOUT THIS TIME, YOU’VE BEEN VERY CAREFUL TO BUILD INTO THE LAW A RESPECT FOR CONFIDENTIALITY AND AN UNDERSTANDING OF THE OVERWHELMING BURDEN IT CAN BE FOR A PERSON TO LEARN THAT HE OR SHE HAS AIDS...AND WILL SOON DIE.
I'VE SAID IT MANY TIMES, THAT WE ARE FIGHTING A TERRIBLE DISEASE...WE ARE NOT FIGHTING THE PEOPLE WHO HAVE IT. AND BY YOUR ACTIONS, YOU HAVE MADE THE GOVERNMENT OF THIS STATE A STRONG ALLY IN THE CAMPAIGN TO MAKE SURE THAT AMERICANS KNOW AND RESPECT THE DIFFERENCE.

I THINK CALIFORNIA HAS DONE WELL IN THE WAY IT HAS EXPENDED ITS SOCIAL AND POLITICAL CAPITAL SO FAR ON THE ISSUE OF AIDS.

BUT IT'S ONLY BEEN A FEW YEARS...AND THIS DISEASE WILL BE A BURDEN TO US FOR THE REST OF THIS CENTURY AT LEAST.

WE NEED, THEREFORE, TO GIVE SOME THOUGHT TO THE WAY WE WILL CARE FOR THE RISING TOLL OF AIDS VICTIMS. AMONG THEM WILL BE THOSE WITH HIGH RISK BEHAVIOR -- HOMOSEXUAL AND BISEXUAL MEN AND IV DRUG ABUSERS, BUT MORE AND MORE HETEROSEXUAL VICTIMS WILL BE IDENTIFIED. MANY OF THOSE WILL HAVE BEEN UNKNOWINGLY INFECTED BY BISEXUAL MEN OR PROMISCUOUS PARTNERS.

ONE OF THE SPIN-OFFS FROM THE HIGH PROFILE OF NANCY REAGAN'S ANTI-DRUG CAMPAIGN WILL BE REDUCING THE SPREAD OF AIDS. ANYTHING THAT WILL STOP DRUG ABUSE, STOPS THE SPREAD OF THE AIDS VIRUS.
The number of babies born with AIDS will certainly rise. Some will die within the first year or two of life. We're seeing that occur already.

But other children will carry the virus and may not exhibit any symptoms of an AIDS-related illness until they are well into their school years.

Frankly, I don't think society has yet worked out how it wants to respond to the plight of these innocent young victims. Some have had to take the brunt of the anger and resentment directed at their parents...who've been better able to step out of the way.

Other children, abandoned by parents, have had to appeal through advocates for medical and social services that would have been routinely given children with any other disease.

We must generate a concern for these youngsters such as the first lady has done with her campaign against drugs.
I do not believe that these examples will prove to be the rule. But the fact that they may have happened at all is reason enough for us all to feel some pain and contrition.

And the costs in dollars and cents is also going to mount. The federal contribution this year is $416 million. About $300 million of that is research...nearly $100 million is for public education and information...and about $10 million is for patient care.

As you well know, California by itself has spent nearly half the total dollars expended by all state governments on AIDS since 1983...some $56 million so far, apportioned among patient care, public information, and research.

Some of our experts estimate that, by 1991, the total national bill for the care of AIDS patients will be $16 billion a year...or nearly twice what we’re spending this year to support all the programs of the entire U.S. public health service.

How will we apportion those costs? What will be the federal government’s share? What share is reasonable for the states to carry? And how much can we ask the individual and his or her family to pay?
COMMERCIAL INSURORS -- BOTH LIFE AND HEALTH -- HAVE RAISED QUESTIONS ABOUT COVERAGE FOR PERSONS KNOWN TO BE CARRYING THE AIDS VIRUS. . . OR WHO ARE MEMBERS OF ONE OR ANOTHER GROUPS PRACTICING HIGH RISK BEHAVIOR. WHILE WE CAN UNDERSTAND THEIR CONCERNS, FROM A STRICTLY FINANCIAL POINT OF VIEW, WE NEED TO ASK OURSELVES HOW THOSE CONCERNS FIT IN WITH GOOD PUBLIC POLICY IN GENERAL.

IN OTHER WORDS, WILL OUR DECISIONS REGARDING THE WAY WE PAY TO CARE FOR AIDS PATIENTS CONTAMINATE OUR ENTIRE SOCIAL AND POLITICAL DECISION-MAKING PROCESS ITSELF? WE MUST NOT ALLOW THAT TO HAPPEN. SUCH AN EFFECT ON OUR PUBLIC LIFE WOULD BE IN ITSELF AN "AIDS-RELATED COMPLEX."

THERE IS, OF COURSE, GENUINE ALARM THAT THE COSTS OF AIDS COULD MUSHROOM AND BANKRUPT OUR HEALTH CARE ECONOMY. MY ADVICE IS TO TAKE THE ISSUE SERIOUSLY, BUT DON'T BE FRIGHTENED INTO TAKING ACTION INCONSISTENT WITH AMERICAN VALUES.
IN ADDITION, WE MUST NOT LET FEAR SO PARALYZE US THAT WE FAIL TO DO CERTAIN SENSIBLE AND PRAGMATIC THINGS, SUCH AS DEVELOPING ALTERNATIVES TO THE HIGH-COST TERMINAL CARE THAT'S GIVEN AIDS PATIENTS IN OUR COMMUNITY AND GENERAL HOSPITALS.

IN ANY CASE, THE CENTRAL QUESTION BEFORE US TODAY...AS IT HAS BEEN FOR OVER 200 YEARS...IS STILL THIS:

HOW CAN WE LIVE SO THAT WE MAY BE A HUMANE AND CIVILIZED PEOPLE?

I CAN’T IMAGINE THIS COUNTRY EVER BECOMING FINANCIALLY BANKRUPT. BUT OUR SOCIETY -- LIKE EVERY OTHER SOCIETY IN HUMAN HISTORY -- ALWAYS RUNS THE RISK OF BECOMING MORALLY AND ETHICALLY BANKRUPT.

AND WE MUST NEVER LET THAT HAPPEN.

ORDINARILY, THE SURGEON GENERAL OF THE UNITED STATES DOESN’T WORRY ABOUT SUCH THINGS. HE OR SHE MAY BE A MORAL AND AN ETHICAL PERSON -- AND CERTAINLY EACH OF MY PREDECESSORS WAS THAT KIND OF PERSON AND I HOPE I WILL BE JUDGED TO HAVE BEEN ONE, ALSO -- BUT YOU KNOW IT’S NEVER BEEN A REQUIREMENT, AS SUCH, FOR HOLDING THIS JOB.
BUT SOME THINGS HAVE APPEARED ON MY WATCH AS YOUR SURGEON GENERAL THAT HAVE TESTED NOT ONLY MY UNDERSTANDING OF MEDICINE AND HEALTH... BUT ALSO MY UNDERSTANDING OF THE NATURE OF THE AMERICAN PEOPLE.

OVER THE PAST 5 YEARS I’VE HAD TO WRESTLE WITH THE ETHICAL ISSUES RAISED BY “BABY DOE” AND “BABY FAE”... BY LITTLE KATIE BECKETT... BY OUR ABILITY TO TRANSPANT ORGANS AND PROLONG LIFE FOR THE TERMINALLY ILL.
MY LATEST CHALLENGE WAS GIVEN TO ME A YEAR AGO, IN FEBRUARY 1986, WHEN PRESIDENT REAGAN ASKED ME TO GATHER TOGETHER ALL THE INFORMATION ON AIDS THAT WAS THEN AVAILABLE AND PUT IT INTO A PLAIN-ENGLISH REPORT TO THE AMERICAN PEOPLE.

AND THAT'S WHAT I DID FOR THE NEXT 8 MONTHS. IN THE PROCESS, I MET NOT ONLY WITH DOCTORS AND NURSES AND PUBLIC HEALTH PEOPLE, I ALSO MET WITH REPRESENTATIVES OF CONCERNED GROUPS FROM ACROSS THE SPECTRUM OF SOCIETY...

GROUPS LIKE THE NATIONAL EDUCATION ASSOCIATION AND THE NATIONAL P.T.A....

THE NATIONAL COUNCIL OF CHURCHES AND THE CHRISTIAN LIFE COMMISSION OF THE SOUTHERN BAPTIST CONVENTION...
I talked with the representatives of 26 groups in all. Most of them knew quite a bit about the health threat posed by AIDS. But what they were deeply trouble about were the moral and ethical issues raised by this disease.

Yes, we all agreed that the only real weapon we had to fight with at this time -- since we lacked a vaccine or an effective drug -- was the weapon of education.

That's where we all agreed. Where we had some differences of opinion, was the substance and the direction of that education.
EVERYBODY HAD SAID, YES, WE SHOULD TEACH ABOUT THE DANGERSPOSED
BY THE AIDS VIRUS.

MOST PEOPLE SAID, WELL, MAYBE WE SHOULD TEACH ABOUT THE METHODS
BY WHICH AIDS IS TRANSMITTED.

AND QUITE A FEW PEOPLE SAID THAT, OF COURSE, WE MIGHT POSSIBLY
TEACH YOUNG PEOPLE SOMETHING ABOUT THEIR SEXUALITY TO BEGIN WITH.

I LISTENED TO EVERYBODY AND TOOK VERY GOOD NOTES.

YOU MAY RECALL THAT MY ENTIRE REPORT IS NOT VERY LONG. AND I
ONLY DEVOTED 92 WORDS TO THE TOPIC OF EDUCATION. BUT THOSE 92 WORDS
HAVE CAPTURED MOST OF THE ATTENTION OF THE MEDIA, OF PARENTS, OF
EDUCATORS, AND OF PUBLIC OFFICIALS AT ALL LEVEL OF GOVERNMENT.

THE REASON IS CLEAR ENOUGH: THE ISSUE GOES TO THE HEART OF EACH
PERSON’S OWN SYSTEM OF MORAL AND ETHICAL VALUES...OR LACK THEREOF.
I introduced the subject in a straightforward way. I said in my report that...

"Education about AIDS should start in early elementary school and at home so that children can grow up knowing the behavior to avoid to protect themselves from exposure to the AIDS virus. The threat of AIDS can provide an opportunity for parents to instill in their children their own moral and ethical standards."

Some people were unduly alarmed by that phrase, "early elementary school." Would that include kindergarten? I'm afraid so.

I know of good, caring approaches to sex education that can be used -- and in fact are used -- in kindergarten and first grade.

However, I recognize that it's more difficult to do and, therefore, I would be willing today, some 4 months after publication, to make that single change in the report...that is, I would agree, albeit reluctantly, to take out the word "early" and just let the sentence read..."education about AIDS should start in elementary school."
I CONCLUDED THE REPORT WITH EXACTLY THE SAME THOUGHT. I SAID...

"EDUCATION CONCERNING AIDS MUST START AT THE LOWEST GRADE POSSIBLE AS PART OF ANY HEALTH AND HYGIENE PROGRAM... THERE IS NOW NO DOUBT THAT WE NEED SEX EDUCATION IN SCHOOLS AND THAT IT MUST INCLUDE INFORMATION ON HETEROSEXUAL AND HOMOSEXUAL RELATIONSHIPS. THE THREAT OF AIDS SHOULD BE SUFFICIENT TO PERMIT A SEX EDUCATION CURRICULUM WITH A HEAVY EMPHASIS ON PREVENTION OF AIDS AND OTHER SEXUALLY TRANSMITTED DISEASES."

AND I WOULD NOT CHANGE ANY OF THE WORDS IN THAT PARAGRAPH.

I AM AWARE THAT THE PEOPLE OF CALIFORNIA, THROUGH THEIR EDUCATIONAL ORGANIZATIONS, HEALTH ORGANIZATIONS, AND THROUGH THEIR REPRESENTATIVES IN LOCAL AND STATE GOVERNMENT, HAVE ENDORSED THE NEED TO BEGIN TEACHING ABOUT AIDS NO LATER THAN THE 7TH GRADE.
I think they’re absolutely right and I applaud them for being clear-headed and public-minded on the issue.

I know, also, that many school districts in this state have adopted one or another curriculum elements that introduce human sexuality and reproductive health in a positive and caring way to children in elementary grades -- generally speaking the 5th or 6th grades and that should mean that local community standards, consistent with parental values, have been taken into account which is as it should be.

And by the way, the School Health Task Force for Los Angeles County came to the same conclusion in January 1986, a good 10 months before my own report was published. In their report, the task force members recommended the general adoption of a comprehensive school health education curriculum that routinely included sexuality right along with accident prevention, nutrition, and an understanding of the cardiovascular and gastrointestinal systems.
IT'S AN EMINENTLY SENSIBLE RECOMMENDATION. AND IT IS AN ETHICALLY POSITIVE RECOMMENDATION AS WELL. IF WE ADULTS KNOW SOMETHING THAT COULD SAVE THE LIFE OF A CHILD, THEN CHILDREN HAVE A RIGHT TO THAT INFORMATION. AND WE HAVE THE OBLIGATION TO TELL THEM.

IF IT MAKES US UNCOMFORTABLE...IF IT IS AWKWARD TO DO...IF IT APPEARS TO CONFLICT WITH OTHER INFORMATION WE MIGHT HAVE, THOSE ARE PROBLEMS THAT WE HAVE TO RESOLVE IN A WAY THAT ENABLES US TO NEVERTHELESS TELL OUR CHILDREN WHAT THEY NEED TO KNOW AND HAVE A RIGHT TO KNOW.

I'M NOT SAYING IT'S EASY. BUT IT'S FAR FROM IMPOSSIBLE.

FOR EXAMPLE, I GAVE JUST THESE TWO PRECAUTIONS IN MY REPORT. THE FIRST ONE IS SIMPLE ENOUGH. IT ADVISES YOU TO...

FIND SOMEONE WHO IS WORTHY OF YOUR RESPECT AND YOUR LOVE...GIVE THAT PERSON BOTH...AND STAY FAITHFUL TO HIM OR HER.
IN OTHER WORDS, SHORT OF TOTAL ABSTINENCE, THE BEST DEFENSE AGAINST AIDS IS TO MAINTAIN A FAITHFUL, MONOGAMOUS RELATIONSHIP IN WHICH YOU HAVE ONLY ONE CONTINUING SEXUAL PARTNER...AND THAT PERSON IS AS FAITHFUL AS YOU ARE.

MY SECOND MESSAGE IS FOR PEOPLE WHO DON'T YET HAVE A FAITHFUL MONOGAMOUS RELATIONSHIP FOR WHATEVER REASON. THAT MESSAGE IS...

CAUTION: IT'S IMPORTANT THAT YOU KNOW WITH ABSOLUTE CERTAINTY THAT NEITHER YOU NOR YOUR PARTNER IS CARRYING THE AIDS VIRUS. IF YOU'RE NOT ABSOLUTELY CERTAIN, THEN YOU MUST TAKE PRECAUTIONS. AND THE BEST ONE AVAILABLE -- THOUGH FAR FROM PERFECT -- IS TO USE A CONDOM FROM START TO FINISH.
FROM MY VIEWPOINT, AS A PUBLIC HEALTH OFFICER, I TELL PEOPLE THAT WHEN THEY HAVE SEX WITH SOMEONE, THEY'RE ALSO HAVING SEX WITH EVERYONE ELSE WITH WHOM THAT PERSON HAS EVER HAD SEX. NATURALLY, IF THE "EVERYONE ELSE" IS ONLY YOU...YOU'RE VERY WELL PROTECTED FROM DISEASE ...AND FROM A LOT OF OTHER UNPLEASANT SURPRISES AS WELL.

THIS ALL SEEMS TO BE INFORMATION THAT IS CLEAR ENOUGH AND STRAIGHTFORWARD ENOUGH TO TELL CHILDREN. THERE'S NOTHING TERRIBLY ESOTERIC ABOUT IT. YET, MANY ADULTS -- PARENTS AND TEACHERS ALIKE -- ARE HAVING TROUBLE COMING TO TERMS WITH IT ALL.

THE MORE I’VE THOUGHT ABOUT THIS PHENOMENON, THE MORE I’VE COME TO BELIEVE THAT THE DIFFICULTY IS NOT IN THE FACT THEMSELVES CONCERNING SEXUALITY, HUMAN REPRODUCTION, AND AIDS. THE DIFFICULTY IS IN THE SIGNIFICANCE OF THOSE FACTS RELATIVE TO THE TOTALITY OF A SENSITIVE AND AFFIRMATIVE HUMAN RELATIONSHIP.
SUCH A RELATIONSHIP WILL INCLUDE SOME FULFILLING SEXUAL ACTIVITY, BUT IT IS NOT DEFINED ONLY BY THAT ACTIVITY. THERE'S MUCH MORE TO A LOVING, CARING, RESPECTFUL, AND TOLERANT HUMAN RELATIONSHIP THAN JUST "GOOD SEX." A RELATIONSHIP DEVOID OF LOVE AND RESPONSIBILITY IS LIKE A PIECE OF PIE THAT'S ALL CRUST AND NO FILLING. AND YOUNG PEOPLE OUGHT TO BE ADVISED OF THAT.

NOVELISTS CALL IT "TRUE LOVE." SOCIOLOGISTS CALL IT "MARITAL FIDELITY." THE SURGEON GENERAL CALLS IT "MONOGAMY." BUT WHATEVER YOU CALL IT, WE ALL WANT THAT WELL-ROUNDED, BALANCED, LOVING, AND FULLY CONSIDERATE RELATIONSHIP...A RELATIONSHIP THAT'S ENRICHED BY SEX, NOT OVERWHELMED BY IT OR DEVOID OF IT EITHER.

SUCH A RELATIONSHIP IS AN IDEAL...BUT "REAL LIFE" ISN'T ALWAYS LIKE THAT. IT'S IMPERFECT...IT'S GIVE-AND-TAKE.
GROWN-UPS KNOW AND COME TO ACCEPT HUMAN IMPERFECTION. BUT CHILDREN DON'T...AND WON'T.

WITHOUT A COMPASSIONATE UNDERSTANDING OF THE IMPERFECT NATURE OF MANY HUMAN RELATIONSHIPS, A CHILD'S EDUCATION WILL BE...ITSELF...VERY IMPERFECT.

SO IF PARENTS ARE TO EDUCATE THEIR CHILDREN ABOUT HUMAN RELATIONSHIPS -- SEXUAL AND OTHERWISE -- THEY MUST FIRST UNDERSTAND AND ACCEPT THE NATURE OF THEIR OWN. FOR MANY, THAT'S HARD TO DO.

PARENTS -- AND ADULTS IN GENERAL -- ARE NOT VERY GOOD ABOUT TALKING TO EACH OTHER ABOUT THEIR SEXUALITY. THEY FEEL FRUSTRATED, GUILTY, AND EVEN ANGRY BECAUSE THEY ARE UNABLE TO DO THE THING THAT THEY KNOW -- INTELLECTUALLY AND EMOTIONALLY -- THEY SHOULD DO.

BUT THEY CAN'T.
IS IT ANY WONDER, THEN, THAT MANY PARENTS HAVE DIFFICULTY TELLING CHILDREN ABOUT THE FULL-DIMENSIONAL NATURE OF AN IDEAL HUMAN RELATIONSHIP.

NEVERTHELESSS, I WANT PARENTS TO TRY. I WANT PARENTS TO DO THIS WITH COMPASSION...WITH RESPECT AND WITH LOVE...AND WITH SOME UNDERSTANDING NOT JUST OF THE CHILD WHO'S LISTENING...BUT ALSO OF THE ADULT WHO IS SPEAKING.

STILL, IT REMAINS AS MY SINCEREST WISH THAT THE PARENTS OF THIS COUNTRY WILL BE THE PRIMARY TEACHERS OF SEX AND HUMAN RELATIONS TO THE CHILDREN OF THIS COUNTRY.

I SAY THAT, KNOWING FULL WELL THAT MANY PARENTS SIMPLY CAN'T DO IT. BUT THE TASK SHOULD NOT THEREFORE BE LEFT, BY DEFAULT, TO THE MOVIES...TO TELEVISION...OR TO THE STREET-CORNER. WE CAN'T DO THAT, AND STILL PROTECT THE MILLIONS OF YOUNG LIVES THAT ARE AT RISK OF AIDS.
AND FOR ME, THAT'S THE COMPELLING REASON WHY OUR SCHOOLS, CHURCHES, SYNAGOGUES, AND OTHER COMMUNITY INSTITUTIONS MUST DO WHATEVER POSSIBLE TO PROVIDE OUR CHILDREN WITH THE BEST AVAILABLE INFORMATION...PHYSICAL, SEXUAL, EMOTIONAL, AND PSYCHOLOGICAL...TO HELP THEM NEGOTIATE THEIR OWN WAY THROUGH THE HUMAN CONDITION.

YOU, AS RESPONSIBLE LEGISLATORS, ARE BEING CALLED UPON TO CONTRIBUTE TO THAT PROCESS, ALSO. AND I KNOW THAT THIS LEGISLATURE IS INDEED WRITING SUCH A RECORD IN THE INDELIBLE INKS OF COMPASSION AND DUTY.

I'VE DELIVERED THIS MESSAGE -- AND VARIATIONS OF IT -- MANY TIMES IN THE PAST FEW MONTHS. BUT IT DOESN'T GET ANY EASIER.

IT'S ESSENTIALLY A GRIM MESSAGE AND I GUESS I'M SOMETHING OF A GRIM COURIER.

MY ONLY HOPE IS THAT EVERY AMERICAN WHO HEARS OR READS MY MESSAGE, WILL BELIEVE IT AND DO HIS OR HER PART TO STOP THE SPREAD OF AIDS...TO PROTECT AND SAVE THE LIVES OF PEOPLE AT RISK, INCLUDING AND ESPECIALLY OUR UNSUSPECTING YOUNG PEOPLE...AND THAT THEY WILL HELP RETURN SEXUALITY BACK TO ITS RIGHTFUL PLACE IN THE SPECTRUM OF HUMAN EXPERIENCE: HAVE IT AGAIN BE A PART OF THE TOTAL COMPLEX OF HUMAN, CARING, INTERPERSONAL RELATIONS.
SUCH RELATIONS, IN MY BOOK ANYWAY, ARE KNOWN AS "TRUE LOVE."

WHICH LEADS ME TO MY FINAL WORD. IT'S NOT MINE REALLY. IT'S THE LAST SENTENCE OF THE BRIDGE OF SAN LUIS REY, THE LITTLE NOVEL WRITTEN BY THE LATE THORNTON WILDER, ONE OF OUR GREATEST NOVELISTS AND PLAYWRIGHTS.

WILDER CONCLUDED THAT NOVEL BY OBSERVING...

"THERE IS A LAND OF THE LIVING AND A LAND OF THE DEAD AND THE ONLY BRIDGE IS LOVE...THE ONLY SURVIVAL, THE ONLY MEANING."

THANK YOU.

# # # # #
Diane Abbitt, Esq.
Co-Chair
No on 64 Campaign
c/o Abbitt & Bennett
12121 Wilshire Boulevard, Suite 1100
Los Angeles, California 90025

Mr. Larry Sprenger
Treasurer
No on 64 Campaign
7985 Santa Monica Boulevard, Suite 109-251
Los Angeles, California 90046-5112

Re: No on 64 Campaign

Dear Diane and Larry:

The purpose of this letter is to outline several outstanding matters for your immediate attention relative to the No on 64 Campaign.

CAMPAIGN STATEMENTS

On February 2, 1987, this office filed the No on 64 Recipient Committee Campaign Statement on your behalf covering the period October 19, 1986 through December 31, 1986, based on information supplied by John Brown of the Abbitt & Bennett law firm. A copy of the report was sent to Larry in care of Abbitt & Bennett. Because Larry had advised us that he would be out of town during the month of January and unable to sign the campaign statement as treasurer, I executed the campaign statement as assistant treasurer. The Political Reform Act of 1974, as amended, requires the signature of the treasurer be on each campaign statement. Enclosed please find FPPC Form 405, the amending report for the campaign statement to identify your signature on the report. Larry, please execute Form 405 and return it to me for filing.

The December 31, 1986 balance was $5,273. The committee must continue to file campaign statements until all debts are extinguished by payment to the payees or resolution to
inform the payees that payment will never be made or surplus funds, if any, have been spent. In 1987, the committee will be required to file semiannually. Once all activity is completed, the committee must file a Statement of Termination (FPPC Form 415) which will terminate its filing responsibilities.

POST ELECTION AUDIT

As we advised you during the course of the campaign, all statewide ballot measures are required to be audited by the Political Reform Audit Division of the Franchise Tax Board. This audit will take place sometime in late 1987 or early 1988. This audit will be conducted to insure the provisions of the Political Reform Act have been complied with and proper accounting procedures and full disclosure has been made on the campaign statements.

In October, 1986, we discussed with you the eventuality of this audit. We advised you that we would request an advance payment to our trust account in the amount of $12,500 to prepare records and undertake the responsibility for the audit. To date, the committee has not authorized us to take responsibility for the audit nor has any payment been made. We assume you do not wish us to conduct the audit of the campaign statements. Please affirmatively advise us so we may transfer the No on 64 records in our possession to you for audit purposes.

TAX EXEMPT APPLICATION

During the course of the campaign, we advised the committee that in order to protect its assets, under federal and state tax laws, it would be necessary for the organization to affirmatively seek application as a tax exempt organization under Internal Revenue Code Section 501(c)(4). We were initially authorized to proceed with this process by Bruce Decker and then by David Mixner, and we filed Articles of Incorporation for the campaign committee under the name Center for Health Policy and Education (copy of Articles of Incorporation attached). We repeatedly asked David to provide us with a list of names of those who would constitute a Board of Directors so that we could proceed with the application in a timely fashion. The application has been completed in draft with the exception of the names of the Board of Directors. Additionally, the draft Bylaws which we provided David Mixner in September, 1986, have never been formally approved. Attached is a copy of those draft Bylaws which must be approved and must be included with the Tax Exempt Application. There are a number of matters which must be attended to in the establishment of the corporation and an agenda is included outlining those items. We suggest the meeting of
members of the Board be done by conference telephone to avoid additional cost to the committee.

OUTSTANDING BALANCE OWED TO NIELSEN, HODGSON, PARRINELLO & MUELLER

In addition to the retention of our services regarding the post election audit and the proposed amount for those services, which is discretionary on your part, there still remains an outstanding balance of $5,164.64 which is owed to this firm for work completed through November, 1986. In addition, during the months of December and January, fees in the amount of $3,387 and expenses in the amount of $6,138.36 (statement enclosed) have accrued for a total amount owed to our firm of $14,690. As you may recall, this firm has already written off significant fees against actual time spent during the campaign and believe these fees and costs currently owed are due and payable.

FUTURE SERVICES

It appears from past correspondence that the committee may not desire our legal services to wrap up the committee and corporation. If you will be using other legal counsel to represent you with these activities, please let us know and we will send our files to such attorney.

Although we have discussed with Larry his obligations under the Political Reform Act of 1974, as amended, it is important to reiterate his duties and obligations as treasurer of the committee. Attached please find a copy of the Fair Political Practices Commission Regulation 18427 which outlines the duties of treasurer with respect to campaign statements.

We look forward from hearing from you as soon as possible.

Very truly yours,

Sherry C. Levit

SCL:ryb
Enclosure
cc: David Mixner
      Harry Britt
      Bruce B. Decker
Hon. March Fong Eu  
Secretary of State  
P.O. Box 1467  
Sacramento, CA 95807

February 17, 1987

Dear Madam Eu and Other Filing Officers:

Enclosed herewith please find the original and one copy of the following for NO ON 64

for the period 10-19-86 through 12-31-86:

- Form 405
- Form 415
- Form 420
- Form 425
- Amendment to the above
- Report sent with Certificate of Mailing
- Other

Please endorse this transmittal letter as acknowledgment of receipt and return it in the envelope provided.

Sincerely,

NIELSEN, HODGSON, PARRINELLO & MUELLER

cc: San Francisco County (2)  
Los Angeles County (2)
AMENDMENT TO CAMPAIGN DISCLOSURE STATEMENT

For use by persons amending statements filed pursuant to Government Code Section 84200—84217. This form must be filed with all filing officers who received the statement being amended.

(TYPE OR PRINT IN INK)

I. The information required in Section I must correspond to the information provided on the campaign statement.

NAME OF FILER:

NO ON 64

ADDRESS OF FILER: NO. AND STREET CITY STATE ZIP CODE AREA CODE PHONE NUMBER

3670 Wilshire Blvd., 3rd Floor, Los Angeles, CA, 90010 (213) 738-8240

NAME OF TREASURER (IF APPLICABLE):

Larry Sprenger

PERMANENT ADDRESS OF TREASURER (IF APPLICABLE): NO. AND STREET CITY STATE ZIP CODE AREA CODE PHONE NUMBER

Same as above

II. The following information amends campaign disclosure statement, Form No. 461, Executed on 2/2/87 for the period 10-19-86 to 12-31-86.

III. The amended information affects items on the:

[X] Front Page  [ ] Summary  [ ] Schedule(s)

IV. Describe the changes below. Include in detail all information you wish to become a part of your official campaign statement.

Signature of Sherry C. Levit, Assistant Treasurer replaced by signature of Larry Sprenger, Treasurer.

V. Reason for amendment:

Treasurer's signature was unavailable at time of filing.

Include additional information on reverse side or on appropriately labeled continuation sheets. (Number of pages attached 1)

C  VERIFICATION

I declare under penalty of perjury that to the best of my knowledge this statement and its schedules are true, correct and complete and that I have used all reasonable diligence in their preparation.

D  Executed on 3/ /87 at Los Angeles, CA. by

E  (DATE) (CITY AND STATE)  (SIGNATURE OF TREASURER)

F  A candidate or officeholder who controls a committee must also verify the campaign statement.

I declare under penalty of perjury that to the best of my knowledge this statement and its schedules are true, correct and complete and the treasurer of this committee has used all reasonable diligence in the preparation of this statement and its schedules.

Executed on n/a at n/a by n/a

(SIGNATURE OF CANDIDATE OR OFFICEHOLDER)

For information required to be provided to you pursuant to the Information Practices Act of 1977, see "Information Manual on Campaign Disclosure Provisions."
RECIPIENT COMMITTEE
CAMPAIGN STATEMENT
(Government Code Sections 84200-84217)
Type or Print in Ink

Statement covers period 10-19-86 through 12-31-86

CHECK ONE OF THE FOLLOWING BOXES TO INDICATE THE TYPE OF STATEMENT BEING FILED.
☐ 1ST SEMI-ANNUAL STATEMENT
☐ 2ND SEMI-ANNUAL STATEMENT
☐ SUPPLEMENTAL PRE-ELECTION STATEMENT
☐ 1ST PRE-ELECTION STATEMENT
☐ 2ND PRE-ELECTION STATEMENT
☐ BALLOT MEASURE QUALIFICATION STATEMENT

NAME OF COMMITTEE: NO ON 64
I.D. NUMBER: 861373

ADDRESS OF COMMITTEE: NO. AND STREET CITY STATE ZIP CODE AREA CODE/PHONE NUMBER
3670 Wilshire Blvd, 3rd Flr., Los Angeles, CA. 90010 (213) 738-8240

NAME OF TREASURER: Larry Sprenger

PERMANENT ADDRESS OF TREASURER: NO. AND STREET CITY STATE ZIP CODE AREA CODE/BUSINESS PHONE NUMBER
Same as above

II IS THIS A SPONSORED COMMITTEE? (See definition on reverse) ☐ YES ☒ NO

III IS THIS A CONTROLLED COMMITTEE? (See definition on reverse) ☒ YES (If yes, candidate or officeholder must verify the campaign statement) ☐ NO
DATE OF ELECTION (Mo., Day, Yr.) (If applicable): November 4, 1986

TOTAL PAGES 273

IV CANDIDATES OR STATE MEASURE PROPONENTS CONTROLLING THIS COMMITTEE; CANDIDATES, STATE MEASURE PROPONENTS OR COMMITTEES WITH WHICH THIS COMMITTEE ACTS JOINTLY. NOTE: If this committee is controlled by more than one candidate, the name of each controlling candidate must be listed below.

<table>
<thead>
<tr>
<th>NAME OF CANDIDATE, STATE MEASURE PROPONENT OR COMMITTEE</th>
<th>IF AFFILIATED WITH ANOTHER COMMITTEE, IDENTIFICATION NUMBER OF COMMITTEE OR TREASURER'S NAME AND PERMANENT STREET ADDRESS</th>
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<td>n/a</td>
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V CANDIDATE(S) OR MEASURE(S) FOR WHICH THIS COMMITTEE IS PRIMARILY FORMED:

<table>
<thead>
<tr>
<th>NAME OF CANDIDATE OR MEASURE</th>
<th>SUPPORT</th>
<th>OPPOSE</th>
<th>OFFICE OF CANDIDATE</th>
<th>OR BALLOT MEASURE NUMBER OR LETTER AND JURISDICTION</th>
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</thead>
<tbody>
<tr>
<td>Acquired Immune Deficiency</td>
<td>XXX</td>
<td></td>
<td></td>
<td>Proposition 64 Statewide Ballot</td>
</tr>
<tr>
<td>Syndrome Initiative Statute</td>
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</tbody>
</table>

VERIFICATION

I have used all reasonable diligence in preparing this Statement. I have reviewed this Statement and to the best of my knowledge the information contained herein and in the attached schedules is true and complete. I certify under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on 3/7/87 at Los Angeles, CA. by Larry Sprenger, Treasurer

A candidate or officeholder who controls a committee must also verify the campaign statement.

I have used all reasonable diligence and to the best of my knowledge the treasurer has used all reasonable diligence in preparing this statement. I have reviewed the Statement and to the best of my knowledge the information contained herein and in the attached schedules is true and complete. I certify under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on n/a at n/a by n/a
I, MARCH FONG EU, Secretary of State of the State of California, hereby certify:

That the annexed transcript has been compared with the record on file in this office, of which it purports to be a copy, and that same is full, true and correct.

IN WITNESS WHEREOF, I execute this certificate and affix the Great Seal of the State of California this JUN 18 1986

March Fong Eu
Secretary of State
ARTICLES OF INCORPORATION

OF

CENTER FOR HEALTH POLICY AND EDUCATION

I

The name of this corporation is Center for Health Policy and Education.

II

A. This corporation is a nonprofit mutual benefit corporation organized under the Nonprofit Mutual Benefit Corporation Law. The purpose of this corporation is to engage in any lawful act or activity for which a corporation may be organized under such law.

B. The specific purpose of this corporation is to promote the social welfare in the State of California through the following purposes:

(1) The corporation shall promote civic betterment and social improvement by (a) promoting educational and research activities consistent with the purposes of medical and constitutional interests; and b) educating the public concerning a balanced approach to combatting the spread of acquired immune deficiency syndrome and related health concerns.

(2) The corporation will seek to promote these objectives through direct and indirect communication with the public concerning ballot measures, legislation, administrative regulations and judicial decisions.

(3) In order to accomplish these objectives, the corporation shall sponsor educational programs through public forums, panel lectures, radio, television, direct mail and other similar activities.

III

The name and address in the State of California of this corporation's initial agent for service of process is:

Kirk Alan Pessner
650 California Street, Suite 2650
San Francisco, CA 94108
IV

A. This corporation is organized and operated exclusively for social welfare purposes within the meaning of section 501(c)(4) of the Internal Revenue Code.

B. Notwithstanding any other provision of these Articles, the corporation shall not carry on any other activities not permitted to be carried on by a corporation exempt from federal income tax under section 501(c)(4) of the Internal Revenue Code.

C. Notwithstanding any of the above statements of purposes and powers, this corporation shall not, except to an insubstantial degree, engage in any activities or exercise any powers that are not in furtherance of the specific purpose of this corporation.

V

The property of this corporation is irrevocably dedicated to social welfare purposes and no part of the net income or assets of this corporation shall ever inure to the benefit of any director, officer or member thereof, or to the benefit of any private person.

VI

Upon the dissolution or winding up of the corporation, its assets remaining after payment, or provision for payment, of all debts and liabilities of this corporation, shall be distributed to a nonprofit fund, foundation or corporation which has established its tax exempt status under section 501(c)(4) of the Internal Revenue Code.

DATED: June 16, 1986

Kirk Alan Pessner

I hereby declare that I am the person who executed the foregoing Articles of Incorporation, which execution is my act and deed.

Kirk Alan Pessner
BYLAWS OF
CENTER FOR HEALTH POLICY AND EDUCATION

A California Nonprofit Corporation

ARTICLE I
NAME, OFFICE AND PURPOSES

The name of this corporation is and shall be CENTER FOR HEALTH POLICY AND EDUCATION (hereinafter referred to as "the corporation").

The principal office of the corporation shall be located in the City and County of San Francisco. The principal office and additional offices may be located in such other places as may be determined from time to time by the Board of Directors.

The purposes of the Corporation shall be:

A. To engage in any lawful act or activity for which a corporation may be organized under such law.

B. To promote the social welfare in the State of California through the following purposes:

(1) The corporation shall promote civic betterment and social improvement by (a) promoting educational and research activities consistent with the purposes of medical and constitutional interests; and b) educating the public concerning a balanced approach to combatting the spread of acquired immune deficiency syndrome and related health concerns.

(2) The corporation will seek to promote these objectives through direct and indirect communication with
the public concerning ballot measures, legislation, administrative regulations and judicial decisions.

(3) In order to accomplish these objectives, the corporation shall sponsor educational programs through public forums, panel lectures, radio, television, direct mail and other similar activities.

ARTICLE II
DISSOLUTION

This corporation is not organized, nor shall it be operated, for pecuniary gain or profit, and it does not contemplate the distribution of gains, profits, or dividends to its members and is organized solely for nonprofit purposes. No part of the profits or net income of this corporation shall ever inure to the benefit of any director, officer, or member thereof, or to any individual. Upon the dissolution or winding up of the corporation, its assets remaining after payment of, or provision for payment of, all debts and liabilities of this corporation, shall be distributed to a nonprofit fund, foundation, or corporation which has established its tax exempt status under section 501(c)(4) of the Internal Revenue Code.

ARTICLE III
MEMBERS

Section 1. Membership and Voting Rights.

The corporation shall have no members. Any references herein to "members" are to the Board of Directors. Each Director shall be entitled to one vote.
ARTICLE IV
BOARD OF DIRECTORS

Section 1. General Powers.
Subject to the limitations of these Bylaws, the Articles of Incorporation, and the laws of California, the affairs of the corporation shall be managed, and all corporate powers shall be exercised by, or under the direction of, a Board of Directors.

Section 2. Number, Tenure and Qualifications.
The corporation shall have not less than three (3) nor more than thirteen (13) directors, who shall be unrelated persons. The exact number within the specified limits, shall be fixed by the Board which shall elect or appoint all directors. Each director shall hold office until the next annual meeting of the Board of Directors, which shall elect all directors, or until a successor shall have been elected. The Board may accept a resignation prior to filling that vacancy with a successor. The first directors shall be those individuals who organized the corporation.

Section 3. Regular Meeting.
Regular meetings of the Board shall be held without other notice than these Bylaws at any place designated from time to time by resolution of the Board.

Section 4. Special Meetings.
Special meetings of the Board of Directors may be called by or at the request of the Chairman, the Secretary or a majority of the actual directors. Unless approved by the Chairman for an alternative location, the place will be the office of the corporation.
Section 5.  Notice of Special Meetings.

Notice of any special meeting of the Board shall be given at least two (2) days prior thereto either personally or by telephone or telegram or four (4) days' notice by first-class mail, subject to waiver of notice as provided in Article V of these Bylaws. All such notices shall be given or sent to the director's address or telephone number as shown on the records of the corporation. The attendance of a director at any special meeting shall also constitute a waiver of notice of such meeting.

Section 6.  Quorum.

A majority of the directors holding office at any point in time shall constitute a quorum. The directors may continue to transact business during a meeting at which a quorum is initially present, notwithstanding the withdrawal of directors, if any action is approved by at least a majority of the required quorum for that meeting.

Section 7.  Manner of Acting.

Action by the Board shall be by a majority of the directors present at a meeting duly held at which a quorum is present unless a greater number is required by law.

Section 8.  Action Without a Meeting.

Any action required or permitted to be taken by the Board of Directors may be taken without a meeting if all members of the Board shall individually or collectively consent in writing to such action. Such action by written consent shall have the same force and effect as a unanimous vote of the Board. Such written consent or consents shall be filed with the minutes of the proceedings of the Board.
Section 9.  Participation in Meetings by Means of Conference Telephone.

Members of the Board may participate in a meeting of the Board by means of a conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

Section 10.  Vacancies.

Any vacancy occurring in the Board of Directors and any directorship to be filled by reason of an increase in the number of directors shall be filled by a majority of the remaining directors, though less than a quorum, or a sole remaining director. A director elected to fill a vacancy shall hold office during the unexpired term of his or her predecessor in office and until his or her successor is elected.

Section 11.  Compensation.

Directors shall not receive compensation for their services as members of the Board. Nothing herein shall be construed to preclude any director from serving the corporation in any other capacity as an officer, agent, employee, or otherwise, and receiving compensation therefor or from receiving reimbursement for reasonable expenses, as may be fixed or determined by resolution of the Board.

Section 12.  No Interest in Assets.

No director shall possess any property right in or to the property of the corporation. In the event the corporation owns or holds any property upon its dissolution and winding up, after paying or adequately providing for its debts and obligations,
the directors shall dispose of the remaining property in accordance with the provisions of the Articles of Incorporation and these Bylaws.

ARTICLE V
COMMITTEES

Section 1. Executive Committee.

At such time that the size of the Board of Directors exceeds three (3) members, the Board shall create an Executive Committee. The Executive Committee shall consist of the Chairman, the Secretary, the Treasurer, and two (2) at-large members chosen from the remaining directors.

Section 2. Duties of the Executive Committee.

The Executive Committee shall have the power to approve all educational plans, budgets and creative executions. The Executive Committee shall be responsible for such other specific duties as may be assigned to it by the Board of Directors. The Executive Committee shall report all actions taken to the next meeting of the Board of Directors. A majority of the members of the Executive Committee present at a meeting shall constitute a quorum. The Chairman of the Executive Committee shall be the Chairman of the Board of Directors.

ARTICLE VI
OFFICERS

Section 1. Officers.

The officers of the corporation shall be a Chairman, a Secretary, a Chief Fiscal Officer who shall be the Treasurer, and
such other officers as may be elected to offices created by the Board. Officers shall have powers and duties as specified herein and as may be additionally prescribed by the Board. One person may hold two or more offices, except one person shall not be both Chairman and Secretary, or Chairman and Chief Fiscal Officer but no officer shall execute, acknowledge, or verify any instrument in more than one capacity, if such instrument is required to be executed, acknowledged, or verified by two or more officers.

Section 2. Election and Term of Office.

The officers of the corporation shall be elected annually by the Board of Directors at the regular annual meeting of the Board of Directors. If the election of any officer shall not be held at such meeting, such election shall be held as soon thereafter as conveniently possible. New offices may be created and filled, and vacancies may be filled, at any meeting of the Board of Directors. Each officer shall hold office until a successor shall have been elected, unless otherwise removed.

Section 3. Removal.

Subject to the rights, if any, of an officer under any contract of employment, any officer elected or appointed by the Board may be removed by the Board with or without cause, whenever in its judgment the best interests of the corporation would be served thereby.

Section 4. Resignation.

Any officer may resign at any time by giving written notice to the corporation. Any resignation shall take effect at the date of the receipt of that notice or at any later time specified in that notice; and, unless otherwise specified in that
notice, the acceptance of the resignation shall not be necessary to make it effective. Any resignation is without prejudice to the rights, if any, of the corporation under any contract to which the officer is a party.

Section 5. Chairman.

The Chairman shall, if present, preside at all meetings of the corporation. He shall serve as Chief Operating Officer and have general supervision, direction and control of the business of the corporation.

Section 6. Secretary.

The Secretary shall be responsible for the mailing of notices and see to the proper recording of proceedings of meetings of the corporation.

Section 7. Treasurer.

The Treasurer shall be responsible for the corporation's funds and financial records. The Treasurer shall collect and report, or supervise collection and reporting, of all income and expenditures, shall establish proper accounting procedures for the handling of the corporation's funds, and shall be responsible for the keeping of the funds in such banks as approved by the Board. The Treasurer shall report on the financial condition of the corporation at meetings of the Board and at other times when called upon by the Chairman.

At the end of each fiscal year, the Treasurer shall prepare, or cause to be prepared, an annual financial report which shall, if required by the Board, be reviewed by a certified public accountant. At the expiration of the Treasurer's term of office, or upon removal, the Treasurer shall immediately deliver
over to the person designated by the Chairman all books, money
and other property in his or her charge.

ARTICLE VII

INDEMNIFICATION OF DIRECTORS, OFFICERS

AND OTHER CORPORATE AGENTS

The corporation may, to the extent allowed by appli-
cable state and federal laws, indemnify and hold harmless its
officers, directors, agents and employees from and against any
and all claims, actions, proceedings, whether threatened, pending
or completed, brought by reason of their respective position with
or relationships to the corporation, including, without limita-
tion, all reasonable attorneys' fees, costs and other expenses
incurred in establishing a right to indemnification under this
Article VII.

Section 1. Definitions.

For the purposes of this Article VII, "agent" means any
person who is or was a director, officer, employee, or other
agent of the corporation, or is or was serving at the request of
the corporation as a director, officer, employee, or agent of
another trust, or other enterprise, "proceeding" means any
threatened, pending, or completed action or proceeding, whether
civil, criminal, administrative, or investigative; and "expenses"
includes without limitation attorneys' fees and any expenses of
establishing a right to indemnification under Section 4 or 5(b)
of this Article VII.
Section 2. Indemnification in Actions by Third Parties.

The corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any proceeding (other than an action by or in the right of the corporation to procure a judgment in its favor, an action brought under section 5233 of the California Nonprofit Public Benefit Corporation Law, by reason of the fact that such person is or was an agent of the corporation, against expenses, judgments, fines, settlements, and other amounts actually and reasonably incurred in connection with such proceeding if such person acted in good faith and in a manner such person reasonably believed to be in the best interests of the corporation and, in the case of a criminal proceeding had no reasonable cause to believe the conduct of such person was unlawful. The termination of any proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in the best interests of the corporation or that the person had reasonable cause to believe that the person's conduct was unlawful.

Section 3. Indemnification in Actions by or in the Right of the Corporation.

The corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action by or in the right of the corporation, or brought under section 5233 of the California Nonprofit Public Benefit Corporation Law, to procure a
judgment in its favor by reason of the fact that such person is or was an agent of the corporation, against expenses actually and reasonably incurred by such person in connection with the defense or settlement of such action if such person acted in good faith, in a manner such person believed to be in the best interests of the corporation and with such care, including reasonable inquiry, as an ordinarily prudent person in a like position would use under similar circumstances. No indemnification shall be made under this Section 3.

(a) In respect of any claim, issue, or matter as to which such person shall have been adjudged to be liable to the corporation in the performance of such person's duty to the corporation, unless and only to the extent that the court in which such proceeding is or was pending shall determine upon application that, in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for the expenses which such court shall determine;

(b) Of amounts paid in settling or otherwise disposing of a threatened or pending action, with or without court approval; or

(c) Of expenses incurred in defending a threatened or pending action which is settled or otherwise disposed of without court approval, unless such action concerns assets held in charitable trust and is settled with the approval of the Attorney General.

Section 4. Indemnification Against Expenses.

To the extent that an agent of the corporation has been successful on the merits in defense of any proceeding referred to
in Section 2 or 3 of this Article VII, or in defense of any claim, issue, or matter therein, the agent shall be indemnified against expenses actually and reasonably incurred by the agent in connection therewith.

Section 5. Required Determinations.

Except as provided in Section 4 of this Article VII, any indemnification under this Article VII shall be made by the corporation only if authorized in the specific case, upon a determination that indemnification of the agent is proper in the circumstances because the agent has met the applicable standard of conduct set forth in Section 2 or 3 of this Article VII, by:

(a) A majority vote of a quorum consisting of directors who are not parties to such proceeding; or

(b) The court in which such proceeding is or was pending upon application made by the corporation or the agent or the attorney or other person rendering services in connection with the defense, whether or not such application by the agent, attorney, or other person is opposed by the corporation.

Section 6. Advance of Expenses.

Expenses incurred in defending any proceeding may be advanced by the corporation prior to the final disposition of such proceeding upon receipt of an undertaking by or on behalf of the agent to repay such amount unless it shall be determined ultimately that the agent is entitled to be indemnified as authorized in this Article VII.

Section 7. Other Indemnification.

No provision made by the corporation to indemnify its directors or officers for the defense of any proceeding, whether
contained in the Articles, Bylaws, a resolution of the directors, an agreement, or otherwise, shall be valid unless consistent with this Article VII. Nothing contained in this Article VII shall affect any right to indemnification to which persons other than such directors and officers may be entitled by contract or otherwise.

Section 8. Forms of Indemnification Not Permitted.

No indemnification or advance shall be made under this Article VII, except as provided in Section 4 or 5(b), in any circumstances where it appears:

(a) That it would be inconsistent with a provision of the Articles, these Bylaws, a resolution of the directors, or an agreement in effect at the time of accrual of the alleged cause of action asserted in the proceeding in which the expenses were incurred or other amounts were paid, which prohibits or otherwise limits indemnification; or

(b) That it would be inconsistent with any condition expressly imposed by a court in approving a settlement.

Section 9. Insurance.

The corporation shall have power to purchase and maintain insurance on behalf of any agent of the corporation against any liability asserted against or incurred by the agent in such capacity or arising out of the agent's status as such whether or not the corporation would have the power to indemnify the agent against such liability under the provisions of this Article VII.
ARTICLE VIII
FISCAL YEAR

The fiscal year of this corporation shall be July 1 through June 30.

ARTICLE IX
BOOKS AND RECORDS

The corporation shall keep at its principal office correct and complete books and records of account, written minutes of the proceedings of its meetings, the original or a copy of the Articles and Bylaws as amended to date, and a record giving the names and addresses of all Directors.

ARTICLE X
WAIVER OF NOTICE

Whenever any notice is required to be given under the provisions of the California Nonprofit Corporation Law or under the provisions of the Articles of Incorporation or by the Bylaws of the corporation, a written waiver thereof, signed by the person or persons entitled to such notice, whether before or after the time stated therein, which is made a part of the minutes, shall be deemed equivalent to the giving of such notice.

ARTICLE XI
RULES OF ORDER

The rules contained in Robert's Rules of Order Newly Revised or as may be amended from time to time, shall govern the corporation in all cases in which they are applicable, and in
which they are not inconsistent with these Bylaws, the Articles of Incorporation, or then existing law.

ARTICLE XII
AMENDMENTS TO BYLAWS

New bylaws may be adopted, or these bylaws may be amended or repealed, by an affirmative majority vote of the Board of Directors at which a quorum is present, provided, however, that no amendment changing the authorized number of directors of the corporation may be adopted until duly approved by vote or written consent of the directors of the corporation. A copy of the proposed amendment or new bylaws shall be included in the notice of meeting given to each director.

CERTIFICATE

I, ______________________, hereby certify:

That I am the duly elected and acting Secretary of CENTER FOR HEALTH POLICY AND EDUCATION, a California Nonprofit Corporation; and

That the foregoing Bylaws, consisting of fifteen (15) pages, including this one, constitute the Bylaws of said corporation, as duly adopted by the Board of Directors at a meeting held on ________________ at __________________________.

IN WITNESS WHEREOF, I have hereunto set my hand this ___ day of __________________.
AGENDA OF FIRST MEETING
OF THE
BOARD OF DIRECTORS
OF
CENTER FOR HEALTH POLICY AND EDUCATION
Scheduled:

1. Establish that all directors were given notice of the meeting.

2. Elect directors and accept resignation of incorporator.

3. Ratify the Articles of Incorporation.

4. Adopt the Bylaws.

5. Resolve that a Minute Book shall be kept at the principal office of the corporation.


7. Authorize a corporate seal.

8. Establish the bank account and adopt the bank resolution necessary to open the account.

9. Select a fiscal year (July 1 - June 30).

10. Resolve that organizational expenses and other expenses incurred prior to this date are assumed as corporate obligations.

11. Select Nielsen, Hodgson, Parrinello & Mueller as corporate counsel and instruct the firm to file tax exemption applications with the IRS and FTB.

12. Select accountant, if necessary.

13. Establish a two-year budget, which shall become part of the tax exemption application.

14. Schedule regular meetings, if a regular schedule is desired.

15. Establish that the first project of the Center is to defeat the Acquired Immune Deficiency Syndrome Initiative Statute on the November, 1986 ballot.

16. Establish that the name of the project and the campaign committee is "No on 64 - Stop LaRouche."
17. Direct preparation of all political reports required by law.

18. Ratify the location of campaign offices.

19. Ratify contract with David Mixner as campaign manager.

20. Ratify contract with Bruce Decker as finance chairman.

21. Ratify contract with Peter Scott as media consultant.

22. Ratify hiring of other employees of the campaign.

23. Conduct any other business required by the corporation.

March 12, 1987

Center for Health Policy and Education
c/o Larry Sprenger, Treasurer
7985 Santa Monica Boulevard, Suite 109-251
Los Angeles, California 90046-5112

Professional services rendered during the months of December, 1986 and January, 1987 by matter number.

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<td>.01</td>
<td>General Legal Matters including preliminary preparation of Federal and State Tax Exempt Applications for 501(c)(4) status; filing Statement of Domestic Non Profit Corporation; reviewing IRS employment tax refund; telephone conversations with John Brown:</td>
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<td>Campaign Compliance. Preparation of year end campaign statement, extensive computer input, $5,000 contribution letters to contributors; numerous telephone conversations with John Brown and Pat Moody; reconcile media buys with Action Media and disclose on campaign statement:</td>
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<td>Ballot Measure Litigation:</td>
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TOTAL FEES FOR THE CURRENT PERIOD: 3,387.00

Costs advanced for telephone, photocopy, postage, outside computer services, and messenger: 6,138.36

TOTAL CURRENT CHARGES: 9,525.36

Previous balance per our January 13, 1987 statement: 5,164.64

TOTAL DUE: $14,690.00

PAYABLE UPON PRESENTATION

SCL: ryb
6146.01
18427. Duties of Treasurers and Candidates With Respect to Campaign Statements.

(a) Treasurers. The treasurer of a committee must verify that to the best of his or her knowledge the committee campaign statements are true and complete and must use all reasonable diligence in the preparation of such statements. To comply with these duties the treasurer shall:

(1) Establish a system of record keeping sufficient to ensure that receipts and expenditures are recorded promptly and accurately, and sufficient to comply with regulations established by the Commission related to record keeping;

(2) Either maintain the records personally or monitor such record keeping by others;

(3) Take steps to ensure that all requirements of the Act concerning the receipt and expenditure of funds and the reporting of such funds are complied with;

(4) Either prepare campaign statements personally or review with care the campaign statements and underlying records prepared by others;

(5) Correct any inaccuracies or omissions in campaign statements of which the treasurer knows, and cause to be checked, and, if necessary, corrected, any information in campaign statements which a person of reasonable prudence would question based on all the surrounding circumstances of which the treasurer is aware or should be aware by reason of his or her duties under this regulation and the Act.

(b) Candidates with respect to candidate campaign statements. A candidate must verify that to the best of his or her knowledge his or her own campaign statements are true and complete and must use all reasonable diligence in the preparation of such statements. To comply with these duties the candidate shall be subject to the same duties imposed upon treasurers as stated in (a) above.

(c) Candidates with respect to campaign statements of committees they control. A candidate must verify to the best of his or her knowledge that the campaign statements filed by a committee he or she controls are true and complete and that the treasurer has used all reasonable diligence in preparation of such campaign statements. To comply with these duties, the candidate shall:

(1) Ascertain whether the treasurer is exercising all reasonable diligence in the performance of his or her duties including those duties specified under (a);

(2) Take whatever steps are necessary to replace the treasurer or raise the treasurer's performance to required standards, if the candidate knows or has reason to know that the treasurer is not exercising all reasonable diligence in the performance of his or her duties;

(3) Review with care the campaign statements prepared for filing by the committee;

(4) Correct any inaccuracies and omissions in campaign statements of which the candidate knows, and cause to be checked, and, if necessary, corrected, any information in campaign statements which a person of reasonable prudence would question based on all the surrounding circumstances of which the candidate is aware or should be aware by reason of his or her duties under this regulation and the Act;

(5) Perform with due care any other tasks assumed in connection with the raising, spending or recording of campaign funds insofar as such tasks relate to the accuracy of information entered on campaign statements;

(6) Unless such steps are required to meet the standards set forth in the foregoing paragraphs (1) through (4), a candidate is not responsible for establishing a record keeping procedure for a committee, monitoring committee record keeping, reviewing campaign finance records other than campaign
§ 18427  

FAIR POLITICAL PRACTICES COMMISSION  

TITLE 2  

(Reg. 86, No. 10—3-86)  

statements, or personally taking steps to corroborate any information contained on a campaign statement.

(d) Committees where no treasurer is designated. If a committee fails to designate a treasurer as required by Government Code Section 84100, the person who is primarily responsible for initiating and implementing the political activity of the committee will be considered the treasurer and will be subject to all the duties set forth in paragraph (a) of this regulation.

COMMENT. This regulation sets out the duties of candidates and treasurers only with respect to campaign statements. Among the duties imposed by this regulation on candidates and treasurers with respect to committee campaign statements is to "cause to be checked, and, if necessary, corrected, any information . . . which a person of reasonable prudence would question based on all the surrounding circumstances of which the treasurer [candidate] is aware or should be aware by reason of his or her duties under this regulation and the Act." The circumstances that trigger a duty to inquire under this standard are limited to those actually known to the candidate or treasurer and to those of which he or she should be aware by carrying out his or her duties under the Act and regulation. They do not include circumstances a candidate or treasurer "might" or "should have known" if he or she had gone beyond his or her required duties. For example, Mr. Jones may give Mr. Smith $100 in cash and instruct him to write a check to the candidate's controlled committee and to conceal the true source of the contribution. The committee reports the contribution as received from Smith. If neither the candidate nor treasurer has any knowledge concerning the questionable nature of the contribution and neither, through performance of their respective duties (such as monitoring campaign records or reviewing campaign statements), could have learned any facts that would lead one to question the contribution, the candidate and treasurer have no duty of inquiry with respect to the contribution. There is no duty of inquiry even though if Smith were asked he would have revealed the true source of the funds.

Once the known circumstances are such that a question is raised concerning the accuracy of information on a campaign statement, an inquiry is required. It is not possible in a regulation to describe with particularity every factual situation that might trigger such an inquiry since the variety of circumstances that could arise with respect to any particular campaign transaction are endless. By way of example, however, such circumstances might include the following in the case of a contribution: The size of the contribution, the reported source, the likelihood of that source making a contribution of the size reported, the circumstances surrounding receipt, and the manner in which the contribution is recorded in campaign records.

The burden of inquiry is likely to fall more heavily upon the treasurer because it is he, rather than the candidate, upon whom the major record keeping and reporting responsibility falls. Therefore, the treasurer is more likely than the candidate to be the person who, by reason of performance of duties, is aware of or should be aware of facts which would give rise to a duty of inquiry.


HISTORY.

1. New section filed 12-13-77 as an emergency; effective upon filing (Register 77, No. 51). For prior history, see Register 77, No. 17.
2. Repealed 4-13-78 by operation of Section 11422.1(e), Government Code. (Register 79, No. 16).
3. New section filed 4-20-79; effective thirtieth day thereafter (Register 79, No. 16).
4. Amendment of subsection (d) filed 1-25-80; effective thirtieth day thereafter (Register 80, No. 4).
5. Editorial correction of section title filed 1-9-81 (Register 81, No. 2).
6. Amendment of section heading filed 2-17-82; effective thirtieth day thereafter (Register 82, No. 8).
Visit by:

Robert E. Windom, M.D.
Assistant Secretary for Health
U.S. Department of Health and Human Services

to Los Angeles

Wednesday, June 24, to Friday, June 26, 1987

Weather advisory: Patchy overcast in mornings, sunny in afternoons, 60's, 70's and 80's

Advance contact: Bruce B. Decker

(O) 213/278-9355
(H) 213/306-3632
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Wednesday, June 24, 1987

**Driver:** 8:01pm Dr. Windom and Mr. Brown arrive Los Angeles International Airport - Braniff #507/Closed to press

**Met by:** Bruce B. Decker, Chairman, Chairman California AIDS Advisory Committee

8:45pm Arrive at The Biltmore Hotel, 506 S. Grand St. Los Angeles, CA 90071 213/624-1011

Briefing by Richard Robertson

Remain overnight

Thursday, June 25, 1987

**Driver:** 8:00am Depart Biltmore Hotel - en route El Centro Human Services

**Advance:** 8:30am Arrive El Centro Human Services, 972 South Goodrich, East Los Angeles for tour and briefing followed by informal remarks (10 minutes)/Open press coverage (Estimated attendance: 25)

**Press:**
- Contact: Genevive Lopez 213/725-1337

**Met by:** Rev. Carl Bean 213/936-4949

**Driver:** 9:30am Depart El Centro Human Services - en route KABC

**Advance:** 9:45am Arrive KABC/Radio Studio, 3321 S. La Cienega

**Press:**
- Met by: Lyle Gregory Michael Jackson Show 213/931-3204

10:00am Michael Jackson Show (1 hour) Live Interview/Call-in

**Driver:** 11:00am Depart KABC - enroute Biltmore Hotel

**Advance:** 11:30am Arrive Biltmore Hotel - Staff time (30 minutes)

(1)
12:00am  | Arrive Crystal Ballroom/Biltmore Hotel for Luncheon honoring Abigail Van Buren and business leaders. Co-sponsored by Business Advisory Council of APLA.  
          | (Estimated attendance: 200)  
1:00pm  | Program begins, Dr. Windom introduced by Michael Gottlieb, M.D./prepared remarks (20 minutes)/Open press coverage  
Driver: 2:00pm | Depart Biltmore Hotel - en route Los Angeles Times  
Advance: 2:15pm | Arrive Los Angeles Times 202 W. First St. at Spring St. for Editorial Board interview  
           | Met by: Tony Day, Editor of Editorial Pages 213/237-7928  
Driver: 3:15pm | Depart Los Angeles Times enroute Los Angeles County Hall of Administration  
Advance: 3:30pm | Arrive Los Angeles County Hall of Administration, Room #822, 500 W. Temple St. for meeting with Supervisor Deane Dana and Supervisor Ed Edelman/Closed to press/213-974-4444  
Press: 4:00pm | Attend reception on 8th Floor balcony for other Supervisors and County health officials/Informal remarks/Open press coverage  
          | (Estimated attendance: 40)  
Driver: 5:00pm | Depart Hall of Administration - enroute Los Angeles County Medical Association  
Advance: 5:30pm | Arrive Los Angeles County Medical Association - 1925 Wilshire Blvd. Proceed to Board Room to meet with Executive and AIDS Committees/Closed to press  
          | (Estimated attendance: 20)  
           | Met by: David Zeitlin 213/483-1581  
Driver: 6:30pm | Depart Los Angeles County Medical Association en route to Le Bel Age Hotel  
Advance: 7:00pm | Arrive Le Bel Age Hotel, 1020 San Vicente Blvd., for MECLA reception  
          | (Estimated attendance: 100)  
Press: Met by: Paul Froman  
         | Lynn Shepodd  
         | 213/650-1128  
          | (2)
Introduced by: Bruce Decker

Formal remarks (20 minutes)/Q & A/Open press coverage

Driver: Ogle
8:00pm Depart Le Bel Age en route Biltmore Hotel
8:30pm Arrive Biltmore Hotel - remain overnight

Friday, June 26, 1987

Driver: Decker
7:15am Depart Biltmore Hotel en route Good Samaritan Hospital (briefing in car)
Advance: Ogle
7:30am Arrive Good Samaritan Hospital, Moseley Salvatori Conference, 637 S. Lucas Ave., for AIDS community based organization breakfast
(Estimated attendance: 75)
Press: Smith
Met by: Rev. Albert J. Ogle
Diocesan Coordinator for AIDS Ministry 213/482-9959

Breakfast is served followed by presentation made by representatives/ Formal remarks (15 minutes)/Q & A/Open press coverage

Driver: Decker
9:00am Depart Good Samaritan Hospital - enroute Los Angeles County/University of California (LAC/USC) Medical Center (briefing in car by Jack Buckingham, Executive Director)
Press: Smith
9:30am Arrive LAC/USC Medical Center, 1200 N. State St., For tour of AIDS Clinic and briefing in the General Hospital Auditorium/Informal remarks (10 minutes)/Q & A/Open press coverage

Met by: Richard Pacheco
Chief Operating Officer
John E. Bethune, M.D.
Chief of Internal Medicine
213/226-6851

Driver: Decker
11:00am Depart LAC/USC Medical Center - enroute Biltmore Hotel
Advance: Epstein
11:30am Arrive Biltmore Hotel - staff time (30 minutes)
12:00am  Arrive Crystal Ballroom for Town Hall Luncheon  
(Estimated attendance: 300)

Met by: Fran Spears  
213/688-8141

12:45am  Dr. Windom introduced by Steven Gamble,  
President, Hospital Council of Southern California/Formal remarks (20 minutes)/  
Q & A (20 minutes)/Open press coverage

1:45pm  Depart Crystal Ballroom - en route to private meeting

Informal meeting with Jackie Goldberg, President of the Los Angeles City School Board (possibly Alan Gershman, Board Member)/Closed to press  
Contact: Ruby Takki 625-6386

2:15pm  Staff time (1 hour)

3:15pm  Depart Biltmore Hotel en route Herald Examiner

3:30pm  Arrive Herald Examiner 1111 S. Broadway

Met by: James Kinsella  
Editorial Page Editor  
213/744-8466

4:30pm  Depart Herald Examiner - en route  
Michael Roth, M.D. residence (possible: LA Times interview in car)

5:30pm  Arrive Roth residence for staff time (1 hour)  
(time for swim and change into informal clothes)

6:30pm  Informal dinner reception with AIDS physicians/  
Closed to press

8:30pm  Depart Roth residence en route LAX

9:00pm  Arrive LAX

9:50pm  Depart LAX Continental # 896 en route Washington, D.C.
ACCOMODATIONS

Biltmore Hotel
506 South Grand Street
Los Angeles, CA 90071
213/624-1011

Check in: 6/24/87 8:45 pm
Check out: 6/26/87 12:00 noon

Manifest: Robert Windom, M.D.       Room #515
Jim Brown               Room #520
Richard Robertson       Room #552

Credit Card Guarantee: Diners Club
Rate: $75.00

Baggage Call: 3:00pm, Friday 6/26/87
This is an East Los Angeles minority (black/latino) AIDS prevention and pilot treatment project primarily focused on IV drug abuse.

Your host will be Rev. Carl Bean whom you recently met in Washington.

You will be given a tour and a briefing. It is open press coverage so you should be prepared to acknowledge minority AIDS concerns and answer press questions.
MEDIA STOPS

KABC/Michael Jackson Show

Very Smart-quasi gadfly but basically liberal - very courteous but look for zinger late in the interview - callers from whole spectrum - fun!

Los Angeles Times/Editorial Board -
Anthony Day, Editorial Page Editor

Very sophisticated and relatively conservative - not particularly sympathetic with the Administration especially on AIDS.

Herald Examiner/Editorial Board
James Kinsella, Editorial Page Editor

Young Turks and relatively liberal - interesting contrast with LA Times - openly hostile to Administration, particularly on AIDS.
You will first meet with Supervisor Deane Dana (R) and Ed Edelman (D). They will present you with plan and request for 87/88 funding. It will be a private meeting.

You will then be escorted to the 8th floor balcony for a reception with leading County Health Department officials and the other Supervisors (Antonovich and Shebarum, Hahn is disabled). You will be introduced by Supervisor Dana and should thank them for the proposal indicating that you will take it home and look it over.

We will then depart en route to the Los Angeles County Medical Association. There you will meet privately with the AIDS committee and several Executive Committee Members. We will be shown their HIV test counselling film.
MECLA

They will gather at 6:30pm, have refreshments and we will arrive at approximately 7:00pm.

The audience will be predominantly gay, upscale and male. MECLA is 10 years old and is recognized as a very powerful fundraising organization which has seriously impacted the Los Angeles and Sacramento political situation.

I will introduce you and have advised you speechwriters of my recommendations. You should be open, relaxed and establish a trust relationship with the audience in an effort to minimize controversy during Q & A period.

I will moderate the Q & A portion and will be assisted by Thomas M. Mundy, M.D., Assistant Professor of Pediatrics/Immunology, Principal Investigator of Natural History of HIV infection in neonatal recipients of blood products, Cedar Sanai Medical Center, Los Angeles, and a Member of the MECLA Board of Directors.

I will screen question for appropriate content. If I choose to pass or reject one and you want to be a hero, overrule me and answer it. Dr. Mundy will assist with technical questions or as a third party endorser.

They will have a brief business meeting at the conclusion of your remarks. You have the option of departing immediately or staying and socializing.
BRIEFING

LOS ANGELES AIDS ORGANIZATIONS AND HEALTH CARE PROVIDERS

In March 1986, 75 AIDS-related organizations were called together by Reverend Albert Ogle, then Director of Planning at the AIDS Project Los Angeles, to develop a countywide 4 year long term plan in response to the AIDS epidemic in Los Angeles. Prompted by the growing unmet needs of people with AIDS/ARC and the lack of particular services such as hospice, home health and residential care, the care providers met together in 15 different focus groups over a period of 3 months.

Reverend Ogle was assisted by Dr. Michael Gorman, an epidemiologist formerly with the Centers for Disease Control in Atlanta. Each Focus group developed a needs assessment in their particular area, i.e. mental health, black community, hospice, home health, etc. and developed a 5 year strategy for meeting the expected increased needs. A control coordinating Task Force representing the chairs of the focus groups, AIDS project Board members, the County Board of Supervisors, business, religious, and other interested parties develop a proposal which was unanimously agreed upon by the 75 agencies and submitted as 2 grant proposals to the Robert Wood Johnson Foundation and the Public Health Service. Los Angeles, like San Francisco and New York were targeted as a recipient of one of the 10 Robert Wood Johnson's 3 year grants. The request from the organization was to have a comprehensive and community supported AIDS plan. The Los Angeles community submitted one proposal while cities like New York submitted 20 proposals.

The energy and interest generated by the process was soon dissipated when the Robert Wood Johnson Foundation did not award a grant to Los Angeles. Shortly thereafter $2.3 million was channeled through the Public Health Service to the County Health Department, although these positions were direct care positions. The Robert Wood Johnson proposal was designed to create a coordinated AIDS resource center for Los Angeles, staffed by 16 specialized resource developers and technical staff who would work with the existing service providers to create new services, new resources, and implement necessary policy changes which were impediments to care. The total grant requested was $2.2 million over 4 years with the provision for generating private sector funding to augment public funding.

The lack of significant coordination where the caregivers, the policy makers, and the private sector could work together to solve problems and develop long term planning was further reinforced by a failure to obtain this grant. The consortium of care providers was never called together again, either by AIDS Project Los Angeles or by the County Health Department. The position which created the consortium was eliminated in October, 1987, and 12 months after the submission of the grants to the Robert Wood Johnson Foundation and the Public Health Service, Los Angeles is still fragmented, crisis oriented, and more deeply distrusting health care system. Many of the issues raised

(12)
12 months ago have still to be addressed. No hospices, nursing homes, one significant shelter to open in July, 1987 for 30 people, no coordinated casemanagement system, and no commitment from respected organizations to take a significant leadership role. The needs and concerns of the Hispanic and Black communities remain unanswered. A recent fracas with the County Board of Supervisors and the Minority AIDS Project which is in process of a law suit against the County has shown the lack of will to seriously address the long term implications of AIDS in this County. (A $20,000 grant to the Minority AIDS Project was not renewed for minority AIDS education).

Revered Ogle and Dr. Gorman recently completed a 5 year Treatment and Prevention Plan for the State of California under the auspices of the Health Policy and Research Foundation, "The Myers Report" in memory of Professor Beverlee Myers, prioritizes the recommendations of the Surgeon General's report and the National Institute of Medicine report relevant to California. The report outlines model treatment and prevention programs with projected costs over 5 years. The report was Co-Chaired by 5 leading public health experts in the State and endorsed by an evaluation of 130 experts in the spectrum of AIDS care and education providers.

Los Angeles and the wider community look to the Federal Government for some leadership in this very frustrating situation.

Resources are needed to develop the expertise required to create new services through expansion of existing programs in every aspect of AIDS services. Existing care providers are so overwhelmed by the current levels of need, they do not have time to plan for next year never mind the next 5 years.

Resources are needed to assist public and private entities to work in conjunction with the existing care providers who have done a wonderful job of working together under tremendous duress. Dr. Windom should specifically mention and pay tribute to the community based agencies, particularly the non profit and voluntary organizations. One hundred and twenty community based organizations have been invited to the breakfast. This is the first time since the Robert Wood Johnson process this group has reconvened. Of particular interest to these organizations will be hearing Dr. Windom on the Federal Government's response to AIDS and the financial, educational and technical resources which will be made available to providers. Another area of interest will be how the Federal Government can help California and in particular Los Angeles with moving beyond the present political impasse to renew the spirit of cooperation and optimism expressed by this community 12 months ago.

(13)
You will be briefed in the car enroute from breakfast by Jack Buckingham, Executive Director.

You will be met by Richard Pacheco (Chief Operating Officer) and John Bethune, M.D. (Chief of Internal Medicine), and given a tour of the AIDS clinic. Note: We want to get picture of you looking into microscope. It is set up.

You will then proceed to auditorium for briefing and should acknowledge the importance of their fine work. If we have time for questions, we will take them.

They are particularly concerned about AZT or other expensive drugs availability to those not eligible for MEDICAL/MEDICAID, outpatient care issues, OB and minority issues.
TOWN HALL

Your speech will be broadcast of public radio and mailed to their membership of 4500.

Note that it is Co-Hosted by the Hospital Council of Southern California and the Los Angeles Unified School District.

We will meet privately with the President of the School Board. They should be acknowledged for their courageous AIDS education efforts.
Robert E. Windom, M.D., Assistant Secretary for Health, U.S. Department of Health and Human Services tours Los Angeles AIDS facilities, meets with involved organizations and commends leadership of business, medical and private sector participants.

Events open to the press are as follows:

Thursday, June 25, 1987

8:30 - 9:30 AM  Tour of Agency oriented to the minority community dealing with AIDS/Open press coverage

El Centro Human Services
972 South Goodrich
East Los Angeles, 90022
(2 blks East of Atlantic/1 blk S. of Whittier)

1:00 - 1:30 PM  Luncheon speech honoring Dr. Michael Gottlieb, Abigail Van Buren and business leaders/Open press coverage

Biltmore Hotel/Crystal Ballroom
506 South Grand Street
Los Angeles, 90013

4:00 - 5:00 PM  Reception with members of Los Angeles Board of Supervisors and County health officials/Open press coverage

Hall of Administration
8th Floor Balcony
500 West Temple Street
Los Angeles, 90012

7:00 - 8:00 PM  Speech and Q & A with Municipal Elections Committee of Los Angeles (MECLA)/Open press coverage

Le Bel Age Hotel/Grand Salon
1020 San Vicente Blvd.
West Hollywood, 90069

(continued on next page)
MEDIA ADVISORY
WINDOM VISIT
6/17/87
PAGE TWO

Friday, June 26, 1987

7:30 - 8:30 AM Breakfast meeting with representatives of Los Angeles community based AIDS organizations/Open press coverage

Good Samaritan Hospital
Moseley Salvatori Conference Room
637 S. Lucas Ave.
Los Angeles

10:00 - 11:00 AM Tour of AIDS Clinic and medical briefing/Open press coverage

Los Angeles County/University of Southern California Medical Center
1200 N. State Street, Room 1602
Los Angeles, 90033

12:45 - 1:30 PM Speech and Q & A with Town Hall/Open press coverage

Title: "The Need for a Public-Private AIDS Partnership"

Biltmore Hotel/Crystal Ballroom
506 S. Grand Street
Los Angeles

Note to Editors:

"The Assistant Secretary is the highest ranking Federal official to come to California to address the issue of AIDS" said Bruce B. Decker, Chairman of the California AIDS Advisory Committee, "A public-private partnership is essential in combating this disease. I hope Dr. Windom's visit will encourage our elected officials, corporate executives, and philanthropic leaders to recognize the urgency in joining the "War against AIDS" with all the resources available to them."

###
Here is some background on the NEAED concerning the contract.

Please hold this until I tell you whether or not we need to let the powers that be know now this sits.

Also treat it as a confidential document.

Put your thoughts to work. Submit a MERIT AWARD SUGGESTION.
Suggested Press Response:

Investigators of the San Francisco Men’s Health Study were notified today that their study was to be terminated by the National Institute of Allergy and Infectious Diseases of the National Institute of Health today.

This study, which is the only prospective epidemiological study of AIDS in single men which is based on a population based survey sample rather than venereal disease clinic or other volunteers, has received widespread recognition for the rigor of its design. Similarly designed studies have only recently been proposed on a national basis to better ascertain the level of infection in the general population, but not as yet been conducted. Samples of minority groups and women would have been added to the current San Francisco study had funding been continued.

The investigators were shocked by the announcement, which was a reversal of previous indications on _______, that there study would be continued for another 4 years. This cancellation may represent another chapter of a long standing dispute between the University investigators and the NIH over how best to conduct AIDS research. This dispute had resulted in a previous attempt on the part of NIH to cancel the study in _______, however NIH reversed its decision at that time after careful review of the relevant documentation. The major issue with the University is whether this project should be conducted independently or under rigid control from NIH.

Scientific productivity would be reduced under the NIH system according to the UC investigators, who detailed their concerns as early as November 1983. The four sister studies in other cities which adopted the rigid NIH protocol have all together produced fewer major publications, despite 4 times the funding and staff, of the UC Berkeley group. The issues are not scientific but administrative, and this dispute calls into question the management of not only the major AIDS epidemiological studies, but also the management of AIDS treatment studies which have also had major delays as a result of NIH management decisions. While delaying funding and attempting to change studies, delaying a cure is costly.
MEMORANDUM

To: Whom it may concern
From: Warren Winkelstein, Jr.
Subject: Termination of NIAID contract support of the San Francisco Men's Health Study (SFMHS).
Date: 23 July 1987

At approximately 8:00 A.M. on 21 July 1987, during a telephone conversation between NIAID contracting officer Mary Anne Glitz and U.C. research administrator Mary S. Meikle, it was revealed that the U.C.B. proposal in response to "RFP" NIAID-AIDSP-87-28-72635 had been disapproved and that negotiations for an "orderly phase out" of our contract supported research would begin immediately. This information was subsequently confirmed by our project officer, Harold Ginsburg, and by a brief letter received today (copy attached). According to Ms. Glitz and Dr. Ginsburg, this action was taken on the advice of a "source selection committee" which, reportedly, met on 20 July 1987 in Bethesda. To date, no information has been made available to us regarding the composition of this committee or the substance of their considerations of our response to 21 questions submitted to us after the committee's initial review and conditional approval of our proposal (referenced letter, 21 questions, and our response attached). In the following paragraphs, I will briefly outline the major events leading up to this action. For your information, I am also attaching the summary which prefaced our response to the RFP and a brief account of previous problems with the contract.

In the spring of 1986, we were site visited by Dr. John R. LaMontagne who had been newly appointed as our project officer and who subsequently became chief of the AIDS Program when it was established in the NIAID. During that visit, I discussed the prospects for contract renewal after the conclusion of the current contract and alternative sources of support. At the time, Dr. LaMontagne was unable to make any statement regarding the prospects for contract renewal, and we discussed the feasibility of a program-project grant which then seemed to be the most prudent approach to long-term support. However, preparation of a program-project proposal is a very considerable undertaking and, of course, its submission is no guarantee of its approval. Close contact was, therefore, maintained with Dr. LaMontagne. When the deadline for initiating the preparation of the proposal, mid-July 1986, arrived, Dr. LaMontagne advised me that prospects for renewal of the contract were excellent and that my colleagues and I should devote our efforts to research and await instructions regarding renewal of funding for the SFMHS.

In early fall, 1986, our new project officer, Dr. Harold Ginsburg, asked us to prepare a document containing our views on the desirable "scope of work" for a new contract. This was to be part of the preparation for a meeting in Bethesda in November to discuss contract renewal procedures. On 30 October 1986 we
submitted a lengthy letter reviewing the accomplishments of our research and our plans for the future. At the meeting in Bethesda on 2-3 November 1986 (also attended by the four principal investigators of the Multi-Center AIDS Cohort Study, MACS) we were given additional instructions regarding the preparation of materials for use by NIAID to establish the justification for renewal of our various contracts on a non-competitive basis. This material was submitted on 10 November 1986. In January 1987, a meeting of the MACS principal investigators was held in Los Angeles, with representation from our study staff, at which time the contract renewal procedures were reconfirmed.

On January 15, 1987 the non-competitive RFP, referenced above, was issued and our proposal was submitted on March 3, 1987. On May 26, 1987, we were notified that our proposal had "...been reviewed and approved pending clarification of the attached list of technical questions..." (see attached letter from contracting officer, Glitz). Our response to the technical questions was submitted on 26 June 1987 (attached). As indicated above, official notification of disapproval was received on this date, 23 July 1987 (attached).

Commentary:

I have been advised by staff of our Sponsored Projects Office that the disapproval of our proposal and the phaseout of our research support is not subject to appeal according to NIH official procedures. Nevertheless, I cannot acquiesce to this action without exhausting every possible measure to get the decision reversed and the contract negotiations resumed. Before outlining some of the measures which might be taken, I would like to comment on the NIAID decision.

According to the May 26, 1987 letter from the NIAID contracting officer, our proposal was approved pending clarification of certain questions. That letter also indicated that a site visit was "...being planned for the purpose of discussing your response....as well as any other questions which may be (sic) arise.". One must wonder how a decision as drastic as that under discussion here could be made without a site visit, or, at least, a discussion of the questionable issues with the principal investigator. Furthermore, according to contracting officer Glitz, the source selection committee made its recommendation on 19 July, either the same day or one day before the NIAID decision was taken (telephone conversation between Ms. Glitz and Ms. Meikle, 21 July 1987). Again, one must wonder how such a drastic decision could be adequately reviewed and approved by responsible NIAID staff in a day or less. (In our experience obtaining approval for the purchase of a freezer or other item of equipment can take as long as three months but never as short as one day.) Finally, the conclusions of a source selection committee are advisory only, unless that committee has been designated as the "source selection authority"; contract decisions must be made by the authorized member of the NIAID staff, contrary to the statement in the July 21, 1987 letter from
contracting officer Glitz.

The objectives outlined in the technical proposal included maintenance of the original cohort including detailed studies about progression to disease, and the initiation of a new seroepidemiological survey of single, largely minority, men and women in the 20 census tracts adjacent to the 19 already sampled. Because it was based on a random probability sample, the original cohort represents a unique sample where results can be generalized to the whole geographical area from which the sample was derived. This is in contrast with volunteer samples where links cannot readily be made between participants and larger populations. Our longitudinal data becomes more valuable over time if the integrity of the cohort is maintained. Our new study survey would represent the first population-based heterosexual sample in the world and would enable researchers and public health officials to better ascertain the true level of infection in the general population.

With respect to our specific responses to the 21 questions submitted by the contracting officer on May 26, I would comment as follows after carefully reviewing them. Many of the responses merited simple reiterations of portions of the original technical proposal or represent simple clarifications of material included therein. Examples of such responses are: 1, 7, 14, 16, 19, and 20. I find nothing in our responses to these questions which could justify the drastic action of terminating our study. Some questions address issues not included in the original proposal. Examples of such responses are: 2, 4, 5, 6, 7, 18, and 21. I can detect no serious issues arising out of our responses to these questions.

A potentially serious problem is apparent in our response to questions 8-11, where we propose to eliminate the neuro-psychiatric component of our proposal. However, this action was taken, for the reasons given in our response, after lengthy and repeated consultations with the project officer who assured us that this could be done without prejudice to the remainder of the proposal. This information should have been included in our response and certainly should have been brought to the attention of the source selection committee by the project officer.

Other responses which I believe could raise serious questions are: 3, 12, 13, 15, and 17. Question 3 deals with the collection of clinical information for study subjects who develop serious HIV infection related conditions. Clearly, our response to this question is inadequate because our study was not originally designed to follow participants after they develop AIDS. However, this could easily be corrected and has minor, if any, budgetary implications. Questions 12 and 13 deal with quality control of laboratory procedures. It is possible that the source selection committee wanted more information than we provided. However, we have repeatedly assured our project officer, and indeed, other MACS investigators, that we are prepared to participate in quality control procedures although we
are not prepared to take the lead in organizing such efforts preferring to expend our energies on other issues. We do recognize the importance of quality control and should have given it more emphasis in our response to question 13.

Questions 15 and 17 deal with our sample and participation rates and imply that our cohort is so biased that our findings are invalid. I think that our response indicates that this is not the case and that, indeed, we have a good sample. Other scientific peers who have reviewed our papers and used our data for public health purposes apparently have a different view of the validity of our data than the particular source selection committee which advised NIAID to terminate the SFMHS. This issue has been repeatedly raised by critics of our research all of whom, if they are involved in AIDS related epidemiological research, depend on "haphazard" or "grab" samples for their data.

It seems to me that the responses to the 21 questions, while admittedly imperfect, hardly merit complete reversal of the prior decision to approve the proposal and negotiate a contract for renewed support of our studies.

Before turning to a discussion of measures to be taken to reverse the NIAID termination action, I would like to draw your attention to an aspect of the SFMHS which is important for those who would support its continuation. That aspect is our publication record. These publications are the most important, although not the only, vehicle for making the results of research available to public health workers and other scientists concerned with the control of this most unusual and terrible epidemic. Seventeen publications have now appeared reporting findings from the SFMHS. Half of these are in the form of letters and all but two appeared in refereed journals. I have attached copies of four of our major publications to illustrate the quality of our research.

Proposed Measures to Reverse NIAID Termination Decision:

1. Immediately after confirming the termination decision with our project officer on 21 July 1987, I called the Acting Deputy Director of the NIAID, Dr. James Hill, to ask him to look into the decision and, hopefully, bring about its reversal. Dr. Hill works very closely with the Director of the NIAID, Dr. Anthony Fauci, and can be trusted to conduct a thorough inquiry and to fully inform Dr. Fauci. The fact that Dr. Hill admitted a lack of information regarding the decision during a subsequent telephone conversation suggests that he and Dr. Fauci were not consulted in advance regarding the termination decision. At the time of preparation of this memorandum, Dr. Hill had not informed me of the results of his inquiry or of any action he or Dr. Fauci would take. I believe we should take no further action in this matter until we have received a response from Dr. Hill. However, if no response is received by noon Friday, 24 July, or Dr. Hill and Dr. Fauci endorse the termination, we should initiate additional actions.
2. Dr. Weingarten, Director of the National Institutes of Health, should be called and asked to look into the matter and intervene on our behalf to obtain a reversal of the termination decision.

3. Dr. Robert E. Windom, Assistant Secretary for Health of the Department of Health and Human Services should be called and asked to look into the matter and intervene on our behalf to obtain a reversal of the termination decision.

4. The following persons should be asked to give Dr. Fauci their opinions of the scientific and public health importance of the SFMHS:

* Dr. Walter R. Dowdle, Public Health Services AIDS Coordinator

* Dr. Roy Widdus, Director of the Division of International Health of the Institute of Medicine of the National Academy of Science and Project Director of the Institute's Committee on a National Strategy for AIDS.

* Dr. James Chin, Special Consultant, AIDS Programme, World Health Organization, Geneva.

* Dr. Donald Francis, Special Consultant AIDS, Centers for Disease Control.

* Dr. James Curran, Chief, AIDS Program, Centers for Disease Control.

* Dr. Mervyn Silverman, Director, American Foundation for AIDS Control.

* Dr. David Werdegar, Director, Department of Health, City and County of San Francisco.

* Dr. Palmer Beasley, Dean, School of Public Health, University of Texas Medical Center, Houston.

* Dr. Marcus Conant, Chairman, Governor's Task Force on AIDS, California.

5. The following persons should be asked to give Dr. Fauci their opinions regarding the public policy importance of the SFMHS:

* Senator Pete Wilson, California.

* Senator Alan Cranston, California.

* Various other members of the California Congressional delegation.

* Bruce B. Decker, President and Acting Director, Health Policy and Research Foundation of California.

* Philip R. Lee, Professor and Director, Health Policy Institute,
University of California, San Francisco.

6. A major press conference to announce the action of NIAID and to present the cause of the SFMHS should be organized for early next week.

7. A small delegation of investigators should seek an early meeting with Dr. Fauci to urge a renewal of contract negotiations.

8. Various organizations should be asked to express their support and concern for the research supported by the NIAID contract.
I.A.3.a. Budgetary problems:

After the University of California at Berkeley had been selected as one of five contractors to implement RFP-NIH-NIAID-MIDP-83-11, the NIAID indicated that major reductions in the total budget for the proposed four-year contract would be necessary in order to implement an award. The reduction amounted to approximately $1,000,000, 25 percent of the proposed budget. After vigorous negotiation and assurances that adjustments could be made after the contract became operational, the contract was signed and the project began. However, within the first six months it became apparent that substantial cost over-runs would occur and on April 20, 1984 a "stop work" order was issued by the contracting officer, the first step in a contract termination procedure. Fortunately, the director of the NIAID interceded and the contract was reactivated within a few days. Nevertheless, the projected cost over-run remained unacceptable to NIAID and in early 1985 the scope of work was reduced for the third and subsequent examination cycles. In addition, it became necessary to consider the probability that projected examination cycles five and six would be abandoned. Fortunately, again, funding was made available in the fall of 1986 to permit implementation of these examination cycles. At present, funding appears to present no major problems.

I.A.3.b. Nature of contractual relationship

At the first meeting between the five contractors' staffs and the NIAID staff in October 1983, it became apparent that the various contractors had proposed, and the NIAID had approved, widely disparate study designs. Nevertheless, at that time NIAID indicated that maximum uniformity in implementation of the contracts was expected. We felt that this policy was not consistent with our expectations based on the RFP and that it was unwise for scientific reasons. Our arguments were laid out in an extensive letter dated 11 November 1983 but they were unavailing and the Multi Center AIDS Cohort Study (MACS) was established with our group participating. However, continued disagreements over the nature of the multicenter collaboration culminating in an unreconcilable disagreement over a proposed publication policy lead to a separation of the San Francisco Men's Health Study from the other four MACS studies in early 1985. Since that time, and particularly since the establishment of the AIDS Program in NIAID, administrative problems have been minimal.
July 21, 1987

Our Ref: Contract No. N01-AI-32519 and RFP No. NIH-NIAID-AIDSP-87-28-72635, "The Natural History of AIDS"

The Regents of the University of California
Attn: Mary S. Meikle, Research Administrator
Sponsored Projects Office
M-11 Wheeler Hall
University of California
Berkeley, CA 94720

Dear Ms. Meikle:

This letter will confirm our conversation this morning regarding the source selection review of your revised proposal in response to RFP-NIH-NIAID-AIDSP-87-28-72635. As I informed you earlier by telephone, we regret that your proposal was determined to be unacceptable by the source selection group.

Therefore, there will be no further negotiations on the contract renewal project. Within the next week we will contact you regarding the possibility of negotiating a phaseout plan for Contract No. N01-AI-32519.

Sincerely,

Mary Anne Glitz
Contracting Officer
National Institute of Allergy and Infectious Diseases

cc: Dr. Winkelstein, U.C. Berkeley
Dr. Ginzburg, NIAID Project Officer
May 26, 1987

Our Reference: RFP NIH-NIAID-AIDSP-87-28-72635

The Regents of the University
of California
Attn: Ms. Mary Meikle, Research Administrator
Sponsored Projects Office
M-11 Wheeler Hall
University of California
Berkeley, California 94720

Dear Ms. Meikle:

This is to advise you that your proposal entitled "The Natural History of Acquired Immunodeficiency Syndrome (AIDS)" submitted in response to RFP-NIH-NIAID-AIDSP-87-28-72635 has been reviewed and approved pending clarification of the attached list of technical questions (Attachment A), and a list of business/budget questions (Attachment B), which will be forwarded to you next week.

It is requested that you respond to both Attachment A and Attachment B so that these responses are received in this office no later than 5:00 P.M. EDT on June 23, 1987. Your response should be in the form of an addendum to your original proposal and should contain an original and five (5) copies.

A site-visit is being planned for the purpose of discussing your response to these items as well as any other questions which may be arise. You will be notified once the specific date has been set, however, we do expect that it will be during the last week of June or sometime early in July--most likely during the week of July 5th.

Should any further questions arise as a result of the site visit, you will be afforded a reasonable time-frame in which to respond. If you have any questions concerning this matter, please contact Mr. Thomas C. Porter on (301) 496-0993.

Sincerely yours,

Mary Anne Glitz
Contracting Officer
Contract Management Branch
National Institute of Allergy and Infectious Diseases

Attachment A

Cc: Dr. Warren Winkelstein, Jr.
Introduction

This addendum to the Technical Proposal entitled, "The Natural History of Acquired Immunodeficiency Syndrome (AIDS)" submitted in response to RFP-NIH-NIAID-AIDSP-87-28-72635 has been prepared in response to a list of technical questions submitted by the Contracting Officer in a letter dated May 26, 1987. In the body of the addendum, each question is listed with the response following. In addition, the addendum includes a series of attachments which are referenced in the main text. References are also made to the original Technical Proposal and its Appendices.

This addendum has been prepared under the direction of Nancy Padian, Ph.D., Project Coordinator, and is the sole responsibility of the co-principal investigators.

Warren Winkelstein, Jr., MD, MPH
Professor of Epidemiology

James Wiley, PhD
Assistant Director
Survey Research Center

University of California, Berkeley
26 June 1987
I. What efforts will be made to ensure a continued high level of participation by current (and supplemental) members of the cohort? How many individuals have attended each follow-up visit? How many have had specimens collected and stored at both the local and national repository?

The follow-up procedures were described in the annual report of September, 1986, and on pages III-2 and 3 of the Technical Proposal. The pertinent passages are included herein as Attachment 1. The actual participation is shown in Table 1 taken from the annual report of May 1987.

SFMHS Participation by Examination Cycle

<table>
<thead>
<tr>
<th>Status</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
<th>Cycle 4</th>
<th>Cycle 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/86</td>
<td>2/85</td>
<td>7/85</td>
<td>1/86</td>
<td>7/86</td>
</tr>
<tr>
<td></td>
<td>4/85</td>
<td>8/85</td>
<td>2/86</td>
<td>6/86</td>
<td>2/87</td>
</tr>
</tbody>
</table>

1. Complete clinic visit 1044 841 749 729 746
2. Phone interview complete* 27 71
3. R unable to participate for some other medical reason 1 7 8 6
4. R deceased 2 4 11 25
5. R moved out the area 27 52 55 8
6. Unable to locate 4 15 21 28
7. R refused 67 103 111 61
8. Pending cases** 98 109 78 95

TOTAL 1044 1044 1044 1044

* Phone interviews were completed with a respondent (R) for a variety of reasons, including R has AIDS (and unable to come to clinic), R no longer lives in the San Francisco area, R unable to come to clinic at this time, and R refused.

** Those respondents who were unable to complete their clinic visit in the designated time period were carried over to the next examination cycle.

Several aspects of the data are of particular note. First, participation in examinations has been stable since the third examination cycle. Second, the number of deaths increased exponentially during the first 30 months of the study. Third, we are in periodic contact with most study subjects who have moved out of the area and are continuing to explore mechanisms for obtaining specimens from them and for examining them. Fourth, although
the number of subjects we are unable to locate (including those who have moved out of the area) has continued to increase over the first 30 months of the study, the number remains low, 2.7% of the original cohort. Fifth, the number of refusals fluctuates substantially at each examination cycle. The reason for this is that all subjects are contacted at each examination cycle and some who refuse examination at one time agree at another. At any particular point in time, we consider the "lost to follow-up" to include those unable to participate for some medical reasons unrelated to HIV infection, the deceased, those we are unable to locate, and the current refusals. Thus at the end of examination cycle 5, there were 120 subjects lost to the cohort of whom 40 had died and, therefore, had contributed to the data base.

All participants have provided specimens for the local and national repository in accordance with the original protocol and subsequent approved modifications.

We plan to continue current procedures to obtain ongoing high levels of participation of the existing cohort. In addition to those described in Attachment 1 and in the Technical Proposal, we will continue the issuance of periodic newsletters, participation in community forums, and maintenance of general community support by active involvement in such activities as the AIDS Foundation and the monthly public "AIDS Grand Rounds" sponsored by the county Health Department.

With respect to the supplemental heterosexual seroepidemiological survey, we plan to obtain substantial media coverage, utilize newspaper advertising, conduct focus groups, contact community organizations, obtain endorsements from local community leaders, and explore payments to respondents.

2. What consideration has been given to the issue of cohort members participating in clinical trials or treatments as: (a) asymptomatic-well individuals, (b) PGL/ARC, (c) AIDS (d) some other clinical stage?

Since March 1987, we have been actively considering the establishment of clinical trial protocols for infected members of the SFMHS cohort. In May we held preliminary discussions with the Director of the San Francisco AIDS Treatment Evaluation Unit (ATEU) regarding inclusion of eligible SFMHS subjects in the NIAID supported multicenter trial of Zidovudine for asymptomatic HIV infected persons. The logistics of this participation have yet to be worked out.

We are also planning to offer participation to SFMHS subjects participation in the clinical trial of Zidovudine for HIV infected persons with less than 200 CD4 T lymphocytes/ul. This will include participants with PGL and ARC.

Because the SFMHS does not include follow-up of subjects after they have developed clinical AIDS, no plans for treatment of these subjects have been contemplated. Of course, SFMHS subjects who are found to have AIDS at periodic examinations are appropriately referred to treatment centers.
3. What are the precise procedures for tracing the clinical status of patients with respect to HIV-related outcome: What is the feasibility of determining the presence of MAC cohort participants on state or Federal AIDS registries and/or obtaining hospital records, autopsy findings, including slides or blocks?

The clinical status of cohort members is determined twice yearly at the Children's Hospital clinics. A manuscript describing the development of clinical and immunological findings during the first 24 months of observation has just been submitted for publication and is included herein as Attachment 2. Other sources of case ascertainment include obituaries and death certificates.

We have established the feasibility of ascertaining reported cases of AIDS in the SFMHS cohort by comparing "Soundex" coded identifiers with similarly coded listings of reported cases in the Department of Health Services in Sacramento and at the CDC in Atlanta. However, we have not implemented these procedures because of confidentiality concerns. We are, however, planning to check our "lost to follow-up" cohort members against the California Automated Death Registry and the National Death Index.

4. While it is acknowledged that the supplemental sample of heterosexuals is chosen appropriately, are the responders significantly different from the non-participants-- what is the nature of the refusal to participate?

Because we have not yet begun recruitment of our heterosexual cohort, it remains too early to evaluate whether respondents differ significantly from non-participants. However, because of our sampling scheme, we already know that we will be able to compare characteristics of our participants with various demographic characteristics available from the census and other neighborhood reports. Thus, although we may not be able to interview non-participants, we will be able to assess the representativeness of our sample as compared to the designated target population living in the census tracts that define the geographic area where the sampling will occur. This procedure is discussed in detail under #15 below.

5. How will the ethnic/racial/linguistic ability of subjects affect participation in the additional proposed studies?

As with Question 4, it is difficult to assess the effects of ethnic diversity on our supplemental heterosexual cohort, because we have not yet begun recruitment of this sample. However, we are preparing to cope with anticipated problems in the following ways:

a. Our interviewers will include bilingual individuals of varied ethnic and racial backgrounds.

b. We are soliciting community support and endorsements from local leaders who may already be known by potential participants.
c. In our pilot phase we will test the feasibility and efficacy of offering respondent payments as incentives for participation. This will be tested by sampling with and without this inducement so that we can compare results.

d. All recruitment procedures that are detailed in the Technical Proposal and in our supplemental budget (approved as Modification 14) will be tested and evaluated in our pilot phase before we implement them on a large scale. We are currently working with a local research organization SAMHA (Substance Abuse and Mental Health in AIDS) funded by NIMH that has been developed to specifically address issues related to AIDS research among minorities. This group is comprised of local researchers and community leaders. We are open to suggestions and guidance from this and other community groups and individuals in developing our final procedures.

6. Discuss feasibility of recruiting regular discordant sexual partners.

Thirty-two steady sexual partner couples (12 of these couples are monogamous, the median number of sexual partners in addition to their live-in partner for the others = 2) are included among our homosexual/bisexual participants in the SFMHS. Nine of these couples are discordant for HIV serostatus. We have only begun to evaluate transmission and infection among these men over the last week and hope to complete this examination in a few months. Based on our findings, if we need to evaluate more partners to increase statistical power to evaluate various hypotheses, we are prepared to advertise for recruitment of steady partners in our periodic newsletter.

We have also encouraged bisexual participants to refer their female sexual partners to an on-going heterosexual partners' study funded by the University of California Universitywide Task Force on AIDS, and also run by Drs. Winkelstein and Padian. We have not actively solicited participation in this study because we did not want to influence or pressure our SFMHS participants in a way that might jeopardize their future participation in the SFMHS. Two SFMHS participants referred their female partners to this study, and we are currently considering more active recruitment. Obviously, in any of these substudies, there is no way to predetermined which partners will represent the other half of a discordant or a concordant couple.

Seropositive participants in the heterosexual supplemental sample will also be encouraged to refer their sexual partners to the on-going heterosexual partners' study. Once again, there is no way to determine which of these partners will be discordant or concordant for HIV serostatus. We do however feel confident in our ability to recruit these partners regardless of serostatus. The partners' study has been recruiting such individuals for over two years, and now represents the largest heterosexual partner study being conducted in this country. Because most of our new participants will be heterosexuals, we feel that issues surrounding future participation in this cohort will be less important than in the SFMHS, and thus recruitment should be easier in this sample than in the SFMHS where bisexuality may be somewhat covert.

-4-
7. Discuss plans to differentiate between drug-induced side effects and interactions from HIV-related pathology for patients on prophylactic/therapeutic drug trials and regimens. Will supplemental questions be necessary for the next wave? What would be the nature of such questions? It was felt by the peer reviewers that greater specificity may be required than already exists for similar questions in the current wave of the MAC?

Since the beginning of the fifth cycle of examinations in July 1986, we have collected extensive information from participants regarding use of putative chemotherapeutic and antibiotic agents for the control of HIV and its consequences as well as information regarding participation in any clinical trials. The coded information which is available is included herein as Attachment 3. Many such agents are available in San Francisco on the "black market".

The availability of this information will allow us to stratify our analyses of outcome variable according to drug usage data. However, because of the probable haphazard use of such agents and the large number of different agents available, we recognize the limitations of such analytic solutions. We have added additional questions on the interview to assess use of specific drugs as we become aware of their use and popularity. Obviously, this list will be updated at each subsequent visit.

8-11. Since submission of the Technical Proposal responding to RFPNIH-NIAID AIDSP-87-28-72635, the scientific staff of the SFMHS has been considering the feasibility and desirability of introducing a major neuropsychiatric substudy in to this research effort. We have also devoted a very considerable amount of time and effort to the development of a screening instrument and we have contacted several other investigators who have been active in neuropsychiatric investigations of HIV infected persons to obtain some insight into the problems and requirements of such investigations. As a result of these activities, we have come to the conclusion that the addition of such a substudy, properly designed and implemented, would be a major undertaking that would jeopardize the effective continuation of our basic efforts to elucidate the epidemiology and natural history of HIV infection in homosexual/bisexual men and to evaluate the spread of infection among heterosexuals and ethnic minorities in areas of San Francisco adjacent to areas where the AIDS epidemic has been most intense. We are, therefore, withdrawing those portions of the Technical Proposal (and budgetary provisions which relate to neuropsychiatric studies).

12. Identify the laboratories which are going to conduct routine and experimental viral isolation studies, and describe those studies. Describe the anticipated quality control system for viral isolation.

Viral isolation will be conducted in the laboratories of Dr. Jay Levy at the Cancer Research Institute, University of California, San Francisco, and at the Viral and Rickettsial Disease Laboratory, California Department of Health Services under the direction of Dr. Michael Ascher. Specific studies and/or routine procedures to be conducted in these laboratories have been described
in the Technical Proposal. Dr. Levy employs the following procedures for quality control of his viral isolations.

a. He controls for false positive results by comparing these results with isolation attempts from normal cells.

b. He controls for false negative results by testing all isolations with an antigen detection assay. Positive results on the assay can then be retested for viral isolation.

Dr. Ascher employs the following procedures to insure quality control for viral isolations from his laboratory:

Peripheral blood lymphocyte (PEL) cultures are inoculated and cell free supernatent is tested for reverse transcriptase (RT) activity on days 11, 18, 25, and 32 of culture. Inoculated and uninoculated cultures are maintained in parallel and considered positive if the RT activity in the inoculated culture is > 10X the RT activity in the uninoculated culture. The specimen is reported as positive for HIV isolation if the RT activity is unequivocally positive on two consecutive weekly tests. If RT activity is low or negative and HIV serologic test are positive, isolation cultures are held and tested for two additional weeks before a negative results is reported. Cultures that give low RT activity are considered potential false positives and are tested using a DNA template. A high level of DNA dependent transcription is considered evidence of a false positive RT.

13. How do you propose to coordinate your quality control studies with those of the four MAC sites? No resources for this purpose are described in your proposal. Describe quality control issues you feel should be handled outside your contract and subcontracts. Describe what is necessary to accomplish this.

Quality control measures for cell separation are being conducted by Dr. Herb Perkins at the Irwin Memorial Blood Bank. However, we would be pleased to run cell surface phenotyping by flow cytometry on any samples sent to us by direction of the NIAID as an external proficiency test. We will test for any marker so requested providing they are among those we routinely identify. We will report the results of the typing as directed.

14. The proposed Children's Hospital Subcontract:

a. The effort proposed for the following positions appears excessive:

   25% Clinical Director
   100% Project Director
   100% Administrative Assistant
   50% Unit Coordinator

Describe in detail the proposed tasks of this project for each.
b. Specify and describe leased/rented equipment and discuss cost efficiency of leasing/renting vs. purchasing. Which items are under service contract; provide cost information.

c. Identify, justify and describe benefit to the contract for the following proposed items:
   -- speakers' honoria
   -- volunteer x-mas gifts
   -- petty cash--source and purpose

Desks and chairs are unallowable for purchase under the contract; please delete from the budget.

(a) The effort for the clinical director is necessary to cover his responsibilities. Dr. Lang supervises our physician's assistants and oversees all clinic functions including physical examinations, sample collection, collaborative clinical research, and the Children's Hospital laboratory and repository. The Children's Hospital project director acts as Dr. Lang's assistant and coordinates all laboratory, repository, and clinical functions. His position is equivalent to a U.C. administrative assistant. He also acts as a conduit between the Children's hospital administrative unit and the project including budget and hiring considerations. He also performs clerical responsibilities as needed. A 50% secretary will be needed to complete clerical tasks such as managing laboratory results and informing participants of their results by letter. We are cutting back the administrative assistant and unit coordinator. Starting in the fall, we will place a Survey Research Center employee in the clinic to oversee interviewers and general clinic flow. This person will also be in charge of preparing charts, scheduling visits and maintaining up-to-date identifying information on participants. This will be a full-time position that will come out of the Survey Research Center budget.

(b) Children's Hospital is renting the Merlin phone system from AT&T and the copy machine. These items are being leased upon the advice of the Children's Hospital purchasing agent. The advice was based on two major factors. First, the rental costs include a service agreement, whereas parts for the copy machine are not guaranteed beyond a few months time if the machine is purchased. Second, these items are likely to become out-of-date within a relatively short period of time. When leases are renewed they can be renegotiated for newer systems. Other items under service agreements include all computer equipment including the Sanyo PC and keyboard, the Taxan monitor, and the Deck terminal, keyboard and printer. This service agreement costs $61.88/month.

(c) We are deleting the speakers' honoria, and the volunteer X-mass gifts from the budget. Petty cash is for miscellaneous expenses when immediate purchases under $50.00 are necessary and can't wait for a purchase order. Examples of such items include: a screw driver, an extension cord, and various stationery items.

(d) Desks and chairs have been deleted from the budget.
15. On page I-2 of the proposal, it is stated that of a sample of 1,750 eligible men, 1,034 (59.2%) completed the first examination cycle. Describe the demographics, lifestyle and other characteristics of the 719 people who did not complete the first examination cycle. Describe how the people who refused to participate in the study differed from those who participated. What reasons for refusal to participate did they offer?

In many surveys, information is not available for non-respondents. Although efforts were made during the initial enumeration of the 3343 households drawn for the SFMHS to obtain some information on all eligible study subjects the data is incomplete except for age, sex, and marital status, the criteria for entry into the study. We elected to evaluate the representativeness of the cohort by comparing the frequencies of various characteristics among study participants with these same characteristics as determined by the census. The results of this comparison were reported on page 322 and discussed on page 324 of one of the publications included in Appendix IX.A of the Technical Proposal [Winkelstein W, et al: Sexual Practices and Risk of Infection by the Human Immunodeficiency Virus: The San Francisco Men's Health Study. JAMA 1987, 257:321-325].

The variables compared were; age, occupation, and education. For age, the 25-29 year old age group was over represented in the sample by 8.2% and the 35-44 year age group was over represented by 8.9%. The other age groups, i.e., 30-34 and 45-54 years, were both within 3% of the census distributions. For occupations, census data are available only for all men over the age of 16 years. Executive and professional managers constituted 43.5% of the sample, 9.5% more than the census. For the combined categories of technical and sales, administrative support, and service personnel, the sample included 2.2% less than the census. For education, reported by the census for all men over the age of 25, the sample included 89.8% with one or more years of college, 24.6% more than the census. We concluded that these differences were insufficient to seriously impair the representativeness of the sample. We do not have data regarding the reasons for refusing to enter the SFMHS.

16. No information is given regarding the adequacy of the sample size for the proposed substudies and for the cohort study. Describe the rationale supporting the adequacy of the sample size of the prospective cohort. What is the associated power to test the key hypotheses? Provide the rationale for the choice of the number of heterosexuals in the study. What statistical power will be achieved with these sample sizes?

Figure 1 depicts the minimum relative risk and statistical power obtainable given the prevalence of a particular risk factor in the uninfected members of the cohort. This Figure was derived from a comparison of seronegative and seropositive homosexual/bisexual participants (N=300 in each group) because to date most of our assessments have been based on this comparison. As is shown on the Figure, even with the lowest parameters: a prevalence of the risk factor of .1, and power set at .8, we could still detect a minimum relative risk of about 1.8. Thus, we have had no problem assessing risks such as sexual behaviors or drug use associated with infection. Similarly, we anticipate having adequate power to detect risk factors associated with progression to disease among HIV-infected participants. As shown in the following table, we will have sufficient sample
sizes to conduct a variety of case-control studies where risk factor prevalences and sample sizes vary. We are assuming a matched pair model with a Type I error of <0.05% and a Type II error of <0.10. The results are shown in the following tabulation:

<table>
<thead>
<tr>
<th>Prevalence of Variable</th>
<th>Difference to be detected</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>25%</td>
<td>37 pairs</td>
</tr>
<tr>
<td>40%</td>
<td>20</td>
<td>63 pairs</td>
</tr>
<tr>
<td>30%</td>
<td>15%</td>
<td>104 pairs</td>
</tr>
<tr>
<td>20%</td>
<td>10%</td>
<td>188 pairs</td>
</tr>
</tbody>
</table>

The sample size for the heterosexual survey was based on an overall population size of approximately 30,000 eligible participants living in the additional 20 census tracts. The following Table shows the sample size necessary for various population rates of infection, sampling errors, and confidence limits.

<table>
<thead>
<tr>
<th>Population rate</th>
<th>Sampling error</th>
<th>Confidence limits</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>.5%</td>
<td>90%</td>
<td>1071</td>
</tr>
<tr>
<td>2%</td>
<td>.5%</td>
<td>90%</td>
<td>530</td>
</tr>
<tr>
<td>2%</td>
<td>1%</td>
<td>95%</td>
<td>752</td>
</tr>
</tbody>
</table>

As is obvious from the Table, the necessary sample size varies between 500 and 1000. Thus we thought an overall sample of 1000 would be sufficient to detect low levels of infection. Note that the sample size calculations do not vary if the overall population was 15000 which is a likely assumption if we examine rates in females and males separately.

17. The investigators recruited an initial sample of 1,034 men from among 1,750 men who were eligible for inclusion in the study for a sampling rate of 59 percent. The men in the study were 25-54 years old and were selected by multistage stratified cluster sampling from the 19 census tracts in San Francisco with the highest cumulative incidence of AIDS. Heterosexual, bisexual, and homosexual men were included in the sample. Of the original cohort of 1,034 men, 800 remain under observation. The sample is unique among the MACS studies in that it was selected by rigid statistical methods. The investigators believe that they will thus be able to extrapolate the sample results to a defined population, the 23,000 single men living in the 19 census tracts sampled. The study is designed to allow an estimation of the infectivity of HIV.

Weaknesses highlighted by the peer reviewers: one weakness of the study is that the sample includes only 50 percent of the 1,750 men who were eligible for inclusion. Thus, the bias introduced by this low sampling rate is impossible to estimate and severely limits the generalizability of the sample results to the target population.
Another serious weakness is the apparent intention of the investigators not to pool the results of this study with those of the other MACS centers. This, and differences in sampling methodology, impose limitations on the statistical power provided by the sample. A final major weakness of this proposal relates to the fact that the investigators state that 700 to 800 subjects will be attending each examination cycle. This represents approximately 50 percent of the original sample, and approximately 75 percent of those who completed the first examination. With a seroconversion rate of approximately 2 percent per year, the loss of 20-25 percent of subjects will make data from this center inconclusive.

Please address each of these issues including your apparent intent not to pool study results/data and/or use protocols common to the other four sites.

A low response rate does not necessarily result in a biased sample just as a high response rate does not necessarily produce an unbiased sample. Thus, it is always necessary to evaluate the representativeness of the sample according to some external criteria. As described above in #15, we evaluated the SFHMS sample by comparing selected characteristics of the sampled men with the same characteristics determined by the census for the census tracts from which the sample was drawn. Our conclusion that the sample was reasonably representative may be open to question. However, it has been accepted by reviewers and editors of at least the three journals which have published our first four major papers, viz., Journal of the American Medical Association, American Journal of Public Health, and the Journal of Infectious Disease. (These papers are included in the Appendices to the Technical Proposal and were numbered: I.C.8., I.C.10., I.C.11., I.C.12. in the Technical Proposal). In each of them, extrapolations to the sampled populations were made.

We have placed no obstacles in the way of utilization of our data by other MACS investigators including NIAID staff. On 26 January 1985, we wrote Dr. Frank Polk (copies to project and contract office staff of NIAID) as follows:

"Despite Article I.B.2.c.2. of our negotiated contract, (Article I.B.2.c.2. of the negotiated contract specifies delivery of a "cleaned, edited, and documented tape containing all clinical, epidemiologic and laboratory data acquired under the contract" at its completion), we are planning to transfer data in machine readable form (or other form if requested) to NIAID in a timely fashion upon request. It is our understanding that this data may be pooled with data from other MACS centers for various analyses. We trust that when this is done, we will be given the opportunity to participate in the planning and interpretation of such analyses as well as in the preparation of publications arising therefrom."

We continue to affirm this position. We have been transferring data regularly to NIAID in the format designated by project office personnel.

We continue to believe that the study design of the SFHMS, based on the area probability sample, is appropriate and has already provided important information which could not be obtained by other designs. For example, we have been able to estimate the HIV seroconversion rates among seronegative
homosexual/bisexual men in San Francisco since 1982 and demonstrate important and substantial declines in these rates. Furthermore, we have been able to relate these declines to changes in sexual behavior and to extrapolate these findings to the 18,000 homosexual/bisexual men who live in the target area (Winkelstein W, et al: The San Francisco Men's Health Study: III. Reduction in human immunodeficiency virus transmission among homosexual/bisexual men, 1982-86. AJPH; 77:685-690.) Many local and national public health professionals have indicated the significance of these observations as they demonstrate the potential for control of the epidemic by behavioral modification. As for statistical power, this has been discussed in §16 above.

Finally, the reviewers indicate concern that only 700 to 800 subjects are attending each examination sample. We too are concerned about the representativeness of the continuing participants. In each of our analyses we have taken note of the possibility of selection bias and have analysed the data accordingly. Thus, in the paper referenced in the preceding paragraph, we evaluated the possibility that the lower seroconversion rates observed over time were due to selection bias by examining the participation rates for each examination cycle according to risk factor status of seronegative subjects on entry into the study. This analysis revealed that participation in subsequent examination cycles was unrelated to this risk status. In the paper just submitted (Attachment 2) we devoted a considerable amount of space to the presentation of data and discussion of the possible effect of selection on the findings.

With respect to seroconverters, to date 32 have been observed in the SFMHS (all among homosexual/bisexual members of the cohort). Although this number, plus any additional seroconverters is modest, it will permit some useful observations. For example, it should be sufficient to permit us to evaluate the CD4 T cell response to infection. We realize that our observations with respect to seroconversion must be limited.

18. Discuss the feasibility of increasing the size of the cohort (sample) in order to achieve adequate power for the various studies, including the heterosexual study.

As of this date, we do not consider it necessary to increase the size of the SFMHS cohort although we do anticipate adding HIV seropositive participants from the heterosexual seroepidemiological study and some seronegative "controls". Statistical power issues have been discussed in §16 above. We believe that is is more important to increase our efforts to achieve complete follow-up of the original SFMHS cohort than to expend funds and energy on adding new study subjects. As far as feasibility is concerned, increasing the size of the cohort would be possible but would be a very costly undertaking.

19. The investigators' curriculum vitae are not all current. The principal investigator's last reference is a paper published in 1982. Please provide updated/current CVs.

Updated curriculum vitae are provided in Attachment IV.
20. Please describe the role(s) of staff and their use(s) of laboratory facilities for the MAC study, the ATSU and other NIH funded HIV-related research, by sources of financial support.

This question appears to be directed to the participating Multi Center AIDS Cohort Study (MACS) investigators. The SFMHS was separated from the MACS by Dr. A. Fauci, Director of the NIAID, on 22 February 1985.

21. Describe the phase-out plans for the fourth year of the contract.

We plan to follow the same phase-out plan for the new contract that was utilized for the current contract. During the latter half of the third year of the contract, we will initiate discussions with NIAID staff concerning the prospects for continued funding of the SFMHS. If those discussions indicate that a renewal of the contract is likely, as they did for the present contract, we will proceed in accordance with guidance from project and contract personnel at NIAID. If not, we will seek support from other sources.

Our first alternative will be to prepare and submit a program-project grant application to NIH for continued support of the cohort and associated studies. This was our plan for the present contract until July 1986 when we were advised that provision for renewal was being made. The second alternative, which will be pursued simultaneously with the first (and third, to be described), will be to seek support from the California University Task Force on AIDS, the mechanism by which the State of California funds AIDS research. Third, if none of the foregoing succeed, we will seek support from appropriate non-profit Foundations.

We hope to be able to know our prospects for continued support by April of the final year of the contract, six months before its scheduled termination. If at that time, continued support appears unlikely, we will proceed with the usual termination procedures, i.e., notification of collaborating institutions and investigators, staff, and study subjects. The repository will be offered to NIH and/or local collaborating investigators. Hopefully, continued support for this valuable resource will be found. We intend to maintain the data obtained from the SFMHS indefinitely.

When the SFMHS was designed, in 1983, it was confidently believed that the epidemiology and natural history of AIDS could be comprehensively investigated in four years. As time has passed, it has become increasingly apparent that both the epidemiology and natural history of infection by the HIV will require continued investigation over a very long period of time. We believe that the SFMHS cohort will continue to provide important information for that long-term effort and it is for this reason that we do not seriously contemplate termination of the project in the foreseeable future.
Figure 1

MINIMUM DETECTABLE RELATIVE RISK
N cases = N controls = 300; alpha = .05
Summary

In July 1984 the San Francisco Men's Health Study (SFMHS) began recruitment of a cohort of single men 25-54 years of age for studies of the epidemiology and natural history of acquired immunodeficiency syndrome (AIDS). The cohort was obtained by multistage stratified cluster sampling from 19 census tracts in San Francisco with the highest cumulative AIDS incidence through December 1983. One thousand thirty-four men entered the SFMHS, of whom more than 800 remain under observation. Subjects visit the study clinic twice yearly for physical examination, provision of materials for laboratory study, and intensive interview.

Major accomplishments include the estimation of the infectivity of human immunodeficiency virus (HIV) for sexual transmission in homosexual/bisexual men. This required: 1) establishing the relationship between the numbers of sexual partners and the risk of HIV infection, 2) determining the mechanism (sexual practices) by which HIV is sexually transmitted among homosexual/bisexual men, 3) estimating the frequency of such practices, 4) measuring the prevalence of HIV infection in the population, and 5) ascertaining the rate of seroconversion in a defined period of time. Other epidemiological findings include the observation of a substantial decline in HIV infection rates in San Francisco since 1984, resulting from substantial decreases in the prevalence of high risk sexual behaviors among homosexual/bisexual men, and the estimation of the potential for spread of infection from the homosexual population through bisexual men to heterosexual women in San Francisco. Clinical and immunological findings include the observation of a unimodal uniform depression of Leu 3a T lymphocytes in HIV infected men and the subsequent uniform decrease in these cells over time, the association between Leu 3a cells and subsequent development of clinical symptoms and AIDS, and the establishment of predictive values of a variety of clinical signs and symptoms for HIV infection. To date, 16 publications (7 letters) have resulted from the study (10 published, 6 in press).

The objectives of this proposal are to continue the study of the epidemiology and natural history of HIV in the SFMHS. In addition, a seroepidemiological survey of single men and women in 20 census tracts adjacent to the 19 already sampled is proposed in order to determine the degree of spread of HIV infection into the heterosexual population and to examine factors associated with such spread if it is occurring. This survey will also be based on area probability sampling. Persons testing positive in the survey, along with suitably matched controls, will be recruited into the SFMHS cohort so that the natural history of infection in heterosexual men and women can be examined. Substantial increases in immunological, virological, neuropsychiatric, genetic and epidemic modeling studies are also anticipated.

The SFMHS is unique among studies of the epidemiology and natural history of HIV infection and AIDS in that its subjects have been recruited by rigorous sampling, thereby permitting the findings to be extrapolated to a defined population and minimizing the possibility that observed associations are spurious.
Original Contributions

Sexual Practices and Risk of Infection by the Human Immunodeficiency Virus

The San Francisco Men's Health Study

Warren Winkelman, Jr, MD, MPH; David M. Lyman, MD, MPH; Nancy Padian, MS, MPH; Robert Grant, MPH; Michael Samuel, James A. Wiley, PhD; Robert E. Anderson, MD; William Lang, MD, John Riggs, PhD; Jay A. Levy, MD

The San Francisco Men's Health Study is a prospective study of the epidemiology and natural history of the acquired immunodeficiency syndrome in a cohort of 1034 single men, 25 to 54 years of age, recruited by multistage probability sampling. At entry, June 1984 through January 1985, the seropositivity rate for human immunodeficiency virus (HIV) infection among homosexual/bisexual study participants was 48.5%. No heterosexual participants were HIV seropositive. Among homosexual/bisexual men reporting no male sexual partners in the two years before entry into the study, seropositivity was 17.6%. For those reporting more than 50 partners, seropositivity was 70.8%. Only receptive anal/genital contact had a significantly elevated risk of HIV infection. Douching was the only ancillary sexual practice that contributed significantly to risk of infection.

AMONG homosexual/bisexual men, large numbers of sexual partners and receptive anal/genital contact have been the most consistently reported risk factors for infection by the retroviruses associated with the acquired immunodeficiency syndrome (AIDS). However, all of the previously reported studies of risk factors for AIDS virus infection have been based on selected clinical or volunteer samples. These investigations may be biased in unknown ways and, therefore, their findings can only be cautiously extrapolated to larger populations. Reported herein are observations based on a large study population selected by area probability sampling so that the results can be generalized to the entire population from which the sample was derived. Furthermore, this design reduces the possibility that observed associations are the result of unknown biases.

The San Francisco Men's Health Study (SFMHS) is a prospective study of a random sample of single men 25 to 54 years of age who live in the 19 census tracts of San Francisco where the AIDS epidemic has been most intense. The objectives of the study, begun in June 1984, are to elucidate the epidemiology and natural history of AIDS. In this article, the sexual practices and serologic evidence of infection by the human immunodeficiency virus (HIV) in the 809 homosexual/bisexual men free of AIDS in the cohort at the beginning of the study are presented.

METHODS

The Sample

A cohort of 1034 single men 25 to 54 years of age was obtained by multistage stratified cluster sampling. The 19 census tracts of San Francisco with the highest cumulative AIDS incidence through December 1983 defined the area from which the sample was drawn. A two-stage procedure was used to obtain the sample. First, a sample of blocks was drawn in each tract directly proportional to the size of the tract. Second, a sample of households was selected inversely proportional to the size of the sampled block. This procedure resulted in a sample of households in which each household had an equal probability of selection. In each selected household, all single men 25 to 54 years of age were invited to participate in the study.

Data Collection

Each participant visits the study clinic twice yearly for physical examination, provision of materials for laboratory study, and intensive interview. The...
questionnaire used to obtain data concerning sexual practices and selected covariates was developed for the Multi-center AIDS Cohort Study, sponsored by the National Institute of Allergy and Infectious Diseases. Interviews are carried out by professional staff of the University of California Survey Research Center, Berkeley. The independent variables included in the analyses reported herein are (1) numbers of sexual partners during previous two years, (2) patterns of anal and oral/genital sexual contact, and (3) ancillary sexual contact activities.

Physical examinations are performed by two physician’s assistants, using standardized procedures and forms for recording findings.

Serologic status was determined by the indirect immunofluorescent antibody assay (IFA), using the HUT 78 human T-cell line infected with HIV (formerly AIDS-associated retrovirus ARV-2). The serum samples, obtained from June 1984 through January 1985, were tested in the laboratories of the University of California Cancer Research Institute in San Francisco and the Viral and Rickettsial Disease Laboratory of the California Department of Health Services in Berkeley. Discrepant results were retested in each laboratory. The IFA test has been shown to be as sensitive as the enzyme-linked immunosorbent assay and more specific. It gives results similar to those of immunoblot assays.

Statistical Procedures
Prevalence of HIV seropositivity in the sample was adjusted for numbers of male sexual partners by the direct method. Comparisons between independent variables and the outcome variable, HIV serostatus, were evaluated by the chi-square test or the chi-square test for trend when such variables were ordered. Relative risks were calculated directly and were adjusted for number of male sexual partners by the method of Mantel and Haenszel. Confidence intervals for the relative risks were calculated by the method of Greenland and Robins. The multiple logistic regression analysis was carried out using a standard statistical package.

Population prevalence estimates and their confidence limits were calculated from the sample, using weights based on response rates and sampling fractions for each census tract.

RESULTS
Sample Response
The sampling procedure yielded 1245 households with 1750 eligible men. Of these, 645 (36.9%) refused to partici-

pate, 71 (4.1%) did not participate for other reasons, and 1034 (59.1%) entered the study. Since no information was available from nonparticipants, the representativeness of the sample was evaluated by analysis of the distribution of selected characteristics among study participants compared with these characteristics as determined for the 19 census tracts by the census for 1980.

With respect to age among single men (obtained from the census by special request), the 25- to 29-year age group was underrepresented in the sample by 8.2% and the 35- to 44-year age group was overrepresented by 8.9%. Other age groups, 30 to 34 years and 45 to 54 years, were both within 3% of the census distributions. With respect to occupations, the census data are available only for all men over the age of 16 years. Executive and professional managers constituted 45.3% of the sample, 9.5% more than reported by the census. For the combined categories of technical and sales, administrative support, and service personnel, the sample included 46.0%, 2.2% less than the census. With respect to education, reported by the census for all men over the age of 25 years, the sample included 89.8% with one or more years of college, 24.6% more than the census.

There were also small differences in response rates between tracts. When the 19 tracts were ranked, those with lower educational achievement had response rates averaging 7.5% lower than average, whereas tracts with higher educational achievement had response rates averaging 9.5% higher than average.

Reliability of HIV Serologic Status
Of 980 IFA tests run by both laboratories, 894 yielded identical results initially. Of the 86 discrepant results, all but one were reconciled after one repeated test. An additional 25 tests were only run by the Cancer Research Institute laboratory and two by the Viral and Rickettsial Disease Laboratory. Thus, serologic status of 1006 men, 97.3% of the cohort, was determined. Of these, 799 were homosexual/bisexual, 204 heterosexual, and three gave no information on sexual orientation. None of the heterosexual men was seropositive; they do not receive further consideration in this report. Seropositivity among homosexual men (49.2%) and bisexual men (46.2%) was essentially the same, allowing the data to be pooled.

Association of Multiple Sexual Partners With HIV Seropositivity
Because of the previously indicated association of multiple sexual partners with infection by the AIDS virus, we analyzed the relationship between reported numbers of sexual contacts during the two years preceding entry into the study and the HIV serostatus of the homosexual/bisexual members of the cohort. The data show a strong positive association between numbers of male sexual partners and seropositivity (Table 1). The extent of seropositivity varied in a graded fashion, from 17.6% among homosexual/bisexual men with a history of no male sexual partners during the two years before entry to 70.8% in those reporting 50 or more partners. This trend was statistically significant (P<.001). The overall seropositivity rate was 45.5%. These prevalence rates are quite similar to those reported in a preliminary report from this study.10

To the extent that the cohort is a representative sample of the target population, approximately 18,000 homosexual/bisexual men 25 to 54 years old living in the 19 census tracts, the population is distributed among partner categories in the same proportions as in the sample. Thus, the prevalence of seropositivity in each of the partner categories may be extrapolated to this population with defined confidence intervals (Table 1). The weighted prevalence rates for each of the partner categories for the whole population are similar to those in the study cohort. The overall weighted prevalence of seropositivity among all homosexual/bisexual men living in the 19 census tracts was 48.2%, with a 95% confidence interval of 44.3% to 52.0%.

Association of Sexual Practices With HIV Seropositivity
The most common sexual practices of homosexual/bisexual men, excluding kissing, for which no data are available from this study, are anal and oral/genital contact. Among the 809 homosexual/bisexual men in the study cohort, 774 (95.7%) gave a history of one or the other practice during the two years before entry into the study. Thirty-five had engaged in neither type of contact. Of the 809, sixty-five gave a history of needle sharing within the past five years. Among them, the rate of HIV seropositivity was 82.8%. Thus, all needle sharers were eliminated from subsequent analyses in this report.

Anal/Genital Contact
Table 2 shows HIV serostatus according to two-year pattern of anal/genital contact (with ejaculation) in 729 homosexual/bisexual members of the cohort. Ninety-nine (13.6%) gave a history of no anal/genital contact during

Human immunodeficiency virus—Winkeinstein et al
Table 1—Association of Number of Male Sexual Partners in Previous Two Years and Human Immunodeficiency Virus (HIV) Serologic Status

<table>
<thead>
<tr>
<th>No. of Male Partners</th>
<th>% HIV Antibody Positive</th>
<th>% HIV Antibody Positive</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Exposed</td>
<td>17.6</td>
<td>17.2</td>
<td>5.2-41.5</td>
</tr>
<tr>
<td>None</td>
<td>17</td>
<td>19.2</td>
<td>5.2-41.5</td>
</tr>
<tr>
<td>1</td>
<td>66</td>
<td>17.9</td>
<td>9.5-29.0</td>
</tr>
<tr>
<td>2-9</td>
<td>206</td>
<td>31.9</td>
<td>25.2-39.0</td>
</tr>
<tr>
<td>10-49</td>
<td>312</td>
<td>53.7</td>
<td>47.4-59.6</td>
</tr>
<tr>
<td>≥50</td>
<td>185</td>
<td>70.8</td>
<td>62.7-76.8</td>
</tr>
<tr>
<td>Total</td>
<td>796</td>
<td>48.5</td>
<td>44.3-52.0</td>
</tr>
</tbody>
</table>

*Subjects with missing data (n = 13) were excluded. The y2 for trend of the association of number of partners and HIV antibody seropositivity in the sample is .867. P < .0001.

*Weighted for sampling fraction and difference in participation rates between census tracts.

Table 2—Association of Human Immunodeficiency Virus Serologic Status and Relative Risk According to Two-Year Pattern of Anal/genital Contact

<table>
<thead>
<tr>
<th>2-y Pattern</th>
<th>No. of Subjects</th>
<th>% Seropositive</th>
<th>Adjusted %</th>
<th>Adjusted Relative Risk, % (95% Confidence Interval)</th>
<th>P</th>
</tr>
</thead>
</table>
| None        | 99              | 17             | 17.2       | 20.6                                                | 1.0 (1.0) | ...
| Inse. only  | 116             | 32             | 27.6       | 26.7                                                | 1.3 (0.7-2.2) | .38 |
| Rece. only  | 72              | 29             | 40.3       | 44.6                                                | 2.1 (1.2-3.6) | .004 |
| Both        | 442             | 252            | 57.0       | 53.3                                                | 2.5 (1.6-4.0) | <.001 |
| Total       | 729             | 330            | 45.3       |                                                     |              |     |

*Subjects with a history of needle sharing (n = 65) and subjects with missing data (n = 15) were excluded.

Table 3—Association of Human Immunodeficiency Virus Serologic Status and Relative Risk According to Two-Year Pattern of Oral/genital Contact

<table>
<thead>
<tr>
<th>Oral/genital Contact</th>
<th>No. of Subjects</th>
<th>% Seropositive</th>
<th>Adjusted %</th>
<th>Adjusted Relative Risk, % (95% Confidence Interval)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>44</td>
<td>8</td>
<td>18.2</td>
<td>22.0</td>
<td>1.01 (0.47-2.18)</td>
</tr>
<tr>
<td>Some</td>
<td>171</td>
<td>41</td>
<td>24.0</td>
<td>24.7</td>
<td>1.01 (0.47-2.18)</td>
</tr>
<tr>
<td>Total</td>
<td>215</td>
<td>49</td>
<td>22.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Subjects reporting no receptive anal/genital contact in previous two years.

years before entry; 116 (15.9%), insertive contact only; 72 (9.9%), receptive only; and 442 (60.6%), both insertive and receptive anal/genital contact. The contact. The prevalence of HIV seropositivity, adjusted for numbers of sexual partners, was similar among those reporting no anal/genital contact and insertive contact only, 20.6% and 26.7%, respectively. The prevalence among those reporting receptive anal/genital contact only, or both receptive and insertive anal/genital contact, was substantially higher, 44.6% and 53.3%, respectively.

After adjusting for numbers of sexual partners, the relative risks of HIV infection for study subjects practicing various patterns of anal/genital contact during the two years before entry was compared with the relative risks of those who did not. The relative risk of 1.3 for insertive anal/genital contact only was not statistically significant (P = .88). For those practicing receptive contact, whether exclusively or combined with insertive contact, the adjusted relative risks of 2.1 and 2.5 were significantly elevated (P = .004 and P < .001, respectively).

Effects of Ancillary Sexual Practices on Risk of HIV Infection

To assess the possibility that certain ancillary sexual practices enhanced the risk of infection among those practicing receptive anal/genital contact, we examined the associations of four such practices with HIV serologic status. Five hundred fourteen men who gave a history of receptive anal/genital contact during the two years before entry were studied. The practices for which data were analyzed included partner inserting finger in subject's rectum (finger), partner inserting hand or fist in subject's rectum (fist), partner inserting dildo or other device in subject's rectum
(dildo), and use of douche or enema before having sexual contact (douche) (Table 4). After adjusting for numbers of sexual partners during the two years before entry into the study, only subjects giving a history of use of either dildo or douche showed significantly elevated relative risks over those with no history of any of the four practices (P < .05 and P < .01, respectively).

The effects of the four ancillary sexual practices were evaluated along with numbers of receptive anal/genital partners in the previous two years in a logistic model (Table 5). Interaction terms were not significant and were omitted from the model as shown. Douching was again shown to be significantly associated (P < .001), but none of the other three practices approached statistical significance (P = .58, P = .68, and P = .23, respectively). Statistically significant associations between numbers of receptive anal/genital contacts and HIV seropositivity were revealed by the logistic analysis (P = .04, P < .001, and P < .001, respectively). These associations were ordered (odds ratios, 1.7, 3.3, and 9.2, respectively).

**COMMENT**

The low response rate of 59% in the sample raises questions regarding its representativeness. However, the degree of agreement between the age and occupational distributions of the sample and the census is reassuring. The somewhat higher educational status of the sample in comparison with that of the census may reflect a higher educational status among homosexual/bisexual men who are more recent migrants to San Francisco and who make up a large proportion of the male population of the 19 census tracts. The small differences in response rates between tracts, grouped according to various census characteristics, were judged to be insufficient to introduce serious biases in the findings. This conclusion is supported by the very small differences between prevalence estimates for HIV seropositivity in subgroups of the sample and the weighted prevalence estimates for the population (Table 1). We have concluded that these differences were not sufficient to impair seriously the representativeness of the sample.

To date, reported prevalence rates for AIDS virus antibodies have been based on selected samples of various populations. For example, in San Francisco, 67.4% of homosexual men who had been recruited from a sexually transmitted disease clinic in 1978 to participate in epidemiological studies of hepatitis B (San Francisco City Clinic Cohort) were reported seropositive in 1984. Because of the particular selection of this sample, the investigators anticipated that the prevalence of infection in that cohort would be exaggerated. For a comparable time period, the prevalence determined in the SFMHS probability sample was 48.5%, with 95% confidence limits of 45.0% to 51.9%. Accurate determination of the prevalence of infection in populations at risk is important in monitoring and predicting the course of the epidemic as well as in understanding the natural history of any disease resulting from infection.

In the SFMHS information concerning sexual practices, the independent variables under study in this communication were obtained by interview. The interviewers were experienced staff of the University of California Survey Research Center, thoroughly trained and closely supervised. Thus, we believe that interviewer bias was minimized. We had no direct way to validate the responses of the study subjects and cannot evaluate the possibility of recall or other respondent bias. However, the respondents did not know their HIV serostatus at the time of the interview, and strong positive associations between certain independent variables and the reliably determined outcome variable, HIV serostatus, were observed. Thus, we believe that substantial respondent bias did not occur.

An increased number of sexual partners has been the most consistently reported risk factor for HIV infection. Except for a preliminary report from the SFMHS and a report from Denmark, none of the other studies has indicated specific levels of risk according to specified numbers of partners in particular time periods and places. This information is useful for predicting and evaluating the effects of behavioral intervention strategies. In the present study, homosexual/bisexual men reporting no partners or a single partner during the two years before entry had relatively low levels of HIV seropositivity (18.1%). Among those reporting two to nine partners, the prevalence almost doubled (31.6%), while for those reporting more than 50 partners in the two years before entry, the prevalence increased by a factor of approximately four (70.8%). The actual prevalence rates in the cohort resulting from various numbers of partners depend on the levels of infection in the population at various points in time.

The data from the SFMHS confirm that receptive anal/genital contact is the major mode of transmission of HIV infection. In fact, there was no evidence of epidemic spread due to any other sexual mode of transmission. This conclusion was made possible because the sample included men who had practiced insertive anal/genital contact exclusively during the two years before entry.
into the study and because the sample also included men who had not practiced receptive anal/genital contact during these same two years but had been potentially exposed to infection by oral/genital contact. Furthermore, the sample was large enough to permit the associations to be controlled for numbers of sexual partners and to allow for the elimination of subjects whose needle-sharing practices might have confounded the results.

It is important to note that even though certain sexual practices, i.e., insertive anal/genital contact and oral/genital contact, were not implicated as modes of transmission responsible for epidemic propagation of HIV infection, they could not be eliminated as possible transmission modalities. The sizes of the subsamples under study for these practices were insufficient to provide the necessary statistical power to reject the possibility of even the small relative risks demonstrated for these practices. This fact is shown in Table 2 and 3 by the upper boundaries of the 95% confidence intervals of 2.2 for the relative risks from insertive anal/genital contact only and oral/genital contact, respectively. Nevertheless, our data show no demonstrable independent contribution of these practices to elevated risk.

The data from the SFMHS indicate that of four types of rectal trauma studied, only douche or enema before sexual contact contributed to risk of infection by receptive anal/genital contact. This finding is consistent with observations of an association between douching and hepatitis B infection. No data regarding finger or dillo use and HIV infection have been previously published, to the best of our knowledge. Contradictory evaluations of "fisting" are available. 10-12

The findings reported here, along with the other reports from the SFMHS, 13,14 support the inference that sexual transmission of HIV infection in homosexual/bisexual men in San Francisco, during the current AIDS epidemic, has been largely a function of the numbers of sexual contacts and the practice of receptive anal/genital contact among them. These epidemiological findings are consistent with biological studies showing a low level of HIV in seminal fluid and its presence primarily in infected cells. Thus, more frequent exposure to infected semen in the presence of an anal mucosa compromised by frequent contact or douching would increase the chance of infection. The implications of this knowledge for control of the epidemic are apparent. In fact, before this knowledge was rigorously demonstrated, extensive efforts had already been made in San Francisco to encourage homosexual/bisexual men to limit their numbers of sexual partners and the practice of unprotected anal/genital contact. There is evidence that these efforts resulted in substantial changes in sexual practices among homosexual/bisexual men and a reduction in other sexually transmitted diseases. 15 In a subsequent communication, the effects of these changes on HIV seroconversion rates in the SFMHS since 1984 will be reported.

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References
Clinical, Immunologic, and Serologic Findings in Men at Risk for Acquired Immunodeficiency Syndrome

The San Francisco Men's Health Study

William Lang, MD; Robert E. Anderson, MD; Herbert Perkins, MD; Robert M. Grant; David Lyman, MD, MPH; Warren Winkelstein, Jr, MD, MPH; Rachel Royce, MPH; Jay A. Levy, MD

Forty-nine percent of homosexual/bisexual men were positive for antibody to the human immunodeficiency virus (HIV) in a population-based probability sample of 1034 single men recruited from San Francisco. All heterosexual men were negative. Among seropositive men, marked lymphadenopathy was present in 29%, and 16% had at least two other symptoms or signs suggestive of HIV infection. However, lymphadenopathy alone failed to indicate severity of immune impairment. The occurrence of two or more clinical signs and symptoms, except for marked lymphadenopathy, correlated with HIV infection, diminished skin test reactivity, and reduction in Leu 3a T cells. Twenty-nine percent of seropositive men had fewer than 400 absolute Leu 3a T helper cells per microliter (<0.4 x 10^9/L). Seronegative homosexual/bisexual men did not differ from heterosexual men in any clinical or laboratory variables except for increased numbers of suppressor Leu 2a T suppressor cells per microliter.

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MORE than 2000 cases of acquired immunodeficiency syndrome (AIDS), with a mortality rate of 55%, were reported to the San Francisco Department of Public Health by July 1, 1986. These cases were largely confined to homosexual/bisexual men living in 19 census tracts located in the central part of the city. The San Francisco Men's Health Study (SFMHS), begun in 1984, is a prospective study of single men, 25 to 54 years of age, recruited from these census tracts by multistage probability sampling. This study includes homosexual, bisexual, and heterosexual men. The objectives of the study are to elucidate the epidemiology and natural history of AIDS.

From the Children's Hospital of San Francisco (Drs Lang and Anderson); the Irwin Memorial Blood Bank, San Francisco (Dr Perkins); the School of Public Health, University of California, Berkeley (Drs Lyman and Winkelstein, Mr Grant, and Ms Royce); and the Cancer Research Institute, University of California, San Francisco (Dr Levy).

Reprint requests to School of Public Health, University of California, Berkeley, CA 94720 (Dr Winkelstein).

Since the outbreak of the AIDS epidemic in 1981, prodromal clinical syndromes and patterns of immunologic dysfunction have been widely recognized.4,4 Lymphadenopathy in people at risk for AIDS has been described by several authors and appears to be strongly associated with clinical and laboratory features of human immunodeficiency virus (HIV) infection.5,6 Lymphadenopathy could be predictive of disease progression, an appropriate immunologic response, or one of many manifestations of infection with the HIV.6 These issues have not been clarified.

Dermatologic findings, including seborrheic dermatitis, bullous impetigo, and herpes zoster, have also been associated with HIV infection and frank AIDS, but their place in the spectrum of this disease has not been established. Other clinical features, such as oral hairy leukoplakia and oral candidiasis, appear to be more clearly predictive of the development of AIDS.7,8

Abnormalities in subsets of T lymphocytes, in particular an elevation in Leu 2a T cells (suppressor) and a decrease in Leu 3a T cells (helper), resulting in a reduction in the Leu 3a–Leu 2a ratio, have been documented in groups at risk for AIDS, individuals with prodromal syndromes, and patients with AIDS itself.9 Leukopenia, hypergammaglobulinemia, skin test anergy, antilymphocyte antibodies, and a number of other abnormalities have also been associated with AIDS-related conditions.9,10

The discovery of a retrovirus associated with AIDS and the development of antiviral antibody testing now allow identification of infected individuals.11-13 Numerous investigators have examined the relationship between virus exposure, laboratory abnormalities, immune dysfunction, and clinical disease, but to our knowledge none has done so in a systematic fashion on a large, population-based cohort.14-18

In this report, the relationships of symptoms, physical findings, and laboratory values to the presence of antibody to HIV are examined. The question of whether lymphadenopathy is a predictor of immune function is addressed, and the characteristics of individuals in whom disease progression will be monitored are described. This is the initial report of clinical and laboratory findings in the SFMHS, which will be the basis for elucidating the natural history of AIDS in this sample of men from a population at high risk for AIDS.
METHODS
Selection and Examination of Subjects
A probability sample of single men 25 to 54 years of age was recruited from the 19 census tracts of San Francisco with a previously reported high incidence of AIDS. Participants are being examined, interviewed, and followed up at six-month intervals in the outpatient clinic of the Children’s Hospital of San Francisco. At the first visit, a comprehensive questionnaire was administered, covering history and symptoms of immunologic disease, sexually transmitted diseases, AIDS, and AIDS-related conditions, as well as history of sexual behaviors, exposure to blood products, use of medicinal and recreational drugs, tobacco use, alcohol use, nutritional patterns, and psychological factors. Men were categorized as either heterosexuals or homosexual/bisexuals based on their history of sexual behaviors.

Symptoms of AIDS-related conditions in the six months before the visit were determined without interviewer or subject knowledge of HIV serostatus and were defined as follows: (1) lymphadenopathy: tender or enlarged glands or lymph nodes (not counting the groin) for at least two weeks; (2) new rash: a new rash lasting for at least two weeks; (3) fatigue: persistent fatigue (feeling tired all the time) for at least two weeks; (4) diarrhea: diarrhea for at least two weeks; (5) night sweats: sweating at night for at least two weeks; (6) weight loss: an unintentional weight loss of at least 4.5 kg (unrelated to dieting); (7) persistent fever: persistent or recurring temperatures higher than 38°C for at least two weeks. A history of worsening herpes virus infection, thrush (oral candidiasis), shingles, or bullous impetigo in the six months before the visit was determined by direct yes/no questions.

A physical examination focusing on the skin and lymphoid system was performed by two specially trained physician’s assistants. Seven skin tests with a glycerin control were applied simultaneously by the Merieux method. Skin test reactions were read at 48 hours, and the size of induration was recorded. The skin test score was calculated by the sum of the average diameter of induration of each reaction greater than or equal to 2 mm to each of seven antigens (tetanus toxoid, diphtheria toxoid, streptococcus, old tuberculin, Candida albicans, Trichophyton mentagrophytes, and Proteus mirabilis). Total lymphoid mass was calculated as follows: the average diameter of lymph nodes greater than or equal to 1 cm at any given site was multiplied by the number of nodes at that site to create a node score for each site; node scores for all sites were then summed.

Blood Cell Studies
Peripheral blood mononuclear cells (PMCs) were prepared for subset analysis by Ficoll-Hypaque separation. A complete blood cell count was obtained on an ethylenediaminetetraacetic acid whole-blood specimen using a whole blood cell (ELT-8 Hematology) counter. A manual white blood cell differential cell count was performed. Absolute values for the different types of white blood cells were calculated by multiplying the white blood cell count by the fraction of cells from the differential cell count.

Analysis of lymphocyte subpopulations was also performed on Ficoll-Hypaque-separated PMCs by two-color fluorescence, using the Becton-Dickenson Immune Monitoring Kit and a cell counter (Becton-Dickenson FACs research analyzer). The percentage of lymphocytes in the separated PMCs was determined after subtracting the monocytes, identified by anti-Leu-M3 conjugated with fluorescent isothiocyanate. The specimens were analyzed for the percentage of T cells (Leu 2a positive plus Leu 3a positive), B cells (HLA-DR positive, Leu 2a and Leu 3a negative), Leu 3a-positive and Leu 2a-positive T cells, and large granular lymphocytes (Leu 7a positive). All were expressed as a percentage of total lymphocytes. The T and B, Leu 2a and 3a, and Leu 2a and Leu 7a cells were run in pairs, one monoclonal antibody conjugated with fluorescent isothiocyanate and the other with phycoerythrin. Absolute counts were obtained by multiplying the percentage of lymphocyte subsets by lymphocyte counts, which were calculated from the white blood cell differential cell count.

Serologic Studies
Antibodies to the HIV were measured using an indirect immunofluorescent antibody technique performed in parallel in the laboratories of the Cancer Research Institute at the University of California, San Francisco, and the Viral and Rickettsial Disease Laboratory of the California Department of Health Services, Berkeley, as described elsewhere.

Statistical Analysis
Statistical analyses were performed using the SPSS package. Differences in percent positivity were tested with the x² test, using Yates’ correction. Differences between means were evaluated by the t test, and trends of means were tested using linear contrasts and analysis of variance, adjusted, where appropriate, for multiple comparisons using Bonferroni’s inequality.

RESULTS
Relationship of Clinical Findings to HIV Antibody Status
One thousand thirty-four men were evaluated. All but three who were

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Heterosexuals (Seronegative) (N = 201-204)</th>
<th>Seronegative (N = 406-411)</th>
<th>Seropositive (N = 382-386)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms in last 6 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>5 (2.5)</td>
<td>9 (2.2)</td>
<td>76 (19.6)§</td>
</tr>
<tr>
<td>New rash</td>
<td>7 (3.4)</td>
<td>31 (7.5)</td>
<td>53 (13.7)§</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6 (0.9)</td>
<td>17 (4.1)</td>
<td>36 (9.3)§</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (2.5)</td>
<td>9 (2.2)</td>
<td>24 (6.2)§</td>
</tr>
<tr>
<td>Night sweats</td>
<td>3 (1.5)</td>
<td>5 (1.2)</td>
<td>19 (4.9)§</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1 (0.5)</td>
<td>3 (0.7)</td>
<td>12 (3.1)§</td>
</tr>
<tr>
<td>Persistent fever</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (2.1)§</td>
</tr>
<tr>
<td>Infections in last 6 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worse diseases</td>
<td>9 (4.5)</td>
<td>17 (4.2)</td>
<td>37 (9.7)§</td>
</tr>
<tr>
<td>Thrush (oral candidiasis)</td>
<td>2 (1.0)</td>
<td>5 (1.2)</td>
<td>24 (6.2)§</td>
</tr>
<tr>
<td>Shingles</td>
<td>0 (0)</td>
<td>1 (0.2)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Bullous impetigo</td>
<td>0 (0)</td>
<td>3 (0.7)</td>
<td>6 (1.6)</td>
</tr>
<tr>
<td>Physical findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoid mass ≥10 cm</td>
<td>3 (1.5)</td>
<td>8 (2.0)</td>
<td>112 (29.0)§</td>
</tr>
<tr>
<td>Oral hairy leukoplakia</td>
<td>2 (1.0)</td>
<td>2 (0.5)</td>
<td>29 (7.5)§</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>2 (1.0)</td>
<td>3 (0.7)</td>
<td>23 (6.0)§</td>
</tr>
</tbody>
</table>

*HIV indicates human immunodeficiency virus.
†Subjects with complete data.
§Tests for differences between adjacent proportions were performed by x² adjusted by Bonferroni’s method such that α is not greater than .05 in each row.
§There is a significant difference (P<.05) between this value and the value to the left.
Table 2.—Degree of Lymphoid Mass by Sexual Preference and Human Immunodeficiency Virus Antibody Status

<table>
<thead>
<tr>
<th>Lymphoid mass, cm</th>
<th>Heterosexual (Seronegative)</th>
<th>Homosexual/Bisexual Seronegative</th>
<th>Seropositive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>105 (52.0)</td>
<td>197 (48.0)</td>
<td>48 (12.4)</td>
</tr>
<tr>
<td>1-4</td>
<td>65 (32.2)</td>
<td>171 (41.6)</td>
<td>119 (30.8)</td>
</tr>
<tr>
<td>5-9</td>
<td>29 (14.4)</td>
<td>34 (8.3)</td>
<td>107 (27.7)</td>
</tr>
<tr>
<td>≥10</td>
<td>3 (1.5)</td>
<td>8 (1.9)</td>
<td>112 (29.0)</td>
</tr>
<tr>
<td>Total</td>
<td>202 (100)</td>
<td>410 (100)</td>
<td>386 (100)</td>
</tr>
</tbody>
</table>

*Subjects with complete data.

Table 3.—Relationship of Lymphadenopathy and Immune Function to Sexual Preference, Human Immunodeficiency Virus Antibody Status, and Clinical Status

<table>
<thead>
<tr>
<th>Clinical and Laboratory Parameters*</th>
<th>Seronegative Men (N = 149-204)</th>
<th>Seropositive Men (Heterosexual/Bisexual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid mass, cm</td>
<td>1.9 (2.8)</td>
<td>2.2 (3.0)</td>
</tr>
<tr>
<td>Skin test score, mm</td>
<td>17.5 ± 6.8</td>
<td>11.4 ± 6.8</td>
</tr>
<tr>
<td>White blood cells/µL</td>
<td>6300 ± 1600</td>
<td>5400 ± 1600§</td>
</tr>
<tr>
<td>(x 10⁹/L)</td>
<td>(6.3 ± 1.6)</td>
<td>(5.4 ± 1.6)</td>
</tr>
<tr>
<td>Lymphocytes/µL</td>
<td>2292 ± 780</td>
<td>1931 ± 658§</td>
</tr>
<tr>
<td>(x 10⁹/L)</td>
<td>(2.2 ± 0.7)</td>
<td>(1.9 ± 0.6)</td>
</tr>
<tr>
<td>T cells/µL</td>
<td>1532 ± 589</td>
<td>1120 ± 449§</td>
</tr>
<tr>
<td>(x 10⁹/L)</td>
<td>(1.5 ± 0.5)</td>
<td>(1.1 ± 0.4)</td>
</tr>
<tr>
<td>Leu 3a cells/µL</td>
<td>950 ± 390</td>
<td>569 ± 249§</td>
</tr>
<tr>
<td>(x 10⁹/L)</td>
<td>(0.9 ± 0.3)</td>
<td>(0.5 ± 0.2)</td>
</tr>
<tr>
<td>Leu 2a cells/µL</td>
<td>636 ± 268</td>
<td>759 ± 351§</td>
</tr>
<tr>
<td>(x 10⁹/L)</td>
<td>(0.6 ± 0.2)</td>
<td>(0.7 ± 0.3)</td>
</tr>
<tr>
<td>Leu 3a-Leu 2a ratio</td>
<td>1.60 ± 0.59</td>
<td>0.82 ± 0.345</td>
</tr>
</tbody>
</table>

*There is a significant trend across all the rows. Trends across the row and differences in adjacent means were tested using linear contrasts adjusted by Bonferroni's method such that α is not greater than .05 in each row. Values given are means ± SDs.
†Subjects with complete data.
‡Findings refer to any of the clinical parameters in Table 1 except lymphadenopathy, lymphoid mass, and fatigue.
§There is a significant difference between this value and the value to the left.

Cumulative frequency distributions of heterosexual men, seronegative homosexual/bisexual men, and seropositive homosexual/bisexual men according to numbers of Leu 3a T cells. HIV indicates human immunodeficiency virus.

Table 4.—Cumulative Frequency Distribution of Leu 3a T Cells

<table>
<thead>
<tr>
<th>T-Helper Cells/µL (x 10⁹/L)</th>
<th>Cumulative % of Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>500 (0.5)</td>
<td>80</td>
</tr>
<tr>
<td>1000 (1.0)</td>
<td>60</td>
</tr>
<tr>
<td>1500 (1.5)</td>
<td>40</td>
</tr>
<tr>
<td>2000 (2.0)</td>
<td>20</td>
</tr>
</tbody>
</table>

Acquired Immunodeficiency Syndrome—Lang et al

unclassified as either heterosexual or homosexual/bisexual, 20 who did not consent to phlebotomy, and one whose serostatus was not resolved are included in the analysis. All 204 heterosexual men were HIV seropositive. Of 796 homosexual/bisexual men, 386 were HIV seropositive, yielding a 45.5% seropositivity rate. Seven patients had AIDS at entry to the study, all of whom were excluded from this analysis.

Symptoms

Table 1 presents the history of AIDS-related symptoms and infections reported by participants according to sexual preference during the six months before entry into the study. Physical findings and HIV antibody status on entry are also shown in Table 1. The frequency of symptoms and prior infection was essentially the same among seronegative heterosexual and homosexual/bisexual study participants. Each symptom suggestive of HIV infection, including swollen lymph nodes, new rash, fatigue, diarrhea, night sweats, weight loss, and fever, occurred more frequently in HIV-seropositive men than HIV-seronegative men in the six months preceding their clinic visit. Histories of worsening of herpetic skin lesions, thrush (oral candidiasis), shingles, and bullous impetigo were also observed more often in HIV-seropositive subjects.

Physical Findings

The frequency of physical findings (Table 1) was similar in both seronegative heterosexual and homosexual/bisexual subjects. Physical examination demonstrated the presence of oral hairy leukoplakia and oral candidiasis more frequently in seropositive men than in seronegative men. Lymphadenopathy, defined as total lymphoid mass greater than 9 cm, was seen in 2% of seronegative men and 29% of seropositive men.

Because lymphadenopathy was the most frequent finding on physical examination and because it is clearly an important feature of HIV infection, the distribution of varying degrees of lymphadenopathy in relation to sexual orientation and serostatus was examined (Table 2). The amount of lymphoid mass was similar in heterosexual and homosexual/bisexual seropositive study subjects; only 2% exhibited lymphadenopathy equal to or greater than 10 cm of total lymphoid mass. By contrast, 29% of seropositive homosexual/bisexual men had greater than or equal to 10 cm of lymphoid mass.

The most widely cited criteria for lymphadenopathy require lymph nodes greater than 1 cm at more than one extragastric site to be present for three
to six months.\textsuperscript{5,6} While we do not know the duration of lymphadenopathy in our cohort because these are baseline data, 70.9% of homosexual/bisexual seropositive men met these size and location criteria at the time of examination. Twenty-three percent of homosexual/bisexual seronegative men and 30% of heterosexuals, however, also met these criteria (data not shown).

**Table 4.—Relationship of Immune Function to Amount of Lymphadenopathy in HIV* Antibody—Positive Men Without AIDS**

<table>
<thead>
<tr>
<th>Immune Function Indicator</th>
<th>No Nodes (N = 41-47)</th>
<th>1-4 (N = 102-115)</th>
<th>5-9 (N = 91-99)</th>
<th>≥10 (N = 95-105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin test score, mm</td>
<td>10.6 ± 6.0</td>
<td>11.2 ± 6.3</td>
<td>12.0 ± 7.8</td>
<td>9.6 ± 6.6</td>
</tr>
<tr>
<td>Leu 3a cells/μL (× 10^9/L)</td>
<td>536 ± 269</td>
<td>553 ± 271</td>
<td>602 ± 249</td>
<td>518 ± 249</td>
</tr>
<tr>
<td></td>
<td>(0.5 ± 0.2)</td>
<td>(0.5 ± 0.2)</td>
<td>(0.6 ± 0.2)</td>
<td>(0.5 ± 0.2)</td>
</tr>
<tr>
<td>Leu 3a–Leu 2a ratio</td>
<td>0.81 ± 0.33</td>
<td>0.78 ± 0.35</td>
<td>0.84 ± 0.37</td>
<td>0.71 ± 0.31</td>
</tr>
</tbody>
</table>

*HIV indicates human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome. tValues given are means ± SD. §Subjects with complete data.

**Table 5.—Predictive Values of Selected Individual Clinical and Laboratory Findings for HIV* Antibody Status in Homosexual/Bisexual Men**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Negative Predictive Value t</th>
<th>Positive Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent fever</td>
<td>52.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>56.4</td>
<td>89.4</td>
</tr>
<tr>
<td>Weight loss</td>
<td>52.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Night sweats</td>
<td>52.4</td>
<td>79.2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>52.5</td>
<td>72.7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>52.8</td>
<td>67.9</td>
</tr>
<tr>
<td>New rash</td>
<td>53.1</td>
<td>63.1</td>
</tr>
<tr>
<td>History of infections</td>
<td>51.7</td>
<td>83.3</td>
</tr>
<tr>
<td>Shingles</td>
<td>52.7</td>
<td>82.9</td>
</tr>
<tr>
<td>Thrush (oral candidiasis)</td>
<td>52.7</td>
<td>82.9</td>
</tr>
<tr>
<td>Extensive lesions</td>
<td>53.0</td>
<td>68.5</td>
</tr>
<tr>
<td>Bullous impetigo</td>
<td>51.6</td>
<td>66.7</td>
</tr>
<tr>
<td>Physical findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy &lt;10 cm</td>
<td>59.5</td>
<td>93.3</td>
</tr>
<tr>
<td>≥1 node</td>
<td>80.4</td>
<td>61.3</td>
</tr>
<tr>
<td>Oral hairy leukoplasia</td>
<td>53.3</td>
<td>93.5</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>52.9</td>
<td>88.5</td>
</tr>
<tr>
<td>T helper cells &lt;400/μL (&lt;×10⁹/L)</td>
<td>58.6</td>
<td>86.3</td>
</tr>
<tr>
<td>Skin test score &lt;.4 mm</td>
<td>55.5</td>
<td>81.2</td>
</tr>
</tbody>
</table>

*HIV indicates human immunodeficiency virus.
\(t\)Negative predictive value equals the number of seronegative homosexual/bisexuals without the finding divided by the number of all homosexual/bisexuals without the finding.

\(\ddagger\)Positive predictive value equals the number of seropositive homosexual/bisexuals with the finding divided by the number of all homosexual/bisexuals with the finding.

**Relationship of Immune Function to HIV Antibody Status and Clinical Findings**

Table 3 shows the relationship of lymphoid mass, skin test reactivity, and selected laboratory findings to HIV antibody status and clinical findings. Seronegative homosexual/bisexual men differed from heterosexual men only by an increase in Leu 2a cells and a resultant decrease in the Leu 3a–Leu 2a ratio. Seropositive men were divided according to the presence or absence of two or more of the clinical findings in Table 1 (excluding fatigue, lymphadenopathy by history, and lymphoid mass by physical examination). Both groups of seropositive individuals had significantly lower skin test scores, counts of white blood cells, lymphocytes, T cells, and Leu 3a T cells than seronegative men. They also had lower Leu 3a–Leu 2a T-cell ratios than seronegative men. The seropositive men with two or more clinical findings had lower mean skin test scores and lower Leu 3a–Leu 2a ratios than seropositive men with fewer than two of these findings. These two groups did not differ in mean lymphoid mass. Except for numbers of Leu 2a T cells, a gradient of increasing abnormality was noted for all variables in Table 3 from seronegative men through relatively symptom-free seropositive men to seropositive men with two or more clinical findings.

**Population Frequency Distributions of Numbers of Leu 3a T Cells**

The Figure shows the cumulative frequency distribution of numbers of Leu 3a T cells in heterosexuals (n = 204), seronegative homosexual/bisexuals (n = 410), and seropositive homosexual/bisexuals (n = 386). The cumulative distributions for the two seronegative groups (heterosexual and homosexual/bisexual) are almost identical, as are their means and SDs (950 ± 398/μL [0.9 ± 0.3 × 10⁹/L] and 945 ± 387/μL [0.9 ± 0.3 × 10⁹/L]). The cumulative distribution for the seropositive participants is shifted toward lower values, and the mean and SD are significantly lower than those of the other groups (573 ± 484/μL [0.5 ± 0.4 × 10⁹/L]). All of the distributions are unimodal, as indicated by the uniform rate of rise of the three slopes. Twenty-nine percent of seropositive men have fewer than 400 Leu 3a T cells per microliter (<×0.4 × 10⁹/L) whereas 4.4% of the seronegative homosexual/bisexual men and 2.0% of the heterosexuals fall below this level. The difference between the means of the two seronegative groups is not significant (\(P = .29\)), while the difference between seronegative and seropositive men is significant (\(P < .0001\)). In spite of the significant differences between seropositive and seronegative men, a number of HIV-infected individuals have normal Leu 3a T-cell numbers.

**Relationship of Degree of Lymphadenopathy to Immune Function**

We evaluated the relationship of degree of lymphadenopathy measured by lymphoid mass and immune function in HIV-seropositive subjects by examining skin test scores, Leu 3a cells per microliter, Leu 2a–Leu 3a ratio, and B cells per microliter (Table 4). No statistically significant trends were shown for any of the associations examined.

**Predictive Values of Selected Clinical and Laboratory Findings for HIV Antibody Seropositivity in Homosexual/Bisexual Men Without AIDS**

Table 5 shows the predictive values that selected symptoms, physical findings, and immunologic parameters had for HIV infection in the homosexual/bisexual study subjects. Negative predictive values indicate the likelihood of
being HIV seronegative given the absence of the clinical or laboratory value examined. For example, absence of one or more enlarged lymph nodes 1 cm or greater in size predicts an 80.4% likelihood of being seronegative. All other negative predictive values fall below 80%.

Positive predictive values indicate the likelihood of HIV seropositivity given the presence of the same parameters. Extensive lymphadenopathy on physical examination, the presence of oral hairy leukoplakia, or persistent fever predict more than a 90% risk of HIV seropositivity in a homosexual/bisexual man from our study area. Several other clinical and laboratory findings predict greater than an 80% likelihood of HIV seropositivity. We attempted without success to improve predictive value by combining several of these findings.

COMMENT

The sampling techniques and size of the SFHMS provide a comprehensive and reliable data base for evaluation of the clinical and laboratory spectrum of HIV-associated disorders. The findings not only corroborate previous reports but also provide first estimates of the prevalence of many symptoms and signs of HIV infection in a defined population. The HIV-seronegative homosexual/bisexual men and seronegative heterosexuals serve as controls. These data indicate that seronegative homosexual/bisexual men do not differ clinically from heterosexual men. By our evaluation, they differ immunologically only by an increase in Leu 2a T cells. This finding may reflect an increased frequency of other infections, such as sexually transmitted diseases, in this group or possibly a small number of homosexual/bisexual men with HIV exposure who have not yet demonstrated antibody.

Lymphadenopathy, defined as the presence of one lymph node of more than 1 cm, is the single most common physical finding in the cohort and is present to some degree in 87% of seropositive men. Using another definition, the presence of greater than 9 cm of lymphoid mass has a positive predictive value of 93% for the presence of antibody to HIV in homosexual/bisexual men (Table 5). However, the presence or degree of lymphadenopathy does not correlate with changes in measures of clinical status or immune function among seropositives. This finding suggests that lymphadenopathy is not a good marker for severity of disease and, therefore, probably will not be a good marker for disease outcome.

Other symptoms (rash, fatigue, night sweats, and weight loss) and other signs (oral candidiasis and oral hairy leukoplakia) are also predictive of HIV seropositivity and constitute an important part of the syndromes of both acute HIV infection and AIDS-related conditions. Persistent fever, oral hairy leukoplakia, and oral candidiasis are particularly good predictors of antibody status. Moreover, the data in Table 3 indicate that the occurrence of two or more clinical symptoms or signs correlates with depressed immune function as well as HIV antibody seropositivity. Although these findings do not predict antibody status definitively (and therefore are insensitive in predicting latent infection), they help define clinically detectable disease and might serve as predictors of progression to AIDS. Future follow-up of this cohort will determine this possibility.

The data presented in the Figure relate the way in which numbers of Leu 3a T cells distribute among HIV-seropositive and -seronegative men. Finding a unimodally depressed distribution among HIV-infected men suggests that the loss of Leu 3a T cells occurs uniformly throughout this population. A slow progressive loss of Leu 3a T cells with attendant progressive immune dysfunction in all HIV-infected individuals is a disturbing interpretation of these data.

Ongoing prospective evaluation of this cohort will provide data on the correlates of seroconversion and disease progression, the rates of disease progression, the evolution of immunologic changes, and the occurrence of late disease sequelae.

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References

The San Francisco Men's Health Study: III. Reduction in Human Immunodeficiency Virus Transmission among Homosexual/Bisexual Men, 1982–86

WARREN WINKELSTEIN, JR., MD, MPH, MICHAEL SAMUEL, NANCY S. PADIAN, MS, MPH, JAMES A. WILEY, PhD, WILLIAM LANG, MD, ROBERT E. ANDERSON, MD, AND JAY A. LEVY, MD

Abstract: The prevalence and incidence of infection by the human immunodeficiency virus (HIV) has been understudy in a cohort of 1,034 single men recruited by area probability sampling from a six kilometer square area of San Francisco where the epidemic of acquired immunodeficiency syndrome (AIDS) has been most severe. Prevalence of infection among homosexual/bisexual study subjects increased from an estimated 22.8 per cent during the last half of 1982 to 48.6 per cent during the period July through December 1984. During three subsequent six-month periods, prevalence remained stable at approximately 50 per cent. Annual infection rates, measured by seroconversion among seronegative study subjects, decreased from an estimated 18.4 per cent per year from 1982 to 1984, to 5.4 and 3.1 per cent during the first and second halves of 1985, and to 4.2 per cent during the first six months of 1986. These declines were associated with reductions of 60 per cent or more in the prevalence of high-risk sexual practices associated with both acquiring and disseminating infection by the human immunodeficiency virus. (Am J Public Health 1987; 77:685-689.)

Introduction

From the beginning of the epidemic of acquired immunodeficiency syndrome (AIDS) in San Francisco through December 1986, more than 2,700 cases and 1,600 deaths were recorded. In June 1984, the San Francisco Men's Health Study (SFMS) was started. It is a study of the epidemiology and natural history of AIDS in a cohort of single men aged 25 to 55 recruited by area probability sampling from a six kilometer square area in San Francisco where the epidemic has been most intense. The design of the study as well as baseline epidemiological and clinical findings have been reported previously. 1,2 In this article, we present rates of seroprevalence and seroconversion to the human immunodeficiency virus (HIV) and factors affecting these rates in the SFMS cohort from 1982 until mid-1986. The findings from this study may provide useful insights into the epidemiology and control of the current pandemic of AIDS.

Methods

The sampling, data collection, laboratory, and statistical procedures of the SFMS have been reported in a previous communication. 1 Briefly, 19 census tracts defined the six kilometer square area from which the sample was drawn. Within each tract, blocks and households were selected so that the probability of any household entering the sample was equal throughout the area. All single men aged 25 to 55 years old living in each selected household were invited to participate in the study. One thousand thirty-four men, representing 59 per cent of eligibles, entered the study. A comparison of selected characteristics of these men with characteristics of comparable men as determined by the census for the 19 tracts, revealed minor differences which were judged insufficient to impair the representativeness of the sample. 1

Address reprint requests to Dr. Warren Winkelstein, Professor of Epidemiology, School of Public Health, University of California, Berkeley, CA 94720. Mr. Samuel and Ms. Padian are also with the School of Public Health; Dr. Wiley is with the Survey Research Center, U-CA, Berkeley; Dr. Lang is with Children's Hospital of San Francisco; Dr. Anderson is with the California Department of Health Services, Sacramento; and Dr. Levy is with the Cancer Research Institute, U-CA, San Francisco. This paper, submitted to the Journal November 24, 1986, was revised and accepted for publication January 13, 1987.

Data collection takes place twice yearly at the Children's Hospital of San Francisco. A lengthy questionnaire is administered by staff of the University of California Survey Research Center and study subjects are given a standardized physical examination by specially trained physician assistants. A variety of specimens are collected for storage in a long-term repository as well as for immediate laboratory examination.

Serological status for antibodies to HIV is determined by an indirect immunofluorescent antibody assay (IFA). 3,4 Serum samples are examined independently in the laboratories of the University of California, Cancer Research Institute (CRI) and in the Viral and Rickettsial Disease Laboratory (VRD) of the California Department of Health Services. When antibody to HIV is detected, immunoblot tests are performed for confirmation of the seroconversion as well as on the previous seronegative sample. 5

Confidence intervals for prevalence estimates of HIV serostatus in the population from which the sample was drawn were weighted for differences in sampling fractions and response rates between census tracts.

Results

Time Trend of HIV Seroprevalence

The prevalence of seropositivity to HIV in the sample of 799 homosexual/bisexual men and 204 heterosexual men, for whom complete data are available on entry into the SFMS, was determined for each examination cycle. Because no HIV seropositive heterosexual subjects were detected up to July 1986, they are given no further consideration in this article. However, they are being followed and studied as a part of the cohort. The prevalence data for the cohort and the values for the estimated 18,000 homosexual/bisexual men living in the study area were evaluated (Table 1). In addition, an estimate was made of seropositivity among homosexual/bisexual members of the cohort two years before entry into the study.

This estimate was made possible because 215 members of the cohort gave no history of activities which would put them at risk of acquiring HIV infection, i.e., receptive anal/genital contact with ejaculation or needle sharing, during the 10 years prior to entry into the study. 1 Forty-nine (22.8 per cent) of them were, however, infected on entry into the SFMS. We infer that the prevalence of HIV seropositivity

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among these 215 subjects is the prevalence for the entire cohort during the period, July through December 1982.

These 215 subjects, when compared to the remainder of the cohort, were older (mean age 37.1 vs 34.5 years); better educated (68.0 per cent had completed two years of college vs 61.2 per cent); less likely to have used nitrites or nitrates as a recreational drug during the previous two years (64.8 per cent vs 77.3 per cent); and to have a history of less lifetime male sexual partners (median of 150 vs 200).

To determine how the 49 subjects could have been infected, a special survey of a subset of 71 of the 215 was undertaken. Fifteen of these subjects gave a history of no sexual contacts during two years before entry, yet three (20 per cent) were seropositive to HIV. Among 56 subjects whose sexual practices were limited to oral/genital contact during the two-year period—a practice not associated with risk of infection of HIV—11 (20 per cent) were HIV seropositive. Of the 14 seropositive subjects in the subsample, 100 per cent gave a history of receptive anal intercourse with ejaculation prior to two years before entry into the study compared to 48 per cent of those who were HIV seronegative at that time. From these data it was inferred that the 49 had been infected by receptive anal/genital contact prior to two years before entry into the SFMHS.

The prevalence of HIV seropositivity among homosexual/bisexual members of the cohort rose from an estimated 22.8 per cent during the period July through December 1982 to 48.6 per cent during the first cycle of examinations, July through December 1984 (Table 1 and Figure 1). Since then, the prevalence of HIV seropositivity has been stable in the cohort: 49.6 per cent during the second examination cycle, 49.3 per cent during the third and fourth cycles.

The prevalence rates for HIV seropositivity extrapolated from the cohort to the homosexual/bisexual population of the study area during the four six-month time periods of observation since the beginning of the SFMHS in July 1984 were quite stable: 48.2 per cent (95 per cent confidence interval [CI], 44.4–52.0 per cent) during the last six months of 1984, to 48.5 per cent (95 per cent CI, 44.1–52.9 per cent), during the first six months of 1986 (Table 1).

To demonstrate the differences between prevalence rates derived from data generated by probability sampling and from selected volunteer samples, prevalence estimates from the San Francisco City Clinic Cohort are also shown in Figure 1. The City Clinic Cohort was obtained by sampling from 6,875 homosexual/bisexual men recruited from sexually transmitted disease clinics in 1978 for ongoing studies of the prevalence, incidence, and prevention of hepatitis B virus infections.

The prevalence of antibody to HIV in the City Clinic Cohort was determined at five time intervals between 1978 and 1985. Prevalence increased from 4 per cent in 1978 to 69 per cent during the interval January through August 1985. The rate of increasing seropositivity was roughly parallel in the two cohorts, although the prevalence of HIV seropositivity in the City Clinic Cohort was 35 to 50 per cent higher than the prevalence in the SFMHS. In both cohorts, however, the rate of increasing seropositivity was greatest earlier in the epidemic.

**Time Trend of HIV Seroconversion**

In the SFMHS, estimates of the seroconversion rates were made for four time intervals (Table 2). Between July 1982 and December 1984, the annual seroconversion rate was estimated to be 18.4 per cent. During the second, third, and fourth six-month intervals of observation, from January 1985 through June 1986, the observed annual seroconversion rates were 5.4, 3.1, and 4.2 per cent, respectively. The difference between the estimated annual seroconversion rate between 1982 and 1984 and the observed rate during the first six

**FIGURE 1—HIV Seropositivity in the SFMHS and City Clinic Cohorts, 1978–86**

**TABLE 1—Per Cent Prevalence of HIV Seropositivity at Various Time Intervals, Homosexual/Bisexual Men, SFMHS, 1982–86**

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Study Sample</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Examined</td>
<td>% HIV AB+</td>
</tr>
<tr>
<td>7/82–12/82</td>
<td>799</td>
<td>22.8†</td>
</tr>
<tr>
<td>7/84–12/84</td>
<td>677</td>
<td>49.6</td>
</tr>
<tr>
<td>1/85–6/85</td>
<td>606</td>
<td>49.3</td>
</tr>
<tr>
<td>7/85–12/85</td>
<td>611</td>
<td>49.3</td>
</tr>
<tr>
<td>1/86–6/86</td>
<td>611</td>
<td>49.3</td>
</tr>
</tbody>
</table>

*San Francisco Men's Health Study.
**HIV antibody positive.
†Weighted for sampling fraction and differences in participation rates between census tracts.
**Estimated as described in text.

**TABLE 2—HIV Seroconverters and Seroconversion Rates (per Year) by Time Period, SFMHS, July 1982–June 1986**

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Seroconverters Observed through Time Periods</th>
<th>Mean Number of Days between Cycles</th>
<th>Seroconversions No. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/82–12/84</td>
<td>615</td>
<td>NA</td>
<td>205</td>
</tr>
<tr>
<td>7/84–12/84 to 1/85–6/85</td>
<td>352</td>
<td>212</td>
<td>11</td>
</tr>
<tr>
<td>1/85–6/85 to 7/85–12/85</td>
<td>312</td>
<td>188</td>
<td>5</td>
</tr>
<tr>
<td>7/85–12/85 to 1/86–6/86</td>
<td>317</td>
<td>191</td>
<td>7</td>
</tr>
</tbody>
</table>

NA = Not applicable.
*Estimated as described in text.
†Number of seroconversions/number seronegative at beginning of interval × fraction of year observed > 100.
months of 1985 represents a 71 per cent decrease. Since the beginning of 1985, the trend has leveled off.

Factors Influencing the Reduction in HIV Seroconversion

The substantial reduction in infection rates could have been the result of one or more of the following circumstances:

- Study subjects at high risk of seroconversion may have participated in the SFMHS in disproportionately smaller numbers than those at low risk of seroconversion, a type of selection bias.
- Members of the cohort who engaged in high-risk behavior might have become infected early in the epidemic leaving only low-risk persons available for infection during the study, the so-called saturation effect.
- The prevalence of high-risk activities could have declined. Reducing the prevalence of high-risk activities also results in depletion of susceptibles from the population at risk for infection.

The possibility that the low seroconversion rates were due to selection bias was evaluated by examining the participation rates for each examination cycle according to risk factor status of seronegative study subjects at the beginning of the study (Table 3). Risk status, for this purpose, was defined by the number of reported male sex partners with whom receptive anal/genital contact with ejaculation had occurred during the six months prior to entry into the study. Receptive anal/genital contact with ejaculation has been demonstrated to be the principal mode of transmission of HIV infection in homosexual/bisexual men. In the second, third, and fourth examination cycles, the participation rate was unrelated to this risk status.

The possibility that the low seroconversion rates during the first 24 months of the SFMHS are attributable to the exhaustion of high-risk susceptibles from the study cohort before entry into observation was evaluated by assessing the number of high-risk seronegative men who entered the cohort during the first cycle of examinations. Fifty-nine (14 per cent) of homosexual/bisexual subjects who were HIV seronegative on entry gave a history of more than two partners with whom they had experienced receptive anal/genital contact with ejaculation during the six months prior to entry into the SFMHS (Table 3). In order to maintain the annual seroconversion rate of 18.4 per cent, estimated for the cohort during the year prior to the beginning of the study, at least 75 seronegative subjects would have to be infected during the first year of observation (184 × 410 seronegatives). Thus, there were not enough HIV seronegative subjects in the high-risk group at entry to maintain the original estimated annual seroconversion rate. Therefore, at least part of the decline in seroconversion could be due to the unavailability in the cohort of persons at high risk of infection. Persons not meeting this high-risk criterion were also at risk of infection if they were exposed to any seropositive sexual partner by receptive anal/genital contact with ejaculation.

It is noteworthy that eight of the 11 study subjects who seroconverted during the first six months of observation were among the 59 seronegative subjects who practiced high-risk activities during the previous six months. Thus, for this high-risk subset of HIV seronegative study subjects, the annualized HIV seroconversion rate was 23.3 per cent (8/59 × 356/212 × 100).

The possibility that the decline in HIV seroconversion rates was due to changes in the prevalence of high-risk behavior was examined in several ways. To evaluate the risk of acquiring infection by HIV, the proportion of HIV seronegative study subjects giving a history of two or more partners with whom they had practiced receptive anal/genital contact with ejaculation during the six months prior to each cycle of examinations was evaluated (Figure 2). The proportions of such subjects reporting this practice in each of the four examination cycles were: 14.4, 5.9, 4.9, and 5.8 per cent, respectively. The difference between the prevalence during January through June 1984, and July through December 1984 represented a 59 per cent decline. However, the trend in prevalence from July 1984 through June 1986 was level.

To evaluate the risk of disseminating infection by HIV, the proportions of HIV seropositive study subjects giving a history of two or more partners with whom they had practiced insertive anal/genital contact with ejaculation during the six months prior to each cycle of examinations were also evaluated (Figure 2). Among these study subjects, 39.6, 25.6, 16.8, and 13.3 per cent reported more than two insertive anal/genital contacts with ejaculation during the six months previous to each examination cycle, an overall reduction of 66 per cent.

---

**TABLE 3**—Participation by Seronegative Men in Examination Cycles 1–4 According to Risk Status* on Entry, SFMHS

<table>
<thead>
<tr>
<th>Examination Cycles</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Status*</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>266</td>
<td>100</td>
<td>239</td>
<td>89.8</td>
</tr>
<tr>
<td>1</td>
<td>85</td>
<td>100</td>
<td>76</td>
<td>89.4</td>
</tr>
<tr>
<td>2 or More</td>
<td>59</td>
<td>100</td>
<td>56</td>
<td>94.9</td>
</tr>
<tr>
<td>Total</td>
<td>410</td>
<td>100</td>
<td>371</td>
<td>90.5</td>
</tr>
</tbody>
</table>

*Number of partners with whom seronegative subjects practiced anal/genital contact with ejaculation during the six months prior to entry into the study.

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The prevalence of high-risk activities (more than 10 sexual partners during the six months prior to each examination cycle, and two or more sexual partners with whom insertive and/or receptive anal/genital contact with ejaculation) has been estimated, without regard to HIV serostatus, from the total experience of the study cohort (Figure 3). For each of the three high-risk activities for which prevalence estimates were generated, declines of 60 per cent or more occurred during the 24 months of observation, July 1984 through June 1986.

Discussion

Despite the severity of the AIDS epidemic in the United States, only three studies (at this writing) provide published data regarding the time trend of the prevalence and cumulative incidence of HIV infection in defined population groups in the United States. All of these studies were conducted in cohorts recruited from homosexual/bisexual men at high risk of acquiring a sexually transmitted disease. Presumably, such samples would yield prevalence estimates biased toward higher values. Thus, it was not unexpected to observe substantially lower prevalence estimates for HIV infection in the SFMHS cohort than in the San Francisco City Clinic Cohort. Nevertheless, the patterns of the time trends of prevalence are essentially parallel although the data from the SFMHS do not provide information prior to 1982. By that time the prevalence of infection was already estimated to have been 23 per cent in the 19 census tracts in which the SFMHS is being conducted.

This estimate of HIV seroprevalence in the SFMHS cohort two years before the beginning of the study was possible because a substantial number of subjects who were seropositive on entry had no history of activities by which infection could be acquired during that period, July 1982 to June 1984. Presumably, they had acquired their infections previously. This was supported by a substudy which showed that those who were infected had engaged in high-risk activities prior to that time at a higher rate than those who remained uninfected. Unfortunately, we did not ascertain when high-risk activities had been curtailed in this group. If the change in activity occurred long before the two-year period, then the cumulative incidence in the group is likely to be an underestimate of the prevalence of HIV seropositivity in the cohort two years before the study began. Furthermore, this group differed from those giving a history of high-risk activity during the two years before the study began in being older, more educated, less involved in recreational use of certain drugs, and having fewer lifetime male sexual partners. These differences, although small, might also have biased the estimate of HIV seropositivity downwards. Thus, we should consider the 23 per cent estimate of seroprevalence in the cohort two years before the study began as a minimum value.

The relatively rapid increase in the prevalence of HIV seropositivity early in the epidemic in both the San Francisco City Clinic cohort and the SFMHS cohort (also indicated by declining seroconversion rates in HIV seronegative subjects in the SFMHS after 1983) is consistent with epidemic theories of infectious diseases spread by contact. According to such theories, an epidemic of HIV infection is eventually exhausted from an infected population by acquisition of immunity after infection. They are then unable to transmit the causal agent or be infected by it. The rate at which this occurs is a function of the number of contacts between infected and uninfected individuals and the infectivity of the agent. In general, the curve of acquisition of infection assumes a logistic form. Although the infectivity of HIV has been shown to be relatively low, the number of potentially contagious contacts was very high early in the epidemic in San Francisco. HIV infection, however, does not assure immunity from disease in the usual sense. Many seropositive individuals may be virus carriers. Therefore, the declining rates of HIV seroconversion during the past 24 months have been attributed to either exhaustion from the cohort by either infection of persons practicing high-risk activities, or by reduction of such activities (e.g., receptive anal/genital contact with ejaculation). The SFMHS supports both explanations. Furthermore, the data indicate a substantial reduction in the practice of insertive anal/genital contact with ejaculation among infected persons who could, thereby, disseminate HIV infection.

However, the continued potential for HIV transmission in populations still practicing high-risk sexual activities was also evident from the data. The annualized HIV seroconversion rate during the first six months of the study among 59 HIV seronegative subjects continuing to practice high-risk sexual practices (23 per cent) was even higher than the estimated annual seroconversion rate for the whole cohort during the year prior to the beginning of the study (18 per cent).

The possibility that the decline in high-risk activities among members of the cohort was the result of participation in the SFMHS could not be substantiated. Although no special educational efforts were made by study staff to modify high-risk activities, educational materials produced by the San Francisco AIDS Foundation and by the San Francisco Health Department were made available in the clinic waiting room. However, these health education materials were also widely disseminated in the community. Moreover, independent evidence from two sources supports the conclusion that the changes in prevalence of high-risk activities in the cohort represent changes in the population.

First, from the last six months of 1982 through the last six months of 1984, the cumulative incidence in newly infected subjects was not different between the two years. Second, the cumulative incidence in the study cohort was essentially the same as that of the general population's during this period.

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months of 1985, the monthly number of cases of anal/rectal gonorrhea reported to the San Francisco City Health Department declined from between 200 and 300 to less than 50. Second, in a follow-up study of 655 homosexual/bisexual men recruited by advertising from a variety of local settings (bars, bathhouses, and AIDS-related investigations), the average number of different male sexual partners per month declined from 6.3 in November 1982 to 3.9 in May 1984 and the average number of times each subject engaged in anal/genital contact with ejaculation with each partner declined from 1.9 to 0.7 in the same time interval. 

Findings from a study based on a probability sample, such as the SFMHS, may be extrapolated to the entire population of 23,000 single men, 25 to 55 years of age, living in the study area. Of these, 18,000 were estimated to be homosexual/bisexual. Data from the SFMHS indicate that, in this population, the prevalence of high-risk activities for acquiring and disseminating HIV infection has declined substantially during the 24 months of observation. July 1984 through June 1986. Nevertheless, seroconversion for HIV infection continues in this population at about 5 per cent per year. This finding indicates that in the presence of a high prevalence of HIV infection in a population, even a low prevalence of high-risk activities can propagate the epidemic. Alternatively, other modes of transmission may be superseding the currently established modes. These possibilities are under study.

ACKNOWLEDGMENTS

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REFERENCES


Kellogg Fellowships in Management for Clinicians

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CONCISE COMMUNICATIONS

Infectivity of the Human Immunodeficiency Virus: Estimates from a Prospective Study of Homosexual Men

A key parameter for understanding the epidemic spread of an infectious agent is the infectivity of the agent. Infectivity is defined here as the proportion of persons who become infected after being exposed in defined circumstances. In this report we present estimates of the infectivity of the human immunodeficiency virus (HIV) associated with the practice of unprotected receptive anal intercourse among homosexual men living in San Francisco. This practice has been established as the principal mode of sexual transmission of HIV infection among homosexual and bisexual men [1, 2].

Studies of the partners of infected persons have provided estimates of infectivity in one risk group, the female sex partners of men seropositive for antibody to HIV [3–7]. These studies consistently found that 6.8% [3] to 14% [5] of exposed women were seropositive, except for one small study [7] that selected couples who had been married for two or more years, and found that 71% (five of seven) of the wives of patients with AIDS or AIDS-related complex were seropositive. Partner tracing has proved less useful among homosexual men because of their relatively high rate of multiple partners. We propose here an alternative method of estimation, a version of which has been used previously to investigate the heterosexual transmission of gonorrhea [8, 9]. This method uses a mathematical model and the sex histories of susceptible persons whose partners are selected from groups in which the prevalence of infection can be estimated.

Subjects and Methods

Subjects and sera. Data from the San Francisco Men’s Health Study (SFMHS) were used to calculate HIV infectivity. As described elsewhere [1], the SFMHS is a prospective cohort study of single men (25–54 years of age) selected at random from all eligible men living in the 19 census tracts of San Francisco that had the highest incidence of AIDS before 1984, when the cohort was established. Of the 1,750 eligible men, 1,034 were enrolled in the study, a response rate of 59.1%. The differences between responders and nonresponders, inferred by comparing 1980 census data with SFMHS cohort data [1], are not expected to bias the calculations presented in this report. The participants in the study are seen at six-month intervals, at which times information about intravenous needle use and numbers of sex partners by type of sex activity (but not numbers of contacts per partner) is obtained. In addition, blood samples are tested for antibodies to HIV in parallel in two laboratories by using the indirect immunofluorescence assay [10]. Tests that indicate seroconversion are confirmed by western blot assay [11]. The sera collected during the first cycle (June 1984–December 1984) and the second cycle (January 1985–June 1985) were used to estimate the prevalence of infection; sera collected during the second cycle were used to determine the number of new infections.

Derivation of the model. To calculate an estimate of infectivity, we assume that the sex partners of homosexual and bisexual men are selected at random from a pool of men with a known prevalence of infection (p). Given that a susceptible man selects an infected partner, the probability that the sexual union with that partner will result in transmission of the agent is defined as infectivity (f). Multiple partners are treated like independent trials in a binomial experiment, with a probability (fp) of HIV transmission on each trial. Accordingly, the probability that the ith susceptible man will become infected after sexual contact with ni partners is 1 – (1 – fp)ni, or one minus the probability of remaining uninfected. In a population of N susceptible men, the expected number of new infections (S) is the sum of the N individual probabilities:

$$S = \sum_{i=1}^{N} [1 - (1 - fp)^{n_i}]$$  \(1\)

The value of f that satisfies equation (1) is a moment estimate of infectivity calculated on a per-partner basis. Alternatively, the likelihood function associated with the model can be used to estimate infectivity. The likelihood function is written as follows:

$$L = \prod_{i=1}^{N} [1 - (1 - fp)^{n_i}]^{x_i}[1 - fp]^{1-x_i}$$  \(2\)

where xi is 1 if the ith man is a seroconverter and is 0 if otherwise. The maximum likelihood estimate (MLE) of infectivity is the value for infectivity that maximizes the likelihood function. In addition to the infectivity estimate, the maximum likelihood method provides a way of calculating the standard error of the estimate on the basis of the asymptotic information score [12] (equations not shown).
The moment estimate is easier to compute than the MLE and is useful as an initial estimate for the iterative solution of the maximum likelihood equation. In practice, the two methods yield very similar estimates of infectivity of HIV from the data used in this report. The MLE is used here because it is a more-efficient large-sample estimate.

Statistical methods. A likelihood ratio \( \chi^2 \) test was used to test whether the seroconversions expected under the model were significantly different from those observed. In constructing this test, equation (1) is regarded as a special, or restricted, case of a more-general model in which the infectivity \( f \) is permitted to vary according to number of partners. This model can be written as follows:

\[
S = \sum_{i=1}^{N} \left(1 - (1 - f_{ni})^m\right),
\]

where the subscript of the \( f \) indicates the infectivity varies by the number of partners. The likelihood ratio test, defined as \(-2\) times the natural log of the ratio of the likelihood of the restricted model over the likelihood of the general model, is asymptotically arranged as a \( \chi^2 \), with the degrees of freedom equal to the number of parameters removed in restricting the model. Because equation (3), the general model, exactly predicts the number of seroconversions in each partner category, it is an appropriate basis for testing the goodness-of-fit of the infectivity model developed above.

Results

Of the 672 homosexual and bisexual men who participated in the first and second cycles of the study, 343 (49.4%) were initially seronegative for antibodies to HIV (N = 343). Eleven of these susceptible individuals seroconverted before the second cycle (S = 11). The seroprevalence in the cohort was 0.49 at the first cycle and 0.51 at the second cycle, with an average seroprevalence over the first six months of follow-up of 0.50 (\( P = .50 \)) Each of the initially seronegative men reported the number of partners with whom they had had unprotected receptive anal intercourse during the period between the first and second cycles (\( n_i = 0, \ldots, 10 \)). Two of the seroconversions occurred in men who denied any unprotected receptive anal intercourse in this period. Because both of these men had had unprotected receptive anal intercourse (with one and two partners) in the six months before their first visit to the clinic, it is reasonable to assume that they were infected before entry into the cohort and that they seroconverted later. Such delays have been reported [13]. Similarly, it is likely that some seroconversions occurred after the second cycle, as a result of sex contacts before the second cycle. Assuming an average time from infection to seroconversion of one month, the number of partners \( n_i \) for the infectivity calculations could be estimated as the weighted average of the number of partners in the six months preceding the first cycle (\( n_{a1} \)) and the number of partners between the first and second cycles (\( n_{a2} \)): \( n_i = (1/6)(n_{a1}) + (5/6)(n_{a2}) \).

When using the weighted average for \( n_i \), the MLE of infectivity is 0.097. The standard error of the MLE is 0.30, a value yielding a 95% confidence interval of 0.041–0.153. The estimate derived by simply setting \( n_i = 1 \) for the two previously exposed men who seroconverted is 0.102 (95% confidence interval, 0.043–0.160). The simpler method of estimating \( n_i \) is used in the remainder of this paper because of its close agreement with the more-rigorous method and to avoid using intuitively difficult fractional numbers of partners, as are produced by calculating \( n_i \) as a weighted average.

Table 1 shows the distribution of initially seronegative men by the number of partners reported between the first and second cycles (with the previously exposed seroconverters listed with one partner each, as discussed above).

The value of 0.102 for infectivity may be more readily believable if one considers the 94 men who reported only one partner. Of the 94 partners, 47 are expected to have been seropositive. There were 5 seroconversions among the 47 men expected to have been exposed, a number yielding an approximate infectivity of 5/47 = 0.106, which is close to the value calculated by using the model and the entire set of data.

A comparison of the observed and expected seroconversions in table 1 indicates that the model fits the observations well. The likelihood ratio \( \chi^2 \) test, calculated after grouping men with four or more partners into one category to avoid indeterminate log-likelihoods produced in
partner categories with no seroconversions, provides no evidence of a lack of fit ($\chi^2 = 0.58, df = 3, P = .90$).

Although parenteral exposure to HIV-contaminated needles is known to transmit the virus [14], this mode of transmission is not important among the susceptible men being analyzed here. None of the seroconversions occurred among men who had shared needles, and only six (1.8%) of the 332 persistently seronegative men had shared needles. Of these men, only one had shared needles in the six-month period before the second cycle.

Discussion

Among the men studied, the infectivity of HIV associated with unprotected receptive anal intercourse was calculated to be 0.102. The MLE of infectivity had a 95% confidence interval of 0.043–0.160.

This estimate is subject to a number of important qualifications. (f) The seroprevalence among the partners of susceptible men in this cohort was estimated to be the seroprevalence in the cohort as a whole by assuming that the susceptible men selected their partners without respect to serostatus, from the population from which the cohort was selected. The true seroprevalence among the partners may be lower, to the extent that partners were chosen from surrounding census tracts with a lower incidence of AIDS and a presumed lower incidence of HIV infection. Alternatively, the true seroprevalence may be higher than the seroprevalence of the cohort as a whole because men with many partners are more available to be selected as a partner and are more likely to be infected with HIV. For example, the seroprevalence of the population of partners might be estimated as the seroprevalence in the SFMHS cohort, with each participant weighted by the number of partners with whom they were inserted. This procedure yields a seroprevalence of 0.7. Fortunately, the model reported in this report is robust to variation in seroprevalence ($p$) over the plausible range of $P = .3 – .7$ and yields estimates of infectivity ranging from $f = 0.072$ to $f = 0.17$.

(f) The estimate of infectivity reported here is really the average infectivity for all pairs of men without regard for differences in susceptibility due to ancillary sex practices (e.g., douching, fisting) [1] and to sexually transmitted diseases [15, 16]. As more seroconversions are observed in the SFMHS, we will analyze infectivity in various subgroups of the sample to determine how behavioral and biologic characteristics of susceptible men affect the infectivity of HIV.

(3) The definition of infectivity used here pertains to contact between seronegative and seropositive individuals and, in effect, assumes that all seropositive men are infectious. A more-refined definition of infectivity (i.e., the risk of infection associated with unprotected receptive anal intercourse with a man who is shedding virus) would yield higher estimates of risk. For example, Levy et al. [17] reported isolating virus from four (21%) of 19 samples of semen from seropositive men. If a similar percentage of seropositive men in the SFMHS shed the virus during the first six months of follow-up, the infectivity of HIV associated with unprotected anal intercourse with an infectious man is 0.102 divided by 0.21, or 48%. The less-than-perfect sensitivity of HIV assays implies that 0.21 may be a low estimate of the proportion of seropositive men who shed virus at any given time. The actual rate is expected to be between 0.21 and 1.0 and to yield estimates of infectivity ranging from 0.102 to 0.48.

(4) The estimate of infectivity is calculated on a per-partner basis rather than on a per-event basis. At present we do not have sufficient data to estimate risk of infection associated with a single episode of unprotected receptive anal intercourse with a man positive for antibodies to HIV. Because the number of events must be at least as large as the number of partners for each individual, however, estimation on a per-partner basis will yield higher infectivities than will estimation on a per-event basis.

This result can be demonstrated by estimating infectivity per contact under plausible assumptions about the number of sex episodes between partners. If each susceptible man has some number of contacts (c) with each of his n partners, the infectivity of HIV per contact ($f_c$) can be estimated, using the parameters defined above, by solving the following equation:

$$S = \sum_{i=1}^{N} \sum_{j=1}^{n_i} (p^i)^j (1 - p)^{n_i-j} [1 - (1 - f_c)^{c_j}].$$

(4)

It can be shown that the infectivity per contact ($f_c$) defined in equation (4) is equal to the infectivity per partner ($f$) defined in equation (1) when $c = 1$. Table 2 shows the moment estimates of $f_c$ that are calculated under various assumptions about the number of contacts with each partner (c). These calculations demonstrate that $f_c$ is equal to $f$ when $c = 1$ and that $f_c$ becomes substantially less than $f$ as c increases. The very small values of infectivity ($f_c$)

**Table 2. Simulation of per-contract infectivity ($f_c$) under various assumptions about the number of sex contacts in the six months before the second cycle.**

<table>
<thead>
<tr>
<th>Assumption</th>
<th>No. of partners (ni)</th>
<th>f_c</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 contact/partner</td>
<td>1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1</td>
<td>0.102</td>
</tr>
<tr>
<td>2 contacts/partner</td>
<td>2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2</td>
<td>0.0503</td>
</tr>
<tr>
<td>3 contacts/partner</td>
<td>3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3</td>
<td>0.0351</td>
</tr>
<tr>
<td>1 contact/month</td>
<td>6 3 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1</td>
<td>0.0280</td>
</tr>
<tr>
<td>2 contacts/month</td>
<td>12 6 4 3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2</td>
<td>0.0142</td>
</tr>
<tr>
<td>4 contacts/month</td>
<td>24 12 8 6 5 4 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3</td>
<td>0.00716</td>
</tr>
<tr>
<td>8 contacts/month</td>
<td>48 48 16 12 10 8 7 6 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5</td>
<td>0.00358</td>
</tr>
</tbody>
</table>

NOTE. Table entries represent the number of contacts per partner (c).
calculated when assuming frequent contact could represent a truly low efficiency in the transmission of HIV even with high-risk sex practices, an overestimation of the frequency of contact, a low rate of viral shedding (see qualification 3), or any combination of the above.

(5) A key assumption underlying our calculations is that partner selection with respect to HIV serostatus is random, or nearly so, within the homosexual and bisexual population. To examine the effect of the assumption of random sexual mixing on our calculations, we formulated an alternative model in which men select partners at random from among men with the same number of partners per six-month period. The probability of infection, given n partners, is 1 - (1 - fpnj)m, where the subscript on the p indicates that seroprevalence varies according to the number of partners, as shown in table 3. The MLE of infectivity under the revised model is f = 0.080 (95% confidence interval, 0.034-0.126). This alternative stratified model of random bonding yields estimates of infectivity that are less than those calculated with the simple random-bonding model and reflects the higher seroprevalence among sexually active men relative to the seroprevalence in the cohort as a whole. Nevertheless, comparing these two models indicates that our estimates are robust for this sort of variation in the selection of sex partners.

Knowledge of the infectivity of HIV is useful for several purposes. First, it permits predictive models to be constructed to study the epidemic spread of HIV. Second, if infectivity is found to decrease during the course of the epidemic, selection of virus according to host susceptibility is suggested. Third, the value of infectivity per partner calculated here (f = 0.102) for homosexual intercourse is similar to the infectivity per partner derived from partner studies of the female sex partners of seropositive men [3-7], a finding suggesting that the predominance of AIDS in homosexual men in the United States has been due primarily to their greater number of partners rather than to differences between rectal and vaginal mucosa, noninvasive drug use, or immunologic competence. This information emphasizes the importance of targeting "safe-sex" public education to the entire sexually active population.

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References

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Table 3. Seroprevalence of antibody to HIV by the number of partners with whom the men in the study practiced unprotected receptive anal intercourse.

<table>
<thead>
<tr>
<th>No. of partners (ni)</th>
<th>Seroprevalence of antibody (pi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.38</td>
</tr>
<tr>
<td>1</td>
<td>0.53</td>
</tr>
<tr>
<td>2</td>
<td>0.58</td>
</tr>
<tr>
<td>3</td>
<td>0.76</td>
</tr>
<tr>
<td>4-9</td>
<td>0.83</td>
</tr>
<tr>
<td>≥10</td>
<td>0.95</td>
</tr>
<tr>
<td>Overall</td>
<td>0.50</td>
</tr>
</tbody>
</table>