

DRAFT LETTER TO THE EDITOR OF
THE LANCET
AIDS INCIDENCE IN SAN FRANCISCO
1980-1982

TO THE EDITOR OF THE LANCET:

Sir---Homosexual men, along with Haitian immigrants, intravenous drug users, hemophiliacs, and now perhaps children of drug users, have all been reported to be at high risk for diseases of the Acquired Immune Deficiency Syndrome (AIDS).^{1,2} In San Francisco, where AIDS surveillance is maintained by the Bureau of Infectious Disease Control, only small numbers of cases have been reported among Haitians and intravenous drug users; the majority of cases have been reported among homosexual and bisexual men. Ninety-two cases of Kaposi's sarcoma and/or opportunistic infections defined by the Center for Disease Control as associated with the AIDS syndrome were recorded in metropolitan San Francisco among men reported to be gay or bisexual, and aged 60 and under, in the period 1980-82. This number is approximately ten percent of the U.S. nationwide total reported by the CDC.

Although no accurate estimates exist for the size of the gay population in San Francisco, information from the 1980 census on numbers of never-married men aged 15 and over may be used to give approximate denominator populations by census tract. This category excludes the estimated 20% of gay men who have been married;³ it includes all heterosexual men aged 15 and over who have never been married. (These biases are in opposite directions.) This number will thus approximate to the size of the gay population in predominantly gay areas, and will approximate less well in more heterosexual neighborhoods.

Seventeen San Francisco census tracts had a cumulative incidence of AIDS diseases, as defined above, of greater than 200 per 100,000 never-married men aged 15 and over in the period 1980-82. Fifteen of these tracts form a contiguous area in the center of the city which includes several of the principal gay neighborhoods. (Area A in figure I). Twenty census tracts had cumulative incidence rates of between 50 and 200 per 100,000, and these, along with the remaining two high incidence tracts, are shown as Area B in figure I. Area B surrounds Area A and includes some of the other predominantly gay neighborhoods in the city.

Table I gives incidence rates per 100,000 never-married men aged 15 and over for Area A, Area B, and San Francisco as a whole. Incidence rates are also given for all men aged 25-44, an age range which includes a sizeable fraction of the gay population. Clearly, these latter rates must underestimate the rates among gay men.

Table I suggests that in a sizeable part of San Francisco, the incidence of AIDS diseases among gay men had reached the rate of approximately 250 per 100,000 by the end of 1982.

If the proportion of gay men among all men in Area B is assumed to be about forty percent of that in Area A, the two sets of rates are comparable. However, there is reason to suppose that incidence rates of AIDS are different among different groups of gay men, depending on aspects of lifestyle and previous exposure to infectious diseases.^{4,5} Thus the lower rates in Area B may represent a combination of (1) different lifestyles and (2) the smaller proportion of gay men among all men in Area B.

It should be noted that the incidence of AIDS in San Francisco is following an epidemic pattern. Figure 2 shows the cumulative numbers of AIDS cases reported by quarter, 1980-82, for the city as a whole and for Area A. About half of all cases reported in the period 1980-82 were reported in the last two quarters of 1982. On an annualized basis, the annual incidence of AIDS in the last quarter of 1982 was running at 285 per 100,000 never-married men aged 15 and over in Area A, and 102 per 100,000 in the city as a whole.

Although incidence rates are given here by geographical area, it is not suggested that geographical proximity is associated with risk, or that Area A is a focus of infection in the classical sense. It is our belief that rates are high in Area A and Area B because they contain the principal gay neighborhoods of the city, and most San Francisco cases are among gay or bisexual men. Given the large numbers of cases among gay or bisexual men in these areas, the small numbers of reported cases among heterosexual men and among women suggests, perhaps, that AIDS is not easily transmitted by non-sexual personal contact. As of January 1, 1982, there were no known AIDS cases in San Francisco that did not appear to fall into the categories cited at the beginning of this letter.

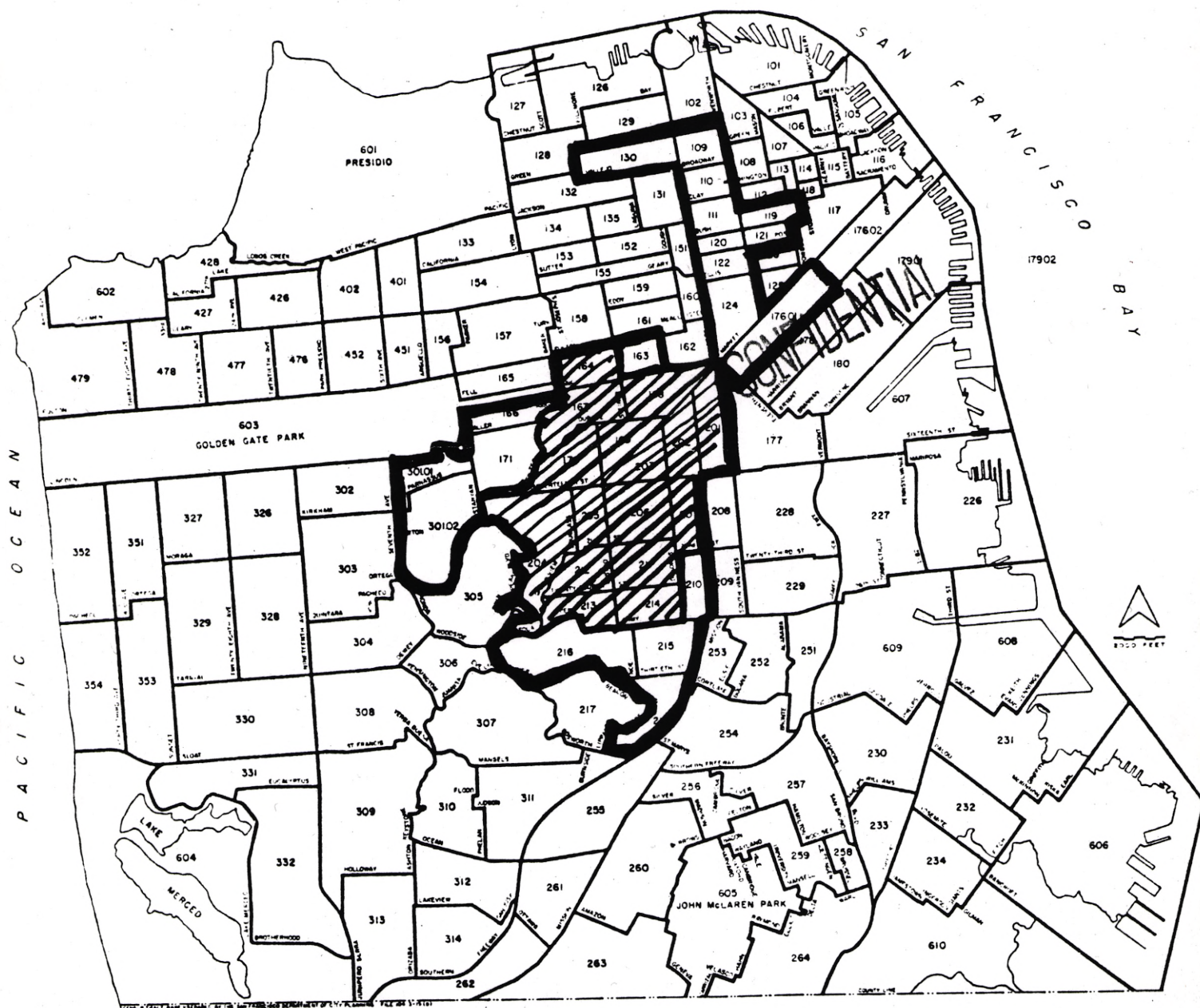
(SIGNATURES)

TABLE I

INCIDENCE OF AIDS, 1980-1982
 AMONG NEVER-MARRIED MEN AGED 15
 AND OVER, AND AMONG ALL MEN AGED 25-44

CONFIDENTIAL

	AREA A	AREA B	OTHER SAN FRANCISCO	ALL SAN FRANCISCO
CASES 1980-82	56	24	12	92
NEVER-MARRIED MEN AGED 15 & OVER	19,518	21,685	56,892	98,095
RATE PER 100,000 NEVER-MARRIED MEN AGED 15 AND OVER	287	111	21	94
CASES AGED 25-44	50	16	11	77
MALES AGED 25-44	19,271	19,461	82,203	120,935
RATE PER 100,000 MEN AGED 25-44	259	82	13	55



1980 CENSUS TRACTS

FIGURE I: AREA A (HATCHED)
AND AREA B

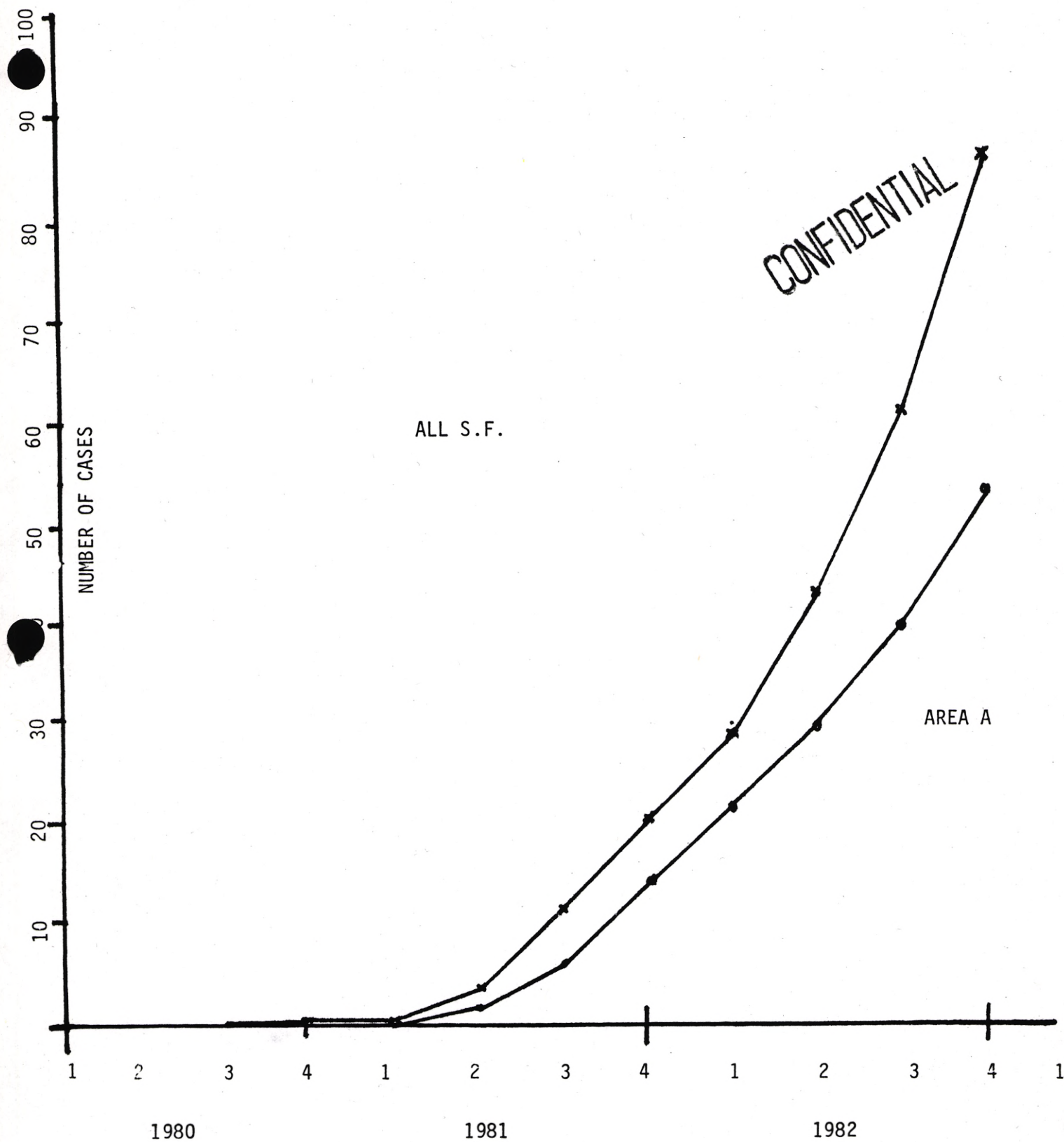


FIGURE 2.

CUMULATIVE NUMBER OF AIDS CASES BY QUARTER: AREA A AND ALL SAN FRANCISCO: 1980-1982



10 March 1982

Marcus A. Conant, M.D.
350 Parnassus Avenue
San Francisco, CA 94117

Dear Doctor ^{Marc}Conant:

I would like to suggest a new track to add to the many we are following in the search for answers to the "Gay Immunosuppression Syndrome", if you are not already following it.

1. All or most of the persons we have interviewed appear to be extremely sexually active, but at least preliminary analysis shows the cases to be much more so than the controls.
2. Is it possible that this hyperactivity elevates or otherwise disturbs relative levels of corticosteroid, which are thought to have some immunosuppressive action?
3. If premise number two above is accepted, it is possible that at a critical level a trigger effect permits the development of the rest of the immunosuppressive sequence by CMV, EBV, HSV, etc..
4. On those bloods which we have available on patients and controls, would you consider laboratory studies for pertinent corticosteroid levels?
5. Am I truly way out in left field?

Sincerely,

A handwritten signature in cursive script, appearing to read "Selma".

Selma K. Dritz, M.D.
Assistant Director
Bureau Communicable
Disease Control

SKD:hs

Marcus Augustine Conant M.D.

A PROFESSIONAL CORPORATION
DERMATOLOGY

(415) 661-2614

*350 Parnassus Avenue, Suite 808,
San Francisco 94117*

March 10, 1982

TO: Kaposi Sarcoma Study Group

FROM: Marcus A. Conant, M.D. *Marc'*

The next meeting of the Kaposi Sarcoma Study Group will be held on Thursday, March the 18th, at 11:00 o'clock in the Dermatology Clinic.

At that meeting Dr. Marvin Garovoy and Dr. Beth Colombe will review with us the HLA findings that they have made in their laboratory on our patients.

Everyone will want to read:

Goedert, J.J., Greene, M.H. and Strong, D.M.: Amyl Nitrite May Alter T Lymphocytes in Homosexual Men.
The Lancet, Sat. 20 Feb. 1982 Vol 1

March 11, 1982

Professor Bernhard Fleckenstein, M.D.
Institut fur Klinische Virologie
8520 Erlangen, LoschgestraBe 7
Nuremberg, Germany

Dear Doctor Fleckenstein:

Thank you so much for your kind letter of February the 11th.
Dr. Larry Drew, who is the chief microbiologist and virologist at
Mt. Zion Hospital here in San Francisco, is supervising all of the
virological studies on our patients with Kaposi's sarcoma.

I have relayed your interest to Dr. Drew and he will be delighted
to correspond with you about performing studies that are not
currently being done here in San Francisco or in Seattle or
Chapel Hill.

We look forward to working with you in the future.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:jb

cc: Dr. Larry Drew

Marcus Augustine Conant M.D.

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DERMATOLOGY

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*350 Parnassus Avenue, Suite 808,
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Institut fur Klinische Virologie
8520 Erlangen, LoschgestraBe 7
Nuremberg, Germany

Dear Doctor Fleckenstein,

Thank you so much for your kind letter of February the 11th. Dr. Larry Drew is a virologist on our staff here at the University of California, who is supervising all of the virological studies on our patients with Kaposi's sarcoma. I have relayed your interest to Dr. Drew and he will be delighted to correspond with you about performing studies that are not currently being done here, in Seattle and in Chapel Hill.

We look forward to working with you.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:ig

cc: Dr. Larry Drew

March 19, 1982

D. A. Lopez, M.D.
353 H Street, Suite DD
Chula Vista, CA 92010

Dear Tony,

Just a note to tell you what an excellent job I think you did in organizing the program on skin cancer update for this year's meeting of the dermatology section of the California Medical Association meeting. All of the comments that I heard were favorable and I felt that the entire presentation was well conceived and well executed.

I was flattered that you asked me to present our material on Kaposi's sarcoma, and the audience seemed genuinely interested in this new and exciting area of viral oncogenesis. Hopefully the next time you hear me present this material, I can report that we not only feel we know what the viral inducer is, but that we have found some way to reverse the basic immunosuppression in these unfortunate patients.

If I am asked to serve as the program director for the 1984 meeting, I will certainly need all of your experience and help in trying to organize a program as successful as that which you produced.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:ig

March 11, 1982

Kitty Brody
San Francisco Foundation
425 California St., Rm 1602
San Francisco, CA 94104

Dear Ms. Brody:

C
O
P
Y
The Kaposi Sarcoma Clinic at U.C. was established in May of last year to coordinate efforts to study and treat patients diagnosed with K.S. As you might already be aware, there has been a sudden appearance of Kaposi's sarcoma in the gay male populations of New York, San Francisco and Los Angeles. The disease previously affected only older men of Jewish and Italian descent and has been seen in certain populations in Africa. The suddenness of its appearance in young gay men in certain geographical areas raises many serious questions as to the reasons for and nature of this disease. The team of specialists in the Clinic are searching for answers.

Funding has been applied for from the National Cancer Institute. So far the staff position of nurse coordinator has been funded for the Clinic by the American Cancer Society. Funding seems to be slow because: 1) this is a new disease; 2) Federal cutbacks have curtailed certain sources of assistance as well as the epidemiological efforts of the Centers for Disease Control; 3) a "gay" disease does not affect the general population. The Clinic itself is in full swing, with 15 patients being seen and treated, and active research projects being developed all the time.

We are in the process of applying for further funding to support the studies being done, which include extensive virologic and immunologic workups on the patients.

We are finding that the sooner the disease is diagnosed and treatment begun, the better the prognosis for the patient. We have, therefore, been anxious to disseminate information both to the medical community and to the gay community to encourage screening for early diagnosis. Thus as an interim measure, before additional research funds are obtained, we would like to apply for \$3,000 from the S.F. Foundation to cover expenses such as office supplies, slides for lectures, typing and graphics. We have been doing much outreach financed personally by the investigators.

I spoke with Melinda Marble regarding the category technical assistance grant, and she felt this was probably not the appropriate channel to pursue. Perhaps you have suggestions as to the form our proposal should take. I look forward to speaking with you.

Sincerely,

Helen Schietinger, RN, MA
K.S. Clinic Coordinator

HS:jb

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SANTA BARBARA • SANTA CRUZ

HOSPITALS AND CLINICS

SAN FRANCISCO, CALIFORNIA 94143

March 15, 1982

Dear Patient:

Being told that you have a serious illness is a shock to most people. It is not uncommon to feel anxious, depressed, angry, or frustrated. Patients often find that it is helpful to be either in individual or group supportive counseling and to have information on the disease. The following resources are available:

- Individual Counseling: free individual counseling is offered by Shanti Project. Contact Jim Geary 415-849-4980.
- Support Group: Shanti Project offers a free support group in San Francisco for gay men who have cancer. The group, which meets weekly, focuses on crucial issues related to the impact of the disease. Additional information may be obtained from Jim Geary 415-849-4980.
- Telephone Network: An informal telephone support network is available to those who wish to speak to other cancer patients. Please contact Jim Geary for additional information 415-849-4950.
- Mixed Support Group: San Francisco Advent Center offers an ongoing support group for cancer patients. Members of the group are female/male and gay/straight. Additional information may be obtained from Rev. William Tye 552-7760.
- Hot Line: American Cancer Society provides information upon request 800-638-6694.
- Recommended Reading:
 - Cousins, Norman. Anatomy of an Illness. Norton, New York, 1979. The book is a patient's reflections on healing and regeneration.
 - Simonton, Carl, et al. Getting Well Again. Tarcher, Los Angeles, 1978. Step-by-step, self help guide to overcoming cancer.
- Other: Further information regarding community resources, discussion of your current emotional situation, or referral may be obtained from Paul Dague, Ph.D. 415-647-8895.

We hope that this information and resource list will be useful.

Marcus A. Conant, M.D.
Director
Kaposi's Sarcoma Clinic

Paul B. Dague
Paul B. Dague, Ph.D.
Consulting Psychologist
Kaposi's Sarcoma Clinic

MITCHELL H. FRIEDLAENDER, M.D.
OPHTHALMOLOGIST
95 KIRKHAM STREET
SAN FRANCISCO 94122
(415) 731-1075

March 16, 1982

Marcus Augustine Conant, M.D.
350 Parnassus Avenue
Suite 808
San Francisco, California 94117

Dear Marc:

Thank you very much for your letter regarding the Kaposi's sarcoma clinic patients. I will make an "insurance only" charge as you requested. I think it would be an excellent idea to send a brief communication once I've examined fifteen patients. I think I have seen about six Kaposi's patients so far.

I will probably not be able to attend the conference on Thursday. I will however, review the articles you recommended.

With best regards.

Sincerely,



MITCHELL H. FRIEDLAENDER, M.D.

MHF:kb

Norman Goldstein, M.D. Inc.
Dermatology

The Stangenwald Building
Downtown

March 16, 1982

Marcus Conant
Dermatology Department
350 Parnassus Avenue
San Francisco, California 94124

Dear Marc:

I have been asked to give some lectures on Kaposi here in Hawaii.

Gerry Gellin sent me one of your brochures. I can use 35 copies of them now. I will write to Neutrogena to see if they have any extra copies available.

I have been asked to put together a Symposium on sexually transmitted diseases in February 1983. Any possibility of your coming and participating at that time? The specific dates are not yet confirmed. ✓

I reviewed our statistics in Hawaii. We have had very few cases from 1946 to date. The last recent one was in an elderly Filipino man which was detected in 1977. More recently, a dermatologist discovered a case of Kaposi in a 29-year-old male homosexual. His case is of interest in that it presented itself as urticaria, and incidentally, the dermatologist detected the solitary nodule of Kaposi. It is being prepared for publication. I will send a copy to you when it is available to me. ✓

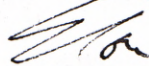
Marcus Conant
Page 2
March 15, 1982

If you have any slides of histiopathology or clinical Kaposi that I could use, I would greatly appreciate receiving them.

I look forward to hearing from you.

Aloha.

Sincerely yours,


Norman Goldstein, M.D.

NG:bm

P.S.: Just in case you missed the attached, I am sending a copy of the Wall Street Journal article to you.
Mahalo again.

mailed

file

March 18, 1982

TO: Dr. John Luce
Dr. Vincent Pons

FROM: Dr. Marcus Conant

RE: Pneumocystis Questionnaire

Word has reached me indirectly from Dr. Selma Dritz that Drs. Dodick and Coleman are working with Dr. Dritz to send out a questionnaire to patients who have had pneumocystis, to assay the reliability of open lung biopsy as a diagnostic technique.

I am certain that the two of you will want to speak to Drs. Dodick and Coleman to add your expertise and counsel.

MAC:jb

consent to examination by a medical practitioner rather than the station sergeant falls a long way short of full, free, and informed consent. In the case of intimate body samples the Bill does provide that consent must be given and the sample has to be taken by a medical practitioner. Nevertheless, the Bill refers simply to "written consent," and this does not leave the doctor the discretion to satisfy himself that the suspect has given full, free, and informed consent to the sample being taken. This should be a required precondition to taking intimate body samples for the purpose of providing evidence for a criminal prosecution.

The most unsettling aspect of the powers affecting the doctor-patient relationship in this Bill is that no case has been made out for their justification. No evidence has been provided that the police have experienced any serious difficulty in securing the cooperation of doctors when circumstances justify it. So far as the disclosure of confidential information is concerned, an informal agreement reached between the

Association of Chief Police Officers and the BMA was in the process of being adopted nationwide and had already provided the police with important information in some well known cases. The procedure worked speedily and effectively. The possibilities of abuse of the powers provided in this Bill are considerable, and, as a joint letter to *The Times* from the secretaries of the BMA and Law Society pointed out recently,³ the police themselves are not adequately protected against the consequences.

J D J HAVARD

Secretary,
British Medical Association

¹ Hailsham of Saint Marylebone, Quintin McGarel Hogg, Baron. *The dilemma of democracy: diagnosis and prescription*. London: Collins, 1978: ch 20.

² Royal Commission on Criminal Procedure. *Report*. London: HMSO, 1981. (Cmnd 8092.)

³ Havard JDJ, Bowron JL. Concern at proposed body searches. *The Times* 1983 Feb 17: 11 (col 5-6).

Regular Review

Acquired immune deficiency syndrome

A P WATERTON

New patterns of infectious disease are always interesting and sometimes alarming. The appearance of a syndrome with a high mortality and including not one but a whole range of infections is both interesting and alarming.¹⁻³ The interest is heightened by the syndrome including an unusual manifestation of an uncommon form of cancer, Kaposi's sarcoma.⁴ The syndrome occurs principally in homosexual men and first surfaced about 1979 in the form of major foci in the urban United States, particularly in New York and California.⁵⁻⁷ Of the first 300 patients described, 291 came from the United States and only nine from six other countries, but several of these had recently been in the United States.⁸⁻¹² More recently new reports have shown that the disease is now no longer confined to the United States nor entirely to homosexuals, nor to the male sex.¹³ Pathologically its essential basis is an acquired cellular immune deficiency, but the cause of this deficit at present eludes investigators, and, perhaps for this very reason, the malady excites an interest far beyond the columns of the medical press.¹⁴

The clinical picture is difficult to describe, or even to define, because of the diffuseness and incoherence of the syndrome.¹⁵ Of the first 300 patients, 290 were men, of whom over four fifths were under 45, and most were homosexuals.³ The 10 women were predominantly heterosexual. Patients may present with a pneumonia eventually diagnosed as due to *Pneumocystis carinii* or with Kaposi's sarcoma, or with both. Many patients, however, appear to have had fever, lymphadenopathy, loss of weight, and diarrhoea before the principal illness, especially before the pneumocystis pneumonia. Of the 300 patients mentioned above, 135 had pneumocystis

pneumonia as the principal illness, 115 had Kaposi's sarcoma, and 28 had both. The remaining 22 had various opportunistic infections.³ Some two fifths of the earlier patients are now dead, and the overall mortality is expected to reach 70%. A few patients have presented with autoimmune disease, particularly thrombocytopenic purpura, with antibodies directed against the platelets.¹⁶ These patients have reduced helper:suppressor T cell ratios. This may be a clinical pathway alternative to the main syndrome, which seems to end in Kaposi's sarcoma if the patient has not been picked off on the way by a fatal opportunistic infection, of which pneumocystis pneumonia appears to be the commonest. Either pneumocystis pneumonia or Kaposi's sarcoma may be accompanied by various other infections.

The cardinal feature is the occurrence of infections which test the host's cellular rather than humoral immunity and which are normally seen only in patients who are naturally or artificially immunocompromised—since their common denominator is the dependence of the host on an effective cellular immunity to combat them. Abnormal or florid forms may also be seen of infections which occur in a more usual guise even in normal people. A striking feature is the range of infectious agents that have been identified. These include protozoa (for example, *P. carinii*¹⁷⁻¹⁹ and *Entamoeba histolytica*; yeasts (for example, *Candida albicans* and *Cryptococcus neoformans*); bacteria (for example, *Mycobacterium avium-intracellulare*)²⁰; and viruses (for example, *Herpesvirus hominis*, genital warts, and cytomegalovirus). Even Kaposi's sarcoma²¹ is not entirely out of step with this pattern, because there is growing evidence for its association with a virus,

possibly cytomegalovirus, and it occurs in the train of immunosuppressive treatment, particularly in the form seen in these patients.²² American Burkitt's lymphoma has been reported in one case.²³ In contrast with the defect in cellular immunity, antibody mediated immunity to infectious disease appears to be working normally in these patients. The severe autoimmune thrombocytopenic purpura^{16 24} which may figure in the overall syndrome is antibody mediated, though its ultimate basis is likely to be a defect in T suppressor cells.

Communicability

The most sinister feature of this acquired immune deficiency is that it appears to be communicable,⁷ perhaps principally by intimate physical contact. The evidence for this conclusion is the explosive occurrence of the syndrome among those who have ample and exceptional opportunities for the spread of infection from person to person; the few who are not homosexuals can mostly be traced back to such a contact. The cellular immune deficiency distorts the clinical picture, so that abnormal, florid, and frequently progressive forms of infection are seen—for example, with *H. hominis* infection occurring as a rectal and anal ulceration; infections occur in ostensibly fit people which are usually seen only in the immunocompromised. Pneumocystis pneumonia rarely if ever occurs in healthy people.^{5 25} Kaposi's sarcoma^{4 24 26} is now occurring in the United States more frequently than ever before, sometimes in association with pneumocystis infection; as a component of this syndrome it appears in a more fulminant guise, not just with multiple vascular nodules but also with visceral lesions, particularly of the lymph nodes. In the past the picture seen so floridly in these patients has been observed as a result of congenital immunodeficiencies or as a product of the artificial state created by the administration of immunosuppressive drugs, whereas now it appears to come out of the blue. On examining "the blue," however—the supposedly previously healthy state—there is more even than at first meets the eye. The patients are mostly male homosexuals or drug abusers, or both,¹³ and they are not so physically healthy as has been supposed, particularly in their immunological state.

The results of immunological investigations have been reported in a substantial number of patients with varying types of the syndrome, including pneumocystis pneumonia and other opportunistic infections (for example, candidiasis, herpesvirus infections, and Kaposi's sarcoma), and also in members of the unaffected homosexual population.²⁷ Four principal immunological features have been identified. Firstly, the helper:suppressor cell ratio among the T lymphocytes is reversed. Secondly, natural killer cell activity is diminished. Thirdly, autoimmune phenomena are seen—for example, lupus erythematosus and thrombocytopenic purpura. The most striking feature, however, might be described as quantitative rather than qualitative. It is the degree of the immunodeficiency which is extraordinary and certainly far beyond that seen in patients having long term treatment with steroids, cyclophosphamide, or cyclosporin A. This serious disturbance of cell mediated immunity contrasts with a largely normal humoral immunity. It is reflected in a lymphopenia, in defective skin sensitivity to various antigens, and in defective lymphocyte transformation.^{17 19 28}

When the lymphocytes come under closer scrutiny a deficiency of T lymphocytes is seen, located in the T helper and inducer subsets—for example, OKT4—as opposed to the T suppressor cytotoxic subsets—for example, OKT8. The

ratio between the two is reversed from the normal by an absolute deficiency of the T helper cells rather than by a change in both subsets, though some studies have found that the number of suppressor cells was absolutely raised.²⁹ These findings are not surprising in view of the clinical picture, but a survey of unaffected homosexuals in New York showed that over 80% had a detectable abnormality in the helper: suppressor T cell ratio.^{27 28} An attempt was made at treatment with thymic extract in one case.³⁰ In this instance the helper: suppressor T cell ratio was restored to normal for a time, but the effect was not lasting. This failure suggests that the defective T cells are under the influence of some persistent agent, or some agent which had a persistent and irreversible effect, or perhaps of a combination of factors, both chemical and microbial. It is the search for such a cause which is at present so baffling, and the choice lies between "recreational" drugs, particularly nitrites,²⁹⁻³¹ and a viral cause, which may be a known immunosuppressive virus—for example, cytomegalovirus—or a hypothetical agent yet to be isolated and characterised. These possibilities are not mutually exclusive, and they may be in action severally or together.

Cause of immunodeficiency

In searching for the cause of the acquired immunodeficiency, one fact that needs to be borne in mind is the high prevalence of homosexuals in the two areas at first concerned (that is, New York and California). This is certainly paralleled by increased homosexual social activity in homosexual bars, restaurants, and so on, and presumably by increased sexual activity. One statistic of note is that the average number of male sexual partners for a life time reported by patients is 1160 as compared with 524 for matched homosexual controls.³² There may, too, be new ventures in the type of "sexual" practice.³³ This raises the question of the use of drugs such as nitrites—said to be the only group of drugs whose use by homosexuals had risen in the 1970s. Nitrites have an effect on T lymphocytes, but the part they play in the syndrome is uncertain if only because their use by homosexuals, if not universal, is widespread. On the other hand, at least one of the Danish patients⁸ and two French patients¹⁰ are said not to have used nitrites at all. These drugs alone seem hardly likely to have caused an irreversible and catastrophic immunodeficiency, but work by Goedert and others²⁹ has suggested that their immunosuppressive effect may be enhanced by repeated viral antigenic stimulation. The raised tempo and facility of transfer of material from person to person may furnish an underlying ecosystem in which they may make their individual contribution and in which a virus hitherto confined to relatively few individuals could find its way around more easily.

So far as microbiological causes are concerned, the difficulty is not so much to find a candidate as to evaluate the possible contributions of several. Comparison of patients having this syndrome with non-affected homosexuals has shown that cytomegalovirus is isolated more often from the urine, that the antibody titre to cytomegalovirus is above 1/128, that there is a raised titre to Epstein-Barr virus, and that there is more seropositivity for syphilis. Enteroviruses are also isolated more often.³ Gonorrhoea, hepatitis B, amoebiasis, and cytomegalovirus infections may be said to be endemic among homosexual, as opposed to heterosexual, men. The difficulty is to decide which, if any, of these infections could have contributed. One possible analogy is with the diseases of overcrowded poultry or calves, in which two or more pathogens

may be needed to produce a particular syndrome. In those circumstances outbreaks of disease cannot be attributed to any one agent³⁴ but to simultaneous infection with more than one—a state of affairs facilitated by the opportunities for transfer of micro-organisms from one individual to another.

So far as single organisms are concerned, however, cytomegalovirus has come under the most suspicion.³² Various viruses of man have an immunosuppressive effect, and cytomegalovirus is one of them. In mice it causes an increased mortality from bacterial and fungal infection,³⁵ and in man it can produce the T helper:suppressor cell ratio so characteristic of this disease.^{27 36} In addition it is closely associated with classical Kaposi's sarcoma in homosexuals³⁷ and with pneumocystis pneumonia.¹⁸ In recipients of renal allografts most opportunistic bacterial and fungal infections occur in patients with evidence of concurrent active cytomegalovirus infection, though such cytomegalovirus infections are common in these patients. It might be argued that even if active cytomegalovirus infection causes immunosuppression this is quite a different matter from a severe irreversible selective loss of T cell function. Nevertheless, there might be a kind of "cascade" effect, with depressed cellular immunity leading to further infection, and so on. The main difficulty in assessing the aetiological role of cytomegalovirus in the homosexuals with acquired immunodeficiency is that (like the use of nitrites) it is rife among them anyway.³⁸

Nevertheless, the case for the syndrome being linked with an infective agent of some kind is strong. Viruses such as hepatitis B virus³⁹ take good advantage of the homosexual drug abuser ecosystem to make up for the lack of facilities for transfer between humans with a less promiscuous sex life. The most likely picture, and it is at present no more than a conjecture, is that an unrecognised agent, probably a virus, has been enabled by one or more of several circumstances to spread in a way it had previously found impossible. The principal factor is a locus of greatly increased homosexual activity, with a background of specifically and overt homosexual bars, clubs, and so on, combined, perhaps, with the acquisition of new techniques of homosexual activity. This may have been compounded by drug abuse, with the syringe playing its part in boosting parenteral spread from person to person. Certainly this has been found to be a common factor where the disease has appeared in women. A virus—perhaps present in the blood, intestinal secretions, or semen of some carriers—may not until recently have had the chance to "take off." Once on its way, a vicious circle could have been set up in which patients with this acquired immune deficiency are more susceptible to reinfection and further replication and enhanced immunodeficiency. The agent could "jump" from the main cycle if, for example, an infected man has heterosexual intercourse. This model could include also a more or less prolonged symptomless phase after first infection, and there is already evidence that subclinical cellular immunodeficiency is far more common among homosexual men than had been realised until recently.²⁷

The question of "newness" of an infectious disease and the emergence of unrecognised agents raise in themselves intriguing issues. These invite comparison with such agents as human T leukaemia virus, Marburg virus, and hepatitis B virus. The first of these is a virus unearthed by present day techniques for a well characterised disease and which must have been in circulation in some form for many years.⁴⁰ The Marburg virus,⁴¹ which infected laboratory workers preparing poliovaccine from vervet monkey kidney cell cultures, might not have come to light at all but for the technical procedures

requiring extensive processing of kidney cells of this species. To this day, its ultimate origin is uncertain, but it may have been in circulation in the African jungle for centuries, only to make its debut in human medicine in 1967 with a few brief but tantalising occurrences since then. Hepatitis B virus is somewhat nearer home. Human convalescent serum had not been used for prophylaxis against measles and other viral infections until about 1920.⁴² At the same time blood transfusion was becoming a practical reality, to be followed soon by the use of freeze dried pooled human plasma. Once these particular procedures became widespread, hepatitis B virus could emerge as a serious problem in infectious disease caused by the human to human transfer of material by this as well as other means, such as improperly sterilised syringes. It was some three decades before its clinical course was realised, however, and even then the nature of the agent was unknown. If it had *not* been for the use of blood and blood products hepatitis B might well have appeared first, at least in any prominence, as a sexually transmitted disease, brought to light by increasing activity³⁹ in the homosexual and drug abusing fraternities of the conurbations where it is now so rife.

Unanswered questions

Clearly there are still more questions than answers about this syndrome. What is it? It is a communicable (or "community acquired"¹³) cellular immune deficiency. Is it "new"? Yes. Why has it appeared? This is still an open question, best answered by asking two more questions—What is the cause? and Why is it able to cause it? Three answers have been suggested.

Firstly, the "hot bed" theory argues that the traffic in human material in certain quarters by abnormal routes has reached such a level that, combined with the effects of drug abuse of various kinds, the sheer weight of chemical and microbial insult to the body in general, and to T lymphocytes in particular, goes beyond the tolerable limit. Eventually irreparable damage is sustained, which becomes manifest clinically in one or other of the variety of components of the syndrome.

Secondly, the drug theory points to drug abuse as the common denominator between the non-homosexuals and the main mass of patients. Much attention has focused on amyl and butyl nitrite as relative newcomers to the scene, but they are scarcely enough alone to cause all the damage.

Thirdly, the virus theory argues that the apparent communicability of the immune defect points to a microbial origin. Various viruses affect the lymphocytes—for example, measles, cytomegalovirus, and Epstein-Barr virus. That there may be another is not surprising.

The first and second of these theories are worth considering; the factors are undoubtedly relevant. Whether or not an unknown virus, perhaps formerly held at bay by adequate cellular immunity, is a reality is still conjecture. One possibility is the introduction of an animal virus into the homosexual system.³ The list of those at risk, now that haemophiliacs have been added,⁴³⁻⁴⁵ and also prisoners,⁴⁶ has a familiar ring to those acquainted with the control of hepatitis B.

This brings us to the last question of all. What is to be done? Towards the end of 1982 the tally of cases was 788,⁴⁷ but this may be more than the tip of a large and rather chilling iceberg yet to come. Specific treatment for the various aspects of the syndrome has been weighed in the balance and mostly found wanting. Antimicrobial chemotherapy for the infections

has proved ineffective in some cases and somewhat disappointing in many others. Anticancer treatment for Kaposi's sarcoma has been hampered by the leucopenia. The results of attempts at thymic supplementation have not been long lasting, and bone marrow transplantation has been suggested and tried in at least one case.³

The absence of any effective treatment for these patients underlines the importance of a preventive approach. If there is a microbial agent, and if it is present in patients' body fluids and particularly their blood,⁴⁸ this means that there is a greater need than ever for care in handling human materials⁴⁹ and in monitoring artificial human to human transfer of any kind. Human blood may carry, among other things, hepatitis B virus, at least two non-A, non-B hepatitis viruses, and

cytomegalovirus; and the possibility of transmission of human T cell leukaemia virus in blood has recently been aired.⁵⁰ Prevention raises issues larger than those simply of cross infection. Ironically, despite all the uncertainties, this disease (like genital herpes, which has also attracted much attention in the American lay press) is essentially preventable. The abandonment of promiscuity, homosexuality, and drug abuse could eventually stop both diseases in their tracks—though that is hardly likely to prove an acceptable solution.

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AIDS: Hemophiliacs

A total of 2,157 AIDS cases have been reported to the CDC as of late August 1983. In July 1983, 53 AIDS cases a week were reported, compared with 24 a week on January of this year and 11 a week in July 1982.

Of the 2,157 cases, 16 (0.7%) occurred in hemophiliacs, who—along with homosexual males, heterosexuals who take illegal IV substances, and Haitian immigrants—are considered at high risk for the syndrome. (This proportion has remained constant.) Depending on both the time from diagnosis and the opportunistic disease(s) contracted, reported mortality from AIDS ranges from 20% to over 50%; of the 16 hemophiliacs reported with AIDS, 12 have died (75%).

Lymphocyte abnormalities found in hemophiliacs receiving frequent clotting-factor treatment: Significance unclear.

Lymphocyte abnormalities in the absence of opportunistic infection have been found in a number of hemophiliacs. This phenomenon is similar to one found in many healthy homosexuals.

Jonathan C. Goldsmith, M.D., and colleagues studied lymphocyte abnormalities among 12 apparently healthy adults with hemophilia who ranged in age from 16 to 71 years. Eleven had severe hemophilia (plasma levels less than 0.01 U/ml of Factor VIII or Factor IX and lifelong recurrent spontaneous hemarthroses), and one had a Factor IX level of 0.04 U/ml and moderately severe bleeding. All were heterosexuals born in the U.S. and none had used illicit intravenous narcotics.

The average ratio of helper to suppressor T cells for the study group was $0.86 \pm 0.14:1$. Age- and sex-matched non-hemophiliac adult men had, in contrast, a ratio of $1.96 \pm 0.24:1$.

The 12 patients were divided into 2 distinct groups. Three had normal T cell ratios, whereas 9 had a ratio of less than $0.82:1$, with decreased absolute numbers of helper cells and either normal, or markedly increased, absolute numbers of suppressor cells. All 9 with abnormal T cell populations had been receiving weekly treatment with commercial products containing clotting factors. In contrast, none of the 3 patients with normal subpopulations of T cells had such continued, frequent exposure.

Preliminary studies have shown that hemophiliacs treated with concentrates have a higher risk of developing not only lymphocyte abnormalities but also AIDS symptoms, than do those treated with cryoprecipitate. Dr. Goldsmith said in an interview, "The intensity of therapy probably predicts fairly well for lymphocyte subpopulation abnormalities, and intensity correlates with the use of concentrate lyophilized Factor VIII."

However, he also noted that all 12 patients in his study are well, and none has shown signs of AIDS. In a more recent study of hemophiliacs by Dr. Goldsmith and others, 1 patient did develop herpes zoster, but the infection did not disseminate.

Dr. Goldsmith said, "So it's likely that this patient won't develop AIDS. I don't think these lymphocyte abnormalities necessarily signify the development of AIDS. There has not been an explosion of cases of

AIDS among the hemophiliac population, which is what one might have anticipated if the lymphocyte abnormalities were going to code for AIDS. AIDS, however, has a long incubation period, and the most important thing is that we're acquiring background data on a circumscribed population. At the very least, we'll learn whether these tests are accurate markers for the development of AIDS, whether they will be applicable to screening blood donors.

"I would recommend to physicians that they treat patients for bleeding episodes as they have in the past. If a patient has moderate hemophilia (only a few episodes in a lifetime), treatment should be restricted to products from pools derived from fewer donors (e.g., cryoprecipitate) or plasma. There is no point in not being safe with that group. But the average adult on home therapy receives 50-100,000 units of Factor VIII a year, either cryoprecipitate or lyophilized concentrate. So there are thousands of donor exposures no matter which way," Dr. Goldsmith told the BULLETIN.

Dr. Goldsmith is Co-Director of the Great Plains Regional Hemophilia Center, Iowa City, Iowa.

See *Ann. Int. Med.*, March 1983, pp. 294 ff.

Patient may have acquired syndrome from Factor VIII infusions: *M. avium-intracellulare* diagnosed.

A pathogen in Factor VIII concentrate appears responsible for the occurrence of AIDS in an Ohio man with hemophilia.

According to James Elliott, M.D., and associates, the 27-year-old patient presented with *Pneumocystis carinii* pneumonia (PCP) and developed numerous episodes of pharyngeal candidiasis over the next 4 months, followed by disseminated

Syphilis

Benzathine penicillin G effective: 100% seronegativity and complete healing of ulcer, rash.

Treatment with benzathine penicillin G is effective against both primary and secondary syphilis, provided there is no prior infection, according to Nicholas J. Fiumara, M.D.

Dr. Fiumara treated 500 patients (452 men, 48 women, mean age 30.2) who had primary syphilis and 522 patients (342 men, 175 women, mean age 28.1) who had secondary syphilis. All primary syphilis patients had, in addition to clinical symptoms, a reactive rapid plasma reagin circle card test (RPR-CT) and a positive fluorescent treponemal antibody absorption (FTA-ABS) test. Criteria for the diagnosis of secondary syphilis were a rash; hard, discrete, and nontender lymphadenopathy; a reactive quantitative RPR-CT, and a positive FTA-ABS test.

Patients allergic to penicillin were excluded from the study and received oral tetracycline 500 gm, 4 times daily for 12 days. Patients with a history of prior treatment for syphilis or signs of previous infection were excluded, and those who became reinfecting during the study were withdrawn from the group.

All patients in the study received benzathine penicillin G, 2.4 million U intramuscularly in 2 sites, and a second course of 2.4 million U 1 week later.

All patients treated for primary syphilis became seronegative within 1 year (median interval, 4 months), and all those treated for secondary syphilis became seronegative within 2 years.

According to Dr. Fiumara, an erosive chancre is nearly healed by 1 week after treatment, and the larger, deeper hunterian chancre within 3 weeks. The rash of secondary syphilis—even pustular lesions—heals completely within 4 weeks. In

his opinion, physicians treating primary or secondary syphilis should inform patients about time required both for healing and for seroconversion. "After the initial shock of receiving a syphilis diagnosis, the average patient has 2 questions: how fast a rash or ulcer will disappear, and how soon the blood test will be normal. These are universally asked," he told the BULLETIN.

Dr. Fiumara also noted that this 2-course schedule calls for twice the

amount of penicillin recommended in current CDC treatment guidelines for STDs. However, research has shown that CDC-recommended levels are associated with less than 100% seronegative rates 2 years after treatment, for both primary and secondary syphilis.

Dr. Fiumara is Director, Division of Communicable and Venereal Diseases, Massachusetts Department of Public Health, Boston.

See *Am. Fam. Physician*, Feb. 1983, pp. 185 ff.

Herpes

Sequential genital infections by HSV-1, HSV-2 can occur: But double or triple infections infrequent.

Two distinctly different herpes-viruses can initiate genital infections in 1 individual, according to Saul Kit, Ph.D., and colleagues.

The investigators saw a 35-year-old woman who presented with a small, painful lesion on the distal site of the right labium majus. Four, 7, and 9 months after the first infection, she returned with new genital lesions.

Restriction nuclease analysis identified the first episode as herpes simplex virus 1 (HSV-1), and testing for IgM antibody to HSV indicated that the patient had recently contracted a new HSV infection.

However, virus microneutralization and the micro-solid phase radio-immunometric test for IgG showed that she had had prior infection with herpes simplex virus type 2 (HSV-2).

Restriction nuclease analysis identified the latter 3 episodes as HSV-2. The isolates were of an identical strain of HSV-2 and were not recombinants or a mixture of the viruses.

Some investigators have cautioned that, since HSV-2 can undergo genome variation while adapting to a new patient, the reported isolation of apparently different viruses from genital herpes infections does not

always mean 2 independent infections. In this case study, however, there was no doubt that the 2 viruses were totally different from each other.

In an interview, Dr. Kit said, "The bad news is that the patients with 1 genital herpes infection and antibodies to that infection and other forms of immunologic resistance are still at risk for a second infection, which might have the potential for a more virulent virus.

"But the good news is that the probability that a patient with 1 infection will have a second infection and recurrences is small. Since recent studies have shown that double or triple infections are infrequent, a first infection must be fairly protective against a second. It can be argued, therefore, that preventive measures for high-risk groups are indicated and may be feasible. The whole picture is pointing toward a rationale for preventive measures such as vaccines," Dr. Kit told the BULLETIN.

Dr. Kit is Professor and Head, Division of Biochemical Virology, Baylor College of Medicine, Houston.

See *Sex. Transm. Dis.*, April-June 1983, pp. 67 ff.

ID/IC BULLETIN

Infectious Diseases and Infection Control, University of California, S.F.

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ACQUIRED IMMUNODEFICIENCY SYNDROME

The appearance of a profound immunodeficiency syndrome in previously healthy homosexual males, Haitians, and hemophiliacs has raised considerable interest in the medical community and American press.

The University of California San Francisco (U.C.S.F.) first began treating these patients in August 1981. The number of patients has been steadily increasing and questions concerning treatment modalities and infection control measures have been frequently posed. This bulletin concentrates on the infectious aspects of this syndrome and presents guidelines for infection control in U.C.S.F. Hospitals and Clinics.

EPIDEMIOLOGY

Between June 1, 1981 and September 3, 1982 the Centers for Disease Control received reports of 578 cases of Kaposi's Sarcoma (KS), *Pneumocystis carinii* pneumonia (PCP) and other serious opportunistic infections (OI) occurring in previously healthy persons. Of the 578, 435 (75%) were homosexual or bisexual men, 83 (14%) heterosexual males, 28 (5%) males of unknown sexual orientation and 32 (6%) women. Almost 90% of the cases were 25-49 years old. Approximately 60% were white not Hispanic, 20% black not Hispanic, and 13% Hispanic.

Cases have been reported from 27 states; however, approximately 50% of the reports have come from New York City. California, Florida, New Jersey and Texas have also reported a large number of cases. (CDC, MMWR, 31:294, 1982). Nine foreign countries have reported at least one case. Some of these individuals had been to New York City prior to becoming ill. There also appears to be a large number of seemingly similar cases occurring in Haiti and there have been 34 diagnosed cases in Haitian refugees in the United States.

Table 1 is a breakdown of disease and mortality of United States cases as of September 3, 1982. (CDC, Task Force on Acquired Immunodeficiency Syndrome, weekly report).

Table 1. Disease and Mortality, United States

	Cases	Percent of total	Deaths (percent)
KS without PCP	177	30.6	34 (19.2)
PCP without KS	291	50.4	137 (47.1)
Both KS and PCP	43	7.4	29 (67.4)
OI without KS or PCP	67	11.6	33 (49.3)
Total	578	100.0	233 (40.3)

The San Francisco Public Health Department first received reports of cases with onset in 1980. There have been 100 cases reported as of September 5, 1982. Ninety-nine were male homosexuals and 1 was a heterosexual male. Fifty-one of the 100 cases have had onset in 1982 and the number of reported cases is continuing to increase. Table 2 summarizes the cases in San Francisco. (personal communication, Selma Dritz MD, Disease Control, San Francisco Public Health Dept).

Table 2. Disease and Mortality, San Francisco

	Cases	Percent of total	Deaths (percent)
KS without PCP	45	45.0	7 (15.6)
PCP without KS	37	37.0	15 (40.5)
Both KS and PCP	8	8.0	5 (62.5)
OI without KS or PCP	10	10.0	5 (50.0)
Total	100	100.0	32 (32.0)

Initially reported cases were in bisexual or homosexual males; however, there has been a small but continuing increase of cases in heterosexual males and in

women. In one study, 63% of the heterosexual men and 57% of the women reported using intravenous drugs, compared with 14% of the homosexual men (CDC, MMWR, 31:294, 1982). In July the Centers for Disease Control released reports of 3 cases of PCP in patients with hemophilia A but no other underlying disease. All 3 patients had received multiple doses of factor VIII concentrate but none of the patients had received concentrate from the same lot (CDC, MMWR, 31:365, 1982).

IMMUNOLOGY

The common denominator explaining the multiplicity of presentations in these patients appears to be a severe disorder of immunoregulation, termed acquired immunodeficiency syndrome (A.I.D.S.) These findings have recently been described (AS Fauci, Ann Intern Med, 96:777, 1982). Patients present with a spectrum of immune dysfunction. This is most often characterized by anergy to skin testing, lymphopenia, and an often profound reversal in the ratio of two populations of T-lymphocytes, termed the helper-cell to suppressor-cell ratio or OK-T4 to OK-T8 cell ratio. Immunoglobulin levels are most often normal, although in some cases elevated IgA and/or IgG levels have been noted. In addition, at least in a few patients, the B-lymphocytes do not appear to be responding normally; this may be a secondary manifestation of abnormalities in the T-lymphocyte population.

This disorder of immune function impairs the body's "surveillance" to both infectious and non-infectious illnesses. The appearance of Kaposi's sarcoma, Burkett's lymphoma, Hodgkin's disease and some mucocutaneous malignancies represents a defect in these patient's ability to recognize or to eradicate malignantly-transformed cells. The recently reported observation of several cases of autoimmune thrombocytopenic purpura probably represents an additional manifestation of this disorder of immunoregulation.

The underlying cause of this disorder is unclear and it is difficult to sort out which risk factors (e.g. environmental, use of street drugs such as nitrites, genetic predisposition, etc.) may be contributory rather than causative. The most current theories include an infectious agent, possibly a virus which is transmitted like hepatitis B virus. It is suggested that this agent might infect T-lymphocytes and be responsible for immunosuppression. This may be a new agent or a mutated form of an old virus. Currently there is some speculation that cytomegalovirus may be involved. Others postulate a "chronic antigenic stimulation" theory which hypothesizes that repeated infections with gonorrhea, syphilis, hepatitis, amoeba and cytomegalovirus (CMV) "exhaust" the immune system.

CYTOMEGALOVIRUS INFECTIONS

Cytomegalovirus is a herpes DNA virus which is found ubiquitously. It is well recognized as a cause of a mononucleosis-like syndrome in adults, neonatal and congenital infection, and illness in immunosuppressed patients. Patients receiving organ transplantation, in particular, are at risk. This infection may manifest as a pneumonitis, hepatitis, gastroenteritis, or retinitis. Recently it has been noted that 93% of sexually-active gay men have cytomegalovirus IgG antibody and approximately 50% have IgM antibody (LW Drew et al., J Infect Dis, 143:188, 1981). In addition, a number of these patients have been found to excrete CMV in their urine and semen. The diagnosis of CMV usually is made on clinical, serological, culture, and often pathological criteria.

A.I.D.S. patients have serological evidence of past infection. The virus has been found in cultures from biopsy specimens and microscopic evidence has been seen in biopsies of lung, bowel and tumor (LW Drew et al., Lancet, II:125, 1982). Speculation regarding the role of this virus as a possible etiological factor in this syndrome remains controversial. The association of this virus and Kaposi's sarcoma was reported in African patients prior to this current epidemic (Geraldo G and Beth E, **The Role of Viruses in Human Cancers**, Elsevier — North Holland, 1:57, 1980). In addition, the laboratory evidence for a transient immunosuppressive state following CMV mononucleosis in otherwise healthy patients has been reported independently. (CR Rinaldo Jr., J Infect Dis, 141:488, 1980).

No efficacious therapy has been defined to date. However, interest in a number of antiviral drugs and interferon has led to ongoing clinical trials with a variety of agents.

PNEUMOCYSTIS CARINII PNEUMONIA

Pneumocystis carinii is a protozoan also found ubiquitously worldwide. By the age of 4, approximately 80% of immunocompetent children have serological evidence for past infection. However, this organism has been identified as a cause of often fatal pneumonitis in several subpopulations. These include protein-malnourished children in European orphanages and immunosuppressed patients. The appearance of this infection and Kaposi's sarcoma in homosexual adult males alerted the medical communities in New York City, Los Angeles, and San Francisco to this syndrome. The organism is most often limited to the lungs. It presents as a diffuse pneumonitis with few findings on physical examination, but often profound hypoxia and dyspnea. Occasionally the organism has been found to disseminate to multiple sites, including the retina. Diagnosis is made by silver methenamine staining of tissue obtained from lung biopsy. To date, attempts at culture and serological diagnosis have been disappointing.

Treatment is provided by either high dose trimethoprim-sulfamethoxazole (TMP-SMX), given either orally or intravenously, or with pentamidine, administered intravenously or intramuscularly. No comparative trials in this population have been reported, and in some cases a combination of these drugs has been given. Although the mortality from this infection in patients with hematological malignancies has decreased with the advent of appropriate chemotherapy from over 50% to 5-10%, the mortality from pneumocystis in patients with A.I.D.S. has been in the range of 50% despite drug therapy. In addition, a number of cases of recurrence have been described. Therapy with oral trimethoprim-sulfamethoxazole should include documentation of adequate absorption by obtaining peak serum concentrations of either trimethoprim or sulfamethoxazole. Problems with both drugs are common. Skin rash and fluid overload with intravenous TMP-SMX are not absolute contraindications to therapy, but must be monitored. The usefulness of prophylactic TMP-SMX in this syndrome has not yet been investigated.

OTHER INFECTIONS

A number of additional infections of varying severity have been reported. Thrush (candida pharyngitis and esophagitis) is nearly universally seen. This infection is unusual in patients not taking antibiotics or known to have an underlying chronic illness. Although occasionally difficult to manage, a number of treatment options are available. These include oral nystatin, mycostatin oral tablets, ketoconazole, and intravenous amphotericin B.

Perianal ulcerations secondary to herpes simplex virus have been described. These can be quite extensive, causing the patient a great deal of discomfort. On occasion this has required the antiviral drug acyclovir for control.

A few cases of disseminated *Mycobacterium tuberculosis* and atypical mycobacteria have been reported. These have presented as diffuse tissue involvement with poor host cellular response. Treatment outcome with as many as five anti-tuberculosis medications has generally been poor.

Disseminated cryptococcus and cryptococcal meningitis have also been seen. These infections may present as pulmonary infiltrates, skin rash, or diffuse headache and photophobia, suggesting meningitis. Treatment with amphotericin B and 5-flucytosine has cured the infection in many cases, but some of these patients have gone on to relapse.

Other infections noted include recurrent bacterial sepsis, follicular impetigo, herpes zoster, *Nocardia* pneumonitis, and cryptosporidiosis colitis. Severe and fatal toxoplasmosis has also been seen. In summary, each new sign or symptom in these patients must be taken seriously and investigated fully for the broadest spectrum of possible infectious agents.

INFECTION CONTROL ASPECTS

The following guidelines were derived through discussion with members of the U.C.S.F. Kaposi's clinic and personnel caring for the patients and have been approved by the Infection Control Committee. They were established in consideration of a potentially transmissible agent being responsible for this syndrome and may be changed as further information becomes available.

All Patients: Private room not necessary (see exceptions below); however, A.I.D.S. patients are immunocompromised and should not be placed in a room with infected patients. Patients should be placed on "Blood" Precautions; i.e. blue sign; gloves required for contact with blood, secretions, excretions; gown and mask not necessary. A needle box should be placed at the bedside for immediate disposal of used sharps. Pregnant women should avoid direct patient contact because many of these patients are excreting cytomegalovirus.

Pneumocystis Patients: Private room not necessary but patients cannot be in the same room with high-risk patients or other A.I.D.S. patients because of the theoretical potential for *P. carinii* airborne spread to immunosuppressed patients. High-risk patients are defined as persons receiving radiation therapy, or other immunosuppressive treatments, cortisone derivatives in a dose greater than 100mg hydrocortisone equivalent per day or diagnosed as having leukemia, lymphoma, aplastic anemia, etc.

Kaposi's Sarcoma Patients: A private room not necessary but it is desirable to have private room and bathroom if the patient has diarrhea.

Compromised Host: Patients with WBC <1000 or PMN <500 should be placed on Compromised Host Precautions.

Materiel Services: Instruments and other items grossly contaminated with blood or excreta should be rinsed under running water in the utility room and sent to Materiel Services in a plastic bag labelled "contaminated."

Environmental Services: Rooms need not routinely be high-cleaned; questions concerning exceptions should be directed to Infection Control.

Dietary: Isolation trays are not necessary.

Linen: Double bag linen only if grossly contaminated with blood or excreta.

Laboratory: Blood specimens should be handled with caution as with known hepatitis B carriers; however, it is important to remember that blood from any patient may be infectious and appropriate infection control measures should always be followed.

Addendum: Frequently patients present with other infectious processes (e.g. hepatitis, herpes, enteric pathogens) and should be placed on appropriate precautions. *NOTE: Individuals who appear to have this syndrome can be seen in the Infectious Disease - Tropical Disease Clinic on the U.C.S.F. campus (x5787).*

Master



University of California San Francisco
Division of Infectious Diseases and
Hospital Infection Control
San Francisco, California 94143

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MARCUS A CONANT
350 PARNASSUS #808
SAN FRANCISCO CA

94117

FEDERAL REPUBLIC OF GERMANY AIDS CASE SURVEILLANCE (8-7-83)

<u>PRIMARY DISEASE</u>	<u>CASES</u>	<u>% OF TOTAL</u>	<u>DEATHS</u>	<u>% DEAD</u>
Kaposi sarcoma (KS) without opportunistic infections (OI)	10	25,0	0	0
Pneumocystis carinii Pneumonia (PCP)	13	32,5	7	53,8
Both KS and PCP or OI	5	12,5	1	20,0
Other OI or tumors related to AIDS (or PCP only clinically suspected)	12	30,0	3	25,0
<u>TOTAL</u>	<u>40</u>	<u>100</u>	<u>11</u>	<u>27,5</u>

<u>AGE</u>	<u>CASES</u>	<u>% OF TOTAL CASES (28) (WRITTEN REPORTS)</u>	<u>RISK GROUPS - (ALL BUT 1 MALES)</u>	<u>CASES</u>	<u>% OF TOTAL</u>
under 20	0	0	Homo- or Bi- sexual	35	89,7
20 - 29	3	10,7	iv-Drug User (only)	0	0
30 - 39	15	53,5	Haitians or Africans	0	0
40 - 49	8	28,5	Hemophiliac	1	2,5
over 50	2	7,1	To little information	3	7,7
no written report	12				
<u>TOTAL</u>	<u>40</u>	<u>99,8</u>	<u>TOTAL</u>	<u>39</u>	<u>100</u>

L'AGE-STEHR

EPIDEMIOLOGY OF TRANSFUSION CASES

Patient	Donors (No.)	Donors Evaluated (No.)	AIDS risk group	Lymphadenopathy	T _H /T _S
1	3	3	None	Yes	0.6
2	28	18	Homosexual man	Yes	0.8
3	20	13	Intravenous drug user	No	1.5
			None	No	0.9
4	6	6	Homosexual man	No	0.5
5	3	1	Homosexual man	No	0.4
6	2	2	Homosexual man	Yes	0.7
7	4	4	Homosexual man who used intravenous drugs	Yes	1.7
8	4	2	None	No	0.6
9	6	3	Homosexual man	No	0.7
10	16	11	None	No	0.3
11	31	28	No high-risk donor identified		
12	34	26	Homosexual man	No	0.6

Jaffe, H. W., "Transfusion-Associated AIDS:
Serologic evidence of human T-cell leukemia
virus infection of donors", Science, 1984,
223:1309

Patient	Diagnosis	Time from transfusion to illness onset (months)
1	PCP	44
2	PCP	15
3	PCP	16
4	PCP	28
5	KS	17
6	PCP	35
7	PCP	40
8	PCP	34
9	PCP	18
10	PCP	27
11	PCP	13
12	PCP	18

**California Medical Association's
111th Annual Session
features**

Skin Cancer Update

March 13

**Allergic and Immunologic
Skin Reactions**

March 14, 1982

Disneyland Hotel, Anaheim

Saturday, March 13

Section on Dermatology and Section on Allergy present

Skin Cancer Update

\$15.00 Luncheon Fee

Cosponsored by

The American Cancer Society, California Division

Program Planner: D. Antonio Lopez, MD, Chula Vista

Educational Objective: This course will update physicians specializing in the treatment of skin cancer on the current advances in the management of various forms of cutaneous malignancies. Emphasis will be given to the indications for selection of the various treatment modalities available for the different types of skin cancers, their proper use, complications, assessment of results, recognition of problem areas and problem tumors, and the detection and management of recurrent carcinomas. Upon completion of this program, the practicing physician should have an up-to-date knowledge of the current treatment modalities, their indications for specific tumor types and locations, as well as knowledge of complications, proper follow-up and expertise in the management of recurrences.

- 8:20 Introduction and Pre-Test**
Dr. Lopez
- 8:30 Environmental Carcinogens and Skin Cancer**
John H. Epstein, MD, San Francisco
- 9:00 Sunlight Protection and Precancerous Conditions**
Joseph F. Walter, MD, San Diego
- 9:20 Skin Cancers—Epidemiology and Prognosis**
Richard G. Glogau, MD, San Francisco
- 9:50 Cryosurgery for Premalignant and Malignant Lesions**
Roberts B. Pappenfort, MD, San Diego
- 10:10 Break**
- 10:30 Electrosurgery in the 80's**
Richard B. Odom, MD, San Francisco
- 10:50 Surgical Equipment and Emergency Preparedness**
Theodore A. Tromovitch, MD, San Francisco
- 11:10 Simple Surgical Excisions for Skin Cancers—
Recognition of Problem Types and Areas**
Samuel J. Stegman, MD, San Francisco
- 11:30 Malignant Melanoma—Staging and Management**
Kenneth Gross, MD, San Diego

- 12:00 Luncheon
Viral Oncogenesis—Current Status of Kaposi Sarcoma
Marcus A. Conant, MD, San Francisco
- 1:30 **Mohs Chemosurgery and Microscopically Controlled Fresh Tissue Chemosurgery**
Dr. Tromovitch
- 2:00 **Flaps, Grafting and Newer Modalities for Skin Cancers—Current Status of Laser Surgery**
Dr. Stegman
- 2:30 **Chemotherapy and Immunotherapy for Skin Cancers and Keratocanthomas**
Dr. Odom
- 2:50 **Mycoses Fungicides and Cutaneous Lymphomas**
Norman M. Price, MD, Walnut Creek
- 3:20 Break
- 3:40 **Radiation Therapy for Skin Cancers**
Douglas K. Pay, MD, San Diego
- 4:10 **Therapeutic Panel**
Moderator: Dr. Lopez
- 5:25 **Post-Test and Evaluations**

Acceptable for up to 8 hours of Category I Credit.

Acceptable by the American Academy of Dermatology for Category Iae Credit

Approved for 8 contact hours, California Board of Registered Nursing provider number 00370.

Sunday, March 14

Section on Allergy and
Section on Dermatology present

Allergic and Immunologic Skin Reactions

\$20.00 Luncheon Fee

Program Planner: Roger M. Katz, MD, Los Angeles

Educational Objective: Physicians including allergists, dermatologists, family physicians, pediatricians, and internists attending this program should be able to apply recent methods of diagnosis and treatment to common allergic and immunologic skin disorders in clinical practice.

- 8:30 **Allergic and Immunologic Mediators—From Where to When**
Stephen Wasserman, MD, San Diego
- 9:15 **Atopic Dermatitis—How to Fix the Itch**
Roger C. Cornell, MD, La Jolla
- 9:45 **Immunologic Diseases of the Skin—Blisters—Sisters**
Razzaque Ahmed, MD, Los Angeles
- 10:15 Break
- 10:30 **Delayed Hypersensitivity—Contact Dermatitis, Enzymes, Metals, and Other Skinitis**
Howard Maibach, MD, San Francisco
- 11:00 **Immune Deficiency and Skin Diseases—PPP**
Michael E. Miller, MD, Torrance
- 11:30 **Break for Keynote Speaker**
- 12:30 Luncheon
Urticaria, Welts or Hives—Where, How or Why
Sheldon Spector, MD, Los Angeles

Acceptable for up to 3½ hours of Category I Credit.

Approved for 3½ contact hours, California Board of Registered Nursing provider number 00370.

Acceptable by the American Academy of Dermatology for Category Iae Credit.

Advance Registration Form

111th Annual Session

March 12-17, 1982

Advance Registration Closes February 12, 1982

CMA ALPHA ID (as shown on member card)

Members please insert. If not available, leave blank and CMA will complete.

MEMBER ID NUMBER

[illegible]

Name

[illegible]

Street

[illegible]

City

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State

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Zip

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Specialty _____

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- ☐ California Medical Association
- ☐ American Medical Association
- ☐ California Medical Association Political Action Committee



GENERAL REGISTRATION FEES:

There is no general registration fee for CMA members or their families. For all others, please indicate category:
(Check only one)

- E ☐ Nonmember Physician — Fee \$100
K ☐ Medical Student — no fee
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R ☐ Exhibitor — no fee
T ☐ News Media — no fee
F ☐ Resident, Fellow, or Intern — no fee
M ☐ Allied Health — no fee
Q ☐ CMA Staff — no fee
S ☐ Speaker — no fee
X ☐ Other — Describe

CME COURSE REGISTRATION AND LUNCHEON FEES

Courses and luncheons with fees (only general registration is required for courses without fees).

Please indicate ☒ those you plan to attend:

- | | | |
|----|---|----------|
| 11 | ☐ Skin Cancer Update
(Luncheon fee only) | \$ 15.00 |
| 02 | ☐ Allergic and Immunologic Skin
Reactions (Luncheon fee only) | \$ 20.00 |

Total Remittance

(Include both CME Course and any General Registration fee due)

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**IF SPOUSE AND/OR CHILDREN ARE TO BE REGISTERED,
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[illegible]

All checks should be made payable to California Medical Association.

Please return this form with appropriate remittance to:

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MARCUS A. CONANT, M.D.
350 PARNASSUS AVENUE
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March 19, 1982

Henry Roenigk, Jr., M.D.
Chairman, Department of Dermatology
Northwestern Medical School
303 East Chicago Avenue
Chicago, IL 60611

Dear Henry,

I will be happy to speak at the symposium of all Cutaneous Tumors
at the AAD meeting in New Orleans on Monday afternoon, December the 6th.

I will be with Al Friedman-Kein at the International Meeting in Tokyo
and perhaps we can decide how best to present our material.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:ig

Fairlane

1940 Hubbard Drive
Dearborn, MI. 48126
(313) 336-2100

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March 24, 1982

Marcus A. Conant, M.D.
350 Parnassus Avenue
San Francisco, California 94117

Dear Dr. Conant:

It was a great pleasure speaking with you on the telephone last week. As we discussed, I am planning to review Kaposi's sarcoma and the GRID infections at the Michigan Dermatology meeting at Henry Ford Hospital on April 21, 1982. To date we have not seen any cases of Kaposi's or infections suggestive of underlying immunodeficiency in our department. I have, however, heard of a few cases of men with suspicious symptoms in the Detroit area and would not be surprised if this number increases.

In the meantime however, I lack the clinical slides to illustrate the dermatologic aspect of these diseases. I greatly appreciate you allowing me to present your slides at the meeting. We will be happy to cover any duplication costs involved.

As you will agree, it is of utmost importance that all physicians be alerted to the early recognition of signs and symptoms that may precede progressive disease.

Thank you so much for your help.

Sincerely yours,

Jeff Karaban

Jeffrey E. Karaban, M.D.
Chief Resident
Department of Dermatology

JK:iag

Tours, le

1^{re} février 1982

Vous seriez très aimable de me faire parvenir un tiré à part de votre travail intitulé
Will you please send me a reprint of your article entitled

Squamous cell Carcinoma In Sexual
Partner Of Kaposi's Sarcoma Patient

paru dans
published in

The Lancet, January 30, 1982

Avec tous mes remerciements.
Thank you.

EXPEDITEUR

LABORATOIRE DE MICROBIOLOGIE

Alain COUDEAU

Faculté de Médecine et de Pharmacie

Boulevard Tonnellé

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France

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D^r Marcus A. Conant
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ROBERT T. PLUMB, M.D.
UROLOGY

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SAN DIEGO, CALIFORNIA 92103
(714) 295-4134

171 "C" STREET
CORONADO, CALIFORNIA 92118
(714) 435-9308

March 26, 1982

Marcus A. Conant, M.D.
350 Parnasseus
San Francisco, Calif., 94117

Dear Dr. Conant:

I appreciated very much you talking to me regarding
the Kopsi slides.

You did a brilliant job with this at the C.M.A.
Meeting.

I will give you full credit if you would forward
the slides to me so they would be available for my May
16th., 1982 lecture at the A.U.A.

Many Thanks in advance.

Sincerely,

Robert T. Plumb, M.D.
Robert T. Plumb, M.D.

RTP:amw

May 6

7/20/82 Regard for slides back

March 27, 1982

Assemblyman Art Agnos
350 McAllister St., Rm 1064
San Francisco, CA

Dear Assemblyman Agnos:

Just a note to thank you for your kindness in meeting with me to discuss the recent outbreak of Kaposi's sarcoma and pneumocystis pneumonia in the gay community here in San Francisco.

I have this morning attended to the various items that we discussed, and in the next day or two, I will dictate a memo for your records detailing these conditions.

Enclosed please find a brochure that we prepared for physicians, who attended the American Academy of Dermatology meeting here in December, which gives in simple medical terms a brief summary of this problem.

Again, let me thank you and your staff for your help.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:jb

cc: Mr. Cleve Jones

Enc.

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HOSPITALS AND CLINICS

SAN FRANCISCO, CALIFORNIA 94143

March 29, 1982

Assemblyman Art Agnos
350 McAllister Street, Room 1064
San Francisco, CA

RE: Kaposi's Sarcoma

Dear Assemblyman Agnos,

Attached please find a memo summarizing the current knowledge on Kaposi's sarcoma.

Research is resulting in rapid changes in this body of knowledge, and if major discoveries are made which alter the content of this report, I shall let you know.

Sincerely yours,

Marcus A. Conant, M.D.

MAC:ig

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HOSPITALS AND CLINICS

SAN FRANCISCO, CALIFORNIA 94143

March 29, 1982

MEMORANDUM

TO: Assemblyman Art Agnos

FROM: Marcus A. Conant, M.D.
Chief, Kaposi Sarcoma Clinic *Mac*

RE: Kaposi Sarcoma Background Paper

Kaposi's sarcoma is a rare malignancy that was originally described by a Hungarian dermatologist, Moritz Kaposi, in 1873. The disease generally affects elderly men and is usually seen on the lower legs. This form of cancer is slow growing, and patients usually live about 13 years after the initial diagnosis is established. In the late 1960's and early 1970's, it was recognized that individuals whose immune system was suppressed (Kidney transplant patients), had a 400 times greater chance of developing Kaposi's sarcoma than do individuals with normal immune mechanisms. At the same time an endemic focus of Kaposi's sarcoma was found in equatorial Africa. In this one location, the disease accounts for 10% of all deaths from cancer.

In late 1979, the Center for Disease Control in Atlanta began to receive reports that Kaposi's sarcoma and another condition which is only seen in immunosuppressed individuals (pneumocystis pneumonia) were being seen in young homosexual men in New York, San Francisco and Los Angeles. To date there have been about 200 cases. Approximately 120 cases of pneumocystis pneumonia have been seen and 50% of these patients have died with the first attack of the disease. About 80 cases of Kaposi's sarcoma have been seen and 20% of these patients have died within the first year. This makes this form of Kaposi's sarcoma one of the most aggressive malignancies in our society. About 15% of the patients have developed both Kaposi's sarcoma and pneumocystis pneumonia. Twenty-seven cases of pneumocystis pneumonia have been described in heterosexuals. Twenty-one of these patients were men and six were women. All of these patients were heavy drug abusers who used intravenous medications such as heroin and methadone. Whether this is the same condition that is being seen in homosexual men or not, is still under investigation.

The distribution of the cases suggests that the condition may be arising from a point source. Numerous cases have been seen in New York, San Francisco and Los Angeles. Very few cases have been seen in other metropolitan areas with large homosexual populations. Of note is the fact that no cases have been described in London, Rome, Athens and other international capitals that are known to have large homosexual populations.

The primary event, that leads to this new syndrome of Kaposi's sarcoma and pneumocystis pneumonia, appears to be severe unexplained destruction of parts of the immune system. A better understanding of these diseases may assist us in understanding the human immune system in general and certain forms of cancer in particular. A number of possible causes for this severe immunological breakdown have been suggested. These include a new virus, certain recreational drugs such as amyl nitrite, other sexually transmitted diseases, or certain medications.

Of the suggested causes, the two best bets are cytomegalovirus or amyl nitrite. Cytomegalovirus is a member of the herpes group of viral agents which infects man and then becomes latent in his body for the rest of his life. It has been shown that cytomegaloviral infections are very common in homosexuals, and the virus is probably transmitted through sexual contact. Research performed by members of the Kaposi's Sarcoma Clinic at U.C. San Francisco has shown a relationship between cytomegalovirus and this new cancer in gay men. Amyl nitrite is a drug that has been used for twenty years as a sexual stimulant. It has not been shown to be harmful but has been implicated as a possible cause of this new syndrome because of its frequent use by homosexuals.

The Kaposi Sarcoma Clinic at the University of California Medical Center was established in the summer of 1981 in response to the sudden appearance of Kaposi's sarcoma and pneumocystis pneumonia. Dr. Marcus Conant (Dermatology) and Dr. Paul Volberding (Cancer Specialist) are chiefs of this Clinic. The Clinic includes Dr. John Ziegler, an eminent oncologist who has worked with cancers caused by viruses; Dr. Larry Drew, a microbiologist, who has done extensive study of cytomegalovirus; Dr. William Epstein, the Chairman of the Department of Dermatology, and a leading authority on allergic reactions of the skin; Dr. Richard Sagebiel, a pathologist, who is one of the authorities in the United States on the microscopic appearance of Kaposi's sarcoma; Dr. Scott McNutt, a pathologist, who is studying Kaposi's sarcoma under the electron microscope; Dr. Arthur Ammann and Dr. Conrad Casavant who are doing immunological studies on patients with Kaposi's sarcoma; Dr. Marvin Garovoy and Dr. Beth Colombe who are studying the genetic makeup of patients who contract Kaposi's sarcoma; and, Dr. Selma Dritz the chief epidemiologist of the City of San Francisco. The Kaposi's Sarcoma Clinic is a multidisciplinary study group designed to study and treat this new cancer syndrome in an effort to discover its cause as soon as possible before the condition spreads to others in our society. It is anticipated that study of this cancer will result in major advances in our understanding of immunology, cancer and virology.

At the present time, initial treatment consists of cancer chemotherapy that has been shown to be effective in Kaposi's sarcoma. We are also testing a new experimental drug, thymizine which stimulates the patient's immune system.

Marcus Augustine Conant M.D.

A PROFESSIONAL CORPORATION
DERMATOLOGY

(415) 661-2614

*350 Parnassus Avenue, Suite 808,
San Francisco 94117*

March 29, 1982

MEMORANDUM

TO: Kaposi's sarcoma Study Group
FROM: Marcus A. Conant, M.D. *Mar*
RE: Kaposi's sarcoma clinic

The next meeting of the Kaposi's sarcoma clinic will be held on Thursday, April 1, 1982 at 11:00 A.M. in the Dermatology Clinic.

Dr. William Wara and Dr. Marcus Conant will review the results of thymosin treatment.