DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
Atlanta GA 30333

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Dr. Ruhakana Rogunda
Minister of Health
Uganda Ministry of Health
P. O. Box 8
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East Africa

Dear Dr. Rogunda:

Thank you very much for the invitation to visit Uganda to assess the AIDS epidemic in your country. As you know, my trip was funded by the Agency for International Development--Washington, D.C. (Wash-AID), and my objectives were 1) to review all information collected to date on AIDS in Uganda, 2) to provide consultation concerning an AIDS study proposal that will be submitted to Wash-AID, and 3) to provide general recommendations to the Ministry regarding surveillance, epidemiologic studies, and prevention and control of AIDS in Uganda.

During my stay in Uganda from July 8 to 16, I met with Dr. S. I. Okware, Assistant Director for Medical Services PH; Dr. J. G. M. Jagwe, Senior Consultant Physician and Deputy Director of Medical Services, Ministry of Health; Dr. C. L. Sezi, Senior Consultant Physician to the Ministry of Health; Dr. Roy D. Mugerwa, AIDS Coordinator and Staff Physician--Mulago Hospital; Drs. Wilson Carswell, Nelson Sewankambo, Peter Kataaha, and Frederick Kigozi, Mulago Hospital; Professor Tarsis Kabwagerya, Department of Sociology--Makerere University; and Professor Donald Hillman, Dr. Elizabeth Hillman, Dr, Margaret Carswell, and Dr. Mworozi from the Department of Pediatrics--Makerere, the Child Health and Development Center and UNICEF. I also met briefly with Dr. J. H. Kyabaggu, Assistant Director for Medical Services, PHC; Dr. J. T. Lema, WHO representative, Entebbe; and Dr. Sylvester Sempala, Director, Uganda Virus Research Institute. Dr. Mugerwa and I traveled to Masaka and the Rakai district on July 12. On that day I was able to meet Dr. A. Lwegaba, former District Medical Officer, Rakai district, who was instrumental in reporting the first AIDS cases in that region; and Sister Dernadette O'Brien from Kitovu Hospital in Masaka. I was not able to meet Drs. David Serwadda and Richard Goodgame, both of whom have been active in AIDS work in Uganda but were out of the country during my visit.

On my return trip through London, I met with Graham Lloyd, Special Pathogens Laboratory, Public Health Laboratory Service, Porton Down, U.K., who has performed virtually all the serologic testing on blood samples from Ugandan patients. Additionally, I spoke with Dr. Robert Downing, also from Porton Down, who has performed virologic studies on many of these samples.

The AIDS situation in Uganda is very serious. AIDS in African adults is relatively easy to diagnose on clinical grounds alone using a case definition proposed by WHO for use in Africa (Attachment A). Using this or a similar definition, cases in Uganda were first noted in the Rakai district in 1982 and have become increasingly common in that area (32 cases seen at Kitovu Hospital in Masaka in 1984, 72 in 1985 and 167 in the first 5 months of 1986). In Kampala, 1-2 cases of AIDS per month were being seen at Mulago Hospital in 1984, versus 1-2 per week in early 1985, 1 per day in late 1985, and 3-4 per day in mid-1986. Cases have been reported from virtually every part of the country, although those from the North and West are less numerous. Most cases are of the "enteropathic" type i.e. they are characterized by weight loss, diarrhea, and other signs and symptoms. However, cases of disseminated Kaposi's sarcoma have also been seen with increasing frequency.

A better indication of the extent of the AIDS epidemic may be given by the number of persons who are seropositive for antibody against the AIDS virus, since seropositivity indicates infection with the virus, and many seropositive persons (perhaps a majority, perhaps all) can be expected to develop clinical AIDS in the next few years. In a study of 1,011 pregnant women attending an antenatal clinic at Nysambia Hospital in Kampala in 1986, 137 (13.6%) were seropositive for antibody against the AIDS virus. In a study of 793 blood donors at Mulago and Nysambia Hospitals (most of whom are males in sexually active age groups) 96 (12.1%) were seropositive. When the pregnant women data were analyzed by ethnic group, seropositivity rates were highest in the Southwest, average in Kampala, and lower in the North and West. Seropositivity has now been documented in all areas of the country. From my review of AIDS cases in which seropositivity was also demonstrated, age and sex information indicate the male:female ratio to be approximately 1:1. The ages most affected are 13-45 (median 20-24) in females, and 16-60 (median 25-29) in males.

Dr. Kigozi of the Department of Psychiatry--Makerere has interviewed approximately 50 AIDS patients and 60 controls selected from the general medical wards at Malago regarding sexual practices and numbers of sexual partners. He found that cases reported approximately twice the number of lifetime sexual partners as controls (approximately 20-30 in cases versus half that number in controls). Case men were more likely to report a history of gonorrhea than controls. Only one person--a case man--admitted to a history of homosexuality.

Cases of AIDS have also being seen in at least five infants (see WHO clinical case definition for children--Attachment B). All the mothers of these children have been found to be seropositive for antibody against the AIDS virus. AIDS virus has been isolated from the cord blood of one infant who was ill at birth and died at 4 months of age. The mother of that child also died of AIDS.

AIDS appears to be absent in the geriatric population. Of 91 sexually inactive residents in old folks homes in Kampala, no cases of seropositivity were found.

Another important study has shown that of 141 household contacts of 23 seropositive AIDS patients, only 13 were seropositive. Ten were sexual contacts of the AIDS patients, 2 were other adults in sexually active age groups, and 1 was a child born to a seropositive woman. None of the other 69 children less than 16 years of age were seropositive.

I have reviewed the laboratory work performed on specimens from Uganda with Graham Lloyd at Porton Down, U.K. The screening test currently in use is the competitive ELISA (Wellcome Diagnostics), which appears to be highly specific for use in Africa. Of approximately 400 sera tested positive by the ELISA and also tested by Western blot, all were positive in the confirmatory test. A handful of false-negative ELISA results have been documented in persons with clinical AIDS who were negative in the ELISA test but positive by Western blot. Approximately 90 isolates of the AIDS virus have been obtained by Dr. Robert Downing at Porton Down. At CDC, we will be working with Dr. Downing to help characterize some of these isolates to see how they compare with others obtained in Africa and in North America.

A number of other studies concerning AIDS in Uganda have been completed, are in progress, or are still being planned. I have listed the most important ones (including those described above) with the investigators responsible for them in Attachment C.

I conclude from reviewing all the data above that as many as 10-15% of sexually active adults in the Kampala area may be infected with the AIDS virus; the percentages are probably higher in the Southwest, and probably much lower in the North and in the West. Heterosexual transmission appears to be the major mode of spread of the virus in the country. Blood transfusion and maternal-child transmission are probably also important. Transmission by unsterilized needles may also account for some transmission of the virus.

In terms of control measures, the Ministry is currently engaged in printing and distributing educational material directed toward the lay public and also toward health workers; I helped review some of this material at a meeting on July 8. Radio and television have also been used, although I was not able to see or hear any of this material during my visit.

A major contribution to preventing transmission of AIDS by blood transfusion has been orchestrated by Dr. Wilson Carswell. Units of blood donated at Mulago and Nysambia Hospitals are now being screened for AIDS virus antibody by the Wellcome ELISA test at Nysambia Hospital. This was accomplished by a

great deal of personal effort (and expense) on the part of Dr. Carswell, as well as by a great deal of outside help (the British Residents' Association, Wellcome Diagnostics, and Sabena Airlines). Additional ELISA machines and test kits, donated by the British High Commission and the European Economic Community are planned for Mulago, Rubaga, and Kitovu Hospitals. Dr. Peter Kataaha will be responsible for setting up the testing at Mulago.

My recommendations concerning the approach to the AIDS problem in Uganda, presented to Dr. Okware and others on July 16, are given in detail in Attachments D and E (surveillance), F (epidemiological studies), and G (prevention and control). I will summarize the most important recommendations, as well as a few additional ones, here.

1. Nationwide surveillance of AIDS disease is paramount to an AIDS program, since it provides a "yardstick" of the epidemic and also provides baseline information from which to assess the efficacy of future public health programs. Surveillance should be instituted using the WHO clinical case definitions (Attachments A and B) in all hospitals in the country actively engaged in patient care (Attachments D and E). I would strongly encourage enlisting the aid of Dr. Carswell, who is familiar with most of the mission hospitals and can help identify a key person in each hospital who can be responsible for surveillance in that hospital. Because of the relatively small size of the country and the enthusiasm of some of those persons who have been working on AIDS, I believe that there exists in Uganda the potential for the best national surveillance of AIDS of any country in Africa.

2. The Ministry should report cases of AIDS, based on surveillance of the disease, to WHO on a systematic basis. Such reporting will enhance the image of Uganda as a country which acknowledges its AIDS problem and is attempting to do something about it. Such an "image" may be important in soliciting assistance from WHO (see #7 below) and from other outside organizations.

3. Epidemiologic studies should focus on seroprevalence (with particular attention at this time given to a good community-based study and also to studies of primary school-aged children), and on the natural history of AIDS virus infection in Uganda (see Attachment F). Such studies provide important information concerning the nature of the AIDS epidemic in Uganda. A community-based study in the Rakai district, which will encompass seroprevalence, risk factors for infection, natural history of infection, and risk factors for disease will be the basis of a study proposal that will be submitted to Wash-AID (Attachment C).

4. Prevention and control activities (Attachment G) should focus on persons in sexually active age groups and, especially, youngsters approaching these ages (pre-pubescent children). Use of condoms should be actively promoted. Attitudes towards sexuality and use of condoms should be explored in Ugandan men and women. Screening of blood products, already instituted at Nysambia Hospital, should be actively promoted, and

physicians (and patients) should be cautioned against inappropriate use of blood and needles.

5. The Ministry should encourage the continued efforts of those in the community who have been most active in generating the data I have reviewed (Attachment C), and it should enlist the aid of these persons in ongoing AIDS programs.

6. The assistance of outside organizations--dramatically demonstrated by the institution of blood screening at Nysambia Hospital--should be actively pursued by the Ministry. As indicated above, support may be available from Wash-AID for an epidiomiologic study in the Rakai district. WHO has earmarked at least $1,000,000 for support of surveillance and prevention and control of AIDS in Africa. UNICEF is supporting, at least initially, the maternal-child study in Kampala (Attachment C). Many other outside organizations have already provided assistance or are eager to help. Assistance should be sought for surveillance, research, prevention and control measures, and treatment of AIDS patients (medication for thrush, diarrhea, intravenous fluids, etc.). Stationery and postage stamps are cheap compared with the results that may be obtained. Again, the help of those in the community who have been dealing with these organizations and are familiar with them should be sought.

7. Regarding possible assistance from WHO, I would encourage you to send me a detailed list of items (equipment, salaries, etc.) that would be needed to implement the surveillance and prevention and control programs I have suggested. I will forward the request to Dr. Jonathan Mann at WHO in Geneva.

Finally, it was apparent during my visit that there is a great deal of concern regarding recent articles in foreign newspapers about AIDS in Uganda. Contrary to the feeling that the image of Uganda as a "promiscuous" society is being transmitted around the world, it has been my impression that these articles have had a very positive effect. People in the United States feel that Uganda has been more open about its AIDS problem that other countries in Africa, and that as a result, the prospects for a good program in AIDS surveillance and control may be better in Uganda than in other African countries. This is not to say that AIDS material should be indiscriminately given to the press. One person should be designated as a press contact, and that person should be in the Ministry.

Thank you again for the invitation to come to Uganda, and especially for making the final arrangements that allowed me to proceed with my trip on July 6. I hope we can meet again soon.

Sincerely yours,

Jonathan E. Kaplan, M.D.
Medical Epidemiologist
Division of Viral Diseases
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copies: Dr. S.I. Okware
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Attachment A: WHO clinical case definition of AIDS in African adults

AIDS in an adult is defined by the existence of at least 2 of the major signs associated with at least 1 minor sign, in the absence of known causes of immunosuppression such as cancer or severe malnutrition or other recognized etiologies.

Major signs

1. Fever for at least one month (intermittent or constant)
2. Diarrhea for at least one month
3. Significant weight loss (10% of body weight)

Minor signs

1. Oro-pharyngeal candidiasis (thrush)
2. Pruritic maculopapular rash
3. Herpes zoster
4. Agressive or chronic (>1 month) herpes simplex infection
5. Generalized lymphadenopathy
6. Cough for at least 1 month without tuberculosis

The presence of generalized Kaposi's srcoma or cryptococcal meningitis are sufficient by themselves for the diagnosis of AIDS.

Attachment B: WHO clinical case definition for AIDS in African children

Pediatric AIDS is suspected in an infant or child presenting with at least 2 of the following major signs associated with at least 2 of the following minor signs in the absence of known causes of immunosuppression such as cancer or severe malnutrition or other recognized etiologies.

Major signs

1. Fever for at least 1 month
2. Diarrhea for at least 1 month
3. Weight loss or abnormally slow growth

Minor signs

1. Oro-pharyngeal candidiasis (thrush)
2. Generalized dermatitis
3. Repeated common infections (pharyngitis, otitis, etc.)
4. Generalized lymphadenopathy
5. Persistent cough
6. Confirmed maternal AIDS virus infection

Attachment C: Aids Research Projects in Uganda

Completed Projects:

1. First description of Slim disease (AIDS) in Uganda. Serwadda et al., Lancet, October 19, 1985.

2. Kaposi's sarcoma in Uganda. Bayley et al., Lancet, February 16, 1985; and Serwadda et al., British Journal of Cancer, 53:497, 1986.

3. Post-mortem findings in AIDS patients. Wamukota et al, in press.

4. Endoscopic findings in AIDS patients. Sewankambo et al, in press.

5. Absence of AIDS in geriatric Patients. Carswell et al., Lancet, May 24, 1986.

6. Seropositivity among blood donors. Sewankambo, Carswell, et al., in preparation.

7. Seropositivity among women attending an antenatal clinic. Mworozi, Hillman, Hillman, Carswell, et al., in preparation.

8. Seropositivity among members of households of AIDS patients. Sewankambo, et al., in preparation.

9. Patterns of sexual behavior in AIDS patients. Kigozi, et al., in preparation.

Studies in Progress:

1. Follow-up of seropositive pregnant women and their offspring. Mworozi, Hillman, Hillman, Carswell, et al.

   This study will assess the rate of transmission of infection from seropositive mothers to their offspring, risk factors for transmission, natural history of AIDS virus infection in mothers, natural history of AIDS virus infection in their children, risk factors (cofactors) for progression to disease among seropositives, and risk factors for seroconversion among a seronegative control group of mothers. Follow-up for at least 2 years is planned, and support from UNICEF is initially available.

2. Tuberculosis and AIDS. Nambuya et al.

3. CNS manifestations of AIDS. Sewankambo et al.

Attachment C (continued)

4. Seropositivity among sickle cell sufferers. Morozi et al.

5. Cryptosporidiosis study. Katabira et al.

6. Prevalence of AIDS virus antibodies in babies who have received breast milk from multiple donors. Mworozi et al.

7. Skin biopsies in AIDS patients. Ddumba et al.

8. Use of filter paper in diagnosing the presence of AIDS antibodies in blood. Lloyd, Downing, et al.

9. Viruses recovered from AIDS patients. Downing et al, in cooperation with CDC.

Studies in the Planning Stage:

1. Rakai community study.

   This study will focus on a sample of the 250,000 persons living in the Rakai district. The objectives will be

   (a) to determine seroprevalence rates of AIDS virus antibody by age and sex in this rural population.
   (b) to assess risk factors for seropositivity.
   (c) to assess the clinical spectrum of disease among seropositive persons.
   (d) to determine the natural history of AIDS virus infection among seropositives in follow-up visits for at least 1 year after the initial visit.
   (e) to assess risk factors (co-factors) for progression to disease among those who are seropositive.
   (f) to assess risk factors for seroconversion among those who are initially seronegative.

   A study proposal will be drafted by Dr. Nelson Sewankambo and others, with Dr. Kaplan in the United States acting as consultant. This proposal should be submitted to Wash-AID by October 1986.

2. Seroprevalence among newborn children.

3. Seroprevalence among children of primary school age.

Attachment D: Surveillance

National surveillance of AIDS disease should be hospital-based, i.e. every hospital actively engaged in patient care in Uganda should be asked to participate. A tentative list of these hospitals, drawn up with the assistance of Dr. Wilson Carswell, is as follows:

Government Hospitals	Mission Hospitals
Mbale	Angal
Gombe	Ishaka
Mbarara	Namasagali
Nakaseke	Villa Maria
Iganga	Nkozi
Jinja	Naggalama
Moyo	Kagondo
Kabale	Maracha
Kawolo	Kaborole
Entebbe "A"	Mutolere
Soroti	Vivika
Turoro	Kamuli
Entebbe "B"	Kitgum Mission Hospital
Masaka	Matany
Mulago	Kitovu
	Nyakibare
	Kitgum
	Kuluva
	Aber
	Kisiizi
	Ngora
	St. Anthony's
	Lacor
	Kalongo
	Rubaga
	Nysambia

At each hospital, a person responsible for the identification and reporting of AIDS cases should be designated. Cases should be defined using the clinical criteria proposed by WHO (Attachments A and B). A case report form should be completed for each patient (Attachment D). These forms should be submitted to a surveillance officer, who should be salaried. This person should be one who will actively seek the participation of all hospitals, is knowledgeable concerning the AIDS epidemic, and is able to collect, organize, and analyze surveillance data. Given the communication problems within the country, "couriers" who travel to Kampala from outlying areas should be used to transport case report forms directly to the surveillance officer in Kampala.

When possible, serum specimens should accompany case report forms so that the accuracy of the WHO clinical case definition (currently thought to be excellent in studies in Zaire and Uganda, at least in adults) can continue to be evaluated.

Attachment E: AIDS CASE REPORT FORM

Demographic

Name_____Age____ Sex: M____ F____ Marital Status_____
Residence_____Tribe_____Hospital_____
Occupation (give details regarding foreign travel)_____
_____

Clinical

Onset of illness:_____/____ Presenting complaint:_____
Month/Year
Diagnosis of AIDS:_____/____ Report received_____/____
Month/Year Month/Year

Symptoms/physical findings

____Weight loss ≥ 10%
____Diarrhea ≥ 1 month
____Fever ≥ 1 month

____Oro-pharyngeal candidiasis (thrush)
____Pruritic maculo-papular skin rash
____Herpes zoster
____Aggressive or chronic (≥1 month) herpes simplex
____Cough ≥ 1 month without tuberculosis
____Generalized lymphadenopathy

____(Children) Generalized dermatitis
____(Children) Repeated common infections (pharyngitis, otitis, etc)

Other Diagnoses/syndromes suggestive of AIDS

____Disseminated Kaposi's Sarcoma
____Crytococcal meningitis
____Cryptosporidiosis
____Tuberculosis
____Bilateral pneumonia unresponsive to treatment
____Chorioretinitis
____Other

Epidemiologic

Within the 5-year period before onset of symptoms, did the patient

1) Have a sexually transmitted disease, such as gonorrhea, syphilis, or chancroid? (Yes or No)_____If yes, how many episodes?_____
2) Have sexual contact with a person who had, or who has since developed AIDS? (Yes or No) _____
3) Travel to a foreign country? (Yes or No)____ If Yes, which country(ies)?_____
4) Have sex with a person from another country? (Yes or No)____ If Yes, from which country(ies)?_____
5) (Men only) Have sex with a prostitute(s)? (Yes or No) _____
6) (Women only) Engage in sexual activity in return for money or goods? (Yes or No)_____
7) Receive a blood transfusion? (Yes or No) _____
8) Receive any material intravenously other than blood? (Yes or No) _____
9) Receive an injection (not including i.v. injections)? (Yes or No) _____
10) (Children only) has the patient's mother had an AIDS-like illness or been found to be seropositive for AIDS antibody? (Yes or No) _____ If yes, give details._____

Attachment F: Epidemiologic studies

1. Seroprevalence

A community-based seroprevalence study should be undertaken to assess infection rates by age and sex. The Rakai district is an obvious choice for such a study, given the apparently high rates of infection in that region. Dr. Nelson Sewankambo is currently drafting a proposal for this study that will be submitted for funding to Wash-AID (Attachment C). This study will be designed to assess risk factors for infection in addition to seroprevalence rates. Consideration should also be given to a community study in an urban area such as Kampala. Studies of school-aged children should be undertaken to assess whether children are infected, and at what age seropositivity rates rise in relation to heterosexual activity.

2. Natural history

The proportion of seropositive individuals who progressed to clinical AIDS and the time intervals involved should be assessed in longitudinal studies of seropositive persons. The Rakai proposal will include a follow-up visit at one year, and the maternal-child study being conducted by Professor Hillman and others from the Child Health and Development Center (Attachment C) will attempt to follow seropositive pregnant women and their offspring for at least 2 years. Both of these studies will attempt to discover risk factors for progression to disease among seropositive persons (cofactors for disease). Other prospective studies of "captive audiences" of seropositive persons should be considered.

Attachment G: Prevention and control

1. Heterosexual transmission--Pamphlets, posters, and radio and television announcements should be used to educate the public about the AIDS epidemic and the need to decrease the number of one's sexual partners, preferably to one. The use of condoms should be encouraged, and condoms should be made widely available in the country. Pending the results of additional seroprevalence studies, the appearance of clinical AIDS in women as young as 13 and in men as young as 16 suggests that children aged 10-12 should be specifically targeted for educational efforts. Attitudes toward sexuality, and toward use of condoms should be explored in men and women. Professor Tarsis Kabwagerya of the Dept. of Sociology--Makerere has expressed an interest in such studies.

2. Transmission by blood--AIDS virus antibody testing should be instituted in a sufficient number of locations such that all units of donated blood can be screened. All units containing AIDS virus antibody should be discarded. Physicians (and patients) should be cautioned concerning inappropriate use of blood; the use of hematinics and plasma expanders should be encouraged.

3. Transmission by contaminated needles--Physicians (and patients) should be cautioned concerning the inappropriate use of injections. Medications should be given by mouth when possible. When their use is required, needles should be sterilized, or at least placed in boiling water for 2-5 minutes.

4. Maternal-Child transmission--No advice at this point.

5. Health care workers should be educated, perhaps through a series of seminars, concerning the AIDS epidemic, the modes of transmission of the virus, and ways to minimize transmission within the health care setting. Gloves must be made available for persons who handle blood and other body fluids; gowns should also be available for workers such as surgeons, obstetricians, and midwives who are apt to have extensive contact with blood.