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MIPR NO: 92MM2550

TITLE: RETROSPECTIVE STUDY OF HIV INFECTION IN HUMAN TISSUES

**SUBTITLE: Computer Survey of the AFIP Repository for Cases of
Acquired Immunodeficiency Preceding the HIV Pandemic**

**PRINCIPAL INVESTIGATOR: Ann Marie Nelson, M.D.
Adolfo Firpo, M.D., Florabel G. Mullick, M.D., Patrick E. Lorenz,
William R. Rohland, Joyce C. Manus**

**CONTRACTING ORGANIZATION: Armed Forces Institute of Pathology
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AIDS Pathology
Washington, DC 20306-6000**

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**PREPARED FOR: U.S. Army Medical Research and
Development Command, Fort Detrick
Frederick, Maryland 21702-5012**

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13. ABSTRACT (Maximum 200 words) To seek, review, identify, and retrieve repository materials (slides, blocks, wet tissues, and information) of cases fulfilling the CDC definition of AIDS in the absence of demonstrable HIV infection. Identify cases for potential use in basic research on the chronology of HIV retroviral infection in human tissues.				
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FOREWORD

For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR56.

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FY93 RESEARCH PROGRESS REPORT

TITLE: Computer Survey of the AFIP Repository for Cases of Acquired Immunodeficiency Preceding the HIV Pandemic

PROJECT NUMBER: UBGA

DEPT: Infectious and Parasitic

SUPPORTED BY: AFIP/USA MRDC

INVESTIGATORS:

Adolfo Firpo.M.D.*

Ann Marie Nelson, MD

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*Dr. Firpo left the AFIP and Dr. Nelson has replaced him

OBJECTIVE: To seek, review, identify, and retrieve repository materials (slides, blocks, wet tissues, and information) of cases fulfilling the CDC definition of AIDS in the absence of demonstrable HIV infection. Identify cases for potential use in basic research on the chronology of HIV retroviral infection in human tissues.

METHODOLOGY: The AFIP's master data base in the mainframe computer will be searched for cases accessioned before 1959 with any diagnosis indicative of immunodeficiency in the absence of proven HIV infection (MMWR, August 14, 1987/Vol. 36/No. 1S -- revised MMWR, 1992/41:1-19). Case selection criteria will be: clinical, pathological, and demographic information available for correlation with pathological diagnoses, geographic origin, anatomic source, patient's age, and medical and social factors demonstrated to influence the spread and distribution of HIV infection and AIDS. Cases will be transferred onto a floppy disk for importation into a custom-designed data base for additional analysis at the Division of AIDS Pathology. Cases with adequate materials and sufficient clinical documentation will be identified and retrieved for review at the AIDS Pathology Division. Records from cases accessioned before 1970 will be reviewed manually for entry into the study data base. Records on microfilm will be scanned into digitized images and, when possible, translated into word processing files for conversion into other suitable formats for import into data base records.

We plan to develop and implement a simplified and more practical approach to data retrieval from the AFIP mainframe computer for importation into personal computer work stations, thereby maximizing efficiency in reviewing and retrieving pathological material that is suitable for collaborative research in all aspects of pathology and basic science and potentially usable by other AFIP investigators.

RESULTS: Computer equipment and software has been purchased for the project and installed. The project implementation phase (Phase I) is in progress, and the level of technical support and the infrastructure requirements for the project at the AIDS Division and AMS are being defined by Drs. Lorenz, Firpo, and Angritt. Mr. Rohland and Mrs. Manus produced two early prototypes for the data retrieval and format conversion strategies, which are currently being tested with all HIV/AIDS cases received at the AFIP.

A pilot study was conducted on repository cases of material collected in Zaire prior to the onset of the HIV pandemic. Dr. Jerome Smith aided in evaluation of the material which he sent from Zaire between 1973 and 1975. A total of 125 autopsy cases were identified in the repository, 85 sent by Dr. Smith and 40 from rural hospitals. There are 26 possible cases of HIV/AIDS.

PRESENTATIONS: The preliminary results were presented at the AFIP and WRAIR (Jackson Foundation) quarterly meeting (attached).

PUBLICATIONS: None.

FUTURE PLANS: A complete computer network will be implemented at the AIDS Pathology Division that will maximize the efficiency of interactions between all investigators. A systems specialist consultant will be hired to establish and run operations at the AIDS Pathology Division and to fine-tune the entire computer-based process. An research clerical technician will be hired to assume responsibility for retrieving and transporting case materials from all locations to the AIDS Pathology Division. The same technician will tabulate information as required by the system specialist at the AIDS Pathology Division to maintain current records of the exact location and processing status of every case under review and update all clinical, demographic, and diagnostic data on the computer data base (serve as data entry person) for the project.

**TITLE: Computer survey of the AFIP repository for cases of
Acquired Immunodeficiency preceding the HIV pandemic: Zaire.**

PROJECT NUMBER:

ORIGINAL APPROVAL DATE:

SOURCE OF SUPPORT:

REPORT PERIOD: 20 TO 25 JULY 1992

INVESTIGATORS:

ESTIMATED COMPLETION DATE:

Ann Marie Nelson, M.D.

Jerome H. Smith, M.D.

Adolfo Firpo, M.D.

Florabel G. Mullick, M.D.

OBJECTIVE: To identify probable case of AIDS or HIV-infection among cases accessioned at the AFIP referred by pathologists and clinicians from the Republic of Zaire in 1980 and earlier.

METHODOLOGY:

1. The AFIP's mainframe computer master data base was searched for autopsies from Zaire during the years 1965 through 1980.

2. The cardfile of the Department of Infectious and Parasitic Disease Pathology was searched for autopsies sent by Dr. Smith which were not retrieved by the above method.

3. The cardfile of the Department of Infectious and Parasitic Disease Pathology was searched for selected surgical specimens recalled by Dr. Smith thought to have been sent to the AFIP and having diagnoses accepted by the CDC/WHO as indicative of immune deficiency.

4. Records, slides and blocks on all cases identified by the above methods were pulled. A database was established to catalogue available material.

5. All available records and slides are reviewed and cases categorized by index of probability of AIDS in the following classification:

1-One or more diseases listed in CDC criteria of AIDS were found in the available material.

2-One or more diseases listed in CDC criteria of AIDS were strongly suspected but not confirmed in the available material. Additional testing may permit confirmation of such diseases.

3-One or more diseases associated AIDS but not listed in CDC criteria of AIDS were found in the available material.

4-Infectious Disease not usually associated with AIDS/HIV infection.

5-No indicator diseases or associated conditions of AIDS found in the available material or the presence of histopathologic constellations incompatible with AIDS (evidence of intact immune response) or inadequate material available to rule in or rule out AIDS.

PRELIMINARY RESULTS (July 25 1992):

Of 104 autopsy cases sent by Dr. Smith to the AFIP between 1973 and 1975, 85 cases were identified by the mainframe search. Of these, records were found on 65 cases, slides on 38 cases and blocks on 72 cases. Two of 12 cases in which records and slide review were complete fell into category 1 (both were in infants less than 1 year old); 2/12 were category 2 and 2/12 were category 3. The remaining six were category 4 and will not be included in future studies of historic AIDS.

Nineteen cases submitted by Dr. Smith in shipments in which we have other cases (indicating that these cases are probably retrievable); among these 19 cases are at least two which would be classified in categories 1 or 2 (see above).

Material from 7 of 15 cases from Kimpese Hospital was found. Slides from two cases were reviewed both fall into category 2. The twenty-five cases from the Equateur Province (1975-1980) have yet to be retrieved, three have AIDS by WHO clinical criteria.

One surgical case was identified which would fit into category 1; material has been requested but not yet received. Material from an additional 12 surgical cases with diagnoses of Kaposi sarcoma, atypical vascular proliferation or lymphoid hyperplasia were also requested but not yet received.

All the above information has already been entered into the database.

Thus, to date, we have identified 26 possible cases of AIDS/HIV associated pathology from Zaire which occurred prior to 1980.

PRESENTATIONS: (AFIP/WRAIR MEETING)

PUBLICATIONS: None

FUTURE PLANS:

1. Find the 19 missing autopsies and review material for categorization.
2. Complete review of all records not yet retrieved.
3. Complete review of slides from remaining cases which meet the WHO clinical criteria or have a CDC indicator disease.
4. Review material on all other cases with suspected HIV-associated pathology.
5. Prepare research proposal for further study of material on cases from categories 1 through 3.
6. Compare Dr. Smith's Mama Yemo Hospital autopsy series (1973-1974) with Dr. Nelson's series of AIDS autopsies from the same hospital (1989-1991).

MILITARY RELEVANCE:

Defining the chronology of retroviral tissue infection would help to understand the natural history of HIV disease and help to evaluate military and public health policies for therapeutic interventions in seropositive, immunocompetent patients. It would also help to identify tissues harboring potentially stable or high frequency recurrent genomic sequences coding for viral proteins that might become targets of immune therapy and assist the military effort of anti-HIV vaccine development.

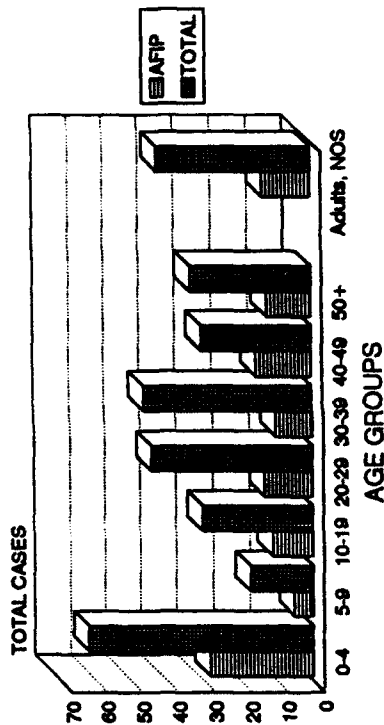
RETROSPECTIVE STUDY OF HIV-INFECTION
IN HUMAN TISSUES

THE MAMA YEMO HOSPITAL SERIES
Kinshasa, Zaire 1973 - 1974

Ann Marie Nelson, M. D.
Adolfo Filipo, M. D.
AIDS Registry, AFIP

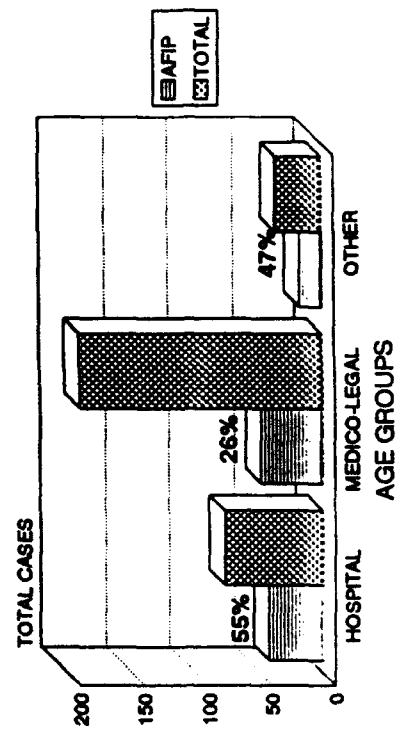
Jerome H. Smith, M.D., M.S.
University of Texas Medical Branch
(formerly of Mama Yemo Hospital)

AUTOPSY CASES SENT TO THE AFIP BY AGE GROUP



33% OF CASE WERE SENT TO THE AFIP

AUTOPSY CASES SENT TO THE AFIP BY CATEGORY



MATERIAL FOUND ON IDENTIFIED CASES

- **CASE RECORDS - 80 (73%)**
- **SLIDES - 49 (45%)**
- **BLOCKS - 79 (73%)**

CASE CATEGORIES

- 1 - *Fulfills CDC criteria for AIDS*
- 2 - *Highly suspicious for AIDS*
- 3 - *AIDS related diagnosis*
- 4 - *Other Infectious Cases*
- 5 - *Definitely not AIDS*

CASES IN EACH CATEGORY

CATEGORY	N
1	2
2	4
3	26
4	32
5	34
?	11

CATEGORY 1 AND 2 CASES

- Female, 5 mos. - PCR, CMV, FTT, thymic atrophy (blks)
- Female, 21 yrs. - Miliary tuberculosis, cachexia (blks)
- Male, Adult - Miliary tuberculosis, diarrhea
- Male, 40 yrs. - Chronic diarrhea, weightloss, Staph Colitis (1 blk)
- Male, 26 yrs. - Pneumonia, colitis (blks)
- Female 5 mos. - CMV, thymic atrophy (blks)

ZAIRE LOOKBACK STUDY

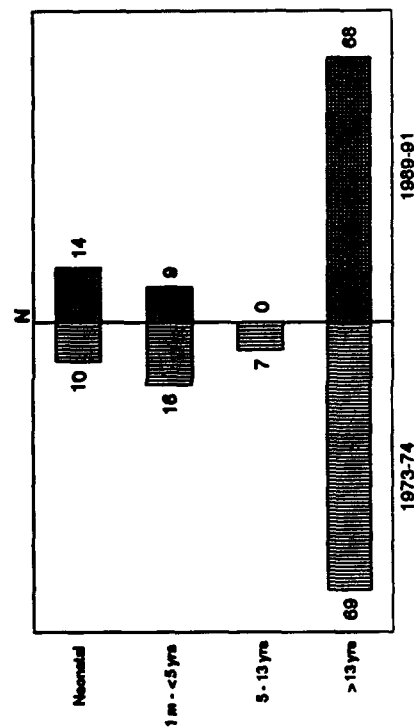
Comparison of 2 autopsy series
at Mama Yemo Hospital:



SMITH 1973 - 1974
and
NELSON 1980 - 1981

CASES REVIEWED

BY AGE GROUP



AGE DISTRIBUTION

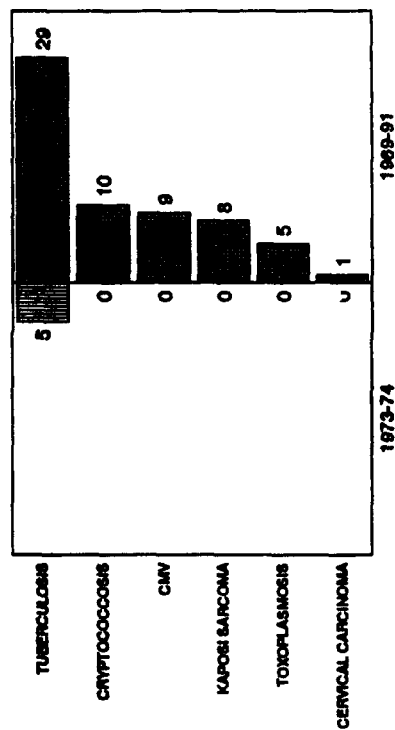


mean age = 40.35

mean age = 35.08

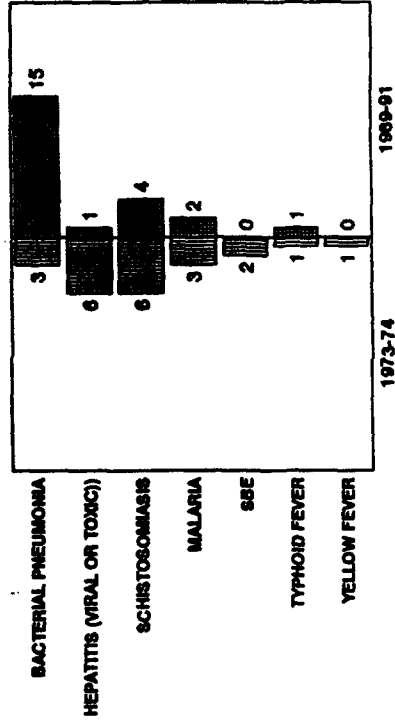
AUTOPSY DIAGNOSES - ADULTS

AIDS RELATED



AUTOPSY DIAGNOSES - ADULTS

INFECTIOUS



AUTOPSY DIAGNOSES - ADULTS

NON-INFECTIOUS

