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An effective new prognostic staging system for acquired immunodeficiency syndrome (AIDS)

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by

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CONTENTS

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> A sower went out to sow his seed; and as he sowed, some fell along the path, and was trodden under foot, and the birds of the air devoured it. And some fell on the rock; and as it grew up, it withered away, because it had no moisture. And some fell among thorns; and the thorns grew with it and choked it. And some of it fell into good soil and grew...
>
> --Luke 8: 4-8, R.S.V.

With heartfelt thanks to those who provided me with good soil, moisture, and frequently freed me from choking thorns:

Dr. Alvan Feinstein, my mentor, advisor, chief editor, and best advocate.

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Ms. Mary Newbury, without whom the tables here contained would be much less legible.

The Medical Records Department at YNHH for finding nearly every medical record I needed.

And to my fiancé, Joseph T. King, Jr., who kept me going when the hour grew late and the time grew short.

ABSTRACT

AN EFFECTIVE NEW PROGNOSTIC STAGING SYSTEM FOR ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

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To evaluate promising new treatments for acquired immunodeficiency syndrome (AIDS), without the ethical dilemma of concurrent placebo controls, an effective system is needed for prognostic staging. Such a system has not been developed, because investigators have either concentrated on the prognostic transition from HIV-positivity to overt AIDS, or have staged the overt syndrome mainly according to morphologic evidence. In 76 consecutive patients with AIDS treated at Yale-New Haven Hospital during 1981-86, 3 major functional deficits were found to be important predictors of death. They were: substantial neurologic deficit (e.g. seizures, severe lethargy, aphasia); severe hypoxemia (arterial $pO_2 \leq 50$); or any 1 of 3 cytopenias (Hematocrit <30, WBC <2,500, or platelets <140,000). Stage III was assigned to patients with "bone marrow" failure, classified as any 2 of the 3 cytopenias; Stage II was assigned for any of the neural, respiratory, or single hematologic deficits; and Stage I had none of the deficits. For the "development set" of 76 patients, 4-month survival rates in the three stages were I, 25/28 (89%); II, 19/38 (50%); and III, 3/10 (30%). The corresponding median months of survival were 10.8, 3.85, and 2.3. The next 42 consecutive patients during 1986-87 were used as a "challenge set". The corresponding survival rates for 16, 19, and 7 persons in each stage were I, 69%; II, 42%; and III, 29% at 4 months, with median survival times of 7.2, 1.6, and 0.7 months. The challenge set results thus confirmed the prognostic gradient.

This prognostic staging system, based on functional deficits, is simple to use, noninvasive, and inexpensive. It offers an effective way to predict prognosis for individual patients, and to improve evaluations when treatments are compared with or without the use of randomized trials.

INTRODUCTION

This thesis concerns the development and testing of a prognostic classification system for Acquired Immunodeficiency Syndrome (AIDS). The system, which is founded on functional criteria, will be useful in predicting individual patient prognosis and in evaluating therapeutic trials.

The introductory discussion contains two parts. The first part gives a brief historical account of the characterization of AIDS, its causal agent and current predictions of the ensuing epidemic. The second part considers the potential applications of a prognostic stratification and offers a critical review of currently proposed classification systems and prognostic variables.

Historical Background

Initial Description and Recognition of Risk Groups:

Less than seven years ago AIDS was completely unknown. In the summer of 1981 the Center for Disease Control (CDC) reported five cases of Pneumocystis carinii and 26 cases of Kaposi's sarcoma in young, previously healthy, homosexual men.[1-2] The CDC recognized the importance of clearly defining this syndrome to allow consistent reporting. By 1983, the CDC had published guidelines for a clinical definition based on the presence of reliably diagnosed disease at least

moderately predictive of an underlying cellular immunodeficiency.[3] At this time the CDC excluded known causes of underlying immunodeficiency or host defense defect, such as immunosuppressive therapy or lymphoreticular malignancy. The CDC criteria, recognizing that the causative agent seemed to be transmitted in blood and blood products, defined certain high risk groups that included homosexual men, intravenous drug abusers (IVDA's), persons who had received large transfusions of blood or blood products, and sexual partners of anyone known to be at high risk. (Haitians were originally included as a separate risk group but were later excluded.)[3-4] A distinct syndrome, AIDS-related complex (ARC), was subsequently recognized and described as a symptom complex that frequently preceded AIDS but did not always progress to the full-blown syndrome.[5]

Identification of the Virus:

In the spring of 1984 Robert Gallo and Luc Montagnier, working in separate laboratories, identified what was eventually named the Human Immunodeficiency Virus (HIV) as the causative agent of AIDS.[6-8] HIV is a human retrovirus that selectively infects and destroys T helper (T_4) lymphocytes. Recent work has shown that the membrane glycoprotein CD_4 is the cellular receptor for HIV. This receptor is found on T_4 lymphocytes, macrophages, natural killer cells, some B lymphocytes and neuronal cells.[9-10]

Once the virus was identified, both laboratories quickly developed assays for human antibodies to major core proteins of the virus. These

assays allowed reliable identification of infected individuals even when asymptomatic.[11-13]

The CDC soon integrated antibody screening into the case definition,[14] as shown in Appendix Ia. Once an asymptomatic state of "HIV positivity" has been identified, an immediate emphasis was placed on describing prognostic indicators for the transitions from HIV positivity to ARC, and from ARC to AIDS. Relatively little attention was given to prognostic indicators for the outcome of overt AIDS.

Epidemiologic Predictions:

AIDS has rightfully been called a modern day plague. Conservative predictions are that 270,000 people in the United States will have AIDS by 1991 or will have already died from the disease.[15]

The potential human and economic costs are staggering. In New York City AIDS is already the leading cause of death among men and women ages 25-34 years; and 87% of people diagnosed with AIDS before 1983 are dead.[16] The New York City Department of Health currently estimates that by 1991 between 25-50% of New York City medical-surgical beds will be constantly occupied by AIDS and ARC patients.[16]

As of now, AIDS has no curative therapy and no prophylactic vaccine. Although "safe sex" campaigns seem to have slowed the rate of rise in the homosexual community, warnings to use clean needles or

abstain from intravenous drug abuse have generally gone unheeded among the IVDA population.[17] Drug abusers, a particularly difficult group to reach with new health measures, have become the most frequent victims of AIDS in New York City,[17] and other cities will undoubtedly follow this trend.

Historical Conclusions:

This brief historical review shows that AIDS research has made remarkable progress in seven short years, but serious therapeutic needs remain. Although some treatments are available for particular opportunistic infections, none eradicate the virus itself. One drug, azidothymidine (AZT, now also called zidovurine[18]) has been made available for treating HIV infection,[18-19] but at best it is palliative, not curative.[18-20] The need for a reliable prognostic stratification system is illustrated by problems in the AZT trial, described in the next section.

Purpose of Prognostic Classification in AIDS

Problems in the AZT Trial:

In July 1987 Fischl et al. published a double-blind randomized placebo controlled trial of AZT.[20] Although originally designed to follow subjects for 24 weeks of therapy, the study was prematurely ended, with only 10% of its subjects having been followed for 24 weeks, when a special screening panel found a significant difference in mortality between the control and experimental groups. The mortality rates were 9/137 (6.6%) in the control group and 1/145 (0.7%) in the experimental group ($P < 0.001$). Because of the difference in mortality, the panel[18] believed that continuation of the trial would be unethical.

AZT was then made generally available to all AIDS and ARC patients at a yearly cost[21] per patient of about $11,000.00. In a companion article Richman et al.[22] warned that AZT had serious toxicity among the patients in their study. Severe anemia, with hemoglobin levels <7.5 grams per deciliter[22], was found in 24% of AZT recipients but in only 4% of controls. Furthermore, the patients who were initially sicker, i.e. with already suppressed hematologic counts, were more likely to experience serious toxicity from AZT.[22] Because the eligibility criteria for the clinical trial demanded that the AIDS patients be both within 120 days of their first bout of Pneumocystis carinii and free of any other opportunistic infection or neoplasm, the treated group contained only relatively healthy AIDS patients. The potentially high morbidity and mortality associated with

AZT in more severely ill AIDS patients has subsequently been demonstrated.[23]

Purposes of Prognostic Stratification in Therapeutic Trials:

The AZT trial illustrates several roles for a reliable prognostic staging system: it can help prevent bias that may arise by chance in randomized trials; it can improve the identification of the historical control group when randomized placebo controlled trials are not possible or ethically permissible; and it can improve both therapeutic decisions for individual patients and therapeutic research for appropriate patient populations. These roles are discussed in the sections that follow.

Randomized Controlled Trials: False Positives

Double-blind, randomized placebo controlled trials are the "gold standard" of clinical research, but are not free from bias. The "luck of the draw" during randomization can produce prognostic disproportions in the groups being compared, and can thus create false positive results.[24] Feinstein and Landis,[25] using computer simulations for two ineffective therapies, showed that without prognostic stratification, a major statistical discrepancy can occur in about 25% of randomized trials with sample sizes of 100. These discrepancies were more likely to occur when patients in the different prognostic stages had sharp differences in the survival rates.[25]

In the AZT trial, Fischl et al.[20] made careful efforts to distribute AIDS and ARC patients evenly; and to compare the groups for age, body weight, Karnofsky performance score, number of symptoms, and mean T_4 cells at entry. Nevertheless, certain major prognostic indicators may not have been included. For example, a particular symptom such as severe anemia might lead to a nadir survival rate of 0% at four months. If such prognostic factors are ignored, and if the treated groups are not evenly distributed for the factors, the results might seem to show significantly different post-therapeutic effects even if the treatment itself was ineffective.[24] These differences could be particularly emphasized by a short period of follow up, before sufficient time had elapsed for a real therapeutic effect.

Historic Controls in the Absence of Randomized Controls

Although randomized controlled trials can be significantly improved, an even more persuasive need for good prognostic stratification occurs when placebo controlled trials are regarded as unethical. Since this problem arose in the AZT trial, any further research with AZT will require historic controls rather than concurrent placebo controls. In the absence of concurrent placebo controls, prognostic staging can allow the compared historic controls to be adjusted for the severity of illness of the treated new group. In light of the pressing need for more comprehensive therapeutic research in AZT[18,22-23] and the ethical difficulties of sham therapies in fatal diseases such as AIDS, reliable prognostic stratification could help solve some of the current ethical and scientific dilemmas.

Different Therapeutic Effects Among Strata: False Negatives

False negative results may occur when prognostic strata are similarly distributed in compared cohorts but are affected differently by the compared treatments.[24] The trial of AZT showed that its toxic effects were highest in the sickest patients. Because the trial included patients who were relatively healthy, it is possible that the apparently favorable response of early AIDS/ARC patients might be reversed in more severely ill patients. If future AZT testing does not include prognostic stratification, a false negative result might be produced as the bad outcomes in the sicker patients obscure a beneficial effect in the relatively healthy patients. For example, consider two prognostic strata being tested with two treatments, AZT and an ineffectual other drug. Suppose that AZT has a beneficial effect in healthy AIDS patients and a detrimental effect in sick cases. We might find the following data for 6 month survival rates:

	Treatment	
	AZT	Ineffectual Agent
"Healthy" AIDS:	50/50 (100%)	35/50 (70%)
"Sick" AIDS:	0/50 (0%)	15/50 (30%)
Total:	50/100 (50%)	50/100 (50%)

If the groups were not prognostically separated, the similar 50% survival rates in the total results would make the researchers falsely conclude that AZT was no more effective than the ineffectual agent. A suitable prognostic separation would prevent this problem and

would yield a valuable insight into the type of patient who could greatly benefit from AZT.

Another aspect of better prognostication is its personal benefit to the patient. The results can help in plannig for the future, in choosing more appropriate therapies, and also in difficult decisions about when to stop heroic treatment.[26]

Current Classification Systems

Two principles of prognostication should be recognized before beginning a review of current prognostic research on HIV.

Basic Principles:

The first important prognostic principle is that AIDS is a complex syndrome. It affects multiple organ systems and has multiple infectious and oncologic processes.[28] This complexity cannot be effectively studied in isolated subsets that consider only patients with one particular manifestation of AIDS.[27] Many papers have been written on isolated aspects of HIV infection (e.g. individual forms of opportunistic infections, various cancers, manifestations in different individual organ systems). These isolated accounts, however, do not provide for combinations and interactions of the varied individual processes.

A second principle of prognosis is that the prediction must be aimed at a specific phenomenon or target event.[24] In the case of HIV infection, prognostic research has emphasized two transitions: the change from membership in a high risk group to HIV infection; and the change from HIV infection to overt AIDS. Relatively little research attention has been given to the outcome of AIDS itself: the transition from AIDS to survival or death. It is the latter target event--survival with overt AIDS--with which this review is concerned.

In general, a single prognostic variable or prognostic system cannot reasonably be expected to predict several different target events.[24] The prediction of the transition from risk group membership to HIV positivity is therefore beyond the scope of this review. The factors that predict initial infection are unlikely to differentiate survival among those already infected. Most persons who develop frank ARC or AIDS will probably have already demonstrated lymphadenopathy, fevers, or other factors that predict the progression. In addition, the virus itself cannot be held responsible for co-morbid factors (such as previous hepatitis B infection) or demographic factors (such as residence in New York city) that increase the predisposition to an initial infection.

On the other hand, the features that predict progression from HIV infection to AIDS may offer important hints about the pathologic effects of the virus's activity. If these predictive factors reflect or correlate with an actual pathologic process of immunologic decline,

they may also affect the patient's ultimate survival after AIDS becomes clinically overt.

This review is therefore concerned with two groups of studies. The first group consists of classification systems and clusters of variables designed to differentiate HIV infection and predict its transition to AIDS. The second group consists of the few studies that have considered survival in AIDS.

CDC Definition of AIDS/ARC:

The most influential current classification system for HIV infection has been the CDC definition of AIDS and ARC[4-5] (Appendix Ia). The goal of the AIDS definition was to encompass a syndrome of several features. The first feature is opportunistic infections (OI). They include the following: intestinal cryptosporidiosis; Pneumocystis carinii pneumonia (PCP); strongyloidosis beyond the gastrointestinal tract; toxoplasmosis in sites other than the spleen, liver, or lymph nodes; esophageal candidiasis; cryptococcosis beyond the lungs and lymph nodes; Mycobacterium avium or intracellulare (MAI) beyond the lungs and lymph nodes; cytomegalovirus (CMV) beyond the liver, spleen, or lymph nodes; disseminated herpes simplex virus; and progressive multifocal leukoencephalopathy (caused by the papilloma virus). A second feature of the AIDS syndrome is the occurrence of certain special neoplasms, such as lymphoma limited to the brain and Kaposi's sarcoma (KS). Both OI's and certain special neoplasms are believed to indicate underlying cellular immunodeficiency. In the

absence of other known underlying causes for the immunodeficiency, the CDC decided that these features are alone sufficient evidence of AIDS without a positive HIV titer. Other opportunistic infections and special neoplasms, when accompanied by a positive HIV titer, are also included in the case definition (see Appendix I).

The goal of the CDC's definition of ARC was to describe a prodrome of unexplained lymphadenopathy, rashes, fatigue, anorexia, oral candidiasis, weight loss, fever, night sweats, dyspnea, and diarrhea that frequently preceded AIDS, but did not always progress to it.[5] Nevertheless, only demographic descriptions, diagnostic components of AIDS (i.e. PCP, MAI, KS, etc.) and a single yes/no category for "wasting syndrome due to HIV" were included in the CDC reporting form (Appendix Ib) for ARC. No systemized approach for reporting symptoms was instituted. Thus, OI's, secondary cancers, risk factors, and routine demographic information became the major variables used in studies considering the ultimate prognosis of AIDS.

The Study by Kaplan et al. for Staging ARC:

Working in conjunction with Gallo, Kaplan et al.[30] developed a six stage system that was intended to reflect a progressive decrease in T-helper cell number from group 1 to 4. The scope of the system ranged from asymptomatic HIV infection (group 0) to AIDS (group 4). Group 5 included patients who were positive for HIV while undergoing chemotherapy for cancer; and group 6 included HIV positive patients with lymphoma.

Important variables in The Kaplan stages of ARC included persistent lymphadenopathy, hypergamma-globulinemia, oral candidiasis and exaggerated infections (such as severe tinea versicolor of the skin; extensive molluscum contagiosum; prolonged ptyriasis rosea; severe tinea cruris; recurring condyloma accuminata; extensive secondary syphilis; or prolonged CMV). AIDS developed in 3 of 7 subjects in group 3; and 4 of 32 patients in group 4 progressed to group 6 disease.

The Study by Haverkos et al.:

After a survey searching for consensus among more than 80 investigators, Haverkos et al.[31] developed a seven-stage stratification which ranged from asymptomatic HIV infection to AIDS. Only stages 6 and 7 involved full-blown AIDS. Stage 6 contained AIDS with only KS; and stage 7 contained AIDS with an OI, with or without KS. Important variables in the earlier stages of the Haverkos system included immune thrombocytopenic purpura, unexplained lymphadenopathy, low grade fevers or night sweats, minor opportunistic infections (such as thrush or herpes zoster), high fevers ($>38.5^{o}$ C or 101.3^{o} F), watery diarrhea, and sustained weight loss of 10% or more of body weight. Haverkos et al. hoped that their stratification would be useful for evaluating therapeutic trials, but did not test the system and warned that it was not intended to convey prognostic implications.

The Walter Reed System:

Perhaps the best documented staging system for HIV infection is the Walter Reed (WR) Classification.[32] Its intent to reflect T cell function was stated as follows:

> This classification system is based on two central observations: the fact that the T-helper cell is the principal target cell of HTLV-III, and the clinical observation that the functional integrity of the T-helper cell determines the clinical presentation.[34]

The Walter Reed system contains seven stages that range from absence of HIV infection to full-blown AIDS. Important variables include asymptomatic HIV positivity, chronic lymphadenopathy, T-helper cells $<400/mm^3$, partial and complete anergy, and oral candidiasis.

In a preliminary study of 39 sequential patients followed for 18 months, Redfield et al.[32] demonstrated that the patients in Walter Reed stages 3 to 6 had a "slow but progressive course to the next stage or death". A different group of investigators[33] later substantiated this stratification by classifying 358 subjects and documenting progression of disease in 8 of 181 seropositive subjects in Walter Reed stages 2-5. These investigators, noting that severe thrombocytopenia was present in 19 cases, suggested that it be added to the WR staging. Redfield, of the Walter Reed staging, concurred.[33]

CDC Composite Classification:

The most recent efforts at staging occurred when the CDC convened a panel that included Redfield (of the Walter Reed Staging) and Gottlieb (of the Haverkos et al. staging) as well as representatives from several branches of The National Institutes of Health. The panel jointly proposed a classification system (see Appendix II) to be used for purposes of reporting and surveillance. The new system incorporates most of the features of the previous systems.[34]

Subsets of Variables:

In several studies, subsets of the foregoing variables were identified as individually prognostic for the transition from a pre-AIDS state to AIDS. In the largest study, in a cohort of 1,835 homosexual men who were seropositive for HIV[35], multivariate analysis showed the following independent predictors: increased T suppressor lymphocytes, a low level of antibody to HIV, a high titer of CMV antibody, and a history of sexual contact with someone in whom AIDs developed. Predictors found in other, smaller studies were: T_4 cell counts,[36] number of homosexual partners,[36] presence of oral candidiasis,[37-38] elevated erythrocyte sedimentation rate,[38] peripheral cytopenias,[38] and previous history of herpes zoster.[38]

Still other studies have directly examined the relationship between clinical presentation in AIDS/ARC and T cell function as reflected by T cell counts (T_4, T_8, and T_4/T_8 ratios). The Multicenter AIDS

Cohort study (n = 2,646), using multiple logistic regression techniques, found certain ARC symptoms strongly associated with low T_4 cell counts.[39] The converse was not true, however: low T_4 counts were not helpful in predicting clinical involvement. Fever, oral candidiasis, low hematocrit, and low neutrophil counts were strongly predictive of low T_4 cell counts. Fatigue and low platelet counts were also correlated (although, less strongly).[39]

Lane[40] studied 38 patients, of whom 17 presented with OI's; 12 with KS alone; and 9 with ARC. The mean number of T_4 cells in these three groups respectively were 34/mm^3, 231/mm^3, and 703/mm^3. Lane concluded that OI's represent a subgroup of patients with a more severe immunologic abnormality than KS. He suggested that KS may represent an earlier manifestation of AIDS in patients predisposed to developing KS.

Despite all of the efforts in classification, none of these staging systems was tested for predicting the survival of AIDS. Their main intent was to use clinical parameters, reflective of T cell function, in predicting which ARC patients were most likely to progress to AIDS.[29-31] The predictive variables in these systems consistently included: demographic risk group characteristics,[28,30-31,36-37] OI's and secondary cancers,[28,31-32,35] minor OI's,[30-36,39] lymphadenopathy,[30-36,39] oral candidiasis,[30-35,38-40] weight loss,[30-31,33-35] diarrhea,[30-31,33-35] fevers,[30-31,33-35,40] night sweats,[30-31,33,35] platelets,[30-31,33-35,40] cytopenias,[39-40]

T cell counts,[30-31,34-37] anergy,[30-31,34-35] and HIV titers.[28,30-31,34-36]

Prognosis for Survival with AIDS:

Four studies have considered overall mortality in AIDS. The San Francisco study by Moss et al.[41] examined 168 reported cases of AIDS before May, 1983. The United Kingdom study[42] examined 168 patients with AIDs reported to the Public Health Laboratory Service Communicable Disease Surveillance Centre between 1982 and June, 1985. An earlier New York City study[43] was subsumed in a later study[44], which contained 5,833 AIDS patients reported during July, 1981 to January, 1984. In all four studies, survival was calculated from time of diagnosis. For comparison here (see Appendix III) all survivals were converted to 30 day months and tenths of months (3 days = 0.1 month).

All four studies found KS to have the best prognosis, with median survivals ranging from 29.2 months[43] to 21.0 months[41]. PCP had the worse prognosis in all studies, with median survivals ranging from 12.5 months[42] to 8.2 months [43]. The combination of KS and PCP had median survivals that ranged from 12.7 to 6.6 months[44,42]. Other OI's also showed a wide range of medians: from 13.3 months[42] to 4.2 months[43]. Only the New York studies checked the combination of KS and other: 15.2 months,[43] 10.8 months[44]; and PCP and other: 10.3 months,[43] 10.0 months[44]. (In both instances, "other" refers to any

OI or neoplasm qualifying for the AIDS diagnosis, but not to PCP or KS).

The recent New York study[44] examined several demographic factors (sex, race, ethnic background, age and risk group) in addition to diagnosis of OI or secondary cancer. Although age, race, risk group, and sex had prognostic significance, the effects were much smaller than those of particular disease manifestations (such as KS, PCP, MAI, etc.). The diagnostic manifestations were 4.6 times more predictively influential (accounting on the average for 56.3% of the excess risk) than the most significant demographic variable, age (which accounted for only 12.2% of the excess risk).[44] The authors concluded:

> Ideally, a study of survival with AIDS would attempt to take into account all manifestations of the disease in each subject, the order in which the manifestations occurred, the intervals between occurrences or relapse, and the type of treatment used. Such detail is not available through routine methods of surveillance; however, our data suggest a broad spectrum of survival based on patterns of disease acquisition.[44]

Functional Prognostic Stratification

Lessons from Cancer Research:

A great deal can be learned from the extensive experience of researchers studying prognostic staging systems for cancer. Feinstein and colleagues have consistently shown that the most effective prognostic staging systems include clinical manifestations as well as

paraclinical data and conventional anatomical staging.[45-47] More recently these investigators also showed that the results of clinical staging tends to remain constant, but anatomical (or morphologic) staging is prone to the "Will Rogers effect".[48] This effect occurs when diagnostic technologies cause a lead-time bias and a resultant morphologic stage migration. The lead-time bias occurs when new diagnostic technologies (e.g. computed tomography) detect tumors in a smaller or "earlier" condition than the same tumor would have been detected by more "primitive" technology (e.g. chest X-ray). The stage migration occurs when the staging is solely dependent upon morphology (e.g. presence or absence of tumor) rather than functional loss (e.g. increasing respiratory distress). The resulting improvements in survival rates do not reflect any real improvement in survival, but merely stage migration within an anatomical staging system.

The same stage-migration effect might also be produced by paraclinical tests that are not ordered routinely. For example, after a particular test, such as a bone marrow biopsy, is found to have prognostic significance, the test may be performed more often than previously. With the increased testing, many asymptomatic patients with a bone marrow infiltrate, such as MAI, will be moved into a poorer prognostic category before they show signs of hematologic compromise or even suppressed peripheral counts. As in the Will Roger's effect, the asymptomatic patients would migrate to a worse prognostic stage and survival rates would be falsely improve.

Conclusions from Prognostic Review:

Experience in cancer research suggests that when staging systems depend on morphology alone, the results may become unreliable if the diagnostic tests become more sensitive or are performed more frequently than before. On the other hand, a system that depends on overt functional effects should not be affected by changes in technology, particularly if the functional effects are manifested in overt clinical findings and routine paraclinical data. In addition to consistency, such a system would be less expensive, invasive, and painful than a morphologic system requiring biopsy or radiologic scans with contrast media.

The work reported in this thesis is an innovative attempt to develop the desired prognostic staging system for adult patients with AIDS. The system depends on routinely collected historical information, clinical manifestations and basic paraclinical data. Because of the relatively small number of patients under study, the results cannot be documented as a definitive staging system for AIDS. Nevertheless, the results show that the functional effects manifested by certain signs, symptoms, and paraclinical data offer a simple, effective, and clinically plausible system of prognostic staging. Further research at this institution and elsewhere can help validate the system and provide any desirable improvements.

MATERIALS AND METHODS

Selection of Patient Population:

The inception cohort in this study consists of all adult AIDS patients who were originally diagnosed or first treated at Yale New Haven Hospital (YNHH) during the period from October, 1980 (when the first YNHH case was identified) to April 20, 1987. The latter closing date was the time at which the roster of AIDS cases at YNHH had been most recently updated when this study began. The AIDS office at YNHH maintains the roster, reports new AIDS patients to the Centers for Disease Control (CDC), and administers an AIDS clinic with routine follow-up on all patients.

The medical record of each patient listed on the roster was obtained and reviewed. To be entered in this study, each patient had to fulfill all of the following eligibility criteria (for a decision flow chart, see Figure 1):

1. The patient must have been diagnosed as having AIDS clinically in accordance with the WHO/CDC criteria[4] of March 1986 (Appendix Ia).

2. The patient must have been diagnosed while alive (i.e. not at autopsy alone).

3. The patient must not be pregnant (pregnancy is known to affect immune response and human investigation on pregnant patients is restricted).

4. The patient must be at least 19 years old.

5. Sufficient data must be available, including a reasonably complete history and physical examination, as well as a complete blood count performed within one month before zero time (as defined below).

6. The patient must not have been immediately lost to follow up after zero time.

Of the 156 patients listed on the roster for the cited time period, 39 were ineligible: 3 patients' records were unavailable or lost; 4 failed to meet the CDC criteria; 3 were not diagnosed until autopsy; 1 was pregnant; 12 were below 19 years of age; 10 had insufficient baseline data; and 6 were lost to follow up almost immediately after zero time. The remaining 117 patients form the inception cohort for this study.

Selection of Zero Time (ZT):

Zero time (ZT), the point from which all serial time intervals were measured for each patient, was determined in a stepwise approach in each eligible medical record (for decision flow chart see Figure 2). The first step was to find the date at which the patient would have first fulfilled the WHO/CDC criteria (of March 1986) for the diagnosis of AIDS. If that date occurred while the patient was being treated at YNHH, either as an inpatient or as an outpatient, and if there was sufficent data collected for an extraction, the day of definitive diagnosis was the date of ZT. If the patient was first definitively diagnosed somewhere other than YNHH or if the data at the first YNHH diagnosis were insufficient, zero time was the first date of YNHH admission (to AIDS clinic or inpatient services) after sufficient data had become available to fulfill the diagnostic criteria for eligibility. Patients with a "delayed" zero time (i.e. ZT assigned at some time after the patient first fulfill the criteria for an AIDS diagnosis, rather than on the

day of diagnosis) were given special identifications. Their results would later be analyzed separately to check for the possibility of prognostic differences between patients with "prompt" and "delayed" zero times.

Extraction/Coding of Medical Record Data:

The primary source of data was each patient's medical record for both inpatient and/or outpatient status at YNHH. Additional information was sometimes obtained from the patient's personal physician or from the AIDS clinic director or coordinator. In no instance was the patient or any member of the patient's family contacted directly.

The data for each patient were extracted in four general categories: demographic; clinical; paraclinical; and co-morbid. This taxonomic system, which had been used in previous prognostic studies at YNHH[49-52], and was designed to include all of the diverse types of data that had been reported as significant in previous AIDS research.

The extraction form went through many different drafts before a final format was selected (as shown in Appendix IV). The extraction of data for each patient required a complete reading of the patient's medical record and any available clinic notes. The process took an average of about four hours for each patient.

After the first 76 extractions were completed, a special new form was designed that could be used both for extracting the remaining medical

records and for computer coding of extracted data. The form is shown in Appendix V, and the associated coding manual is shown in Appendix VI. Data from all previous extractions were transferred to the new form, and the last 42 medical records were all extracted directly onto it.

The comments in the text that follows are confined to a discussion of pertinent major decisions made during the data extraction and coding (details of the coding techniques are described in Appendix VI). The extraction form was organized around the ZT date and the patient's status at zero time. Sections were provided for data concerning the "pre-ZT" interval that preceded ZT; for the ZT admission or clinic visit, labeled "ZT"; and for the "post-ZT" interval thereafter until the patient's death or the last date of follow up.

The extracted demographic data included age, race, sex, and documented risk factors for AIDS, such as homosexuality, drug abuse, multiple blood transfusions, and sexual partners with AIDS. In the chronologic account of clinical and paraclinical manifestations of AIDS, special attention was paid to severity and timing of ARC/AIDS symptoms, and to co-morbid states such as endocarditis or documented alcohol abuse. Each extraction included a detailed account of the ZT history and physical examination, as well as routine laboratory findings (complete blood count, sedimentation rate, chest X-ray, etc). The post-ZT interval ended with the date of death or last follow up, and the corresponding data included autopsy findings, and major post-ZT

clinical events as well as clinical decisions, such as initiation of AZT therapy or a do-not-resuscitate order.

Follow up information was obtained from inpatient charts, AIDS clinic charts, or private physicians. An assessment of survival status for each of the 118 patients was made as of December 31, 1987, which was the closing date of the research.

Analytic Methods:

For data analysis, the patients were divided into two sets. One set, called the development set, contained the first 76 patients eligible for the study. This development set was analyzed to form a prognostic classification system. The second set, called the challenge set contained the next 42 consecutive eligible patients. The challenge set was used for a validating test of the previously developed prognostic staging system. The challenge set data were not analyzed until the staging system was ready for testing.

After the test was completed (with successful validating results), all the data were then combined and re-analyzed to see whether any further cogent prognostic factors might be identified.

The prognostic staging system was developed by a "targetted cluster" method of stratification.[53] Conventional statistical methods of multivariable analysis using the proportional hazard function (Cox regression) procedure were then carried out as confirmation and to check whether any important variables had been overlooked.

Data Processing Methods:

In order to ensure accuracy, the coded data were double entered into the computer, and verified using a program which compares pairs of records character by character.

Computerized data analysis was performed using the SAS (Statistical Analysis System)[54-55] collection of packaged statistical procedures, version 5, run under MVS on the IBM 4341 computer at the Yale Computer Center. The specific statistical procedures employed were:

PROC FREQ--for univeriate frequencies, crosstabulations with specific survival targets, contrasts of distributions between the two population and associated x^2 and Fisher's exact tests;

PROC UNIVARIATE--to generate distributional data for dimensional variables, and median survival times within subsets of data;

PROC T TEST--to test the baseline differances for dimensional variables between development and challenge groups;

PROC CORR--to assess the correlations of survival time with dimensional variables;

PROC LIFETEST--to generate life table estimates of survival for the prognostic strata and to test that calculated curves were statistically different from each other using the Wilcoxon test for homogeneity over strata;

PROC PHGLM--to generate Cox proportionate hazard models. The Cox analyses were conducted using a stepwise algorithm, with statistical criteria for entry and deletion set at $P < .05$.

RESULTS

Data analysis proceeded in three main phases. Phase one was concerned with the development set (i.e. the first 76 consecutive eligible patients.) This information was used to explore and arrange the prognostic variables into a staging system. In phase two, data from the challenge set (the next 42 eligible patients) were used to test and validate the staging system. In phase three, the two data sets were combined for further analysis and evaluation.

Phase One: Analysis of Development Set

The analysis of data for the development set began with a simple statistical overview of each variable for which data had been collected. Each baseline categorical variable (expressed as binary or ordinal ratings) was cross tabulated with survival at 4, 6, 8, 10, and 12 months (Tables 1-6). A particular category was identified as potentially important if the data contained 4 or more subjects within that category, and if the comparison with other categories in the same variable showed a consistent survival gradient over the 12 month period. A category that contained too few patients was also retained as potentially important if the category could be logically combined with other similar categories and if the combination had a distinctive prognostic gradient. Dimensional variables were analyzed by linear

correlation with survival (Table 7). Dimensional variables were regarded as potentially important if the correlation was statistically significant ($p < .05$).

For clarity in this presentation, no statistical numbers will be cited in the text for the initial elemental data, which are all listed in Tables 1-7. In the description that follows, potentially important variables will be discussed according to their data type, and their apparent univariate impact on survival. The location of the Table with the corresponding data is noted for each variable. The citations of negative and positive predictors are listed according to trends in the data, without calculations of statistical significance, which are reserved for the combined categories discussed later. The associated survival was reduced by a negative predictor and increased by a positive predictor.

Note that, at this stage, all variables that fulfilled the above criteria for "potential significance" were included whether or not they seemed to make "clinical sense." Later on these variables will be subjected to more rigorous clinical and statistical filtration.

Demographic Data/Table 1: Negative predictors: Hispanic race and homosexual male. Positive predictors: heterosexual exposure, and exposure by blood transfusion.

AIDS Diagnostic Category/Table 2: Negative predictors: MAI, Cryptococcus, KS, and other. Positive predictors: PCP and Candida esophagitis.

Historical Data/Table 3: Negative predictors: weight loss, constant diarrhea, KS, any Herpetic lesions, any encephalomeningeal symptoms (stiff neck, new seizures, severe lethargy/confusion, and photophobia), any "other" neurologic symptoms (dysarthria/aphasia, paralysis, and dementia). Positive predictors: enlarged lymph nodes.

Co-morbid Data/Table 4: Negative predictors: previous diagnosis of endocarditis, and previous suicidal gestures/attempts. Positive predictors: smoking history of >1 pack per day for ≥ 10 years, and history of gonorrhea.

Physical Exam Data/Table 5: Negative predictors: oral thrush, retinal abnormalities, encephalomeningeal signs (stiff neck, new seizures, severe lethargy, and/or photophobia), and other neurologic signs (dysarthria/ aphasia, paralysis, dementia). Positive predictors: detectable lymphadenopathy.

Paraclinical Data/Table 6: Negative predictors: positive serologies for CMV, cavitary lesions on chest X-ray, lobular infiltrate on chest X-ray and ring-enhancing lesions

on computed tomography of the head. Positive predictors: normal or "partial" result on anergy test.

Dimensional Data/Table 7: Negative statistically significant correlations: none. Positive statistically significant correlations: hematocrit, lymphocyte count, and duration of diarrhea.

One pertinent feature of Table 7 was that T cell counts were not significant in linear correlation with survival ($P \leq .05$). T_4 counts came closer to significance than T_4% (percentage of T_4 cells among total lymphocytes) or T_4/T_8 ratio (T_4, $P = 0.2$; T_4%, $P = 0.8$; T_4/T_8, $P = 0.4$). The expected correlation of survival with T cell counts was probably not found because of sparse data. Only 28/76 (37%) of the development set patients had their T_4 cells measured. A separate problem in the T cell measurments was their timing. Even when done, the measurement was seldom obtained at or near zero time. In the analysis of data, we used the T cell measurements that were closest to ZT, but their timing was often substantially earlier or later than ZT. For these reasons--lack of significance in linear correlation, small numbers of patients, and temporal discordance--T cell count was not included in our staging system.

Ordinalization of Dimensional Data and Formation of Prognostic Unions

In the next step of the phase one analysis, we gave further attention to variables that were considered prognostically promising, either because of previous clinical beliefs or because of the results of our initial univariate analysis.

Because we wanted to develop a staging system based on categories, the dimensional variables were "ordinalized" into categorical groupings as shown in Table 8. Several boundaries for these groups were explored during the process of ordinalization. The final choices depended on both the particular data being analyzed and on conformity with reasonable clinical customs. Table 8 shows a summary of the most striking results found with the ordinalized categories of the dimensional variables. No P values are cited for this preliminary exploration of survival gradients. Tests of significance will be reserved for the final staging evaluation.

The power of ordinalization and binary partitions is particularly well shown for room air arterial pO_2 and WBC's. Although pO_2 did not have a striking statistical effect when linearly regressed against survival, a marked prognostic gradient is shown in the binary partition (4 month survival was : 4/12 (33%) with $pO_2 \leq 50\%$; and 43/64 (67%) without)(Table 8). White blood cell count (WBC) was also unimpressive in linear regression but showed a marked prognostic

difference in patients with WBC's <2,500/ml and in those with higher values (4 month survival: 1/6 (17%) vs. 46/70 (66%)).

As might be expected from the significant regression with survival, hematocrit categories also showed a marked difference in survival. (4-month survival was: 10/22 (45%) for patients with hematocrits below 30 vs. 37/54 (71%) for hematocrit of 30 or above).

Platelet counts are often reported in ordinal categories (such as "low") by the laboratory at YNHH. The "low" designation, which represents counts below 140,000/ml, was prognostically important. The 4-month survival was 4/11 (36%) for patients with low platelet counts and 43/65 (66%) for those with higher values.

The next step was to combine the ordinalized dimensional data and the important categorical variables into clustered unions. In the first set of analyses an attempt was made to combine categories that had nadir and zenith survival results (Table 9). Past history of ring enhancing lesions on head CT, cavitary lesions on chest X-ray, and endocarditis were put into unions because each category seemed to reflect a nadir prognosis. (Respective 4-month survival rates were: 1/4 (25%); 0/4 (0%); 2/6 (33%).) These three variables formed a union with a 4-month survival of 3/11 (27%). The zenith union comprised patients with blood transfusion as their risk factor or with $\geq$150,000 lymphocytes per ml. (4-month survival: 5/5 (100%) and

11/14 (79%), respectively). The union of this set of categories produced a zenith survival of 9/9 (100%) at 4 months.

Construction of "Functional" Unions

We were concerned that the variables contained in the zenith and nadir unions were largely either morphologic (such as ring enhancing lesions on head CT and cavitary lesions on chest x-ray) or demographic (such as blood transfusion exposure). Because morphologic and demographic attributes may not directly reflect the functional severity of a disease's impact, the next step in the phase one analysis was to form functional groupings (or unions) of variables that might indicate the known pathologic processes of AIDS. The four unions that we first explored were: respiratory failure; neurologic failure; bone marrow failure; and nutritional failure.

Several variables were considered for inclusion under respiratory failure: degree of reported dyspnea (Table 3), respiratory rate (Table 7), and pO2 (Table 8). Of these, only pO2 showed a real difference in survival. Thus pO2$\leq$50 mm Hg (or hypoxemia) became the pertinent prognostic variable for respiratory function.

For neurologic compromise, the main functional variables were those of neurologic symptoms and signs. These variables were contained under the headings of encephalomeningeal symptoms, other neurologic symptoms, encephalomeningeal signs, and other neurologic

signs. In preliminary analysis of data in Tables 3 and 5, symptoms were superior to signs for prognosis because more patients had symptoms than documented signs although nearly all patients with signs also had symptoms. Thus all symptom manifestations under the headings of encephalomeningeal symptoms and other neurologic symptoms, except "other", were incorporated into a functional union of neurologic deficit. The manifestations included a history of stiff neck, new seizures, lethargy or confusion, photophobia, dysarthria/aphasia, paralysis, or dementia. This union had a 4-month survival rate of 7/19 (37%) in patients with nerologic deficts vs. 40/57 (70%) in patients free of such deficits.

Bone marrow compromise/failure was determined from paraclinical data because patients did not routinely demonstrate the traditional clinical manifestations of bleeding, petechiae, etc. The complete blood counts collected on all patients avoided the selection bias that might arise in technologic decisions such as getting a CT scan for certain patients but not for others. The binary partition values of hematocrit (<30), platelets (<140,000/ml.), and WBC's (<2,500/ml.) (Table 8) were then grouped into a union of cytopenias (Table 8). Any one cytopenia qualified a patient for inclusions in the union. Because two or more cytopenias seemed ominous, such patients were placed in a separate category of bone marrow failure (4-month survival rates were: 0 cytopenias= 35/48 (73%); 1-of-3 cytopenias= 9/18 (50%); 2 of 3 cytopenias= 3/10 (30%). At 8 months of survival time, all of the

10 patients with 2 of 3 cytopenias were dead, contrasted with only 56% of those patients without cytopenias.

Because weight loss and diarrhea occur commonly in AIDS patients, a concerted effort was made to explore variables that might reflect compromised nutritional function. The variables analyzed for this purpose were: reported weight loss, percent weight lost below a standardized normal weight, average weight, admission weight, serum albumin, and duration and severity of diarrhea (Table 10). Because weight status, and features of weight loss had been poorly reported or recorded, no reliable relationship could be established for the weight variables. The only promising prognostic variable in the "nutrition" group was constant diarrhea. 4-month survival was 7/18 (39%) for patients with constant diarrhea , and 39/57 (68%) for those without (Table 10). In the 18 patients with constant diarrhea, only four had had diarrhea for at least a month. The survival gradient, shown in Table 10, was not particularly striking over 12 or 4-month durations. Combinations of degree of diarrhea and weight loss were explored as well as combinations of diarrhea and low serum albumin. None of the combinations seemed prognostically important. Consequently a union based on "nutritional failure" was not included in the staging system.

The many other variables individually explored in the early analyses were not included in any unions. Their prognostic gradients or numbers of patients were too small; or the variables did not reflect

functional impairment. some of these variables were set aside for further evaluation in the entire data set after the challenge set tests were completed.

Final Staging in Phase One

The three successful functional unions: hypoxemia ($pO_2 \leq 50$ mm Hg), neurologic deficit (any one of the following: stiff neck, new seizures, severe lethargy/confusion, photophobia, dysarthria or aphasia, partial or complete paralysis, or dementia), and cytopenias (any one of the following: hematocrit < 30, white blood cell count $< 2{,}500$/ml, or platelet count $< 140{,}000$/ml) were then arranged into prognostic stages (Table 11).

Stage I consisted of patients who had none of these functional deficits. Stage II consisted of patients having any one of the functional deficits, but no more than one cytopenia. Stage III patients had at least two of the three cytopenias. The survival rates at 4 months in the three stages respectively were 25/28 (89%); 19/38 (50%); and 3/10 (30%) at 6 months. The corresponding median survival times were 11.2, 3.9, and 2.3 months, respectively. Figure 3 shows the life table analysis of the developmental group by stages.

Phase Two: Comparison of Development and Challenge Sets

With the staging system developed, phase two was devoted to checking its performance in the challenge set of 41 patients. The analysis of the challenge set requires some additional explaination because many members of the challenge set had their zero times in 1987, and (at the time of this analysis) had not yet had the opportunity to live 12 months after zero time. All 41 members of the challenge set have been followed for a minimum of 6 months but when 8, 10, and 12-month survival rates are cited for the challenge set, some patients will be "censored", because they have not yet been followed that long. When censoring occurs, it is noted with an asterisk and footnote in all pertinent tables.

For the same reasons, some of the median survival times are conservative figures. They were determined from the latest duration of survival, and might be lenghtened as certain patients have the opportunity to survive longer. These conservative citations are noted in bold print and with appropriate footnotes whenever they are displayed.

For the sake of direct comparison with the developmental set, only 4 and 6-month survivals will be reported in the text. Cited gradients will be chosen to bset illustrate the particular observation. As in the phase one results, pertinent tables are indicated in parenthesis.

In demographic characteristics and in AIDS diagnostic components (Tables 12- 13 vs. Tables 1-2) the development and challenge groups are quite similar. Their only major dissimilarity (by t-test) is in the number of Hispanic subjects (15 subjects in the developmental group and 1 in the experimental, $P < .05$). The two groups were not significantly different in 4 or 6-month survival rates.

Validation of Staging System

Table 14 shows the results of the challenge set partitioned into the proposed staging system. The results show the same prognostic gradients that were found in the development set with 4-month survival rates of: I, 11/15 (73%), II, 8/19 (42%), and III 2/7 (29%). Median survival times were **7.2**, 1.6, and 0.7 months, for stage I-III respectively. (Note that the median for stage one is a conservative estimate due to censoring.) Figure 4 shows the life table analysis of the challenge set and offers a visual display of the prognostic gradients.

In contrast, the nonfunctional unions were not effective forecasters in the challenge set (Table 15). The previous "nadir" set actually reversed itself and did better than patients without its attributes (6-month survival rates: 6/10 (60%) for nadir and 10/31 (32%) for non-nadir subjects). Two of the three component variables in the nadir set lost their negative effect. The results in Table 15 show ring enhancing lesions on head CT: 6-month survival l2/5 (40%) vs. 14/36 (39%), and history of endocarditis: 6-month survival 3/4 (75%) vs. 13/37 (35%).

Only one patient in the challenge set had a cavitary lesion on chest x-ray.

The zenith set fared better than non-zenith set subjects in the challenge set group. 6-month survival rates were: 67% vs. 34% in non-zenith patients, but only half of the component variables in the zenith set remained as positive predictors in Table 15, blood transfusion risk still predicted longer survival (only 2 subjects, 6-month survival: 1/2 (50%) vs. 15/39 (38%) in non-transfusion risk subjects). The high-lymph patients actually fared worse than those with lower values (6 month survival 5/10 (50%) for high lymphs, 10/30 (33%) for those without).

Thus, the non-functional variables and unions (Table 15) that had been sugested by the development set did not remain prognistically effective in the challenge set. On the other hand, the challenge set confirmed the prognistic gradients previously found in the functional variables and unions (Tables 14 and 16).

Phase Three: Combination of Data Sets

After the staging had been validated in the challenge group, the two data sets were combined for descriptive purposes and to provide a larger group for certain methodologic tests. The Tables 17-23 show the elemental data for all 117 patients previously listed only for the development set (Tables 1-7). These are included for descriptive

completeness, but demonstrate no new phenomona and will not be discussed.

Examination of Patients with "Delayed" Zero Time

Table 24 is addressed to a previously mentioned concern about patients with a "delayed" zero time. In some patients, ZT was the date of their first definitive AIDS diagnosis at YNHH, whereas other patients, for whom AIDS had originally been diagnosed elsewhere, were assigned ZT for the date of their first "admission" to the clinic or hospital of YNHH. The latter patients were included in the cohort to augment its numbers, but we were concerned that the "delayed-ZT" group might have different survival patterns from those of the "prompt-ZT" group.

In Table 24, the patients are listed according to the three main prognostic stages, but are divided into the groups with prompt and delayed zero times. The subtotal results for the two ZT groups show identical median survival times (5 months) and almost identical survival rates (prompt ZT/delayed ZT) at 4 (58%/58%), 6 (44%/42%), 8 (34%/31%), 10 (24%/22%), and 12 (22%/16%) months. The total results thus appear to justify the combination of the two ZT groups into a single cohort.

On the other hand within the individual stages, some interesting differences appear between the two ZT groups for survival in stages II

and III. For the prompt-ZT group, the survival statistics are quite similar in stages II and III, whereas the delayed-ZT groups have a markedly different survival pattern in these two stages. Compared with the prompt-ZT group, patients in the delayed-ZT group have better survivals in stage II and worse survivals in stage III. The distinction may arise because the disease is less virulent in patients who can remain in Stage II despite a delay in ZT, and more virulent (or closer to death) in stage III patients whose survival duration is shorted by assignment of a delayed ZT.

The distinction should also be borne in mind when this staging system is applied in prognosticating for future patients. If zero time is promptly established, the most significant survival gradients may be between Stage I and the other two stages, rather than among all three stages.

Appraisal of AZT Therapy

Another concern in the phase three analysis arose because the new drug, azidothymidine had become available as a possibly effective treatment for AIDS. This drug was received by 1 patient in the developmental set and by 7 patients in the challenge set. All 8 patients were alive at the date of last follow-up. Stage I contained 4 AZT patients: 1 alive at 12 months, 1 alive at 10 months, and 2 alive at 8 months. Stage II contained 3 AZT patients: 1 alive at 12 months, 1

alive at 10 months, and 1 alive at 8 months. Stage III contained 1 AZT patient who was alive at 8 months.

Although the results at first appear encouraging, the effectiveness of AZT is difficult to analyze from these data. Not only are the numbers small, but AZT was not given at zero time. Because AZT was started after zero time in these patients when they might have altered their clinical stage. A patient in stage II at ZT, because of a low white count or hematocrit might have had spontaneous improvement after ZT before the AZT was initiated. For these reasons, the AZT results in this population cannot be analyzed. The apparently high survival of all 8 patients may be due to AZT, but may also arise from selection bias in the way the patients were chosen for AZT therapy. Decisions about the efficacy of the drug would require further study for of a larger group of patients, classified into appropriate stages when AZT therapy was initiated.

Overall Staging in Comparison with Other Predictors and those Used by Rothenberg et al.

Table 28 and Figure 5 show the final results of the three functional stages for the entire population of 117 patients. The overall median survivals in the stages were I: 9.2 months; II: 3.5 months; and III: 2.1 months with a total median survival of 5.0 months (note that the stage I median is conservative due to incomplete follow up). The three stages show marked gradients of survival rates throughout the 12 month period.

For contrast, Table 29 compares the survival results of these three functional stages, with the results of the prognostic variables used by Rothenberg et al.[44] as noted in the CDC reporting forms. For each cell in Table 29, the numbers show N (the size of the group), the 6-month survival rate, and the median survival in months. The table clearly shows that the stages discriminate survival rates much more strongly than the demographic and morphologic-etiologic variables examined by Rothenberg et al.

To demonstrate the impact on survival of competing variables, we used Cox regression. In the regression analysis the three group staging system was entered as one variable, and the other entries included: the nadir and zenith set variables, MAI, and Candida esophagitis, and the Rothenberg et al.[44] demographic and diagnostic component variables. None of these variable were contained in the three stages but had looked promising during analysis. The results, which show the variables that emerged in their order of importance in the regression were as follows:

1.	Staging System	$p < 0.00001$	$R = 0.166$
2.	Constant Diarrhea	$p = 0.0008$	$R = 0.109$
3.	Candida Esoph.	$p = 0.0192$	$R = 0.067$
4.	Hispanic Race	$p = 0.0375$	$R = 0.055$

The Cox regression analysis was then repeated, with the staging system eliminated as a single variable, and replaced by its component elements. All the additional variables were entered into the analysis as before. The sequence of important variables was as follows:

1.	Bone Marrow Failure	p=0.0001	R=0.129
2.	Low pO2	p=0.0003	R=0.121
3	Neurologic Manifestations	p=0.0019	R=0.100
4.	Constant Diarrhea	p=0.0010	R=0.107
5.	Candida Esophagitis	p=0.0121	R=0.075
6.	Hispanic Race	p=0.0396	R=0.054
7.	High Lymphocyte Count	p=0.0300	R=-0.059

(In the Cox results, a posititve R value implies a negative effect on survival.) Thus, high lymphocyte count, with a negative R value, was a positive predictor, although its effect was relatively small when compared with the other cited variables.

In both sets of Cox regression analyses, the staging system or its component elements was much more prognostically effective than any of the variables not included in the staging. Only one functional variable, constant diarrhea, that was not included in the staging, showed an impressive effect (with R values$\geq$.05). This variable should be considered as an additional possible component of the functional

staging when its value can be confirmed in larger numbers of patients than were available for this analysis.

Summary

In summary, the functional staging system developed in a single set of subjects was substantiated in a separate challenge set, as well as in comparison with predictor variables used in the most authoritative previous prognostic study. The results clearly demonstrate that functional variables are superior to demographic or morphologic-etiologic variables in predicting survival of patients with AIDS. The main functional variables were indications of hypoxemia, neurologic deficit, or compromised bone marrow.

DISCUSSION

Three issues remain for discussion: 1. Comparison of this study's results with those of previous studies, and possible explanations for the differences; 2. Possible problems in this study; and 3. Potential applications for the proposed staging.

Review of Previous Studies of Predictive Variables

In previous research with AIDS, two types of prognoses had been evaluated. In one type of study, the prognostic transition was from ARC to overt AIDS--a transition not assessed in this research but potentially pertinent to it. The second type of prognostic study was aimed at the same goal as the current research: predicting survival among patients having overt AIDS.

Functional Variables Vs. Non-functional Variables:

An interesting finding in the prognostic transition from ARC to AIDS was the proposed importance of what we have called "functional" variables: lymphadenopathy, weight loss, diarrhea, fevers, night sweats, platelets, hematocrit, lymphocyte count, white blood cell count, T cell counts, and anergy.[28-40] In studies of survival among patients with overt AIDS, however, very few of these functional variables were examined. The analysis was focused solely on demographic or morphologic-etiologic variables: sex, race, age, risk

group, and diagnostic components (i.e. PCP, KS, MAI, etc.).[41-44] The current results, showing the powerful prognostic impact of functional variables (hematocrit, platelets, white blood cell count, pO_2, neurologic manifestations, and diarrhea) do not require explanation or reconciliation with these former studies, because the functional variables were not included in the previous studies of survival.

Another important feature of previous studies is that none of their prognostic data were taken directly from the patients' medical records (as in the current research). Instead, the previously analyzed information came from infectious-disease reporting forms [41-44] (see also Appendix Ib) that included only morphologic-etiologic data (such as AIDS diagnostic components) or demographic data. The demographic-morphologic-etiologic variables make no distinction between patients who are symptomatic or asymptomatic, and between those who have major functional deficits or none. By emphasizing and classifying the functional consequences of AIDS, we were able to distinguish major prognostic gradients despite the statistical handicap of working with a relatively small number of patients.

Immunologic Functional Variables:

Because AIDS is an immunologic disease that selectively attacks T_4 lymphocytes,[9] previous investigators have assumed that "the functional integrity of the T_4 cell determines clinical presentation."[34] Three variables measured in the present study--T_4 cell count, anergy, and lymphocyte count--might have been reasonably expected to reflect

functional integrity of the T_4 lymphocyte. In fact, these variables were found to be individually significant in previous studies[30-34] of the transition from ARC to AIDS. Yet none of these variables were included in our staging system. Each variable, and our reasons for excluding it, will be discussed separately.

T_4 Lymphocyte Count:

T_4 cell count would appear a promising variable. It is, after all, a direct measure of the presence of T_4 cells. Nevertheless, it could not be included in our staging because T cell counts were not done routinely, and the relatively few that were done, were not done at zero time. Only 28/76 (30%) of the development set and 3/41 (7%) of the challenge set ever had T cell counts done. Almost none of the counts were done on or near the patient's ZT, and many counts occurred were 6-12 months before or after ZT. Thus, the T_4 values could not be included in our staging The two main reasons were the potential for selection bias when decisions were made to get the T-cell test for some patients but not others; and also the ineligibility ("off limits") feature of information obtained either after zero time, or too early before ZT to be pertinent for a ZT classification.

Nevertheless, during certain Cox Regressions of the entire data set, the T_4 cell count emerged as a significant prognostic variable. When T_4 count was compared as a single variable with the staging system as a single variable in the 31 uncensored patients with T cell counts, the staging emerged first ($X^2 = 9.84$; $P = 0.0017$; $R = 0.232$) and T_4 count

emerged second ($X^2 = 5.56$; $P = 0.0183$; $R = 0.156$). Thus, even among the 31 patients for whom T cell tests were recorded, the staging system was prognostically more effective than the T-cell counts.

This distinction is especially noteworthy with respect to costs.[54] The routine paraclinical tests in our staging (ABG + CBC + differential + platelet count) cost a total of $43.45, whereas a single T cell study costs $142.50. Another important distinction is that the data used in our staging came from tests that are done in the course of routine patient care, whereas T cell tests are not routinely required and their use in prognostic staging would substantially increase the routine costs of AIDS patient care.

Anergy:

Anergy failed to show prognostic value in this study, possibly because of small numbers. Only 31% (34/117) of the patients had anergy panels placed and read. The 6-month survival rates in these 34 patients showed an impressive prognostic distinction. Of those with normal readings or only partial anergy, 75% (6/8) were alive at 6 months compared with 36% (9/26) of those with complete anergy. When compared simultaneously with the other variables in the Cox regression analysis, however, anergy was not significant, perhaps because of covariance and small sample size. The prognostic role of anergy should be reappraised in future studies containing larger numbers of patients.

Lymphocyte Count:

In contrast to T_4 cell counts and anergy, lymphocyte counts were not handicapped by small sample sizes. The counts were available in 97% (114/117) of the patients. Although lymphocytes initially seemed important as an isolated variable, they emerged as only weakly predictive because they were found to co-vary with a strong predictor, hematocrit.

Another reason for the prognostic weakness of lymphocyte counts may be that they are low in almost all patients with AIDS. (The median count for all 117 patients in our series was 533.) For measurements that are almost all at one extreme of a normal Gaussian distribution, the laboratory tests themselves may not provide an effective differentiation of the extreme values. The results may then show little prognostic discrimination, despite their diagnostic importance.

Furthermore, because HIV is known to selectively attack lymphocytes, a lowered lymphocyte count might well be prognostic[39] for the transition from ARC to AIDS, but the count may be too low for further clinical distinctions after AIDS has become overt. In contrast, other cytopenias--such as low hematocrit, WBC's or platelets--may be more accurate reflections of bone marrow infiltration and compromise, a secondary process associated primarily with MAI.[53]

Possible Problems in this Study

Several problems may arise from the methodology of this study. They include: definition of zero time (ZT), the effects of AZT therapy, reversibility of staging, changes in prognosis as physicians become more adept at treating AIDS, and the limitations of a medical record review.

Definition of ZT:

The comparison of prompt and delayed zero-time groups (Table 28) shows both encouraging and discouraging results. On the one hand, the total results in these two groups seemed to show almost identical prognoses. The two groups were therefore reasonably combined into a single cohort. On the other hand, after a staging system was developed for that cohort, the delayed zero-time group had a more striking survival gradient between stages II and III than the prompt group.

The emergence of this distinction helps demonstrate the importance of prognostic staging for patients with AIDS. The differences between the prompt and delayed zero-time groups became apparent only after the staging was imposed. The differences also can shed light on how the staging system might be improved in the future. The delayed ZT patients have obviously already "survived a round". After their initial diagnosis elsewhere, they lived long enough to be admitted to YNHH. All the patients who would have died elsewhere

during their 1st hospital admission for AIDS did not live long enough to reach YNHH and become a delayed-ZT member of our cohort. If a patient who survives a first admission is thereafter more likely to live 6 months than a patient who has not yet passed the test of a first admission, then the delayed ZT patients could be expected to live longer than prompt-ZT patients even when in the same composite clinical stage. At the other end of the spectrum, however, delayed-ZT patients with Stage III severe illness may be less likely to recover and may die sooner than prompt-ZT patients in the same severe stage of disease.

The prognostic effect of pre-therapeutic duration of disease within patients in the same stage should be checked in the future when larger numbers of patients are available. In the meantime, however, users of the current prognostic system should bear in mind that its major discrimination is between Stage I and the other two stages. Whether Stages II and III continue to create distinctive prognostic differences remains to be confirmed in future research.

Effects of AZT Therapy:

The preliminary results of AZT therapy among the 8 patients in this study are attractive but cannot be interpreted. The numbers are too small and the treatment was given after their zero-time status. There is a strong probability of post-ZT selection bias, because AZT was given only to patients who were able to survive and recover somewhat from their first AIDS diagnostic infection or cancer. The only conclusion

that can be reached about AZT therapy is that it alone has not been conclusively shown to improve our survival results.

Reversibility of Stages:

The possibility that AIDS patients might reverse their staging (i.e. go from stage II to stage I) deserves more discussion. During the extraction of the medical records we noted that certain post-ZT events--such as development of adult respiratory distress syndrome, recovery from a cytopenia, or a response to trimethoprim-sulfamethoxazole (Bactrim) therapy--seemed to have an important influence on survival. Because we were trying to predict survival from a defined point in time, our study design precluded inclusion of such post-ZT events. In future studies, valuable results might emerge if patients are "restaged" after susequent but significant prognostic events may prove productive.

Improved Prognosis with Improved Treatment:

Another concern about the timing of this study is the possibility that prognosis will improve as physicians become more adept at treating various opportunistic infections. Despite this possibility, the challenge group, which represented a more recent patient population than the development group in this study, actually had a similar survival patterns. This result is in contrast to what was found by Rothenberg et al.[44] in New York City. In that study, cumulative probability of one year survival with PCP increased from 18.2% (in 1981) to 48.2% (in 1985). However, most 78% of the secular increase in probability of survival (from 18.2%-41.7%) occurred during the period from 1981

to 1983. Only 13/117 (11%) of the patients in our study had zero time during the 1981-1983 period. The remaining patients were diagnosed after 1983--a secular interval for which Rothenberg et al. found much less of a secular increase (from 41.7-48.2%) in the survival rates.[44]

Limitations of a Medical Review:

Medical record reviews present special problems in data collection.[49-52] The extractor can only collect data that were recorded, and the accuracy of the extracted data will be limited by the accuracy with which the information was originally inscribed. Further, the data are subject not only to observer bias occurring during the original doctor-patient interchanges that led to the recorded information, but also to bias in the person extracting the record. Nevertheless patient records can be and have been invaluable sources of information, particularly when standardized methods[49-52] are used for maximizing the consistency and accuracy of the extraction process. Since a review of the medical record is used both in research activities and in communication among clinicians, the information is particularly applicable for the purpose of clinical staging.

Potential Applications for the Proposed Staging System

Aside from its prognostic discrimination, the new staging system has the major advantage of being simple, non-invasive, and inexpensive. The staging information does not require special forms of imaging, invasive procedures, or expensive paraclinical tests. The classification makes use of information that is obtained routinely for all patients via history, physical examination, and an ordinary complete blood count. The arterial puncture required to measure $p0_2$ is not necessarily a routine test, but is almost always obtained today whenever a patient shows any significant respiratory impairment. In the absence of any clinical manifestations of such impairment, $p0_2$ can safely be assumed to exceed the boundary value of 50 mm Hg.

The most obvious and compelling application for the new staging system will be to improve the evaluation of new drugs for AIDS. In view of the grave prognosis of AIDS, placebo controlled trials are no longer considered ethical. All patients will probably receive some form of presumably active treatment. When compared with a previous treatment or with no treatment, the results of a new treatment may be highly deceptive or distorted if the patients are not suitably classified for prognostic expectations. An effective treatment may show poor results if given mainly to patients in Stage III; an ineffectual treatment may show apparently good results if given mainly to patients in Stage I.

This type of inadvertent deception may be occurring today when the results of AZT are evaluated without proper prognostic staging.

Because of the pre-therapeutic criteria that make patients "eligible" for AZT treatment, the patients who receive it will usually be "healthier" (i.e in Stage I) than those who do not. Unless AZT (or any other active treatment) has many lethal side effects, the post-therapeutic survival results in the Stage I treated group will inevitably be superior when compared with results of the untreated patients in Stages II and III.

When other new active treatments arise to be compared against AZT in randomized trials, a suitable prognostic staging system can enhance the efficiency with which the trials are designed, and the precision with which the results are analyzed.[24]

A different compelling reason for developing accurate prognostic staging, is the doctor's role in the lives of the patients who suffer from this tragic disease. This study was originally conceived during a medical student's rotation on the Fitkin Service of YNHH. As she cared for her newly diagnosed AIDS patient, a young woman about the student's age with two children, the student was struck by what little useful information the medical community had to offer the patient. Although it was clear that the patient would die of this disease, no one knew if death would come in 2 months or 2 years. It was clear to the student in talking with her patient and her patient's family that such knowledge would help them face the disease and plan how best to make the most of the life that remained. Such plans would include arrangements for the patient's children as well as decisions about when

the patient's comfort would be more important than attempts to eradicate whatever opportunistic infection was currently compromising her health.

It is the hope of that medical student that this research project might in some way facilitate the future development of new effective therapies and in the meantime encourage frank discussions of individual prognosis with AIDS patients and their families.

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TABLE # TITLE

TABLE 1

DEVELOPMENTAL SET: DEMOGRAPHICS

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Race:						
White	27 (36%)	19 (70%)	14 (52%)	11 (41%)	8 (30%)	8 (30%)
Black	34 (45%)	22 (65%)	16 (47%)	11 (32%)	10 (29%)	9 (26%)
Hispanic	15 (20%)	6 (40%)	5 (33%)	3 (20%)	3 (20%)	2 (13%)
Gender:						
Male	56 (74%)	34 (61%)	26 (46%)	18 (32%)	15 (27%)	14 (25%)
Female	20 (26%)	13 (65%)	9 (45%)	7 (35%)	6 (30%)	5 (25%)
Risk Factors[1]:						
IVDA:						
No	38 (50%)	23 (61%)	18 (47%)	13 (34%)	10 (26%)	10 (26%)
Yes	38 (50%)	24 (63%)	17 (45%)	12 (32%)	11 (29%)	9 (24%)
Homosexual Male:						
No	43 (57%)	29 (67%)	21 (49%)	15 (35%)	14 (33%)	13 (30%)
Yes	33 (43%)	18 (55%)	14 (42%)	10 (30%)	7 (21%)	6 (18%)
Heterosexual Exposure:						
No	63 (83%)	38 (60%)	27 (43%)	19 (30%)	15 (24%)	13 (21%)
Yes	13 (17%)	9 (69%)	8 (62%)	6 (46%)	6 (46%)	6 (46%)
Transfusion Exposure:						
No	71 (93%)	42 (59%)	31 (44%)	21 (30%)	17 (24%)	15 (21%)
Yes	5 (7%)	5 (100%)	4 (80%)	4 (80%)	4 (80%)	4 (80%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

TABLE 2

DEVELOPMENTAL SET: AIDS DIAGNOSTIC COMPONENTS

Baseline Disease In Establishing Diagnosis[1]	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
PCP Pneumonia:						
No	25 (33%)	15 (60%)	9 (36%)	5 (20%)	5 (20%)	5 (20%)
Yes	51 (67%)	32 (63%)	26 (51%)	20 (39%)	16 (31%)	14 (27%)
MAI:						
Yes	70 (92%)	45 (64%)	34 (49%)	25 (36%)	21 (30%)	19 (27%)
No	6 (8%)	2 (33%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)
Kaposi's Sarcoma:						
No	67 (88%)	42 (63%)	32 (48%)	23 (34%)	19 (28%)	17 (25%)
Yes	9 (12%)	5 (56%)	3 (33%)	2 (22%)	2 (22%)	2 (22%)
Crytococcus Infection:						
No	71 (93%)	45 (63%)	33 (47%)	24 (34%)	20 (28%)	18 (25%)
Yes	5 (7%)	2 (40%)	2 (40%)	1 (20%)	1 (20%)	1 (20%)
Toxoplasmosis:						
No	73 (96%)	45 (62%)	34 (47%)	24 (33%)	21 (29%)	19 (26%)
Yes	3 (4%)	2 (66%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)
Brain Cancer:						
No	75 (99%)	46 (61%)	34 (45%)	25 (33%)	21 (28%)	19 (25%)
Yes	1 (1%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Candida Esophagitis:						
No	71 (93%)	42 (59%)	32 (45%)	22 (31%)	19 (27%)	17 (24%)
Yes	5 (7%)	5 (100%)	3 (60%)	3 (60%)	2 (40%))	2 (40%)
Other Dx[2]:						
No	68 (89%)	43 (63%)	33 (49%)	24 (35%)	21 (31%)	19 (28%)
Yes	8 (11%)	4 (50%)	2 (25%)	1 (13%)	0 (0%)	0 (0%)
TOTAL	76	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

2 Other included: CMV, cryptosporidiosis, disseminated herpes zoster, disseminated camphlobacter , progressive multifocal leukoencephalopathy, invasive Candida albicans, diffuse immunoblastic leukemia.

TABLE 3

DEVELOPMENTAL SET: HISTORY (SYMPTOMS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Weight Loss:						
No	15 (20%)	11 (73%)	8 (53%)	6 (40%)	6 (40%)	5 (33%)
Yes	60 (80%)	36 (60%)	27 (45%)	19 (32%)	15 (25%)	14 (23%)
Systemic Symptoms[1]:						
None	23 (31%)	12 (52%)	10 (43%)	7 (30%)	7 (30%)	6 (26%)
Fever	46 (61%)	31 (67%)	22 (49%)	16 (35%)	12 (26%)	11 (24%)
Chills	26 (35%)	18 (69%)	12 (46%)	7 (27%)	6 (23%)	6 (23%)
Night Sweats	36 (48%)	25 (69%)	17 (47%)	12 (33%)	11 (31%)	10 (28%)
Lymphadenopathy:						
No	45 (60%)	26 (58%)	18 (40%)	12 (27%)	10 (22%)	9 (20%)
Yes	30 (40%)	21 (70%)	17 (57%)	13 (43%)	11 (37%)	10 (33%)
Skin Lesion[1]:						
None	45 (60%)	31 (69%)	24 (53%)	16 (36%)	13 (29%)	13 (29%)
Kaposis	11 (14%)	6 (55%)	4 (36%)	3 (27%)	2 (18%)	2 (18%)
Herpetic	11 (14%)	6 (55%)	3 (27%)	2 (18%)	2 (18%)	2 (18%)
Rash	12 (15%)	5 (42%)	5 (42%)	5 (42%)	5 (42%)	3 (25%)
Oral Thrush:						
No	46 (61%)	28 (61%)	21 (46%)	14 (30%)	13 (28%)	11 (24%)
Yes	30 (39%)	19 (63%)	14 (47%)	11 (37%)	8 (27%)	8 (27%)
Diarrhea:						
None	37 (49%)	25 (68%)	17 (46%)	15 (41%)	13 (35%)	11 (30%)
Intermittent	20 (27%)	14 (70%)	13 (65%)	7 (35%)	5 (25%)	5 (25%)
Constant	18 (24%)	7 (39%)	5 (28%)	3 (17%)	3 (17%)	3 (17%)
Diarrhea Severity:						
Not Significant	71 (95%)	44 (62%)	33 (46%)	24 (34%)	20 (28%)	18 (25%)
Significant	4 (5%)	2 (50%)	2 (50%)	1 (25%)	1 (25%)	1 (25%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

[This table is continued on the next page]

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

TABLE 3 (Continued)

DEVELOPMENTAL SET: HISTORY (SYMPTOMS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Cough & Chest Pain[1]:						
None	20 (26%)	15 (75%)	11 (55%)	5 (25%)	4 (20%)	4 (20%)
Cough	55 (72%)	31 (56%)	23 (42%)	19 (35%)	16 (29%)	14 (25%)
Non-Pleuritic CP	2 (3%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pleuritic	20 (26%)	10 (50%)	10 (50%)	9 (45%)	8 (40%)	8 (40%)
Dyspnea:						
None	30 (39%)	19 (63%)	13 (43%)	7 (23%)	6 (20%)	5 (17%)
On Exertion	38 (50%)	23 (61%)	18 (47%)	15 (39%)	14 (37%)	13 (34%)
At Rest	8 (11%)	5 (63%)	4 (50%)	3 (38%)	1 (13%)	1 (13%)
Eye Sx:						
None	72 (95%)	45 (63%)	33 (46%)	25 (35%)	21 (29%)	19 (26%)
Visual Blur	4 (5%)	2 (50%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)
Encephalomeningeal Sx:[1]						
None	61 (80%)	43 (70%)	33 (54%)	24 (39%)	20 (33%)	18 (30%)
Stiff Neck	5 (7%)	1 (20%)	1 (20%)	1 (20%)	1 (20%)	1 (20%)
Seizures	5 (7%)	2 (40%)	2 (40%)	1 (20%)	1 (20%)	1 (20%)
Lethargy/Confusion	12 (16%)	4 (33%)	2 (17%)	1 (8%)	1 (8%)	1 (8%)
Photophobia	3 (4%)	1 (33%)	1 (33%)	1 (33%)	1 (33%)	1 (8%)
Any	15 (20%)	4 (27%)	2 (13%)	1 (7%)	1 (7%)	1 (7%)
Other Neurological Sx:[1]						
None	68 (89%)	41 (60%)	33 (49%)	25 (37%)	21 (31%)	19 (28%)
Dysarthria/Aphasia	4 (5%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Paralysis	6 (8%)	4 (67%)	2 (33%)	0 (0%)	0 (0%)	0 (0%)
Dementia	3 (4%)	2 (67%))	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Any	8 (11%)	6 (75%)	2 (15%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

TABLE 4

DEVELOPMENTAL GROUP: COMORBIDITY DATA

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
History of Related Diagnosis[1]:						
None	38 (50%)	22 (59%)	17 (45%)	13 (34%)	11 (29%)	11 (29%)
Hepatitis B	28 (37%)	18 (64%)	11 (39%)	10 (36%)	6 (21%)	6 (21%)
CMV	2 (3%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Syphillia	3 (4%)	3 (100%)	2 (67%)	0 (0%)	0 (0%)	0 (0%)
Gonorrhea	11 (14%)	8 (73%)	6 (55%)	4 (36%)	4 (36%)	4 (36%)
Endocarditis	6 (8%)	2 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Alcohol Abuse:						
None or Social	54 (71%)	32 (59%)	26 (48%)	18 (33%)	14 (26%)	12 (22%)
"Noted"	20 (26%)	14 (70%)	8 (40%)	6 (30%)	6 (30%)	6 (30%)
"Evidence Sd Eff"	2 (3%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Cigarette Smoking:						
None	30 (39%)	18 (60%)	12 (40%)	8 (27%)	6 (20%)	5 (17%)
≤1 ppd × 10 yrs	23 (30%)	14 (61%)	10 (43%)	7 (30%)	6 (26%)	5 (22%)
>1 ppd × 10 yrs	23 (30%)	15 (65%)	13 (57%)	10 (43%)	9 (39%)	9 (39%)
Psychiatric Problems[1]:						
None	64 (84%)	40 (63%)	31 (48%)	22 (34%)	19 (30%)	17 (27%)
Related to IVDA	1 (1%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
"Psychotic"	2 (3%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Depression/Suicide	9 (12%)	5 (56%)	2 (22%)	2 (22%)	1 (11%)	1 (11%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

TABLE 5

DEVELOPMENTAL SET: PHYSICAL EXAMINATION (SIGNS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Oral Thrush						
No	23 (30%)	17 (74%)	14 (61%)	11 (48%)	10 (43%)	9 (39%)
Yes	53 (70%)	30 (57%)	21 (40%)	14 (26%)	11 (21%)	10 (19%)
Lymphadenopathy:						
No	24 (32%)	12 (50%)	6 (25%)	3 (13%)	3 (13%)	3 (13%)
Detectable	47 (63%)	32 (68%)	26 (55%)	21 (45%)	17 (36%)	16 (34%)
Pronounced	4 (5%)	3 (75%)	3 (75%)	1 (25%)	1 (25%)	0 (0%)
Kaposi's Sarcoma:						
None	64 (84%)	40 (63%)	30 (47%)	21 (33%)	18 (28%)	17 (27%)
<10 Lesions; or 1 Location	1 (1%)	1 (100%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)
≥10 Lesions; or 2 Locations	5 (7%)	2 (40%)	2 (40%)	1 (20%)	1 (20%)	0 (0%)
>2 Locations	6 (8%)	4 (67%)	2 (33%)	2 (33%)	2 (33%)	2 (33%)
Eye Lesions:						
None	70 (92%)	45 (64%)	33 (47%)	23 (33%)	20 (29%)	18 (26%)
Retinal Abnormality	6 (8%)	2 (33%)	2 (33%)	2 (33%)	1 (17%)	1 (17%)
Encephalomeningeal Signs[1]:						
None	69 (91%)	44 (64%)	33 (48%)	24 (35%)	20 (29%)	18 (26%)
Stiff Neck	4 (5%)	2 (50%)	2 (50%)	1 (25%)	1 (25%)	1 (25%)
Seizures	1 (1%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Severe Lethargy	5 (7%)	2 (40%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Any	7 (9%)	3 (43%)	2 (29%)	1 (14%)	1 (14%)	1 (14%)
Neurological Signs[1]:						
None	69 (91%)	43 (62%)	33 (48%)	24 (35%)	20 (29%)	18 (26%)
Dysarthria/Aphasia	4 (5%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Paralysis	6 (8%)	2 (33%)	2 (33%)	1 (17%)	1 (17%)	1 (17%)
Dementia	3 (4%)	2 (67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Any	7 (9%)	4 (57%)	2 (29%)	1 (14%)	1 (14%)	1 (14%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

TABLE 6

DEVELOPMENTAL SET: PARACLINICAL DATA (LABORATORY DATA)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Serologies[1]:						
None Positive	48 (63%)	28 (53%)	21 (44%)	16 (33%)	14 (29%)	14 (29%)
Hepatitis B	23 (30%)	17 (74%)	13 (50%)	9 (39%)	7 (30%)	5 (22%)
CMV	5 (7%)	1 (20%)	1 (20%)	1 (20%)	0 (0%)	0 (0%)
Toxoplasmosis	4 (5%)	3 (75%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)
Crytococcosis	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anergy[1]:						
Not Tested/Unknown	45 (59%)	28 (62%)	22 (58%)	14 (35%)	12 (30%)	10 (25%)
Normal	3 (4%)	2 (67%)	2 (67%)	2 (67%)	1 (33%)	1 (33%)
Partial	4 (6%)	3 (75%)	3 (75%)	2 (50%)	2 (50%)	2 (50%)
Complete	24 (34%)	14 (58%)	8 (33%)	7 (29%)	6 (25%)	6 (25%)
Chest Xray Findings[1]:						
Not Done	3 (4%)	2 (67%)	2 (67%)	2 (67%)	2 (67%)	2 (67%)
Normal	21 (28%)	12 (57%)	7 (33%)	4 (19%)	4 (19%)	4 (19%)
Diffuse Infiltrate	43 (57%)	27 (63%)	21 (49%)	14 (33%)	10 (23%)	8 (19%)
Lobular Infiltrate	14 (18%)	8 (57%)	7 (50%)	6 (43%)	6 (43%)	5 (36%)
Cavitary Lesion	4 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Head CT[1]:						
Not Done	57 (75%)	37 (65%)	29 (51%)	21 (37%)	17 (30%)	16 (28%)
Normal	12 (16%)	7 (58%)	4 (33%)	3 (25%)	3 (25%)	3 (25%)
Ring Enhancing Lesion	4 (5%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mass Effect	2 (3%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Other[2]	3 (4%)	2 (67%)	2 (67%)	1 (33%)	1 (33%)	0 (0%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

• Percent of total.

1 Patients could have >1 of these characteristics.

2 Other included: right cerebellar low density lesion; hypodense area in left frontoparietal area; and atrophy.

TABLE 7

DEVELOPMENTAL SET: DIMENSIONAL VARIABLES

Variable	N•	Mean	Median	Range	Coefficient of Correlation with Survival in Mos.
Demographics:					
Age	76	35.1	33.0	22-59	-.02
History Intervals(mos):					
From first Sx to ZT	76	13.1	8.1	0.1-99.9†	.11
Duration Syst Sx	57	3.1	0.7	0-99.9	.07
Duration Diarrhea	65	3.1	0.1	0-99.9	.30*
Duration Pulm Sx	64	2.6	0.9	0-24	.22
Weight Loss(lbs):					
Amount	66	22.0	20.0	0-96	-.07
Period (mos)	51	6.68	4.1	1-25	.24
% Wt Loss	60	5.7	3.0	0-25	.15
Normal State[1]	31	11.4	9.0	-14-79	-.12
Adm State[1]	32	-12.0	-15.0	-58-49	.07
Highest Fever(F):	33	103.1	103.0	100-106	-.26
Physical Exam:					
Temperature	65	100.5	101.0	96-106	-.01
Respiratory Rate	65	25.0	24.0	12-56	.005
Paraclinical Data:					
T Cell Studies[2]:					
T4 Count	28	63.0	32.5	0-463	-.26
T4 %	27	12.4	11.0	0-73	.05
T8 Count	26	232.9	174.5	8-896	-.07
T8 %	27	43.0	40	8-82	.30
T4/T8	40	0.4	0.3	0-1.0	-.19
Complete Blood Count:					
Hematocrit	76	33.0	33.8	18.7-51.6	.32**
WBC	75	5.2	4.8	1.5-9.9	-.04
Calc Lymphs	73	758.5	520.0	0-7020	.26*
Platelets	46	241.4	236.5	8-566	-.12
Sedimentation Rate	34	52.2	54.0	17-78	-.11
Arterial Blood Gas (Rm Air)					
pH	57	744.2	744.0	728-755	.03
PCO_2	57	31.4	32.0	19-45	-.04
PO_2	57	72.4	75.0	28-122	.17
Albumin	42	2.5	2.5	1.2-4.0	.19

NOTES:

• Percent of total; * = $P \leq .05$; ** = $P \leq .01$; † = Maximum coding value was 99.9

1 Normal State refers to normal weight & Admission State refers to admission weight. Patients weights were subtracted from their ideal body weight (IBW; Appendix III) to determine if they were above (+) or below (-) IBW.

2 Some patients only had %'s or T4/T8 ratios given rather than a full T cell count.

TABLE 8

DEVELOPMENTAL SET: STAGING COMPONENTS AND UNIONS

ponents	N (%)*	Median (Survival in Mo.)	Number (and %) Surviving at Cited Period 4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
rologic ifestations:							
No	57 (75%)	7.0	40 (70%)	32 (56%)	24 (42%)	20 (35%)	13 (32%)
Yes	19 (25%)	2.1	7 (37%)	3 (16%)	1 (5%)	1 (5%)	1 (5%)
oxia:							
$PO_2 > 50$ or Not Tested	64 (84%)	6.0	43 (67%)	32 (50%)	23 (36%)	20 (31%)	18 (28%)
$PO_2 \leq 50$	12 (16%)	2.9	4 (33%)	3 (25%)	2 (17%)	1 (8%)	1 (8%)
openias:							
atocrit:							
>30	54 (71%)	6.4	37 (69%)	28 (52%)	22 (41%)	18 (33%)	17 (32%)
<30	22 (29%)	2.8	10 (45%)	7 (32%)	3 (14%)	3 (14%)	2 (9%)
:							
≥2,500	70 (92%)	5.7	46 (66%)	34 (49%)	25 (36%)	21 (30%)	19 (27%)
<2,500	6 (8%)	2.1	1 (17%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)
telets:							
≥140,000 or Not Tested	65 (86%)	6.1	43 (66%)	33 (51%)	24 (37%)	20 (31%)	18 (28%)
<140,000	11 (14%)	3.1	4 (36%)	2 (18%)	1 (9%)	1 (9%)	1 (9%)
penic erity:							
None	48 (63%)	6.9	35 (73%)	27 (56%)	21 (44%)	17 (35%)	16 (33%)
Cytopenia[1]: 1 of 3	18 (24%)	3.9	9 (50%)	6 (33%)	4 (22%)	4 (22%)	3 (17%)
BMF[2]: ≥2 of 3	10 (13%)	2.3	3 (30%)	2 (20%)	0 (0%)	0 (0%)	0 (0%)
L	76 (100%)	5.5	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

:

rcent of total.

topenia refers to any 1 of 3 possible cytopenias (HCT <30; WBC <2,500; PLTS <150,000).

F (bone marrow failure) refers to the presence of ≥2 cytopenias.

TABLE 9

DEVELOPMENTAL SET: NADIR AND ZENITH COMPONENTS AND UNIONS

Components	N (%)	Median	Number (and %) Surviving at Cited Period				
			4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
avitary Lesion n Chest X-Ray:							
No	72 (95%)	5.7	47 (65%)	35 (49%)	25 (35%)	21 (29%)	19 (26%)
Yes	4 (5%)	2.1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ing Enhancing T Lesion:							
No	72 (95%)	5.7	46 (64%)	35 (49%)	25 (35%)	21 (29%)	19 (26%)
Yes	4 (5%)	1.7	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ndocarditis:							
No	70 (92%)	5.3	45 (64%)	35 (50%)	25 (36%)	21 (30%)	19 (27%)
Yes	6 (8%)	2.5	2 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ligh Lymphs:							
< 1500	59 (81%)	6.6	34 (58%)	25 (42%)	17 (29%)	14 (24%)	12 (20%)
≥1500	14 (19%)	3.6	11 (79%)	8 (57%)	6 (43%)	5 (36%)	5 (36%)
Blood Tranfusion:							
No	71 (93%)	5.0	42 (59%)	31 (44%)	21 (30%)	17 (24%)	15 (21%)
Yes	5 (7%)	14.9	5 (100%)	4 (80%)	4 (80%)	4 (80%)	4 (80%)
Unions							
Nadir Group[1]:							
No	65 (86%)	6.4	44 (68%)	35 (54%)	25 (38%)	21 (32%)	19 (29%)
Yes	11 (14%)	2.4	3 (27%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Zenith Group[2]							
No	67 (88%)	5.0	38 (57%)	28 (42%)	18 (27%)	14 (21%)	12 (18%)
Yes	9 (12%)	14.9	9 (100%)	7 (78%)	7 (78%)	7 (78%)	7 (78%)
TOTAL	76 (100%)	5.5	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:

1 Nadir Group: Cavitary lesions on CXR, or Ring Enhancing lesions on Head CT scan, or Endocarditis.

2 Zenith Group: Lymphs ≥1500 or blood tranfusion risk

TABLE 10

DEVELOPMENTAL SET: NUTRITIONAL STATUS

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Wt. Loss Hx:						
No	65 (86%)	38 (58%)	28 (43%)	20 (31%)	16 (25%)	15 (23%)
Yes	11 (14%)	9 (82%)	7 (64%)	5 (45%)	5 (45%)	4 (36%)
Reported Loss:						
Unk	21 (28%)	13 (62%)	9 (43%)	6 (29%)	6 (29%)	5 (24%)
<20	20 (26%)	16 (80%)	14 (70%)	10 (50%)	8 (40%)	7 (35%)
≥20	35 (46%)	18 (51%)	12 (34%)	9 (26%)	7 (20%)	7 (20%)
% Calculated:						
Unk	50 (68%)	31 (62%)	23 (46%)	16 (32%)	15 (30%)	14 (28%)
≤10%	9 (12%)	5 (56%)	4 (44%)	2 (22%)	2 (22%)	2 (22%)
>10%- ≤15%	9 (12%)	6 (67%)	5 (56%)	4 (44%)	2 (22%)	1 (11%)
>15%	8 (11%)	5 (63%)	3 (38%)	3 (38%)	2 (25%)	2 (25%)
Normal State:						
Unk	46 (61%)	27 (59%)	19 (41%)	13 (30%)	12 (26%)	12 (26%)
Nl/Thin	20 (26%)	14 (70%)	12 (60%)	8 (40%)	6 (30%)	5 (25%)
Obese	10 (13%)	6 (60%)	4 (40%)	4 (40%)	3 (30%)	2 (20%)
Adm. State:						
Unk	44 (58%)	27 (61%)	19 (43%)	13 (30%)	12 (27%)	12 (27%)
Nl/Thin[1]	28 (37%)	18 (64%)	14 (50%)	10 (36%)	7 (25%)	6 (21%)
Obese[2]	4 (5%)	2 (50%)	2 (50%)	2 (50%)	2 (50%)	1 (25%)
Albumin:						
< 2.5	54 (71%)	31 (57%)	23 (43%)	18 (33%)	14 (26%)	14 (26%)
≥2.5	22 (29%)	16 (73%)	12 (55%)	7 (32%)	7 (32%)	5 (23%)
Diarrhea:						
None	37 (49%)	25 (68%)	17 (46%)	15 (41%)	13 (35%)	11 (30%)
Intermittent	20 (27%)	14 (70%)	13 (65%)	7 (35%)	5 (25%)	5 (25%)
Constant	18 (24%)	7 (39%)	5 (28%)	3 (17%)	3 (17%)	3 (17%)
Diarrhea Class:						
Not Significant	71 (95%)	44 (62%)	33 (46%)	24 (34%)	20 (28%)	18 (25%)
Significant	4 (5%)	2 (50%)	2 (50%)	1 (25%)	1 (25%)	1 (25%)
Unions						
Obese, ≤10%↓	6 (20%)	3 (50%)	2 (33%)	2 (33%)	2 (33%)	1 (17%)
Obese, >10%↓	4 (13%)	3 (75%)	2 (50%)	2 (50%)	1 (25%)	1 (25%)
Nl/Thin, ≤10%↓	7 (23%)	6 (86%)	6 (86%)	3 (43%)	3 (43%)	3 (43%)
Nl/Thin, >10%↓	13 (43%)	8 (62%)	6 (46%)	5 (38%)	3 (23%)	2 (15%)
TOTAL	76 (100%)	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTE:

• Percent of total.

1 Nl/Thin was defined as ≤20 lbs. over actual weight as per Appendix VII.

2 Obese was defined as >20 lbs. over ideal weight as per Appendix VII.

TABLE 11

DEVELOPMENTAL SET: FINAL STAGING SYSTEM

STAGE[1]	N (%)•	Median (mos.)	Number (and %) Surviving at Cited Period				
			4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
I	28 (37%)	11.2	25 (89%)	21 (75%)	18 (64%)	15 (54%)	14 (50%)
II	38 (50%)	3.9	19 (50%)	12 (32%)	7 (18%)	6 (16%)	5 (13%)
III	10 (13%)	2.3	3 (30%)	2 (20%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	76 (100%)	5.5	47 (62%)	35 (46%)	25 (33%)	21 (28%)	19 (25%)

NOTES:
• Percent of total.

[1] The staging system had the following components and arrangements:

COMPONENTS OF STAGING OF OVERT AIDS

-- Hypoxemia: $PO_2 \leq 50$.

-- Neurologic Deficit: stiff neck; seizures; severe lethargy or confusion; photophobia; dysarthria or aphasia; partial or complete paralysis; or dementia.

-- Cytopenias: hematocrit <30; WBC <2,500; Platelets <140,000.

STAGING ARRANGEMENTS

STAGE I: None of the functional deficits listed above.

STAGE II: Any one of the deficits listed above, but no more than one cytopenia.

STAGE III: Bone Marrow Failure: any two (or more) of the three cytopenias.

TABLE 12

CHALLENGE SET: DEMOGRAPHICS

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Race:						
White	24 (59%)	11 (46%)	9 (38%)	9 (38%)	4*(20%)	2*(11%)
Black	16 (39%)	9 (56%)	7 (44%)	4*(29%)	0*(0%)	0*(0%)
Hispanic	1 (2%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gender:						
Male	33 (80%)	15 (45%)	11 (33%)	9*(28%)	3*(12%)	1*(4%)
Female	8 (20%)	6 (75%)	5 (63%)	4*(57%)	1*(20%)	1*(20%)
Risk Group[1]:						
IVDA:						
No	23 (56%)	13 (57%)	10 (43%)	10 (43%)	2*(13%)	1*(7%)
Yes	18 (44%)	8 (44%)	6 (33%)	3*(19%)	2*(13%)	1*(7%)
Homosexual Male:						
No	21 (51%)	13 (62%)	10 (48%)	7*(37%)	3*(19%)	1*(7%)
Yes	20 (49%)	8 (40%)	6 (30%)	6 (30%)	1*(7%)	1*(7%)
Heterosexual Exposure:						
No	36 (88%)	17 (47%)	13 (36%)	10*(29%)	4*(14%)	2*(7%)
Yes	5 (12%)	4 (80%)	3 (60%)	3 (60%)	0*(0%)	0*(0%)
Transfusion Exposure:						
No	39 (95%)	20 (51%)	15 (38%)	12*(32%)	4*(14%)	2*(7%)
Yes	2 (5%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)
TOTAL	41 (100%)	21 (51%)	16 (39%)	13*(33%)	4*(13%)	2*(7%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 13

CHALLENGE SET: AIDS DIAGNOSIS

Baseline Disease Establishing Dx[1]	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
PCP Pneumonia:						
No	16 (39%)	8 (50%)	6 (38%)	5 (31%)	1*(8%)	1*(8%)
Yes	25 (61%)	13 (52%)	10 (40%)	8*(35%)	3*(17%)	1*(6%)
MAI:						
Yes	37 (90%)	20 (54%)	16 (43%)	13*(37%)	4*(15%)	2*(8%)
No	4 (10%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Kaposi's Sarcoma:						
No	37 (90%)	19 (51%)	14 (38%)	11*(31%)	4*(14%)	2*(7%)
Yes	4 (10%)	2 (50%)	2 (50%)	2 (50%)	0*(0%)	0*(0%)
Crytococcus: Infection:						
No	36 (88%)	17 (47%)	12 (33%)	10*(29%)	3*(11%)	1*(4%)
Yes	5 (12%)	4 (80%)	4 (80%)	3 (60%)	1*(33%)	1*(33%)
Toxoplasmosis:						
No	36 (88%)	20 (56%)	15 (42%)	13*(37%)	4*(15%)	2*(8%)
Yes	5 (12%)	1 (20%)	1 (28%)	0*(0%)	0*(0%)	0*(0%)
Brain Cancer						
No	41 (100%)	21 (51%)	16 (39%)	13*(33%)	4*(13%)	2*(7%)
Yes	--	--	--	--	--	--
Candida Esophagitis:						
No	37 (90%)	19 (51%)	15 (41%)	12*(34%)	4*(15%)	2*(8%)
Yes	4 (100%)	2 (50%)	1 (25%)	1 (25%)	0 (0%)	0 (0%)
Other Dx[2]:						
No	40 (98%)	20 (50%)	16 (40%)	13*(34%)	4*(13%)	2*(7%)
Yes	1 (2%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	41 (100%)	21 (50%)	16 (39%)	13 (33%)	4 (13%)	2 (7%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

2 Other included: See Table 2 and text.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 14

CHALLENGE SET: FINAL STAGING SYSTEM

STAGE[1]	N (%)•	Median (mos.)	Number (and %) Surviving at Cited Period				
			4 Mo.	6 Mo.	8 Mo.†	10 Mo.††	12 Mo.†††
I	15 (37%)	**7.2**	11 (73%)	9 (60%)	8 (53%)	2*(20%)	1*(11%)
II[2]	19 (46%)	1.6	8 (42%)	5 (26%)	4*(22%)	2*(13%)	1*(7%)
III[3]	7 (17%)	0.7	2 (29%)	2 (29%)	1*(17%)	0*(0%)	0*(0%)
TOTAL	41 (100%)	4.2	21 (51%)	16 (39%)	13*(33%)†	4*(13%)††	2*(7%)†††

NOTES:

1 For description of the stages, see Table 11 and text.

• Percent of total.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

Median values in bold print (Stage I) are conservative estimates that assume patients died on date of their last follow-up while alive.

† At 8 months, a total of 2 patients are censored: 1 in Stage II; 1 in Stage III.

†† At 10 months, a total of 10 patients are censored: 5 in Stage I; 3 in Stage II; and 2 in Stage III.

††† At 12 months a total of 12 patients censored: 6 in Stage I; 4 in Stage II 2 in Stage III.

TABLE 15

CHALLENGE SET: NADIR AND ZENITH COMPONENTS AND UNIONS

Components	N (%)•	Median	Number (and %) Surviving at Cited Period				
			4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
avitary Lesion n Chest X-Ray:							
No	40 (98%)	4.2	20 (50%)	15 (38%)	12*(32%)	3*(10%)	2 (7%)
Yes	1 (2%)	10.2	1 (100%)	1 (100%)	1 (100%)	1 (100%)	--
ing Enhancing I Lesion:							
No	36 (88%)	4.4	19 (53%)	14 (39%)	12*(34%)	3*(11%)	1*(4%)
Yes	5 (12%)	3.1	2 (40%)	2 (40%)	1*(25%)	1*(25%)	1*(25%)
ndocarditis:							
No	37 (90%)	3.2	17 (46%)	13 (35%)	12*(33%)	3*(11%)	1*(4%)
Yes	4 (10%)	7.1	4 (100%)	3 (75%)	1*(33%)	1*(33%))	1*(33%)
igh Lymphs:							
<1500	30 (75%)	4.6	15 (50%)	10 (33%)	8*(29%)	3*(13%)	1*(5%)
≥ 1500	10 (25%)	4.3	5 (50%)	5 (50%)	5 (50%)	1*(14%)	1*(14%)
lood Tranfusion:							
No	39 (95%)	4.3	20 (51%)	15 (38%)	12*(32%)	4*(14%)	2*(7%)
Yes	2 (5%)	5.0	1 (50%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)
nions							
adir Group[1]:							
No	31 (76%)	3.2	14 (45%)	10 (32%)	10 (32%)	1*(4%)	0*(0%)
Yes	10 (24%)	6.1	7 (70%)	6 (60%)	3*(38%)	3*(38%)	2*(29%)
enith Group[2]							
No	35 (54%)	4.0	17 (49%)	12 (34%)	9*(27%)	3*(11%)	1*(4%)
Yes	6 (15%)	8.8	4 (67%)	4 (67%)	4 (67%)	1*(25%)	1*(25%)
OTAL	41 (100%)	4.2	21 (51%)	16 (39%)	13*(33%)	4*(13%)	2*(7%)

OTES:

Nadir Group: Cavitary lesions on CXR, or Ring Enhancing lesions on Head CT scan, or Endocarditis.

Zenith Group: Lymphs ≥ 1500 or blood tranfusion risk .

Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 16

CHALLENGE SET: STAGING COMPONENTS AND UNIONS

omponents	N (%)•	Median	Number (and %) Surviving at Cited Period 4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
eurologic anifestations:							
No	29 (71%)	5.0	17 (59%)	12 (41%)	10*(36%)	3*(14%)	1*(5%)
Yes	12 (29%)	2.1	4 (37%)	4 (33%)	3*(27%)	1*(11%)	1*(11%)
ypoxia:							
$PO_2 > 50$	38 (93%)	4.8	21 (55%)	16 (42%)	13*(36%)	4*(14%)	2*(08%)
$PO_2 \leq 50$	3 (07%)	0.1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ytopenias:							
ematocrit:							
≥ 30	29 (71%)	4.5	16 (55%)	13 (45%)	11*(39%)	3*(14%)	2*(10%)
< 30	12 (29%)	2.2	5 (42%)	3 (25%)	2*(18%)	1*(10%)	0*(0%)
BC:							
≥ 2,500	36 (88%)	4.4	19 (53%)	15 (42%)	13*(37%)	4*(15%)	2*(8%)
< 2,500	5 (12%)	2.7	2 (40%)	1 (20%)	0*(0%)	0*(0%)	0*(0%)
latelets:							
≥ 140,000	30 (73%)	5.1	18 (60%)	13 (43%)	11*(38%)	4*(17%)	2*(10%)
< 140,000	11 (27%)	0.7	3 (27%)	3 (27%)	2*(20%)	0*(0%)	0*(0%)
ytopenic everity:							
None	21 (51%)	6.1	13 (62%)	11 (52%)	10 (40%)	3*(20%)	2*(14%)
Cytopenia[1]							
1 of 3	13 (32%)	1.6	6 (40%)	3 (23%)	2*(17%)	1*(9%)	0*(0%)
BMF[2]: ≥ 2 Of 3	7 (17%)	0.7	2 (29%)	2 (29%)	1*(17%)	0*(0%)	0*(0%)
OTAL	41 (100%)	4.2	21 (51%)	16 (39%)	13*(33%)	4*(13%)	2*(7%)

OTE:

• Percent of total.

1 Cytopenia refers to any 1 of 3 possible cytopenias (HCT < 30; WBC < 2,500; or PLTS < 150,000).

2 BMF (bone marrow failure) refers to the presence of ≥2 cytopenias.

Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 17

TOTAL SET: DEMOGRAPHIC DATA

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Race:						
White	51 (44%)	30 (59%)	23 (45%)	20 (39%)	12*(26%)	10*(22%)
Black	50 (43%)	31 (62%)	23 (46%)	15*(31%)	10*(23%)	9*(20%)
Hispanic	16 (14%)	7 (44%)	5 (31%)	3*(19%)	3*(19%)	2*(13%)
Gender:						
Male	89 (76%)	49 (55%)	37 (42%)	27*(31%)	18*(22%)	15*(19%)
Female	28 (24%)	19 (68%)	14 (50%)	11*(41%)	7*(28%)	6*(24%)
Risk Group[1]:						
IVDA:						
No	61 (52%)	36 (59%)	28 (46%)	23 (38%)	12*(22%)	11*(21%)
Yes	56 (48%)	32 (57%)	23 (41%)	15*(28%)	13*(26%)	10*(19%)
Homosexual Male:						
No	64 (55%)	42 (66%)	31 (48%)	22*(35%)	17*(29%)	14*(25%)
Yes	53 (45%)	26 (49%)	20 (38%)	16 (30%)	8*(17%)	7*(15%)
Heterosexual Exposure:						
No	99 (85%)	55 (56%)	40 (40%)	29*(30%)	19*(21%)	15*(17%)
Yes	18 (15%)	13 (72%)	11 (61%)	9 (50%)	6*(40%)	6*(40%)
Transfusion Exposure:						
No	110 (94%)	62 (56%)	46 (42%)	33*(31%)	21*(21%)	17*(17%)
Yes	7 (6%)	6 (86%)	5 (71%)	5 (71%)	4 (57%)	4 (57%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

[1] Patients could have >1 of these characteristics.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 18

TOTAL SET: AIDS DIAGNOSTIC COMPONENTS

Baseline Disease[1]	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Establishing Dx:						
PCP Pneumonia:						
No	41 (35%)	23 (56%)	15 (37%)	10 (24%)	6*(16%)	6*(16%)
Yes	76 (65%)	45 (59%)	36 (47%)	28*(37%)	19*(28%)	15*(22%)
MAI:						
Yes	107 (91%)	65 (61%)	50 (47%))	38*(36%)	25*(26%)	21*(22%)
No	10 (9%)	3 (30%)	1 (10%)	0*(0%)	0*(0%)	0*(0%)
Kaposi's Sarcoma:						
No	104 (89%)	61 (59%)	46 (44%)	34*(33%)	23*(24%)	19*(20%)
Yes	13 (11%)	7 (54%)	5 (38%)	4 (31%)	2*(18%)	2*(18%)
Crytococcus Infection:						
No	107 (91%)	62 (58%)	45 (42%)	34*(32%)	23*(23%)	19*(20%)
Yes	10 (9%)	6 (60%)	6 (60%)	4 (40%)	2*(25%)	2*(25%)
Toxoplasmosis:						
No	109 (93%)	65 (60%)	49 (45%)	37*(34%)	25*(25%)	21*(21%)
Yes	8 (7%)	3 (38%)	2 (25%)	1*(14%)	0*(0%)	0*(0%)
Brain Cancer:						
No	116 (99%)	67 (58%)	50 (43%)	38*(33%)	25*(24%)	21*(20%)
Yes	1 (1%)	1 (100%)	1 (100%)	0*(0%)	0 (0%)	0 (0%)
Candida Esophagitis:						
No	108 (92%)	61 (56%)	47 (44%)	34*(32%)	23*(23%)	19*(20%)
Yes	9 (8%)	7 (78%)	4 (44%)	4 (44%)	2 (22%)	2 (22%)
Other Dx[2]:						
No	108 (92%)	63 (58%)	49 (45%)	37*(35%)	25*(26%)	21*(22%)
Yes	9 (8%)	5 (56%)	2 (22%)	1 (11%)	0*(0%)	0*(0%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

1 Patient could have >1 of these characteristics.

2 Other included: See Table 2 and text.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 19

TOTAL SET: HISTORICAL DATA (SYMPTOMS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Weight Loss:						
No	98 (84%)	54 (55%)	40 (41%)	30*(31%)	18*(20%)	15*(17%)
Yes	19 (16%)	14 (74%)	11 (58%)	8*(44%)	7*(41%)	6*(35%)
Systemic Symptoms[1]:						
None	36 (31%)	20 (56%)	17 (47%)	13*(36%)	10*(32%)	8*(27%)
Fever	71 (61%)	42 (59%)	30 (42%)	23*(49%)	13*(25%)	6*(11%)
Chills	41 (35%)	24 (59%)	16 (39%)	11*(37%)	6*(19%)	6*(19%)
Night Sweats	51 (44%)	30 (59%)	19 (37%)	13*(35%)	11*(28%)	10*(24%)
Lymphadenopathy:						
No	70 (60%)	40 (57%)	29 (41%)	21*(30%)	13*(20%)	11*(17%)
Yes	46 (39%)	28 (61%)	22 (48%)	17*(38%)	12*(29%)	10*(24%)
Skin Lesion[1]:						
None	74 (63%)	47 (64%)	36 (49%)	25*(35%)	15*(23%)	15*(23%)
Kaposis	15 (13%)	8 (53%)	6 (40%)	5 (33%)	2*(15%)	2*(15%)
Herpetic	11 (9%)	6 (55%)	3 (27%)	2 (18%)	2 (18%)	2 (18%)
Rash	21 (18%)	9 (43%)	8 (38%)	8 (38%)	7*(35%)	3*(17%)
Oral Thrush						
No	62 (53%)	39 (63%)	31 (50%)	22*(36%)	16*(29%)	13*(24%)
Yes	55 (47%)	29 (53%)	20 (36%)	16*(30%)	9*(18%)	8*(16%)
Diarrhea:						
None	59 (51%)	38 (64%)	27 (46%)	22*(39%)	16*(30%)	13*(25%)
Intermittent	34 (29%)	22 (65%)	19 (56%)	13 (38%)	6*(21%)	5*(18%)
Constant	24 (21%)	8 (33%)	5 (21%)	3 (13%)	3 (13%)	3 (13%)
Diarrhea Class:						
Not Significant	109 (93%)	65 (60%)	49 (45%)	37*(35%)	24*(24%)	20*(21%)
Significant	8 (7%)	3 (38%)	2 (25%)	1 (13%)	1 (13%)	1 (13%)
Cough & Chest Pain[1]:						
None	36 (31%)	27 (75%)	21 (58%)	12*(35%)	7*(23%)	6*(20%)
Cough	79 (68%)	40 (51%)	29 (37%)	25 (32%)	17*(23%)	14*(19%)
Non-Pleuritic CP	4 (3%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pleuritic	25 (21%)	12 (48%)	11 (44%)	10 (40%)	8*(33%)	8*(33%)
TOTAL	117 (100%)	68 (53%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

[This table is continued on the next page]

NOTES:

• Percent of total.

1 Patient could have >1 than one of these.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 19 (Continued)

TOTAL SET: HISTORICAL DATA (SYMPTOMS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Dyspnea:						
None	50 (43%)	30 (60%)	22 (44%)	14*(29%)	9*(20%)	7*(16%)
On Exertion	56 (48%)	33 (59%)	25 (45%)	21*(38%)	15*(29%)	13 (26%)
At Rest	11 (9%)	5 (45%)	4 (36%)	3 (27%)	1 (9%)	1 (9%)
Eye Sx[1]:						
None	110 (94%)	65 (59%)	48 (44%)	37*(34%)	25*(26%)	21*(22%)
Visual Blur	7 (6%)	3 (43%)	3 (43%)	1 (14%)	0*(0%)	0*(0%)
Encephalomeningeal Sx[1]:						
None	94 (80%)	60 (64%)	45 (48%)	34*(37%)	23*(26%)	19*(22%)
Stiff Neck	6 (5%)	2 (33%)	2 (33%)	2 (33%)	1*(20%)	1*(20%)
Seizures	5 (4%)	2 (40%)	2 (40%)	1 (20%)	1 (20%)	1 (20%)
Severe Lethargy	19 (16%)	7 (37%)	5 (26%)	3*(17%)	2*(12%)	1*(6%)
Photophobia	5 (4%))	33 (60%)	3 (60%)	3 (60%)	2*(50%)	2*(50%)
Any	23 (30%)	8 (35%)	6 (26%)	4*(18%)	2*(10%)	2*(10%)
Other Neurological Sx[1]:						
None	100 (85%)	61 (61%)	48 (48%)	38*(38%)	25*(27%)	21*(24%)
Dysarthria/Aphasia	6 (5%)	2 (33%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)
Paralysis	10 (9%)	5 (50%)	3 (30%)	0*(0%)	0*(0%)	0*(0%)
Dementia	9 (8%)	3 (33%)	1 (11%)	0*(0%)	0*(0%)	0*(0%)
Any	17 (15%)	7 (41%)	3 (18%)	0*(0%)	0*(0%)	0*(0%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

1 Patient could have > 1 than one of these.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 20

TOTAL SET: COMORBIDITY DATA

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
History of Related Diagnosis[1]:						
None	60 (52%)	31 (52%)	24 (40%)	20 (33%)	12*(22%)	11*(20%)
Hepatitis B	34 (29%)	20 (59%)	15 (44%)	10*(30%)	8*(24%)	6*(18%)
CMV	1 (1%)	1 (100%)	1 (100%)	1 (100%)	--	--
Syphillia	10 (9%)	6 (60%)	5 (50%)	3 (30%)	2*(22%)	2*(22%)
Gonorrhea	15 (13%)	9 (60%)	7 (47%)	5 (33%)	4*(29%)	4*(33%)
Endocarditis	10 (9%)	6 (60%)	3 (30%)	1*(11%)	1*(11%)	1*(11%)
Alchohol Abuse:						
None or Social	84 (74%)	48 (57%)	37 (44%)	28 (33%)	17*(22%)	14*(18%)
"Noted"	25 (22%)	17 (68%)	11 (44%)	7*(30%)	6*(26%)	6*(26%)
"Evidence Sd Eff"	5 (4%)	2 (40%)	2 (40%)	2 (40%)	1*(25%)	1*(25%)
Cigarette Smoking:						
None	47 (42%)	27 (57%)	19 (40%)	14 (30%)	9*(20%)	7*(16%)
≤1 ppd × 10 yrs	38 (55%)	21 (55%)	15 (39%)	11*(30%)	6*(18%0	5*(15%)
>1 ppd × 10 yrs	27 (24%)	18 (67%)	16 (59%)	12*(46%)	9*(38%)	9*(38%)
Psychiatric Problems[1]:						
None	95 (83%)	54 (57%)	42 (44%)	31*(33%)	21*(24%)	18*(21%)
Related to IVDA	1 (1%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
"Psychotic"	3 (3%)	1 (33%)	1 (33%)	1 (33%)	1 (33%)	1 (33%)
Depression/Suicide	16 (14%)	10 (63%)	6 (38%)	5*(33%)	2*(14%)	2*(14%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

1 Patient could have >1 than one of these.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 21

TOTAL SET: PHYSICAL EXAMINATION (SIGNS)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Oral Thrush						
No	38 (32%)	27 (71%)	23 (61%)	19 (50%)	14*(41%)	11*(34%)
Yes	79 (68%)	41 (52%)	28 (35%)	19*(25%)	11*(15%)	10*(14%)
Lymphadenopathy:						
No	44 (38%)	21 (48%)	13 (30%)	9 (20%)	6*(14%)	5*(12%)
Detectable	69 (59%)	44 (64%)	35 (51%)	28*(42%)	18*(30%)	16*(27%)
Pronounced	4 (3%)	3 (75%)	3 (75%)	1 (25%)	1 (25%)	0 (0%)
Kaposi's Sarcoma:						
None	102 (87%)	60 (59%)	45 (44%)	33*(33%)	22*(24%)	19*(21%)
≤10 Lesions; or 1 Location	3 (3%)	2 (67%)	2 (67%)	2 (67%)	0*(0%)	0*(0%)
>10 Lesions; or 2 Locations	5 (4%)	2 (40%)	2 (40%)	1 (20%)	1 (20%)	0 (0%)
>2 Locations	7 (6%)	4 (57%)	2 (29%)	2 (29%)	2 (29%)	2 (29%)
Eye Lesions:						
None	105 (91%)	61 (58%)	46 (44%)	34*(34%)	24*(25%)	21*(22%)
Retinal Abnormality	10 (9%)	4 (40%)	3 (30%)	2*(22%)	1*(11%)	1*(11%)
Other	1 (1%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0 (0%)
Encephalomeningeal Signs:[1]						
None	103 (88%)	62 (60%)	46 (45%)	35*(34%)	23*(24%)	19*(20%)
Stiff Neck	6 (5%)	3 (50%)	3 (50%)	2 (33%)	1*(20%)	1*(20%)
Seizures	1 (1%)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Severe Lethargy	11 (9%)	4 (36%)	3 (27%)	1*(10%)	1*(10%)	1*(10%)
Photophobia	2 (2%)	2 (100%)	2 (100%)	2 (100%)	1*(100%))	1*(100%)
Any	14 (12%)	6 (43%)	5 (36%)	3*(23%)	2*(18%)	2*(18%)
Neurological Signs:[1]						
None	101 (86%)	62 (61%)	47 (47%)	36*(36%)	24*(26%)	20*(22%)
Dysarthria/ Aphasia	4 (3%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Paralysis	9 (8%)	4 (44%)	3 (33%)	1*(13%)	1*(13%)	1*(13%)
Dementia	10 (9%)	3 (30%)	1 (10%)	0*(0%)	0*(0%)	0*(0%)
Any	16 (14%)	6 (38%)	4 (25%)	2*(13%)	1*(6%)	1*(6%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

1 Patient could have >1 than one of these.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 22

TOTAL SET: PARACLINICAL DATA (LABORATORY DATA)

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Serologies[1]:						
None Positive	69 (59%)	37 (54%)	28 (41%)	23 (33%)	16*(25%)	15*(23%)
Hepatitis B	36 (31%)	23 (64%)	16 (44%)	10*(29%)	7*(21%)	5*(15%)
CMV	9 (8%)	4 (44%)	3 (33%)	3 (33%)	0*(0%)	0*(0%)
Toxoplasmosis	5 (4%)	4 (80%)	3 (60%)	1*(25%)	0*(0%)	0*(0%)
Cryotococcosis	5 (4%)	4 (80%)	4 (80%)	3 (60%)	1*(33%)	1*(33%)
Anergy[1]:						
Not Tested/Unknown	83 (71%)	47 (57%)	36 (43%)	25*(33%)	16*(23%)	12*(18%)
Normal	4 (4%)	3 (75%)	3 (75%)	3 (75%)	1*(33%)	1*(33%)
Partial	4 (4%)	3 (75%)	3 (75%)	2 (50%)	2 (50%)	2 (50%)
Complete	26 (23%)	15 (58%)	9 (35%)	8 (31%)	6*(24%)	6*(24%)
Platelets:						
Not Done	9 (8%)	6 (67%)	5 (56%)	3 (33%)	2 (22%)	2 (22%)
Adeno	73 (62%)	47 (64%)	38 (52%)	30*(42%)	21*(32%)	18*(28%)
Decreased	22 (19%)	7 (32%)	5 (23%)	3*(14%)	1*(5%)	1*(5%)
Increased	13 (11%)	8 (62%)	3 (23%)	2 (15%)	1 (8%)	0*(0%)
Chest Xray Findings[1]:						
Not Done	12 (10%)	9 (75%)	9 (75%)	8 (67%)	5*(45%)	4*(44%)
WNL	32 (27%)	19 (59%)	12 (38%)	8*(26%)	4*(15%)	4*(15%)
Diffuse Infiltrate	60 (51%)	33 (55%)	24 (40%)	16*(27%)	11*(19%)	8*(14%)
Lobular Infiltrate	18 (15%)	10 (56%)	8 (44%)	7 (39%)	6*(35%)	5*(29%)
Cavity Lesions	5 (43%)	1 (20%)	1 (20%)	1 (20%)	1*(25%)	0*(0%)
Head CT[1]:						
Not Done	83 (71%)	52 (63%)	39 (47%)	30 (36%)	20*(26%)	17*(22%)
Normal	18 (15%)	11 (61%)	8 (44%)	6*(35%)	3*(21%)	3*(21%)
Ring Enhancing Lesion	9 (8%)	3 (33%)	2 (22%)	1*(13%)	1*(13%)	1*(13%)
Mass Effect	2 (2%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Other[2]	7 (6%)	2 (29%)	2 (29%)	1 (14%)	1 (14%)	1 (14%)
TOTAL	117 (100%)	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTES:

• Percent of total.

1 Patient could have >1 than one of these.

2 Other included: enlarged ventricles; right cerebellar low density lesion; marked atrophy; shrinkage with increased ventricular size; hypodense area in left frontoparietal area; air fluid level in ethmoid; atrophy.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 23

TOTAL SET: DIMENSIONAL VARIABLES

Variable	N•	Mean	Median	Range	Coefficient of Correlation with Survival in Mos.
Demographics:					
Age	117	35.6	34.0	22-65	-0.05
History Intervals(mos):					
From first Sx to ZT	112	12.3	7.3	0.1-99.9†	0.08
Duration Syst Sx	90	2.8	0.5	0-99.9	0.05
Duration Diarrhea	99	3.0	0.1	0-99.9	0.25*
Duration Pulm Sx	98	2.0	0.7	0-24	0.22*
Weight Loss(lbs):					
Amount	97	19.2	15.0	0-96	-0.05
Period (mos)	74	6.5	4.1	0.3-25	0.21
% Wt Loss	91	5.3	3.0	0-25	0.16
Normal State[1]	41	+10.4	+ 8.0	-28-+79	-0.06
Adm State[1]	41	- 9.7	-13.0	-58-+60	0.05
Highest Fever(F°):	58	102.0	103.0	100-106	-0.12
Physical Exam:					
Temperature	114	100.7	101.0	96-106	0.02
Respiratory Rate	96	24.8	23.0	12-80	-0.05
Paraclinical Data:					
T Cell Studies[2]:					
T4 Count	31	66.3	36.0	0-463	-0.28
T4 %	31	13.3	11.0	0-73	0.03
T8 Count	29	237.8	180.0	8-896	-0.10
T8 %	30	44.5	42.0	8-82	0.23
T4/T8	45	0.3	0.3	0-1	-0.13
Complete Blood Count:					
Hematocrit	117	33.1	33.7	15.6-51.6	0.30**
WBC	117	5.1	4.5	1.1-9.9	-0.05
Calc Lymphs	114	758.9	533.0	0-7,020	0.21*
Platelets	77	219.5	210.0	8-566	0.03
Sedimentation Rate	51	52.5	54.0	10-99	-0.21
Arterial Blood Gas (Rm Air)					
pH	85	7.4	7.4	7.28-7.55	0.07
PCO_2	85	30.9	32.0	19-45	0.04
PO_2	85	74.2	77.0	28-123	0.14
Albumin	71	2.6	2.6	0.7-4.4	0.25*

NOTES:

• Percent of total; * = $P \leq .05$; ** = $P \leq .01$; † = Maximum coding value was 99.9

1 Normal state refers to normal weight & admission state refers to admission weight Patients weights were subtracted from their ideal body weight (IBW; Appendix III) to determine if they were above (+) or below (-) IBW.

2 Some patients only had %'s or T4/T8 ratios given rather than a full T cell count.

TABLE 24

TOTAL SET: SURVIVAL RESULTS, WITHIN STAGES, FOR PATIENTS WITH PROMPT OR DELAYED ZERO TIME

	N•	Median	4	6	8†	10††	12†††
Stage I:							
Prompt ZT	34 (42%)	**9.2**	28 (82%)	23 (68%)	20 (59%)	14*(45%)	12*(40%)
Delayed ZT	9 (25%)	8.3	8 (89%)	7 (78%)	6 (67%)	3*(43%)	3 (43%)
Stage II:							
Prompt ZT	37 (46%)	2.4	15 (41%)	9 (24%)	6 (16%)	4*(11%)	4*(11%)
Delayed ZT	20 (56%)	5.0	12 (60%)	8 (40%)	5*(26%)	4*(22%)	2*(12%)
Stage III:							
Prompt ZT	10 (12%)	2.6	4 (40%)	4 (40%)	1*(11%)	0*(0%)	0*(0%)
Delayed ZT	7 (19%)	1.9	1 (14%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Subtotals:							
Prompt ZT	81 (69%)	5.0	47 (58%)	36 (44%)	27*(34%)	18*(24%)	16*(22%)
Delayed ZT	36 (31%)	5.0	21 (58%)	15 (42%)	11*(31%)	7*(22%)	5*(16%)
TOTAL	117 (100%)	5.0	68 (58%)	51 (44%)	38† (33%)	25†† (23%)	21††† (20%)

NOTES:

• Percent of total.

Bold printed medians are conservative estimates that assume patients die on date of last follow-up.

† At 8 months of total of 2 people censored: 1 at Stage II; 1 at Stage III.

†† At 10 months a total of 10 people censored: 5 at Stage I; 3 at Stage II; 2 at Stage III.

††† At 12 months a total of 12 people censored: 6 at Stage I; 4 at Stage II; 2 at Stage III.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 25

TOTAL SET: STAGING COMPONENTS AND UNIONS

Characteristic	N (%)•	Number (and %) Surviving at Cited Period				
		Median	4 Mo.	6 Mo.	8 Mo.	10 Mo.	12 Mo.
Neurologic Manifestation:							
No	86 (74%)	6.2	57 (66%)	44 (51%)	34*(40%)	23*(29%)	19*(25%)
Yes	31 (26%)	2.1	11 (35%)	7 (23%)	4*(13%)	2*(7%)	2*(7%)
Hypoxia:							
$PO_2 > 50$	102 (87%)	5.3	64 (63%)	48 (47%)	36*(36%)	24*(26%)	20*(22%)
$PO_2 \leq 50$	15 (13%)	1.0	4 (27%)	3 (20%)	2 (13%)	1 (7%)	1 (7%)
**Cytopenia:							
Hematocrit							
≥ 30	83 (71%)	5.8	53 (64%)	41 (49%)	33*(40%)	21*(28%)	19*(26%)
< 30	34 (29%)	2.6	15 (44%)	10 (29%)	5*(15%)	4*(13%)	2*(6%)
WBC							
$\geq 2{,}500$	106 (91%)	5.3	65 (61%)	49 (46%)	38*(36%)	25*(26%)	21*(22%)
$< 2{,}500$	11 (9%)	2.5	3 (27%)	2 (18%)	0*(0%)	0*(0%)	0*(0%)
Platelets							
$\geq 140{,}000$	95 (81%)	5.5	61 (64%)	46 (48%)	35*(37%)	24*(27%)	20*(23%)
$< 140{,}000$	12 (19%)	2.0	7 (32%)	5 (23%)	3*(14%)	1*(5%)	1*(5%)
Cytopenic Severity:							
None	69 (59%)	6.7	40 (70%)	38 (55%)	31 (45%)	20*(32%)	18*(29%)
Cytopenia [1] 1 of 3	31 (26%)	3.6	15 (48%)	9 (29%)	6*(20%)	5*(17%)	3*(11%)
BMF[2] ≥ 2 of 3	17 (15%)	2.1	5 (29%)	4 (24%)	1*(6%)	0*(0%)	0*(0%)
TOTAL	117 (100%)	5.0	68 (58%)	51 (44%)	38*(33%)	25*(23%)	21*(20%)

NOTE:

• Percent of total.

[1] Cytopenia refers to any 1 of 3 possible cytopenias (HCT < 30; WBC < 2,500; or PLTS < 150,000).

[2] BMF (bone marrow failure) refers to the presence of ≥ 2 cytopenias.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

TABLE 26

TOTAL SET: STAGING SYSTEM

STAGE[1]	N (%)•	Median (mos.)	Number (and %) Surviving at Cited Period				
			4 Mo.	6 Mo.	8 Mo.†	10 Mo.††	12 Mo.†††
I	43 (38%)	**9.2**	36 (84%)	30 (70%)	26 (60%)	17*(45%)	15*(41%)
II	57 (49%)	3.5	27 (47%)	17 (30%)	11*(20%)	8*(15%)	6*(11%)
III	17 (15%)	2.1	5 (29%)	4 (24%)	1*(6%)	0*(0%)	0*(0%)
TOTAL	117 (100%)	5.0	68 (58%)	51 (44%)	38 (33%)†	25 (23%)††	21 (20%)†††

NOTES:

1 For description of the stages, see Table 11 and text.

• Percent of total.

* Some of data are "censored" because the patients have not yet had a chance to live this long. The percentages have been calculated for the appropriate denominator of people followed for at least as long as the cited period of time.

Median values in bold print (Stage I) are conservative estimates that assume patients died on date of their last follow-up while alive.

† At 8 months, a total of 2 patients are censored: 1 in Stage II; 1 in Stage III.

†† At 10 months, a total of 10 patients are censored: 5 in Stage I; 3 in Stage II; and 2 in Stage III.

††† At 12 months a total of 12 patients censored: 6 in Stage I; 4 in Stage II 2 in Stage III.

TABLE 27

TOTAL SET: ROTHENBERG VARIABLES VS. STAGING SYSTEM

Note: Each cell of this table has three components. The first is N, the number of members in the cell. The second shows the percentage who have survived six months or more. The third number shows the median survival in months.

Variable	Stage I	Stage II	Stage III	Total
Sex:				
Male	31: 71%, 9.2	45: 29%, 3.5	13: 15%, 1.9	89: 42%, 5.0
Female	12: 67%, 9.3	12: 33%, 4.0	4: 50%, 5.1	28: 50%, 6.0
Race:				
White	17: 65%, 9.2	26: 42%, 4.6	8: 13%, 2.2	51: 45%, 5.1
Black	19: 79%, 9.2	23: 22%, 3.5	8: 38%, 2.3	50: 46%, 5.1
Hispanic	7: 57%, 7.8	6: 13%, 1.8	1: 0%, 0.5	16: 31%, 3.3
Age:				
< 30	7: 100%, 13.2	16: 31%, 4.6	4: 0%, 2.0	27: 44%, 5.1
30-34	16: 63%, 8.1	13: 8%, 3.1	6: 17%, 1.8	35: 34%, 4.1
35-39	10: 50%, 6.2	11: 73%, 9.8	2: 50%, 3.6	23: 61%, 6.6
≥ 40	10: 80%, 9.9	17: 18%, 2.1	5: 40%, 3.1	32: 41%, 4.2
Exposure:				
Homosexual	14: 64%, 8.8	24: 38%, 3.3	6: 0%, 1.8	44: 41%, 4.7
IVDA	17: 76%, 8.2	22: 23%, 3.7	8: 38%, 2.7	47: 45%, 5.1
Homosexual & IVDA	4: 50%, 7.1	4: 0%, 2.4	1: 0%, 2.7	9: 22%, 3.2
Other Only††	8: 75%, 12.2	7: 43%, 4.1	2: 50%, 4.3	17: 59%, 8.3
Presenting Diseases:				
KS Only	3: 67%, 9.2	4: 25%, 1.5	1: 0%, 5.5	8: 38%, 5.3
KS & PCP Only	0: -- , --	2: 50%, 4.0	0: -- --	2: 50%, 4.0
KS & Other†	1: 100%, 8.3	0: -- , --	1: 0%, 1.9	2: 50%, 5.1
PCP Only	31: 71%, 9.2	24: 33%, 4.2	9: 33%, 1.9	64: 52%, 6.3
PCP & Other†	1: 100%, 10.0	7: 14%, 2.4	1: 0%, 2.7	9: 22%, 2.7
1 Other Only	7: 57%, 6.1	20: 30%, 3.9	4: 25%, 2.3	31: 35%, 4.2
2 or More Other†	0: -- , --	0: -- , --	1: 0%, 0.7	1: 0%, 0.7
TOTAL	43 (37%)	57 (49%)	17 (15%)	117 (100%)

NOTES:

† In Rothenberg et al., other MAI, Candida esophagitis, Crytococcus, toxoplasmosis, brain Ca, and "Other Dx".

†† In Rothenberg et al., Other included transfusion exposure, heterosexual exposure.

TABLE OF APPENDICES

APPENDIX Ia

WHO/CDC CASE DEFINITION FOR ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

For surveillance purposes, a relatively precise case definition is required that includes the most characteristic manifestations of HIV[1] infections. WHO recently adopted the case definition of AIDS in adults and children developed by the Centers for Disease Control (CDC) and endoresed by the participants at the Second Meeting of the WHO Collaborating Centres on AIDS held in Geneva 16-18 December 1985. The WHO/CDC definition, to be applied incountries where appropriate diagnostic techniques are available specifies that a case of acquired immunodeficiency syndrome (AIDS) is an illness characterized by:

I. one or more of the opportunistic diseases listed below (diagnosed by methods considered reliable) that are at least moderately indicative of underlying cellular immunodeficiency: and

II. absence of all known underlying causes of cellular immunodeficiency (other than HIV infection) and absence of all other causes of reduced resistance reported to be associated with at least one of those opportunistic diseases.

Despite having the above, patients are excluded as AIDS cases if they have negative results on testing for serum antibody to HIV,* do not have a positive culture for HIV and have both a normal or high number of T-helper (OKT4 or LEU3) lymphocytes and a normal or high ratio of T-helper to T-suppressor (OKT8 or LEU2) lymphocytes. In the absence of test results, patients satisfying all other criteria in this definition are included as cases.

This general case definition may be made more explicit by specifying:

I. the particular diseases considered at least moderately indicative of cellular immunodeficiency, which are used as indicators of AIDS: and

II. the known causes of cellular immunodeficiency or other causes of reduced resistance reported to be associated with particular diseases, which would disqualify a patient as an AIDS case.

I. Diseases at least moderately indicative of underlying cellular immunodeficiency:

In the following list of diseases, the required diagnostic methods with positive results are shown in parentheses. "Microscopy" may include cytology.

A. Protozoal and helminthic infections:

1. cryptosporidiosis, intestinal, causing diarrhoea for over 1 month (on histology or stool microscopy):

2. Pneumocystis carinii pneumonia (on histology, or microscopy of a "touch" preparation, bronchial washings, or sputum);

3. strongyloidosis, causing pneumonia, central nervous system infection, or infection disseminated beyond the gastrointestinal tract (on histology);

4. toxoplasmosis, causing infection in internal organs other than liver, spleen, or lymph nodes (on histology or microscopy of a "touch" preparation).

B. Fungal infections:

1. candidiasis, causing oesophagitis (on histology, or microscopy of a "wet" preparation from the oesophagus, or endoscopic or autopsy findings of white plaques on an erythematous mucosay base, but not by culture alone);

2. cryptococcosis, causing central nervous system or other infection disseminated beyond lungs and lymph nodes (on culture, antigen detection, histology, or Indian ink preparation of CSF).

C. Bacterial infections:

1. Mycobacterium avium or intracellulare (M. avium complex), or M. kansasii, causing infection disseminated beyond lungs and lymph nodes (on culture).

D. Viral infections:

1. cytomegalovirus causing infection in internal organs other than liver, spleen, or lymph nodes (on histology or cytology, but not by culture or serum antibody titre);

2. herpes simplex virus, causing chronic mucocutaneous infection with ulcers persisting more than 1 month, or pulmonary, gastrintestinal tract (beyond mouth, throat, or rectum), or disseminated infection (but not encephalitis alone) (on culture, histology, or cytology);

3. progressive multifocal leukoencephalopathy (presumed to be caused by papovavirus) (on histology).

E. Cancer:

1. Kaposi's sarcoma (on histology);

2. lymphoma limited to the brain (on histology).

F. Other opportunistic infections with positive tests for HIV.** In the absence of the above opportunistic diseases, any of the following diseases is considered indicative of AIDS if the patient had a positive test for HIV:**

1. disseminated histoplasmosis (on culture, histology, or cytology);

2. bronchial or pulmonary candidiasis (on microscopy or visualization grossly of characteristic white plaques on the bronchial mucosa, but not by culture alone);

3. isosporiasis, causing chronic diarrhoea (over 1 month) (on histology or stool microscopy).

G. Chronic lymphoid interstitial pneumonitis:

In the absence of the above opportunistic diseases, a histologically confirmed diagnosis of chronic (persisting over 2 months) lymphoid interstitial pneumonitis in a child (under 13 years of age) is indicative of AIDS unless test(s) for HIV are negative.** The histological examination of lung tissue must show diffuse interstitial and peribronchiolar infiltration by lymphocytes, plasma cells with Russell bodies, plasmactoid lymphocytes and immunoblasts. Histological and culture evaluation must not identify a pathogenic organism as the cause of this pneumonia.

H. Non-Hodgkin's lymphoma with postive test for HIV:**

If the patient had a positive test for HIV, then the following histological types of lymphoma are indicative of AIDS regardless of anatomic site:

1. small non-cleaved lymphoma (Burkitt's tumor or Burkitt-like lymphoma), but not small cleaved lymphoma;

2. immunoblastic sarcoma (or immunoblastic lymphoma) of B-cell or unknown immunological phenotype (not of T-cell type). Other terms which may be equivalent include: diffuse undifferentiated non-Hodgkin's lymphoma, large cell lymphoma (cleaved or non-cleaved), diffuse histiocytic lymphoma, reticulum cell sarcoma, and high-grade lymphoma.

Lymphomas should not be accepted as indicative of AIDS if they are described in any of the following ways: low grade, of T-cell type (immunological phenotype), small cleaved lymphoma, lymphocytic lymphoma (regardless of whether well or poorly differentiated), lymphoblastic leukaemia (acute or chronic), or Hodgkin's disease (or Hodgkin's lymphoma).

II. Known causes of reduced resistance:

1. Systemic corticosteroid therapy:

Any infection diagnosed during or within 1 month after discontinuation of the corticosteroid therapy, unless symptoms specific for an infected anatomic site (e.g.,dyspnea for pneumonia, headache for encephalitis, diarrhoea for colitis) began before the corticosteroid therapy;

or any cancer diagnosed during or within 1 month after discontinuation of more than 4 months of long-term corticosteroid therapy, unless symptoms specific for the anatomic sites of the cancer (as described above) began before the long-term corticosteroid therapy.

2. Other immunosuppressive or cytotoxic therapy:
Any infection diagnosed during or within 1 year after discontinuation of the immunosuppressive therapy, unless symptoms specific for an infected anatomic site (as described above) began before the long-term corticosteroid therapy.

or any cancer diagnosed during or within 1 year after discontinuation of more than 4 months of long-term immunosuppressive therapy, unless symptoms specific for the anatomic sites of the cancer (as described above) began before the long-term therapy.

3. Cancer of lymphoreticular or histiocytic tissue such as lymphoma (except for lymphoma localized to the brain). Hodgkin's disease, lymphocytic leukaemia or multiple myeloma.

   Any infection or cancer, if diagnosed after or within 3 months before the diagnosis of the cancer of lymphoreticular or histiocytic tissue.

4. Age 60 years or oder at diagnosis:
   Kaposi's sarcome given that the patient has a positive test for HIV.

5. Age under 28 days (neonatal) at diagnosis:
   Tomoplasmosis or herpes simplex virus infection as described above.

6. Age under 6 months at diagnosis:
   Cytomegalovirus infection, as described above.

7. An immunodeficiency atypical of AIDS, such as one involving hypogammaglobulinaemia or angioimmunoblastic lymphadenopathy; or an immunodeficiency of which the cause appears to be a genetic or developmental defect, rather thay HIV infection:
   Any infection or cancer diagnosed during such immunodeficiency.

8. Exogenous malnutrition (starvation due to food deprivation, not malnutrition due to malabsorption or illness).

   Any infection or cancer diagnosed during or within 1 month after discontinuation of starvation.

Notes:

1 From the Weekly Epidemiological Record of the World Health Organization, March 7, 1986 issue.

2 For simplicity, HIV has been substituted throughout this copy where LAV/HTLV-III was originally used. They are equivalent terms.

* A single negative test for HIV may be applied here if it is an antibody test by ELISA immunofluorescent, or Western blot methods, becuase such tests are very sensitive. Viral cultures are less sensitive but more specific, and so may be used only if positive but not if negative. If multiple antibody tests have inconsistent results the result applied to the case definition should be that of the majority. A positive culture, however would overrule negative antibody tests.

** A postive test for HIV may consist of a reactive test for antibody to HIV or a positive culture (isolation of HIV from a culture of the patient's peripheral blood lymphocytes). If multiple antibody tests have inconsistent results, the result applied to the case definition should be that of the majority done by the ELISA immunoflorescent or Western blot methods. A positive culture, however, would overrule negative antibody tests.

tient's Name: _____ Telephone No.: (___) _____

ddress: _____

ACQUIRED IMMUNODEFI
ADULT CONFIDEN
(Patients ≥13 years of

EPARTMENT OF HEALTH AND HUMAN SERVICES
UBLIC HEALTH SERVICE
ENTERS FOR DISEASE CONTROL
IDS PROGRAM, CID, ATLANTA, GEORGIA 30333

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) ADULT CONFIDENTIAL CASE REPORT

(Patients ≥13 years of age at time of diagnosis)

FORM APPROVED
OMB NO. 0920-0009

This report is authorized by law (Sections 304 and 306 of the Public Health Service Act, 42 USC 242b and 242k). Response in this case is voluntary for federal government purposes, but may be mandatory under state and local statutes. Your cooperation is necessary for the understanding and control of AIDS. Information in the surveillance system that would permit identification of any individual or establishment is collected with a guarantee that it will be held in confidence, will be used only for the purposes stated in the assurance on the reverse of the form, and will not otherwise be disclosed or released without the consent of the individual or the establishment in accordance with Section 308(d) of the Public Health Service Act (42 USC 242m).

DATE FORM COMPLETED Mo. ☐☐ Day ☐☐ Year ☐☐

CDC PATIENT NUMBER ☐☐☐☐☐☐☐

HEALTH DEPARTMENT USE ONLY

SOUNDEX NAME CODE ☐☐☐☐

STATUS OF THIS REPORT
1 New Case
2 Update Report

REPORTING HEALTH DEPARTMENT
State _____
City/County _____

STATE PATIENT NUMBER ☐☐☐☐☐☐☐☐☐☐

CITY/COUNTY PATIENT NUMBER ☐☐☐☐☐☐☐☐☐☐

I. BASIC PATIENT INFORMATION

DATE OF BIRTH Mo. ☐☐ Day ☐☐ Year ☐☐

AGE AT DIAGNOSIS OF AIDS Years ☐☐

CURRENT STATUS
1 Alive 2 Dead
9 Unknown

DATE OF DEATH Mo. ☐☐ Day ☐☐ Year ☐☐

SEX
1 Male 2 Female

RACE/ETHNICITY
1 White (not Hispanic) 2 Black (not Hispanic) 3 Hispanic
4 Asian/Pacific Islander 5 American Indian/Alaskan Native 9 Not Specified

COUNTRY OF BIRTH
1 U.S. 2 Canada 3 Dominican Republic 4 Haiti
5 Mexico 8 Other (specify) _____

RESIDENCE AT ONSET OF ILLNESS SUGGESTIVE OF AIDS:
City _____ County _____
Zip Code ☐☐☐☐☐
State/Country _____

HOSPITAL WHERE DIAGNOSIS OF AIDS ESTABLISHED:
Name _____
City _____ State/Country _____

II. SOCIAL AND RISK FACTORS

AFTER 1977 AND PRECEDING THE DIAGNOSIS OF AIDS, DID THIS PATIENT: (check all that apply)

	Yes	No	Unk
• Have sexual relations with a male partner?	1	0	9
• Have sexual relations with a female partner?	1	0	9
• Use needles for self-injection of drugs not prescribed by a physician?	1	0	9
• Receive any blood products (i.e., factor VIII or IX, cryoprecipitate, or fibrinogen) for the treatment of a coagulation disorder?	1	0	9
• If yes, specify disorder: 1 Hemophilia A (factor VIII) 2 Hemophilia B (factor IX) 8 Other, specify: _____			
• Have heterosexual relations with any of the following: (check all that apply)			
• I.V. drug abuser	1	0	9
• Bisexual man	1	0	9
• Person with hemophilia/coagulation disorder	1	0	9
• Blood transfusion recipient with AIDS or documented HIV infection	1	0	9
• Person with AIDS or documented HIV infection	1	0	9
• Person born in a country where heterosexual transmission predominates, (e.g., African or Caribbean country) Specify country: _____	1	0	9
• Has patient received a transfusion of blood/blood components?	1	0	9
• If yes, and this is only risk factor, give date of first and last transfusion: First Mo. ☐☐ Yr. ☐☐ Last Mo. ☐☐ Yr. ☐☐			
• Work in a health-care or clinical laboratory setting?	1	0	9
• If yes, specify occupation: _____			

SYNDROME (AIDS)
SE REPORT
ne of diagnosis)

Physician's Name: _____ Telephone No.: (___) _____

Hospital: _____ Medical Record No.: _____

Person Completing Form: _____ Telephone No.: (___) _____

III. DISEASES INDICATIVE OF AIDS (check all that apply)

DISEASE	DIAGNOSIS Definitive*	DIAGNOSIS Presumptive
idiasis, bronchi, trachea, or lungs	1	NA
idiasis, esophageal	1	2
idioidomycosis, disseminated or xtrapulmonary	1	NA
itococcosis, extrapulmonary	1	NA
itosporidiosis, chronic intestinal	1	NA
megalovirus disease (other than in liver, pleen, or nodes)	1	NA
megalovirus retinitis (with loss of vision)	1	2
encephalopathy	1	NA
es simplex: chronic ulcer(s) (>1 mo. duration); onchitis, pneumonitis, or esophagitis	1	NA
plasmosis, disseminated or extrapulmonary	1	NA
poriasis, chronic intestinal (>1 mo. duration)	1	NA

DISEASE	DIAGNOSIS Definitive*	DIAGNOSIS Presumptive
Kaposi's sarcoma	1	2
Lymphoma, Burkitt's (or equivalent term)	1	NA
Lymphoma, immunoblastic (or equivalent term)	1	NA
Lymphoma, primary in brain	1	NA
Mycobacterium avium complex or *M. kansasii*, disseminated or extrapulmonary	1	2
M. tuberculosis, disseminated or extrapulmonary	1	2
Mycobacterium, of other species or unidentified species, disseminated or extrapulmonary	1	2
Pneumocystis carinii pneumonia	1	2
Progressive multifocal leukoencephalopathy	1	NA
Salmonella septicemia, recurrent	1	NA
Toxoplasmosis of brain	1	2
Wasting syndrome due to HIV	1	NA

*Refer to instructions on back for definition of definitive diagnosis.

Of diseases checked above, date first disease diagnosed: Mo. ☐☐ Yr. ☐☐

IV. LABORATORY DATA

IV SERUM ANTIBODY TESTS:

	Pos	Neg	Inc*	Not Done
ELISA	1	0	8	9
Western blot/immunofluorescence assay	1	0	8	9
Other (specify) _____	1	0	8	9

*Inc = Inconclusive

IV DETECTION TESTS:
Applicable only if serum antibody tests are not positive.)

	Pos	Neg	Inc*	Not Done
Culture of HIV confirmed by both specific HIV antigen test and reverse transcriptase detection	1	0	8	9
HIV serum antigen test	1	0	8	9
Other HIV test (specify) _____	1	0	8	9

*Inc = Inconclusive

HIV tests were not positive or were not done, does this patient have an immunodeficiency that would disqualify him/her from the AIDS case definition?

Yes	No	Unk
1	0	9

S ABSOLUTE T-HELPER LYMPHOCYTE COUNT <400 per mm^3 ?
(Applicable only if tests results are negative for HIV infection.)

Yes	No	Unk
1	0	9

V. ADDITIONAL INFORMATION OR COMMENTS

APPENDIX II

CDC COMPOSITE CLASSIFICATION SYSTEM FOR HIV INFECTIONS

Group I	Acute Infection: HIV positive with an acute, mononucleosis-like symdrome.
Group II	Asymptomatic Infection: no history of any ARC symptoms. Subclassifications include lymphopehia, thrombocytopenia, and decreased numbers of T_4 cells.
Group III	Persistent Generalized Lymphadenopathy: palpable lymphadenopathy (nodes $\geq$ to 1 cm).
Group IV	Other HIV Disease: (each subgroup may include patients who are minimally symptomatic as well as patients who are severely ill.)
Subgroup A	Constitutional Disease: one or more of the following: fever > 1 month, weight loss > 10% of baseline, diarrhea > 1 month, and absence of concurrent illness other than HIV to explain findings.
Subgroup B	Neurologic Disease: one or more of the following: dementia, myelopathy, or periferal neuropathy; and the absence of a concurrent illness or condition, other than HIV infection to explain the findings.
Subgroup C	Secondary Infectious Diseases: the diagnosis of an infectious disease associated with HIV infection or at least moderately indicative of a defect in cell-mediated immunity.
C-1	Any of the 12 OI's that qualifies for the diagnosis of AIDS.(see appendix I).
C-2	One of the 6 following diseases: oral hairy Leukoplakia, multidermal herpes zoster, recurrent salmonella bacteremia, nocardiosis, tuberculosis, or oral candidiasis.

Subgroup D	Secondary Cancers: one of the following: K.S., non-Hodgkins lymphoma (small noncleaved lymphoma or immunoblastic sarcoma), or primary lymphoma of the brain.)
Subgroup E	Other Conditions in HIV Infection: chromic lymphoid interstitial pneumonitis, or signs and symptoms attributable to HIV infection or co-exisiting disease the course or management of which may be complicated or altered by HIV infection.

APPENDIX III

SUMMARY OF SURVIVAL STUDIES IN AIDS
(All survivals in Months and Tenths of Months)

	San Francisco[41] May'83 n=165	U.K.[42] June'85 n=168	N.Y.C. #1[43]* Jan.'84 n=1,410	N.Y.C. #2[44]* Jan.'86 n=5,833
KS	21	21.2	29.2	25.0
PCP	9	12.5	8.2	10.6
KS+PCP	--	6.6	14.2	12.7
Other **	9	13.3	4.2	7.2
KS+Other	--	--	15.2	10.8
PCP+Other	--	--	10.3	10.0

Notes:

* Rivin et al.'s data was subsumed in Rothenberg et al. It is reported here because the earlier medians were different than Rothenberg et al.'s findings.

** Other was defined as any OI or neoplasm that qualified for the AIDS diagnosis excluding PCP or KS.

__Form Complete:

__Clinic Chart
__In-patient Record:
# of Volumes_____
Volumes done:

__Other Records to Review
__Records Not Available

Code Number_____

Date Begun_____

-EXTRACTION FORM-

EMOGRAPHICS

D.O.B._____ Age_____ Race_____
Sex: M F Marital Status: S M W D Sep
Religion:_____
Residence:_____
Cohabitants:_____
Occupation:_____
Occupational Status:_____

ISK CATEGORY

__Homosexual Male __IVDA __Blood Trans.
__Haitian __Sexual Partner __N.K.R.
Last known Exposure:_____
notes:

NTERVALS

Zero Time_____ Date of Death_____
Date Last Doc. Alive_____
Source_____
* to Admission_____ *to ZT_____
= to admission_____ = to ZT_____
Adm to ZT_____ ZT to end_____

ZT DIAGNOSIS

__P.C.P. __P.C.P. & R.F. __M.A.I.
__K.S. __Other (_____)

NECROPSY

#_____ date_____

(was the brain evaluated?)

Co-Morbidity

__Hepatitis Exposure:

__Cigarette Smoker __ppdx ___yrs.
__complications

__EtOH Abuse ___/d. x _____yrs.
__complications

__IVDA
__complicaitons

__Psychiatric Hx.

__Other

Medications
(close to ZT steroids?, antibx?,
drugs known to alter C.B.C.'s?)

Pre-Zero Time Line

History

Chief Complaint:

Weakness
Fatigue
Malaise

Anorexia

Weight Loss

Fever
Sweats
Chills

Dysphagia

Myalgias
Arthralgias

Lymphadenopathy: by hx / by pre-ZT exam / other poss. causes / site & size / period present

GI Sx's: cramps / pain / nausea / vomiting / diarrhea: previous w/u / frequency / amount / period present

Rash: by hx / by pre-ZT exam / dx'd as: / site / period present

Pulmonary Sx's: dyspnea / cough: prod / non-prod / hoarseness / chest pain: pleuritic / nonpleuritic / period sx's present:

Neurologic Sx's: headache / personality/cognitive / dementia / altered level of consciousness / convulsions / focal sensory/motor / retinitis

Other Sx's:

notes:

ZT Exam

overall appearance:

Temp._____ Resp. Rate_____

__Oral Thrush? __ K.S.-like lesions?

___Lymphadenopathy?
__"shotty cervical"
__cervical
__submandibular
__axillary
__inguinal

ZT Paraclinical Data

T Cell Studies:

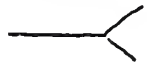
T_4_____ T_8_____ T_4/T_8_____

date_____ source_____

time before ZT_____

Cutaneous Anergy:
__anergic __normal
__Tetanus __Trichophyton
__Mumps __Candida __PPD
date placed_____ &read_____

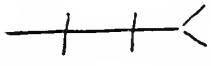
C.B.C.&Diff:



S/ B/ L/ M/ E/

Plts: Sed. Rate:

PT / PTT /

Chemistry: 

Rm Air Blood Gas: / / /
pH CO_2 O_2

Diffusion Capacity:

Nutr. Consult? date_____

Weight

Reported Ave Wt_____ Calc Ave Wt_____
Adm Wt_____ Calc Wt Loss_____
Reported Wt Loss_____ %Wt Loss _____
Height_____ Index B. Wt_____

T.protien/albumin_____

Radiology:

D.N.R. STATUS

__Never Discussed
__Discussed
  __Not Established
  __Established, date_____
    __antibx
    __pressors
    __intubation
    __C.P.R.
    __other

    __est. prior to code
    __est. s/p code
      __pt unresponsive
      __pt responsive
__Discussed with patient
__Discussed with patient's family

__Patient died
  _____time after status established

notes:

BRONCHOSCOPIES

findings	date	source

BIOPSIES

tissue	findings	date/source

RADIOLOGIC STUDIES

study	findings	date	source

O.I.'s AND CANCER TABULATION SHEET note pzt or s/pzt

-viral-

Adenovirus

Cytomegalovirus

Herpes Simplex chronic mucocutaneous
other

JC Virus (papova virus) progressive multifocal leukoencephalopathy

Oral Hairy Leukoplakia

-fungal-

Aspergillus fumigatus (& other species)

Candida albicans

Cryptococcus neoformans

Coccidioides immitis

Histoplasma capsulatum

Zygomycosis (several species)

-protozoal & helminthic-

Cryptosporidia spp chronic enterocolitis
other

Isospora belli chronic enterocolitis
other

Pneumocystis carinii

Strongyloides stercoralis

Toxoplasma gondii

-bacterial-

Non-tuberculin mycobacteria avium
kansasii

Tuberculin mycobacteria

Nocardia asteroides

Lysteria monocytogenes

Salmonella

-N.B. for each of the O.I.'s above note site of infection (i.e. pneumonia, meningitis, encephalitis, esophagitis, disseminated, other or not known), source of evidence of infection (i.e. blood cx on 9/17/84 / 999 : for candida 1/3 one dream., info taken directly from lab slip, dc)

-cancers-

Kaposi's Sarcoma < 10 lesions or one anatomic site oral lymph nd
> 10 lesions or > one anatomic site cutan/visceral
systemic signs/sx's: fever (37.8 ? sks no IO'd infect)
weight loss (10% BW)

Non-Hodgkin's Lymphoma (histologic grade?)

Primary lymphoma of the brain

Other:

Notes:

FORM COMPLETED: Date:

AIDS EXTRACTION FORM

CLINIC CHART _____
INPT CHART _____

NOTES

CODING

ID

CODE	AGE	RACE	SEX
[ ] [ ] [ ] [ ]	[ ] [ ]	[ ] 1 W	[ ] 1 M
(1) (2) (3) (4)	(5) (6)	(7) 2 B	(8) 2 F
		3 H	
		4 O	

RISK

IVDA	HOMOM	HETERO	BLOOD TRANS
[ ] 0 NKR	[ ] 0 NKR	[ ] 0 NKR	[ ] 0 NKR
(9) 1 +	(10) 1 +	(11) 1 +	(12) 1 +

ZT Hx Date & Dx:

PCP	MAI	KS	CRYPTO	TOXO
[ ] 0 None	[ ] 0 None	[ ] 0 None	[ ] 0 None	[ ] 0 None
(13) 1 +	(14) 1 +	(15) 1 +	(16) 1 +	(17) 1 +

CC:

BRAIN CA	CANDIDA ESOPHAGITIS	OTHER
[ ] 0 None	[ ] 0 None	[ ] 0 None
(18) 1 +	(19) 1 +	(20) 1 +

* → ZT	WT LOSS	RPT LOSS/PERIOD
[ ] [ ] .[ ] mo	[ ] 1 None	[ ] [ ] lbs in [ ] [ ] .[ ] mo
(21) (22) (23)	(24) 2 +	(25) (26) (27) (28) (29)

SYSTEMIC Sx's:

F/C/NS	HIGHEST F	PERIOD OF S. Sx's
[ ] 0 None	[ ] [ ] [ ] F	[ ] [ ] .[ ]
(30) 1 Fever	(31) (32) (33)	(34) (35) (36)
2 Chills		
4 Night Sweats		

LN & SKIN:

LN	SKIN LESIONS	EXTENT
[ ] 0 None	[ ] 0 None	[ ] 0 None
(37) 1 +	(38) 1 KS-like	(39) 1 One Loc, ≤ 10 Lesions
	2 Herpetic	2 Two Loc, or > 10 Les
	4 Rash	3 > Three Loc

GI:
(Sig Diarrhea= Constant × ≥1 mo)

Hx OF THRUSH	FREQ DIARRHEA	PERIOD OF D	CLASS OF D
[ ] 0 None	[ ] 0 None	[ ] [ ] .[ ] mo	[ ] 1 not sig
(40) 1 +	(41) 1 Intermit	(42) (43) (44)	(45) 2 sig
	2 Constant		

PULMONARY:

COUGH/CP	DYSPNEA	PERIOD OF P Sx's
[ ] 0 None	[ ] 0 None	[ ] [ ] .[ ]
(46) 1 Cough	(47) 1 DOE	(48) (49) (50)
2 CP-NP	2 At Rest	
4 CP-P		

NEURO:

EYE	ENCEPHALOMENIGEAL	OTHER NEUROLOGIC SYMPTOMS
[ ] 0 None	[ ] [ ] 0 None	[ ] [ ] 0 None
(51) 1 Cotton Wool	(52) (53) 1 Stiff Neck	(54) (55) 1 Dysarthria Aphasia
2 Visual Blur	2 Seizures	2 Paralysis
	4 Severe Lethargy/Conf	4 Dementia
	8 Photophobia	

NOTES:

COMORBIDITY

Hx of REL DZ (56) (57)
0 None
1 Hep B
2 CMV
4 Syph
8 Gono
16 Endocarditis

SEROLOGIES (58) (59)
0 None
1 Hep B+
2 CMV+
4 Toxo+
8 CRYPTO+

ETOH ABUSE (60)
0 None, Social
1 Noted
2 Evidence sd eff (Note)

CIG SMOKING (Note) (61)
0 None
1 < 1 ppd × 10 yrs
2 >1 ppd × 10 yrs

PSYCH Hx (62) (63)
0 None
1 Rel to Homosex
2 Rel to IVDA
4 "Psychotic"
8 Depression/Suicide

ZT EXAM

OVERALL ASSESSMENT:

INPT/OUTPT (64)
1 Inpt (Yale)
2 Outpt
4 Delayed ZT

TEMP (65) (66) (67) F

R.R. (68) (69)

SPECIFIC FINDINGS:

THRUSH (70)
0 None
1 +

LN (71)
0 None
1 Detectable
2 Pronounced

KS (72)
0 None
1 < 10 Lesions One Loc
2 > 10 Lesions Two Loc
3 > Two Loc

EYE (73) (74)
0 None
1 Retinal Abn
2 Other

ENCEPHALOMENIGEAL SIGNS (75) (76)
0 None
1 Stiff Neck
2 Seizures
4 Severe Lethargy
8 Photophobia

OTHER NEUROLOGIC SIGNS (77) (78)
0 None
1 Dysarthria, Aphasia
2 Paralysis
4 Dementia
8 Other

MASS EFFECT (79)
0 None
1 Papill Edema
2 Pupil Dilation

GROUP (80)
1 Devel
2 Chall

T PARACLINICAL DATA

IMMUNOLOGICAL DATA:

CODE # (1) (2) (3) (4)

ANERGY (5)
0 Not Tested
1 Norm
2 Partial
3 Complete

REL TO ZT (6) +0 -1 (7) (8) . (9)

T_4 % (10) (11)

T_4 /µl (12) (13) (14)

T_8 % (15) (16)

T_8 /µl (17) (18) (19)

T_4/T_8 (20) (21) (22)

REL TO ZT (23) +0 -1 (24) (25) . (26) mo

TECH LAB (27)
1 Yale
2 Other

EMATOLOGIC DATA:

	S	B	L	M	E
BC:	/	/	/	/	/

alc Lymp=WBC___ * %L___=___

HCT
[ ] [ ].[ ]
(28) (29) (30)

WBC
[ ] .[ ]
(31) (32)

CALC LYMPHS
[ ] [ ] [ ] [ ]
(33) (34) (35) (36)

PLTS ADEQ?
[ ] 0 Not Measured
(37) 1 ADEQ
2 ↓'d
3 ↑'d

PLTS
[ ] [ ] [ ] K
(38) (39) (40)

BMF
[--] Revised
(41) 1 Single Line Fail
2 Two Lines Fail
3 3 Lines Fail

SED RATE
[ ] [ ] [ ]
(42) (43) (44)

LAB
[ ] 0 ?
(45) 1 Yale
2 Other

ESPIRATORY DATA:
m Air ABG/CXR

pH
[ ] [ ] [ ]
(46) (47) (48)

PCO_2
[ ] [ ]
(49) (50)

PO_2
[ ] [ ] [ ]
(51) (52) (53)

CXR
[ ] [ ]
(54) (55)
0 ?
1 Wnl
2 Diffuse Infilt
4 Lobular Infilt
8 Cavitary Lesion

EUROLOGIC DATA:

HEAD CT
[ ] [ ]
(56) (57)
0 None
1 Wnl
2 Ring Enhancing Lesion
4 Mass Effect
8 Other

T LOSS DATA:
PRO/ALB:
T: → 1BW:
VE WT:
DM WT: → CALC WT LOSS:

ALB
[ ] .[ ]
(58) (59)

NL STATE
[ ] 0+ [ ] [ ]
(60) 1- (61) (62)

ADM STATE
[ ] 0+ [ ] [ ]
(63) 1- (64) (65)

% CALC WT LOSS
[ ] [ ]
(66) (67)

INTERVALS
ZT:
DEATHS:
LAST ALIVE:

ZT
[ ] [ ] / [ ] [ ] / [ ] [ ]
(68) (69) (70) (71) (72) (73)

ALIVE/DEAD
[ ] 0?
(74) 1 Alive
2 Dead

ZT → END
[ ] [ ] .[ ]
(75) (76) (77)

AUTOPSY #_____
Major Dx's:

AUTOPSY
[ ] 0 None
(78) 1 +

SURPRISES ?
[ ] 0 None
(79) 1 +

AZT Dates of Therapy

AZT
[ ] 0 None
(80) 1 +

DNR Date:
Specifications:

Pt_____ Family_____

APPENDIX VI

MANUAL FOR COMPLETION OF EXTRACTION/DATA ENTRY FORM

ORIENTATION:

The form has a space at the top for bookkeeping, a space on the left hand margin for longhand notes, and a coding area on the right for data entry. The numbers underneath spaces on the data-entry portion correspond to columns in a computer format. the numbers go from 1-80 and then repeat.

DEFINITIONS:

Throughout this manual certain definitions apply:

Zero time (ZT): This is the time with which all intervals are measured, including survival. Zero time is either the day upon which the patient was diagnosed as having AIDS by CDC criteria (see Appendix I), or an YNHH admission to medicine or neurology or a visit to the AIDS clinic at YNHH following the actual date of diagnosis. For a more specific explanation see "determining Zero Time" below and Appendix VII.

Interval (*-): An interval is the time elapsed between two date points (one of which is always zero time). It is recorded in 30-day months and tenths of months (.1 month equals 3 days, 2 days are rounded up to .1, 1 day is rounded down to 0.) For example, if a patient had ZT 6/23/83 and died on 9/30/83, the patient's survival interval would be recorded as 3.2 months.

Recent: any history or physical examination recorded within one month of ZT.

Sufficient data for an extraction: There must be a recent history and physical exam that are reasonably complete and at least a complete blood count.

Additive: Certain variables such as F/C/NS are noted as "additive". This simply means that a given patient may have more than one of the symptoms or signs listed. Simply add up the score and enter the total. A patient with fevers and chills would have a score of 3, a patient with chills and night sweats would have a score of 6, and a patient with all three symptoms would have a score of 7.

BOOKKEEPING:

The top section of the form is used to keep track of the progress of the extraction. It includes the date the extraction began, and the number of inpatient volumes that exist and that have been reviewed. Note the existence of and reviewed status of an outpatient file (designated by a yellow sticker on its outside). A separate index card is kept for each patient's identification number and name. This card can be used to note any problems in completing the extraction and the final outcome (i.e. "extraction complete" or "lost to follow up" or "volume V never found therefore extraction done after original diagnosis" etc.)

DETERMINATION OF ZERO TIME (ZT):

Locating the "zero time admission" involves several steps (see Figure 2). First, using the WHO/CDC criteria in Appendix I, determine the time at which the patient first meets the criteria for the AIDS diagnosis. If this diagnosis was made at YNHH, either as an inpatient or as an outpatient, and if there are sufficient records for an extraction, then ZT is the date on which the CDC criteria were satisfied. If the data are insufficient, or if the patient was originally diagnosed at an outside hospital, then ZT is the date of the first recorded visit after diagnosis to the YNHH AIDS Clinic or admission to YNHH, for which sufficient data are available for an extraction.

Note that all information available up to the designated zero time can be used in extraction of the ZT history, ZT physical exam, and ZT paraclinical data. Any data that becomes available after ZT is not eligible for classifying patients at ZT, but pertinent post-ZT events and findings should be noted within the left margin if they shed light on the patient's eventual outcome.

Patient's height, AZT therapy, DNR status, T cell studies, Anergy Panel and Autopsy data should be coded whether or not it occured at ZT. Be sure to note the interval between the time of the anergy panel, the T cell studies, and the AZT therapy and ZT. This data will have to be analyzed separately since it was not collected prior to or on ZT.

IDENTIFICATION AND DEMOGRAPHIC DATA (1-8):

1-4. ID Code: write the patient's full 7 digit hospita unit number in left margin of the form. Enter last four digits on code sheet in these columns.

5-6. Age: calculated from birth date on ER sheet or ID card. Cite as age on last birthday before ZT.

7. Race: the consensus of the emergency room sheet and what is reported on the history and physical exams.

8. Sex: as reported in physical exam.

ZT HISTORY:

Any history, physical exam or paraclinical tests performed prior to ZT are available data for ZT history. Also any history recorded on ZT is available. If a specific symptom is occassionally mentioned, but not uniformly, and is not specifically denied in any history, assume it is present. If histories have conflicting accounts of specific symptoms, time periods, etc, give most weight to the medical student's history and to those histories that seem most complete. If there seems to be a great deal of controversy take a consensus account and note the controversy in the left margin.

RISK (9-12):

for each category of risk code 0 for No Known Risk (NKR), 1 for a positive history.

9. IVDA: any record of intravenous drug abuse.

10. HOMOM: any record of male homosexual intercourse.

11. HETERO: heterosexual partner of an individual known to be at high risk (i.e. to be an IVDA, Homom, Blood Trans) or known to be HIV positive.

12. BLOOD TRANS: any hemophiliac or anyone else receiving large amounts of blood or blood products within the last 10 years.(Note within left margin nature of transfusions and when they were recieved.)

ZT DIAGNOSTIC COMPONENT (13-20):

13. PCP: Pneumocystis carinii identified via gram stain or silver stain of sputum, bronchial washings, or bronchial biopsy.

14. MAI: Cultures from blood, urine, sputum, or surgical specimens positive for any strain of atypical mycobacterium (and not considered merely a contaminate).

15. KS: Skin punch biopsy proven Kaposi's Sarcoma.

16. Crypto: Cryptococcus identified in either cerebral spinal fluid via a positive india ink test or a positive antigen titer, or Cryptococcus cultured or identified on smear of blood.

17. Toxo: Toxoplasmosis identified in brain biopsy specimen or in organs other than liver, spleen, or lymph nodes.

18. Brain Ca: Brain biopsy proven lymphoma or progressive multifocal leukoencephalopathy (PML).

19. Candida Esophagitis: Endoscopic biopsy positive for fungal elements.

20. Other: (see WHO paper in Appendix I) Any other opportunistic infection that qualifies for the diagnosis of AIDS.

21-23. *-ZT: Interval from first symptoms attributable to AIDS or ARC, to ZT.

SYSTEMIC SYMPTOMS (24-36):

24. Wt Loss: 1-(None) if patient reports no weight loss; 2-(present) if he/she reports any.

25-26. Rpt Loss: Record number of pounds reported lost.

27-29. Period: Interval over which weight was lost.

30. F/C/NS: (additive) Fever, chills, and/or night sweats. Positive if symptoms reported in any history within the *-ZT interval.

31-33. Highest F: Highest fever by patient's report or previous physical exam or admission fever if it is highest.

34-36. Period of S.Sx's: Period over which systemic symptoms (fever/chills/night sweats) have been present.

LN & SKIN (37-39):

37. LN: Positive if lymph nodes are enlarged by patient's account or on physical examination prior to ZT.

38. Skin Lesions: (additive) KS-like lesions positive if patient reports purplish maculo-papular lesions, Herpetic positive if clustered vesicular lesions reported, and Rash positive if purpuric lesions present.

39. Extent: if KS-like lesions present record only extent of KS; if no KS, but Herpetic lesions record only for Herpetic lesions; if only rash present, record for rash. One location equals one arm, one leg, or one quadrant of dorsal or ventral torso.

GI (40-45):

40. Oral Thrush: positive if present by previous exam or if patient reports dysphagia or actually seeing white plaques on the inside of his/her mouth.

41. Freq Diarrhea: 1 if diarrhea described as occasional or intermittent; 2 if described as loose, watery or requiring persistent use of opioids (e.g. Lomotil).

42-44. Period of Diarrhea: Interval over which diarrhea has been a problem.

45. Class of Diarrhea: If #41 = 2 and #42 through 44 $\geq$ one month than class is "significant" (#45 = 2). If data missing or period of severity less, than #45 = 1.

PULMONARY (46-50):

46. Cough/CP: (additive) +1 if cough reported; +2 if non-pleuritic chest pain reported; +4 if pleuritic chest pain reported.

47. Dyspnea: 1 if short of breath on exertion, 2 if short of breath at rest.

48-50. Period of P Sx's: interval of longest pulmonary symptoms presence.

NEUROLOGIC SYMPTOMS (51-55):

51. Eye: (additive) +1 if white spots seen on funduscopic exam; +2 if patient reports visual blurring.

52-53. Encephalomenigeal: (additive) +1 if patient complains of neck stiffness; +2 if patient has developed new onset seizures in past 6 months; +4 if patient or patient's family reports new severe lethargy or confusion; +8 if patient complains of photophobia.

54-55. Neurologic Deficits: (additive) +1 if patient has newly developed difficulty with speaking; +2 if patient complains of complete or partial paralysis of any extremity; +4 if patient or family complains of inappropriate behavior or extreme disorientation, or if history taking is made extremely difficult secondary to patients compromised mentation; +8 if other noteworthy neurologic deficits are present.

CO-MORBIDITY (56-63):

56-57. Hx of Rel Dz: (additive) +1 if history of hepatitis B infection; +2 if history of cytomegalovirus (CMV) infection; +4 if history of syphilis; +8 if history of gonorrhea; +16 if patient had multiple positive blood cultures without a clear alternative source (such as an infected central line). Be sure to note all evidence for and against endocarditis and record date of blood cultures as well as organisms grown.

58-59. Serologies: (additive) +1 if positive titer for Hepatitis B; +2 if positive titer for CMV; +4 if positive for Toxoplasmosis; +8 if positive titer for Cryptococcus.

60. ETOH Abuse: 1 if abuse noted in chart at any time; 2 if evidence of side effects (PE, liver biopsy positive for fatty liver or cirrhosis, evidence of cerebellar compromise, etc.)

61. Cig Smoking: 1 if less than or equal to 10 pack years, or if patient stopped smoking over 2 years ago; 2 if greater than 10 pack year history.

62-63. Psych History: (additive) +1 if related to homosexuality (i.e. if patient sought psychiatric counselling for problems associated with homosexuality); +2 patient was placed in drug rehabilitation program; +4 if patient was considered psychotic; +8 if patient was considered suicidally depressed or had actually attempted suicide.

ZT EXAM (64-80):

Any physical exam sign described within one month of ZT is recordable. If there are conflicting reports of a particular finding give most weight to house officer with the most seniority and expertise in the area of the finding. For example, a pulmonary fellow would give the most authoritative account of the lung exam, etc.

64. ZT: 1 if ZT is as inpatient at YNHH; 2 if ZT is as outpatient at YNHH; 4 if ZT is not at time of original CDC AIDS dx.

65-67. Temp: If ZT is within 2 days of admission use ER temp. If no ER temp, use highest PE temperature.

68-69. RR: record highest respiratory rate given. If range given (i.e. 30-40) pick mean of range (i.e. 35).

70. Thrush: 1 if present.

71. LN: 1 if lymph nodes detectable; 2 if ≥3cm. or "pronounced".

72. KS: record if house officer believes lesions suspicious for KS, locations determined in same manner as #39.

73-74. Eye: (additive) +1 if abnormality seen on fundoscopic exam; +2 if other abnormalities of eye(s) observed (periorbital swelling, conjunctivitis, etc.)

75-76. Encephalomenigeal Signs: (additive) +1 if stiff neck or painful to touch chin to chest; +2 if seizure witnessed; +4 if patient is difficult to keep awake during examination or described as lethargic, obtunded, or stuporous; +8 if patient unable to tolerate bright light during exam.

77-78. Other Neurologic Signs: (additive) +1 if patient has difficulty speaking during exam;+2 if patient demonstrates significant lower extremity weakness or paralysis; +4 if patient not oriented to person, place, and/or time; +8 if other neurologic deficits (i.e. abnormalities in neuro exam) are present.

79. Mass Effect: (additive) +1 if papilledema present; +2 if one or both pupils dialated (without benefit of sympathomimetics).

80. Group: if patient placed on AIDS Clinic list up to and including July 24, 1986 code as 1; if patient added after, code as 2.

ZT PARACLINICAL DATA(1-65):

1-4. Same ID code as 1-4 under identification.

5. Anergy: 1 (normal) if PPD negative and all controls positive; 2 (partial) if PPD negative and at least one but not all controls positive; 3 (complete) if all tests negative.

Anergy Rel to ZT (6-9):

6. 0 if anergy tested after ZT; 1 if anergy tested before or on ZT.

7-9. Interval: record period between panel and ZT.

T Cell Panel (10-27):
preference given to panel closest to ZT.

10-11. T4 percent

12-14. T4 per microliter

15-16. T8 percent

17-19. T8 per microliter

20-22. T4/T8 ratio

T Cell Rel to ZT (23-27):

23. 0 if tested after ZT; 1 if tested before or on ZT.

24-26. Interval between ZT and T Cell test.

27. 1 if tested at YNHH; 2 if tested elsewhere.

Complete Blood Count(28-45):

Manual differential to be noted in left margin. Use CBC closest to ZT prior to any blood transfusions. If patient is receiving marrow suppressing medications such as trimethoprim sulfamethoxazol (i.e. Bactrim), amphotericin, pentamidine, etc. compare current CBC with one prior to treatment and if CBC is lower after treatment than use old CBC, if not use current CBC.

28-30. Hematocrit record directly.

31-32. White Blood Count/1000. If greater than 9.9 record as 9.9 and note actual count on the side.

33-36. Calculated Lymphocytes = (WBC) x (percent lymohicytes) x 10

37. Platelets: if listed only as "ADEQ" or "DECREASED" or "INCREASED" so record. If actual count given: $\leq$ 140,000 = decreased; > 400,000 = increased; all others are adequate.

38-40. Platelet Count: record actual count if given

41. Bone Marrow Failure (this category revised, ignore.)

42-44. Sedimentation Rate record directly.

45. Lab: 0 if unknown; 1 if YNHH; 2 if any other hospital.

Respiratory Data(46-55):

46-53. Room Air Arteriolar Blood Gas: Use the room air ABG with the lowest pO2 value prior to ZT.

54-55. Chest X-Ray: (additive) +0 if not ordered or misplaced; +1 if read as "normal chest" or "no acute change"; +2 if "diffuse infiltrate," "multinodular interstitial pattern," or "cannot rule out P.C.P."; +4 if specific lobular infiltrate identified; +8 if cavitary lesion" is specified.

56-57. Head CT: (additive) +0 if not obtained or misplaced; +1 if read as "within normal limits"; +2 if contrast and non-contrast studies are done and ring enhancing lesions are identified; +4 if "mass effect" noted; +8 if anything else of significance is noted (specify on left).

Nutritional Data(58-67):

This section cannot be completed without documentation of the patient's height. Use the weignt/height chart (Appendix VII) to determine ideal body weight for patient.

58-59. Albumin: record directly, value closest to ZT.

60-62. Normal Weight State: Subtract ideal weight from weight reported as patient's normal or usual weight.

60. If result of calculation is positive, code 0 if negative code 1.

61-62. Record number of pounds of difference. If no difference, code 0.

63-65. Admission Weight State: subtract ideal weight from weight recorded on or near admission or ZT (give priority to weight closest to ZT).

63. If difference of above is positive,0; if negative code 1.

64-65. Record number of pounds of difference; if no difference, code 0.

66-67. % Calculated Weight Loss: subtract admission weight from normal weight and divide the difference by normal state. Record as %. If no weight loss or if weight gain, record 0.

INTERVALS (68-77):

68-73. Record the date of ZT by month/date/year.

74. ? equals lost to follow up. Look at last date at which patient is known to be alive or dead and so record.

75-77. Subtract ZT date from date of death and record difference in months and tenths of months. If patient alive or, if state unknown leave these spaces blank.

AUTOPSY (78-79):

Find final report of autopsy if done. Record autopsy number and major diagnoses. If any major diagnoses were unsuspected when patient was still alive code 1 in column 79.

78. 0 if no autopsy done or report not found; 1 if report found.

79. Surprises: (see above and so note).

AZT DURATION (80):

Look at outpatient chart and summary list of AZT therapy from AIDS office and so record. If no AZT administered code as 0. If AZT given at any time, code as 1. Note date therapy started.

DNR (Do Not Resuscitate) STATUS:

Determine date of DNR status (if established) and note who was consulted as well as any specifics of the order.

APPENDIX VII

IDEAL BODY WEIGHT IN POUNDS[1]

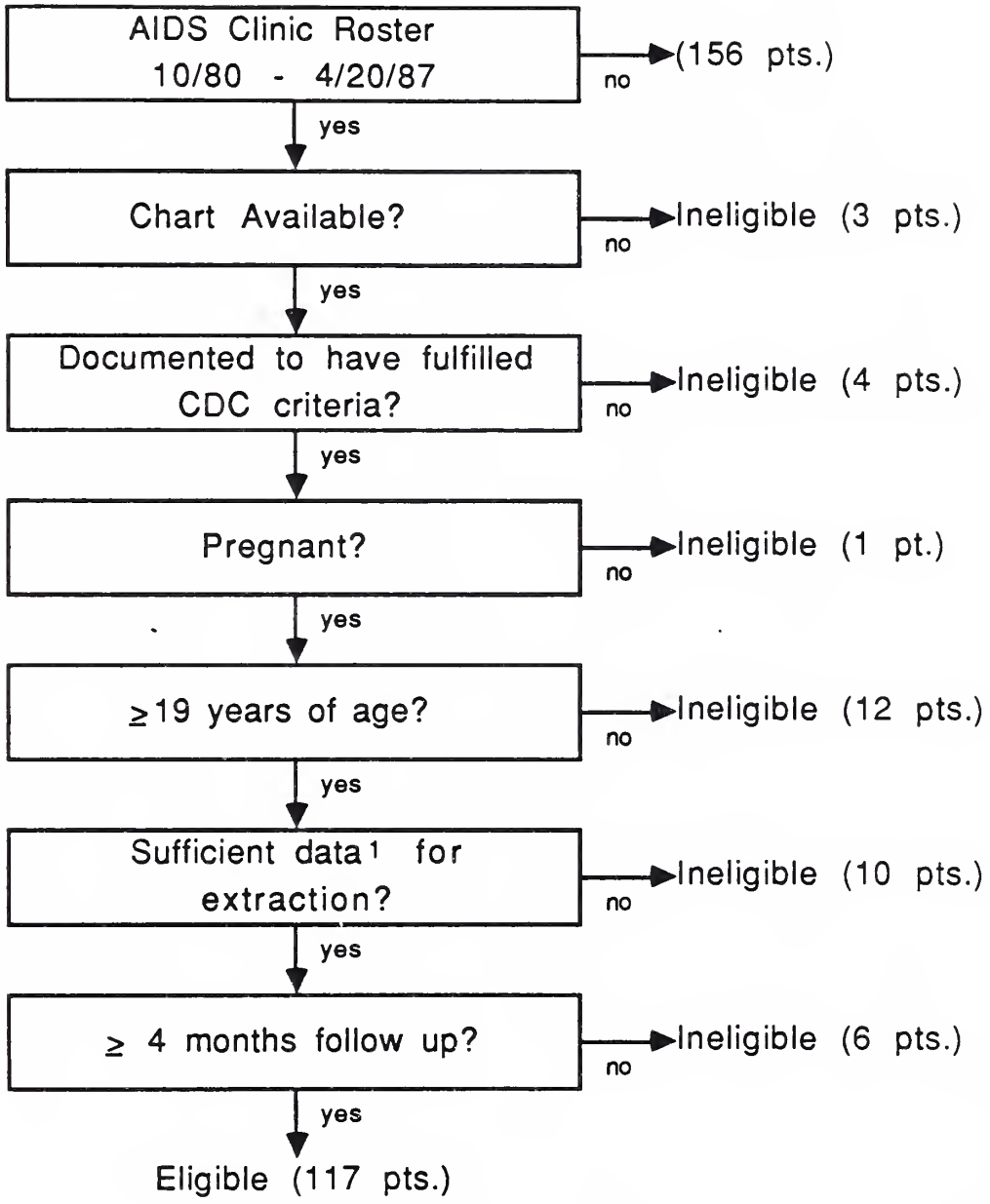
Height (in feet & inches)	*Age* 20-29	30-39	40-49	50-59	60-69
			Men		
5'3"	125	129	130	131	130
5'6"	135	140	142	143	142
5'9"	149	153	155	156	155
6'0"	161	166	167	168	167
6'3"	176	181	183	184	180
			Women		
4'10"	97	102	106	109	111
5'1"	106	109	114	118	120
5'4"	114	118	122	127	129
5'7"	123	127	132	137	140
5'10"	134	138	142	146	147

Notes:
1 Taken from The Pacific Mutual Life Insurance Company Tables (updated 1986).

TABLE OF FIGURES

Figure 1.

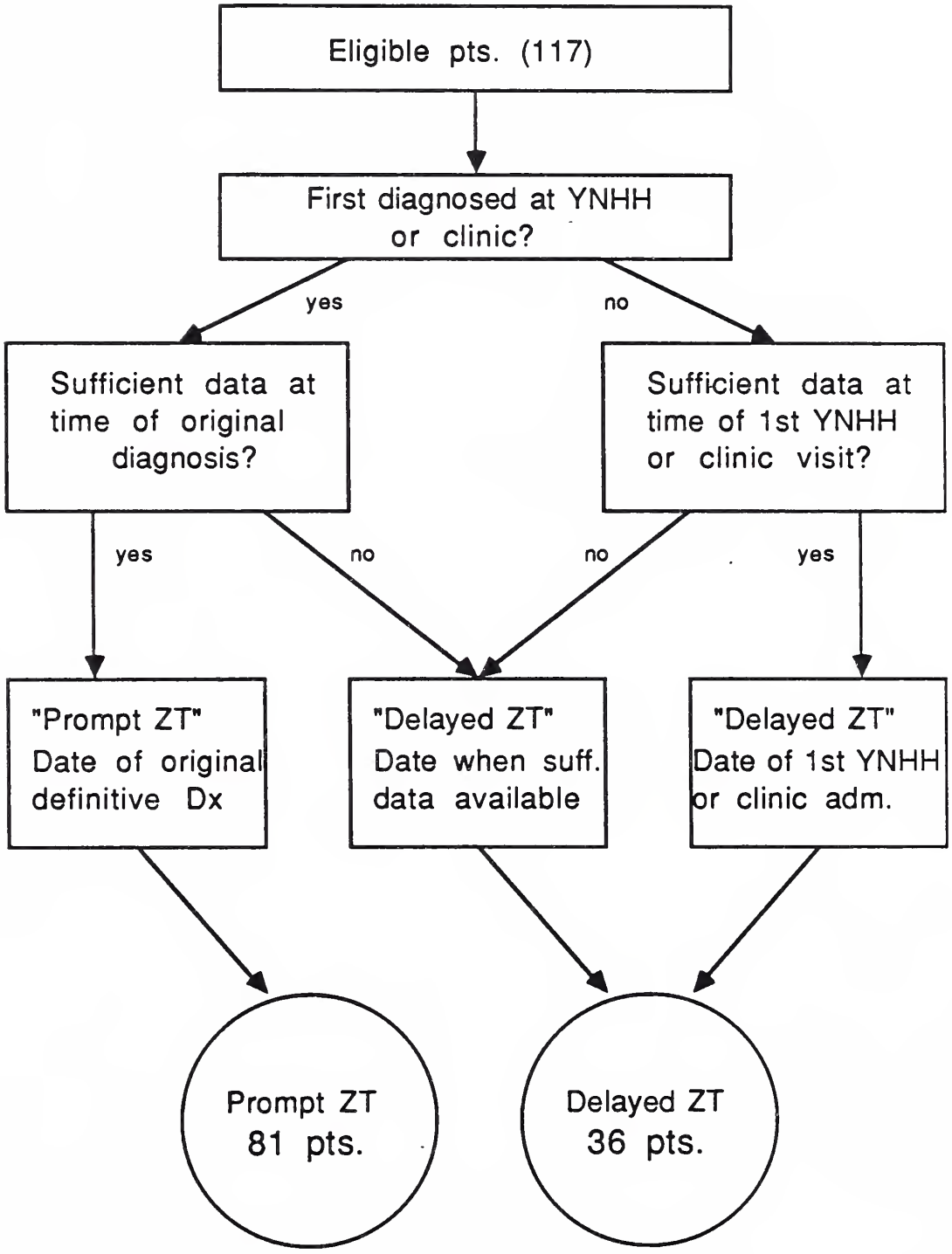
ELIGIBILITY CRITERIA



1. Sufficient data = Reasonably complete history and physical exam with a complete blood count done within 1 month of zero time. The complete blood count must not be suspected of being depressed secondary to ongoing therapy with known myelosuppressive agents such as trimethoprim-sulfamethoxizole, pentamidine, amphotericin, etc.

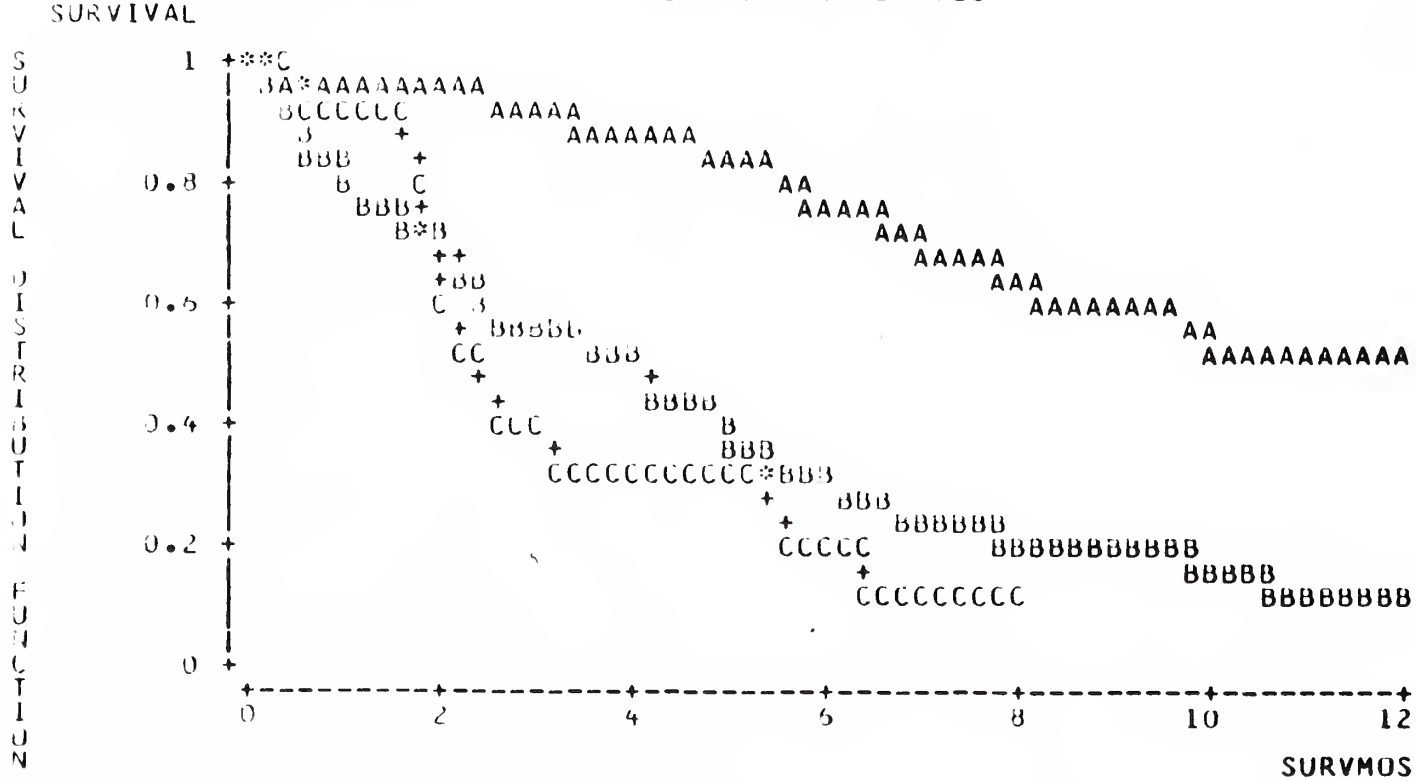
Figure 2

ZERO TIME ASSIGNMENT



LIFE TABLE ANALYSIS: DEVELOPMENT SET

SURVIVAL ESTIMATES

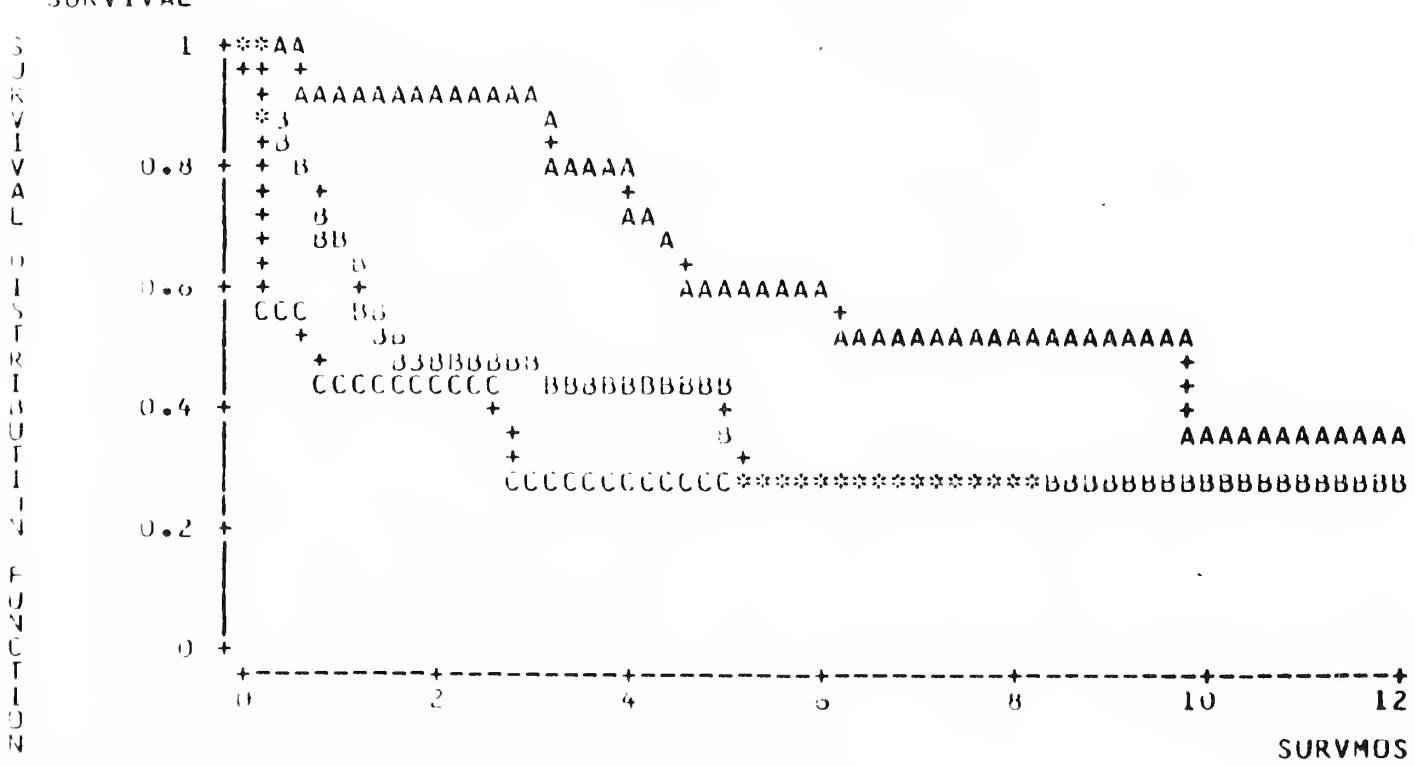


LEGEND FOR STRATA SYMBOLS

	STAGEC	STAGEC	STAGEC
A=	1	B= 2	C= 3

LIFE TABLE ANALYSIS: CHALLENGE SET

SURVIVAL ESTIMATES

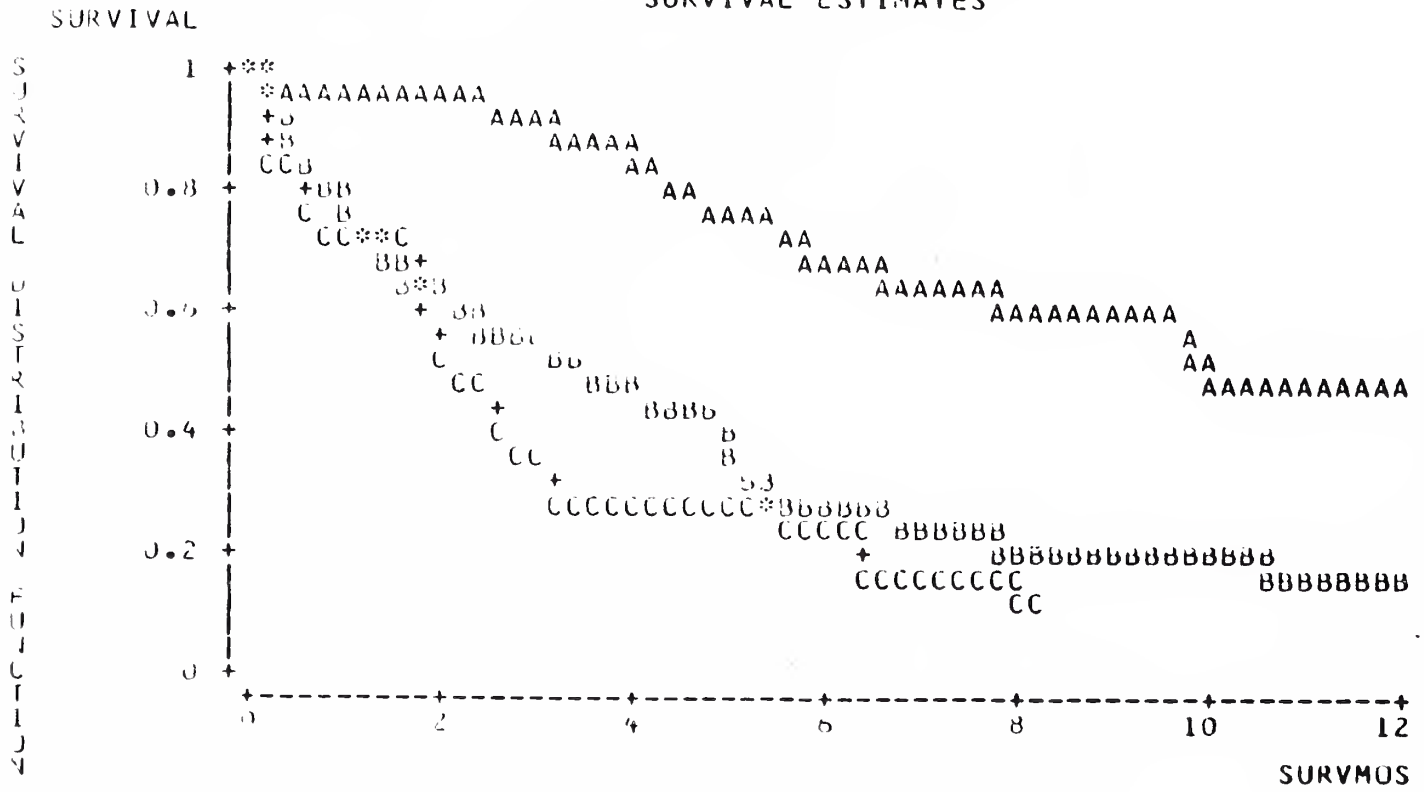


LEGEND FOR STRATA SYMBOLS

STAGEC	STAGEC	STAGEC
A= 1	B= 2	C= 3

LIFE TABLE ANALYSIS: TOTAL POPULATION

SURVIVAL ESTIMATES



LEGEND FOR STRATA SYMBOLS

A = STAGEC 1 B = STAGEC 2 C = STAGEC 3

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Vinita Sehgal 2/24/89

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