



## To Study the Hematological parameters as predictors of morbidity in patients with HIV infection

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GJMEDPH 2014; Vol. 3, issue 1

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Conflict of Interest—none

Funding—none

### ABSTRACT

**BACKGROUND:** HIV infection is a multisystem disease and is associated often with a wide range of hematological abnormalities, including impaired haematopoiesis, immune mediated cytopenias and coagulopathies, particularly in the later part of the disease. Bone marrow findings are highly variable depending on the clinical severity of the immune-deficient state. Here we study the haematological abnormalities and bone marrow findings in 100 HIV infected individuals. Hence all HIV patients were investigated for hematological abnormalities as it has a significant impact on the clinical outcome and treated accordingly to reduce morbidity and mortality and improve the quality of life.

**METHODOLOGY:** A prospective study was conducted on 100 cases detected to be HIV positive as per WHO criteria attending Department of Medicine/ART Centre, K.R. Hospital, Mysore.

**RESULTS:** HIV affected the highly productive age group of 21-40 years (74%) and predominantly males (80%) in the present study. Among the hematological manifestations, anemia (89%) was the commonest. The frequency and severity of anemia worsened with declining immune status (CD<sub>4</sub> count). Leucopenia was seen in 40 cases (40%) and Thrombocytopenia was seen in 30 cases (30%). Bone marrow study showed normocytic and hypercellular in 6 cases and hypocellular in 2 cases.

**CONCLUSION:** The frequency and severity of these hematological manifestations increased with decline in CD<sub>4</sub> count and had got significant impact on clinical outcomes and quality of life. Hence all HIV patients should be investigated for hematological abnormalities and treated accordingly to reduce morbidity and mortality.

**Keywords:** HIV, CD<sub>4</sub> count, CD<sub>8</sub> count, Anemia, Leucopenia, Thrombocytopenia, Pancytopenia

### LIST OF ABBREVIATIONS:

TLC	→	Total Leucocyte Count
DA	→	Dimorphic anemia
NHA	→	Normocytic hypochromic anemia
NNA	→	Normocytic normochromic anemia
PA	→	Pancytopenia

## INTRODUCTION

Human Immunodeficiency Virus (HIV) attacks the body's immune system. Normally, the immune system produces infection fighting cells called T-cell lymphocytes. Months to years after a person is infected with HIV, the virus destroys all the T-cell lymphocytes. This disables the immune system to defend the body against diseases and tumors. Various opportunistic infections take advantage of the body's weakened immune system. These infections which normally do not cause severe or fatal health problems will eventually cause the death of the HIV patient.<sup>1</sup>

HIV infection is a multisystem disease. Hematological abnormalities are among the most common clinic-pathological manifestations of HIV infection. HIV infection is associated often with a wide range of hematological abnormalities, including impaired haematopoiesis, immune mediated cytopenias and coagulopathies, particularly in the later part of the disease.<sup>2,3,4</sup>

Bone marrow findings are highly variable depending on the clinical severity of the immunodeficient state. The prevalence of anemia increases to 30% to 40% in those with early disease and 75% to 90% in those with AIDS.<sup>5</sup>

### Objectives of the Study

1. To study the blood picture of HIV infected patients.
2. Analyze specific laboratory determinations of anemia, leukopenia, and thrombocytopenia and correlate with CD<sub>4</sub> lymphocyte count.
3. Identify the clinical manifestations of altered hematopoiesis related to HIV.

## METHODS

### Method of collection of data

**Sample size:** One hundred (100) cases detected to be HIV positive as per WHO criteria were taken up for the study.

**Sampling method:** Simple random sampling.

### Inclusion Criteria

HIV positive patients as per WHO criteria criteria irrespective of their antiretroviral treatment status, attending to Department of Medicine/ART Centre, K.R. Hospital, Mysore were included in the study after obtaining ethical committee clearance.

### Exclusion Criteria

1. Patients with previously known hematological disorders.
2. Congenital hematological disorders.
3. Age < 12 years.

Data was collected by using pre-tested proforma meeting the objectives of the study. Purpose of the study was carefully explained to the patients and consent was taken.

All patients were interviewed, detailed history was taken with respect to risk factors and detailed physical examinations were carried out. Appropriate investigations were carried out.

### Investigations

- a. Complete hemogram including peripheral smear.
- b. Bone marrow biopsy whenever indicated.
- c. CD<sub>4</sub> lymphocyte counts by FLOW CYTOMETRY by standard technique using Becton-Dickinson FAC Scan.
- d. Lymphnode biopsy, ultrasound abdomen, CT scan/MRI scan if needed.

The results were analysed by calculating percentages, the mean values, standard deviation, standard error, unpaired 't' test, Chi-square 'χ' test and proportion test. Proportions were compared using Chi-square test of significance. A 'p' value of less than 0.05 was considered statistically significant.

## RESULTS

- Peripheral and bone marrow abnormalities were common in HIV related disease and have gotten significant impact on clinical outcomes and quality of life (QOL).
- The variation in the prevalence of hematological abnormalities in different stages of disease are due to number of factors which includes – CD<sub>4</sub> count, clinical disease status, drug therapy,

- opportunistic infections and malignancy.
- HIV infection affected the highly productive age group of 21-40 years of age (74%) and predominantly males (80%) in the present study.
  - The most common symptom was fatigue (86%) and fever (80%), and among the signs pallor (75%) and oral thrush (48%) were common. This may be due to the advanced clinical disease status and worsening immunity (88% of cases were in clinical stages III or IV). But there was no statistical significance in relation to CD<sub>4</sub> count.
  - Among the hematological manifestations, anemia (89%) was the commonest. The frequency and severity of anemia worsened with declining immune status (CD<sub>4</sub> count).
  - The commonest type of anemia in present is normocytic normochromic (49%), which is on par with the earlier studies.
  - Normocytic normochromic and normocytic hypochromic anemia were seen commonly with the worsening of immune status and clinical stage. But there was no statistical significance of any particular anemia in relation to reduction in CD<sub>4</sub> count.
  - Leucopenia was seen in 40 cases (40%) which had significant correlation with CD<sub>4</sub> count ( $p = 0.019$ ).
  - Thrombocytopenia was seen in 30 cases (30%) in correlation with CD<sub>4</sub> count. But there was no statistical significance ( $p = 0.262$ ).
  - Bone marrow study showed normocytic and hypercellular in six cases and hypocellular in two cases.

**Table 1. Age and sex distribution of HIV positive patients**

Age (in years)	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
<20	0	0	2	10	2	2
21-30	20	25	10	50	30	30
31-40	40	50	4	20	44	44
41-50	10	12.5	2	10	12	12
51-60	7	8.75	2	10	9	9
>60	3	3.75	0	0	3	3

**Table 2. Signs and symptoms distribution**

Symptom or sign	Number of patients	Percentage
Fatigue	86	86
Fever	80	80
Weight loss	78	78
Pallor	75	75
Anorexia	48	48
Oral thrush	48	48
Dyspnoea	46	46
Cough	44	44
Emaciation	40	40
Adenopathy	40	40
Diarrhoea	24	24
Temperature	12	12
Edema	12	12
Clubbing	8	8
Petechiae /Purpura	6	6
Palpitation	5	5
Jaundice	3	3
Cyanosis	3	3

Table 3. Frequency of hemoglobin percentage

Hb% (in gms%)	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
≤6*	10	12.50	2	10	12	12
>6≤9*	28	35	7	35	35	35
>9≤13*	35	43.75	11	55	46	46
>13*	7	8.75	0	0	7	7

$$*\chi^2 = 0.166; p < 0.415$$

Table 4. Frequency of Total leucocyte count(TLC)

TLC cells /μl	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
<4000*	36	45	4	20	40	40
4000- 11,000*	42	57.5	14	70	56	56
>11,000*	2	2.5	2	10	4	4

$$*\chi^2 = 0.152; p = 0.306$$

Table 5. Frequency of neutrophil count

Ne utrophil count in %	Males (n=80)		Females (n=20)		Total (no=100)	
	Number	% of males	Number	% of females	Number	%
<50*	4	5	3	15	7	7
50-70*	66	82.5	12	60	78	78
>70*	10	12.5	5	25	15	15

$$*\chi^2 = 0.218; p < 0.082$$

Table 6, Frequency of lymphocyte count

Lymphocyte count in %	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
<20*	34	42.5	4	20	38	38
20-40*	40	50	12	60	52	52
>40*	6	7.5	4	20	10	10

$$*\chi^2 = 0.172; p < 0.217$$

**Table 7. Frequency of platelet count**

Platelet count in lakhs/cumm	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
<1.50 <sup>*</sup>	26	32.5	5	25	31	31
1.5-4 <sup>*</sup>	52	65	12	60	64	64
>4 <sup>*</sup>	2	2.5	3	15	5	5

<sup>\*</sup> $\chi^2 = 0.225$ ;  $p < 0.069$

**Table 8. Frequency of CD4 count distribution**

CD4 count	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Numbers	% of females	Number	%
$\leq 50$ <sup>*</sup>	34	42.5	10	50	44	44
$>50 \leq 200$ <sup>*</sup>	32	40	6	30	38	38
$>200$ <sup>*</sup>	14	17.5	4	20	18	18

<sup>\*</sup> $\chi^2 = 0.082$ ;  $p < 0.711$

**Table 9. Frequency of type of anemia**

Type of anemia	Males (n=80)		Females (n=20)		Total (n=100)	
	Number	% of males	Number	% of females	Number	%
Normocytic <sup>*</sup> normochromic anemia(NHA)	32	40	6	30	38	38
Normocytic <sup>*</sup> hypochromic anemia(NNA)	38	47.5	11	55	49	49
Macrocytic <sup>*</sup> hypochromic anemia(MHA)	6	7.5	1	5	7	7
Dimorphic <sup>*</sup> anemia (DA)	2	2.5	1	5	3	3
Pancytopenia (PA) <sup>*</sup>	2	2.5	1	5	3	3

<sup>\*</sup> $\chi^2 = 0.118$ ;  $p < 0.842$

Table 10: Correlation of cellularity of bone marrow with peripheral blood picture

Bone marrow cellularity	Peripheral blood picture		
	Hb%	Total leucocyte count	Platelet count
<b>Hypercellular/Normal</b>			
Decreased	6	2	4
Normal	0	4	2
<b>Hypocellular</b>			
Decreased	2	2	1
Normal	0	0	1

Table 11: Hb% in relation to CD4 lymphocyte count

Hb in gms%	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
≤6*	5	6.25	3	15	8	8
>6≤9*	30	37.5	3	15	33	33
>9≤13*	38	47.5	10	50	48	48
>13*	7	8.75	4	20	11	11

$$*\chi^2 = 0.235; p < 0.119$$

Table 12: TLC in relation to CD4 Count

TLC cells/mm <sup>3</sup>	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
≤4000*	36	45	4	20	40	40
4000-11000*	43	53.75	13	65	56	56
>11000*	1	1.25	3	15	4	4

$$*\chi^2 = 0.272; p < 0.019$$

Table 13: Neutrophil count in relation to CD4 count

Neutrophil Count %	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
≤50*	6	7.5	1	5	7	7
50-70*	62	77.5	16	80	78	78
>70*	12	15	3	15	15	15

$$*\chi^2 = 0.039; p < 0.925$$

**Table 14: Lymphocyte count in relation to CD4 count**

Lymphocyte Count %	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
<20*	40	50	3	15	43	43
20-40*	24	30	14	80	38	38
>40*	16	20	3	15	19	19

$$*\chi^2 = 0.123; p < 0.466$$

**Table 15: Platelet count in relation to CD4 count**

Platelet count in lakhs/mm <sup>3</sup>	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
<1.5*	27	33.75	3	15	30	30
1.5-4*	50	62.5	16	80	66	66
>4*	3	3.75	1	5	4	4

$$*\chi^2 = 0.162; p < 0.262$$

**Table 16: Type of anemia in relation to CD4 count**

Type of anemia	≤200 (n=80)		>200 (n=20)		Total (n=100)	
	Number	% of cases	Number	% of cases	Number	%
NNA*	44	55	5	25	49	49
NHA*	25	31.25	13	65	38	38
MHA*	6	7.5	1	5	7	7
DA*	2	2.5	1	5	3	3
PA*	3	3.75	0	0	3	3

$$*\chi^2 = 0.322; p < 0.021$$

#### HEMATOLOGIC PARAMETERS IN CORRELATION WITH CD4 COUNT

**Table 17: Correlation of hematological parameters with respect to CD4 lymphocyte count**

Hematologic parameter	CD4 ≤ 200	CD4 ≥ 200	Significance
Hb%			
Normal (n=11)	7	4	(p = 0.11)
Decreased (n=89)	73	16	
Total Leucocyte Count (TLC)			
Normal (n=80)	44	16	(p = 0.19)
Decreased (n=20)	36	4	
Neutrophil count			
Normal (n=93)	74	19	(p = 0.925)
Decreased (n=7)	6	1	
Lymphocyte count			
Normal (n=77)	40	17	(p = 0.466)
Decreased (n=23)	40	3	
Platelet count			
Normal (n=70)	53	17	(p = 0.262)
Decreased (n=30)	27	3	

## DISCUSSION

### Hematologic Manifestations of HIV infection

Impaired hematopoiesis, immune-mediated cytopenias, and altered coagulation mechanisms have all been described in HIV infected individuals. These abnormalities may occur as a result of HIV infection itself, as sequelae of HIV-related opportunistic infections or malignancies, or as a consequence of therapies used for HIV infection and associated conditions.

### Anemia

Anemia is a very common finding in patients with HIV infection. In a study of patients receiving no myelosuppressive therapies, 8% of asymptomatic HIV-seropositive patients, 20% of those with symptomatic middle-stage HIV disease, and 71% of those with Centers for Disease Control (CDC)-defined AIDS were anemic<sup>6</sup>. Investigation of a cohort from a longitudinal study of HIV disease found anemia in 18% of asymptomatic HIV-seropositive patients, 50% of those with symptomatic middle-stage HIV disease, and 75% of those with CDC-defined AIDS.<sup>7</sup>

HIV infection alone, without other complicating illness, may produce anemia in some. Other studies have suggested that soluble factors in the serum of HIV-infected patients may inhibit hematopoiesis, or that direct HIV infection of marrow progenitor cells may play a role in producing anemia and other hematologic abnormalities associated with HIV infection<sup>8,9</sup>

### Anemia Caused by Bone Marrow Infections

Infection with *Mycobacterium avium* complex (MAC) is another common cause of anemia in advanced HIV disease. This infection, diagnosed in up to 18% of patients with advanced HIV disease during the course of their illness.<sup>10</sup>

Tuberculosis, Histoplasmosis, Cryptococcosis, Pneumocystosis and Non-Hodgkin's lymphoma can all infiltrate the bone marrow, generally causing pancytopenia.

### Other causes of anemia

Anti-erythrocyte antibodies produce a positive direct antiglobulin test in approximately 20% of HIV-infected patients with hypergammaglobulinemia<sup>11</sup>

### Pancytopenia

The main identified mechanisms were:

1. HIV infections of the bone marrow CD34+ population.
2. Viral persistence infection of stem cells, and stromal cells (EBV, PV-B19, CMV, HHV8, HTLV I, II).
3. Disturbance of cytokines and interleukin synthesis and activity.
4. Bone marrow involvement by Lymphoma, Kaposi's angiosarcoma and Granulomatous diseases.
5. Myelotoxic effects of Anti-retroviral (ARV) therapy.

### Thrombocytopenia

Thrombocytopenia is frequently associated with HIV infection. Possible etiologies include immune-mediated destruction, Thrombotic thrombocytopenic purpura, impaired hematopoiesis, and toxic effects of medications.

### HIV-Related Immune Thrombocytopenic Purpura

A patient with thrombocytopenia has true HIV-ITP if there is no other condition or treatment that could cause thrombocytopenia. Thrombotic

### Other causes of thrombocytopenia in HIV infection

Alcohol use, splenomegaly and liver disease, or drug effects (Heparin, Quinidine).

### Granulocytopenia and Abnormal Granulocyte Function

The pathogenesis of granulocytopenia in patients with HIV infection is multifactorial. An autoimmune mechanism involving antigranulocyte antibodies<sup>12</sup> and impaired granulopoiesis,<sup>13,14</sup> infiltrative process involving the bone marrow (infection, malignancy) and drug toxicity.



### Lymphopenia

Increases in both CD<sub>4</sub> and CD<sub>8</sub> cell death and impairment in function are the sine qua non of HIV infection.

### CD<sub>4</sub>+ T Cells

Progressive depletion in numbers of circulating CD<sub>4</sub>+ T cells occurs in almost all cases of untreated HIV infection. The number of circulating CD<sub>4</sub>+ T cells is widely used as a measure of global "immune competence" and provides a predictor of the immediate risk for opportunistic illnesses.<sup>15</sup>

### CD<sub>8</sub>+ T Cells

In early HIV infection, CD<sub>8</sub>+ T-cell numbers tend to increase, reflecting expansion of memory CD<sub>8</sub>+ T cells, particularly HIV-reactive cells. CD<sub>8</sub> cell expansions persist until far advanced stages of HIV disease, when all T-cell numbers tend to fall.<sup>16</sup>

### Hemostatic Abnormalities

Thrombosis reportedly occurs in upto 2% of HIV-infected patients. Factors associated with venous thromboembolic complications include age over 45 years, advanced stage of HIV infection, the presence of Cytomegalovirus(CMV) or other AIDS-defining opportunistic infections, hospitalization, and therapy with Indinavir or Megestrol acetate.<sup>17</sup>

### The bone marrow in Human Immunodeficiency Virus (HIV) Infection

Morphologic abnormalities can be found in the majority of bone marrow samples from HIV-1 infected patients, but most are non-specific except in opportunistic infections like *M. avium* intracellulare, Tuberculosis, or Fungal infection or as part of staging for malignancy.<sup>18</sup>

The histopathologic findings in the bone marrow of HIV-1 infected patients are varied -includes hypercellular marrow, myelodysplastic changes, hypocellular marrow and fibrosis of bone marrow.<sup>18</sup>

## AGE AND SEX DISTRIBUTION

**Table 18: Sex distribution of cases in various studies in relation to present study**

Sex	Manisha et al n=416	Thripati et al n=54	Antonio et al n=54	Present study n=100
Males	83.2%	79.72%	89.79%	80%
Females	16.8%	21.28%	10.31%	20%

## HEMATOLOGICAL MANIFESTATIONS

### ANAEMIA

**Table 19: Percentage of anemia in various studies**

Study	Aboulafia		Zon		Spivak		Manisha		Present study	
	No.	%	No.	%	No.	%	No.	%	No.	%
% of anemia	54	75%	106	64%	124	71.5	416	90.8%	100	89%

(p=0.119)

## TOTAL LEUCOCYTE COUNT AND DIFFERENTIAL COUNT

Table 20: Percentage of total leucocyte counts in various studies

Study	Murphy MF et al.		Zon LI et al.		Ellaurie M et al.		Castella A et al.		Present study	
	No.	%	No.	%	No.	%	No.	%	No.	%
% of leucopenia	105	75	106	65	55	70	55	75	100	40

36 cases of leukopenia had CD4 counts less than 200 cells/mm<sup>3</sup> definitely showing the severity of the disease.

TABLE 21. Platelet count

Study	Murphy MF et al.		Zon LI MF et al.		Jost J et al.		Kaslow RA et al.		Present study	
	No.	%	No.	%	No.	%	No.	%	No.	%
% of Thrombocytopenia	105	30	106	40	321	9	1411	6.7	100	30

## TYPE OF ANEMIA

Table 22: Percentage of anemia in various studies

Type of anemia	Zon LI et al	Murphy MF et al	Jost J et al	Kaslow RA et al	Present study
NHA	5	14	22	8	0.024
NNA	4	9	20	5	
MHA	0	4	3	1	0.5
DA	0	2	1	0	
PA	0	1	2	0	

## CONCLUSION

- In the present study, out of 100 patients, the commonest haematological manifestations found were anemia, leucopenia and thrombocytopenia..
- The frequency and severity of these hematological manifestations increased with decline in CD4 count and had got significant impact on clinical outcomes and quality of life.
- Hence all HIV patients should be investigated for hematological abnormalities and treated accordingly to reduce morbidity and mortality.

## REFERENCES

1. Rombauts B. Farmaceutische Microbiologie (met inbegrip van de farmaceutische technologie van steriele geneesmiddelen). Cursus 1 ste graad apotheker VUB 1997;11:14-16.
2. Cohen PT, Sande MA, Volberding P. The AIDS knowledge base: A textbook of HIV disease from the University of California, San Francisco General Hospital. Boston: Little, Brown; 1994.
3. Sande MA, Volberding (eds). The medical management of AIDS. 4<sup>th</sup> ed. Philadelphia: WB Saunders; 1995
4. Spivak JL, Bender BS, Quin TC. Hematological abnormalities in the acquired immune deficiency syndrome. Am J Med 1984;77:224-8

5. Zauli G, Davis BR, Re MC. Fat protein stimulates production of transforming growth factor – beta-1 by the bone marrow macrophages: A potential mechanism for human immunodeficiency virus-1-induced hematopoietic suppression. *Blood* 1992; 80:3036-43.
6. Zon LI, Groopman JE. Hematologic manifestations of human immune deficiency virus (HIV). *Semin Hematol* 1988;25:208.
7. Rogel ME, Wu LI, Emerman M. The human immunodeficiency virus type 1 vpr gene prevents cell proliferation during chronic infection. *J Virol* 1995; 69:882-8.
8. Stella CC, Ganser A, Hoelzer D. Defective in vitro growth of hematopoietic progenitor cells in the acquired immunodeficiency syndrome. *J Clin Invest* 1987; 80:286-93.
9. Folks TM, Kessler A, Orenstein JM. Infection and replication of HIV-1 in purified progenitor cells of normal human bone marrow. *Science* 1988; 242:919-22.
10. Hawkins CC, Gold JW, Whimbey E. Mycobacterium avium complex infections in patients with acquired immunodeficiency syndrome. *Ann Intern Med* 1986; 105:184-8.
11. McGinniss M, Macher AA, Rook A. Red cell autoantibodies in patients with acquired immunodeficiency syndrome. *Transfusion* 1986; 26:405-9.
12. Kovacs JA, Vogel S, Albert JM. Controlled trial of interleukin-2 infusions in patients infected with the human immunodeficiency virus. *N Engl J Med* 1996;335:1350-6.
13. Willey RL, Maldarelli F, Martin MA. Human immunodeficiency virus type 1 Vpu protein induces rapid degradation of CD4. *J Virol* 1992;66(12):7193-200.
14. Klimkait T, Strebel K, Hoggan MA. The human immunodeficiency virus type 1-specific protein vpu is required for efficient virus maturation and release. *J Virol* 1990;64:621-9.
15. Masur H, Ognibene FP, Yarchoan R, Shelhamer JH, Biard BF, Travis W et al. CD4 counts as predictors of opportunistic pneumonias in human immunodeficiency virus (HIV) infection. *Ann Intern Med* 1989;111:223-31.
16. Margolick JB, Munoz A, Donnenberg AD, Park LP, Galai N, Giorgi JV, et al. Failure of T-cell homeostasis preceding AIDS in HIV-1 infection. The Multicenter AIDS Cohort Study. *Nat Med* 1995;1:674-80.
17. Love PE, Santoro SA. Antiphospholipid antibodies: Anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and in non-SLE disorders. Prevalence and clinical significance. *Ann Intern Med* 1990; 112:682-98.
18. Karcher DS, Frost AR. The bone marrow in human immunodeficiency virus (HIV)-related disease. Morphology and clinical correlation. *Am J Clin Pathol* 1991;95:63-71.