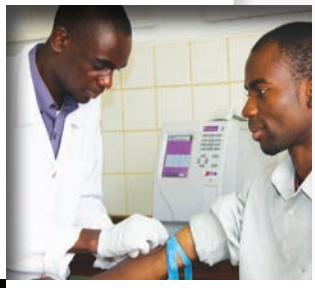
PointCare®

THE POINTCARE NOW SYSTEM AND DIAGNOSTIC MANAGEMENT OF HIV PATIENTS IN RESOURCE-POOR SETTINGS



Clinical management of patients with HIV is complex and has presented numerous challenges to healthcare providers in the developed world for more than 20 years. Today, an estimated 90 percent of HIV-infected people live in developing regions. Caring for these HIV patients has presented two additional challenges for the global medical community. First, HIV patients in resource-poor settings typically present with serious opportunistic infections, such as parasitic disease, not seen routinely in wealthy countries. These conditions need appropriate diagnosis and treatment for antiretroviral therapy programs to succeed. Second, HIV patients require years of long-term care. Although managing HIV as a chronic-disease is common in wealthy nations, such long-term care practices are not widespread in economically disadvantaged regions, where medical care is generally limited to acute care, with the goal that patients be "re-oriented toward recovery" in a single visit to a health worker.

Further complicating delivery of effective HIV patient care in these settings is the lack of appropriate diagnostic tools. Much of the clinical testing used to support delivery of antiretroviral therapy was developed in the industrialized world, using samples obtained from patients in medically "uncomplicated" populations. As the fight against AIDS went global, so did the tests, which were deployed into areas where medical and other resources are scarce, and opportunistic infections are common. Unfortunately, clinicians and laboratory personnel are finding that tests optimized in high-resource environments often provide less-than-optimal results in resource-poor settings. No area of HIV patient testing has proved more challenging than CD4 testing.

CD4/CD4% and Hematology Parameters Plus Onboard Storage of Results Enable Better HIV Patient Care

PointCare Technologies designed its FDA-cleared PointCare NOW system working closely with clinicians and laboratory personnel on the front lines of HIV care in developing regions to optimize testing procedures to meet the specific needs of the patient population and to address the challenges unique to their clinical environment. Accordingly, the system has a larger test menu than the traditional CD4 counter to give greater insight into the patient's overall health. In just eight minutes, and from one patient sample, the PointCare NOW system delivers 12 results in one easy report:

- *CD4 count and CD4% (expressed as a percent of total lymphocytes);*
- *WBC differentials;*
- *Hemoglobin;*
- *Lymphocyte, neutrophil, monocyte, eosinophil (count and percent for all).*

As programs to combat HIV continue to expand, the need for a comprehensive diagnostic picture of **each** *patient extending over many years of the patient's life has become acute. In industrialized countries, clinicians usually have access to additional diagnostic tests beyond CD4 counts and medical records for each*

patient. In many remote HIV-treatment settings, these patient records are not readily available, impeding successful antiretroviral therapy. Because diagnostic pictures of patients evolve over time, and chronic clinical care is necessary, the PointCare NOW system stores all patient test results onboard the instrument, enabling clinicians to view all results for any patient at any time. This feature allows clinicians to trend results for each patient and view results from previous visits along with current test results.

Clinicians who use the system have found that the eight-minute PointCare NOW results and onboard access to all previous test data provide increased options for improved diagnosis and treatment of their HIV patients. **The purpose of this guide is to explain how the parameters on the PointCare NOW system can be useful in the clinical management of HIV patients in developing regions.**

Technical Factors Affecting CD4 Counts: Uses of CD4%

Highlights

Many factors in addition to HIV-status can influence CD4 counts. CD4% values provide useful cross-checks on CD4 counts and can normalize factors other than HIV-status that alter CD4 counts. *If both CD4 counts and CD4% values change in parallel, the changes are probably HIV-related. If CD4 counts and CD4% values do not change in parallel, the changes are probably not HIV-related.* Non-HIV related changes in CD4 counts include:

- Opportunistic infections, including syphilis
- Infection with tuberculosis (TB)
- Time of day
- Recent rest
- Recent stress

World Health Organization (WHO) guidelines indicate that clinicians use CD4% values in initiating and monitoring antiretroviral therapy in pediatric HIV cases. However, many clinicians have found that CD4% values are also useful in *adult* HIV care.

For many years, CD4 counts have been recognized as important parameters for tracking progress of HIV infection. CD4 counts have been used as indicators for both initiation and management of antiretroviral therapy in HIV patients. However, many studies have shown that common conditions, including infection with TB and/or other opportunistic infections, stress factors, and circumstances of sample collection, affect CD4 counts. In addition, CD4 counts exhibit day-to-day variability approaching 40 percent. Variability in CD4 counts can mislead clinicians responsible for delivery of antiretroviral therapy. A clinically useful addition to CD4 counts is the ratio of CD4 lymphocytes to total lymphocytes in peripheral blood, or "CD4%." Many factors that impact CD4 counts *do not* affect CD4% values. Patient management can be improved by simultaneous monitoring of both CD4 count and CD4%.

Cells bearing CD4-antigen are a sub-population of all T-lymphocytes. Estimates are that only about two percent of CD4-bearing lymphocytes are circulating in blood. The remaining 98 percent of these cells are sequestered in tissue compartments. Two important tissue compartments where lymphocytes are found in abundance are connective tissue and lymphatic tissue.

Laboratory procedures for CD4 testing are designed and optimized for blood samples. This means that CD4 lymphocyte counts are based on the relatively small fraction of CD4 cells found in circulating or peripheral blood at the moment of sample collection. Consequently, values associated with CD4 lymphocyte counting are subject to problems common to all "small-sample" counting situations, namely, high variability. Several factors, in addition to HIV-infection, can alter CD4 counts in peripheral blood. Understanding these factors will enhance interpretation of CD4 counts. Failure to understand these factors and how to compensate for them, may lead to poor management of HIV patients.

Numerous studies conducted using samples of peripheral blood from patient populations in the industrialized world provided the evidence-base for current guidelines for HIV patient management.[1] In general, these patients presented with relatively uncomplicated HIV disease; they had few if any opportunistic infections, and conditions under which their blood samples were collected were well-controlled.

Today, worldwide focus on HIV-patient management has shifted to resource-poor environments where opportunistic infections, including TB, anemia, and neutropenia, are common, and conditions under which blood samples are collected cannot be well-controlled. This means that it is difficult to obtain reliable CD4 results.

In patients where HIV-infection is the only disease condition, numbers of circulating CD4 lymphocytes *decrease* during the progression of HIV disease and *increase* with successful delivery of antiretroviral therapy. In resource-poor settings, it is rare to find patients where HIV is the only disease condition. Thus, in these settings, interpretation of CD4 counts is more complex than in the original studies. In the global epidemic, clinicians regularly see HIV patients who present with opportunistic infections that dramatically affect lymphocyte counts, and hence CD4-lymphocyte counts. In these patients, changes in CD4 counts may have nothing to do with HIV-infection, and clinicians often welcome additional information before making treatment decisions.

Fortunately, many difficulties associated with CD4 counts can be resolved by cross-checking CD4 counts with parallel measurement of CD4% values to help rule out non-HIV-related causes that could affect CD4 counts. In many situations, when CD4 counts change, CD4% values do not change. In these cases, CD4% can be used to exclude non-HIV-related sources of variability. Cross-checking CD4 counts in parallel with CD4% allows clinicians to normalize CD4 testing for some factors. Examples are described below.

Tuberculosis

As the global burden of TB increases, evidence accumulates that TB-status alters CD4 counts. In 2006, a study in South Africa[2] followed progression of pulmonary TB in 21 newly smear-positive patients, none of whom were HIV-positive. Participants were monitored closely for several parameters, including CD4 counts, as they progressed into early stages of acute disease. The authors observed that numbers of total lymphocytes decreased from 2,300 cells/μL to 1,300 cells/μL as patients entered early stages of acute disease. Because TB affects all lymphocytes, CD4 lymphocytes are also affected. In this study, CD4 counts dropped from a mean of 1,100 cells/μL to 600 cells/μL as patients entered early stages of acute disease. Although both lymphocyte counts *and* CD4 counts climbed during 26 weeks of successful treatment, neither count reached "healthy control" levels. Thus, CD4 counts are affected by both progression and treatment of TB infection.

HIV-infection is a significant risk factor for TB.[3] Cross-checking CD4 counts with CD4% values can normalize effects of non-HIV factors influencing CD4 counts, including progression of TB. In the example above, "healthy controls" displayed mean CD4% values of 48 percent (1,100/2,300), whereas patients in early stages of acute disease displayed mean CD4% values of 46 percent (600/1,300). After 26 weeks of successful treatment, the mean CD4% was 44 percent. Even though CD4 counts showed significant changes during treatment, CD4% values did not change. There was almost no difference between CD4% values for healthy controls versus patients in early stages of acute disease and at the end of successful treatment.

Changes in CD4 counts in patients where TB may be present should be confirmed by changes in CD4% values. If CD4% values do not change, then clinicians may assume there have been no HIV-induced changes in CD4 counts.

Diurnal Variation

Another commonly cited source of lymphocyte (and thus CD4 count) variability is diurnal (time-of-day) variation. In 1990, Malone and coworkers[4] performed what continues to be the most comprehensive study of diurnal variation in lymphocytes and lymphocyte subsets. Comparing diurnal variation in lymphocyte and CD4 counts between HIV-infected and uninfected patients, they found:

- In uninfected patients, lymphocyte counts increased from 1,902 cells/μL to 2,242 cells/μL, between the hours of 8 a.m. and 4 p.m. During the same interval, CD4 counts increased from 818 cells/μL to 970 cells/μL. *CD4% values remained constant at 43 percent.*
- In HIV-infected patients, all of whom had CD4 counts below 500 cells/μL, lymphocyte counts increased from 1,452 cells/μL to 1,698 cells/μL between the hours of 8 a.m. and 4 p.m. During the same interval, CD4 counts increased from 384 cells/μL to 447 cells/μL. *CD4% values remained constant at 26 percent.*

This study is often cited to show that CD4 counts change less during the day in more-advanced-stage HIV patients than in early-stage patients (change of +63/μL compared to +152/μL). Perhaps more interesting is that CD4% values *did not change at all during the day*, providing additional support for cross-checking CD4 counts with CD4% values in HIV-patient monitoring. This study shows that CD4% values can normalize time-of-day variations in sample collection. In many resource-poor settings, time-of-day for sample collection using typical testing procedures is either unknown or uncontrolled.

Closer review of Malone's data reveals that CD4% values can also be used to normalize "between-day" monitoring of CD4 counts. Patient samples were collected at 8 a.m. on three consecutive days. The authors compared between-day variability in testing for total lymphocytes, CD4 counts, and CD4% values. In patients with AIDS (Stage IV HIV-infection), lymphocyte counts showed between-day coefficients of variation (CVs) of 40 percent, and CD4 counts showed between-day CVs of 35 percent. In contrast, CD4% values showed a between-day CV of just 10 percent. Thus, in addition to being useful parameters for during-the-day monitoring, CD4% values are also useful for between-day monitoring.

Pediatric HIV Care

Measurement of CD4% values is essential for optimal care and treatment of pediatric HIV patients. Lymphocyte counts are very high in children, and thus CD4 counts are also very high. In 2010, the World Health Organization released recommendations for initiation and monitoring of pediatric HIV.[5] Changes from previous recommendations include earlier initiation of antiretroviral therapy in children between the ages of two and five with CD4% values ≤ 25 percent, or CD4 counts of ≤ 750 cells/μL.

Antiretroviral Therapy

A final observation about use of CD4 counts and CD4% is warranted. In 2006, Hulgan *et al*.[6] studied a large, multi-center HIV patient cohort to find relative prognostic values of CD4% versus CD4 counts for decisions to initiate antiretroviral therapy. The study not only showed considerable ranges of CD4% associated with specific CD4 counts – but also that CD4% correlated well with probabilities that patients would have an AIDS Defining Event (ADE) within six years. For example, patients in the group defined by CD4 counts of 200 cells/μL had CD4% values ranging from five to 40 percent. Patients near the CD4% range of five percent in this group had 60-percent probabilities of six-years-free of an ADE, while patients near the CD4% range of 40 percent in this group had 85-percent probabilities of six-years free of an ADE. Even more interesting were patients in the group defined by higher CD4 counts (300 cells/μL). These patients also had CD4% values ranging from five to 45 percent. *While these patients had similar CD4% values to those in the lower CD4 count group, they showed increased probabilities of six-years-free of an ADE.* Patients near the CD4% range of five percent in this group had 75-percent probabilities of six-years-free of an ADE; patients near the CD4% range of 45 percent in this group had 90 percent probabilities of six-years-free of an ADE. *Hulgan and coworkers concluded that CD4% at initiation of antiretroviral therapy can predict disease progression independently of CD4 counts. They proposed that CD4% values be used to determine timing of therapy.* Studies like these indicate expanded uses for CD4% beyond the current cross-check functions are on the horizon.

In summary, although CD4 counts are used routinely to monitor HIV patients, when used alone, CD4 counts can be misleading. This is because many common conditions interfere with routine CD4 counts and can present difficulties for clinician interpretation of the values. *Variability in CD4 counts can be cross-checked by parallel measurements of CD4% values, which can help rule-out non-HIV-related influences in situations where CD4 counts change and CD4% values do not.*

Direct Effects of HIV on the Hematology Profile

Highlights

In addition to reducing both CD4 counts and CD4% values, HIV-infection also reduces production of other blood cells, specifically:

- Red blood cell (RBC) production in bone marrow is reduced in HIV-infected patients. Reduced RBC production results in anemia, which is predictive of poor outcomes for HIV patients.
- Neutrophil production in bone marrow is reduced in HIV-infected patients. Reduced neutrophil production compromises defense against opportunistic infections, which left untreated, can delay or complicate delivery of antiretroviral therapy.

Routine tracking of hemoglobin values and neutrophil counts in HIV clinics allows clinicians to detect onset and progression of anemia and/or neutropenia. In patients in advanced stages of HIV disease, bacterial infection is a serious and often life-threatening complication. By "trending" neutrophil counts in HIV patients, clinicians will better understand patient risk for bacterial infection.

Although values for both CD4 counts and CD4% decrease during progression of HIV, these are not the only hematology profile components to do so; reductions in numbers of both red blood cells and neutrophils also correlate with progression of HIV. In 2007, Mildvan *et al*.[7] reported a 36 percent prevalence of anemia in HIV patients. Friel and Scadden[8] reported that 50 to 70 percent of HIV patients became neutropenic in late stages of their disease. Anemia and neutropenia are serious complications for HIV patients.

Clinicians managing delivery of antiretroviral therapy for HIV patients in well-funded settings expect routine hematology profiling for each patient, and consequently, anemia and neutropenia are usually detected early and managed appropriately. That is typically *not* the case in low-resource settings, such as remote HIV clinics, where hematology instruments are not routinely available. Even where instruments are available, technical and financial obstacles often get in the way of reliable hematology profiling. Thus, two serious hematological conditions, anemia and neutropenia, generally go undetected.

Anemia

Several studies have shown that monitoring hemoglobin levels is essential to optimal HIV-patient management. In 1999, Mocroft *et al*.[9] studied correlations between hemoglobin levels and survival of HIV patients. These authors used hemoglobin levels (in g/dL) as quantitative measures of anemia and found that, among patients with similar CD4 counts and viral load, most-recent values of hemoglobin were strong independent prognostic markers for death. In their study, a 1 g/dL decrease in most-recent hemoglobin levels increased risk of death by 57 percent. In fact, risk hazards for just a 1 g/dL decrease in hemoglobin levels were approximately equal to those for 50-percent decreases in CD4 counts and a full-log increase in viral loads. *These data illustrate that measuring hemoglobin is just as important as measuring CD4 counts and viral loads.*

Although origins of HIV-associated anemia are not well understood, there are links with antiretroviral therapy. In 1995, Moore[10] reported drug treatments, infections, and neoplasms as sources of anemia in HIV patients. In 1999, Sullivan *et al*.[11] reported that 22 percent of anemias they encountered were related to therapeutic drugs used in treatment of HIV patients. Sullivan *et al.* also showed that patients who developed anemia before their CD4 counts dropped below 200 cells/μL were 2.5 times more likely to die than patients who developed anemia after their CD4 counts dropped below 200 cells/μL. *Thus, early onset of HIV-associated anemia can be viewed as an added risk factor in progression of HIV. This increased risk argues strongly for early tracking of hemoglobin in HIV patients.*

Anemia undermines quality of life. Anemic patients are often perceived as lazy or irresponsible when, in fact, they have low hemoglobin levels (and thus low oxygen-transport capacity). Consequently, they often have difficulty maintaining jobs, and caring for themselves and their families. Only patients who have adequate energy can remain vital parts of their communities. If anemia could be identified and treated, then anemic patients would not have these additional burdens. *Optimal management of HIV patients would include routine monitoring of hemoglobin levels at the time of CD4 testing.*

Neutropenia

Among the first white blood cells to concentrate at sites of infection, neutrophils, comprise 50 to 70 percent of the white blood cell population and serve as "first lines of defense" against bacterial infections. In contrast to RBCs that may live for a month, neutrophils live for only a few hours. After arriving at sites of infection, neutrophils form extracellular "nets" to capture and ingest bacteria, in a process known as phagocytosis. After ingesting invading bacteria, neutrophils die quickly and form pus. Neutrophils are constantly replaced in healthy individuals.

Several reports have described correlations between neutropenia and HIV-infection. Moore *et al*.[12] described neutropenia as an independent risk factor for bacterial infection in HIV patients with the same CD4 counts. Patton[13] studied 516 HIV patients in various stages of disease and found that 27 percent were neutropenic. In 1987, Zon *et al*.[14] reviewed hematology records of a well-characterized HIV cohort and found that 50 percent were neutropenic. Jacobson *et al*.[15] published a retrospective study of neutropenia in approximately 2,000 HIV patients, which found that risk of hospitalization for bacterial infection correlates closely with degree of neutropenia.

Unexplained anemia (hemaglobin levels of < 8 g/dL), and/or neutropenia (neutrophil counts of < 500/cells/μL) are both indicators for World Health Organization Stage III HIV infection. Thus, regular measurement of both hemoglobiln levels and neutrophil counts can be useful in long-term HIV patient monitoring. Reductions in neutrophil counts provide early indications of severe neutropenia.

Hematology Profiles for TB Infection in HIV Patients

Highlights

HIV patients are often co-infected with other diseases, including TB. Diagnosis of TB in HIV-positive patients is more complicated than in HIV-negative patients. Relatively "low-tech" methods of TB diagnosis, such as skin tests and chest X-rays, do not work well in HIV patients. Relatively "high-tech" methods of TB diagnosis do not work well in remote settings.

Recent observations about progression of TB in HIV-negative patients may also be useful for HIV patients. Changes in neutrophil and monocyte counts are used to monitor both progression of disease and success of treatment in patients with pulmonary TB. In pulmonary TB patients who are HIV-negative, the product of neutrophil counts and monocyte counts (NM product) can be used to monitor response to treatment:

- Sudden spikes in NM products may indicate development of TB and need for treatment.
- Downward trends in NM products during treatment indicate treatment success

TB Management

Approximately one-third of the world's population (or two billion people) is infected with *Mycobacterium tuberculosis*, the bacterium that causes TB. In patients who develop pulmonary TB, disease progression is characterized by pulmonary clinical symptoms such as severe coughing, often with sputum or blood, and chest pain. TB is termed "inactive" or "latent" when patients' immune systems can control the bacterium and clinical symptoms are unapparent. Although latent TB is not contagious, people with latent tuberculosis are frequently termed "carriers." TB is termed "active" when patients' immune systems are unable to suppress the bacterium. Diagnosis of TB infection usually begins with skin tests and chest X-rays. TB skin tests are simple to administer and react positively for both active and latent disease. Patients who are TB-skin-test positive are referred for chest X-rays. Sites of local inflammation are visible in chest X-rays of patients with active TB.

TB is a leading cause of death of HIV patients, according to the World Health Organization.[16] TB Infection usually occurs before HIV-infection or early in progression of HIV. In HIV patients, latent TB disease can become active disease as HIV progresses and patients' immune systems are impaired. Although knowledge of TB infection-status is especially important for treatment of HIV patients, *obtaining* information about TB infection-status is extremely difficult, particularly in patients in resource-poor settings.[17]

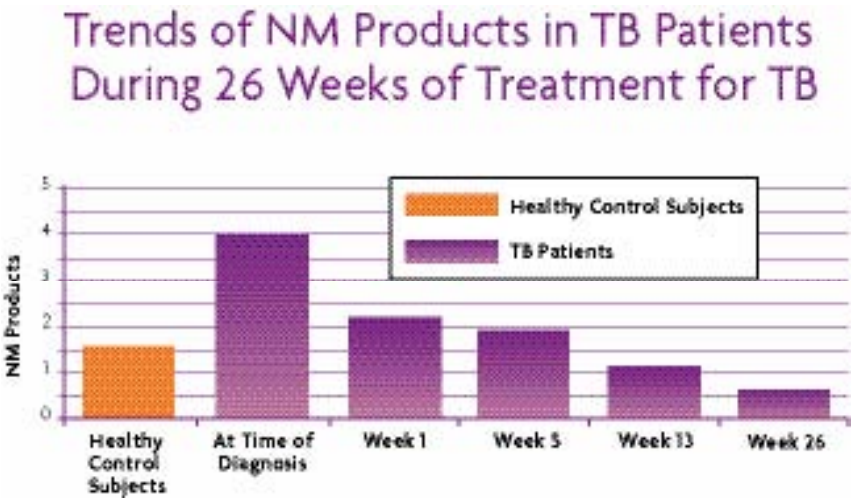
Until recently, undiluted-sputum-smear microscopy has been the primary diagnostic method for TB in resource-poor settings. However, the method is recognized as having high false-negative rates for *all* TB diagnoses and these high false-negative rates are exacerbated in HIV patients.[18] Many methods for screening and diagnosing pulmonary TB work even less well in HIV patients, who often have extra-pulmonary TB. Indeed, clinicians have found both TB skin tests and chest X-rays to be notoriously misleading in HIV patients. Weakened patient immune systems are unable to mount inflammatory responses to infection. Recently, Cain *et al.*[17] presented evidence for an algorithm of interview questions for screening and diagnosing TB in HIV patients.

The definitive method for diagnosis of active TB in HIV patients is culture of sputum. Unfortunately, access to this method is very limited in resource-poor settings. Even in places where access is possible, logistics for this method are formidable. In places where most HIV patients live, establishing facilities to culture TB is a daunting task and locating patients after culture results are available is time-consuming. Under such limitations, patients with clinical symptoms of TB are frequently assigned to therapy presumptively.

A simple hematology method may buttress presumptive diagnoses of TB. This method arises from work conducted in the 1920s and 1930s,[19] when Florence Sabin studied TB in rabbit models and observed that monocyte counts in blood rose from "normal" levels of eight percent to 15 percent a few days after rabbits were infected with TB. In 2006, Veenstra *et al.*[2] confirmed Sabin's work using human subjects in a study of healthy subjects and those in successful treatment for active TB.

The graph on the following page shows trends in NM products (neutrophil counts multiplied by monocyte counts) of TB patients during 26 weeks of treatment for TB, as derived from Veenstra *et al.*[2] data. The first bar shows NM products for healthy controls. The second bar shows NM products at the time of diagnosis of pulmonary TB. NM products at the time of diagnosis are 2.5-fold higher than those of healthy controls. During the 26-week treatment, NM products trend downward (bars three through five).

Upon completion of therapy, values for all NM products of TB patients were below those of healthy-control levels. Total white cell counts and other white cell subsets, including total T cells, B cells, and NK cells, were also at reduced levels upon completion of therapy. Simple automated white cell differential counts were all that was needed to monitor these events.



NM products at the time of diagnosis are 2.5-fold higher than those of healthy controls. During treatment, NM products trend downward. Upon completion of therapy, NM products were below those of healthy controls.

Using Eosinophil Monitoring to Manage Helminth Infection in HIV Patients

Highlights

Helminth infection (worms) affects millions of people in regions where HIV is prevalent. Thus, HIV patients in these regions often suffer from co-infections with helminths. Because helminth infections can adversely affect progress of antiretroviral therapy, helminth diagnosis and treatment should be part of routine HIV-patient management. Characteristics of patients with helminth infection include:

- Persistently elevated eosinophil counts.
- Declines in eosinophil counts (back to normal ranges) when treatment is successful.

Eosinophil counts coupled with fecal diagnosis of helminth infection may be a useful tool to help improve management of helminth infections. High eosinophil counts can be used as prompts to obtain and examine stool samples for helminth infection. If stool samples are positive or presumptive for worms, anti-helminth therapy can be initiated and success of therapy can be monitored using eosinophil counts.

Estimates are that one-third to one-half the people who live in poverty are chronically infected with helminths. School-age children are disproportionately affected because helminth infection causes cognitive impairment, poor memory, physical weakness, and stunts growth. Helminth infection commonly accompanies HIV-infection. A recent study by Modjarrad *et al*.[20] in Lusaka, Zambia, showed that 25 percent of HIV patients were co-infected with helminths. These authors suggested that helminth diagnosis and treatment should become a routine part of HIV care.

Borkow *et al*.[21] have reviewed relationships between progression of HIV and helminth infection. These authors concluded that well-documented effects of helminth infection on immunity should raise concerns about management of HIV patients. The authors demonstrated correlations between helminth infection and HIV viral loads, showing that when helminths were eradicated in HIV patients, viral loads for these patients decreased significantly. (Their attempts to find correlations between CD4 counts and helminth infection were not successful.)

In a separate study, in Nigeria, Uwah *et al.*[22] demonstrated further correlations between helminth infections and HIV viral loads. In this study, *when helminth infections were eradicated in HIV patients, viral loads for these patients decreased and the patients displayed improvement in clinical symptoms associated with HIV.*

The most common method for diagnosis of helminth infection is microscopic examination of feces. A World Health Organization publication by P.C. Beaver[23] contains a definitive statistical analysis of the direct-smear method and concentration techniques for diagnosis of helminth infection. Beaver concluded that although the direct-smear technique should be sufficient to detect helminths, it is not capable of providing quantitative estimates of helminth load. This means that current techniques for detection of helminthes are not sufficiently quantitative to track success or failure of therapy.

In endemic areas, helminth infections are the most typical reason for elevated eosinophil counts or eosinophilia.[24] *Although elevated eosinophil counts are not in themselves diagnostic for helminth infections, they can be very useful when coupled with diagnosis by fecal examination. After diagnosis, regular monitoring of eosinophil counts is a powerful tool for monitoring success of anti-helminth therapy.* Eosinophil counts are simple to obtain from peripheral blood samples. Loutfy *et al*.[25] demonstrated utility of this tool for monitoring treatment of strongyloidiasis. Harries *et al.*[26] reported on a group of 119 travelers who returned to England with eosinophilia. Even though only 39 percent of the group had definitive fecal sample diagnosis for parasite infections, all were presumptively treated for parasite infections and all experienced decreased eosinophil counts.

SUMMARY AND CONCLUSIONS

When viewed globally, more than 90 percent of all HIV patients live in resource-poor settings. The World Health Organization is encouraging decentralization of clinical testing to support HIV management of these patients. Many challenges are associated with decentralization – perhaps the most significant is reliable CD4 testing and access to test results that paint a broader picture of the patient's overall health in a single visit. Most HIV patients seeking antiretroviral therapy in developing regions present with complex medical conditions not often encountered where CD4 testing was developed. Opportunistic infections common in resource-poor settings can interfere with CD4 counts, requiring additional hematology testing for optimal mangement of antiretroviral therapy.

Clinician-friendly, the PointCare NOW system addresses the challenges of reliable CD4 testing in decentralized settings. The system is easy to operate with minimal training, and fully automated, capped-tube sampling means that the operator is never exposed to contaminated blood. Flexible power options enables reliable testing anywhere, anytime, with fast, easy set-up for clinic and mobile use.

The PointCare NOW system offers significant advantages for clinicians:

- It is the only point-of-care system currently available that bolsters and cross-checks CD4 counts by providing CD4% values with each test – a fast, easy, and cost-effective way for clinicians to normalize many non-HIV-related variables associated with CD4 testing, including opportunistic infections and timing of blood-sample collection.

- Onboard results storage gives clinicians ready access to patient data at all times, enabling long-term trending of patient hematology profiles that are integral to effective management of many chronic conditions, such as anemia (hemoglobin), HIV-induced neutropenia (neutrophils), helminth infections (eosinophils) and pulmonary tuberculosis (monocytes, lymphocytes, and neutrophils), in addition to HIV disease (CD4 counts and CD4% values).

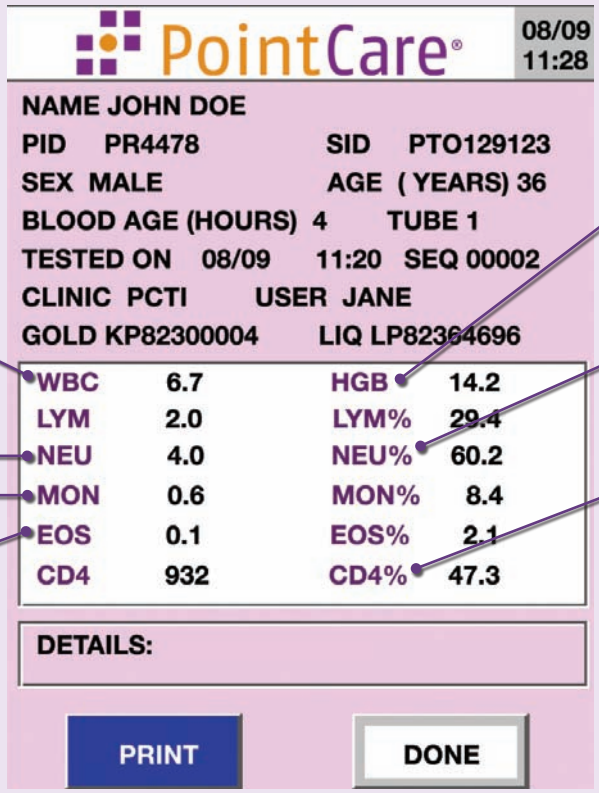
With one sample, one visit – and in just eight minutes – the PointCare NOW system delivers 12 results in one report for better disease management. Clinicians providing HIV care around the globe can have easy access to the essential diagnostic information they need to make vital treatment decisions before the patient has left the clinic.

POINTCARE NOW PARAMETERS FOR BETTER DISEASE MANAGEMENT

White blood cell count monitoring can help detect opportunistic infection.

Neutrophil-Monocyte (NM) product may help flag HIV patients co-infected with tuberculosis.

Eosinophils can be a valuable marker to flag and monitor parasitic infection.



Hemoglobin concentration can help identify anemia early to improve health outcomes.

Low **neutrophils** put HIV/AIDS patients at increased risk for bacterial and fungal infection.

CD4% is a critical parameter in pediatric *and* adult care
Unlike absolute CD4 values, CD4% values remain constant within the increasing or decreasing lymphocyte population. When viewed together, **CD4, CD4%, and lymphocyte** can be a more-accurate indicator of immune status than CD4 count alone, facilitating internal cross-checking of each CD4 patient report.

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