

## Chapter 12

***Integration of Palliative Care with ART******Overview***

Prior to the advent of ART, HIV/AIDS was characterized by progressive damage to the immune system, with increasingly frequent occurrences of opportunistic infections (OIs) and AIDS-related cancers and ultimately death.

Recent advances in treatment have significantly reduced AIDS-related morbidity and mortality and provided the means to transform HIV infection into a manageable chronic disease. But HIV/AIDS remains a significant cause of serious illness and death for young adults even in the era of ART because:

- ART is not a cure for HIV/AIDS
- The majority of people with HIV have limited access to ART
- HIV/AIDS is a chronic, debilitating disease
- HIV-related illness is cumulative, causing an increasing burden over time
- Treatments for HIV often have toxic side effects

The biomedical paradigm of ART as the cornerstone of treatment has resulted in a more narrow focus and a de facto separation of disease-specific (curative) and symptom-specific (palliative) care for patients, who survive longer in the latter stages of the disease. However, patients need increasingly comprehensive symptom management, as well as psychosocial, family, spiritual, and end-of-life care (Selwyn, 2003).

With ART, HIV/AIDS can be transformed into a chronic, manageable, yet still incurable disease. It is of increasing importance that HCWs in HIV care familiarise themselves with all aspects of HIV care, including the HIV-specific therapies. In this way, the HCW can make management decisions based on clinical and laboratory evidence, whilst providing holistic care for the patient's physical, psychosocial, and spiritual needs. HCWs must keep up to date with the rapid advancements in this field in order to provide current, comprehensive education and advice to the patient, allowing for informed treatment choices.

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### Model of Integrated Care

People with HIV require a holistic model of care that integrates curative and palliative services from diagnosis of HIV to death. The proportion of integration depends on the:

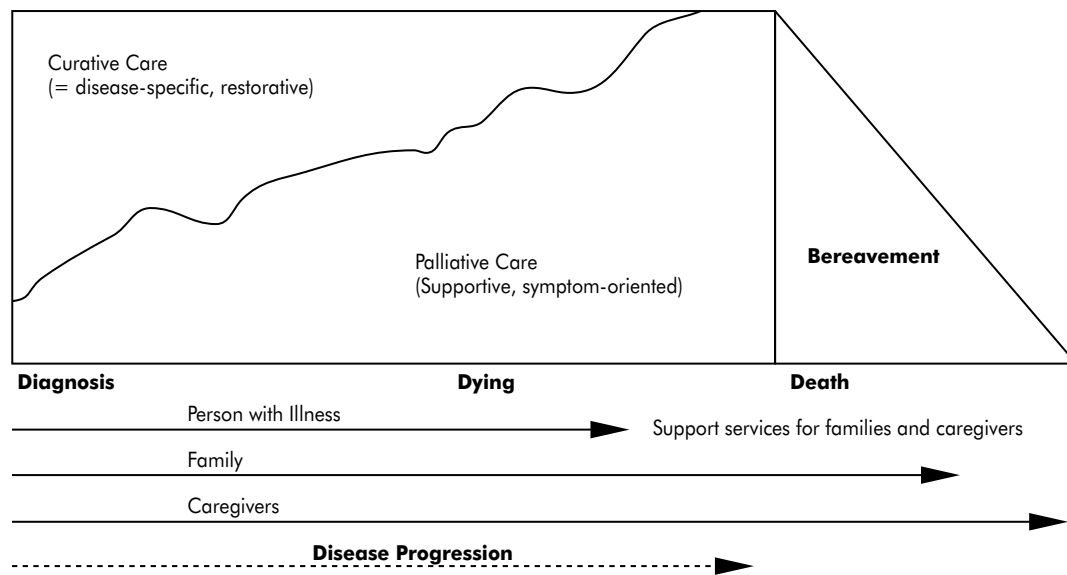
- Patient’s biomedical status on presentation
- Level of health care available to the patient
- Psychosocial and spiritual needs of the patient and family
- Level of support from family, friends, and community
- Availability of various support organisations (e.g., community-based organisations that provide food security and orphan care)
- Availability of accessible, affordable analgesia for symptom control during all stages of the disease

Good patient care is delivered by competent health care workers (HCWs) and those trained in palliative care who network with relevant services to offer holistic care to patients and families (see Figure 12.1). It is the responsibility of the primary care team leader, whether a physician, nurse or nurse practitioner, or clinical officer, to adopt this integrated approach, having ensured that all HCWs acquire the relevant competencies, knowledge, and skills.

An integrated approach is inherent in the working definition of palliative care:

Palliative care is patient- and family-centred care. It optimises quality of life by active anticipation, prevention, and treatment of suffering. It emphasises use of an interdisciplinary team approach throughout the continuum of the illness, placing critical importance on the building of respectful and trusting relationships. Palliative care addresses physical, intellectual, emotional, social, and spiritual needs. It facilitates patient autonomy, access to information, and choice.

**Figure 12.1: Integrated Model of Palliative Care**



## Current Role of HIV-Specific Therapies

### *Treating Reversible Causes*

HIV-specific medical treatment includes:

- treatment for OIs and AIDS-related cancers
- primary and secondary prophylaxis for OIs
- highly active antiretroviral therapy (ART)

The treatment of OIs and some cancers in patients with HIV may not mirror that provided to patients who are HIV-negative. The drugs of choice may differ, as may dosages and duration of treatment. With AIDS-related cancers the prognosis is influenced by the CD4 level (lower CD4 equating with a poorer prognosis) and the fact that these cancers tend to be more aggressive in HIV disease.

The current role of prophylaxis regimens, whether primary or secondary, is to provide the patient with increased protection against specific OIs once the immune system has suffered significant damage.

- Primary prophylaxis for PCP: where testing is available, with CD4 count  $<200$  cells/mm<sup>3</sup>
- Secondary prophylaxis for PCP: after a confirmed episode of PCP

ART is meant to significantly reduce plasma viral load and increase CD4 levels, allowing for immune recovery, and reducing the frequency and severity of OIs, thus improving quality of life. This modifies the course of HIV/AIDS, giving it a more chronic nature.

### *Palliative Management*

The role of palliative care is of equal importance in HIV care, and includes:

- Pain and symptom control during all stages of the illness, including at the end of life
- Physiotherapy to restore body function
- Occupational therapy to assist patients to cope with functional restrictions, to adapt the home environment, and to provide assistive equipment such as walkers and wheelchairs
- Nutritional assistance and guidance
- General counselling and spiritual care

Whilst these services may not always be accessible to patients through a health system, much can also be provided by the family and the community. Integrating palliative treatment with HIV treatment provides the patient and family with holistic care, whereas HIV treatment alone does not optimise quality of life.

## Reasons to Integrate Palliative and HIV Care

**Palliative care enhances HIV care.** Patients may be referred for palliative care at various stages of their illness. Proper assessment and diagnosis by the palliative care team is vital to assuring optimal care at the correct level of health facility. The palliative care team must build a foundation of HIV knowledge, integrated with their knowledge of pain and symptom control, in order to appropriately manage patients with HIV.

**Side effects of HIV treatment require symptom management.** HIV therapies affect quality of life (QOL). Numerous pills (pill burden), food restrictions, side effects, toxicities, drug-drug interactions, and complex regimens are aspects of HIV therapy that affect QOL. Improving QOL is a key facet of comprehensive palliative care.

- Neuropathic pain is a good example of an ART toxicity that can be irreversible and impact negatively on QOL. Knowledge of pain management (one of the cornerstones of palliative care, and one poorly managed by curative care) is necessary to address this problem.
- Lipodystrophy and lipoatrophy are other examples of toxicities causing changes to body image. A change of ART coupled with dietary and counselling interventions will assist the patient to adjust to living with this condition.

**The phenomenon of pill-sharing requires that HCWs recognize that other family members may be taking some of the patient's medicine.** Under programmatic approaches, ART is offered in prescribed regimens to a limited sector of the community (e.g., specific employees), thereby excluding family members and leading to pill sharing. Under sponsorships, individuals receive ART through a benefactor (may even be a drug company), which may be shared with other HIV-positive family members who are excluded from care.

**Palliative care is about good communication.** Adherence is pivotal to the success of ART, and good provider–patient communication is pivotal to adherence. Communication skills between patient and HCW, and between members of the interdisciplinary team, are one of the hallmarks of palliative care. Because curative care places the focus more on technical skills than on communication skills, integrating palliative care provides an important contribution.

**Psychosocial factors affect health and well-being.** A purely biomedical approach to care focuses on laboratory markers and clinical symptoms, yet several studies (Farinpour, 2003; Kalichman, 2002; Leserman, 2002) document the effects of psychosocial factors on patient morbidity and mortality. Palliative care has always recognised the benefits of a holistic approach.

**Disease progression causes emotional distress.** Changes in laboratory results such as the viral load have been associated with changes in patients' emotional well-being (Leserman, 2002). HCWs need to be able to assess and manage patients who become depressed in response to treatment failure or other causes.

**HIV care involves dealing with patients at the end of life.** The physical and psychological results of treatment failure and drug resistance require that HCWs be equipped to deal with end-of-life issues when necessary.

**The divide between curative care and palliative care is often unclear.** Only an integrated approach provides continuity of care throughout the course of the disease

## Why Patients With HIV on ART Still Die

Although many people assume that ART cures AIDS, a wide range of factors, many preventable, can lead to treatment failure (Mascolini, 2004).

**Drug-resistant virus:** Primary resistance to antiretroviral drugs is more common in countries where there is significant access to ART with subsequent transmission of drug-resistant virus from one person to another. Secondary resistance occurs because of poor adherence, suboptimal dosing (resulting from financial inability to sustain uninterrupted therapy), or malabsorption of drugs (although this is rare and manifests as early rather than late treatment failure).

**Poor adherence to ART:** Poor adherence to treatment regimens leads to treatment failure. Intermittent therapy (defined as filling 75% of prescriptions) accounts for a 2.9-fold increase in the risk of death. Patients eventually die of classic AIDS-related diseases.

**Starting ART when disease is already advanced:** A large proportion of people still remain undiagnosed until their disease is advanced and not reversible.

**Tuberculosis:** TB is a major cause of death in people on ART, especially when patients have advanced HIV disease, extrapulmonary TB, and very low CD4 counts. ART should not be initiated until TB has been ruled out or treated for two months (see Chapter 6: Respiratory Symptoms).

**Liver disease:** People with HIV who are co-infected with hepatitis B virus (HBV) are more likely to have chronic HBV infection. People co-infected with hepatitis C tend to have more aggressive liver disease.

**AIDS-related and other cancers:** As more people are treated for OIs, there may be a relative increase in AIDS-related cancers such as non-Hodgkin's lymphoma, with resultant deaths. As people on ART live longer, there is an increased risk of their getting other cancers, such as lung cancer if they smoke.

**Heart disease:** As people on ART live longer, many will reach the age when heart disease becomes a problem. Risk factors for myocardial infarction include current or previous smoking, older age, previous heart disease, and male gender.

**Care by HCWs with limited HIV experience:** In studies, people with HIV who were cared for by physicians with more HIV experience tended to live longer. HCWs must have clinical experience and knowledge of available resources. Also, potent drugs in the hands of inexperienced HCW may serve to promote viral resistance.

**Renal failure:** Renal disease is caused not only by co-morbid conditions and toxic drug reactions but by HIV itself. For example, acute tubular necrosis may be a result of diarrhoeal disease or sepsis (Wilson, 2002).

**Suicide and homicide:** People living with HIV around the world die from suicide and domestic violence. Violent or self-inflicted death of people living with HIV is not uncommon in societies where the stigma of HIV is great, where women have minimal or no power in the sexual relationship, and where homosexuality is taboo.

**HIV psychosis and dementia:** People who suffer from HIV psychosis or dementia are especially vulnerable, and may die early if they lack the care and support of a protected and structured environment.

**Chronic substance abuse and chronic use of some traditional medicines:** Whilst liver-toxic drugs should be avoided in chronic alcohol abusers with cirrhosis and abnormal liver function, this may not be possible where laboratory testing and drug formularies are limited. Some traditional medicines interact with antiretroviral drugs (such as St. John's wort with protease inhibitors) or have toxic effects (such as potassium dichromate, which has been used in enemas) (Wilson, 2002).

## Core Competencies Required to Integrate Care

It is not the purpose of this chapter to provide details of HIV care, but rather to highlight the information that palliative care professionals should be aware of in order to integrate palliative care with ART. Integration of palliative care with ART requires knowledge in the following areas.

### *Diagnosis of HIV*

Knowledge about and access to HIV testing and care is highly variable, both within and between countries in Africa. The high prevalence of HIV can result in erroneous diagnosis of HIV/AIDS in patients that actually have TB, are malnourished, have endemic Kaposi's sarcoma, or are thyrotoxic. A firm diagnosis of HIV is desirable where possible, as a basis for all future management decisions, especially with regard to HIV-specific therapies.

Certain clinical conditions should prompt the HCW to offer HIV testing. These include herpes zoster, chronic herpetic ulcers, oral hairy leucoplakia, eosinophilic folliculitis, multiple molluscum contagiosum, and TB.

HCWs should understand the various HIV-related laboratory tests where available and be familiar with their interpretation, specificity, and sensitivity. These include antibody, antigen, RNA, and DNA tests.

The ability to communicate test results to patients may also assist with problems relating to denial, disclosure, and fears of imminent death.

Pre- and post-test counselling skills are necessary even in palliative care, especially when patients enter care late in the disease process.

Careful interpretation of HIV ELISA assays in children is of particular importance in regions where malnutrition is prevalent and must be differentiated from HIV infection. Maternal HIV antibodies can cause positive ELISA tests in an HIV-negative infant until the age of 18 months. The polymerase chain reaction (PCR) test for HIV DNA can provide definitive diagnosis in almost 100% of infants within three to six months of birth, but is expensive and not widely available in Africa. (See Chapter 28: Integration of Palliative Care with ART in Children.)

### *Staging and Monitoring HIV Disease*

Staging assists with knowledge of the range of possible OIs and cancers, eligibility for HIV-specific therapies, prognostication, monitoring response to therapy, determining early toxicities, and treatment failure. Laboratory testing can be prohibitively expensive, but with expanding access to treatment programmes, HCWs need to understand their significance.

Where CD4 tests are not available, using the full blood count (FBC) may prove helpful for making decisions (see Figure 12.2).

*If available*, CD4 tests and viral load tests can be used to assess the patient's prognosis. To understand the relationship between the two tests in estimating prognosis in HIV disease, consider a bus whose brakes have failed that is speeding towards the edge of a cliff (see Figure 12.3). The speed of the bus represents the viral load, the distance from the cliff is the CD4 count, and the bus tumbling down the precipice represents the onset of full-blown AIDS.

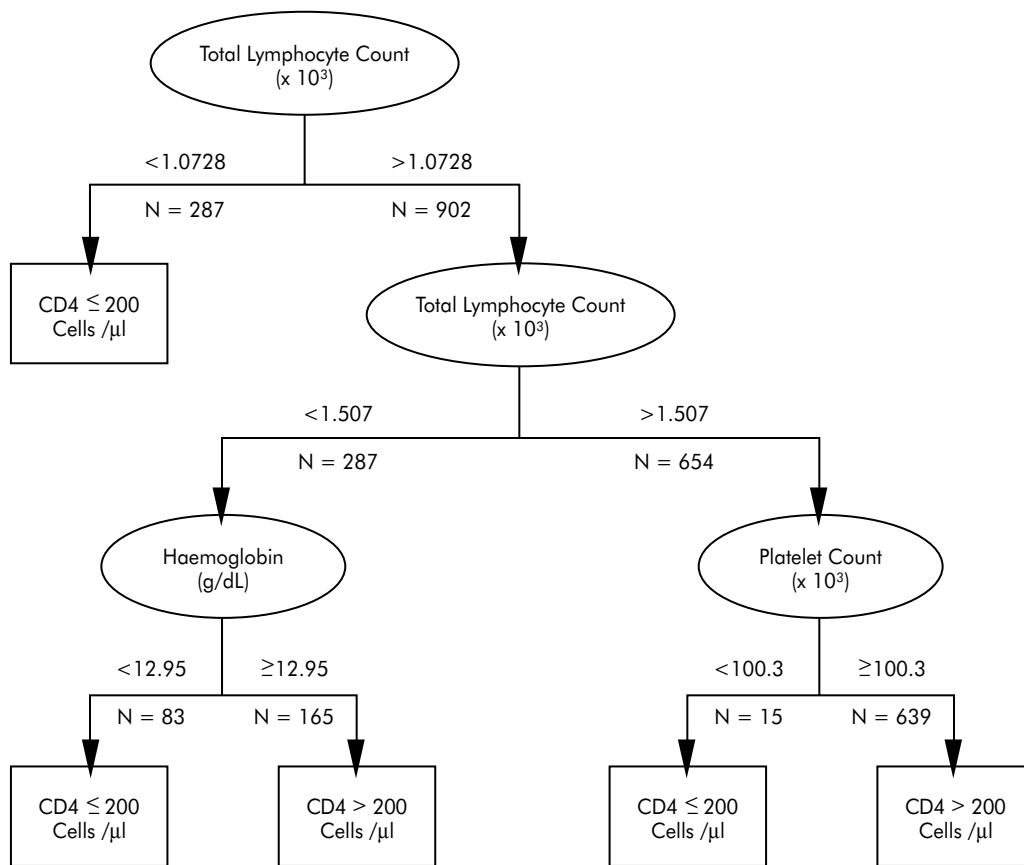
Proper assessment, and knowledge of clinical and immunological staging (according to the local access to laboratory markers), heightens awareness that current symptoms may be indicative of:

- New OI/AIDS-related cancers
- Deterioration of the underlying HIV/AIDS
- Side effects of HIV-specific therapies or other treatments
- Immune restoration syndromes
- Concomitant unrelated pathologies

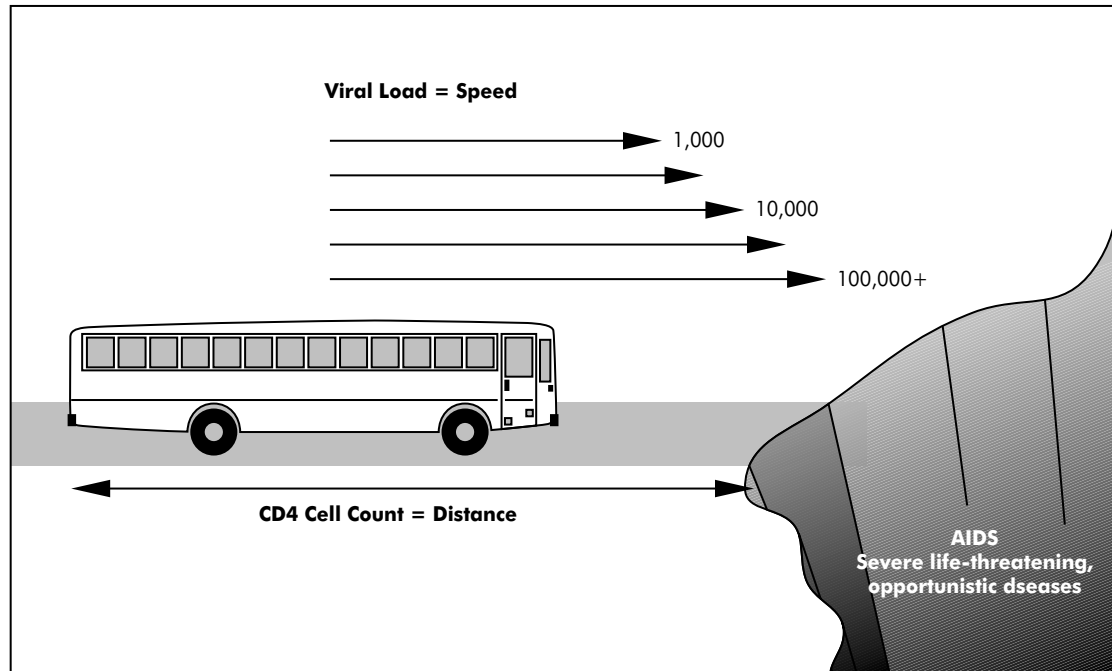
These in turn can provide valuable prognostic indicators and assist in determining the ratio of curative to palliative care for each individual patient.

A full assessment also enables the HCW to decide whether and when to initiate ART in a patient referred for palliative care. Knowledge of prognostic indicators specific to OIs and AIDS-related cancers is also vital for this purpose and well-defined in the literature.

**Figure 12.2: The Full Blood Count Decision Tree**



Source: Chen, 2003.

**Figure 12.3: Relationship Between Viral Load and CD4 Cell Count**

Source: Adapted from Evian, 2000.

### ***Details of HIV-specific Therapies***

Palliative care HCWs need to know the patient's previous medical illnesses that may impact on ART, such as diabetes mellitus and renal, liver, and cardiac diseases. They must also be familiar with the patient's HIV therapy, including:

- Drugs, including dosages
- Duration of each treatment
- Eligibility criteria for initiation and cessation of treatment
- Probable drug interactions and side-effect profiles (see Table 12.1: Properties of antiretroviral drugs)

This knowledge helps to determine:

- Which medications are essential
- Whether symptomatology is due to treatment
- Whether treatment needs to be discontinued based on intolerability
- Whether laboratory testing is necessary to ascertain toxicities, and
- Which treatment to choose for symptom control without impairing the therapeutic levels of ART (see Box 12.1)

HCWs need to understand the interaction of TB drugs and ART. They also should know which ARVs are safe for women of child-bearing age. The interaction of ARVs with contraceptives is not fully known. Nevirapine decreases the area under the curve for ethinyloestradiol by 29%, suggesting that hormonal contraception should not be used as the sole method of family planning. See Chapter 11: Pharmacology and Box 12.2 for more information on ART.

**Box 12.1:**

**Risk Factors For Life-Threatening Clinical Events**

There are numerous risk factors for the potential development of life-threatening clinical events in patients on ART (Reisler, 2003) including:

**HIV/host interactions:** Viral load and CD4 count levels as related to OIs and cancers.

**Stage of HIV disease:** Patients with lower CD4 counts are more likely to experience side effects, toxicities, and drug interactions when started on ART. Conversely, women with higher CD4 counts of >250 have a 12-fold increased risk for severe hepatotoxicity with the use of nevirapine.

**Other lab markers:** Low baseline creatinine levels; low CD4 level after 4 months of ART; low haemoglobin level (where new OIs are more likely to occur ) (Creagh, 2001); and elevated transaminase level (Lewden, 2002).

**Specific combinations of antiretroviral drugs:** For example, lactic acidosis caused by didanosine + stavudine.

**Genetic predisposition:** Some people whose disease progresses rapidly (rapid progressors) are in this category.

**Older age:** Older patients exhibit a less robust response of CD4 to ART than younger patients (Florence, 2003).

**Co-morbid conditions:** For example, patients with disseminated KS have a poorer prognosis than those with focal cutaneous KS, even with ART.

**Co-infections:** For example, patients with hepatitis B receiving ART have a greater likelihood of hepatotoxicity.

**Specific concomitant medications:** Drugs given with ART may cause increased hepatotoxicity or reduced levels of an ARV or interacting drug, increased likelihood of drug-drug interactions or poor adherence due to pill burden.

**Poor nutritional status:** Weight loss of 3–5% from baseline on ART is the best independent predictor of poor prognosis (Tang, 2002).

**Use of recreational drugs and alcohol:** Use of these increases the chance of non-adherence leading to treatment failure.

**Other social behaviours and practices.**

**Lack of HCW experience with HIV (WHO, 2002).**

**Table 12.1: Properties of Antiretroviral Drugs**

	AZT	DDI	D4T	3TC/FTC	TDF	LOP/RIT	NEV	EFF	Prevention of Side Effects
Taken with food					+	+			
Cell cycle activity	active	resting							
CNS penetration	60%	20%	30/40%	10%	13%	?	<45%		
Half-Life — Intracellular	3 hrs.	25–40 hrs.	3.5 hrs.	12/39 hrs.	10–50 hrs.	T1/2= 5–6 hrs.	T1/2= 25–30 hrs.	T1/2= 36–100hrs.	
Side Effects:									
Anemia	+								
CNS • Headache • Insomnia • Dizziness • Vivid dreams • Depression	+							+	Take at bedtime
GI • N/V • Bloating • Diarrhea • Pancreatitis • Hepatic necrosis	+	+			+	+	+	+	Prescribe Anti-emetic; Anti-diarrheal
		(original formulation-diarrhea)				+ 15–25%	(body ≥ 250 CD4)		
Rash				(occasional hyper-pigmentation-soles/palms)			15–30%	15–27%	
Nail-bed changes	+								
Fatigue/ Asthenia	+	+	+			+			
Peripheral Neuropathy		+	+						
Body Habitus • Facial wasting • Fatty deposits: Post. Neck & Abdomen	+	+	++			+			
Long Term • Lactic Acidosis • ↑lipids	+	+	+++			+		+	
CYP34A • Inhibiter • Inducer						+	(Both)	+	(Both)

AZT-Zidovudine; DDI-Didanosine; D4T-Stavudine; 3TC/FTC-Lamivudine/Emtricitabine; TDF-Tenofovir; LOP/RIT-Lopinavir/Ritonavir;

Nev-Nevirapine; EFF-Efavirenz (Stocrin)

### *Significance of Adherence in Treatment Success*

Adherence is an essential component of treatment success, with good adherence resulting in higher blood levels of drugs and improved virological and clinical outcomes. Greater than 95% adherence, defined as < 3 missed doses per month, is desirable to maximise the benefits of ART. Adherence is crucial in resource-limited settings, or where the programmatic approach does not allow for regular viral load testing.

Adherence counselling and support are key elements of success, and a patient-centred, rather than a provider-centred, approach is vital (see Box 12.2). A poor provider-patient relationship will negatively affect adherence.

Adherence in pregnant and immediately post-partum women is a special consideration. 'Morning sickness', the concerns over effects of ART on the fetus, physical and psychological changes after delivery, and the demands of caring for a newborn may all compromise maternal drug adherence (WHO, 2002).

Adherence in children is a special challenge given that poor health or economic conditions are likely to disrupt the family unit. Lack of disclosure to children can lead to their refusing to take medication. Failure to notify at least one person other than the primary caregiver, or all caregivers with access to the child, may result in missed doses should the primary care giver no longer be available or be incapacitated. Family-based care programmes, other peer supporters, and a holistic approach that addresses socio-economic, psychological, and biomedical factors may help to overcome this (WHO, 2002).

#### **Box 12.2:**

##### **Keys to Successful Adherence**

- Proper education and counseling BEFORE initiation of therapy
- Information on HIV and its manifestations, benefits and side effects of drugs
- Taking into account pill burden, dosing frequency, pill packaging, food precautions to fit the patient's lifestyle where possible
- Involvement of peer supporters in patient's treatment
- Awareness of 'pill fatigue' in previously adherent patients on treatment for a long time; pro-active enquiry into adherence and ongoing adherence support in ALL patients on treatment
- Cost-sharing (between patient and programme) is controversial with varied success depending on country and duration of treatment
- Family-based care when more than one family member is affected (prevents pill-sharing and provides immediate peer support)
- Use of pill boxes and other reminders
- Directly observed therapy (DOT) or modified DOT, especially allied to TB treatment
- Accessibility and availability of clinic staff and treatment
- Psychosocial support to minimise stigma
- Culturally appropriate adherence programs

*Significance of Treatment Failure*

HCWs must be aware of the criteria for treatment failure (available in HIV literature). Whether it is a first or subsequent treatment failure is important, as treatment options are limited with successive treatment failures. When options are exhausted, patients may be continued on treatment for immunological rather than clinical benefit. HCWs must assess the degree of clinical benefit expected and weigh it against the burden of long-term toxicities. Patient preference must also be considered.

Treatment failure has psychological consequences, especially if treatment options have been exhausted. End-of-life issues and advance planning need to be pro-actively discussed with patients before clinical decline ensues (see Chapters 14, 17, 29, and 32).

HCWs also need support during this time, as treatment failure in several patients may lead to despair over their role in the provision of ART, how their relationships with patients may have influenced compliance, failure to 'cure' the patients, and wondering whether the treatment is worth pursuing in other patients.

A pregnant woman who has failed treatment has her own and her child's illness and potential death to consider, and needs special support during treatment decisions.

HCWs need to be aware that treatment failure in children can result in severe psychological and spiritual consequences for families, as with the death of young cancer patients, and refer families for emotional support early, preferably before the crisis evolves.

Patients who have experienced treatment failure whilst on certain ARVs, such as tenofovir and lamivudine, may opt to continue these in conjunction with a new regimen for the benefits gained against previous hepatitis B infection, if resistant hepatitis B is not evident.

*When to Address End-of-life Issues*

End-of-life issues need to be addressed with patients before ART is initiated. Patients with drug-resistant virus will be more common as ART becomes more widely available. These patients will experience treatment failure early in their treatment and will have limited treatment options from the outset. With programmatic approaches or sponsorships, using four or more ARVs may not be an option.

End-of-life issues need to be discussed when a patient is well, free of the pressures of imminent death or marked illness, and practically able to initiate plans for the future. HCWs often avoid this discussion for fear that the patient will think that treatment has failed, death is imminent, or the HCW has no faith in the treatment. Also, the perception still abounds that if an issue is discussed it may become a self-fulfilling prophecy. A good provider-patient relationship and an interdisciplinary approach form the basis for discussing end-of-life issues with patients whilst they are well.

*When to Recommend a Pure Palliative Approach*

Pure palliation suggests a cessation of all HIV-specific therapies, including treatment for acute OIs and cancers, primary and secondary prophylaxis, and ART (see Box 12.3). As in patients with cancer, when to discontinue and what to discontinue should be decided in conjunction with the entire care team, including the patient and family. Decisions should take into account the following:

**Clinical and immunological stage of the disease** (the present biological prospects of the patient)

**Previous treatments and current treatment options** with expected benefits and burdens

**The desires of the patient and family caregivers**, who have been provided unbiased information on the patient's current biological prospects and the treatment benefits/burdens

**Treatment failure of all available treatment options**, with loss of immunological benefit and deterioration of clinical status

The use of mono- or dual therapy for symptom relief (e.g., clinical improvement of AIDS dementia complex on AZT alone) is controversial. Triple therapy is still recommended in these situations. Because patients on monotherapy are likely to have lower CD4 counts and therefore be more susceptible to side effects, monotherapy for pure symptom control must be embarked upon only if monitoring is possible (e.g., bone marrow suppression with AZT).

The laboratory tests should be done when patients are relatively stable. Other clinical features that indicate that end-of-life care should begin include:

- A WHO performance scale of 4: bedbound for more than half the day for a month
- No reversible underlying illness
- Encephalopathy and wasting syndrome
- Cryptosporidiosis, cytomegalovirus infection, progressive multifocal leukoencephalopathy, or primary central nervous system lymphoma

**Box 12.3:**

**Guidelines for Withdrawing Treatment and Beginning Pure Palliative Care**

No antiretroviral therapy options

*and*

Laboratory evidence of severe immune suppression (CD4 count  $<50$  cells/mm<sup>3</sup> or total lymphocyte count  $<0.75 \times 10^9$ /L)

*and*

Poor quality of life with NO reversible illnesses

*Note: all these should be present*

Source: Maartens, 2001.

**Post-exposure Prophylaxis Regimens for Occupational Exposure**

Where ARVs are available, programmes should have up-to-date protocols and drugs available to address post-exposure prophylaxis (PEP) for occupational exposure to HIV. HCWs need to understand and keep up to date with PEP protocols.

**Willingness to Keep up with Rapid Developments in the Field of HIV/AIDS Medicine**

As HIV/AIDS science is a rapidly developing field, HCWs need to keep up to date in order to have relevant, unbiased, scientifically based evidence for treatment choices for their patients.

**Immunisation in HIV Disease**

Recommendations for immunisation of patients with HIV are based on weighing benefits against risks, as HIV can alter the efficacy and safety profile of vaccinations and the susceptibility to the diseases for which immunisation can confer protection (Hecht, 1998).

**Efficacy:** HIV alters immune function so that vaccination may not confer the same protection to a person with HIV that an immunocompetent person would achieve. Whether the levels of antibodies thought to confer protection to immunocompetent individuals are adequate to confer protection to immunocompromised individuals is unknown.

**Effect on disease progression:** Activated CD4 cells are more susceptible to HIV infection than 'resting' CD4 cells. Exposure to an antigenic stimulus such as a vaccine activates CD4 cells. This suggests that vaccination could accelerate the course of HIV. Certain studies have shown an increase in viraemia post-vaccination, but whether the temporary increases might alter the long-term course of the disease is unknown. No studies to date have evaluated effects on HIV viraemia in patients on ART, but it is likely that ART would control the effects of vaccination on stimulating HIV replication.

**Safety of live attenuated virus vaccines:**

Concern has been generated over the development of disseminated disease in patients who received live vaccines.

***Specific Recommendations:***

**BCG:** BCG is not recommended as a standard vaccine with the possible exception of asymptomatic children in high endemic areas.

**Live vaccines:** The majority of live vaccines should be avoided in immunocompromised patients.

**Pneumococcal vaccine:** NOT recommended. Several studies have shown reduced responses to pneumococcal vaccine in HIV-infected patients, with those with advanced disease showing lower antibody responses than those with asymptomatic infection. Pneumococcal strains in sub-Saharan Africa have not been fully identified to recommend specific vaccination on the subcontinent.

***Immune Reconstitution Syndromes***

HCWs must be aware of, and hypervigilant about, the immune reconstitution syndrome in patients on ART to avoid misinterpretation of worsening symptoms as progression of underlying AIDS secondary to treatment failure. This syndrome occurs as a result of improved immune cell responses, causing worsening of OIs usually between two weeks and even up to six months of beginning treatment in some patients (Conway, 2004).

Immune reconstitution syndrome is characterised by fevers, lymphadenopathy, worsening clinical picture (TB on chest X-ray, expanding CNS lesions in toxoplasmosis), and weight loss. Transaminitis may occur as a result of a reconstituted immune response against underlying chronically infected hepatocytes in patients with hepatitis B, and needs to be distinguished from ART-induced hepatitis.

The HCW needs to distinguish between a new OI as the immune system recovers on ART, treatment failure with subsequent OI as the immune system deteriorates, concomitant disease, and the inflammation of immune reconstitution syndrome. The syndrome is typically self-limiting and may require corticosteroids to reduce inflammation. The presenting apparent OI may be documented in the past history, but may also be a masked previously undiagnosed entity.

Of note, a 'paradoxical reaction' in patients on TB treatment and ART is well established, in which symptoms worsen and in pulmonary TB, the chest X-ray shows signs of deterioration. However, sputa that have converted to negative on TB treatment will remain negative. Supportive treatment and steroids are recommended. Positive sputa should result in enquiries into whether the patient 1) is adhering to TB treatment, or 2) has developed multi-drug-resistant TB.

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