COMMUNITY OF SANT’EGIDIO

DREAM

Drug Resource Enhancement against AIDS and Malnutrition

Treating AIDS in Africa

A model for introducing antiretroviral treatment of HIV into healthcare systems in limited resource countries

LEONARDO INTERNATIONAL
TREATING AIDS IN AFRICA
DREAM, a total-approach program for treating AIDS in Africa, has been active in the field since March 2002, after two years of preparation work. Given its innovative approach, including antiretroviral therapy, and its initial choice of Mozambique – a country with low economic resources – as its institutional partner, raising the funds needed to start up and develop the project has become a central problem.

Time and funding have been the two poles – at times conflicting – within which we have acted, in the need to get the infrastructure, professional figures, and intervention models into the field with the urgency that the pandemic and lack of therapy demand. This is why DREAM was started with scant initial funding, sufficient for the first phase but not for its development: in the hope and conviction of being able to attract more substantial resources once the entire project becomes more understandable, effective, and verifiable on the field. And this has happened.

DREAM would not have been possible without a prompt opening of credit – at times of small proportions and at times more substantial – and trust from sponsors of all kinds that, although contributing in different amounts, were each for their own part important in subsequent development phases: UniCredito Italiano, Trenta Ore per la Vita, Sue Ryder Care, Fondazione Monte dei Paschi di Siena, Generalitat de Catalunya, Messaggero di Sant’Antonio, Zecchino d’Oro, Dopolavoro Ferrovie dello Stato, Accenti, Viva gli Anziani, Il Paese dell’Arcobaleno, Regione Campania, Regione Emilia Romagna, CEI, Action Medeor, Ferrovie dello Stato, Farmindustria, Misericordia di Siena, Caritas tedesca, Flanders, GTZ, Fons Català de Cooperació al Desenvolupament, Comuni dell’Umbria per l’Africa, the Finnish Embassy in Mozambique, Wine for Life, Merck Sharp e Dohme Italia, the Province of Naples and Rissho Kosei-Kai.

DREAM’s main sponsor is UniCredito Italiano – a partnership decisive for the whole program’s rapid development on Mozambican territory. This solid, transparent joint venture of broad social reach is a centrepiece for other alliances and collaborations that are now enabling DREAM to grow quickly, yielding important results for the population of Mozambique and for similar projects in other countries in sub-Saharan Africa.

Many common citizens have also made their contribution to making DREAM a dream come true. Therefore, on behalf of all Mozambicans, and of all those who will benefit from the DREAM program elsewhere in Africa in the future, we would like to thank:
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Rissho Kosei-Kai
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LEONARDO INTERNATIONAL
The Community of Sant’Egidio began in Rome in 1968, in the period following the Second Vatican Council. Today it is a movement of lay people and has more than 40,000 members, dedicated to evangelisation and charity, in Rome, in Italy and in more than 60 countries throughout the world. The Community of Sant’Egidio is a “Church public lay association”. The different communities, spread throughout the world, share the same spirituality and principles which characterise the way of Sant’Egidio:

**Prayer**, which is an essential part of the life of the community in Rome and in communities throughout the world. Prayer is central to the overall direction of community life.

**Communicating the Gospel**, the heart of the life of the Community, which extends to all those who seek and ask for a meaning for their life.

**Solidarity with the poor**, lived as a voluntary and free service, in the evangelical spirit of a Church that is the “Church for all and particularly the poor” (Pope John XXIII).

**Ecumenism**, friendship, prayer and search for unity among Christians of the whole world.

**Dialogue**, recommended by Vatican II as a way of peace and co-operation among religions, and also a way of life and as a means of resolving conflicts.

The Community has as its center the Roman Church of Sant’Egidio, from which the Community takes its name. From its very beginnings, the Community has maintained, in the area of Trastevere and in Rome, a continuous presence of prayer and welcome for the poor and for pilgrims.
The Community of Sant’Egidio is a Non-Governmental Organization (NGO) headquartered in Rome and active on all continents, with programs including development cooperation in support of human rights, and supporting and facilitating peace and reconciliation processes. Amongst NGOs, the Community of Sant’Egidio is known for the total commitment (96-98%) of its resources to the projects, and the very low overhead and expenses for supporting the structures (2-4%). This is made possible by the free, voluntary work of all the directors and many of the highly professional and specialized employees. This is why all the Community’s programs have an extremely low overall cost in comparison with their impact and results. The Community of Sant’Egidio has a long history in Mozambique, from the humanitarian aid sent in the early 1980s to the official mediation between the guerrillas and the government leading to the General peace agreement signed in Rome on 4 October 1992 after 27 months of negotiations. Today, Mozambique is a major example of democratic rebirth in sub-Saharan Africa. This special link with Mozambique has led the Community of Sant’Egidio to choose this country as the first where to pilot the Global Program to fight AIDS in Africa, called DREAM (Drug Resource Enhancement against AIDS and Malnutrition).
Why DREAM?

DREAM (Drug Resource Enhancement against AIDS and Malnutrition) is a control, prevention, and treatment program – in other words, a global program to fight HIV infection in limited resource countries.

DREAM reflects the Community of Sant’Egidio’s way of thinking

The Community of Sant’Egidio places central importance on the person and on each and every life. For many long years, an exclusively prevention-based strategy has been the paradigm of all large international agencies – and of the scientific community – for attacking AIDS in developing countries. This strategy has shown its limits: tens of millions of HIV positive Africans and the epidemic’s alarming growth curve (steady until at least 2010) require extraordinary efforts to recover lost time and, at last, to allow prevention to be accompanied by therapy; this is the only way to avoid that the entire struggle against AIDS in the southern areas of the world fail, and much of Africa, today and tomorrow, disappear. The program was therefore created with the objective of going back to bringing prevention and therapy together, convinced that we must save as well as prevent, gaining new time to live for as many people as possible.

DREAM: conceived for excellence

Excellence in care, and in diagnosis, organization, and information. Thus, as will be illustrated in the following pages,
DREAM proposes to apply in Africa the state of the art of Western standards, by using viral load evaluation routines, or by introducing the Highly Active Anti-Retroviral Therapy (HAART), the current gold standard in HIV treatment, for all patients that need it. For the Community of Sant’Egidio, people are never simple “emergencies” – bodies to be clothed, sores to treat, mouths to feed. They are always people, always friends. This is why we are guided by that simple, age-old secret: do unto others as we have them do unto us. Who wouldn’t want excellence for himself? This approach is profoundly efficient: it provides great motivation for the personnel involved; it earns maximum patient collaboration; it makes the patients themselves promoters of knowledge in the surrounding environment; it eliminates waste and interruption of the therapy in progress; and it raises the quality of the service that is offered. In the area of AIDS, the minimalism in international aid and cooperation so often proposed risks resulting in perilous – if not outright lethal – consequences in an environment already exposed to too much weakness and in the face of a complexity that at root resists any sector-based or reductive approach.

DREAM: based on partnership

The Community of Sant’Egidio does not have the role of a distant donor that, by its ownership, grants its funds and lets things be, seeing mostly to the financial reports: not a patronizing approach but rather a responsible one. Being able to work together provides yet another opportunity. Working together means supplying all the means necessary for achieving the objectives, in collaboration with – and with respect for – the local institutional framework. Thus, while hundreds of the Community’s members are devoted to activities promoting the project in the West, more than 120 qualified volunteers – physicians, nurses, lab technicians, computer experts, educators, and administrators – work in rotation, with overlapping and direct transfer of knowledge, all year long, alongside the local personnel involved in the program.
DREAM: a participatory program

Although it was created only in the world’s more industrialized nations, DREAM has a rock-solid social base in Africa; in Mozambique, a country counting more than 60 Sant’Egidio communities, for instance, there are five thousand youths and adults working alongside the most impoverished. Everyone lends a hand: no one is so poor as to be unable to help someone even poorer. These communities are active in the program in two strategic areas: health education and nutritional support. Tens of thousands of Mozambicans in the most deprived areas draw stable benefits from this daily activity. But DREAM is also open to participation from those living in the West. While scientific institutions and various subjects from the industrial and economic world have become stable partners in the program, offering their scientific and economic resources, a large number of private citizens are also taking part in the program, receiving detailed information and providing their support in many ways.

DREAM: modulated for rapid scaling–up

Excellent services along with reduced economic resources have not set a limit on the possibility of bringing treatment to a vast number of people and, in the future, to all. The main problem lies rather in the difficulty of implementing, in limited-resource healthcare systems such as those in Africa, the complex assistance required for HIV/AIDS. An innovative road in this field must be built, taking these special features into account and satisfying the need for light, agile facilities. DREAM has now shown itself to be a functioning model that must face the challenge of its growth. The issue is to broaden and spread all the system’s aspects together, one alongside the other, from training technical and medical personnel (in countries, with a chronic shortage of personnel aggravated by the pandemic) to creating suitable infrastructures; from diagnostic facilities to suitable assistance in
childbirth; and from monitoring and supervising therapies to evaluating the results. Co-ordinated, harmonious growth of the various components is critical and requires exceptional commitment, now and in the future. And in any event, the fight against AIDS must come to grips with this inescapable large-scale transit of therapies if it is to aim to become a nation-wide battle and, later, a model for limited-resource countries. Indeed, it is impossible to offer everything to everyone at the same time. This requires priority-setting. Thus, in the first phase, DREAM has given precedence to pregnant women, single mothers, and some key interventions in such strategic sectors of development as healthcare (physicians, nurses, and auxiliary personnel) and education (teachers at mandatory school). Program directors have been frequently asked whether it is ethical to privilege one population segment over another. But unfortunately, the starting situation in much of Africa is that of non-choice accompanied by immobility, impotence, and total resignation before the expanding epidemic.

Not choosing in order to avoid the ethical risk of choosing the necessary priorities at the start of any program with global ambitions (like those of containing, combating, and defeating AIDS in Africa) truly opens up the very opposite to the ethical risk, in a sort of ethical limbo that is responsible for the disappearance of entire generations.

This is why priority-setting introduces a starting ethic in a dramatically marked north/south imbalance.

DREAM has not forgotten other population sectors with difficulty accessing treatment, such as prison inmates or children in institutions. It is thus rapidly expanding in central and northern Mozambique and across Africa.

DREAM: a public health program

DREAM has been conceived to become a stable component of national healthcare systems. In Mozambique, for instance, its facilities – at hospitals, healthcare centers, and maternity wards – are those of the healthcare system. And already lo-
cations will also include private facilities of great public and social importance – managed by religious congregations, NGOs, and other solidarity agencies – which are already effective in helping scale up the program. All healthcare services, from diagnosis to nutritional support, from health education to conventional therapy for opportunistic and sexually transmitted infections (like HAART) are offered completely free of charge, at least for the populations in the centers’ user basins. The possibility is being studied of guaranteeing access to these services for those farther away geographically, and cost-sharing mechanisms based on out-of-pocket expenses have been proposed, to cover the costs of diagnosis reagents, for example.

DREAM: an operating research project

DREAM is also used for the purposes of research in public healthcare, epidemiology of services and their impact, in clinics, and in therapy in developing countries. The acquisition of new knowledge in research dedicated to development interventions in impoverished countries is a sound contribution in the fight against AIDS. In this sense, the program has strong connections with the scientific world and is oriented towards gathering data for epidemiological and clinical studies, both as routine and for ad-hoc investigations. Much attention has been given to the need to give life to an efficient internal communications system. A computerized, wired network links all the centers and connects them to servers on site and in Europe, thereby facilitating the coordination and supervision work, allowing immediate remote consultation for DREAM clinics, and providing the data produced by the individual facilities in real time.

These pages were written for two reasons. The first is to provide simple, detailed information about the first steps and conquests of a program that has shown convincingly – and against the grain – that AIDS can be defeated in Africa. The second is that DREAM aims to be an open channel for those who wish to take part in this engaging battle but lack the
means to do so – a collector of energy and resources for all of Africa. And in fact, DREAM – and this is its last characteristic – needs everyone and is available to those who think they can expand it to other situations in the struggle against AIDS in Africa.

Defeating AIDS in Africa is really possible. We hope that awareness of this can become contagious, spreading among those who can multiply the effectiveness of this decisive battle for the future of Africa and of the whole planet. Support from many people makes it possible to grow better and faster. And against AIDS, time is of the essence.

Even as these pages are printed, DREAM has been active for more than a year, and the first results were presented at the Tenth CROI (Conference on Retroviruses and Opportunistic Infections - Boston 2003).
1. The human immunodeficiency virus pandemic

Starting in the early 1980s, AIDS had a development without comparison in the history of human pathologies. With AIDS, something new and hitherto unheard of was developing in the world. And the tens of millions of people stricken in every country in the world bear witness to a pandemic that can truly lay claim to being the first pathology of the era of globalization.

A radically new situation such as this requires radically new responses. Models must be identified that take into account both the features of the illness and the available possibilities for treatment.

More than two thirds of those with HIV/AIDS – tens of millions of people – live in Africa. And only a very small number of these people, mostly those with some economic means, have access to antiretroviral treatment. With such a serious emergency, while intervention must be quick, what is needed immediately is to start laying the foundations for building a medium- and long-term response.

2. Antiretroviral therapy

The advent of HAART (Highly Active Anti-Retroviral Therapy) in the mid-1990s radically changed the natural history of the illness, transforming AIDS into a chronic pathology. But at the same time, antiretroviral therapy cre-
ated new needs. To yield optimum results, this therapy requires technologically advanced monitoring and diagnostic methods, and must reach the population extensively, where it lives. The availability of highly specialized centers must be combined with the greatest possible spread and accessibility. Here is the first contradiction – one apparently difficult to solve, because the impact of the therapeutic intervention can only be limited. In brief, here lies the challenge: treatment with antiretrovirals must be based on advanced diagnostic methods, by necessity localized in a large city; at the same time, to be effective, treatment has to rely on extensive distribution.

Over time, it became clear that AIDS could not be fought with prevention alone; treatment was needed as well. Ongoing prevention is as necessary as ever, but on its own, it is clearly not enough. In fact, the lack of hope for access to and availability of therapy risks drastically to reduce the effectiveness of prevention, thereby lowering interest in knowing one’s own condition vis-à-vis the infection: awareness without an available therapy would risk creating the dramatic and unbearable knowledge of a premature demise, often preceded by isolation and social condemnation.

These needs imply wide-ranging economic and political interventions, as well as highly articulated and innovative healthcare planning and organization of services. The millions of deaths, infected persons, and orphans require immediate intervention, without getting bogged down in non-essential preparatory phases. Likewise, however, the emergency intervention should be designed from the beginning with a view to developing stable facilities capable of waging the battle over the long term. To put it briefly, intervention in the struggle against AIDS must be based on immediacy and farsightedness.

3. A public health intervention

It was starting from these assumptions that the Community of Sant’Egidio developed its methodology in the fight against
AIDS, which in Mozambique is already expressed through the DREAM Program. This horizontal public health intervention aims to take action in the various areas of the country. To be quickly operative and effective in order to respond to emergencies, DREAM has created a bureaucratically and administratively streamlined intervention model. This particularly agile system makes it possible to maintain administrative costs – including those for non-local personnel, who work exclusively free of charge – at a minimum percentage of the overall budget at all times. In other words, the whole budget is used exclusively to fund activities in the country.

Day hospital and home assistance
Antiretroviral therapy is administered to the population through day hospital and home assistance activities. In this way, lacking specialized facilities spread throughout the territory, the program is allowed to be in direct contact with the population, thereby guaranteeing the necessary control over the therapy. When the people to be treated cannot come closer to the possibility for therapy, it is DREAM that brings them closer.

However, AIDS cannot be combated exclusively with antiretroviral drugs. It requires a more wide-ranging intervention taking into account the person’s overall needs. The package of services ordinarily offered to the patient on a stable basis is comprised of voluntary counseling and testing, lab tests (biochemical, haemochrome, CD4+, and viral load), antiretroviral therapy, treatment of opportunistic infections and sexually transmitted diseases, nutritional support, basic health education, and social support.

Caring for mothers and prevention of vertical transmission
An original aspect of the DREAM program is caring for pregnant women in accordance with the Mother & Child Prevention & Care (MCPC) scheme. Pregnant HIV positive women are given the following services:
Evaluation of nutritional status and supplementation, where necessary, for mother and newborn
– Testing & counseling for HIV infection
– Health education
– Diagnosis and treatment of sexually transmitted diseases
– Diagnosis and treatment of opportunistic infections
– Prophylaxis of mother-to-child transmission with antiretroviral drugs
– Treatment of the mother in accordance with protocols with antiretroviral drugs both for treating the HIV infection, and for mother-to-child transmission.
– Support and monitoring of feeding and caring for the newborn

Care for mothers is one of the special features of the model proposed through DREAM. In fact, the offer of antiretroviral therapy to mothers – which is not interrupted but continues even after childbirth – is essential. It is the only way for a mother, who has given birth to a child in which infection has been prevented, from dying of AIDS shortly thereafter. Until now, this kind of intervention has not been used in Africa. On the other hand, it is well known that in Africa, the survival of orphaned children, even HIV negative ones, is lower than that of other children. They also have fewer possibilities to attend school. Thus, not only is the vertical transmission of the infection prevented, but a mechanism of survival – and of increased chances for and in life – is created for the newborn and the entire family.

**Training**

DREAM places great importance on training personnel, and has in fact developed its intervention taking exclusively local personnel (physicians, medical technicians, nurses, biologists, lab technicians, and social workers) as its basis. This is one of the essential aspects for the future sustainability of any intervention. However, the use of local personnel requires strong human investment in and commitment to theoretical and practical training, both on site and abroad. And this is what DREAM foresees in the short, medium, and long term. Given the need to intervene as soon as possible, an ongoing training program has been provided for and prepared, right from the beginning. This is why DREAM has
developed an original model for partnership between local personnel and staff from other countries. Non-local personnel is always present in the country in regular shifts, thus guaranteeing the necessary technical and training support for local personnel, without ever replacing it in any way. DREAM has already led a number of training courses for home care assistants, nurses, and physicians on treating and assisting persons living with HIV. It also organizes public conferences on issues of treatment and advanced diagnostics in HIV infection. Several times a year, supervision missions reserved for the activity of the project’s medical personnel are held.

A major part of personnel training is seeing to the quality of the relationship with the patients, who must at all times be received courteously, openly, and with respect. Counseling does not end with the first examination, but continues in subsequent visits through direct contact with patients and support to all. Similarly, the facilities where patients are treated must always be well cared for and cleaned in accordance with high health and sanitary standards – this also applies to the case of essential facilities. These are two important aspects in order to guarantee, in addition to personal dignity, the effectiveness of interventions – such as that against AIDS – that require much time and good collaboration with the patient.

The laboratory
To be effective, antiretroviral treatment requires strong lab support. This is why the DREAM program has included the development of highly specialized molecular biology labs, where the CD4+ count and the viral load measurement (in accordance with the indications of the diagnostic and therapeutic protocols), in addition to the basic biochemistry and haemochrome, are regularly performed, acting as the technological core of the whole program. Labs of this kind are needed in order to respond quickly and effectively to the development of drug-resistant viral strains. This is an invest-
ment for the country’s future, both in training highly specialized human resources and in equipment.

**Computerization**

All the DREAM program’s activities are monitored through a computer network linking the various centers to one another and to the reference labs. This system guarantees efficient monitoring of the treated patients – including adherence to the therapy – and becomes an important source of data that can be used to continue improving the quality of the interventions, through applied research too. And it is applied research that makes it possible to perfect the forms of intervention and helps guarantee that the finest, most effective help is offered, even in sub-Saharan Africa countries.
1. Introduction

In October 2001, the DREAM program began its activities to treat persons with HIV/AIDS, opening the first home care and day hospital assistance service in a suburb of Maputo, Mozambique’s capital. With the help of consulting from specialists in the sector, protocols were developed for care with antiretroviral drugs to be used to treat the sick and prevent mother-to-child transmission. The issue was to adapt to the particular situation of a limited resource country like Mozambique those clinical and pharmacological indications already trialled in the United States and Europe that had completely changed the natural history of the disease from 1996. In such a way was reduced patient mortality even in the most advanced phase of infection.

Administration of antiretroviral drugs to patients began in February 2002, when these drugs became available in Mozambique.

The therapeutic protocols developed, which of course can be perfected, have sought to take into account the problems posed by the context being worked in:
– the possibility of using generic drugs in fixed combinations of three active principles within the same pill: although it limits the variety of medications and therapeutical schemes that may be used in comparison with the range available in the United States and Europe, at the same time it may pro-
vide an important opportunity to simplify therapy and improve adherence;
– the high prevalence of such pathological conditions as HIV/TB co-infection, malaria, or simple malnutrition-based anemia, that condition therapeutic choices;
– the percentage of women in childbearing years among the infected (more than 50% of therapy candidates), which further conditions therapeutic choices given the possibility of pregnancies;
– the need to blend high patient management standards with cost containment (for lab diagnosis, for example);
– the problem of prophylaxis for opportunistic infections (which ones, how many, for how much time, how to avoid excessive difficulties in taking the therapy);
– the frequent need for nutritional support accompanying therapy, particularly for pregnant women.\textsuperscript{1-2-3}

These are just some of the questions that accompanied the development of the protocols which, although still having ample space for improvement, have so far yielded spectacular results and have represented a first, important contribution to the fight against AIDS in developing countries.

The April, 2002 publication by the World Health Organization of the document entitled: “Scaling up Antiretroviral treatment in limited resource setting” marked a point of no return in the debate on access to care for persons with HIV/AIDS in Africa\textsuperscript{3}. This document was a theoretical reference point, in many cases confirming the orientations that DREAM had already taken on and provided more points for reflection on treatment for persons living with HIV/AIDS in Africa.

The WHO document had the following objectives:
– to increase the use of antiretroviral drugs to meet the needs of persons living with HIV/AIDS in limited resource countries;
– to standardize and simplify antiretroviral therapy to permit it to be spread widely and easily;
– to ensure that treatment is based on the available scientific evidence, to keep the use of protocols far from the finest
clinical and therapeutical standards from causing damage to individual patients and fostering the emergence of resistant strains.

The same WHO document saw public health programs as the framework most suited for achieving the objectives that had been set. Along with this document, the guidelines for using antiretroviral therapy in Europe and the United States, and broad examination of the latest scientific literature, constituted the scientific background against which DREAM’s protocols were developed.

2. Eligibility criteria for treatment

**When to begin antiretroviral treatment** is still an open issue. While there is general agreement concerning patients with less than 200 CD4+/mm³, or with evident symptoms of disease,⁴⁻⁵ this is not true for asymptomatic patients with CD4+ greater than 200. It is true however that potentially mortal infectious diseases, even in non-immunocompromised hosts, are more widespread in Africa than in Europe or the U.S. An example may be Malaria which is one of the leading causes of mortality both in HIV positive and HIV negative patients.⁶ On the other hand the percentage of subjects with CD4+ between 200 and 350, which develops AIDS within 3 years is around 38.5% with a peak of 60% when viral loads are greater than 55,000 copies/ml.⁷ These considerations seem to justify the choice of an aggressive approach, which DREAM considers to be the extension of antiretroviral therapy to those patients with CD4+ between 200 and 350 and with viral loads greater than 55,000 copies/ml.
Tab. 1 – *Eligibility criteria for treatment with ARV Drugs*

<table>
<thead>
<tr>
<th>WHO clinical classification</th>
<th>CD4+ count</th>
<th>Viral Load</th>
<th>Current EU and US guidelines</th>
<th>WHO guidelines for LRS*</th>
<th>DREAM Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stages III – IV</td>
<td>Any value</td>
<td>Any value</td>
<td>Treatment</td>
<td>Treatment</td>
<td>Treatment</td>
</tr>
<tr>
<td>Stages I-II</td>
<td>&lt; 200</td>
<td>Any value</td>
<td>Treatment</td>
<td>Treatment</td>
<td>Treatment</td>
</tr>
<tr>
<td>Stages I-II</td>
<td>200-350</td>
<td>Any value</td>
<td>Treatment/observation</td>
<td>Observation</td>
<td>Treatment/observation</td>
</tr>
<tr>
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<td>&gt; 350</td>
<td>&gt;55.000</td>
<td>Treatment/observation</td>
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<tr>
<td>Stages I-II</td>
<td>&gt;350</td>
<td>&lt;55.000</td>
<td>Observation</td>
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<td>Observation</td>
</tr>
</tbody>
</table>

*LRS: Limited Resource Setting.*
3. Treatment regimens

In setting up the treatment protocols the following different aspects (not in order of importance) were taken into account.

The first was related to the choice of drug combinations. Very many exist, but use of no less than three drugs was decided since it is the current golden standard in the treatment of HIV/AIDS patients. Several clinical trials have shown that different treatment regimens are basically equivalent in terms of antiviral potency.\(^8-15\).

The second aspect regards simplicity of administration. This limits the range of possible choices. Adherence to drug therapy has always been one of the major problems linked to treatment in Africa since errors in taking the drugs may easily lead to the emergence of resistant strains. Besides their high costs and the structural flaws in the Health Systems, this is one of the reasons why many consider HIV/AIDS therapy in Africa as impracticable or unadvisable. There is no doubt that the patient’s adherence to drug therapy is crucial and can influence efficacy of treatment even in those countries where drugs have always been available. It is therefore important that where the patient is obliged to interrupt taking a drug or simply forgets to, he/she should interrupt all three drugs in order to curb the risk of the emergence of resistant strains. Pharmacological preparations which unite all three drugs in a single pill are very important in improving adherence to drug therapy and reducing the risk of antiretroviral resistant strains. On the one hand treatment is greatly simplified: from many (up to 10-15) pills a day for a European patient down to two; on the other hand, where treatment is interrupted it necessarily involves all three drugs. Moreover these preparations, on average, cost twenty times less than the corresponding treatment regimens schemes in Europe or the U.S saving up to 95%.

The two basic treatment regimens chosen as the first line of treatment are:
1) zidovudine (AZT) 300 mg – lamivudine (3TC) 150 mg – nevirapine (NVP) 200 mg 
2) stavudine (d4T) 30 o 40 mg – lamivudine 150 mg – nevirapine 200 mg. 
The annual cost per person of these two regimens is currently 330 USD. 
The choice between these two regimens is based on an element often present in HIV patients, especially in highly endemic malaria areas in Africa: a hemoglobin concentration lower than 8 g/dl would indicate the use of stavudine. Instead if hemoglobin concentration is greater or a peripheral neurological disorder is present the regimen with zidovudine is preferred. There is also a third possibility i.e. peripheral neurological disorder and anemia together. This infrequent but not impossible case would require yet another scheme with abacavir (ABC) – didanosine (ddi) – nevirapine, for which pharmacological preparations such as those previously mentioned do not yet exist. Another aspect which in theory influences the choice of drugs, even when starting treatment, is tuberculosis (a problem which will be discussed further on). However, on the basis of an overall widespread anemia in African people the best regimen, without doubt, would be stavudine-lamivudine-nevirapine. In case of failure of this regimen the alternatives are greater than those available for the regimen with zidovudine. In fact even the use of abacavir in patients resistant to treatment with zidovudine and lamivudine is limited by frequent cross resistance.3 The alternative to nevirapine, i.e. efavirenz (EFV), does not seem feasible due to potential teratogenicity in a patient population where more than 50% are women, all in childbearing age and not used to taking contraceptives. Moreover, further doubts arise when considering the drug’s pharmacokinetics: they show a longer half-life compared to other drugs thus calling for special attention in administration or interruption.3-5 For the same reason the combination stavudine-didanosine should not be used unless there are no alternatives, because of some deaths of pregnant women who had used the drugs throughout pregnancy16. Finally the
use of protease inhibitors seems more appropriate in second-line regimens considering the difficulties linked to greater daily amounts of pills (no protease inhibitors have been combined in a single pill with other drugs). In the future the availability of once-daily drugs combination may lead to reconsider this therapeutic approach. Safety: the drugs used are among the best so far used in combating HIV infection. Side effects or adverse events are not many (except for nevirapine) and their toxicity, in most cases is spread over time and can be detected even when periodical checks are not very frequent. This is very important in those areas where travel is neither rapid nor simple and contact with patients is less frequent than in other areas.

As far as second line regimens are concerned choice depends on the reasons for changing the initial regimen. Reasons are basically two: allergy or intolerance of some kind and treatment failure.

1) Allergy-intolerance-adverse events attributable to one of the drugs included in the first line regimen. If nevirapine is responsible it can be replaced by a protease inhibitor (for example indinavir (IDV) or Nelfinavir (NFV) or with a third NRTI (Nucleoside Reverse Transcriptase Inhibitor) such as abacavir.  

2) Treatment failure: definition of treatment failure can be clinical (development of AIDS-related diseases after ART has been administered for a time sufficient to restore immune functions), immunological (30% fall in number of CD4+ lymphocytes or return to CD4+ levels prior to treatment), or virological (viral load still present after 6 months of treatment or, viral load greater than 10,000 copies after 6 months of treatment for those patients with a viral load of 500,000 copies before treatment). Some degree of variability however exists and must be assessed over time and one result only should not influence decisions. Once this is clear, where clinical conditions are stable, evaluation aimed at changing the therapy should be carried out after at least 6 months of treatment.
In this case the whole treatment should be changed: possible alternatives would be zidovudine-didanosine together with indinavir or Nelfinavir, if initial regimen were stavudine-lamivudine-nevirapine. If instead the initial regimen included zidovudine the alternative regimen would be the triple didanosine-stavudine-indinavir. Resistance to antiretroviral drugs represents a substantial threat for future therapies, due to the cross resistance among many of the drugs available. Altough this is a concern for developed countries as well, this issue cannot be a factor limiting the spread of antiretroviral therapy in Africa. At the same time, however, the implementation of systems that limit the development of cross-resistance will be highly considered, in a way similar to developed countries. Among them, quick therapy switch at the time of early failure, that is before mutations conferring resistance to antiretroviral drugs are fully developed, is the main criterium. Implementation of systems to detect resistance mutations (from simple and easy-to-use methods, to sophisticated methodologies based upon sequencing) represents an objective for future efforts. As far as prophylaxis of opportunistic infections is concerned, the only treatment in the protocol is administration of co-trimoxazole daily for 6 months in patients with less than 200 CD4+ at enrollment. No other kind of prophylaxis is at the moment considered without further details on prevalence of opportunistic infections in AIDS patients in sub Saharan Africa. The treatment protocol thus designed looks simple and homogeneous. Candidates for treatment are almost all people who have not received any previous antiretroviral treatment. Therefore efficacy is potentially greater than that reported for the same treatment in European or North American patients who had previously received different regimens which later turned out to be sub-optimal. Such efficacy may already be observed from the first results of the treatment in cohorts of African patients who have had the opportunity to receive it. Homogeneity and treatment on a large scale would further help to combat the emergence of resistance since the patients tend to take always the same drugs.
Tab. 2 – Treatment Regimens included in the DREAM protocols

<table>
<thead>
<tr>
<th>First Line</th>
<th>Second Line due to allergy/adverse events</th>
<th>Second line due to treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>d4T – 3TC – NFV</td>
<td>d4T – 3TC – NFV</td>
<td>AZT – ddI – NFV</td>
</tr>
<tr>
<td>d4T – 3TC – NVP</td>
<td>d4T – 3TC – NVP</td>
<td>d4T – ABC – NFV</td>
</tr>
</tbody>
</table>

4. Caring for the mother and preventing vertical transmission

If the main aim of treatment in people with HIV/AIDS is to contrast the progression of infection, in pregnant women with HIV the aim is also to avoid transmission to the fetus. In this respect viral load is even more important. It is in fact the key element in the risk of infection being transmitted from mother to child although it is not clearly the only one. Other risk factors include malnutrition, Sexually Transmitted Diseases (STD), genital ulcers, prolonged rupture of membranes, vaginal laceration and postnatal feeding.3-20-26 All these elements must be considered and action taken where possible.

In order to significantly reduce transmission risks, the viral load must be cut down to less than 1,000 copies per ml.1 With highly efficient treatment such as with the three-drug combination an average reduction of at least one log per month of treatment of the viral load may be obtained.19 This means that average antenatal treatment should be carried out for two months or more to be reasonably sure that the viral load in most cases will fall below the 1,000 copies per ml. Another aspect to be considered is proneness to pre-term delivery of HIV positive women. On the basis of all this, beginning of treatment at week 25 has been decided for all women. For those women who at enrollment present CD4+ counts less than 200/mm³, or a viral load greater than 55,000 copies/ml (DNA 3.0), or symptoms (WHO clinical
staging system level 3), treatment shall commence before week 25 but always after week 14 of pregnancy. Choice is based on much of the same criteria as those already mentioned for adults/adolescents. The chosen regimen is zidovudine-lamivudine-nevirapine due to greater experience acquired in the use of these three drugs in pregnancy. In women with less than 8 mg/100 ml of hemoglobin stavudine is preferred. The latter has been involved in three cases of death of pregnant women due to lactic acidosis; in all, three cases the patient had been taking the drug together with didanosine since the beginning of pregnancy. Other cases of lactic acidosis have been reported for other NsRTI drugs with or without stavudine but none were lethal. Lactic acidosis is a rare event which may occur in pregnant women treated with this kind of drug. However since this is rare, stavudine should be maintained as an option in treatment to prevent mother to child transmission. However, unless there is no alternative, association with didanosine should be avoided. The same considerations may be made in the case of NRTI-related mitochondrial toxicity except that no cases of death due to mitochondrial toxicity have been reported in the literature following use of these drugs. During pregnancy, the mother receives nutritional support (rice, beans, oil, sugar) and multivitamin supplementation in order to combat malnutrition and anemia, to reduce the proportion of pre-term deliveries (vitamine A) and the qualitative and quantitative incidence of low birth weight. Moreover, if the proteic and energetic strain induced by HIV on the body is considered, supplementation plays a fundamental role in the battle against the virus. Within 72 hours of birth, the newborn receives one dose of nevirapine syrup to protect it during breastfeeding, in which he/she is most vulnerable. Pharmacological treatment is continued at full dosages after childbirth in women who, upon enrollment, corresponded to the therapy criteria identified by the DREAM program (see above). Should this condition not exist, therapy is suspended a month after childbirth, if it is certain that the woman has lost her milk. To create safe feeding conditions,
women are provided with a filter for water (ceramic and active charcoal), a bottle and, periodically, the amount of artificial milk the child needs. Brief health education courses during pregnancy and individual instruction at childbirth have the objective of fostering formula feeding. The mother continues to receive nutritional and vitamin support during the post-partum period. From the 4\textsuperscript{th} - 6\textsuperscript{th} month, weaning begins, to be completed by about the 12\textsuperscript{th} month.

\textbf{Saving the future of Africa}

Caring for mothers is one of the special features of the model proposed through DREAM. Offering antiretroviral therapy to mothers with the objective of curing them even after childbirth is essential. It is the only way to prevent the exponential increase of orphans. HIV orphans are already estimated at about 14,000,000 – of whom 11,000,000 live in sub-Saharan Africa. Being orphaned in Africa is not simply an unfavorable condition from a psychological or from a human standpoint. It is a risk factor: the risk of dying more easily than other children, and the risk of not going to school because the family cannot manage to guarantee what is needed for enrolment. In southern Africa, the percentage of orphaned children attending school falls on average by about two thirds.

DREAM’s choice to offer mothers both prevention for mother-to-child transmission and treatment for their disease also has the effect of ensuring better adherence to the program. For prevention projects to work, a message has to be spread out among people in general and women in particular: the desire to fight against AIDS, and above all the hope that this struggle can be won. Now that this is possible at relatively contained costs, care for the mothers is not just an ethical imperative. It makes good sense.
| Type of patient | Stages 3 - 4 | Stages 1 - 2 | Stage 0+
|----------------|--------------|--------------|----------------|
| **Ante natal** | II Quarter  
AZT 300 mg 2/day  
3TC 150 mg 2/day  
NVP* 200 mg for 13 days and after 400 mg/day  
If CD4+<200 or viral load >55,000  
see stages 3-4 | Week 25  
AZT 300 mg 2/day  
3TC 150 mg 2/day  
NVP* 200 mg for 13 days and after 400 mg/day  
If CD4+<200 or viral load >55,000  
see stages 3-4 | Continue ongoing treatment  
AZT 600 mg + 300 mg 8/day  
3TC 150 mg 2/day  
NVP 200 mg for 13 days and after 400 mg/day |
| **At Childbirth** | Continue ongoing treatment | Continue ongoing treatment |  
AZT 600 mg + 300 mg 8/day  
3TC 150 mg 2/day  
NVP 200 mg for 13 days and after 400 mg/day |
| **Post natal** | Child: Nevirapine  
2mg/Kg/day within 48-72 hours of birth  
Mother: Continues ongoing treatment | Child: Nevirapine 2mg/Kg/day  
within 48-72 hours of birth  
Mother: Continues ongoing treatment |  
Child: Nevirapine 2mg/Kg/day  
within 48-72 hours of birth  
Mother: Reclassified in one of the previous stages |

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5In anemic patients (Hb<8) AZT replaced by d4T: 30 mg 2/day for bodyweight less than 60 Kg; 40mg 2/day for bodyweight over 60 Kg. All will be advised to formula feed.

*In cases of intolerance NVP will be replaced by Indinavir or Nelfinavir.

+Women visited for the first time at childbirth.
5. Haart treatment in patients with tuberculosis in intensive treatment

The indication for using the therapy for HIV infection in patients in intensive treatment for tuberculosis regards those who have a CD4+ count of less than 200: it is absolute for patients with less than 50 CD4+ per mm³, and conditioned upon the clinical and immunological situation for those with CD4+ greater than 50 but less than 200.¹ When antiretroviral therapy starts being administered to a patient with HIV in intensive treatment for TB, there may be paradoxical reactions that fall under the name of immuno-reconstitution.³⁵ Moreover, the many reactions between anti-TB and antiretroviral drugs are to be taken into consideration if we are to conduct two treatments at the same time.³⁶ Lastly, simultaneous administration of anti-TB and antiretroviral therapy may create confusion in taking the drugs. It is thus often preferable to wait for the first two months of anti-TB therapy before starting administration of antiretroviral drugs; however, below 200 CD4+, the infection progresses so rapidly that it is often fatal to put off therapy. As a rule, patients with less than 200 CD4+ must be very closely monitored, especially if the decision is made not to start antiretroviral therapy. Otherwise, the course of action would appear to be that of substituting the nevirapine in first line therapy schemes due to its interferences with rifampicine, a drug almost always present in anti-TB therapy schemes in African countries. But the alternatives involve considerable difficulties, first among which adherence to the therapy, as the number of pills to be taken on a daily basis increases – doubled in the best of circumstances. This is a difficulty that regards one of the main alternatives ABC¹ – whose formulation in a single pill with zidovudine and lamivudine is available only at prices that are at least triple that of the other three-drug formulations in developing nations. A second alternative, efavirenz, raises – if this is possible – a greater number of doubts due to the difficulty of using it, particularly in the population of women in childbearing years, given its already mentioned possible teratogenetic effects:³ and it should be kept in mind that this
type of population represents more than 50% of the HIV positive persons in developing nations. Lastly, the third recommended alternative – substituting nevirapine with saquinavir/ritonavir – is impractical due to its scarcity. On the other hand, the therapeutic scheme with nevirapine may be used – albeit with some caution given the approximately one-third reduction of the bio-availability of nevirapine when administered at the same time as rifampicin. This choice saves the features of easy administration of the drug formulations with nevirapine and uniformity in treatment, and appears to be the most appropriate when unable to wait for the conclusion of the intensive phase of TB treatment (the first two months). In fact, TB-HIV co-infection has a rather high prevalence in Africa, and the use of rifampicin is consequently just as high. Conditioning the use of nevirapine would require re-examining the first lines of treatment in a highly significant percentage of therapy-candidate HIV cases, thereby considerably compromising the feasibility of the proposed model. The possible availability of other drug combinations (in particular that with three NsRTI including abacavir) in a single pill at prices comparable to those currently in force for other three-drug formulations could offer a useful alternative in treating TB-HIV co-infection.

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Chapter 3

The DREAM program and the struggle against malnutrition

1. Background and justification

Since the early 1980’s, the humanitarian efforts of the Community of Sant’Egidio have been characterised by a constant commitment to bringing relief to people in critical situations such as wars and natural disasters; this commitment has often meant fighting hunger and malnutrition. These efforts have sought to respond quickly to the needs found: humanitarian emergency programs have been carried out, with food distribution and support for therapeutic and supplementary nutritional centers; in other situations, we have intervened with agricultural aid programs, distributing seeds and implement kits so that cultivation could be resumed; and lastly, wherever and whenever the country’s internal situation has allowed, we have conducted long-term public health programs oriented towards fighting malnutrition and infectious diseases. The Community of Sant’Egidio views the struggle against malnutrition in the broadest sense: from prevention to treatment, from controlling protein-energy malnutrition to the more hidden forms of micronutrient deficiency. It has always been clear to us that hunger and mal-
nutrition must be fought in order to prevent possible epidemics at critical times. Sant’Egidio’s DREAM program, backed up by these years of experience in fighting hunger and malnutrition, now faces what may be an even greater, and lesser known, challenge: malnutrition coupled with HIV/AIDS infection. At the heart of this challenge lies the knowledge that in Sub-Saharan Africa much of the population is vulnerable to both of these conditions, and that there exists a synergy between the two that to date has been little studied but is very dangerous in terms of human life and the deterioration of social and community life.

2. Malnutrition, infection, and the HIV/AIDS epidemic

In addition to having some 30 million people living with HIV/AIDS, in Sub-Saharan Africa most of the population lives under the threat of poverty and food insecurity.

<table>
<thead>
<tr>
<th>Country</th>
<th>% of adults with HIV</th>
<th>Poverty (% of population living on less than $2 a day)</th>
<th>% Malnourished children (0-5 years weight for age&lt;2 Zscore)</th>
<th>% of population undernourished</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>15%</td>
<td>76%</td>
<td>25.4%</td>
<td>33%</td>
</tr>
<tr>
<td>Zambia</td>
<td>21%</td>
<td>87%</td>
<td>25.0%</td>
<td>50%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>13%</td>
<td>78%</td>
<td>27.0%</td>
<td>63%</td>
</tr>
<tr>
<td>Tanzania</td>
<td>17%</td>
<td>50%</td>
<td>29.0%</td>
<td>47%</td>
</tr>
</tbody>
</table>

This shows that a broad segment of the African population is extremely vulnerable to the independent or synergetic effects of malnutrition and infection with HIV/AIDS.

2. The malnutrition, infection, and HIV/AIDS epidemic complex

In 1968 the international scientific community recognised with reason and clarity the synergetic re-
relationship linking nutrition of status to infections, and that nutritional deficiencies, increase the mortality, severity and duration of many infectious diseases. Therefore public health programs were forcefully directed towards intervening in both directions: correcting states of malnutrition and combating infection.

Malnutrition is almost always the result of combination of infectious diseases and dietary deficiencies interacting in a mutually reinforcing manner. Malnutrition lowers immune defences and increases the risk and severity of infections. While an inadequate diet may in and of itself cause death and, likewise, infectious diseases may be lethal regardless of nutritional status, most frequently the cause of death in poor African countries is due to the interaction between insufficient food intake and infective pathology. The infection process exacerbates of nutrients, loss, because of the host’s metabolic response and because of the loss of tissue, such as intestinal tissue. These factors worsen malnutrition and further damage the organism’s defences. This cycle is responsible for the high rates of mortality and morbidity in those African populations heavily exposed to infectious diseases and food shortages. The complex nature of these interactions makes it truly difficult to distinguish cause from effect. These facts leads us to reflect on the huge scale of the HIV/AIDS epidemic in Sub-Saharan Africa and, while we know that the poorest and most malnourished populations tend to be the hardest hit by HIV, clearly show that malnutrition is one of the decisive risk factors in the spread of the epidemic.

The vicious circle linking malnutrition, AIDS, immune-system deficit and other infectious diseases functions very smoothly in favourable environments like these fragile African societies, causing millions of deaths each year.
This shows that:

- HIV begins the circle by weakening the immune system
- Immune deficiency leads to an increase in infectious diseases, which worsen malnutrition.
- Malnutrition leads to a greater deficit of the immune system, whose weakness worsens the effects of the HIV infection.
- The cycle speeds up the progress of infection from HIV to AIDS.

3. DREAM’s objectives for combating malnutrition

As a public health program, DREAM’s priority is to interrupt the vicious circle linking HIV/AIDS infection to the immune system and to malnutrition. For DREAM, it is essential to slow down this vicious circle by combating malnutrition, so as to maintain good nutritional status in at-risk populations or in those already living with HIV/AIDS.

Obviously good nutrition does not cure AIDS, but it is a basic aid that complements HAART: it will help to maintain and improve health status of those living with HIV/AIDS by
delaying the progression from HIV to AIDS, fighting opportunistic infections and improving patients’ quality of life. The most frequent result of HIV/AIDS infection is weight loss, a major reduction in muscular tissue, and the consequent shortening of patient survival. The scale of this weight loss is dramatic: a person afflicted by HIV/AIDS may lose up to 30-50% of his body mass before succumbing to the disease. One of the most common and feared manifestations of the disease is Wasting Syndrome; its clinical signs are profound involuntary weight loss >10% of baseline body weight plus either chronic diarrhea (at least two loose stools per day for >30 days) fever, and marked weakness (≤30 days, intermittent or constant). This syndrome, which was included in the list of AIDS-associated pathologies in 1987, disfigures the patient’s body, reduces his functional capacity and prevents even a minimal social life, and, above all, increases the risk of death. In Africa, Wasting Syndrome was recognised early on, and infection with HIV/AIDS quickly came to be known as “slim disease.” It is well known that the leading cause of weight loss in people with HIV is insufficient food: diet is often hypocaloric and hypoproteic in the face of increased metabolic requirements due to the infection.

The energy and protein needs of people with HIV/AIDS are increased.

HIV infection increases the energy requirement: it is recommended that an HIV+ adult increase his caloric intake by 10-15%.
An additional 400 calories per day need to be provided for men, and 300 calories per day for women.

HIV infection increases protein requirements: it is recommended that an HIV+ adult increase his protein intake by 50-100%.
It is necessary to go from a recommended protein intake of 0.8-1.0 g/kg of body weight for the healthy population to 1.2-2.0 g/kg of body weight.
For a 70kg adult, this translates into a daily protein intake of between 84 and 140 grams. This broad range
of recommended protein intake obviously depends on the patient’s ability to consume a diet with such a high protein level.
(Source: Woods 1999)

The disease’s progression is also associated with shortages of micronutrients such as vitamin A and zinc. Increased requirements for vitamins A, C, E and B6, selenium and zinc have been found in persons afflicted with HIV/AIDS. Studies are still under way to establish adequate intake levels for these and other micronutrients, but a diet that increases patients’ daily intake has been recommended for some time now. It has been confirmed that a vitamin A deficiency increases mother-to-child transmission, whilst other studies are necessary to understand the role of other micronutrients or of multiple nutritional deficits in mother-to-child transmission.

In conclusion, there is clearly room in the treatment and prevention of HIV/AIDS for nutritional therapy, and the DREAM program has included this in its own prevention and therapy measures as an integral part of its approach.

In keeping with FAO’s recommendation included in the nutritional support manual for people with HIV/AIDS, the objectives of this nutritional therapy are to be found in the following points:

- Maintaining body weight and physical strength
- Improving nutritional status with recovery of weight lost during infective episodes
- Ensuring adequate levels of intake for each nutrient, in particular vitamins and other micronutrients that have an impact on the immune system
- Improving and maintaining immune system functions
- Delaying the transition from HIV to AIDS
- Improving response to drug treatments
- Proper dietetic management of symptoms associated with the disease, such as: anorexia, digestive problems and poor absorption
- Maintaining the work capacity, physical performance and independence of those living with HIV/AIDS
4. DREAM’s approach to nutritional support for people with HIV/AIDS

*Education to promote an healthy and balanced nutrition*

Every DREAM service features times and places devoted to health education, especially education that promotes a wholesome and balanced diet; the educators, who are trained periodically, possess a unique tool for working effectively: the book “How’s Your Health”. This book enables even those who cannot read to learn how to manage their own health and diet. The sessions are held on various occasions, at the day hospital, at the Mother & Child center (also for learning and consolidating basic nutritional information for children), and sometimes even in patients’ homes, involving the family and neighbours. Every meeting with the patient can be an opportunity to convey information and advice on how to improve diet and food hygiene. Who handles dietary education? All of DREAM’s operators are trained in this area, but promoting proper diet is mainly the job of the activists. Some activists are people with HIV/AIDS, DREAM patients, who have tested the program’s efficacy and work within it to help others. Their presence has a positive influence on others and encourages those who have trouble regaining their hope and will in combating the disease.

Certain topics, such as checking for symptoms such as diarrhoea, nausea, anorexia and vomiting due to the disease or treatment are dealt with by the physicians and nurses.

*Assessment and monitoring of nutritional status*

DREAM offers a simple assessment that provides dietary, anthropometric, clinical and laboratory information.

**Nutritional case history and clinical exam:** the doctor conducts a detailed survey of the patient’s dietary history and evaluates the quality and quantity of the diet, trying to identify any mistakes, shortages and needs for education and assistance. During the clinical exam, the doctor looks for signs
and symptoms such as: anorexia, nausea, vomiting, diarrhoea, steatorrhea, dysphagia, etc.

**Anthropometric parameters:** Taking the weight and height and calculating the BMI are basic elements that are checked periodically so that they can be monitored constantly. Measuring the arm circumference and the tricipital skinfold supplements the basic parameters for better assessment of body composition.

Special attention is paid to the correct measurement of these parameters, with periodic calibration of the instruments. For children, the anthropometric assessment is done according to UNICEF’s instructions, particularly in the first two years, by calculating the weight by age in relation to the NCHS/WHO reference values, monitoring growth using the growth curve.

**Biochemical parameters:** The laboratory provides routine indications with regard to albuminaemia, revealing the severity of protein-energy malnutrition; the results of the haemochrome make it possible to evaluate the anaemia. Specific parameters are required for more in-depth assessments, especially those involving interactions between metabolism and HAART therapy.

**Computer support:** An essential element of DREAM. It helps the physician in assessing and monitoring nutritional status by complementing the reading of the anthropometric data with the other clinical and nutritional parameters, allowing the viewing of the anthropometric indicators chosen in relation to the cutoff points identified for the screening of individuals at high risk for malnutrition.

At the end of this assessment process, the physician assigns a nutritional regime to the patient to optimise his diet and nutritional status.

**Food aid to people with HIV/AIDS and their families.**

DREAM has chosen to donate food to people with HIV/AIDS and their families in order to ensure food security and contribute to a wholesome and balanced diet. Based on the assessment of his nutritional status and his so-
cial and family needs, every DREAM patient is included in the program of food assistance for himself and his family.

The means chosen by DREAM to improve the diet of those with HIV/AIDS and their families are:

1. Monthly food deliveries in the form of dry rations to be taken home.
2. Distribution of small meals during day hospitals and visits to Maternity.
3. Delivery of meals and nutritional supplements in Hospital for hospitalised patients.

The DREAM program has chosen to donate foods that are part of the local diet and that complete their nutritional requirements.

Tab. 2 – Foods most commonly distributed to families by DREAM.

<table>
<thead>
<tr>
<th>Grain</th>
<th>Legumes and nuts</th>
<th>Flour mixes and fortified oils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice</td>
<td>Peas</td>
<td>Corn Soy Blend</td>
</tr>
<tr>
<td>Corn and Corn flour</td>
<td>Lentils</td>
<td>Wheat Soy Blend</td>
</tr>
<tr>
<td>Cookies</td>
<td>Beans</td>
<td>Soybean oil</td>
</tr>
<tr>
<td></td>
<td>Peanuts</td>
<td></td>
</tr>
</tbody>
</table>

The amount distributed is calculated on the family’s size, economic conditions, and the number of people with HIV/AIDS and their health status.
Each distribution is accompanied by correct information on the nutritional characteristics and the best means of conserving and cooking each foodstuff distributed. The DREAM staff is responsible for giving recipes and advice for improving the flavour and maintaining the nutritional qualities of the food. Finally, the staff regularly samples the opinions and ideas of the beneficiaries regarding the acceptability and approval of the foods distributed.

The food storage-transport-distribution chain
Proper health and hygiene management of the food storage-transport-distribution chain is a basic requi-
site for DREAM. Special care is taken to ensure proper conservation of the foodstuffs; the warehouse and the premises where the foods are prepared and distributed must be suitable and secure to prevent any sort of damage to these commodities. The foods distributed must all be high in nutritional quality, and their source must be such as to guarantee the wholesomeness and safety of the product, based on international food hygiene and safety standards.

Supplementation with vitamins and other micronutrients, nutritional counselling

The physician is responsible for prescribing and controlling supplements of vitamins and other micronutrients. Therefore every supplement is administered free of charge and under the physician’s control, for a period of time that is limited to actual requirements and in any case until the body’s need has been replenished.

The physician is also responsible for the nutritional counselling that is intended to lead to proper management of nutritional symptoms and signs, such as anorexia, diarrhoea, nausea and vomiting, stomatitis and dysphagia, dryness of the mouth, constipation, etc., caused either by the disease or as adverse and side effects of the HAART therapy and/or other therapies. The meeting with the patient is also aimed at intervening in a specific nutritional and therapeutic situation, to avoid those foods that interfere with the therapy and to increase the consumption of foods or of vitamins and minerals depleted by the drug therapies.

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1. Home care

Home care is for patients whose clinical conditions do not let them have access to outpatient and day hospital services: it is a service for those patients who are clinically and socially the weakest, and it expresses the choice of guaranteeing care for all. In developing countries, reaching healthcare centers is even more difficult for those patients with neither the energy nor the resources to do so on their own. Besides difficulties in transportation and structural shortcomings of public services inadequately sized in proportion to real needs as a consequence of insufficient resources, an often determining factor of poor compliance is the condition of economic and general weakness of many inhabitants. This service thus provides the concrete possibility of bringing care even where it would never get, ensures all patients of their right to health, makes it possible to conquer the isolation to which so many are relegated, rebuilds a network of personal relationships, and involves families in the care and recovery processes.

Organization

The home care service headquarters is part of the day hospital structure; in fact, a close relationship between these two services is necessary to facilitate the patient’s transfer from one mode of assistance to another. In its first months of activity, DREAM saw a rapid shift of patients from home assistance to day hospital – a first step forward made possible for many by improved clinical conditions, recovered independence of movement, and the renewed hope for life.
The assistance team
The team consists of Mozambican social workers and healthcare personnel and a coordinator. Everyone is required to have, and is furnished with, specific training in home care for persons with AIDS. The service receives consulting services from a physician for diagnostic and therapeutic aspects in patient care.

Access
The home care service is for patients residing in an area near its headquarters. Patients are indicated by families, hospital facilities, healthcare centers, and service personnel present in the territory.

Services
The services respond to the needs emerging from a multi-dimensional evaluation taking into consideration the economic and social conditions of the patient’s family, as well as his or her clinical conditions and residual functional capacities. This service was structured taking into account the drama that many families experience with one or more ill persons. Reduced economic resources; malnutrition; inability to maintain ordinary household hygiene; failure to make civil registration entries; dropping out of school; and the inability to access even basic care: the accumulation of these circumstances is often a fact from the outset, and home care is associated with interventions aimed at seeking an environmental sustainability indispensable for improving life conditions and for the therapy to work.

The services contemplated by the program are as follows:
– assessment evaluation of the social situation;
– assessment of the health situation;
– home care (cleaning the home, preparing meals, disinfecting water, providing a water filter);
– social support for keeping minors in school, cutting through red tape, seeing to legal matters, running the household;
– transporting the patient to healthcare facilities for medical consultations and diagnostic exams;
– health education and counseling to the patient and his or her family;
– improving the quantity and quality of the nutrition of the patient and his or her family;
– personal care and hygiene services;
– home nursing;
– medical consultation;
– supply of antiretroviral and basic drugs.

Modes of operation
1. During the first home visit, the patient’s case history is gathered, an initial clinical evaluation made, and nutritional, social, and living conditions assessed. At that time, analyses, counseling, the doctor’s visit, and other clinical checks are planned.

2. During the weekly meeting of the social/healthcare team, an overall evaluation of each patient is made to define the number of weekly visits by personnel and the type of activities to be carried out.

3. Each social/healthcare worker going to the patient’s home reports the visit in the social section of the patient’s file, notifies the physician of any changes in the state of health, and reports to the service coordinator any changes in social and living conditions.

The DREAM program places great importance on the relationship established between workers and patients. Training courses stress that maximum respect is required when entering the patients’ homes with the delicate task of caring for the many aspects described above. Courtesy, privacy, and discretion in proposing solutions and interventions are essential for respecting the dignity of all and for the program to succeed.

2. Day hospital

Day hospital is for patients that are HIV positive or with full-blown AIDS. The population accessing the service is composed of both children and adults.
Organization
The service headquarters has:
a) a patient’s waiting area, with chairs and benches to ensure comfort;
b) a room near the entrance for reception, with a computer to gather data;
c) a room for medical examinations;
d) a counseling room;
e) a room for tests and samples to be taken;
f) a pharmacy area;
g) a warehouse storing foods for nutritional support;
h) a meeting area, or a multifunctional room that can be set up as a meeting room.

The assistance team
The day hospital is manned by healthcare and social workers (physicians, nurses, social workers). Operators receive ongoing training and are coordinated by a management team chief who, as already pointed out, has specific highly professional features gained in Europe and refined on site, is strongly integrated with all team members. A group meeting is held once a week to discuss clinical cases and problems related to the service.

Access
Patients access DH on their own or as indicated by physicians from health care service. An objective of the DREAM program is to foster care for entire households.

The path
The path begins with reception/waiting in an area for this purpose, which may be a yard or room. During the wait, the day hospital’s social workers concentrate on creating a cordial, relaxed atmosphere: patients are offered soft drinks and fresh water, there is conversation, and a collective reading of the book “Como vai a saúde” (Guerini e Associati Editore-Milan-1999) – The Community of Sant’Egidio’s basic health education course – is proposed, to introduce the concepts that will become necessary.
The patient then accesses the reception room – an initial entry at which operators gather personal data and open the clinical file. Special attention is given to translation: many persons need the mediation of operators for local languages. Once the clinical file is opened, a nurse proposes HIV testing to the patient (pre-test counseling) in the room for this purpose. Those who test negative are invited to counseling and informed as to how the illness is transmitted and the rules for prevention. Those testing positive are invited to counseling and, once informed of their state of health, to take part in the DREAM program. They are given a card, which they are told to keep with care, with their ID code (univocal identification number) and the center’s telephone numbers that may be called for any problem.

After informed consent, the patient gives samples for initial analyses, and the service coordinator schedules the first medical examination.

Based on the results of the lab tests and the clinical examination, the physician chooses the therapeutic path in accordance with the DREAM protocols. Simplifying communication and procedures is a decisive element for the whole intervention to be effective. As already seen, language problems, reading difficulties or illiteracy, and lack of experience with written instructions and taking note of what must be done, can – without paying specific attention to how to transmit information – become insurmountable obstacles. This is why, to simplify subsequent visits, patients are given cards of a different colour for each type of appointment (red for testing, yellow for nutritional support, green for the medical examination, and blue for medication). This is how the patient accesses the center for testing, medical examinations, picking up medication, and nutritional support.

Additional attention is devoted to distributing the therapy. Each patient receives the medication in named envelopes indicating, even by symbols (the sun for the morning, the moon for the evening), when it is to be taken. At that time, the patient is given a small plastic package, hermetically sealed for proper conservation.

The clinical file is computerized.
Privacy
Although operating in situations of health emergency, the diagnosis and treatment centers and the labs that take part in the DREAM program are required to devote special attention to safeguarding privacy.

*At diagnosis and treatment centers, tests and counseling are carried out by healthcare workers bound by professional secrecy. The clinical file is designed to guarantee separate access for healthcare personnel and social/assistance workers: data on HIV positivity and the stage of the illness thus remain confidential.

To improve compliance (adherence to the diagnostic-therapeutic program), the patient is required to authorize home visits or the use of his or her phone number if he or she misses the appointments set by the center.

*Upon reception, the analysis labs assign to the samples an identification code, thereby preventing treatment of personal data and the possible consequent spread of private information.

*Data are computerized, gathered, and sent to the centralized archive for the remote medicine service solely by ID codes. The computerization program scrambles the patient’s data automatically, thereby ensuring maximum confidentiality while permitting the transmission of information useful for improving diagnosis and care from one end of the world to the other.

3. The mother/child healthcare center: preventing vertical transmission

This service is performed at the maternity wards located at the healthcare centers. Its purpose is to test pregnant women, prevent mother-to-child transmission, and care for mothers in accordance with the pre-established protocols (see chap.2). All women going to the healthcare centers when pregnant are informed as to the existence of the DREAM program.
**Organization**
The mother/child healthcare center has a minimal structure as well, corresponding to the functional requirements:

a) a waiting area, suitably equipped, with seats and benches;
b) a room for HIV testing and for counseling;
c) a room for taking samples;
d) a room for the medical examination and delivering medication;
e) a pharmacy.

**The assistance team**
As with the other services, the assistance team consists of physicians, nurses, and social workers. The presence of a nurse and a physician with pediatric qualifications is recommended.

**Access**
Pregnant women going for prenatal checkups at the healthcare center are informed as to the possibility of accessing the service: schedules, characteristics, and the fact that it is free of charge.

**The path**
A qualified nurse performs pre-test counseling, in which the woman is informed as to how the illness is transmitted, particularly from mother to child, and is made aware of the existence of the DREAM program, and above all of the possibility — and benefit — of being able to receive all the necessary care in the event she is HIV positive.

Those who wish to do so are tested for HIV. In this population group, DREAM has recorded 100% compliance — a confirmation of the effectiveness of the communication, combined with the actual possibility of therapeutic support in case of need. This particularly encouraging fact has few precedents or similar events in other African experiences.

Women with positive test results are sent to counseling, informed of their health status, and invited to take part in the DREAM program, which allows them to be treated with antiretroviral drugs and to prevent transmission to their child.
Women deciding to take part in DREAM give a sample and undergo a medical examination. The physician chooses the therapeutic path in accordance with the protocols predefined based on the clinical and lab results. From the moment of entry into the program, for the following months of the pregnancy, the woman is followed constantly until childbirth. She accesses the service for medical examinations and samples; she can pick up medication and receive health education for artificial feeding; nutritional support is available. After childbirth, the service covers both mother and child.

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Compliance

For a long time, adherence to therapy has been one of the main obstacles to introducing antiretroviral therapy in limited resource countries. DREAM’s experience points out an effective, viable way towards overcoming the stumbling block of adherence to therapies and alleviating these concerns. During its first months of life, DREAM has recorded very high compliance. These encouraging results are no accident. They are rooted in the careful communication of positive messages.

1. Being HIV positive is not a death sentence: during testing and counseling, each patient is explained that the drugs available today allow effective care guaranteeing a good standard of living. Thanks to the therapy, being HIV positive is no death sentence.
2. DREAM guarantees therapy to all those that need it, free of charge.
3. No patients are left on their own, but are accompanied on their clinical and diagnostic itinerary: they receive explanations as to the type of analyses to be performed and how they are important for identifying the most effective therapy; therapy is simplified as much as possible to guide them in taking their medication regularly; patients are invited to contact the center for any problem that may arise, by phone if they can, or in person.
4. The guarantee of privacy, the respect that surrounds each person, the courtesy and availability of operators, and introduction into a pleasant, welcoming environment: these are all factors that contribute to the choice of coming back.

5. The rediscovered hope for life, the rapid improvement of clinical conditions, and the possibility for many to return to a normal social and working life: these all key factors for the entire environment in which the patient lives, and are the best guarantee of adherence to prevention programs.

Caring for pregnant women
DREAM privileges pregnant women and the mother/child pair: this is the choice for Africa’s future. Women are encouraged to be tested with the security that they will receive care for themselves and the hope that they will bear healthy children free of HIV. Nutritional support is essential for facing the delicate gestation period, and is often an aid for sustaining the other children.

Throughout pregnancy, each contact with the center is an occasion for getting advice, support, encouragement, and friendship, for women in a difficult period in their lives, and at times without support from men (deceased, away working, etc).

We take particular care in explaining to the future mothers the need for artificial feeding: short health education courses are effective and useful to gain familiarity with water filters, bottles, and dosages of powdered milk.

While waiting, and with the help of the center’s staff, fears and confusion can be overcome by meeting other women going through the same experience and seeing them feed artificially.

When childbirth is near, each woman receives an important basic kit: water filter, bottle, and powdered milk, along with an information sheet using drawings and simple graphics to depict the procedures to be fol-
allowed. This is no minor safety device for the program: some women may be unable to reach the center for their childbirth and must be ready to put what they have learnt into practice, to keep their healthy baby HIV free.

All the same, each women knows that it is important to reach the center within three days after childbirth, for the child to receive the specific therapy, plus all the care he or she might need. The first arrival of the new mother and her newborn at the DREAM center stresses the new birth and the victory over the virus by appropriate means (party, gifts), which help strengthen the bonds that are decisive for the entire duration of the treatment.
Chapter 5

The molecular biology laboratory for antiretroviral treatment in Africa

1. Introduction

The DREAM program for treating AIDS in developing countries places particular importance on diagnosis – understood both as level I diagnostics and as such advanced diagnostics as, for example, quantifying the viral load and evaluating the CD4+ lymphocyte sub population. Although leukocyte immuno-phenotyping in monitoring HIV in the West has been routine for years, in Africa this possibility, within the context of the services performed by the national health systems, is quite limited – if not absent altogether – in the vast majority of countries. But having a reliable CD4+ count of the patient’s blood is at present an indispensable factor in the administration of antiretroviral therapy. In addition to the physician’s strictly clinical observations, the exact clinical picture of a patient with HIV is also made up of analysis results, which must be solid and reliable. Methods of molecular biology measuring viral DNA or RNA also make it possible to effectively monitor the therapy in subjects treated with drugs inhibiting virus replication. This is why the DREAM program includes a molecular biology lab as a specific support to the HIV diagnosis and care service. The lab exams deemed necessary for these purposes are those that make it possible to monitor the therapy and the related toxic effects that it may have, and see to perfecting
and using a variety of analytical techniques with differing levels of complexity and specialization. The first level involves the careful determination of the **haemochrome** and of the complete **leucocyte formula**. This exam is crucial for the utility of the final report, given HIV’s characteristic of specifically attacking and killing CD4+ lymphocytes, and in monitoring the toxic effects of drugs being used for the first time, such as zidovudine. The second level corresponds to the need to monitor the state of **kidney and liver functions** and to measure the concentration of **specific ions such as Fe++**.

The third level involves the double platform instrument count of the lymphocyte sub populations, specifically **CD4+ and CD8+**, an essential support for monitoring antiretroviral therapy and the patient’s state of health. The fourth level of specialization consists in applying the analytical methods needed to quantify the plasma viral load – a parameter that is an indicator of the state of infection and, along with the CD4+ count, one of the major parameters for evaluating the therapy to be administered.

The classification that is made cannot ignore other lab practices which, although they cannot be catalogued in terms of specialization and complexity, make real contributions to making the lab’s service a sound one. These are:

1. the possibility of carrying out rapid tests on HIV positivity on whole blood, plasma, or serum;
2. the possibility of producing analytical grade distilled water for the dilutions and preparations envisaged by the various diagnostic kits used;
3. the use of an effective sterilization and waste elimination system;
4. keeping the proper temperature of reactives and samples of whole blood, plasma, or serum, also for establishing a serum bank;
5. developing and implementing a proprietary software program for managing the exams.

Separate thought must be given to instrument maintenance. In a limited resource country, the introduction of a
molecular biology lab often raises for the first time the problem of maintenance of sophisticated lab equipment. Specific training must thus be planned for local maintenance personnel, to ensure over time the indispensable technical assistance. At the same time, lab workers must acquire a minimum technical ability in order to carry out at least basic instrument maintenance, to allow a certain degree of laboratory self-sufficiency when intervention by the maintenance technician cannot be guaranteed quickly and in every circumstance.

2. The facility

The use of advanced methods poses problems as to the adequacy of the facility in which to house the laboratory. In this regard, the minimum requirements necessary for the premises of the labs are listed below, taking into account that facilities of this kind may be installed at medium-large centers.

*Condition of the premises*

The areas must guarantee the possibility of suitably deploying the various moments of analysis. In particular, there must be a room for reception and reporting, also to be used as an office/archive. There must also be a confined area in which to treat infected waste with an autoclave. It will be necessary to have a warehouse area, or at least to keep the surplus material in boxes and cartons in a place where samples are not processed. Virology areas must be large enough to permit the unidirectional flow of the sample, in order to prevent contamination. Lighting surfaces must not permit opening to the outside. Windows, if any, are to be sealed and provided with curtains in a washable, non-absorbent material (plastic is ideal). It is important that the flooring be in a washable, non-porous material (e.g. linoleum treated with waxing products). Walls and casings shall, where possible, be treated with washable paints.
Work stations surfaces shall be washable and acid resistant. All areas shall be air conditioned. The size of the air conditioning system in the area where the cytofluorimeter and the –80°C freezer are to be deployed shall take into account the heat produced by the machines. It should be ensured that the electrical system has an earthing system; otherwise, a grounding cable should be provided, since the lab has electrical equipment using water. Constant, continuous electric power is indispensable. Given the environmental conditions and the quite possible occurrence of voltage rushes or temporary absence of power (which may be prolonged), an autonomous electric generator must be provided that can intervene automatically, even at night, given that some of the methods require overnight incubation and the freezers for conservation at –80°C cannot maintain such low temperatures for long; samples and expensive reagents would risk being made unusable. The freezer must be connected to the general electric board directly, to keep the motor’s absorption from interfering with the remaining equipment. Current stabilizers for the more sophisticated equipment – such as the cytometer, which uses a laser source – are useful.

3. Analysis parameters

It should be kept in mind that the laboratory is exclusively for monitoring antiretroviral therapy. Therefore, although screening tests may occasionally be performed, this is not its specific function. The use of rapid HIV testing frees the lab from such practices as ELISA or the Western Blot, which are more burdensome in terms of time, cost, and necessary manipulation. In fact, the rapid tests completely free the lab worker, since they may be carried out anywhere so long as the minimum requirements necessary to effectively safeguard the worker are kept in mind. A kit can be equipped with single-use lancets (needles are not recommended), cotton wool, disinfectant, and disposable gloves, and can be used to perform the test anywhere. The screening tests
adopted in the program have thus been chosen bearing in mind their use chiefly at the diagnosis and care centers, thereby providing the possibility of organizing work in order to be able to carry out the HIV testing and the counseling on the same day, sending the specialized lab only the samples from positive patients.

The essential parameters to be determined are as follows:
1. Hemochrome and complete leucocyte formula
2. Liver function
3. Kidney function
4. Iron
5. CD4+ and CD8+, percentage and absolute levels
6. Viral load as level of plasma RNA

**Analytical determinations**

**HAEMATOLOGY**

The erythrocyte and leucocyte count is to be performed with automatic equipment permitting the two cellular types to be counted separately. Leucocytes are counted after the erythrocytes are lysed. The equipment must also be able to count in a differentiated fashion, both as a percentage and in absolute values, the leucocyte sub-populations and the platelets. It is good to have printed reports available for every determination.

The equipment needed to count the lymphocyte sub-populations is the flow cytometer, or cytofluorimeter. From the standpoint of determining for diagnostic purposes the CD4+ and CD8+ lymphocytes, the type of cytofluorimeter most widely used in the West is with blue laser, perhaps associated with an optional red laser. This is the only kind of machine that enables routine, accurate, and realistic – albeit surely not the most affordable – determination of lymphocyte sub-populations. Other machines on the market try to avoid the considerable costs of purchasing a blue laser cytofluorimeter to the detriment of the number of determinable parameters. For example, using green or red lasers makes it possible to reduce costs considerably, but with the loss of the ability to use a series of fluorochromes that are important for internal controls and for the overall evaluation of the ac-
quisition. Another market tendency is to reduce the fluids and optics, making these cytofluorimeters virtually transportable. But these machines’ fluid ducts clog more easily and the flow is more unstable than in a fixed machine. Moreover, instability problems are found in the light source due to the difficulty in controlling the cytofluorimeter’s internal temperature. This is why, to equip a reference laboratory, an argon laser, cytometer, one of the standards in the West, has been chosen. The system also has a carousel mechanism making it possible to automate the operations for inserting the test tubes containing the blood to be tested, thereby diminishing manipulation of the sample. Lastly, the cytofluorimeter communicates with a computer that sets up its activities and stores the results obtained, thereby obtaining an important database at the same time.

The absolute CD4+ and CD8+ count is made in double platform. Samples are processed by the lyse non-wash method, using a generic lysant and reduced volumes of antibody.

**BIOCHEMISTRY**

These determinations are made using colorimetric methods and require a spectrophotometer. Instrumentation with interchangeable filters permitting the selection of three or four wavelengths – those needed for the colorimetric determination of the most frequently required parameters – is sufficient. The following are usually measured:

1. transaminases
2. albumin
3. amylases
4. direct and total bilirubin
5. creatinine
6. iron.

It is important for the photometer to have a multiple or single self-sampling system, to eliminate the risk deriving to the operator from movement of the cuvette in the system’s housing. The photometer should also have a data entry and/or storage system; display only machines should be avoided. Micro-methods have been perfected to enable the use of reduced volumes of reagents and serum. The micro-methods
were validated in-house and are periodically verified. The acceptability of the method is subordinated to a value $r>0.9$ of the regression lines.

**Development of methods for biochemistry**

The clinical biochemistry performed in the lab uses well-known, trialled diagnosis kits. These are colorimetric kits developed in such a way as to simplify their use as much as possible. The samples are normally prepared in accordance with standardized protocols that involve using automatic pipettes with fixed volumes of 100, 250, 500, and 1000 µl. This solution is certainly useful where a photometer is used requiring cuvettes with a volume of 3 ml, or where it is impossible to work accurately with reduced and variable volumes.

However, methods employing smaller volumes (micro-methods) are more convenient. By evaluating the cell’s useful volume, micro-methods may be developed that, by using volumes tailored to the machine, considerably reduce the fixed cost of the reagents needed for each determination. The other advantage found is the possibility of reducing sample volumes, particularly in pediatrics and neonatology, where large quantities of venous blood are hard to draw.

This is made possible by a complete serious of automatic micro-pipettes, and above all by the technical know-how of lab workers perfectly capable of working with micro-volumes on a routine basis. Other advantages are the reduction of infected material to be eliminated, and less manipulation of the sample by the lab worker.
**Viral load**

The plasma’s viral RNA is measured by bDNA (branched DNA). This method has the advantage of being based on amplifying the signal and not the target as with the methods using PCR (polymerase chain reaction), and therefore of being less susceptible to the problem of contamination. Currently, the bDNA system appears to be the one that offers greater coverage for the various extant HIV subtypes. Furthermore, bDNA is not subject to the errors typical of the PCR procedures (amplification of contaminant RNA, mutations induced by the polymerase). This results in a reduced level of sterility necessary for the analyses to be performed. The method is relatively easy to perform, although it involves the use of micro-volumes and requires two working days, with rigid timing for carrying out the various steps. The method’s disadvantages certainly lie in the extremely high cost for the kit, plus the fact that single samples cannot be processed (to optimize the kit’s use, many samples must be processed at the same time, and the response awaited at the clinic). Furthermore, the bDNA technique is influenced by the instability of the reagents, and particularly of the control RNAs that are employed to determine the standard curve from which to obtain the viral load of the samples in question. The luminescent substrata used by the detection system are also extremely light sensitive and to be kept carefully. Experiments are currently under way to research and validate alternative, less expensive systems to quantify the viral load using the dosage of viral antigens.

**4. Work flow**

Blood is normally transported the same morning to the laboratory in slightly refrigerated insulated containers.

*Receiving specimens*

Specimens must always be sent together with a form containing at least the case clinical history record number, name of the patient, provenance, signature of the director of the
Health Center, number of vials collected from each patient. The Reception office will check that the number of vials corresponds to the amount declared and that they are all labeled.

Using the appropriate laboratory software a progressive number will be assigned to each specimen and this number must be attached to the specimen and written on the accompanying form. Thus the specimen will be unequivocally identified throughout its life in the laboratory and will guarantee the patient’s privacy.

The aliquots are normally two vacutainers: one with a violet cap containing K(3)EDTA, for haematology and evaluation of plasma RNA and one with a red cap without anticoagulants for biochemical analysis.

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**Distant Centers**

When specimens come from centers which are very far from the reference laboratory (several hours of driving), some precautions must be taken to ensure the quality of analysis.

If CD4+ cell counts need to be assessed it is important to find out if there is an automatic blood cell counter in the center where the specimen was collected. If so it is better for the center to carry out the Complete Blood Count (CBC) analysis itself and either email the report or, time allowing, attach it to the aliquot to be sent to the reference laboratory. If CBC is routinely performed by microscopy it is better to send this aliquot too to the reference laboratory. In fact although in order to assess CBC, specimens should be processed within a few hours from collection, automatic counting makes it possible to evaluate a much greater population and thus compensates underestimation due to delay in analysis. If this option is preferred, attention should be paid to haemolysis. In fact if only the aliquot for CD4+ analysis is sent, haemolysis is a minor problem (the specimen is lysed to allow the reading of the different lymphocyte sub-populations); if both aliquots are sent greater care should be taken in transport. Vials should
be placed in insulated containers in appropriate vial racks possibly placed on material which will absorb shocks (polystyrene, foam rubber).

**Sorting the aliquots**

**SEROLOGY**

Vials for serological analysis are processed using normal centrifuges. Centrifugation must be carried out immediately. The following analyses must be performed the same day:

- Albumin
- Creatinine

The following analyses can be carried out the morning after:

- Bilirubin Total
- Bilirubin Direct
- GOT
- GPT
- Iron

Specimens to be processed the following day must be stored at +4°C.

**HEMATOLOGY**

One of the 2 aliquots with the anticoagulant will be used for the Complete Blood Count. Then, if necessary, an aliquot will be processed for Flow Cytometry. Flow Cytometry analysis may be performed even the day after blood collection. In this case the aliquot with whole blood and EDTA will be stored in a dark place at room temperature. The following day analysis will be performed according to the protocol.

**VIROLOGY**

The second aliquot with anticoagulant will be centrifugated in order to separate the plasma necessary to determine the viral load. All the plasma will be kept in the freezer at –80°C. A list of samples present in the freezer is to be kept and properly updated.

**Reports**

The results of the different tests will be recorded electronically
the day after, at the latest. The report will be printed and delivered only when all the requested analyses have been performed. Only the results of viral load determination may be given at a later date and should be printed on labels with patient identifier and result. Reports shall be folded and stapled and filed in appropriate folders, one for each center of provenance.

5. Waste disposal

Waste disposal is a public health issue. Contaminated material may be burnt but one should make sure that all the material has actually been destroyed. Alternatively, where there is no efficient sterilization and waste disposal system, an autoclave set according to international standards, i.e. at least 15 minutes at 120 degrees centigrade and saturated with vapor may be used. Treatment is confirmed by adhesive tape containing a substance which changes color with heat. Waste thus treated may be disposed of together with non-infectious material. Fluids (supernatant, excess sera) are collected in rigid plastic containers with 100/200 ml of 5% bleach solution (sodium hypochlorite), left overnight and later disposed of.

6. Safety

In each laboratory safety measures should be implemented to protect personnel. The main rules regarding laboratory practice, specimen handling and use of equipment should be stressed.

Safety Rules

General rules

– *It is forbidden to eat or drink in the laboratory and to store food or drinks in refrigerators where laboratory products are stored.*
– *Personnel must wear laboratory coats to be taken off before leaving.*
– Access to laboratory premises is forbidden to unauthorized personnel. Suppliers and agents must be received at the reception or in the chief’s office. – Never use glassware which is cracked and/or splintered. Never wash or reuse microscopy slides. Never wash and reuse disposables. – When blood specimens are handled, personnel must use disposable gloves to be removed and thrown away each time processing is interrupted, no matter the reason. Personnel who are last to leave the laboratory in the evening must check that everything is in proper order and that equipment has been turned off.

Precautions when using electrical equipment
– Immediately report any malfunction of equipment, presence of worn out wires, damaged plugs or sockets. – Equipment run electrically should not be placed near explosive or inflammable material.

Precautions when processing biological materials
Infectious agents may be parasites, helminths, fungi, bacteria and viruses. Therefore all biological material processed and not only that coming from positive patients should be treated as infectious. An efficient disinfectant should be present in each room. A dispenser of a 5% bleach solution (sodium hypochlorite) is useful. – Never pipette by mouth. – Hands must be washed before leaving the laboratory.

Precautions when using Ultraviolet Rays
– Avoid direct exposure to UV rays.

Rules for use of centrifuges
Personnel who use centrifuges must know exactly how they work and are run. In particular before use: – Check that all centrifuges have safety devices which do not allow them to start with the lid open.
– Observe recommended maximum speed and sample density ratings.
– Check that containers are accurately balanced.
Moreover:
– clean centrifuges and rotors after use so that they may be used later without risk;
– immediately switch off a centrifuge that vibrates or produces strange sounds.

7. Quality control of the diagnosis circuit

An effective quality control for such a complex procedure as determining diagnostic parameters involves establishing rules for each individual step. That is to say that it is necessary to analyze and validate the whole diagnostic circuit process and not merely one aspect of it. Towards these ends, key steps for a blood sample’s entire path have been assessed, from withdrawal to reporting, to transport and effective use in instrument methods, thus highlighting operative moments requiring validation.

No kind of quality control may be considered apart from a representative sample, both in terms of number and quality of the population to be investigated, and only thus yielding a statistically meaningful result.

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**Sampling:**
Sampling is performed using exclusively vacutainers – the only containers capable of ensuring the conditions of safety and sterility necessary for carrying out analyses of this kind.
The vacutainers are filled to capacity. Smaller volumes may influence the analytical result.

**Preparation of aliquots:**
Aliquoting blood specimens must take into account the spontaneous precipitation of haematic cells; vials must always be kept gently agitating to avoid clotting (coagulation). Only vials containing $(K_3)$ EDTA should be used. If clotting (coagulation) occurs, the specimen cannot be processed. Even micro-coagulation due to incomplete or insufficient mixing of blood and anticoagulant may influence test results.

**Storage and transport of aliquots:**
Blood should not be exposed to heat shock but must be stored at room temperature to avoid haemolysis or loss of representativeness of the white cell component. Blood must be sent to the test center as soon as possible within acceptance time set by the laboratory.

**Storage of specimens in the laboratory:**
Specimens must be accepted when they are delivered. Specimens, which have not been registered, cannot be stored in the laboratory. Storage of specimens to be used for the different tests shall follow the laboratory workflow. Vials should always be hermetically sealed and stored at room temperature for hematology, at $+4^\circ C$ for serology and at $-80^\circ C$ for virology.

**Tests:**
**HAEMATOLOGY**
Complete Blood Count is carried out with an automatic blood cell counter. Instrument performance is checked daily using a standard synthetic serum and plotting a graph with deviations from the standard. The percentage of lymphocyte sub-populations is assessed using a flow cytometer with an argon laser (488 nm), in double platform by the “lyse non-wash” method. This ensures that error in reproducibility is not greater than 15%. Frequency of quality control depends on the amount of tests.
performed. The laboratory is part of an external quality control circuit.

**Blood Chemistry**

Clinical biochemistry is performed by spectrophotometer using diagnostic kits to which reductions in volume are applied. Periodically, control normal and pathological sera are tested in every determinable parameter.

**Reports**

Results are recorded on a master program for laboratory management. The program handles a data bank containing all results generated in the laboratory thus allowing a comparison with previous results from the same patient. Moreover the program permits differential printing of parameters whose results and subsequent reports are generated at different times. It also allows to check printed reports or those undergoing validation and indicates date of print.

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1. Introduction

In order to manage and monitor patients correctly, software has been developed to enable real-time analysis of each person’s clinical situation. This software is in fact not a mere archive, but a working tool used whenever the patient reaches one of the diagnosis and care centers. “DREAM_prg” this is the name of the program - manages not only the clinical and chemical portion with detailed medical logs, but also each contact the patient has with the various services. Each patient is automatically assigned an ID (univocal identification number), identifying him or her in all subsequent accesses and becoming his or her reference and file number. The identification number is an alphanumerical code with two letters indicating the care center of reference followed by 6 digits. The identification number of children born within the MCPC vertical prevention scheme will be the same as that of the mother, with the code “P1” added.

At each medical examination, all the clinical annotations are entered directly into the computer. For each new access, a log is created indicating each patient’s symptoms, diagnosis, and therapy. Each symptom and diagnosis is followed by a notes space where the physician can freely write any annotations. The program can show the type of antiretroviral therapy and separate it from the remaining therapeutic treatment. After each medical examination, a new log is printed and inserted in the clinical file.
Laboratory exam reports reach our care centers in hard copy and by such computerized means as e-mail, diskettes, or digital pens. DREAM_prg therefore stores all the haematocochelical examinations undergone by the patients, in order to easily monitor biohumoral variations over time. With each arriving report, an updated report is printed summarizing all the laboratory levels, and added to the file.

A portion of the program also manages such social interventions as distributing water filters and delivering mosquito netting. From time to time, DREAM_prg will indicate the need to replace water filters.

2. Mother/child monitoring

DREAM_prg also has a section dedicated to monitoring the prevention of mother-to-child HIV infection. When a pregnant woman’s week of gestation is entered, the due date is automatically indicated, and will be indicated again as the event approaches.

This feature allows us to forecast the number of childbirths in a given period, thereby facilitating the prompt administration of Nevirapine by the time the newborns are 72 hours old. This session will also report peri-partum information (type of childbirth, APGAR, etc). Each newborn will thus have a neonatological, and subsequently a pediatric log.

Dream also has a graphic portion displaying the growth curve in percentiles, in order to follow growth deficits – and if necessary correct them with drugs and/or nutritional support.

Although from the clinical standpoint, artificial or breast feeding regards the newborn exclusively, it is a datum always reported, of course, by the mother during the examination. DREAM_prg sees that this datum, when reported on the mother’s log, will also be available in the newborn’s, and the other way around. This simple feature makes it possible not to lose indispensable information on the mother-to-child prevention program.
3. Agendas

All appointments for samples, medication, medical examinations, or for other purposes are made by information technology. In fact, DREAM_prg has electronic agendas that plan the various accesses and automatically signal each day’s appointments. Thus appointments are computerized for medical examinations, for giving samples, for delivering medication, and for providing nutritional support. A special agenda is devoted to urgent checks; it is used when a patient has not come to the center and must be tracked down, with the grounds for his or her absence checked. DREAM_prg is therefore a tool capable of monitoring each patient’s adherence to the care program and promptly indicating those who, for a number of reasons, have failed to show up on the appointed days.

4. Remote medicine, remote consultation

The remote medication service makes it possible to provide remote consultation for special clinical cases; simply by supplying the patient’s ID code, it is in practice possible to remotely consult the entire clinical file in Jpeg format. Remote consultation is currently active with physicians from a number of centers of reference. DREAM_prg thus enables us to remotely monitor the clinical conditions of all our patients. Moreover, being able to remotely obtain an updated version of all the data allows us to promptly identify any errors in data entry, or to see which patients have failed to show up for their appointments. This kind of control is performed on a weekly basis. The data are completely separated from the program, and this makes it possible to download updates of DREAM_prg from the Internet without interfering with the data bank at all.

5. Technical features

At the larger care centers, the program is on line over local
networks, thereby making it possible to access all the data from a number of PCs: one for the physician, one for the nurses, one for the coordinator and social workers. In this way, the passage of clinical data, drug prescriptions, and the planning of interventions is made on line, thereby cutting down paperwork and reducing the possibility for error. The data files are backed up on a daily basis, whether or not the operators give the command. Thus this backup creates 7 security files a week, thereby guaranteeing 7 copies of updated data at all times. Once a week, each center’s PC server will automatically e-mail to a local server a scrambled and anonymous copy of each care center’s archive. The program deletes the personal data of the patients, who will be identifiable only by their ID code. This local server will gather the archives from all the care centers, which may be consulted or sent to the Comunità’s physicians. A high-speed Internet connection is not required to perform this remote medicine service. A 33 Kbyte/sec modem connection is sufficient. These technical features make the model reproducible even in those areas without high-speed lines, where only a phone line is available. Training courses for using the program have been developed, attended by physicians, nurses, and social workers. DREAM_prg is easy to use, and will soon be available in various languages that the operator may select when starting the program.

6. DREAM-laboratory

Computerizing the molecular biology lab
The computerization of the molecular biology lab is by means of a database that interacts with hematology, spectrophotometry, cytofluorimetry, and branched Dna. The program uses modern control systems to manage the reporting of the analytical parameters, thereby eliminating the error percentage typical of manual reporting.
This software controls the reception, processing, and reporting of each blood sample. Reporting is dual: hard copy and in electronic format, through interfacing, via Internet or using simple floppy disks, with the DREAM_prg program. The analytical data will thus be automatically downloaded into the program, thereby erasing once again any manual reporting errors. Internet reporting is protected by password and, in any event, as discussed in the observations on privacy, contains no patient personal data, but only the univocal identification code. Telematic reporting allows centers distant from the lab to receive results, thereby limiting transport problems only to the delivery of the blood samples. In reporting the results, a remote validation has been created. Criteria have been established by which some parameters may require outside validation. For this purpose some dedicated software packages, such as those managing the cytofluorimeter or the bDNA, can be used off line by European professionals remotely validating and reporting the acquisition data. This mechanism, the only one of its kind, makes continuous supervision possible, particularly of the parameters most important for monitoring the therapy.
1. Personnel

DREAM includes the participation of both local and non-local personnel.

*Non-local personnel*
A feature of the Community of Sant’Egidio’s programs in developing countries is that non-local personnel, as volunteers, are unpaid. Constant presence in the country is guaranteed by a regular system of shifts. Workers – for the most part healthcare personnel (physicians with various specialties, university researchers, biologists, nurses, and rehabilitation therapists) – are from a number of countries. There are also social workers and other professional figures with administrative and logistical supervision tasks, as well as people of good will, who are as useful as all the others. Again on a voluntary basis, members of the Community of Sant’Egidio are helped by medical and lab personnel from various European scientific and healthcare institutions.

*Local personnel*
Local personnel is employed in the medical/healthcare, social, and administrative area, or with logistical support responsibilities. Salary levels correspond with the standards of other international agencies present in the country. Healthcare and social personnel are trained before hiring and, on a regular basis, are brought up to date at specific training seminars.
2. Costs

The laboratory
As discussed above, to prepare a lab capable of effectively monitoring antiretroviral therapy and its possible toxic effects, a suitable facility is needed. The following is a list of the various items that are the essential units for setting up the laboratory, with a general indication of the costs, to which will be added any costs for restructuring the premises.

I. Furnishings
II. Machinery for basic diagnosis
III. Machinery for advanced diagnosis

The total estimated cost for equipping a molecular biology lab is now equal to US$ 330,000.
The relatively high initial cost is justified by the need to purchase machinery that ensures solidity and reproducibility of results over time. Cost reduction is to be sought in the ordinary management of the reagents, by developing, for example, devices aimed at using the volumes that are actually needed, and methods making it possible to reduce operating expenses.
The analytical costs for monitoring a patient based on the clinical/diagnostic protocols used by the DREAM program (cf. Annex II) were calculated. A laboratory out-of-pocket costs estimate is equal to about US$ 170 per year for patients in antiretroviral therapy, and US$ 95 per year for HIV positive patients not in antiretroviral therapy. These costs may be attributed mainly to determining the viral load and the CD4+, whose reagents are still excessively expensive. As regards the mother-child pair, the average cost for carrying out the necessary analyses during the first year, according to the protocols used (see Annex III), is about US$ 400. In subsequent years it comes to US$ 200 per year.

Cost of antiretroviral drugs
At present, the yearly cost of antiretroviral drugs per person is about US$ 330. The introduction of medications not included in the two first-choice schemes results in a higher cost, which in any event comes to an average of US$ 350.
Total costs
To the personnel, lab, and antiretroviral drug costs are to be added the costs for non-antiretroviral drugs, single-use material, artificial milk, nutritional support, water filters, transport, computerization, and the expenses for the equipment and for operating the various facilities. However, these costs do not exceed 30% of the total budget and will tend to diminish considering the processes of the economy of scale that will occur as the various activities are developed.
Annex I
CASE HISTORY RECORD

Center:________________________

ID________________________

Name________________________________________

Surname________________________________________

Date of birth________/_____/______ Sex M F

Starting date of assistance ______/_____/______
Admittance

Center _______________________________ Date __/__/______

Patient's name ________________________ ID __________________

Date of birth __/__/______ age ____ sex: ____ marital status: ________________

Address _______________________________ Town __________________

Telephone _______________________________ Occupation __________________

HIV Test

Quick diagnosis test pos ☐ neg ☐ Confirmation Test pos ☐ neg ☐

Counselling

______________________________

Personal data

General Data

Children: _______ Alive _______ Dead _______ Aborted _______

Number of family members in the same house _______

Reference person: family member ______ neighbour ______ none ______

House in bricks ______ cone ______ sheet iron ______ bathroom inside the house: yes ______ no ______

Running water: yes ______ no ______ Electricity in the house: yes ______ no ______

Time it takes to get to the health center: ______

With what kind of transportation: on foot ______ bicycle ______ car ______ public transportation ______

School attended: none ______ primary ______ intermediate ______ high school ______ university ______

For children: father: alive ______ deceased ______ due to __________________________

mother: alive ______ deceased ______ due to __________________________

Reference person: __________________________

For pregnant women:

dil: __/__/______ week of pregnancy ______ date foreseen for birth ______

Where does the husband usually live:

At home ______ abroad ______ in another city ______ in another region ______ does not know ______

Husband's occupation: __________________________
## MEDICAL HISTORY

**Name and surname**

<table>
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<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Alcohol</td>
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<td></td>
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<tr>
<td>Drugs</td>
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<table>
<thead>
<tr>
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<th>Yes</th>
<th>No</th>
<th>Which</th>
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<tbody>
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<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>Previous hospitalization</th>
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<table>
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<tr>
<th>Operations</th>
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<td></td>
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</table>

<table>
<thead>
<tr>
<th>Accidents</th>
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<tbody>
<tr>
<td></td>
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### Diseases

<table>
<thead>
<tr>
<th>Diseases</th>
<th>When - Comments</th>
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<tbody>
<tr>
<td>Skin</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
</tr>
<tr>
<td>Gastroenteric</td>
<td></td>
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<tr>
<td>Urogenital</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
</tr>
<tr>
<td>Of the Nervous system</td>
<td></td>
</tr>
<tr>
<td>Exanthematous</td>
<td></td>
</tr>
<tr>
<td>Other Pathologies/Diseases</td>
<td></td>
</tr>
</tbody>
</table>

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**Date**
# Medical Check-Up

**Name and surname**: 

**Overall conditions**:  
- Good 
- Average  
- Not good  

| Height (cm) | Weight (Kg) | BMI | Nutritional status:  
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tricipital fold (cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Arm circum. (cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Head circum. (cm)</td>
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</tbody>
</table>

| Vital parameters:  
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>AP</td>
<td>Fr (R/min)</td>
<td>Fc (b/min)</td>
</tr>
</tbody>
</table>

**Skin**: 

**Lymphnodes**: 

**Mouth**: 

**Head and neck**: 

**Thorax**: 

**Abdomen**: 

**Genital organs**: 

**Musculoskeletal system**: 

**Nervous system**: 

**Other**: 

---

**Diary**

**Name and surname**: 

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>Height (cm)</th>
<th>BMI</th>
<th>Tricipital fold (cm)</th>
<th>Arm circum.</th>
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</thead>
<tbody>
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</tbody>
</table>

P: A ______  

Tc (°C) ____  

Fc (b/min) ____  

Fr (R/min) ____  

**Symptoms**:  

**Lesions of the mouth**:  

**Cough** with catarrh  

with blood  

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<th>Symptom</th>
<th>Frequency</th>
<th>Symptom</th>
<th>Frequency</th>
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</thead>
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<tr>
<td>Dyspnea</td>
<td>at rest</td>
<td>Dysuria</td>
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</tr>
<tr>
<td>Nausea</td>
<td>times per day</td>
<td>Leucorrhea</td>
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<tr>
<td>Vomiting</td>
<td>times per day</td>
<td>Asthenia</td>
<td></td>
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<tr>
<td>Anorexia</td>
<td></td>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>times per day</td>
<td></td>
<td></td>
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<tr>
<td>Lymphadenopathy</td>
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</tbody>
</table>

**Diagnostic examination**

- Kaposi sarcoma
- Oral candidiasis
- Candidiasis of the oesofagus
- Bronchitis
- Pneumonia
- Tuberculosis
- Malaria
- Cystitis

**AIDS STAGE**

- Karnofsky Index

**CD4**

**DRUGS**

**ARV THERAPY**

**NON-ARV THERAPY**

**Notes**
<table>
<thead>
<tr>
<th>DATE</th>
<th>DRUGS</th>
<th>SIGNATURE</th>
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<tr>
<td>LAB EXAMS</td>
<td>Name and Surname</td>
<td>ID</td>
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<tr>
<td>DATE</td>
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<tr>
<td>Leucocytes</td>
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<td>Erythrocytes</td>
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<td>Platelets</td>
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<tr>
<td>Lin x 10^3/ml</td>
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<tr>
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<tr>
<td>Lin [W-SRB]/%</td>
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<td></td>
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<tr>
<td>Neut [W-SRB]%</td>
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</tr>
<tr>
<td>Mxd [W-SRB]%</td>
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<tr>
<td>CD4/µl</td>
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<td>CD8/µl</td>
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<tr>
<td>CD4 (%)</td>
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<tr>
<td>CD8 (%)</td>
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<tr>
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<tr>
<td>HIV Viral Load</td>
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<tr>
<td>Creatinine</td>
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<tr>
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<tr>
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<td>Direct bilirubin</td>
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<tr>
<td>GOT</td>
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<td>Albuminemia</td>
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<tr>
<td>Sideremia</td>
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<tr>
<td>Plasmodium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BK</td>
<td></td>
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</tr>
<tr>
<td>Weight</td>
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</tr>
<tr>
<td>Temperature</td>
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WHO Clinical Stage (SIDA Estdio)
### WHO Clinical Stage

<table>
<thead>
<tr>
<th>Clinical stage I</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Asymptomatic</td>
</tr>
<tr>
<td>2. Persistent generalized lymphadenopathy</td>
</tr>
<tr>
<td>Performance scale 1: asymptomatic, normal activity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage II</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Weight loss, &lt;10% of body weight</td>
</tr>
<tr>
<td>4. Minor mucocutaneous manifestations (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)</td>
</tr>
<tr>
<td>5. Herpes zoster within the last five years</td>
</tr>
<tr>
<td>6. Recurrent upper respiratory tract infections (i.e. bacterial sinusitis)</td>
</tr>
<tr>
<td><em>And/or performance scale 2: symptomatic, normal activity</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Weight loss, &gt;10% of body weight</td>
</tr>
<tr>
<td>8. Unexplained chronic diarrhoea, &gt;1 month</td>
</tr>
<tr>
<td>9. Unexplained prolonged fever (intermittent or constant), &gt;1 month</td>
</tr>
<tr>
<td>10. Oral candidiasis (thrush)</td>
</tr>
<tr>
<td>11. Oral hairy leukoplakia</td>
</tr>
<tr>
<td>12. Pulmonary tuberculosis within the past year</td>
</tr>
<tr>
<td>13. Severe bacterial infections (i.e. pneumonia, pyomyositis)</td>
</tr>
<tr>
<td><em>And/or performance scale 3: bedridden &lt;50% of the day during the last month</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. HIV wasting syndrome, as defined by the Centers for Disease Control and Prevention*</td>
</tr>
<tr>
<td>15. Pneumocystis carinii pneumonia</td>
</tr>
<tr>
<td>16. Toxoplasmosis of the brain</td>
</tr>
<tr>
<td>17. Cryptosporidiosis with diarrhoea &gt;1 month</td>
</tr>
<tr>
<td>18. Cryptococcosis, extrapulmonary</td>
</tr>
<tr>
<td>19. Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes</td>
</tr>
<tr>
<td>20. Herpes simplex virus infection, mucocutaneous &gt;1 month, or visceral any duration</td>
</tr>
<tr>
<td>21. Progressive multifocal leukoencephalopathy</td>
</tr>
<tr>
<td>22. Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis)</td>
</tr>
<tr>
<td>23. Candidiasis of the oesophagus, trachea, bronchi or lungs</td>
</tr>
<tr>
<td>24. Atypical mycobacteriosis, disseminated</td>
</tr>
<tr>
<td>25. Non-typhoid Salmonella septicaemia</td>
</tr>
<tr>
<td>26. Extrapulmonary tuberculosis</td>
</tr>
<tr>
<td>27. Lymphoma</td>
</tr>
<tr>
<td>28. Kaposi’s sarcoma</td>
</tr>
<tr>
<td>29. HIV encephalopathy, as defined by the Centers for Disease Control and Prevention.</td>
</tr>
<tr>
<td><em>And/or performance scale 4: bedridden &gt;50% of the day during the last month</em></td>
</tr>
</tbody>
</table>

Note: both definitive and presumptive diagnoses are acceptable.

a. HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).

b. HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

### Karnofsky Performance Status Index

100 Normal, no evidence of disease

90 Able to carry normal activity, minor signs or symptoms of disease

80 Normal activity with effort, some signs or symptoms of disease

70 Cares for self, unable to carry on normal activity or to do work

60 Requires occasional assistance from others but able to care for most needs

50 Requires a considerable assistance from others but able to care for most needs

40 Disabled, requires special care and assistance

30 Severely impaired, required hospitalisation

20 Very sick, hospitalisation necessary, active supportive treatment necessary

10 Moribund

0 Dead
Annex II

Protocol for antiretroviral treatment for HIV infected people

First Contact. Rapid test for HIV infection (pre-test counseling) is offered to the patient eventually followed by a confirmatory test. Post-test counseling is offered the same day and results of exam are given to patient. If the exam is negative, the patient record is filed. If the exam is positive, blood specimen is collected from the patient and tested for: CBC, glucose, serum BUN, serum creatinine, transaminases, proteins and protein electrophoresis, Iron, CD4+ and viral load. Medical follow-up will be arranged for the week after: exam results will be given then.

First Medical Examination: patient’s clinical history is assessed, and beginning of antiretroviral treatment is evaluated on the basis of the following criteria:

a) if CD4+ are less than 200 or symptoms related to HIV-infection are present (WHO Clinical staging: stages 3,4) treatment shall begin;

b) if there are no symptoms and CD4+ are more than 200 but less than 350 wait for results of viral load: if viral load is greater than 55,000 copies/ml begin treatment. Otherwise, wait one month and then repeat CD4+ and Complete Blood Count. If CD4+ numbers fall begin antiretroviral treatment. If they remain stable or increase the person should be enrolled for regular follow-up every three months;

c) if CD4+ are greater than 350 and there are no symptoms of
disease, irrespective of viral load, an appointment will be arranged for three months later (CD4+ and CBC check and medical examination). If CD4+ have remained above 350, patient will be enrolled in a follow-up program every six months. d) if CD4+ are greater than 500, irrespective of viral load, the patient will be enrolled in a follow-up program every six months (see above).

If treatment must be started
Treatment regimens:
First Choice:
a) Duovir (AZT 300 mg + 3TC 150 mg) 1 pill for two per day + NVP 200 mg 1 pill per day for 15 days. Then two pills a day for NVP, too (Duovir-N 1 pill for two per day)
b) D4t 30 mg + 3TC 150 mg (if body weight over 60 kg use D4t 40 mg) + NVP 200 mg 1 pill per day for 15 days. Then two pills per day for NVP, too (Triomune 1 pill per day)
If allergic or adverse reactions arise replacement of AZT with D4t or NVP with IDV should be evaluated
c) prophylaxis with cotrimoxazole if CD4+ count is lower than 200/mm³.
Supply drugs for a week

Control schedule during treatment
After 1 week; CBC. If, at the moment of drawing blood, the patient has some kind of difficulty or shows for the first time symptoms such as diarrhea, fever, vomit, rash or other he must be examined by a doctor.
Supply drugs for a week
After 2 weeks:
Routine medical examination and CBC
Supply drugs for a week
After 3 weeks:
Routine medical examination
Supply drugs for a week
After 4 weeks:
CBC and transaminases
Supply drugs for a week
After 5 weeks:
medical examination and arrange for next follow up. If the patient is feeling well:
Supply drugs for two weeks
If the patient is not feeling well, frequency and type of examination must be decided case by case

After 7 weeks:
supply drugs for three weeks
After 9 weeks:
CBC and transaminases
After 10 weeks:
medical examination
Supply drugs for three weeks
After 13 weeks:
Supply drugs for three weeks
CBC, transaminases, CD4+
After 14 weeks:
medical check up
After 16 weeks:
supply drugs for 4 weeks
After 20 weeks:
supply drugs for 4 weeks
After 24 weeks:
collect blood specimen for CBC, serum BUN, glucose, serum creatinine, transaminases, iron, proteins and protein electrophoresis, CD4+ and viral load.
supply drugs for 4 weeks
After 25 weeks:
medical examination
After 28 weeks
medical examination, result of test for viral load, assessment of clinical conditions.
Supply drugs for 4 weeks

If the patient is feeling well, CD4+ count is over 350, viral load is undetectable or below 10,000 copies/ml in those patients who had 500,000 copies/ml at the beginning of treatment, check-up may take place after 6 months but drugs for more than 4 weeks should not be supplied so that the patient is obliged to come back and have his conditions checked.
Follow-up every Three or Six Months

1st appointment: collection of blood specimen for CD4+ and CBC (once a year, besides CD4+ and CBC, also transaminases and viral load);
2nd appointment: medical examination and review of results according to which beginning of treatment may be decided or not.

Whether or not undergoing treatment, each contact the patient has with the center (blood collection or to get drugs) is an opportunity for the DREAM operators (nurses and social care personnel) to assess his/her conditions. If the patient presents new or serious clinical symptoms, he/she must be sent to the doctor for an examination even if not scheduled according to the protocol.
Pregnancy

First contact:
Pre-test counseling, HIV test
If test is negative provide only post-test counseling
If test is positive:
1) post test counseling
2) blood specimen will be collected from the patient to assess: CD4+, Viral load, Complete Blood Count, Serum Creatinine, Glucose, GOT, GPT, Albumin, Iron, Bilirubin Total and Bilirubin Direct
3) medical examination, counseling for treatment and labor, Antiretroviral treatment shall begin immediately for
   – all women at week 25 or more of pregnancy
   – women between week 14 and 25 of pregnancy at WHO clinical stages 3,4)
Antiretroviral treatment shall not begin before the end of week 14
4) supply tin of formula and sealed baby’s bottle and water filter
5) supply nutritional support
6) lesson in health education (description of the program, instructions on formula feeding, use and management of baby’s bottle which must remain sealed until birth, instructions on the use of water filter and information on the risks linked to use of unfiltered water. The educator may add other subjects).
7) For women who begin treatment:
– Supply treatment for 15 days
– Arrange appointment for the week after for the first control blood specimen
– Arrange appointment for 15 days later for medical examination and supply of treatment

8) For women before week 25 of pregnancy who do not meet criteria for initiation of treatment, arrange appointment for 3 weeks later for results of analysis and to assess the beginnings of antiretroviral therapy.

For women before week 25 of pregnancy who at first contact do not meet criteria for initiation of treatment arrange for three weeks later:
Medical check-up to assess results of analysis:
Women with less than 200 CD4+ and/or viral load greater than 55,000 copies/ml shall immediately begin treatment. For the others an appointment shall be arranged at week 25 of pregnancy to start antiretroviral treatment

After beginning of antiretroviral treatment

After 1 week
Collect blood specimen for CBC

After 2 weeks
Medical examination
Supply treatment for 2 weeks
Supply nutritional support if necessary
Arrange appointment for a week later for collection of blood
Arrange appointment for 2 weeks later for medical examination and supply of treatment

After 3 weeks
Collection of blood specimen for CBC, GOT, e GPT.
For women who began treatment from week 32 onwards of pregnancy (because they arrived for their first check at this moment of pregnancy) blood shall be collected also for CD4+ count and viral load
After 4 weeks
Medical examination. If all is well:
supply nutritional support
Arrange appointment for 2 weeks later to supply treatment
Arrange appointment for 4 weeks later for collection of blood specimen
Arrange appointment for 5 weeks later for medical examination

After 6 weeks
Supply treatment for 3 weeks
Supply nutritional support

After 8 weeks
Collection of blood specimen for CD4+, Viral Load, CBC, GOT, GPT
Supply nutritional support

After 9 weeks
Medical examination
Supply treatment for 4 weeks (if patient has demonstrated good adherence to control and treatment protocols, otherwise supply treatment for 2 weeks and arrange another appointment)
Arrange appointment for 4 weeks later for check up with the doctor

Post-Partum.

At Delivery
Administration of nevirapine to child (2 mg/kg)
Fill in Child’s case history
Supply milk for two weeks and one bottle of mineral water
New instructions on use of milk and baby’s bottle. Instructions on how to control and inhibit lactation onset
Supply treatment for 2 weeks
Arrange appointment for 2 weeks later for infant and mother for medical examination. Clinical assessment must be more frequent in low-weight newborns.
After 2 weeks
Medical examination
Check weight and clinical conditions of infant
Supply treatment for 2 weeks
Supply milk for 2 weeks
Supply nutritional support
Arrange appointment for 2 weeks later for medical examination and collection of blood specimen.

After 4 weeks
Collection of blood specimen from mother for CD4+ count, viral load, CBC, GOT and GPT
Collection of blood specimen from infant for viral load
Check weight and clinical conditions of infant
Medical examination to decide whether or not treatment of mother should be continued
1) Mothers with CD4+ >350 and with no symptoms at beginning of treatment may interrupt ARV treatment if they no more have milk
2) Mothers with CD4+ between 200 and 350 and viral load below 55,000 copies/ml and with no symptoms of disease before beginning treatment may interrupt treatment, if they no more have milk
3) All the others shall continue ARV treatment
Supply treatment for 3 weeks (to those who continue)
Supply milk for 3 weeks
Supply nutritional support if necessary
Arrange appointment for 3 weeks later for medical examination
Arrange appointment for 3 weeks later to supply milk.

After 7 weeks.
Check weight and clinical conditions of infant
Medical examination, results of blood test for infant, check conditions of mother and child. If infant has been infected, collect blood specimen for CD4+ count, CBC and blood chemistry. If infant has been infected arrange appointment for medical examination 21 days later to assess test results for infant
Supply treatment for 3 weeks (if mother is continuing treatment)
Supply milk for 3 weeks
Supply nutritional support
Arrange appointment with mother to collect blood 3 weeks later
Arrange appointment with mother 3 weeks later to supply milk and eventual treatment
Arrange appointment with mother for 12 weeks later for medical examination (results of tests at 12 weeks).

**After 10 weeks**
Check weight and clinical conditions of infant
Medical examination if infant has been infected (results of blood test for infant), evaluate and plan eventual ARV
Collect blood specimen from mother (CD4+, CBC, GOT, GPT)
Supply treatment for 2 weeks (if mother is continuing treatment)
Supply milk for 2 weeks
Supply nutritional support
Arrange appointment for 2 weeks later for medical examination for mother and child.

**After 12 weeks**
Check up for mother (test results) and child
Check weight and clinical conditions of infant
Supply treatment for one month to mother (if undergoing treatment)
Supply milk for 4 weeks
Supply nutritional support
Arrange appointment with mother for 4 weeks later to supply milk and treatment
Arrange appointment for 4 weeks later for child if infected.

**After 16 weeks**
Medical examination of child (if infected)
Check child’s weight
Supply milk and treatment for mother for 4 weeks (if undergoing treatment).
Supply nutritional support
Arrange appointment for 4 weeks later to supply milk and treatment

After 20 weeks
Medical examination of child (if infected)
Check child’s weight and clinical conditions
Supply milk and treatment for 4 weeks to mother (if on treatment)
Supply nutritional support
Arrange appointment for 4 weeks later:
– to supply milk and treatment
– to collect blood specimen from mother and child (if infected)
– for medical examination.

After 24 weeks
Collect blood specimen from mother (CD4+, Viral Load, Blood chemistry, CBC)
Collect blood specimen from child (Viral Load) and CD4+, blood chemistry, CBC if child has been infected
Medical examination for both mother and child
Supply milk (type 2) and treatment to mother (if undergoing treatment) for 4 weeks
Supply nutritional support
Arrange appointment for 4 weeks later to supply milk and treatment
Begin weaning the child

Arrange appointments once every 4 weeks to supply treatment, milk and nutritional support and to follow up weaning until child is 18 months old (check weight and clinical conditions of child).

CD4+, CBC and blood chemistry checks each six months for mother (if no problems have arisen in the meantime).

Check viral load of mother 12 months after childbirth.

Tests for infected children at 9, 12, 18 months (CD4+ and CBC)
Viral Load at 12 months.
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