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NEWSLETTER
Version 14
January 2008

Editors Note

By: Silas Nunu

It is the beginning of a new year after all the fun and festivities of the holiday season. As if we need any reminding, the old year has come and gone and left us with a list of things to do and all our hopes and aspirations from the last year are upon us like a bad rash. I have to admit that at these early stages it does look daunting, but on the other hand you can't wait to sink your teeth into this New Year and find out what it holds for you.

For me the festive season which has just passed means three main things. These are; the festivities and all that comes with them. That is the eating and more eating which brings with it its own ills; the weight gain, the stress etc. Don't worry about the weight gain. We have you covered. We have articles on failed weight strategies and how to truly take off that unwanted weight. So not to worry, you'll soon lose that weight that you gained and be back to your svelte self in no time.

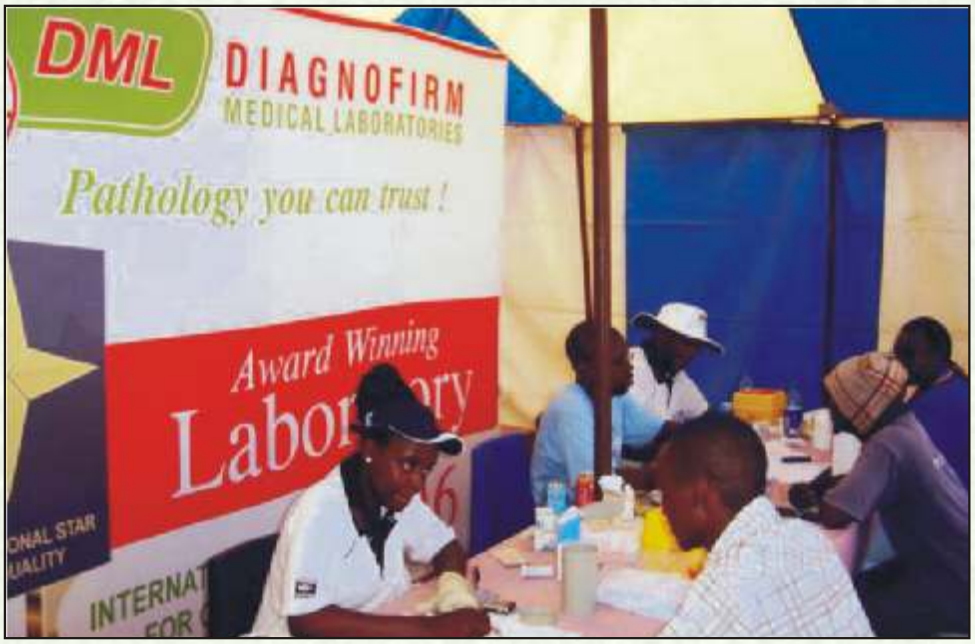
Secondly, December marked the commemoration of World Aids Day. I hope everyone did their part in "Keeping the promise" and will continue to do so in 2008. And I don't mean just wearing the red ribbon. I mean observing AIDS all year by abstaining or at least practising safe sex. It is all too easy for us to be complacent about the impact this disease is having on us because it is mentioned all too regularly, but believe me, the AIDS message cannot be emphasised too much!

Also the end of a year and the dawn of a new one puts me or if I can speak for everyone, puts us in a reflective mood. The end of year provides an opportunity to reflect on our achievements and our failures. But to you I say, let not our failures put a damper or underestimate our positives of our past year. Let those failures be merely lessons to better results this year.

Have a prosperous year 2008!!!

Inside this Issue

Tiger Design and Graphics



Lillian, Blessing and Nicholas doing some testing in Selebi-Phikwe

DIAGNOFIRM MEDICAL LABORATORIES

Diagnofirm Management and staff would like to say; compliments of the New Year, Ngwaga o mosha and Goledzwa to everyone.

Recent And Upcoming Events @ Diagnofirm

Greetings to you all. And hope the festive season has been kind to one and all and not left you dreading entering the year 2008. We are going to look back and reflect at some things that took place at Diagnofirm at the later part of last year.

The Diagnofirm Selebi-Phikwe and Village laboratory branches were also fully accredited with SANAS, which means the now the whole Diagnofirm family is an accredited member of SANAS operating at internationally recognized and standardized levels.

We were also been busy with wellness assessments all over the country so as to build a better nation in compliance with Vision 2016 strategic goals. During the past quarter, Diagnofirm has been to Jwaneng, Selebi-Phikwe and around Gaborone promoting maintenance of better health.

Also, Diagnofirm was present to help commemorate World Diabetes Day at Game City which turned out to be a very successful event. All thanks to all the people who participated. We look forward to better things this year.

Please send any questions or suggestions for topics to be covered to silas@diagnofirm.co.bw / lab@diagnofirm.co.bw

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Botswana's fight against HIV

In the interest of public knowledge, here are some studies that are being carried out in Botswana to try and curb this scourge of HIV.

The studies are designed to fight HIV whilst on the other hand some are finding ways of improving the quality of lives of those already infected or affected by this disease.

HIV Prevention

Mashi Study: Prevention of Mother to Infant Transmission Study

The Mashi study is a clinical trial investigating novel approaches in the prevention of mother-to-child-transmission of HIV (PMTCT).

Mma Bana Study

The Mma Bana Study is a treatment trial to determine the optimal HAART regimen to prevent mother-to-child HIV transmission (MTCT).

Netefatso Study: HSV-2/HIV Transmission

The Netefatso Study is the first study to evaluate whether it is possible to reduce transmission of HIV-1C by treating genital herpes with acyclovir.

Vaccine Development/Maiteko a Tshireletso Vaccine Initiative

Along with the laboratory investigations dedicated to developing a safe and effective HIV vaccine for southern Africa, the BotswanaHarvard AIDS Institute Partnership is currently collaborating with local, regional and international institutions and organizations to develop the necessary infrastructure and community awareness to conduct vaccine trials in Botswana.

HIV Care and Treatment

Basadi Treatment Study

The Basadi Treatment study is investigating how HSV-2 co-infection influences genital tract shedding of HIV-1C among women taking anti-retroviral therapy.

Cost-Effectiveness Study

The Cost Effectiveness Study will address key questions related to the costs and cost-effectiveness of implementing HAART at a national level in Botswana.

Micronutrient Study

The Micronutrient Therapy Study will investigate the importance of micronutrients in relation to HIV disease progression.

OCTANE Study

The OCTANE Study is investigating whether women starting anti-retroviral treatment will have a better response to a regimen containing nevirapine versus a regimen containing a protease inhibitor.

Tshepo Study: Adult Antiretroviral Treatment and Resistance

The Tshepo Study examines the use of antiretroviral therapy for the treatment of HIV-1C infection in Botswana.

Social and Behavioral Studies

Behavioral Studies

Researchers working with the Botswana-Harvard Partnership are investigating behavioral and social components associated with HIV infection and AIDS.

HIV Molecular Research

Cytotoxic T Lymphocytes (CTL) and Human Leukocyte Antigens (HLA)

Two studies investigating cytotoxic T lymphocytes (CTL) and human leukocyte antigens (HLA) suggest that the mapping of CTL epitopes, on the basis of common HLA specificities among the target population, will contribute to the design of a more efficient HLA-based AIDS vaccine.

Genomic Analysis of Genetic Characteristics of HIV-1C

In order to better understand how HIV is passed from mother- to-infant, virus isolated from HIV-infected infants is being compared to virus isolated from samples of blood, breast milk, and cervicovaginal fluid from their mothers.

Molecular Characterization of HIV-1C

More than 50 different isolates of the HIV-1C virus have been isolated from different regions in Botswana and researchers have characterized their molecular and biologic traits.

Tshedimoso Study

The Tshedimoso Study is investigating the immune characteristics of individuals who are newly infected with HIV-1C.

Other studies and projects have included:

- The Teacher Capacity Building Program (TCB) is a partnership between ACHAP, The Ministry of Education, Botswana Television (BTV) and the UNDP. The TCB project is an interactive teacher education program which targets Botswana's teachers with information about HIV/AIDS in an effort to build their capacity to effectively address HIV/AIDS issues in the classroom.
- The Blood Safety and Youth HIV Prevention Program is a two-pronged HIV prevention program aiming to increase the supply of HIV negative blood in Botswana by encouraging more youth to become regular blood donors and remain HIV negative.
- Free condom distribution, Resource centres at District Hospitals and Support for HIV counseling and testing.

There are many other programmes taking place around the country. For more information, you can contact the National Aids Coordinating Agency and organizations such as BOTUSA and ACHAP that are actively involved in these projects.

Information in this article has been obtained from the websites of: The Botswana-Harvard AIDS Institute, ACHAP and BOTUSA

Interlude

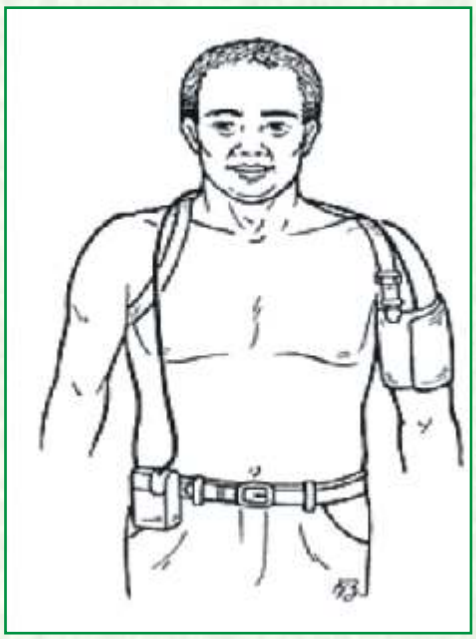
The patient awakened after the operation to find herself in a room with all the blinds drawn.

"Why are all the blinds closed?" she asked her doctor.

"Well," the surgeon responded, "They're fighting a huge fire across the street, and we didn't want you to wake up and think the operation had failed."

by: Professor Kiran Bhagat, Cardiac Clinic.

Prognostic value of Ambulatory blood Pressure



Ambulatory blood pressure shows a superior correlation with cardiovascular morbidity and mortality in treated hypertensive patients. This also holds true after the adjustment brought from of all possible risk factors including office blood pressure.

Therefore, it is recommended to record ambulatory blood pressure in all hypertensive patients at regular intervals, even when office blood pressure is well controlled.

For many years, hypertension has been recognised as a major risk factor in the development of cardiovascular diseases. One of the main problems in hypertension is its definition. Many mistakes are made at the time of blood pressure measurements and these mistakes can have far reaching consequences.

They may be generated from using a faulty manometer, a non adapted cuff, from stenosis at the level of the brachial artery or, as it is most often the case, from misinterpretation of the readings by the physician.

Also, one must realise that blood pressure is not a constant value. Blood pressure varies from one moment to the next, day readings are different from night readings etc. These variations are largely due to the conditions encountered in real life and also depend on the circumstances at the time of blood measurements themselves (whether at the doctor's office, at home or at work …).

Consequently, blood pressure measurements should no longer be seen as a set of numbers, but rather, as forming a curve that is permanently "floating" over 24 hours and is influenced by all factors acting on the cardiovascular system.

Thus, to define someone's "real" blood pressure, one should overcome all technical problems but also provide the observer with information on the variations of blood pressure over a certain period of time (for ex. 24 hours).

In the last thirty years, several techniques have been developed to try to achieve this. First intra-arterial recordings were made on an ambulatory basis. Because of the risk linked to this technique, non-invasive techniques were set up to enable the recording of blood pressure in normal life conditions over 24 hours and even longer.

The definition of blood pressure is reached by recording either the Korotkoff sounds or the oscillations at the level of the brachial artery. Inflation and deflation of the cuff is fully automated and data are stored in a memory chip placed inside a portable recorder. Results must then be checked and fully validated according to international guidelines.(1).

An example of such 24 hour ambulatory recordings is given in fig.1. You may clearly see that blood pressure rapidly increases in the early morning, decreases in the afternoon and increases again at the end of the afternoon and evening, and dips during the night. Recording 24 hour ambulatory blood pressure fully illustrates the large variations of blood pressure; it can easily be understood that there are large differences when compared to data collected from the few readings at the doctor's office.

The real question that follows such an observation is: what are the blood pressure readings that really matter for the patient? Which pressure determines long term prognosis and with what pressure to proceed in the clinic to define and follow up someone's overall blood pressure.

Many aspects of this question have been answered in a recent study which compares over a long term, office pressure and 24-hour ambulatory pressure in treated hypertensive patients (the Office versus Ambulatory blood pressure study, OvA) (2).

A group of 1963 patients with mild to moderate hypertension were followed over a period of at least five years, yielding approximately 10.000 patient/years; all events were carefully recorded, analysed and reviewed by an expert committee. All patients were treated according to international guidelines; the choice of antihypertensive drugs was left to the discretion of the physician.

At yearly intervals, all data obtained were reviewed and control examinations were made on office and ambulatory blood pressure. Close attention was given to obtain, through treatment, an office blood pressure control down to 140/90 mm Hg. To determine whether office or ambulatory pressure is best to predict events, correlations were calculated between events and office pressure on one hand and between events and ambulatory pressure on the other hand.

Quite clearly, all blood pressure figures, including the simple office readings, correlate with long term prognosis. This is a confirmation of many previous studies and makes clear that whatever the type of blood pressure measurement, the level of blood pressure is related, step by step, to long term prognosis.

However, when office and ambulatory blood pressure are compared vis-a-vis their relation to long term prognosis, it comes out that ambulatory blood pressure predicts prognosis much better than ("over and above") office pressure. This also holds true after an adjustment is made from all existing risk factors.

Besides this main message, many other pieces of information came out of this study. Systolic blood pressure does clearly better in predicting prognosis than diastolic blood pressure. This also holds true in several recent studies amplifying the importance of systolic blood pressure elevation (3) One should not, nevertheless, deny the role of diastolic blood pressure.

Lastly, elements of information are yielded in a new class of patients - i.e. in those whose office pressure is lower than ambulatory pressure-; this new entity is often called "reversed" or "masked" hypertension.

The clinical value of reversed hypertension was clearly illustrated in this study as shown by the following finding: prognosis of patients with high office

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By Dr. Debashish Gangopadhyay, Specialist Physician, Cardiac Clinic

HIV/AIDS and Weight Loss

AIDS-associated wasting has been defined variously as a reduction in body weight since disease onset or as a reduction in body weight below ideal body weight, normal body mass index or lean body mass. Before the advent of HAART, up to 10% of HIV-infected individuals in the developed world fulfilled the US CDC definition of AIDS because of wasting, and this is a very common presentation in resource-poor countries. However, it is clear that significant weight loss is usually associated with an underlying opportunistic infection (OI) or tumour and most wasting in sub-Saharan Africa is caused by either severe oesophageal candidiasis or concomitant cryptosporidiosis.

CAUSES OF WEIGHT LOSS

Most wasting in those infected with HIV does not fit neatly into either a starvation model or a cachexia model. In the former, there is an appropriate response to poor caloric intake with raised insulin levels and mobilization of fat stores involving a predominant loss of fat mass but preservation of lean body mass. In such individuals, the resting energy expenditure is reduced or normal. The wasting associated with cryptosporidiosis in AIDS fits this model best, with the prominent cause of weight loss being a poor caloric intake, aggravated by the mal-absorption associated with cryptosporidial infection and, possibly, by anorexia induced by nutrient-rich chyme passing over the terminal ileum. In the cachexia model of weight loss, there is disturbed body metabolism, perhaps induced by cytokine release associated with an underlying infection, which leads to increased resting energy expenditure and preferential loss of lean body mass. This model most closely fits that seen in those infected with opportunistic infections such as MAI.

An analysis of the causes of weight loss in HIV-infected patients is complicated because resting energy expenditure is raised in all sero-positive individuals. This is usually balanced by a reduction in total energy expenditure (reduced exercise). Thus, asymptomatic HIV-positive individuals, whatever their CD4 T-cell count, do not progressively lose weight or lean body mass. Compared with control subjects, there is a small reduction in fat mass, which is not progressive and might be associated with anorexia at around the time of seroconversion, possibly related to stress at this time. In general, nutritional intake is appropriate for the total energy expenditure. The effects of HIV infection on protein metabolism are controversial. However, there is probably increased protein turnover but an appropriate response to intravenously infused amino acids.

PATTERNS OF WEIGHT LOSS

One of two patterns predominates in the weight loss experienced in HIV infection. An inexorable progressive weight loss is seen in those with gut infections, whereas with other OIs, sudden drops in weight coincide with active disease, followed by incomplete and variable recovery of weight and of lean body mass.

It is not clear whether weight loss itself predisposes the patient to the development of OIs. In other malnourished states, immunological abnormalities that may exacerbate the underlying problems in HIV disease do result from a low caloric intake, and some studies, but not others, have shown that weight loss may precede the development of overt AIDS by some months. It is also unclear whether deliberate weight gain and improvements in lean body mass by taking regular exercise and increasing caloric intake during the asymptomatic phase of HIV infection have any effect on the rate of subsequent progression to AIDS.

TREATMENT

The most important single goal in the treatment of wasting is to restore lean body mass to improve body function. However, a subsidiary and positive goal is to improve body weight and so body image for many individuals. The most important aspect of the treatment of wasting is to diagnose OIs early and treat them rigorously. For example, lean body mass can be regained by treatment of CMV infection.

Many people in the asymptomatic phases of diseases wish to prevent wasting and so seek dietetic advice. However, they find it difficult to accept that this advice includes eating large amounts of high-energy foods such as fats, which they have come to believe are unhealthy.

Mineral supplementation may be an important component of treatment in resource-poor countries where vitamin deficiencies are common and may accelerate the development of AIDS.

Attention to caloric intake is crucial during periods of weight loss. Unfortunately, oral supplementation is likely to be inadequate in many individuals who are anorexic as part of the infectious process. Equally, because the body's homeostasis is often disturbed during infection, simple caloric supplementation may not be sufficient to reduce the effects of cachexia in those individuals with gut disease or with continuing infections such as CMV of MAI, which may not be treatable.

Tube feeding to increase caloric intake may be helpful, although sometimes difficult because of the associated malabsorption. Nasogastric feeding is difficult to tolerate in the long-term, despite new and much more user-friendly tubes, and many patients now opt to be fed by a percutaneously inserted gastrotomy tube. Such feeding can be successful in replenishing body weight, particularly if the diet is carefully tailored to avoid diarrhoea. The body weight regained by such supplementation is mainly body water and fat. Lean body mass is only likely to be regained if the patients are ambulant and able to exercise. Parenteral feeding has also been shown to improve body weight although, again, increases in lean body mass are modest. There is a high risk of sepsis with long-term intravenous catheters and so parenteral feeding is usually regarded as a temporary measure to overcome profound but short-lived episodes of anorexia.

Appetite stimulants such as megesterol acetate have been shown to increase food intake in several controlled trials but, again, this mainly results in the deposition of fat rather than lean body mass. The role of anabolic steroids in the treatment of wasting is controversial and has been studied poorly. About 10% of individuals with advanced HIV infection are deficient in testosterone and replenishment of this may produce increases in lean body mass. However, the wider role of anabolic steroids associated with exercise in laying down muscle and its value in fighting wasting remain to be definitively

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By: Silas

Battle of the Bulge

Diary of a man against the flab

It's an early Tuesday morning and I decide to weigh myself "for the fun of it". Well, needless to say what I saw was not fun. I had gained a whopping 7kg from the beginning of the year.

You must just be wondering to yourself what the big deal is. The big deal is that for as far as I can remember, I have always prided myself on my good metabolism and the fact that I needed no exercise because my body was that good at taking care of my several indulgences. Like my high school teacher once pointed out "if you indulge, you bulge".

So, I then took it upon myself that I should at all accounts lose that shame of a 7kg before the year ends. My target, two weeks of fighting the bulge. My struggle began in earnest on one Monday morning about 2 weeks later when I woke up early and couldn't get back to sleep.

1ST WEEK

Monday
I started the exercise at about 4:30am. It felt very good. I was at it for about 2 hours. Nothing like taking a shower after having sweat all over you and that feeling of accomplishment. Rest of the day, I was as bright as a 100watt bulb.

Tuesday
Was expecting a little soreness. Nothing! I could get used to this. I do my exercises as, run around the block. This time it's a little over an hour. I am in the zone, I feel pumped.

Wednesday
Well, you know that soreness I was awaiting? It finally came, and boy did it come! So, you can understand my hesitation at waking up and going through the whole exercise routine. But I finally do go through with it. And once I start, it gets a little better.

Thursday
Four straight days. I am very much chuffed with myself. I feel a sense of accomplishment. And I get on with the job. Yeah that's what it's become, a job!

Friday
Starting to feel a little sorry for my body, so, I do a light exercise. Anyway, it's Friday!

We are still on Friday, but this is evening now. I figure, 'let me have a drink or two, anyway, I deserve it'. So, I do have the drink or two. And the next day is Saturday; I give myself a day off with exercise. Sunday, same thing. I mean, who wants to be exercising their on a Sunday morning. They don't call it 'easy like a Sunday morning' for nothing!

2ND WEEK

Monday
Back to the grind. Feeling a little guilty about letting myself go over the weekend, I exert myself a little extra.

Tuesday
I get on with it. By now my efforts are getting somewhere because I can't do anymore sit-ups. So, those stomach muscles must be beginning to firm up; so I think.

Wednesday
Now, I'm feeling a little fatigued, the sit-ups getting a little harder. Am thinking of giving it all up. Or alternatively, I could get a running mate. Then I think to myself, I don't need an overzealous person who'll start waking me up even when I don't feel like it. I hope you can grasp the irony there!

Anyway, I get on with it. Painful!

Thursday
I can't get up in the morning. Tired to the bone. So I decide to shift my exercises to the evenings after work.

I exercise after work and it good. Because later on I can shower and go to sleep all refreshed. And getting to sleep is a breeze; I'm out like a light bulb.

Friday
In the morning I do some exercises. I the evening the jog. Tomorrow, Saturday, it's my day off. It's the same old story again; a few drinks.

Sunday;
It's a day of rest. And just like that, the two weeks is over.

Monday,
Feeling all accomplished, I do no exercises.

Tuesday,
I then go for the big weigh-in.

I have managed to lose 1.5kg over the past two weeks. I'm a little sad, since I had set out to lose all of 7kg. So, I decide to write this article of my tribulations!

So, what have we learnt?

1. Don't exercise alone. All it is does is make you slacken up. Excuses are easy to come by when you have only yourself to convince. So get a partner and sweat it out.
2. Change your lifestyle; this is what got you here in the first place.

    a) Change your eating habits. You really don't expect to lose weight when you gobble down food like it's the end of the world even when you are exercising.
    b) You social outings have to change. When you consider that 3 beers have the same calorific value as a large order of fried chips at a fast food restaurant.
    c) The friends you hang out with. Peer pressure. And you thought high school was the last time you'd hear that phrase!! The fastest way to lose weight; hang out with very chubby guys! Seriously though, don't hang-out with people who are enablers of bad dietary and lifestyle habits if you are seriously planning of getting rid of that flab.
3. Have an action plan. At the beginning of your exercise regime, weigh yourself, measure your vital stats, then have a target of what you want to achieve. Also regularly check yourself and make sure you are still holding true to your game plan. This will also help you to not get obsessive.

To quote Cecil B. De Mille, "the person who makes a success of living is the one who sees his goal steadily and aims for it unswervingly"

So, with visions of savoury meals and oceans of drinks dancing in your mind, why not lift some weights, run some miles and do some push-ups beforehand.

That will make a bit more caloric room in your diet for splurges and make sure all the work you have done all year to stay in shape doesn't go to "waist".

By: Kiran Bhagat, Cardiac Clinic. Prof@cardiacclinic.co.bw

Peripheral Arterial Disease - a Cardiologist's Perspective

Summary

PAD tends to coexist with atherosclerotic lesions in other vascular beds, especially in the elderly. The most frequent PAD symptom is intermittent claudication, however, typical symptoms of intermittent claudication in patients with diagnosed PAD are rather uncommon.

History and physical examination are much less accurate than objective measurements, such as the ankle/brachial index (ABI). ABI measurement is a simple examination that takes 10-15 minutes and that can be performed in every outpatients clinic.

Patients with PAD should then undergo thorough medical evaluation to exclude or confirm the coexistence of coronary heart disease, carotid artery stenosis or other lesions.

Peripheral arterial disease (PAD) is not always atherosclerotic in origin, but in today's cardiology practice it is usually a sign of generalised, multilevel atherosclerosis.

I - PAD tends to coexist with atherosclerotic lesions in other vascular beds, especially in the elderly.

In a study of 1802 men and women, mean age 80 years, 68% of subjects with PAD had coexistent CAD and 42% had prior ischemic stroke (1).

Patients with PAD have an increased risk of angina, myocardial infarction, stroke, congestive heart failure and death compared to patients without PAD. In this group, the risk of non-fatal myocardial infarction is increased by 20-40%, and of heart failure by 60%. Mortality in patients with PAD is two to seven times as high as in those without PAD. A 5-year follow-up in Edinburgh Artery Study showed a comparable increase in risk of coronary events and death in both patients with symptomatic and asymptomatic PAD (2).

Both incidence and prevalence of PDA increase with age. Criqui et al. (3) estimated that PAD is present in 5.6% of subjects aged 38 to 59 years, in 15.9% of those aged 60 to 69 years, and in 33.8% of those aged 70 to 82 years.In individuals aged ≥ 65 years without cardiovascular disease, included in the Cardiovascular Health Study (4), the prevalence of PAD was 13.9% in men and 11.4% in women. However, in the oldest group, symptomatic PAD was present in 20% of male (mean age 80), and in 13% of female subjects (mean age 81).

II - The most frequent PAD symptom is intermittent claudication.

The most frequent PAD symptom is intermittent claudication, that is defined as **muscle pain or weakness induced by exercise and relieved with rest, which occurs distal to the arterial obstruction**.

Atherosclerotic lesions most commonly involve the **superficial femoral and popliteal arteries,** and therefore, the pain of intermittent claudication is **usually localized in the calf**.

When atherosclerotic obstruction affects the **distal aorta and its bifurcation into the two iliac arteries**, the **pain** is localized both **in the buttocks or thighs,** and in the legs (5).

III - However, typical symptoms of intermittent claudication in patients with diagnosed PAD are rather uncommon.

Intermittent claudication is not the only symptom of lower extremities atherosclerosis, and limb pain elicited by walking **may be relieved when exercise is continued** or pain **may be chronic, with mild exacerbation upon exercise** (6)

Results of the PARTNERS study indicate that less than 11% of patients with PAD have "typical" intermittent claudication, while more than half have atypical symptoms of lower limb discomfort present at rest (7).

With the progression of the disease; patients might have **pain at rest, which is most prominent with leg elevation, and can be relieved by dependency.**

In subjects with most advanced stages of PDA, **tissue hypoperfusion may lead to ischaemic ulcerations and necrosis.** In consequence, in more than 30% of these patients major amputation is required (8).

Contrary to a common belief, typical symptoms of intermittent claudication in patients with diagnosed PAD are rather uncommon. According to different authors they occur in 20-30% of patients (3).

Asymptomatic atherosclerotic narrowings are present in almost 20% of persons above 55 years of age, which makes it the most prevalent form of atherosclerosis (9).

Although symptoms typically occur as the luminal obstruction is in excess of 50%, even patients with severe disease may remain asymptomatic if extensive collateralisition in the lower extremity has developed (10).

IV- History and physical examination are much less accurate than objective measurements, such as the ankle/brachial index.

Persons with advanced PAD of the lower extremities have diminished or absent arterial pulses, the diagnosis seems easy. However, history and physical examination are much less accurate than objective measurements, such as the ankle/brachial index. **Pulses palpation is neither sensitive nor specific for peripheral arteries disease.**

In a study of males and females of mean age 66 years, among whom 11% had PAD; sensitivity of abnormal pulses examination was 77%, whereas specificity of normal pulses in the absence of disease was 86% (11).

Noninvasive tests used to asses lower extremity arterial blood flow include :

1. measurement of ankle and brachial artery systolic blood pressures
2. characterisation of velocity wave form
3. duplex ultrasonography

Measurements of ankle and brachial artery systolic blood pressure using a Doppler probe and blood pressure cuffs allow calculation of the ankle/brachial index (ABI), which is normally 0.9 to 1.2. An ABI of less than 0.90 is 95% sensitive and 99% specific for the diagnosis of PAD (3).

Using the ankle-brachial index (ABI) of less than 0.95 as indicative of PAD, the prevalence of 6.9% was observed in patients aged 45-74 years, and only 22% of them had symptoms. (8).

The discrepancy between typical symptoms and the presence of PAD defined by ABI was shown in the Rotterdam study, a population-based

analysis of 7715 patients (2). Although a prevalence of intermittent claudication ranged from about 1% in the group aged 55-60 years to 4.6% in the group aged 80-85 years, the PAD diagnosed on the basis of ABI was found in 16.9% of men and 20.5% of women aged 55 and older.

ABI measurement should be widely used to detect PAD. According to Hirsch (12), this test should be done at least in the following patient categories:

1. patients with discomfort in lower limbs after exercise
2. patients with non-healing wounds
3. patients above 70 years of age
4. smokers and/or diabetics above 50 years of age.

Conclusions

PAD remains unrecognised too often or is discovered in advanced stage. ABI measurement is a simple examination that takes 10-15 minutes and that can be performed in every outpatients clinic.

Early diagnosis of PAD allows for immediate implementation of measures to reduce atherosclerotic risk.

The presence of PAD should be considered as an index of systemic atherosclerosis, as patients with PAD have a higher incidence of coronary heart disease and atherosclerotic abnormalities of cerebral circulation.

Thus, patients with PAD should undergo thorough medical evaluation to exclude or confirm the coexistence of coronary heart disease, carotid artery stenosis or other lesions.

References available on request

Interlude

Morris was removing some engine valves from a car on the lift when he spotted the famous heart surgeon Dr. Chris Barnard, who was standing off to the side, waiting for the service manager. Morris, somewhat of a loud mouth, shouted across the garage, "Hey Barnard...Is dat you? Come over here a minute."

The famous surgeon, a bit surprised, walked over to where Morris was working on a car. Morris in a loud voice, all could hear, said argumentatively, "So Mr. fancy doctor, look at this work. I also take valves out, grind 'em, put in new parts, and when I finish this baby will purr like a kitten. So how come you get the big bucks, when you and me are doing basically the same work?"

Barnard, very embarrassed, walked away and said softly, to Morris, "Try doing your work with the engine running."

By N. Bozongwana, D. Ndlovu & E. Molojwane

QuantiFERON TB Gold Test

Introduction

The number of people infected with tuberculosis in Botswana and the rest of the world has been increasing as a result of the increase the number of immuno-compromised HIV patients with reduced ability to fight infection. A reliable reproducible method of diagnosing tuberculosis infection with a shorter turn-around time (time it takes to get results) is therefore necessary. Infection with *Mycobacterium tuberculosis* bacterium is the most common cause of tuberculosis. The Mantoux test in conjunction with chest radiographs, physical evaluation and diagnostic microbiology i.e. culturing the bacterium from a patients clinical specimen such as sputum has been used to diagnose tuberculosis in patients. In the Mantoux test, a *M. tuberculosis* protein (PPD) is injected into the top layer of skin in the forearm. Formation of a firm, raised, red area surrounding the test site within 48 to 72 hours (as assessed by a health care worker) is indicative of infection with tuberculosis bacteria.

While the Mantoux is considered the most accurate skin test for tuberculosis, there are some problems associated with it. False-negative results may occur due to conditions such as cancer and AIDS in its late stages that weaken the immune system. False-negatives may also be the result if infection has occurred less than six weeks before the test or if the patient simply fails to have a reaction (as a small number of infected people do). Patients may falsely test positive if they have previously been given the Bacillus Calmette- Guerrin, BCG, vaccination which is given to people who are at risk of contracting tuberculosis. People who have previously had a positive Mantoux test face a very small risk of severe redness and swelling of the arm should they repeat the test. Few cases of previously untested individuals have an adverse reaction to the test.

QuantiFERON TB Gold is an FDA approved test for tuberculosis infection and disease and latent tuberculosis infection. QuantiFERON is different from the Mantoux in that it is performed in vitro on whole blood and tests for tuberculosis indirectly.

How does it work?

ESAT-6 and CFP-10 are two *M. tuberculosis* proteins. They are antigens i.e they elicit an immune response in infected patients. In the QuantiFERON test, patients' whole blood is incubated with ESAT-6 and/or CFP-10 for 16 to 24 hrs. This must occur within 12 hours of the blood being drawn. Interferon-ã is produced by white blood cells called T- lymphocytes as part of the immune response. If a patient has been previously exposed, the T- lymphocytes present in their blood sample recognize these antigens. The amount of interferon-ã released by their white blood cells in response to challenge with *M. tuberculosis* antigen is then assayed or measured. The patient will test positive or negative for tuberculosis depending on the amount of interferon-ã produced in their blood. Since ESAT-6 and CFP-10 are only found in mycobacteria that cause tuberculosis and not others, this test is able to detect latent TB infection i.e. infection that has not yet progressed to active TB disease. However, it is not able to predict when the infection will progress to active tuberculosis.

Limitations of the test

Blood must be drawn and processed within 12 hours while white cells are still viable. Laboratory and clinical experience, with the assay is limited.

Advantages of the test

The test is not subject to reader bias, is not affected by prior BCG vaccination and it does not boost responses measured by subsequent tests as may occur with tuberculin skin tests. Only one patient visit to draw blood is required, following which results can be ready within 24 hours.

Evaluation of effectiveness of the test

To be able to validate the test results, large numbers of samples need to be assayed in parallel with the Mantoux test to be able to allow accurate statistical analysis. Thus far, we have performed the assay three times using a handful of blood samples each time which means that no meaningful statistical analysis can be applied. The extent to which results produced by the QuantiFERON test tally with those from the Mantoux test is yet to be determined as well as its reproducibility. Repeated analysis of blood samples has given early indication that the test has good reproducibility. As such, patients are encouraged when having a Mantoux test done, to submit a blood sample for QuantiFERON testing.

Diagnofirm in Pictures

Dr. Bhagat and Mr. Mphathi from BCL in Selebi-Phikwe

Dr. Gangopadhyay and Lesego from Cardiac Clinic in Jwaneng

Silas doing some testing in Jwaneng

Joy Crosbie from Diabetes Botswana with some participants on World Diabetes Day at Game City

Diagnofirm at Game City World Diabetes Day

Blessing an Nicholas testing in Phikwe

Participants at Jwaneng Mine Health Awareness Day

ng

Diabetic children playing action golf on World Diabetes Day

y

Participants take part in a health walk in Selelbi-Phikwe

By Chishamiso Mudenyanga, Virology Department.

Challenges of Relying on CD4 Count in HIV/ AIDS Management

There has been a tremendous progress in the successful management of individuals who are on Antiretroviral (ARV). The good use of these drugs has improved lives of a great number of HIV+ people the world over. This is clearly seen by the lower death rates in countries where drugs are readily available compared to those which do not have them readily available.

A lot of documentation has been done on HIV management and we will definitely agree that the key tests to successful management are CD4 counts and HIV viral load. This does not mean that one can do away with Liver Function tests, Full Blood Counts, Lipid profiles, etc which are also key in this regard. It is the CD4 in most cases that clinicians are interested in when it comes to HIV even though HIV viral load may be considered. This is simply because in HIV cases, it is the immunologic rather than the virologic response that seem to matter a lot. However, there are some challenges associated with relying on CD4 count only without considering the clinical presentation of HIV infected persons.

A number of factors do exist which affect CD4 counts. These range from analytical variation, seasonal and diurnal variations, drugs and many more. A look at these factors might help us in understanding how diverse HIV management is.CD4 counts are said to be at their lowest levels at 12:30pm and at their highest at 8:30pm although this does not have any bearing as to what time CD4 counts must be done. What is important is for an individual to maintain consistent collection times for blood samples for the test. Literature also suggests that in successful treatment of HIV, CD4 may rise by about 50cells/mm3 in 4 8 weeks and 50-100 cells/mm3/year thereafter. In most cases the laboratory results do not show this trend. In three months CD4 count may rise by more than 100cells.

It might be that sometimes the CD4 values that are obtained in the laboratory are not a very good representation of patients' immune status. If a patient is told that they are HIV positive, the first thing that would happen to them is worry and getting stressed even with successful counseling. This on its own then will cause a marked drop in CD4. This then gives an incorrect baseline CD4, hence the suggestion by some to have more than one CD4 count before a baseline can be established. There are conditions that are related to HIV which cause drop in CD4 as much as 200cells/mm3 such as bacterial infections, parasitic infections, sepsis, tuberculosis, malnutrition, psychological stress and intravenous injections of foreign proteins. Over-exercising and pregnancy also have similar effects. It then appears that low CD4 counts are not necessarily due to depletion by the HIV but a common reaction to many kinds of physical and psychological stressors. The question then would be, “How then can we rely on CD4 counts?”

This brings us to the fact that HIV is everyone's responsibility. The doctor can give good treatment but it will take the patient's full participation by informing the doctor all that may not be well with them. Bacterial and parasitic infections are to be treated successfully. There is no need to wait long before other illnesses are attended to because during that time CD4 counts will be affected. Away from the doctor, there is need for social support from friends and family members so as to avoid social isolation. The affected persons also need to have a positive approach to living with HIV so that their immune status is not affected. This will mean that with good ARV treatment, a positive approach to life and positive support from people around should cause the immune system to improve significantly.

There are cases of HIV positive people who have very normal CD4 counts like those of HIV negative persons and with suppressed viral loads. Of course we can never rule out the need for adherence to treatment as key to ARV therapy success. Having mentioned the above, one would then think that it is vital to maintain a high CD4 count when HIV positive. The truth is YES! What we need to understand is that the best rise in CD4 would be the one done by the body itself due to viral suppression by ARV and management of other conditions mentioned afore. It is not very recommended to use immune boosters like the African potato and Canova to raise CD4 levels. In most cases these raised CD4 counts have not been proved to be functioning normally and even though one may have a good CD4 count, it may not serve a good purpose in the system. This explains scenarios where a patient with a good CD4 count would still be prone to opportunistic infections. In any case patients are highly discouraged from using immune boosters without their doctor's permission.

Is it possible then that there could be cases of persons that have been put on ARVs with low CD4 counts which were not a true picture of their immune status, either due to stress or other infections? Could this then explain why CD4 counts can rise by over the documented rise in a year because as people get to accept their condition and become positive, the immune system responds better? Or could it be the fact that support groups are encouraging people to live positively and that societies have learnt to see HIV infection as any other disease, thus giving positive social support to the affected?

In any case, until other tests other than CD4 are available we need to do the best we can to get reliable information from CD4 counts. That is why treatment and prevention of TB, pneumocystis carinii pneumonia (PCP), fungal infections, mycobacterium avium complex (MAC) and Cytomegalovirus (CMV) are critical. This does not mean that HIV negative persons do not experience fall in CD4.In a study that was done in 1990 (Malone et al. 1990), a comparison of diurnal variation in HIV negative and positive people showed that there were greater variations in HIV negative people. Both groups showed a pattern that coincides with known daily fluctuations of cortisol, with minimum CD4 levels occurring between 8am and 10am, and maximums occurring around 10pm. Cortisol also causes low CD4 and T-lymphocyte counts. In this study HIV negative people had an average variation of 506cells/mm3 per day while HIV positive people had only about 60cells/mm3 variation. Of interest was the fact that 25% of HIV positive people had counts below 200cells/mm3 in the morning but had greater than 200cells/mm3 in the afternoon. That would mean that in the morning they would be diagnosed with AIDS but in the afternoon they would be just HIV positive. This goes to show how much variation there is in CD4 counts even though they are crucial in the management of HIV/AIDS. Despite these challenges, CD4 remain one of the best ways to manage this disease.

Ten things to know about HIV

Having a test to find out if you have HIV could save your life.
If you're HIV-positive, the sooner you find out, the sooner you can receive medical care. Many people die because they found out they were HIV-positive so late that treatment couldn't work. HIV test are done at laboratories and voluntary counseling and testing centres.

HIV testing and treatment is confidential.
Your HIV clinic won't tell anybody that you have HIV without your permission.

HIV care can be given at hospitals and general practitioner offices
HIV doctors, hospitals and clinics will regularly check your health to see how HIV is affecting your immune system and explain what treatment you need to take.

Taking HIV treatment can mean a longer, healthier life.
Even though there's no cure for HIV, doctors are now hopeful that you can live a more or less normal lifespan if you take a combination of anti-HIV drugs.

You need to take all your anti-HIV drugs as instructed.
If you don't, there's a risk that the drugs you are currently taking, and any similar drugs,won't work.

HIV treatment is there to protect and improve your health.
However anti-HIV drugs can cause side-effects. Make sure you tell your doctor, as there's a good chance you'll be able to do something about them.

HIV is readily available in Botswana.
If you are a member of medical aid scheme you can get HIV treatment through your scheme. If you are not you may enroll with the government schemes that are available

You may still be able to pass on HIV to somebody else even if you are taking anti-HIV treatment.
Condoms effectively prevent the transmission of HIV and other sexually transmitted infections. Never share needles or other injecting equipment.

Mother to baby transmission of HIV can be prevented in nearly all cases.
The use of anti-HIV treatment, having a caesarean delivery, and not breastfeeding can reduce the risk of a mother passing on HIV to her baby to less than 1%.

There's a lot you can do to look after your own health.
You can help yourself by eating well, reducing stress, not smoking, and exercising. Make sure you get good quality, impartial information about HIV to help you make good decisions regarding your health and treatment.

The Drug Development Process

It usually takes ten or more years for a promising candidate to wind its way through the drug development process (although activists have succeeded in speeding up development of medications for HIV and other life-threatening diseases).

According to the Food and Drug Administration (FDA), only one in 1,000 compounds makes it from the laboratory to clinical trials in humans, and only one in five that enters human trials is ever approved.

The earliest stage of drug development takes place in the laboratory. Traditionally, large numbers of candidate agents are screened by combining them with disease causing organisms and cell cultures in a test tube or Petri dish to see how they interact. Such preclinical work is known as in vitro research (Latin for "in glass").

Today, drug companies increasingly use a process called rational drug design in which computers guide the construction of custom-made compounds that have a desired action.

If a candidate shows good activity in the lab, preclinical testing continues with animal studies (in vivo research, Latin for "in a living organism"). Different tests are done to see what side effects an agent causes and what doses are safe.
It is not unusual to see specific toxicities in animals but not in humans, and vice versa. If all goes well, the candidate then enters human clinical trials. Before a drug is approved for marketing, it is called an investigational new drug (IND).

Phase I trials - are usually conducted in a small number of healthy HIV-negative volunteers (typically 10-100); sometimes testing in people with HIV may begin in Phase I.

These early trials establish the pharmacokinetics of a drug (how it is absorbed, processed, and excreted by the body), its safety and tolerability, and the best doses.

Phase II trials - involve a larger number of participants with the disease under study (typically 50-500). While researchers continue to look for toxicities, they also seek preliminary indications of effectiveness, or efficacy.

Sometimes Phase I and II or Phase II and III trials are combined to speed the development process.

Phase III trials - include the largest number of participants (typically hundreds or thousands). These trials are designed to determine whether a drug is effective.

They also continue to monitor toxicity, especially longer-term side effects. Once Phase III trials are complete, a company may submit a New Drug Application (NDA) to the FDA.

The agency uses results from these studies to determine whether a drug should be approved for marketing.

Phase IV trials - are post-marketing studies conducted after an agent has been approved. They are intended to further confirm efficacy and safety under "real world" conditions, and are especially valuable for detecting long-term and uncommon side effects that do not show up in Phase III trials. Since many

HIV drugs have been given accelerated approval, activists have complained that companies often neglect to do these follow-up studies.

Traditionally, drugs are tested against a placebo (an inactive substance such as a sugar pill), but this is now less common in HIV trials.

However, randomized, double- blind trials in which participants are assigned by chance to receive different treatments and neither the researchers nor the participants know who is getting what remain the "gold standard."

New agents are often compared to an existing standard of care, such as the best currently available drugs.

Interlude

"Doctors at a local hospital have gone on strike.

Hospital officials say they will find out what the Doctors' demands are as soon as they can get a pharmacist over there to read the picket signs!"

by Suzanne Crowe from http://hivroundtable2002

Monitoring Of Hiv Infection In Resource-constrained Countries.

Monitoring of HIV infection in both the developed world and in resource-constrained settings involves both laboratory tests and clinical examination. In the developed world, where resources are generally plentiful, laboratory monitoring includes regular assessment of both HIV viral load and the CD4 T lymphocyte count. The CD4 count is an indication of the degree of damage that has been done to the immune system; the HIV viral load provides quantification of the level of HIV within the blood and as such is an indicator of how quickly one might expect to see damage to the immune system.

These parameters provide independent indication of prognosis as well as guidance regarding the need for, and response to, antiretroviral therapy. Both tests are performed in laboratories with access to expensive equipment that requires maintenance including flow cytometers and polymerase chain reaction (PCR) machines. In resource-constrained settings, the total lymphocyte count, together with clinical assessment, is often used as a surrogate for the CD4 count and has been recently shown to correlate well with the predicted onset of HIV-related opportunistic infections. Viral load is rarely available.

The clinical assessment of the patient, including the very important weight assessment, is critical for the management of HIV infection, regardless of the availability of laboratory tests.The WHO has provided a staging system for management of HIV infection which includes both clinical and laboratory parameters. This is generally only used in resource-constrained countries. The clinical axis provides a list of conditions of prognostic significance, subdividing the course of HIV infection into four stages.

The laboratory axis further subdivides each clinical stage into three strata, according to CD4 count or total lymphocyte count. Thus in stage 1, in which the patient is generally asymptomatic with normal performance of daily activities, if the CD4 count is >500 cells/ul, this would be hold better prognosis (WHO stage1, stratum I) than if the CD4 count was <200 cells/ul (WHO stage 1, stratum III). This modified WHO staging system has been evaluated and validated in a number of countries; further modifications include additional low-cost tests such as the haematocrit which may provide even stronger predictive values, particularly in those individuals with a low CD4 count.

While these tests are useful, it is still felt that where financially and technically possible, countries should try and establish CD4 testing methods in order to assess prognosis and guide the requirement for therapy. The gold standard for quantifying the CD4 count is via staining of these cells in a fresh blood sample with fluorescently labeled monoclonal antibodies and their subsequent quantification using a flow cytometer.

Dual platform technology has largely been replaced with single platform methodology. Whilst less expensive technology (eg the FACSCount) has been successfully introduced into a number of resource-constrained settings the initial price of the equipment is still a major obstacle.

Thus with successful introduction of antiretroviral therapies into resource-constrained countries comes an urgent need for inexpensive laboratory infrastructure to support such a move. Over recent years, a number of low-cost manual assays to measure CD4 T cell counts have been evaluated. Two assays in particular, using immunobead technology, have received encouraging results.

These are the assays developed by Coulter and Dynal. In both assays, the technology includes either the removal of monocytes from the sample (Dynal) or the labeling of monocytes within the sample (Coulter) in order to ensure that these cells, which also express CD4 on their surface, do not falsely increase the CD4 T cell count. Both assays require very little equipment basically a good microscope and a haemocytometer, and the Dynal assay additionally requiring a magnet and a rotating wheel. The Coulter manual CD4 count kit (Coulter Corporation) uses latex cytospheres coated with antibodies to Cd4.

Smaller latex spheres with antibodies to CD14 are used to identify and exclude monocytes The anti-CD4 cytosphere binds to the CD4 T cell forming a rosette which, following addition of a crystal violet counter stain, can be counted under a microscope. This assay has an excellent association with CD4 counts assessed by flow cytometry.

The Dynabeads T4-T8 Quantification System (Dynal) uses Dynabeads which are magnetic beads coated with anti-CD4 (anti-CD8 beads are also available but are not required for monitoring). Magnetic beads which are coated with anti-CD14 are used to remove monocytes from the blood sample. The remaining CD4 cells (T cells) are lysed and their nuclei stained with Sternheimer Malbin stain for enumeration under a light microscope. The method can also be used with fluorescence microscopy, with a different stain (acridine orange) and this is a little easier for the scientist to visualize with less eye strain. Again this method has been shown to correlate well with flow cytometry.

One of the concerns is whether these assays can be used on blood samples that cannot be immediately assayed (eg the sample needs to be transported long distances to reach the laboratory). There are a number of stabilizers that can be added to blood (eg TransFix) in order to prolong the time between collection and assay. These have been validated for flow cytometric methods and are currently undergoing evaluation for the manual bead technologies. In addition, the stability of the blood sample at ambient temperatures which may be in excess of 30 degrees C needs to be evaluated.

There are currently no point-of-care assays to measure CD4 counts. These assays would be ideal for remote clinics where laboratory facilities are non-existent or rudimentary.

Such as assay may only provide limited information (e.g. greater or less than 200 CD4 cells/ul) but would be sufficient to apply the WHO criteria, should antiretroviral therapies be available. (Current guidelines suggest institution of therapy, if available, when the CD4 count is less than 200 cells/ul. Better resourced countries have increased this level to less than 350 CD4 cells/ul).

A number of other immunologic assays have been evaluated to determine their value as surrogate markers for HIV disease progression.

One of these, serum levels of beta-2-microglobulin, has been found to increase as a result of HIV infection and to predict a decline in the CD4 T cell count as part of disease progression. However it has been found to be of limited overall value as a number of other infections, many of which

are common in tropical countries or in individuals with HIV infection, may also raise the level. These include tuberculosis, syphilis and other sexually transmitted infections.

In developed countries HIV viral load is measured using one of several molecular methods. The most common is the RT-PCR assay (Roche Amplicor). This requires a high degree of technical skill as contamination of the sample is very easy without appropriate precautions. The assay is also very expensive. Two newer assays, both manual and less technically demanding, are currently being evaluated. These include the Cavidi ultrasensitive reverse transcriptase assay and the Perkin Elmer ultrasensitive p24 assay.It is generally felt that the transfer of technology to quantify viral load is of lower priority than that to monitor CD4 counts.

When considering what assays are appropriate to establish in a resource-constrained setting the following needs to be considered. First, how large is the population that might require monitoring. For example, if only 5 to 10 CD4 counts are likely to be performed per week a manual method is preferable and more cost-effective than eg FACSCount.

Conversely, if 20 or more analyses are being performed per day an automated method is required. Second, what technical skills are locally available. And third, what funding is available, both to transfer the technology and to continue the assay after that.

Sustainability of the introduced technology is fundamentally important. It is likely that in many countries there will eventually be a tiered system, with larger cities providing monitoring for larger populations of HIV-infected persons using automated technology (eg FACSCount or single platform flow cytology) and participating in national or international quality assurance programs, regional laboratories caring for smaller numbers of patients providing manual CD4 assays with quality assurance checks through the reference laboratory and isolated regional clinics performing point of care assays, once these are available.

References

Turnbull S, Dunne S, Crowe S et al. Monitoring HIV infection in resource-constrained countries. Clin Inf Dis 2003 (in press).

Crowe SM, Carlin JB, Stewart KI, Lucas CR, Hoy JF. Predictive value of CD4 lymphocyte numbers for the development of opportunistic infections and malignancies in HIV-infected persons. J Acquir Immune Defic Syndr 1991; 4:770-776.

Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus:

Suggested Baseling Laboratory Tests (I.e tests to be done after testing positive for HIV)

Complete Blood Count with differential and platelets
Comprehensive metabolic profile
Urinanalysis
G-6-PD qualitative
Hepatitis B surface antigen
Hepatitis B core antibody
Hepatitis C virus antibody
Hepatitis A virus antibody (optional unless HCV or HBV+)
Syphilis serology
Fasting lipid profile
Cellular immune profile (CD4-lymphocytes) x 2
HIV-1 RNA load by PCR (Viral Load)
Tuberculin skin test / Quantiferon Test
***Toxoplasma gondii* IgG antibodies**

These tests are done as to establish the condition the patient's body and system Is in and to anticipate any complications that may arise

Proper Use of HIV-Specific Laboratory Evaluations

HIV Viral Load	1. Possible acute retroviral syndrome to confirm diagnosis 2. Newly diagnosed HIV infection to establish baseline and confirm diagnosis 3. Periodically to follow the course of HIV treatment (see below)
HIV Resistance Assay (see below)	1. Prior to initiation of therapy when pre-existing antiretroviral drug resistance is known or suspected - acute or chronic HIV infection. This recommendation includes most patients in whom antiretroviral therapy is initiated. Suspect pre-existing antiretroviral drug resistance in the setting of recently acquired infection especially in a metropolitan are. 2. During antiretroviral therapy after loss of virologic suppression (while on antiretroviral drug therapy)
CD4-Lymphocyte Assay	1. Prior to initiation of therapy and periodically thereafter to evaluate the indirect effects of virologic suppression and the need for opportunistic infection antimicrobial prophylaxis (see below) 2. At the time of intercurrent febrile illnesses to evaluate for the possibility of opportunistic infection

Suggested Laboratory Tests to Evaluate Antiretroviral Therapy

HIV Viral Load	Monthly until undetectable; then every 3 months
Ultrasensitive HIV Viral Load	1-2 months after undetectable on regular sensitivity assay and every 3-6 months thereafter
Complete blood count	Monthly for 3-4 months, and then every 2-3 months
Comprehensive metabolic profile	Monthly for 3-4 months, and then every 2-3 months
Fasting lipid profile	Every 3 months
Serum lactic acid level	No routine testing recommended; perform test in correct clinical contest [malaise, nausea, myalgia, anion gap acidosis, NRTI therapy]
***Antiretroviral drug levels**	This may provide information about drug absorption, distribution, metabolism, excretion, and adherence in persons with suboptimal virologic response

* test not currently being done at Diagnofirm

Continued from page 3

Prognostic value of Ambulatory blood Pressure

pressure but with low ambulatory pressure is better than prognosis of patients with low office but with high ambulatory pressure.

One must realise the clinical repercussions of this finding: the first situation is regularly quoted as bad blood pressure control since office readings are above the goal values described in the guidelines; the second situation is precisely the opposite as it shows good control of office pressure. Yet, prognosis is worse in the latter situation. Several conclusions can be drawn from this study. First, it confirms previous studies that have shown that, in a vertical relation, ambulatory blood pressure correlates better than office readings with parameters of organ damage such as left ventricular hypertrophy (4). But the present study goes far beyond this statement yet as it clearly shows that this better correlation also has long term repercussions and ambulatory blood pressure recordings predict cardiovascular morbidity and mortality significantly better than office readings.

Second, this leads to a revision in the indications for ambulatory blood pressure recordings. Up to now, it was stated that ambulatory recordings should be made whenever there is a contradiction between office readings and clinical symptoms or parameters of organ damage (for example high office values and no left ventricular hypertrophy), in patients with so-called resistant hypertension (many of them have much lower ambulatory readings that can be predicted from office readings), patients showing many side effects on even low doses of antihypertensives (as their blood pressure often is very much lower than anticipated) and of course, in research conditions. However the present data give a much broader scope for ambulatory blood pressure recordings.

There is a clear argument that such recordings should be made in all hypertensive patients on treatment whatever their achieved office blood pressure is. Such recordings should be repeated at regular intervals. In all, one can hope that the implementation of these conclusions should be made possible by making the technique easier and cheaper. Social security and/or insurance systems should work at a proper reimbursement of the technique.

Also there could come an appealing association with home blood pressure recordings that could provide a filter to define in which patients ambulatory pressure should be recorded so as to yield optimal clinically useful information (5).

References available on request

Continued from page 13

Monitoring of HIV infection

introduction. USPHS/IDSA Prevention of Opportunistic Infections Working Group. Clin Infect Dis 1995; 21 (Suppl 1):S1-11.

Lyamuya EF, Kagoma C, Mbena EC, et al. Evaluation of the FACScount, TRAx CD4 and Dynabeads methods for CD4 lymphocyte determination. J Immunol Methods 1996; 195:103-112.

Brando B, Barnett D, Janossy G, et al. Cytofluorometric methods for assessing absolute numbers of cell subsets in blood. European Working Group on Clinical Cell Analysis. Cytometry 2000; 42:327-346.

Janossy G, Jani I, Gohde W. Affordable CD4(+) T-cell counts on 'single-platform' flow cytometers I. Primary CD4 gating. Br J Haematol 2000; 111:1198-1208.

WHO. Scaling up antiretroviral therapy in resource-limited settings. 2002 http://www.who.int/docstore/hiv/scaling/.

Yamey G. Drug companies cut HIV drug prices in the developing world. BritishMedical Journal 2000,320:1357.

Didier JM, Kazatchkine MD, Demouchy C, *et al.* Comparative assessment of five alternative methods for CD4+ T- lymphocyte enumeration for implementation in developing countries. *J Acquir Immune Defic Syndr* 2001; **26**:193-195.

Ferreira OC, Jr., Suleiman G, Brites C, et al. A rapid and reliable assay to enumerate CD4+ T lymphocytes in whole blood. J Acquir Immune Defic Syndr 1994; 7:1224-1227.

Gernow A, Lisse IM, Bottiger B, Christensen L, Brattegaard K. Determination of CD4+ and CD8+ lymphocytes with the cytosphere assay: a comparative study with flow cytometry and the immunoalkaline phosphatase method. Clin Immunol Immunopathol 1995; 76:135-141.

Landay A, Ho JL, Hom D, et al. A rapid manual method for CD4+ T-cell quantitation for use in developing countries. AIDS 1993; 7:1565-1568.

Nicholson JK, Velleca WM, Jubert S, Green TA, Bryan L. Evaluation of alternative CD4 technologies for the enumeration of CD4 lymphocytes. J Immunol Methods1994; 177:43-54.

Denny TN, Jensen BD, Gavin EI, et al. Determination of CD4 and CD8 lymphocyte subsets by a new alternative fluorescence immunoassay. Clin Diag Lab Immunol 1995; 2:330-336.

Jani V, Janossy G, Iqbal A, et al. Affordable CD4+ T cell counts by flow cytometry. II. The use of fixed whole blood in resource-poor settings. J Immunol Methods 2001; 257:145-154.

Kumarasamy N, Mahajan AP, Flanigan TP et al. Total lymphocyte count (TLC) is a useful tool for the timing of opportunistic infection prophylaxis in India and other resource-constrained countries. J Acquir Immune Defic Syndr 2002; 31:378-383.

Badri M, Wood R. Usefulness of total lymphocyte count in monitoring highly active antiretroviral therapy in resource-limited settings. AIDS 2003; 17:541-545.

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HIV/AIDS and weightloss

explored. Recombinant growth hormone has been shown to increase lean body mass and to reduce fat mass in both HIV-positive and HIV-negative subjects. Short courses of up to 12 weeks have been associated with significant functional improvement in grip strength and treadmill tests, but this treatment has failed to gain widespread acceptance.

The reasons for this are several-fold and include the facts that the treatment is extremely expensive, case reports have suggested that the treatment may encourage rapid growth of Kaposi's sarcoma and the reductions in fat mass may render the patient liable to catastrophic loss of lean body mass during the next OI because little energy is stored in any of the body's other compartments.

Growth hormone treatment is associated with increased insulin resistance, a major disadvantage in patients who are currently taking PI therapy.

INVESTIGATIONS OF WEIGHT LOSS

Regular weighing of the patient at clinic visits on accurate scales is helpful in predicting those in whom underlying OIs should be sought. Measuring the patient's height allows calculation of the body mass index, which may give a more accurate guide to significant wasting. Anthropometry provides a surprisingly accurate guide to fat mass and, by subtraction, lean body mass.

Although absolute values obtained by this method may not be accurate, changes in such measurements do accurately reflect changes in body composition. Unfortunately, in HIV infection, changes in body water may make this an unreliable guide to absolute values.

Dual x-ray absorptiometry (DEXA), provides a good opportunity for the measurement of lean body mass, both of the appendicular skeleton and viscerally. Such measurements correlate well with assessments made by the use of the distribution of heavy water, which is still regarded as the standard measurement of body composition, but is too expensive to use in most routine settings.

By: Kgomotso P. Vasco (Dietitian RD) - Abundant Life Dietetics Services

Health Benefits Of Olive Oil

With effect from this issue Diagnofirm will be dedicating a section of the Newsletter to healthy eating and dietary information

With the rise of diet related diseases in this generation, most people are interested in following healthy dietary principles. Fat has been one of the food items singled out as the culprit to risks of obesity, coronary heart disease, atherosclerosis, heart attacks, Diabetes Mellitus, cancers and many more other diseases.

However, moderate usage and the right choice of fat in our diet will help prevent ailments related to excessive consumption of fat.

Olive oil has been found to be the healthiest oil to opt for. You will find different types of olive oil sold in your local food stores such as

Virgin Olive Oil

The oil is extracted in a more natural way by grinding the olives into a paste, and then cold pressing to squeeze the oil out.

Extra Virgin Olive Oil

Has a lower acidity level of less than 1o acidity, which is less than 1% free fatty acids.

Fine Virgin Olive Oil

Has about 1.5° acidity.

Ordinary Virgin Oil

May contain up to 3° acidity.

Industrial Virgin Olive Oil.

Has more than 3° acidity. It is not addible because of its strong taste. It needs to be refined before it can be used.

Refined Olive Oil -

It has more free fatty acids than virgin olive oil because of the hot pressing process or if poor olive fruits had been used. This means it is more acidic than virgin olive oil. Most of the vitamins and phytosteroids are lost during the hot pressing process.

Pure Olive Oil

Is produced by mixing virgin and refined olive oils. This is the most common oil in the market.

Olive oil is healthier than other seed oils such as sunflower, palm, canola (rape seed), safflower seed oils because:

- Olive oil is more natural since it is extracted in a more natural way than most of the other oils. Virgin olive oil is not refined and there are no solvents used to extract it.
- It is rich in iron (0.38mg/100g) as it is produced in a more natural way. The natural extraction process preserves the iron. Other oils do not provide iron.
- Its fatty acid composition distribution favors a healthy heart. Olive oil is composed of 77.1% as monounsaturated fatty acid mainly in the form of oleic acid, 8.8% of olive oil is polyunsaturated fatty acid, whilst 14.1% being saturated fat.

  The American Heart Asso-ciation recommends that daily intake of fat should be 50% as mono-unsaturated fat. Therefore, olive oil meets this recommen-dation and far exceeds it.
- Olive oil does not contain trans fatty acids. Trans fatty acids are known to promote formation of cholesterol which favour athero-sclerosis. Olive oil also raises high density lipoproteins (HDL), the beneficial cholesterol. It is therefore protective of coronary heart diseases and arteriosclerosis than any other oil.
- This oil is more stable than other oils due to its low content of polyunsaturated fatty acids. It remains stable in very high temperatures of 160-200oC. Therefore it is safer to use when frying than other oils. When other oils are exposed to heat they form free radicals such as peroxides and hydroperoxides which promote arteriosclerosis and cancer formation. Olive oil will resist this effect unless if heated above 200oC.
- Olive oil also inhibits oxidation of low density lipoprotein(LDL) which is the main process that leads to arteriosclerosis. This is because it is high in oleic acid which is effective in inhibiting oxidation of lipoproteins.
- Olive oil protects the heart and reduces the likelihood of thrombosis. Olive oil is as effective as fish oils in reducing fibrinogen which is responsible for blood clotting.
- Olive oil reduces the risk of breast cancer whilst the use of margarines is a high risk of this disease.
- It also acts as a laxative if taken on an empty stomach. About 1-2 table spoons will help relieve constipation.
- Even though it is a healthy fat to opt for, take care when using olive oil as excessive use of fat in general will lead to weight gain. Fat is a major source of energy, providing 9kcals per gram of energy as compared to 4kcals per gram of carbohydrate.
- It provides a better flavor and aroma than other oils.

Even though it is an expensive food commodity, it is worth having olive oil in your kitchen to give you all the health benefits discussed above. It is never too late to start. Start this new year with a new ingredient in your diet.

Live life to the fullest this year. Here are a few choice quotes about the beginning of a new year;

- "Year's end is neither an end nor a beginning but a going on, with all the wisdom that experience can instill in us." --Hal Borland
- "We will open the book. Its pages are blank. We are going to put words on them ourselves. The book is called Opportunity and its first chapter is New Years Day." Edith Lovejoy Pierce
- "An optimist stays up until midnight to see the new year in. A pessimist stays up to make sure the old year leaves." --Bill Vaughn. Which one were you this year?!

HIV Update from the WHO

Improvements in surveillance increase understanding of the epidemic, resulting in substantial revisions to HIV estimates

New data show global HIV prevalencethe percentage of people living with HIVhas levelled off and that the number of new infections has fallen, in part as a result of the impact of HIV programmes. However, in 2007 33.2 million [30.6 36.1 million] people were estimated to be living with HIV, 2.5 million [1.8 4.1 million] people became newly infected and 2.1 million [1.9 2.4 million] people died of AIDS.

There were an estimated 1.7 million [1.4 2.4 million] new HIV infections in sub-Saharan Africa in 2007a significant reduction since 2001. However, the region remains most severely affected. An estimated 22.5 million [20.9 24.3 million] people living with HIV, or 68% of the global total, are in sub-Saharan Africa. Eight countries in this region now account for almost one-third of all new HIV infections and AIDS deaths globally.

While the global prevalence of HIV infectionthe percentage of people infected with HIV has levelled off, the total number of people living with HIV is increasing because of ongoing acquisition of HIV infection, combined with longer survival times, in a continuously growing general population.

Global HIV incidencethe number of new HIV infections per yearis now estimated to have peaked in the late 1990s at over 3 million [2.4 5.1 million] new infections per year, and is estimated in 2007 to be 2.5 million [1.8 4.1 million] new infections, an average of more than 6 800 new infections each day. This reflects natural trends in the epidemic, as well as the result of HIV prevention efforts.

The number of people dying from AIDS-related illnesses has declined in the last two years, due in part to the life prolonging effects of antiretroviral therapy. AIDS is among the leading causes of death globally and remains the primary cause of death in Africa.

Progress seen but more needs to be done HIV prevalence among young pregnant women (15 24) attending antenatal clinics has declined since 2000/2001 in 11 of the15 most-affected countries. Preliminary data also show favourable changes in risk behaviour among young people in a number of countries, (Botswana, Cameroon, Chad, Haiti, Kenya, Malawi, Togo, Zambia, and Zimbabwe). These trends suggest that prevention efforts are having an impact in several of the most affected countries.

In sub-Saharan Africa, continued treatment scale-up and HIV prevention efforts are also bringing results in some countries, but mortality from AIDS remains high in Africa due to the extensive unmet treatment need.

Cote d'Ivoire, Kenya and Zimbabwe, among others, have all seen downward trends in their national prevalence. Beyond sub-Saharan Africa, declines in new HIV infections have also occurred in South and South-East Asia, notably in Cambodia, Myanmar and Thailand.

There is a need to adapt and revive HIV prevention efforts as some countries are seeing a reversal of declining trends. Burundi's declining trend from the late 1990's did not continue beyond 2005 and HIV prevalence started to increase again at most surveillance sites.

Despite achievements in reversing the epidemic in Thailand, HIV prevalence is rising among men who have sex with men and has remained high among injecting drug users over the past 15 years, ranging between 30% to 50%.

UNAIDS and WHO officials point out that the new estimates do not change the need for immediate action and increased funding to scale up towards universal access to HIV prevention, treatment, care and support services.

JOKES CORNER

Patient: I'm in a hospital! Why am I in here?

Doctor: You've had an accident involving a bus.

Patient: What happened?

Doctor: Well, I've got some good news and some bad news. Which would you like to hear first?

Patient: Give me the bad news first.

Doctor: Your legs were injured so badly that we had to amputate both of them.

Patient: That's terrible! What's the good news?

Doctor: There's a guy in the next ward who made a very good offer on your slippers.

A doctor is talking to a car mechanic, "Your fee is several times more per hour then we get paid for medical care."

"Yeah, but you see, doc, you have always the same model, it hasn't changed since Adam; but we have to keep up to date with new models coming every month."

At the height of mad cow disease scare, a couple goes to dinner at an exclusive restaurant in London.

The man orders a fillet steak, prepared rare.

The waiter asks politely, "What about the mad cow, sir ?"

"Oh don't worry," answers the man, "she'll order for herself ..."

Doctor: I have some bad news and some very bad news.

Patient: Well, might as well give me the bad news first.

Doctor: The lab called with your test results. They said you have 24 hours to live.

Patient: 24 hours! That's terrible! What could be worse? What's the very bad news?

Doctor: I've been trying to reach you since yesterday.