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NEWSLETTER
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Editorial

QUALITY THE WAY FORWARD! Quality is critical to the success of every service-providing organisation. For it make an impact, good quality practice must be accepted at senior management level and then instilled within the whole organisation. It must become a culture, not just about implementing a system or working towards set standards. Quality is an attitude, a way of working, which improves services as well as the way people work and live.

The newly established Diagnofirm Medical Laboratories Quality Management System is aimed at becoming a major force in pursuit of quality and is now making a key contribution to the services provided at DML. The Quality Management System is facilitating and promoting the use of quality standards to add value to the organisation and encourage the standing of quality professionals.

In this issue and those to follow an effort shall be made to try and make fellow scientists and professional colleagues conscious of the irresistible force that is 'QUALITY' which is sweeping the health care delivery system. It is high time we all embraced the idea of providing quality services to our clients.

The response to our first newsletter was overwhelming and we would like to extend our sincere gratitude to all those who supported and gave us their constructive critism and gave us the will power to go on producing this newsletter. This is the 2nd edition of our newsletter and the 3rd edition will be coming out on the 1st of September. As usual, your opinions, on what is in the current issue or what you would like to see in future editions, are most welcome. The contributions can be sent to lab@diagnofirm.co.bw. Efforts will be made to address all your concerns ◀

"Learn to share information, that's the only way we can improve ourselves."
Dalai Lama

Moonya Mangwendeza
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Inside this Issue

DML's Lab Manager Desire Mhlabi shares a joke with Dr S Belcher of Abbott

DML DIAGNOFIRM MEDICAL LABORATORIES

By Silas Nunu

Recent events @ DML

Installation of the NucliSens EasyQ

Diagnofirm laboratory, realizing the ever-increasing need for HIV monitoring successfully installed a new HIV viral load analyzer, the NucliSens EasyQ from Biomeriuex and OmniMed Diagnostics. This also incorporated the training of an initial group of 4 Laboratory Scientists in January and then 3 more in February. This new machine has greatly improved the result turnover for HIV monitoring results from more than 3 days to only 24 hours.

The new machine is located at the new Virology Lab premises along Independence Ave(Plot 881). This new department now exclusively looks at tests involved in HIV monitoring (T-cell profile and viral load). The Director of Health, Dr. Mazonde (on behalf of the Minister of Health), and a host of local medical practitioners, bank officials, and Medical aid representatives officially toured these new premises at the end of February. Diagnofirm also took the opportunity to demonstrate the functions of the HIV monitoring machines during this tour.

Installation of the Bact-Alert

Still in the month of February DML acquired a Bact-Alert blood culture machine from OmniMed Diagnostics. This machine will enhance detection capabilities in blood cultures. The principle of this analyzer is based on carbon dioxide production during bacterial growth, which brings about pH change and subsequent colour changes of the indicator in the bottle. The machine then detects this and it alerts the operator who then identifies the organism. It thus

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Part one

By Moonya Mangwendeza

Interpretation of Clinical Chemistry Laboratory Results

IMPACT OF ANALYTICAL AND PRE-ANALYTICAL VARIATIONS.

Laboratory test results are used to confirm a clinical suspicion or make a more definitive diagnosis. Once a diagnosis has been made, tests are used to monitor the patient's condition. Laboratory test results are used as a screening tool, which is designed to confirm or exclude the presence of a particular disease. Many non-analytical and analytical factors affect test results thus leading to interpretive difficulties. A laboratory result reflects a biochemical 'snapshot' of a patient's physiological state at the time of specimen collection hence it is up to those who use the test results to be aware of the factors affecting the test results so that the physiological state is truly represented at the time when the specimen was collected. Discussed below are some of the factors affecting laboratory results, which we need to be aware of.

Analytical variations are due to the analytical process and can be determined from the analytical method or the instruments used to perform the test. Accuracy, precision, analytical sensitivity and specificity are all included in analytical variations. However a closer look will be given to imprecision. Imprecision is the amount of random analytical error present in an analytical method. Sources of such variations include temperature fluctuations, inconsistent handling of materials, and changes in the analytical environment and variability in the analytical environment. Imprecision can be quantified by calculating the mean, standard deviation (SD) and the Coefficient of variation (CV). Results from analytical methods with only small amounts of imprecision will produce a small SD and CV.

Physiological variations are basically biological variations and occur prior to the analytical process. Table 1 shows some of the controllable and uncontrollable sources of physiological variation.

Diet and recent food intake affect laboratory results. Most changes resulting from recently ingested food are not clinically significant. However, some are for example the lipaemia after a meal will affect the serum sodium levels due the reduction in the water content of the specimen because of the high triglyceride concentration. Cortisol levels are affected by the intake of coffee. Certain dietary restrictions need to be enforced before certain tests are done for example the restriction of meat rich meals before doing occult blood tests. Dietary habits may affect serum constituents for example a high protein diet leads to higher levels of urea, cholesterol and phosphate. In nutritionally deprived people protein levels, albumin, cholesterol and trigycerides are reduced as well as the activity alkaline phosphatase. Dietary differences between cultures are one very important reason why it is important to come up with local reference ranges. The effect of alcohol on tests is dependent on whether the patient is an abuser of alcohol or not, the time of specimen collection after alcohol intake, the quantity consumed and the patient's response to alcohol. Enzymes like CK, AST and LDH are elevated after alcohol intake. Posture affects results due to the changes in blood volume that occur when an individual changes from a lying to a standing position. The changes are observed in those plasma components that do not change components with the water hence rises in levels up to 10% can be observed with proteins, albumin, cholesterol, bilirubins, triglycerides, AST, ALT, iron and hormones. These changes are of great importance especially to patients who change from being outpatient to inpatients or vice versa. Exercise has a dramatic effect on biological composition of blood depending on the type of exercise, its intensity and duration. Exercise will increase levels of pyruvate and lactate due to increased skeletal muscle metabolism. Changes that occur in cell membrane permeability during exercise will result in higher serum levels of enzymes like CK, AST and LDH.

Stress is an important factor in the assessment of plasma cortisol levels as it can cause the levels to rise ten times. Stress due to surgery or heart attack can cause a fall in serum iron and a rise in

PHYSIOLOGICAL SOURCES OF VARIATION

CONTROLLABLE	UNCONTROLLABLE
Diet	Gender
Alcohol intake	Age
Posture	Race
Stress	Rhythmic influences
Pregnancy	Fever
Exercise	
Hospitalization/immobilization	
Drugs	
Previous medical and surgical care	

ferritin. Pregnancy causes hormonal and non-hormonal changes. The non-hormonal changes are mainly due to the increase in plasma volume, which has a dilutional effect on constituents. Many hormones especially progesterone, hCG as well as urinary hormones are elevated in pregnancy. The higher levels of thyroxine and cortisol experienced are mainly due to the high levels of hormone binding proteins experienced in pregnancy. Immobilization increases calcium and phosphate levels but without affecting the serum levels. Drugs can either have a direct effect on the laboratory test itself or have a physiological effect on the constituent. Drug references are too many to be covered here but there is need to know how they affect a result otherwise they will result in wrong patient management. Blood transfusions result in increased levels of bilirubin just as intramuscular injections will cause a rise in CK, LDH and AST

Specimens need to be collected from a well-informed and prepared patient. The time at which a specimen is collected should be noted. Some constituents demonstrate cyclical changes over the course of the day (circadian) or even the course of the year as a result of seasonal influences (cirannual). For example the concentration of cortisol can vary as much as 50%between specimens collected in the morning and those collected in the evening. Others like rennin, aldosterone, TSH and growth hormone also show a similar phenomenon. Calcium exhibits a circannual variation. Calcium serum concentrations are higher in summer when there is more frequent exposure to sunlight and a corresponding increase in vitamin D. Some of the analytes show changes as a result of the changes in diet and physical activity associated with the changes in seasons.

Other pre-analytical factors apart from physiological variations should also be considered. Blood collection site is a contributing factor in variations experienced in lab results. Blood specimens should not be collected from the arm where infusions are also being administered because the specimen will be a mixture of the blood and whatever will be being infused. For example for a patient on a dextrose drip, if the sample is collected from the same arm where infusion is taking place, the glucose levels will be too high while all the other analytes will be abnormally low. There is need to question specimen collection when levels are too high or too low. Contamination certainly affects results. An example is the use of an ethanol swab to clean a site for blood collected to measure alcohol levels. Air bubbles and froth affect pH and blood gas analysis. The type of anticoagulant affects the test results. For instance, blood collected in potassium EDTA tubes will result in lower calcium and magnesium levels as well as alkaline phosphatase. Some specimens require special conditions an example being plasma rennin activity assay, which requires the use of a pre-cooled tube. In correct collection techniques cause haemolysis and falsely elevated results of potassium, phosphate, AST and LDH. Tourniquets must be applied for as short a time as possible because of the effects of venous occlusion, which causes changes in proteins, and protein bound constituents.

A laboratory result is only as good as the sample analyzed. Hence it becomes imperative that we minimize as much as possible the factors discussed in this article and others not mentioned so that laboratory results can truly represent the conditions they are meant to. Test results are used to base medical decisions on, so we must be fully aware of the limitations of the tests and educate our medical colleagues on the variations inherent in laboratory results

References

1- David G. Grenache, PhD. Imprecision and Physiological variation. Clinical Laboratory News March 2004

2- Thistle QA. Interpretation of Clinical Chemistry Laboratory Data 2004.

BRAIN TEASERS

A 15-year old girl with known portal hypertension (due to a previous portal vein thrombosis) was admitted with bleeding oesophageal varices. Her U & Es the next day were as follows :

Na	K	Cl	Co2	Urea	Creatinine
140	3.8	106	30	12.6	84
Mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	umol/L

Questions

- What does the elevated urea signify?
- What other factors influence plasma urea?

Explanation

Uraemia due to gastrointestinal haemorrhage

Urea is an unreliable marker of renal function and hydration status since its value is affected by changes in protein load and hepatic function.

Creatinine is a better marker of renal function but you should remember that it has a non-linear relation to decrease in GFR - a large change in GFR can occur with only a small rise in creatinine.

By Kiran Bhagat

Should I Be Taking Vitamins?

The Clinical Problem

Medical teaching has been that, in generally healthy persons, nutritional needs can be readily met by diet alone. However, recent evidence shows that the use of folic acid supplements in early pregnancy can dramatically reduce the incidence of neural-tube defects; thus, at least in some circumstances, vitamin intake can be sub-optimal without there being any clinical evidence of deficiency. Public interest in vitamin supplements is enormous. In the US alone 30 percent of the population is currently using such supplements. Political pressures have led to a highly unregulated industry with limited control by the Food and Drug Administration over marketing and quality.

Strategies and Evidence

Ideally, vitamin supplements would be evaluated in randomized prevention trials with measurable clinical end points. However, such trials are complicated, and the results could be misleading. First, everyone has some level of consumption of vitamins, so the effect of a supplement depends on the amount of a given vitamin that is already being consumed. Because trial participants often have good diets, the results of a study finding no effect of a vitamin supplement might not apply to those with poorer diets. Moreover, a trial may be too short for an effect to be detected, particularly in the case of the evidence of cancer. In addition, to enhance their statistical power, many studies focus on persons at high risk for a disease or those with existing disease. If diet is not responsible for the elevated risk, clearly positive results would be compelling, but negative results would be difficult to interpret.

One approach is to discourage the use of vitamin supplements unless benefits are proved in randomized trials with measurable clinical outcomes. An alternative is to use all the available evidence to weigh the likelihood of a benefit against the likelihood of harm, while also considering the costs. Evidence should include the results of animal studies, randomized trials examining intermediate biologic markers, and observational epidemiological studies with clinical end points. For example, a low intake of several micro nutrients may cause DNA damage, although the clinical effect of this damage is not known. Epidemiological studies demonstrating a relation between low intake of a nutrient and the risk of disease suggest that at least part of the population has sub-optimal intake.

Because foods contain many nutrients, distinguishing among the effects of various nutrients in the same foods can be difficult. For example, the observation that high-dose beta carotene supplementation in smokers did not reduce the risk of lung cancer and may even have increased risk highlights the potential dangers of extrapolating from epidemiological studies of food consumption (the consumption of fruits and vegetables, in this case) to concentrated forms of a single chemical. Epidemiological studies of vitamin-supplement use per se are more directly relevant, but careful statistical adjustment for other lifestyle factors is essential because users of supplements may have healthier behaviour in general than nonusers. This review highlights the potential effects of commonly used vitamins, recognizing that the relevant literature is far greater than what can be cited here.

Folic Acid

Several epidemiological studies have found that periconceptional folic acid supplementation is associated with a substantially reduced risk of neural-tube defects by 70 percent. A randomized trial of a multivitamin that included folic acid (800 ug daily) in pregnant women without a history of an affected pregancy was stopped early because of a clear benefit. This is the only definitively proven benefit of a multivitamin.

Although this relation has not been tested in randomized trials, substantial evidence suggests that low folic acid intake increases the risk of cardiovascular disease and several types of cancer. In many studies, high blood homocysteine leves have been associated with higher risks of coronary disease. Inadequate intake of folic acid and, to a lesser extent, of vitamin B6 and vitamin B12 increases homocysteine levels. Higher folic acid intake, the use of multivitamin supplements, and higher blood folate levels are all associated with a lower risk of coronary disease.

Higher intake of folic acid is associated with a lower risk of colon cancer and breast cancer, particularly among persons who are at increased risk because of daily alcohol consumption. Also, a polymorphism in the gene for methylenetetrahydrofolate reductase (which is involved in folate metabolism) has been associated with an increased risk of colon cancer in some studies, providing additional evidence that the relation between low folic acid intake and an increased risk of colon cancer is causal. Alcohol interferes with folate absorption and metabolism, perhaps accounting for increased folate requirements among drinkers. When folate levels are low, uracil is inappropriately incorporated into DNA, and folic acid supplementation reverses this process.

The optimal folic acid intake remains uncertain. An intake of 400 ug per day minimizes blood homocysteine levels in most people, but more may be needed to reduce the risk of cancer.

Vitamin B6

Vitamin B6 intake below the recommended daily allowance (RDA) of 2 mg is associated with an increased risk of coronary disease, but it is unclear whether this association is independent of folic acid intake. Meat and legumes are the major food sources of vitamin B6; persons who reduce their consumption of red meat without increasing their consumption of legumes may have low vitamin B6 intake.

Vitamin B12

Low blood levels of vitamin B12 (serum cobalamin level, <258 pmol per liter) , caused primarily by reduced absorption in elderly persons with low gastric acidity, are also associated with higher blood homocysteine of marginal vitamin B12 status remain unclear, but they may include increased risks of vascular disease and cancer.

Crystalline vitamin B12, the form that is used in supplements, does not require gastric acid for absorption, so a multivitamin can ensure that intake is adequate for most people.

Vitamin D

In Botswana it is likely that sun exposure alone may provide adequate vitamin D. The effect of supplement depends on the amount of sun exposure a person receives and his or her dietary intake. However, reasonable evidence suggests that many Americans would benefit from supplemental vitamin D to reach the RDA of 400 IU, and double this amount mount may be desirable for some persons. 23 A vitamin D intake of up to 2000 IU per day is believed to be safe.

Vitamin A

Because vitamin A helps regulate cell differentiation, higher intakes could potentially reduce the risk of cancer. However, blood levels are tightly controlled, and greater intake in well-nourished persons has only a minimal effect on these levels. Both intake and blood levels of vitamin A have generally been shown to be unrelated to the risk of cancer. Supplemental beta carotene, a vitamin A precusor, has consistently failed to reduce the risk of cancer in randomized trials.

Intake of up to twice the RDA of vitamin A of 5000 IU is thought to be safe. However, an intake of preformed vitamin A (retinol) in the range of 10,000 IU per day or higher - which might be attainable from foods rich in vitamin A (especially liver, fortified breakfast cereals, and dairy products) in combination with a multivitamin containing the RDA of retinol - might be undesirable. Intakes of preformed vitamin A in this range have been associated with an increased risk of high fracture, and daily intakes of appropriately 10, 000 IU during pregnancy have been associated with specific birth defects, but confirmation of these associations is needed

Multivamin Preparations

The most common supplements are multivitamins that typically include the RDA of thiamin, riboflavin, niacin, folic acid, and vitamins A, C, B6, B12, D, K, and E. Few studies have evaluated the effects of multivitamin has been associated with a lower risk of coronary disease, colon cancer, and breast cancer, particularly among regular consumers of alcohol. In a randomized trial involving elderly persons, a multivitamin-multimineral combination reduced the number of days of illness due to infections by half. A similar supplement reduced the incidence of stroke, primarily among men, in a nutritionally deficient population in China. The results must be replicated in other settings.

Vitamin E Supplements

Vitamin E supplements, most os which contain 200 to 800 UI, lead to intakes far greater than the RDA of 30 IU and well beyond those attainable by diet. High doses of vitamin E block the oxidative modification of low-density lipoprotein cholesterol and have additional effects that might reduce the risk of coronary disease. However, the value of vitamin E for the prevention of cardioscular disease is controversial. In prospective, observational studies involving persons without known cardiovascular disease, the use of vitamin E supplements for two or more years - most commonly at a dose of 400 IU per day - has been associated with 20 to 40 percent reduction in the risk of coronary disease. The one negative prospective study included few users of the supplements, and information on the duration of use was not collected.

The published randomized trials, in contrast to these observational studies, have focused primarily on persons with existing coronary disease, and their results are inconsistent. Although the incidence of recurrent infarction was reduced by half in one study, supplementation with vitamin E (400 IU daily) had no effect on cardiovascular events in the substantially larger Heart Outcomes Prevention Evaluation trial. The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico found on significant differences in the overall cardiovascular end points, but there was a significant reduction in the rate of death due to cardiac causes. One recent trial showed a significant halving of the rate of cardiovascular outcomes among patients on dialysis, and another demonstrated a large reduction in the rate of progression of intima-media thickness among men (but not women) randomly assigned to receive a combination of vitamin E and vitamin C. No effect of vitamin E was seen among high risk patients in a recent trial, but the intervention ended at 3.6 years.

Thus, the weight of evidence is against an important short-term benefit of vitamin E supplements among patients with existing cardiovascular disease who are being treated with multiple pharmacologic agents. The long-term benefits of vitamin E supplementation for primary prevention remain unclear.

It has also been hypothesized that vitamin E supplements reduce the risk of cancer. No benefit has been found in terms of the risk of breast cancer, and data on the risk of colon cancer are mixed. The randomized Alpha-Tocopherol Beta Carotene Cancer Prevention Study found an unexpected, significant reduction in the incidence of prostate cancer but not in the incidence of other types of cancer. Because many cancer sites were examined, this may represent a chance finding. Sparse evidence suggests that vitamin E may slow the progression of Alzheimer's disease.

Vitamin E intake of up at least 1000 IU per day is generally considered safe. A nonsignificant increase in the incidence of hemorrhagic stroke was seen in the Alpha-Tocopherol Beta Carotene trial, which included only men who smoked, but such an increase was not observed in a cohort composed primarily of nonsmokers. Vitamin E supplementation may accelerate the progression of disease in patients with retinitis pigmentosa.

Vitamin C Supplements

Little evidence supports the existence of a benefit of vitamin C supplementation beyond the range of the typical diet in the United States or the current RDA of 90 mg for Men and 75mg for women (35 mg higher for smokers) a minimal effects might be expected from supplementation because tissues become saturated at about these levels of intake. Vitamin C supplements have been associated with a lower risk of coronary disease in one cohort study, but the analysis did not control for the use of vitamin E supplements.

Many studied have found an association between a low dietary intake of vitamin C and an increased risk of stomach cancer, but the effects of vitamin C supplements have not been specifically evaluated. Even long term supplementation with vitamin C was not associated with a lower risk of breast cancer. Fewer data are available on associations with other types of cancer, but there is no compelling evidence of a benefit.

Areas of Uncertainty

Few of the many possible associations between specific vitamins and specific diseases have been examined in randomized clinic trials. The evidence that folic acid reduces the risk of coronary disease and of colon cancer is strong, although not definitive. Even in instances in which a benefit has been proved, and in the incidence of neural-tube defects by folic acid supplementation, the optimal dose is uncertain. Requirements for nutrients may be influenced by genetic variations, and this is a focus of ongoing research.

Guidelines

Guidelines from some professional societies or governmental panels recommend attempting to obtain vitamins and minerals from food sources rather than from supplements. The American Dietetic Association and the U.S. Dietary Guidelines also note that some people may need vitamin or mineral supplements in addition to a good diet to ensure that their nutritional needs are met. The U.S. Preventive Services Task Force emphasizes the needs for folic acid supplements for women planning pregnancy, and the centres for Disease Control and Prevention recommend supplemental folic acid for premenopausal women who could potentially become pregnant. The Food and Nutrition Board of the Institute of Medicine notes that there has been no resolution of the question regarding the effect of antioxidant vitamins on the risk of chronic disease.

Conclusions and Recommedations

Given the greater likelihood of benefit than harm, and considering the low cost, we conclude that a daily multivitamin that does not exceed RDA of its component vitamins makes sense for most adults, including the woman in the case vignette. Substantial data suggest that higher intakes of folic acid, vitamin B6, vitamin B12, and vitamin D will benefit many people, and a multivitamin is especially important for women who might become pregnant; for persons who regularly consume one or two alcohol drinks per day; for the elderly, who tend to absorb vitamin B12 poorly and are often deficient in vitamin D; for vegans, who require supplemental vitamin B12; and for poor urban residents, who may be unable to afford adequate intakes of fruit and vegetables.

Many multivitamins also include essential minerals, although these doses of some of these minerals, such as calcium, are well below the RDA. Although we have not discussed minerals here, there is less evidence supporting the existence of a benefit for mineral supplements, with the exception of the additional iron required by some premenopausal women.

Although one could measure blood levels to identify those who would benefit most from multivitamins, this would be much more expensive than simply recommending that all adults take a supplement. Education regarding nutrition is vitally important, but it has been far less effective than supplementation or the fortification of food in raising blood folic acid levels. However, a vitamin pill is no substitute for a healthful lifestyle or diet, because foods contain additional important components, such as fibre and essential fatty acids. In particular, a vitamin supplement cannot begin to compensate for the massive risks associated with smoking, obesity, or inactivity. The cost of a multivitamin supplement is so low - similar to that of about a quarter of a serving of fruit or vegetables - that it is unlikely to displace healthful foods in most persons' budgets.

Finally, although we do not recommend additional vitamin supplements at present, the relevant evidence remains far from complete ◀

BRAIN TEASERS

Clinical Cases.

The following biochemical results were recorded in a 29-year-old female who attended her GP complaining of tiredness.
There was no previous relevant history.

FT4	8 nmol/L
TSH	12.6 IU/L

Questions

- What is the diagnosis?
- What other clinical features might be present?
- What other tests might be abnormal?

Explanation

Hypothyroidism

This is a typical picture of hypothyroidism with low FT4 and raised TSH.
Typically patients have a bradyycardia and show signs of weight gain. They may complain of cold intolerance.
In some cases the assessment of antibody status can be helpful as anti-thyroid autoantibodies can be cause thyroid gland damage. In patients with positive anti-thyroid peroxidase antibodies there is a 5% chance per year of developing hypothyroidism.
It is unnecessary to measure FT3 in this case as it will not give us additional diagnostic information.

By Desire B. Mjabi

Implementing New Kidney Disease Testing Guidelines

The Clinical Lab's Role in Identifying At-Risk Individuals

According to the U.S. National Kidney Foundation (NKF) the prevalence of kidney failure is surpassed only by an even higher prevalence of early-stage chronic kidney disease (CKD), and despite its debilitating nature, it remains under-diagnosed and under-treated in the US and worldwide. Evidence indicates that some of the adverse effects of CKD, especially cardiovascular disease can be slowed down or prevented altogether with the initiation of treatment earlier in the disease process. Because of these implications, the role of the clinical laboratory in the diagnosis of CKD is critical to ensuring that patients who are at risk are properly identified so that life-sustaining treatments can be initiated.

One of the main reasons for the under-diagnosis of kidney disease is a lack of agreement on a standard definition and classification of stages in the progression of CKD, irrespective of the underlying disease. However using the Glomerular filtration rate (GFR) as the major factor for classification, NKF set out guidelines which define CKD as the presence of kidney damage or decreased level of kidney function with GFR < 60 ml/min/ 1.73m2 for three months or more, irrespective of the specific renal disease diagnosis. The most widely used endogenous marker for GFR is measurement of creatinine or creatinine clearance. Serum creatinine alone is really not sufficient to assess GFR because it has a large between-individual variation hence the use of an equation based on serum creatinine, age, body size, gender and race. Creatinine production is also closely related to muscle mass hence men have higher serum creatinine levels than women.

Labs have therefore been advised to focus on the new definition and stages of CKD and also the estimation of GFR as tools to monitoring and evaluation strategies. All individuals should be assessed as part of routine health encounters to determine whether they are at increased risk of developing CKD, based on clinical and socio-demographic factors. Those found to be at an increased risk of developing CKD should undergo testing for markers of kidney damage and to estimate the level of GFR from their serum creatinine.

Laboratories are also encouraged to assess proteinuria for increased excretion of albumin in adults, total protein in children, as well as confirm a positive dipstick result by quantitative measurement of the protein to creatinine ratio. Estimation of GFR together with measurement of microalbuminuria is also recommended for the monitoring of slowly progressing nephropathies such as that associated with Diabetes. Urine chemistry, serum creatinine, creatinine clearance and microalbumin studies are all available at Diagnofirm Medical laboratories.

Shown below are the Equations recommended by NKF for predicting GFR

Adults

$$GFR = \frac{(140\text{-age}) \times 2.12 \times \text{weight} \times (0.85 \text{ if female})}{Scr \times SA}$$

From Cockcroft and Gault (Nephron 1976)

Children

$$GFR = \frac{0.55 \times \text{height (cm)}}{Scr}$$

From Counahan-Barrett (Arch Dis Child 1976)

Abbreviation
Scr = Serum creatinine
SA = Body surface area

To augment existing tests and formulae a new potential marker for CKD called Serum Cystatin C appears promising as an index for GFR but there is not much data now to support its widespread clinical use. It is independent of age and may form the basis for standardization of reference ranges for both children and udults. In studies Cystatin C has been found to have a better correlation with GFR than either serum creatinine or the Cockcroft and Gault equation. Only studies in large populations of individuals with very mild kidney disease would offer a better validation of this. This test is however still not available in routine laboratories.

Table 2 shows progression of chronic kidney disease and the Clinical action plan. As shown on the table it is always better to identify at risk individuals and implement intervention strategies to avoid end stage renal failure.

Conclusion

The assessment of renal disease requires the successful integration of a wide range of pathology disciplines. A decline in GFR may be identified by serum creatinine measurement but establishing diagnosis requires radiological, histopathological, immunological and haematological support. Improving methodology and the discovery of new markers of GFR and glomerular or tubular damage will continue to provide important contributions to early diagnosis of renal disease. Intervention treatments can then slow down the progression of CKD and significantly reduce CVD risk when kidney damage is present with normal or elevated GFR (~90 ml/min/1.73m2).

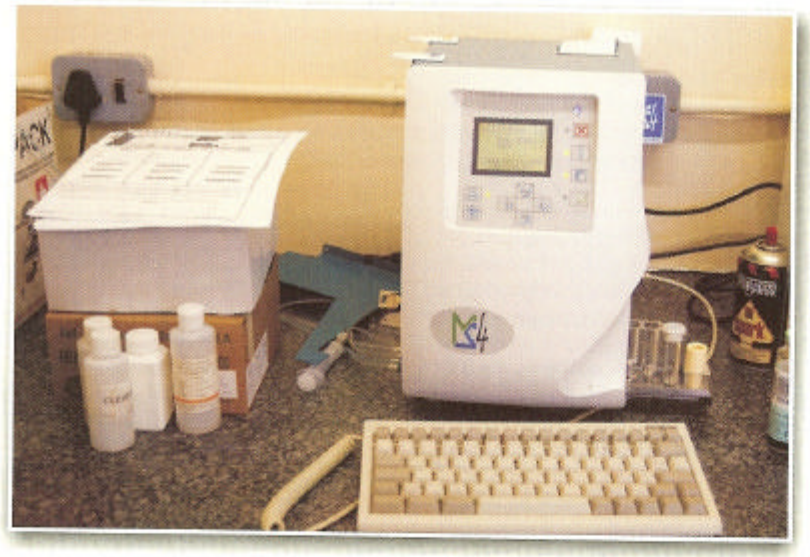
Adapted from Clinical lab news 2002 and LabMedica international 9-10/ 2003.

Table 2

STAGE	DESCRIPTION At increased Risk	GFR (ml/min/1.73m2 >=90(with CKD risk Factors)	ACTION Screening, CKD risk reduction
1	Kidney damage with normal or increased GFR	>=90	Diagnosis and treatment, treatment of comorbid conditions, slowing progression, CVD risk reduction
2	Kidney damage with mild or decreased GFR	60-89	Estimating progression
3	Moderately decreased GFR	30-59	Evaluating and treating complications
4	Severely reduced GFR	15-29	Preparation for kidney replacement therapy
5	Kidney failure	<15	Replacement (if uremia present) or dialysis

By Maanya Mangwendeza, QA Officer, DML

Acquiring a New Analyser



MS 4 analyser at DML Phikwe Branch

To keep up with technological advances, medical laboratories have to acquire new technology every 5-10 years. Purchasing laboratory instrumentation, like many other aspects of healthcare, has changed dramatically over the past decade. Yet some things never change: those purchasing want the most for their money, and manufacturers want to make sales. Here are some guidelines on how to select the system that's right for your needs. Any instrument purchase involves 3 phases: planning, acquisition, and implementation.

Planning

Obvious the first step is to identify the need for a new analyzer. The core of the planning process is to get a realistic, complete picture of your current testing situation and determine your needs. Sample handling, test volume and throughput, turnaround time (stat and routine), data management, send outs, and labor requirements are obvious variables to analyze and consider. Warranties, service contracts, maintenance and repair records, and other documentation for the laboratory's existing instrumentation should be gathered and scrutinized. Make sure there is enough space in the laboratory to add in the new analyzer without compromising on-going operations. Are ventilation, electrical supply and water supply available for the new analyzer? Confirm the availability of IT requirements for the new analyzer such as interfaces, computers and servers. If the laboratory is ready for a new analyzer then it is time to go shopping.

Prior to purchase of an instrument there is need to talk to the manufacturer have them explain the analyzer to you in detail and see the analyzer in operation. You should also make enquires about the maintenance requirements of the analyzer and the operation details. Make it a note as well to get the details of the technical assistance offered by the manufacturer and at what times the technical assistance is available in the event the analyzers needs to be repaired.

Acquisition

The planning phase should provide the details for selecting the actual instrumentation. You should now have a clear understanding of what your needs are, what you can afford, what features are absolutely essential, and what extras you can live without.

Basic information on available and state-of-the-art instrumentation can be obtained from trade journals, sales representatives, and on the Internet. Don't be too impressed by the most advanced technology, the most advanced robotic automation, or the most powerful capabilities unless they directly answer the needs identified in your planning phase. Cutting-edge innovations may be cost-effective for your particular situation, but then again, 4- or 5-year-old technology may do the job just as well for the foreseeable future.

Don't just choose an instrument choose a company. The company will be your chief resource, for better or worse, in getting the most value and efficiency from an instrument. Check out track records. Once you have identified a manufacturer talk to satisfied, or unsatisfied, users. The more closely a colleague's laboratory situation mirrors your own (in terms of volume, type of institution, personnel level, and so on), the more valuable his or her comments will be. Ask about the instrument, of course its reliability, performance, user-friendliness, data handling, and other relevant concerns; but also dig for feedback on the manufacturer's ongoing commitment to service and customer satisfaction. Are repair technicians easy to reach on the phone? Were training resources adequate? Has the manufacturer met the sales representative's promises? Is reagent delivery hassle-free?

Implementation: Instrument validation

Quality Assurance standards recommend that laboratories should characterise the baseline performance of each instrument prior to conducting patient testing.

Every laboratory must be able to prove that prior to releasing a patient's test result, it can be able to obtain performance specifications for accuracy, precision, and reportable range of patient test results, comparable to those established by the manufacturer of the instrument. The laboratory must also verify that the manufacturer's reference range is appropriate for the laboratory's patient population. Other critical factors such as specimen types, specimen volumes, and time required for analysis, rate of

analysis, personnel required, efficiency, and safety must be considered during the selection of the instrument.

The approach to instrument validation will be to perform a series of experiments designed to estimate certain types of analytical errors e.g., a linearity experiment to determine reportable range, a replication experiment to estimate imprecision or random error, a comparison of instruments to estimate inaccuracy or systematic error, or interference and recovery experiments to specifically estimate constant and proportional systematic errors (analytical specificity) and a detection limit experiment to characterize analytical sensitivity.

1- The linearity or reportable range experiment: a minimum of 5 specimens with known or assigned values should be analysed in triplicate to assess a reportable range.
2- The replication experiment: a minimum of 20 replicate determinants on at least two levels of control materials are recommended to estimate the imprecision or random error of the instrument
3- The comparison of instruments experiment: a minimum of 40 patient specimens should e analysed by the new instrument and an established instrument to estimate the inaccuracy or systematic error of the new instrument.
4- The interference and recovery experiments: common interferences like lipaemia, haemolysis and elevated bilirubin are usually tested, along with potential that are specific to certain tests. Recovery experiments are used to test competitive interferences, such as possible effects of proteins and metabolics in the specimens.
5- The detection limit experiment: generally, a blank specimen and a specimen spiked with the amount of analyte in the manufacturer's claim for the limit of detection are each analysed 20 times.

The data collected in the different experiments needs to be analysed to provide an estimation of the analytical errors that are focus of each experiment. The acceptability of these errors is judged by comparison to standards of quality i.e., recommendations for the types and amounts of analytical errors that are allowable without invalidating the medical usefulness of the test results.

A critical review of literature is a good place to start when selecting and evaluating an instrument. The literature includes scientific papers as well as manufacturer's descriptions. However it is necessary to impose your own system of organisation, data analysis, and data interpretation. After this, resolve any differences between your conclusions and those of the manufacturer. Document the validation process. If the instrument is acceptable prepare an SOP to standardize the use of the instrument. Prepare teaching materials for in-service training. Select appropriate QC materials, control rules and numbers of control measurements to monitor routine performance.

Acquiring a new analyser provides the opportunity for improvement in the laboratory's performance and patient care. A well-formulated plan will allow laboratories to better schedule for instrument replacements, as well as periodic revalidations that will guarantee high quality testing and continuous adoption of new technology into the future◀

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By Nicholas Mburungu

DML in Selebi Phikwe

Mr Nicholas Mburungu validating results

Situated in the BCL Mine hospital, DML Phikwe branch is a highly equipped modern laboratory with machinery for routine Hematology, Biochemistry and Microbiology work. The lab mainly serves the BCL Mine hospital and Doctors in Selebi Phikwe and surrounding areas on 24 hours on call services thanks to the tireless Lab scientist Mr. Nicholas Mburungu. Specialised tests not done in Phikwe are referred to the main lab in Gaborone by an overnight express service and results are sent back electronically, thus ensuring timely release of results to the clinicians.

The lab also works hand in glove with the BCL Mine HIV coordinator Mr. Habangana who is pleased with the partnership especially the timeous dispatch of HIV monitoring results. The Senior Medical Doctor for BCL Mine hospital Dr F Le Roux has described the service from Diagnofirm as Efficient and Reliable. Our warm gratitude to the Phikwe community for this partnership◀

By Maoriya Mangwendeza, QA Officer, DML

The Quest for Quality Excellence

SIX SIGMA AND THE MEDICAL LABORATORY

"Quality is never an accident; it is always the result of high tension, sincere effort, intelligent direction; it represents the wise choice of many alternatives" Will A Foster

From Total Quality Management (TQM) to Continuous Quality Improvement (CQI) to Improving Organizational Performance (IOP) to ORYX and now Six Sigma! Six Sigma is the current sensation in Quality Management programmes and the rate at which the QM programmes are being changed shows the important position Quality has taken in service provision.

The different QM Programme names reflect a change in what each programme emphasizes on not a change in the overall principles. TQM emphasizes on a broad perspective for QM. It identifies the importance of customers and their needs and then focuses on the processes as the critical mechanism for producing the desired quality. CQI puts emphasis on the fact that quality is not static but needs to be improved on an on-going basis. Teamwork and group problem solving are important in CQI. IOP emphasizes that QM applies not only to work processes but also to management processes that determine how the various parts of an organisation work together to deliver quality to their customers. ORYX emphasizes that outcome measurements help an organisation measure how well it is doing. Six Sigma emphasises on making QM a more quantitative science. It provides a quantitative definition of the desired specifications for the production processes and allows those specifications to be related to customer needs or requirements. Quality can truly be measured and managed in a more quantitative way if Six-Sigma is recognised as a fundamental goal process.

Six sigma is mainly about process improvement, a process being the most fundamental unit of a business, which can be managed and describes how the business produces value. The six-sigma principle encourages the first step to be the analysis of the processes in a business to determine how they work and a well-designed process being critical to achieving quality.

To have a better insight into Six-Sigma, we shall look at where it all began. Motorola used Six Sigma quality as the foundation of its Continuous Improvement Programme and the goal was to have Total Customer Satisfaction and it achieved a dominant market position in pagers and cell phones. In 1985 Bill Smith at Motorola demonstrated a correlation between how often a product was repaired during manufacture and its life in the field. Defect levels in the defects per million rather than defects per hundred were needed to improve the reliability of semiconductors and electronic products in order to compete with the Japanese. Hence the development of the Motorola six-sigma quality programmes and with its land mark quality level of 3 defects per million. Six sigma was intended to improve the quality of processes that are already under control i.e. the major special causes of processes problems have been removed.

Mr. Silas Nunu in Haematology Dept

The output of these processes usually follows a Normal Distribution with the process capability defined as +/- 3 sigma. Process capability or sigma capability is an industrial term that characterises how the tolerance specification of a product relates to the centering (bias) and variation (SD) of the process. High capability means that the process can readily produce a product within the tolerance specifications. Low capability means that the process will likely produce products outside the tolerance specifications i.e. defective products or defects.specifications i.e. defective products or defects.

They observed that the process mean would vary every time a process is executed using different equipment, different personnel, different materials, and e.t.c. The observed variation in the process mean was +/- 1.5 sigma. Motorola decided on a design tolerance of +/-6 sigma was needed so that there will only be 3.4 dpm. This was the defined as the six-sigma quality.

Six Sigma deals with Define, Measure, Analyse, Improve and Control. Process sigma is the primary unit of measure. It is determined from an analysis of the number of defects observed in a process. Performance is compared to the best in class sigma for that process to determine whether the process needs to be improved or the product service needs to be redesigned. When improvement is necessary, design of experiments is used to determine which product or process parameters are most important and specific parameter values that will give the best performance. Statistical Process Control is used to continually monitor product and process performance. Customer requirements, design quality, measures, and continuous improvement are key elements of Six-Sigma process improvement.

Most of the total quality improvement programmes do not achieve their

SIX SIGMA METHODOLOGY

objectives because there is lack of commitment to the specific improvement actions and to their effective implementation. Six sigma as a system overcomes that weakness by

- Focusing on the common commitment to meeting customer requirements
- Developing a consensus set of improvement actions
- Prioritising those actions
- Establishing measures that assume accountability in implementation.

PHASE 1

Define the failure or defect from the customer's point of view and then investigate the process of interest that needs to be improved. Senior personnel analyse customer, financial, operational, and quality data to identify improvement opportunities and quantify possible improvements. Improvement goals are then aligned with strategic business objectives.

PHASE 2

Collect data regarding all the various process involved

PHASE 3

Product line teams use value analysis style workshops to develop and evaluate specific products/service and process improvement needed to meet quality, productivity and cost objectives. It is necessary to determine those process attributes that have the greatest relation to the defects and those that have a causative relation.

PHASE 4

Multi-functional teams analyse products and processes in depth and develop implementation plans for improvements. Here the processes are redefined to remove the causes of defects.

PHASE 5

Full documentation of the new control procedures. Strong management support is essential in making significant and lasting improvements. Decision-making needs to be crisp. Follow-up needs to be relentless. Improvement goals and the implementation schedule must be met to achieve the projected returns.

process and training methods is done to control the new process. A process control scheme is established to obtain key process measures and to track them for each time a process is performed. These are quality control procedures. Strong management support is essential in making significant and lasting improvements. Decision-making needs to be crisp. Follow-up needs to be relentless. Improvement goals and the implementation schedule must be met to achieve the projected returns.

Any process done has two inherent types of variation, random variation and bias. A six sigma-capable process has so little random variation that the standard deviation when multiplied by 6, gives a quantity that meets the customer's requirements for that process. In other words 6D is equal or less than the process specification.

If the assay shifted off target by 1.5sd, this would leave 4.5 SD for random variation within the bounds of customer satisfaction. This is the basis for Six Sigma.

Once the sigma capability of the process is known, one can then determine what level of improvement is necessary. However not all processes can be improved to this ideal but the closer one gets to six sigma, the fewer the defects and the lower the cost of production. A better process means higher efficiency saving of money and effort and better customer satisfaction.

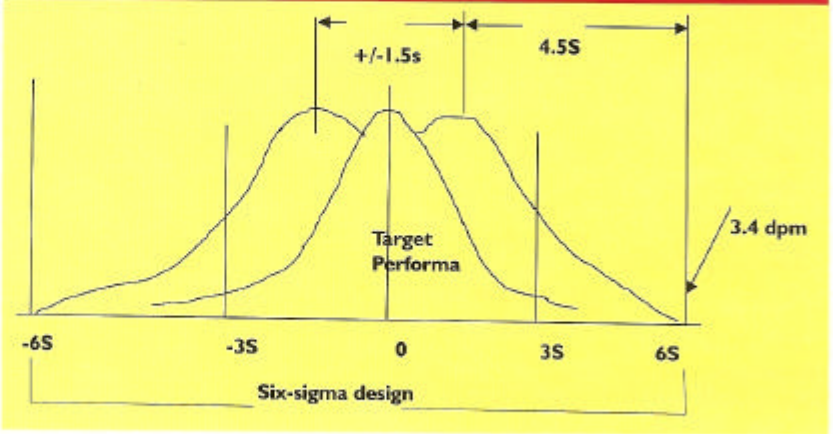
Although started in other industries, Six Sigma is very much applicable to health care delivery systems. It characterises process performance and one can understand the magnitude of defects in healthcare process.

Service production specification will also differ when it comes to medical laboratories. It is difficult to improve on a test as it comes with manufacturers specifications otherwise a better more expensive method will have to be used. A better alternative will be to make improvements to the quality control procedures to match their error detection capabilities to the performance of the testing process. This improvement of detection of errors will be through careful selection of quality control procedures, and then one will reduce the number of defective test results. With properly designed controlled procedures, one will also minimise false reject-ions, which reduces the number of repeat tests, saves time in trouble shoot-ing or mini-mises inter-ruptions or de-lays in the delivery of test results.

Quality design in a laboratory mu-st begin with analy-tical quality because it is the most essential quality characteristic of any laboratory test. For example turnaround time is an important quality characteristic, but it doesn't matter how fast the result is reported if the result is wrong. The laboratory must first be able to produce a correct test result before any other quality characteristic becomes important.

For the medical laboratory, six sigma provides an opportunity to communicate measures of performance quality in a common format that is understood by people outside the laboratory◀

SIX SIGMA PERFORMANCE



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Continued From page 1

Recent events @ DML

Nicholas and the Humalyser 900

avoids the intrusive method of sub-culturing the blood cultures and thus avoiding laboratory contamination. It also improves identification of blood pathogens timeously.

Installation of the Option 2 Plus Coagulation machine

Diagnofirm also moved to automated Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) studies. This was through the installation of the Option 2 Plus machine. This machine will relieve the lab scientist of the tedious manual method and also improve the accuracy and precision of results sent out to doctors. The machine has already found a home in the Haematology department, where it is performing a number of coagulation studies for patients. The principle of the machine is based on the detection of clot formation after addition of the appropriate reagents(eg calcium chloride or thromboplastin). This it does through a photodiode that measures the variations in the optical density of the reaction medium. Quite state of the art, hey?

Presentation on HIV and Hepatitis mutations

DML' s department of continuing health education sponsored a lecture on HIV sub-types and Hepatitis mutants by Dr. Stephen Belcher, Abbott's area Business Development Manager for Hepatitis, Retrovirus and TSE in Africa, Europe and Middle East. During his presentation, Dr Belcher pointed out the different test kits used in HIV and Hepatitis testing and this was very informative in that he also pointed out the different stages at which detection of virus is possible and more importantly when it can produce false negatives. He also then pointed on which test would be best to use in such instances.

The end of the presentation was marked by the presentation of certificates of accomplishment for

Dr. S. Belcher at Gaborone Sun

Nuclisens EasyQ training to Messers D. Mhlabi, W. Mpofu, N. Bozongwana, and C. Mudenyanga by Mrs. W. Chand. Further testimony to Diagnofirm's

Motto:
" Pathology you can trust"

Jokes Corner

Did you know that

Diamonds are thought to be made from dead bacteria.

The main constituent of diamonds is carbon and those suspected to have an organic origin are the so-called "eclogitic" diamonds. These diamonds may have obtained their carbon from bacterial communities that once lived around hydrothermal vents and were turned into diamonds by metamorphism (heat and pressures). So those sparklers of yours may just be clumps of billion-year-old bacterial corpses...

How do you tell the difference between male and female chromosomes

Pull down their genes

A man after having his healthy serving of steak then asks for a tooth pick from the maid. The maid returns to tell him there are no toothpicks left. The man, puzzled at this saying to the maid: "I bought these toothpicks only recently, don't tell me they all finished" To which the maid replies: "I'm also baffled. It must be these kids wasting them. I always make sure I return them after using!!"

Can u believe things people do. I was in church when this guy next to me started smoking. U know, I was so shocked I nearly dropped my beer.