DIAGNOSTICS UPDATE .COM

NEWSLETTER
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From my Keyboard

I must say I am having the time of my life, doing the job I love and at the same time able to pursue my number one passion, dissemination of information. I am one of those people who believe that information must be shared for the benefit of all mankind, which can turn to be one of the main ways to combat the spread of disease. Forearming people with information can help them take the necessary precautions and hence stop diseases before they set in. In that regard, I sincerely hope this newsletter, to some extend, has been of great help.

The science of genetic testing has come a long way and has emerged as on of the most valuable tools in diagnostic laboratory medicine. Genetic testing can be used in the medical field to diagnose and treat diseases as well as solve cases in the legal world with extremely high levels of accuracy and precision. With so many options now available as a result of genetic testing, it would be of great benefit to find out from the laboratory how genetic, in all its different forms, can help in your particular situation.

Great and wonderful things are in store at Diagnofirm and in our next issue, we will give you an in-depth look into the new look Diagnofirm Medical Laboratories.

Till then, stay informed!

Munyaradzi Mangwendeza Ed.
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Inside this Issue

Mr & Mrs Chand hold the International star for quality presented by BID in paris France

DIAGNOFIRM MEDICAL LABORATORIES

by Desire B Mhlabi

Recent Events @ Diagnofirm

Diagnofirm Leads in the fight against Hypertension

The world Hypertension Day 2006 was commemorated on Saturday 13th of May and Batswana from all walks of life converged at the Main Mall (Gaborone) for the various festivities lined up for the day. The commemoration was organized by Diagnofirm Medical laboratories in conjunction with other healthcare providers like The Cardiac clinic, Bhorheinger Ingelheim, Roche Diagnostics and Pharmaceuticals, Medswana and Pfizer.

The theme for this year's event was "Treat to goal" and it was in realization of the fact that many Hypertensives are inadequately treated and don't receive full benefit of either Lifestyle modification or drug therapy. The goal was basically to underscore the health consequences of Hypertension (high blood pressure) and encourage people to have their Blood pressure tested and then do something about the results. Hypertension combined with other conditions like Diabetes mellitus, obesity and high blood cholesterol is by far the largest risk factor for heart disease, stroke and kidney diseases (Hypertension if untreated may lead to end stage renal failure). In the modern world, due to rapid lifestyle changes characterized by highly refined foodstuffs and sedentary patterns (lack of exercise) obesity, type two Diabetes mellitus and hypertension are emerging as health risks of grave proportions. Many people no longer exercise, walk their pets but instead spend the whole day in low activity events like internet browsing, television watching and driving around, some consuming alcohol and even smoking.

The World hypertension Day commemoration therefore was to basically raise awareness, test people and offer advice on what action to take. Several speakers among them Professor Kiran Bhagat and

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Tiger Design and Graphics

By Munyaradzi Mangwendeza

DISPUTED PARENTAGE ANALYSIS (DNA PATERNITY TESTING)

DNA parentage analysis or testing allows for the determination of the true biological parent of the child. This method is highly accurate and has become the method of choice in resolving the conflict of child parentage dispute. Additionally, DNA parentage testing can be submitted as acceptable evidence in a court of law.

DNA (deoxyribonucleic acid) is the genetic blueprint, which contains all the information necessary to make a living being. It is responsible for determining the physical and physiological attributes of an organism. DNA is a unique and complicated structure because it remains constant for a lifetime. It can be obtained from body cells and various bodily fluids such as blood, urine and synovial fluid. DNA is wound into tight threadlike structures called chromosomes, which are found in every cell in the human body. Humans have 46 chromosomes in total. Half of these come from the mother in the egg and the other half from the father in the sperm.

Certain regions of human DNA show variations between people. At each of these regions a person possesses two genetic types known as alleles, one inherited from each parent.

By looking at a number of these variable regions in a person, a DNA profile is produced. By comparing the DNA profiles of a mother and child it is possible to determine which half of the child's DNA was inherited from its mother (maternal alleles). The other half must have been inherited from the biological father (paternal alleles). The alleged father's profile is then examined to determine whether he has DNA types in his profile that match the paternal alleles in the child. If the man's DNA types do not match the child's, he is excluded from being the biological father, if it matches, he is not excluded as the father.

If a man is not excluded as being the biological father of a child, a probability of paternity is reported. The figure is usually greater than 99.5%. It is never possible to prove 100% that a man is definitely the biological father of a child, as there is always a chance however remote, that another man in the population may have DNA types which match that child. A total of 15 independent tests are done in the profiling. If a man does not match in two or more tests, then it is usually accepted that he is not the true father of the child. Our testing provides a probability of paternity of 99.9%.

In order to determine parentage, the child, the father and/or the mother must participate. Information such as name, address, and birth date and identity card numbers will be gathered from each participating individual. To maintain quality control, specimens are collected form our laboratory facility. However in cases where coming to the laboratory is not feasible because of medical conditions or location, specimens can be collected in a qualified medical facility. You can contact the laboratory to accommodate any special needs. Specimens of blood will be collected from each individual. The mother the child

Table I

In this report, the numbers that the child shares with the mother are in bold type and the numbers that the child shares with the father are in italics. This is an example of a report for a man who is the biological father of the child.

	MOTHER	CHILD	PUTATIVE	FATHER
SURNAME	**DOE**	**DOE**	**DOE**	
FIRST NAME	**JANE**	**JONNY**	**JOHN**	
ID No	**1522155555**	**NA**	**254615565**	
LOCUS	MOTHER	CHILD	FATHER	MATCH
D3S1358	**14**/17	**14**/*16*	16/*16*	YES
vWA	**20**/23	*16*/**20**	*16*/17	YES
FGA	**21**/21	**21**/*31.2*	*23*/*31.2*	YES
AMELOGENIN	XX	XY	XY	
D8S1179	**14**/16	**14**/*15*	13/*15*	YES
D21S11	**28**/29	**28**/*35*	27/*35*	YES
D18S51	**17**/17	*16*/**17**	15/*16*	YES
D5S818	8/9	8/*12*	*12*/12	YES
D13S317	**11**/12	**11**/*11*	*11*/12	YES
D7S820	**11**/13	*10*/**11**	8/*10*	YES
D16S539	10/**11**	**11**/*11*	*11*/11	YES
THO1	8/8	7/8	7/9.3	YES
TPOX	9/11	9/*11*	9/*11*	YES
CSF1PO	9/10	9/*11*	9/*11*	YES
Penta D	**10**/11	*2.2*/**10**	*2.2*/9	YES
Penta E	8/9	*5*/**8**	*5*/9	YES

PROBABILITY OF PATERNITY
99.999 %
(Prior Probability = 50%)
Note: The Probability of Paternity calculation assumes a Prior
Probability of 50%, thus making 2 assumptions, namely:
1) The biological father is EITHER the alleged father
2) OR someone who is entirely unrelated.
Before considering the DNA evidence the probability is 50% either
way.
A calculated Probability of Paternity greater than 99.800% is considered
proof of paternity.Maternal match: the results show that the maternal profile matches the child's DNA profile .PATERNAL MATCH: The results of DNA profiling analysis of the 3 persons identified above indicates that JOHN DOE cannot be excluded as the biological father of JONNY DOE. The child exhibits a compatible obligatory paternal allelic profile with that of JOHN DOE. ANALYSIS METHOD PowerPlex 16 STR kit manufactured by Promega Corp., Madison, WI. analysed on an ABI Prism 3100 Genetic Analyser.

and the father should all be tested. If the mother is not available, DNA tests can still be performed, however the results will be less informative than when both parents are tested. When the mother's profile is available it is possible to determine which half is of the child's DNA was inherited from the father. Without this information the chance of detecting that a non-father is excluded is decreased. In cases without the mother, the probability of exclusion is decreased. Single parent testing is performed in exceptional cases. If the child is under 18 years of age, consent must be obtained from the child's mother or legal guardians before testing can be performed on a sample from the child. There is no need for a doctor or lawyer's order for DNA parentage testing. Clients can come into our facility for counseling and testing. If there is any need for us to communicate with any involved relations, doctors or lawyers, the clients should authorize us to do so.

As soon as a child is born, it is possible to perform DNA parentage testing. The test result reports are typically ready within 21 working days following receipt of the specimen. Results are given to the mother, alleged father or their legal representatives. No results will be issued over the phone. Information of any kind regarding a case will not be released to anyone other than the tested parties and their named representatives without written order. It is also important to note that paternity testing is not considered to be a medically necessary procedure; therefore it is not covered by medical aid societies.

For any further information on paternity testing or any other form of DNA testing please contact Diagnofirm Medical Laboratories Biochemistry department.

Understanding the Paternity results.

To understand your paternity test results, it is important to remember that a child receives equal amounts of genetic material from its father and mother. In the paternity test, several locations on the tested DNA are used to determine the likelihood that the tested man is the father. These locations are listed in the locus column on the left side of the paternity test results. For each location tested, the mother, child and alleged father's result (or phenotype) is represented by a number in the final report. When you read the result, it is important to first compare the numbers for the child and mother. Because the child received half of its DNA from the mother, one of the numbers in the child's column must match one of the numbers in the mother's column. Once you have determined which number of the child's matches the mother, the child's remaining number must match one of the father's numbers. If the tested man has the same number as the child, he cannot be excluded as the biological father of the child. If the tested man does not share that number with the child, the man can be excluded as the father of the child for that location on the DNA. If the father is excluded for two (2) or more locations in the DNA, the man cannot be the biological father of the child.

Table 1 and 2 show examples of paternity testing results

References

Genes, Genome and Human Genetics - Department of Genetics, Division of Biological Sciences, Rutgers University and Waksman Institutes

UK Health Department Code of Practice and Guidance on Genetic Paternity Testing 2001

Table 2

In this report, the numbers that the child shares with the mother are in bold type. It is easy to see that the child does not share its remaining number with the tested man, indicating that the child did not receive its DNA from the tested man

SURNAME	MOTHER DOE	CHILD DOE	PUTATIVE DOE	FATHER
FIRST NAME	JANE	JONNY	JOHN	
ID No	1522155555	NA	254615565	
LOCUS	MOTHER	CHILD	FATHER	MATCH
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D7S820	**11**/13	*10*/**11**	8/*9*	no
D16S539	10/**11**	**11**/*11*	9/1	no
THO1	8/8	7/8	9/9.3	no
TPOX	9/11	9/*11*	9/*10*	no
CSF1PO	9/10	9/*11*	9/*13*	no
Penta D	**10**/11	*8*/**10**	*2.2*/9	no
Penta E	8/9	*5*/8	*8*/9	no

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ANALYSIS METHOD

PowerPlex 16 STR kit manufactured by Promega Corp., Madison, WI. analysed on an ABI Prism 3100 Genetic Analyser.

GUIDELINES FOR GENETIC TESTING

Chromosomal and genetic-biochemical analyses as well as DNA-based testing are being used clinically as a part of laboratory tests in modern day genetic medicine. We expect that genetic information from such testing will play an increasingly important role in diagnosis, treatment, prevention, and genetic counseling modalities. On the other hand, because the testing conveys important genetic information that remains unchanged through an individual's life time, there are some important issues for discussion, such as informed consent at testing, protection of an individual's genetic information, handling of specimens used in testing, and genetic counseling before and after testing. In addition, as individual's genetic information reflects genetic characteristics involving not only the individual but also the individual's relatives, the establishment of bioethical guidelines is required.

With future progress in genetic medicine and genetic testing, it is hoped that these guidelines also move forward, subject to appropriate and timely revision. Testing guidelines differ from country to country (due to social and cultural differences). Below are some generalized guidelines applicable in most countries.

I. Testing to be directed by the guidelines

These guidelines concern genetic testing (chromosome analysis, biochemical testing and DNA-based testing) for gene mutations, chromosomal aberrations or their related germline abnormalities. The tests include those for clinical diagnosis, carrier detection, presymptomatic diagnosis, disease susceptibility estimation (including so-called diathesis diagnosis), pharmacogenetic diagnosis, prenatal diagnosis, and newborn screening for inborn errors of metabolism. However, the guidelines do not cover tests for gene mutation, gene expression and chromosome abnormality which are confined to somatic cells such as cancer cells nor those for infectious agents, e.g., bacteria and viruses, and DNA testing for forensic medicine such as determination of parentage (paternity testing).

II. Practice of Genetic Testing

1. Genetic testing should be carried out only when considered clinically and genetically appropriate and useful, as a part of comprehensive genetic medicine systems.

   (a) Medical facilities that offer genetic testing must provide systems for comprehensive genetic medicine, including genetic counseling.

   (b) When performing genetic testing, its analytical and clinical validity, and clinical utility that stand at the sufficient levels should be guaranteed.

   (c) Facilities that carry out genetic testing must conscientiously pursue new data in medical genetics and concordantly must show a measurable improvement in diagnostic accuracy.

   (d) Because of technological ease of sampling, genetic testing may be able to be performed bypassing standard medical procedures such as blood sampling. Nevertheless, genetic testing bypassing medical facilities should never be performed.

2. Those health-care professionals involved with genetic testing and its related genetic counseling should take great care to respect the human rights of individuals of being tested (further referred to as examinees) and their relatives and family members. All efforts should be made to protect examinees and/or relatives from possible discrimination (genetic discrimination) on the basis of their genetic information, such as specific karyotypes (chromosome constitutions), genotypes, haplotypes and/or phenotypes. In addition, all efforts should be made to offer appropriate medical care, clinico-psychological and societal support to these individuals.

3. The directing physicians involved with genetic testing should obtain informed consent on the genetic test from examinees prior to the testing.

   (a) Informed consent requires understandable explanations of the following elements to examinees: the purpose, method, implications (including expected merits and demerits to examinees), accuracy (particularly regarding unavoidable diagnostic limitations), alternative choice other than the testing, and accurate information on any discomfort and/or medical risks of the testing. All these require written explanation in addition to oral explanation.

   (b) Decision on whether or not to undergo genetic testing should be made on the basis of a free right of autonomy for examinees. The directing physicians should explain the individual rights of not being tested, the freedom to withdraw at any time, and to refuse disclosure of data after testing. Also individuals being tested must be informed that they have the right to receive unrestricted health care, even if their decision is not to participate or to withdraw from the test process. However, in these cases, it should be explained that the medical benefits that may be available from genetic testing will not be used as a treatment modality.
   Physicians are enjoined to offer the most appropriate medical care while respecting the decisions of examinees.

4. Genetic testing may not be indicated in the following cases:

   (a) When the directing physicians conclude that a test is ethically and/or socially inappropriate, or when against their personal, moral, ethical principles, the physicians may, with thorough explanations, refuse to carry out the genetic testing, even though examinees request it. Instead, the physicians should seek to introduce examinees to other alternative health-care providers.

   (b) Pediatric genetic testing for an adult-onset disease that has no preventative or therapeutic options should be fundamentally avoided.

   (c) In view of protection of future individual's autonomous decision making, genetic testing in minors should be postponed until adulthood, except for diseases for which therapeutic and/or preventive options are available based upon test results, or for urgent cases.

5. In principle, samples obtained for genetic testing (further referred to as samples) should not be used for

purposes other than the test at hand.

(a) In the case where samples are expected to be used for other genetic tests that may be of potential future benefit to examinees or their families, new informed consent on storing of samples should be obtained with clear explanation of the implications of the tests and sample storing method.

(b) When stored samples are used for new genetic testing, new informed consent for the new testing should be obtained.

6. Samples for genetic testing must be stored with utmost care. Confidentiality of personal, identifiable information as well as of individual genetic information resulting of the testing must be a top priority.

(a) As a fundamental rule, regular medical information and genetic information linked to specific individuals must be stored separately.

(b) Information regarding personal identification and individual genetic information must be kept confidential. Directing physicians, genetic counseling providers and/or any responsible officials of medical facilities should strive to prevent such information from leaking to any third party.

(c) When a part of the results of genetic testing is to be entrusted to another laboratory testing facility or institution, samples should be rendered anonymous before commission, and personal, identifiable information must be kept confidential.

Disclosure of Genetic Test Results

1. The rights of examinees to know or not to know test results should be equally respected.

2. When disclosing genetic test results, the wishes of examinees to have results disclosed or to refuse them should be respected. Individual genetic information gained from testing must be subject to confidentiality, and therefore fundamentally should never be disclosed to relatives or any third party without obtaining permission from the examinees themselves. Even when the examinees agree, individual genetic test results should be protected from access by employers, health insures and schools.

3. When disclosing test results to examinees, the directing physicians should explain the results with adequate, understandable language. In the cases where the test was unsuccessful or unsubstantial for diagnosis, examinees should be so informed.

4. Those who engage in genetic testing should be constantly vigilant against the use of test results for social discrimination.

5. When the directing physicians judge that the accompanying of trusted person(s) is more suitable than the examinees alone regarding disclosure and explanation of test results, they should so recommend.

Genetic Testing and Genetic Counseling

1. Genetic testing should be carried out after adequate and thorough genetic counseling.

2. Genetic counseling should be practiced by a clinician, e.g., a clinical geneticist , who is experienced in genetic counseling and has appropriate expertise in genetic medicine. Genetic counseling providers should have a good grasp of the examinees' psycho-emotional condition. Genetic counseling providers may seek cooperation from psychiatrists, clinical psychologists, genetic nurses and social workers, to work as a team.

3. Genetic counseling providers should work as hard as possible to provide accurate, most current, disease-related information to examinees. This includes information on the frequency, natural history, and recurrent risk (genetic prognosis) of the disease, as well as information on the implications of carrier detection, prenatal diagnosis and disease susceptibility tests. Genetic counseling providers should pay enough attention to heterogeneity in gene mutations, clinical manifestations, prognosis, and effects of treatments, even in the same disease.

4. During genetic counseling, genetic counseling providers are responsible for providing examinees with thoroughly understandable explanations in clear, simple language, and should confirm that examinees sufficiently understand the matters at hard. When examinees request attendance of accompanying people or when judged for its necessity, other people may be present during genetic counseling sessions.

5. Pretest and post counseling should be adequately provided .

IN CONCLUSION

However, those who are expected to respect the guidelines may remain limited principally within the members of these societies. In other words, even if unethical, antisocial and inappropriate genetic testing is being practiced, the guidelines have no jurisdiction to regulate or prevent this kind of testing, when people other than the society members perform it. In this way, examinees can receive medical benefits and avoid the potential suffering incurred by unwarranted, meaningless genetic tests. The absolute necessity of enforced confidentiality of individual genetic information is another important issue, calling for utmost care in application. Unless genetic testing is carried out under the aforementioned considerations, some people may refuse to be tested, because of fear of such discrimination. We finally hope that, with these guidelines as the foundation, a more effective genetic testing system based on both human rights and legislation can be established.

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By Dr. Debashish Gangopadhyay, Physician Specialist, Cardiac Clinic

Women and Heart Disease: A Global Perspective

The Global impact of cardiovascular disease in Women

The common view that CVD is a men's health problem has overshadowed the recognition of the significance of CVD for women's health. Of the 27 million deaths worldwide in women each year, almost 10 million result from CVD and, of these, two thirds occur in developing countries. Rheumatic heart disease is a significant component of CVD.

Not only are coronary heart disease and stroke the first and second leading causes of death worldwide, but they will remain so in the next 20 years and beyond. Although ranked fifth and sixth now in terms of disability, estimates suggest that, by 2020, heart disease and stroke will rank second and third. The majority of the burden of disability associated with heart disease and stroke already falls in low and middle income countries, not high income countries where most of the resources are concentrated.

Results from a major international collaborative study, the WHO MONICA Project, confirm the gender differences in mortality statistics. The same variation is observed for coronary heart disease and stroke event rates. This major international collaborative study, which measured trends over 10 years, suggested that approximately two thirds of the decline in mortality in heart disease and one third of the decline in stroke could be explained by fewer new events. Reduction in event rates was related to both improvements in the major risk factors and improvements in treatment.

Patterns and Trends in Modifiable Risk Factors

Patterns between countries reflect to a large extent, the profiles of the major risk factors that heart disease and stroke share:

1. Smoking
2. High blood pressure
3. Cholesterol
4. Body mass index (BMI).

Although the prevalence of hypertension in middle age (35-64 years) is similar in men and women, there are wide variations in smoking prevalence between women and men; smoking prevalence remains low for women in many countries.

The pattern is changing, however. Data from the MONICA study show 10-year trends in cigarette smoking in women and men ages 35-64. In men, in most populations, a decline in smoking was noted, the exception being in 4 populations:

1. Yugoslavia
2. Russia
3. Canada
4. China

In these 4 countries, smoking in middle-aged men increased by 15%. In women, however, a decline was registered in about only half of the populations, and there was a tendency toward an increase in a number of populations. In 5 of these countries, Russia, Germany, Belgium, Spain, Poland, the increase was as much as 10%.

In summary, the MONICA risk factor trend data show that over 10 years, smoking rates were most often down in men but mixed in women. Other main modifiable risk factors show varying patterns. Blood pressure was mostly down in both men and women, total cholesterol also declined slightly in most populations, and BMI is on the increase, more so in men than in women in these populations.

The Aging of Populations

One of the major achievements in the past half-century has been the dramatic improvements in life expectancy; improvements are projected to be even more steep in less developed countries than in developed countries. The decline in fertility combined with a decline in CVD mortality rates is the main reason for improvements in life expectancy and the growth of the older population. The older population in large countries in rapid economic transition, such as Indonesia, India, and China will increase 3-to-4 fold in the next few decades, compared with a relatively small increase in the United States, Australia, New Zealand, and Europe. Aging alone will tend to increase the burden of CVD unless prevention is taken seriously.

Hearts and Hormones

Menopause is a universal process that occurs in women who are around 50 years old in both developed and developing countries. In developed countries, most women are in good health at this age. In many developing countries, by the time a woman reaches menopause, her health may already have been undermined, not by her hormonal state but by the aftermath of health problems associated with reproduction and by the social and environmental conditions under which she lives.

It is ironic that the increased attention to the subject of heart disease in women is mainly a consequence of the promotion of hormone replacement treatment to women. Less widely known is the impact of smoking on the onset of menopause. Women who smoke, on average, reach menopause 2 years earlier than nonsmokers.

Menopause has been promoted in many western countries to such a degree that large proportions of perimenopausal and postmenopausal women use hormone treatment, not just for relieving distressing hormonal symptoms but in the belief it will prevent heart disease. There is a widespread notion that when the decline of estrogen levels occurs at menopause, the risk of heart disease increases, but there is no steep increase in heart disease in women around the time of menopause. Instead, there is a gradual increase in age-specific rates in women starting around age 50, which parallels the increase in men. Only at the oldest age group (85+ years) do the rates in women begin to converge towards those of men. A plethora of observational studies over the past few decades lend weight to the notion that hormone replacement is protective of women's hearts.

Should women be prescribed hormone replacement therapy (HRT) for the prevention of primary and secondary coronary heart disease? If not, why not? What are the physiologic mechanisms responsible for the scientific data? What have the data from observational studies shown? What do the data from both primary and secondary prevention clinical trials show?

Note: Most studies cited here used the following hormones:

Estrogen: Conjugated equine estrogen (CEE)- 0.625 mg/day
Progesterone: Medrooxyprogesterone

(MPA)-2.5 mg/day;

These medications should be assumed in the following discussions unless otherwise specified. In women without an intact uterus, estrogen is given alone—unopposed estrogen therapy—sometimes known as ERT. In women with an intact uterus, progesterone is added to the estrogen to prevent uterine hyperplasia- opposed estrogen therapy. Thus the combination therapy is often CEE-MPA. This is often referred to as HRT.

A number of basic science studies have demonstrated a favourable effect of estrogen on lipids and vascular function. Whether these changes result in clinical benefits, however, can only be determined in clinical trials.

Clinical Trials

After 20 years of observational studies, the first clinical trials examining the role of HRT in CHD prevention are emerging. The 1998 release of the Heart and Estrogen Replacement Study (HERS), a secondary prevention clinical trial in 2736 women with established coronary disease found no significant differences between the women in the experimental (CEE+MPA) and control groups. The primary end point was the occurrence of nonfatal myocardial infarction (MI) or death from CHD. Data show an early increase in coronary events in the HRT group, which tapered off after 2 years and was balanced by a decline over the next 2 years.

Another secondary prevention clinical trial (an angiographic and not a clinical endpoint study), the Estrogen Replacement and Atherosclerosis (ERA) trail, presented below by Dr. David Herrington, showed similar findings to the HERS trial, eg, no difference between the experimental (CEE or CEE+MPA) and the control (Placebo groups)

The Women's Health Initiative (WHI), a primary prevention trial of over 27,000 women with no known coronary disease, again uses CEE or CEE+ MPA.

WHI comprised 2 HT trials: estrogen plus progestin (Prempro) for women with an intact uterus (E+P) and estrogen alone (E-alone) (Premarin) for women with prior hysterectomy. The trials were not intended to explore treatment of menopausal symptoms. Rather, they addressed the value of long-term HRT in the prevention of major chronic conditions of women after menopause. The primary outcomes were all-cause mortality, coronary mortality, and several major conditions: coronary disease, breast cancer, hip and other fractures, pulmonary embolism, and colorectal cancer

Neither intervention had an impact on total mortality. Coronary disease, breast cancer, and pulmonary embolism rates were significantly increased by E+P, but this was not seen with E-alone. Both interventions caused an increase in stroke rates and a decrease in hip fracture rates. E+P caused a decrease in colon cancer rates, but this was not seen with E-alone. Dementia rates were increased with E+P; a similar trend was seen with E-alone, but this was not statistically significant. There was a significant overall increase in dementia outcome rates when the findings from both trials were combined.

In the case of differential effects between E+P and E-alone, it has been suggested that the progestin (medrooxyprogesterone) may be responsible for some of these differences. This may be correct, but this issue will require further study.

The WHI has made critically important contributions to our knowledge of disease prevention in postmenopausal women and has challenged current clinical practice and prevention policies. Many women seek advice on the value of HRT at the time of menopause, and provision of counseling is now more complex.

The evolving story of women, heat disease and hormone illustrates the importance of sound epidemiologic research in advancing the health of women.

Future Global Challenges

The main driving force of the CVD epidemic is the aging of populations combined with rapid urbanization and global changes in nutrition and smoking patterns. Regrettably, from the sparse data that are available, the risk factor profiles of many populations in developing countries is changing in an adverse direction. We need to monitor the coming epidemic of CVD in poorer countries and reassess our responses, placing greater focus on the population approach to prevention. Only this strategy can being to confront the underlying social, economic, and cultural determinants of the global CVD epidemic.

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Diagnofirm Leads in the fight against Hypertension

Specially elected MP Hon Botsalo Ntuane alluded to the fact that a lot still needs to be done in Botswana to raise awareness and promote the proper management of Hypertensives. They also called on the Government and other stakeholders to take a proactive stance towards a condition that in 2010 may overtake HIV/ AIDS as the leading cause of death in our population. Hon Ntuane shared his own personal experience and encouraged all present to exercise, go to the gym, take walks and basically take better care of themselves in order to live a better quality of life as these conditions may not only lead to death but also diminish one's quality of life.

Diagnofirm Medical laboratories in conjunction with Roche Diagnostics offered Free blood Glucose testing while the Cardiac Clinic, Bhoreinger, Roche Pharmaceuticals and Pfiezel were testing for blood pressure and Body Mass index. The campaign was a huge success as 2245 people were tested with more than 200 new people discovering that they have unacceptably high blood pressure and another 50 discovering for the first time that they could be Diabetic. Two of the participants were surprised to find out that their blood sugar was too high that they were in danger of Hyperglycemic shock. The Blood pressure statistics were almost in line with the World Hypertension league's estimation that 20% of the world adults are Hypertensive. People who tested were given souvenirs like T-shirts and Caps donated by Diagnofirm and Mascom.

The big lesson to be learnt on the day was that Hypertension and other associated conditions are slow and silent killers which may encroach over years and when fully blown are untreatable but are otherwise avoidable at an earlier stage. This means that we all need to love ourselves and make sure that we are aware of any health risks that might be slowly building in our bodies. This is enshrined in the Diagnofirm policy of promoting Good health by taking Wellness assessment to the people as we have seen with campaigns at Parliament and in Serowe already this year.

Underconstruction !

Diagnofirm medical laboratories is growing bigger and new and better facilities are underconstruction in Partial Gaborone and the project is expected to be through in July. Watch this space for more info!

DIAGNOFIRM

WHO representative Dr. Kalua Giving his speech on World Hypertension Day

Hon. M.P Botsalo Ntuane emphasizes a point on World Hypertension Day

Pro K. Bhagat of the Cardiac Clinic explaining important issues to do with Hypertension

Dr. Kalua having his blood pressure checked

Desire performing tests on Dr. Kalua as Tapiwa looks on

Mr & Mrs Chand with BID President Jose E. Prieto

Zakiyyah Chand discussing a result with Joy from Cardiac Clinic

IN PICTURES

Mr & Mrs Chand receiving the International Star for quality from BID President Jose E. Prieto

Tapiwa, Crispen and Gibson on World Hypertension Day

Delene from Bayer Health Care with her colleagues awaiting Patients coming for blood pressure measurements

Under construction - The New Diagnofirm Medical Laboratories Headquaters at Middle Star

People queuing for free testing on World Hypertension Day

Mr. Tyrone checks the patient glucose level

Zakiyyah Chand with a patient on World Hypertension Day

Mr. Chand, Zakiyyah, Desire and Donald from Gabz FMwith the winner of the holiday in South Africa Diagnofirm Sponsores Raffle Mrs Selebaleng Keitlhokile

THYROID FUNCTION TESTS.

Well Trained Laboratory Staff can significantly enhance the choice of appropriate tests and the accuracy of clinical response in any kind of disease investigation. However this is a fact that can only be supported by appropriate training and relevant information from the clinicians. Testing for disorders of thyroid function should be done whenever there are clinical findings suggestive of thyroid disease. In addition there are certain circumstances when there is an increased risk of thyroid disease, and it is appropriate to test for abnormalities of thyroid function. Risk factors for hypothyroidism include: age over 50 years, female sex, goitre, previous hyperthyroidism, history of thyroiditis, family history of thyroid disease, history of head or neck cancer, Down Syndrome, other auto-immune diseases, treatment with lithium or amiodarone, or elevated serum cholesterol.

Thryroid stimulating hormone (TSH) measurement is the cornerstone of thyroid function testing. Nevertheless, an abnormal TSH concentration alone is never an adequate basis for initializing of treatment. This should be based on the typical relationship between trophic and target gland hormones i.e. TSH, T3 and T4. Thyroid testing in the laboratory uses six basic assumptions which are:

1) Steady state conditions prevailing during testing
2) Normal trophic-target hormone relationship.
3) Tissue response proportional to serum FT4 concentration.
4) Accurate estimation of active hormone concentration.
5) Appropriate reference ranges.
6) Adequate assay sensitivity.

Presentations of thyrotoxicosis and hypothyridism are so diverse that it is difficult to rule out these conditions clinically, or to make a conclusive diagnosis until the disorder is far advanced.

Laboratory tests are definitely needed in the following instances: -

1) Thyroid dysfunction suspected cases
2) Groups with an increased risk of Thyroid dysfunction.
3) Neonatal congenital hypothyroidism
4) Thyroid Dysfunction is sufficiently common in women over 50 to justify routine testing at presentation for medical care.
5) The finding of significant intellectual impairment in the offspring of women who were mildly hypothyroid early in pregnancy.

The distinction between "overt" and "sub clinical" hypothyroidism or thyrotoxicosis is based on whether an abnormal serum TSH concentration is associated with abnormal levels of circulating Thyroid hormones T3 and T4 or whether serum TSH alone is abnormal

Prevalence of Thyroid Dysfunction

1.9 – 2.7 % people routinely tested show overt thyrotoxicosis with 1.4-1.9 % cases of overt hypothyroidism in women, with progressive increase in age, values which are 10times lower in men. Sub clinical hypothyroidism occurs 4-5 fold higher in women with about 10% women over 50 showing an increase in serum TSH with progressive increase with age. Thyroid dysfunction also appears common when younger women are tested post-partum. In general, hypothyroidism is more common with abundant iodine intake, with goiter and sub clinical thyrotoxicosis more common with low iodine intake. It is important to note that one third of all the patients who have been evaluated and treated only on clinical presentation have had a revision of the clinical assessment after laboratory tests have been carried out hence underlining the importance of laboratory tests. Laboratory tests facilitate early detection before clinical features are obvious.

Measurement of Serum TSH.

Secretion of TSH from the arterial pituitary is regulated by negative feedback from the serum free thyroid hormone concentration. Serum TSH can be precisely measured to at least 0.03 mu/l so that the lowest concentrations in normal subjects are clearly distinguishable from those formed in thyrotoxicosis. The serum TSH response to changes in serum FT4 is logarithmic, meaning a 2- fold change in FT4 induces inverse 10-100 fold changes in TSH. This feedback amplification of the Serum TSH response as the serum FT4 increases or decreases, accounts for the fact that serum TSH can fall outside the reference interval several years before there is a diagnostic change in Serum FT4. Values associated with thyrotoxicosis either overt or sub clinical are suppressed (<0.03 mu/l) and need to be distinguished from subnormal detectable values in the range 0.05 – 0.4 mu/l that do not indicate Thyrotoxicosis.

Subnormal but detectable values are common in patients with goiter, only a few who develop thyrotoxicosis, for example during severe illness, serum TSH is often subnormal without indicating any persistent abnormality of thyroid function. Suppressed TSH values <0.03 mu\l can occur during critical illness without indicating any intrinsic abnormality of thyroid function and transient to above normal can occur during the recover phase.

Table I shows conditions that need confirmatory clinical featuresverses measures of serum TSH

Common to both	Thyrotoxicosis	Hypothyroidism
Classical presentations	Heart failure	Anaemia
Goiter	Arrhythmia	Constipation
Postpartum	Eye disease	Depression
Menstrual	Anxiety state	Dementia
Neonatal	Weight loss	Myalgia
Incident finding	Diarrhea	Nerve entrapment
	Apathetic hyperthyroidism	Hyperlipidaemia
	Myopathy	Hypoventilation
	Periodic paralysis	Galactorrhoea
	Dermopathy	Infertility
	Itch	Puberty, precocious or delayed
	Thyroid storm	Delayed growth
		Hypothermia, coma

TSH and T4 Relationship

Serum TSH and serum Free T4 are both necessary for definitive assessment of thyroid status. The common types of thyroid dysfunction can be identified in a single sample from characteristics diagonal deviations in the normal Free T4 and TSH relationship (**Figure 1**)

1) N- Normal

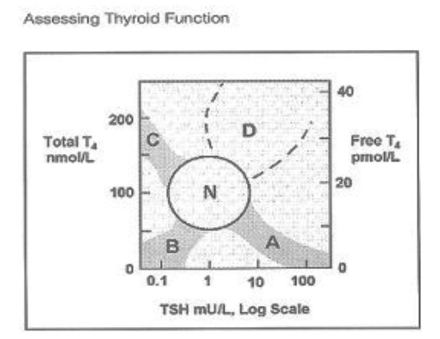

Figure 1 the relationship between serum TSH and total free T4 concentration in normal subject (N) and in various typical abnormalities of thyroid function; primary hypothyroidism (A); central or pituitary dependent hypothyroidism (B); thyrotoxicosis due to autonomy or abnormal thyroid stimulation (C); and TSH dependent thyrotoxicosis or generalized thyroid hormone resistance (D). Note that linear free and total T4 responses correspond to logarithmic TSH changes finding at A and C represent primary thyroid abnormalities, while result in B and D suggests a primary pituitary abnormality. Result in the intermediate areas are more often due to non steady state sampling conditions or an altered T4-TSH relationship.

2) Central or Pituitary – dependant hypothyroidism
3) thyrotoxicosis due to autonary or abnormal thyroid stimulation
4) TSH – dependant thryotoxicosis
5) Generalized thyroid hormone resistance.

Either TSH or FT4 can be used for initial screening and case finding but TSH gives better first line testing than FT4. However, these are some important situations in which TSH alone can give a misleading or ambiguous assessment of Thyroid Status.

Clinical Applications of TSH testing differ depending on the test group. i.e.

1) Testing of untreated subjects in whom clinical features suggest Thyroid dysfunction
2) Screening or case finding in a risk group
3) Evaluation of the response to treatment
4) Assessment when associated illness or drug therapy are likely to complicate both clinical and laboratory assessment

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Indications for thyroid diagnostic testing

For untreated Subjects

- begin with measurement of TSH alone with T4 and T3 added if TSH is abnormal or if an abnormality of TSH secretion is suspected.
- FT4 should be measured to distinguish between overt and sub clinical hypothyroidism when serum TSH is elevated.
- A suppressed or subnormal TSH level should be followed by assay of both FT4 and FT3 to distinguish sub clinical from overt thyrotoxicosis and to identify T3 thyrotoxicosis.

For response to Treatment

- In patients with newly treated thyrotoxicosis, TSH may remain suppressed for several months after normalization of FT4 and FT3. Serious over-treatment may result if TSH alone is used for adjusting anti-thyroid drug dosage.
- During long-term treatment, TSH generally gives a reliable guide to optimal drug usage.
- During long-term replacement or suppressive therapy with T4, serum TSH is the best single index of appropriate dosage.
- During early phase of treatment of hypothyroidism FT4 should also be measured because TSH may remain inappropriately elevated for many months after normalization of FT4.
- During TSH suppressive therapy with T4 e.g. in thyroid cancer FT4 and FT3 in addition to TSH should be measured to limit the degree of thyroid hormone excess because over treatment can have important adverse effects in the cardiovascular system and bone density.
- In treatment of hypothyroidism due to pituitary or hypothalamic disease, serum TSH is of no value in assessing T4 dosage, which should be judged from clinical response and serum Free T4.

For difficult diagnostic situations

- In hospital practice interpretation of thyroid function is often compromised by associated illness or by medications. There is a high prevalence of FT4 or TSH in patients with acute medical or psychiatric illness ,but when FT4 and TSH are considered together, few of these conditions shows true thyroid dysfunction.

For effects of medication

- Effects are mostly physiological on TSH and methodological on FT4. measurement e.g., iodine and lithium rich compounds cause abnormal thyroid functions.
- Lithium, which is used in the management of bipolar illness, has multiple effects in pituitary-thyroid axis hormone release. It can increase or initiate autoimmune thyroid disease with development of goiter and eventual hypothyroidism.TSH, FT4 and FT3 assays generally give a true index of thyroid status during lithium treatment.

Antibody Measurements

- For patients with sub-clinical hypothyroidism and presence of TPO antibodies, there is a 4-5 times chances of developing overt hypothyroidism. In pregnant women there is a high likelihood of developing post-partum thyroiditis.
- Persistently positive receptive abtibodies (TR ab) is a useful indicator in (1) that apparent remission of Graves diseases is unlikely to be sustained. (2) Possibility of neonatal or intra uterine thyrotoxicosis in the infant of a mother with auto immune thyroid disease (3) Defining the aetiology of atypical eye disease **Thyroglobulin**
- Serum thyroglobulin concentration should always be interpreted in relation to the prevailing level of TSH which is responsive to alterations in thyroid hormone dosage.

Comments from the laboratory on laboratory results can significantly improve clinical response to treatment of thyroid dysfunction patients. However the quality if the assistance depends on both the training and experience of the lab scientist and the available clinical information. Non-specialist users of endocrine assays are most likely to benefit from laboratory based assistance in the interpretation of the results. Sometimes lab scientists may see results that are uninterpretable or ambiguous unless the relevant clinical information is unavailable hence the need to always include clinical information on the results. Clinical correlation inevitably has an effect on the precision and reproducibility of laboratory tests and hence the diagnostic accuracy of methods employed in the laboratory. As a result clinical feedback remains a key aspect of Quality Assurance in laboratory testing

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Use of angiotensin-converting-enzyme inhibitors in renal insufficiency

The use of inhibitors of the renin angiotensin system (RAS) can significantly reduce mortality and morbidity in patients with cardiovascular disease. In addition, in patients with and without diabetes, angiotensin-converting-enzyme inhibitors (ACE-I) and angiotensin II type 1 receptor blockers (ARB) slow progression of nephropathy.

However, in clinical practice the use of inhibitors of the RAS in appropriate doses is limited due to dose-related changes in serum creatinine and potassium levels in patients with advanced renal insufficiency.

Why do ACE-I increase serum creatinine levels? ACE-I reduce the intraglomerular pressure. In combination with a decreased effective arterial blood volume which results in a reduced pressure in the afferent arteriole, the single nephron is no longer able to maintain glomerular filtration pressure and filtration rate (GFR). The combination of ACE-I therapy and hypoperfusion of the kidneys (e.g. after aggressive diuretic therapy in patients with low output heart failure) with the loss of the kidneys' ability for pressure autoregulation, are the most common causes for an acute rise in serum creatinine following RAS inhibition .

In large-scale prospective clinical ACE-I trials, patients with advanced renal insufficiency were excluded for the above mentioned reasons and consequently data on renal outcome and change of cardiovascular risk has not been determined in this group of patients.

Hou and colleagues recently investigated the effect of benazepril in 422 Chinese patients with non-diabetic renal insufficiency. The patients were divided according to their creatinine levels: Group 1 included patients with creatinine levels of 1.5 to 3.0 mg/dl (n=104) while group 2 included patients with levels of 3.1 to 5.0 mg/dl (n=224). After a 8 week run-in, patients in group 1 received 10mg benazepril bd whereas patients in group 2 received 10mg benazepril or placebo (n=112 each). Patients were followed for a mean of 3.4 years. In order to achieve a blood pressure of less than 130/80 mmHg the use of antihypertensive drugs other than ACE-I or ARB was allowed. The primary outcome was a combined end point consisting of a doubling of serum creatinine levels, end-stage renal disease or death. Secondary end points were the rate of urinary protein excretion, and the progression of renal disease (creatinine level, clearance, GFR).

102 patients (22%) in group 1, 44 patients (41%) in group 2 (benazepril), and 65 patients (60%) in group 2 (placebo) reached the primary endpoint. Treatment with benazepril significantly reduced the occurrence of the primary endpoint compared to placebo. However, patients with creatinine levels of 1.5-3.0 mg/dl (group 1) had a significant better outcome with benazepril treatment compared to patients with creatinine levels between 3.1 and 5.0 mg/dl (group 2) under the same dose of benazepril (p=0.003). Compared with placebo treatment, benazepril resulted in a significant risk reduction (43%, p=0.005) in group 2 patients independently of blood pressure reduction (p=0.009). Interestingly, benazepril was able to reduce the risk for end-stage renal disease by 40% (p=0.02) and significantly improved secondary endpoints.

The results of the study demonstrate that benazepril mediates renal protection even in advanced stages of renal disease in non-diabetic patients. This effect was blood pressure independent.

Health care providers may reconsider the restricted use of inhibitors of the RAS in patients with chronic renal disease. By any means, treatment with ACE-I in renal insufficiency requires close monitoring of renal function and serum potassium levels.

Absolute contraindications for ACE-I are bilateral renal stenosis, and serum potassium levels of >5.5 mmol/L.

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Cardiovascular Diseases in Women

Risks, symptoms, age of onset, and response to therapy are different in women than they are in men. These facts need to be taken into account more so than in the past.

Trials do not involve women enough and women's' heart conditions are not taken seriously enough. This needs to change. Fifty-five percent of all female deaths are caused by cardiovascular diseases. While research should become more gender-specific, doctors should also take these differences into account in their daily practice.

1) Epidemiology

Cardiovascular disease is the leading cause of mortality for both men and women. Worldwide about 55 percent of all female deaths are caused by cardiovascular diseases, especially coronary artery disease and stroke.

2) Risks

Unfortunately, the risk of women is underestimated because of the perception that females are "protected" against cardiovascular disease but this protection fades after menopause. Indeed, women are better protected than men against heart disease before menopause thanks to oestrogen, which increases their HDL and decreases their LDL cholesterol levels, but this advantage disappears in the postmenopausal period leaving women with untreated risk factors vulnerable to develop myocardial infarction, heart failure and stroke. This explains why the incidence of CHD in women increases dramatically in middle age.

If we analyse the SCORE charts for the 10-year risk of fatal cardiovascular events it may appear that women are at lower risk than men. However, the only difference is that women's' risk is delayed by 10 years: a 60-year old woman has an almost identical risk as that of a 50-year old man.

Furthermore, women who already had a heart attack - especially if they are diabetic, are twice as likely as their male counterparts to have another heart attack. Smoking while taking the contraceptive pill put women at an even greater risk of CHD.

3) Symptoms

The symptoms of CVD in women may be different from men's symptoms. The most common symptoms in women with a heart attack are :

in the prodromal phase: unusual fatigue, sleep disturbance, shortness of breath, indigestion, anxiety, heart racing and weak or heavy arms;

during the acute heart phase: shortness of breath, weakness, unusual fatigue, cold sweat, dizziness, nausea, weak or heavy arms.

Yet this difference is poorly recognised.

4) Diagnosis and Therapy

Due to the low number of *ad hoc* trials to study CVD in women:

CVD in women is often not promptly and well diagnosed - the majority of drugs are tested for safety and efficacy in male populations. Yet response to therapy in women may be different from those observed in males.

The Euro Heart Survey on angina has shown that women are

significantly less likely to be referred for functional testing for ischaemia, in particular for exercise testing

less likely to receive angiography even after adjustment for the results of non invasive tests, and were less likely to be referred for revascularization.

A smaller percentage of women receive secondary preventive therapies (aspirin or statin) while in fact the female gender is strongly associated with an increased risk of death and myocardial infarction, independently of age and other predictors of adverse outcome.

5) Steps to be taken

The understanding of all the differences is necessary for the improvement of the clinical management of cardiovascular diseases and for the development of possible new gender-specific diagnostic and therapeutic options.

It would be advisable to move to more focused evaluation in females. Thus, it is recommended that based on the specific question addressed, clinical trials enrolling only female patients or clinical trials enrolling a significant proportion of women - to allow for pre-specified gender analysis - should be conducted. Medical textbooks should underline the different prevalence of male and female symptoms in heart attack in women and doctors should be trained to recognise the symptoms.

Table. I

A review of cardiovascular trials conducted between 1986-1997.

Trial	Enrolled patients	% females	Reference
GISSI-1	11711	25%	Lancet 1986; 1:397-402
ISIS-2	17187	23%	Lancet 1988; 2:349-360
GISSI-2	12490	20%	Lancet 1990; 336:65-71
GISSI-3	18023	22%	Lancet 1994; 343:1115-22
4S	4444	19%	Lancet 1994; 343:1383-89
ISIS-4	58050	26%	Lancet 1995; 345:669-685
SMILE	1556	27%	NEJM 1995; 332:80-85
EMIAT	1486	16%	Lancet 1997; 349:667-674
GISSI-P	11324	15%	Lancet 1999; 354:447-52
CIBIS-2	2647	19%	Lancet 1999; 353:9-13
CHARM	7601	31%	Lancet 2003; 362:759-766

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By Munyaradzi Mangwendeza

Biological variations, laboratory results interpretation and the quest for quality

The interpretation of a patient's laboratory results varies from doctor to doctor and institution to institution. The level of interpretation covers levels from simple methods such as comparing the results to a decision limit to other more complicated computer aided interpretations. However simple decision limit interpretations are more common. With simple interpretation of laboratory data, all results are compared to some reference:

- One or more previous results from the patient
- A reference group i.e. a healthy population with a certain disease or both
- a decision limit

With this in mind, the objective of a laboratory should be to create the best basis for the best interpretation of results by limiting those factors that result in bad interpretations. The information generated by a laboratory should be fit for the purpose and error free. By fit for purpose meaning, doctors can use the results for the best benefit of the patient. Total eradication of error cannot be done but the laboratory can limit the prospect for error through having an effective management system intended and operated to achieve quality. ISO describes quality as the "totality of characteristics of an entity that bear on its ability to satisfy stated and implied need". But for laboratory medicine quality, this should be viewed to mean enabling doctors to practice good medicine through providing correct and usable laboratory results. The management system should be for the collection examination and reporting of human samples in a way that:

- Supports diagnosis, prevention and management of disease.
- Generates information having clinical use and optimal impact on health outcomes.
- Meets predetermined targets of accuracy, reproducibility and traceability
- Strives to minimize error.
- Is timely, efficient and cost effective
- Focuses on client satisfaction and continual improvement.

Before, we can control, practice, assume or improve laboratory quality; one must know exactly what level of quality is needed to ensure adequate clinical decision-making. Quality parameters should involve an effective quality control program, establishment of reference interval, allowance for biological variation, determination of allowable total error and consciousness of measurement uncertainty. Internal QC will then be used for verifying intervals used as a guide for the end user of the results to assist in interpretation of the results.

This need of quality begins and ends with the patient. This is because doctors order tests and rarely question them. Hence, assuming that these results and the tests are 100% specific and sensitive, the onus is then left to the laboratory to make sure that after all these assumptions are made, the doctors will still have the best results which will result in the best service to the patient.

Many analytes of clinical interest vary over time in an individual's lifetime, which is all part of the ageing process. These variations occur rapidly at the critical points in the life cycle for example during neonatal period, puberty, childhood, menopause and old age. The knowledge of predictable rhythms or cycles is vital for good patient care. The absence of an expected rhythm can also be indicative of disease. Biological variations can be split into several groups.

1. Over the span of life
2. Predictable biological cyclical rhythms
   a. Daily
   b. Monthly
   c. Seasonal
3. Random inherent biological variation
   a. Pre analytical difference in patient preparation, sample collection, sample handling
   b. Analytical associated with imprecision and bias.

It is essential to collect within-subject biological variation and analytical precision. This data will need to be used for determining the change that must occur in an individual serial result before the change is significant and also to determine the statistical probability that a change in individual's serial results is significant.

Comparing within-subject and between-subject biological variations will enable one to decide the good use of population based reference values and to clarify why stratifying reference values according to age and sex improves clinical decision-making. Ultimately this information can be used for deciding the best way to report test results, the best sample to collect and the test procedure of greatest potential use.

Data on the components of biological variation can be applied to set quality specifications for

a) Precision
b) Bias
c) Total allowable error
d) Allowable difference between methods
e) Use in proficiency testing programs and external quality assessment schemes
f) Use of reference methods and ranges

Ultimately, it is the well being of the patient that guides the decision on how good a test or test protocol needs to be for in reality a laboratory is rarely provided with the clinical data specific to each patient and so it must second guess the needs of the end user of the results as well as the patient. This

can be overcome in several ways. One method is the patient outcome determined test protocols. An example can be found in investigations for myocardial infarctions. By introducing tests with increasing specificity for the purpose one can determine the best tests to include in protocol e.g., introducing AST then CK then CK iso-enzymes then to Troponin-T and Pro-BNP. These procedures are essential for the improvement of diagnostics methods and knowledge about the best treatment of patients. The other method would be to analyse patient's results based on more detailed understanding of the biological and clinical variability and elucidation of the basic data. The focus here is on reducing sources of error by use of other information then the laboratory results themselves and by careful evaluation of biological and clinical distributions of patient results. This is done through the use of factors such as age, gender, and race and to reduce controllable factors such as patient population, standardization of sampling, reduction of analytical errors. Here the uncontrollable factors are the patients biological or diseased set points and within subject variation.

Interpretation of laboratory data will always be a complex process which can however be made easier by taking into consideration all the various possibilities that can make a result meaningful or not. If biological variations are ignored in making clinical decisions then there is always a chance of introducing errors and ultimately not giving the patient the best practice of medicine.

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Erectile dysfunction (ED) and Heart Disease

For a man to get a natural erection , he has to become sexually excited a process which allows blood flow to the arteries to increase and the smooth muscles in the penis to relax and the tissue, acting like sponges, to fill with blood and make the penis erect. As a result damage to the blood vessels or nerves can cause ED or impotence. ED is the persistent failure to get an erection firm enough to start or finish sexual intercourse. Blood circulation problems are the most common causes of ED in men over 50 since they prevent or reduce blood flow to the penis. However, not every case of ED is linked to circulation problems.

ED can be a wake-up call that you are at risk for heart disease. The same factors that attribute to heart disease which are smoking, high cholesterol, diabetes, obesity, high blood pressure can also cause sexual problems.

1. Atherosclerosis: Coronary arteries are narrow and stiff and blood supply cannot be sufficient to fill the penis to allow a suitable erection. Because the arteries supplying the penis are smaller than the one to the heart, symptoms may first show up as ED. Risk factors include diabetes, Obesity, high cholesterol and smoking.
2. Medications: High Blood pressure medications and diuretics can result in ED. Although you cannot stop taking your medications, there may be other drug options that are less likely to cause ED which can be discussed with your doctor.
3. Anxiety and Depression: Men who have had a heart attack or surgery to the heart are often anxious about resuming an active sex life. Intercourse seldom causes heart attacks. Sexual activity with a usual partner in a familiar setting does not lead to a particularly high blood pressure level or heart rate. If you have medication for depression and have sexual side effects, you may be able to a different drug.

A relationship has been shown to exist between high blood levels of homocysteine an amino acid marker for heart disease and erectile dysfunction; Patients with high homocysteine levels have also been found to have ED. Hence testing for homocysteine may be able to identify patients with the risk of erectile dysfunction and the levels may be a sign of how severe the erectile dysfunction is. Patients with erectile dysfunction also have higher levels of C-reactive protein, also another marker of heart disease. Of the heart diseases which are common, chronic angina seems more directly linked to ED. The best predictors of ED are old age, prior heart-attack and a diagnosis of 2-3 blocked arteries. A study has shown that 54.8% of patients with chronic heart disease present with ED and they exhibit more severe chronic heart disease and left ventricular dysfunction than those without ED. Thus questioning of erectile dysfunction may be a useful tool for stratifying risk in individuals with suspected coronary heart disease.

If you have erectile dysfunction and it persists for 3-6 months, you need to get treated, not only for erectile dysfunction, at the same time get good crucial assessment of blood pressure, weight and other blood tests. It is vital not to just write-off ED as being tired or very stressed, its usually part of a vascular issue. Going to doctors at the first experience of erectile dysfunction will allow cardio-vascular diseases to be picked up at a much earlier time.

Patients who have erectile dysfunction should be seen by doctors who have the capacity to evaluate them for coronary heart disease. Erectile dysfunction can help save a life, although developing it could be distressing, the condition may help alert you and the doctor of possible cardio vascular disease.

References:

1 *Steven Reinberg: Erectile trouble may signal Heart Disease*

2 *James K MD et al: Prediction of Coronary Heart Disease by erectile Dysfunction in Men referred for Nuclear Stress Testing.*

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24 May 2005
Patrick J. Mulrow, M.D.
Secretary General, World Hypertension League
Medical College of Ohio
Department of Medicine - RHC
3120 Glendale Avenue
Toledo, OH 43614-5809 USA
Dear Professor Mulrow:

RE: COMMEMORATION OF WORLD HYPERTENSION DAY 14th MAY 2005

I am writing on behalf of Botswana, its people, and practitioners that we are indeed delighted to inform you that for the first time in this country's history we have managed to mark this event with considerable public awareness and media coverage, both within the tabloids as well as formal television and radio press.

Botswana has a population of approximately 1.8 million and no firm body of literature documenting the prevalence or incidence of hypertension. Cross-sectional surveys, as well as retrospective analysis from government records (Bhagat K, et al. 1999, World Health Organization Consultancy Report), indicates that above the age of 35, between two or three out of ten individuals within urban areas suffer from hypertension.

Botswana, by definition, has the status of a medium income country with one of the highest GDP's in sub-Saharan Africa. Until the advent of HIV/AIDS it had largely conquered communicable diseases. However, it now has one of the highest incidences of HIV/AIDS in the world and as a result the mind of the public, patient and practitioner has shifted towards this disease. This has notably been at the expense of the silent but rising epidemic of cardiovascular disease in sub-Saharan Africa. Indeed, it is estimated by the Southern African Hypertension Society that by 2015 cardiovascular diseases will exceed, in terms of morbidity and mortality, that of HIV in the region. In this respect we have been attempting through regular media coverage, as well as public print, to expose this silent but ravaging epidemic.

We took the opportunity of World Hypertension Day as a landmark event for future public advocacy.

I enclose copies of our media coverage for your records. The event has gone a long way towards sensitizing the nation and we do hope that greater public/private partnership in Botswana will lead to appropriate emphasis of hypertension in its primary, secondary and tertiary management.

Kind regards,
Kiran Bhagat
Consultant Cardiologist and Professor of Clinical Pharmacology

Editor's winter health tips

1. Take time for reflection. The meditative nature of winter provides an outstanding opportunity for greater reflection and self-assessment. Take an honest look at where you are. At the same time, be gentle with yourself. If you are somewhat worn-out, you may also feel more vulnerable and more susceptible to illness. Your emotions may be high, or you may be more sensitive than usual. See if you are able to accept yourself more fully in as many areas of your life as possible.
2. Reduce stress. That will help you conserve energy and slow down unnecessary drains on your energy. Assess the type of stress you are experiencing - is it physical or emotional? Are you feeling stress from your environment, an illness, your work, or your relationships? Write down a few tips to help with your stress.
3. Get quality sleep. Sleep involves both your state-of-mind and body chemistry. If you go to bed feeling stressed or weighed down with worries, even if you don't normally have sleeplessness, your sleep may not have the quality it does when your mind is relaxed.
4. Increase the relaxation in your life. Learn some relaxation exercises or practice. These gentle practices can be done almost anywhere, regardless of the weather.
5. Nourish yourself. In this still cold time of winter, provide your body with the extra raw materials it needs. Emphasize warming foods - more concentrated sources of fuel and nutrients, including whole grains and beans, nuts and seeds, and quality proteins. In cold or damp weather, you also require a few more calories and spices such as ginger and garlic, to heat your body.
6. Be sure you're getting enough essential nutrients. You also need some nutrient enhancement to protect you from the stresses of cold, wind, dampness, and the decrease in sunlight. The antioxidants are important, especially vitamins A, E, and C. Nutrients that address stress include the B complex vitamins (with B5 and B12), Make sure you get enough fats and oils - the essential fatty acids you all need to operate the nervous system, rebuild and protect your cells, and assure good brain function.
7. Avoid over-indulgence. If you feel like you're continually hungry, it makes sense to give yourself a little extra nurturing. But don't confuse self-care with self-indulgence. Continue to minimize sweets and simple starches and avoid the empty calories of junk food. Portion sizes may also be a factor. Provide yourself with quality nutrition and supplements rather than constantly jump-starting yourself with caffeine containing drinks.
8. Have fun. Laugh. Hang out with your most fun-loving and light-hearted friends. Simple pleasures are stress reducing and very healing.
9. Make time for love. Touch and intimacy are good for your health. If you're not in an intimate relationship, get a massage, renew an old friendship, or make time for some close emotional interchanges with a trusted friend or family member.
10. Nourish others. Notice how very deeply that nourishes you in return. Build giving into your life. Another important aspect of giving is remembering to keep reasonable limits or boundaries, so you don't feel swallowed up or depleted by your generosity.