Editor's Note

Hi to you all and welcome to a new and refreshing version of our widely distributed *Diagnostics-Update.Com*. With the constant changes we experience with communication in our times, it is imperative that we as communicators also change or risk losing relevance. The deliverance of information has evolved tremendously, people now want their information in little bite sizes and want to understand a whole topic in just one sentence, so what we will endeavour to do in this and subsequent issues is to sectionalize so that a particular topic can be covered in a concise and refreshing way. To this end we have introduced a 'Hot Topics' column which will explain several medical/health topics in a paragraph or two. And we shall also be seeking to reflect a greater dynamism in our publication by moving away from the more formal presentation along structural lines of material aimed at the non-medical-professional readers and instead will pick and run with material of greater enthusiasm and relevance to our community. But this does not mean we will become 'all gloss and no depth.' On the contrary, with the sectionalizing, we will then have some other feature articles that will be aimed at primarily the medical professionals or those seeking an in-depth understanding of a particular subject.

We have also included a section of some word games, so as to keep the mind sharp and also help those who come to enjoy our publication in waiting rooms to pass the time and keep the informative pieces for later when more relaxed.

Finally, we invite your suggestions for other improvements to *Diagnostics-Update.Com*. What type of material would you like to see? How should it be presented? We need your ideas to make sure that *Diagnostics-Update.Com* remains something that people actually want to read.

Let us know what you think of this Newsletter by writing, emailing, phoning, and using the Forum or Feedback page on the Website www.diagnostics-update.com. And, please send all your health queries and we'll forward them to our health experts and feature the answers in *Diagnostics-Update.Com* issues to come.

I trust you shall continue to enjoy this and other editions

> "It takes a lot of courage to release the familiar and seemingly secure, to embrace the new. But there is no real security in what is no longer meaningful. There is more security in the adventurous and exciting, for in movement there is life, and in change there is power."
>
> *Alan Cohen*

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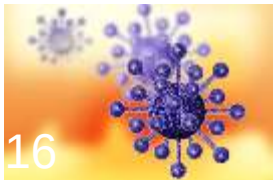
What's Inside



feature article

Malaria

Critical role of Diagnostics

Mark D. Perkins and David R. Bell
Summarized from www.pubmedcentral.nih.gov

> ***An African child has on average between 1.6 and 5.4 episodes of malaria fever each year. And every 30 seconds a child dies from malaria.***

Malaria control has recently seen a long-overdue resurgence in interest and funding, a belated recognition that malaria is still dominating the lives and health of millions, and holding whole populations in poverty. In places where these renewed efforts have been systematically applied, insecticide-treated bed nets, indoor residual spraying, and artemisinin-based combination therapy (ACT) have demonstrated their capacity to reduce both incidence and mortality from malaria. For the first time in decades, the idea of elimination of malaria as a public health problem, and perhaps complete interruption of transmission across whole regions, is being considered. However, although modern prevention and treatment tools for malaria are shown to be effective, long-term success in controlling malaria, and in reducing the morbidity and mortality of fever in the tropics, will require a fundamental change in the way fever is managed, and in the specificity with which malaria care is allocated. This article argues that the role of diagnosis must be prioritized, both for case management and for surveillance, and that progress toward malaria elimination will only increase the need for good diagnostic information.

Malaria is caused by a parasite called Plasmodium, which is transmitted via the bites of infected mosquitoes. In the human body, the parasites multiply in the liver, and then infect red blood cells.

> **Symptoms**
> Symptoms of malaria include fever, headache, and vomiting, and usually appear between 10 and 15 days after the mosquito bite. If not treated, malaria can quickly become life-threatening by disrupting the blood supply to vital organs. In many parts of the world, the parasites have developed resistance to a number of malaria medicines.

> **Intervention**
> Key interventions to control malaria include: prompt and effective treatment with artemisinin-based combination therapies; use of insecticidal nets by people at risk; and indoor residual spraying with insecticide to control the vector mosquitoes.
>
> *World Health Organization*

Background

Most causes of fever in the tropics are transient, non-fatal illnesses. The utility of microscopy in tropical fevers, and the availability of life-saving treatment for malaria, led to the wide advocacy of microscopy-based case management as the standard of care. When microscopy was found to be hard to extensively provided in many parts of the world, due to the massive effort and resources required to maintain such a service in close proximity to the rural and poor populations widely at risk, syndromic management, classifying all 'malaria-like' fevers as malaria, again became the de facto standard of practice. This has lead to the medical community treating most fevers in malaria-endemic countries as malaria and thus forgoing the diagnostic process. This practice has been codified into national and international recommendations and training manuals for health workers, especially for fever in children. The common teaching has been 'fever equals malaria unless proven otherwise'. Clearly many lives have been saved by pushing for rapid, even community or home-based access to antimalarial therapy, regardless of diagnostic testing. In the many communities in which malaria has accounted for the majority of potentially fatal causes of fever, it has been hard to imagine any other approach, given the poor performance and relative unavailability of microscopy. Over the past decade, though, a number of important changes have taken place in the epidemiology and control of malaria and in the diagnostic techniques available that dramatically alter the balance of rational action in favour of parasite-based diagnosis over blind therapy of fever with anti-malarial drugs. Specific diagnosis of malaria is now not only possible, but necessary, and scaled up malaria control efforts, including elimination plans, must include expanded and quality assured use of parasite-based diagnostic testing and reporting of results.

Overdiagnosis of malaria and fever mismanagement

Unfortunately, the clinical presentation of malaria is highly variable and overlaps with that of a number of other common illnesses, including

pneumonia, which are associated with significant morbidity and mortality. The 2008 World Malaria Report estimates well below a third of fevers in endemic areas of Africa are due to malaria, and much less again in other regions. In India, for instance, slide positivity rates, based on approximately 100 million slides examined, are about 2%. Even when WHO criteria for severe malaria are met, an important fraction of patients may be found to have an alternative cause of fever on post-mortem or other careful investigation. Unfortunately, not enough is known about the causes of non-malarial fevers in the tropics. During a period when inexpensive drugs such as chloroquine were available, widespread overtreatment for malaria was accepted as a means to improve treatment coverage and decrease mortality. With rising drug resistance, national malaria control programmes are moving to more expensive and more effective artemisinin combination therapy (ACT), and the cost of drugs wasted on treatment of non-malarial fever become substantial. Malaria misdiagnosis and subsequent mis-management has individual as well as societalrepercussions. At the individual level, misdiagnosis results in: wasted resources on drug purchase, especially in the private sector, exposure to drug side effects, and most importantly morbidity due to improper management of the true cause of fever.

Early treatment with effective drugs is vital in acute respiratory tract infections, meningitis, and other differential diagnoses of malaria, in the same way that early, appropriate and effective treatment is fundamental to reducing malaria case fatality rates. Due to the cost of drugs and of complications from inappropriately managed illness, and to the limitations in access to good microscopy services in remote and resource-poor locations, impoverished individuals are disproportionately affected by malaria misdiagnosis.

At a societal level, mismanagement of fever: erodes patient's faith in the health system, wastes drug resources, augments drug pressure toward resistance, and contributes to ignorance of the true causes of illness in these populations.

In the face of this, it should be disturbing that less than 20% of suspected malaria cases receive a confirmatory diagnosis in 75% of African countries. One of the drivers of presumptive treatment is fear of rapid mortality of untreated malaria, especially in young children. Increasing evidence suggests that where accurate parasite-based diagnosis is present, febrile children with negative malaria examinations may safely be cared for without antimalarial treatment. A carefully performed study in Uganda examined whether, in a setting of low to moderate transmission, microscopy-directed therapy would result in excess mortality from unrecognized and untreated malaria. Of 2,359 medical visits by children <10 years of age presenting with fever, 1,608 (68%) were microscopy-negative and were not given anti-malarial drugs.

During seven days of follow-up, only 13 (0.8%) were subsequently diagnosed with malaria. There were no deaths, and no episodes of severe malaria. Similarly, Ngasala and colleagues found that microscopy-based treatment was safe and effective in children under five years old, even where less expert microscopy was used for screening. Modeling studies suggest that even at high parasite prevalence the benefits of improved management of non-malarial illness make parasite-based diagnostic methods cost-effective. WHO is currently developing evidence-based recommendations in this area.

Development of rapid diagnostic tests (RDTs)

Microscopy services for the diagnosis of malaria are not widely available, especially at the community level where most urgent care takes place. In the hands of many microscopists in low-income settings where training, equipment and reagents may be substandard, the accuracy of microscopy is poor.

But while microscopy standards may vary it remains invaluable for diagnosis, ensuring the quality of microscopy as a system-wide approach has proved beyond the capability of most malaria control programmes. For these reasons the development, in the early 1990s, of lateral flow immunochromatographic tests that could detect malaria parasite antigens in a fingerprick blood sample was a major advance. These rapid diagnostic tests (RDT) are based on the ability of monoclonal antibodies to bind to parasite antigens in lysed blood and immobilize them along a defined line on nitrocellulose for detection with a colored label (most commonly colloidal gold). All existing commercial RDTs target one or more of well characterized Plasmodium protein targets: histidine rich protein 2 (HRP2), parasite lactate dehydro-genase (pLDH), or aldolase). RDTs have the obvious advantage of requiring less training, being easily performed in remote or village settings, and putting most of the quality control responsibility in the hands of the manufacturer instead of the user.

These tests are in relatively wide use in many South American and Asian countries, where use has been scaled up, to accompany ACT. Use is now also increasing in a number of African countries. There are several sources of monoclonal antibodies against the common antigen targets, and companies making lateral flow tests for other indications such as pregnancy testing, screening for illicit drugs or diagnosis of infectious diseases can, without much difficulty or expense, add malaria to their test portfolio. The profusion of malaria test manufacturers, many of them small, combined with their difficulty obtaining reference

Facts on malaria

About 3.3 billion people - half of the world's population - are at risk of malaria. Every year, this leads to about 250 million malaria cases and 880 000 deaths.

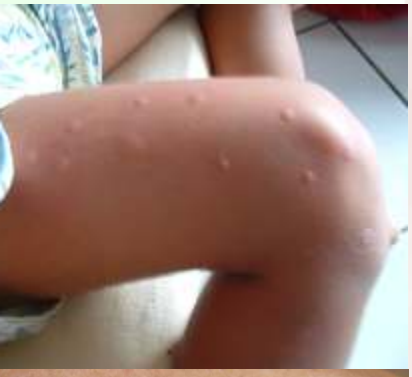
People living in the poorest countries are the most vulnerable. Malaria is especially a serious problem in Africa, where one in every five (20%) childhood deaths is due to the effects of the disease.

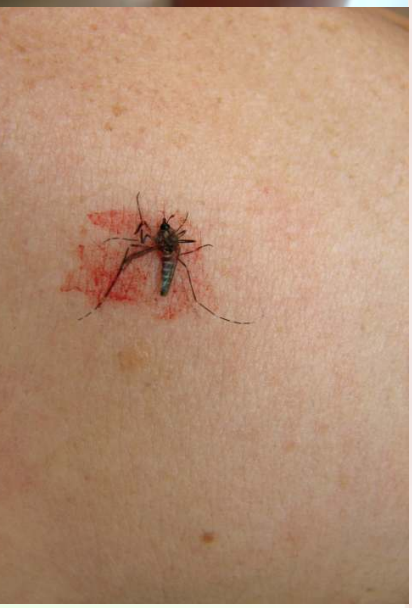
This fact file presents the extent and effects of malaria and how it can be prevented and controlled.

World Health Organization

> Sustained malaria control will depend on the global capacity to accurately detect malaria and map its distribution.

> The specific detection of malaria parasites is now possible even at the village level with high quality rapid diagnostic tests.





clinical materials from well-characterized malaria patients and the lack of biologic reference standards, has resulted in significant variability in the quality of tests being manufactured. Many RDTs have been shown to perform well, detecting over 90% of malaria cases, including those with relatively low parasite density (200 parasites/µl). Several RDTs distinguish between falciparum and non-falciparum malaria, and in ideal conditions bring the power of reliable expert microscopy (detection, species identification, and to a much lesser extent, quantitation) and put it in the hands of village health workers. Unfortunately, though these tests have been shown to be useful, cost-effective, and safe in the direction of antimalarial therapy, health care workers frequently ignore results, either because of ingrained treatment habits, pressure to treat from patients and family members, or doubt about the accuracy of the RDT results. Clearly, if RDTs are going to shift the global paradigm of fever management from reflex antimalarial treatment to diagnostic-directed treatment, systems will need to be in place to: ensure the confidence of the health worker in the performance of the diagnostic test, and provide capacity to appropriately and effectively manage the illnesses of RDT-negative patients.

Diagnostics in the malaria elimination campaign

Now 40 years after the failure of the first Global Malaria Eradication Campaign in the 1960s, there are new calls for malaria elimination, and in a few settings advanced degrees of control have already been accomplished. At the recent 2008 Millennium Development Goals Malaria Summit, an ambitious new Global Malaria Action Plan was endorsed and nearly $3 billion committed towards reducing the number of malaria deaths to near zero by 2015.

A drive towards malaria elimination will increase the need for broad use of quality assured diagnostics for malaria, and possibly the development of novel assays to address specific needs such as the sensitivity at low parasite densities and minimal invasiveness required for population-based surveys for parasite reservoirs. The imperative for parasitologic diagnosis will be dramatically increased where malaria incidence falls, and where reflex treatment of fever with antimalarial drugs would be ineffective and even harmful in the vast majority of cases.

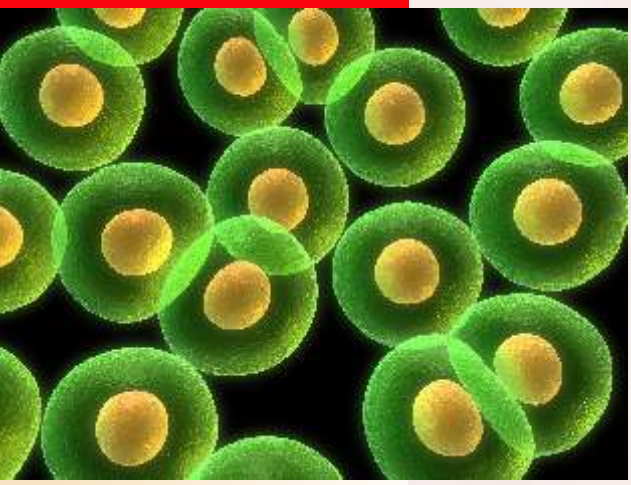
More important perhaps, is the role of routine malaria testing as a surveillance method. Mapping malarial cases will be critical to understanding the effectiveness and impact of different control policies that are being implemented. Though this is currently done through testing at sentinel sites or in large population-based surveys, much more accurate and real-time information can be gathered through the development of reporting systems that capture the results of RDT testing at village level. Currently, very few RDT results are recorded and transmitted back to centralized levels of the health system in a way that could serve surveillance needs. For both HIV and tuberculosis, relatively robust systems are in place that capture the results of testing in peripheral settings and establish the basis for national reporting. Though this will be a greater challenge for malaria, recent developments, including the existence of RDTs, the strengthening of malaria services with a rapid increase in funding, and the drive toward elimination, make such planning feasible. System-wide reporting would also highlight outbreaks, and could serve as early harbinger of emerging drug resistance or increased insecticide resistance in mosquitoes. Elimination planning and monitoring will require faster and more accurate information about the incidence and distribution of disease than is currently available.

Ultimately, the Global Malaria Eradication Campaign died in the 1960s from donor fatigue. Elimination campaigns are costly and difficult, even when highly effective tools are available. Without clear and detailed evidence of the impact of donor spending on malaria case rates and geographic distribution, donors cannot be expected to continue to fund control campaigns.

Conclusion

Sustained malaria control will depend on the global capacity to accurately detect malaria and map its distribution. The specific detection of malaria parasites is now possible even at the village level with high quality rapid diagnostic tests. Driven by the extent of over-diagnosis and misdiagnosis of malaria when syndromic approaches are used, global efforts are underway to increase the utilization of parasite-based diagnosis, and to ensure the quality of tests that are used. Elimination efforts will not only increase the need for widespread RDT use, but may drive the development of new tests with enhanced performance. Implementation of the Global Malaria Action Plan, proposed regional initiatives towards elimination of malaria, and the reductions in mortality from malarial and non-malarial illness necessary to achieve Millennium Development Goals will require an increased emphasis on building systems for parasite detection as an integral part of malaria case and programme management.

Hot Topics



Stem Cells

These are the root cell of the body and all other cells 'stem' or are derived from them. Stem cells have certain characteristics that distinguish them from other cells in the body.

They are unspecialized cells with the capability of dividing even after long periods of inactivity and when they divide each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.

Under certain conditions (physiological or experimental), they become organ or tissue specific cells. Meaning they can be induced to produce new organs or tissues for grafting elsewhere.

Researchers are still learning how the body uses these cells to restore or regenerate tissue and hope to harness the power of stem cells and make them a human "repair kit." There are three major types of stem cells - embryonic stem cells, embryonic "fetal" germ cells, and adult stem cells - but scientists mainly work with adult and embryonic stem cells from animals and humans.

According to Robert Goldstein, Chief Scientific Officer of the Juvenile Diabetes Research Foundation, "Embryonic stem cells could serve as replacement cells for those that have been lost or destroyed because of disease." And he also adds, "If (science) can discover the biological cues that make an embryonic stem cell develop into a specialized cell - like an insulin-secreting cell in the pancreas - then we could try to reproduce these signals in the lab and create a source of replacement cells for many afflictions."

The great controversy lies in deriving these embryonic stem cells and thus destroying an embryo and this has raised ethical and moral issues such as those raised for abortion. Mainly that is: “when does life begin?” and “does killing an embryo not constitute murder?”

> “Embryonic stem cells could serve as replacement cells for those that have been lost or destroyed because of disease.”
>
> *Robert Goldstein*

Allergies

Allergy is also known as hypersensitivity and can be described as a harmful, increased susceptibility to a specific substance. What is happening during an allergic reaction is that the specific substance that is causing the allergy (also known as an allergen), when introduced to the system will bind to allergic antibodies (IgE antibodies) present on the hosts immune cells. These cells will then release chemicals such as histamine into the blood stream which will then result in the allergic reaction.

Some allergies can be termed as atopic. This state of atopy is defined as an inherited tendency towards the hyperproduction of IgE antibodies to common environmental allergens. Loosely explained it refers to the genetic predisposition to specific or general allergies. Examples include a child suffering from asthma and one of the parents also suffering from it or a child suffering from atopic eczema with one or both of the parents or their lineage having asthma or some other allergy.

Many common allergies such as asthma have seen huge increases in recent years, and many studies appear to show a correlation between this and our increasingly affluent and therefore clean lifestyles. This has led some researchers to conclude that it is our "too clean" upbringing that is to blame for the lack of immune system stimulation in early childhood. Many children have a natural tendency, for example, to consume soil - a practice that often provokes an equally natural tendency in parents to stop them. However, it appears that this may have a valuable function in priming the immune system, and is one way to ensure that allergies are less likely to develop in later life.

Allergic symptoms can vary from mild itching, wheezing, runny eyes and nose, to severe anaphylactic shock and death.

> “Many studies appear to show a correlation between allergies and our increasingly affluent and therefore clean lifestyles.”

Male Menopause

M.A. Naeem

Once it was common belief that men stay virile throughout their lives and the myth of "ageless male" was alive and well. No more, though, as studies become more and more focused on what is now commonly dubbed as "male menopause". While some shrug male menopause aside as simply a case of "mid-life crisis", many doctors believe that male menopause is a physiological phenomenon, rather than just a psycho-social adjustment.

> "Some men experience a significant drop in testosterone levels by the age of forty."

Male menopause, more appropriately called andropause, refers to a gradual decline in a man's testosterone levels. Some men experience a significant drop in testosterone levels by the age of forty. Almost half of the men experience such drop by the age of fifty. It must be stated that the other half maintain their hormone levels well into their eighties.

Testosterone is the hormone responsible for stimulating sexual development in male infants. It helps with bone and muscle growth and keeps muscles strong. It is also responsible for creating and releasing sperm and for maintaining an overall healthy sexual drive.

A decrease in the production of male hormone leads to a variety of ailments. The symptoms of andropause are similar to the ones experienced by menopausal women. These include poor sex drive, lethargy (tiredness and fatigue), depression, irritability, mood swings, hot flushes, insomnia, loss of body mass, loss of bone mass, general aches and pains, and in some cases, impotence.

Symptoms Include

- poor sex drive
- lethargy (tiredness and fatigue)
- depression
- irritability
- mood swings
- hot flushes
- insomnia
- loss of body mass
- loss of bone mass
- general aches and pains
- and in some cases impotence

While it occurs naturally in some men, more often andropause is caused by physical or psychological issues, such as, anaemia, thyroid gland dysfunction, depression, dementia, and obesity. Men with autoimmune disorders, cancer, diseases that attack heart and lungs, or other degenerative illnesses, also suffer from andropause. External factors that contribute to this condition are excessive alcohol consumption, smoking, poor diet, lack of exercise, prescription and non-prescription medications, and family or job related problems.

Strictly speaking, andropause is not similar to menopause. Female menopause is defined as the time at which menstruation ceases altogether, followed by complete disappearance of the female hormone oestrogen. This results in acute symptoms in women and leads to complete loss of fertility. All women go through menopause, while only some men go through andropause. Even then andropausal men don't lose their fertility. Testosterone is still being produced, even though at a reduced level, as well as sperm, thus allowing all men to stay fertile well into their late years.

Patients with andropausal complaints should be checked for serum FAT (Free Available Testosterone), which is measured in a pooled early morning blood sample. If the level is low, then the patient may be diagnosed with andropause. Such diagnosis can only be performed by a very responsible physician, and only after taking into account all the other aspects of a patient's life. Even though the symptoms of "mid-life crisis" and andropause overlap considerably, only careful analysis can determine if andropause is the ailment.

The primary treatment for andropause is Testosterone Replacement Therapy (TRT). Main purpose of TRT is to bring hormone levels back up to a healthy level, the way estrogen replacement does this for women. However, TRT has a lot of side effects and it must be administered by a competent physician under strict case selection criteria and supervision.

Testosterone is available in many forms, such as oral, injectable, trans-dermal, and implants. Patches, pellets, creams, and gels are also available. Oral uptake is discouraged because it can lead to liver toxicity. Some newer forms bypass the liver and are absorbed through the lymphatics, thus reducing liver toxicity. Injectable testosterone is safe but blood levels are not uniformly maintained.

Any excess testosterone in the body is converted to estrogens, which is counter productive because it changes the testosterone-oestorgen balance. Oestrogen is commonly associated with prostate cancer, which is one of the major side effects of TRT. Other side effects include thrombophlebitis and hypercoagulability of blood.

While testosterone replacement therapy does show a significant improvement in symptoms, its dosage must be tailored to the needs of the patient. Before starting TRT, a thorough general check up must be carried out, including haematocrit tests, lipid profile, cardiac function test, liver functions tests, measurement of prostate specific antigen, and trans-rectal ultrasound. These tests must be repeated at regular intervals all through the treatment.

Cervical Cancer

Use of HPV Testing

Silas Nunu

Cervical cancer is the second most common cancer in women worldwide with approximately half a million new cases every year and 250 – 300 thousand deaths. Approximately 85% of these cases occur in developing countries (including Botswana) where women do not have access to effective cervical cancer screening.

> "Cervical cancer is the second most common cancer in women worldwide."

> "Primary screening test can detect approximately 50% more high-grade lesions than the Pap test."

Cervical cancer is known to be caused by the Human Papilloma Virus. Human papillomavirus (HPV) is the name of a group of viruses that includes more than 100 different strains or types. Approximately 40 of these viruses are sexually transmitted, and they can infect the genital area of men and women including the skin of the penis, vulva (area outside the vagina), or anus, and the linings of the vagina, cervix, or rectum. Most people who become infected with HPV will not have any symptoms and will clear the infection on their own. About 13 of these HPV genotpes are strongly associated with the development of cervical cancer and have been designated as the HR-HPVs (high risk HPVs). By contrast some other genital HPV types are associated with benign genital warts but not cervical cancer and have been classified as low risk. Cervical infections due to HR-HPVs cause virtually all cervical cancers. They also are the cause of their immediate precursor, cervical intraepithelial neoplasia grade 3 (CIN3), a precancerous condition. Despite a persistent infection with the HR-HPVs, most HPV infections will resolve themselves before progressing to the precancer stage of CIN3.

It is this recognition that cervical cancer is caused by HR-HPV that has led to the development of several new technologies for cervical cancer prevention such as HPV DNA testing and HPV vaccination. Most cervical cancer screening is currently based on the Pap smear. The Pap smear involves a brushing of the cervix which is then analyzed to detect any aberrant cell growth. An HPV test uses a similar technique but checks for viral infection.

However, the Pap smear is far from a perfect screening test as it is highly subjective and the recognition of cytological abnormalities varies widely from one laboratory to the next with the sensitivity and specificity ranging from 30 to 87% and 86 to 100%, respectively. But this is not meant to knock down the effectiveness of Pap smear screening, because as studies show a lack of Pap screening has been identified as the single most common attributable factor in the development of invasive cervical cancer.

But, as much as organized Pap smear screening is or isn't effective for the prevention of cervical cancer infection, HPV testing is better. A number of large-scale randomized controlled trials have shown that HPV testing as a primary screening test can detect approximately 50% more high-grade lesions (such as CIN3) than the Pap test.

In one study Researchers randomly assigned more than 130,000 women age 30 to 59 in rural India to one of four equal-sized groups. Three of the groups underwent cervical cancer screening either through, a test for HPV strains known to cause cervical cancer; a Pap smear; or visual cervical examination. Women in a fourth group, the control group, were advised to seek medical care on their own. If any test showed a woman had an HPV infection or abnormal cell growth on her cervix, she was given a full exam and treated further as necessary. Thorough removal of precancerous lesions prevents cervical cancer.

The results showed that women who received HPV screening were less likely to develop any advanced-stage cervical cancer over the course of the study. By the end of the study, 34 women who got the HPV screening had died of cervical cancer, compared with 54 in the Pap smear group, 56 in the visual exam group and 64 among the controls.

These results have also been confirmed by other studies such as one in the *British Medical Journal (BMJ)* about the long term predictive value of cytology and HPV testing in cervical cancer that showed that HPV test positivity is more predictive of cervical cancer than cytology.

What this all means is that eradication of HPV infection can very likely lead to a wiping out of cervical cancer. This can likely take place through the standardized use of recently developed HPV vaccines. It is envisaged that by continued use of these vaccines will reduce incidence of cervical cancer and this will be very effective in resource poor communities as it shall reduce the amount of doctor visits required currently where women need repeated screens to determine in the first place their likelihood to get cervical cancer.

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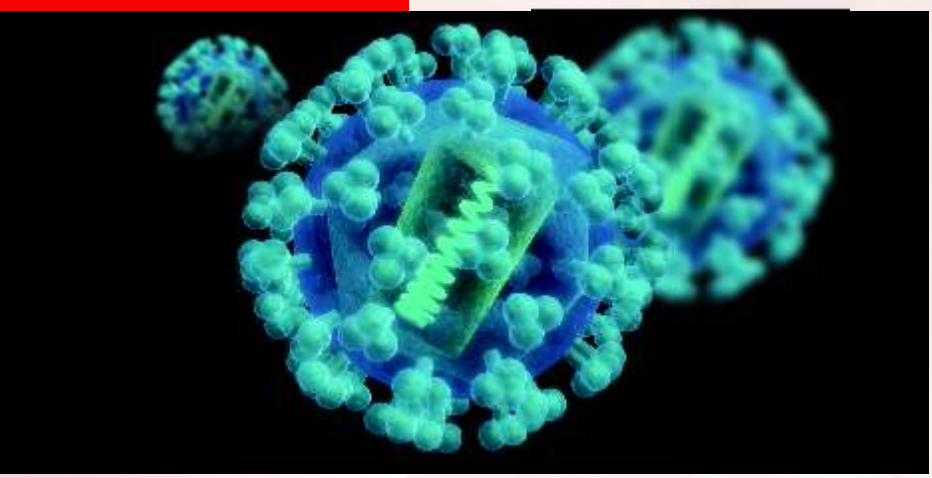
1. A guest speaker at the Parliament wellness week opening
2. Vice chancellor of the UB Prof Bojosi Otlhogile giving a vote of thanks at the UB walk for HFB
3. Prof Sheila Tlou (former Health Minister) was part of the attendees of Parliament wellness week opening
4. Testing during Parliament wellness week
5. Dr Saleshando, a kidney specialist, addresses the World Kidney Day gathering
6. Dr Mazonde(2nd Left) and Hon Speaker Balopi(3rd Right) were among the dignitaries at the Parliament wellness week opening
7. WHO country representative for Botswana giving a speech at the Main Mall
8. Dignitaries at the UB walk for Heart Foundation Botswana included Prof Otlhogile, Commissioner Tsimako and Prof Bhagat
9. Students from the Department of Environmental Sciences at the UB who organised the walk together with their organiser Bontle Mbongwe
10. Commissioner Thebeyame Tsimako of the Botswana Police giving the keynote address
11. Tyrone, Desire, Bozongwana and Nkiwane from Diagnofirm were present to perform some testing.
12. Participants to the World kidney day commemoration

feature article

HIV Related Malignancies

Dr. J. Kasese
Gaborone Oncology Clinic



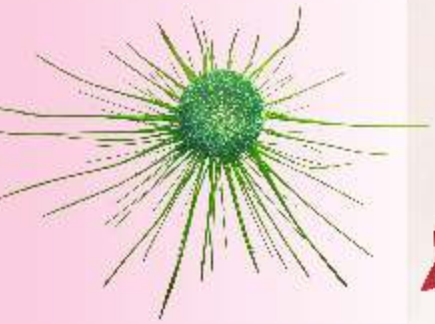
> ***HIV patients have increased incidence of certain tumours. In fact 30% to 40% will develop a malignancy during their lifetime.***

> HIV related malignancies are caused by oncogenic viruses. HIV is not a direct oncogene virus as it does not result in genetic modifications affecting cellular replication, but it facilitates the development of cancers by removing the immune system.

Cancer and HIV are both pandemics. They have shared characteristics in that they both have social and emotional impact that goes beyond the physical disruptions that they cause. They both attract billions in research funds and also receive priority over heart and mental health topics in news coverage.

The problems currently being faced in tackling this growing epidemic are that although research is wide and extensive, data collection worldwide takes years to compile and this results in problems with topicality and redundancy in that a title prepared in 2005 may lose relevance in 2009. Also, specific anticancer therapies for HIV related malignancies have not been addressed. The other issues affecting management of this correlation are that there's no combined research effort. The major publications on HIV are concerned with research and epidemiology, which is where drug companies spend a lot of their budgets, whilst radiotherapy and chemotherapy, though they have a big role to play, have only a limited number of published articles and chapters in books on the subject

> Kaposi's Sarcoma has been shown to be associated with gamma-2-herpes virus, known as HHV-8, whice is transmitted in saliva and recent evidence from Africa suggests infection is acquired through normal social contact within the family.



Current facts are that HIV patients have increased incidence of certain tumours, i.e. Kaposi's sarcoma, Non-Hodgkin's lymphoma, cervical cancer, SCC conjunctiva, ano-rectal carcinoma and leiomyosarcoma in children. Cancer is a significant cause of mortality and morbidity in people infected with HIV; in fact 30% to 40% will develop a malignancy during their lifetime. Cancers such as non-Hodgkin's lymphoma, Kaposi's carcinoma and invasive cervical cancer are referred to as AIDS-defining cancers. These are the majority of cancers affecting HIV-positive people. The other types of cancer also appear to be more common among those infected with HIV. While not classified as AIDS-defining, these malignancies are affecting the HIV/AIDS community greatly and have been referred to as "AIDS-associated malignancies" or "opportunistic" cancers. Analyses have revealed a 2- to 3-fold increase in overall risk of developing these cancers.

What is now evident is, over the past decade, that HIV related malignancies are caused by oncogenic viruses. HIV is not a direct oncogene virus as it does not result in genetic modifications affecting cellular replication, but it facilitates the development of cancers by removing the immune system. The cancers developed during HIV infection do not necessarily contribute to the final cause of death of the patient because of other competing risks of mortality, ranging from infection to other causes, such as treatment.

To better understand the complications involved in the co-existence of HIV and cancer, it is imperative that one understands the individual specific tumours.

Kaposi's Sacroma

We will start with Kaposi's sarcoma, which was the first malignancy to be associated with HIV by Hymes in 1981, and was at one time the most frequent neoplasm in AIDS patients before the advent of antiretrovirals. It was first described by Moriz Kaposi in 1872 on patients presenting with 'sarcoma idiopaticum multiple haemorrhagicum'. In 1912 it was then described as classical Kaposi's sarcoma and was seen as an indolent tumour seen typically in men of Mediterranean or East European Jewish origin. In 1960 the first case of KS, following organ transplant and subsequent

immunosuppressive therapy, was documented. This was then significantly followed by its association with AIDS in 1981.

KS has been shown to be associated with gamma-2-herpes virus, known as HHV-8, also referred to as KSHV (Kaposi's sarcoma associated Herpes virus). HHV-8 is transmitted in saliva and recent evidence from Africa on HHV-8 prevalence in children suggests infection is acquired through normal social contact within the family. People infected with HIV have been shown to be 100 to 300 times more likely to be infected with KS and the risk and severity of KS increases in the presence of low CD4 T cell counts, as people with intact immune systems tend not to develop KS when infected with HHV-8. KS develops from HHV-8 infection through a combination of factors, including analogues of cyclin D and BCL-2, which increase cell production and prevent cell apoptosis.

The clinical features of KS are the classic raised lesion which may also coalesce with other lesions into plaques and ulcerate and bleed. Oedema is also always associated with individuals with KS.

Treatment for KS is achieved through either local or systemic therapy. Local treatment includes cryotherapy, which is therapy that involves the use of low temperatures or the removal of heat from certain body parts; photodynamic therapy (treatment that combines a light source and a photosensitizing agent [a drug that is activated by light] to destroy cancer); intralesional injection; and radiation therapy. Sytemic therapy involves interferon alpha immunotherapy and chemotherapy.

Studies have unequivocally demonstrated significant declines in the incidence of KS following the introduction of HAART. Furthermore, the incidence rates for KS are 5 times lower in HIV-positive patients who have received HAART compared to those patients who have not. Presently, most patients who develop KS while taking HAART show evidence of virologic treatment failure. Importantly, HAART may also have a positive effect on treating established KS.

There are also some experimental approaches being developed. These include anti-angiogenesis with thalidomide and interleukin 2.

Non-Hodgkin Lymphoma

The other common malignancy in HIV infection is non-Hodgkin lymphoma (NHL). It is characteristically aggressive and its association with HIV was recognized in 1982. NHL encompasses several types of lymphoma, including primary lymphomas of the central nervous system (PCNSL), diffuse large cell lymphoma (DLCL), Burkitt's lymphoma and primary effusion lymphomas.

Lymphomas develop against a background of chronic antigenic stimulation and most are of B-cell origin. Cytokines will stimulate the expansion of the tumour once malignant transformation has occurred. The cytokines involved are interleukin 6, tumour necrosis factor beta (TNF-β) and interleukin 10. Chemokines produced by HIV infected macrophages and monocytes will then produce autocrine stimulation of the abnormal clone cells, hence the tumour.

The degree and duration of HIV affects the type of lymphoma that will develop. Data also indicate that high-grade lymphoma is more prevalent in the HIV-positive community compared to low-grade lymphoma. Many agree that the risk of developing NHL, particularly PCNSL, increases with lower CD4 T cell counts and further progression of HIV infection. Moreover, NHL is more prevalent in HIV-positive women compared to high-risk HIV-negative women, indicating that immunosuppression, rather than other risk factors, is associated with the increased incidence of NHL in the HIV-positive community.

The relative risk associated with these different lymphomas to HIV positive individuals compared to the general population are as follows: Burkitts – 261, High grade diffuse – 652, Intermediate grade – 113, and Low grade – 14.

There are different types of treatments for non-Hodgkin's lymphomas. These include radiotherapy for CNS lymphomas; other lymphomas are generally treated with CHOP and R-CHOP for CD20 positive patients. On the issue of HIV treatment with the presence of NHL, no definitive conclusions can be drawn regarding the effect of HAART on the incidence of NHL, even though it continues to be one of the most common malignancies afflicting those with HIV infection. Some studies have demonstrated significant decreases in incidence of NHL following the introduction of HAART, whilst, however, other studies fail to show any substantial change.

But there are suggestions that a patient's response to HAART may provide insight into their cancer prognosis. Regardless, unlike for KS, there has not been a dramatic decrease in the number of cases of AIDS-related lymphomas following the introduction of HAART.

Cancer of the cervix

Cancer of the cervix is the most common cancer in women in Sub-Saharan Africa. Its association with HIV was noted in 1983, but criteria for defining AIDS were modified to include cervical cancer in 1993. Human papilloma virus (HPV), especially genotypes 16 and 18, is involved in almost all cases of cervical cancer regardless of HIV status, and is strongly associated with

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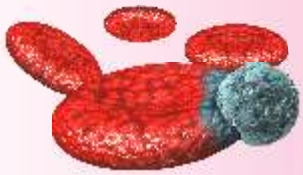

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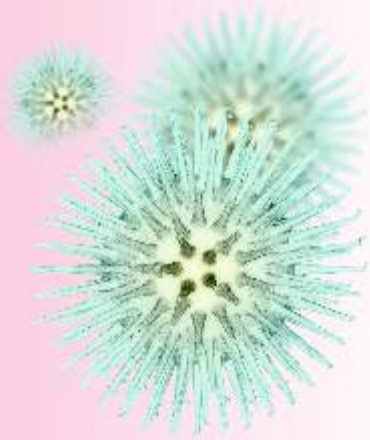
"Human papilloma virus, especially genotypes 16 and 18, is involved in almost all cases of cervical cancer regardless of HIV status. Women infected with HIV are more likely to be co-infected with HPV."



Cervical Cancer Symptoms

- post-coital
- bleeding
- inter-menstrual bleeding
- excessive menstrual bleeding vesico-vaginal or
- recto-vaginal fistulae.

"Fowl smelling discharge and backache are considered late symptoms."

cervical intraepithelial neoplasia (CIN) and squamous intraepithelial lesions (SIL), which are precursors to invasive cervical cancer (ICC). Women infected with HIV are more likely to be co-infected with HPV, possibly because of similar risk profiles and mode of transmission, as well as interactions that could putatively result in immune dysfunction and abnormal cytokine expression and growth factor production. Decreased CD4 T cell counts are associated with increased risk of acquiring HPV.

Clinical features of cervical cancer are: post-coital bleeding, inter-menstrual bleeding, excessive menstrual bleeding and vesico-vaginal or recto-vaginal fistulae. Fowl smelling discharge and backache are considered late symptoms. Its diagnosis is through Pap smear analysis, colposcopy and biopsy.

Treatment can be as drastic as hysterectomy if fertility is not an issue or if the cancer is at an advanced stage. Other forms of management are radical radiotherapy, brachytherapy and diathermy. There are possible future advances in the production of a vaccine, but this avenue is still to be evaluated.

There have been studies that have tried to find associations between HAART treatment and cervical cancer regression. However a majority of studies have shown HAART was not associated with decreased prevalence or persistence of HPV infection, but a significant reduction in the incidence of new cases of HPV-16 and HPV-18 was detected in HAART-treated women, suggesting that HAART may have an effect on acute HPV infection, but not on advanced infection. Of note, women taking HAART who experienced disease regression had higher CD4 T cell counts, suggesting some level of immune restoration.

Other Tumours

The other tumours that are associated with HIV (anal cancer, lung cancer, testicular germ cell tumours and SCC of conjunctiva) are not that common and not that much research has been done with these malignancies and their association with HIV.

The cancer prognosis for people infected with HIV tends to be worse compared to seronegative cancer patients, regardless of the type of malignancy. Perhaps because of a suppressed immune system and impaired immune surveillance, malignancies take a more aggressive clinical course in those infected with HIV. HIV-positive patients typically present with more advanced cancer at the time of diagnosis, and the average age at diagnosis is usually younger in HIV-positive patients compared to seronegative patients; this is particularly true with lung and testicular cancers.

Conclusion

In conclusion, in addition to the cancers discussed in this article, the risk of developing a multitude of other cancers appears to be slightly increased in the HIV-positive community. Regardless of whether these cancers are directly related to HIV-induced immunosuppression, treating cancer in HIV-positive patients remains a challenge because of drug interactions, compounded side effects, and the potential effect of chemotherapy on CD4 T cell count and viral load. Moreover, treatment compliance tends to be poor among HIV-positive patients with cancer, perhaps because of the increased responsibility of taking drugs for both diseases. The question of whether to suspend HAART during chemotherapy depends on several factors, particularly the type and stage of malignancy and the status of HIV infection.

Heart Foundation of Botswana - Slaying a Killer

"Heart Disease is sadly a huge problem right here in Botswana, and being silent, with no obvious stand alone symptoms, this killer is reaping a healthy harvest. This is made even more alarming by the fact this is all preventable and manageable. Heart disease and related issues such as hypertension should not be killing our nation.

The facts show that Heart Disease is way ahead of HIV/AIDS, Malaria and other diseases, and that it is in fact the biggest killer world wide."

Please see the HFB website for details on all events and programs mentioned, or contact Heart Foundation Botswana, Coordinator Michelle Theron Jay at hfb@cardiacclinic.co.bw

This year will see a wealth of activities and campaigns being championed by the Heart Foundation Botswana. We'll show you that even very small changes can make a huge difference in your well being. We will also prove that living a healthy lifestyle can be fun.

We need support from corporate entities and institutions so that we can reach everyone with this vital information. All brands will receive due recognition for their support.

The Heart Foundation Botswana (HFB) calendar '09 is focusing on two key areas: Women and children.

Reaching the Children

The heart of any community is the children. HFB '09 will target children and encourage them to research their home and community lifestyles, learning important lessons on the way and involving those around them. This will be done primarily through Heart Art Competition, which was launched in 2006 with a mandate of to deliver, through our schools nationally, the concepts of healthy eating, exercising and heart disease.

The Heart Art Competition was awarded an acknowledgement from the Botswana Postal Services and Philately Association in 2008 for one of the stamps designed by our children. This stamp was developed as a National Commemorative Stamp.

HFB will also be launching a Fun Kids Club and will also be mobilizing other activities such as Skip Rope challenges, Wear red days, and others to show the children that being healthy can be fun. We are also on a mission to get school tuck shops to stock healthier foods for the children.

GO RED for women

The leading cause of death in women worldwide, including Botswana, is heart disease and stroke. Therefore, increasing awareness of the impact of heart disease in women is also a mandate of HFB. Women are our primary caregivers, home makers, and a large part of our workforce, making it imperative that we get all women to look after themselves. We will be using a wealth of mediums to get the messages across. This campaign is partnering with many organizations to empower women. We are going to use the faces and stories of women across Botswana to motivate other women. We will be involving the press actively as well as employers. GO RED '09 will culminate in a Women's Wellness Expo.

Annual Events

HFB is involved in a number of annual events, through our international affiliations. Some of these are World Hypertension Day, World Heart Day, World Kidney Day, World Diabetes Day, and many more. HFB is also originating additional events such as Walk for Heart Day. All these events will boast a flurry of activity, with hopefully tremendous motivation for all to take more interest in their bodies and ways they can look after themselves.

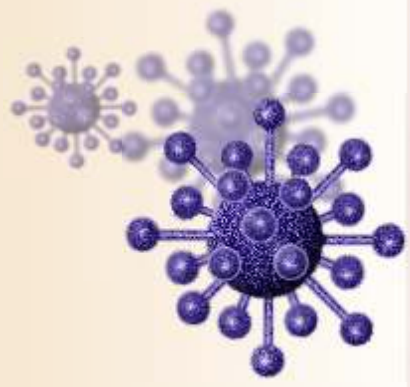
Stomach Flu

Q Hie. I recently went to the doctor with my son suspecting he had cholera. I was informed he had stomach flu and I was given a prescription for those oral re-hydration sachets…….. Could you please explain this further for me?

Thanks, Gontle

A *Thanks very much Gontle for getting in touch with Diagnostics Update.com. We forwarded your query to Dr Ritalin, consultant pathologist at DML, who responded with an article. We hope this article answers your question and any other that you or anyone else might have on the subject.*

Ed.



Stomach flu or Gastroenteritis (also known as gastric flu, although it is unrelated to influenza), is inflammation of the gastrointestinal tract, including stomach and intestines. The inflammation is caused by infection with certain viruses, bacteria, parasites, or toxins. Inadequate treatment of gastroenteritis kills 5-8 million people per year worldwide, especially infants and children under 5 years of age.

Half of the cases of gastroenteritis as food borne illness are due to noravirus infection and majority of severe cases in children are due to rotavirus infection. Other significant viral agents include adenoviruses and astroviruses.

Symptoms and Signs

The main symptoms are watery diarrhea, nausea and vomiting. There may also be headache, fever, and abdominal cramps. Symptoms generally start 1-2 days following infection and may last up to 10 days. Most people recover from infection completely without long-term problems. It is severe for people unable replenish lost fluids and electrolyte. Infants, young children, disabled and elderly people are particularly at risk of dehydration.

Immune compromised persons are more prone to dehydration because they are more vulnerable to get a serious infection with severe vomiting or diarrhea. They may need hospitalization for appropriate treatment to correct dehydration.

Is it contagious? How does it spread?

Viral Gastroenteritis is contagious. It is spread through close contact with infected persons e.g. by sharing food, water and eating utensils. One can also get infected by eating or drinking contaminated food and beverages.

Food may get contaminated by food preparers and handlers who have the infection, especially if they do not wash their hands regularly after using the bathroom. Shellfish and fish harvested from contaminated water may also cause infection. Drinking water contaminated with sewage can also be a source of infection.

Particular care should be taken with young children in diapers who may have diarrhea. Some people may even continue to be contagious for as long as 2 weeks after recovery. Therefore, it is particularly important for such people to follow strict hygienic protocol.

Who? Where? When?

Viral gastroenteritis affects people of all age groups or backgrounds in all parts of the world. Rotavirus and Noravirus infections are more common among children and Noravirus infection in particular among older children and adults. There are many different strains of the same virus, which makes it difficult for a person's body to develop long lasting immunity. Recurrence can therefore occur during a person's lifetime even after suffering an infection.

The viruses are also known to have seasonal activity. Rotavirus and Astrovirus infections are more common in cooler months, whereas Adenovirus infection can occur all year round. Noravirus outbreaks can occur in institutional settings, such as schools, childcare facilities, nursing homes, banquet halls, cruise ships, etc.

Tests and Treatment

Laboratory tests include stool examination, stool culture, microscopic examination to excluse parasites, their ova and cysts, and ELISA to detect viral antigens and antibodies.

Principal treatment is rehydration. This treatment should begin at home and excludes sports drinks which do not replace the nutrients and minerals. Medications, including antibiotics and other treatments should be avoided unless specifically recommended by a physician. Currently, there is no antiviral medication that works against Noravirus and there is no vaccine to prevent infection.

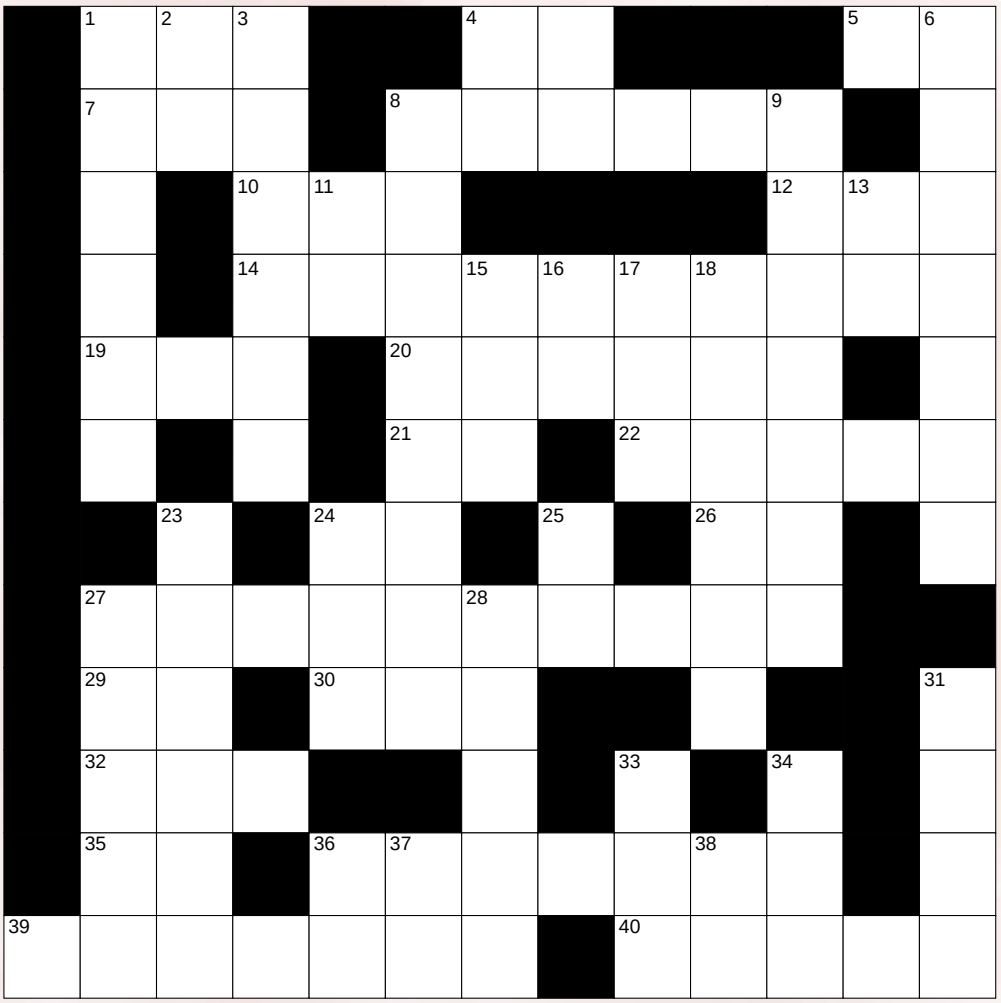
Prevention

Persons can reduce their chance of getting infected by frequent hand washing, prompt disinfection of contaminated surfaces with household chlorine bleach based cleaners, and prompt washing of soiled articles of clothing.

Remember

- Frequently wash your hands, especially after toilet visits and changing diapers, before eating and preparing food.
- Carefully wash fruits and vegetables, and steam oysters before eating them.
- Thoroughly clean and disinfect contaminated surfaces immediately after an episode of illness by using bleach based household cleaner.
- People who are infected should not prepare food while they have symptoms and for 3 days after they recover.

Crossword



Decrypt

Associate a number with a letter, then substitute that letter above the number below to form a phrase.

A	
B	
C	
D	
E	
F	
G	
H	
I	
J	
K	9
L	19
M	
N	3
O	
P	
Q	
R	
S	
T	20
U	
V	
W	
X	
Y	26
Z	

21 15 4 14 23

T 20 8 10 25 6 14

25 N 3 8 18 14 3

2 21 3 23 1 15 20

2 Y 26 1 17 25 21 3

K 9 14 18 20

24 25 L 19 19 21 3 13

8 15 20 .

Scramblers

Unscramble each of the clue words
Copy the circled letters to form mystery word

DAPRI

ARALMAI

LAYLERG

MOUNSPAEE

NERCCA

WEYGAGR

RALFEUR

Across

1 Boy offspring [3]
4 Nitric oxide [1.1]
5 Gaborone (colloquial) [1.1]
7 Mimic [3]
8 Accumulated [6]
10 Epidemiology and Public Health [1.1.1]
12 Alcoholic spirit [3]
14 A Botswana medical lab [10]
19 Lots of Love [1.1.1]
20 Aid [6]
21 Millilitre (Abbr) [2]
22 Roman language [5]
24 Calcium chemical symbol [2]
26 In response to (when writing a letter) [2]
27 Doctor wrote a pharmacy note [10]
29 Operating Room [1.1]
30 For Your Information [1.1.1]
32 On which to lay down on [3]
35 Operating System [1.1]
36 SMS = Short ____ Service [7]
39 Verge / Radical [7]
40 Container used for medicine [5]

Down

1 A portion of / Unit tested in lab [6]
2 Operation (Abbr) [2]
3 Pierces skin & vein during blood collection [6]
4 Response in the negative [2]
6 An Order [7]
8 Medication dispensary [8]
9 Roamed aimlessly [7]
11 Coagulation test / Detective [2]
13 “you are” in SMS language [2]
15 Jelly-like substance used to style hair [3]
16 National Laboratory [1.1]
17 Precious combustible liquid [3]
18 Was afraid [6]
23 Heart attack = Cardiac ___ [6]
24 Cerebrospinal fluid [1.1.1]
25 Hello [2]
27 Postal address [1.1.3]
28 Final wash to remove soap [5]
31 Brick and mortar built structure [4]
33 Cervical cancer screen test [3]
34 Hawaiian flower wreath [3]
36 ___, myself and I [2]
37 Electromagnetic [1.1]
38 Growth Hormone [1.1]

Why I just might quit meat!

Silas Nunu

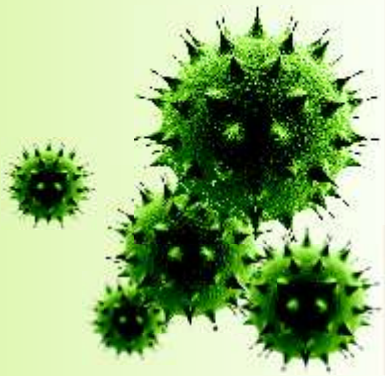
The mention of 'flu' has always brought about visions of cold, clammy winter days, but never did I imagine that one day the word 'flu' would be tied down to my food or, more specifically, my meat choices.

First there was bird/avian flu, which made me temporarily forego the occasional binge on takeaway chicken and the hearty egg breakfast. "Not too bad" I told myself, "I can always get my meat nutrition from elsewhere: after all there is beef, pork, mutton and so on."

Now there is "swine flu", said to be a mixture of swine, human and avian flu viruses; which we are told is more virulent and harder to contain than the other flues. Why do I get the sneaky feeling that there is a bovine flu coming along that will kill you as slowly as grilling your beef over some mildly hot coals?! But come to think of it, there has been Bovine Spongiform Encephelopathy (BSE), more commonly known as 'mad cow disease' to disturb those beef aficionados. Though it's not flu, its cause is virus-like. So, the question is: 'is it all doom and gloom?'

As of now, it's difficult to say, because there is quite a bit of misinformation out there and the answers are hard to come by. Just ask Mrs. Hernandez, the mother of the first recorded sufferer, Edgar Hernandez. She had this to say: "If the people who are supposed to be familiar with this didn't know what it was, how will we ever know how my son got it?"

The minute you **"google"** swine flu, you have some sites advising you to go around wearing face-masks, others predicting a pandemic of immense proportions, while still other sites merely calling it a variant of our seasonal flu, and on it goes; all of them claiming to be official sources with the latest updates.



What we do know is this: the reason swine flu is dangerous and has pandemic potential written all over it is that it has symptoms similar to those of our common "normal garden variety" flu, and hence, hard to distinguish. So, what may start out as some sniffles, can then progress for longer than normal, and by the time the diagnosis is made that it is swine flu, you have spent too much time unnecessarily sipping flu syrups and treating the wrong thing.

Swine flu is said to be caused by a virus with a mix of bird, pig and human genes (yes, it is the Frankenstein of flues), and humans have limited immunity to it. As I write this, about 160 people in Mexico have died from suspected swine flu infections. Of these, 44 have so far been confirmed as having being caused by the "H1N1 influenza A" virus (a.k.a. swine flu). Outside of Mexico it is confirmed to have claimed many lives as well. The World Health Organisation has declared it a Phase 5 outbreak; the second highest on its threat scale before it is declared a pandemic.

This though is not the first swine flu outbreak the world has had to deal with. There have been others previously; in 1918, 1976 and 1988. Although most of these swine flu infections will resolve themselves without the need for any treatment, the virus is said to mutate quickly and significantly and thus could become even more virulent.

The problem we now face with swine flu is that it can be harder to contain than other respiratory pandemics we have had lately. This is because its incubation period is up to seven days, so, there is a pre-symptomatic infectious period; which means, sufferers are infectious before symptoms appear—up to 24 hours before symptoms appear. Up to one-third of sufferers do not show signs of sickness; however, they can still spread the disease even if they do not show symptoms. Also, sufferers are at their most infectious at the start of the infection. That means, during that stage when you are still wondering if you got the flu or you are just suffering from the effects of your car air-con, you are in fact busy incubating the swine flu virus in your body! Aaaaah!

Also, to add fuel to the fire, there are no vaccines available so far for prevention of exposure to this virus. So, in the meantime, reduction in transmission will have to be through good old courteous healthy behaviour. That is: (a) Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it. (b)Wash your hands often with soap and water, especially after you cough or sneeze. Alcohol-based hand cleaners are also effective. (c) Avoid touching your eyes, nose or mouth. Germs spread that way. (d) Stay home if you get sick. It is recommended that you stay home from work or school, and limit your contact with others to keep from infecting them.

Also make sure that if your job involves continuous contact with people, like with nurses and doctors, disinfection after every patient or customer must be practiced.

That said, I'm left wondering what zoonotic flu will be visited upon us next year. To all of you who eat dog, donkey or rodent meat; beware of canine, equine and murine flu.

Tell me what you think.