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From the President's Pen

Colleagues,

I greet you in the great name of the Almighty God. May His peace descend on you and His love and mercy, the garment in which you are clothed.

It had not been long since I handed the mantle of leadership of this August association to Hon. Past President Dr Mojela who also passed it on to our immediate past President Dr McPherson.

Indeed, if someone had told me that just two years after that handover I would be called back to the horses' saddle and be given the responsibility once again of being the one to direct and spur it on as it gallops ceaselessly to the great heights it sets itself to reach in life, my response automatically and unequivocally would have been "OH! Is it really me once again who is being requested to step into this challenging position of onerous responsibility?" Despite my current tight professional and official schedule I feel more obliged to listen to the voice of the people to lead them as the president of our great association. Of course saying "NO" was my spontaneous reaction but saying that NO, it later dawned on me, would again be tantamount to letting down the people who have reposed immeasurable measure of confidence in me.

My interpretation of you colleagues calling me back to take once again the mantle of leadership of the Lesotho Medical Association is that of you putting your trust in me. By this action you make me believe that words from my mouth to you or words I disseminate to you through the President's Pen of this journal as I am doing now are words that you cherish and are ready to assimilate and make part of your own thoughts as you turn things in your minds with respect to what you can do as an individual to promote the good name of this association.

Colleagues, if my interpretations of your calling me back to captain this ship is understood in the same vein as indicated above, then I can never thank you enough, for the great honour bestowed on me.

Past presidents Dr Mojela and Dr McPherson as we all can truthfully testify to, very capably led this association efficiently, effectively and efficaciously for the past two years. The styles of leadership of these two immediate past dynamic presidents can be likened to that of a father who in the face of all odds worked very assiduously to maintain the unity and pride of his family.
We were that family and the odds they faced were none other than lack of funds, disunity, low attendance at meetings, and members disinterest and apathy towards activities organized by the association.
To my feeble mind and for the good of this noble association of ours the collective, collateral and institutional member skills and efforts possessed by members are more than adequate in unified manner to champion the cause of all its members and objectives of the body.

In view of this, there is no point for the formation of subgroups or appendages to the association under which we all fall since any of such moves may be detrimental to the hard fought long standing unity and cohesion which have been built within the pillars of the association over the years by our predecessors.

These odds are cancers that eat the fabrics of societies and hence harbingers of associations' disintegration. They have plagued the Lesotho Medical Association for sometime now and colleagues, if we mean business with regard to lifting this association to levels commensurate with our professional status and obligations to the society we serve, then we need to rise above such petty sectional interests which may serve as centripetal forces to the well being of our association.

My dear colleagues I entreat members to actively participate in continuous programmes of the association including our participation in continuous professional development. As far as my conviction of the benefits members stand to gain as the quality of services they render to the community is concerned, my office pledges to make organization of continuous educational programmes a focal area of attention.

I preach to you love, peace and unity. We need these for the sustenance of ourselves as an association and for the fortification of our spirits as we extent welcoming hands to those that are in distress and in want of health.

I take this opportunity to remind colleagues of our expected role in this society. We are mandated by our profession to safeguard the health needs of the people. We interact with the sick, many of whom may benefit from treatment we provide not only through medicines we give but also the love we show to them through assurance we give and ways and manners in which we show concerns about the states of their health. Let us remain united in our actions and pronouncement and be professional to acceptable levels of satisfaction and standard the society demands of us.

GOD BLESS US ALL.

Thank You.

Dr C.K Hoedoafia

26/08/2009

Editors

Instructions for Authors

The Lesotho Medical Association Journal accepts editorials, original research papers, review papers, case discussions, clinical guidelines, letters and Lesotho medical news reviews.

The author should submit both an electronic and hard copy of the manuscript to the address below:

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Breast Feeding

M MOKETE, MD

A month of breastfeeding (August) has just been commemorated in all countries of the world boosting and encouraging those who breastfeed to continue to do so and those who shun or have other reasons not to do so to start and continue to breastfeed at least for six months.

Breastfeeding advantages for the child and mother are well known, among which mention may be made of: the normal and ideal temperature of the milk, the full nutritional content, the protection of the baby immunologically at least in the first six months and further the bonding with the mother and the avoidance of contamination of any feeds by bottle feeding.

Lesotho Medical Association acknowledges the hurdles engendered by the work situation in which mothers have to stay away from home for a greater part of the day in factories, offices, etc. We are saying why wont Governments attach Nurseries/Kindergartens to all work centres so that kids can always be next to their mothers and have regular feeds? We are questioning why Governments and private sector cannot give sufficient maternal leave of a minimum of three months or even six months like in some Nordic countries in order to provide cover for the development of the future human capital?

We must also be aware of the dilemma created by HIV and AIDS pandemic wherein some mothers are reluctant to have mother to child transmission of HIV through breastfeeding. L.M.A says mothers, as internationally agreed, should continue to breast feed for six months with adequate triple ARV treatment to prevent transmission of viruses to the children.
With the questioned efficacy of the triple prescription of ARV's containing NEVIRAPINE, why can't the authorities who are responsible for the WHO strategy (NEVIRAPINE, Zidovudine and Lamivudine) adopt an improved strategy (Tenofovir, Zidovudine, Lamivudine) which has had successful results of prevention of transmission in some centers in Europe?

Governments in the early nineties slowly embarked on a campaign of knowing your status (KYS), most successful in the new millennium, among the most vulnerable, the fourteen year olds to the forties and perhaps beyond. The campaign, which is very difficult, left out the babies who were being made and being born in those years.

Today many infected children have been born and many countries are waking up to the problem of mother to child infection which has increased exponentially as an additional burden to the diagnosis, care and treatment of these cohorts of the population, let alone manpower needs to contain the problem.

The bottom line is in the political will of facing reality and awareness of the fact that time and tide wait for no man. TB programmes were shelved or taken with less intensity, but today time is overwhelming us with multiple health burdens. Let us wake-up and overcome.

Mycobacterium tuberculosis and Human Immuno-deficiency Virus Co-infection:

Is this not a medical emergency?

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Mycobacterium tuberculosis

Introduction

Infection with Mycobacterium tuberculosis (MTB) is widespread throughout the world, and tuberculosis is one of the leading causes of death in developing countries [1]. Although M. tuberculosis is the most common cause of tuberculosis, other Mycobacteria such as M. bovis, M. africanum, M. carnetti, and M. microtti are also implicated but their prevalence is uncommon [40]. Despite advances in diagnosis and treatment, tuberculosis remains a major worldwide health problem, and, in developing countries, the epidemic of TB is further exacerbated by the presence of a large group of HIV-1 co-infected individuals [6]. According to Harries et al, one of every four human immunodeficiency virus type 1 (HIV-1)-infected persons in the world is diagnosed with active TB [32]. As summarised by De Cock et. al, various studies have reported a prevalence of HIV infection among tuberculosis patients in sub- Saharan African countries to range from 20- 67% [38].

The success of MTB as a pathogen is evidenced by its parasitism of approximately one-third of its target population: mankind [2]. Attempts to control TB are exacerbated by long-term persistence of MTB, TB-HIV co-infection, and the emergence of multidrug-resistant (MDR) MTB strains. One factor that may be important in moderating the interactions of M. tuberculosis with alveolar macrophages is pulmonary surfactant, a complex mixture of lipids and specific proteins that is synthesized, packaged, stored, and secreted by type II epithelial cells in the alveolar lining [3],- [5].

Pathogenesis M. tuberculosis

Infection with M. tuberculosis most commonly occurs via the respiratory route by inhalation of droplets that contain the bacilli but a previous infection may also be reactivated. In areas of low prevalence of tuberculosis, it is generally thought that most TB cases arise from latent infections, because only few new infections are occurring [39]. About one in ten of these latent infections will eventually progress to active disease if left untreated [40]. The number of bacilli expelled into air, the concentration of bacteria in air, and the length of time exposed to bacilli determine the likelihood of infection. Once infected the progression into an active disease depends on immune status. Of those individuals with normal immunity 90% will not progress into active disease [40]. Some of those at risk because of decline in immunity are children less than 5 years, elderly, diabetic and individuals infected with HIV. Other risk factors include silicosis, use of immunosuppressive drugs and patients on chemotherapy.

Inhaled bacilli are engulfed by alveolar macrophages, the first line of host defense against the pathogen, within which MTB survive by arresting phagosome maturation and avoiding fusion with lysosomes [2]. Thus the interactions between M. tuberculosis and pulmonary macrophages are crucial in the disease process caused by this microorganism. Marchal et al deduces that the importance of infection is the formation of a caseus granuloma, a cellular formation which results from phagocytosis of MTB by alveolar macrophages and recruitment of other mononuclear cells from neighbouring blood vessels [53]. Also local immunity may have a significant impact on the clinical features of the disease, as type-1 immunity predominates in non-cavitary TB, whereas a type-2 response is associated with lung cavitations and extensive tissue necrosis [7].

Tumour necrosis factor alpha (TNF-α) and inflammatory chemokines produced by the infected macrophages recruit white blood cells, which phagocytise bacilli and by returning to the bloodstream may cause haematogenic dissemination that may lead to systemic manifestation of the disease [2]. Tubercle bacilli can also spread by the lymphatic route to regional lymph nodes; from the hilar lymph nodes tubercle bacilli spread through the thoracic and vertebral lymph nodes and reach the blood through the thoracic duct. This may lead to infection of other organs such as the upper areas of the lungs, kidneys, brain, and bones. Despite the increased frequency of unusual forms of TB in persons with HIV infection, respiratory forms of TB infection tends to dominate in most cases [41], and are therefore associated with increased mortality if a patient does not present earlier for treatment.

Common symptoms of tuberculosis include chronic cough with blood stained sputum, night sweat, loss of weight and loss of appetite.

Immune response against MTB

Cellular immunity to MTB requires a coordinated response between the innate and adaptive arms of the immune system, resulting in a type 1 cytokine response, which is associated with control of infection. Although macrophages are identified as main targets of infection by M. tuberculosis, it has been postulated that other cell populations, such as Langerhans cells by their TLR expression profile that help them recognize bacterial cells [51], are still susceptible to infection and hence important in the progress of the disease. Neutrophils are among the first recruited to the site of infection and are important in the production of chemokines [8], and granuloma formation [9].

Mast cells are found in the mucosa of the gastrointestinal tract, respiratory, urinary and lymph and blood vessels. They have a role in allergic reactions [10] and are responsible for development of T Helper 2 response [11]. They express a receptor with high affinity for immunoglobulin E (IgE) and upon binding of an antigen with active sites of IgE and mast cell complex, several immune mediators are released and they aid in recruitment of other immune cells and hence add to local damage. Besides interaction of antigen with IgE, other agents are able to directly activate mast cells and induce release of cytokines and other mediators. Such are microbial products that stimulate mast cells through activation of two types of Toll-like-receptors (TLR), TLR-2 and TLR-4 [12], [13].

On entrance of tuberculosis bacilli into the alveoli, macrophages initiate the primary response against bacilli through interactions with cellular receptors such as those for the Fc portion, complement [14], mannose [15], surfactant protein [16], CD14 [17], and CD43 [18]. TLR-2 and TLR-4 present on the surfaces of immune cells are activated by several mycobacterial components such as the 19 kDa lipoprotein and lipoarabinomanann (LAM) which activate macrophages through TLR-2, promoting the production of IL-12, IL-6, TNF-α and inducible nitric oxide synthase (iNOS) [19]. When MTB bacilli are inhaled and phagocytised by macrophages, they remain and even replicate in the cell because they are able to arrest phagosome and avoid fusion with lysosomes [2].

Dendritic cells function as antigen presenting cells and they recognize, capture and process antigens, thus being able to present them in the form of major histocompatibility complex (MHC) molecules, as well as through CD1 [20]. Dendritic cells bind antigens via C-type lectin receptors and Fcγ/Fcε receptors, and internalize them by endocytosis [21], which in MTB is carried out through C-type lectin receptors such as dendritic cell-specific intercellular-adhesion-molecule-grabbing non-integrin (DC-SIGN) [22]. DC-SIGN interacts with mannose capped-LAM, present on the cell wall of the MTB [23], inducing release of IL-10. Furthermore, peripheral blood dendritic cells and immature dendritic cells derived from monocytes express TLR-2 and TLR-4 [24], with which MTB interacts. Natural killer cells are among the first cytotoxic cells recruited to the site of infection and they are associated with secretion of Interferon gamma (IFN-γ) and enhancement of CD8+ T lymphocytes to produce IFN-γ and lyse cells infected with M. tuberculosis.

Specific immunity can be divided into cell mediated immunity, which coordinates maturation and action of cytotoxic T cells; and humoral immunity that controls maturation of B-cells and antibody production. As for intracellular infection, as in MTB, immune

response is mainly cell mediated. However, MTB is resistant to cell-mediated microbicidal agents that clear the phagocytised material [2]. It also produces agents that hinder macrophage activation by IFN-γ and IL-12, which both activate macrophages and promote bacterial destruction.

Since bacilli reside within the macrophage [53], their antigens are presented by MHC class II molecules to CD4+ T lymphocytes. These cells play an important role in the protective response against MTB through production of cytokines such as IFN-γ and their absence therefore renders growth of bacilli difficult to control [25]. They also help in developing the CD8+ T cell-mediated response [26]. Additionally, CD4+ T cells may participate in the induction of apoptosis of infected cells and the subsequent reduction of bacterial viability through the CD95 Fas ligand system [27]. From Serbina et al, CD8+ T cells showed the ability to secrete IFN-γ through activation of the T-cell receptor or by interaction with infected dendritic cells in the lungs of infected mice [28]. In addition, CD8+ T cells proved to be efficient in lysing infected cells and in reducing the number of intracellular bacteria [29]. The mechanisms of control of the bacterial load seem to be associated with granular exocytosis involving perforin and granzymes. Still, granulysin, which is found in CD8+ T granules, is the molecule responsible for killing the bacterium [30].

Human-immunodeficiency virus

Introduction

Since the discovery and isolation of HIV by Robert Gallo and Luc Montagnier in 1984, the origin of HIV-1 among non-human primates has been traced to a simian virus, SIVcpz, which infected several geographically isolated chimpanzee communities in Southern Cameroon [31]. HIV is a single-stranded RNA and enveloped virus that belongs to the genus Lentivirus of the family Retroviridae [40]. Retroviruses derive their name from the Latin retro (backwards) because they transcribe DNA from a viral RNA template [35]. Efforts to prevent HIV infection, which largely focus on altering human behavior, have had some notable successes in some parts of Sub Sahara yet have failed to halt the spread of the AIDS pandemic, with 22.0 million people reported to be living with AIDS by the end of 2007 (UNAIDS, 2007). Many infections seem to be acquired through unprotected sexual intercourse. From a study done amongst women at high risk of HIV infection in Durban and Hlabisa, Tanzania and Zambia, Ramjee et al commends that high-risk sexual behaviours were common, and consistent condom use remained low despite ongoing counselling conducted during the study [55].

Pathogenesis

The chief cell targets of HIV are CD4+ T lymphocytes, macrophages and monocytes which only support HIV replication when activated as in an immune response [35]. However viral cDNA can persist in resting lymphocytes for a long time as a latent infection. In terms of infections through genital secretions, the first cells to become infected may be immature dentritic cells, Langerhans cells or submucosal lymphocytes in the genital tract or rectum [36]. The virus may then be transported to lining lymphocytes where it replicates extensively and infects more cells. At about one to twelve weeks following infection by HIV, most patients develop non-specific flu-like illness characterised by fever, pharyngitis, lymphadenopathy, rash and fatigue. This is known as acute retroviral syndrome and it is associated with increased viral population in the blood and a decline in CD4+ cells [58]. Beside viral induced apoptosis of infected cells [33], CD8+ cytotoxic T cells, natural killer cells, and antibody dependent cytotoxicity may contribute to decline of CD4+ cells by lysing infected cells while neutralising antibodies clear free virions [35].

A long asymptomatic period known as clinical latency, lasting from 1-15 years, then follows before any clinical evidence of infection appears. During this period, only low viral titres are demonstrable in blood by conventional culture techniques. Although frequent, at CD4 counts greater than 500cells/mm3 many clinical symptoms match those observed in common bacterial illnesses like tuberculosis, pneumonia and minor skin conditions. However, at CD4 counts between 200cells/mm3 and 500cells/mm3, additional symptoms begin to appear such as Kaposi's sarcoma, Candidal infections and Herpes Zoster. The last stage is an end AIDS stage in which in-

dividuals develop severe symptoms associated with additional infections.

Immune response against HIV

Due to abnormalities and decline in T lymphocytes, patients have an increased susceptibility to opportunistic infections and increased incidence of neoplasms such as Kaposi's sarcoma.

Langerhans cells (LC), a unique dendritic cell-type, are ideally suited for their function as antigen presenting cells that capture invading viruses and induce anti-viral immunity because they are located in mucosal stratified squamous epithelium and skin epidermis [36] and they express receptors with affinity to those on the viral membrane. They are able to interact directly with microorganisms at the periphery to produce effector cytokines and initiate activation of T and B lymphocytes through antigen presentation since they express different pattern recognition receptors such as C-type lectin receptors (CLR) and Toll-like receptors [36]. Langerhans cells and immature dentritic cells are more important in HIV-1 transmission because they express high levels of CCR5. But on maturation, CCR5 is down-regulated and CXCR4 up-regulated resulting in reduced infectability by R5 (CCR5 binding) viral strains, which are shown to be predominant during sexual transmission [37]. Mature LC migrate to the lymph nodes where they are directly or indirectly involved in presentation of pathogen derived antigens on MHC Class I and II to T cells, resulting in activation of antigen-specific T cells [52].

HIV replication

The virus invades CD4+ cells by attachment via its extracellular glycoprotein receptor, gp120, to a primary receptor, CD4, which CD4+ cells possess on their membrane [35]. Cellular entry of HIV-1 requires binding to both CD4 and to one of the chemokine receptors that act as co-receptors (CCR-5 or CXCR-4) [57]. CCR5 and CXCR4 were identified in 1996 as the major co-receptors for HIV-1 cell entry [56]. Entry into the cell then occurs by direct pH independent fusion of trans-membrane protein, gp41, with plasma membrane hence allowing the core of the virion to be liberated into the cell cytoplasm [35]. The viral nucleocapsid consists of two viral RNA strands and three replication enzymes (Reverse transcriptase, Integrase and Protease). With the genome available for reverse transcription and using the host cell nucleotides, Reverse Transcriptase changes ssRNA for dsDNA with long terminal repeats composed of sequences duplicated from the 3′ (U3) and 5′ (U5) ends of viral RNA. Integrase then cleaves a dinucleatide from each prime end of the DNA creating two sticky ends. It then incorporates the viral DNA into the cell nucleus and integrates it into the host cell genome. The host genome, containing the viral genetic information, gets activated and this induces transcription of proviral RNA into messenger RNA (mRNA). In the cytoplasm of the host cell, mRNA produces poly-protein chains that are processed and cleaved into smaller molecules by Protease. A nucleocapsid is then formed by two viral RNA and replication enzymes which leave the cell acquiring a new membrane. Complete reverse transcription and integration of the DNA provirus into a chromosome occur efficiently only in activated and proliferating T lymphocytes which is brought about by mitogens, cytokines or transactivating proteins encoded by certain other viruses such as HTLV-1, HSV and HHV-6.

Treatment in the TB-HIV co-infection

Drugs that are used to treat patients with human immunodeficiency virus (HIV) infection are classified according to their target in the HIV replication or life cycle. Antiretroviral drugs that inhibit reverse transcriptase fall into two groups; namely, Nucleoside reverse transcriptase inhibitors (NRTIs) and Non-nucleoside reverse transcriptase inhibitors (NNRTIs) [42]. The first to be developed were NRTIs, which lead to premature termination of the nascent DNA chain; and NNRTIs, which bind and inhibit reverse transcriptase [43]. The viral protease inhibitors were next to be generated, which in combination with NRTIs and NNRTIs produce a combination of highly active antiretroviral therapy (HAART) [44]. Other targets, such as the CCR5 receptor, the fusion peptide, and viral integrase, have recently yielded promising molecules. However, current guidelines recommend initiating anti-retroviral therapy with two NRTIs in combination with either an NNRTI or a protease inhibitor [45]. According to a study done by Riddler et al, Hirschel et al summarises that efavirenz plus two NRTIs provides a good

combination, however, Etravirine (an NNRTI) [46], Raltegravir (an integrase inhibitor) [47], and Maraviroc (a CCR5 inhibitor) [48] are targeted to patients with drug resistant HIV.

Some people find it difficult to cope with taking a large number of pills which unfortunately is a daily required for treatment of both HIV and tuberculosis. Concerning drug interactions and toxicities associated with anti-TB and anti-retrovirals, options are to defer HIV treatment until completion of anti-TB regimen or commence anti-retrovirals in the late course of TB treatment. However, from a study done by Velasco et al, simultaneous HAART and TB treatment in HIV patients with TB is associated with improved survival [49]. This supports the South African treatment study done at CAPRISA eThekwini TB-HIV Clinic which showed that mortality among TB-HIV co-infected can be reduced by 55% when TB and antiretroviral treatments are initiated simultaneously [50]. Moreover, from the Sizonq'oba study done in rural South Africa [54], Gandhi et al concludes that TB and HIV treatment in a rural setting can be integrated using concurrent home-based therapy resulting in excellent adherence and TB and HIV outcomes. These models show success in simultaneous management of both diseases despite toxicities that may be brought by combined therapy.

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Keynote Address to the Lesotho Medical Association Research Workshop at Lesotho Sun on 16th to 17th May 2009

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INTRODUCTION

Greetings and thank you for the invitation

This keynote address touches on the importance of strengthening developing countries' involvement in research for health and the consequent role of research. It recognizes that research is central to progress in Global health and outlines ways in which WHO can work with countries and Partners to harness science, technology and broader knowledge in order to produce research evidence and tools for improving health outcomes globally and at national levels. Research is vital for sound policy decisions.

In all countries, increasing demands are being placed on research to provide opportunities for resolving current and emerging health problems. In meeting the challenge of resolving priority problems across the spectrum of public health – whether it be tackling diseases of poverty, responding to the global epidemiological transition to chronic diseases, ensuring that mothers have access to safe delivery practices, or preparing for global threats to health security – research in indispensable.

In a global environment of competing demands for limited resources, it is especially important that health policies and practices should be informed by the best research evidence.

Although the value of research is widely recognized, exploiting research optimally to resolve priority health problems is not a straight forward matter. The complex nature of the health problems confronting societies, the rapid advances in knowledge and technologies related to health, the shifting expectations and concerns of the public in respect to research, and changes in the organization and management of research within and across countries, are among the many factors that must be taken into account.

Importantly, much progress has been made in recent decades. In parallel to the growing importance attached to health globally, attention is increasingly being focused by the broader research community on the health problems of the poor and disadvantaged. Significant research efforts, involving public-private partnerships and other innovative mechanisms, are being concentrated on neglected diseases in order to stimulate the development of vaccines, drugs and diagnosis where market forces alone are insufficient.

Despite this progress, there is growing awareness that research systems are not responding optimally to the diverse demands that they face. Investments in health research are insufficient; further, they are not appropriately directed towards tackling priority health problems. In addition, when complex challenges are being met, such as tackling food insecurity or the effects of climate change, there has been a failure to draw on resources available for research in other sectors. Low income countries are faced with a diverse range of donor-driven research agendas that often weaken national priorities, and many countries are facing significant challenges in training and retaining researchers.

Work in support of the ethical review and public accountability of research is not keeping pace with best practices. The opportunity of creating a shared framework for storing and sharing research data, tools and materials has not been seized with the same energy in the area of health as it has in other scientific fields, and policy-makers are neither contributing to research priorities nor using evidence to inform their decisions.

In view of the rapid changes taking place in public health and research, there is an urgent need for a systematic and comprehensive approach to organizing and managing research for health, especially in developing countries.

The ethics of research related to health care in developing countries

WHO states that all research involving human participants must be conducted in a manner that respects the dignity, safety and rights of research participants and that recognizes the responsibilities of researchers.

The WHO Manual defines research with human subjects as 'any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge, in which human beings i) are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment, or ii) become individually identifiable through investigator's collection, preparation, or use of biological material or other records.'

The term "research for health" reflects the fact that improving health outcomes requires the involvement of many sectors and discipline and contribute to the achievement of the Millennium Development Goals, heath equity and better health for all.

Research for health covers the full spectrum of research, which spans the following five generic areas of activity:

- Measuring the magnitude and distribution of the health problem
- Understanding the diverse causes or the determinants of the problem, whether they are due to biological, behavioural, social or environmental factors.
- Developing solutions or interventions that will help to prevent or mitigate the problem.
- Implementing or delivering solutions through policies and programme.
- Evaluating the impact of these solutions on the level and distribution of the problem.

Many people from the developing world suffer from poor health and reduced life expectancy. The role of research that contributes to the development of appropriate treatment and disease prevention measures is vital. However, lack of resources and weak infrastructure means that many researchers in developing countries have very limited capacities to conduct their own clinical research. They therefore often take research in partnership with groups from developed countries. A sound ethical framework is a critical safeguard to avoid exploitation of research participants in this circumstance.

The need for research

Each year £ 35-40 billion is spent on healthcare research worldwide. But only 10 percent of this is devoted to the health problems of the developing countries which is home to 90 percent of the world's population. Developing countries urgently need research to help prevent and treat diseases such as TB and malaria. But many countries have limited funds and a lack of trained staff to conduct their own research. It is vital that the public and private sectors in developed countries should sponsor research to help bridge this gap.

Social and cultural issues

Misunderstandings can occur when sponsors of research are unfamiliar with the cultural traditions of the country in which it is conducted. There will often be cultural differences between those organizing of funding the research and the participants, for example, differing perspectives in respect for family and individuals, and the role of the community.

Setting priorities

National resources for research are often lacking in developing countries and it is therefore particularly important for each country to ensure that research is appropriate and relevant for its health needs. It is recommended that all countries should set national priorities for healthcare, the research should be justified to the appropriate research ethics committees.

Ethics guidelines in research

The ethical and scientific standards for carrying out biomedical research on human subjects have been developed and established in international guidelines including the (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects, and the WHO and ICH Guidelines for Good Clinical Practice. Compliance with these guidelines helps to ensure that the dignity, rights, safety, and well-being of research participants are promoted and that the results of the investigations are credible.

These guidelines are intended to facilitate and support ethical review in all countries around the world. They are based on a close examination of the requirements for ethical review as established in international guidelines, as well as on an evaluation of existing practices of ethical review in countries around the world. They do not, however, purport to replace the need for national and local guidelines for the ethical review of biomedical research, nor do they intend to supersede national laws and regulations.

Consent

For research to be ethically acceptable, participants should be given the relevant information in a comprehensible manner, and must take part voluntarily. However, differences in social and cultural contexts in developing countries mean that some procedures may be ineffective or inappropriate. The way in which information on the potential risks and benefits or research is provided is particularly important.

- Who should give consent?
- How should consent be obtained?
- How should consent be recorded?
- Are inducements acceptable?

All these questions are important and should be based on National guidelines and laws.

Standard of care

A particularly controversial issue concerns the 'standard of care' that should be provided to participants during research in developing countries. Much of the debate has focused on the level of care provided to the control group in clinical trials. Should participants in developing countries receive the same standard of care that participants in wealthier countries would receive if the research was conducted there? Yes of course.

What level of care should be provided for those in the control group?

Some argue that when research is externally sponsored, participants in developing countries should receive the same standard of care as participants would receive if the research was conducted in the sponsor's country. Others argue that this could prevent some forms of potentially beneficial research from being undertaken.

Is it ethically acceptable to conduct research in a country that may not be able to afford to provide the treatment if it is effective? This is not always a straightforward issue. For example, sometimes the cost of treatments can drop dramatically after research, or an agreement may be reached with pharmaceutical company that the treatment will be provided for free for a certain period.

Who should be responsible for making a successful intervention available?

We consider that the provision of new medicines or improved healthcare is primarily the responsibility of national governments. However, researchers and sponsors should address the issue before starting research. They may also play a role by contributing to the development of local healthcare facilities.

Where participants have chronic diseases, who should be responsible for providing continuing care after the research is over?

Participants in research may have conditions that require continuing treatment. In such cases, it may be suggested that there is an obligation to continue to provide an intervention that has been shown to be effective. Researchers should try to secure post-trial access for effective interventions for all participants before the trial begins.

Other important issue that must be considered relate to :

- Adverse affects that occur as a result of an intervention under evaluation;
- Long-term surveillance of participant after the research is over;
- The responsibility of researchers, sponsors, international agencies and governments; and
- The continued provision of a higher of healthcare.

The majority of biomedical research has been predominantly motivated by concern for the benefit of already privileged communities. This is reflected by the fact that the WHO estimated that 90% of the resources devoted to research and development of medical problems are applied to diseases causing less than 10% of the present global suffering. The establishment of international guidelines that assist in strengthening the capacity for the ethical review of biomedical research in all countries contributes to redressing this imbalance.

Ethical committee

An effective system for ethical review of research proposals is a crucial safeguard for participants. However, properly functioning research ethics committees (RECs) are often absent, ineffective or underresourced in developing countries. In addition, there may not be enough trained and independent people to serve on a committee.

What types of review should be required?

It is recommended that each proposal should receive three levels of assessment:

- Relevance to healthcare priorities within the country;
- Scientific validity; and
- Ethical acceptability.

Who should fund Research Ethics Committee (REC)?

Many RCEs in developing countries have very limited financial and administrative support. Some may receive funding from government, while others levy fees for reviewing protocols.

It is crucial that RECs are independent. There is therefore need for creative approaches for providing support for RECs, without compromising their independence. Sponsors could meet the costs of reviewing externally sponsored research in an appropriate manner.

Developing capacity

Local expertise in healthcare-related research is generally very limited. Externally sponsored research has the potential to allow regional scientist to develop skills and expertise. Partnerships between scientists from developed and developing countries can help to build capacity. The development of expertise in ethical review is also urgently required. We recommend that sponsors of research should require that the development of local expertise in healthcare is an integral component of research proposals.
Consideration should also be given to longer term issues – it is important to ensure that improvements to healthcare facilities are sustainable once the research is over. We recommend that international organizations should help to strengthen research ethics committees by expanding initiatives that assist with training and monitoring.

Establishing a System of Ethical Review

Countries, institutions, and communities should strive to develop ECs and ethical review systems that ensure the broadest possible coverage of protection for potential research participants and contribute to the highest attainable quality in the science and ethics of biomedical research.

States should promote, as appropriate, the establishment of ECs at the national, institutional, and local levels that are independent, multi-disciplinary, multi-sectorial and pluralistic in nature. ECs require administrative and financial support.

Procedures need to be establishment for relating various levels of review in order to ensure consistency and facilitate cooperation.

The Nuffield Council following an International Workshop published the ethics of research related to healthcare in developing countries in April 2002.

The discussions that took place at a follow-up Workshop held in Cape Town in February 2004 were published in a Discussion Paper in March 2005.

The role of WHO in research ethics

WHO's role in research for health is executed through its six core functions, one of which is: "shaping the research agenda and stimulating the generation, translation and dissemination of valuable knowledge".

The other five functions involve providing leadership, setting norms and standards, articulating evidence-based policy options, providing technical support, and monitoring the health situation.

Research Ethics in WHO is overseen by the WHO Research Ethics Review Committee, known as the WHO ERC, and is housed within the Research Policy and Cooperation (RPC) Department. The ERC secretariat manages the committee, provides initial review of research projects, facilitates ethics review, and liaises with technical units.

The ERC secretariat also supports capacity strengthening, through the ethics review process, and through the development of checklists, templates and other guidance documents that support research proposal development. Capacity building workshops are also organized at regional, country and HQ level.

Department of Research Policy & Cooperation

The Department of Research Policy and Cooperation (RPC) works to strengthen the informational, scientific and ethical foundations of health research. It aims to contribute to health systems development and to health improvement, particularly in the world's poorer countries.

As part of WHO's Information, Evidence and Research (IER) Cluster, the Department of RPC cover a wide spectrum of research functions from setting priorities to formulating policies and guidelines, and from developing interventions to implementing and evaluating programmes. The Department places emphasis on improving the health of the world's poorer populations.

CONCLUSION

Developing countries urgently need research to help relieve the enormous burden of disease that they carry. It is vital that those in wealthy countries, both in the public and private sector, help fund this research.

Countries should set national priorities for healthcare research. If external sponsors propose research which falls outside the national priorities, the research should be justified to the appropriate research ethics committees.

While researchers and sponsors are subject to international declarations, guidelines and regulations, developing countries should develop their own national policy and guidelines to promote ethically sound research.

All efforts should be mobilized to ensure that national research ethics committees are strengthened through training and monitoring.

Research must be appropriately planned, taking account of local context, and effectively reviewed on scientific and ethical grounds.

Collaboration between researchers of developing and developed countries can provide opportunity to assist developing countries to strengthen expertise in conducting and reviewing research.

THANK YOU!

The Role of the Public and Patient Engagement in Quality Healthcare

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This is a modified account of a presentation made at the 12th Association of Medical Councils of Africa (AMCOA) in Maseru in October 2008

Abstract: The aim of the presentation was to consider the experience of the public in our health institutions, both private and Government. This paper attempts to consider these experiences under the following headings:

- Achieving a seamless, co-ordinated experience in our centres
- Monitoring and responding to these experiences
- Health information dissemination to the public
- Handling of complaints from the public, if any

ACHIEVING AN INTEGRATED, SEAMLESS, CO-ORDINATED PATIENT EXPERIENCE

First, it might be useful to define what I understand by the above phrase. I understand it to mean easy access to a healthcare service provider, be they primary health care worker, general medical practitioner or specialist. Hopefully the patient and this provider would be able to communicate in the same language; the provider would be able to deal with the patient's problems or refer them to somebody else who could. The patient should leave the provider having an understanding of his/her illness and the rationale for investigations, treatment options and further referral, if any. The investigations, treatment modalities and specialists would be easily accessible, and the patient would leave feeling satisfied.

Obviously, the above is an ideal scenario, but parts of it are achievable to varying degrees if we consider the different patient settings in Lesotho: private doctors' consulting rooms; health centre/clinic whether government, CHAL or other non-governmental body; district level hospitals, and finally the main referral hospital, Q.E.11 in Maseru. The discussion will focus on the out-patient experience.

PRIVATE DOCTORS' ROOMS AND PRIVATE HOSPITALS AND CLINICS

Those patients who can afford it visit private practitioners of their choice, so in theory part of their wish for their treatment has already been fulfilled. The waiting rooms in most private surgeries are generally pleasant and comfortable (indeed, are designed to be). In many patients are seen by appointment and therefore waiting times, if any, are minimal to moderate, certainly in contrast to public institutions. Consultation time is adequate in general, and since in Lesotho most are Basotho, language is not an issue. Drugs and dressings are often available on site; if other investigations have to be obtained elsewhere instructions are usually clear as to where to go. Referral to government hospitals for specialist treatment may be accepted but only if the patient cannot afford R.S.A. private hospitals.

All in all, the private patient's experience goes along way towards being at least a partially seamless experience, especially in the urban setting, which is where most private doctors are

HEALTH CENTRE PATIENT EXPERIENCES

The health centres may be run by government, CHAL, or private nurse practitioners. The discussion will refer mainly to the CHAL and government health centres. (This discussion excludes filter clinics, whose full-time staff includes doctors) these are primarily nurse driven, with periodic doctor visits, and as such present particular challenges well known to both the patients and the staff.

The clinics are often not easily accessible in the mountainous areas of the country; there are often a large number of patients for the few health staff

available, therefore long waiting times are the norm. Irregular drug stocks may contribute to an unsatisfactory patient experience and outcome. Investigations in this setting are minimal since specimen collection is also periodic. Referrals are done in an ad-hoc manner, with patients often sent to the hospital with little or no explanation of what to expect, and how or when they are likely to return (even in a non-emergency). All in all, the Health Centre experience is a long way from being seamless or co-ordinated in many respects, varying with the complexity of the presenting illness.

DISTRICT HOSPITAL EXPERIENCES.

In the district hospitals, patients have a more disparate, rougher experience than at the Health Centre. This is because:

- Queues are longer
- In most cases the hospital is a bigger physical structure with no central enquiry point and so patients get lost. Additionally the signage is very poor, and even where it does exist, not all patients are literate.
- Referrals, except in emergencies, are cumbersome logistically and a lot of patients do not get a clear explanation of why they are being referred.
- Central to this may be the fact that most doctors in these hospitals do not speak Sesotho.
- T.B. and H.I.V services are still in separate areas though there is such a high rate of co-infection.

These few factors pointed out here, which in fact overlap with the ones mentioned under Health Centre experiences, suggest the public's experiences in hospitals are not integrated and seamless.

H.I.V./AIDS SERVICES

At this point it might be worth digressing slightly to discuss H.I.V services with respect to the above-mentioned indices. Several aspects of H.I.V. services could be positive models of the integrated co-ordinated experiences which we think our patients should have. For example, Senkatana H.I.V Centre has the Botsabelo T.B. Centre at least nearby even though the services are not yet integrated. Similarly, Baylor Paediatric H.I.V. Centre treat children for H.I.V. and T.B.; blood investigations are done on site. The families of the children are also offered counselling, testing and referral as indicated . Co-ordination of nutritional assistance for families, as needed, is also done on site, thus providing another aspect of seamless service.

PATIENT EXPERIENCES AT Q.E. 11 HOSPITAL

Patients' experiences as out-patients in the referral hospital can be extrapolated from their experiences at the District/H.S.A. hospital. The negative factors are largely similar. Even though patients who come to Q.E.11 have specific departments to go to, again there are no signs to indicate where these various clinics are to be found, and there is no central enquiry point. Rather, there are a lot of rather hostile security guards who are disinclined to allow anybody into the hospital except at visiting time.

A lot of referring doctors do not inform the patients that specific clinics are held on only certain days of the week, resulting in wasted transport money that patients can ill afford, and further reinforcing negative feelings that members of the public already have about Q.E.11., rightly or wrongly. However, some specialty clinics in Q.E.11 are booked in advance; this at least means that all patients are seen, with enough consulting time. This should improve some patients' experiences.

Central again to the signage issue is the fact that the other essential services (pharmacy, radiology, dressing room, etc) are all in different areas with inadequate signs as to how to get to them.

A major challenge is that it is the patent's responsibility to take any investigative specimens to the laboratory (no signs) and to subsequently collect the results and bring them back to the doctor who ordered them! This process is fraught with misunderstanding, especially with elderly patients. Needless to say, it often goes wrong, much to everybody's frustration.

For physically disabled patients, experiences in most of our health facilities must be worse than those of their able-bodied counterparts, given all the problems outlined above.

DISCUSSION.

The full topic of which this paper is part involves the public and patients on the one hand, and the providers of quality healthcare on the other, considered un-

der the headings set out at the beginning of the article.

I have centred the discussion on only the first of these, and have highlighted the more gross areas of deficiencies, especially in our government institutions. As healthworkers, we become involved with the strictly clinical/technical minutiae and yet feel helpless in improving the other aspects of our hospitals and clinics' lack of consideration for the patient, even where this seriously affects the quality of care we render.

The role of Helicobacter Pylori in Perforated Peptic Ulcers

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INTRODUCTION

Much has been learnt about the special microbe known today as helicobacter pylori since its isolation in 1983 by Marshall and Warren[1]. Now there is firm evidence that the microbe is not present as a mere contaminant or commensal[2]. Many health professionals are still doubtful about the pathogenic role of this microbe. The overall association between H. pylori and acid related disorders in the upper GIT is impressive[3].

There are three important risk factors for peptic ulcers and related serious upper GIT events; these are: NSAIDs, H. pylori and cigarette smoking[4]. More than 95% of patients suffering from duodenal ulcers and about 70-80% of patients with gastric ulcers are H. pylori positive[5&6].

It is well stated in the literature that medical treatment for peptic ulcer is based on a combination of proton pump inhibitors (PPIs) and antibiotics to eradicate the H. pylori infection. This treatment is associated with a high rate of immediate success and a low rate of recurrence at 12 months[7].

After increasing steeply at the beginning of the twentieth century, ulcers perforation incidence has declined during the last decades in young children and in men; however, it has increased in elderly[8]. Ulcers perforation was frequently treated by gastric resection in the former days, whereas suturing, being the first method introduced in 1887 is the method of choice today[9].

Significant risk factors that led to complications after surgery were perforation that had been present more than 24 hours, the co-existence of significant associated illnesses, and resection surgery. The significant risk factors that led to death were presence of shock at admission, the co-morbid illnesses, and resection surgery. There was no statistically significant difference concerning morbidity and mortality between simple closure of perforation and definitive surgery (VT + Dr) (truncal vagotomy + drainage) ulcer relapse was significantly less common in patients treated with anti-helicobacter therapy than those who received omeprazole alone-4.8% vs. 38.1%[9&10] .

The aim of this study is to furnish data on prevalence of H. pylori in perforated peptic ulcers.

METHODOLOGY

All adult patients diagnosed with and operated for perforated peptic (gastric and duodenal) ulcers from May 2007 to April 2008 were prospectively entered in this study. Cases were excluded if the perforation was due to causes other than peptic ulceration (e.g. tumors). All the demographic data was charted on a Performa.

Per-operatively the perforation site was determined. A mucosal biopsy was obtained through the perforation. A second biopsy was taken from the ulcer edge.

No patient diagnosed as suffering from perforated peptic ulcer was treated conservatively during this period. Identification of H. pylori in biopsied material was performed using urease test. The urease test is well evaluated in the clinical setting. Its reported specificity and sensitivity are both close to 90-100% [10&12].

H. pylori serology was also performed on blood samples and they have sensitivity 80-98% and specificity of 90-100% and are non-invasive.

Serological tests for H. pylori infection circulating (IgG & IgA) measured by immunology show that H. pylori infection is low in children, but rises dramatically in fifth and subsequent decades[12&13].

25 patients with peptic ulcer were recruited.

RESULTS

TABLE 1: Prevalence of Antibodies

AGE (Yrs)	Present %	Positive%
	IgG	IgA
0-9	<2	2
10-19	3	11
20-39	3	8
40-59	40	50
>60	52	50

TABLE 2: Age – Gender Characteristics

Age group (years)	Male	Female
15-20	3	-
21-30	5	-
31-40	2	-
41-50	9	-
51-60	5	1

TABLE 3: Urease and serology tests

No. of patient	Biopsy antrum	Urease ulcer edge	Serology
10	Positive	Positive	Positive
8	Positive	Negative	Positive
7	Negative	Negative	Negative

Percent of patients at one site positive= 72%

Details about drug consumption and other risk factors like smoking and diabetes mellitus is shown in Table 4.

TABLE 4: Drug Consumption Data

	No. of patients	Percentage (%)
NSAIDs	5	20
Steroids	4	16
Anti-ulcer drugs	11	44
Smoking (plus other forms of tobacco)	19	76
Diabetes	1	1

Eleven patients had anti-ulcer treatment previously. None of the patients had previous perforated duodenal ulcer. Five patients had used NSAIDs and 19 patients were using tobacco in one or another form.

All patients who had positive urease test were given H. pylori eradication therapy. All the patients underwent repeat urease test at 6 weeks post-operatively and by that time 16 patients were H. pylori negative, giving a success rate of 90%.

DISCUSSION

In 25 patients presenting with acute perforation of a gastric or duodenal ulcer, prevalence of H. pylori is 72%. Data regarding H.pylori infection in perforated peptic ulcers are conflicting. Indeed, H.pylori infection rates range from 0-92%[14-23]. Some reports show that eradication of H. pylori can prevent recurrent ulcer disease complications such as bleeding [10, 21, 23 & 24]. This has recently been demonstrated by Ng et al[15] in perforated peptic ulcers. These researchers showed in a randomized clinical trial that eradication of H. pylori prevents ulcers recurrence in patients with H. pylori-associated perforated duodenal ulcers. After one year, ulcer relapse was significantly treated with an anti-H.pylori therapy; likewise, Chu et al 16 concluded that recurrent ulcer disease in patients with a history of perforated duodenal ulcer is related to H. pylori infection.

None of our patients had to undergo repeated surgery for recurrent peptic ulcer disease after simple closure of perforated ulcer and successful H. pylori eradication. The discrepancy between infection rates found in the literature[13-22] may be attributed in part to different populations studied. For example, Sebastian et al[16] reported an infection rate of 83% in a small group of young male smokers from India with acute perforated peptic ulcer; this result is comparable to our findings. Another small study from India[21] with 15 perforated duodenal ulcer patients show on the contrary that all patient were negative for H. pylori; while Sharma et al[14] found a prevalence of 61% among 44 patients from Chhat-

tisgarh region, India. Reinbeck et al[17] claimed that perforated ulcers might have a different pathogenesis because in their study only 47% of perforated duodenal ulcer patients were positive for H. pylori. Forty-four percent of their patients were on NSAIDs and their study showed no difference between NSAID users[23]. Matsukura et al[24] showed that there were no significant differences between perforated and non-surgical peptic ulcer groups for H. pylori serum and gene markers. Ng et al[18] on the other hand found a 70% infection rate (n = 73) in perforated duodenal or pre-pyloric ulcer patients; their figures are similar to ours. This is barely higher than the prevalence of H. pylori in local population.

It would be beyond the scope of this paper to discuss the different H. pylori eradication regimens and their success rates. Our eradication rate was 90%, which is excellent[22-27]. While elective ulcer surgery declined significantly the percentage of emergency operation for complicated ulcers has recently increased from 60-90%. Simple closure of perforation gained popularity in the presence of potent acid suppressing and H. pylori eradication agents[28-30]. The high age of patient population with its co morbidity and the availability of efficient H. pylori eradication regimens may accounts for this move away from extensive surgery[30&31]. A variety of laparoscopic techniques for closure of perforated peptic ulcer have recently emerged[32-35].

Lan et al[31] carried out a randomized study comparing laparoscopic versus open surgery for perforated peptic ulcers. They reported that laparoscopic repair followed by peritoneal washout had become standard treatment. They found no significant difference in morbidity, re-operating rate and mortality between laparoscopic and open repair. Hospital stay and time needed to resume normal activity was similar in broth groups. In contrast to elective laparoscopic surgery such as cholecystectomy or fundoplication patients do not seem to benefit from a less invasive approach.

The main complications of acute perforated peptic ulcers are the consequences of peritonitis, development of septicemia and reduced gastrointestinal motility. Therefore, irrespective of the way in which the perforation is repaired, patients probably need some period of time to recover[33&34]. However, overall treatment of the total peritoneal surface is essential if abscess for motion within the abdominal cavity is to be avoided as much as possible. Hence, open surgery may be needed, especially if the perforation has been there for some hours.

In summary this study shows that there is an evident association between H. pylori infection and acute perforated peptic ulceration. A temple H.pylori eradication therapy in successful and yields a response rate of 90%.

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Case Report: Recurrent Laryngeal Papillomatosis in a Child with HIV

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A 5 year old girl was referred to Children's Medical Ward, QEII Hospital, on 18th August 2009 with a 3 day history of shortness of breath and hoarse voice. Her appetite was decreased over the same time period. There was no history of recent TB contact, no cough or fever and no diarrhoea or vomiting.

The patient was known to be HIV positive but had defaulted HAART in October 2006. She was admitted to Universitas, Bloemfontein in October 2008 with upper airway obstruction and the diagnosis of recurrent laryngeal papillomatosis was made. During this admission, treatment for pulmonary TB was initiated because of bilateral patchy infiltrates on her chest X-ray. She underwent surgical excision of the papillomata on 14th October 2008 which was successful, with no problems.

She had been delivered by normal vaginal delivery at full-term, no prevention of maternal to child transmission (PMTCT) was given, there were no neonatal problems and there is no information about maternal papillomata.

Her developmental milestones were normal and her immunisations were up to date. Her parent's HIV statuses were unknown and she has no siblings. The mother is a housewife and the father is unemployed.

On examination, she was conscious and alert. She was afebrile and acyanotic. She was tachypnoeic at 35 breaths/minute, with biphasic stridor, but there were no other signs of respiratory distress. Her heart rate was 147 beats/minute and oxygen saturations were 94%. Her weight was 12.5kg and her height was 98cm, giving her a Z-score of -1/-2 SD. She had multiple small axillary and inguinal lymph nodes.

Investigations & Management:

Her CD4 absolute count was 712/mm3 (22%). A rapid Haemoglobin was 11.1g/dL. A full blood count and urea and electrolytes were within the normal range.

On admission, immediate management included dexamethasone 1mg/kg IV QID and nebulized adrenaline (1:1000) 1ml on a needs basis. The ENT team recommended direct laryngoscopy and removal of papillomata under general anaesthetic but her mother wished to discuss the operation with the father as she felt unable to give consent. On the 20th August she was comfortable, chest was clear bilaterally and respiratory rate was 28 breaths/minute. Management was continued, with the patient made nil by mouth from midnight with an elective procedure planned for the 21st after consent had been gained from the father.

On the morning of the 21st she was gasping, had decreased level of consciousness and had severe airway obstruction requiring immediate intervention. This was discussed with the ENT consultant, who explained the operation and the risks involved with the mother, who gave consent. An urgent tracheostomy was carried out under local anaesthetic, followed by successful removal of the papillomata. Her post-operative course was complicated by facial oedema, thought to be surgical emphysema which gradually resolved. Over the next few days the patient improved and at ENT review on the 24th her surgical emphysema was found to be decreasing and she was discharged for out-patient follow-up.

Summary:

This patient presented with upper airway obstruction secondary to recurrent laryngeal papillomatosis. She had moderate malnutrition and was HIV positive with a CD4 count of 712/mm3. Elective intervention was offered but initially refused; life saving intervention was later carried out after she developed acute upper airway obstruction.

Discussion:

Recurrent laryngeal papillomatosis or recurrent respiratory papillomatosis (RRP) is a histologically benign disease of the larynx, trachea and bronchi. RRP is caused by human papilloma virus (HPV) types 6 and 11 and has a tendency to recur.

The incidence in the paediatric population is 3.96 per 100,000. A maternal history of genital warts during pregnancy is the single most important risk factor for children developing RRP and approximately 7 out of every 1000 children born to mothers with a history of vaginal condyloma develop RRP. Patients with HIV have an increased risk of HPV disease which is related to the degree of immunosuppression.

In a retrospective analysis of cases of paediatric RRP in the USA it was found that the average age of diagnosis was 4.0 years and that young age was the most important determinant of disease severity. Most paediatric patients with RRP experience spontaneous disease regression at some point later in life, but some do not.

Common presenting symptoms of RRP include: hoarseness, cough, stridor and aphonia, of which hoarseness is the most common.

Management options include: surgical debulking or excision, CO2 laser therapy and adjuvant medical therapies, including cidofovir given systemically or intralesionally. Due to the tendency for papilloma to recur, multiple surgeries may be carried out; paediatric RRP patients included in the American National Registry had an average of 5.1 surgeries annually.

The patient in this case report presented with shortness of breath and a hoarse voice, typical presenting symptoms of RRP and she had previously had surgery to remove papilloma. It is unknown whether her mother had vaginal condyloma during the pregnancy.

Limited literature is available regarding the interaction between HIV and RRP and the potential effects of HAART on disease progress. In a case report of RRP in a HIV positive patient, initiation of HAART caused an immune reconstitution-like syndrome, leading to the development of RRP. Although the authors state that the association of RRP with HAART is speculative, they are keen for clinicians to be aware of RRP as a potential cause of airway symptoms. It is unclear whether the disease process in the patient described in this case report would have been affected by her initiation of HAART in 2006; it is possible that immune reconstitution could have had an adverse effect on the RRP. Alternatively, the compromised cell-mediated immune response that may be associated with repeated or persistent HPV infections may be improved by HAART, thus improving the clinical course of RRP. Given this life threatening event, consideration will be given to re-initiation in this five year old child.

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Every encounter is not an ICD, PID and PTB:

A brief clinical encounter to affirm the need for well trained family doctors in Lesotho

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At the outset I want to thank the Lesotho-Boston Health Alliance (LeBoHA) for giving me an opportunity to come to Lesotho for a second visit, this time as (stand in) faculty/preceptor for the newly started MOHSW/LeBoHA Family Medicine Specialty Training Program at Leribe hospital.

My expectation was to not only participate in the teaching activities of the registrars but also to learn about the prevalent diseases and clinical conditions that one would encounter in Lesotho.

Though I did see a good number of patients afflicted with PTB, HIV, (designated as ICD+ in Lesotho), as well as PID & other STD's, there were to my surprise an equally good number of patients suffering from other non-infectious, chronic illnesses such as HTN, DM, CHF and yes even depression, all of which are common clinical conditions that a US-trained family physician should be well versed in.

My daily experience in precepting the registrars in their outpatient clinics as well as rounding with them on the inpatient wards has strengthened my belief that a solid family medicine residency program like the MOHSW/LeBoHA program needs to be supported and strengthened.

The following clinical encounter is just one small example that illustrates this.

A 21 year old female presents to the outpatient department (OPD) with intermittent headache for 4 months. She states that her headache has worsened over the last 6 days, is localized to the frontal region and not associated with any visual changes. The headache is described as continuous and she has mild relief with NSAIDs & paracetamol.

She denies any nasal drainage, cough, or fever. She has been seen 5 times since March this year for the same complaint. She has regular periods and no surgical history.

She was diagnosed as having a viral URI and was treated at varying times with Pen VK, Erythromycin. Her ICD status is negative.

She is pale, BP =133/86, PERLA, no focal neurological deficits; otherwise her physical exam is unremarkable.

The initial impression was headache from an unknown cause and the differential diagnosis included anaemia, elevated blood pressure and possibly tension headache.

I encouraged the registrar to elicit a social history, upon which the patient started sobbing uncontrollably. The patient explained that for the last several months, after both her parents died, she & her only other sibling live with an aunt who has been verbally and emotionally abusive. The patient works at a local factory for 12 hours, then is abused as a house maid upon return to her aunt's home. She is unable to sleep and does not eat well.

The registrar showed patience in eliciting the social history, empathy in providing comfort, and compassion in counselling the patient. The patient was referred to a social work counsellor at the district hospital and prescribed low dose TCA both as an antidepressant and sleep aid. The whole visit lasted a little under 30 minutes, but it was time well spent and worth the effort.

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