A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO DEVELOPMENTS IN DIAGNOSIS AND MANAGEMENT AVAILABLE AS FULL-TEXT (SOME FREE, SOME REQUIRING PAYMENT)

Selection of readings made by A/Prof Goh Lee Gan

CHRONIC HEPATITIS B MANAGEMENT

Reading 1 : Barriers in management

Tan NC, Cheah SL. What barriers do primary care physicians face in the management of patients with chronic hepatitis B infection in primary care? Singapore Med J. 2005 Jul;46(7):333-9.

URL: http://www.sma.org.sg/smj/4607/4607a4.pdf (free fulltext)

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ABSTRACT

INTRODUCTION: Asymptomatic chronic hepatitis B virus (HBV) carriers, followed-up in primary care, present a challenge to primary care physicians as they encounter problems in monitoring this group of patients. The study aims to explore the barriers faced by primary care physicians in the management of patients with chronic hepatitis B infection in primary care.

METHODS: Qualitative analysis of eight focus group discussions with 43 primary care physicians in Singapore was conducted.

RESULTS: Primary care physicians highlighted the HBV carriers' poor compliance to disease monitoring as a major hurdle, attributing to their lack of understanding of the disease, state of denial, fear of stigmatisation in society, failure to perceive benefits, costs and reluctance of investigations due to physical discomfort. The carriers' health-seeking behaviour, such as doctor hopping and the use of traditional medication, were other barriers. The investigators noted that the physicians placed emphasis on passive disease monitoring, focusing on the investigation results when they reviewed the carriers. They were less proactive in explaining the disease's natural history nor discussing the possibility of definitive anti-viral treatment for suitable carriers. These physicians varied in their approaches in disease monitoring of chronic HBV infection. The fees-for-service healthcare system allowed the carrier to seek consultation from different doctors, which could result in disruption of disease surveillance. This was further compounded by the differential cost of investigations in private practices and government-aided polyclinics. The absence of a national HBV registry and recall system and waiting time for referral to specialist clinics in restructured hospitals, were other barriers.

CONCLUSION: The management of HBV carriers in primary care could be enhanced by measures that eliminate the barriers involving the patient, doctor and healthcare system.

Reading 2 : Approach to management

Hu KQ. A Practical Approach to Management of Chronic Hepatitis B. Int J Med Sci. 2005;2(1):17-23. Epub 2005 Jan 5

URL: http://www.pubmedcentral.gov.libproxy1.nus.edu.sg/articlerender.fcgi?tool=pubmed&pubmedid=15968335 (free fulltext)

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ABSTRACT

Chronic hepatitis B (CHB) is one of the important public health problems worldwide. Major advances have been made in the treatment of CHB during the past several years. This article systemically reviews advances in the application of HBV DNA quantitation and three approved drugs for HBV treatment, and presents an updated and practical clinical approach to managing CHB. Highly sensitive PCR-based quantitation of HBV DNA makes it possible to precisely determine pre-treatment HBV load and monitor HBV DNA response during treatment. HBV DNA level, HBeAg status, degree of hepatic histological activity and fibrosis, and serum transaminases are the most important parameters in determining indication, regimen, and duration of HBV treatment. Although interferon alfa-2b, lamivudine, and adefovir are all approved as initial HBV treatment, understanding the advantages and advantages of each agent is important in choosing the best treatment for each individual patient with CHB.

BENIGN PROSTATIC HYPERPLASIA

Reading 3 : Noninvasive management

Kuritzky L. Noninvasive management of lower urinary tract symptoms and sexual dysfunction associated with benign prostatic hyperplasia in the primary care setting. Compr Ther. 2005 Fall;31(3):194-208.

URL: http://www.ingentaconnect.com.libproxy1.nus.edu.sg/content/hum/comp/2005/00000031/00000003/ (payment required)

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ABSTRACT

Most men who live to middle age and beyond will ultimately develop lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH), and many will also experience sexual dysfunction. Clinical studies indicate that most patients will experience improvement in BPH-related LUTS with alpha-adrenergic blockade or 5alpha-reductase inhibition. Recent studies suggest that alpha-blockers and 5alpha-reductase inhibitors may help to slow the progression of LUTS; 5alpha-reductase inhibitors reduce the need for surgery and complications, such as acute urinary retention. Third-generation alpha-blockers (alfuzosin, tamsulosin) are infrequently associated with cardiovascular side effects, in contrast to their predecessors (doxazosin, terazosin, prazosin). This may provide an advantage for consideration as firstline therapy. Alpha-Blocker therapy may also improve sexual functioning, with the exception of ejaculation disorders, predominantly associated with subtypeselective alpha-blockers. By contrast, 5alpha-reductase inhibition is not recommended for men without demonstrable prostatic enlargement, may be associated with a long delay between treatment initiation and LUTS improvement, and is clearly associated with sexual side effects, including decreased libido, ejaculatory dysfunction, and erectile dysfunction. When choosing appropriate pharmacotherapy, the clinician should consider not only the expeditious relief of the presenting symptoms but also the patient's quality of life, including sexual function and potential long-term outcomes, such as acute urinary retention and the need for surgical intervention.

Reading 4 : Alpha-adrenoceptor antagonists

Milani S, Djavan B. Lower urinary tract symptoms suggestive of benign prostatic hyperplasia: latest update on alpha-adrenoceptor antagonists. BJU Int. 2005 Jun;95 Suppl 4:29-36.

URL: http://www.ingentaconnect.com.libproxy1.nus.edu.sg/content/bsc/bju/2005/00000095/A00401s4/art00005?token=006219a95965c635f333f25703568293c62207d673f232f27375f2a67232d45237b6d24247b423b2041287670443013a1f (payment required)

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ABSTRACT

An update of a systematic review of alpha1-adrenoceptor (AR) antagonists in the treatment of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) showed that these agents have comparable efficacy. The total symptom score is improved by 30-45% and maximum urinary flow rate by 15-30% vs baseline. alpha1-AR antagonists that can be started at their therapeutic dose have a more rapid onset of action than alpha1-AR antagonists that have to be titrated. Alpha1-AR antagonists can be differentiated according to their tolerability. Alfuzosin (especially the 10 mg once daily dose) and tamsulosin (especially the 0.4 mg once daily dose) are better tolerated than doxazosin and terazosin. However, alfuzosin might induce more cardiovascular adverse events (AEs) in the elderly and/or patients with cardiovascular comorbidity and/or comedication. Tamsulosin tends to interfere less with blood pressure regulation and induce less vasodilatory AEs than alfuzosin, especially in the elderly, and is well tolerated in patients with cardiovascular comorbidity and/or comedication. Cardiovascular AEs might lead to potentially serious complications such as falls, fractures and institutionalization. Abnormal ejaculation has mainly been reported in placebo-controlled trials with tamsulosin but in direct comparative trials its rate with tamsulosin 0.4 mg was similar to, or only slightly higher than, the rate with alfuzosin. In addition, abnormal ejaculation is not reported as bothersome by the patient or associated with serious complications. It can be concluded that an alpha1-AR antagonist with a low potential to interfere with blood pressure regulation and to induce cardiovascular AEs, also in patients with cardiovascular comorbidity and/or comedication, can be considered a first-choice treatment option in LUTS/BPH.

Reading 5 : Progression of symptoms

Trachtenberg J. Treatment of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in relation to the patient's risk profile for progression. BJU Int. 2005 Jun;95 Suppl 4:6-11.

URL: http://www.ingentaconnect.com.libproxy1.nus.edu.sg/content/bsc/bju/2005/00000095/A00401s4/art00002?token=005c1933ff41fc8ba6b64277b687627502b333e3568793c62207d677e442f20675d3e763f447b3a4a5f7b733887c (payment required)

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ABSTRACT

Lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) is a slowly progressing disease, with some patients progressing more rapidly than others. In 80% of patients who progress this is caused by the worsening of symptoms. The physician can predict the risk of progression from the patient's clinical profile; increased symptom severity, a poor maximum urinary flow rate (Qmax), and a high postvoid

residual urine volume (PVR), are major risk factors for overall clinical progression of LUTS/BPH. A large baseline prostate volume and a high serum prostate-specific antigen (PSA) level are the predominant risk factors for developing acute urinary retention. After predicting risk, the most appropriate treatment should be established by balancing the benefits of treatment against the possible risks and bother resulting from adverse events. From the Medical Therapy Of Prostatic Symptoms study it can be concluded that monotherapy with an alpha1-adrenoceptor (AR) antagonist is an appropriate treatment for many patients with LUTS/BPH. However, for those at high risk of progression (those with a large prostate volume and high PSA level), it appears more appropriate to add a 5alpha-reductase inhibitor to the alpha1-AR antagonist to obtain maximum relief of symptoms, and ideally to halt the progression of the disease. This was confirmed by the RAND Appropriateness Method study, in which 12 urologists determined the most appropriate treatment for patients with LUTS/BPH based on their clinical profile, combination of clinical variables and/or risk factors. This study also indicates that patients at very high risk of progression, with severe obstruction (poor Qmax and high PVR), are potential candidates for immediate surgery.

HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER

Reading 6 : Cervical screening

Sheary B, Dayan L. Cervical screening and human papillomavirus. Aust Fam Physician. 2005 Jul;34(7):578-80.

URL: http://www.racgp.org.au/document.asp?id=17400 (free full text)

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ABSTRACT

BACKGROUND: Cervical screening in Australia has been successful in reducing the incidence and mortality of cervical cancer. Human papilloma virus (HPV) is a common sexually transmitted infection and an integral agent in the development of cervical cancer.

OBJECTIVE: This article discusses cervical screening, HPV infection and counselling women with low grade abnormalities on cervical cytology.

DISCUSSION: For most women, detectable HPV infection is transient and subclinical. While HPV is a precursor to cervical cancer, this is a rare outcome of HPV infection. Minor abnormalities on cervical cytology reflecting acute HPV infection are common. Women with low grade Pap test abnormalities require reassurance and education about the prevalence and natural history of HPV.

Reading 7 : Human papillomavirus vaccine

Mahdavi A, Monk BJ. Vaccines against human papillomavirus and cervical cancer: promises and challenges. Oncologist. 2005 Aug;10(7):528-38.

URL: http://theoncologist.alphamedpress.org.libproxy1.nus.edu.sg/cgi/content/full/10/7/528 (free full text)

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ABSTRACT

Cervical cancer and precancerous lesions of the genital tract are major threats to the health of women worldwide. The introduction of screening tests to detect cervical cancer precursor lesions has reduced cervical cancer rates in the developed world, but not in developing countries. Human papillomavirus (HPV) is the primary etiologic agent of cervical cancer and dysplasia. Thus, cervical cancer and other HPV-associated malignancies might be prevented or treated by HPV vaccines. Two vaccine strategies have been developed. First, prevention of HPV infection through induction of capsid-specific neutralizing antibodies has been studied in clinical trials. However, because the capsid proteins are not expressed at detectable levels by infected basal keratinocytes or in HPV-transformed cells, a second approach of developing therapeutic vaccines by targeting nonstructural early viral antigens has also been developed. Because two HPV oncogenic proteins, E6 and E7, are critical to the induction and maintenance of cellular transformation and are coexpressed in the majority of HPV-containing carcinomas, most therapeutic vaccines target one or both of these gene products. A variety of approaches is being tested in therapeutic vaccine clinical trials, whereby E6 and/or E7 are administered in live vectors, as peptides or protein, in nucleic acid form, or in cell-based vaccines. The paradigm of preventing HPV infection through vaccination has been tested, and two vaccines are currently in phase III clinical trials. However, current therapeutic vaccine trials are less mature with respect to disease clearance. A number of approaches have shown significant therapeutic benefit in preclinical papillomavirus models and await testing in patient populations to determine the most effective curative strategy.

ROTAVIRUS GASTROENTERITIS

Reading 8 : Burden of rotavirus disease in Malaysia

Hsu VP, Abdul Rahman HB, Wong SL, Ibrahim LH, Yusoff AF, Chan LG, Parashar U, Glass RI, Bresee J. Estimates of the burden of rotavirus disease in Malaysia. J Infect Dis. 2005 Sep 1;192 Suppl 1:S80-6.

URL: http://www.journals.uchicago.edu/JID/journal/available.html (payment required)

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ABSTRACT

BACKGROUND: Accurate national estimates of the disease burden associated with rotavirus diarrhoea are essential when considering implementation of a rotavirus vaccination program. We sought to estimate rotavirus disease-associated morbidity and mortality in Malaysia, using available sources of information.

METHODS: We analyzed national data from the Ministry of Health (Kuala Lumpur, Malaysia) to derive rates of hospitalization, clinic visits, and deaths related to acute gastroenteritis (AG) among children <5 years of age. The

number of events attributable to rotavirus infection was estimated by multiplying age-stratified rates of detection of rotavirus from 2 hospital surveillance sites by national data.

RESULTS: In 1999 and 2000, an average of 13,936 children (1 in 187 children) were hospitalized annually for AG. Surveillance of visits to outpatient clinics for AG identified an average of 60,342 such visits/year between 1998 and 2000. The AG-associated mortality rate was 2.5 deaths/100,000 children. On the basis of the finding that 50% of children were hospitalized for rotavirus diarrhoea, we estimated that 1 in 61 children will be hospitalized for rotavirus disease and that 1 in 37 children will seek treatment as an outpatient.

CONCLUSIONS: Among Malaysian children, there is a significant burden associated with AG- and rotavirus disease-related hospitalizations and outpatient visits, and this burden potentially could be prevented by the use of rotavirus vaccines.

Reading 9 : Rotavirus gastroenteritis in Denmark

Olesen B, Neimann J, Bottiger B, Ethelberg S, Schiellerup P, Jensen C, Helms M, Scheutz F, Olsen KE, Krogfelt K, Petersen E, Molbak K, Gerner-Smidt P. Etiology of diarrhea in young children in Denmark: a case-control study. J Clin Microbiol. 2005 Aug;43(8):3636-41.

URL: http://jcm.asm.org/cgi/content/full/43/8/3636?view=long&pmid=16081890 (payment required)

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ABSTRACT

Infectious gastroenteritis is one of the most common diseases in young children. To clarify the infectious etiology of diarrhea in Danish children less than 5 years of age, we conducted a 2-year prospective case-control study. Stools from 424 children with diarrhea and 870 asymptomatic age-matched controls were examined, and their parents were interviewed concerning symptoms. Rotavirus, adenovirus, and astrovirus were detected by enzyme-linked immunosorbent assay, and norovirus and sapovirus were detected by PCR. Salmonella, thermotolerant Campylobacter, Yersinia, Shigella, and Vibrio spp. were detected by standard methods. Shiga toxin-producing (STEC), attaching-and-effacing (A/EEC), enteropathogenic (EPEC), enterotoxigenic, enteroinvasive, and enteroaggregative Escherichia coli were detected by using colony hybridization with virulence gene probes and serotyping. Parasites were detected by microscopy. Overall, a potential pathogen was found in 54% of cases. More cases than controls were infected with rotavirus, Salmonella, norovirus, adenovirus, Campylobacter, sapovirus, STEC, classical EPEC, Yersinia, and Cryptosporidium strains, whereas A/EEC, although common, was not associated with illness. The single most important cause of diarrhea was rotavirus, which points toward the need for a childhood vaccine for this pathogen, but norovirus, adenovirus, and sapovirus were also major etiologies. Salmonella sp. was the most common bacterial pathogen, followed by Campylobacter, STEC, Yersinia, and classical EPEC strains. A/EEC not belonging to the classical EPEC serotypes was not associated with diarrhea, underscoring the importance of serotyping for the definition of EPEC.

Reading 10 : Projected cost-effectiveness of Rotavirus vaccination

Podewils LJ, Antil L, Hummelman E, Bresee J, Parashar UD, Rheingans R. Projected cost-effectiveness of rotavirus vaccination for children in Asia. J Infect Dis. 2005 Sep 1;192 Suppl 1:S133-45.

URL: http://www.journals.uchicago.edu/JID/journal/available.html (payment required)

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ABSTRACT

BACKGROUND: New rotavirus vaccines may soon be licensed, and decisions regarding implementation of their use will likely be based on the health and economic benefits of vaccination.

METHODS: We estimated the benefits and cost-effectiveness of rotavirus vaccination in Asia by using published estimates of rotavirus disease incidence, health care expenditures, vaccine coverage rates, and vaccine efficacy.

RESULTS: Without a rotavirus vaccination program, it is estimated that 171,000 Asian children will die of rotavirus diarrhea, 1.9 million will be hospitalized, and 13.5 million will require an outpatient visit by the time the Asian birth cohort reaches 5 years of age. The medical costs associated with these events are approximately $191 million; however, the total burden would be higher with the inclusion of such societal costs as lost productivity. A universal rotavirus vaccination program could avert approximately 109,000 deaths, 1.4 million hospitalizations, and 7.7 million outpatient visits among these children.

CONCLUSIONS: A rotavirus vaccine could be cost-effective, depending on the income level of the country, the price of the vaccine, and the cost-effectiveness standard that is used. Decisions regarding implementation of vaccine use should be based not only on whether the intervention provides a cost savings but, also, on the value of preventing rotavirus disease-associated morbidity and mortality, particularly in countries with a low income level (according to 2004 World Bank criteria for the classification of countries into income groups on the basis of per capita gross national income) where the disease burden is great.