Abstracts of Dissertations
December 2002 Exit Assessment Exercise

THE ADVERSE PROGNOSTIC FACTORS OF ACUTE CENTRAL NERVOUS SYSTEM INFECTION IN ADULTS

Dr Au Yeung Tung Wai, Department of Medicine & Geriatrics, Tuen Mun Hospital (December 2002 AIM Exit Assessment Exercise)

This dissertation reviewed the acute central nervous system infection in adults including bacterial, tuberculous and fungal meningitis, viral encephalitis, and brain abscess. The epidemiology of the diseases in Hong Kong and overseas were described and compared, followed by a summary of the current understanding of the pathogenesis of various types of CNS infection.

A series of 128 patients suffering from acute CNS infection in Tuen Mun Hospital from 1996 to 2002 was analysed. The crude hospital mortality was 15.6% with a residual morbidity rate of 10.2%. Ten (7.8%) patients had a history of radiotherapy in the past, seven of which were for nasopharyngeal carcinoma. Streptococcus was the commonest pathogen in bacterial meningitis, accounting for 41.4% of the bacteria-positive group. Among them five were due to streptococcus suis. Tuberculous meningitis was common with an incidence about half of that of its bacterial counterpart. The clinical features of tuberculous meningitis differed from the others with more confusion and altered conscious level on initial presentation. There were six cases of cryptococcal meningitis in this series. Four patients were previously healthy; one was later confirmed to be HIV seropositive and the remaining patient had been taking steroids for eczematous skin condition.

The adverse prognostic factors that were associated with hospital mortality were: altered conscious level, convulsion, high CSF protein level and usage of steroid as adjunctive therapy. Interestingly, the presence of headache and meningism were associated with less mortality. There was no statistical meaningful difference in mortality among the various pathogen groups.

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ROSIGLITAZONE IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS: A CRITICAL REVIEW AND LOCAL EXPERIENCE

Dr Kwan Yiu Keung, Department of Medicine and Geriatrics, Tuen Mun Hospital (December 2002 AIM Exit Assessment Exercise)

This dissertation will be divided into 3 parts

1 To review the pathophysiology of type 2 diabetes mellitus and insulin resistance. Moreover it will discuss how to manage diabetes by manipulating the pathophysiologic mechanism that contribute to the disease. It will also introduce a new direction in treating diabetes by improving peripheral insulin sensitivity.

2 Critical review of rosiglitazone, the second generation of thiazolidinedione. The pharmacology, pharmacokinetics, clinical efficacy, and adverse effects of rosiglitazone will be reviewed.

3 Local experience in the use of rosiglitazone. Diabetic patients who had taken rosiglitazone were recruited into the study. Totally there were 28 patients, 17 men and 11 women. The mean age was 58.4 ± 13.4. The mean treatment duration was 10.8 ± 4.5 months. The mean baseline HbA1c was 10.4 ± 1.8%. Most of them (75%) required combination therapy for glycemic control. The most common combination (36%) was sulphonylurea and metformin. Rosiglitazone was added to the previous regimen. Some of them had medications adjusted afterwards. Finally most of them (61%) were put on either triple therapy (combination of rosiglitazone, sulphonylurea and metformin) or quadruple therapy (triple therapy and acarbose). The mean reduction in HbA1c was 0.29% at 3-month and 0.74% at 6-month compared with the baseline. Sub-group analysis on patients put on triple or quadruple therapy showed that the mean reduction in HbA1c was 0.24% at 3-month and 0.91% at 6-month compared with the baseline. Rosiglitazone was discontinued in 5 patients. The reasons were poor diabetic control in 3 patients, fluid retention in 1 patient and no apparent reason in 1 patient. Most of the patients tolerated the medication well. None of them reported liver toxicity. It is concluded that rosiglitazone seems to be safe and effective, even as triple combination.

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ADULT BACTERIAL MENINGITIS – APPLICATIONS OF A PROGNOSTIC MODEL

Dr Shum Yuk Wah, Department of Medicine and Geriatrics, Tuen Mun Hospital
(December 2002 AIM Exit Assessment Exercise)

Background Bacterial meningitis is a serious infection of the central nervous system. It carries high mortality and survivors often develop neurological sequelae. A prognostic model has been developed by Aronin et al to predict chance of adverse clinical outcome.

Objective To collect local data and apply the prognostic model to our patients and see if the model can predict adverse outcome for them.

Patients and methods A retrospective chart review of all patients with bacterial meningitis treated in Tuen Mun Hospital from 1995 to March 2002 was performed. Diagnosis was confirmed either by culture of cerebrospinal fluid (CSF), or a positive blood culture plus suggestive CSF results. Information concerning clinical features, causative organisms, bacterial antigen results, complications and outcome were obtained. There were 16 episodes with charts reviewed. Those arising after neurosurgery and hospital-acquired cases were excluded.

Results For this small series of patients, mortality was 19%. Another 19% developed neurological complications. The most prevalent organisms were *Streptococcus pneumoniae* and *Streptococcus suis*, each causing 3 episodes. On classifying these patients by means of the prognostic model designed by Aronin et al, 9 were in stage I, 5 in stage II and 1 in stage III. The proportion of patients having adverse outcome were 22% in stage I and 80% in stage II. There was only one patient in stage III, who survived without neurological sequelae. Corresponding figures in the original cohort were 9%, 33% and 57% respectively.

Conclusion In this local series of adult community-acquired bacterial meningitis.

The Aronin model can predict adverse clinical outcome. However, for stage I and II patients in the local series, a much higher proportion of patients had adverse outcome than the original cohort.

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THE EFFECTS OF HORMONE REPLACEMENT THERAPY ON ENDOTHELIAL FUNCTION IN TURNER'S SYNDROME

Dr Chan Nor, Norman, Department of Medicine & Therapeutics, Prince of Wales Hospital (December 2002 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Objective To examine the effect of HRT on vascular reactivity of forearm resistance vessels in women with Turner's syndrome.

Methods Seven women with Turner's syndrome (mean age of 29.3 ± 2.1 years) were studied. Forearm blood flow in response to intra-brachial infusion of bradykinin, 10, 30, 100 pmol/min (endothelium-dependent vasodilator), glyceryl trinitrate, 4, 8, 16 nmol/min (GTN; endothelium-independent vasodilator), noradrenaline, 60, 120, 240 pmol/min (NA, α-adrenergic receptor agonist) and N^G-monomethyl-L-arginine, 1, 2, 4 μmol/min (L-NMMA; NO synthase inhibitor) was assessed by bilateral venous plethysmography. Subjects were studied on three occasions, on their usual HRT (study 1), then after 6 weeks off HRT (study 2) and finally after a further 6 weeks on HRT (study 3).

Results The vasodilator response to bradykinin, expressed as the within-subject mean difference in area under the dose-response curve (AUC) between study 2 and study 1, was significantly diminished (-744.2±287.2, p=0.04), but improved 6 weeks after HRT recommencement. However, there was no significant change in response to GTN (between study 2 and 1, 189.5±247.8, p=0.47). The vasoconstrictor response to L-NMMA was also diminished in study 2 when compared to study 1 (-100.4 ± 35.4, p=0.039) and was restored after HRT was recommenced (between study 3 and 2, 117.5±69.3, p=0.17) whereas there was no significant difference in response to NA between study 2 and 1 (76.7±50.6, p=0.18) or study 3 and 2 (-70.8±71.1, p=0.38).

Conclusions HRT is associated with an improvement in bradykinin-stimulated and basal NO endothelium-dependent vasodilatation in women with Turner's syndrome.

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HORMONAL MALE CONTRACEPTION: LONG-ACTING TESTOSTERONE AND PROGESTAGEN IMPLANTS

Dr Lee Ka Kui, Department of Medicine, Queen Mary Hospital (December 2002 Endocrinology, Diabetes & Metabolism Exit Assessment Exericse)

Previous studies supported by the World Health Organization showed that high or above physiological levels of testosterone (T) appear to be necessary to achieve azoospermia or severe oligozoospermia for effective male hormonal contraception comparable with the currently available female methods. Other studies showed that adding a progestagen to T enhanced the efficacy of suppression of spermatogenesis. Our long-term goal is to develop a long-lasting male contraceptive with long-acting T

and progestagen implants with high efficacy and minimal side effects. During my overseas training at the Harbor-UCLA Medical Center, I actively participated in a two-center clinical trial to compare the efficacy of suppression of spermatogenesis with progestagen implants (Norplant II) in combination with androgen implants (T pellets) versus androgen implants alone. The preliminary data of the study showed that T pellets in combination with the Norplant II system were more effective in the suppression of spermatogenesis than T pellets alone. The treatment was also relatively free of adverse events with no significant changes in body weight, cholesterol levels and clinical biochemistry. We believe that with modifications of the androgen to be delivered, long acting androgen plus progestagen implants might provide a viable long lasting method of hormonal male contraception.

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SECOND-LINE THERAPY ON H PYLORI

Dr Cheung Yuen Cheong, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2002 Gastroenterology & Hepatology Exit Assessment Exercise)

Proton pump inhibitor based triple therapy eradicated *H. pylori* in about 90% of patients. Treatment failure was often attributed to antibiotic resistance. There had been studies reporting more than 80% eradication rate of metronidazole resistant *H. pylori* strain with ranitidine bismuth citrate, metronidazole and tetracycline, as initial therapy. However there were only a few reports on the use of this combination as second-line treatment regimen.

Aims

1. To study the antibiotic sensitivity / resistance pattern of *H. pylori* in eradication treatment failure patients.
2. To evaluate the efficacy and tolerability of ranitidine bismuth citrate, metronidazole and tetracycline used as a second-line regimen.

Methods Patients aged 18 to 80 who had failed previous eradication therapy for *H. pylori* eradication were recruited. *H. pylori* infection was documented by positive C13 urea breath test, histological staining and culture. Four samples of biopsy were taken from the antrum and the corpus, respectively. Samples were subjected to histology with H&E +/- immunohistochemical staining. Minimum inhibitory concentration (MIC) of amoxicillin, clarithromycin, metronidazole and tetracycline were determined by E-test. Isolates were considered to be resistant when MIC values exceeded 4μg/ml in amoxicillin,8μg/ml in clarithromycin,8μg/ml in metronidazole and 8μg/ml in tetracycline. A seven-day course of ranitidine bismuth citrate 400mg bd, metronidazole 400mg qid and tetracycline 500mg qid was prescribed. Successful eradication was defined as absence of *H. pylori* at the 8th week, being confirmed by a negative C13 urea breath test, histological staining and culture. The study was approved by Ethics Committee in Princess Margaret Hospital and an informed consent was obtained from every patient after thorough explanation of the details of the study.

Results The study period was two years from November 1999 to November 2001.2550 patients were screened. 27 male and 31 female patients with a mean age of 48 (18-69) were recruited. The percentages of patients of previous exposure to amoxicillin, clarithromycin, metronidazole and tetracycline were 69%, 96%, 38% and 3% respectively. 6 patients had received dual therapy/therapies and 37 patients had

received 1 course of proton pump inhibitor (PPI) based triple therapy with or without dual therapy. The remaining 15 patients had received multiple courses of eradication therapies of different combinations.30 patients were given PPI+amoxicillin+clarithromycin regimen and. In the beginning of the study, 81 % of the isolates showed clarithromycin resistance and metronidazole resistance was demonstrated in 64% isolates. One patient was harbouring amoxicillin resisitant *H.pylori* strain but tetracycline resistant strain was not detected. 34 patients had *H. pylori* strains showing resistance to both clarithromycin and metronidazole while one patient had *H.pylori* strain showing triple resistance to clarithromycin, metronidazole and amoxicillin. One patient defaulted follow-up. The overall eradication rate for all patients was 88 % by intention-to treat (ITT) and 89% by per-protocol (PP) analysis .For the 37 patients who had received only one course of PPI-based triple therapy, the eradication rate was 86% ITT and 88% PP respectively. The presence of metronidazole resistant *H.pylori* strain had no statistical significant impact on the treatment efficacy. Ranitidine bismuth citrate (RBC) with metronidazole and tetracycline regimen was also found to be safe and well tolerated to most of the patients.

Conclusion There was a high rate of resistance to clarithromycin and metronidazole in treatment failure patients. Second-line treatment with RBC 400mg bd, metronidazole 400mg qid and tetracycline500mg qid resulted in 88% and 89% eradication rate by ITT and PP analysis respectively and this regimen was safe and well tolerated.

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ASSESSMENT OF COAGULATION IN LIVER DISEASE WITH THROMBELASTOGRAPHY: CITRATED WHOLE BLOOD VERSUS NATIVE BLOOD AND LITERATURE REVIEW

Dr Fung Tang Tat, Konrad, Department of Medicine and Geriatrics, Kwong Wah Hospital (December 2002 Gastroenterology and Hepatology Exit Assessment Exercise)

Background and Aims Thrombelastography (TEG) enables a complete evaluation of the process of clot initiation and the structural characteristics of the formed clot and its stability. Using native blood sample, it is necessary to start the procedure within four minutes after sampling. In two recent studies, both in subjects with normal coagulation, a correlation was shown between native and citrated blood. The aim of this study was to compare the TEG parameters from native and citrated blood in patients with liver disease, whose baseline coagulation is abnormal.

Patients and methods TEG parameters of patients with liver cirrhosis or fulminant liver failure were studied prospectively. TEG was performed within four minutes using native blood and, after recalcification, within one to two hours of citrate storage at room temperature. TEG variables (reaction time, clot formation time, alpha angle and maximum amplitude) between native and citrated blood were compared using Mann- Whitney U test and correlation was assessed by determining the Pearson coefficient of correlation (correlation statistically significant if $P<0.01$).

Results 32 patients were recruited, 20 were of Child class C. There was no significant difference between citrated and native blood for all the variables. Correlation between native and citrated blood for each of the variables was significant

($P<0.01$).

Conclusion Citrated blood can substitute native blood using TEG in cirrhotics, being that it allows more time between sampling and the TEG measurement.

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ACUTE NON-VARICEAL NON-PEPTIC ULCER UPPER GASTROINTESTINAL BLEEDING: AN EIGHT-YEAR REGIONAL HOSPITAL EXPERIENCE IN HONG KONG

Dr Kung Kam Ngai, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (December 2002 Gastroenterology & Hepatology Exit Assessment Exercise)

Upper gastrointestinal bleeding (UGIB) is a common gastrointestinal emergency. Among the various groups of UGIB, non-variceal non-peptic ulcer aetiologies account up to 33% of severe bleeding cases in western countries. There is scanty data concerning this group of diseases in our population. A retrospective study of non-variceal non-peptic ulcer haemorrhage was performed for consecutive patients with acute UGIB, who underwent upper endoscopy in Pamela Youde Nethersole Eastern Hospital from 1st January 1994 to 31st December 2001. A total of 6,408 patients were recruited for data collection, 25% suffered from non-variceal non-peptic ulcer bleeding and 1.5% was classified as severe non-variceal non-peptic ulcer bleeding. Gastritis, duodenitis, Mallory-Weiss syndrome, gastric and duodenal erosions were the commonest endoscopic diagnoses of non-variceal non-peptic ulcer bleeding. Clinical severe bleeding occurred in 6.3% of this group of patients. Mallory-Weiss syndrome, Dieulafoy's disease, upper gastrointestinal angiodysplasia and gastric antral vascular ectasia were the main causes of severe bleeding. Those patients with Dieulafoy's disease and upper gastrointestinal angiodysplasia contributed the greatest proportion of patients presenting as clinical severe bleeding. Endoscopic therapy was generally noted to be effective in controlling bleeding for these diseases in our patients. The overall mortality rate was 7.5% in patients with severe acute non-variceal non-peptic ulcer UGIB. Deaths in these patients were due to underlying co-morbidities rather than directly attributed to the bleeding episode.

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EUS IN PORTAL HYPERTENSION

Dr Lai Siu Wing, Lawrence, Department of Medicine & Geriatrics, Caritas Medical Centre (December 2002 Gastroenterology & Hepatology Exit Assessment Exercise)

Background: As endoscopic ultrasound (EUS) can come into close range with the portal vein, its assessment by EUS is possible. Previous case report showed that EUS might be superior than USG and CT in evaluating portal venous system thrombosis (PVST). In addition, there is no ideal method for measurement of portal pressure.
Objectives: To study the role of EUS in the evaluation of portal hypertension.

Hypothesis: (1) EUS is a sensitive and accurate investigation tool for the detection of PVST. (2) EUS guided portal pressure measurement is safe and feasible.
Methods: This project consists of 3 parts. *Part A* was a retrospective analysis of 56 patients undergoing EUS, CT and surgery for evaluation of portal and splenic veins at Massachusetts General Hospital between 1995-2001. *Part B* was a prospective

blinded local study comparing EUS and CT/USG in the detection of PVST between 1-10/2002. *Part C* was an animal study of 21 pigs to evaluate EUS guided portal pressure measurement. This was compared with transhepatic portal pressure measurement at 1) baseline, 2) induced portal hypertensive state, 3) after heparinization and 4) after octreotide. The pigs were later sacrificed to assess safety issues.

Results: *Part A* Both EUS and CT confirmed PVST in 3 of 4 patients with PVST, and 27 of 29 patients without PVST as shown by surgery. In addition, EUS identified 13 of 14 CT proven thrombosis patients. There were 11 patients with EUS only evidence of PVST, although 3 of them had indirect evidence of PVST on CT scan. After excluding patients without proof of PVST, the sensitivity was 84.2%, the specificity was 93.1% and the accuracy was 89.6%. *Part B* EUS agreed completely with CT in the diagnosis of PVST in 10 patients (κ=1.0, p=0.002). *Part C* The mean difference between the pressure measured by the EUS and the transhepatic catheter was 0.28mm Hg (95% C.I. –0.43 – 0.89mmHg). There was close correlation between the pressure obtained by EUS catheter and the transhepatic portal vein catheter(r=0.95, p=0.01). No significant complication was encountered in EUS guided portal vein catheterization.

Conclusions: EUS is probably at least as sensitive as CT in the diagnosis of PVST in human, and EUS guided portal pressure measurement is accurate and at least as safe as transhepatic portal vein catheterisation in pigs. Further studies are warranted.

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NON-MYELOABLATIVE STEM CELL TRANSPLANTATION - A STUDY OF NON-MYELOABLATIVE MATCHED UNRELATED DONOR TRANSPLANT IN PATIENTS OVER 55 YEARS OLD WITH HEMATOLOGICAL MALIGNANCIES & A LITERATURE REVIEW OF THE BIOLOGICAL BASIS AND INDICATIONS OF NON-MYELOABLATIVE TRANSPLANT

Dr Wong Siu Ming, Raymond, Department of Medicine & Therapeutics, Prince of Wales Hospital (December 2002 Haematology & Haematological Oncology Exit Assessment Exercise)

Traditionally, allogeneic hematopoietic stem cell transplantation (ASCT) involves intensive chemoradiotherapy as conditioning regimen to achieve cure and engraftment. The high treatment related morbidity and mortality limit allogeneic stem cell transplant to young patients with good medical conditions. Recent studies have shown that the therapeutic benefits of allogeneic stem cell transplant are closely related to the immune mediated graft-versus-malignancy effects of the allograft. Successful engraftment has been demonstrated with non-myeloablative conditioning regimen. This strategy permits allogeneic transplantation to be used in older patients and those with comorbidities. In the first part of this article, we studied 55 patients older than 55 years of age receiving non-myeloablative conditioning followed by matched unrelated donor stem cell transplantation. The diagnoses were AML (n=13), MDS (n=7), CML (n=9), CLL (n=9), NHL (n=8), mantle cell lymphoma (n=3), myeloma(n=3), ALL (n=2) and myelofibrosis (n=1). About two-third of the patients had comorbidities. The overall survival and progression free survival at 1 year was 35.2% and 32.1% respectively. Transplant related mortality were 45.1% at 1-year. Patients with CML and AML/MDS had the best outcomes and these were comparable to those reported with unrelated donor stem cell transplant in younger patients. Our results suggested that MUD transplant with non-myeloablative conditioning could be an option for older patients with hematological malignancies. The use of non-myeloablative

conditioning regimen and graft-versus-malignancy effect of the allografts may provide a new paradigm for ASCT. The second part of this article is a comprehensive literature of the biological basis and indications of non-myeloablative transplant.

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NON-TYPHOIDAL SALMONELLOSIS: A REVIEW OF LOCAL EPIDEMIOLOGY AND CHARACTERISTICS OF EXTRA-INTESTINAL DISEASES

Dr Choi Kin Wing, Department of Medicine & Geriatrics, Princess Margaret Hospital
(December 2002 Infectious Disease Exit Assessment Exercise)

Aim of the study (1) To evaluate the prevalence of different serogroups of non-typhoid *Salmonella* in causing gastroenteritis and extra-intestinal diseases; (2) to address the local trend of antibiotic sensitivity; (3) to study the characteristics of patients having bacteraemia and extra-intestinal infections; (4) to identify the risk factors for acquisition and predictors of adverse outcomes.

Method Retrospective cross-sectional study of cases of non-typhoidal salmonellosis admitted to a regional hospital in Hong Kong during the period of 01/01/1996 to 31/12/2001 inclusive. Cases were identified by retrieval of laboratory record. Analysis of the distribution of serogroups was performed for those with positive stool culture. Cases admitted to the adult medical services during the same period of time and having positive culture from specimens other than stool were recruited for further analysis with respect to the aims of study.

Results 1924 positive stool isolates were identified. Serogroup B (35.8%) was most prevalent, and this was followed by serogroup D (26.1%). In 32 patients with bacteraemia, 17 cases had concomitant illnesses or therapies that predisposed to immunosuppression. Serogroup D accounted for 87.6% of cases, and half of them belonged to the serotype *S. enteriditis*. Less than 10% of the isolates exhibited intermediate to high level of resistance to ampicillin, chloramphenicol, cotrimoxazole or gentamicin. Intermediate level of resistance to ceftriaxone was identified in 1 isolate. All the organisms were sensitive to fluoroquinolones, which were the definitive antimicrobial therapy for 86.5% of cases. Complications occurred in four patients: two developed septic shock, one had secondary infection and leaking of co-existing aortic aneurysm, and another developed mycotic aneurysms of internal iliac arteries. Mortality rate was 12.5%. Advanced age was the only factor that demonstrated statistically significant association to adverse outcomes. In the 22 patients presented with focal extra-intestinal infection, urinary tract infection was the predominant focal infection in this series (63.6%). Serogroups B and D were equally prevalent and each accounted for 36.4% of cases. Fifty three percent of patients had concomitant illnesses or therapies that predisposed to immunosuppression. Antibiotic sensitivity pattern was similar to those with bacteraemia and over 95% of cases received fluoroquinolones as definitive treatment. Two patients developed septic shock and died, and the mortality was 9.1%

Conclusion Non-typhoidal *Salmonella* is an important enteric pathogen in Hong Kong. Most of the cases with extra-intestinal diseases had identifiable causes of immunosuppression. Resistance to third generation cephalosporins is emerging. Advanced age is a predictor of adverse outcomes.

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CHOICES OF EMPIRICAL THERAPY FOR GRAM-NEGATIVE BACTEREMIA – ONE YEAR ANTIMICROBIAL SUSCEPTIBILITY ANALYSIS IN A REGIONAL HOSPITAL IN HONG KONG

Dr Lee Lai Shun, Nelson, Department of Medicine & Therapeutics, Prince of Wales Hospital (December 2002 Infectious Disease Exit Assessment Exercise)

A retrospective, observational study was performed to investigate the in-vitro antibiotic susceptibility pattern of all gram-negative blood culture isolates in one year in a regional hospital in Hong Kong. The prevalence of different drug-resistant bacterial subgroups was determined; and antibiotics were evaluated in their relative ability to provide effective empirical coverage (in terms of susceptibility rates) in community-acquired and hospital-acquired gram-negative septicemia. A total of 585 cases of gram-negative septicemia were analyzed: median age of patients was 74 years; *diabetes* (20-25%), *malignancy* (17-31%) and end-stage renal failure (10-12%) were the commonest associated systemic diseases. While overall crude mortality rate was 30%, it was up to 50% in nosocomial infections. *E. coli, Klebsiella* and *Proteus* species constituted majority of the blood isolates, but potentially drug-resistant pathogens including *Pseudomonas*, *Acinetobacter* and E.C.S.M.P. (*Enterobacter, Citrobacter, Serratia, Morganella* and *Providencia*) species were prevalent among hospital-acquired infections (total 27%). Up to 24% and 21% of nosocomial infections were classified as 'primary bacteremia' and 'polymicrobial' respectively. Imipenem and amikacin had the highest susceptibility rates in both community-acquired and hospital-acquired infections; all other antibiotics tested had lower susceptibility in hospital-acquired infections. A rank order of antibiotics was noted especially among hospital-acquired infections: imipenem (97%) and amikacin (94%) > piperacillin/tazobactam (82%) and cefoperazone/sulbactam (77%) > ceftazidime or ciprofloxacin (below 66%) > cefotaxime or cefuroxime (below 50%). This rank order was not as apparent among community-acquired infections, as most antibiotics had over 80% susceptibility. These observations were congruent with the nosocomial prevalence of ESBL-producers (27%); ceftazidime non-susceptible *Acinetobacter* and E.C.S.M.P. species (6%); and cefotaxime non-susceptible *Acinetobacter, Pseudomonas* and E.C.S.M.P. species (17%), resulting a total of 33-44% cephalosporins non-susceptible isolates. Rational prescription of empirical therapy against gram-negative septicemia should depend on local prevalence of these resistant pathogens.

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A REVIEW OF CLINICAL CHARACTERISTICS, DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH CHRONIC HEPATITIS C IN A REGIONAL HOSPITAL IN HONG KONG

Dr Tsang Tak Yin, Owen, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2002 Infectious Disease Exit Assessment Exercise)

Hepatitis C infection is an important infection worldwide. In Hong Kong, the prevalence is about 0.5%. The predominant genotypes of hepatitis C in Hong Kong are 1b and 6a. However, information on the clinical characteristics and management of patients with chronic hepatitis C in Hong Kong is lacking. Moreover, no intervention study has been performed so far. Therefore, a retrospective review

targeting on the above characteristics and a prospective treatment study were performed. 105 men and 83 women were recruited. Their mean age was 53 with range from 16 to 85. Diabetes mellitus was present in 16% of patients. HCV infection was acquired by blood transfusion in 73%, while previous intravenous drug addiction was responsible in 8% of patients. Most transfusion related HCV infected patients acquired their disease 16-30 years before the diagnosis. 6 patients (3.3%) presented with acute hepatitis and 23.6% (39/165) patients had ultrasound evidence of cirrhosis. Male is more likely to have ultrasound evidence of cirrhosis. Splenomegaly & stigmata of chronic liver diseases were the commonest clinical findings. Mortality was 1.6% and was resulted from hepatic encephalopathy or gastrointestinal bleeding. However, these outcomes were not associated with patient's race, co-morbidity, duration of illness, risk factors for hepatitis C, other hepatitis status or genotypes. The mean alanine aminotransferase (ALT) level was 122 U/Litre (U/L). Diabetic patients had a significant higher ALT than the non-diabetic, and patients with daily alcoholic intake also had a higher ALT than non-alcoholic. Genotypes 1b was identified in 73.3%(44/60) and 6a in 13.3%(8/60) of HCV infected patients. Diabetic patients were significantly associated with more advanced histological staging. 51 patients were given antiviral treatment. 31 patients had completed treatment by 31 August 2002. The overall end-of-treatment biochemical response was 80.6%. The sustained biochemical response was 78.6% and sustained virological response was 74%. There was no significant difference between the responses for genotype 1b, 6a or non-1b/6a.

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AN EPIDEMIOLOGICAL INVESTIGATION OF THE EMERGENCE AND SPREAD OF HIGHLY TRANSMISSIBLE CLONES OF MULTI-RESISTANT ACINETOBACTER AT HAMMERSMITH HOSPITALS NHS TRUST

Dr Tso Yuk Keung, Eugene, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2002 Infectious Disease Exit Assessment Exercise)

The number of *Acinetobacter* isolates has been increasing in Hammersmith Hospitals NHS Trust. A retrospective study was performed to investigate their evolution and spread.

1332 isolates from 511 patients were identified. Commonest sources were wound, respiratory tract, central venous catheter tip and blood. Incidence rose in summer. The most significant risk factors for death were the presence of isolates in the respiratory tract (odds ratio 3.9, p=0.0003) and age (odds ratio 1.021, p=0.003).

Six major clones (CX1-5, H2) had emerged, all resistant to ceftazidime, cefotaxime and ciprofloxacin. CX1 had been present in Charing Cross Hospital for 3 years and 2 months. Its dominance in the intensive care unit was superseded by the gentamicin-resistant but tobramycin-sensitive CX3 in 2000. CX3 became widespread in Charing Cross Hospital and spread to Hammersmith Hospital. The rise in incidence was correlated with an increase in inpatient tobramycin expenditure (r_s=0.571, p=0.0002). However, CX4 (gentamicin-sensitive but tobramycin-resistant) was identified more often afterwards, coinciding with a significant rebound in the hospital expenditure on gentamicin for all inpatient. A pattern of increased incidence following increased meropenem expenditure was observed. 13 meropenem-resistant isolates (including CX1) were identified, mostly after a marked increase in carbapenem expenditure.

This is the first report of polyclonal *Acinetobacter* spread in the hospital. *Acinetobacter* major clones have evolved in response to a change in the antibiotic-hostile environment. They are difficult to be eradicated. Strict infection control measures including the controlled use of broad-spectrum antibiotics such as carbapenem are important.

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ULTRAFILTRATION FAILURE IN LONG TERM PERITONEAL DIALYSIS

Dr Lam Man Fai, Fei, Department of Medicine, Queen Mary Hospital (December 2002 Nephrology Exit Assessment Exercise)

The peritoneal dialysis (PD) has now become an established mode of renal replacement therapy for end stage renal disease patient. In Hong Kong, this mode of disease has already become the first line therapy. However, there are still a substantial morbidity and mortality due to peritonitis and loss of ultrafiltration (UF) capacity which resulting in fluid overload and inadequate dialysis. Furthermore, it may require a change of mode of dialysis, which further increase the burden of hemodialysis in our limited availability of resources.

The rate of peritonitis has been much used after the use of twin bag system. However, the problem of loss of UF capacity has been increase recently since more patients have stayed in PD for longer time. Not only do the mechanical cause like mal-position of Tenckhoff catheter and abdominal adhesion, but also the membrane dysfunction could result in loss of UF capacity. By understanding, firstly, the structural changes of peritoneal dysfunctions, such as increased number of blood vessels and amount of fibrosis in the peritoneum and secondly, the molecular mechanisms, such as elevated growth factors like vascular endothelial growth factor and increased enzyme activity of nitric oxide synthase resulting in an increase nitric oxide production would help us to understand the underlying mechanism and plan the management plan and more important is to prevent the development of UF failure. Interventions that target to these functional and structural changes may help to solve the problem in future.

A standard peritoneal equilibration test (PET) has been commonly used to assess the peritoneal membrane characteristics and to quantify the amount of UF capacity. A retrospective analysis of PET has been performed to investigate the incidence of UF in a local center. UF failure was defined as UF volume less than 200ml in a standard PET (2.5% glucose solution). There were total 1036 of PET performed for 389 patients receiving the PD within these 7 years. The PET was categorized into yearly interval for comparison. The initial D/P Cr was higher than the later assessments (0.74 ± 0.11 vs 0.70 ± 0.10, $p < 0.001$). The UF volume was also lower in initial assessment and increased back in the following serial measurements with similar trend as D/P Cr. The proportion of patient had UF failure was found to be higher in the first assessment about 16%. The proportion was about 11% in each year-interval. In sub-group analysis, for 136 patients (F =72) with consecutive PET (272 tests) performed for the first 2 years. The D/P Cr for the first year and second year were 0.74 ± 0.11 and 0.71 ± 0.10 respectively ($p = 0.001$) suggesting that the change of solute transports is due to the patient factor rather than any patients dropped out from the dialysis. Patients having PD more than 3 years were also analyzed separately. We found that about 13.8% of the patients has UF less than 200ml. These patients were found to have a higher small solute transport than patients with normal UF (D/P Cr at

4 hr, 0.74 ± 0.12 vs 0.69 ± 0.11, p = 0.02). However, the duration of dialysis was similar in both groups (Median 64 vs 73 months, p = 0.17). However, diabetic patients were found to have a higher risk of UF failure compared to non-diabetic patients (25.6% vs 11.0%, p = 0.013, 95% CI 1.22- 6.37).

In conclusion, patients on long term PD would develop UF problems and about 10% for each year interval. However, the PET might not truly reflect the real problems as many patients might have developed clinical problems well before a schedule PET and the standard PET may not be a good assessment tool to delineate the problem of UF failure and its underlying causes. The current management of UF failure has been well discussed in the literatures. For patient with high solutes transport rate, a short dwell time for the conventional glucose dialysate solution and or usage of glucose polymer solution may be useful. Temporary hemodialysis with peritoneal resting may also help. Different pharmacological approach to improve the ultrafiltration capacity has been studied in the animal model but still require further study before it could be well applied to human subject. To prevent the development of peritoneal membrane dysfunction, patients should be advised not to use high concentrated glucose solution if possible. Further study should be done to investigate the causes for the UF problems in the initial stage of PD so that high glucose concentration could be avoided at the earlier stage. A combination of different non-glucose based dialysate solution and using a more biocompatible solution may also help to prevent the problem.

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PROPHYLAXIS OF GRAM-POSITIVE ORGANISMS EXIT SITE INFECTION AND PERITONITIS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS BY APPLYING MUPIROCIN OINTMENT AT THE CATHETER EXIT SITE

Dr. Wong Sze Ho, Sunny, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2002 Nephrology Exit Assessment Exercise)

Objectives To evaluate the effectiveness of local application of mupirocin ointment at the catheter exit site in preventing exit site infection and peritonitis due to gram-positive organisms in continuous ambulatory peritoneal dialysis patients.

Methods This prospective randomized controlled trial included 154 patients. They were randomly allocated into a mupirocin treated group (group M) and a control group (group C). Group M included 73/154 patients (47.4%) and they were instructed to apply mupirocin ointment to the catheter exit site once daily after the routine daily exit site dressing. Group C included 81/154 patients (52.6%) and they continued their usual daily exit site care without applying mupirocin. The two groups were followed up to see whether there would be any difference in the frequency and the organisms of exit site infection and peritonitis.

Results Interim data was collected at 5 months after the start of the study and it showed that there was significant decrease in the incidence of exit site infection and peritonitis due to gram-positive organisms in group M compared with group C. The incidence of gram-positive exit site infection in group C was 0.33 episode/patient/year while that of group M was 0 ($p<0.05$). The incidence of gram-positive peritonitis in group C was 0.30 episode/patient/year, while that of group M was 0.03 episode/patient/year ($p<0.05$). For exit site infection and peritonitis due to other

organisms, mupirocin treatment had no significant effect on the incidence. The incidence of exit site infection due to other organisms in group C was 0.06 episode/patient/year while that of group M was 0.13 episode/patient/year. The incidence of peritonitis due to other organism in the group C was 0.06 episode/patient/year, while that of group M was 0.16 episode/patient/year. Before mupirocin treatment, we saw a trend towards higher infection rate in the diabetic patients and the nasal carriers of staphylococcus aureus compared with non-diabetic patients and non-nasal carriers of staphylococcus aureus. Mupirocin brought the infection rate of the diabetic and non-daibetic, nasal carrier and non-nasal carrier of staphylococcus aureus to an equally low level. No adverse effect of local application of mupirocin was reported.

Conclusions Local application of mupirocin ointment at the catheter exit site is a safe and effective method in preventing exit site infection and peritonitis due to gram-positive organisms.

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URAEMIC AUTONOMIC NEUROPATHY IN NON-DIABETIC CAPD PATIENTS IN HONG KONG - A CROSS-SECTIONAL STUDY OF ITS PREVALENCE AND PREDICTIVE FACTORS

Dr Jonathan Yung, Department of Medicine, Alice Ho Miu Ling Nethersole Hospital
(December 2002 Nephrology Exit Assessment Exercise)

Objectives The purpose of this study was to evaluate the prevalence of autonomic neuropathy in non-diabetic CAPD patients and to investigate its risk factors.

Methodology We performed a cross-sectional study on 114 non-diabetic CAPD patients. All patients underwent a standard battery of autonomic function tests including the sympathetic skin response, blood pressure and heart rate response to orthostasis, R-R interval variation test and the valsalva maneourve test.

Results Patients were categorized into two groups according to the results of the autonomic function tests. The baseline clinical data, nutritional and dialysis adequacy indices were compared. Definite autonomic neuropathy was noted in 53% of cases. Patients with autonomic neuropathy were significantly older (60.81 ± 12.53 vs 55.80 ± 12.43 yrs, p= 0.041) and both measures of residual renal function as well as dialysis dose were significantly lower in the autonomic neuropathy group. All other variables measured were not significantly different. Multivariate analysis using logistic regression identified the weekly renal Kt/V as the sole predictor of the presence/absence of autonomic neuropathy. A one unit reduction in residual renal function is predictive of a 10 times increase in the chance of having autonomic neuropathy (odds ratio = 0.100, CI= 0.030 - 0.335, $p<0.001$).

Conclusion Autonomic neuropathy is common in non-diabetic CAPD patients. Residual renal function, as calculated by the weekly renal Kt/V remains the most powerful predictor of autonomic neuropathy, underlining the importance of preservation of residual renal function in patients on CAPD. Prospective study is warranted to investigate the reversibility of autonomic dysfunction after an increment in dialysis dose.

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A PROSPECTIVE STUDY ON THE OUTCOMES AND ASSOCIATED FACTORS OF ELDERLY HIP FRACTURES UNDER A MODEL OF GERIATRIC HIP FRACTURE PROGRAM

Dr Chow Siu Lun, Eddie, Department of Medicine, Ruttonjee Hospital (December 2002 Rehabilitation Exit Assessment Exercise)

This is a prospective study describing the outcomes of Geriatric hip fracture patients under a model of care involving a Geriatric Hip Fracture Program (GHFP) and implementation of a clinical protocol. 44.4% of the recruited population were community walkers and 74% was living at home at the time of fracture. The reported in-patient, 6-month and 12-month mortality were 7.4%, 18.5% and 29.6%, respectively. Among those living at home before fracture, 55% remained at home at 6-month and 50% remained so at 12-month. For premorbid community ambulators, progressive improvement in the functional state was noted after discharge, with 67% of pre-fracture community ambulators resumed community walking at 6 months. The BADL also improved progressively after discharge. Despite the improvement of functional status, the institutionalization rate was not reduced. The factors associated with the hip fracture rehabilitative outcomes included mainly functional, cognitive and demographic factors. With the exception of haemoglobin levels, most of the surgical and medical factors were not shown to have significant association with 6-month and 12-month outcomes. The use of 20-point Barthel index (SBI) and Elderly Mobility Scale (EMS) seemed to be a flexible tool as assessment at different time frame were associated with outcomes. A review of local data and literature with their implications on current practice were discussed. Literature and local studies with limited data supported benefits of the models of Geriatric Hip Fracture Programs and Clinical Protocols with respect to hospital length of stay and cost savings. Further studies are required to delineate the important components of such models and consolidate their impact on rehabilitation outcomes.

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PULMONARY REHABILITATION FOR PATIENTS WITH COPD

Dr Lo Kwok Man, Department of Medicine & Geriatrics, United Christian Hospital (December 2002 Rehabilitation Exit Assessment Exercise)

Background Pulmonary rehabilitation has been shown to improve the exercise capacity and quality of life in patients suffering from chronic obstructive pulmonary diseases (COPD). However, individual responses are variable.

Objective To identify factors that may distinguish responders from non-responders in exercise capacity and health-related quality of life after pulmonary rehabilitation.

Subjects 102 patients with COPD entering the pulmonary rehabilitation programme in Haven of Hope Hospital from April 1998 to March 2001

Method The baseline characteristics of responders and non-responders of maximal exercise capacity, functional exercise capacity and quality of life were compared. Responders of maximal exercise capacity were defined as more than 12% increase in maximum workload during incremental cycle ergometry after pulmonary rehabilitation. Responders of functional exercise capacity were defined as patients

with more than 6% increase in 6-minute walk distance. Responders of quality of life were defined as improvement of more than 10 points in the Chronic Respiratory Disease Questionnaire. (CRQ)

Results Responders of maximal exercise capacity had significant lower initial maximum workload compared with non-responders (31.5 W vs. 39 W, p = 0.05). Responders of functional exercise capacity had significant smaller initial six-minute walk distance compared with non-responders. (272.7 m vs. 328.9 m, p = 0.001). There was a trend that responders of quality of life had lower initial CRQ score (76.2 vs. 83.6, p = 0.07), higher albumin level (39.9 g/L vs. 38.4 g/L, p = 0.08), and had a lower proportion of using long-term oxygen therapy (8.3% vs. 22.9%, p = 0.09) compared with non-responders, but the differences were not statistically significant.

Conclusion Patients with poorer initial exercise capacity and quality of life are more likely to be responders of the programme. They should have a higher priority of admitting to the programme.

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POSTSTROKE URINARY RETENTION – INCIDENCE AND OUTCOME

Dr Tsang Mei Ling, Department of Rehabilitation and Extended Care, Wong Tai Sin Hospital (December 2002 Rehabilitation Exit Assessment Exercise)

Objective

1) Document the incidence of poststroke urinary retention in a rehabilitative unit
2) Determine the clinical variables associated with it
3) Study the pressure-flow study in those with poststroke urinary retention and the possible management
4) Document the outcome of those with poststroke urinary retention

Design Cohort of consecutive patients admitted from 19 November 2001 – 13 April 2002

Setting Inpatient setting of a rehabilitation and extended care hospital

Participants Consecutively eighty-seven patients (49 male, 38 female; mean age of 75.6yr) with a principal diagnosis of stroke, admitted to the hospital for rehabilitation and convalescence.

Main Outcome Measures Postvoid residuals (PVR) were measured via a bladder scan within 96 hours of admission. Urinary retention was defined accordingly.
Pressure-flow study of cytometrogam with electromyography were performed in consented patients with urinary retention

Results Urinary retention was found in 33 (37.9%) patients. It was significantly associated ($p < 0.05$) with cognitive impairment on admission, lower functional status on admission, presence of constipation & faecal impaction, presence of urinary symptom before stroke and presence of urinary tract infection after stroke in acute hospital. It was not found to be associated with diabetes mellitus, dysphasia or the use of anticholinergic drugs. On discharge, 26 patients had urinary retention resolved. 17 patients of those with urinary retention underwent pressure-flow study of cytometrogram with surface EMG electrode. The patients were managed accordingly.

15 out of 17 patients had urinary retention resolved on discharge. 2 patients were put on long-term catheterization because of acontractile bladder.

Conclusion Urinary retention is common in patient with stroke. It should be addressed as part of the stroke rehabilitation management.

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MICROSCOPIC POLYANGIITIS: EXPERIENCE IN REGIONAL HOSPITALS AND REVIEW OF THE DISEASE

Dr Kwok Man Leung, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2002 Rheumatology Exit Assessment Exercise)

Microscopic Polyangiitis, previously known as a variant of classic Polyarteritis Nodosa, was only recently reclassified as a distinct disease entity. It is a rare disease which carries both significant mortality and morbidity. This dissertation describes the findings of a group of patients from two regional hospitals in respect to clinical features, laboratory findings, prognostic factors, morbidity and mortality.

A group of 14 patients who were diagnosed with vasculitis and whose diagnosis was compatible with the Chapel Hill Consensus Conference criteria for the diagnosis of Microscopic Polyangiitis were identified and their medical case notes were retrospectively reviewed.

The mean age at diagnosis was 62.29 (range 27-77). Mean duration of symptoms before diagnosis was 9.2 months (range 0.5- to 36 months) and the mean duration of follow up were 29.34 months (range 1-123 months). The most common presenting features were constitutional symptoms (85.6%), followed by renal (78.6%) and respiratory symptoms (50%). Musculoskeletal and gastrointestional symptoms were rare in this group of patients. Non-specific markers for the presence of inflammation were frequently found to be elevated. Anti-nuclear factor and rheumatoid factor were elevated in most of the patients during the active phase of the disease. These markers normalised when disease was in remission phase. The anti-myeloperoxidse antibody were all positive. None of the patients had positive anti-proteinase 3 antibody. Our mortality rate of 21.4% was comparable with the published literature. There was no relationship between mortality and the Five Factor Score. In this study, the percentage of patients with brochiectasis was 71.4 %. This relatively high prevalence warrants further study to evaluate its effect on the pathogenesis of the disease.

Note: For obtaining the full dissertation, please contact the author directly.