

## **Abstracts of Dissertations**

### **December 2004 Exit Assessment Exercise**

#### **DARIER'S DISEASE (KERATOSIS FOLLICULARIS) - A LOCAL SURVEY, STUDY OF LIFE IMPACT, MUTATION ANALYSIS OF THE ATP2A2 GENE AND REVIEW**

Dr. Chan Yiu Hoi, Department of Health, Hong Kong (December 2004 Dermatology & Venereology Exit Assessment Exercise)

This is a study which consists of two parts. Part I is a multi-clinic, 20-year, retrospective study to review the clinico-pathological features, life impact, treatment and disease outcomes of patients with Darier's disease in the Social Hygiene Service, Hong Kong Special Administrative Region, China. Part II is a genetic study on the patterns of mutation of ATP2A2 gene in the aforesaid patients. Data were collected from 32 affected patients (15 males and 17 females with approximately equal sex ratio) and the mean age of onset was 15. Twenty patients had positive family history. The estimated incidence of DD in Hong Kong is 0.025 per 100,000 per year. The life impact of DD on our patients which was measured by the DLQI score was found to be low in our locality. The average DLQI score was 6.43 with the majority (27/28=96%) scoring less than 15. Most patients lived with the disease without major problems. The major symptom experienced was itching. Keratotic papules were invariably present in our patients and mixed pattern with seborrhoeic plus flexural involvement was the commonest phenotypic variation. All of them had acral signs; 38% had oral mucosal lesions. Lesions were most frequently found on face, neck, front chest and ears. There was no full remission. Focal acantholytic dyskeratosis with corps ronds and grains were the usual histopathological findings. Systemic retinoid was the most effective therapy for our patients although minor side effects were common. Mutation analysis in the ATP2A2 gene on chromosome 12 had been performed in 28 Chinese patients with DD. These patients had mild to severe skin symptoms. DNA extraction followed by polymerase chain reaction (PCR) amplification of the exons and flanking regions of the ATP2A2 gene were performed. Mutation detection strategies included heteroduplex scanning by denaturing high performance liquid chromatography (DHPLC) and nucleotide sequencing. We found four distinct mutations, all of which were novel. DHPLC in normal controls further verified the mutations. Three sisters within a family had a new T insertion at nucleotide 3022 in exon 20 resulting in a premature termination codon (PTC) at codon 1008. This mutation only affected SERCA2b. A 68-year-old gentleman with moderately severe DD had a novel T deletion at nucleotide 216 resulting in a PTC at codon 72. Another 22-year-old gentleman with mild disease had a new frameshift deletion mutation (2918-2920delCCT) in exon 20 resulting in deletion of serine at position 973. A further novel altered splice site mutation IVS10+1G>T resulting in exon skipping PTC was detected in a 35-year-old pregnant woman who had severe DD. Conclusions: Darier's disease is a rare dermatosis in HKSAR. Systemic retinoid is the most effective therapy and well tolerated in our patients despite minor side effects are common. Most DD patients can live with minimal life impact. Four pathogenic mutations in the ATP2A2 gene were identified in 19 Chinese pedigrees. All of these mutations are private with nonsense type being the commonest. No mutation hotspots and clear-cut genotype-phenotype association could be identified.

Keywords: Darier's disease; Keratosis follicularis; ATP2A2 gene mutation; Hong Kong; Chinese

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## **CUTANEOUS MELANOMA: A REVIEW OF 32 PATIENTS IN THE SOCIAL HYGIENE SERVICE, 99 PATHOLOGICAL REPORTS FROM MAJOR HOSPITALS AND DATA FROM THE HONG KONG CANCER REGISTRY**

Dr Hui Shiu Kee, Department of Health, Hong Kong (December 2004 Dermatology and Venereology Exit Assessment Exercise)

Cutaneous melanoma (CM) is an important disease entity for its potential fatality and its urgency of management. No systematic study on this entity had been conducted locally. This study is conducted in three scopes: (1) a population based study focusing on the epidemiology; (2) a review of 99 pathology reports from five major hospitals; (3) a review of 32 patients in dermatology clinics of the Social Hygiene Service (SHS). A case-control study was also conducted to assess the significance of the seemingly higher prevalence of diabetes mellitus among patients with CM.

The incidence of CM was double than that of Japan and triple than that of Mainland China but it was lower than that of Caucasians. The case fatality was ten times than that of non-melanoma skin cancer. Males had a higher incidence, mortality and case-fatality. Unlike the findings in Caucasians, the crude incidence and mortality rates in this study had a steep increase with age without any birth cohort adjustment. The feet were the commonest site of predilection. Change in size and colour were the commonest presenting symptoms. Acral lentiginous melanoma was the commonest type. The prevalence of diabetic history was higher in patients with CM, though it did not reach statistical significance.

Comparing our data with that of Caucasian, two major differences were found: (1) melanoma predominantly occurred on the feet in Chinese patients, and (2) a much steeper increasing trend in crude age-specific incidence rate without any birth cohort-adjustment.

Keywords: cutaneous melanoma, epidemiology, Chinese, diabetes mellitus

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## **HEALTH-RELATED QUALITY OF LIFE AMONG CHINESE PEOPLE WITH PSORIASIS IN HONG KONG**

Dr Tse Chi Tat, Department of Health, Hong Kong (December 2004 Dermatology and Venereology Exit Assessment Exercise)

**Background** Psoriasis is a common skin disease that can considerably impair health-related quality of life (HRQOL). However little is known about the HRQOL among local psoriasis patients and its relationship with clinical severity.

**Objectives** The objectives of this study were: (1) to describe the HRQOL of Chinese people with psoriasis by three different HRQOL instruments and to compare it with HRQOL of healthy individuals and people with other illnesses in Hong Kong (2) to examine the relationship between the three HRQOL instruments and also the relationship between HRQOL and clinical severity.

**Methods** A total of 182 Chinese adults with psoriasis were recruited in 6 government dermatology clinics from October 2003 to March 2004. We used the Chinese (HK) SF-36 Health Survey (SF-36) to evaluate the generic HRQOL, the Hong Kong Chinese version of Psoriasis Disability Index (PDI-HK) to evaluate the psoriasis-specific disability and Global Single Question (GSQ) to evaluate the overall disability. While higher SF-36 scores indicated better HRQOL, higher PDI or GSQ score indicated poorer HRQOL. Concurrently, physicians rated the clinical severity by a modified Psoriasis Area and Severity Index (MPASI). It was a

summation of extent and lesional severity (erythema, desquamation and induration) with higher value indicating worse clinical status. Finally, the relationships between the SF-36 summary scores, PDI (%) [percentage of maximum possible disability revealed by PDI-HK], GSQ score and MPASI were examined by correlation coefficient.

**Results** SF-36 showed that the greatest disability among psoriasis patients was the impairment in social functioning. The SF-36 physical summary score and mental summary score of psoriasis patients were significantly ( $P < 0.01$ ) lower than that of the sex- & age-matched 2410 HK healthy controls. The reduction of physical and mental functioning in psoriasis was comparable to that of Severe Acute Respiratory Syndrome or bronchiectasis. PDI-HK showed that hairdressing was the worst psoriasis-specific problem. The GSQ showed that most patients had mild to moderate overall disability. The SF-36 summary scores had strong and significant correlations with PDI (%) [ $r_s = -0.46$  &  $-0.47$ ;  $P < 0.01$ ] and GSQ score [ $r_s = -0.46$  &  $-0.40$ ;  $P < 0.01$ ]. However, MPASI had weak correlations with SF-36 summary scores [ $r_s = -0.14$  &  $-0.12$ ], PDI (%) [ $r_s = 0.27$ ] and GSQ score [ $r_s = 0.15$ ].

**Conclusions** This study confirmed the negative impact of psoriasis on HRQOL among local Chinese people. The degree of disability was comparable to two debilitating respiratory diseases. Health policy makers should recognize the importance of psoriasis and allocate appropriate resources to improve the HRQOL. Clinicians should pay attention to the impairment in social functioning and scalp psoriasis that can cause substantial hairdressing problem. Our findings supported the construct validity of the PDI-HK and GSQ. These two are useful HRQOL instruments that are applicable to Chinese patients and simple to use. The poor correlation between HRQOL and MPASI suggested that patient-reported HRQOL and physician-assessed clinical severity were two independent outcome measures.

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## **GASTROINTESTINAL STROMAL TUMORS – EXPERIENCE OF A REGIONAL HOSPITAL IN HONG KONG**

Dr. Chan Kam Hoi, Division of Gastroenterology & Hepatology, Department of Medicine, Yan Chai Hospital (December 2004 Gastroenterology and Hepatology Exit Assessment Exercise)

**Background** Gastrointestinal stromal tumors (GISTs) are relatively uncommon mesenchymal tumors with a lot of controversies regarding their nomenclature, cellular origin, diagnosis and prognosis. Recent studies suggested that GISTs have unique histological, immunophenotypical and molecular genetic features that set them apart from typical smooth muscle tumors. The precise cellular origin of GISTs has recently been proposed to be the interstitial cell of Cajal. Following is a report on the experience in a cohort of Chinese patients with GISTs managed in a local hospital. Their clinical and pathological characteristics, survival pattern as well as recurrence were reviewed..

**Methods** All Chinese patients diagnosed of GISTs in Yan Chai Hospital between September 1995 to December 2003 were studied. The clinical information were obtained from the medical records, including both inpatient and outpatient records. Before final recruitment and analysis, the diagnosis of GIST was reconfirmed by a designated pathologist who reviewed all the histology slides of the case retrieved.

**Results** In total, 47 patients with GISTs, 26 male and 21 female, mean age 66.6 years at the time of diagnosis (SD 13.1, range from 29 to 87) were identified. The stomach (34 patients, 72.3%) was the most common location for the tumor, followed by the small intestine (8 patients, 17.0%), esophagus (2 patient, 4.3%), omentum (2 patient, 4.3%) and colon (1 patient, 2.1%).

31 patients (66%) had complete tumor resection, 7 patients (15%) underwent incomplete resection and 5 patients (10%) were inoperable. There were totally 16 mortalities. Among them, 11 deaths (23%) were tumor related. The median survival time was 26 months. Five year survival probability was 61.3%. By Cox Proportional Hazard Model, the significant factors associated with adverse outcome include incomplete resection, tumor size 5cm or above, invasion to the adjacent organ or presence of metastasis.

**Conclusions** The clinical and histological features of gastrointestinal stromal tumors in a regional hospital in Hong Kong were similar to reports in the literature. The survival of the completely resected tumors is good.

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### **CLINICAL OUTCOMES OF CHINESE PATIENTS WITH LIVER CIRRHOSIS WHO DEVELOPED SPONTANEOUS BACTERIAL PERITONITIS IN A REGIONAL HOSPITAL**

Dr. Chan Wai Man, Department of Medicine & Geriatrics, Kwong Wah Hospital, (December 2004 Gastroenterology & Hepatology Exit Assessment Exercise)

Spontaneous bacterial peritonitis (SBP) was considered a serious complication in patients with liver cirrhosis. Nowadays studies carried out in Western countries showed that the hospital mortality of SBP lied between 20-40 per cent. Due to relative lack of studies in Chinese patients, the aims of this study were to determine the characteristics and outcomes of Chinese patients with liver cirrhosis who were admitted for spontaneous bacterial peritonitis, and to identify parameters that might affect hospital mortality. A retrospective study was carried out for patients with spontaneous bacterial peritonitis patients who were admitted to Kwong Wah Hospital between 1997 and 2003. Forty-seven consecutive episodes of SBP were identified. The mean age of the patients was 60.8 years. 85.1 per cent were male patients. 55.3% of the cases were hepatitis B surface antigen (HBsAg) positive and the mean Child-Puge score was 10.7. There were 21 classical SBP episodes (44.7%) and 20 of these were caused by gram-negative bacilli, with *Escherichia coli* accounting for 81% of these. The most frequent presenting features were increased abdominal distension (80.9%) followed by fever, chills and rigors (74.5%) and abdominal pain (68.1%). Thirty-seven parameters were recorded to evaluate their relationship with the hospital mortality. The overall hospital mortality was 34% and the 2 year survival was 25.7%. Ten parameters were found to be related to a higher in-hospital mortality on univariate analysis (female gender, positive ascitic fluid culture, renal impairment (serum creatinine level > 133  $\mu\text{mol/L}$  or 1.5mg/dl) before SBP treatment, gastrointestinal bleeding, failed response to antibiotic treatment, progressive hepatic encephalopathy, shock, symptom onset-treatment time gap and pre-treatment serum urea and creatinine levels). All patients with shock, progressive hepatic encephalopathy and failed response to antibiotic treatment died during hospitalization ( $p < 0.001$ ). On multivariate analysis, shock ( $p < 0.001$ ), failed response to antibiotic treatment ( $p < 0.001$ ), progressive hepatic encephalopathy ( $p < 0.001$ ), pre-treatment serum creatinine level ( $p = 0.016$ ), positive ascitic fluid culture ( $p = 0.029$ ) and female gender ( $p = 0.041$ ) were significantly associated with in-hospital mortality. This study re-confirmed that spontaneous bacterial peritonitis had a significant hospital mortality and a poor long term survival.

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### **NON-SURGICAL MANAGEMENT OF SMALL SINGLE HEPATOCELLULAR CARCINOMA**

Dr. Cheung Wai Ching, Department of Medicine, Queen Elizabeth Hospital (December 2004 Gastroenterology & Hepatology Exit Assessment Exercise)

Hepatocellular carcinoma (HCC) is one of the most common malignancies world-wide. Ultrasonography (U/S) screening allows early detection of subclinical HCC which are assessable to a variety of therapeutic modalities. Therefore, the number of patients presented with small single HCC is increasing. Non-surgical management of small single HCC will be reviewed and discussed. In addition, the management outcome in the local situation will be analysed retrospectively from a group of patients in Queen Elizabeth Hospital (QEH).

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### **PYOGENIC LIVER ABSCESS: PATIENT CHARACTERISTICS AND EXPERIENCE IN MANAGEMENT FROM A REGIONAL HOSPITAL**

Dr Lok Ka Ho, Department of Medicine & Geriatrics, Tuen Mun Hospital (December 2004 Gastroenterology and Hepatology Exit Assessment Exercise)

Pyogenic liver abscess is a major hepatobiliary infection with significant morbidity and mortality. Current literatures suggest that the mortality rate is 10-25% in the era of ultrasound and CT scan. Over the past two decades, there have been significant developments in the management of this disease. The objective of this dissertation is to retrospectively review the experience in Tuen Mun Hospital over a period of 6 years and to identify any risk factors associated with unfavorable patient outcomes.

**Study methods** All patents with diagnosis of pyogenic liver abscess hospitalized to Tuen Mun Hospital from July 1998 to June 2004 were included. The medical records of eligible patients were reviewed to obtain demographic, clinical, laboratory, microbiological and radiological data. Management strategy and final outcome were studied.

**Results** A total 111 patients were included in the study. Fever, chills and right upper quadrant pain were the most common presenting symptoms. Low albumin level, elevated alkaline phosphatase and leukocytosis were the most common laboratory features. Klebsiella pneumoniae was the most common etiological agent detected in cultures of blood and abscess aspirates. 53% of liver abscesses are cryptogenic in origin and 22.5% had biliary pathology. The mortality rate was 11.7%. By multiple logistic regression analysis, malignancy ( $p=0.001$ ), requirement for open surgical intervention ( $p=0.01$ ) and delay in diagnosis ( $p=0.0019$ ) were independent risk factors associated with mortality. Requirement for open surgical treatment ( $p=0.004$ ) and septicemic shock ( $p=0.04$ ) were independent risk factors associated with the need of ICU care.

**Conclusion** Although advances in imaging and therapeutic modalities lead to substantial improvement of patient outcome, mortality still occur in patients with chronic illnesses and those requiring open surgical intervention. Delay in diagnosis can cause fatal outcome. High index of suspicion with prompt institution of treatment is the cornerstone of successful treatment in patients with pyogenic liver abscess.

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### **A RETROSPECTIVE STUDY OF TREATMENT OUTCOME IN PATIENTS WITH NEWLY DIAGNOSED OR FIRST –RELAPSE ACUTE PROMYELOCYTIC LEUKEMIA: EXPERIENCE IN REGIONAL HOSPITALS IN HONG KONG**

Dr Lau Ching Wa, Department of Medicine, Tuen Mun Hospital (December 2004

**Objective:** This study reviewed treatment outcome of newly diagnosed and first-relapse acute promyelocytic leukemia (APL) in two regional hospitals in Hong Kong retrospectively; analyzed the relationship between clinico-biological features and treatment outcome; and summarized evidence on pathogenesis, diagnostic approach, treatment consensus, and disease monitoring.

**Main outcome measures:** hematological complete remission rate in newly diagnosed APL patients, their hematological relapse rate, hematological complete remission rate in first-relapse APL patients, toxicity associated with treatment, and overall survival status.

**Results:** A total of 28 newly diagnosed APL patients were treated in the study period from 1991 to 2004 in Tuen Mun Hospital and Prince Margaret Hospital. Hematological complete remission achieved in 24 patients (86%), including 82% receiving all-*trans* retinoic acid-based induction therapy and 4% receiving anthracycline-based chemotherapy alone. Refractory disease happened in 1 patient (4%), whom achieved hematological remission after receiving re-induction treatment with arsenic trioxide. 6 patients (24%) relapsed. Second hematological complete remission achieved in 5 of them (83%). For newly diagnosed APL patients, early fatal hemorrhagic complication was reported in 4%; treatment associated lethal cardiotoxicity and infective complications were both 7%. In first-relapse APL patient, early fatal infective complication was reported in 17%; no treatment associated lethal toxicity was observed. The median follow-up was 36 months. 3-year OS, EFS and DFS were 75% ± 9%, 49% ± 11% and 51% ± 11% respectively. OS, EFS and DFS were unfavorably influenced by presenting WBC count greater than  $10 \times 10^9/L$  ( $P = 0.038, 0.013, 0.005$  respectively).

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## **MULTIPLE MYELOMA: EVALUATION OF PROGNOSTIC FACTORS FOR HONG KONG CHINESE PATIENTS**

Dr Law Man Fai, Department of Medicine, Tuen Mun Hospital (December 2004 Haematology & Haematological Oncology Exit Assessment Exercise)

**Introduction** Multiple myeloma is a common haematological malignancy, especially in the elderly. We would like to evaluate the prognostic information for survival in 53 myeloma patients in Tuen Mun Hospital

**Method** This is a retrospective cohort study of patients diagnosed with multiple myeloma from 1/1/1995 to 30/6/2002. We evaluated the clinical and laboratory characteristics of these patients at the time of diagnosis, including age, sex, co-morbidity, staging of myeloma, presence of bony lytic lesion, blood hemoglobin level, white cell count, platelet count, serum levels of creatinine, globulin, albumin, corrected calcium, urate, beta2-microglobulin, C-reactive protein, and immunoglobulin type. The initial treatment and any use of bisphosphonate for patients with lytic bone lesions were also evaluated. The survival status of these patients were assessed on 30/6/2004.

**Results** A total of 53 Chinese patients were recruited in the review. 43 patients (81%) died at the end of the study. Fourteen clinical and laboratory parameters were studied for their prognostic significance. We found that age at presentation was a statistically significant parameter to survival. Beta2-microglobulin and CRP could not be evaluated because of high missing rate of these parameters.

**Conclusion** Among the 14 clinical and laboratory parameters analysed in the 53 Chinese

patients , age of presentation was found to be significant prognostic markers for survival. The usefulness of beta2-microglobulin , CRP and cytogenetics in Chinese patients may need further study

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## **DECLINING MORTALITY AND MORBIDITY OF ADVANCED HIV DISEASE WITH THE USE OF HAART IN HONG KONG**

Dr Chan Chi Wai Kenny, Integrated Treatment Centre, Centre for Health Protection, Department of Health, Hong Kong (December 2004 Infectious Disease Exit Assessment Exercise)

**Background** Morbidity and mortality of advanced HIV infection have declined in Western industrialized countries since the availability of HAART. It is unclear if this has also happened in Hong Kong.

**Objective** To assess the mortality and morbidity of AIDS in Hong Kong and their relationship with the use of HAART.

**Study Design** Retrospective clinic cohort of patients with advanced HIV disease in Hong Kong.

**Methods** There were three parts to the study. First, the mortality of advanced HIV disease per year was evaluated for the decade 1993 to 2002. Patient observation was then divided into that prior to 1997 and that in 1997 and thereafter. Their respective mortality was compared. Second, patients were divided into those of the pre-HAART (1984-96) and HAART (1997-mid2003) eras. Their respective progression to AIDS or death was assessed by life table analysis. Cox proportional hazards model was also used to estimate the adjusted relative hazards of AIDS and death by era of diagnosis. Third, observation period of patients with advanced disease was divided into that on HAART and that which was not. After the events rates were estimated for the clinical end points of AIDS and death, they were adjusted for covariates including calendar year and baseline CD4 cell count.

**Results** Crude mortality rate of advanced HIV disease declined in the decade 1993-2002, coinciding with the rising use of HAART since 1997. Overall, it decreased from 10.8 - 30.4/100 patients in 1993-96, to 0.8 - 6.9/100 patients in 1997-2002. When grouped according to follow up before 1997 and in 1997 or later, the death rate decreased from 9.2 to 2.4 per 1000 patient-months, a rate ratio of 4.04 (95% CI, 2.52-6.47). On the basis of life table analysis, patients who were diagnosed with HIV in the HAART era (1997 to mid-2003) had improved prognosis compared to patients in the pre-HAART era (1984-1996). Median survival after AIDS increased from 29.8 months to >70 months, and times to AIDS and death after reaching a CD4 count <200/ $\mu$ l both increased to >130 months from 47.7 and >120 months respectively. The adjusted HRs of these clinical end points were 0.15 (95% CI, 0.08-0.26), 0.38 (95% CI , 0.24-0.60) and 0.25 (95% CI, 0.15-0.40). Similar benefits were shown when patient observation was categorized according to actual use of HAART. In a multivariate model where baseline CD4 count and calendar period were adjusted, there was an independent reduction of clinical events with use of HAART but not calendar period.

**Conclusions** In conclusion, the mortality of advanced HIV disease has declined in the last decade in Hong Kong. Patients who were diagnosed with HIV in 1997 or later had delayed progression to AIDS and death. This improved prognosis was attributable to the use of HAART.

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## **THE ROLE OF BACTERIAL PATHOGENS AND USE OF ANTIBIOTICS IN ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (AECOPD): A REVIEW OF CURRENT MEDICAL LITERATURE AND GUIDELINES AND REPORT ON A LOCAL STUDY**

Dr Wu Ka Lun Alan, Division of Infectious Diseases, Department of Medicine & Therapeutics, Prince of Wales Hospital (December 2004 Infectious Disease Exit Assessment Exercise)

Chronic obstructive pulmonary disease (COPD) exacerbation is associated with significant morbidity and mortality worldwide. The role of bacterial infection was once thought to be controversial, and many people believed that bacteria isolated from sputum represent colonization only. Likewise, the efficacy of antibiotics in treatment of AECOPD has been viewed with skepticism, and there is a wide variation in the suggestion of specific choice of antibiotic in different guidelines. Although AECOPD is a heterogeneous disease, available evidence suggest that at least 80% of AECOPDs are infectious in origin. There is now increasing evidence for specific roles of bacterial pathogens in the etiology and pathogenesis of AECOPD. This new knowledge includes the following: 1) New lines of evidence demonstrate that bacterial isolation from sputum during exacerbation in many instances reflects a causal relationship. 2) Exacerbations contribute to the progressive deterioration of lung function that is characteristic of COPD. 3) Bacterial colonization of the lower airway in COPD is associated with inflammatory responses that may contribute to progressive lung damage. 4) Effective antibiotic therapy leads to bacterial eradication, increase in exacerbation-free interval, and improved quality of life in COPD patients; it is recommended for patients with at least two cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence. The current review will focus on some of the emerging evidence that suggest specific roles of bacterial pathogens in AECOPD, as well as the evidence and current guidelines regarding use of antibiotics in AECOPD.

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## **RETROSPECTIVE STUDY ON DIALYSIS-RELATED AMYLOIDOSIS (DRA) AMONG PATIENTS RECEIVING HEMODIALYSIS IN PRINCESS MARGARET HOSPITAL WITH LITERATURE REVIEW**

Dr Cheuk Au, Renal Unit, Department of Medicine & Geriatrics, Princess Margaret Hospital (December 2004 Nephrology Exit Assessment Exercise)

**Aim** Dialysis-related amyloidosis (DRA) is a serious and inevitable complication approached 100% in patients dialyzed > 15 years. There is lack of local study on the prevalence, risk factors, clinical course, treatment and outcome of DRA. I review the literatures and perform a retrospective study to give the locals result on DRA.

**Method** We retrospectively analyzed 30 clinically probable and 14 histologically confirmed DRA patients out of a total of 251 patients on haemodialysis, followed-up by Princess Margaret hospital in the last 10 years.

**Result** The age of starting hemodialysis is relatively young in our DRA patients due to the fact that peritoneal dialysis is the first mode of dialysis in Hong Kong. All 44 DRA patients are on haemodialysis and there is no case in patients on haemodialysis < 6 years nor in our peritoneal dialysis patients. Carpal tunnel syndrome (CTS) is the earliest and commonest presentation followed by arthropathy, pathological fractures and finally extra-articular involvement. The severity of symptoms increases in direct proportion to the number of years on dialysis. The diagnostic test of choice is the histology of synovial tissue from release



surgery for CTS. Magnetic resonance imaging of the affected bone and joint also have a high positive yield of diagnosis. The optimal treatment is to offer renal transplantation if possible. Other symptomatic treatment modalities include parathyroidectomy, high flux dialysis and haemodiafiltration, which should be considered in long-term hemodialysis patients who are unfit to have renal transplantation in the future. DRA carries significant morbidity. Renal transplantation is the only way to improve mortality in this group of patients.

**Conclusion** The management strategy of DRA includes 1. DRA is not a major clinical concern in patients whose life expectancy on dialysis is expected to be less than 5 years. 2. In all patients on long-term hemodialysis, renal transplantation should be the best option to avoid this complication. 3. To consider parathyroidectomy, use of high-flux haemodialysis or haemodiafiltration for symptomatic improvement in those patients who have little chance for renal transplant in future.

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### **EFFECT OF ANDROGEN, RECOMBINANT HUMAN ERYTHROPOIETIN (rHuEPO) AND COMBINATION OF ANDROGEN AND rHuEPO IN DIALYSIS PATIENTS: A LOCAL EXPERIENCE\**

Dr Wong Chi Kwan, Renal Team, Department of Medicine, Alice Ho Miu Ling Nethersole Hospital (December 2004 Nephrology Exit Assessment Exercise)

**Background:** Anemia and malnutrition are the universal complications in chronic dialysis patients. Prior to the introduction of recombinant human erythropoietin (rHuEPO), androgen and blood transfusion were the mainstay treatment of anemia. The availability of recombinant human erythropoietin had completely changed the use of androgen. However, the generalized use of recombinant human erythropoietin was limited by the high cost. Not every anemic patient in chronic dialysis can afford the cost of the treatment by rHuEPO.

**Objective:** In this study, we try to evaluate the effect of androgen, rHuEPO and in combination in treatment of anemia in chronic dialysis patients in Chinese population.

**Methods:** All the patients recruited into the dialysis program of the Alice Ho Miu Ling Nethersole Hospital between January 1999 and January 2004 were reviewed. Patients who received androgen therapy and fulfilled the following criteria were recruited into the study. The criteria were: 1) who had completed at least 6 months androgen therapy, 2) there was no evidence of gastrointestinal bleeding, 3) no history of chronic inflammation or infection, 4) no history of malignancy. According to the mode of treatment, the patients were divided into 2 groups: Group A received androgen therapy alone. Group B received combination of androgen and rHuEPO therapy. Furthermore, a group of matched subjects selected from the list of rHuEPO therapy, Group C, was selected in order to compare with the effect of androgen. The clinical parameters, hematological and biochemical parameters were collected from medical records and analyzed.

**Results:** There were total 61 anemic renal failure patients who had received androgen therapy (nandrolone decanoate) in our hospital. Among of them, 21 cases were excluded from analysis because they did not fulfill the inclusion criteria. It ended up 20 patients in group A and 20 patients in group B. The mean dosages of androgen were  $92.5 \pm 18.3$  mg and  $97.5 \pm 11.2$  mg per month in group A and group B respectively. Group C patients had better residual renal function, lower parathyroid hormone level and shorter duration of dialysis. The hemoglobin and hematocrit were significantly increased in those 3 groups after 6 months of therapy. The hemoglobin was increased from  $7.26 \pm 0.79$  to  $9.58 \pm 1.32$  gm/dL in group A ( $p < 0.001$ ),  $7.46 \pm 1.0$  to  $9.39 \pm 1.33$  gm /dL in group B ( $p < 0.001$ ) and  $7.08 \pm 0.73$  to  $9.0 \pm 1.2$  gm/dL in group C.

The increment among those 3 groups was comparable. Nutritional parameters, as reflected by albumin level, body weight and ferritin level, did not change after 6 months of therapy of androgen.

**Conclusion:** We found that nandrolone decanoate used alone and combination rHuEPO were efficacious in treatment of anemia in chronic dialysis. Nandrolone decanoate achieved erythropoietic results which were similar to that of rHuEPO but with a lower economic cost. Lack of nutritional status improvement in present study may be related to low dosage of nandrolone decanoate used. Nandrolone decanoate may be considered as an effective alternative therapy or as adjunct for the anemia patient on chronic dialysis.

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### **DETECTION OF ASYMPTOMATIC DIABETIC DISTAL SYMMETRIC POLYNEUROPATHY WITH CLINICAL EXAMINATION AND NERVE CONDUCTION STUDY IN PATIENTS WITH NON-INSULIN DEPENDENT DIABETES MELLITUS (NIDDM)**

Dr Lau Siu Wah, Herrick, Kwong Wah Hospital (December 2004 Neurology Exit Assessment Exercise)

**Background:** Non-insulin dependent diabetes mellitus (NIDDM) is highly prevalent in our local population. Yet, local data concerning diabetic neuropathy are lacking. The problem of diabetic neuropathy, of which distal symmetric polyneuropathy comprises the majority, can be sizeable. Hence, the physical and social burden brought forward can be enormous. Since active treatment may improve prognosis of neuropathy, it is crucial to apply accurate diagnostic tool and achieve early detection of neuropathy or individuals at risk.

**Method:** 80 voluntary NIDDM patients without symptoms of neuropathy were examined for evidence suggestive of peripheral neuropathy using standard clinical examination tools and nerve conduction study (NCS). Risk factors possibly associated with neuropathy were evaluated. Accuracy of the two methods were compared and discussed. A control sample served as normal references for NCS parameters.

**Results:** Clinical examination identified abnormality in 5% patients. It showed high specificity when compared with NCS, which revealed abnormality suggestive of polyneuropathy in 23.8%. High HbA1c level (  $p=0.000$  ) and presence of nephropathy (  $p= 0.011$  ) are independent risk factors for neuropathy. Abnormalities of lower limb NCS parameters and minimum F-latency are the most consistent findings in patients with abnormal NCS. Delay of tibial F-latency is observed in a significant proportion (13.1%) even in diabetic subjects with normal standard NCS findings.

**Conclusion:** A significant proportion of asymptomatic prevalent NIDDM patients already have neuropathy detectable at neurophysiological level. There is no good consensus as to accuracy of clinical examination in diagnosis of neuropathy. Clinical foot examination including monofilament tests on dorsum and plantar aspect of feet, vibration threshold at big toes measured with neurothesiometer and ankle reflexes may not provide sufficient sensitivity for neuropathy screening in certain patients. NCS may be supplemented to routine foot examination for this purpose in patients at high risk for development of neuropathy. F-latency should be valuable parameter to be assessed in all diabetics with suspicion of early neuropathy.

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## **REHABILITATION OUTCOMES IN PATIENTS WITH RECURRENT HIP FRACTURE**

Dr Cheung Tak Cheong, Rehabilitation Medicine, Kowloon Hospital (December 2004 Rehabilitation Exit Assessment Exercise)

**Objective** To evaluate the in-patient rehabilitation outcomes in elderly patients suffered from recurrent hip fracture.

**Methods and design** Retrospective cohort study. Between April 2001 and Mar 2002, 327 patients admitted to a regional rehabilitation hospital for hip fracture rehabilitation were recruited. A total of 21 out of 327 were admitted for rehabilitation of second hip fracture, and the remaining 306 cases were admitted for rehabilitation of their first hip fracture. Baseline demographic data were compared. Rehabilitation outcomes included length of stay, changes in Functional Independence Measure (FIM), discharge FIM score and discharge residency were evaluated.

**Results** Admission FIM score was significantly lower in the recurrent hip fracture group. There was no statistically significant difference in the discharge FIM score, total FIM gain, FIM gain per day, length of hospital stay and discharge placement between the two groups of patients.

**Conclusion** This study did not find a deleterious effect of a previous hip fracture in functional recovery and rehabilitation outcomes. Patients with recurrent hip fracture benefit from in-patient hip fracture rehabilitation program to the same degree as the patients with first hip fracture.

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## **FUNCTIONAL OUTCOMES AFTER HIP FRACTURE IN THE ELDERLY**

Dr Leung Chung Ping, Department of Rehabilitation, Wong Tai Sin Hospital (December 2004 Rehabilitation Exit Assessment Exercise)

This was a prospective study on the ambulatory status, basic self-care ability, mortality and discharge disposition of 62 elderly hip fracture patients in a local rehabilitation hospital. The patients were aged over 65 (mean age 82.4) and 34% had cognitive impairment. They were transferred from the orthopedic unit of a local acute hospital for rehabilitation after surgical intervention. Assessment of outcomes was made on admission to the rehabilitation unit, on discharge and at 6 months after the fracture.

By 6 month, 4 patients out of 62 (6%) had died, 27 patients out of 35 (77%) had entered nursing homes and 37 patients were successfully followed up. Among those follow up patients, 22 patients out of 37 (59%) had satisfactory self care abilities and were independent in ambulation.

Predictors of poor outcome in ambulation included residence in institution after discharge ( $p=0.025$ ) and re-hospitalization ( $p=0.002$ ). Predictors of poor outcome in self-care was cognitive impairment ( $p=0.045$ ). Predictors of discharge to institution were living alone before fracture ( $p=0.002$ ) and low self care score on admission ( $p=0.048$ ). Predictor of mortality was residence in institution after hospital discharge ( $p=0.031$ ). Knowledge of the predictors of outcomes could facilitate hospital discharge and shorten the length of hospital stay.

Cognitively impaired patients benefit from in-patient rehabilitation and they should not be excluded from it. Although their gain in motor FIM score (6.95 points) was smaller than that in cognitively intact patients (14.7 points), the gain after rehabilitation was statistically significant ( $p=0.000$ ). The ability of dressing lower garment and toileting deteriorated significantly after discharge ( $p=0.049$  and  $p=0.004$  respectively) and more emphasis should be put on these activities during in-patient rehabilitation and subsequent follow up. While for the cognitively intact patient, more emphasis should be put on climbing stairs and bathing as they had a low score at 6 months after discharge from hospital (both scores were below 5 over 7).

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## **ASSOCIATION AND RISK FACTORS FOR POST-STROKE HEMIPLEGIC SHOULDER PAIN: A PROSPECTIVE STUDY FROM A CONSECUTIVE COHORT OF CHINESE STROKE PATIENTS**

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**Objective** To describe prospectively the incidence of hemiplegic shoulder pain after stroke, in a stroke population over a 6-month period, characterize the neurological deficits, identify parameters associated with pain and investigate the outcome and prognosis of shoulder pain.

**Methods** All consecutive patients, over a 6-month period admitted to Tung Wah Eastern Hospital for stroke rehabilitation were screened. Full neurological examination assessment was undertaken, with sensation and limb power was studied and particularly patients were examined whether one could elevate the shoulder against gravity. The score of Functional Independence Measure (FIM), Barthel Index (BI), Gross Motor Function (GMF) and Geriatric Depression Score (GDS) were recorded. Other parameters like side of hemiplegia, presence of shoulder subluxation and hemispatial neglect were also noted. Follow up examinations at 3 and 6 months post-stroke were made after discharge from hospital, with pain sufferers were asked whether pain had improved or worsened. Patients who developed shoulder pain within the post-stroke 6-month period was compared with the control group i.e. patients without pain. The general parameters and the above mentioned clinical factors were compared, with the dependent variable being the development of shoulder pain. The FIM gain from discharge to 6 months post stroke were compared between two groups to investigate whether shoulder pain would adversely affect the rehabilitation progress.

**Results** A total of 94 patients formed the basis of the study. 32 patients (34%) developed shoulder pain during the six months study period. The mean onset of shoulder pain was 6.13 weeks post-stroke. There was significant statistical difference between the pain and non-pain groups in relation to arm weakness (i.e. could not abduct shoulder against gravity)(23/32cases in pain-group (72%) vs 5/62 cases in non-pain group (8%), chi-square 41.1,  $p<0.001$ ), admission Functional Independence Measure (FIM)(64.3 SD 22.5 vs 80.2 SD 20.2,  $p=0.001$ ), Barthel Index (BI)(47.5 SD 24.5 vs 65.2 SD 22.4,  $p=0.001$ ) and Gross Motor Function (GMF) score (37.4 SD 20.8 vs 53.4 SD 19.0,  $p<0.001$ ). For those patients with the admission FIM > 80 are at less risk of developing shoulder pain (chi-square:6.8,  $p=0.009$ , negative predictive value 80%). Though the number of cases is small, the presence of shoulder subluxation (7 cases vs 1 cases, chi-square=11.1,  $p=0.001$ ) and hemispatial neglect (6 cases vs 0 cases, chi-square=12.4,  $p<0.001$ ) is highly indicative for developing hemiplegic shoulder pain. 7 cases with shoulder pain (22 % of pain group) showed evidence of complex regional pain syndrome (CRPS). Other factors like age, recurrent stroke, side of hemiplegia, diabetes and GDS score were not significantly related to shoulder pain. 22 cases (69%) reported pain persisted and not much improved during the 6 months study period, while 8 cases (25%) improved or had resolution of symptoms.

**Conclusions** Hemiplegic shoulder pain after stroke occurred in 34% of patients in the study. Patients with increasing severity of impairment and disability due to stroke and inability to abduct shoulder against gravity are more at risk of developing shoulder pain after stroke. Significant proportions of patients with persistence of pain up to 6 months and the occurrence of complex regional pain syndrome underline the importance of careful repeated assessments and follow-up of stroke patients.

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## **IDIOPATHIC INFLAMMATORY MYOPATHIES – A RETROSPECTIVE COHORT STUDY WITH EMPHASES ON INTERSTITIAL LUNG DISEASE, MALIGNANCY AND PREDICTORS OF MORTALITY**

Dr Chau Shuk Yi Lucia, Department of Medicine, Queen Elizabeth Hospital (December 2004 Rheumatology Exit Assessment Exercise)

**Introduction** Idiopathic inflammatory myopathies (IIM) are characterized by proximal muscle weakness, elevation in muscle enzymes, rash and various other features. It is associated with interstitial lung disease (ILD) and malignancy. The latter mandates cancer screening but the best strategy has yet to be developed. The purposes of this study are to describe a group of local patients with this condition and to look for predictive factors for mortality, clinical features and outcomes of patients with ILD, pattern of malignancies, and to formulate the strategy of cancer screening.

**Method** Medical records with the ICD-9 CM codes for myopathies, myositis, polymyositis, dermatomyositis in the period 1<sup>st</sup> January 1997 – 30<sup>th</sup> September 2003 were retrieved. Data on demographic characteristics, presentation, clinical features, investigations, treatment, clinical course and outcome were extracted and statistical analyses performed.

**Result** Sixty-eight patients were identified (45 dermatomyositis, 20 polymyositis, 3 amyotrophic dermatomyositis). The mean age of the patients was 56.0, and female: male ratio was 1.43:1. Most patients had mild proximal myopathy. Heliotrope rash and Gottron's papule were common. The diagnosis was frequently confused with dermatological conditions, other connective tissue diseases and infection. Treatment response to corticosteroids with or without immunosuppressants was similar in the three subgroups. Thirty-one patients (45.6%) died. The median survival was 34.9 months and the 2-year survival rate was 54.4%. Survival of less than 2 years was associated with advanced age and the presence of ILD. Most of the mortality was due to infectious complications, ILD and malignancy. Twenty-five patients (36.8%) were diagnosed to have ILD. Patients with ILD responded less well to treatment and had poorer survival. The subset of rapidly progressive interstitial lung disease was invariably fatal but no predictive factor was found. Malignancy was diagnosed in 20 patients (29.4%) within two years of onset of IIM. Nasopharyngeal carcinoma and carcinoma of ovary were over-represented. A delay in diagnosis of cancer was frequently due to inadequate initial screening. The median survival for patients with malignancy was not particularly poor.

**Conclusion** Idiopathic inflammatory myopathy is an uncommon disease. It carries high mortality, especially in patients with interstitial lung disease. Nasopharyngeal carcinoma and carcinoma of ovary were particularly associated with the condition.

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## **OSTEOPOROSIS IN RHEUMATOID ARTHRITIS ROSS-SECTIONAL STUDY IN HONG KONG EAST REGION**

Dr Lee Ka Lai, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (December 2004 Rheumatology Exit Assessment Exercise)

Rheumatoid arthritis (RA) is a common inflammatory arthropathy of unknown etiology. The effects of rheumatoid arthritis on bone causing erosion, periarticular osteoporosis and generalized osteoporosis were well established. The latter may lead to increased risk of fractures that are associated with significant morbidity and mortality. A review of the epidemiology, risk factors and pathogenesis of osteoporosis in RA will be discussed. Management in terms of early identification of osteoporosis and updated treatment regimen will be highlighted.

A local study of osteoporosis in RA was conducted. One hundred and ninety-five cases were identified from a RA registry, those fulfilled the 1987 ACR diagnostic criteria and aged sixty or above were included. The overall prevalence of osteoporosis in RA female age 60 or older was 63.9% which was double than healthy general population. The rate of osteoporotic fracture was 46.7%, with incident of vertebral fracture (33.6%) higher than non-vertebral one (18.9). Risks factors of osteoporosis in RA identified in this cohort were increasing age, lower body weight, higher number of swollen joint count and prior history of fragility fracture. Knowledge and treatment in osteoporosis were found to be inadequate and education was highly suggested.

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## **THE INCIDENCE AND PATTERN OF MALIGNANCY IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN TWO REGIONAL HOSPITALS IN KOWLOON WEST CLUSTER OF HONG KONG**

Dr. Lee Kwok Fai, Tony, Department of Medicine, Yan Chai hospital (December 2004 Rheumatology Exit Assessment Exercise)

The aim of the study was to examine the incidence and pattern of malignancy in patients with rheumatoid arthritis (RA) in two regional hospitals in Kowloon West cluster of Hong Kong. Methodology: retrospective study. Results: 240 patients (196 women and 44 men) who were diagnosed of RA and were followed-up in the medical clinic/rheumatology clinic of Yan Chai and Princess Margaret hospitals from 1993 to 2003 were included. The mean age of diagnosis of RA was 49.3 years (range: 22-85 years). There were totally 1252 patient-years of follow-up and a median duration of follow-up of 63 +/- 38.8 months (range 1-120 months). There were 234 (97.5%) patients who have been treated with DMARDS. Among these 234 patients who have been treated with DMARDS, 113 patients (56.8 %) have been given immunosuppressive agents as DMARDS. There were totally 13 cases of malignancy (5.4%) identified in twelve patients (5%) during the follow-up period. One patient developed two malignancies. These malignancies included 2 colon, 3 breast, 1 stomach, 1 nasopharynx, 1 lung, 1 thyroid cancer, 1 retroperitoneal fibromyxoid sarcoma, 1 skin and 2 lymphoma (1 Hodgkin and 1 non-Hodgkin). The incidence of malignancy was 12.6 cases/1000 patient-years for male RA patients and 9.9 cases/1000 patient-years for female patients. When compared with the general population of Hong Kong, the sex and age specific incidence rate of the RA patients was higher, with the incidence rate ratios 1.76 - 5.1.

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## **A CROSS-SECTIONAL DESCRIPTIVE STUDY OF FOOT AND ANKLE PROBLEMS IN RHEUMATOID ARTHRITIS IN ONE REGIONAL HOSPITAL IN HONG KONG**

Dr. Woo Wai Shan, Sandy, Department of Medicine, Ruttonjee Hospital (December 2004 Rheumatology Exit Assessment Exercise)

Foot and ankle joint complex involvement is common in rheumatoid arthritis (RA) patients, but is often neglected by clinician compare to upper limb disease. Thirty two percent of patients (n=47) in a regional hospital had foot and ankle problem at some time since diagnosis of rheumatoid arthritis. Rheumatoid forefoot in terms of metatarsal phalangeal joint synovitis, dorsal subluxation of proximal phalanges, hallux valgus and hammertoes deformity is most common in our group of patients. Valgus heel is the most common hindfoot deformity and subtalar joint is more frequently involved than tibiotalar joint. Midfoot disease is less common clinically.

Compare to those RA patients without foot and ankle diseases, this group of patient had longer disease duration (mean 9.21+/-8.29 vs 5.59+/-3.93 years, p=0.013), and are more commonly female (80.9 vs 59.3%, p=0.044). They had more radiologically erosive disease (68.1 vs 37.0%, p=0.009) and upper limb deformities are more prevalent (76.6 vs 33.3 %, p=0.000). Total number of DMARDS used currently is more in this group of patients despite not statistically significant (2.13+/-1.03 vs 1.93+/-0.83, p=0.479). Foot and ankle involvement is associated with higher level of physical disability and poorer functional level in terms of significantly higher scores in disability scales in Health Assessment Questionnaires (mean HAQ score 0.617+/-0.577 vs 0.245 +/-0.254, p=0.003) and attainment of higher functional class (class 1.7 +/-0.78 vs 1.30+/-0.61, p=0.014) . This is consolidated by a significant Foot Function Index scoring.

Most of our studied patients had never been referred to podiatrist or prosthetic and orthotic department so education of proper foot wear and foot care is lacking. The use of orthotics and special shoes is infrequent inspite several studies suggested their use might be effective in pain reduction and pressure relief. None of our patients had received corrective surgery for severe foot and ankle deformities. Study in effectiveness of surgical correction of foot and ankle deformities compare to conservative management is lacking and inputs from orthopedic surgeons, podiatrists and orthotists are invaluable in providing best foot care in rheumatoid arthritis patients.

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