

Selected Abstracts of Articles Published Elsewhere by Authors in Kuwait

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Secular Trends in Susceptibility Patterns of Mycobacterium Tuberculosis Isolates in Kuwait, 1996-2005

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Objective: To determine the incidence and trends of drug resistance among all Mycobacterium tuberculosis strains isolated during a 10-year period in Kuwait.

Design: Drug susceptibility data for M. tuberculosis isolates recovered from all pulmonary and extra-pulmonary tuberculosis (TB) patients in Kuwait from January 1996 to December 2005 were collected and analysed. Patients were divided into Kuwaiti nationals and expatriates. Prior treatment status was not recorded.

Results: From 1996 to 2005, 5399 non-repetitive culture-positive TB cases (56% from pulmonary sites and 44% from extra-pulmonary sites) among 917 (17%) Kuwaiti nationals and 4482 (83%) expatriates were identified throughout Kuwait. Overall resistance rates were as follows: any drug 12.5%, isoniazid (INH) 9.1%; rifampicin (RMP) 1.1%, ethambutol (EMB) 2.0%, streptomycin 4.3% and multidrug resistance (MDR) 0.9%. The resistance rates over the 10-year period remained nearly same. However, significant differences were noted in resistance rates for RMP and MDR among pulmonary vs. extra-pulmonary cases and for any drug, INH and EMB among isolates from Kuwaiti vs. expatriate patients.

Conclusions: Moderate and stable single drug resistance (<10%) and low MDR rates (<1%) were found among TB cases in Kuwait. These findings highlight the importance of ongoing control measures to limit the development and spread of drug-resistant M. tuberculosis in Kuwait.

Psychological Distress and Associated Risk Factors in Bronchial Asthma Patients in Kuwait

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Context: Recent literature shows a high prevalence of psychological distress in bronchial asthma.

Aim: To find the extent of psychological distress and associated risk factors in bronchial asthma patients in Kuwait.

Design: Case-control study. **Materials and Methods:** In a study at Kuwait's allergy center, 102 patients aged 20-60 years with asthma (67%), asthma with allergic rhinitis (33%) completed a self-

administered questionnaire (WHO-Five Well-being Index). A score below 13 was considered as psychological distress; and 13 and above, as normal. An equal number of controls, matched for age, gender, nationality, were also enrolled.

Statistical Analysis: The data were analyzed using SPSS software, and proportions were tested with Chi-square or Fisher's test. Odds ratio (OR) with 95% confidence interval (CI) was calculated to quantify the risk factors. Results: A significantly large proportion (69%) of patients were found to be psychologically distressed, compared to 24% among controls (P).

Conclusions: We found a high rate of poor well-being and psychological distress in patients suffering from asthma. Young patients and those with relatively short duration of illness, as well as asthmatic females, are more vulnerable to distress and need further psychological evaluation.

Spectral Analysis of HIV Seropositivity among Migrant Workers Entering Kuwait

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Background: There is paucity of published data on human immunodeficiency virus (HIV) seroprevalence among migrant workers entering Middle-East particularly Kuwait. We took advantage of the routine screening of migrants for HIV infection, upon arrival in Kuwait from the areas with high HIV prevalence, to 1) estimate the HIV seroprevalence among migrant workers entering Kuwait and to 2) ascertain if any significant time trend or changes had occurred in HIV seroprevalence among these migrants over the study period.

Methods: The monthly aggregates of daily number of migrant workers tested and number of HIV seropositive were used to generate the monthly series of proportions of HIV seropositive (per 100,000) migrants over a period of 120 months from January 1, 1997 to December 31, 2006. We carried out spectral analysis of these time series data on monthly proportions (per 100,000) of HIV seropositive migrants.

Results: Overall HIV seroprevalence (per 100,000) among the migrants was 21 (494/2328582) (95% CI: 19 -23), ranging from 11 (95% CI: 8 - 16) in 2003 to 31 (95% CI: 24 -41) in 1998. There was no discernable pattern in the year-specific proportions of HIV seropositive migrants up to 2003; in subsequent years there was a slight but consistent increase in the proportions of HIV seropositive migrants. However, the Mann-Kendall test showed non-significant ($P = 0.741$) trend in de-seasonalized data series of proportions of HIV seropositive migrants. The spectral density had a statistically significant ($P = 0.03$) peak located at a frequency (radians) 2.4, which corresponds to a regular cycle of three-month duration in this study. Auto-correlation function did not show any significant seasonality (correlation coefficient at lag 12 = - 0.025, $P = 0.575$).

Conclusion: During the study period, overall a low HIV seroprevalence (0.021%) was recorded. Towards the end of the study, a slight but non-significant upward trend in the proportions of HIV seropositive migrants was recorded. A significant rhythmic cycle of three-month duration was observed in the proportions of HIV seropositive migrants. The underlying factors for a consistent upward trend towards the end of study period and for a significant quarterly cycle in the proportions of HIV seropositive migrants merit further investigations.

The Importance of Determining the Aggressiveness of Prostate Cancer Using Serum and Tissue Molecular Markers

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Incidental prostate cancer (PCa) has been demonstrated at autopsy in about 80% of men aged 80 years and above and also in 10%-15% of younger men aged 30-50 years in the United States. These data imply a wide variation in aggressiveness of prostate cancer, from indolent tumors to aggressive cancers that kill the patients. The use of prostate specific antigen (PSA) in screening for PCa may detect even indolent disease for which radical prostatectomy may not be necessary. Currently available criteria such as histological grade, PSA level, stage of the disease do not always predict outcome. Furthermore, only about 80% of men with metastatic PCa will respond to first line hormone manipulation and once the patient develops hormone resistant prostate cancer (HRPCa), survival remains poor. Recent genomic and proteomic studies have provided many novel molecular markers that may help to redefine prognostic parameters. This paper is a review of studies using these novel markers in order to determine whether prostate cancer patients with the following characteristics have more aggressive cancer than those without: a) high serum levels of cathepsin B, survivin, Her-2 / neu, IGFBP-2; b) low serum stefin A, IGFBP-3, c) positive immuno-staining of primary tumors for Her-2/neu, survivin and cathepsin B / stefin A ratio > 1 and d) gene expression of AMACR, HER-2/neu, high Bcl-2: Bax ratio and EZH2 in cancer cells. These markers have been chosen for review because they are among the most promising markers emerging currently.

Geroderma Osteodysplastica/Wrinkly Skin Syndrome: Report of Three Patients and Brief Review of the Literature

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Geroderma osteodysplastica and wrinkly skin syndrome are rare autosomal recessive disorders. Due to the many phenotypic similarities in these two conditions, it has been proposed that they represent the same disorder. Both conditions are well delineated in the genetic literature, but despite skin involvement being a striking feature, they are rarely reported in dermatology journals. In this report, we describe three Arab children from two consanguineous families who exhibit overlapping features of geroderma osteodysplastica and wrinkly skin syndrome. All the patients had dysmorphic facial features, wrinkled skin more marked on the hands and feet, hyperextensible joints, intrauterine growth retardation, developmental delay, congenital dislocation of hips, and osteoporosis. Our observations also support the contention that geroderma osteodysplastica and wrinkly skin syndrome have the same clinical spectrum; however, this needs to be confirmed at the molecular level.

Public Knowledge and Attitudes toward Epilepsy in Kuwait

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Purpose: The study was conducted to determine the familiarity with, knowledge of, misunderstandings, and attitudes toward epilepsy among the Kuwaiti population. **Methods:** A pretested questionnaire was used to collect data from a sample of 784 Kuwaiti individuals, selected from five governorates in Kuwait using a multistage stratified clustered sampling.

Results: Seven hundred fifty-five subjects were interviewed, and 97.6% reported their awareness about epilepsy. Of these, 51.8% knew someone who had epilepsy, 56.4% had witnessed an epileptic seizure, 45.9% believed that epilepsy is a hereditary disease, 60.4% reported that "all epileptic fits manifest symptoms of generalized tonic-clonic seizure," 88.3% indicated that putting an object into the patient's mouth to prevent tongue biting during a seizure is appropriate, and 57.1% stated that drug therapy was the only treatment available for epilepsy. Objections to shake hands with, working with, marrying, and employing epileptic patients were reported by 16.0%, 24.8%, 71.6%, and 45.2%, respectively. Childbirth by epileptic women and allowing children to play with an epileptic child were opposed by 56.3% and 27.7%, respectively. A total of 370 (50.2%) agreed that epilepsy is equivalent to psychiatric disorder. **Discussion:** The present findings have demonstrated that epilepsy is a well-known disease in Kuwait, and that negative attitudes toward epilepsy do prevail in Kuwait. The majority of the negative attitudes were significantly associated with the misunderstanding of epilepsy. Continuing effective educational interventions would be needed in order to improve the appropriate understanding of epilepsy, and to ameliorate the social discrimination and misconceptions against epileptic patients.

Primary Immunodeficiency Disorders in Kuwait: First Report from Kuwait National Primary Immunodeficiency Registry (2004-2006)

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Primary immunodeficiency disorders are heterogeneous group of illnesses that predispose patients to serious complications. Registries for these disorders have provided important epidemiological data and shown both racial and geographical variations. The clinical features of 76 patients with primary immunodeficiency disorders registered in Kuwait National Primary Immunodeficiency Registry from 2004 to 2006 were recorded. Ninety-eight percent of the patients presented in childhood. The prevalence of these disorders in children was 11.98 in 100,000 children with an incidence of 10.06 in 100,000 children. The distribution of these patients according to each primary immunodeficiency category is: combined T and B cell immunodeficiencies (21%), predominantly antibody immunodeficiency (30%), other well defined immunodeficiencies (30%), diseases of immune dysregulation (7%), congenital defects of phagocyte number, function or both (8%), and complement deficiencies (4%). The consanguinity rate within the registered patients was 77%. The patients had a wide range of clinical features affecting different body systems. Primary immunodeficiency disorders are prevalent in Kuwait and have a significant impact into the health system.

Cytokine Imbalance in Pregnancy Complications and its Modulation

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The phenomenon of pregnancy can be compromised by a number of complications, such as threatened abortion, recurrent spontaneous miscarriage, preeclampsia, and preterm delivery. Research conducted during the last decade has opened up the possibility that cellular immune effectors may underlie such pregnancy complications. Particularly interesting are the effects of pro-inflammatory and anti-inflammatory cytokines on the conceptus and thus on the success or failure of pregnancy. This review focuses on the association between cytokines and the different complications of pregnancy as well as on the possible pathways of the effector function of cytokines in pregnancy loss. This review also goes on to discuss the redirection of the cytokine profile towards one that is more conducive to pregnancy. Among the most promising agents for the modulation of the Th1/Th2 balance are progestogens such as progesterone and dydrogesterone. Recently published studies lead us to propose that a therapeutic approach worth pursuing would be to assess the individual cytokine profiles of women with pregnancy complications and then to adjust individual therapy using the most effective progestogen.

Histopathological and Ultrastructural Studies of a Mouse Lung Model of *Campylobacter Jejuni* Infection

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Campylobacter jejuni is a major cause of diarrhoea in humans. However, the pathogenesis of *C. jejuni* diarrhoea is poorly understood due to the lack of a good animal model of infection. Many animals have been tried with limited success, but a mouse lung model of infection has been found to be satisfactory previously; however, the lung pathology of this model has not been studied. For the purpose of characterizing the histopathological and ultrastructural lesions in the lung of the mouse pulmonary model of *C. jejuni* infection, *C. jejuni* strain 81-176 or sterile PBS was intranasally inoculated into BALB/c mice. The infection resulted in a mild illness only, and in an initial predominance of polymorphonuclear cells, followed by the accumulation of macrophages and later the prominence of epithelioid cells. Focal peribronchial pneumonia appeared on day 3, granuloma-like reaction on day 4 and bronchopneumonia on day 5 post-infection. These features developed until day 5 post-infection, but were less consistent afterwards when histopathology was monitored up to 9 days post-infection. Intracellular structures resembling bacteria were observed on days 3 and 5 post-infection, but not on day 7 post-infection. On days 3 and 5 post-infection, degenerative changes were also observed by transmission electron microscopy. The histological changes were not associated with acid-fast bacteria or any fungal elements. The infection was systemic as *C. jejuni* was isolated from blood and all organ homogenates (lung, spleen, liver, and small and large intestines) at 24 h post-infection. Thereafter, the organism was recovered from the intestine only, thus indicating its predilection for this location. This characterization of pathology should contribute to a better understanding of the animal model and pathogenesis of *C. jejuni* infection.

Patient Demographics and Disease Variables Correlate with Distinct Cytokine Patterns in Mitogen-Stimulated Peripheral Blood Mononuclear Cells from Rheumatoid Arthritis Patients

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There is paucity of literature on the association of peripheral blood cytokine patterns with patient demographics and disease variables in rheumatoid arthritis (RA). We test the hypothesis that there may be differences in peripheral blood levels of inflammatory cytokines in RA subjects according to various disease variables. In this case, we could identify peripheral blood cytokine markers that correlate with different disease variables. Forty-two seropositive RA patients were characterized according to the age at onset, gender, disease duration, severity, activity and ACR functional class. The production levels in mitogen-stimulated PBMCs of five pro-inflammatory cytokines (IFN γ , TNF α , TNF β , IL-8, IL-18) and three anti-inflammatory cytokines (IL-4, IL-10, IL-13) were evaluated in these patients and in healthy controls. Several new findings emerge: (1) higher levels of IL-4 correlate with female gender, milder disease, non-erosive disease, and earlier age at onset; (2) higher levels of IL-10 correlate with the requirement of ≤ 2 DMARDs; (3) higher levels of IL-18 correlate with non-erosive disease and younger age at onset; (4) higher TNF β levels correlate with older present age of patients; and (5) higher IL-8 levels correlate with established/late disease. There are several interesting differences in cytokine patterns with respect to age at onset, current age, disease severity, and the number of DMARDs the patients require.