

## Journal Scan

**U. C. Ojha**

Senior Specialist & Head – Department of Respiratory Medicine, E.S.I Hospital, New Delhi

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*Indian J Sleep Med 2012; 7.1, 29-32*

*1. J Rheumatol Suppl. 2011 Nov;88:36-42.*

### **Fatigue and quality of sleep in patients with immune-mediated inflammatory disease.**

**Graff LA, Walker JR, Russell AS, Bissonnette R, Bernstein CN.**

Department of Clinical Health Psychology, University of Manitoba, 771 Bannatyne Avenue, Winnipeg, Manitoba, Canada. lgraff@hsc.mb.ca

Fatigue, a systemic feeling of exhaustion, is a common symptom of many chronic illnesses, including immune-mediated inflammatory diseases (IMID). IMID-related fatigue is associated with disease activity and pain and has detrimental effects on patient quality of life and overall well-being. Thus, routine assessment and management of fatigue in clinical practice is important. This article provides an overview of the prevalence, correlates, and predictors of fatigue in IMID. There is also discussion of the effects of different treatments on fatigue outcomes, as well as management recommendations.

*2. J Clin Sleep Med. 2011 Oct 15;7(5 Suppl):S31-3.*

### **Association of inflammatory markers with cardiovascular risk and sleepiness.**

**Miller MA.**

University of Warwick, Warwick Medical School, Division of Metabolic and Vascular Health, Coventry, UK. Michelle.Miller@warwick.ac.uk

There is emerging evidence suggesting that disturbances in sleep and sleep disorders play a role in the morbidity of chronic conditions including obesity and hypertension as well as in the development of type-2 diabetes. This brief review examines the role of inflammation in the development of atherosclerosis. Furthermore, it outlines the utility of inflammatory markers and, in particular, adhesion molecules as biomarkers for cardiovascular risk and the factors that affect their level in the circulation. It then discusses the relationship between sleep and markers of inflammation and the role of sleep in immune function.

*3. J Occup Health. 2011 Dec 9;53(6):413-6.*

### **Noise and health—sleep disturbance in adults.**

**Kawada T.**

Department of Hygiene and Public Health, Nippon Medical School, Japan. kawada@nms.ac.jp

Factors modifying the effect of environmental noise on sleep include sex, age, susceptibility, personality and the health status, including past and present history of

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*Address for correspondence*

**Dr. U. C. Ojha**

Senior Consultant and Head of the Department Specialist & Head, Dept of Respiratory Medicine E.S.I. Hospital, Basaidarapur, New Delhi  
Email: ucojha@rediffmail.com

disease. Objective: The effects of noise on sleep and habituation of sleep to noise were summarized. Results and conclusions: 1) The effect of noise on sleep is associated with physical changes, such as changes in heart rate, blood flow volume, breathing and the immune and neurocirculatory systems. During sleep, specific changes in these indicators are noted during different sleep stages. There are individual and sex differences, and it is important to understand the effects of noise on sleep considering several related factors. 2) Habituation to noise is also an important phenomenon that must be addressed while considering the effects of noise on sleep. Habituation is dependent on the type and sound level of the noise. In occupational fields, shift work and job stress should be considered to determine the association between noise and sleep, which is important to retaining a good quality of working life.

4. *Clin Exp Med.* 2012 Sep;12(3):181-94.

### **Comparison of circadian characteristics for cytotoxic lymphocyte subsets in non-small cell lung cancer patients versus controls.**

**Mazzoccoli G, Sothorn RB, Parrella P, Muscarella LA, Fazio VM, Giuliani F, Polyakova V, Kvetnoy IM.**

Department of Internal Medicine and Chronobiology Unit, Scientific Institute and Regional General Hospital "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Foggia, Italy, g.mazzoccoli@tin.it.

Lymphocyte subsets are major cellular components of the adaptive immune response and in most cases show 24-h (circadian) variations in health. In order to determine overall levels and circadian characteristics of cytotoxic natural killer (NK) and T and B lymphocyte subsets, blood samples were collected every 4 h for 24 h from eleven male controls (C) without neoplastic disease and nine men with untreated non-small cell lung cancer (NSCLC) and analyzed for 3 hormones (melatonin, cortisol, and interleukin 2 [IL2]) and for 11 lymphocyte subpopulations classified by cell surface clusters of differentiation (CD) and antigen receptors. Circadian rhythmicity for each variable was evaluated by ANOVA and 24 h cosine fitting and groups compared. Rhythms in melatonin and cortisol (peaks near 01:30 and 08:00 h)

indicated identical synchronization to the light-dark schedule and probable persistent entrainment of rhythms for both groups in metabolism or proliferation of healthy tissues normally tightly coupled to the sleep-wake cycle. Twenty-four hours means were significantly higher in NSCLC for CD16, CD25, cortisol, and IL2 and lower for CD8, CD8bright, and  $\gamma\delta$ TCR. A significant circadian rhythm was found in C with daytime peaks for CD8, CD8dim, CD16, V $\delta$ 2TCR, and cortisol and nighttime peaks for CD3, CD4, CD20, and melatonin, and in NSCLC, with daytime peaks for CD16,  $\gamma\delta$ TCR, V $\delta$ 2TCR and cortisol, and nighttime peaks for CD4, CD25, and melatonin. Thus, NSCLC was associated with significant increases or decreases in proportions for several lymphocyte subsets that may reflect disease development, but peak times were nevertheless similar between C and NSCLC for each variable, suggesting that timed circadian administration (chronotherapy) of immunotherapy and other cancer treatments may improve efficacy due to persistent circadian entrainment of healthy tissues.

5. *Am J Physiol Gastrointest Liver Physiol.* 2011 Nov;301(5):G749-61.

### **Liver-brain inflammation axis.**

**D'Mello C, Swain MG.**

Snyder Institute of Infection, Immunity, and Inflammation, Liver Unit, Department of Medicine, University of Calgary, Alberta, Canada.

It is becoming increasingly evident that peripheral organ-centered inflammatory diseases, including chronic inflammatory liver diseases, are associated with changes in central neural transmission that result in alterations in behavior. These behavioral changes include sickness behaviors, such as fatigue, cognitive dysfunction, mood disorders, and sleep disturbances. While such behaviors have a significant impact on quality of life, the changes within the brain and the communication pathways between the liver and the brain that give rise to changes in central neural activity are not fully understood. Traditionally, neural and humoral communication pathways have been described, with the three cytokines TNF $\alpha$ , IL-1 $\alpha$ , and IL-6 receiving the most attention in mediating communication between the periphery and the brain, in the setting of peripheral inflammation.

However, more recently, we described an immune-mediated communication pathway in experimentally induced liver inflammation whereby, in response to activation of resident immune cells in the brain (i.e., the microglia), peripheral circulating monocytes transmigrate into the brain, leading to development of sickness behaviors. These signaling pathways drive changes in behavior by altering central neurotransmitter systems. Specifically, changes in serotonergic and corticotropin-releasing hormone neurotransmission have been demonstrated and implicated in liver inflammation-associated sickness behaviors. Understanding how the liver communicates with the brain in the setting of chronic inflammatory liver diseases will help delineate novel therapeutic targets that can reduce the burden of symptoms in patients with liver disease.

6. *Ind Health*. 2011;49(5):597-604.

### **Influence of shift-work on selected immune variables in nurses.**

**Copertaro A, Bracci M, Gesuita R, Carle F, Amati M, Baldassari M, Mocchegiani E, Santarelli L.**

Healthcare Workers Service, Regional Health Administration, Loreto Hospital, Ancona, Italy. alfredo.copertaro@sanita.marche.it

Shift-work, particularly night-work, interferes with the physiological circadian rhythm and has the potential to induce psycho-physiological disturbances. A nurse population was investigated to establish whether shift-work can induce changes in a number of immune variables. Lymphocyte immunophenotype and proliferative response, NK cytotoxicity, cytokines and cortisol were determined in 68 shift-working and 28 daytime nurses at baseline and at 12 months. None of the variables studied differed significantly between shift and daytime workers, either at baseline or at 12 months, except IL-1 $\alpha$  and TNF- $\alpha$ , which were significantly higher among daytime nurses at baseline, but not at follow-up. No effect of shift-work on immune variable and cortisol levels was seen at 12 months after adjustment for baseline values and job seniority. The specific work schedule as well as job type likely influenced our results, suggesting that rotational shift-work does not necessarily affect the immune system adversely. The immune changes reported

by other studies in shift-workers should not be generalized.

7. *J Occup Health*. 2011;53(5):312-9.

### **Effects of fatigue on immune function in nurses performing shift work.**

**Nagai M, Morikawa Y, Kitaoka K, Nakamura K, Sakurai M, Nishijo M, Hamazaki Y, Maruzeni S, Nakagawa H.**

Department of Epidemiology and Public Health, Kanazawa Medical University, Japan. m-long@kanazawa-med.ac.jp

**OBJECTIVES:** We investigated the effects of fatigue on NK cell function and lymphocyte subpopulations in nurses performing shift work using a longitudinal design.

**METHODS:** Fifty-seven female nurses engaged in shift work at a hospital in Japan were selected for our study cohort. The hospital used a counter clockwise rotating three-shift system. Night shifts followed day shifts after a seven-hour interval. Immune parameters measured at the beginning of the day shift through to the end of the night shift were compared between two groups stratified by their level of fatigue. Statistical differences were evaluated after adjusting for baseline immune values and other demographic features.

**RESULTS:** Subjective feelings of fatigue increased progressively from the beginning of day shifts to the end of night shifts. From the beginning of day shifts to the end of night shifts, NK cell activity and CD16(+)CD56(+) lymphocytes decreased, while CD3(+) and CD4(+) lymphocytes increased. The group with the greater increase in fatigue showed a larger decrease in NK cell activity and a larger increase in CD4(+)lymphocytes when compared with the group reporting less fatigue. These findings did not change after adjusting for demographic factors and sleep hours.

**CONCLUSION:** Our data suggest that shift work has deleterious effects on NK cell function and that the effects depend on the degree of fatigue. Proper management of shift work may lessen fatigue in workers and also ameliorate many health problems experienced by shift workers.

8. *Scand J Work Environ Health*. 2012 Jan;38(1):56-64.

### **Association of overtime work with cellular immune markers among healthy daytime white-collar employees.**

**Nakata A, Takahashi M, Irie M.**

Division of Applied Research and Technology, National Institute for Occupational Safety and Health (NIOSH), Cincinnati, OH 45226, USA. [cji5@cdc.gov](mailto:cji5@cdc.gov)

**OBJECTIVE:** Even though overtime work has been suspected to be a risk factor for ill health, little research has been done to determine the underlying immunological mechanisms. This study investigated the association between overtime work and cellular immunity among Japanese white-collar workers.

**METHODS:** A total of 306 healthy, full-time, non-shift, daytime employees (165 men and 141 women), aged 22-69 (mean 36) years, provided a blood sample for the measurement of circulating immune [natural killer (NK), B, and T] cells and NK cell cytotoxicity (NKCC) and completed a questionnaire survey including overtime/month. Blood samples were collected between 09.00-11.00 hours during working days and participants completed the questionnaire within the two weeks prior to the blood sampling. Stepwise linear regression analyses controlling for confounders were carried out to examine the relationship between overtime work and immune markers.

**RESULTS:** Overtime work was mainly related to short sleep duration, increased weight, and reduced job satisfaction, and it was more prevalent among men than women and among younger and married employees. Amount of overtime was inversely associated with NK (CD3-CD56+) cell counts ( $\alpha=-0.145$ ;  $P=0.032$ ) but was not associated with NKCC, NKCC/NK cell ratio, or T or B cells.

**CONCLUSIONS:** The NK cell is a lymphocyte that possesses killer activity against tumor and virus-infected cells and constitutes a major component of the innate immune system. A decrease of NK cell counts from overtime work suggests a dampened innate immune defense. However, the finding needs to be further validated with a well-designed study using objective overtime measures.

9. *Open Respir Med J*. 2011;5:31-43. Epub 2011 Jun 23.

### **Metabolic, endocrine, and immune consequences of sleep deprivation.**

**Aldabal L, Bahammam AS.**

Department of Pulmonary Medicine, Rashid Hospital, Dubai Health Authority, United Arab Emirates.

Over the last three to four decades, it has been observed that the average total hours of sleep have decreased to less than seven hours per person per night.

Concomitantly, global figures relating to obesity and diabetes mellitus have increased in an alarming fashion in adults and children, and it has been hypothesized that neuro-hormonal changes accompanying this behavioral sleep deprivation may lead to insulin resistance and, subsequently, to diabetes mellitus. Sleep deprivation has been associated with multiple physiological changes, including increased cortisol and ghrelin levels, decreased leptin levels and impaired glucose metabolism. Experimental studies have also shown an increase in inflammatory and pro-inflammatory markers, which are indicators of body stress, under sleep deprivation. This review elaborates further on this hypothesis, exploring the molecular basis for the link between both entities and the underlying pathophysiology that results in insulin resistance and diabetes mellitus. We review the results of experimental and epidemiological studies, specifically examining the relationship between sleep duration and the immune and endocrine systems.