urothelial cell permeability barrier and infection. A major intrinsic cellular mechanism for protection against stress is provided by the heat shock proteins (hsp) which are induced by a wide range of stimuli. This study examines the expression of hsp 27, 60 and 70 in normal human bladder and in bladder specimens obtained from patients with IC. Immunohistochemical methods were utilized to determine the localization of hsps in paraffin-embedded bladder specimens. Western blotting and reverse transcriptase polymerase chain reaction were used to confirm gene expression in normal bladder tissue samples. In normal bladder, the expression of hsp 27 was high in the transitional epithelium whereas the expression of hsp 60 was moderate. Heat shock protein 70 was present only in basally located transitional epithelial cells. The expression of hsp 27 was not altered significantly in the transitional epithelium of IC patients, though its intensity increased in smooth muscle cells and vessel walls of IC bladder specimens. In patients with IC, there was reduced expression of hsp 70 in basal transitional epithelial cells. The expression of hsp 60 was absent in the urothelial cells or smooth muscle cells from patients with IC. These results suggest that hsp 70 and 60 are down regulated in the bladder or patients with IC.

239 THE SUPPRESSIVE EFFECTS OF CORTEX MORI ON NO, TNF-α AND IL-1 PRODUCTION BY MACROPHAGE.

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Cortex Mori (*Morus loba L.*), the root bark of mulberry tree has been used as an autiphlogistic, diuretic and expectorant in herbal medicine. Recently, a few papers reported that phenolic extract of Cortex Mori had the hypotensive, hypolglycemic, antiviral and anticancer effects, and hot water extract of Cortex Mori had inhibitory effect on the degranulation and histamine release from activated mast cells. These previous studies suggest a possibility that CM has an antidotal activity against inflammation which was mediated mainly by macrophage-secreting inflammatory factors. This study was performed to evaluate the influences of Cortex Mori on carrageenan-induced edema *in vivo* and release of inflammatory mediators such as NO, TNF and IL-1 by macrophages stimulated with LPS or IFN-γ *in vitro*. Subcutaneous njections of carrageenan into the mouse paw rapidly induced local edema by increasing vascular permeability, but single intraperitoneal injection of CM extract at 30 minutes before carrageenan suppressed the development of edema. NO- and TNF production from macrophage stimulated by LPS or INF-γ were significantly suppressed, especially TNF secretion by up to 3-4 folds. LPS stimulated IL-1 production was also inhibited, but not significantly. Cell viability assay verified that the inhibition was not due to general cell toxicity. These results suggest that reduction of NO, TNF and IL-1 production may be one of the means by which Cortex Mori prevent inflammation associated diseases.

240 DECREASED RESPONSE TO ENDOTOXIN CHALLENGE BY PRE-TREATMENT WITH ERGOTAMINE.

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The objective of this experiment was to investigate whether the ergot alkaloid, ergotamine (ET), an alkaloid used to model fescue toxicosis in cattle, increases the response of cattle to endotoxin (LPS) challenge. Steers (n=16) were divided into the following treatment groups: control (C), ergotamine (ET), endotoxin (LPS), and ET+LPS. ET and ET+LPS groups received a single bolus i.v. injection of ET (40 μ g/kg/BW), whereas C and LPS steers received a single bolus injection of sterile vehicle. Thirty minutes after ET/vehicle administration, a single bolus i.v. injection of LPS (0.2 μ g/kg/BW) was given. Blood was collected at various time points for 48 h post LPS. Endotoxin alone increased the circulating levels of tumor necrosis factor alpha (TNF-α), cortisol, the acute-phase protein haptoglobin (Hp), thromboxane B_2 (TXB_2), and rectal temperature (RT), and decreased plasma glucose and insulin-like growth factor-1 (IGF-1). Importantly, haptoglobin, TNF-α , and TXB_2 increases were blunted by pretreatment with ET compared to LPS. The combination ET+LPS resulted in hyperglycemia followed by profound hypoglycemia. Ergotamine alone, increased RT, plasma urea nitrogen, packed cell volume and glucose and decreased serum prolactin (PRL). Therefore, administration of LPS to steers resulted in a typical metabolic and endocrine response. The combination of ET+LPS attenuated major effects of LPS alone. Thus, acute administration of ET appeared to be anti-inflammatory as it decreased the inflammatory response to LPS.

241 PLASMA INTERLEUKIN-10 AND NITRATE/NITRITE CONCENTRATIONS IN THE HUMAN ENDOTOXIN MODEL.

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I.v. administration of *E.coli* lipopolysaccharide (LPS, U.S. Standard Reference Endotoxin, CC-RE-Lot 2) to healthy volunteers has been used as a safe reproducible model of sepsis. To further characterize this model, studies were performed to evaluate patterns of plasma interleukin-10 (IL-10) and products of nitric oxide metabolism. **Methods**: To elicit the inflammatory response, two doses of LPS (20 EU/kg) were administered on two consecutive days to 15 men, and clinical responses (temperature/pulse) were monitored and compared to responses after a saline injection. At 4 time points after saline and 10 time points after the LPS injections, plasma IL-10 and NO_2/NO_3 concentrations were assayed. TNF-α and IL-6 were also assessed. **Results:** Expected clinical signs after each LPS injection were observed with mean temperature rise of 3.1 ±1.0 ^{0}F and pulse rise of 30 ± 9 bpm. Peaks of IL-10 concentration were found at 3.5 hr after each dose of LPS (176 ± 36 and 198 ± 30 pg/ml respectively). Baseline IL-10 after saline ranged from 32 to 60 pg/ ml. Unlike TNF-α and IL-6, the IL-10 peak after the second LPS dose was higher than after the first dose. Plasma NO_2/NO_3 profiles showed approximately 2-fold elevations after LPS with a delayed peak of 74 ± 12 μM at 12 hr after the first dose and an earlier 3 hr peak of 75 ± 13 μM after the second dose. NO_2/NO_3 concentrations after the saline injection ranged from 24 to 40μM. **Conclusions:** These data are the first to characterize the increases in plasma IL-10 and NO_2/NO_3 in the human endotoxin model of sepsis.

242 PERSISTENT PULMONARY INFLAMMATION AFTER INTRATRACHEAL INSTILLATION OF ABRASIVE BLASTING AGENTS.

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Use of silica sand in abrasive blasting is associated with pulmonary disability due to silicosis. However, the pulmonary toxicity of substitutes for silica sand in abrasive blasting remains incompletely investigated. Therefore, Sprague Dawley rats received a single intratracheal instillation (IT) dosage of 2.5 or 10 mg of the respirable fractions of abrasive blasting agents collected from the air during blasting of a steel bar. Four weeks post-IT, the right lung lobe was lavaged to isolate bronchoalveolar lavage cells and acellular bronchoalveolar lavage fluid (BALF); the left lung was processed for histopathology. Polymorphonuclear leukocyte (PMN) cell yield and alveolar macrophage (AM) chemiluminescence (CL) were significantly increased above control levels in rats instilled with coal slag (2.5 and 10 mg), silica sand (10 mg), staurolite (10 mg), and treated sand (10 mg). Rats which received garnet (10 mg) also had increased PMN numbers versus control but AM CL was not increased. Lactate dehydrogenase (LDH) was significantly elevated in the BALF of rats instilled with coal slag (2.5 and 10 mg), garnet (2.5 and 10 mg), silica sand (2.5 and 10 mg), staurolite (10.0 mg), and treated sand (10 mg), whereas BALF albumin was not increased in any of the exposed rats versus control. Hydroxyproline was significantly elevated over saline controls only in the rats receiving coal slag (10 mg). However, trichrome stained lung sections showed focal to multifocal, minimal fibrosis in 6 of 6 silica exposed rats (10 mg) and 3 of 6 coal slag exposed rats (2.5 and 10 mg). Only specular hematite (iron oxide) failed to increase some measure of pulmonary toxicity.

243 EFFECTS OF OZONE EXPOSURE ON CYTOKINE EXPRESSION IN HUMAN NASAL EPITHELIAL CELLS.

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Ozone is an oxidant pollutant gas that has been shown to induce adverse respiratory effects in humans, including airway inflammation. Although the mechanisms are poorly understood, airway epithelium is thought to play an active role in ozone-induced inflammation, since it is one of the first cellular targets to come into contact with inhaled ozone and/or its free radical

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshop, roundtable, and poster sessions of the 38th Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.

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