
2007 Health Sciences SIPs

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The Disproportionately High Number of Female ACL Tears to Male ACL Tears Exhibited During Noncontact Activity

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Anterior cruciate ligament (ACL) tears are detrimental injuries that plague countless sports participants. The cost of reconstructing and rehabilitating the ACL is approximately \$17,000 per patient. In addition, there are psychological costs as well as the potential for loss of entire seasons of sports participation, possible loss of scholarship funding, and significantly lowered academic performance. Female athlete ACL injuries occur with a 4- to 6-fold greater incidence compared with male athletes playing the same landing and cutting sports. This paper specifically focuses on why females are more at risk for ACL injuries. The greater incidence of ACL tears in females is a result of differences in: anatomy, hormones, muscle strength, and neuromuscular training. These factors tend to combine during activity and result in ACL injuries. The common mechanism of injury for a noncontact ACL injury involves deceleration of the subject with internal rotation of the femur, valgus knee positioning, and internal tibial rotation usually on a pronated, externally rotated foot. In order to prevent this injury, neuromuscular and plyometric training must be incorporated into female athletes' workouts.

Early diagnosis and treatment of mild cognitive impairment

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Due to the increasing number of Americans affected by Alzheimer's disease (AD), there is continual interest in understanding the pathology of the disease and its progression. A fairly novel diagnosis relating to AD, mild cognitive impairment (MCI), has furthered this understanding and also holds promise for a better diagnosis and treatment of the disease in the future. MCI is a transition state that exists between normal aging and Alzheimer's disease. Many studies have proven that some of the known degenerative changes that exist in AD patients are able to be seen in the beginning stages in MCI patients. There are three categories of MCI including amnesic MCI, multiple domain MCI, and single domain non-memory MCI. The amnesic form of MCI has the most information known and the most research being conducted on it. For AD and MCI early diagnosis is crucial because there is not yet a treatment method that is able to reverse the effects of the disease, only to slow the progression. Therefore, the goal is to achieve early diagnosis at which point the individual still has a fairly high cognitive level. An important component in the diagnosis of MCI is diagnostic tests. They examine multiple cognitive domains in an effort to increase specificity in the diagnosis. Biomarkers also play an integral role in the process as they can help the clinician understand more about how the disease is progressing and how to treat the individual most efficiently. Imaging is currently the most accurate tool in detecting MCI. There are a multitude of types of imaging and each one allows the clinician to get a clearer picture of the disease progression. Each of these diagnostic categories are constantly changing and developing as more scientific innovations are proven effective. Currently there are no approved treatments for MCI specifically. However, with a diagnosis of MCI it is common practice to prescribe treatments approved for AD. These include acetylcholinesterase inhibitors or N-methyl-D-aspartate (NMDA) receptor antagonists. Again, these treatments have only been shown to slow the progression and relieve some of the behavioral symptoms of AD, however, very promising research is being conducted on other treatment options that could treat AD, and eventually MCI, from a different angle.

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*An Analysis and Assessment of Nine Recent Studies on the
Alcohol-Aggression Relation that Generally Leads to Violence*

ABSTRACT

Perpetrators under the influence of alcohol commit a significant amount of violent crimes. This led to the belief that alcohol induces aggression. However, studies show that not all, but only some individuals become aggressive after alcohol consumption. These individuals are usually those with high dispositional aggressivity, hostility, impulsiveness, or other similar personality traits. Yet, others claim that aggressive behavior more likely results from the pharmacological effects of alcohol on the brain. Still, some even suggest that the expectancy of aggressive behavior after alcohol consumption causes a person to behave accordingly. The alcohol-aggression relation has been studied for many years, yet there does not seem to be a clear and definite understanding of the true cause of aggression in some individuals who consume alcohol. However, with new discoveries and approach methods, recent studies will give more insight on and a better understanding of the alcohol-aggression relation. Hopefully then a course of action can be developed to more effectively decrease frequency of violent acts associated with alcohol-induced aggression. An examination of nine recent studies shows that the alcohol-aggression relation is mediated by many psychological, behavioral, and biological factors. The individual's personality, life history, family relations and environment also interplay into how alcohol may nudge an individual towards a more aggressive tendency after alcohol consumption. Although many variables affect and regulate the alcohol-induced aggression, each should be studied independently and more carefully so that measures can be taken to lessen their roles in the alcohol-aggression relation.

The Pharmaceutical Influence, Clinical Analysis, and Managerial Treatment of Bisphosphonate-associated Osteonecrosis

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Incidence of skeletal diseases has increased concomitantly with other degenerative diseases. In response, pharmaceutical companies have begun using bisphosphonates, which were originally employed in the industrial sector over a century (Licata, 2005). However, since bisphosphonates also have a strong affinity to hydroxyapatite, they are useful in the medical field (Tech Rpt of Zometa[®], 2005). Yet, post-market research has uncovered adverse effects associated with bisphosphonate therapy. These side-effects are only associated with the nitrogen-based bisphosphonate derivatives and are part of a larger disorder called bisphosphonate-associated osteonecrosis (BON). The complications associated with BON include oral lesions, non-healing gingival wounds, and osteonecrosis of the jaw, yet these side-effects are only observed in 0.7 out of everyone 100,000 patients undergoing bisphosphonate therapy (ADASCA, 2006). Treatment options for symptoms of BON are very limited, because of its rarity and infrequency. Beside sequestrectomies, no treatments have been successful after BON fully develops. Therefore, a preventive treatment plan is the most effective measure in the fight against BON. The preventive care hinges on cooperation between both dentists and physicians. Without proper communication between clinicians, the probability of developing BON increases. To decrease the chance of developing BON, patient's cancer treatments and osteoporosis therapies should be approved by both practitioners. This protocol will reduce the amount of future oral trauma, which is one of the steps of the pathobiological development of BON.

The Necessity of Podiatric Care for People with Diabetes Mellitus

By Ian Renton

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Abstract:

Diabetes Mellitus is a disease that is caused by the inadequate production and use of insulin in the body. This can cause various health problems. Some of the major health problems caused by diabetes can occur in the feet. Infections, ulcers, and neuropathy are some of the major problems in the feet that stem from diabetes. Infection also leads to a higher than normal likelihood of the need for amputation.

For these reasons, as well as others, it is very important for people that have diabetes to go to a podiatrist regularly for podiatric care. It is so important, in fact, that it should be a necessity for diabetics to see a podiatrist, at least for routine checkups.

The Diagnosis and Management of Malignant Gliomas

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Abstract

The treatment of malignant gliomas remains one of the great challenges in clinical medicine. The most aggressive form of malignant glioma is glioblastoma multiforme (GBM), which is also the most prevalent primary central nervous system tumor. Many investigator initiated studies related to the treatment of malignant gliomas are currently underway in this country and throughout the world. One organization conducting such research is Carolina Neurosurgery and Spine Associates in Charlotte, North Carolina, the nation's largest community-based neurosurgical group. Dr. Anthony L. Asher, MD, FACS directs a research staff at CNSA that is presently involved in numerous clinical trials related to brain tumors and other neurosurgical disorders. During a ten-week internship under the guidance of Dr. Asher, I became involved in an ongoing investigator initiated study designed to assess the efficacy of a combination of therapies in the treatment of malignant gliomas. This study used temozolomide as a neoadjuvant treatment with chemo-radiotherapy and Gliadel® (BCNU) wafers. In addition to assisting with data collection related to this study, I was involved in other activities during this experience including independent research, observation during procedures, and participation in patient care conferences. What follows is a summary of malignant gliomas treatment options associated with these tumors, an overview of clinical trials and a detailed description of the protocol, Temozolomide as Neoadjuvant and Chemo-radiotherapy Following Resection and GLIADEL® Wafer Placement in Patients with Newly Diagnosed High-grade Glioma. Additional concepts that were explored during this internship, in addition to and other work-related experiences, are detailed in the SIP journal.

ER-targeted Bcl-2 Mitigates Ethanol Toxicity More Significantly Than Wildtype or Mitochondria-targeted Bcl-2

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ABSTRACT

The Bcl-2 family of proteins, which includes both pro- and anti-apoptotic members, is responsible for the regulation of apoptosis through control of caspase activity. Bcl-2 protects cells from apoptosis by inhibiting Bax and Bak (both pro-apoptotic members) from releasing cytochrome c, an important co-factor for caspase activation, from mitochondria. Previously, Bcl-2 was thought to be subcellularly localized only to the mitochondria, however recent work suggests that Bcl-2 is distributed in the endoplasmic reticulum as well. Prior *in vivo* studies have shown that overexpression of wildtype Bcl-2 is protective against ethanol toxicity, a known inducer of apoptosis; nonetheless, it is unclear whether protection is mediated through the mitochondria or the ER. Chinese hamster ovary cells (CHO695) were transiently transfected with GFP: Bcl-2 wildtype, GFP: Bcl-2 MAOB (mitochondria target) or GFP: Bcl-2 Cb5 (ER target) in order to confirm the subcellular localization of overexpressed Bcl-2 and to determine differential rescue from ethanol toxicity. GFP: Bcl-2 fusion proteins were appropriately localized, indicating successful organelle-targeting. MTT apoptosis assay was used to measure cell viability in response to ethanol in cells overexpressing wildtype and organelle-targeted Bcl-2. We found that the ER-targeted Bcl-2 significantly rescued CHO695 cells from ethanol toxicity even at normally toxic concentrations, whereas wildtype and mitochondria-targeted Bcl-2 offered more limited protection. Therefore, the present study indicates that Bcl-2's known amelioration of ethanol toxicity is likely mediated through the ER. Future work should clarify the role of the ER in ethanol toxicity.

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Fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD) are characterized by mental retardation, abnormality of the central nervous system, and facial deformation, affect millions of individuals, but its exact mechanism is unknown.

This study investigates the effect of ethanol on pathways of histiotrophic nutrition and the consequences embryonic malnutrition has on cell proliferation. The embryo is nourished via pinocytosis, and following pinocytic uptake, the exogenous matter undergoes proteolysis, and the resulting amino acids are used in protein synthesis in the embryonic and visceral yolk sac (VYS) cells. Malnutrition leads to fewer available amino acids, and less cysteine and its successor, glutathione are produced, leading to free radical formation and a more oxidizing environment, which encourages the initiation of cell death pathways.

Whole embryo culture in media containing FITC-Ab and ethanol will allow for visual morphology assessment, and histiotrophic nutrition will be quantified via fluorescent spectroscopy. Free radical generation will be determined through the evaluation of GSH/GSSG levels and measured by HPLC.

Decreases in embryonic growth and development, the interference of histiotrophic nutrition, and the dose-dependent increase in half-cell redox potential, indicating an increasingly oxidizing environment, were observed. It is therefore concluded that ethanol increases the likelihood of reactive oxygen species (ROS) formation, which produces embryotoxicity by inhibiting pathways of histiotrophic nutrition.

The Effect of Differing Degrees of Vascular Wall Injury on the Regulation of Cell Cycle and Inflammation Marker Proteins

By Shanti Virupannavar

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Abstract

The objective of this study was to investigate the effect of vascular wall injury through stent oversizing on the regulation of cell cycle proteins and inflammation markers. In particular, the amounts of cell cycle regulatory proteins, p27 and FKBP12, and inflammation marker, PCNA, were assessed in high injury, low injury and control treatment groups. Cypher© sirolimus eluting stents and Bx Velocity© (balloon expandable) bare metal stents were implanted in four *Sus scrofa* at high injury (30% balloon to artery ratio, or BAR), and in four swine at low injury (15% BAR). It was hypothesized that PCNA and FKBP12 would be upregulated and p27 would be downregulated in the high injury treatment group as compared to the low injury and control treatment groups.

Arterial tissue samples were taken from stented vessels, and from non-stented vessels, as a control, three days following stent implantation. Following determination of protein concentration in the sample, SDS-PAGE and Western Blot analysis were performed. For statistical analysis, protein values were normalized initially to actin, as a loading control, and then to untreated (non-stented) controls, to account for variation among the pigs.

No significant differences were found for p27 and PCNA, among high injury, low injury and untreated models. For FKBP12, however, we found that as vessel wall trauma became more severe due to stent oversizing, the amount of FKBP12 increased from 1.807 ± 1.473 to 9.952 ± 13.963 ($p=0.0396$). This suggests that with high vessel wall injury, the cell cycle is hyperactivated leading to increased intimal thickening.