with mitotic inhibition. Bovine pulmonary arterial endothelial cells (BECs) were treated with a reversible cell cycle inhibitor (aphidicolin, 1–2μM for 24 hours) to synchronize cells just prior to DNA synthesis. Cells were then washed to initiate cell cycling and exposed to vehicle or MCTP (5μg/ml) for 4 hours, a regimen in which MCTP causes cell cycle inhibition prior to mitosis. To label cells actively synthesizing DNA, BECs were exposed to a 30 minute pulse of bromodeoxyuridine (BrdU, 20μM) starting 23.5 hours after release from aphidicolin. At 24 hours, they were collected and processed to measure DNA content and BrdU incorporation by flow cytometry. Cells exposed to vehicle were uniformly distributed in all cell cycle phases at 24 hours and contained a population of cells incorporating BrdU which spanned S phase. MCTP exposure before and early in DNA synthesis resulted in the inhibition of cell cycle progression at G2/M. A sizable population of MCTP-treated cells incorporating BrdU had a greater than tetraploid DNA content. These data show that MCTP causes cell cycle inhibition prior to mitosis but does not block DNA synthesis. These results suggest that inhibition of proliferation may occur due to disruption of the premitotic checkpoint. *(Supported by NIEHS grant ES02581).*

232 ANTIMONY ATTENUATES MOBILIZATION OF Ca^{2+} DURING EXCITATION AND CONTRACTION IN CULTURED CARDIAC MYOCYTES.

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Industrial and pharmaceutical use of antimony compounds has been linked to altered cardiovascular function and pathology. Antimony compounds induce hypotension, bradycardia, and cardiac arrhythmias all of which can arise from aberrations in myocyte regulation of intracellular free calcium concentration ($[Ca^{2+}]_i$). In order to investigate the effects of trivalent antimony on $[Ca^{2+}]_i$, we developed an in vitro cardiac myocyte model that was exposed for 24 hr to potassium antimonyl tartrate (PAT) at 0–10 μM. Control myocytes were exposed to sodium potassium tartrate. Cardiac myocytes were obtained from neonatal rats and maintained in M199 supplemented with 10% calf serum for 2 days prior to exposure to PAT. Culture concentrations of up to 10 uM PAT were without effect on total DNA and protein content of cultures indicating that PAT exposures were not overtly toxic. Spontaneous beating rate of myocytes was significantly reduced by 5 or 10 μM PAT. $[Ca^{2+}]_i$ transients were monitored with fura-2 during excitation in myocytes paced by electric field stimulation at 0.5 Hz. Myocytes exposed to 8 μM PAT were often not paceable, therefore, the maximum exposure concentration evaluated was 6 μM. PAT significantly reduced systolic $[Ca^{2+}]_i$ in a concentration-dependent fashion, but was without effect on diastolic $[Ca^{2+}]_i$, the first derivative of the transient rise ($d[Ca^{2+}]_i/dt$), or the exponential decay of the transient. Myocytes from control cells responded to epinephrine (10^{-8} -10^{5} M) in concentration-dependent fashion with elevated systolic $[Ca^{2+}]_i$ and an increase in the rate of decay of transients. In PAT-exposed myocytes, the systolic response was blunted while the decay-rate response was maintained. PAT-exposed cells also exhibited a reduced basal $[Ca^{2+}]_i$ when depolarized by 90 mM KCl, and a reduced caffeine-releasable Ca^{2+} pool of the sarcoplasmic reticulum (SR). Both control and PAT treated cells responded to ryanodine in a comparable fashion. Results indicate that a nonlethal exposure to PAT impairs Ca^{2+} mobilization during excitation and contraction. Decreased flux of Ca^{2+} across the sarcolemma and a reduced SR-Ca^{2+} pool appear to be primarily responsible.

233 INITIAL EXPERIENCE WITH THE INTEGRATED TELEMETRY SYSTEM (ITS) FOR CARDIOVASCULAR MONITORING IN DOGS.

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Telemetry has been shown to be valuable for characterizing the acute or chronic effects of pharmaceutical agents on arterial pressure, heart rate, and ECG. We present our initial experience with the new Integrated Telemetry System (ITS) for cardiovascular monitoring in conscious, unrestrained dogs (DISS and RMISS). Cardiac output, aortic blood pressure and ECG were monitored continuously over a 24-hour period. Beagles were chronically instrumented with an active redirection transit time flow probe (ART^2) for measuring cardiac output (Triton Technology) and a solid-state pressure transducer with a biopotential lead (Konigsberg Instruments) for monitoring aortic blood pressure and ECG. Sensor cables were exteriorized to skin buttons, which can be connected to miniaturized electronics and batteries housed in pockets of the dog jackets (Konigsberg). Data was transmitted telemetrically using an infra-red transmitter/receiver system (Moore Instruments LTD) and demodulated at a Konigsberg Base Station. Acquired signal waveforms were processed beat by beat using CA Recorder® and Gateway ECG®. Principle advantages of the ITS system are it's external power source, providing for extended animal use, support of multiple power consuming sensors, and the ability to monitor blood flow by telemetry. Other advantages include: optical data transmission, elimination of cross talk between animal pens and other interferences, and simultaneous data processing on multiple animals. Disadvantages of the system are the high initial cost and the considerable investment of time and effort required to fully understand and utilize this technology in pharmaceutical development.

234 HISTOLOGIC LESIONS IN CATTLE FED TOXIC TALL FESCUE GRASS.

J W Oliver and A E Schultze. *The University of Tennessee College of Veterinary Medicine, Knoxville, TN.*

Tall fescue grass is a perennial, cool season, bunch grass used by many livestock producers as a forage crop. Most tall fescue grass is infected with the endophyte fungus, *Acremonium coenophialum*, which produces toxins that make the plant more drought tolerant and insect resistant. Vasoreactive toxins produced by the endophyte infected forage grass have been incriminated causally in a variety of bovine tall fescue related morbidity and mortality. Several ergot and pyrrolizidine alkaloids predominate in endophyte positive fescue grass and are believed responsible for the toxicity. We examined the tissues of cattle that were fed tall fescue grass, in which mean ergovaline levels ranged from 166 to 287 ppb, for 22 weeks. Necropsy revealed moderate thickening of the medial layer in arterioles of the tail, skin, and lip. Mild thickening of the vascular media was observed in several organs including the lungs, kidneys and dorsal pedal veins. Intimal lesions were minimal. Steers fed in dry lot without exposure to tall fescue grass had no such lesions. The lesions observed in steers fed toxic tall fescue grass were similar to those observed in dairy heifers with ergot toxicity from *Claviceps species*. (Supported in part by The University of Tennessee Centers of Excellence in Livestock Diseases and Human Health.)

235 LOCALIZATION AND EXPRESSION OF HEME OXYGENASE GENE IN THE ISCHEMIC REPERFUSED HEART.

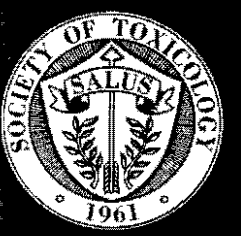
N Maulik. *Molecular Cardiology Laboratory, Department of Surgery, University of Connecticut School of Medicine, Farmington, CT.* Sponsor: V E Kagan.

Heme oxygenases (HO) which are ubiquitously present in mammalian tissues varies in their activities by its differential distribution of two isenzymes, HO-I & HO-II. HO-I has recently been identified as HSP-32 & oxygen free radicals have been found to be one of its inducers. Since reperfusion of ischemic myocardium leads to the development of oxidative stress, we hypothesized that mRNA of HO may be expressed in the ischemic reperfused hearts. To test this hypothesis we used isolated perfused rat myocardium. Hearts were made globally ischemic by terminating the coronary flow followed by 15,30,45,60 min reperfusion. In some experiments hearts were pre-perfused for 15 min with or without SOD and catalase followed by 30 min perfusion with hydroxyl generating system. At the end of each experiment tissues were processed for the Northern blot to evaluate HO gene expression, and immunohistochemistry for the localization of HO. The results of our study indicate that HO is not induced by ischemia but it is induced during reperfusion. The induction of HO is a function of the duration of reperfusion time. The induction was blocked by pre-perfusing the hearts with oxygen free radical scavenger, SOD & catalase. This induction was also blocked by SOD and catalase. This suggests that it is oxygen free radicals that is produced during the reperfusion is the stimulus for the expression of HO in the ischemic/reperfused myocardium. Immunohistochemical localization revealed that HO is primarily accumulated in the perivascular region and in the cardiomyocytes.

236 GLUTATHIONE PEROXIDASE KNOCKOUT MICE ARE SUSCEPTIBLE TO ISCHEMIA REPERFUSION INJURY.

T Yoshida, N Maulik, R M Engelman, Y- S Ho, J- L Magnenat and D K Das. *Univ. of Connecticut School of Medicine, Farmington, CT and Institute of Chemical Toxicology, Wayne State University, Detroit, MI.* Sponsor: V E Kagan.

To test our hypothesis that intracellular antioxidant enzymes constitute a cellular defense against acute stress, we studied myocardial ischemia reperfu-



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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 36th Annual Meeting of the Society of Toxicology, held at the Cincinnati Convention Center, Cincinnati, Ohio, March 9-13, 1997.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 371.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 395.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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