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Manuscripts and inquiries about publication and information about advertising should be sent to the editor: Kenneth J. Curry, University of Southern Mississippi, Post Office Box 5018, Hattiesburg, MS 39406-5018.
601-266-4930 (voice & fax)
kenneth.curry@usm.edu.

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Editorial

We are looking forward to an exciting annual meeting next February. The meeting will be held in Oxford, Mississippi, at the new convention center currently under construction. I made a site visit to the convention center last month. The building was finished, but much of the detail work inside had to be completed. The building features a large front entrance and a generous hallway to accommodate our growing poster sessions. The breakout rooms are generally larger than the smallest rooms at the Biloxi facility, but as is our usual problem, there will be just barely enough breakout rooms for all of our 13 divisions and other special programs.

Our Oxford meeting, like the one in Hattiesburg two years ago, is in a university town. The University of Mississippi will be hosting us, and several programs sponsored by and conducted on the campus are planned. This will be a wonderful opportunity for those of you that have not visited the beautiful campus of Ole Miss or visited the quaint town of Oxford.

This issue of our journal contains the first call for abstracts for the February annual meeting. As you think about what you have been doing during the past year that you would like to present, you should also consider writing your research in a formal manuscript for publication in this peer-reviewed journal. This could be a gratifying first experience with the peer review system for students. Many students gain their first public speaking experience with a formal scientifically profession audience at our annual meetings. This journal could be the place where they get their first experience with a formal peer review system for publication.—Ken Curry

ELECTION RESULTS
Congratulations to

Larry McDaniel, President-Elect
Juan Silva, Board Member

The *sixty-ninth* annual meeting of the

Mississippi Academy of Sciences

will be held on Thursday and Friday, **February 17 and 18, 2005**

Oxford, Mississippi
at the Oxford Conference Center

Dodgen Lecturer for 2005 Annual Meeting of the Mississippi Academy of Sciences
Dr. Bruce Alberts

Bruce Alberts, president of the National Academy of Sciences in Washington, D.C., is known for his work both in biochemistry and molecular biology, in particular for his extensive study of the protein complexes that allow chromosomes to be replicated. Alberts graduated from Harvard College and earned a doctorate from Harvard University in 1965. He joined the faculty of Princeton University in 1966 and after ten years moved to the Department of Biochemistry and Biophysics at the University of California, San Francisco, where he became chair. He is one of the original authors of *The Molecular Biology of the Cell*, through 4 editions the leading advanced textbook in this important field. His most recent text, *Essential Cell Biology* (2003), is intended to present this subject matter to a wider audience. Dr. Alberts has long been committed to the improvement of science education, dedicating much of his time to educational projects such as City Science, a program that seeks to improve science teaching in San Francisco elementary schools.

For the period 2000 to 2005, Dr. Alberts is the Co-chair of the InterAcademy Council, a new advisory institution in Amsterdam governed by the presidents of the science academies of 15 different nations.

2004-2005 Mississippi Supercomputing Research Expedition for High School Students

It is well documented that, in order for the United States to continue as a world leader in research and innovation, we must help our young people to develop an interest and excitement in science and mathematics. It is equally well-documented that our current science and mathematics educational programs are not adequate to meet the needs of the future technological workforce, and that significant improvements and supplements to the traditional educational system must be identified and energized. The State of Mississippi hosts significant resources in the computational sciences, and our new program, the Mississippi Supercomputing Research Expedition, provides a means to leverage these resources to the benefit of our educational system.

Within the State of Mississippi, we have extensive supercomputing resources; we hope to use these powerful computers to challenge interested and motivated students. Our outreach program is intended to establish a relationship between our three Mississippi high performance computing centers and the local high schools, to teach and foster an understanding of high performance computers, to encourage curiosity about current topics in science, and to introduce an exciting computer technology area to our next generation of scientists. Many of the program's volunteer staff will be drawn from the State's population of scientists, engineers, and researchers – providing students with immediate interaction with role models and practitioners in a variety of science disciplines.

During the 2004-05 academic year, we plan to conduct a pilot program with two high schools. Our pilot program will run during the traditional academic school year. During this time, teams of students, along with a sponsoring teacher, will identify and pursue a single computational project, using high performance computers. Throughout the school year, mentoring and help will be provided to the student teams by the organizers, sponsors, and volunteer mentors.

Ultimately, all interested students in grades 9 through 12 will be eligible to participate. Students may be enrolled in any high school curriculum in Mississippi, and we we do not anticipate any requirements for specific grade point averages or previous computer experience.

The Mississippi Center for Supercomputing Research will provide computer accounts for student teams to access remotely. As part of the kick-off of the program in the fall of 2004, the sponsoring computer centers will conduct training workshops such as using high-end computers, writing programs, analyzing data, developing technical reports, and making oral presentations.

The program will conclude in the spring of 2005 with formal judging and awards day activities. Teams are eligible for prizes in areas such as Creativity and Innovation, Best Written Report, Best Oral Presentation, and the Judges' Choice Award.

The program will be sponsored by Mississippi's three Supercomputing centers: our two DoD Major Shared Resource Centers at Stennis and at Vicksburg, and the Mississippi Center for Supercomputing Research at Oxford, using the highly successful New Mexico "Adventures in Supercomputing" program as a model. A partnership of Federal and State agencies, universities, and private industries is currently being formed, to allow us to administer the program at minimal cost to participants. Sponsors' donations will be used for kick-off, awards ceremonies and prizes for winning teams.

For further information, please go to the MSRE website, www.mcsr.olemiss.edu/expedition

The Center for Community Earthquake Preparedness Focuses on Earthquake Preparedness Issues in Mississippi's Medical Community

Terry L. Panhorst and Charles T. Swann
Center for Community Earthquake Preparedness
University of Mississippi, University, Ms 38677

The Center for Community Earthquake Preparedness (CCEP) is one of the newest research centers at The University of Mississippi. The Center's mission is to perform structural, geotechnical, and geological research projects and implement this research through data collection, design, construction, and field investigation activities for the benefit of targeted communities with significant seismic hazards. Center projects focus on quantifying local seismic hazards, dynamic site response properties, and structural response characteristics for critical facilities in the community, and developing and implementing cost-effective mitigation strategies. Dr. Chris Mullen, P.E. and Associate Professor of Civil Engineering, is the Center's director.

On August 7, 2003 the *Medical Aspects of Earthquake Response Workshop* was co-sponsored by CCEP and the Central United States Earthquake Consortium (CUSEC). This event, attended by 24 people, was held at the meeting facilities of The University of Mississippi Field Station.

The workshop consisted of two major elements, first a morning session of presentations by experts in the fields of earthquake events and medical preparedness, followed by an afternoon roundtable discussion.

The morning session speakers included:

- Dr. Eugene (Buddy) Schweig, U.S. Geological Survey (USGS), Memphis, Tennessee
- Dr. Gary Rhyne, Centers for Disease Control (CDC), Atlanta, Georgia
- Mr. John Cartwright, Mississippi Emergency Management Agency (MEMA), Jackson, Mississippi
- Mr. Jim Wilkinson, CUSEC, Memphis, Tennessee
- Dr. Robert Galli, University of Mississippi Medical Center, Jackson, Mississippi
- Dr. Stephanie Van Arsdale, Nursing Consultant, Memphis, Tennessee

Dr. Rhyne opened the morning session with a discussion of the responsibilities of the CDC in the event of a major disaster and their likely response. Dr. Schweig discussed the role of the USGS in earthquake research and presented a short discussion of the liquefaction hazard and its potential for damage in the central United States. Mr. Jim Wilkinson described the role CUSEC plays in earthquake preparedness and how the seven state Board of Directors work for a regional solution to earthquake hazards mitigation and preparedness. Mr. John Cartwright described how MEMA will respond to an earthquake disaster and how MEMA will interface with other agencies.

Dr. Robert Galli, M.D. presented a slide presentation illustrating the damage sustained by the Olive View Hospital in California as a result of two major earthquakes and the measures that were necessary to deal with these disasters. Dr. Galli also described the need of prior preparation and of the required mental attitude necessary for dealing with an internal hospital disaster as well as the surrounding earthquake disaster. Dr. Stephanie Van Arsdale described the role of nurses in the event of an earthquake disaster in a hospital.

The afternoon session began with a presentation by Mr. Jimmy Allgood, Lafayette County, Mississippi, Emergency Manager. Mr. Allgood described a set of recent weather-related disasters in Mississippi and the consequences resulting from them, pointing out the differences between local weather events and regional earthquake events. Following Mr. Allgood's presentation, a roundtable discussion was held with four panelists:

- Dr. Christopher Mullen, CCEP Director, University of Mississippi
- Mr. Carl Magnum, University of Mississippi School of Nursing
- Mr. Jim Wilkinson, Executive Director, CUSEC
- Mr. Jimmy Allgood, Emergency Manager, Lafayette County, Mississippi

The following paragraphs represent a very brief summary of some of the roundtable discussion highlights. Additional information on these discussions is available through CCEP as Open-File Report CCEP-03-02.

- Groups expected to respond to an emergency need to have plenty of coordinated pre-disaster training, because communications are typically a real nightmare during and after the event. Public utilities and the news media are critical members of the communication network and must be included in the pre-disaster training. Emergency planners must also think in terms of what happens when the plans do not work, for example when the generators fail to function.
- Smaller or more rural areas get their emergency services taxed to the maximum very quickly, and will need assistance immediately. The result of a really big emergency, such as a large earthquake, on these areas is uncertain as most resources are likely to be directed toward areas of larger population. After publicly requesting donations, expect some strange things to show up, such as bowling trophies or winter coats during the summer.
- Mass care and housing recovery are going to be important issues in a large seismic event. Estimates are that in a 7.6 magnitude event there is expected to be up to 500,000 displaced persons, and this can only be dealt with on a regional scale. Transportation is another topic where the regional approach is definitely needed. Each state has a unique set of priority routes for evacuations, but often these routes do not match from state to state. Thus seismic retrofitting on a bridge may be of little use if the adjoining state does not treat this same road as a priority evacuation route.
- Some form of reliable identification for qualified volunteers is greatly needed. A similar system is needed so that qualified researchers (psychologists, sociologists, engineers, etc.) can collect necessary data without getting in the way of rescue operations.
- Hospitals will be experiencing their own crises during and after a disaster. Only the largest hospitals can afford a good internal security force. Many small hospitals have no such force, or if they do, it consists of people from plant operations who will be *extremely* busy elsewhere if a large disaster strikes. If a hospital is damaged, personnel may have to perform all emergency functions in a parking lot, which naturally upsets many people. People are willing to (temporarily) accept a lower standard of care during emergencies, but this has to be well organized prior to the need. The most seriously injured patients do not arrive right at first after a disaster occurs. These often arrive 12 to 24 hours afterwards, because individuals were trapped in collapsed structures and had to be extracted using equipment.

Recent CCEP modeling using the HAZUS-MH code (Hazards United States loss estimation code, multi-hazard version, produced by the Federal Emergency Management Agency) has allowed estimates to be made regarding the effect a major earthquake would potentially have on the North Mississippi medical community. These HAZUS-MH results corroborate the major ideas formulated in the August workshop. In support of MEMA's construction of a hazard mitigation plan for Mississippi, CCEP modeled a "worst-case scenario," i.e., a magnitude eight earthquake with its epicenter in the southern end of the New Madrid Seismic Zone (Marked Tree, Arkansas).

The modeling predicts that of the 105 Mississippi hospitals in the HAZUS-MH data base, only 74 are likely to be functional immediately after the earthquake. Only 41% of the total beds will be usable immediately after the event. This 41% must accommodate both the patients with injuries resulting from the earthquake as well patients occupying beds prior to the earthquake (some hospitals routinely have bed occupancy rates above 80 percent). The bed space problem is compounded by model predictions that hospitals nearest the epicenter may sustain 80+ percent structural damage which may require relocation of existing patients as well the earthquake-derived patients to other hospitals. The model estimates that after 30 days 84% of the beds will be back in service. This situation will be further complicated by the expected influx of out-of-state patients from Memphis and the surrounding heavily-damaged areas.

The HAZUS-MH code can also estimate deaths and injuries, which will vary according to the time of the earthquake. The estimates of Mississippi earthquake-related deaths vary from 55 with a 2 a.m. earthquake occurrence scenario to 136 with a 2 p.m. scenario. Injuries not requiring hospitalization vary

from 1,592 in a 5 p.m. scenario to 1,196 in a 2 p.m. scenario. Patients requiring hospitalization vary from 265 at 2 a.m. to 495 in the 2 p.m. scenario. The number of patients requiring hospitalization with life-threatening injuries vary from 29 in the 2 a.m. event to 95 in the 5 p.m. scenario. Like the hospital estimates, these injuries and deaths reflect only those residing in Mississippi. Patients from adjacent states may be relocated into Mississippi, which will rapidly tax the capabilities of existing Mississippi health care facilities.

Many other parameters can be estimated by HAZUS-MH. Total economic loss, for example, is estimated for Mississippi at 3.05 billion dollars for this event. Damage and economic loss to the transportation infrastructure and utility lifeline losses are also parameters of interest to hospitals. The lack of potable water (lifeline loss) or the inability of patients and emergency transport (transport infrastructure) to reach a hospital (or patient) will certainly influence the operations of the facility. The HAZUS-MH code can evaluate these parameters as well as others and guide mitigation efforts.

The numbers generated by this modeling effort is based on default data presently contained in the HAZUS-MH code. Some of these HAZUS-MH default parameters are not completely appropriate for Mississippi. Mississippi, for example, is comprised of more than one soil type (different type soils may amplify or damp seismic vibrations) and liquefaction is not considered in the default HAZUS-MH analysis - despite liquefaction being a potentially serious threat in the "delta" region of western Mississippi. The areas mapped with damaging levels of peak ground acceleration seem unusually small when compared to historical records of the 1811-1812 New Madrid seismic events. This factor alone could significantly change the loss estimates. The CCEP hopes to work with MEMA to "fine tune" the basic HAZUS-MH data base to more accurately reflect existing conditions in Mississippi. Using the modified HAZUS-MH data base will surely change the preliminary results reported here. The important point, however, is that preparedness is of paramount importance and it must begin before the earthquake, not afterwards.

Calcium Channel Blockers Controversy: A Review of the Literature

Ann H. Peden and Hamed A. Benghuzzi
University of Mississippi Medical Center Jackson, MS 39216

Calcium channel blockers (CCBs) are a commonly used cardiovascular drug class. Sales of CCBs have been estimated to be approximately $3.2 billion annually. Clinicians have prescribed calcium channel blockers for the treatment of angina pectoris, hypertension, and cardiac rhythm disturbances since the 1980s (Katzung, 1998). In 2002, the eighth most prescribed drug in the United States was amlodipine, a calcium channel blocker, and several other types of calcium channel blockers are also found among the top 100 prescription drugs (Mosby's Drug Consult, Online). However, the use of calcium channel blockers has not been without controversy. The controversy started with a review written by Psaty et al. in 1995, which showed increased incidence of myocardial infarction in patients taking short acting calcium channel blockers to treat hypertension. In the mid-1990s the popular media sensationalized research that questioned the safety of calcium channel blockers, which resulted in some patients stopping their use of these medications and also spawned lawsuits for libel against some news organizations (Carruthers, 2002).

Calcium channel blockers are used safely by thousands of people, but have also been associated with both adverse effects and poisonings. Calcium channel blocker overdose is one of the most lethal prescription drug ingestions. This paper will examine the actions of calcium channel blockers, how they can be effective in treating certain conditions, their adverse effects in normal (correct) use, and their effects in improper (incorrect) use, such as overdose.

METHODS

Definitions and limitations. A calcium channel blocker (CCB) is a drug that prevents calcium from entering cells and has its chief effects on vascular smooth muscle and the heart. CCBs are also called calcium antagonists and slow channel blockers. Commonly prescribed calcium channel blockers fall into one of three chemical families – dihydropyridine, phenylalkylamine, and benzothiazepine (Lehne, 1998), although newer classes of CCBs are under investigation (Lacolley, Poitevin, Koen, and Levy, 1998).

This paper defines "adverse effects" and "poisoning" according to the *International Classification of Diseases, 9th edition, Clinical Modification* (ICD-9-CM). An *adverse effect* occurs when a medication is prescribed and administered properly (i.e., the right patient, drug, time, dose and route), yet the patient still experiences an untoward reaction. A *poisoning* is the result of improper use of a drug, whether the result of an accidental medication error or of an intentional overdose, as in a suicide attempt (Brown, 2003).

A limitation of this review is that it investigates a sampling of issues related to adverse effects and poisonings due to calcium channel blockers. A comprehensive, in-depth report on every known or suspected adverse effect or poisoning result is beyond the scope of this paper.

Sources. The researchers retrieved articles using various sources, including a search using the abstract and indexing service, MEDLINE, for the years 1996–April 2004. Focusing on the key term, "Calcium Channel Blockers," specifying the subject headings, "adverse effects" and "poisoning" and limiting the search to English language articles dealing with human subjects resulted in a total of 485 articles for this time period. The researchers also utilized the MDConsult database and the search phrases "calcium channel blocker AND adverse effects," which yielded 870 articles from the year 2001 to present, and "calcium channel blocker AND overdose," which found 90 articles from 2001 to present. The author selected articles for inclusion in this paper that provided information related to the usefulness of calcium channel blockers, the potential adverse effects of their use, and the mechanisms and circumstance by which poisoning or overdose of calcium channel blockers cause harm. Textbooks provided general background information.

BODY OF REVIEW

Calcium Channels. Calcium has long been known to plan a diverse and critical role as a mediator of cell function, both as a transmembrane charge carrier and as an intracellular second messenger. Although the cell possesses large stores of calcium, intracellular free calcium is maintained in the

submicromolar range. Low intracellular calcium concentration in maintained by pumps or exchange systems which act to transport calcium from the cytoplasm to the outside of the cell. Transient increases in calcium concentration provide a critical link in cellular activation processes such as excitation-contraction and excitation-secretion coupling. Transient increases in intracellular calcium occur by two mechanisms, both presumably involving calcium channels. The first is the release from internal sites such as the endoplasmic reticulum. The second involves channels in the plasma membrane that allow extracellular calcium to pass down a concentration gradient and enter the cell. The plasma membrane calcium channels can be divided into two subtypes. One type is the receptor operated channel, in which calcium influx is directly coupled to a receptor (Miller, 1987). Less is known about the receptor operated channels than about the second subtype of voltage-sensitive channels.

The voltage sensitive calcium channels have been divided into 3 subtypes (L, N, and T) based upon their conductances and sensitivities to voltage (Schwartz et al., 1988; Tsien et al., 1988). Only the L-type channel is sensitive to calcium channel blockers. The calcium channels in smooth muscles, exocrine glands, and skeletal muscle seem to be dihydropyridine sensitive.

Calcium Channel Blockers' Action on Calcium Channels. It is believed that dihydropyridines bind to only the large α_1 subunit of the calcium channel. Other conventional channel blockers bind to different sites on the L-channel. A recent report by Hering et al. in 2000 showed evidence that the phenylalkylamine class of calcium channel blockers binds to and accesses their receptors from an intracellular site.

In addition to blocking the calcium channel, the dihydropyridines may also inhibit a cyclic nucleotide phosphodiesterases. The increase of serum cyclic nucleotide, in particular adenosine, may also contribute to their greater effects on vascular relaxation than the other classes.

Actions and Uses of Calcium Channel Blockers. Calcium channel blockers have their effects chiefly on the heart (on both the cardiac muscle and the cardiac conduction system) and on vascular smooth muscle. In the heart, the entry of calcium ions into cardiac cells through the slow calcium channels has both inotropic (force of contraction) and chronotropic (rhythm) effects. When calcium ions enter a cardiac muscle cell, this triggers a release of calcium from the sarcoplasmic reticulum, which ultimately allows the actin and myosin cross-bridges needed for contraction of the muscle to form. The fewer the cross-bridges, the more diminished the strength of the contraction (negative inotropic effect) (Proano, Chiang, and Wang, 1995; McKenry and Salerno, 1998). With regard to effects on cardiac rhythm, the cells of the sinoatrial (SA) node depolarize spontaneously, generating action potentials at a faster rate than other cardiac muscle cells, thus making this node the natural pacemaker of the heart (Seeley, Stephens, and Tate, 2003). The spontaneous depolarization of the cells of the SA node is linked to the influx of calcium ions into the cells through the slow calcium channels. Therefore, blocking the slow calcium channels decreases the rate of depolarization, which decreases the rate at which the SA node generates impulses. A similar mechanism affects the atrioventricular (AV) node, slowing the rate at which impulses are conducted across the AV junction and ultimately slowing the rate of ventricular contraction (negative chronotopic effect) (McKenry and Salerno, 1998). The overall effect on the heart of blocking calcium channels, then, is to decrease the heart's force of contraction and to slow its rate of contraction.

In a similar fashion, the contractility of vascular smooth muscle is affected by calcium channel blockade. The reduced rate of influx of calcium ions into vascular smooth muscle cells interferes with the action of actin and myosin, thus inhibiting the ability to contract. This results in relaxation and dilation of arteries (McKenry and Salerno, 1998), which can be helpful in the treatment of several diseases.

As previously stated, there are three chemical families containing commonly used calcium channel blockers. There are numerous drugs in the dihydropyridine family, including nifedipine, amlodipine, felodipine, and so on. Each of the other two families contains only one widely available drug – verapamil in the phenylalkylamine family and diltiazem in the benzothiazepine family. Different types of calcium-channel blockers tend to be used to treat different types of diseases. The dihydropyridines have a greater effect on vascular smooth muscle, specifically on arterioles, and do not depress heart action significantly in normal use. Therefore, the dihydropyridines are frequently used to treat angina pectoris and hypertension, because relaxing the arteries allows blood to flow more easily. Improved blood flow would help to relieve anginal pain by improving oxygenation of heart muscle and hypertension by

decreasing peripheral circulatory resistance. Drugs used in the treatment of angina are used to treat the pain associated with ischemic heart disease. Basically, they provide symptomatic treatment and do not affect the disease course.

Verapamil and diltiazem, however, affect both the heart and vascular smooth muscle at therapeutic doses. The direct effects of these two drugs in slowing the heart are counteracted by the baroreceptor reflex, which increases heart rate and force of contraction, thus counterbalancing the effects of verapamil and diltiazem on the heart. Like the dihydropyridines, these two drugs are used to treat angina pectoris and hypertension. Additionally, they are useful in treating cardiac dysrhythmias because of their direct affects on the heart (Lehne, 1998; Katzung, 1998).

Several studies have shown the benefits of treatment of certain conditions with CCBs. Wang and Staessen (2002) reviewed the results of eleven clinic trials of various medications for hypertension. Compared to conventional therapy (diuretics and beta blockers), calcium channel blockers were more effective in preventing thickening of the intima and media of the carotid artery and also were more effective in preventing mild renal dysfunction.

Studies comparing different calcium channel blockers have been conducted and newer uses of these drugs have been investigated. One animal study compared nifedipine and amlodipine (dihydropyridines) to mibefradil, which is a new calcium antagonist from benzimidazolyl-substituted tetraline derivatives. Because edema can be an adverse effect of dihydropyridine use, the researchers were interested in learning whether there would be differences in fluid filtration with a new class of drug. Their study found that mibefradil had the same effect as the dihydropyridines in lowering blood pressure, yet with lower fluid filtration, suggesting that mibefradil is not as harmful to vascular permeability in hypertensive rats as dihydropyridines. (Lacolley et al., 1998). Dihydropyridines also have been shown to inhibit platelet aggregation and can be used to prevent the formation of thromboemboli in patients with prosthetic cardiac valves (Chou et al., 1999).

Because of the calcium channel blocker "scare" alluded to in the introduction and described more in depth later, there has been interest in developing more long-acting calcium channel blockers. An example of a study of this nature compared nisoldipine-extended release (ER), a second-generation long-acting dihydropyridine, to the popular drug amlodipine. The result of this clinical trial were that both were effective in reducing blood pressure and increasing exercise time in patients with hypertension and angina pectoris. The investigators' description of the results highlights potential adverse effects (to be discussed later): "Neither drug increased heart rate and both decreased frequency of anginal episodes. Adverse events were infrequent, and typically were vasodilator-related effects (including headache and peripheral edema) that occurred with somewhat higher incidence in the nisoldipine-ER group. Thus, nisoldipine-ER and amlodipine provided comparable antihypertensive and anti-ischemic efficacy, and both were generally well tolerated" (Pepine et al., 2003, p. 274).

Calcium channel blockers have been found to be useful in treating hypertension in patients who also have respiratory problems, such as chronic airway obstruction. CCBs have been found not to cause as many respiratory adverse effects as some other hypertension treatments. For example, coughing may occur with treatment using ACE inhibitors, which may also exacerbate asthma. Although diuretics may be the first choice in treatment of hypertension in patients with airway obstruction, CCBs are recommended if response to diuretics is poor. The effects of CCBs on smooth muscle can in some instances be beneficial to patients with airway obstruction by muting hypersensitivity of the airways (Cazzola et al., 2002).

One investigational use of CCBs is in the treatment of migraine headaches. Certain types of migraine headaches are accompanied by a transient hemiparesis (weakness on one side of the body). When this type of migraine is found in several family members, it is called familial hemiplegic migraine (FHM) and when there is no apparent family history, it is termed sporadic hemiplegic migraine (SHM). Gene mutations affecting the calcium channels were discovered to be associated with FHM and so calcium channel blockade has been investigated as a possible treatment. IV verapamil has been used to stop acute attacks of FHM and case reports have shown both oral and IV verapamil to be effective in treating SHM that was refractory to other treatments (Yu and Horowitz, 2003). Flunarizine, an investigational drug (not yet approved by the FDA for routine prescription in the U.S.), is a calcium channel blocker that has been effective in reducing the severity and preventing recurrences of migraines in early trials. (Katzung, 1998).

Several studies have evaluated the use of calcium channel blockers as a means of managing preterm labor. Because the myometrium of the uterus is comprised of smooth muscle, it stands to reason that CCBs could be effective in suppressing early uterine contractions. (The term, "tocolytic" is applied to an agent that effectively stops uterine contractions.) Researchers at Duke University and the University of North Carolina abstracted data from 75 studies of tocolytic agents and conducted a meta-analysis using 24 studies. Their review showed that calcium channel blockers could be used effectively in tocolytic treatment, prolonging the gestational period and improving birth outcomes. The reviews did uncover a pattern of slight increase in risk for minor cardiovascular harm for patients treated with calcium channel blockers in some of the studies (Berkman et al., 2003).

Pharmacokinetics. The CCBs all have similar pharmacokinetic properties. With the exception of amlodipine and the sustained release products, all are rapidly absorbed following oral administration and generally reach peak concentration in 1–2 hours. Amlodipine reaches peak concentrations in 6–9 hours. Absorption is nearly complete after administration, but the bioavailability is reduced because of first pass metabolism. The liver metabolizes the CCBs almost exclusively. All the CCBs also exhibit significant protein binding (70–90%) (Table 1).

Adverse Effects. Adverse effects that can occur at normal therapeutic dosages of CCBs include vasodilator effects such as facial flushing, dizziness, headache, and peripheral edema. However, some of the newer CCBs, such as lacidipine, appear to be less likely to cause ankle edema (Andresdottir et al., 2000). CCBs may also cause gingival (gum tissue) hyperplasia. Verapamil also tends to cause constipation, which is not as much a problem with diltiazem and the dihydropyridines. However, drugs such as nifedipine sometimes cause reflex tachycardia (increased heart rate in response to lowered blood pressure) (Lehne, 1998).

Controversy arose during the 1990s over the safety of calcium channel blockers when meta-analyses by Furberg, Psaty, and Meyer (1995) and Psaty et al. (1995) indicated that rapid acting nifedipine in moderate to high doses was associated with increased risk of mortality. Their studies suggested that people with high blood pressure who had been taking short acting CCBs had a 60% higher risk of heart attack compared to patients on beta blockers and/or diuretics. A subsequent case control study by Pahor et al. (1995) confirmed their findings in elderly hypertensives. The authors hypothesized that other calcium channel blockers may have similar mortality patterns. The attention that these articles received in the mainstream media generated a firestorm caused by headlines such as this one, which appeared in *The*

Table 1. Calcium Channel Blockers (Pharmokinetics).

Class	Agents	Bioavailability	Onset (h)	Protein Binding	Route of metabolism	Route of Excretion
Dihydropyridine	Nifedipine	immediate	0.33	92–98%	Liver	60–80% urine
	Amlodipine	52–88	6	97	Liver	Bile
	Felodipine	10–25	3–5	>99	Liver	70% urine 10% feces
	Isradipine	15–24	2	97	Liver	90% urine 10% feces
	Nicardipine	35	0.33	89–99.5	Liver	60% urine 35% feces
Phenylalkylamine	Verapamil	20–35	0.5	83–92	Liver	70% urine 16% feces
Benzothiazepine	Diltiazem	40–67	0.5–1	70–80	Liver	urine

Data compiled from Goodman and Gilman's *The Pharmacological Basis of Therapeutics* (8th ed.). Pergamon Press (1990).

Washington Post: "Drugs for Blood Pressure Linked to Heart Attacks: Researchers Fear 6 Million Are Imperiled" (Washington Post, 1995; Messerli, 1995). In Canada, the Canadian Broadcasting Corporation (CBC) aired an investigative report that implied that all calcium channel blockers were dangerous and painted an extremely negative portrait of certain physicians who believed in the safety of CCBs. Six years after the airing of the report, two physicians who had been pilloried in the Canadian media won libel lawsuits against CBC (Carruthers, 2002). A similar panic occurred in 2000 when the *New York Times* placed a story questioning the safety of CCBs on its front page. Following the 2000 scare, Norman M. Kaplan expressed the concern of many physicians about the effects of unbalanced presentations of such studies in the mass media: "Hypertension is the most common risk factor for cardiovascular diseases that are the most common cause of disability and death in…all developed societies…. As the 'silent killer,' hypertension will always be difficult to control. It is hard to keep asymptomatic people on daily treatment for life when they recognize no obvious benefit, but rather have adverse effects and often spend large amounts of money for medications…. (W)ide press and media coverage…provoked a great deal of fear and anxiety among patients taking the calcium channel blockers…. Among patients who abruptly stopped their medications without contacting their physicians (after the 2000 scare), heart attacks and strokes likely occurred, as had been noted after the 1995 scare…. Over the subsequent 5 years, multiple, properly controlled trials have attested to the efficacy and safety of long-acting calcium channel blockers" (2001, pp. 759–760).

The meta-analysis that started the controversy in 1995 was based on short-acting nifedipine, which indeed has been recognized to be unsafe in large doses. However, long-acting calcium channel blockers have been found to be generally safe and effective (Eisenberg, Brox, and Bestawros, 2004). For example, researchers with the Framingham Heart Study found that there were no differences in mortality among subjects with hypertension being treated with CCBs and those who were not using calcium channel blockers (Abascal et al., 1998). More recently, a meta-analysis by Opie and Schall in 2002 found the risk of mortality for CCBs to be about the same as for conventional treatment such as diuretics and beta blockers. Although they found a relative increase in the rate of myocardial infarction with CCBs, this was offset by a decreased incidence of stroke among CCB patients. A study of hypertensive diabetic patients also found calcium antagonists to be safe and effective, "although their use is associated with a lesser reduction of risk of heart failure as compared with other treatments for hypertension" (Grossman and Messerli, 2004, p. 44). We see from this discussion that long-acting CCBs compare favorably with other hypertension treatments with regard to mortality, even though some calcium channel blockers may not decrease the risk of adverse cardiac events as much as some other treatments.

What are the other possible risks or adverse effects of CCBs? Butler et al. (2004) studied patients who were experiencing heart failure, and found an increased incidence of declining renal function among patients receiving CCBs. Another less-commonly reported adverse effect is a photosensitive dermatologic reaction (Silvestre and Albares, 2001; Seggev and Lagstein, 1996). Case reports have also described pulmonary edema as an idiosyncratic reaction to calcium channel blockers (Lee-Chiong and Matthay, 2004). Finally, a single case of acute hypoxemia apparently due to nimodipine provides a reason for physicians to carefully monitor patient oxygenation status when using this CCB (Devlin et al., 2000).

Poisoning. Calcium channel blockers often exert their actions on the L-type of calcium channels that are located primarily in the cardiac and vascular smooth muscle cells. CCBs prevent calcium influx into the cell, resulting in a decrease in vascular tone as well as negative cardiac inotropy and chronotropy. In situations of overdose, patients may experience vasodilation and bradycardia (slow heart rate) leading to shock.

When a calcium channel blocker overdose occurs, exaggeration of the effects of the drug on the heart can create serious problems such as bradycardia, atrioventricular block, cardiac arrest, and congestive heart failure (Katzung, 1998). Other manifestations sometimes occur that are related to the nervous system, including lethargy, confusion, and coma (Zimmerman, 2003). Case reports have also described myoclonus (sudden, brief, irregular involuntary movements) as a manifestation of CCB overdose (Vadlamudi and Wijdicks, 2002). Inhibition of insulin secretion resulting in hyperglycemia has also been reported after CCB overdose (Mokhlesi et al., 2003).

Overdose by short acting agents is characterized

by rapid progression to cardiac arrest. Overdose by extended relief formulations result in delayed onset of arrhythmias, shock, sudden cardiac collapse and bowel ischemia. Other physiologic responses to CCB overdose include suppression of insulin release from the pancreas and decreased free fatty acid utilization by the myocardium. These factors produce hyperglycemia, lactic acidosis, and depressed cardiac contractility.

Reports on the frequency of CCB overdose in the U.S. from the American Association of Poison Control Centers (AAPCC) for a four-year period are shown in the table below:

Year	# Cases	# Fatalities	# Major Outcomes
1996	8555	58	225
1997	9077	44	232
1998	8666	61	277
1999	8841	61	243

Approximately 25–28% of cases each year occurred in children under the age of six years (Horowitz, 2004).

Overdose can occur easily in children and so CCBs are rarely prescribed for this population (Barcelona and Cote, 2001). Ingestion of even one tablet by a child can result in vomiting, lethargy, low blood pressure, slow heart rate, and a trip to the emergency department (Abbruzzi and Stork, 2002). Therefore, adults who use calcium channel blockers should be careful to store them safely out of the reach of children.

Of all the calcium channel blockers, verapamil is most commonly associated with serious illness and death when used inappropriately (Zimmerman, 2003). Verapamil has a pronounced negative effect on the force of cardiac contraction, whereas nifedipine has more of a vasodilatory effect. Both verapamil and diltiazem slow the pacemaker and conduction activities of the heart. (Mokhlesi et al., 2003).

Aggressive cardiovascular support is necessary for management of CCB overdose. Although calcium administration may overcome some adverse effects of CCBs, other treatment is generally needed to restore normal cardiovascular status. A number of case reports showed good results from the use of glucagon and inamrinone (Doyon and Roberts, 1993; Fant et al., 1997; Mahr, Valdes, and Lamas, 1997; Stone, May, and Carrol, 1995; Tuncok et al., 1996; Walter et al., 1993). In addition, vasopressor agents are frequently used for adequate resuscitation when hypotension is evident. Recent case reports suggest that the use of high dose insulin, with maintenance of euglycemia by dextrose infusion, may be more efficacious (Yuan et al., 1999; Salhanick and Shannon, 2003; Boyer and Shannon, 2001).

Recommended treatment for overdose of calcium channel blockers includes gastric lavage and whole-bowel irrigation for long-acting CCBs. Hypotension and shock are treated with administration of fluids and glucagon (Mokhlesi et al., 2003). Administration of intravenous calcium raises the level of extracellular calcium and the availability of free calcium. Because the T tubules of the sarcoplasmic reticulum are formed by the infolding of the cell membrane, extracellular calcium can enter the T tubules and stimulate the sarcoplasmic reticulum to release calcium, thus improving the contractility of the myocardium (Proano, Chiang, and Wang, 1995). Intravenous calcium has been used to improve the hemodynamic status of patients presenting with CCB overdose without creating further adverse effects (Lam, Tse, and Lau, 2001). However, mortality rates associated with massive CCB overdose are traditionally quite high (Durward et al., 2003).

CRITICAL DISCUSSION AND CONCLUSION

Calcium channel blockers are generally safe and effective when used correctly for treatment of hypertension, angina pectoris, and cardiac dysrhythmias. However, some have noted a pattern of increased cardiac-related mortality compared to other treatments. Others argue that the lower stroke mortality rates in CCB treatment offset the increase in deaths associated with heart problems so that the net increase in mortality compared to other treatments is zero. Achieving good patient compliance with hypertension treatment extends life expectancy and patients are more likely to be compliant if they have confidence in their treatment and if their treatment does not result in adverse effects. Further study of newer calcium channel blockers may bring about approval of medications that inspire greater confidence from patients and result in fewer unpleasant side effects, thus improving compliance and achieving a longer and better quality of life. Also, further study could provide more evidence regarding the effectiveness of calcium channel blockers for non-traditional uses, for example, in treating migraine headaches or patients with cardiac implants. Finally, caution must be exercised to avoid CCB overdose, which can have serious consequences. In summary,

while calcium channel blockers are generally safe and effective, further investigation of these drugs can result in refinements that improve their selectivity and decrease their toxicity, thus providing health benefits to many patients diagnosed with circulatory disorders.

LITERATURE CITED

Abascal, V.M., M.G. Larson, J.C. Evans, A.T. Blohm, K. Poli, and D. Levy. 1998. Calcium antagonists and mortality risk in men and women with hypertension in the Framingham Heart Study. Archives of Internal Medicine 158(17): 1882–1886.

Abbruzzi, G., and C.M. Stork. 2002. Pediatric toxicologic concerns. Emergency Medicine Clinics of North America 20(1):223–247.

Andresdottir, M.B., H.W. van Hamersvelt, M.J. van Helden, W.J.H.M. van de Bosch, I.M. Valk, and F.T. Huysmans. 2000. Ankle edema formation during treatment with the calcium channel blockers lacidipine and amlodipine: A single-centre study. Journal of Cardiovascular Pharmacology 35(Supplement 1 to Issue 3):S25–S30.

Barcelona, S.L., and C.J. Cote. 2001. Pediatric resuscitation in the operating room. Anesthesiology Clinics of North America. 19(2):339–265.

Berkman, N.D., J.M. Thorp, Jr., K.N. Lohr, T.S. Carey, K.E. Hartmann, N.I. Gavin, V. Hasselblad, and A.E. Idicula. 2003. Tocolytic treatment for the management of preterm labor: A review of the evidence. American Journal of Obstetrics and Gynecology. 188(6):1648–1659.

Boyer, E.W., and M. Shannon. 2001. Treatment of calcium-channel-blocker intoxication with insulin infusion. New England Journal of Medicine. 344(22):1721–1722.

Brown, F. 2003. ICD-9-CM Coding Handbook. Chicago, IL: Health Forum.

Butler, J., D.E. Forman, W.T. Abraham, S.S. Gottlieb, E. Loh, B.M. Massie, C.M. O'Connor, M.W. Rich, L.W. Stevenson, Y. Wang, J.B. Young, and H.M. Krumholz. 2004. Relationship between heart failure treatment and development of worsening renal function among hospitalized patients. American Heart Journal 147(2): 193–194.

Carruthers, S.G. 2002. Calcium channel blocker on trial: Hypertension specialists win landmark libel lawsuits against Canadian Broadcasting Corporation. Journal of Hypertension 20(8):1663– 1666.

Cazzola, M., P. Noschese, G. D'Amato, and M.G. Matera. 2002. The pharmacologic treatment of uncomplicated arterial hypertension in patients with airway dysfunction. Chest 121(1):230–241.

Chou, T.C., C.Y. Li, M.H. Yen, and Y.A. Ding. 1999. Antiplatelet effect of amlodipine: A possible mechanism through a nitric oxide-mediated process. Biochemical Pharmacology 58(10): 1657–1663.

Devlin, J.W., W.M. Coplin, K.R. Murry, S.S Rengachary, and R.F. Wilson. 2000. Nimodipine-induced acute hypoxemia: Case report. Neurosurgery 47(5):1243–1247.

Doyon, S., and J.R. Roberts. 1993. The use of glucagon in a case of calcium channel blocker overdose. Annals of Emergency Medicine. 22(7): 1229–1233.

Durward, A., A.M. Guerguerian, M. Lefebvre, and S.D. Shemie. 2003. Massive diltiazem overdose treated with extracorporeal membrane oxygenation. Pediatric Critical Care Medicine 4(3): 372–376.

Eisenberg, M.J., A. Brox, and A.N. Bestawros. 2004. Calcium channel blockers: An update. American Journal of Medicine 116(1):35–43.

Fant, J.S., L.P. James, R.T. Fiser, and G.L. Kearns. 1997. The use of glucagon in nifedipine poisoning complicated by clonidine ingestion. Pediatric Emergency Care. 13(6):417–419.

Ferberg, C.D., B.M. Psaty, and J.V. Meyer. 1995. Nifedipine: Dose-related increase in mortality in patients with coronary heart disease. Circulation 92:1326–1331.

Gilman, A.G., T.W. Rall, A.S. Nies, and P. Taylor (eds.). 1990. Goodman and Gilman's the pharmacological basis of therapeutics (8th ed.). New York: Pergamon Press.

Grossman, E., and F.H. Messerli. 2004. Are calcium antagonists beneficial in diabetic patients with hypertension? American Journal of Medicine 116(1):44–49.

Hering S., S. Berjukow, S. Sokolov, R. Marksteiner, R.G. Weiss, R. Kraus, and E.N. Timin. 2000. Molecular determinants of inactivation in voltage-gated Ca2+ channels. J Physiol. Oct 15;528 Pt 2:237–49. Review.

Horowitz, B.Z. 2004. Toxicity, Calcium Channel Blocker. *eMedicine* [Online]. Available: http://www.emedicine.com/emerg/topic75.htm [2004, May 25].

Kaplan, N.M. 2001. Another scare about antihypertensive therapy. American Journal of Cardiology 87(6):759–760.

Katzung, B.G. 1998. Basic and clinical pharmacology (7th ed.). Stamford, CT: Appleton and Lange.

Lacolley, P., P. Poitevin, R. Koen, and B.I. Levy. 1998. Different effects of calcium antagonists on fluid filtration of large arteries and albumin permeability in spontaneously hypertensive rats. Journal of Hypertension 16(3):349–355.

Lam, Y.M., H.F. Tse, and C.P. Lau. 2001. Continuous calcium chloride infusion for massive nifedipine overdose. Chest 119(4):1280–1282.

Lee-Chiong, Jr., T., and R.A. Matthay. 2004. Drug-induced pulmonary edema and acute respiratory distress syndrome. Clinics in Chest Medicine 25(1):95.

Lehne, R.A. 1998. Pharmacology for nursing care (3rd ed.). Philadelphia, PA: W.B. Saunders.

Mahr, N.C., A. Valdes, and G. Lamas. 1997. Use of glucagon for acute intravenous diltiazem toxicity. American Journal of Cardiology 79(11):1570– 1571.

McKenry, L.M., and E. Salerno. 1998. Pharmacology in Nursing (20th ed.). St. Louis, MO: Mosby.

Messerli, F.H. 1995. Case-control study, meta-analysis, and bouillabaisse. Annals of Internal Medicine 123(11):888–889.

Miller, R.J. 1987. Multiple calcium channels and neuronal function. Science. Jan 2;235(4784): 46–52. Review.

Mokhlesi, B., J.B. Leikin, P. Murray, and T.C. Corbridge. 2003. Adult toxicology in critical care: Part II: Specific poisonings. Chest 123(3):897–922.

Mosby's Drug Consult. (No date). Top 200 Most Prescribed Drugs 2002. [Online]. Available: http://www.mosbysdrugconsult.com/DrugConsult/Top_200 [2004, April 26].

Opie, L.H., and R. Schall. 2002. Evidence-based evaluation of calcium channel blockers for hypertension: Equality of mortality and cardiovascular risk relative to conventional therapy. Journal of the American College of Cardiology 39(2): 315–322.

Pahor, M., J.M. Guralnik, M.C. Corti, D.J. Foley, P. Carbonin, and R.J. Havlik. 1995. Long-term survival and use of antihypertensive medications in older persons. Journal of the American Geriatrics Society 43(11):1191–1197.

Psaty, B.M., S.R. Heckbert, T.D. Koepsell, D.S. Siscovick, T.E. Raghunathan, N.S. Weiss, F.R. Rosendaal, R.N. Lemaitre, N.L. Smith, P.W. Wahl, et al. 1995. The risk of myocardial infarction associated with antihypertensive drug therapies. JAMA 274(8):620–625.

Pepine, C.J., R.M. Cooper-DeHoff, R.J Weiss, M. Koren, N. Bittar, U. Thadani, M.C. Minkwitz, E.L. Michelson, and H.G. Hutchinson. 2003. Comparison of effects of nisoldipine-extended release and amlodipine in patients with systemic hypertension and chronic stable angina pectoris. American Journal of Cardiology 91(3):274–279.

Proano, L., W.K. Chiang, and R.Y. Wang. 1995. Calcium channel blocker overdose. American Journal of Emergency Medicine 13(4):444–450.

Salhanick, S.D., and M.W. Shannon. 2003. Management of calcium channel antagonist overdose. Drug Safety 26(2):65–79.

Seeley, R.R., T.D. Stephens, and P. Tate. 2003. Anatomy and physiology (6th ed.). Boston: McGraw-Hill.

Seggev, J.S., and Z. Lagstein. 1996. Photosensitivity skin reactions to calcium channel blockers. Journal of Allergy and Clinical Immunology 97 (3):852–855.

Silvestre, J.F., and M.P. Albares. 2001. Photodistributed felodipine-induced facial telangiectasia. Journal of the American Academy of Dermatology 45(2):323–324.

Stone, C.K., W.A. May, and R. Carroll. 1995. Treatment of verapamil overdose with glucagon in dogs. Annals of Emergency Medicine 25(3): 369–374.

Schwartz, A., E. McKenna, and P.L. Vaghy. 1988. Receptors for calcium antagonists. Am J Cardiol. Oct 5;62(11):3G–6G. Review.

Tsien, R.W., D. Lipscombe, D.V. Madison, K.R. Bley, and A.P. Fox. 1988. Multiple types of neuronal calcium channels and their selective modulation. Trends Neurosci. Oct;11(10): 431– 438. Review

Tuncok, Y., S. Apaydin, S. Kalkan, M. Ates, and H. Guven. 1996. The effects of amrinone and glucagon on verapamil-induced cardiovascular toxicity in anaesthetized rats. International Journal of Experimental Pathology 77(5): 207–212.

Vadlamudi, L., and E.F. Wijdicks. 2002. Multifocal myoclonus due to verapamil overdose. Neurology 58(6):984.

Walter, F.G, G. Frye, J.T. Mullen, B.R. Ekins, and P.A. Khasigian. 1993. Amelioration of nifedipine poisoning associated with glucagon therapy. Annals of Emergency Medicine 22(7):1234– 1237.

Wang, J.G., and J.A. Staessen. 2002. Conventional therapy and newer drug classes for cardiovascular protection in hypertension. Journal of the American Society of Nephrology 13 (Suppl 3): S208–215.

Washington Post (1995, March 11). Drugs for blood pressure linked to heart attack. Researchers feel 6 million are imperiled. Cited in F.H. Messerli, 1995. Case-control study, meta-analysis, and bouillabaisse. Annals of Internal Medicine 123 (11):888–889.

Yu, W., and S.H. Horowitz. 2003. Treatment of sporadic hemiplegic migraine with calcium-channel blocker verapamil. Neurology 60(1): 120–121.

Yuan, T.H., W.P Kerns, II, C.A. Tomaszewski, M.D. Ford, and J.A. Kline. 1999. Insulin-glucose as adjunctive therapy for severe calcium channel antagonist poisoning. Journal Toxicology-Clinical Toxicology 37(4):463–474.

Zimmerman, J.L. 2003. Poisonings and overdoses in the intensive care unit: General and specific management issues. Critical Care Medicine 31(12): 2794–2801.

The Effects of Supraphysiological Levels of Cortisol Alone or in Combination with Physiological Levels of Selenomethionine on Kidney Morphology

Michelle Tucci, Ham Benghuzzi, James Hughes, Russell Lyon, and Stevie Adams
University of Mississippi Medical Center Jackson, MS 39216

Chronic increased levels of glucocorticoids (GC) can result in hypertension, which may ultimately lead to impairment of renal function. Recent studies have shown GC excess can elicit serious adverse effects on the vascular system. Glucocorticoid excess causes over production of reactive oxygen species (ROS) and disrupts nitric oxide availability in the vascular endothelium, leading to vascular complications in patients with GC excess. Increases in reactive oxygen species are implicated in a number of disease processes and strategies that are directed at counter balancing the oxidative process could have a potential role in clinical medicine. The use of antioxidants has been shown to reduce ROS as well as renal tubular injury in cases of increased glucocorticoid administration *in vitro*. The objectives of this study were: (1) to establish an animal model of increased glucocorticoid levels by sustained delivery and (2) to determine if sustained delivery of selenomethionine in combination with glucocorticiods can protect kidney tubular structures. Sixteen female rats were divided into four equal groups (control and 3 experimental groups implanted with tricalcium phosphate lysine drug delivery systems (TCPL) charged with either 50mg selenomethionine (Se), 50 mg cortisol (C), or 50 mg of both C and Se). At the end of 24 days, the rats were sacrificed and both kidneys were removed for histological analysis. Quantitative analysis was performed on serum calcium levels, body weights and kidneys weights in all groups. Kidney slides were evaluated for changes in kidney morphology namely change in area and width. Sustained release of Se and Se + C resulted in a significant reduction of glomerular area ($p < 0.05$). Data obtained indicated that C, Se and Se + C administration caused a reduction in serum calcium levels compared with control. The reduction may be in part to changes in calcium-filtered load, changes in glomerular filtration rates or interference of calcium absorption from the gut. In conclusion, high levels of cortisol will modify kidney structure and possibly alter blood pressure.

Cortisol is the major adrenal glucocorticoid (GC) in humans and most mammals, and the kidney is the main site for cortisol metabolism. Rodents do not express adrenal 17 hydroxylase, which is responsible for the production of cortisol, and therefore, corticosterone is the major GC in rats. The enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) converts corticosterone to 11-dehydrocorticosterone in the distal convoluted tubules and cortical collecting ducts in rats, and cortisol to cortisone in humans. The 11β-HSD2 is thought to prevent endogenous glucocorticoids from exerting mineralcorticoid-like effects (Bailey, Unwin, and Shirley, 2001). Impairment of the enzyme has led to sodium retention, volume expansion and hypertension (Stewart et al., 1988) and is believed to contribute to the pathophysiology of hypertension. Defective renal cortisol metabolism could contribute to some of the consequences of renal disease (hypertension and sodium retention) or modify other (hyperkalaemia and decreased glomerular filtration rate (GFR)) (Mangos et al., 2003). In conditions such as Cushing's disease or ectopic adrenocorticotrophin production where GC levels in the plasma are high, the 11β-HSD2 is thought have reached saturation kinetics as opposed to impairment. Cortisol is responsible for increasing renal vascular resistance (RVR), GFR and filtered fraction (FF) while lowering renal blood flow. In addition to these hemodynamic properties, glucocorticoids have additional actions on sodium/phosphate cotransport, sulphate cotransport and amino acid transport. Patients with Cushing's syndrome (CS) have been reported to have a high incidence of kidney stone formation (nephrolithiasis) (Ross et al., 1966). Changes in renal clearance for calcium may also reflect the increase in renal stone formation in CS patients. The underlying pathogenesis in the development of nephrolithiasis in Cush-

ing's syndrome is poorly understood. However, it is thought to occur via a glucocorticoid-dependent mechanism.

Recently, in CS it has been shown that cortisol can stimulate sodium and water reabsorption and increase blood pressure. The dogma is that GC will increase blood pressure by acting on renal type 1 mineralcorticoid receptors to produce water and salt retention. However, experiments by Montrella-Waybill et al. (1991), showed that spironolactone, a competitive antagonist of mineralcorticoids, did not affect cortisol induced sodium retention or blood pressure elevation suggesting that cortisol may not necessarily innervate mineralcorticoid receptors. The data suggest that excess cortisol increases sodium retention via a different mechanism. Faggiano et al. (2002) demonstrated that CS patients have significant changes in serum and urinary concentration of several amino acids and changes in renal clearance of some specific amino acids. Their study also showed that normalization of cortisol levels restored the amino acid profile. Patients with high serum levels of cortisol experience a vast array of complications including decrease healing, osteoporosis, hyperlipidemia, kidney stones and diabetes to name a few.

Ogasawara et al. (1999) studied systemic and nonsystemic stress responses in the male rat kidney. They showed acutely stressed rats had increased serum corticosterone and renal cortical reduced glutathione (GSH) levels. They concluded from their study that increases in endogenous GC directly stimulate the defense mechanism within the kidney by increasing GSH. Glutathione peroxidase is an important enzyme in cellular antioxidant defense systems, detoxifying peroxides and hydroperoxides. As a component of the GSH cycle, it protects from reactive oxygen metabolites. Selenocysteine is present at the catalytic site of glutathione peroxidase, and selenium availability regulates glutathione peroxidase enzyme activity and ultimately GSH. The finding by Ogasawara et al. (1999) are important and suggests the possible need for nutritional supplementation of selenomethionine in chronically stressed patients such as those with CS. Nutritional supplementation may reduce the risk of many important complications associated with increased levels of cortisol. For example, supplementation with selenium, vitamin C, zinc, and fluoride might help offset the inhibitory effect of cortisol on fibroblast and osteoblast function. Antioxidant nutrients could support humoral immunity and neutrophil function. Supplementary selenium could reduce the risk of nephrocalcinosis and nephrolithiasis associated with increased cortisol as seen in CS. Therefore, the objectives of this research was to determine the effect of sustained increased levels of cortisol alone and in combination with selenium for 24 days in adult male rats. Specifically, to determine the effects of these compounds on body weight, serum calcium levels as well as kidney morphology.

MATERIALS AND METHODS

Experimental Design. A total of 16 male adult Sprague Dawley female rats from Harlan Suppliers were randomly divided into four equal groups. A control group receiving no treatment and 3 experimental groups administered sustained delivery devices were used. Animals in groups II, III, and IV were surgically implanted with a TCPL drug delivery devices containing either 50 mg selenomethionine (Se), 50 mg of cortisol (C) or 50 mg of both cortisol and selenomethionine (Se + C). During the investigation, blood samples were obtained via the tail artery bi-weekly and X-rays were performed to evaluate the resorptive properties of the drug delivery system.

Ceramic Capsule Design. Tricalcium phosphate was prepared by the method established by Bajpai and Benghuzzi (1988). The TCP material was sieved through a series of Tyler sieves to obtain sizes of TCP ranging from 1–38 μm. The TCP material was processed by first mixing 70% (w/v) calcium nitrate with 100 mL of one molar ammonium hydroxide. This solution was labeled solution 1. A second solution was prepared separately by adding 27% ammonium hydroxide and 16% ammonium hydrogen phosphate. This solution was labeled solution 2. Solution 1 was slowly added to solution 2 over a period of 20 minutes using a funnel. A precipitate formed and was harvested and centrifuged at 2000 rpm for five minutes, washed three times in water, and then resuspended in 3% ammonium sulfate. The resultant material was then dried for approximately four hours and then calcined for one hour at 1150 °C. The calcined material was placed on the Tyler sieve to obtain TCP particles ranging from 1–38 μm. The TCP powder (1 gram) was combined with 30 mg of lysine for strength and either 50 mg of C, 50 mg of Se, or 50 mg Se + 50 mg of C and pressed with a compression load of 2,500 kgs.

Surgical Procedure. Implantation of ceramic delivery systems was accomplished according to surgical guidelines approved by the University of

Mississippi Medical Center IACUC committee. To ensure sterility of capsules and equipment, they were processed in ethylene oxide overnight. The abdomens of each rat were shaved and scrubbed with povidone iodine. Animals were administered intraperitoneally (IP) a mixture of Ketamine/Xylazine for anesthesia. Using standard aseptic techniques the capsules were implanted intraperitoneally through a 1.5-cm incision. The peritoneum was then closed using a 3-0 silk suture, and the skin utilized four to six wound clips (9mm). Postoperatively animals were injected with 0.1cc of 300,000 units of Penicillin-G/Procaine (IM). Wounds were cleansed daily with povidone iodine. Wound clips were removed after ten days using a surgical staple remover.

Histopathological Evaluation. After 24 days, the animals were euthanized and the organs were removed. The kidneys, adrenals heart, liver, spleen, liver and lung samples were removed and the organs wet weights were obtained and recorded. Organs were placed in 10% buffered formalin. The organs were processed through a dehydration method and then embedded in paraffin blocks. The blocks were then sectioned. Sectioning was performed using a Leica microtome to produce 5µm sections. The sections were floated in a water bath and allowed to adhere to 3 x 3 glass slides and allowed to dry. Slides were then stained using standard hematoxylin and eosin staining procedure for further analysis.

Histomorphometric Analysis. Utilization of Image Pro Software was the primary means of obtaining morphometric analysis of glomerular changes. After proper calibration of the software, images at 40x and 10x were obtained. A total of 4 tissue sections per slide were examined for differences in area and width. Five measurements from each glomerulus were made utilizing the Image Pro Software. A total of 160 measurements were obtained and recorded per group.

Serum and X-ray Analysis. Blood samples were obtained semi-weekly and X-rays were performed to evaluate the efficiency of the drug delivery system. During the investigation, approximately 500 µL of blood was collected into a 3.5 mL autosep blood collection tube and kept on ice for 1 hour. The tubes were then centrifuged at 2,500 rpms for 30 minutes. Serum was collected and placed in labeled microcentrifuge tubes and stored at -20 °C until further analysis.

Calcium Analysis. Calcium serum levels were determined using an endpoint determination assay designed by Pointe- Scientific pre and post operatively. Five milliliter glass culture tubes were labeled "reagent blank," "standard calcium (10 mg/dL)," "control," and "sample." One milliliter of reagent was placed into each tube. Ten microliters (10 µL) of serum were added to the respective tubes. The solution was then mixed and allowed to incubate at room temperature for at least one minute. The spectrometer was blanked with the reagent at 650nm. Then the absorbencies of the samples and supernatant were read and recorded and the results were calculated (Pointe Scientific 2001). Total serum calcium levels were calculated based upon the following equation:

Absorbance of sample/Absorbance of standard x [calcium standard] = calcium (mg/dL)

Data Analysis. Statistical data was analyzed using Jandel's Sigma Stat Software and Microsoft Excel. Slidewrite Software was utilized to convert results to graphs. Descriptive statistics were used to determine the mean, standard deviation, standard error of the mean, range, median, mode and quartile data. Analysis of variance was used initially the compare the four groups to determine differences between the groups. Parametric ad hoc tests were used to determine significant changes between groups. Significance are reported at 95% confidence.

RESULTS AND DISCUSSION

Body Weights. Results from this study indicated that sustained delivery of cortisol and selenomethionine for 24 days did not provoke changes in body weight (Figure 1). Se treated animals' shows a slight insignificant increase in the final body weight analysis (Figure 1B). Control and cortisol body weights were consistent and did not change throughout the experiment. Cortisol excess in man is characterized by abdominal obesity, hypertension, glucose intolerance, and hyperlipidemia as well as contributes to an increase risk for cardiovascular disease (CVD) (Andrews and Walkers, 1999; Colao et al., 1999; Lindholm et al., 2001; Boscaro et al., 2001). In rats, GCs seem to be important in the development of obesity, which can be attenuated with GC receptor antagonists. Livingstone et al. (2000) showed stressed Zucker rats were heavier, hypercorticosteronemic and excreted more corticosterone metabolites than non-stressed or lean rats. The data from our experiment show that sustained continuous administration

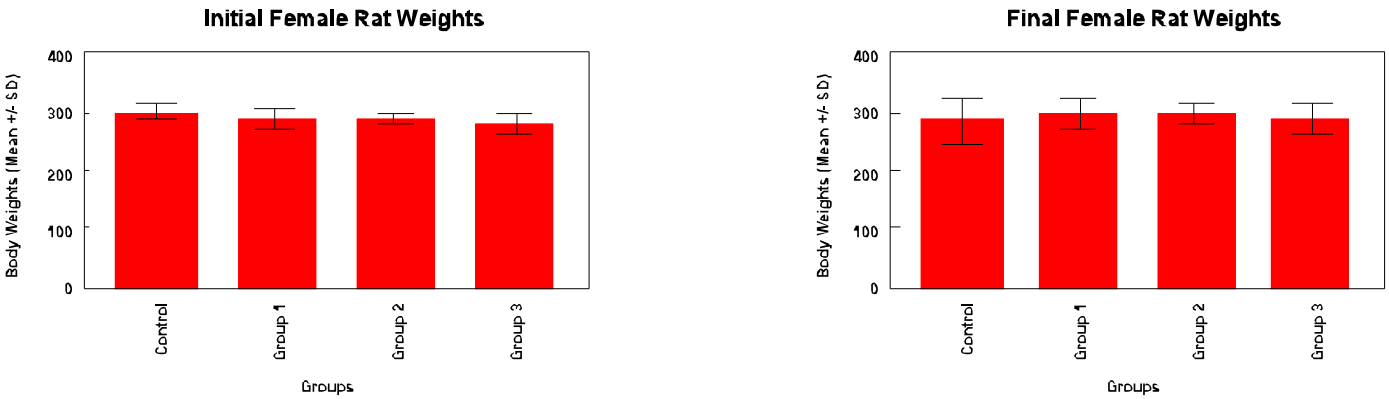

Figure 1. Data are represented as (A; left) the average body weight prior to implantation and (B; right) at the time of necropsy (n = 4).

of cortisol (2–5 ng/day) was not able to increase body weights above the control group for the duration of the experiment. However, it was noted during necropsy a must greater increase in omental fat in the both the C and C + SE treated groups when compared with control and SE treated animals. The data suggests the possibility that GCs cause redistribution of fat similar as to that which occur in CS. In CS patients there is a gain in fat in the back of the neck, supraclavicular area and face and loss of fat from the extremities. Czech and Fain (1972) proposed that the adipose tissue hypertrophies in CS and responds preferentially to the lipogenic and antilipolytic actions of the elevated concentrations of insulin evoked by GC induced hyperglycemia. They also suggest that the adipocytes in the extremities are less sensitive to insulin and more sensitive to the lipolytic effect of other hormones.

Serum Calcium. Sustained delivery of C, Se and Se + C by TCPL significantly ($p < 0.05$) reduced the serum calcium levels when compared with control animals. Se and combination of Se and C caused the greatest depression of serum calcium after 1 week post-op. Serum calcium levels four weeks post-op in selenium treated animals showed the greatest increase back toward control calcium levels (Figure 2). The mechanism of increase is probably due to the body attempting to restore calcium balance by either resorption of calcium via the bone or by altering calcium excretion. It is thought during GC excess abnormal handling of cations, sodium (Na(+)) and calcium (Ca(2+)), occur either primarily or in part by the kidney tubule (Ferrari, 2003). Our data does not show changes in serum calcium concentration in C treated animals from the control suggesting that the sustained release of C was not at a high enough concentration to saturate the enzymes in the kidney which protect against GCs having mineralcorticoid activities. In humans, the mineralcorticoid receptor (MR) in the kidney is protected from GC occupation by the enzyme 11beta-hydroxysteroid dehydrogenase type 2 (11betaHSD2), which converts cortisol to a receptor-inactive form, cortisone. This enzyme allows lower levels of aldosterone to be the agonist of the MR in spite of higher circulating levels of cortisol. Kinetic properties of 11betaHSD2 suggest saturability of this enzyme is achieved with high plasma cortisol levels which can result in overstimulation of the MR by cortisol by GC excess.

The significant decrease in serum calcium concentrations in Se and Se + C treated animals was unexpected. Little information on serum calcium levels are available in the literature to date. However, there is significant research showing a protective effect of selenium for cisplastin induced nephrotoxicity. Francescato et al. (2001) showed lipid peroxidation is one of the mechanisms by which cisplatin induces oxidative injury to kidney tissue. They demonstrated cisplastin increased renal malondialdehyde, renal glutathione, and serum creatinine and decreased creatinine clearance. Selenium treatment decreased the effect of cisplastin on serum creatinine, and renal malondialdehyde levels, but selenium did not affect the other parameters with the exception of kidney necrosis. The concentration of selenium administered was 2 mg/kg (equivalent to 500 µg in a 250 g rat) body weight by gavage which was 1000-fold higher than our daily administered dose of 5 ng/day. However, administration by gavage undergoes first pass metabolism whereas sustained delivery via TCPL avoids first pass metabolism. The bioavailability of selenium may be greater via sus-

tained release and account for the differences observed.

Kidney Histopathology. Average glomerular diameter was determined by taking the average five reference points measured from one point of the glomeruli across the glomeruli to a second point (Figure 3A). A total of eighty measurements were taken per group at 40x magnification. The results show a significant change in glomerular diameter in the Se and the Se + C treated animals when compared to control and C treated animals. The differences were significant at $p < 0.001$. Histological examination showed a reduction in the area of glomeruli as a result of an increased thickening of the inner epithelial layer. Calculation of the area showed significant reduction in the area of Se and Se + C treated animals (Figure 3B). These changes may be due to a compensation mechanism to reduce the renal clearance of calcium by decreasing the glomerular filtration rates in order to reestablish serum calcium balance. Histomorphometric analysis of the tissue revealed changes in glomerular area in Se an Se + C treated animals that may alter GFR. This data is consistent with data reported in the literature for hyperoxaluria rat model. When given selenium and vitamin E to protect against renal injury due to oxidation, urinary excretion of oxalate and calcium were normalized (Santhosh et al., 2003). Figure 4 shows representative photographs of the kidney tissue from the various treated groups showing changes in the area. A more in depth screening of the kidney tissue needs to be performed. Figure 5 shows an increased magnification of the kidney representing proximal/distal tubules, juxtaglomeular apparatus, and macula densa.

CONCLUSION

The results indicate TCPL delivery systems are capable of administering corticosteriods alone or in combination with Se for 24 days. Results also suggest that sustained release of C and Se via TCPL system resulted in a significant change in glomerular area when comparing all groups. The results also conclude both Se and Se + C administration affected calcium levels. The body's homeostasis mechanisms for maintaining calcium concentration were upregulated in Se treated animals. This compensation may be attributed to alterations in GFR.

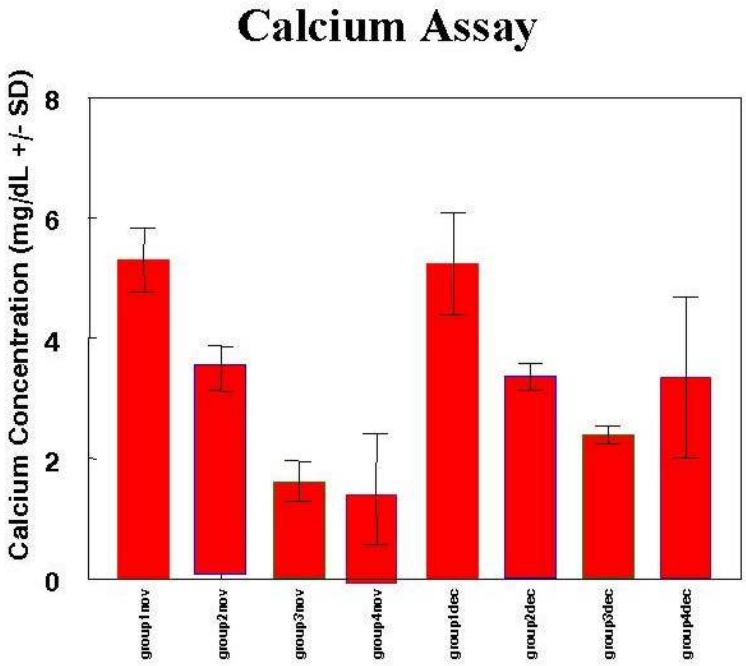

Figure 2. Data are represented for calcium levels 1 week post-op and at time of necropsy. The data are presented as mean mg/dL ± SD (n = 4).

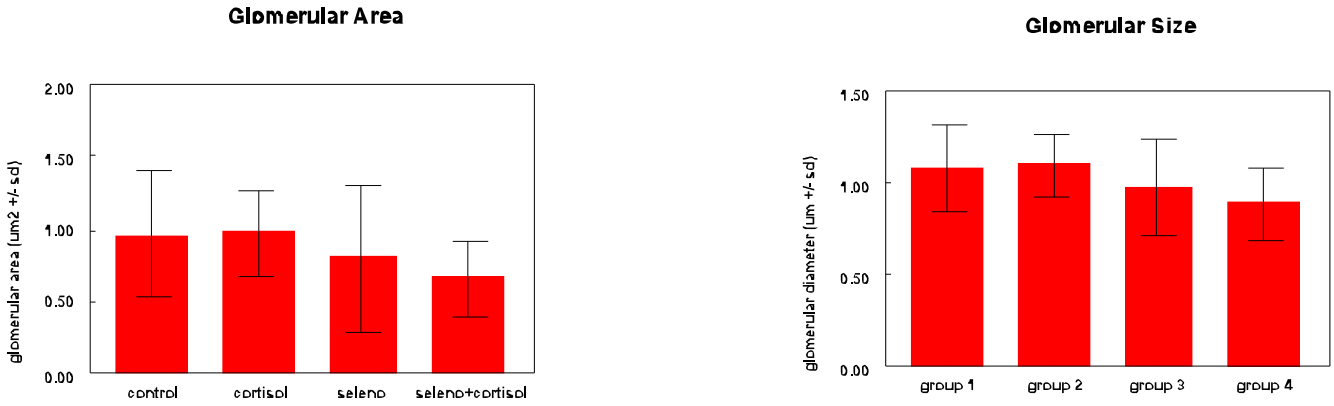

Figure 3. (A) Average glomerular diameter was determined by taking the average five reference points measured from one point of the glomeruli across the glomeruli to a second point. (B) A total of eighty measurements were taken per group at 40x magnification. Glomerular area was calculated as πr^2.

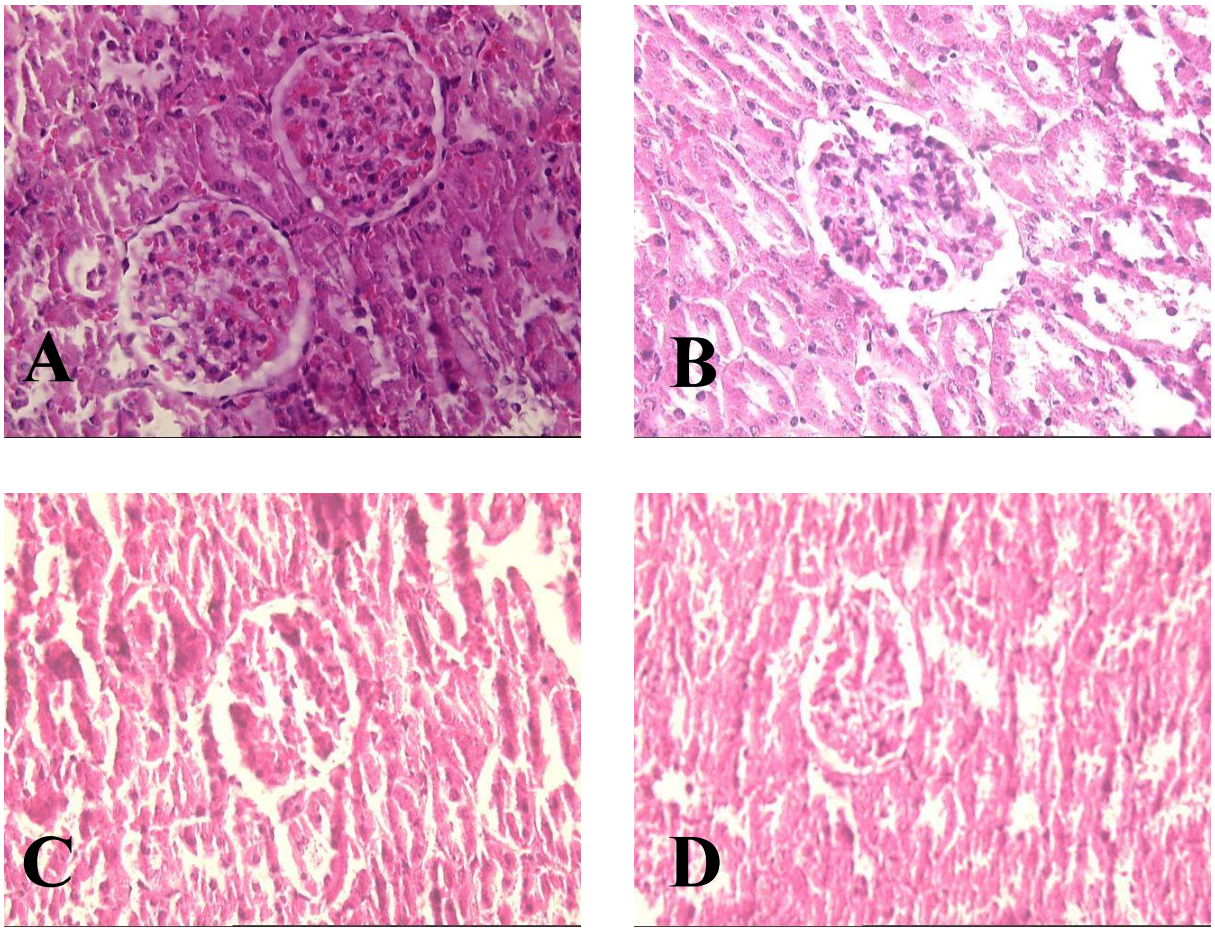

Figure 4. Representative photographs showing changes in glomerular area. (A) control, (B) cortisol, (C) Se, (D) Se + cortisol.

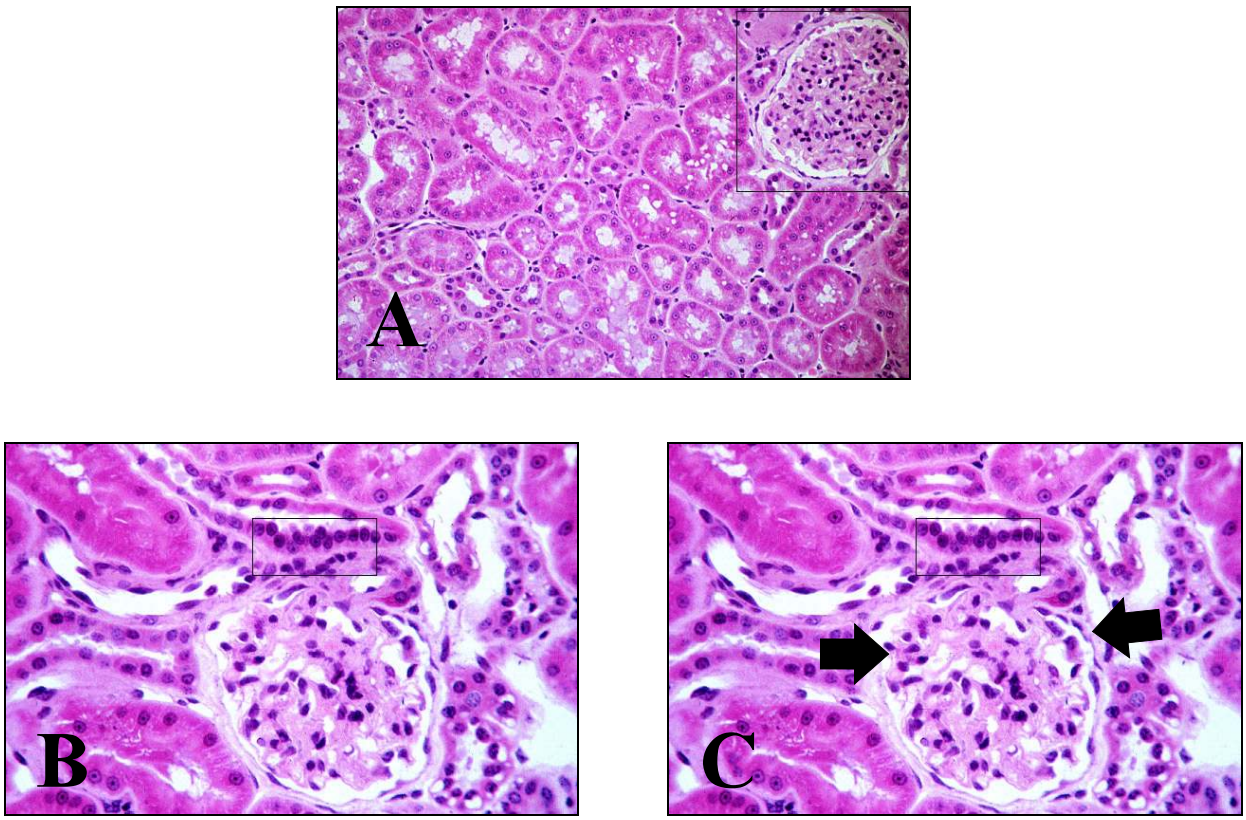

Figure 5. (A) Demonstrates proximal/distal convoluted, (B) Demonstrating macula densa tubules, (C) Arrows represent the juxtaglomerular apparatus.

LITERATURE CITED

Andrews, R.C., and B.R. Walker. 1999. Glucocorticoids and insulin resistance: old hormones, new targets. Clinical Sciences 96:513–523.

Bailey, M.A., R.J Unwin, and D.G. Shirley 2001. *In vivo* inhibition of renal 11beta-hydroxysteroid dehydrogenase in the rat stimulates collecting duct sodium reabsorption. Clin Sci (Lond). Aug;101(2):195–198.

Bajpai, P.K., and H.A. Benghuzzi. 1988. Ceramic systems for long-term delivery of chemicals and biologicals. J Biomed Mater Res. Dec;22(12):1245–1266.

Boscaro, M., L. Barzon, F. Fallo, and N. Sonino. 2001. Cushing's syndrome. Lancet 357:783–791.

Colao, A., R. Pivonello, S. Spiezia, A. Faggiano, D. Ferone, M. Filippella, P. Marzullo, G. Cerbone, M. Siciliani, and G. Lombardi. 1999. Persistence of increased cardiovascular risk in patients with Cushing's disease after five years of successful cure. J Clin Endocrinol Metab. Aug;84(8): 2664–2672.

Czech, M.P., and J.N. Fain. 1972. Antagonism of insulin action on glucose metabolism in white fat cells by dexamethasone. Endocrinology. Aug;91(2):518–522.

Faggiano, A., R. Pivonello, D. Melis, R. Alfieri, M. Filippella, G. Spagnuolo, F. Salvatore, G. Lombardi, and A. Colao. 2002. Evaluation of circulating levels and renal clearance of natural amino acids in patients with Cushing's disease. J Endocrinol Invest 25:142–151.

Fallo, F., A. Scarda, N. Sonino, A. Paoletta, M. Boscaro, C. Pagano, G. Federspil, and R. Vetor. 2004. Effect of glucocorticoids on adiponectin: a study in healthy subjects and in Cushin's syndrome. European Journal of Endocrinology 150:339–334.

Ferrari, P. 2003. Cortisol and the renal handling of electrolytes: role in gluccocorticoid induced hypertension and bone disease. Best Pract Res Clin Endocrinol Metab. Dec; 17(4):575–589.

Francescato, H.D., R.S. Costa, S.M. Rodrigues Camargo, M.A. Zanetti, M.A. Lavrador, and M.D. Bianchi. 2001. Effect of oral selenium administration on cisplstin induced nephrotoxicity in rats. Pharmacol Res 2001 Jan; 43(1):77–82.

Lindholm, J., S. Juul, J.O. Jorgensen, J. Astrup, P. Bjerre, U. Feldt-Rasmussen, C. Hagen, J. Jorgensen, M. Kosteljanetz, L. Kristensen, P. Laurberg, K. Schmidt, and J. Weeke. 2001. Incidence and late prognosis of cushing's syndrome: a population-based study. J Clin Endocrinol Metab. 2001 Jan;86(1):117–123.

Livingstone, D.E., G.C. Jones, K. Smith, P.M. Jamieson, R. Andrew, C.J. Kenyon, and B.R. Walker. 2000. Understanding the role of glucocorticoids in obesity: tissue-specific alterations of corticosterone metabolism in obese Zucker rats. Endocrinology. Feb;141(2):560–563.

Mangos, G.J., J.A. Whitworth, P.M. Williamson, and J.J. Kelly. 2003. Glucocorticoids and the kidney. Nephrology (Carlton). Dec;8(6):267–273.

Mannix, E.T., M.O. Farber, G.R. Aronoff, M.E. Brier, M.H. Weinberger, P. Palange, and F. Manfredi. 1996. Hemodynamic, renal, and hormonal responses to lower body positive pressure in human subjects. J Lab Clin Med. Dec;128(6):585–593.

Montrella-Waybill, M., J.N. Clore, A.C. Schoolwerth, and C.O. Watlington. 1991. Evidence that high dose cortisol-induced Na+ retention in man is not mediated by the mineralocorticoid receptor. J Clin Endocrinol Metab. May;72 (5):1060–1066.

Ogasawara, M., K. Nomura, N. Shibata, M. Ujihara, M. Kobayashi, and H. Demura. 1999. Surgical stress increases renal glutathione content via increased glucocorticoid, and resistance to subsequent oxidative injury in the rat: significant link between endocrine response and cell defense system under the stress. Endocr J. Feb;46(1): 99–106.

Ross, E.J., P. Marshall-Jones, and M. Friedman. 1966. Cushing's syndrome: diagnostic criteria. Q J Med 35:149–154.

Santhosh Kumar, M., and R. Selvam. 2003. Supplementation of vitamin E and selenium prevents hyperoxaluria in experimental urolithic rats. J Nutr Biochem. Jun;14(6): 306–313.

Stewart, P.M., J.E. Corrie, C.H. Shackleton, and C.R. Edwards. 1988. Syndrome of apparent mineralocorticoid excess. A defect in the cortisol-cortisone shuttle. J Clin Invest. Jul;82(1):340–9.

President's Column

Dear Friends,

This has been a marvelous year for The Mississippi Academy of Sciences. I have made it no secret that my top priority has been to work with the membership to organize an exciting meeting for all of us. The reason for my apparent success can be found in the words for an epitaph Andrew Carnegie suggested for his tombstone, "Here lies a man who knew how to enlist in his service better men than himself." When I look back on this year, all the memories of intensity and stress and responsibilities tend to fade, but the memories of the successes shared with colleagues and friends will remain forever. And, at this time I wish to thank those unsung heroes. Their diligent behind the scene efforts are what truly made this past year the success it has been. Thank all of you for allowing me to be apart of your team!

Whereas our meeting had been my top priority, there have been several other exciting developments. Namely, the level of participation by every division was phenomenal. The increase in the number of symposium and mini-symposium arranged by the various divisions this year was outstanding. In addition, the number of student participation and attendance at the various sessions was most encouraging especially since students are our future. Continued support from the faculty is still needed to help MAS thrive. I challenge my friends and colleagues to put forth the efforts to become involved and help to advance our MAS in this fast paced technological world we live in. Our goal as educators and scientist is to provide a conduit for the dissemination of ideas and a forum for their presentation and discussions. Each of us has a lot to offer, and it should be our duty and responsibility as well as an honor to serve as an **active** member in the Academy.

Our membership continues to grow, but the rate is not fast enough to meet our long term goal. We all need to be aware of young talent and encourage them to participate. With membership including on-line access to the Journal, being a member of The Mississippi Academy of Sciences is one of the best bargains in science!

I have appreciated the opportunity to serve you as President of this dynamic academy. My term is ended, but not my loyalty!! See you in Oxford!—Hamed Benghuzzi

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Executive Officer's Column

Perhaps the news item of most interest to MAS members is that the location of the February annual meeting has been selected. The annual meeting will be held February 17–18, 2005, at the Oxford Conference Center, in Oxford, Mississippi. The Conference Center is in the final stages of completion and the MAS meeting should be one of the first to enjoy the new facilities. The Conference Center is easy to find – its located on the northern end of the city, just east of Highway 7 (you can see it from the highway), exit onto Sisk Avenue. The University of Mississippi deserves a special thanks due to the monetary contribution made through the Office of Research and Sponsored Programs. This contribution makes the Oxford meeting possible and it is much appreciated.

The agenda for the 2005 meeting is also beginning to take form. A number of people have mentioned ideas for special symposia. The subject matter varies widely from taxonomy to aspects of the Civil War. The Gulf of Mexico Gas Hydrates Research Consortium has also tentatively agreed to add a day to their winter meeting and present a special symposium at our annual meeting. The Consortium is doing world-class research and a significant amount of the research is being done in Mississippi. If you have ideas you want to put into action at the Oxford meeting, just let us know so we can work you into the agenda.

Of special note, Dr. John Boyle, Mississippi State University, has arranged for Dr. Bruce Alberts, President of the National Academies of Science to make a special presentation to commemorate the MAS on its 75th anniversary. Having Dr. Alberts take time from his busy schedule to address the MAS is certainly an honor. To my knowledge, this is the first time a president of the National Academies of Science has attended an annual MAS meeting. I encourage everyone to make a special effort to hear Dr. Alberts remarks.

The Executive Officer has also been working with Ms. Aimee Lee, Youth Activities Director, to work out the logistics of bringing the Mississippi Junior Academy of Sciences (MJAS) to Oxford. We are using the Biloxi meeting as a model and plan to hold the MJAS meeting just prior to the MAS meeting. This makes it easy for the teachers and students attending the MJAS to also attend the MAS meeting.

On May 10, 2004, the MAS held its usual annual meeting recap. This informal gathering is designed to critique the annual meeting and to determine agenda items to include in the midsummer Board meeting. The comments from the Biloxi meeting were mostly positive. Everyone seemed to enjoy the variety of special events and speakers. The attendance at Biloxi was also the highest in recent years. On the other side of the coin, the MAS needs to improve our internal communications, and improve our coordination at the annual meetings. As our meetings become larger and membership expands, we also need to improve cost control procedures. Three items that will be placed before the Board at the midsummer meeting. These items include an external audit of MAS financial affairs, updating standard operating procedure, and to explore means of formalizing the relationship between the MJAS and the MAS. Details regarding the Board meeting time and place will sent from the MAS office in the near future.

Finally, congratulations to Dr. Sarah McGuire, of Millsaps College. Sarah will be replacing Dr. Hamed Benghuzzi this summer as MAS President. We all look forward to working with Sarah in the coming year.—Charles Swann

Divisional Report

Zoology and Entomology

The Zoology and Entomology Division met on the afternoon of Thursday, Feb 19, 200t. During this sixty-eighth annual meeting of MAS, there was a symposium on "Sickle cell anemia and its prevalence among blacks in some southern states of the USA" which contained four presentations. In addition, four oral presentations and one poster were made. In the report of 2002, it was stated that efforts would be made to involve more graduate and undergraduate students. This objective was achieved as was the case last year. About four oral papers were presented by graduate students, two by undergraduates and a poster, by an undergraduate student. About 25 individuals attended the presentations. The symposium was captivating and generated a lot of questions, discussions and comments. A need to continue this kind of symposium was implicitly expressed. The papers presented were also interesting, informative and excited attention, comments and questions. We anticipate continued interest and participation of Division members and invite new members to join us, and make their contributions.

During the business meeting, a motion was made that the present officers of the Division continue to serve in their respective capacities. The motion carried. So Dr. Alex D. W. Acholonu of Acorn State University, continues to serve as Chair of the Zoology and Entomology Division and Dr. Elgenaid Hamadain of Jackson State University, as the Vice-Chair. I feel deeply honored to be found worthy to serve again as the Chair of the Division.—Alex D. W. Acholonu

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ABSTRACT INFORMATION

Abstract title _____

Name of presenting author(s) _____
(Presenter must be a current (i.e., 2005 membership dues must be paid) student member, regular member, or life member of the MAS)

Telephone _____ Email _____

Check the division in which you are presenting

___ Agriculture and Plant Science
___ Cellular, Molecular and Dev. Biol.
___ Chemistry and Chem. Engineering
___ Ecology and Evolutionary Biology
___ Geology and Geography
___ Health Sciences
___ History and Philosophy of Science
___ Math., Computer Sci. and Statistics
___ Marine and Atmospheric Sciences
___ Physics and Engineering
___ Psychology and Social Sciences
___ Science Education
___ Zoology and Entomology

Type of presentation

___ Poster presentation ___ Workshop
___ Lecture presentation ___ Invited symposium

If the presenting author for this paper is also presenting in another division, please list the other division: _____

Audio-visual equipment needs

___ 2" x 2" slide projector
___ Overhead projector

Other audio-visual equipment including computers and computer projection equipment must be provided by the speaker.

MEMBERSHIP INFORMATION

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PLEASE INDICATE DIVISION WITH WHICH YOU WISH TO BE AFFILIATED _____
Regular member $25 Student member $5 Life member $ 250
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CHECKLIST

The following MUST be DONE:

___ 1. Enclose copy of abstract (even if abstract has been submitted electronically)
___ 2. Complete and enclose abstract form /membership form(this form)
___ 3. Enclose the following payments (make check payable to Mississippi Academy of Sciences):
  ___ $25 per abstract
  ___ $25 regular membership fee OR $5 student membership fee (2005 membership must be paid for abstract to be accepted)
___ 4. You must supply a check # _____ or P.O. # _____ (credit cards are not accepted)

In addition you MAY preregister at this time:

___ Enclose the following payments:
  ___ $25 regular member (after 14 Jan.) ___ $15 regular member (Preregistration before Jan. 14, 2005)
  ___ $10 student member (after 14 Jan.) ___ $ 5 student member (Preregistration before Jan. 14, 2005)
  ___ $50 nonmember (after 14 Jan.) ___ $40 nonmember (Preregistration before Jan. 14, 2005)

NOTE: **Abstracts that are resubmitted for changes will incur a $10 resubmission fee. Late abstracts will be accepted with a $10 late fee during November increased to $25 after that. Late abstracts will be accepted only if there is room in the appropriate division.** They will be published in the April issue of the MAS JOURNAL.

MISSISSIPPI ACADEMY OF SCIENCES—ABSTRACT INSTRUCTIONS
PLEASE READ ALL INSTRUCTIONS BEFORE YOU SUBMIT YOUR ABSTRACT

- Your paper may be presented orally or as a poster. Oral presentations are generally 15 minutes although some divisions allow more time. The speaker should limit a 15 minute presentation to 10–12 minutes to allow time for discussion; longer presentations should be limited accordingly. Instructions for poster presentations are given on the reverse side of this sheet.
- Enclose a personal check, money order, institutional check, or purchase order for $25 publication charge for each abstract to be published, payable to the Mississippi Academy of Sciences. The publication charge will be refunded if the abstract is not accepted.
- The presenting author must be a member of the Academy at the time the paper/poster is presented. Payment for membership of the presenting author must accompany the abstract.
- Attendance and participation at all sessions requires payment of registration.
- Note that three separate fees are associated with submitting and presenting a paper at the annual meeting of the Mississippi Academy of Sciences. (1) An abstract fee is assessed to defray the cost of publishing abstracts and (2) a membership fee is assessed to defray the costs of running the Academy. (3) Preregistration payment ($15 regular; $5 student) may accompany the abstract, or you may elect to pay this fee before January 14th, or pay full registration fees at the meeting.
- Abstracts may be submitted by e-mail or entered directly through the MAS website. The URL is http://www.msacad.org. This abstract submission form and the appropriate fees should be sent by US mail even if the abstract has been submitted electronically.
- Abstracts may be submitted as a WordPerfect, Word, ASCII, ANSI, or .RTF file on a PC readable diskette. *Formatting should be minimal*. This abstract submission form and the appropriate fees should be sent by US mail even if a diskette is used for the abstract.
- Abstracts may be submitted typed or printed on clean white paper. Abstracts received in this form will be scanned into a computer. Leave ample margins and use a sanserif type font to help minimize errors in scanning.
- **Abstracts that are resubmitted for changes will incur a $10 resubmission fee.**
- **Late abstracts will be accepted with a $10 late fee during November increased to $25 after that. Late abstracts will be accepted only if there is room in the appropriate division.** They will be published in the April issue of the MAS JOURNAL.
- Submit your abstract and appropriate fees to the Abstracts' Editor, John Boyle, **TO BE RECEIVED NO LATER THAN NOVEMBER 1, 2004**.
- Late abstracts will be accepted with a $10 late fee and only if there is room in the appropriate division. They will be published in the April issue of the MAS journal.

Dr. John Boyle
Mississippi State University
Dept. of Biochemistry
P.O. Drawer 9650
Mississippi State, MS 39762

FORMAT FOR ABSTRACT

- Your abstract should be informative, containing: (a) a sentence statement of the study's specific objectives, unless this is given in the title; (b) brief statement of methods, if pertinent; (c) summary of the results obtained; (d) statement of the conclusions. It is not satisfactory to state, "The results will be discussed."

- Your abstract, including a concise, descriptive title, author(s), location where work was done, text and acknowledgment, may not exceed 250 words. **Excessively long abstracts will be truncated**.
- The title should be all capital letters. Use significant words descriptive of subject content.
- Authors' names start a new line.
- The institution where your research was done should include city, state, and zip code. Do not include institutional subdivisions such as department.
- The abstract should be one paragraph, single spaced, starting with a 3-space indentation.
- Use standard abbreviations for common units of measure. Other words to be abbreviated, such as chemical names, should be spelled out in full for the first use, followed by the abbreviation in parenthesis. Do not abbreviate in the abstract title.
- Special symbols not on your printer or typewriter must be in black ink.
- Use italics for scientific names of organisms.
- Begin authors' names on a new line. Place an asterisk (*) after the presenter(s), if there are multiple authors.
- Use superscripts for institutional affiliations where necessary to avoid ambiguity.
- Refer to these examples as guides.

EXAMPLES OF TITLES AND AUTHORS:

[single author, no ambiguity about designated speaker or affiliation]
AN EXPERIMENTAL MODEL FOR CHEMOTHERAPY ON DORMANT TUBERCULOUS INFECTION WITH PARTICULAR REFERENCE TO RIFAMPICIN
Joe E. Jones, Mississippi State University, Mississippi State, MS 39762
Abstract body starts here . . .

[two authors, both designated as speakers, different affiliations, but no ambiguity]
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Abstract body starts here . . .

GUIDELINES FOR POSTER PRESENTATIONS

- The Academy provides poster backboards. Each backboard is 34" high by 5' wide. Mount the poster on the board assigned to you by your Division Chairperson. Please do not draw, write, or use adhesive material on the boards. You must provide your own thumb tacks.
- Lettering for your poster title should be at least 1" high and follow the format for your abstract. Lettering for your poster text should be at least 3/8" high.
- Posters should be on display during the entire day during which their divisional poster session is scheduled. They must be removed at the end of that day.
- Authors must be present with their poster to discuss their work at the time indicated in the program.