were assessed using high-resolution time-series analysis, and adenosine triphosphate (ATP) expenditure was calculated.

Results: Immediately after the onset of transient ischemia, there was a brief period when developed pressure (Δ +13±3 mm Hg; $P<.05$ versus baseline) and heart rate (Δ +51±0.12 beats/min) increased. This inotropic and chronotropic reflex occurred within 10 seconds of ischemia. Subsequent cycles of transient ischemia and reperfusion differentially reduced the inotropic (Δ –30±15%; $P<.05$ fourth versus first cycle) and chronotropic (Δ –53±23%; $P<.05$ versus baseline) aspects of the reflex, with eventual diminution of both reflexes after 4 cycles. Attenuation of the compensatory reflex resulted in decreased contractile work and energy expenditure during repeated episodes of global ischemia, with a net ATP savings of 4.3 μmol/g wet weight. The inotropic and chronotropic responses during all cycles of ischemia were attenuated by 10 μM propranolol.

Conclusion: This study reports a novel, locally mediated adrenergic sympathetic response that results in a desperate energy expenditure during global cardiac ischemia. Ischemic preconditioning curtails this reflex after the onset of global ischemia, and the preconditioning effect may be replicated using β-blockade. Blocking this adrenergic response may prevent energy expenditure on potentially futile cardiac contractile work during prolonged global ischemia and prove beneficial in protecting cardiac function during acute ischemic states, such as coronary syndromes, arrest, shock, and trauma.

6 γ-Aminobutyric Acid, but Not Opiate Receptor Agonists Attenuate Organophosphate-Induced Central Respiratory Depression

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Study objectives: Acute organophosphate poisoning causes mortality by 2 discrete mechanisms: (1) peripheral cholinergic crisis; and (2) central respiratory depression. It has further been reported that the respiratory depressant diazepam paradoxically attenuates organophosphate-induced central respiratory depression; however, it is not known whether this is specifically caused by diazepam's actions on the γ-aminobutyric acid (GABA) receptor or a nonspecific effect on respiratory drive. We determine whether the respiratory depressant morphine also attenuates organophosphate-induced respiratory depression.

Methods: Sprague-Dawley rats (n=34) weighing 200 to 250 g were randomized to receive treatment with nothing (controls), glycopyrrolate 3 mg/kg, diazepam 5 mg/kg, morphine 5 mg/kg, glycopyrrolate+diazepam or glycopyrrolate+morphine, 5 minutes before a single subcutaneous injection of the organophosphate dichlorvos (20 mg/kg). A reviewer blinded to the treatment group observed the animals for signs of peripheral cholinergic crisis (salivation, defecation, urination, and retractions) and respiratory arrest for up to 20 minutes after poisoning.

Results: Fasciculations were seen within 3 minutes of dichlorvos injection in all animals, regardless of treatment group. In control animals and those treated solely with diazepam or morphine, fasciculations were followed by signs of severe peripheral cholinergic crisis and respiratory arrest within 6 minutes of poisoning. Rapid respiratory arrest (within 8 minutes of poisoning) also occurred in all animals treated with glycopyrrolate alone; however, it was not preceded by signs of peripheral cholinergic distress. Fifty percent of the animals treated with diazepam+glycopyrrolate survived to the 20-minute endpoint of the study ($P\leq.05$ by χ^2 analysis), suggesting that this combination treatment attenuated both the peripheral and central nervous system manifestations of the poisoning. The beneficial effects of combination treatment with a peripheral anticholinergic+a respiratory depressant were not seen in the cohort receiving morphine+glycopyrrolate (100% mortality by 8 minutes).

Conclusion: These findings suggest that diazepam attenuates central respiratory depression by a GABA-dependent mechanism not related to its respiratory depressive effects.

7 The Inhibition of Apoptosis in Swine Brain by Hyperbaric Oxygen Therapy Following Cardiopulmonary Arrest

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Study objectives: It has been demonstrated that 4 atmospheres of hyperbaric oxygen therapy delivered after a 25-minute cardiopulmonary arrest in swine has produced immediate and sustained (2 hours) spontaneous return of circulation. Recent studies have shown that hyperbaric oxygen can improve neurologic recovery in cerebral ischemia models, but the mechanism remains controversial. This study tested the hypothesis that hyperbaric oxygen therapy delivered during cardiopulmonary resuscitation after a 25-minute cardiac arrest in swine would result in an attenuation of cerebral cortical apoptosis compared with animals resuscitated at surface pressure.

Methods: Eighteen adolescent swine were anesthetized and underwent induced cardiac arrest for 25 minutes, producing a model of complete global ischemia. The animals were randomized to 3 groups, representing 3 pressures of oxygen ventilation provided during the cardiopulmonary resuscitation of the swine. Six animals per group received oxygen ventilation at surface pressure, 2 atmospheres, or 4 atmospheres. After 2 hours of resuscitation, the animals' brains were harvested and flash frozen in liquid nitrogen. The degree of apoptosis in each sample of cerebral cortex was determined through the measurement of DNA laddering, caspase-3 activity, poly(adenosine diphosphate ribose) polymerase (PARP) expression, and nucleosome cleavage. The average degree of apoptosis of the 3 groups was compared.

Results: The relative density of PARP (caspase-3 substrate) was smaller in the group treated at surface depth (5.71) than in the 2-atmosphere group or the 4-atmosphere group (8.39 and 8.63, respectively; P=.04). There was no evidence of DNA laddering in any animals in group 3 (4 ATA), whereas 2 animals in group 1 (surface pressure) and 1 animal in group 2 (2 ATA) showed evidence of DNA laddering. Relative caspase-3 activity in the 4-ATA, 2-ATA, and surface-treated animals was 0.0327, 0.0402, and 0.0407 units/μg protein, respectively, whereas the relative quantity of nucleosome cleavage in the same groups was 0.108, 0.137, and 0.140 $Abs[_{405\ 492}]$, respectively (no statistical significance).

Conclusion: The groups receiving hyperbaric oxygen therapy showed less apoptosis than the group treated at surface pressure, as measured by PARP cleavage. A similar trend exists as measured by the other tests (DNA laddering, caspase-3 assay, nucleosome enzyme-linked immunosorbent assay).

8 The Effect of Age on Outpatient Uropathogen Antibiotic Resistance

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Study objectives: Empiric antibiotic treatment of urinary tract infection (UTI) in adults is based on the local resistance patterns of common uropathogens. Increasing antibiotic resistance has affected empiric antibiotic choice for UTI. Most antibiotic resistance levels report overall inpatient resistance, and there are limited data on outpatient resistance trends. We describe the effect of age on outpatient resistance patterns to common empiric antibiotics.

Methods: This is a multicenter, prospective case series composed of patients with UTI. Participating facilities include 4 emergency departments and 84 outpatient clinics in an urban and suburban environment. All urine samples were collected during a 12-month period from July 2002 through June 2003. Only adult patients with a clean-catch urine containing greater than 100,000 colony-forming units of a uropathogen were included. Uropathogens were tested against levofloxacin, ceftriaxone, trimethoprim/sulfamethoxazole (TMP/SMX), and ampicillin. Resistance data were divided into 5 age groups: 18 to 40, 41 to 50, 51 to 60, 61 to 70, and older than 70 years.

Results: Two thousand seven hundred fifty-one total urine cultures met inclusion criteria. The 2 most common uropathogens were *Escherichia coli* (52% to 76%) and *Enterococcus* sp (11% to 20%) in all age groups. Older patients were less likely to have a UTI caused by *E coli*. *E coli* resistance to ceftriaxone and ampicillin varied little across age (0.2% and 32%, respectively), with the exception of patients older than 70 years, where *E coli* resistance to ampicillin decreased to 23%. *E coli* resistance to levofloxacin showed nonlinear relationships to age, with the highest resistance seen in the sixth decade (0.76% to 4.55%). *E coli* resistance to TMP/SMX decreased with advancing age (14.8% in young adults to 11.5% in adults >70 years). The number of UTIs caused by *Enterococcus* sp increased with advancing age, with older patients having higher resistance to levofloxacin (5.7% in young adults compared with 33% in adults >70 years). *Enterococcus* sp resistance to ampicillin varied across age groups, with the highest resistance seen in adults older than 70 years (0.0% to 9.2%). *Enterococcus* sp was not tested against TMP-SMZ or ceftriaxone.

Conclusion: Outpatient uropathogen antibiotic resistance was affected by patient age. *Enterococcus* sp resistance increased as patient age increased. Empiric antibiotic