140 INHIBITION OF BIOPROSTHETIC (BHV) CALCIFICATION (CALC) WITH COVALENTLY BOUND AMINOPROPANEHYDROXYDIPHOSPHONATE (APD) Catherine L. Webb, James Benedict, Judy Linden, Robert J. Levy, C.S.Mott Children's Hospital, University of Michigan, Ann Arbor, MI.

CALC is the principal failure mode of BHV fabricated from glutaraldehyde pretreated porcine aortic valves or bovine pericardium. Covalent binding of APD to residual glutaraldehyde in pericardial BHV was studied as an approach for the inhibition of CALC. BHV were preincubated in APD (0.14M) at various pH's with and without sodium borohydride (NaBH4) reduction. The bound APD was determined using C14 APD and the CALC was studied with 21 day rat subdermal implants of BHV. APD incorporation was pH dependent with more rapid uptake at higher pH (Table). APD completely inhibited CALC when binding was >30ng/mg, while controls exhibited CALC comparable to several years of clinical implantation. NaBH4 reduction significantly stabilized (p<.001) APD bound to BHV subjected to in vitro incubations (pH 7.4, 37C). In conclusion, APD pretreatment of BHV significantly inhibits CALC and may also be useful with controlled release drug delivery to prevent CALC. Our data suggest that incubation in APD at pH 11.0 for 1 hour during surgical preparation for BHV implant may be all the pretreatment that is necessary to prevent BHV CALC.

APD-BHV and CALC of RAT 21 DAY IMPLANTS

pH	Duration	APD(nM/mg)	Valve Ca++(ug/mg)
7.4	1 hour	8.03	52.6+10.1
9.0	1 hour	19.15	12.7+7.1
11.0	1 hour	33.55	3.1+0.9
control	-	-	141.7+12.8

●141 RECURRENCE OF CONGENITAL HEART DEFECTS IN PROGENY OF AFFECTED MEN VS. WOMEN. Ruth Whittemore, James A. Wells, Margaret R. Wright, Yale University School of Medicine and Yale-New Haven Hospital, Department of Pediatrics, New Haven, Connecticut.

Over the past 25 years, 254 women with congenital heart defects (CHD) originally seen between 1947-1960 have participated in a prospective study of their pregnancies, and repeated examinations of their offspring for the first three years according to a set protocol. The over-all incidence of CHD in these children was 15.6%. Over the past three years, the progeny of men with CHD from this same population have been examined to try to substantiate the hypothesis that offspring of affected women are more likely to have CHD than are the offspring of affected men. To date we have examined 308 offspring of 151 men of whom 12.3% are proven to be affected, but this difference is not statistically significant. The only significant differences are in the greater recurrence among the offspring of women than in the offspring of men with left sided obstruction (23% vs. 9.5%, P<.05) and ventricular septal defect (22.3% vs. 10%, P<.05) but the difference in risk of recurrence of VSD becomes insignificant when one corrects for the number of VSDs that closed during the 3 year period of observation of the maternal offspring. In the offspring of the 15 women with genetic syndrome or strong family history, 56% were affected (15/27) but of the 5 men with similar history, 60% (6/10) are affected to date. Concordance of defects with that of the parent was 51% in the maternal study and 45% to date in the paternal study. The over-all risk of recurrence of CHD does not appear to depend upon the sex of the affected parent.

●142 ESOPHAGEAL DYSMOTILITY: A CAUSE OF CHEST PAIN IN CHILDHOOD MITRAL VALVE PROLAPSE (MVP). Paul K. Woolf, Stuart Berezin, Marvin S. Medow, Leonard J. Newman, Julian M. Stewart, Michael H. Gewitz, (Spon. by Lawrence Shapiro). New York Medical College, Westchester Medical Center, Dept. of Pediatrics, Valhalla, NY 10595.

Since the cause of chest discomfort in patients with mitral valve prolapse (MVP) is controversial, we prospectively measured esophageal motility in 14 children, 10 as normal controls and 4 with MVP and chest discomfort. Ages ranged from 10-14 yrs. All had clinical and echocardiographic evidence of MVP and normal left atrial size. None had rhythm disorders. Esophageal manometry was performed with the station pull-through technique and a triple-lumen perfused polyethylene catheter system. 10 wet swallows (3ml water) given at 30 sec. intervals were used to examine the esophageal body. Bernstein acid perfusion tests were performed on all patients.

3 of 4 with MVP and chest discomfort had manometric abnormalities: Diffuse esophageal spasm was present in 1, hypotensive lower esophageal sphincter (<7mm Hg) in 2. Bernstein tests reproducing chest discomfort were positive in the 2 with hypotensive lower esophageal sphincters. Intensive antacid therapy relieved chest discomfort in 2 patients and dicyclomine was effective in the patient with diffuse esophageal spasm. Control patients had normal esophageal manometric studies with negative Bernstein tests.

Conclusions: 1. In some children with MVP, chest discomfort attributed to MVP may be due to esophageal dysmotility. 2. Children with MVP and chest pain may benefit from esophageal manometry and the Bernstein acid perfusion test prior to the initiation of therapy.

●143 **THE ELECTROPHYSIOLOGIC EFFECTS OF SOTALOL IN THE IMMATURE MAMMALIAN HEART** Hui Xu, Juan Villafane, Jorge McCormack, Adrienne Stolfi, Henry Gelband, Arthur S. Pickoff (Spon. by Arthur S. Pickoff). University of Miami School of Medicine, Dept. of Pediatrics, Miami, FL.

Sotalol (So), a new antiarrhythmic agent, is a beta-blocker that also has been shown to have some class III electrophysiologic (EP) effects. To evaluate the EP effects of So on the immature heart and to assess the relative importance of its class III actions, two groups of neonatal canines, ages 4-15 days, were studied and compared. Group I consisted of 6 puppies in whom EP studies were performed in the control state (C) and following 1.5, 2.5 and 4.0 mg/kg I.V. So. Group II consisted of 6 puppies in whom EP studies were performed prior to and following beta-blockade with 0.6 mg/kg I.V. propranolol (P). So caused a dose dependent decrease in heart rate (181 ± 27 to 125 ± 21 bpm, p < 0.001) while P caused no significant change (169 ± 9 to 159 ± 14, ns). So significantly prolonged atrial refractoriness (AERP: 67 ± 14 C, 117 ± 28 So; AFRP: 102 ± 9 C, 152 ± 31 So, p < 0.001) while P only slightly increased the AFRP (114 ± 12 C, 120 ± 10 P, p < 0.03). While the AV node FRP was prolonged by P (183 ± 9 C, 193 ± 19 P, p< 0.05) So caused a greater increase (171 ± 29 C, 244 ± 57 So, p< 0.01). Similarly, while P slightly increased the VERP (158 ± 12 C to 168 ± 13, p <0.05) So caused a far greater increase in ventricular refractoriness (VERP: 152 ± 26 C, 227 ± 41 So; VFRP: 173 ± 23 C, 253 ± 34 So, p < 0.001). Because the EP changes with beta-blockade in the immature heart are modest, the large changes in myocardial refractoriness induced by So must be largely due to a significant class III antiarrhythmic effect.

●144 CHARACTERIZATION OF SINUS NODE REFRACTORINESS AND SINOATRIAL CONDUCTION DURING ACUTE HYPOXIA. Steven M. Yabek, University of New Mexico School of Medicine, Dept. of Pediatrics, Albuquerque, NM.

Since hypoxia inhibits conduction & automaticity predominantly in tissues dependent on the slow (Ca-channel) current, sinus node (SN) function should be selectively depressed. The effects of acute, severe hypoxia (H) on SN refractoriness and sinoatrial conduction time (SACT) were studied using rabbit SN-right atrial preparations and standard microelectrode techniques. True SN pacemaker cells were identified by intracellular action potentials having low amplitude (65±7mV) and Vmax (3.3±1.0 V/s), and rapid rates of spontaneous diastolic depolarization (51±15 mV/s). Spontaneous sinus cycle length (CL) (control = 460±58ms) increased by 36% with H. Retrograde SACT, measured from the crista terminalis to a true SN pacemaker cell, was rate dependent; increasing at shorter paced CL. SACT increased at all paced CL with H. At a CL of 400ms, SACT increased from 41±12 to 101±19ms (+146%). The minimum paced CL with 1:1 atrio-SN conduction (CLm) increased from 203±34 to 308±41ms (+52%) with H. SACT at CLm increased from 65±19 to 134±30ms (+105%). SN effective refractory period (ERP)(at a paced CL of 400ms) increased from 158±37 to 261±45ms (+66%). All changes in SN function related to H were significant (at least p<0.05). SN pacing from the crista terminalis was never limited by atrial muscle conduction (fast, Na-channel dependent) or refractoriness. Atrial ERP changed from 86±14 to 96±20ms (NS) with H. In summary, acute H adversely affects SN automaticity, conduction and refractoriness; presumably related to alterations in the Ca current. These changes may be responsible for many of the bradyarrhythmias seen clinically during severe H.

●145 THE EFFECTS OF HYPOXIA AND ADENOSINE ON THE ELECTROPHYSIOLOGIC FUNCTION OF THE ADULT AND NEONATAL RABBIT ATRIOVENTRICULAR NODE. Ming-Lon Young, Brian M. Ramza, Ronald W. Joyner (Spon. by Ronald M. Lauer). Univ of Iowa, Depts of Peds. and Phys., Iowa City, IA

We used an isolated perfused heart model to test the effects of acute hypoxia and adenosine (ADO) on the adult (A) and neonatal (N) (1-5 days) rabbit atrioventricular node (AVN). The AVN function was assessed by the AH interval at a constant atrial pacing cycle length (CL) just shorter than the intrinsic CL and by the longest pacing CL resulting in Wenckebach periodicity (WP). When the hearts were sequentially exposed to 0.01, 0.1 and 1 mM ADO, in both groups ADO caused a similar degree of dose-dependent increase in AH (93±53% in A, n=8; 58±24% in N, n=7, after 1 mM ADO) and WP (43±12% in A; 36±18% in N). When the hearts were exposed to 5 min of hypoxia (O_2 replaced with N_2) there was a significant difference in the increase of WP between these 2 groups (128±44% in A; 34±13% in N, p <0.01). The change in WP in A caused by hypoxia was significantly greater (p <0.05) than that caused by 1 mM ADO, a dose that has been previously shown to cause complete AVN block in guinea pigs. In A when 1 mM aminophylline (AMO), a competitive antagonist to ADO, was added, it could attenuate the WP increment caused by 1mM ADO (32±13% by ADO; 19±8% by ADO+AMO, n=8, p <0.01), but it could not attenuate those caused by hypoxia (100±25% by hypoxia; 87±32% by hypoxia+AMO, p=0.38). We conclude that in the rabbit AVN: 1) The response to ADO is similar in A and N. 2) N is relatively resistant to acute hypoxia as compared to A. 3) The response to acute hypoxia in A could not be totally explained by the ADO release theory.