

Effects of Metabolic and Respiratory Acidosis & Alkalosis
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The consequences of respiratory and metabolic acidosis are poorly documented. The consequences of over treatment are not well understood. The responses to metabolic and respiratory acidosis and alkalosis of the pulmonary and systemic vasculature were studied in anesthetized dogs measuring pulmonary and systemic B.P., C.O., R.A. and L.A. B.P. The following is a graphic summary of the measured changes during 15 min. of respiratory manipulation or 10 min. following an infusion of bicarbonate or acid:

	PH	PCO ₂	ΔBP	ΔC.O.	ΔPul.Resis	ΔSyst.Resis
Resp. alkalosis	7.65	14	-31%	-26%	+40%	+10%
Resp. acidosis	7.15	90	+35%	+26%	+1%	+4.5%
Met. alkalosis	7.51	40	+4.5%	+3%	+10%	-22%
Met. acidosis	7.01	44	0	+4.5%	-8%	-9.5%

The major change seen in respiratory alkalosis was a decrease in B.P. and in C. O. with an increase in pulmonary resistance. These are changes which should be avoided with the use of ventilatory assistance. There was an increase in both B.P. & C.O. with respiratory acidosis. The major change with metabolic alkalosis was an increase of C.O. and a decrease in systemic resistance which could be duplicated with the infusion of hypertonic saline. There were very few measurable changes following acid infusion. Caution should be used in the correction of metabolic acidosis.

ENHANCING THE DIAGNOSTIC VALUE OF CARBOXYHEMOGLOBIN (%COHb) DETERMINATIONS. Rolf R. Engel, Siv Modler, William Norberg and Gary Geller. Dept. of Ped., Univ. of Minnesota, Minneapolis.

To capitalize on the equi-molar relation between endogenous carbon monoxide production (\dot{V}_{CO}) and heme turnover, we have evaluated 6 alternative sampling methods for detecting increased \dot{V}_{CO} . The greatest resolution of \dot{V}_{CO} was achieved when %COHb levels were corrected for ambient CO exposure. This correction was based on the CO content of a diffusion chamber that remained at the bedside for 18 hours prior to obtaining a 0.5 cc sample of the patient's blood. The gas space of the chamber (a 100 ml glass syringe) and the area of the diffusion membrane (a loop of silicone tubing) are adjusted according to the patient's CO space and pulmonary function so that the patient's $T_{1/2}$ for CO equilibration with ambient air is duplicated. Our empiric data confirms the theoretical prediction that the effect of ambient CO on %COHb is described by the following equation: $\Delta\%COHb = 0.16 \times CO$ in ppm. The relation between \dot{V}_{CO} and %COHb was derived from the intercept of a plot of %COHb vs ambient CO in normal individuals. Confirmation was obtained with the much more cumbersome tests of in vivo survival of Cr⁵¹ tagged erythrocytes and measurements of \dot{V}_{CO} in a rebreathing apparatus. Serial determinations of \dot{V}_{CO} on patients with Coombs positive hemolytic anemia permitted rapid adjustments of the optimal dose of immuno-suppressive agents. Successive measurements on jaundiced infants demonstrated no increase in \dot{V}_{CO} during phototherapy. Infants who developed bacterial septicemia did have a pronounced rise in \dot{V}_{CO} .

BIOCHEMICAL ASSESSMENT OF CILIARY ACTIVITY IN THE PRESENCE OF CYSTIC FIBROSIS (CF) SERUM. P.M. Farrell, G.N. Fox, and S.S. Spicer, (Intr. by Paul A. di Sant'Agnes), NIH, Bethesda, Md.

Since Spock, *et al.* (Pediat. Res. 1:173, 1967) first observed that serum from CF patients and heterozygotes induced ciliary dysrhythmia, several "CF factor" bioassays have been described. Such methods, however, suffer from several disadvantages in that they are: a) subjective, b) qualitative, and c) difficult to reproduce. We ourselves had consistently negative experiences with both rabbit tracheal (RT) and oyster gill (OG) assays. In an effort to develop a quantitative chemical assay, we have tried a fresh approach by measuring motility-coupled ciliary ATP hydrolysis in the presence of serum. In addition, to characterize the ATPase activity several basic studies were performed with OG and RT cilia. Homogeneous, motile cilia were prepared from the former by mincing in 0.05 M Tris HCl (pH 8.0), 0.3 mM EDTA; this preparation, which on electron microscopy showed intact cilia, hydrolyzed ATP in proportion to calculated beat frequency. A high molecular wt. ATPase was purified from RT cilia and shown to have properties similar to flagellar dynein. The effect of various factors (time, temp., pH, cations, and substrate concentration) on ciliary ATP hydrolysis was determined. Explants, homogenates, and minces of RT and OG were preincubated for 30-45 min with either normal, CF, or CF heterozygote sera; subsequent addition of ATP- γ -³²P and measurement of ³²Pi production revealed that the latter two groups could not be distinguished from normal serum. Studies are continuing but this objective, quantitative assay has thus far failed to demonstrate the "CF factor."

A METABOLIC BASIS FOR SEVERE INTRACTABLE ASTHMA. Philip Fireman, Louie Linarelli, Gilbert A. Friday, Robert A. Bernstein and Allan Drash. Univ. of Pittsburgh Sch. of Med., Dept. of Ped., Pittsburgh, Pa.

We have previously reported that severe asthmatics after receiving catecholamines have decreased urinary cyclic AMP compared to normals. To better define this abnormality, which suggests B-adrenergic blockade, 15 severe asthmatic children were studied prospectively. Whereas, normals had a mean 3.2±0.4 Nm/min/1.73M² increment in 2 hour urinary cyclic AMP, asthmatics had a mean 1.6±0.3 Nm/min/1.73M² increment after 6 µg/Kg of epinephrine. After 12 µg/Kg epinephrine the asthmatics had a mean 2.2±0.4 Nm/min/1.73M² increment in 2 hour urinary cyclic AMP: individually, 7 asthmatics had no increased urinary cyclic AMP excretion with double the epinephrine; whereas, 8 patients had 1.0 to 5.2 Nm/min/1.73M² increment after 12 µg/Kg epinephrine. Clinical evaluation the past 18 months demonstrated that 6 of 7 asthmatics who had no increase in urinary cyclic AMP to 12 µg/Kg epinephrine persisted with severe intractable asthma. However, 5 of 8 asthmatics who demonstrated with the dose response test an increase in urinary cyclic AMP had clinical improvement: their asthma is intermittent and less severe. These data support the hypothesis that severe asthmatic patients have a defect in formation of cyclic AMP after B-adrenergic stimulation. Also, lack of a dose response to epinephrine has delineated a unique group of asthmatics.

RESPIRATORY CENTER OUTPUT IN INFANTS AS INDICATED BY INSPIRATORY PRESSURE DURING AIRWAY OCCLUSION. Ivan D. Frantz, III, William Tausch, Jr., Izzie Wyszogrodski, William Whitelaw, Joseph Milic-Emili, and Mary Ellen Avery. McGill University - Montreal Children's Hospital Research Institute, and Dept. of Physiology, McGill University, Montreal.

The pressure generated by inspiratory muscles against an obstructed airway at functional residual capacity is an index of respiratory center output that is relatively independent of body size and lung mechanics. We have utilized this approach, that also assesses effects of afferent vagal activity, to measure output of the respiratory center in 6 full term infants on 15 occasions during the first week of life. While an infant was breathing room air or rebreathing carbon dioxide in oxygen, the face mask was occluded for 1 to 5 inspiratory efforts. Flow, tidal volume, inspiratory pressure, and carbon dioxide were measured continuously.

Tidal volume, peak inspiratory pressure, inspiratory pressure at 0.1 sec after occlusion, and minute ventilation all increased with increasing carbon dioxide. The sequential increase in pressure during 5 occluded inspiratory efforts serves as an index of respiratory sensitivity to increasing chemical drive. Application of these techniques to infants with respiratory control problems can simultaneously differentiate nervous (vagal) and chemical influences on respiratory center output.

REVERSIBILITY OF CHRONIC OBSTRUCTIVE LUNG DISEASE IN INFANTS FOLLOWING REPAIR OF VENTRICULAR SEPTAL DEFECT (VSD). Allan J. Hordof, Carl N. Steeg, Welton M. Gersony, and Robert B. Mellins. Col. of Physicians & Surgeons, Columbia Univ., Dept. of Ped., N.Y.

The persistence of signs of obstructive lung disease in some infants with VSD and left to right shunt, despite apparent cardiac compensation, suggests underlying or unrelated lung disease. To determine whether the chronic lung hyperinflation and respiratory acidosis seen in these infants is reversible, we analyzed the course of nine infants who presented at 1 month to 7 months of age. All had wheezing and persistent x-ray evidence of hyperinflation, either generalized or lobar, and five had chronic hypercarbia. The increase in heart size and pulmonary vascularity varied from mild to severe; pulmonary to systemic blood flow ratios ranged from 1.8 to 4.1/1, and pulmonary to systemic mean arterial pressure ratios ranged from 0.3 to 0.9. There was no relationship between the severity of cardiac disease and the manifestation of obstructive lung disease. Both chest x-ray and arterial blood gas findings reverted to normal in all of the patients following open heart correction of the VSD at 4 to 12 months of age.

We conclude that the chronic obstructive lung disease in infants with VSD and left to right shunt is directly related to the cardiac disease and is completely reversible when the heart lesion is surgically corrected.