in lymph nodes, spleen, lungs and skin consistent with graft versus host syndrome. A successful marrow graft in posthepatitis aplasia can be achieved.

- 131 *Liberal Versus Restricted Indications for Oxygen in RDS: A Controlled Trial.* ROBERT H. USHER, Royal Victoria Hosp. and McGill Univ., Montreal (introduced by Mary E. Avery).

Oxygen therapy for RDS may improve the course of the syndrome by increasing pulmonary perfusion, improving myocardial, renal and cerebral function, and by preventing lactic acidosis. Conversely, it may aggravate the disease by pulmonary toxicity. In an attempt to assess the balance between benefits and risk, oxygen therapy for RDS was given during the first 72 h of life according to liberal indications in 75 infants (for PaO_2 below 80 or PcapO_2 below 55 mm Hg), and according to more restricted indications in 75 others (for PaO_2 below 40 or PcapO_2 below 35 mm Hg). The 2 groups were well matched and had a similar severity of RDS at 1 h of age. Concentrations of oxygen exceeding 60% ambient were required in 50% of liberal and 10% of restricted oxygen cases.

Mortality was similar among the 45 infants weighing 500–1,250 g (68% liberal vs. 69% restricted). Infants weighing more than 1,250 g had a higher mortality when treated with liberal than with restricted oxygen (2% of 51 vs. 9% of 54). The liberal group developed more severe respiratory distress, more rales, faster respirations and more severe x-ray changes. Their pCO_2 and lactic acid rose to higher levels and they required 30% more bicarbonate to maintain a blood pH of 7.35. Liberal oxygen as defined therefore, conferred no apparent benefit and caused significant pulmonary oxygen toxicity.

- 132 *Pulmonary Pathology in Lambs with Hyaline Membrane Disease Ventilated with Air and 100% O_2 .* J. R. RAYE, R. L. GUTBERLET, G. FAXELIUS, S. SWANSTRÖM, V. S. LEQUIRE and M. T. STAHLMAN, Vanderbilt Med. Sch., Dept. of Ped. and Path., Nashville, Tenn.

There has been increasing controversy over the role of oxygen in the clinical and pathological picture of severe HMD assisted with positive pressure ventilation. For this reason a control study of the effects of 100% O_2 versus room air administered by IPPV to premature lambs with induced HMD was initiated. Ewes of 132–136 days gestation were made hypotensive with pentolinium and delivered 24 h later by cesarean section. Such lambs have previously been shown to develop the pathological sequence characteristic of HMD. Singleton lambs were immediately intubated, suctioned and ventilated with room air. A tracheostomy was performed and the RLL isolated with a Foley balloon catheter. The isolated lobe and remaining lung were ventilated separately with Bird respirators on either O_2 or room air. Twin lambs were intubated and ventilated either with room air or O_2 . Catheters were placed in Ao, SVC and, when feasible, PA and LA. Twin lambs were monitored until one died; the other was then sacrificed (1 ½ to 11 h). Lambs ventilated with 100% O_2 had a striking PAO_2 to PaO_2 gradient, metabolic acidosis, and lower PA pressures. All portions of lung examined showed some slough of alveolar duct and respiratory bronchiolar epithelium, pulmonary edema and arteriolar constriction. Portions of lung ventilated with 100% O_2 showed more advanced cellular slough, further advanced membrane formation

and more alveolar fluid. These findings suggest that, in severe HMD when cellular slough is already occurring, high PAO_2 may cause further direct damage to pulmonary epithelium, as well as increasing exudation of fluid from damaged capillaries by promoting $\text{L} \rightarrow \text{R}$ shunting, resulting in more extensive hyaline membrane formation.

- 133 *The Special Relation Between Oxygen and Nitrogen in Pulmonary Injury.* D. R. SHANKLIN, Pritzker Sch. of Med. Univ. of Chicago, Depts. of Obstet. and Path., Chicago, IL.

The lungs of post-vagotomy newborn rabbits show the lesion of hyaline membrane disease in extent directly proportional to the percentage of oxygen in polybaric (0.2–3.0 Atm. Abs.) mixtures [Lab. Invest. 21: 439, 1969]. At 7% O_2 lesions do not form, but all vagotomized animals die. Comparative gas studies show the direct proportionality to be related to nitrogen itself, probably through physical interaction at the pulmonary interface [South. med. J. 61: 1338, 1968; Fed. Proc. 28: 654, 1969]. In 3% O_2 (1 Atm.) further dissociation between mortality and pulmonary lesion is seen. 3% O_2 in nitrogen is 100% lethal without vagotomy over a time course (0.3–27.0 h) questionably longer ($0.02 > p > 0.01$), but otherwise similar to vagotomy effects. Minimal lesions are seen in both (2–3% extent). 3% O_2 in helium with or without vagotomy shows moderate lesions (19–32% extent); without vagotomy only 7% die by 24 and 40% by 48 h. 3% O_2 in sulfur hexafluoride shows moderate lesions (7–15% extent) after vagotomy; without vagotomy only 15% die by 24 and 26% by 48 h. The protective effect of SF_6 after vagotomy [South. med. J., *ibid*] is thus seen only at 20% + O_2 . The difference in survival without vagotomy between N_2 , He and SF_6 is highly significant ($p < 0.001$), and probably due to better uptake of oxygen. These data suggest a special relation between O_2 and N_2 , enhancing the importance of physical attributes, molecular size, shape, etc. They also suggest a further mediation of blocking by N_2 through physicochemical interaction which is not shown by He or SF_6 in relation to O_2 . The limit of 'hypoxic' tolerance ($> 3\% \text{O}_2$) described by G. AVERY [Pediatrics 32: 801, 1963], *inter alia*, is thus an effect of specific interaction of oxygen and nitrogen. (Supported by the John A. Hartford Foundation, New York.)

- 134 *Continuous Positive Airway Pressure with Spontaneous Respiration: A New Method of Increasing Arterial Oxygenation in the Respiratory Distress Syndrome.* GEORGE A. GREGORY, JOSEPH A. KITTERMAN, RODERIC H. PHIBBS, WILLIAM H. TOOLEY and WILLIAM K. HAMILTON, Univ. of California, San Francisco Med. Center, Depts. of Anesth., Ped. and Cardiovasc. Res. Inst.

Seven infants < 12 hours of age, weighing 1.1–2.8 kg and severely ill with idiopathic respiratory distress syndrome (IRDS) were allowed to breathe spontaneously against a continuous positive airway pressure (CPAP). Before CPAP they were unable to maintain an O_2 tension in the descending aorta (PaO_2) > 50 mm Hg in 100% O_2 , were candidates for mechanical ventilation and had probabilities of survival from 0–0.3 [STAHLMAN *et al.*, New Engl. J. Med. 276: 303, 1967]. After application of CPAP up to 12 mm Hg, PaO_2 rose at once in all. In 6/7 adequate oxygenation was maintained by CPAP until recovery; 1 died of IRDS despite use of CPAP and subsequent mechanical ventilation.