ventilation, alveolar PO_2 and PCO_2, arterial pH, PCO_2 and PO_2, Co_2 respiratory response curves, and sensitivity to O_2. We measured ventilation with a nose piece and a screen flowmeter, using a constant flow-through to eliminate dead space and valves. Analyses were made from 3 to 5 min after the baby began breathing air, 2% or 4% Co_2 in air or 100% O_2. Sensitivity to O_2 was assesed by the change in ventilation when 100% O_2 was substituted for air.

Results:

	$\dot{V}_E$ L/min/kg	$PaCO_2$	$PACO_2$	PaO_2
P[1]	0.230±0.008	41±2	39±1	57±3
R[1]	0.273±0.011	38±2	35±2	66±4
	p<0.001	p<0.025	p<0.005	p<0.001

	PAO_2	pH
P[1]	102±2	7.34±0.01
R[1]	108±2	7.33±0.01
	p<0.001	p>0.5

	CO_2[2]		%$\Delta\dot{V}E$
	Slope	Position[3]	Air .. O_2
P[1]	0.030±0.007	42.7±2.2	−37±11
R[1]	0.035±0.007	36.0±2.7	−20±9
	p>0.2	p<0.001	p<0.025

All values: mean±0.2 S.E.
[1] P = periodic; R = regular.
[2] Response curve in L/min/kg/mm Hg.
[3] $PACO_2$ at 0.300 L/min/kg.

These findings show that periodic breathing in low birth weight infants is associated with hypoventilation, shift of the Co_2 response curve to the right and marked sensitivity to O_2. We suggest that low birth weight infants have increased O_2 chemoreceptor activity, but breathe periodically because of relative central depression.

170 *Ventilatory Disturbance and Arterial-Alveolar N_2 Differences During Recovery from Hyaline Membrane Disease.* A. PATHAK, L. MORRISON, L. M. PRUDENT, R. B. CHERRY and N. M. NELSON, Harvard Med. Sch. and Boston Hosp. for Women, Boston, Mass.

In infants recovering from hyaline membrane disease (HMD) persistent hypoxemia has been identified which seems not to result from venoarterial shunting [ADAMSON *et al.*, Pediatrics *44:* 168, 1969] but which could be due either to pulmonary diffusing defect or to ventilation/perfusion imbalance. Since the arterial-alveolar N_2 difference ($aADN_2$) and venous-alveolar N_2 difference ($vADN_2$) are unaffected by diffusion defect or by venoarterial shunting but are increase by impairment of ventilation with respect to perfusion, we have measured $vADN_2$ in a group of 10 normal low birth weight infants and in 4 infants convalescing from HMD. (Simultaneous comparison of $vADN_2$ and $aADN_2$ in seven infants revealed no significant difference.) In another 4 infants convalenscing from HMD the alveolar-arterial O_2 difference ($AaDO_2$) and arterial-alveolar CO_2 difference ($aADCO_2$) were also examined.

Number of infants	Age (days)	Birth weight (g)	Dx
10	18.5±11.2	1713.6±331.5	normal
4	7 to 16	1644 to 2892	HMD
4	10 to 33	1276 to 2395	HMD

Number of infants	$AaDO_2$ mm Hg	$aADCO_2$ mm Hg	$aADN_2$ mm Hg	$vADN_2$ mm Hg
				14.1±18.6
				77.0±36.8
	59±7.5	9.5±5.5	44.8±4.9	42.8±7.4

Unlike the hypoxemia seen in infants with early and developing HMD (which is due to an inequality of perfusion and a persistence of venoarterial shunting), the present findings suggest that it is inequality of ventilation which is mainly responsible for persistent hypoxemia during convalescence from HMD.

171 *Adjustment of Ventilation in the Newborn.* PETER A. M. AULD, ALFRED N. KRAUSS and JANE SOODALTER, Dept. of Ped., Cornell Univ. Med. Center, New York, NY.

In adapting to extrauterine life, ventilation and perfusion must soon become well-matched. The time course of this process can be assessed by measurement of the urinary-alveolar nitrogen gradient ($uADN_2$). An elevated $uADN_2$ is an indication of the maldistribution of $\dot{V}A/\dot{Q}$, specifically the presence of areas of low $\dot{V}A/\dot{Q}$. Seventeen healthy full-term neonates were studied serially from the first day of life. Values of $uADN_2$ within the range for normal adults were found (less than 10 mm Hg). Serial studies on 3 infants with evidence of aspiration pneumonia revealed $uADN_2$ consistently elevated above the normal. Children and adults with obstructive pulmonary disease were tested as a validation of the method and the expected elevation of $uADN_2$ was found. The studies indicate that (1) ventilation is uniformly distributed in the first days of life in normal infants; (2) maldistribution of ventilation is an important cause of arterial unsaturation in aspiration pneumonia. These results will be considered in the context of other studies of extrauterine pulmonary adaptation.

172 *Immaturity and Enhanced Susceptibility to Acute Hemodynamic Pulmonary Edema.* ELIHU P. REES, DORA A. STINSON, PAUL M. TAYLOR and DORIS W. WATSON, Dept. of Ped., Univ. of Pittsburgh Sch. of Med. and Magee-Women's Hosp.

The hypothesis that the immature lung is more susceptible than the mature lung to the development of acute pulmonary edema (PE), was tested by determining the transmural hydrostatic pressure in excess of whole blood colloid osmotic pressure (COP) necessary to produce PE in pups and adult dogs. Ten pups and ten adults were anesthetized with pentobarbital, parpalyzed with succinylcholine, and artificially ventilated. Transmural pulmonary artery wedge pressure (TPAWP) (as a reflection of vascular filtration pressure) was monitored continuously and whole blood COP intermittently. A balloon catheter in the thoracic aorta was inflated to produce an elevation of TPAWP in relation to COP that was maintained for 30 min by infusion of isosmotic dog blood to maintain a constant differential pressure (TPAWP-COP). Lungs were then removed and the degree of PE assessed by gross and microscopic appearance and determination of water content.

Interstitial edema first appeared with the following range of values:

	TPAWP mm Hg	Total protein g%	COP mm Hg	TPAWP-COP mm Hg
Adult dogs	24–30	5.6–7.0	19–22	6 to 8
Pups	10–15	4.2–5.6	12–17	−2 to +1

Gross edema formed at higher differential pressures. Thus the pups developed minimal PE at lower TPAWP than would have been expected from their T.P. and COP. The data do not permit a choice of the several factors that might explain this finding. Similar susceptibility of the human fetus and newborn in relation to the adult would favor the development of PE during the perinatal period and might thus play a role in the pathogenesis of pulmonary problems of the newborn.

173 The Effect of Thyroxin on Fatty Acid Biosynthesis in Brain. JORGE GRIPPO and JOHN H. MENKES, UCLA Sch. of Med., Los Angeles, CA.

Fatty acid synthesis by chain elongation occurs in microsomal and mitochondrial fractions of rat brain. With myelination (13–16 days of age) the rate at which microsomal particles incorporate malonyl-CoA into saturated fatty acids characteristic for myelin is increased. The present study was undertaken to study control mechanisms of fatty acid synthesis in brain.

Daily injections of triiodo thyronine (60 μg/100 g body wt.) were given from age 1 day to 2 h prior to sacrifice. In the microsomal system incorporation of malonyl-CoA into fatty acids in 5–6-day-old animals was increased from 0.91 ± 0.52 mμM/mg protein to 2.25 ± 0.39 mμM/mg protein. The increase in precursor incorporation occurred almost entirely into saturated fatty acids. Thyroid had no significant effect on fatty acid synthesis by microsomal particles derived from animals sacrificed at other stages of development or from adult rats.

Incorporation of acetyl-CoA into both saturated and unsaturated fatty acids by mitochondria was slightly increased by thyroid in adult animals and at 3–6 days of age, but the differences were not significant.

These studies suggest that thyroid accelerates the normal maturational increase in microsomal fatty acid synthesis. This probably occurs by stimulating the synthesis of the enzyme system involved in the production of fatty acids characteristic for myelin.

174 Mechanisms Responsible for the Sensitivity of Newborn Rats to Pregnanolone. LESTER F. SOYKA, LASZLO GYERMEK and PATRICIA CAMPBELL, Stanford Univ. Sch. of Med., Palo Alto, CA.

The minimum lethal dose of pregnanolone, a potent pharmacologically active metabolite of progesterone, increased about 60-fold from birth to weaning. This was greater than the increase seen with non-steroid hypnotic drugs. The brain concentration of pregnanolone at the onset of hypnosis was 0.35 μg/g in 3-day-old and 7–10$\times$ higher in 23-day-old rats, indicating an elevated receptor threshold. Similarly, older rats awoke at a brain concentration 6$\times$ higher than that maintaining sleep in younger animals. Hepatic biotransformation to sulfate and glucuronic acid esters and more polar steroids was extremely rapid, even in 3 day olds. Seven minutes after i.p. administration of pregnanolone with radioactive tracer only 29 and 37% of the total cpm in blood and liver were present as free pregnanolone. Although metabolism was somewhat faster in older rats, the relative increase was not quantitatively important compared to the extent of newborn sensitivity. A number of metabolites were found in blood, brain and liver of which pregnanediol was a surprisingly small component. Esters in the liver (at 45 min postinjection) were predominantly sulfates. No conjugates were found in brain. Pregnanolone accumulation in brain, as a percentage of the injected dose, was slightly greater in newborns, though far less than predicted assuming uniform distribution. In almost all previous developmental studies, impaired hepatic metabolism has been of sufficient magnitude to explain accentuated pharmacologic responses. These studies may be the first to experimentally verify the concept of altered receptor threshold in the brain as a mechanism for the sensitivity of newborn animals to drugs.

175 Familial Neuromuscular Disease and Non-ketotic Glycinemia. GRANT MORROW III, ASLAN AKSU, WILLIAM BANK, L. P. ROWLAND and L. A. BARNESS, Dept. of Ped. and Neurol., Hosp. Univ. of Pennsylvania and Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.

A family of Lebanese extract is described in which 3 of the 4 children (all males) have neuromuscular disorders and a primary aminoaciduria. The symptoms in those affected began in early childhood and are slowly progressive. In the 2 older siblings (age 22 and 24), the neurological disorder implied dysfunction of both spinal cord and peripheral nerves: weakness, wasting and loss of reflexes of distal muscles, combined with hyperactive reflexes, and spasticity of other muscles. EMG and muscle biopsy indicated denervation but conduction velocity of peripheral nerves could not be estimated because action potentials were not evoked by stimulation. Symmetrical upper motor neuron disease with clonus, spasticity, bilateral Babinski signs, and increased deep tendon reflexes were the clinical picture in the 10-year-old sibling. Examination and EMG in the mother and unaffected 14-year-old sibling were normal. The syndrome has features of both Friedreich's ataxia and Charcot-Marie-Tooth disease.

Urinary amino acids were measured on 6 members of the family. The combination of massive isolated glycinuria and neuromuscular disease was found only in the 3 affected males. Amino acid quantitation of the propositus revealed a plasma glycine of 0.817 μM/ml (normal 0.150–0.300) and urinary excretion of 1720 mg/day (normal <200). None of the patients were clinically acidotic and urinary organic acids were normal. Propionate metabolism in white cells of the entire family was normal. This is the first known example of an inherited neuromuscular disorder associated with a specific amino acid abnormality. (Supported in part by USPHS grants nos. AM-02231 and HD-04837.)

176 A Syndrome of Hypopituitary Dwarfism, Hypoplasia of Optic Nerves, and Malformation of Prosencephalon: Report of 6 Patients. SELNA L. KAPLAN, MELVIN M. GRUMBACH and WILLIAM F. HOYT, Dept. of Ped. and Ophthal., Univ. of California, San Francisco, CA.

We have suggested that 'idiopathic' hypopituitary dwarfism (IHP) is a heterogenous disorder of disparate pathogenesis [New Engl. J. Med. *278:* 57, 1968]. Among a group of 36 children with sporadic IHP (16 isolated GH and 20 multiple pituitary deficiencies) in whom mass lesions were excluded, 6 patients (3F, 3M) had a distinctive clinical entity of dwarfism, optic nerve dysplasia, and midline abnormalities of the prosencephalon. The findings included: congenital diabetes insipidus in 2; bilateral hypoplasia of optic nerves with small optic discs in 6; pendular, dysjunctive nystagmus in 5; bilateral amblyopia in 3; inconstant, irregular field defects in 5; and documented growth