EGF receptor levels in adult rat liver. The present study supports these observations and shows that the developing mouse responds to thyroid hormone with increased levels of endogenous EGF receptors in a known EGF target organ, the skin. Thus, one mechanism for modulation of developmental events by thyroid hormones is the modulation of growth factor receptors.

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Intrauterine Growth-Retarded Rat Pups Show Increased Susceptibility to Pulmonary O_2 Toxicity

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ABSTRACT. We used a nutritional deprivation model to produce intrauterine growth-retarded (IGR) rat pups (birth weight = ~75% of normal). The IGR newborns evidenced a marked reduction in tolerance to >95% O_2 exposure: 10-day survival = 10/47 (21%) *versus* 18/36 (50%) for control pups, and LT_{50} = 7.2 days *versus* 10 days for controls ($p < 0.01$). Various lung parameters at birth and during O_2 exposure were examined to try to define why prenatal undernutrition should compromise the survival of IGR rats in hyperoxia. We found decreased lung glutathione peroxidase and glucose-6-phosphate dehydrogenase activity (with normal superoxide dismutase and catalase levels) in the IGRs at birth; decreased lung disaturated phosphatidylcholine content (even more markedly decreased in 1-day premature pups); and decreased lung surface area/body weight. These factors and other features of newborn IGRs reported in the literature may help to explain how prenatal undernutrition compromises postnatal tolerance to prolonged high-O_2 exposure. (*Pediatr Res* 19: 281–286, 1985)

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Abbreviations

IGR, intrauterine growth retardation
SOD, superoxide dismutase
CAT, catalase
GP, glutathione peroxidase
G-6-PD, glucose-6-phosphate dehydrogenase
DSPC, disaturated phosphatidylcholine
PL, phospholipid
ISA, internal surface area
V_L, lung volume
L_m, linear intercept

Small for gestational age or IGR infants are believed to experience periods of *in utero* undernutrition (produced by a diversity of pathological conditions), and due to perinatal difficulties may require prolonged O_2 therapy after birth (1, 2). Acute and chronic lung damage resulting from prolonged treatment with high concentrations of O_2 is a frequently encountered problem in sick newborns (3, 4). The ability of newborn rat pups to tolerate prolonged exposure to high levels of O_2 is seriously compromised by postnatal undernutrition (5). We wondered if IGR, or prenatal undernutrition, would also have an effect on the newborn's ability to tolerate hyperoxic challenge. We describe herein studies which indicate that nutritional deprivation *in utero* results in significantly compromised neonatal tolerance to hyperoxia. We also discuss the results of studies which were done to try to help us understand why prenatal growth retardation should detrimentally affect postnatal ability to resist pulmonary O_2 toxicity.

METHODS

Pregnant animals. Adult Sprague-Dawley albino female rats were originally obtained from Charles River Laboratories, Wilmington, MA and were maintained in our rat breeding rooms at the University of Miami Animal Care Facility. Timed-pregnancy rats were obtained by housing (2) female rats with a male rat overnight, and using a sperm-positive vaginal smear the next morning to indicate pregnancy. The midpoint of the cohabitation period was considered as the time of conception. The pregnant rats were then housed separately and kept on water *ad libitum* and standard Laboratory Chow (Rodent Lab Chow 5001, Ralston-Purina, St. Louis, MO) either *ad libitum* (normally nourished controls) or from the midpoint of pregnancy (day 11) onward were restricted to ~25% of the dietary intake of the control pregnant rats (IGR group).

Newborn rat pups and exposures to hyperoxia. Within 6 h of birth the normal and IGR pups from all the litters used were pooled together briefly in a specially constructed "rat pup incubator" consisting of a cloth-lined wire box atop a gently rocking shaker bath unit (Dubnoff Metabolic Shaking Bath, Precision Scientific, Chicago, IL). The temperature in the incubator was maintained at 33–35° C with heat lamps. The pooled pups were then randomly redistributed to the individually caged dams in litter sizes of 10–11 pups/dam. (Only dams which had been on an *ad libitum* feeding protocol during pregnancy were used.) Half of the litters with their dams were placed in hyperoxic exposure chambers (>95% O_2), and half were kept in room air chambers. The rat pups were in the chambers continuously for 7–10 days except for a 10- to 15-min period daily when the pups were removed for weighing and the dams were switched between O_2 and air litters. This was necessary to avoid pulmonary O_2 toxicity in the nursing mother rats. Dams were carefully observed, and any dam who appeared to be rejecting a litter was replaced with an extra nursing dam kept especially for this purpose. (This was only necessary once; rat dams are very good "foster mothers").

Exposures were conducted in 3.5 ft^3 chambers constructed from modified clear-plastic nursery isolettes (model 86, Air Shields-Narco, Hatboro, PA). The chamber conditions were carefully monitored throughout the exposures (96–98% O_2—Beckmann oxygen analyzer, model OM-11; <0.5% CO_2—Beckmann medical gas analyzer, model LB-2; 23–26° C, in-chamber thermometers; 50–70% humidity, in-chamber hygrometers).

Lung preparations. The control and IGR pups were monitored daily for survival. After 5 days in >95% O_2 (or 21% O_2) some of the pups were removed and killed by intraperitoneal injection of pentobarbital sodium followed by exsanguination. In some pups the lungs were immediately cleared of blood by perfusion with cold isotonic buffer (0.1 M potassium phosphate, 0.15 M KCl, pH 7.4) through the pulmonary artery, with the left atrial appendage removed for drainage. These lungs were then weighed and homogenized in cold hypotonic buffer (0.005 M potassium phosphate, pH 7.8) (25:1, v/w) for biochemical analyses described below. The lungs of other rat pups were formalin-fixed *in situ* for microscopic study. Ten percent buffered formalin was infused via a tracheal cannula at a constant pressure of 20 cm H_2O to inflate the lungs. After fixation in the inflated state for 48 h, similarly oriented sections of each lobe were prepared for hematoxylin and eosin staining and subsequent microscopic examination (see below). Similar lung preparations were carried out in newborn pups from both groups.

Biochemical analyses. Fresh homogenates from the perfused lungs were assayed for superoxide dismutase (SOD) activity by the ferricytochrome c method (6) and for lung DNA (7), RNA (8), and protein (9) content, using purified DNA, RNA, and bovine serum albumin as standards (Sigma Chemical Co., St. Louis, MO). Analyses for lung catalase (CAT) (10), GP (11), and G-6-PD (12) activity were done on the 15,000 × *g* 10 min homogenate supernatant fluid stored frozen overnight.

Lung PL and DSPC assays utilized initial lipid extraction of lung homogenates by the method of Bligh and Dyer (13). The extracts were dried under nitrogen, reconstituted with chloroform:methanol (2:1), and assayed for total lipid phosphorus following the method of Morrison (14). A portion of the dried lipid extract in chloroform:methanol (2:1) was used to isolate DSPC by the method described by Mason *et al.* (15). An internal standard of [^{14}C]-DSPC was added before extraction to estimate and correct for losses during the isolation of DSPC (New England Nuclear, Boston, MA).

Microscopic studies. Microscopic sections were evaluated by light microscopy at 450× magnification. An eye-piece with a simple square-grid pattern was used (square grid with five horizontal lines and 25 intercept bars, model CPLW 10×/18 eyepiece, Zeiss Optical, West Germany). A minimum of 30 lung

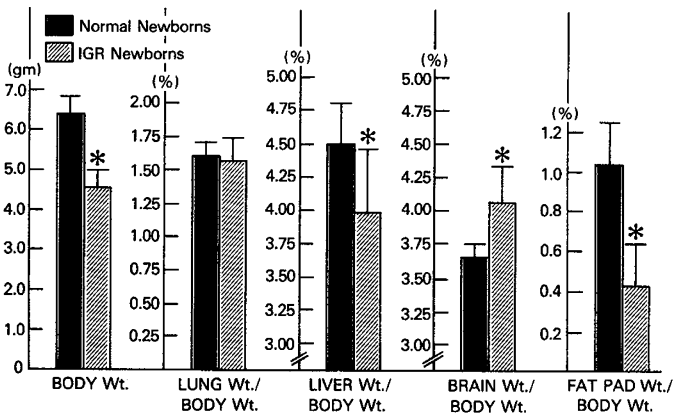

Fig. 1. Body weights and organ weights/body weight in newborn rat pups. The effect of prenatal undernutrition is shown in comparison of gravimetric parameters between IGR newborns and newborns from normally nourished pregnant rats. Values are means (n = 30–36) with 1 SD *bar*; * $p < 0.01$ between newborn groups.

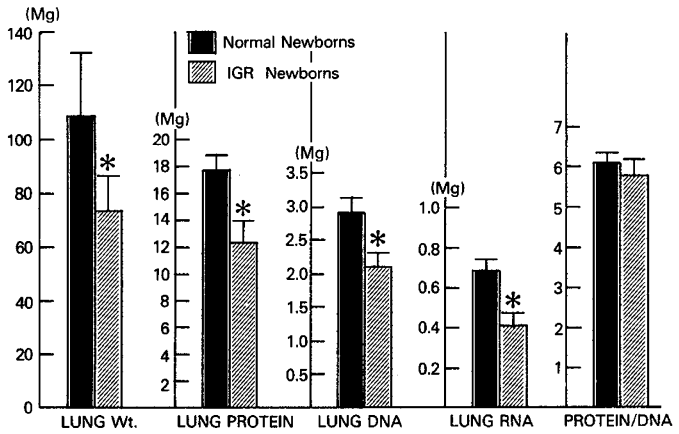

Fig. 2. Lung biochemical parameters in newborn rat pups. The effect of prenatal undernutrition is shown in comparison of lung protein, DNA, RNA contents, and protein/DNA ratio (related to lung cell size) between IGR newborns and newborns from normally nourished pregnant rats. Values are means ($n = 12$) with 1 SD *bar*; * $p < 0.01$ between newborn groups.

fields from each of three different lung sections (left lung, right middle lobe, and right lower lobe) per animal were examined, with four to six animals used per group. To calculate the mean L_m (representing the average distance between alveolar walls) we used the formula $L_m = n \cdot L/\xi i$, where n is the number of lines counted, L is the length of the line, and ξi is the sum of alveolar intercepts (16). To calculate the ISA we used the formula $ISA = 4 \cdot V_L/L_m$ (16), where V_L is the postfixation lung volume by water displacement (17). All of the coded slides were examined by two of the authors.

Statistical analysis. For comparisons of differences between the control and IGR rat pups, Student's unpaired *t* analysis was done; *p* values of <0.05 were considered statistically significant. Differences in survival rates were determined at the $p < 0.05$ level by χ^2 testing (18). The Litchfield-Wilcoxon graphic analysis test (19) was used for calculation of LT_{50} values (lethal time for 50% of the experimental animals in each group), 95% confidence limits, and for determining significant differences in the LT_{50} values at the $p < 0.05$ level.

RESULTS

The experimental model for producing IGR newborn rat pups was quite replicable. There were <10% stillborn fetuses found in the large number of pregnant rats put on the 25% food intake diet. Litter size averaged 10.5 *versus* 11.2 pups/litter in the controls. Figure 1 indicates that the average body weights of IGR pups at birth were ~25–30% lower than for normal pups. While absolute organ weights (lung, liver, brain, dorsal fat pad) were all significantly lower in the IGR pups, when expressed as the ratio of organ weight/body weight (Fig. 1) the lung weights were equivalent in the two groups of pups, while liver and especially fat pad weights were decreased but brain weight/body weight was increased in the IGRs.

Figure 2 shows that the lungs of the IGR pups had significantly depressed protein, DNA, and RNA content compared to the normal pups. However, when these were calculated on a per lung weight basis, lung protein/, lung DNA/, and lung RNA/g lung were similar in both groups, as were the protein/DNA ratios in the IGRs (5.80 ± 0.31) and control pup lungs (6.02 ± 0.29) which suggests that the IGR lungs had fewer cells, but cells of equal size to those of the normal newborn animals.

Figure 3 indicates that prenatal undernutrition did not impair the postnatal growth of the IGR pups nurtured by dietary replete dams. These pups grew as well as the normal pups maintained in air or exposed to hyperoxia, as seen by the parallel growth curves.

Figure 4 shows the comparative survival rates of the two groups of pups simultaneously exposed to hyperoxia. The IGR pups tolerated high O_2 more poorly than the normal pups, with significantly depressed survival rates at all exposure times between days 6 and 10. The LT_{50} (with 95% confidence limits) was reduced from 10 days (8.68–11.52) in the normal rats to 7.2 days (6.21–8.35) in the IGR group ($p < 0.05$). Only 21% of the IGRs survived 10 days in >95% O_2 compared to 50% of the control neonatal pups ($p < 0.005$).

To look for some biochemical/physiological/morphological explanation for the increased susceptibility of the IGRs to O_2 toxicity, we assayed the lung antioxidant enzymes, lung surfactant, and lung morphometry in the two groups at birth. The data in Table 1 indicates no difference in the activities of the antioxidant enzymes SOD and CAT, but significantly reduced GP and

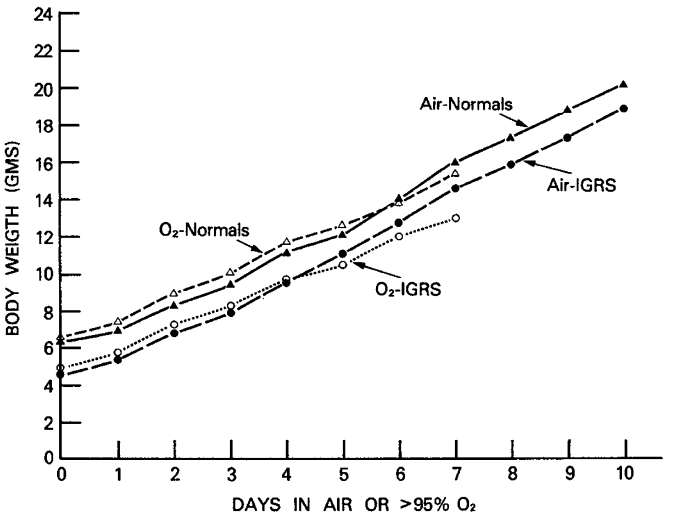

Fig. 3. Growth curves of newborn rat pups. Body weight changes in IGR pups and pups from normally nourished pregnant rats are shown, both for groups maintained in room air environment and for those exposed to >95% O_2 from the time of birth. All pups after birth were nurtured by normally nourished dams. Values represent composite data from ~60 rat pups per group (for the first 7 days of life).

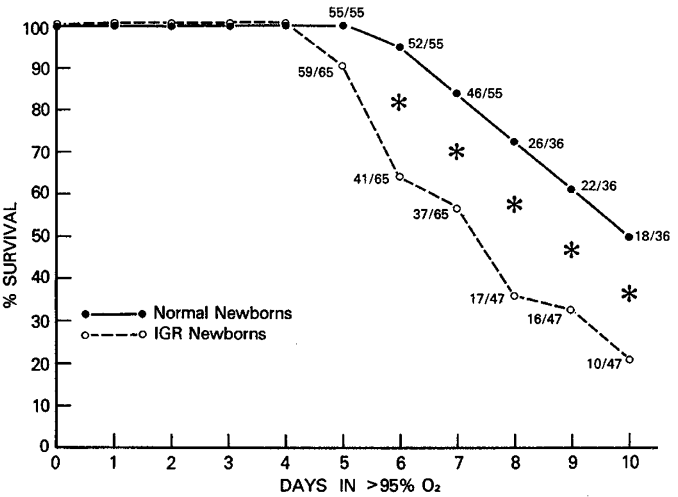

Fig. 4. Survival of normal and IGR rat pups in hyperoxia. Comparative 10-day survival rates in >95% O_2 for newborn IGR pups and pups from normally nourished pregnant rats. Numbers are no. surviving/no. exposed to O_2. * $p < 0.01$ for comparative survival values between groups, days 6–10, by χ^2 testing.

G-6-PD in the lungs of the newborn IGR rats. Lung phospholipid content was apparently unaffected by the intrauterine nutritional deprivation in the IGRs (Table 1), but the DSPC content was decreased by 11–12% in the IGR pups lungs ($p < 0.05$) as was the DSPC/PL ratio. In comparing the lung structure in the two groups of newborns (Table 2), we found that the IGRs had approximately a 25% decrease in lung volume (V_L) which was matched by an approximately 25% decrease in lung ISA for respiratory exchange. When the morphometric values were normalized for the difference in body size between the IGR and control pups (V_L- and ISA-specific), a slight but significant reduction in the normal surface area for respiratory exchange was found in the IGR lungs at birth (Table 2).

We additionally looked at the comparative effects of hyperoxic exposure on lung biochemical parameters including the responses of the protective antioxidant enzyme systems, and also at the effects of high O_2 on the structure of the growing lung in both neonatal pup groups.

The data in Table 3 reflects the anticipated inhibitory effect of hyperoxia on lung biosynthetic processes, with depressions of lung protein, DNA, and RNA in both groups of rat pups to essentially an equivalent degree. The results listed in Table 3 also show that the pulmonary antioxidant enzyme response to hyperoxia in the IGRs was no different than the control neonates' responses, with equivalent significant elevations of SOD (~50%), CAT (~75%), GP (~140%), and G-6-PD (~90%) activities. The morphometric data (Table 4) indicate marked O_2-induced decreases in (specific) lung volume and ISA, but the inhibitory effects of O_2 on the growing lung were comparable in both neonatal pup groups.

Table 1. *Lung biochemical parameters in newborn normal and IGR rat pups**

Group	Antioxidant enzymes†			
	SOD	CAT	GP	G-6-PD
Normal newborns	57.6 ± 3.9	548 ± 42	2.49 ± 0.30	0.990 ± 0.087
IGR newborns	59.4 ± 3.9	517 ± 59	2.02 ± 0.26‡	0.846 ± 0.069‡

Group	PL (μg/mg protein)	DSPC (μg/mg protein)	DSPC/PL (%)
Normal newborns	194 ± 17	53.2 ± 6.8	
IGR newborns	196 ± 16	47.2 ± 5.8‡	24.0 ± 2.1‡

* Values for newborn pups from normally fed pregnant rats and from pregnant rats restricted to 25% of normal food intake throughout second half of pregnancy. Values = mean ± 1 SD for nine to 12 samples per group (three experiments).

† Lung SOD (U/mg DNA), CAT (IU/mg DNA), GP (μmol NADPH oxid/min/mg DNA), and G-6-PD (μmol NADP red/min/mg DNA) activities.

‡ $p < 0.05$ for IGRs compared to normal newborns.

DISCUSSION

Animal model for IGR. In humans, a variety of untoward factors have been associated with the delivery of low birth weight, small for gestational age infants (1, 2, 20, 21). The more common conditions include medical complications of pregnancy such as toxemia, chronic hypertension, continuous medication with corticosteroids and other growth-retardant drugs, and excess cigarette smoking, teen-age pregnancy, and perhaps exposure to environmental toxins. The common denominator in all these conditions, and in experimental IGR, is believed to be compromised blood flow to the fetal-placental unit with consequent depression of nutrient supply to the developing fetus (4, 5, 20–22). Experimentally, unilateral ligation of the uterine artery, chronic exposure of the pregnant animal to hypoxia, partial nephrectomy, and dietary manipulations have all been used to compromise the nutrient (and O_2) supply to the fetuses (20–23). Our choice of IGR dietary protocol, supplying approximately 25% of the normal food intake during the 2nd half of pregnancy, was successful in producing a rather consistent 20–30% reduction in newborn birth weight without producing the excess fetal wastage which is a problem with the surgical and hypoxia models (23).

Effect of nutrition on pulmonary O_2 toxicity. Recently, much overdue attention in the literature is being focused on the influence of altered nutrition on O_2 tolerance/susceptibility; nutritional support of O_2-requiring neonates has been criticized as woefully inadequate, due perhaps to the concentration of time and attention required for ideal respiratory care, and the problems involved in use of the parenteral route for nutrition. Its now been shown in both experimental and clinical studies that failure to provide adequate caloric maintenance may have serious aggravating effects on O_2-induced lung damage (5, 24–26). We have recently demonstrated in normal newborn rats that hypocaloric undernutrition will consistently reduce the tolerance of

Table 3. *Lung biochemical parameters in air and O_2-exposed normal and IGR rat pups**

Group	Lung wt (mg)	Lung protein (mg)	Lung DNA (mg)	Lung RNA (mg)
Normals in air	153 ± 11	21.5 ± 1.3	3.38 ± 0.28	1.61 ± 0.15
Normals in O_2	145 ± 18	19.1 ± 2.8	2.32 ± 0.62†	1.29 ± 0.17†
IGRs in air	106 ± 16	16.2 ± 3.1	2.42 ± 0.22	1.23 ± 0.15
IGRs in O_2	109 ± 10	13.9 ± 0.8	1.63 ± 0.29†	0.99 ± 0.09†

	Antioxidant enzymes			
	SOD	CAT	GP	G-6-PD
Normals in air	61.5 ± 3.8	453 ± 29	2.69 ± 0.31	1.15 ± 0.12
Normals in O_2	94.3 ± 22.5†	837 ± 136†	6.48 ± 1.98†	2.13 ± 0.44†
IGRs in air	62.8 ± 10.0	493 ± 84	2.41 ± 0.52	1.11 ± 0.11
IGRs in O_2	93.8 ± 13.5†	825 ± 204†	5.61 ± 1.17†	2.15 ± 0.42†

* Values for pups exposed to >95% O_2 or 21% O_2 from birth to age 5 days; mean ± 1 SD for six to eight animals per group.

† $p < 0.01$ for comparisons of O_2-exposed to air-exposed pups for each subgroup.

Table 2. *Lung morphometry in newborn normal and IGR rat pups**

Group	V_L (ml)	V_L-specific (ml/100 g body wt)	% Air space	L_m (μm)	ISA (cm^2)	ISA-specific (cm^2/100 g body wt)
Normal newborns	0.256 ± 0.021	4.20 ± 0.36	69.6 ± 1.5	53.8 ± 2.0	18.1 ± 1.6	300 ± 22
IGR newborns	0.195 ± 0.018	3.93 ± 0.33	68.6 ± 2.3	54.9 ± 2.4	13.8 ± 1.2	278 ± 21
	$p < 0.005$	NS	NS	NS	$p < 0.001$	$p < 0.025$

* Values for newborns; mean ± 1 SD for three lung sections (30 hpf/section) from five animals per group.

Table 4. *Lung morphometry in O_2-exposed normal and IGR rat pups**

Group	V_L (ml)	V_L-specific (ml/100 g body wt)	% Air space	L_m (μm)	ISA (cm^2)	ISA-specific (cm^2/100 g body wt)
Normal air	0.63 ± 0.04	5.32 ± 0.08	72.8 ± 0.2	34.8 ± 3.0	72.9 ± 1.9	608 ± 21
Normal O_2	0.55 ± 0.05	4.51 ± 0.28†	78.9 ± 1.3†	46.8 ± 4.8†	47.4 ± 8.9†	390 ± 61†
IGR air	0.50 ± 0.07	5.54 ± 0.38	73.5 ± 0.9	41.0 ± 1.7	53.0 ± 1.1	555 ± 22
IGR O_2	0.39 ± 0.01†	4.53 ± 0.05†	78.5 ± 0.1†	48.4 ± 3.9†	31.4 ± 5.1†	354 ± 105†

* Values for pups exposed to >95% O_2 or 21% O_2 for 5 days; mean ± 1 SD for three lung sections (30 hpf/section) from three animals per group.
† $p < 0.05$ for comparison of air and O_2-exposed pups from same subgroups.

the pups to hyperoxic exposure during the 1st wk of life (mortality increased from 27% in normally nourished rat pups to 56% in the undernourished group) (5). Postnatal undernutrition also has additive effects with hyperoxia in inhibiting lung growth potential and may further compromise the lung's ability to repair O_2-induced damage (5, 25–28). Clinically its been observed that respiratory-distressed infants who were provided with more normocaloric parenteral nutrition had a much better outcome than a control group of similarly sick infants on O_2 therapy whose nutritional support consisted only of sugar and electrolyte solutions early in life (24).

Whether the prolonged stress of prenatal undernutrition might also negatively influence the ability of the newborn to withstand toxic high O_2 challenge, has not (to our knowledge) been previously investigated. Since a proportion of the lower birth weight population which are considered especially prone to suffer serious O_2-associated lung damage (BPD) are likely to have developed in a compromised *in utero* environment, the influence of prenatal nutritional deficiency and growth retardation on the course of these O_2-exposed neonates deserves experimental study.

Reasons for decreased hyperoxic tolerance of IGR rat pups. We consistently found that the IGR rat pups produced by the animal model we used were more susceptible to O_2-induced lethality, with a significantly reduced LT_{50} in hyperoxia of 7.2 days compared to 10.0 days for the rat pups normally nourished *in utero*. We investigated several possible mechanisms to try to define the reason(s) for the impaired O_2 tolerance in the IGR pups. We found the lung surfactant (DSPC) content to be slightly but significantly depressed in the IGRs at birth. Surfactant production had apparently been delayed in maturation since gestational day 21 DSPC values were found to be even more markedly lower in the IGR than in the normally nourished fetal rat lungs [values for 1-day premature pups = 23.6 ± 2.7 (IGRs) *versus* 37.1 ± 7.0 μg/mg protein (normal controls), $n = 8$, $p < 0.01$]. Since O_2 exposure tends to inhibit surfactant synthesis (29, 30), if the O_2-exposed IGRs were less able to compensate for the effect of hyperoxia by increasing surfactant production rates as readily as normally nourished pups, this could compromise their lung function and perhaps contribute to their diminished O_2 tolerance.

The lung's primary defensive system against O_2 toxicity—the antioxidant enzymes—did show differences in the two groups of newborns, with significantly reduced lung GP and G-6-PD activities in the IGRs. GP is believed to play the key role in the lung in detoxifying cytotoxic H_2O_2 and also, together with G-6-PD and the enzyme glutathione reductase, is important for its role in detoxifying lipid peroxides produced by the interaction of reactive O_2 species and unsaturated lipids in the cell (31, 32). These enzyme deficits could have contributed to the early production of O_2-induced lung injury in the IGR pups. Although by 5 days of O_2 exposure the IGR pups had responded appropriately to hyperoxia with adaptive increases of all the antioxidant enzymes (Table 3), nonetheless, even transient early depression of the glutathione detoxification system has recently been reported to seriously compromise tolerance to prolonged O_2 exposure (33).

Except for the changes we found in lung GP and G-6-PD levels at birth, the moderate decrease in lung surfactant (DSPC) content, and the morphometric evidence for reduced specific ISA at birth, we at this point have no clear-cut explanation for the decreased O_2 tolerance of the IGR pups. The cyanotic appearance, gasping respirations, and nasal frothing of the pups just prior to their deaths, together with the grossly swollen appearance of the lungs clearly indicated to us a pulmonary cause for their demise. In examining the literature for other parameters that are different in normally nourished and growth-retarded newborns we have found the following data which could partially explain the accelerated pulmonary O_2 toxicity in the IGR pups: (1) small for gestational age newborns are reportedly in a relatively hypermetabolic state with increased rates of O_2 consumption—experimentally produced hypermetabolism with increased O_2 consumption results in greater O_2-free radical production and an acceleration of O_2 toxicity (30, 32, 34, 35); (2) IGR rat pups reportedly have depressed capacity for ATP synthesis (36), and depressed capacity for DNA synthesis and cell proliferation (37, 38)—both of these characteristics could be important in depressing the repair response to ongoing O_2-induced lung cell injury; and finally, (3) purely postnatal adaptations in other organs (brain myelination) have been found to be altered by malnutrition during the prenatal period only (39).

Further studies will obviously need to be done to understand why prenatal malnutrition appears to have as marked a detrimental effect on tolerance/susceptibility to pulmonary O_2 toxicity as postnatal nutritional deficiency is now known to have.

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Composition and Surface Activity of Normal and Phosphatidylglycerol-Deficient Lung Surfactant

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ABSTRACT. The possibility that pulmonary surfactant, characterized by a phosphatidylglycerol deficiency, as in early fetal life, might have inferior surface properties was evaluated. We obtained this specific surfactant from adult rabbits by withholding glucose and giving them an excess of myoinositol by mouth and intravenously. Controls were given a similar quantity of glucose. The myoinositol resulted in a drastic reduction of surfactant phosphatidylglycerol, from 7.2 to 0.3% of phospholipids, and a corresponding increase in phosphatidylinositol from 4.8 to 11.3%. In addition, the myoinositol treatment increased the myoinositol that was disaturated from 18.5 to 27.3% ($p < 0.05$). The corresponding figures for disaturated phosphatidylcholine were 56.0 and 60.5%, respectively (NS). The myoinositol treatment for 4 days increased the pool size of alveolar surfactant by 32% ($p < 0.01$). The surface activity was studied with modified Wilhelmy balance and the pulsating bubble surfactometer. Surfactant containing phosphatidylinositol rather than phosphatidylglycerol was not inferior, as compared to surfactant that contained phosphatidylglycerol (minimum surface tension: 2.0 *versus* 2.2 $mN \cdot m^{-1}$; collapse rate at 10 $nM \cdot m^{-1}$: 1.85 *versus* 1.95 min^{-1}; rate of adsorption from subphase to surface: 32 *versus* 35 $mN \cdot m^{-1} \cdot 30\ s^{-1}$), nor was there a difference in the ability of the two surfactants to improve lung stability of 27-day-old rabbit fetuses (air retention at 35 cm H_2O: 1.8 *versus* 1.8 ml/30 g; air retention at 0 cm H_2O: 0.8 *versus* 0.9 ml/30 g). We conclude that phosphatidylinositol surfactant does not have inferior surface properties. Myoinositol affects not only the acidic surfactant phospholipids but also increases the pool size of surfactant by an as yet unknown mechanism. (*Pediatr Res* 19: 286–292, 1985)

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