fetus takes place from a relatively small area of capillary bed in which we deduce that hydrostatic pressure is elevated. In the newborn lamb, the results suggest a lower capillary pressure and larger capillary bed than in the fetus. The pulmonary vascular bed of the fetus, we conclude, may contain large unperfused areas; and vasodilation at birth may take place mainly by recruitment of additional areas. There is support for these ideas in the very nonlinear pressure-flow curves characteristic of the fetal and neonatal circulation: they suggest the presence of unperfused areas which are recruited when inflow pressure is increased.

The fluid in the fetal acini is not a plasma filtrate. Its formation depends on active Cl- transport across the alveolar epithelium. The epithelium also forms a barrier to the passive penetration of most plasma solutes and therefore to the passive accumulation of liquid. Absorption of lung liquid at birth requires changes in the pulmonary epithelium, only some of which have yet been identified.

REFERENCES


Pulmonary Vascular Responses during Advancing Gestation in Fetal Lambs in utero*

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PREVIOUS STUDIES on the responses to hypoxemia or vasoactive substances of the fetal pulmonary circulation were performed in exteriorized, anesthetized animals. We designed a study to examine pulmonary vascular responses to graded hypoxemia and to the injection of acetylcholine in fetal lambs in utero during advancing gestation.

METHODS

Time-dated pregnant sheep with gestational periods of 100-138 days were studied. Under low spinal anesthesia to the ewe, polyvinyl catheters were inserted into fetal arteries and veins. Through a left thoracotomy, the main pulmonary artery or the left pulmonary artery was isolated. A snug-fitting, precalibrated electromagnetic flow transducer was placed around one of these arteries (Fig 1). Flow measurements with this technique have been validated previously. Through a purse-string suture in the pulmonary trunk, adjacent to the origin of the main pulmonary artery, a polyvinyl catheter was inserted and directed into the main pulmonary artery (Fig 1). The incisions were closed and all catheters and the transducer cable led to a pouch sewn to the maternal flank. The fetus and ewe were allowed to recover and studies were performed 3-12 days after surgery. Flow, measured with a Statham SP2300 flowmeter, and pressures, measured with Statham P5310R pressure transducers, were recorded on a Beckman dynograph recorder.

Fetal hypoxemia was produced 26 times in 15 animals by lowering the maternal FEO2 from 0.21 to 0.06. Hypocarbia was prevented by adding 5 percent CO2 to the mixture. Acetylcholine was either injected (0.4-5.7 μg/kg) as a slow bolus or infused (7 μg/kg/min) into the superior vena cava in 9 fetuses.

RESULTS

Flow Patterns

Phasic pulmonary arterial blood flow in the fetus was forward only in the first third of systole and backward

FIGURE 1. Diagrammatic view of operative field. The electromagnetic flow transducer has been placed around the main pulmonary artery (Main PA) which arises from the main pulmonary trunk and divides almost immediately into the left main (LPA) and right main (RPA) pulmonary arteries. RV = right ventricle.
during late systole and early diastole. This contrasts with neonatal lambs in which flow is forward throughout systole. These configurations are compatible with a high fetal pulmonary vascular resistance and low pulmonary vascular resistance in the neonatal lamb.

Effects of Hypoxemia

Pulmonary arterial blood pH and Pco2 were normal and unaltered throughout. Po2, averaged 39 mm Hg before and varied from 10-13 mm Hg during hypoxemia. Pulmonary blood flow fell in all fetuses (Fig 2). In the gestational periods 103-104 days and 112-119 days, this was not significant. In the two older groups, the fall was significant (P < 0.05 paired t test), but there was no difference between the groups. Calculated pulmonary vascular resistance increased in all animals (Fig 2), but again was significant only in the two older groups.

The pattern of the increase of pulmonary vascular resistance to hypoxemia was clearly related to gestational age. In the 103-day-gestation lamb, a progressive decrease in pulmonary arterial blood Po2 produced only a small increase in resistance below a Po2 of 12 mm Hg. With advancing gestation the maximal increase in resistance was greater and occurred with progressively smaller Po2 reductions, and the relationship between the percentage of increase in resistance and Po2 was curvilinear. Alpha and beta adrenergic and parasympathetic blockade did not alter the hypoxic response.

Effects of Acetylcholine

Acetylcholine produced an increase in pulmonary blood flow due to a fall in pulmonary vascular resistance. The phasic flow recordings during the infusion of acetylcholine were very similar to those of a neonatal lamb. The response to acetylcholine was also age-dependent with the more mature fetuses showing a greater change than the immature fetuses.

Discussion

These studies were performed on chronically instrumented fetal lambs in utero. The phasic flow pattern closely paralleled the level of pulmonary vascular resistance; forward flow occurred only in early systole when the resistance vessels were constricted and forward flow occurred throughout systole when the resistance was reduced.

Both the constrictor response to hypoxemia and the dilator effect of acetylcholine were age-dependent, the less mature animals showing less effect. The amount of smooth muscle in each resistance vessel does not change during the period of gestation under study; therefore, the decreased responsiveness in early gestation is likely to be due to lack of development of the mechanisms or receptors whereby the pulmonary resistance vessels are controlled.

References

Effects of Prostaglandin Precursors, Prostaglandins, and Prostaglandin Metabolites on Pulmonary Circulation of Perinatal Goats*

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The mammalian lung is capable of synthesizing, reabsorbing, and metabolizing highly vasoactive prostaglandins (PGs) of the E- and F-series.1,2 We have suggested that prostaglandins play a role in regulation of