For studying early development, the mouse embryo provides a convenient experimental model. Of particular interest is the transition from the cleavage (day 2) to the blastocyst (day 3) stage of development, a period of concurrent morphologic and molecular change. In addition to striking alterations in the activities of several enzymes, there is a marked change in the capacity of embryos incubated *in vitro* to take up uridine, a nucleoside precursor of RNA. The incorporation of ^{3}H-uridine into the acid soluble pool follows Michaelis-Menten kinetics, and the maximal uptake (V_{max}) is 8-fold greater in day 3 than in day 2 embryos. During the same time there is also an increase in the incorporation of ^{3}H-uridine into embryonic RNA. To distinguish a real increase in RNA synthetic capacity from an apparent increase resulting from greater precursor uptake, embryos were incubated in the presence of varying concentrations of ^{3}H-uridine. In day 3 embryos, saturation of the RNA synthetic system occurs prior to saturation of the transport system, and incorporation of uridine into RNA is independent of precursor concentration $\geq 1\ \mu$M. However, this is not the case in day 2 embryos: uridine incorporation into RNA parallels the uptake of uridine into the acid soluble pool. Therefore, it appears that the low rate of uridine incorporation into RNA by day 2 embryos is at least partially attributable to the low rate of precursor uptake. Since preimplantation mouse embryos develop *in vitro* in the absence of uridine, the physiological role of the uridine transport system during this period is uncertain. Nonetheless, the preimplantation change in uridine transport is a striking developmental phenomenon and may be important in preparing the embryo for the utilization of exogenous nutrients during postimplantation growth and development.

31 *Circulation and its Distribution in Previable Human Fetuses.* MICHAEL A. HEYMANN, ABRAHAM M. RUDOLPH, KARI TERAMO, CYNTHIA T. BARRETT and NIELS RAIHA, Univ. of California, San Francisco and Helsinki Univ. Central Hosp.

The course of the circulation, distribution of cardiac output and organ blood flow have been extensively studied in fetal lambs. No such information is available in human fetuses. 33 fetuses weighing 12–272 g (estimated gestation 10–20 weeks) were delivered by hysterotomy performed for legal abortion with the mother receiving general anesthesia and 50% O_2. While placental circulation continued, a fine teflon cannula was inserted into the umbilical vein (UV), and nuclide-labeled microspheres were injected (within 3 min in most fetuses) to measure the distribution of blood flow. pH, PO_2 and PCO_2 were measured in arterialized maternal (MA) and in UV and fetal arterial (FA) bloods. Mean values for MA were pH 7.47, PCO_2 23, and PO_2 183, for UV pH 7.41, PCO_2 26, and PO_2 60, and FA pH 7.27 PCO_2 38 and PO_2 34. Distribution of blood flow to each organ was expressed as a percentage of systemic venous return (%CO) in 4 weight groups <50 g, 51–100, 101–150 and >150 g. The % CO to placenta increased from a mean of 16.9 in <50 g to 33.1 in >150 g fetuses; %CO to gut rose from 5.5 to 9.2 and to spleen from 0.4 to 0.9; %CO to kidneys fell from 6.5 to 3.2, myocardium 3.3 to 2.1, and brain 16.0 to 11.3. An average of 51.4% of UV blood passed through the ductus venosus; no significant change with growth was noted. In <50 g fetuses 50.7% of inferior vena caval blood crossed the foramen ovale to be distributed to the upper body, brain and myocardium; this fell to 32.3% in the >150 g group. These studies demonstrate that the pattern of circulation in human fetuses is similar to that of other mammals, but there are quantitative differences in distribution of cardiac output. (Supported by NIH Grant HE 06285).

32 *The Actions of Cardioactive Drugs on Developing Myocardium.* WILLIAM F. FRIEDMAN, CHARLES COOPER, TOMÁS ROMERO, Univ. of Calif.-San Diego, Sch. of Med., La Jolla, Calif.

Clinicians have long recognized age related differences in cardiac pharmacology. These phenomena may reflect altered drug metabolism or disposition in the immature organism and/or an altered sensitivity of fetal and neonatal myocardium per se. The latter possibility was examined by studying the responsiveness to cardioactive drugs of heart muscle isolated from a total of 100 fetal, newborn, and adult sheep and swine. The enhancement of cardiac contractility produced by digitalis was significantly greater in newborn than adult heart. However, newborn myocardium required significantly more digitalis to achieve a peak inotropic effect or to demonstrate evidence of toxicity when compared to the adult. Fetal and adult cardiac muscle was equally responsive to isoproterenol, and acetylcholine. Fetal heart was supersensitive to the positive inotropic effects of norepinephrine. At all ages acidosis attenuated the augmentation of contractility produced by norepinephrine. Propranolol exerted a more profound negative inotropic action on fetal than adult heart, although the effectiveness of beta adrenergic receptor blockade by propranolol was equal in fetal and adult myocardium. Glucagon exerted a negative inotropic effect on fetal cardiac muscle, a small positive inotropic effect in newborns, and a marked augmentation of contractility in the adult. Thus, a marked age-dependency of the myocardial responses to many cardioactive drugs exists that must be considered in any clinical evaluation of cardiac pharmacology in the perinatal period.

33 *Cardiac Responses to Sympathetic and Vagal Stimulation in the Newborn Lamb During Acidosis and Hypoxia.* ELLIOT A. MILGRAM, KATHERINE H. HALLORAN, NORMAN S. TALNER, ALEXANDER G. M. CAMPBELL and S. EVANS DOWNING, Yale Univ. Sch. of Med., Depts. Path. and Ped., New Haven, Conn.

Heart rate (HR) and left ventricular contractility (VC) responses to sympathetic and vagal nerve stimulation were assessed in 15 lambs from <1 to 3 days of during lactic acidemia, hypercapnia and hypoxemia. These were compared with responses under control conditions. In all experiments supramaximal electrical stimulation of the left inferior cardiac sympathetic nerve produced large increases of VC as measured by the dP/dt max from a given end-diastolic pressure (LVEDP) when HR, mean aortic pressure and cardiac output (Medicon) were held constant. With a pH of 7.39 the dP/dt max increased from 3,000 ($\pm$155 SE) to 4,244 ($\pm$147 SE) mm Hg/sec during stimulation, while the LVEDP fell from 7.3 ($\pm$0.73 SE) to 5.8 ($\pm$0.79). During acidemia the increase (1,310$\pm$159 SE) was unchanged. With hypercapnia (PCO_2 69 mm Hg) the responses were less (840 mm Hg/sec) than with low PCO_2 (1,300 mm Hg/sec, $p < 0.01$). Responses during hypoxemia (PO_2 33 mm Hg) were identical to those with normal PO_2. Cardiac slowing in response to stimulation of the right distal vagus N was measured