Mimicking the placenta with computer models

Even with considerable cross-fertilization between scientific specialties, only a handful of chemical engineers are turning from traditional industrial "hard hat" challenges to "green mask" ones—creating biomedical instruments or bringing chemical engineering tools to bear on basic medical questions. One of the more ambitious undertakings of the latter genre is to probe and simulate functions of the placenta in engineering terms. The work was detailed last week at a national meeting of the American Chemical Society in Washington.

Increasing basic medical and clinical evidence indicates that the placenta may be a major source of many difficulties the fetus encounters during gestation or labor. If oxygen exchange is cut off by too many or too prolonged labor contractions, coupled with maternal anemia and umbilical cord difficulties, the baby may be in danger. Brain damage is especially possible, clinical, animal experiment and tissue studies indicate, since the fetus feeds almost entirely off glucose and six oxygen molecules are necessary to oxidize one glucose molecule.

Chemical engineers Daniel Reneau and Eric Guilbeau of Louisiana Tech University and their physician-physiologist co-worker Melvin Knisely of the Medical University of South Carolina have developed a theoretical model of the placenta. They are now planning to undertake animal experiments to test their simulation. The model, linked up with a computer into which many variables can be fed, will help tell them what they should look for in their experiments. They hope to determine, for example, how severe labor contractions must be to deprive the fetus of adequate oxygen and how long each contraction or total labor must be to achieve a similar effect. Many medical researchers believe that extended labor leads to oxygen deprivation. Results of the experiments will then be fed into the placental model via computer, to tell the researchers if their model assumptions correspond to the real-life situation, at least for animals. The model will be revised as necessary. Other variables will be fed in as more experiments are carried out. This breaking down of the real placental spatial dimensions and sequential functions into principles of chemistry, physics and mathematics is known in engineering terms as a systems analysis approach to biology.

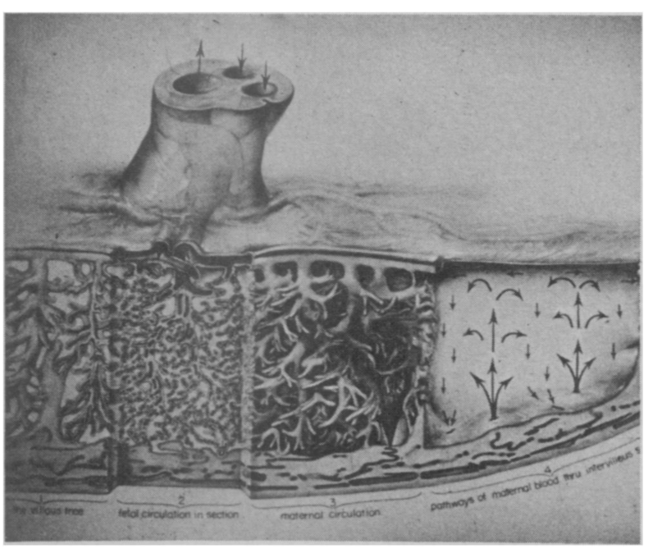
The work of Reneau, Guilbeau and Knisely represents some of the first detailed unsteady-state analyses of placental oxygen transport—analyses that take into account changes in functions of the placenta over time. But Lawrence Longo of Loma Linda University in California is concentrating on steady-state mathematical analyses of the placenta. He and his co-workers are not yet trying to consider time-induced variants in placental functions. They have not yet developed the level of sophistication in their mathematical analyses that the Louisiana researchers have, but they have already started animal experiments to test for certain assumptions incorporated into the placental model. Does resistance to placental diffusion of oxygen slow down oxygen transport to the fetus? Which factors might be most critical in slowing diffusion? What is the average rate of oxygen transfer across a single placental capillary?

To answer such questions the California workers nicked a hole in the uterine wall of a pregnant ewe, inserted a tube into a placental blood vessel, turned off the umbilical flow of blood and oxygen, then pumped oxygen into the blood vessel at different rates to determine how the placental blood vessels would react. They found that the average rate of oxygen transfer in one placental capillary transit is one and a half seconds and that the less oxygen diffusion through the placenta, the less oxygen reaches fetal blood. Results of animal experiments correlate relatively well with their original placental model assumptions.

"Longo's animal experiment work," Reneau affirms, "will help us draw up better mathematical models of the placenta."

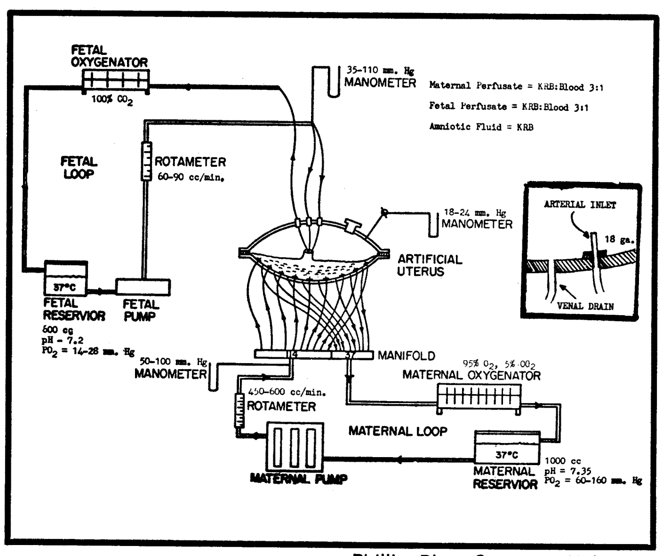
Phillip Rice and his chemical engineering team at Syracuse University are taking a somewhat different approach to placental modeling. Theirs is not just a theoretical model but a three-dimensional artificial uterus hooked up with a real placenta and oxygen perfusion pumps. The Syracuse researchers have found that at first nutrients and wastes diffuse throughout the placenta independently of the rate at which these chemicals feed into it, but that eventually the diffusion becomes dependent on the influx rate. It takes glucose from 40 to 60 minutes to reach a consistent flow between maternal and fetal blood vessels.

When fed into placental models, such data are expected eventually to give not only detailed, mathematically precise explanations of how the human placenta works but also to predict, with the help of a computer, what would happen if the placenta were placed under particular conditions or stresses. Once such models are refined for clinical use, they could provide physicians with tough preventive medicine tools—the ability to predict consequences and select alternatives before making critical medical decisions. Understanding how the placenta works, Rice says, is also necessary before a human fetus can be placed in an artificial uterus, or womb (SN: 7/5/69, p. 12). □



E. M. Ramsey, Carnegie

Placental model indicating maternal blood pathways.



Phillip Rice, Syracuse University

Real placenta-artificial uterus, with oxygen pumps.