FETOLOGY

Watching the unborn

Lambs in a man-made womb unlock secrets of uterine life and aid perfection of artificial lungs

by Barbara J. Culliton

Development of an artificial womb is a research goal that has overtones of science fiction to it. The known problems involved—nutrition requirements, regulation of the environment, the possible need for darkness or periodic motion to simulate conditions in the mother's uterus—are compounded by the many unknowns about the process of fetal development itself.

But the very unknowns are driving scientists to attempt the creation of a laboratory womb, and to study the development of the mammalian fetus in a situation where observation is possible.

A focus of the present effort is a laboratory at the National Heart Institute in Bethesda, Md., where an artificial womb has been used to keep some 35 fetal lambs alive for up to 55 hours. Out of these experiments have already come some indications that the classic theories of fetal circulation may have to be somewhat revised.

The experiments at the heart institute's Laboratory of Technical Development are also testing an artificial lung, an adjunct to the womb research, that is important in its own right.

On a recent Thursday at the NHI lab, an operating table and a clear plastic fish tank were wheeled into the laboratory and surgeons performed a cesarean section on a pregnant ewe. Then Dr. Warren Zapol pulled a squirming, kicking fetal lamb from its mother and plunged it into the waiting tank filled with synthetic amniotic fluid.

Tubes inserted in the unborn lamb's blood vessels during surgery became its umbilical cord. Through one, an intravenous solution of sugars, vitamins, heparin and protein-building amino acids slowly dripped from a jar suspended above the tank. Another connected to a compact artificial lung that supplied oxygen and carried carbon dioxide away.

Monitors showed oxygen and carbon dioxide levels were in good balance and fetal metabolism was normal.

The lamb soon settled comfortably into its new environment, kicking and turning occasionally as it would have inside its mother's body.

About three hours later, Dr. Zapol and his colleagues, Drs. Theodor Kolobow, Joseph Pierce, Gerald Vurek and Robert Bowman, wheeled the lamb to an X-ray room where they transferred it to a smaller tank, about the size of a dish pan, and with some difficulty positioned a long, flexible polyurethane catheter in its heart. While Dr. Zapol squirted radiopaque dye through the catheter, radiologist John Doppman took movies of the fetal circulatory system, showing the routes blood takes through the heart to the animal's head and body and out the umbilical cord.

"What we're seeing," Dr. Zapol enthused, "is that some of the things we learned in medical school about fetal circulation may not be true." Classical physiology holds that in a fetus only minimal amounts of blood circulate through the lungs, which do not function as an oxygen supply house until the creature begins breathing at birth. Instead, according to the theory, the major portion of blood flows from the heart through a wide-open passage called the ductus arteriosis to umbilical arteries into the placenta where it picks up fresh oxygen and deposits carbon dioxide before being recirculated through the fetus. Then, within a few hours of birth, the ductus closes, shutting off the lung by-pass.

"These first films of circulation of a fetus behaving normally in an artificial womb indicate that the ductus is not wide open," Dr. Zapol observes. "Furthermore, raising and lowering the content of oxygen in the fetal blood, we seem to be able to change the size of the ductus. And since it turns out that it is regulated by oxygen concentrations, we may now have a technique for forcing it shut in abnormal babies," he speculates, stressing that evidence at this point is extremely sketchy and will remain so until additional experiments are conducted next fall when more pregnant ewes become available.

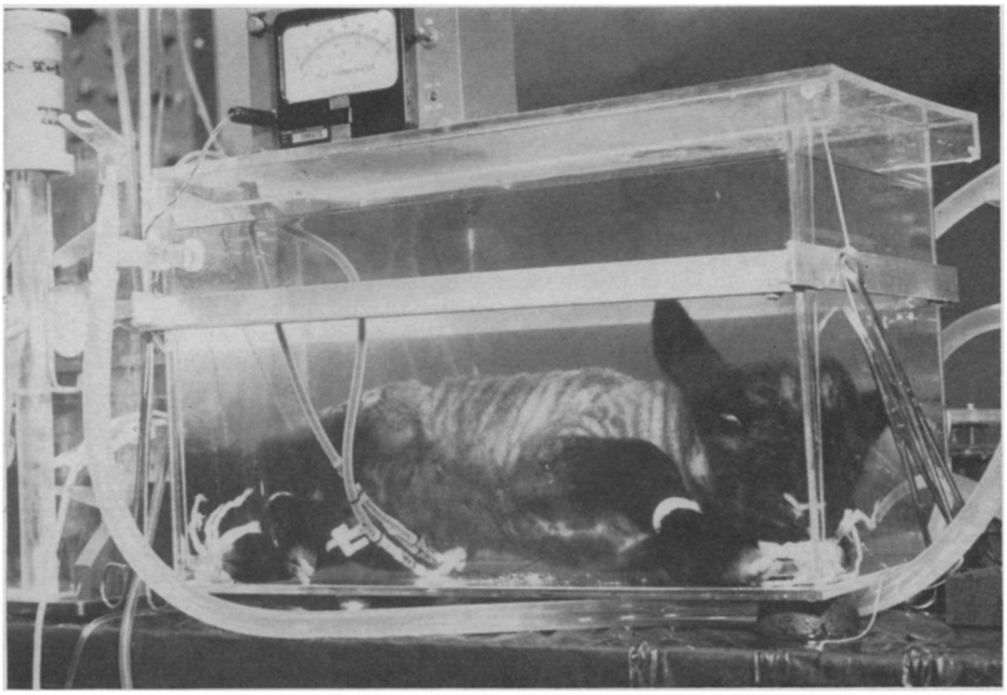
Before any sound prediction of future applications of the womb can be made for either research or human use, the NHI researchers have to show that a fetus can actually grow, not just survive, in their man-made womb. "We will have to keep a fetus alive for a week or more and then deliver it from the tank. We haven't done that," Dr. Zapol declares, though he thinks it may be possible. To date, average survival time in the tank is about 40 hours—the longest survivor lived 55 hours—though death has been unrelated to critical factors such as blood cell breakage from the artificial lung. Infection (conditions are clean but not sterile), pulled plugs and loose cords have accounted for deaths.

Dr. John Doppman

Eventually, it might be possible to place extremely premature infants into such a womb—the offspring, for example, of diabetic mothers who often have difficulty carrying a baby to term—to support them until they can survive on their own. Tempting as it is to speculate, however, development of this artificial uterus is not likely to lead to growing test-tube babies in a brave new world. "First of all," says Dr. Zapol, "our system depends on an umbilical cord. We're talking about supplying oxygen and nutrients to a developing fetus, not providing a home for a newly fertilized egg."

While aimed on the one hand at revealing details of prenatal life, the NHI experiments are also focused on establishing the safety and efficiency of the silicone membrane lung, which could save thousands of infants born in the United States every year with hyaline membrane disease and other disorders in which the infants' lungs fail to supply oxygen to the blood. The pint-sized lung, designed by Dr. Kolobow, had been tested successfully on young lambs (SN: 8/3, p. 109) before its use this year on fetal lambs, two newborn human infants and one adult cancer patient. It appears to have several advantages over standard lung machines

Science Service, Inc. is collaborating with JSTOR to digitize, preserve, and extend access to *Science News*. www.jstor.org



Dr. Raymond Chen

From X-ray studies of unborn lambs, living in a plastic womb where they are supplied oxygen by pint-sized membrane lungs, Dr. Zapol hypothesizes that classic theories of fetal circulation may be somewhat revised.

which can be used only for a matter of hours because they invariably damage delicate blood cells.

The Kolobow lung, powered by a pump that gently transports blood, seems to circumvent this hazard, partly by eliminating severe physical stress and by preventing blood passing through it from coming in direct contact with gases—oxygen and carbon dioxide. The lung itself is a seven-foot-long envelope of silicone rubber membrane coating a flexible skeleton of stretchable nylon knit. The envelope, fitted with inlet and outlet ports for oxygen and carbon dioxide, is wound around a plastic spool the size of a pint bottle. Blood enters the membrane lung through a tube in one end of the spool and flows between the layers of silicone envelope picking up oxygen and depositing carbon dioxide as they diffuse across the walls.

With Dr. Gordon Avery of Washington's Children's Hospital, Drs. Zapol and Kolobow used the lung in attempts to save premature infants whose own blood was being shunted past their lungs. In October, a fatally ill baby boy lived for four hours on the lung, showing temporary signs of recovery—he became alert and turned pink—shortly before death. In December, another premature infant was put on the lung in a desperate effort to save his life; he made it for 12 hours.

NIH

"It's hard to call these two cases either successes or failures," Dr. Zapol comments. "We learned that it is a workable method of getting oxygen into the infant's blood, that we can improve the ratio of blood gases and that there was virtually no damage to blood cells. But the patients died. Because the lung is experimental we selected only those babies with a zero chance of survival. It's hard to judge the lung in such cases. We'd like to try again—infants with underdeveloped lungs are born all the time in this city—but we get few referrals; few doctors know about it." ◇

CLASSIFIED

Classified advertisements are accepted for the following classifications: Books, Business Opportunities, Camps, Colleges, Micro Ads, Personals, Positions Wanted, Schools, Services, Travel. All advertisements must be consonant with the character of Science News.

Rates . . . single insertion 30c a word. Minimum charge is $6.00. For multiple insertions, write for rate card. Classified advertising is payable in advance. Closing date 4 weeks prior to publication (Saturday).

Employment opportunities are accepted at regular display rates, subject to agency commission. Minimum size 1 inch. Minimum charge $23.80 per inch. Rate cards available upon request.

To speed up insertion, address classified advertising . . . Classified Ads, Science News, 1719 N Street, N.W., Washington, D. C. 20036.

BOOKS

MUSHROOMS AND FUNGI. Comprehensive lists. LEW's, 2510 Van Ness Avenue, San Francisco, Calif. 94109.

PAPERBACK CATALOGUE, 270 pages, 15,000 titles, Subject indexed. $2.00. Credited toward order. N.Y. Book, 4S West 43rd St., New York, N.Y. 10036.

MICRO ADS

GOVERNMENT SURPLUS 80-page electronic-optical catalog showing hundreds of bargains galore. Pennies on the dollar. Meshna, Nahant, Mass. 01908.

STROBES, COLOR ORGANS, THE INCREDIBLE STROBIT. See your music in dazzling color. Factory prices, Save 25-50%. Catalog 25c, refunded first order. Teletronics, Box 1266, South Lake Tahoe, CA 95705.

SUPPLIES FOR LIQUID CHROMATOGRAPHY. Miniature Kel-F valves, tees, and other low cost connectors for .030" and .062" Teflon tubing. Flowcells, screens, Teflon discs, colorimeters. Free Catalog. MER CHROMATOGRAPHIC, P.O. Box 1119, Menlo Park, Calif. 94025.

CHEMICALS, Biologicals, Botanicals, $1.00 Quantities Pricelist $1.00 Deductible from First Order. Dept. S Spectro. 1354 Ellison, Louisville, Ky. 40204.

LIVE SEAHORSES, marine specimens, aquarium supplies. Illustrated catalog 15c. Marine Box 248-306 Dania, Florida 33004.

MINIATURE ALUMINUM EXTRUSIONS, Cross sectional area as small as .010. Send prints for immediate quote. Mann Made Inc., Box 307, Fate, Texas 75032.

PERSONALS

WAS NERO A GOOD EMPEROR? Did Vikings settle in North America? Was Stonehenge built by Minoans? Are the legends of Hercules-Medusa-the Phoenix, based on facts? If these questions intrigue you, read (and give) ART AND ARCHAEOLOGY NEWSLETTER, packed with little-known facts about the Pagan world, new finds and deductions, reports from "digs," travel tips. Now in its 4th year. Subscribers include university and other libraries. Send $5.00 for 8-issue subscription to OTTO F. REISS, Publisher, 243 East 39th Street, New York, N.Y. 10016.

SERVICES

AUSTRALIA!!!, AUSTRALIA!!!, AUSTRALIA!!! Jobs Galore! Government assisted Transportation. 1969 Handbook $1.00. Satisfaction Guaranteed!! Associated, Box 17X97, Lafayette, California.

ENGINEERS

Looking for a top position? You can find the right one among leading firms advertising in the

LOS ANGELES HERALD-EXAMINER'S NATION-WIDE HELP WANTED EDITION.

Send for your FREE copy coming out July 6th. Leading firms thruout the country will be represented.

WRITE L.A. HERALD-EXAMINER
Classified Mail Division, Dept. 15
1111 So. Broadway, Los Angeles 90054