

## NOTES FROM ACADEME

**The Rhythm of a Course in Reproductive Biology: Eat, Sleep, Go to the Lab**

By DAVID L. WHEELER

Woods Hole, Mass.

David Sprague, a graduate student in biochemistry and genetics at Texas A&M University, drove here in three days, leaving behind his wife and eight-month-old daughter -- who began to crawl in his absence. Irina Buhimschi, an assistant professor of obstetrics and gynecology at the University of Maryland's medical school, left her 4-year-old son at her home in Columbia, Md., in the care of her parents, who were visiting from Romania. Michael J. Paidas, an academic obstetrician at the New York University School of Medicine, brought his family with him, but had to find other physicians to take over his caseload of 36 pregnant women a day.

The draw wasn't the nearby Cape Cod beaches, but a six-week course in "The Frontiers of Reproduction" held at the Marine Biological Laboratory here. Known as the summer home of biology, the M.B.L. is an independent institution with a stable of year-round staff researchers and a summer influx of graduate students, postdoctoral fellows, and faculty members who show up for intensive introductions to various aspects of biology.

Reproductive biologists say their field isn't as active as it might seem, despite the frequent publicity about cloning, technological aids for infertile couples, and multiple births. Many foundations and pharmaceutical companies dropped their support for further contraception research in the late 1960s, after "the pill" came on the market. Nowadays, senior researchers say, reproductive science could use some rejuvenation, and a few of them organized the M.B.L. course as a step toward that goal. "Reproductive biology needs young people," says Joanne Richards, a professor of cell biology at Baylor College of Medicine and a guest lecturer for the course.

The 16 students in the course benefit from the expertise of about 50 scientists, some of whom drop in for a day and others who stay for a couple of weeks. The students get a chance to test their stamina in the laboratory and at the local pub with Keith Campbell, a British scientist who helped to clone Dolly, the famous sheep. They hear from John C. Herr, a professor of cell biology at the University of Virginia, who is developing a contraceptive vaccine that would create antibodies to prevent fertilization. They learn the latest techniques for tracing the molecular signals in the maze-like biochemical pathways that make reproduction possible.

To produce fertile eggs or energetic sperm, a large cast of hormones has to loop through the brain, the pituitary gland, and the gonads in complex, precisely timed sequences. The students are often left wondering how it is that mammalian reproduction is successful so much of the time.

The course itself has a simple, six-day-a-week rhythm: breakfast, lecture, lab, lunch, lab, dinner, lab or lecture, possible movie break or trip to Captain Kidd's, the local bar. Sleep. Start over.

The long hours are put in within view of a harbor filled with sailboats, and lectures are punctuated by the horns of the ferries to Martha's Vineyard.



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The students sometimes talk to each other about their research. One evening, YanHe Lue, a researcher from China who is now at the Harbor-UCLA Medical Center, gives fellow students a glimpse of his attempt to develop a male contraceptive. Shots of testosterone, he explains, can stop the creation of sperm and are licensed in Europe for use as a contraceptive. But the shots don't take effect for three months. He proposes adding heat, to create a faster-acting contraceptive. The idea was inspired by studies of infertility in men whose testicles, because they have not descended, are subjected to higher temperatures in the body. In an early experiment testing his idea, Dr. Lue gave some rats testosterone shots and dipped their testicles in water heated to 109 degrees Fahrenheit. The results suggested that the concept might work.

The mental image created by that experiment -- Dr. Lue mentions the technical problem of heating only the testes -- proves to be too much even for experienced researchers, who erupt in laughter.

A question meant seriously -- about the effect of saunas on men's fertility -- sets off a new round of giggling. "You guys are laughing," says Kelly E. Mayo, a professor of biology at Northwestern University and one of the course's organizers. "But he's going to be rich if it works."

Dr. Lue takes the hilarity in stride and calmly returns to his point. Combining heat with testosterone would enable the shots' dosage to be lowered, he says, reducing the risk of prostate cancer as a side effect. To a question about the practicality of applying the process to humans, he responds that he has tested the heating procedure himself. "It's not too bad," he says. A fellow student -- male -- walks to the front of the room to high-five Dr. Lue.

The next afternoon, the students are in the laboratory, their attention having shifted to rats' ovaries. Mr. Mayo and a laboratory assistant anesthetize female rats with carbon dioxide, decapitate them, and hand them out to the students, who remove the ovaries and use a syringe to tease out granulosa cells, important players in preparing ova, or egg cells, for ovulation. Under the dissecting microscope, the ovaries look like pink raspberries, and the cells like seeds floating in the solution.

Over the next few days, the students will add new genes to the cells, incubate them, and check to see if the cells have taken up the genes, which have been hooked up to a molecular beacon that glows -- literally -- using the same biochemistry that makes a firefly light up. An instrument that measures the strength of the glow will also reveal how active the genes are. The experiment is designed less to teach students about the particular genes than to give them the ability to take home a new technique.

During breaks in the routine, the students get on the laboratory's computers to check scores in the N.B.A. playoffs, take video tours of the Egyptian pyramids, or search Medline, a bibliographical data base. They also exchange e-mail and instant messages with family and friends. Gabriela Mendeluk, who works at a fertility clinic in Buenos Aires, is in a chat room with her 13-year-old daughter when she is summoned away. A friend takes over on the computer. "Your mum is counting the cells in a rat's ovary," she writes.

The next day, the students try their hand at slicing sections of frozen mouse ovaries. For the procedure, the students need a cryostat, an \$18,000 version of a meat slicer. They are making the sections for "*in situ* hybridization," which can reveal what genes are being used by the cells, and when.

David Sprague, the student from Texas A&M, turned 31 years old the previous day. At the laboratory window, he points out

the spot where he went fishing the night before to celebrate. His friend Dean Betts, a graduate student from the University of Guelph, in Ontario, takes over on the cryostat. Mr. Betts's hands reveal a shade of fingernail polish -- "Mocha Java" -- that was applied in the late stages of the birthday party, after the tequila took hold.

By Saturday of the fifth week of the course, everyone's energy is lagging. The morning's lecturer, Margaret Shupnik, a professor of internal medicine at the University of Virginia Health Sciences Center, has guessed that the students might be tired. She brings clear explanations to her lectures and James Brown-style whoops to the laboratory.

She has a penetrating mind that provides its own peer review, seeking out alternative explanations for experimental results. The cells in the glass dishes and the frozen ovaries, she reminds the students, are all tools to get at one central question: Just how is it that life renews itself?

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