Solving Reproductive Problems with a Computer

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The combination of the computer and a new technique offers support and encouragement to childless couples who want a family.

Introduction

An HP 340 computer is playing a vital role in identifying the problem of recurrent miscarriages among patients of Reproductive Immunology Associates in Encino, California, a suburb of Los Angeles. "It takes us about 10 seconds to collect data on 10,000 cells," says Dr. Bill Matzner, an RIA principal. "And that data can give a childless couple hope of becoming parents."

A Frustrating Problem

Early in pregnancy, a mother-to-be gets signals from the tiny fetus, some of which are direct genetic messages from the father. One of the father's messages includes the tissue type (HLA) antigens that determine "self." Because the father's antigens are different from the mother's, she recognizes the cells as "foreign," and Iymphocytes in her uterus begin to produce a special blocking antibody that coats the baby's cells and protects it from the mother's immune killer cells. In addition, these antibodies send a signal to the placenta to make the baby's cells grow and divide.

"Research by Dr. Alan Beer, Chicago Medical School and others suggests that mothers who suffer repeated miscarriages do not experience this chain of events," says Matzner. "That is because the mother's and father's HLA antigens are too much alike, thereby short circuiting the production of the protective antibodies."

He pauses for a moment. "In other words, the want-to-be mother and father are genetically more like brother and sister than unrelated husband and wife," he points out.

Matzner and his associates, Dr. Penny Chong and Dr. Wendell Ching, use an in-office cell flow cytometer to measure the amount of blocking antibody that a potential mother has in her serum. Their system uses laminar flow fluidics, laser optics and the HP computer to study the cell characteristics.

New Technology is More Sensitive

This combined technology is significantly more sensitive in detecting the lack of blocking antibody than other, more commonly used tests," Matzner says. To study the blocking antibody, the husband's Iymphocytes are mixed with serum from the wife and a particular dye-marked fluorescent antibody, which can be seen by the cytometer. If she has blocking antibody, it attaches to the Iymphocytes.

This entire mixture is placed in the cytometer. Using laminar flow fluidics, where a surrounding sheath of saline keeps the mixture in a narrow path, the cells, in single-file fashion, are sent across the path of a blue, argon laser. When the laser hits the cell, it scatters light. Those cells marked with the fluorescent dye emit a certain color of light.

A series of mirrors and prisms send the light to various photo multiplier tubes, which collect information on the size, granularity and amount of dye on each cell. This data is digitized and sent via cable to a Hewlett-Packard 340 computer. "It takes only about 10 seconds to collect data on approximately 10,000 cells," notes Matzner. "The computer quantifies the amount of light and can tell us the per cent of lymphocytes that have blocking antibody on them."

The program for this study, Lysis II by Becton Dickinson, is Windows-based, acting similar to a Macintosh (although it uses the HP Pascal operating system).

Immunology Associates physicians use in-office cell flow cytometry and an HP 340 computer to study cell characteristics of women with recurrent fetal miscarriage.

Dr.Wendell Ching reviews data to detect the presence of antinuclear and phospholipid antibodies in a serum sample, while Dr. Penny Chong counts white blood cells to determine the viability and quantity of lymphocytes.

How It Works

Matzner, Chong and Ching label either a T of B cell with the orange dye (phycoerythrin) and the blocking antibody with a green dye (FITC). The program plots this data on a contour graph, where the number of cells with a certain characteristic is plotted in color, using contour lines. In the graph, the orange dye is on the Y axis, and the green dye is on the X-axis.

"We are looking at the per cent of cells in the upper right quadrant as a per cent of cells in both the upper left and upper right quadrants," Matzner says. "This gives us the ratio of double labeled cells to orange labeled cells as a per cent (of either the T of B cell population)."

He considers his next point. "A positive response occurs when more than 50 per cent of the T or B cells have antibody attached to them," he notes. "And that negative response means that the couple needs to undergo treatment."

He gestures to emphasize the therapy. "Treatment involves immunizing the mother with the father's leukocytes. This gives a concentrated (10,000 x) message from the father that induces her to produce the protective antibody," Matzner explains. Known as paternal leukocyte immunizations, they are administered twice, a month apart. The increase in blocking antibody is monitored and substantiated through retesting and computer evaluation. Additional vaccinations may be required.

Computer analysis is also being a used by Matzner, Chong, and Ching to evaluate and treat other problems.

"With each pregnancy loss, there is a 10 to 15 per cent chance that the mother will develop an antibody to the fatty molecules, called phospholipids, found on the cell surfaces of the baby that was miscarried,' Matzner says. "During subsequent pregnancies, the antiphospholipid antibodies can cause the mother's blood to clot more easily than normal, resulting in loss of the baby or | growth retardation. Most women with this problem are not sick and appear healthy."

Other women may have autoimmune tendencies or diseases. They may have antinuclear antibodies that can affect their pregnancies.

Treatment For The Problem

Treatment programs for these latter immune problems involve the use of low-dose aspirin, a blood thinner called heparin and corticosteroids, usually the drug prednisone. They are all started during the cycle of planned conception and then continued through most of the pregnancy.

"The success rate of delivery in these couples approaches 86 per cent, with proper diagnosis and therapy," Matzner stresses. "The time has passed for couples who experience repeated pregnancy loss to continue suffering. New technology, pinpoint accurate computer evaluation, identification of problems and successful treatment are now available to physicians and their patients," Matzner concludes.

More information is available from Reproductive Immunology Associates. They are located at 6850 Sepulveda Blvd., Suite 210, Van Nuys, CA 91405, (818) 781-5195

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