

Women's Health Issues Take Center Stage at the IOM

Ever since the Women's Liberation movement was launched in the 1960s, women have been asking to be treated more like men. And in at least one respect they have been—by doctors, who have treated them as if they *were* men. For example, doctors have prescribed drugs for women that have been tested extensively only in men. Recommendations to take aspirin to prevent heart attacks came out of two trials that included only men. Says Leslie Benet, chairman of the department of pharmacy at the University of California, San Francisco (UCSF): "Clinicians generally don't pay attention to gender differences." In

addition, "there are large gaps in our understanding of the health problems of women," agrees Ruth Kirchstein, a physician who is director of the National Institute of General Medical Sciences.

But recently there have been a few hopeful signs that things are changing, and that the medical establishment has begun to lend an ear to the specific medical problems of women. In fact, last week, when the Institute of Medicine held its annual meeting,* the neglect of women's health issues was the main theme. Many speakers agreed that more basic research is needed on diseases that afflict women exclusively, such as breast and ovarian cancer—or that express themselves differently in women, such as AIDS, cardiovascular disease, and lung cancer. They also called for new studies exploring the effects of common drugs on women—such as replacement estrogen after menopause—and the steps, such as changing their diets, that women can take to prevent disease.

At first glance, it may seem like women already are in good shape: In the United States, women live on average 7 years longer than men, and by the time they are 100 years old, they outnumber men five to one. But those extra years aren't necessarily a bonus at the end of a long life. "It's a horrible travesty that women are not so much living longer, but are taking longer to die," says Maureen Henderson, a cancer epidemiologist at the Fred Hutchinson Cancer Research Center at the University of Washington. Of their 7 extra years, she says, at least 4 are "bad ones," because of osteoporosis, dementia, depression, rheumatoid arthritis, and the other health problems that plague older, frail women.

And it was clearly the consensus of the meeting that more research should be directed at understanding why older women suffer from such diseases at the end of life—and, indeed, why women seem to be afflicted in general with more illnesses than men, in spite of the fact that they apparently have stronger immune systems. Women suffer from more autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis, and also are getting infections more than men are, says Leon Rosenberg, president of Bristol-Myers Squibb Pharmaceutical Research Institute. As an example, the fraction of women among AIDS patients globally has gone from 20% percent in 1980 to 40% today and is projected to climb to 50% by the year 2000, according to the World Health Organization.

But no one really knows the basis for these differences, Rosen-



Special treatment needed? Women with AIDS may respond to drugs differently than men.

berg points out. While women's stronger immune responses might account for at least part of their greater susceptibility to autoimmune diseases, it would seem that they ought to be less susceptible to infections. One possibility is that they are simply exposed to more diseases, since they are the ones who usually care for the sick and the young.

But there are clues that more fundamental factors might be at work as well. One place to look might be the hormones that are responsible for sex differences between men and women, says University of Texas Southwestern

Medical Center physician Jean Wilson. Those hormones may influence how males' and females' immune systems respond to stress and disease. What's more, there are signs that the hormones may also regulate the way drugs are metabolized in men and women, which is one reason that drugs may act differently in women.

The hormones in birth control pills, for example, may inhibit a woman's ability to clear many drugs, including prednisolone, which is used as an immunosuppressant for transplant patients, says Benet of UCSF. He cited several studies that indicate that a woman's ability to get rid of a drug may be influenced by whether she is taking hormones, or is postmenopausal, menstruating, or pregnant. In the future, says Benet, we need to discriminate between how men's and women's metabolisms handle drugs before making recommendations about their use—although he added that most drugs have such a wide margin for safety that there is rarely cause for clinical concern.

Another big unknown is how hormones combine with foods—and play a role in disease. Does fat in the diet, for example, stimulate growth factors or interact with hormones in a way that could set the stage for breast cancer? "We need to put a much bigger priority on the behavioral aspects of health and disease," says Henderson.

The National Institutes of Health must agree: Last month, it selected the Fred Hutchinson Cancer Center as the coordinator for a \$625 million study of 150,000 women in the United States over the next 14 years. One goal is to see whether women's rates of heart disease and breast cancer are reduced by a low-fat, high vegetable diet—and how their risk is altered by taking hormones after menopause. "Women need clear and unequivocal answers to lingering questions about the safety of using replacement estrogen," says Kirchstein of NIH. "Is there, for example, a significant link between the use of estrogen in postmenopausal women and the development of breast cancer?"

There are also other signs that the medical and research establishments are getting the message that they must include women in their studies. And as a more concrete sign, the Food and Drug Administration now requires drug companies to include women in clinical trials (although they're still barred from Phase I trials if they are of reproductive age), noted Judy Norsigian, codirector of the Boston Women's Health Book Collective. "There has been progress," she concluded. "We're hoping what will change now is that we won't have to stand up on the table and scream to have research done."

—Ann Gibbons

* The meeting on "Gender Differences in Health," was held on 19 October in Washington, D.C.