A New Mosaic for Women’s Health

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In recent years, interest in and commitment to the improvement of women’s health have burgeoned in the United States and around the world. Over the past twenty-five years in the United States, the women’s advocacy community has successfully argued for a better appreciation of the health of women and increased understanding of and sensitivity about women’s health care needs. This long-standing advocacy effort seemed to blossom more fully in the scientific and health care communities during the 1990s, with unprecedented levels of interest and resources dedicated to elucidating sex (biological characteristics of being female or male) and gender (responses to societal influences based upon sex) differences and similarities in health and disease, as well as in normative development, aging, responses to interventions, and the study of psychosocial and behavioral influences on health.

We saw much progress over the last years of the twentieth century. Today, we can view the progress and the future of women’s health as a new mosaic: one that incorporates research, education of consumers and practitioners of health care, public health policy changes related to new information resulting from research, career development and advancement based upon the new paradigm, and—central to all in the new mosaic—women themselves. This new mosaic addresses emerging public health needs, scientific opportunities, and policy/advocacy concerns through the advancement of women as scientists, administrators, educators, and practitioners of health care.

Just a few years ago, “women’s health” was thought of primarily as that involving the reproductive system. There was little attention given to other areas of women’s health, such as heart disease, dental and oral health, autoimmune diseases, and menopause. Today’s print and visual media show how that has changed over the past ten years. In the process, there has been an explosion of information about and attention to women’s health. We have learned that normal parts of aging, such as menopause, should not be thought of as “diseases” and that prevention can help us to “age successfully” in a healthy manner.

In addition, initiatives to address the recruitment, retention, advancement, and reentry of girls and women into science and research fields, health care careers, health policy positions, and health administration are being developed and designed to attract girls and women into science.

During the past decade, the U.S. government has established new offices or programs within virtually every agency of the Department of Health and Human Services (HHS) to foster biomedical and behavioral research, health care, health policy studies, and other programs designed to address important issues related to the health of women. Today, although considerable scientific data are available on the natural biological and pathologic processes that affect women, substantial gaps in knowledge remain. Considerable efforts are required to further understand the effects of female sex hormones on cellular and organ systems and gender differences in health and disease. Such efforts have been under way for the past decade in the United States through the commitment of the National Institutes of Health (NIH) and its Office of Research on Women’s Health (ORWH).

In September 1990, the ORWH was established at the NIH, the first HHS office dedicated to women’s health issues. The NIH/ORWH is dedicated to expanding medical knowledge through scientific inquiry in order to ensure that every human being enjoys the highest attainable standard of health across
the life span, from earliest childhood to the later years of life, without regard to sex or gender. At the NIH, the imperative to advance women’s status through improved health is generating biomedical research designed to provide a better understanding of how such biological factors as sex and gender, as well as other factors including economic, genetic, geographic, and environmental differences, influence the causes, diagnosis, progression, treatment, and outcome of diseases for diverse populations. The women’s health research agenda stresses the appreciation of the connections between early life activities and experiences that are antecedents for health or disease in later life, with important implications for the health of postmenopausal and elderly women.

In the 1990s, changes in thinking and perceptions transformed how scientific studies are designed and conducted—including who participates in and who conducts such research. Changes in research study design to include sufficient men and women that an analysis by sex/gender of the results are important, as the data resulting from research must be applicable to both men and women of diverse racial and ethnic groups. Broader representation in the inclusion of participants in clinical research can then bring about improvements in public health policy, standards of health care practice, and individual perceptions about how best to preserve health across the life span of women with the understanding that such conclusions are based upon scientific facts.

Traditionally, with women’s health viewed as synonymous with reproductive health, scant attention in research on women was given to issues beyond reproductive capacity, and the male body was viewed as the normative standard for clinical implications for both women and men. The expanded definition of women’s health now fosters research on the totality of biological, genetic, biobehavioral, and environmental factors that influence health across the life span of females, from the prenatal period and birth, through childhood and adolescence and the adult years, to the menopausal, postmenopausal, elderly, and advanced years of life. The ORWH has utilized these expanded concepts to publish two research agendas on women’s health with the full collaboration and participation of the advocacy and biomedical communities.

The NIH’s Research Agenda for Women’s Health: Addressing the Totality of Factors That Contribute to Health

Since the publication of its initial research agenda on women’s health in 1992, the ORWH has emphasized approaches to research that encompass the totality of factors that influence and contribute to health of women across the life span. With the development of the eight-volume Agenda for Research on Women’s Health for the 21st Century published in 1999, increased emphasis has been given to interdisciplinary research, prevention, analysis of research data by sex/gender, and the inclusion of diverse populations of women in clinical studies to determine factors contributing to differences in health outcomes and responses to therapeutic interventions. Health status is influenced by the interactions of genes, human biology, and behavior, as well as the environment, including access to health care, culture, and education. Research priorities published in the agenda, as well as those identified each year by the ORWH for special emphasis, call for studies on connections between early life activities that are antecedents for health or disease in later life and the role of personal behaviors and lifestyle choices in the health and aging processes, focusing on such issues as obesity, exercise, addiction, and smoking cessation.

In the present fiscal year, priority has been given to the study of genetic, infectious, environmental, molecular, and/or hormonal factors as they contribute to multisystemic disorders affecting women, including mechanisms of sex differences in immunological responses and the development of surrogate markers and immune therapy. Prominent is a focus on diabetes, obesity, and cardiovascular diseases, with special emphasis on prevention, including nutrition, physical fitness, medical screenings, and oral and dental care. Attention is also being given to neurobiological and psychological risk and protective factors in the development of mental health and addictive disorders, as well as health consequences of violence and stress. Other areas of em-
phasis include reproductive health, such as meno-
opause, fertility, and benign and malignant gyneco-
logic conditions; care giving and health-related qual-
ity of life issues; infections, including sexually trans-
mitted diseases; cancer; and complementary and al-
ternative medicines and dietary supplements.

With the passage of the NIH Revitalization Act
of 1993, which established the ORWH in law, the
NIH’s strengthened policies for the inclusion of
women and minorities in clinical research studies
became a matter of public law. The new law stipu-
lated that NIH-supported studies must include
women and minorities, unless there is compelling
justification not to do so, including when such re-
search might have a negative effect upon their health.
The ORWH has the responsibility for ensuring the
full implementation of these broader inclusion poli-
cies and for monitoring the inclusion of women and
minorities in clinical trials. Since passage of the Re-
vitalization Act of 1993, investigators have been re-
quired to enroll diverse cohorts of women that re-
fect the populations at risk or that share the
demographic profile of those at risk for the condi-
tion under study. This mandate increases the chal-
lenges for recruitment and retention of women in
clinical studies.

To identify barriers to women’s full participa-
tion in research, the ORWH convened a meeting in
1993 and issued a report, *Recruitment and Retention
of Women in Clinical Studies,* as well as an Out-
reach Notebook for clinical investigators. The
ORWH is also working to ensure that subpopulations
of minority groups are adequately represented in re-
search and that disparities in health among diverse
populations of women are addressed through its re-
search agenda and through its *Strategic Plan to Ad-
dress Health Disparities Among Diverse Populations
of Women.*

A recent ORWH scientific workshop, “Science
Meets Reality: Recruitment and Retention of Women
in Clinical Studies and the Critical Role of Re-
levance,” examined lessons of the past decade, con-
tinuing challenges to ensure that clinical research is
relevant and targets scientific questions important to
the public health, and emerging ethical and policy
issues that present both challenges and opportunities
for women’s health research. Among issues raised
were the need to appreciate how sex differences
should be taken into account in the design of clinical
research; the shift from the ethics of protectionism
to the ethics of inclusion to concepts of justice in
research; and the differences between clinical care
and clinical research. Recommendations from the
meeting will soon be published.

**Threats to Women’s Health: Perception and Reality**

Women’s perceptions and expectations contrib-
ute in important ways to their health-related behav-
ior. It seems rather logical and straightforward that
if girls and women know the real threats to their
health, longevity, and quality of life, they may be
more attuned to behaviors and health practices that
can prevent or alleviate such threats. Therefore, hav-
ing factual scientific information rather than living
with myths or incorrect assumptions is extremely
important for improving women’s health today and
tomorrow. For example, surveys show that more
women worry about breast cancer than any other
form of the disease, but the leading cause of cancer
death in women since the mid-1980s has been lung
cancer, which is mostly related to the increase in ciga-
rette smoking among women. Research has shown
that cigarette nicotine dose is a less important influ-
ence on the subjective and, under some conditions,
reinforcing effects of smoking in women than in men.
Therefore, harnessing social support to foster absti-
nence is important in treating women.

The leading causes of death for all women in
this country are the same as for men: heart disease,
lung cancer associated with smoking, and stroke. Yet,
an American Heart Association Survey found that
61 percent of women consider breast cancer to be
their greatest health threat as opposed to 7 percent
for heart disease and 1 percent for stroke. Among
women twenty-five to thirty-four years of age, only
17 percent named cardiovascular disease and stroke
as the leading causes of death in women. The survey
also reported that, when exercise stress tests are ab-
normal, about half as many women as men are rec-
ommended for further evaluation. Indeed, deaths for
women from heart attacks, strokes, and other cardio-
vascular diseases (CVD) have exceeded those for
men since 1984. Heart disease, stroke, and other
CVD have only recently been recognized as serious
health problems for women, despite the fact that
women have a worse prognosis following a heart
attack than men, due to older age and multiple health conditions, such as smoking-related conditions and diabetes, which pose major threats to public health in the United States.

Diabetes is closely connected with the issue of obesity, which is a major health problem for Americans of all racial and ethnic backgrounds. According to the Centers for Disease Control and Prevention, 33 percent of women in the United States, compared with 28 percent of men, are obese. Obesity is not only a serious threat to good health and longevity by itself, but it also puts individuals at risk for a host of other serious diseases and conditions, including cardiovascular disease and breast cancer. Obesity, for example, is one of strongest known risk factors for non-insulin dependent diabetes mellitus (NIDDM) and has a substantially higher prevalence among minority women. At present, almost 50 percent of adult minority women in the United States are obese, and many of these women will develop NIDDM and its comorbidities, which include heart disease, which is two to four times more common in the obese; stroke, which has a risk 2.5 times higher in the obese; hypertension; blindness; end stage renal disease; neuropathy; amputations; periodontal disease; and congenital malformations and mortality in infants who have obese mothers. Multidisciplinary approaches to research on obesity and its causes and sequella are current priorities for addressing this much too common threat to women’s health.

Successful Aging and Menopause: Findings from the Women’s Health Initiative

Another one of the areas in the NIH’s agenda on women’s health research is to define what constitutes normative development in girls and women as they mature. Despite the fact that menopause is a universal phenomenon in women’s maturation, until the mid-1990s, little research had been conducted on the physiological and behavioral changes preceding and following the permanent cessation of menses. It is important to note that women, on average, now live about one-third of their lives following menopause. Many of ORWH’s efforts, therefore, address the need to increase our knowledge and understanding of a completely normal physiological process in women: menopause. Today more than 35 million women, or one-third of the female population of the United States, has made the transition to menopause.

Menopause-related research supported by the NIH includes the well-known Study of Women Across the Nation (SWAN), a study of the natural history and progression of menopause among diverse populations of American women, as well as the Women’s Health Initiative (WHI). Such large-scale studies are complemented by basic science research conducted throughout the NIH’s constituent institutes. The WHI is a major fifteen-year research program to address the most common causes of death, disability, and frailty in postmenopausal women: cardiovascular disease, breast and colon cancer, and the fractures of osteoporosis. In July 2002, the investigators stopped the estrogen-plus-progestin (E+P) arm of the WHI clinical trial study after finding that the health risks associated with taking E+P outweighed the benefits. The results from the combination E+P arm of the WHI demonstrated that for every 10,000 women during one year, there were seven more heart attacks, eight more strokes, eight more cases of breast cancer, and eight more cases of pulmonary blood clots. There were some benefits, however, in that there were fewer cases of colon cancer and fewer osteoporotic fractures. The findings from this prematurely stopped E+P arm of the WHI seemed to show that, contrary to long-held clinical beliefs, E+P does not protect the heart and may, in fact, increase the risk of coronary heart disease as well as result in an increased risk of breast cancer.

The WHI Memory Study (WHIMS), an ancillary study of the WHI, examined how E+P or estrogen (E) alone affects women’s cognition, including:

- Normal cognitive function (thinking abilities like memory, attention, concentration, language, abstract reasoning, and calculation);
- Mild cognitive impairment (a significant decline or drop in at least one cognitive ability); and
- Dementia (a significant drop in several cognitive abilities, not related to other medical problems, but clearly interfering with day-to-day activities).

Results from WHIMS showed that women aged sixty-five and older taking E+P therapy had twice the rate of dementia, including Alzheimer’s disease (AD), compared with women who did not take the medication. The study also found that the combination therapy did not protect against the de-
Development of Mild Cognitive Impairment (MCI), a form of cognitive decline less severe than dementia.

Because the findings of this controlled clinical trial of E+P of the WHI were at odds with long-held beliefs, there was much controversy and concern among women and their physicians. However, the results of this clinical trial can and do provide information for women to be able to make informed decisions about their individual use of E+P.

Recognizing that the WHI clinical trial for E alone for menopausal hormone therapy is continuing, women must realize that the results from the E+P arm are not necessarily what will be found with the use of E alone, and there is no cause for alarm for women who are taking E. However, the Food and Drug Administration has now required new labels for all E and E+P products that indicate that the approved use of such hormones is for moderate to severe vasomotor symptoms associated with menopause or vulvar and vaginal atrophy associated with menopause, as well as the prevention of postmenopausal osteoporosis but only for women with significant risk of osteoporosis that outweighs the risks of the drug.15

The findings already released from the WHI and those anticipated in the future are prime examples of the importance of research to confirm or refute long-held beliefs related to women’s health and health care that are not based upon scientific findings.

**ORWH Programs to Support Women’s Advancement in Biomedical Careers**

The ORWH has, as a major component of its mission, the charge to address and develop programs to support the recruitment, retention, reentry, and advancement of women in biomedical research careers. Some of the programs that the ORWH has launched also seek to nurture the next generation of investigators in women’s health research. For example, the recently launched Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) Career Development programs support mentored, interdisciplinary research career development of junior faculty members, known as BIRCWH Scholars.16

The BIRCWH program was developed in response to a need expressed during the process of formulating the women’s health research agenda for a way to support interdisciplinary research bridging the completion of training with an independent career in research addressing women’s health. Further, with the women’s health community calling for less fragmentation of women’s health care, the need to encourage interdisciplinary research as a foundation for integrated care seems of great importance. Further, there is a need to provide support for the development of interdisciplinary collaborations as well as a need to fund mechanisms for the development of women’s health researchers in a mentored environment. Therefore, by creating a program that leads to interdisciplinary collaboration and mentoring for research, the stage may be also set to increase the likelihood of interdisciplinary collaboration for women’s health care.

A unique feature of the BIRCWH program is the combination of support from the ORWH, which leads the BIRCWH initiative, and a number of NIH institutes and offices, including the National Institute of Child Health and Human Development (NICHD), which administers the program, and the Agency for Healthcare Research and Quality (AHRQ). By uniting cosponsors from a breadth of scientific areas, the program encourages researchers from different disciplines to apply their knowledge in new ways to study important topics in women’s health, including sex (biologically based) and gender (socially based) factors in health and disease. The institutions that have received BIRCWH awards in 2000 and 2002 are listed in Table 1.

The fact that the ORWH works in partnership with the NIH institutes and centers to carry out the research agenda on women’s health creates opportunities for creative collaborations and innovations. Another such innovative initiative is the Specialized Centers of Research on Sex and Gender Factors Affecting Women’s Health (SCORs), which supports both basic and clinical projects related to research priorities that can advance scientific discoveries from the laboratory to the clinical environment.17 The ORWH recently established eleven SCORs to promote institutional interdisciplinary research in an area important to women’s health. The SCORs are cofunded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), the National Institute of Dia-
The National Institutes of Health (NIH) supports the Beijing International Research Center for Women’s Health (BIRCWH) to advance the participation and advancement of women in biomedical careers. Since its inception in 2000, the centers have received over $200 million in federal funding.

The centers are funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institutes on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), the National Institute of Environmental Health Sciences (NIEHS), and the Food and Drug Administration. The NIAMS provides administrative oversight for the centers.

The eleven centers and their areas of concentration are:

• **Emory University.** Models will be developed for the pharmacology of anti-epileptic and psychotropic drugs during pregnancy and lactation. This information will help physicians provide risk-benefit information to pregnant and lactating women.

• **Medical University of South Carolina.** The role of sex and gender differences in substance abuse relapse will be studied, with particular emphasis on elucidating factors contributing to relapse. Tobacco, cocaine, and alcohol will be studied.

• **Northwestern University.** Genes, androgens, and the intrauterine environment in polycystic ovarian syndrome (PCOS) provide the theme for studies elucidating the pathogenesis of PCOS.

• **University of California, Los Angeles.** Sex and gender factors underlying the pathophysiology of irritable bowel syndrome (IBS) and interstitial cystitis (IC) will be evaluated.

• **University of California, San Francisco.** Mechanisms underlying female urinary incontinence will be studied, using epidemiologic, biologic, and molecular approaches. The impact of diabetes on urinary incontinence will be evaluated.

• **University of Maryland.** The research goals include an understanding of neuronal mechanisms underlying sex differences in pain sensitivity, in particular for visceral and temporomandibular pain.

• **University of Michigan.** Studies will focus on understanding an important clinical issue for women, stress incontinence, and more specifically the effects of childbirth on the development of urinary incontinence.

• **University of Pittsburgh.** Genetic and environmental factors contributing to adverse pregnancy outcomes will be sought, particularly for recurrent pregnancy loss.

• **University of Washington.** The mechanisms by which drugs are transported in the body also control maternal and fetal drug exposure during pregnancy. Alterations in drug transport during pregnancy will be studied. Data should allow predictions on the magnitude of change in exposure likely to be observed when drugs are administered to pregnant women.

• **Washington University.** The molecular and epidemiologic basis of acute and recurrent urinary tract infections (UTIs) in women will be studied. UTIs, which are among the most common infectious diseases in the United States, primarily affect women.

• **Yale University.** Sex, stress, and cocaine addiction will be the focus of a multidisciplinary program leading to sex-specific prevention and treatments.

In addition to collaborating with the NIH institutes and centers to foster women’s participation and advancement in biomedical careers, the ORWH has worked with professional societies in science to identify routes to women’s advancement. In conjunction with the American Society for Cell Biology (ACSB) and the NIEHS, ORWH convened a meeting called Achieving Xxcellence in Science (AXXS 99) to explore the roles of scientific societies in advancing science by building the careers of all women in science. It is the mission of AXXS to make women

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**Table 1. Institutions that have received BIRCWH awards in 2000 and 2002**

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<th>BIRCWH Centers Funded in FY 2000</th>
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<td>Baylor College of Medicine</td>
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<td>University of California, San Francisco</td>
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<td>University of Connecticut Health Center</td>
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<td>University of Kentucky Research Foundation</td>
<td>SUNY Downstate Medical Center</td>
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<td>University of Medicine and Dentistry of New Jersey</td>
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more visible and to advance their careers by increasing the recognition of their scientific accomplishments.

In June 2000, ORWH and ACSB sponsored a follow-up meeting to prioritize and refine the AXSS 99 initiatives and to develop action plans for implementing these initiatives, both within and across scientific societies. In fiscal year 2001, the ACTeam, a task force comprised of a core group of AXSS representatives, was formed to encourage and assist scientific societies and other professional organizations to implement and sustain initiatives to advance the careers of women in science. The ACTeam, working in cooperation with the Committee on Women in Science and Engineering (CWSE) of the National Academy of Sciences (NAS), held a one-and-a-half-day workshop in July 2002, that brought together representatives of more than forty-seven clinical societies to discuss ways to enhance the participation of women scientists in the clinical research workforce. The most recent meeting, AXSS 2002, evaluated the collected recommendations and proposed action items for a forthcoming report. Recommendations focused on initiatives and action items that clinical societies can adopt within their organizations to enhance women’s advancement in the clinical research field; ways for clinical societies to disseminate successful strategies to advance women’s careers; and ways that clinical societies can collaborate to promote women’s contributions to their fields. Many clinical as well as basic science professional organizations and societies participated in addition to many components of the NIH. The AXSS project prepared and has distributed a summary of strategies presented and discussed at the meeting, which is also available on the AXSS website.

Health for the 21st Century: Where Do We Go from Here?

In implementing the recommendations for research and women’s career advancement published in the agenda for research on women’s health, the ORWH is working in concert with the institutes and centers of the NIH, as well as with the scientific community and advocacy and other organizations within and outside the federal government. Such collaborative partnerships are essential to ensuring that the multiplicity of biological, behavioral, social, psychological, cultural, and other issues that contribute to health are integrated into the design of studies supported by the NIH and to ensuring that the results of research are used in changing standards of health care practice to reflect sex/gender factors. Research conducted to date has given the biomedical community a new appreciation of the connections between early life activities that are antecedents for health or disease in later life and the role of personal behaviors and lifestyle choices in the health and aging processes of women. The NIH/ORWH will continue to support and conduct studies that elucidate the role played by sex and gender, as well as the multiplicity of other factors that contribute to the health status of women across the life span. Further goals for enhancing the new mosaic for women’s health research and health care in the twenty-first century include:

- building on biomedical and behavioral research,
- utilizing health professional education and public outreach and education,
- changing standards of health care practice to include sex/gender/racial/ethnic factors,
- influencing personal behaviors for health,
- providing equitable access to health care, and
- increasing the role of women in science and in health care professions.

As women increase in the general population and in entry into science and health care careers, their potential for contributions to advancements in science and health becomes an even more valuable resource for our nations and our world. Overcoming perceived as well as the very real inequities of opportunities for women to advance in scientific and health care careers must be an imperative for our efforts and for the new mosaic.

The path ahead requires us to stress the importance of including women of all races and cultures in science and health care careers, their potential for contributions to advancements in science and health becomes an even more valuable resource for our nations and our world. Overcoming perceived as well as the very real inequities of opportunities for women to advance in scientific and health care careers must be an imperative for our efforts and for the new mosaic.

In the future, we look forward to developing a focused research and education program to expand the science base of accurate information, followed by dissemination of that information about the health
and the diversity of women that make up our nations. Integral to this effort is the incorporation of such information into the education and training of future health professionals, regardless of their discipline. Our ultimate goal is for science, and therefore for all health professionals, to provide the wisdom necessary to provide sex- and gender-appropriate care for those seeking to preserve their health or cure their illnesses. Women, as well as men, and their families and communities can and will benefit from this approach.

REFERENCES