

The Emerging Science of Gender-Specific Emergency Medicine

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INTRODUCTION

It is increasingly evident that sex and gender play an important role in disease and response to medical treatment. Accordingly, the National Institutes of Health (NIH) has begun targeting funding and initiatives toward sex- and gender-specific investigations. Although the field of Emergency Medicine (EM) has lagged behind other fields of medicine in its attention to sex and gender factors in research and clinical practice, the specialty has recently poised itself for significant growth in this area. The impetus for this increased attention to sex- and gender-specific medicine lies in the historical approach to gender in medicine in the United States and recognition of the resulting deficiencies in research, clinical practice, and medical education.

Historical Gender Bias in United States Medical Research

Scientific investigators have traditionally concentrated on the male patient for a number of reasons. First, the U.S. Food and Drug Administration (FDA), with the intention of preventing the abuse of women, categorized them as “protected subjects” in human clinical investigations conducted prior to World War II. The fear of harming women was compounded by fears that including women of childbearing age in clinical trials, particularly drug trials, might result in unforeseen teratogenic harm to the fetus. Further, there was uncertainty surrounding women’s menstrual cycles, and how the fluctuating hormonal environment might affect comparisons made between subjects. For certain types of studies, hormonal differences might require increased sample size in order to allow investigators to control additionally for “stage of cycle.”¹ Compounding considerations of risk, complexity, and cost was the implicit assumption that outcomes in men would be adequate proxies for outcomes in women, despite the fact that physiologic, anatomic, and metabolic differences between the genders argued against this assumption.

By the 1980s, with women’s individualism brought to the nation’s consciousness by the feminist movement, the concept of sex in human biology was revolutionized. In 1985, the National Institutes of Health (NIH) established a Public Health Service Task Force on Women’s Health. Its recommendations for increased attention to women’s health issues led to development of specific guidelines regarding the inclusion of women as subjects in NIH-funded extramural research.² Subsequently, in 1990, the Office of Research



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on Women’s Health was established to ensure that women’s health issues were adequately addressed in research conducted by the NIH and to ensure that women were appropriately represented in all studies supported by the NIH. Further, a Clinical Equity Provision was included in the 1993 NIH Revitalization Act to ensure that the efficacy of treatments for women would be scientifically determined and not extrapolated from data derived from male participants, as had been done previously.³ This legislation formed the basis for the science of gender-specific research.

The new appreciation that single sex studies fail to provide a complete picture of the distinctions between men’s and women’s health and morbidity⁴ has, simultaneously, raised concerns about women’s access to safe, effective clinical treatment.⁵ Viewed from a gender lens, modern medicine is predicated on a startling lack of information about how women respond to treatments tested exclusively on men.³

Defining Women’s Health, Sex and Gender

Initially, the notion of women’s health was limited to issues surrounding reproduction: childbearing, menstruation, breast health and menopause. This archaic view has been termed “Bikini Medicine.” The conceptualization of women’s health has evolved significantly in the past decade and encompasses far more than reproductive issues.⁶ As a result of this evolution, women’s health is seen to depend on complex interactions between individual biology, health behavior and the socio-economic context of women’s lives.⁷

“Sex” refers to biological differences between men and women such as chromosomes (XX or XY), internal and external sex organs and hormonal profiles. “Gender” refers to the socially constructed roles, values and personality traits that vary from society to society and over time. Every cell has a sex. Whether a cell contains an XX or XY chromosome may have an impact on everything from regulation of gene expression in a cell line to efficacy or toxicity of a pharmaceutical in a living human.⁸ The Institute of Medicine (IOM) has stated that “Sex, that is being male or female, is an important basic human variable that should be considered when designing and analyzing studies in all areas and at all levels of biomedical and health related research” (IOM 2001, p.3). Sex and gender are interactive. In real life, there is a continuous interaction between the two; women’s health is determined by the biology of being female and the social context of gender.

Accordingly, in recent years, there has been a shift away from talking about “women” to talking about “gender.” This is evident at institutions of higher education, where “women’s studies” are increasingly being replaced with “gender studies.” This shift signals the end of the “one size fits all” era, in which there was a male norm in biomedicine.⁴ Instead, the concept of sex and gender have now been recognized as determinants of health and disease for both women and men.¹⁰

While some emphasis on women’s health is needed to correct the imbalances created by the historical use of men as the reference point in education, research and health services, this emphasis is not meant to minimize the impact of gender on men’s health. Sex- and gender-specific medicine embraces the concept that differences between men and women encompass the entire organism – not just their reproductive biology – and that these differences have significant implications that will improve the precision and quality of healthcare for both men and women.

Incorporating a Gender Perspective into Medicine

As we begin to compare data obtained from the direct study of female patients with those we had gathered from males over the years, the new science of sex- and gender-specific medicine is emerging. We now have over 20 years of research, mandated by Congress to include women. How are we doing in areas of education, research and the clinical aspect of patient care?

Education

Are the doctors of tomorrow still learning the women’s health of yesterday? Surveys of medical students and residents entering practice demonstrate that their programs lack education in gender-specific women’s health and their examinations are void of questions that bring a women’s health perspective into the thought process.¹¹ A 2003 survey of U.S. medical schools indicated that fewer than half of the respondents reported that they offer a women’s health curriculum.¹²

While 95% of these schools cover sexual and reproductive function specific to women, only a minority taught about the women’s leading causes of death and medical disorders that disproportionately affect women. More recently, a 2006 study reported that 75% of medical schools had women’s health courses, but only 7% offered interdisciplinary courses that offer a solid grounding in women’s health.¹³

Research

Greater awareness of sex and gender medicine – through the increased attention of government agencies, researchers, and journal editors – has helped stimulate new perspectives on conducting research. For many, gender-based research has come to mean more than simply including women and acknowledging gender as a covariate; indeed, sampling and statistical techniques that simply adjust or control for differences in men and women fail to tell us whether the outcomes are the same for men and women. Ideally, researchers will begin to routinely examine how gender modifies or mediates factors related to disease outcomes.

However, recent evidence suggests that there remain barriers to the acknowledgment of sex and gender in funded and published research. Frequently, even the relatively simple steps of gender inclusion and gender-adjusted analyses are not performed. For example, of clinical trials published in the *New England Journal of Medicine* (NEJM) between 1994 and 1999, 86% of 120 did not perform gender-specific analyses.¹⁴ In a review of 239 phase I and II clinical trials, two thirds of the trials excluded women entirely, and 90% did not conduct analyses specific to gender.¹⁵ A 2010 Women’s Health Research report by the IOM identified multiple gaps in the sex and gender-related content of existing research, such as a lack of studies on the social and environmental determinants of disease in women, few investigations into high-morbidity diseases affecting women, and underrepresentation of socially disadvantaged groups of women. They also noted that study findings were not well communicated to women who might benefit from them. These examples suggest that much progress must be made before clinical research comes near to meeting the new federal recommendations regarding gender.

Clinical

Gender-based medicine can only be translated into routine clinical practice if it is well informed by advances in research and systematically included in medical school and residency curricula. Despite attempts to make women’s health curricula easily accessible, recent findings confirm that only a small percentage of healthcare providers incorporate this knowledge into their clinical practices.¹⁶ If the emerging science continues to support the fact that sex and gender is a significant factor in diagnostic reasoning and treatment decisions, all healthcare providers will need to seek a greater understanding of gender-specific research findings in order to provide patients with safe and effective care.

Incorporating a Gender Perspective into Emergency Medicine

EM has come to assume an important role in healthcare in the U.S. EDs receive 120 million visits annually; this number is projected to continue to rise in upcoming years. Like all specialists, EM providers will have to be sensitive to the impact of sex and gender differences on health care delivery; unlike most other health care providers, they must learn to incorporate these considerations in a high-acuity, high-volume care setting. Clearly-articulated information related to the practice of sex and gender medicine will be particularly critical in the practice of EM, where key decisions can lead to large differences in outcome over a short period of time.

Yet to date, the specialty of EM has not been a high performer in inclusion of women in clinical research or analysis of health outcomes by gender. A review of EM literature published in 2011 found that only 2% of the studies reported gender-specific outcomes and only 10% included gender as a covariate or independent variable in the analysis. In 21% of the studies subject gender was not reported.¹⁷ Based on similar reviews of the scientific literature in other fields^{3, 18, 19}; EM seems to be underperforming in its attention to the effect of gender on disease.

However, recent activities have suggested that gender-specific science is becoming a priority area of growth within EM. A number of recent publications have drawn attention to sex- and gender-specific topics or gaps in our knowledge about sex- and gender-specific issues.¹⁷ In 2014, *Academic Emergency Medicine (AEM)*, the journal of the Society of Academic Emergency Medicine (SAEM), selected gender-specific emergency medicine research as the focus of its one-day consensus conference, an annual event designed to shed light on a priority area of emergency care-related research. The same journal instituted a policy to require original investigations to report a breakdown of subjects by gender. The SAEM Academy of Women in Academic Medicine (AWAEM) has established as one of its core objectives the advancement of research that relates “to our understanding of the role of sex and gender in emergency illnesses/injuries and emergency care and practice.”²⁰

Rhode Island is the home of one initiative to expand and sustain knowledge around sex- and gender-specific medicine related to emergency care: in 2011, the Department of Emergency Medicine at The Warren Alpert Medical School at Brown University established a Division of Sex and Gender in Emergency Medicine (SGEM) (formerly called the Division of Women's Health in Emergency Care). The division runs a two-year fellowship-training program in sex- and gender-specific medicine and women's health for EM residency graduates. Division members, who are a multidisciplinary panel of Brown faculty, perform original research focused on sex- and gender-based analyses in a variety of acute care topics including Gender Discrepancies in Time-to-ECG, Chest Pain Unit Stress Test Utilization, and Completion of Resuscitation Bundle in Severe Sepsis and Septic Shock.

Educational activities include instruction of residents in a four-week clinical elective that provides rich clinical opportunities, including at the Women's Cardiac Center at The Miriam Hospital and Hasbro Children's Hospital Adolescent Clinic. A fundamental goal of SGEM is to raise regional and national awareness about sex and gender-based health issues and research by establishing a community advisory board and creating educational programs for SAEM. The intent of this division is to bring national attention to the new science of sex and gender research and ultimately contribute to the effective management of women in the acute care setting.

CONCLUSION

Health care providers are beginning to recognize the need to improve outcomes for women and the importance of understanding the role of sex and gender in clinical practice. Continued progress in research with accompanying curricular advances have the opportunity to translate into improved diagnosis and treatment of both male and female patients. The opportunity exists for emergency physicians to inform the study of sex- and gender-specific acute clinical care and translate this new data into lifesaving outcomes. Recent activities have suggested that sex- and gender-specific medicine is becoming a high priority in the field of Emergency Medicine.

For more information: www.rhodeislandhospital.org/sgem

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