

Invisible

Julie Ann Freischlag, MD, Sacramento, CA

Vice Chancellor, UC Davis School of Medicine, Sacramento, CA

THE ARTICLE “Sex Bias Exists in Basic Science and Translational Surgical Research,” by Yoon et al identifies a major problem of sex bias in biomedical research. This disparity has overarching implications because the results from such studies, similar to the results from other clinical trial studies performed without an adequate number of women, could be erroneous if applied to women patients in a similar manner as men. The authors describe many causes for such lack of reporting and use of female cell lines and animals—overt, inadvertent, situational, financial, or just plain ignorance—but maintain that now with the recent announcement by the National Institutes of Health of the requirement to describe the plan for the use of both sexes when doing preclinical animal research—and their call to arms of other funding agencies to do the same and to include the sex of the cell line as well—that perhaps the situation will slowly but surely be rectified.

I think this policy has been occurring often, because I remember when I was doing animal research, we ordered only male rabbits for our appendicitis model to study peripheral and peritoneal neutrophils to “keep it simple” and to have less variation.¹ That was policy inadvertent and related to ignorance on our part in not considering potential differences between the sexes. (Also, I think I remember that the male rabbits were cheaper!)

Later in my research on arterial and venous endothelial cell function in rabbits exposed to cigarette smoke and a high-cholesterol diet, we used only male rabbits—again for what we thought was less variability—but we overlooked the

opportunity to seek out the difference in male and female rabbits with smoke exposure.^{2,3} We never thought about the importance of the difference that might have occurred if we had compared the two. We even thought at that time that atherosclerosis was more of a male disease because clinically we saw fewer women with peripheral vascular disease, carotid disease, or aneurysms. That thinking was probably situational, inadvertent, and ignorant as well, and we lost a potential opportunity. Indeed, we never thought about it!

Much later, I was involved in a project on developing a new intraluminal device to assess the composition of a carotid plaque in rabbits on a high-cholesterol diet.⁴ My co-principal investigator was a woman biomedical engineer. We used only male rabbits—why didn’t the two of us women even entertain the potential for differences between male and female rabbits? When we used the device in our human clinical trial, we did see male and female patients—less women—probably about 20%—but there were women. The “light” never went off for us—why was that?

I just read an article by Kaatz and Carnes⁵ entitled “Stuck in the Out-Group: Jennifer Can’t Grow Up, Jane’s Invisible, and Janet’s Over the Hill.” This article describes three reasons perhaps why women are still vastly underrepresented in the higher ranks and leadership positions in academic medicine. In large part, sex stereotypes are to blame and society by and large has difficulty abandoning the assumptions of what a great leader looks and acts like. Because of these stereotypes, much of society continues to frame women as too junior (can’t grow up); women often are not noticed and are “invisible” because too many people assume that a man is the leader in the laboratory. Similarly, when women become more senior, they are still part of the out group—men are not necessarily seen that way (ie, as over the hill).

It made me wonder if the issue that Kibbe et al bring to our attention is caused in some part by invisibility. The likelihood of a different outcome in female cells or animals could be to the result of our inability (blindness) to see or recognize the possibility that women could be different—that inability to see the need certainly existed in my

10.1016/j.surg.2014.07.001

Accepted for publication July 9, 2014.

Reprint requests: Julie Ann Freischlag, MD, Vice Chancellor Human Health Sciences and Dean for School of Medicine, UC Davis School of Medicine, UC Davis Health System, 4610 X Street, Suite 3101, Sacramento, CA 95817. E-mail: jafreischlag@ucdavis.edu.

Surgery 2014;156:519-20.

0039-6060/\$ - see front matter

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<http://dx.doi.org/10.1016/j.surg.2014.07.002>

early career as well. Society has reserved certain diseases for certain sexes—such as atherosclerosis being a male disease—and therefore the women with the same diseases were “invisible.”

When I was in medical school, I remember learning the phrase—“Men die and women suffer”—when describing diseases more attributable to men and women. Maybe women suffered because we did not see them as those who could be at risk for the same disease—they were “invisible.” There are many reports about women underestimating their symptoms and doctors underestimating the importance of the symptoms, leading to bad outcomes in women, especially in atherosclerotic-related illnesses such as claudication and angina. More often, women are in charge of the choices of the health care for their family, but they tend to take care of themselves last because the family and children are more of their concern.

How do we make society accept and more importantly understand that both men and women are equal and deserve equal opportunity to be in basic, translational, and clinical research? We have to be sure to call out the need for equal sex representation as has been done in this study—and there should be no acceptable reason for any omission. Female representation should be equal, and females should no longer be invisible. This topic may mandate a change in our culture.

Now that there are equal numbers of men and women going to medical school, we have an opportunity for such a sea change in culture in who leads us as

well. Society needs to acknowledge and then remove the stereotypes of what men and women do—women should no longer be stuck in the out group. There should only be one group with everyone equal in it!

As leaders, we can make the culture change, and we need to thank Yoon et al for bringing this disparity in our past and even current research endeavors to our attention. We all need to help to promulgate this need to include female cell lines, animals, and patients in research. This approach will make the need for the study of females visible. This policy is fair, scientific, and the right thing to do and will aid in making females more visible in other areas as well.

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