Females ignored in basic medical research

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A new study from Northwestern Medicine has found that surgical researchers rarely use female animals or female cells in their published studies—despite a huge body of evidence showing that sex differences can play a crucial role in medical research.

Editors of the five major surgical journals reviewed in this study have responded to this finding and will now require authors to state the sex of animals and cells used in their studies. If they use only one sex in their studies, they will be asked to justify why.

"Women make up half the population, but in surgical literature, 80 percent of the studies only use males," said Melina R. Kibbe, M.D., senior author of the study and a vascular surgeon at Northwestern Medicine.

"We need to do better and provide basic research on both sexes to ultimately improve treatments for male and female patients."

To be published Aug. 28 in the journal *Surgery*, the study follows a "60 Minutes" segment in February about the problem of overlooking sex differences in biomedical research, featuring Northwestern Medicine® scientists Teresa Woodruff and Kibbe.

Following the "60 Minutes" piece, the National Institutes of Health announced that they are developing a policy that will require all of its funded researchers to study both sexes for all pre-clinical research (the animal and cell studies performed before human studies).

Basic science research has shown repeatedly that male and female animals metabolize drugs differently. Accordingly, the research shows that men and women may experience differences in the ways they manifest diseases, experience illnesses and benefit from treatments.

"Requiring the sex of animals and cells is a very small thing to ask of authors," Kibbe said. "It should be a requirement of all medical journals."

Kibbe is a member of the Women's Health Research Institute and is the Edward G. Elcock Professor of Surgical Research at Northwestern University Feinberg School of Medicine.

For the paper, 2,347 studies from *Annals of Surgery*, *American Journal of Surgery*, *JAMA Surgery*, *Journal of Surgical Research*, and *Surgery* from 2011 to 2012 were reviewed. Just over 600 of those articles included animal or cell research.

More highlights from the study:

- 22 percent of publications using animals did not state the sex studied.
- In studies that stated the sex of the animal, 80 percent used male animals, 17 percent used females and three percent used both.
- Most of the studies using cell research did not specify the sex (76 percent).
- In cell research that did specify the sex, 71 percent used only male cells, 21 percent only female cells and seven percent used cells from both sexes.
- Only one percent of studies reported sex-based results.In female-prevalent diseases, 44 percent did not report the sex; when reported, only 14 percent studied females.

A few years ago Kibbe was encouraged to include female rats in her vascular research by fellow Northwestern scientist Teresa Woodruff. Like many researchers, Kibbe only used males because they were "easier" to study—they lacked the hormonal changes of female rats.

Kibbe soon discovered a critical difference between female and male rats, which may be important to human health.

"I started out with ignorance," Kibbe said. "After Teresa enlightened me, I saw in my own research huge differences between the sexes. I immediately became aware of the significance of this problem."

Kibbe hopes a law will be passed, much like the Revitalization Act of 1993, which increased the enrollment of women in clinical trials, to focus on sex disparity in basic and translational research.

"The majority of research is based on the study of male animals and cells and this practice does harm to both sexes," Kibbe said. "By studying therapies and drugs in males and females, we will develop better drugs that will be more efficacious and lead to less adverse effects in both sexes."

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