1335

New York Times
Editorial Page
Letters to the Editor
229 West 43rd Street
New York, NY 10036

To the Editor:

We wish that the headline ("Study Finds No Implant-Disease Links") of your recent (June 16) article on breast implants were true. If true, the tens of thousands of women with silicone-related diseases would have to start believing that their medical problems were caused by something else, and the hundreds of thousands of women currently well but worried about the prospect of getting implant-caused disease would be enormously relieved.

Unfortunately, the headline is patently false, ignoring as it does thousands of women with well-documented problems, unequivocally caused by silicone implants. There have been more than ten thousand women with reported cases of implant rupture, causing many to experience serious local or regional complications such as scar tissue formation, severe pain and migration of silicone to adjacent lymph nodes and organs. It also ignores the clear evidence of delayed diagnosis of breast cancer in women because the implants decrease the ability of mammograms to detect small breast cancers.

Because the Mayo Clinic study did not look for these problems--only for connective tissue diseases (CTDs) such as rheumatoid arthritis and some symptoms referable to these diseases--it could not have found them, the headline writer notwithstanding. The article itself, however, is replete with phrases such as that the results of the study are "reassuring" and quoted the author, referring to women not yet sick with breast implant disease, as hoping that the results would "reduce some of the anxiety that many women with implants feel."

The study was, in fact, greatly oversold by the New England Journal of Medicine which printed it, as well as by the press. The problem lies in the study's small sample size and in the low probability that such a small sample will detect a statistically significant increase in CTDs among women with breast implants. In the study, seven out of one thousand women without implants had developed CTDs. If implants double the risk of these

diseases, an extra 7,000 to 14,000 cases will occur in the approximately one to two million women nationwide who have silicone-gel breast implants.

Given its sample size, the probability that the Mayo Clinic study would have detected a statistically significant doubling of the risk of CTDs among women with breast implants was only 31% (this is usually described as the power of the study). In other words, because of the small size of the study, its power to find a significant doubling of these diseases in women with implants was less than one in three. The study would have had to involve more than three times more women in order to have had an acceptable chance (80%) of finding (or not finding) twice as much CTD in women with implants.

Thus, the study's conclusion, "We found no association between breast implants and the connective-tissue diseases" is highly misleading, although slightly attenuated in the discussion of the paper. Better, the conclusion should have been that because of the limited size of the study, the negative findings should not be taken as an assurance that breast implants are not causing CTDs. When the negative results of any study are reported, it is imperative to put them into perspective by assessing the power of the study as a means of determining how significant the negative findings are. Otherwise, there is a strong likelihood that consumers of this information will have a false sense of security and be reassured and less anxious without cause.

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PUBLIC CITIZEN HEALTH RESEARCH GROUP
Washington, D.C., June 20, 1994

In the recent editorial, "U-Turn on Implants?" (June 20), the Post errs in its interpretation of the recent Mayo Clinic study on breast implants. The editorial states that the study--of 749 women with implants and 1,498 women without implants--failed to show "a systematic pattern of links between the implants and...any of the serious diseases that have been ascribed to implants"

This statement is highly misleading because it ignores thousands of women with well-documented serious problems, unequivocally caused by silicone implants. There have been more than ten thousand women with cases reported to the Food and Drug Administration (FDA) of implant rupture, causing many to experience serious local or regional complications such as scar tissue formation, severe pain and migration of silicone to adjacent lymph nodes and organs. It also ignores the clear evidence of delayed diagnosis of breast cancer in women because the implants decrease the ability of mammograms to detect small breast cancers.

Because the Mayo Clinic study did not look for these problems--only for connective tissue diseases (CTDs) such as rheumatoid arthritis and some symptoms referable to these diseases--it could not have found them.

But even in the context of the diseases that were examined, the study was greatly oversold by the *New England Journal of Medicine* which printed it, as well as by the press. The author was quoted as saying, "We'd be happier if the numbers were bigger." This is understandable, considering the low probability that such a small sample will detect a statistically significant increase in CTDs among women with breast implants. In the study, seven out of one thousand women without implants had developed CTDs. If implants double the risk of these diseases, an extra 7,000 to 14,000 cases would occur in the approximately one to two million women nationwide who have had breast implants.

Given its small sample size, the probability that the Mayo Clinic study would have detected a statistically significant doubling of the risk of CTDs among women with breast implants was only 31% (this is usually described as the power of the study). In other words, because of the small size of the study, its power to find a significant doubling of these diseases in women with implants was less than one in three. The study would have had to involve more than three times more women in order to have had an acceptable chance (80%) of finding (or not finding) twice as much CTD in women with implants. All of this is especially ironic since the Mayo Clinic authors criticized previous studies because of "inadequate statistical power."

Since no one has ever alleged that most women with implants will have serious problems, the editorial's statement that "It could yet turn out that the implants are safe in most cases" is not "reassuring", a comment made by several people to the press when the study was published. If even 5% of women have either CTDs or the other complications such as rupture or infection, this would affect 50,000 to 100,000 women of the one to two million women with implants. A representative nationwide study several years ago, funded by plastic surgeons, did find that 5% of women with

implants for augmentation had experienced ruptures or infections although "most" women in the study were satisfied with their implants.

In addition to misstating the implications of the Mayo Clinic study, the editorial similarly misrepresents the FDA's reasons for the moratorium and, later, the restricted use of silicone gel implants. It states that it is "important to remember" the FDA actions "were responses not to proof of danger but to a lack of the kind of evidence of safety that's now being produced." Thus, the notion is put forward that it was purely the lack of reliable data on autoimmune or connective tissue disease, not positive evidence of other problems, which led the FDA to take action.

In a January 28, 1992 "Background" statement explaining the moratorium, the FDA listed other concerns about silicone gel implants, including leak, rupture, the fate of escaped gel, hardening of the implants, and interference with mammography. Unlike the "possible relationship between the implants and autoimmune disorders" or CTDs for which the proof of causation was still in question, for these other adverse effects the FDA acknowledged causation but was seeking information on how frequently these problems occurred.

The larger issue raised by the Mayo Clinic study is how medical journals, the media, and, most importantly, the public should reliably respond to so-called "negative" studies. Although portrayed as negative, this study actually lacked the statistical power to really put to rest even the considerable concern that a doubling in the incidence of connective tissue diseases would cause. Thus, the study's conclusion, "We found no association between breast implants and the connective-tissue diseases" is highly misleading, although slightly attenuated in the discussion of the paper. Better, the conclusion should have been that because of the limited size of the study and its lack of statistical power, the negative findings should <u>not</u> be taken as an assurance that breast implants do not cause CTDs. When the negative results of any study are reported, it is imperative to put them into perspective by assessing the power of the study as a means of determining how significant the negative findings are. Otherwise, there is a strong likelihood that consumers of this information will have a false sense of security.

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Washington, D.C., June 20, 1994

The Wall Street Journal
Editorial Page
Letters to the Editor
200 Liberty Street
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To the Editor:

Having noted your recent reporting of the Mayo Clinic breast implant study ("Breast Implant Study Finds No Link With Arthritis and Similar Diseases", June 16) and the polemic which it engendered, "The $4.3 Billion Mistake" (Review & Outlook, June 17), we wish to address both.

First of all, your coverage ignores the many diseases which are unequivocally caused by silicone implants. There have been more than ten thousand women with reported cases of implant rupture, causing many to experience serious local or regional complications such as scar tissue formation, severe pain and migration of silicone to adjacent lymph nodes and organs. It also ignores the clear evidence of delayed diagnosis of breast cancer in women because the implants decrease the ability of mammograms to detect small breast cancers.

Because the Mayo Clinic study did not look for these problems--only for connective tissue diseases (CTDs) such as rheumatoid arthritis and some symptoms referable to these diseases--it could not have found them. Your article, however, is replete with misleading phrases such as the author's quote that "[i]f there's a risk, it's very unlikely to be a major one," and that the findings should give women "some peace of mind about their futures," as well as Dow Corning's statement that "the study affirms its position that the implants don't cause the diseases."

The study was greatly oversold by the New England Journal of Medicine which printed it, as well as by the press. As reported by you, the author acknowledged that "the number of women studied was too small to detect differences in some particularly rare diseases such as scleroderma." This is a disingenuous statement, considering the fact that the other CTDs studied are not particularly rare; yet the sample size was insufficient to detect those either. In fact, given its sample size, the probability that the Mayo Clinic study would have detected a statistically significant doubling of the risk of CTDs among women with breast implants was only 31% (this is usually described as the power of the study). The study would have had to involve more than three times more women in order to have had an acceptable chance (80%) of finding (or not finding) twice as much CTD in women with implants, and the detection of a smaller increase would have required an even larger sample.

Thus, the present study's conclusion, "We found no association between breast implants and the connective-tissue diseases" is highly misleading. Better, the conclusion should have been that because of the limited size of the study, the negative findings should not be taken as an assurance that breast implants are not causing CTDs. When the negative results of any study are reported, it is imperative to put them into perspective by assessing the power of the study as a means of determining how significant the negative findings are. Otherwise, there is a strong likelihood that consumers of this information will have a false sense of security and be reassured and less anxious without a valid reason.

More misleading, however, is the June 17 editorial, wherein the author makes the giant leap of concluding that "the linkage [between breast implants and a variety of ailments] simply cannot be established." The editorial goes on to say that "in our era, the scientific method can't compete anymore with lawyers... politically correct mindsets in the media, or Dr. Kessler's Food and Drug Administration." It is ironic that this non-scientist who has decided that the results of three small negative studies are proof that an association does not exist, speaks with an air of authority to the scientific method.

Rather than address the remainder of this editorial chapter and verse, we say: To be sure, we will never have a definitive conclusion about the quantitative risk of autoimmune diseases after exposure to breast implants, until large, multicenter studies are conducted, with at least a 10-year followup. In the meantime, we may take passing notice of small, retrospective studies, funded by those with an economic interest in the outcomes, but we should not hold them up as stellar examples of "the scientific method." And we pose the question: Does anyone think that these powerful corporations would have participated in a $4.3 billion settlement if no linkage had been established thus far between breast implants and disease?

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Washington, D.C., June 20, 1994