Induced Abortion as an Independent Risk Factor for Breast Cancer

The following article is an expanded version of a paper presented by Joel Brind, PhD at the annual meeting of the Association of Interdisciplinary Research in Values and Social Change, Milwaukee, Wis., June, 1993. Dr. Brind is a breast cancer researcher and professor of biology and endocrinology at Baruch College, The City University of New York.

The US Congress has pinned the label, "growing epidemic" on breast cancer, now the single most frequent cause of death among middle-aged American women. To put it in quantitative perspective, 18,000 American women contracted AIDS in the first ten years of that epidemic (1981 - 1991), but this is merely one-tenth number of new cases of breast cancer diagnosed in 1992 alone. Although most breast cancer researchers readily admit that a majority of patients do not fit any known risk profiles, many risk factors have been identified which seem to be related to some form of excess exposure to the predominant female sex steroid hormone, estrogen.

There is, of course, a monthly estrogen surge with the menstrual cycle, and it is well recognized that those women who spend more of their lives cycling, because of early menarche, and/or late menopause and/or having fewer or no children, are at greater risk. But next to the hormonal awakening of puberty, the greatest surge in circulating estrogen occurs in early pregnancy, during which the cells of the breast are again stimulated to undergo a burst of proliferation. This explosive growth is counterbalanced by several hormones of late pregnancy, which serve to differentiate the breast tissue for the task of milk production and to eliminate unneeded growing cells.

There is direct evidence of the ill effects of abortion vis-à-vis breast cancer. Russo and Russo's laboratory studies in rats as far back as 1980 at the Michigan Cancer Foundation showed that full-term pregnancies protected rats from breast cancer, while aborting the pregnancies guaranteed the cancer's occurrence.1 Histological examination of the rats' breasts also established the necessity of full-term pregnancy for full differentiation of the breast tissue for the function of lactation, while early pregnancy serves to stimulate growth of both normal and abnormal, potentially cancerous cells.
In 1983 at the same Michigan Cancer Foundation, Ownby and coworkers also looked at histological differences between surgically removed breast tumors from patients who had had any abortions (spontaneous or induced) and those who had never aborted. Those with any abortions were only half as likely to have well differentiated types of tumors (associated with slower growth and better prognosis). More statistically significant and directly relevant was the finding that among 238 patients diagnosed with primary breast cancer with no metastases or lymph node involvement, twice as many (20.5 vs. 10.5%) of the 39 patients who had one abortion and three times as many (32.3 vs. 10.5%) of the 26 patients who had had two or more abortions had a recurrence of the cancer within three years, in comparison to the 174 patients who had had only live births.2

More disturbing data have recently emerged from studies of 175 young women with premenopausal human breast cancer in the laboratories of Olsson and coworkers at the University of Lund, Sweden. They found that tumors from patients who had aborted (induced or spontaneous) before first full-term pregnancy had a significant, 49% higher index of cellular proliferation (which signifies fast tumor growth and poorer prognosis) compared to patients with no abortions.3 The same group subsequently reported results of a study of genetic markers in premenopausal breast tumors. They found that tumors from patients with any abortions before first full-term pregnancy were (significantly) 26 times more likely to show amplification of the INT2 gene, another indicator of faster tumor growth and lower survival.4

Although the association of abortion and breast cancer is mostly a matter of the disease being a latent, (by years or decades) side-effect of the procedure, there also sometimes occurs a clinical situation in which the two may come together, namely, when the diagnosis of breast cancer occurs during a pregnancy. In 1989, Clark and Chua published the results they compiled on a series of 154 cases of coincidental breast cancer in Toronto, Canada. They found not only a clear difference in survival between those patients who aborted and those who did not, but also between those who aborted spontaneously and those who received a “therapeutic” abortion. Thus, while only 20% of the 116 patients who carried their babies to term were ultimately cured of the cancer, 40% of the 13 who spontaneously aborted were cured. With the fetus out of the way, of course, the cancer can be more aggressively treated. However, of the 21 patients who received “therapeutic” abortions, none escaped death from the breast cancer.5

It has also long been established, since the classic series of World Health Organization sponsored studies under Brian MacMahon in 1970, that an early, full term pregnancy (the earlier the better) affords a woman a measure of lifetime protection against breast cancer.6

In like agreement with known female physiology and endocrinology, pregnancies which are interrupted by spontaneous abortion have, with few exceptions7-11 consistently been associated with increased risk in studies going back as far as 1957.12-22 In 1981, Malcolm Pike and colleagues at the University of Southern California (USC) extended the finding of the risk-enhancing effect of interrupted pregnancy to induced abortion. Specifically, they found that young (less than 33 years of age), white women in southern California were 2.4 times more likely (i.e., relative risk = 2.4) to get breast cancer if they
UNDERSTANDING THE MEANING OF RISK FACTOR

The subtle maneuvers and statistical somersaults some scientists use to "prove" what they want to prove are not obvious to the uninitiated. However, the tricks in the bag are few and well worth the effort to recognize. Here is a brief primer in the principles and pitfalls of epidemiological study design and reporting.

Most studies are of the retrospective, case-control type. The researchers identify (usually from computer records) some hundreds or thousands of recently diagnosed cases of breast cancer. Then they try to identify (either from the same hospitals or from the same local population) women who closely resemble the breast cancer patients (especially for characteristics that are known to affect breast cancer risk) except that they don't have breast cancer. Cases and controls are then subjected to questionnaires and/or interviews to determine important elements of their reproductive history, such as children born and children aborted. Then the frequency of abortion (or abortion at a particular time, such as before the first live birth) is compared in the cases versus controls, and that ratio generates a number known as relative risk. A "relative risk = one" means that the factor (e.g., abortion) does not affect the risk of getting disease; a relative risk of two means the factor doubles the risk; and so on. A relative risk value less than one indicates a protective or risk-lowering effect.

Published relative risk values are generally adjusted for other factors affecting risk that controls are not matched for. This is poor substitute for good case control matching, and it reduces the statistical power of the study. Statistical power refers to the adequacy of the study to show up small relative risk values, and it is dependent both on the closeness of matching and on the number of subjects in the study. Two studies may find the same result, say, a relative risk of two for subjects with a prior abortion, but a study with lower statistical power may ignore it totally in the summary of their findings. Unfortunately, no real relative risk value above one can be considered small for a common disease like breast cancer, even though relative risk values less than two are generally considered small or slight. For example, a relative risk of 1.5 may mean increasing one's chances of getting the disease from 10% to 15% (a 50% increase)! The point here is that there is ample opportunity for researchers with a pro-abortion bias (and/or financial support) to design studies of deliberately low statistical power. Thus, increases in breast cancer risk due to factors such as abortion can be made to disappear.

Not all studies are of the retrospective case-control type. Some are cohort studies, in which large segments of a population are followed for many years, and the incidence of breast cancer and other significant life events are recorded as they occur. At any given time, individuals who have developed breast cancer can be studied and compared to those in the cohort who have not, or to the general population. Since such studies usually rely on computerized records, they cannot be affected by possible recall bias, to which questionnaire-based studies may be subject. However, the lack of a bona fide control group permits considerable distortion, if desired.

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had any history of either spontaneous or induced abortion in the absence of a full-term pregnancy.23

What has since followed the Pike study at USC in the largely "pro-choice" world of epidemiological research, appearing in over a dozen publications from around the world, is a curious mix of studies designed to either prove or disprove the USC study. Most support Pike's 1981 findings, even though many of the researchers showed a pro-abortion bias in designing their studies or presenting their data in ways that would minimize or eliminate the evidence of an increased risk of breast cancer due to abortion, or even show an alleged protective effect. As one recent reviewer, Larissa Remennick put it: "An initial attitude of researchers towards abortion usually determines the way they interpret results".24

One oft-cited study claiming to refute Pike's 1981 findings, published the following year in the same British Journal of Cancer by Vessey and colleagues at Oxford, cites the Pike study in the abstract, which then continues: "Data are presented on 1176 women aged 16-50 years with breast cancer... The results are entirely reassuring, being, in fact, more compatible with protective effects than the reverse." But this is clearly inconsistent with the authors results section of the paper which admits that their data includes "only a handful" of women having a termination (induced or spontaneous) before their first term pregnancy.25

A year later, in the same journal, Brinton and colleagues at the National Cancer Institute (NCI) reported data on 1362 breast cancer cases from 29 screening centers around the US. In their discussion they concluded: "Contrary to Pike, et al. (1981), but in common with Vessey et al. (1982), we observed no excess risk associated with having a first trimester abortion prior to a full-term birth". Actually, from their data they obtained a relative risk estimate of 1.34, but the small number of cases rendered this number statistically insignificant. They also reported that, "al-
though based on small numbers, the finding of excess risk among nulliparous women who experienced an induced abortion is noteworthy". In fact, their relative risk estimate for nulliparous women was 5.5, and close to the statistically significant level. And if the Brinton study had tabulated their data in the same manner as the Pike study, there would have been a close corroboration. Later, in the very same British Journal of Cancer in 1988, Ewertz and Duffy reported their results of a study on 1486 breast cancer cases in Denmark to be "in agreement with the studies of Pike, et al. (1981) and Brinton et al., (1983)". i.e., that first trimester induced abortions significantly increased breast cancer risk in nulliparous women (relative risk = 3.85).

Even associates of Pike at USC have downplayed the adverse affects of abortion on breast cancer. In 1988, Henderson et al. of USC, in collaboration with the University of Shanghai, published the results of their study on Chinese breast cancer patients. They reproduced their own 1981 results exactly, i.e., relative risk = 2.4 for women under 40 years old with a history of induced or spontaneous abortion before first full term pregnancy. But strangely, this remarkably reproduced statistic, which did not quite achieve statistical significance, was not even mentioned in the article's abstract in the American Journal of Cancer Research.

Meanwhile, the preoccupation with disproving Pike's risk increase of 2.4 with abortion before the first full term pregnancy was carried to a new extreme in 1988, when Rosenberg and colleagues, in discussing their finding of a (non-significant) relative risk estimate of 1.3 among nulliparous women from the northeastern U.S. who had had any induced abortions, stated that "the results suggest that an approximate doubling among nulliparous women who had had an induced or spontaneous abortion can be ruled out with 95% confidence". However, a look at the relevant data table shows the contrary: that the upper limit of the 95% confidence interval is 2.6 for women with on induced abortion and 2.2 with women with any number of induced abortions.

**Control for age has been a widespread problem**

There are other serious problems with the Rosenberg study, most notably the egregious age mismatch between patients and controls: 52 v. 40 years respectively. Yet despite this extreme bias in study design, wherein both age and cohort effects served to lower relative risk estimates, their relative risk estimates for both parous and nulliparous women with any induced abortion history still exceeded unity (1.2 and 1.3, respectively), although there was no trend of increasing risk with increasing number of abortions. The authors did adjust for age in the statistical treatment, but only by 5 year intervals, and the result of such a large adjustment renders statistically weak a study with even so large a patient population (3200) as this one.

Age adjustment is, in fact, a widespread problem in this area of epidemiological research. With few exceptions, controls are not age-matched, and the age differences are adjusted for by grouping in 5-year age strata. This is inappropriate for any study dealing with breast cancer in younger patients, since the age-incidence curve is so steep. For example, the incidence of breast cancer among 35 year old women is about 2.5 times higher than that among 30 year olds. Thus the median age of a randomly selected patient population in the 31-35 age range with be 34+, while that of a control group in the same range will be 33. The net effect is a reduction in the resulting relative risk estimate.

In their classical 1959 paper on epidemiological study design, on which the statistical models used in this area are
based, Mantel and Haenszel specifically warned against this pitfall: "It can be shown, for instance, that within a given age interval the average age of individuals with cancer of certain sites will be greater than the average age of individuals from the general population in the same age interval. This can arise when incidence increases rapidly with age and may pose a serious problem with broad age intervals. This effect can be offset by close matching of cases and controls on age in drawing of samples, even though they are classified by a broad age category in the analysis".30

Age matched studies show the clearest association between abortion and breast cancer

... It is therefore not surprising that the clearest association between induced abortion and breast cancer emerges from studies where controls were age matched to patients. Thus, Le, et al. were able to show a statistically significant relative risk of 1.17 for one abortion and 1.64 for two or more in their 1984 study of French breast cancer patients.31 and Howe, et al. found a statistically significant relative risk of 1.9 among upstate New York women with any abortion history (4.0 among those with two consecutive abortions) in their 1989 study that was based entirely on computer registry data.32 A Japanese age matched study also showed a highly significant, continuous increase in risk with number of induced abortions, from 2.45 for one abortion to 4.90 for four or more.33 This echoed the finding of Dvoirin and Medvedev in their 1978 study in the former Soviet Union (where abortion has been legal since 1955), where one or two abortions produced a relative breast cancer risk of 2.0, and 3.4 for three or four abortions.34

It is also important to note that correction for parity and age at first full-term pregnancy has been the general rule in this area of research, which helps to demonstrate the independent effect of abortion in addition to the delay of first full-term pregnancy. Moreover, as noted above, the largest and most consistent risk elevations have been observed among nulliparous women who have had any abortions, compared to nulliparous women who have never been pregnant.

Studies attempting to show abortion is protective are poorly designed

... It is indeed rare in the epidemiological literature to find any potential risk factor so universally associated with any disease as induced abortion has been with breast cancer. There are, in fact, as of this writing, only two reports which go the other way, i.e., which claim to report a slight but statistically significant protective effect of induced abortion, one in Sweden35 and one in Northern Italy.39

The former study, published by Lindefors-Harris et al. in 1989, is a computer registry study (rather than a questionnaire or interview based study) in which a study sample was selected from the Swedish abortion registry, and compared for the incidence of breast cancer with the general Swedish population. There was no explanation for the failure to select an appropriate control group from the general population registry, nor for limiting the study cohort to women who had an abortion before age 30, but enough data are presented to show that correcting either of these defects in study design would have abolished the 23% “protective” effect.

Most noteworthy in this regard is the difference in the proportion of nulliparous women (known to be at higher risk) in the study cohort (41%) compared to the general population (49%). This statistic alone is enough to account for most if not all of the “protective” effect. Simply put, in this study the protective effect of parity masquerades as a protective effect of abortion. Significantly, in comparing women who were nulliparous at the time of...
abortion (i.e., abortion before first full-term pregnancy) to those who were parous, even this study found a relative risk of 1.9, thus corroborating a lengthening list of worldwide studies.35

The not-so-hidden agenda of Lindefors-Harris study is even more obvious in their subsequent 1991 study on “response bias”, which appeared in the American Journal of Epidemiology.36 Their attempt to discredit the general finding of increased risk due to abortion appears therein as the literal bottom line: “this bias may in fact explain the tendency of increased risk of breast cancer associated with induced abortion in many case control studies”. The hypothesis the authors supposedly supported with their data was essentially that breast cancer patients would be more prone to remember and report events in their reproductive history (like abortions) accurately, while healthy (control) women would be more likely to be forgetful or dishonest. Thus they compared the results of their earlier, computer registry study discussed above with another earlier study they had conducted using standard questionnaire methods, also on a Swedish population.36,37 Since the computer registry includes everyone, these patients were also included in the computer registry study, so the accuracy of their responses could be compared. They found that a relative risk of 1.5 (statistically significant) could be explained by “under reporting of previous induced abortions among controls relative to over reporting among cases”. That last phrase means, of course, that patients made up abortions that never happened! And the controls were from a young group of control subjects which had in fact been deleted inexplicably from the case control study under consideration. How such a poorly designed study could find its way into a prestigious, peer-reviewed journal is a good question.

Yet more chicanery is revealed by this “tale of two studies” in Sweden. The case-control study, which supposedly should have shown an exaggerated risk due to abortion, actually reported no risk elevation due to abortion before first full-term pregnancy. But it was the computer registry study which, as noted above, evidenced a 90% increased risk among women who aborted when nulliparous. The explanation lies in the small print footnote of the data table of the case-control study which shows no risk increase: “nulliparous excluded”. It is easy to see why as 50% exaggeration of a 90% increase translates to a relative risk of 2.4 for abortion before first full-term pregnancy, just as Pike had reported in 1981 and so many others had confirmed.

The Italian study is a continuing study of hospital patients in greater Milan. It suffers from the widespread deficiency of control patients tending to be younger than breast cancer patients and crude, 5-year age adjustment. Nevertheless, Parazzini et al. reported in 1991 that induced or spontaneous abortion increased breast cancer risk by 20% (relative risk = 1.2).38 However, their most recent report, published in 1993, negates this finding, instead showing no increase in risk with a single abortion, and a significant, 20% decrease in risk with a history of two or more abortions.39

Closer scrutiny of these two studies reveals trends in the study population that underlie the shift in results. The 1991 study of 2,394 breast cancer cases (of which 18% were nulliparous) and 2,218 control patients (of which 20% were nulliparous) is already a very atypical population, since nulliparous women are, in the general population, over represented among breast cancer patients. (Nulliparity raises risk.) Thus, although the relative risk data are corrected for parity, the correction is essentially nil, since parity appears to provide no protection in this study population. That helps explain the relatively low risk elevation reported in 1991. However, in the 1993 report, while the breast cancer population had been increased by
43% to 3,415 cases (18.8% nulliparous), the control population had been increased by 153%, and 23.3% of controls are now nulliparous. The data tables reveal the strange effect of packing the control population in this way: women with two children appear have a 40% higher risk of breast cancer than nulliparous women. Add to this the fact that the vast majority of Italian women who have abortions already have children, the proverbial "bottom line" is another case of the protective effect of parity masquerading as the protective effect of abortion.

Since breast cancer is such a common disease, and induced abortion such a common procedure, the public health impact of the latter on the former must be devastating by even the most conservative estimation. If we consider only the increased risk associated with abortion in the absence of full-term pregnancy (800,00 induced abortions per year in the US on nulliparous girls and women), ignoring the effect of delaying pregnancy, we may assign the modest, minimum relative risk value of 1.5. If we then assume and average lifetime risk in the absence of abortion of 10% then we can expect abortion to be responsible for at least 40,000 excess cases of breast cancer every year, by the time the cohort of American women who were in their twenties in 1973 reach their eighties in the 2030's. Clearly, many thousands have already been afflicted with breast cancer due to previous abortions, and tens or hundreds of thousands more will be, also from abortions that have already taken place!

There is an opening from some skepticism here, however, when we consider that, of necessity, most of the data linking induced abortion to breast cancer has been gathered on young patients. It may thus be argued that the increased risk may only last during the premenopausal period. After all, the risk of contracting breast cancer by age 50 is only about 2%. Even so, a relative risk of 1.5 would raise incidence by 1% of 800,000, or 8,000 excess per year. But there is every reason to be less optimistic. The many early studies on spontaneous abortion that showed increased risk made no age distinctions among patients. More recently, a most careful and thoroughgoing analysis of a cohort of 3,315 parous women in Connecticut who gave birth between 1946 and 1965, was published by Hadjimichael et al. in 1986. They found not only a significant, independent relative risk of 3.5 for women who had any abortions (all presumed spontaneous in the absence of legally induced abortion), but also a much steeper rise in incidence with age among these women, compared to those with no abortions.40

The good news about abortion and breast cancer, in fact, the only good news - is that induced abortion is an elective procedure; a matter of choice, as it were. A woman can simply elect not to have one. The worst news about the link between abortion breast cancer is that it is news at all, considering the one-sided evidence that has been piling up around the globe for decades now. Even as late as July, 1992, Harris et al. published an apparently thorough, three-part review on breast cancer in the New England Journal of Medicine (perhaps the most quoted source of medical news for the popular media) that was totally devoid of any mention of abortion whatsoever, even as a potential risk factor.41 Aware of the evidence, one of the authors even claimed, as recently as April of this year that "this information has not been suppressed".42 A change in the informational climate in that direction would be most welcome.

Joel Brind, PhD.

FOOTNOTES
nant Breast Tumors in Relation to Early Oral Contraceptive Use and Early Abortions, Cancer, 67:1285-1290