

## New Study Pinpoints Oral Contraceptive-Breast Cancer Link (OCBC link); Resurrects Abortion-Breast Cancer Link (ABC link)

By Joel Brind, Ph.D.

January 3, 2010

In the April, 2009 issue of the prestigious cancer epidemiology journal *Cancer Epidemiology, Biomarkers and Prevention*, appeared a paper by the prestigious Janet Daling group of the Fred Hutchinson Cancer Research Center in Seattle, WA, with first author Jessica Dolle. [1] The paper represents a bombshell in OCBC (oral contraceptives-breast cancer) research in terms of new data; and a bombshell in ABC (abortion-breast cancer) research in terms of admissions about existing data.

The Dolle study is based on a population of 897 cancer patients diagnosed under age 45 and 1,569 controls with a similar age distribution, all from the greater Seattle, WA area. The subjects were all subjects of earlier studies published by the Daling group during the 1990's (diagnosis dates between 1983 and 1992); specifically, the patients for whom breast tumor tissue specimens were still available to do complete analyses for 3 prognostic tumor markers, namely, estrogen receptors (ER), progesterone receptors (PR) and HER2 receptors. [2,3] The present study divides the patients thus examined into two groups: Triple negative breast cancer (TNBC), i.e., those negative for all 3 markers (187 cases) and all other combinations (710 cases; referred to as non-TNBC).

TNBC was first described in 2007, and represents a subset of cases (about 10% - 20% of all breast cancers) with a particularly aggressive and treatment-resistant cancer type. Other studies have shown TNBC to be more prevalent among younger women, those of African-American ethnicity, and those who are overweight.

Although the Dolle study population, for whom full demographic, medical and reproductive history had been collected for the original study, was analyzed on the basis of age and body mass index (BMI), meaningful analysis for ethnicity was precluded by the population's being almost exclusively (94%) Caucasian.

There was found to be no difference between TNBC and non-TNBC in regard to age at diagnosis, but there was a small (though statistically not significant) association between high and low BMI patients and TNBC only.

The real dramatic new finding was a strong association between TNBC and OC (oral contraceptives) use; particularly among those whose first OC use was under age 18: odds ratio (OR) = 3.7, and those who had gone between 1 and 5 years since last use: OR = 4.2. (OR is a measure of relative risk. Hence, OR = 4.2 means a 320% risk increase over those who never used OCs). Importantly, this strong association with OC use did not appear for non-TNBC cancers, which were very weakly related (20% - 30% risk increase) to OC use.

As noted in the literal bottom line of the Dolle study's abstract, such clear findings are strongly indicative of a genuine causal effect of OC's on TNBC, i.e., "lending support to a distinct etiology." While the authors did not suggest anything about the nature of this

“distinct etiology”, it is likely that, rather than simply acting as a tumor promoter (secondary carcinogen), the synthetic estrogen-progestin combination of OCs, or one or more of their metabolites, actually act as primary carcinogens, i.e., cause mutations in breast cells that lead to cancer formation.

As noted above, in terms of the ABC link, there are really no new findings as such; rather, a repeat of the modest but significant prior findings of the studies from the 1990's, i.e. those two studies - Daling et al. 1994 and Daling et al. 1996 - had reported ORs for induced abortion and breast cancer of between 1.2 and 1.5. Hence, the reported OR in the present study of 1.4 was not really new. But what was striking was the way in which the finding of a significant ABC link was characterized. Specifically, abortion appears in the data table which lists the associations found for “known and suspected risk factors”. In the text, the effect of the significant risk factors, including induced abortion, were described as “consistent with the effects observed in previous studies on younger women.” Hence, this paper provides clear support for the existence of the ABC link.

But what is really new here is that one of the coauthors of this study is one Louise A. Brinton of the NCI. Importantly, Brinton was the chief organizer for the 2003 NCI (U.S. National Cancer Institute) “workshop” on “early reproductive events and breast cancer”, a panel which reported that the lack of an ABC link had been “established”. In other words, since 2003, the NCI has firmly maintained the position that there is no ABC link; that the studies which had reported such a link were deemed unreliable. However, two of these prior studies were the very studies by the Daling group (of which one Brinton also was a co-author). [2,3] Now, in 2009, Brinton is on record reiterating findings of the ABC link and reporting them as “consistent” with earlier studies that found induced abortion to be a risk factor.

Can it not therefore be argued that the NCI is backing off its denial of the ABC link? This is big news, to be sure, but no one has challenged the NCI with it, yet.

#### References:

1. Dolle J, Daling J, White E, Brinton L, Doody D, et al. Risk factors for triple-negative breast cancer in women under the age of 45 years. *Cancer Epidemiol Biomarkers Prev* 2009;18(4):1157-1166.
2. Daling JR, Malone DE, Voigt LF, White E, Weiss NS. Risk of breast cancer among young women: relationship to induced abortion. *J Natl Cancer Inst* 1994;86:1584-1592. White E, Malone KE, Weiss NS, Daling JR. Breast cancer among young US women in relation to oral contraceptive use. *J Natl Cancer Inst* 1994;86:505-514.
3. Daling JR, Brinton LA, Voigt LF, et al. Risk of breast cancer among white women following induced abortion. *Am J Epidemiol* 1996;144:373-380.