

### **Breast-fed infants possibly exposed to dioxins in milk, compared to formula-fed infants, have unexpectedly lower incidence of endometriosis in later adult life**

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In Japan, like other industrialized countries, dioxin contamination is a serious public problem now. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and these compounds are resistant to degradation and are ubiquitous environmental pollutants that become concentrated in animal tissues, climb the food chain, accumulate in adipose tissue and are excreted in breast milk in large amounts. The estimated daily dietary intake of these pollutants by breast-fed infants was reported to amount to 170 pg/kg/day at 2 months of ages which is higher than the tolerable daily intake recommended by the WHO-10 (most recently, 1-4 pg/kg/day) Recent Japanese government reports indicated that daily dioxin intake of average Japanese is estimated to be 3.26pg/kg/day and breast milk contains 17.4 pg/g fat, the highest levels among those analyzed all over the world.

Recent fragmentary evidence has suggested a link between TCDD and endometriosis. It has been implied that environmental toxicants might enhance endometriosis through their immunosuppressive and estrogenomimetic activities [1]. In rhesus monkeys, chronic low-dose exposure to TCDD at a dose of 126 pg/kg/day for four years was directly correlated with an increased incidence of the development of endometriosis [2]. Higher levels of dioxin in women with endometriosis have also been reported [3]. It is still not clear whether dioxin is the causative agent of endometriosis in human. The studies may be warranted to see whether lactational exposure to TCDD and related compounds may be involved in the pathogenesis of endometriosis. Therefore we performed an epidemiological study to evaluate a possible link between the breast milk intake of such pollutants in infancy and the later development of endometriosis.

Information on modes of feeding along with other obstetric data was obtained with through a self-administered questionnaire. They all were informed of the purpose of the present study and those who do not know how they were fed as a baby were excluded from this

study. Controls were healthy Japanese volunteers of reproductive age with no complaints of dysmenorrhea (control group) who belong to one of 8 companies willing to cooperate this project. Patients with endometriosis (confirmed by laparoscopy or laparotomy) were those who belong to the Japanese Endometriosis Association or who underwent surgery in the Tokyo University Hospital. There were significant differences in modes of feeding during infancy between controls and patients with endometriosis (Table 1). The percentage of breast-fed infants in control group was 68%, which was significantly higher than the percentage (51%) in the group of patients with endometriosis.

In formula, milk lipids contain a negligible amount of dioxins and the postnatal exposure of dioxins in formula-fed infants is of no concern although they were prenatally exposed to some extent since dioxins can pass through the placental barrier. On the contrary, breast-fed infants are exposed to higher doses of dioxins and, indeed, their body burden of dioxins is much higher than that of formula-fed infants [4]. However, our finding that the percentage of breast feeding was significantly lower in patients with endometriosis suggests that dioxin burden, at least during infancy, is not a risk factor for developing endometriosis in adult life. One possible explanation for this is that the half-lives of dioxins and congeners are shorter in infants (5–months) than in adults (10–years) [4]. Alternatively, present data may call into a question a possible link between dioxins and endometriosis. In addition, we cannot discount the possibility that breast feeding per se decreases the occurrence of endometriosis. It is intriguing to speculate that breast milk might contain some factor(s) that lowers the risk of endometriosis, as is the case in the well-known association of breast feeding with reduced risk of otitis media and other bacterial and viral infections, allergies, childhood cancers, diabetes mellitus, sudden infant death syndrome and so on.

Among the various possible detrimental effects of dioxin and related compounds, development of endometriosis is reported to be caused at a lowest dioxin dose in animal experiments [1]. Despite this, the present finding that breast feeding does not seem to increase the potential for developing endometriosis suggests that dioxin introduced into the body through breast feeding does not increase the risk of dioxin-related harm. Thus, we may well urge mothers to continue breast feeding because the benefits may far outweigh any theoretical risks at present. However, the amount of pollutants in milk should be closely watched and it remains mandatory to reduce the expulsion and dumping of dioxins and related compounds as much as possible to keep breast milk clean for the next generations as well.

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**Table 1.** Modes of feeding during infancy in healthy controls and patients with endometriosis.

Subjects	Total	Breast feeding	Combined	Formula
Controls	2281	1550 (68.0%)	427 (18.7%)	304 (13.3%)
Patients*	567	289 (51.0%)	177 (31.2%)	101 (17.8%)

Modes of feeding during infancy were classified as follows: i) breast feeding (breast milk only for at least three months); ii) combined feeding (breast feeding plus formula milk); and iii) formula (formula milk only). \*P<0.001 compared by chi-square test.

