CORRESPONDENCE

Chemotherapy-related conversion of tumor

To the Editors:

I would suggest that the title of the report by Deppe and associates, "Transformation of endodermal sinus tumor to dysgerminoma following chemotherapy," (AM. J. OBSTET. GYNECOL. 139:970, 1981), is misleading, and that the report does not really compare, as stated in the introduction, with the report of DiSaia and associates,[1] since there really was no "chemotherapy-related conversion." Although the tumor in question is reported by Deppe and associates to be an endodermal sinus tumor in the title of their report, one reads in the body of the report that it was, in fact, a "mixed germ cell tumor with *predominantly* [italics mine for emphasis] endodermal sinus tumor histology, but with some choriocarcinoma elements and a few areas of dysgerminona." It is well known that malignant germ cell tumors are not always purely of one cell type, but often have several cell types, including endodermal sinus tumor, choriocarcinoma, dysgerminoma, or immature teratoma.[2]

The report by Deppe and associates is, therefore, not too surprising in view of the fact that one of the cell types originally present in the tumor seems to have been resistant to the chemotherapy utilized. As stated in the report by the authors themselves, "it is attractive to hypothesize that the chemotherapy destroyed all of the cell lines except the dysgerminomatous elements, allowing these to proliferate." However, what was fascinating in the report by DiSaia and associates was the postulated "retroconversion" of immature teratoma, secondary to chemotherapy, to mature teratoma, or dermoid, which did not happen in the case reported by Deppe and associates, wherein some of the originally immature elements present before chemotherapy were still present in the same immature form after chemotherapy. Malignant immature elements persisted in the report by Deppe and associates, whereas in the report by DiSaia and associates, all immature malignant elements seemingly vanished after chemotherapy, with only benign mature elements persisting, or "retroconverted." A comparison of these two reports is no different than a comparison of ovaries to apples and oranges. Had some speculation been made, or actual performance of in vitro testing of different cell types to different chemotherapeutic agents to determine sensitivities and/or resistances of different cell types to different agents, prior to therapy, as one does with bacteria and antimicrobial agents, then the report by Deppe and associates might well have added to our fund of knowledge. As it is, it is a mildly, perhaps, interesting case report, but without anywhere near the significance attributable to the report by DiSaia and associates.

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2. DiSaia, P. J., Morrow, C. P., and Townsend, D. E.: Synopsis of Gynecologic Oncology, New York, 1975, John Wiley & Sons, Inc., p. 174.

Reply to Dr. Fribourg

To the Editors:

Dr. Fribourg seems to offer the following criticisms: (1) He objects to our use of the term "conversion" because he considers it misleading. (2) He thinks that there is no comparison between our observation and that of Dr. DiSaia. (3) He states that our observation is "not too surprising" and concludes that it is not as significant as that of DiSaia and colleagues, and thus he questions its contribution to the general "fund of knowledge."

We are pleased to address these criticisms individually.

1. We removed a tumor, the dominant cell type of which was endodermal sinus. We treated with chemotherapy. On reexploration, we found no endodermal sinus tumor; instead, we found only dysgerminoma. Whether this observation was due to "conversion" or selective cell destruction is unclear, and, in a semantic sense, Dr. Fribourg might be correct. The process might even be selective cloning.

DiSaia and associates treated a malignant teratoma which had several elements (some of which might have been benign), and, at second look, found only benign

elements. Can Dr. Fribourg state with certainty that this was not selective eradication instead of "retroconversion"? The semantics do not disturb us.

2. We never meant to compare directly with DiSaia and co-workers. In fact, our opening paragraph clearly states that, "we have observed a *different* kind of conversion which we wish to report."

3. Perhaps our observation did not surprise Dr. Fribourg, but it was a new observation for us, and we had not found it described elsewhere. How many patients with endodermal sinus tumor has Dr. Fribourg or any therapist studied by second-look operation after apparently successful chemotherapy? Traditionally, endodermal sinus tumors are considered to be highly virulent, with poor survival, and the opportunity for such study has been limited until the recent advent of improved chemotherapy.

Finally, we make no claim for comparative significance. Instead, we offer this report to suggest that there might be stages in transforming usually lethal neoplasms into benign neoplasms, and that "retroconversion" or "conversion" or "selective cell kill" might all be elements in a complex continuum. Only by encouraging such reports from gynecologic oncologists can enough information be accumulated to justify the prospective in vitro studies which Dr. Fribourg prefers. Perhaps their significance will then be evaluable with perspective and precision.

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Cardiovascular complications of terbutaline for preterm labor

To the Editors:

It was with great interest that I read the article by Katz and colleagues (AM. J. OBSTET. GYNECOL. 139:605, 1981) on cardiovascular complications and terbutaline treatment. The authors found 5% incidence of severe cardiovascular complications in patients treated with infusion of terbutaline for preterm labor.

This figure is surprising. This drug was introduced in our clinic (3,200 deliveries per year) in 1971,[1, 2] and has since been used routinely for treatment of preterm labor. During this period, manifest or suspected pulmonary edema has been recorded in only a few cases, and there have been very few reports about this complication,[3] despite the fact that terbutaline is used in most clinics in Sweden. Drugs with negative inotropic effect or drugs that cause water retention might, together with a beta-receptor agonist, cause cardiovascular problems. This type of complication is also associated with iatrogenic volume overload—and, according to the above-mentioned article, twin pregnancy, also.

However, the authors concluded that they administered terbutaline in a low dose (10 to 30 μg/min) and claimed that the range frequently used is 10 to 80 μg/min. It must be stressed that the maximum rate of infusion is 25 μg/min.[1, 2] Rates of infusion that exceed this have been reported by Wallace and colleagues[4] but cannot be recommended. It can be assumed that the risk of complications of this type is correlated to the maximum rate of infusion of the drug.

Finally, I do agree with the authors' recommendations. Terbutaline is a potent inhibitor of uterine activity but should be restricted to carefully selected patients. Mother and fetus should be carefully monitored during treatment, and immediate withdrawal of the treatment must be considered if pronounced side effects appear.

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3. Notices from the Swedish Adverse Drug Committee.
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Reply to Dr. Ingemarsson

To the Editors:

The 5% incidence of severe cardiovascular complications that was shown by the recent review of our experience with terbutaline tocolysis[1] was initially met by us with the same surprise expressed by Dr. Ingemarsson. Since no other published review, except for a few anecdotal case reports, is available in the obstetric literature, the incidence in other institutions in the United States and Europe remains a matter of speculation. In a recent study by Speroff and associates,[2] an identical 5% incidence of pulmonary edema was found among 99 patients undergoing terbutaline tocolysis. If, indeed, the actual incidence in Sweden is lower, we have no obvious explanation to settle this disparity.

Dr. Ingemarsson's comment about the role of the infusion rate as an etiologic factor in patients with cardiovascular complications deserves clarification. Although our treatment protocol, as well as that of