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Editorial

Hydatidiform moles

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Our increasing knowledge of hydatidiform moles appears to create fresh problems and new dilemmas. Only the most prominent of these will be considered here.

Are complete and partial hydatidiform moles separate entities?

Until recently it appeared that complete and partial hydatidiform moles differed clearly from each other in both morphological and cytogenetic terms, the complete moles having a 46XX or, less commonly, 46XY chromosomal constitution and the partial moles being associated with a fetal triploidy (Szulman and Surti 1978a, b; Jacobs et al. 1980; Surti et al. 1982). Recent flow cytometry results have, however led to a blurring of this apparently sharp division into two discrete entities (Hemming et al. 1987). Thus, some moles which morphologically show a complete pattern have a triploid DNA pattern whilst a significant proportion of morphologically defined partial moles appear to be diploid, this latter finding confirming a previous cytogenetic study of three partial moles with a diploid karotype (Teng and Ballon 1984). Further a number of tetraploid moles have now been described (Surti et al. 1986; Lage et al. 1988), some of these taking the form of a complete mole and others that of a partial mole.

It is not yet known whether triploid complete moles are of purely androgenetic origin or whether they are dispermic or monospermic; the exact nature of diploid partial moles is also currently obscure. Nevertheless it is apparent that it is no longer possible to predict the karotype of a hydatidiform mole from its histological appearances and this raises the question of whether a mole should be classified in morphological or karotypic terms. Is it possible that the vesicular change in some partial moles is so extensive that they appear morphologically to be complete and are there complete moles in which vesicular change does not involve the entire villous population? Is it, in fact, justifiable to continue distinguishing complete from partial moles in routine histopathological practice?

Does a diagnosis of a partial mole necessitate the same follow-up procedure as does that of a complete hydatidiform mole?

There is no disagreement about the principle that all women who have had a complete hydatidiform mole should be carefully followed up with serial hCG estimations. There has been less agreement as to whether or not a similar follow-up surveillance should be a routine procedure of women who have had a partial hydatidiform mole, largely because the natural history of a partial mole is still not fully defined. It is now clear, however, that the incidence of persistent trophoblastic disease following a partial mole is not dissimilar to that encountered after a complete mole (Mostoufi-Zadeh et al. 1987) whilst a number of invasive partial moles have now been reported (Gaear et al. 1986). It is usually stated that there has been no convincing published report of a choriocarcinoma following a partial mole: Looi and Sivanesaratnam (1979) did, however, record an example of an undoubted choriocarcinoma developing after a partial mole. This only proves however that a choriocarcinoma *can* develop in a patient who has had a partial mole and there is currently no evidence that the incidence of choriocarcinoma after a partial mole is any higher than that found after a normal pregnancy.

The available data suggests therefore that the potential for complications, certainly those falling short of an obvious choriocarcinoma, after a par-

tial mole is as great as is that after a complete mole and indicates that follow-up after a partial mole should be as mandatory as after a complete mole. It is though possible that the period of surveillance after return of hCG levels to normal could be shorter for women with partial moles than the two years currently recommended for patients with a complete mole.

Can, and should, prognostic criteria be determined for complete moles?

Approximately ten per cent of women with a complete hydatidiform mole progress to persistent trophoblastic disease whilst between three and five per cent will develop a choriocarcinoma.

It has been suggested that the risk of eventual development of a choriocarcinoma can be estimated by grading the degree of trophoblastic proliferation, it being argued that the greater the trophoblastic proliferation and atypia the higher is the risk of post-molar complications (Hertig and Sheldon 1947). There are, however, many who are unconvinced of the value of such a grading system (Elston, 1987) and, indeed, since all patients with moles should be followed up in the same way, irrespective of the histological appearances of the mole, it is clear that histological grading is now irrelevant. It can, in fact, be argued that any type of grading system for moles is potentially dangerous as it may, in injudicious hands, lead to the unnecessary administration of chemotherapy to some women and to the ill-advised neglect of others.

The fact that histological grading of moles is of little value does not, however, mean that a search for prognostic features indicative of an increased propensity for persistent trophoblastic disease or choriocarcinoma should be abandoned. It is of interest that flow cytometry has failed to identify such features, for the hyperdiploid fraction of moles progressing to persistent trophoblastic disease is the same as in moles with sequelae (Hemming et al. 1988): as the hyperdiploid fraction is an index of cell proliferation this confirms that the degree of trophoblastic proliferation is of very limited prognostic importance. The most significant contribution to our understanding of molar progression has been the demonstration that dispermic (heterozygous) moles are associated with a much higher incidence of subsequent persistent trophoblastic disease than are monospermic (homozygous) moles (Wake et al. 1987). The biological implications of this finding are far from being understood but are clearly considerable.

What is the nature of a hydatidiform mole?

There is a widespread impression that a hydatidiform mole is a benign neoplasm, this belief, usually implied rather than stated, being based solely on the fact that choriocarcinoma occurs more commonly after a molar gestation than after a non-molar pregnancy. It is this attitude which has led to histological grading of moles and to the concept of "malignant change" in a mole. In reality moles are simply a form of abortion and there is nothing to suggest that they are in any way neoplastic. The fact that a mole may become "invasive" is no more an indication of neoplasia than is the invasion of the myometrium by normal placental villi in cases of placenta accreta whilst blood borne spread of trophoblastic tissue, to sites such as the vagina and lungs, occurs in all normal pregnancies and is not confined to molar pregnancies (Attwood and Park 1961).

There is, in fact, a considerable, though largely unacknowledged, hiatus in our knowledge of the events which occur in the time interval between either a normal or a molar pregnancy and the development of a choriocarcinoma. It has recently been suggested that an apparently primary choriocarcinoma occurring after a normal pregnancy may, in fact, be an intramyometrial metastasis from a small intraplacental choriocarcinoma (Fox and Laurini 1988) and it is possible that some post-molar choriocarcinomas are similarly metastases from a small unrecognised intramolar focus of choriocarcinoma. Alternatively, a post-molar conception may be a choriocarcinoma ab initio, the implanting trophoblastic of a fertilised ovum developing directly into a chorciocarcinoma (Acosta-Sisson 1955), the factor, or factors, which predispose to a molar gestation also predisposing to a choriocarcinoma.

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