GUEST EDITORIAL:

CHORIOCARCINOMA — A REAPPRAISAL

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ONE in three hundred pregnant women in this country (Sivanesaratnam and Ng, 1977) may develop a molar pregnancy. A high number of these patients will develop choriocarcinoma. It used to be said that if one had choriocarcinoma and one survived, the diagnosis was wrong. Now, it is a potentially curable disease.

This, together with the easy availability of methotrexate, makes it tempting for specialists (and others) to attempt the management of these cases when they come across them. This is especially so in Malaysia where patients would otherwise have to travel long distances to get to specialist centres (who may not possess all that many extra facilities anyway) particularly as trophoblastic disease can be cured using agents like methotrexate in over 80% of cases (Lewis, 1976).

Unfortunately the truth is slightly different. In the presence of the full-blown, avillous, histologically proven metastatic disease seen so commonly in Malaysia, the survival rate is depressingly low. Though the unit in Singapore is very experienced in treating choriocarcinoma, and though it has modern facilities like radio-immunoassay of B-submit human chorionic gonadotrophin to monitor chemotherapy, Ratnam *et al.* (1976) found that if the patient came with metastatic avillous choriocarcinoma the survival rate was only 46.7%. His cases with early disease had over 80% survival rates. It is of course possible that the disease in this part of the world is biologically different from that in the West, but it is most unlikely that the fate of patients treated at random across the length and breadth of Malaysia is much better than of those in the highly specialised unit in Singapore.

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It is essential, therefore, for the sake of our patients, to examine how workers have been able to report cure rates around 80%, and determine how we, in this country, can achieve comparable results. Two aspects need close examination. The first is early diagnosis, and the second is management. Early diagnosis is very important. It is highly significant that patients diagnosed late are now grouped as high risk cases (Bagshawe, 1976) and require highly toxic combination chemotherapy, sterile rooms, and all the massive paraphernalia of specialised oncology units before they have any chance of cure.

This means that we can only hope to decrease the number of patients who die by catching the disease early. To do this one needs to have units which are capable of conducting the painstaking job of *close follow-up*, and which have facilities for assay of tumour markers to pick up early malignant change. Radio-immunoassay picks up the patient whose human chorionic gonadotrophin levels have dropped below the level of sensitivity of the usual immunological tests for pregnancy, *but have not reached zero, and who is therefore harbouring microscopic amounts of either malignant or potentially malignant trophoblast.*

It is when the disease is picked up at this early preclinical stage that 80% cure rates can be expected, as will be seen by inspecting the results of Ratnam *et al.* (1976).

It is also necessary to keep in mind that full-blown disease can be present even when human chorionic gonadotrophin levels are low, so that one cannot be complacent just because a pregnancy test is negative. It is necessary to be aware that recent work (Singh, J. and Sivanesaratnam, V., in preparation) has clearly shown that an x-ray chest may not reveal the presence of lung metastases, and other radiological monitoring techniques may be required. It is also necessary to be aware that choriocarcinoma invades the

myometrium, and may be present elsewhere than in the uterine cavity, so that *a negative D & C does not indicate absence of disease.*

For the woman who has had a molar pregnancy evacuated and nees to be followed up, there is evidence suggesting (Stone *et al.*, 1976) that the use of the contraceptive pill may lead to a slower removal of trophoblastic tissue from the system. If she unfortunately becomes amenorrhoeic during the period of observation, *it is essential to assume that she has choriocarcinoma until proved otherwise.*

There are few satisfactory ways one can find out whether this is a normal intrauterine pregnancy or choriocarcinoma. The first is the use of ultrasound: the gestation sac can be picked up on grey scale at six weeks' and fetal movements seen on real time at eight weeks' amenorrhoea, already rather late. The second is the use of radio-immunoassay; high human chorionic gonadotrophin and low human placental lactogen levels are rather suggestive of molar trophoblast (Lim *et al.*, 1976). The third is to evacuate the uterus and examine the contents. Finally one can wait, and see whether the patient lives, or dies.

The second problem is that of management. The drugs used in treating the disease are potentially lethal. It is therefore preferable that they are used only as long as necessary. However, if they are not used long enough, recurrence is certain. Incomplete therapy also renders the tumour resistant to chemotherapy and makes subsequent therapy difficult and ineffective.

Figure 1 shows that if one stops after an arbitrary number of courses after the immunologic test for human chorionic gonadotrophin is negative, the chemotherapy may be incomplete. It will be seen therefore that the *usually used immunological assay methods are adequate neither for the follow-up of molar pregnancies nor for monitoring chemotherapy in choriocarcinoma.*

If we review facilities available in this country, one will see that ultrasound is as yet available only in General Hospital, Kuala Lumpur, and radio-immumoassay for human chorionic gonadotrophin while until recently available in Institute of Medical Research, Universiti Kebangsaan and

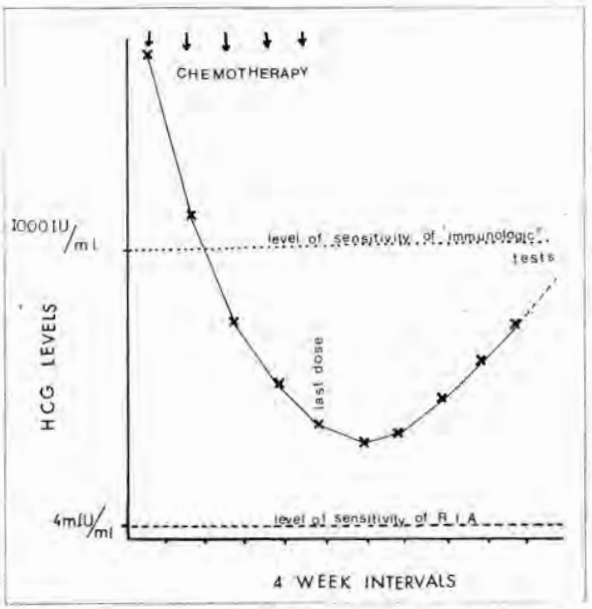

Fig. 1. Levels of human chorionic gonadotrophin (HCG) during course of chemotherapy showing inadequacy of latex agglutination test in monitoring; chemotherapy stopped too early while radio-immunoassays (R I A) would have shown the presence of viable, secreting tumour cells.

University of Malaya is not so far developed at any of these places that they can prepare their own B-submit antibody, and they were certainly *not being deluged by anything like the number of tests that should be asked for to cover all the patients in the country who have had molar pregnancy and should at this moment be on human chorionic gonadotrophin surveillance.* Also, serum for human chorionic gonadotrophin assay *does not travel well;* the hormone breaks down rapidly at room temperature. The facilities needed are beginning to be available. But they need to be developed, and used.

Finally it is essential to understand that follow-up does not just mean doing tests and clinical examinations on patients who come. Adequate follow-up implies tracing defaulters, persuading them to attend, understanding their difficulties, and assisting to overcome these, tracing results, and a general ability and willingness to spend time with and for each patient. This is obviously impossible for a busy specialist, and specialists throughout the country are very busy indeed.

The above is a fairly superficial review of the problem, as it stands. Countries like England long ago realised that adequate experience and care of cases like these can only be achieved by the use of regional centres. It is patently clear that we who have much more of this disease must similarly form and develop regional centres, and concentrate *at least* the serological follow-up of our patients there, NOT AFTER THEY HAVE DEVELOPED CHORIOCARCINOMA, BUT BEFORE.

Unless we do so, and make sure that these regional centres are not just centres in name but have the basic *functioning* facilities outlined above, and have people with enough skill, enthusiasm, and *available time* to cope with these patients we will have to admit, if we are at all honest with ourselves, that we are prepared (for whatever reason it may be) to let a proportion of our women who should have an 80% chance of survival have only a 40% chance to do so.

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