

# Prophylaxis against choriocarcinoma

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## Summary

CHORIOCARCINOMA is a serious malignant disease in which the majority of cases are preceded by the benign hydatidiform mole. Forty-one patients with hydatidiform moles were managed during the period March 1968 to March 1976. All patients received prophylactic methotrexate intravenously during and just after evacuation of the mole or after total hysterectomy. The rationale for this form of prophylaxis against choriocarcinoma is discussed. Thirty-six patients were closely followed up for three years or more. None developed choriocarcinoma.

Although the treatment of choriocarcinoma with chemotherapy has markedly reduced the mortality rate from 80% to 24% (Chun and Ma, 1974), the mortality from the disease is still relatively high. We should, therefore, not only try to improve our management of this condition, but also direct our attention at its prevention. Choriocarcinoma may result from non-molar pregnancies, but the patient with molar pregnancy has a 2,000–4,000 higher chance of developing it (Park and Lees, 1950). As shown in Table I, about 50% to 70% of choriocarcinomas are preceded by molar pregnancies. Therefore, the incidence of choriocarcinoma would theoretically be markedly reduced if prophylaxis against it was taken in the management of molar pregnancies. In this paper, we present our results of a trial of prophylaxis against choriocarcinoma in the management of hydatidiform moles. This trial was carried out in the Obstetric and Gynaecological Unit, University Hospital Kuala Lumpur, Malaysia.

**Table I**  
**Natural History of Choriocarcinoma**

| Author        | Type of preceding pregnancy |          |                 |                   |
|---------------|-----------------------------|----------|-----------------|-------------------|
|               | Mole                        | Abortion | Normal Delivery | Ectopic Pregnancy |
| Hertig (1950) | 50.0%                       | 25.0%    | 22.5%           | 2.5%              |
| Chan (1967)   | 67.5%                       | 17.5%    | 15.0%           | –                 |
| Tow (1965)    | 70.0%                       | 20.0%    | 10.0%           | –                 |
| Chun (1974)   | 57.0%                       | 21.0%    | 22.0%           | –                 |

## MATERIALS AND METHODS

During the period March 1968 to March 1973, forty-one patients with molar pregnancy were treated and followed up till March 1976. The incidence pattern of this disease in relation to normal pregnancies and to abortions is shown in Table 2. Molar pregnancy is thus relatively common in Malaysia, as compared to the West (Jeffcoate, 1969; Novak, 1965).

**Table 2**  
**Incidence of molar pregnancies in relation to pregnancies and abortions**

|                   |
|-------------------|
| 1: 330 deliveries |
| 1: 35 abortions   |

Patients belonging to the "high risk" group (Tow, 1965), i.e. patients aged 40 or more, or para 3 and over, were subjected to hysterectomy. In all other patients, if they were not already aborting, an

oxytocic drip was set up, and as soon as vesicles were passed or vaginal bleeding occurred, a suction/curettage was performed. A methotrexate drip, containing 20 mg methotrexate in 500 ml 5% dextrose, was set up at the commencement of the surgical procedure and continued for 3 to 4 hours thereafter. A second curettage was done about one week after the initial curettage before the patient was discharged if it was felt that the first curettage had been incomplete. All patients were arranged for follow-up for at least 3 years. They were seen at weekly intervals for the first month, then every fortnightly for 2 months, every month for the next 3 months, every 2 months for the subsequent 6 months, and thereafter at 3 monthly intervals. Those who did not have a hysterectomy performed were prescribed contraception for 2 years so that pregnancy would not interfere with the follow-up assessment of the patients. At each visit a full gynaecological examination and a urine Gravindex pregnancy test were carried out. A chest X-ray was done at regular intervals.

## RESULTS

### Ethnic Distribution

Table 3 shows the racial distribution of the patients. Out of a total of 41 patients, 73.2% were Chinese.

**Table 3**  
Racial incidence of molar pregnancy

| Race    | Number | Percentage |
|---------|--------|------------|
| Chinese | 30     | 73.2       |
| Malay   | 10     | 24.4       |
| Indian  | 1      | 2.4        |

### Age and Parity Distribution

The majority of the patients were in the third decade of life (68.4%). There appears to be a significantly higher incidence of molar pregnancy in the nulliparous group (Tables 4 and 5).

**Table 4**  
Age distribution of molar pregnancy

| Age in years | Number | Percentage |
|--------------|--------|------------|
| less than 20 | 2      | 4.8        |
| 21 - 30      | 28     | 68.4       |
| 31 - 40      | 7      | 17.1       |
| 41 - 50      | 3      | 7.3        |
| more than 50 | 1      | 2.4        |

**Table 5**  
Parity pattern of Molar Pregnancy

| Parity    | Number | Percentage |
|-----------|--------|------------|
| 0         | 10     | 24.4       |
| 1         | 7      | 17.1       |
| 2         | 7      | 17.1       |
| 3         | 4      | 9.7        |
| 4         | 8      | 19.6       |
| 5 or more | 5      | 12.1       |

### Definitive Treatment

This was carried out under intravenous methotrexate cover in all patients. In 12 patients who were in the "high risk" group (Tow, 1965) a total hysterectomy was done with the mole in situ. In the remaining 29 patients, a suction/curettage was done with an oxytocic drip running at the same time to keep the uterus contracted and thereby minimise blood loss and the risk of uterine perforation (Table 6).

**Table 6**  
Definitive treatment of molar pregnancy

| Type of treatment                       | Number | Percentage |
|---|--------|------------|
| Hysterectomy and i.v. methotrexate      | 12     | 29.3       |
| Suction/curettage and i.v. methotrexate | 29     | 70.7       |
| Total                                   | 41     | 100.0      |

### Toxic Effects Of Chemotherapy

Except for 3 patients who developed mild stomal ulcers and sore throat, no other toxic complication was noticed.

### Urine Gravindex Results

In about 88% of patients (Table 7), the urine gravindex pregnancy test became negative within the first 4 weeks. There were no instances where the gravindex test became positive again after having been negative. In one patient, however, the test remained positive for as long as 8 weeks after the initial uterine curettage. A repeat curettage was done under intravenous methotrexate cover. The curettings showed residual molar tissue. The gravindex test became negative 2 weeks later and has remained negative for the past 3 years.

**Table 7**  
**Interval between evacuation/hysterectomy and negative Gravindex**

| Duration in weeks | Number | Percentage |
|-------------------|--------|------------|
| 1                 | 4      | 9.8        |
| 2                 | 9      | 21.9       |
| 3                 | 12     | 29.3       |
| 4                 | 11     | 26.9       |
| 5                 | 2      | 4.8        |
| more than 5       | 3      | 7.3        |

#### **Duration of Follow-up and Incidence of Metastasis**

Five patients were lost to follow-up after 2 to 3 months. The remaining 36 cases were followed up closely for at least 3 years, with no clinical or radiological evidence of local or metastatic choriocarcinoma developing.

#### **DISCUSSION**

It is a well-established fact that metastatic choriocarcinoma is found in a large number of patients where no growth is present in the uterus. Thus it appears that hysterectomy as advocated by Tow (1965) in the "high risk" group of cases, is no guarantee against the development of choriocarcinoma at distant sites. Attention has been drawn to the importance of trophoblastic deportation during molar pregnancy or during the treatment of molar pregnancy (Chan, 1965). He suggested the possibility of subsequent malignant transformation of the deported trophoblast after a variable latent period. This latent period was found by him to be 6 months or less in over 40% of cases (Chan, 1967). The presence of pulmonary metastasis worsens the

prognosis and the presence of cerebral metastasis makes it hopeless. Hence, it would appear logical to administer methotrexate by intravenous drip as described in this paper as a prophylactic measure against the development of metastatic choriocarcinoma subsequently. With this form of therapy, we have had no cases of choriocarcinoma following molar pregnancy in 36 patients followed up for 3 years or more, suggesting it is a safe and worthwhile preventive measure against choriocarcinoma.

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