# INVASIVE MOLE

By

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## SUMMARY

**This study highlights the diagnostic role of ultrasonography in invasive mole. A plea is made to employ sonography routinely in post-molar surveillance, not only for monitoring the lutein cysts, but also to locate myometrial nodule.**

**Surgical enucleation of the myometrial nodule of invasive mole under chemotherapeutic cover appears the most optimal treatment for invasive mole. It is also suggested that no sooner a sonographic diagnosis of invasive mole is made chemotherapy should be initiated to obviate the possibility of haemorrhage. Conveniently the nodule can be surgically enucleated on a later date with minimal morbidity and excellent outcome. Fertility potential is very much preserved as observed in one of our subjects.**

'Invasive mole' denotes molar villi found elsewhere than at their original implantation site, and it is usually invasion of myometrium but could also be in other places such as vaginal wall or the lung (Driscoll, 1984). Although this definition does not take into consideration the quality of the associated trophoblast, most invasive moles evidence moderate to marked trophoblastic activity. By their presence in ectopic sites, viable fragments of molar tissue behave as blood-born deposits of a malignant neoplasm. Uterine hemorrhaga, uterine perforation and intra-peritoneal haemorrhage, and bleeding from the vaginal nodule are the dreaded complications of invasive mole.

Since invasive mole is a myometrial invasion it is most difficult to make the diagnosis from curettage material, and this diagnosis till recently was made at the time of hysterectomy (Surwit and Hammond, 1980). Today, invasive mole is diagnosed with excellent precision by employing ultrasonography in post-molar subjects with abnormal beta hCG regression pattern. In this communication we discuss how these two investigative procedures are employed to diagnose invasive mole, and indicate how excision of the myometrial nodule complemented by methotrexate (MXT) therapy is ideally suited for salvaging the reproductive function of the patient.

*Study Design:* If early diagnosis of vesicular mole has meaningful advantages, we feel that the only way to achieve this is to perform routine first trimester sonography by 8 completed weeks of pregnancy. By waiting for a complaint of vaginal bleeding 2/3rds of

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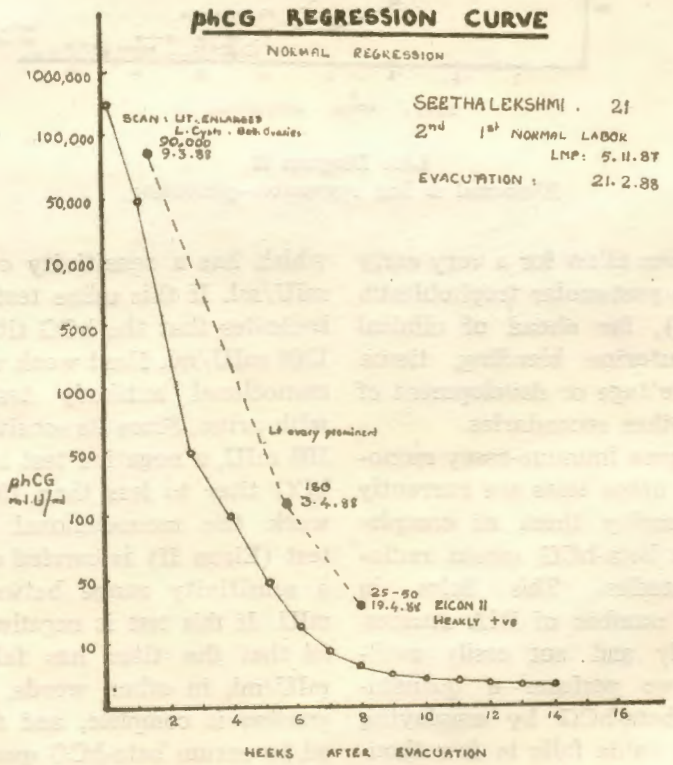
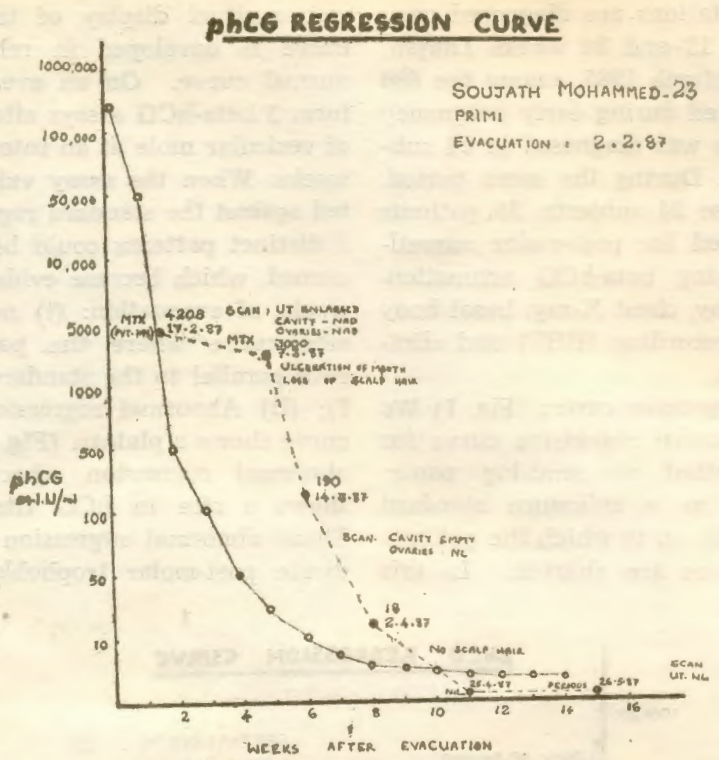
*Accepted for publication on* 11-2-89.

the molar gestations are diagnosed very late, between 13 and 24 weeks (Rajan, 1988). Since March 1985, among the 638 subjects scanned during early pregnancy vesicular mole was diagnosed in 24 subjects (3.76%). During the same period, including these 24 subjects, 33 patients were monitored for post-molar surveillance, employing beta-hCG estimation, ultrasonography, chest X-ray, basal body temperature recording (BBT) and clinical evaluation.

*Beta-hCG regression curve*: (Fig. I) We employ the normal regression curve for beta-hCG plotted on semi-log paper, which serves as a reference standard (Morrow, 1984), on to which the patients beta-hCG values are charted. In this way a visual display of the regression curve is developed in relation to the normal curve. On an average we perform 3 beta-hCG assays after evacuation of vesicular mole at an interval of 1 to 2 weeks. When the assay values are plotted against the standard regression curve 3 distinct patterns could be readily discerned, which become evident by 4 to 8 weeks of evacuation: (i) normal regression curve where the patient's value runs parallel to the standard curve (Fig. I); (ii) Abnormal regression where the curve shows a plateau (Fig. II); and (iii) abnormal regression where the curve shows a rise in hCG titer (Fig. III). These abnormal regression patterns indicate post-molar trophoblastic disease.



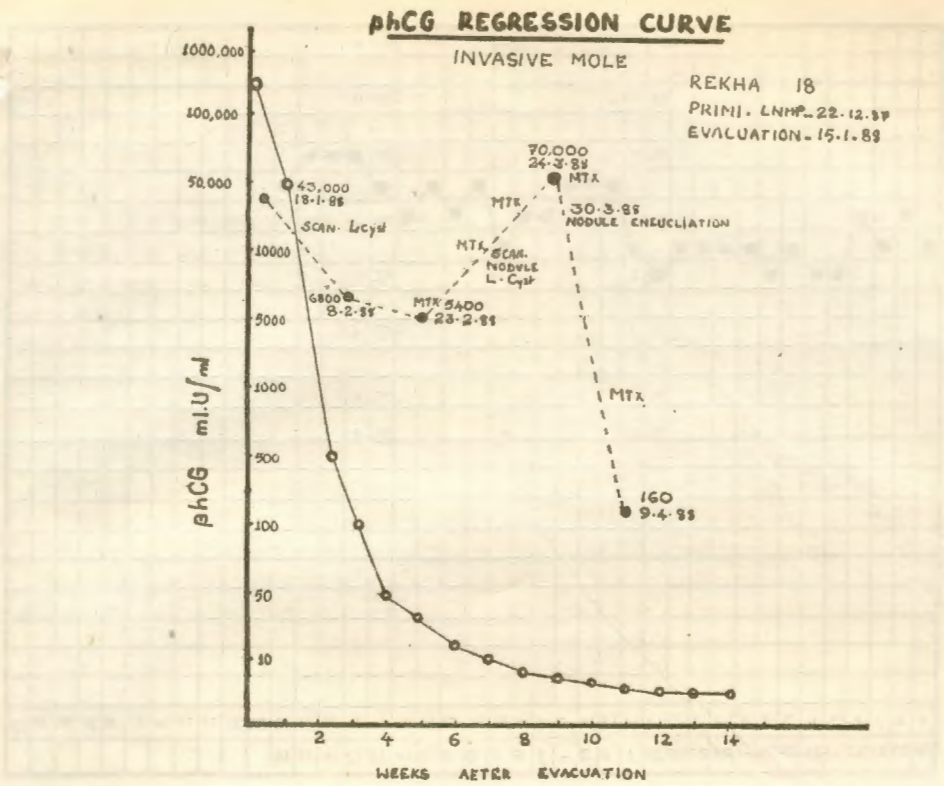

Line Diagram I
Normal ß Lcg regression.




Line Diagram II
Abnormal ß Leg regression—plateauing.

Thus, these curves allow for a very early detection of the post-molar trophoblastic disease (PMTD), far ahead of clinical symptoms of uterine bleeding, tissue diagnosis at curettage or development of pulmonary or other secondaries.

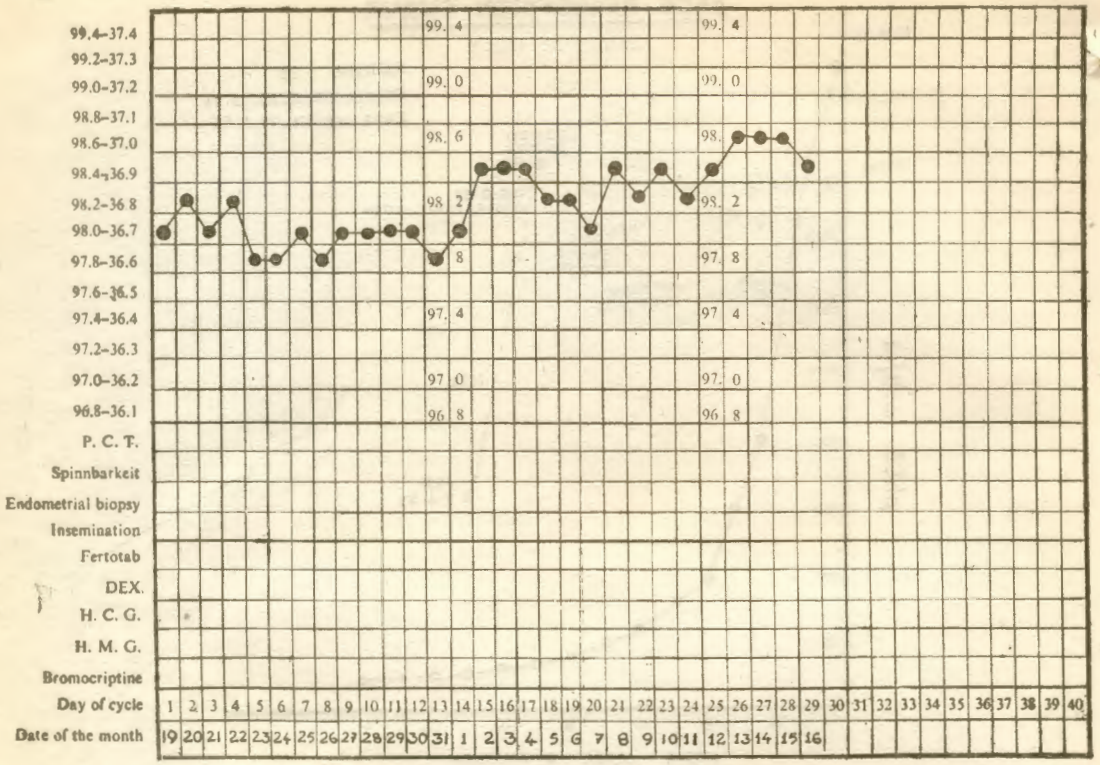
Since the enzyme immuno-assay monoclonal antibody urine tests are currently available we employ them as complementary to the beta-hCG serum radioimmunoassay studies. This helps in minimising the number of RIA studies, which are costly and not easily available. Initially we perform a quantitative study of beta-hCG by employing RIA. When the value falls to few thousand mIU of hCG we perform the 'Gravindex test (immunologic slide test) which has a sensitivity of 1300 to 1700 mIU/ml. If this urine test is negative it indicates that the hCG titer is less than 1300 mIU/ml. Next week we perform the monoclonal antibody test (Pregeolor) with urine. Since its sensitivity is around 100 mIU, a negative test indicates fall of hCG titer to less than 100 mIU. Next week the monoclononal ELISA urine test (Eicon II) is carried out, which has a sensitivity range between 25 and 50 mIU. If this test is negative it is presumed that the titer has fallen below 25 mIU/ml, in other words, the hCG regression is complete, and this is confirmed by serum beta-hCG quantitative RIA. A titer below 15 mIU is considered as indicating complete regression.




Line Diagram III
Abnormal ß Lcg regression—rising level.

By adhering to this monitoring protocol we observed 9 of the 33 post-molar subjects undergoing surveillance had abnormal beta-hCG regression pattern; and this indicates the development of PMTD in 27.27% of subjects followed after molar evacuation. Among the 24 subjects with molar gestation, treated and followed by us 3 subjects (12.50%) had developed PMTD. The high incidence of PMTD in the group recruited for post-molar surveillance (after the molar gestation was evacuated elsewhere) denote the probability that only such of those who had symptoms or abnormal regression were referred. Hence, the true incidence of PMTD developing following molar evacuation should be considered as 12.50%.

*Sonography:* It is well conceived that sonography easily identifies the complete emptying of the uterus after molar evacuation and obviates the need for a check curettage, and also locates the lutein cysts in the ovaries. An equally important role of sonography in subjects with abnormal hCG regression curve is to identify whether the abnormal regression (PMTD) is due to choriocarcinoma or due to invasive mole. Invasive mole is classically diagnosed as a well circumscribed nodule in the myometrium. These nodules could show an echofree area (hemorrhagic) or speckled asppearance of the moles (Fig. IV and V).




**Line Diagram VI**

B.B.T. Evidencing biphasic shift of temperature. This indicates ovulation.

A sonographic evaluation is routinely carried out every 2 weeks in our series, and among the 9 subjects with abnormal beta-hCG regression pattern 4 had invasive moles diagnosed by ultrasound (44.44%). Thus we find an incidence of 44.44% of invasive moles in the total postmolar trophoblastic disease diagnosed by abnormal beta-hCG titer.

In addition to diagnosing invasive mole, sonography precisely locates the site of origin of the invasive mole in the myometrium. This localization is very important because, unless the nodule projects out of the uterus and enlarges the uterus irregularly a laparoscopy/laparotomy diagnosis of invasive mole will be very difficult. Among the 4 subjects in whom invasive mole was diagnosed by ultrasound the nodules were projecting on to the uterine serosal surface and hence easily identifiable at laparotomy in only 2 subjects, and the rest (50%) did not reveal any uterine abnormality, and the nodules could be identified only by following the location indicated by the scan. In one patient (nulliparous) where the nodule was excised, ultrasound enabled the correct localisation of the nodule and accurate placement of uterine incision on the surface of the nodule.

*Invasive Mole*

Invasive mole was diagnosed in subjects with abnormal beta-hCG regression

in whom sonography evidenced a well-circumscribed myometrial nodule or clinical examination revealed a vaginal (suburethral) nodule. Among the 9 subjects with PMTD 4 were identified to be cases of invasive moles (44.44%). Of the 33 subjects undergoing surveillance, identifying 5 cases of invasive mole gives an incidence of 15.15% of invasive mole developing following molar gestation. We also observe that among all those subjects who had molar evacuation done by us and monitored from the very early post-abortal period, (of the 24 subjects) the PMTD developed in all the 3 subjects (12.50%) were in the form of invasive moles. There were no choriocarcinoma in this group. This only suggests that early surveillance of post-molar subjects, within 8 weeks of evacuation, not only promotes an early diagnoses of PMTD but also diagnoses the disease in the stage of invasive mole which is amenable to an optimal treatment described below with almost 100% cure rate.

*Methotrexate:* We employ methotrexate for all subjects wih PMTD. The drug is administered in the standard dose of 0.4 mg/kg body weight, given I.V. for 5 days, every 10 to 15 days. Treatment is initiated as soon as the abnormal hCG regression is noticed. In all those subjects where molar evacuation was done by us and the PMTD detected, the drug was started within 8 weeks of evacuation. For subjects with invasive mole our aims of administering methotrexate are: (i) to achieve immediate regression of proliferation and vascularity, so much so, the threat of uterine rupture could be avoided; (ii) to reduce the vascularity, so much so, the tumor enuceation could be perfected with minimal blood loss. We consider surgical excision of the tumor following 2 to 3 courses of chemotherapy ideal for subjects preferring preservation of reproductive function. Our argument is that following tumour excision there is a precipitous fall of beta-hCG titer and that the duration of chemotherapy could be minimised.

*Nodule Excision*

Among the 5 cases of invasive mole developing following molar gestation 4 were cases of myometrial nodules (80%), and 1 was a vaginal nodule (20%). Of the 4 subjects with myometrial nodules 3 were nulliparous young subjects in whom tumor excision was practised at laparotomy following 2 or 3 courses of methotrexate treatment. Excluding one subject who was operated last week, in the other 2 subjects the beta-hCG titer showed a sharp decline within 1 to 2 weeks of excision of nodule, and complete hCG regression was achieved by just one more course of post-excision chemotherapy. There was one multiparous elderly subject who was subjected to hysterectomy; and the subject with vaginal nodule had excision of vaginal nodule prior to chemotherapy, and was administered 4 courses of methotrexate post-operatively to achieve complete hCG regression.

In addition to the above mentioned 5 subjects with invasive mole there was one elderly parous subject who underwent MTP in the first trimester in the month of March, 1988. She also had an ovariotomy for dermoid of the right ovary. She was admitted during the month of May with complaints of vaginal bleeding. Since she had profuse bleeding a curettage was done (a prior sonography could not be done on her). Curettage further aggrevated the bleeding and

hence hysterectomy was performed. The uterus revealed, hemorrhagic myometrial nodule breaking into the uterine cavity. The uterine cavity was found to be empty. This was another case of trophoblastic invasion of the myometrium which was managed by hysterectomy. Since a scan was not performed, the presence of the nodule was not identified. If the nodule was identified and chemotherapy was ordered immediately the heavy vaginal bleeding and the emergency hysterectomy could have been avoided. Under these circumstances methotrexate treatment could be employed to buy time for deciding on the optimal line of management. The histopathology of the nodule was chorionic villi with no evidence of molar changes. After one week of the surgery her beta-hCG value was recorded as 12 m.IU/ml. She was also given one course of chemotherapy in the post-operative period. Now she is under surveillance.

After the hCG regression is complete and when the patients resume their menstrual cycles, we advocate recording of the BBT for evidence of ovulation (Fig. 6). Atleast 6 regular and ovulatory menstrual cycles could indicate that the subject is fit to attempt next pregnancy.

*Conclusion*

We observe that very early diagnosis of PMTD is certainly possible by employing the beta-hCG regression curve. The practical application of the urine hCG tests as complementary to RIA has been discussed. This protocol identifies PMTD in 12.5% subjects in whom molar evacuation was performed by us and further monitored by us. Among the total 33 subjects undergoing post-molar surveillance the incidence of PMTD is 27.27%, however. Complementary use of sonography diagnoses invasive moles among the subjects with PMTD, and 44.44% of subjects with PMTD are found to have invasive mole. The incidence of invasive mole arising from molar gestation appears to be 15.15%. We also feel that by instituting very early post-molar surveillance the PMTD diagnosed within the first 8 weeks or so of evacuation are in the stage of invasive mole.

We advocate methotrexate to reduce the vascularity, avoid dissemination, and to regress the growth, so much so the immediate threat of uterine rupture could be prevented. Surgical excision of the nodule after 2 or 3 courses of chemotherapy appears to be optimal since beta-hCG remission is very quick following surgery, and the post-operative methotrexate treatment required could be minimised to just one course to achieve complete regression. After complete regression we employ BBT to prove that the cycles are ovulatory which further evidences that the hCG titer is negligible or not increasing. If 6 regular ovulatory cycles could be achieved the patient stands fit to attempt next pregnancy. However, just prior to this a re-confirmation of hCG value will be ideal.

*References*

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*See Figs. on Art Paper II*