CHORIO-EPITHELIOMA AND MALIGNANT HYDATID MOLE

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There seems to be a great deal of confusion in the literature, due to the various terms used to describe these neoplasms. Malignant hydatidiform mole has been called destructive placental mole, invasive mole and chorio-adenoma destruens. Chorio-epithelioma has been referred to as chorioma or as chorio-carcinoma. In order to try to lessen the confusion the following comparative summary has been constructed and from here on only the terms chorio-adenoma destruens and chorio-carcinoma will be used. Benign hydatid mole and syncytioma have only been included in the table in order to complete the group.

<table>
<thead>
<tr>
<th>Benign hydatid mole</th>
<th>Chorio-adenoma destruens (malignant hydatid mole)</th>
<th>Chorio-carcinoma (Chorio-epithelioma)</th>
<th>Syncytioma (Syncytial endometritis)</th>
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<td>Preserved villus pattern.</td>
<td>Villus pattern usually preserved.</td>
<td>Loss of villus pattern.</td>
<td>No villus pattern.</td>
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<td>Moderate trophoblastic proliferation.</td>
<td>Excessive trophoblastic overgrowth.</td>
<td>Trophoblastic overgrowth.</td>
<td>Clumps of normal trophoblasts infiltrate along tissue spaces.</td>
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<td>Stromal oedema.</td>
<td>Increased connective tissue core.</td>
<td>Anaplastic tumour cells?</td>
<td>Inflammatory reaction present.</td>
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<td>Bloodstream metastasis (causes no trouble).</td>
<td>Invasion of uterine wall without destruction.</td>
<td>Invasion, destruction and necrosis of uterine muscle.</td>
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Chorio-adenoma destruens is characterized by the fact that the villus pattern is preserved, with an excessive trophoblastic overgrowth and an increased connective tissue core. Distant metastases are rare. It invades the uterine wall locally and as a result there is a tendency to perforation and death from intraabdominal haemorrhage. The prognosis is good if the condition is treated by hysterectomy.

Chorio-carcinoma, on the other hand, is characterized by the loss of villus pattern in almost every case. Masses of trophoblasts invade and destroy the uterine musculature with resulting haemorrhage and coagulation necrosis. The anaplastic activity of the tumour cells should be mentioned here. However, Novak and Seah report a number of chorio-carcinomas which have metastasized and killed, but in which the cells were remarkably mature and well differentiated, with no mitosis and no hyperchromatosis. Blood stream metastases to the lungs, liver and brain are common. Park and Lees describe it as “an acutely dangerous tumour, probably the most rapidly killing in the whole field of pathology.”

Chorio-adenoma destruens and chorio-carcinoma are very rare tumours which in the majority of cases arise from chorionic epithelium. There has been general agreement that roughly 50% follow hydatidiform moles, 25% abortions and 25% full-term pregnancies. However, Novak and Seah in their recent report on 74 cases of chorio-carcinoma note that 39.2% followed hydatidiform moles and that 37.8% followed abortions. It is thought that about 1-2% of hydatidiform moles become malignant.

These growths may occur at any age during the childbearing period. Durburg reports a case in an 18-year-old; Novak and Seah report 8 cases of chorio-carcinomas in girls under 20 years of age. Medina and Salvatore, on the other hand, report a case in a 66-year-old patient whose last pregnancy occurred 26 years previously and who had been past the menopause for 14 years.

The primary lesion usually occurs in the body of the uterus, but may arise from an ectopic pregnancy or a teratoma. Oliver and Horne added a case after ectopic pregnancy to the 13 they had found in the literature up to 1948.

Park and Lees point out some interesting peculiarities which distinguish these lesions from all other neoplasms. Occasionally there is apparently no primary lesion. This writer has seen a case where the uterus was removed about three months after evacuation of a hydatidiform mole. No primary lesion was found in the uterus but the patient died shortly afterward of metastases to lungs, liver and brain. Complete spontaneous re-
gression of a frank cancer is extremely rare, but it does occasionally occur in cases of chorio-
carcinoma. Except for rare cases in teratomas, it only occurs during or after pregnancy. It is 
always associated with hormonal changes. There is little difference as regards cell type between a 
chorio-adenoma which shows little invasion and a chorio-carcinoma. The cells have a different 
genetic constitution from that of the host. Park and Lees\(^2\) state that it always kills within 12 
months of diagnosis or not at all. However, Novak and Seah\(^1\) reported two cases that did 
survive more than a year.

In making the diagnosis the history of abnormal bleeding after an abortion or a confine-
ment or the passage of molar tissue should always make one think of a chorio-adenoma destruens 
or a chorio-carcinoma. An enlarged boggy uterus and enlarged bilateral cystic ovaries may be of 
significance. On the other hand, vaginal metastatic lesions may be the first indication of 
trouble. Biological tests can be of value in establishing the diagnosis. There is, however, a danger 
of placing too much reliance on them. Park and Lees\(^2\) stress that "all that an Aschheim-Zondek 
reaction affirms is that one of the conditions that produce a reaction to the A-Z test is present. 
The decision whether this condition is specifically pregnancy or chorio-carcinoma or other states, 
depends upon the clinical findings."

Putting too much reliance on a biological test will only lead to a needless sacrifice of uteri.

Klempner\(^6\) emphasizes the importance of making the diagnosis on the clinical and patho-
logical data since the degree of malignancy is not necessarily reflected by the intensity of the 
pregnancy reaction. He reports a case of a benign hydatidiform mole where the spinal fluid 
gave a positive Aschheim-Zondek test. Schugt\(^1\) reported a case of chorio-epithelioma in which 
the Aschheim-Zondek tests were negative. Others have reported positive pregnancy tests in spinal 
fluids in normal pregnancies. Hence, while biological tests are valuable, they must never be 
considered entirely dependable, whether done on the urine, blood or spinal fluid.

The gross and microscopic appearance of material obtained from curettage may make one at 
least suspect a malignant change. Occasionally, however, the tumour may have invaded the 
uterine wall to such an extent that it is missed by the curette, no matter how thoroughly the pro-
cedure is carried out. Novak and Seah\(^1\) point out that making a diagnosis of chorio-carcinoma 
from curettings alone is rather hazardous and note that the correct diagnosis was made in only 
13 of 74 cases.

In the treatment of these lesions let us first consider chorio-adenoma destruens. It has 
already been pointed out that the prognosis is very good in these cases. Total hysterectomy is 
the treatment of choice. In the young woman, preservation of at least one normal ovary seems 
reasonable. Postoperative deep x-ray therapy is not indicated but the patient should be followed up 
for at least one year.

In the case of chorio-carcinoma total hysterectomy and bilateral salpingo-oophorectomy is ad-
vocated, although Stearns\(^8\) feels that unless the ovaries are definitely involved they should 
be preserved. When we know that spread to the ovaries is rare and that death is usually due to 
distant metastasis, leaving the ovaries does seem to be a logical procedure. In the event that 
metastasis has already occurred, removal of the primary lesion is still indicated, since occasionally 
spontaneous regression of the metastatic lesions does occur. Postoperative deep x-ray therapy to 
the pelvis has not been proved valuable. However, it may help in the control of secondaries 
in the inoperable patient. Levi and Haig\(^9\) report two cases in which they felt that x-ray therapy 
led to regression of the primary tumour with spontaneous disappearance of pulmonary meta-
stases. Stearns\(^8\) feels that estrogenic hormonal therapy is valuable for cases of metastatic spread.

Case 1
On July 16, 1952, C.B., a 25-year-old, para 3, gravida 4 was admitted at about 2½ months' gestation because of 

vaginal bleeding. The fundus was not palpable. She was treated as a case of threatened abortion and was 
discharged in a week with no cramps or flow. The following day she was readmitted passing large blood clots. 
A dilatation and curettage was done and the pathologist re-
ported: "products of conception with acute inflammation." She was discharged in five days as cured. Four 
weeks later, on August 25, the patient was readmitted because of intermittent vaginal bleeding and a history of 
severe hæmorrhage just before admission. The uterus was described as being soft and boggy and about the 
size of a two months' pregnancy. The cavity was explored and hydatidiform mole tissue obtained. She was 
discharged, but readmitted three weeks later in shock with severe uterine cramps and excessive bleeding. Her 
condition improved, but while she was being treated for severe blood loss, she went into shock again with evi-
dence of intraabdominal hæmorrhage. At laparotomy an estimated 800 c.c. of blood was found in the abdomi-
nal cavity. The uterus was enlarged and boggy. The right cornus, upper two-thirds of the fundus and right 
ovary were hyperæmic in colour, and a clot was extruding from the right broad ligament below the ovary. A branch 
of the uterine artery was spurring. The left ovary and fallopian tube appeared normal. A total hysterectomy
and right salpingo-oophorectomy was performed. The patient made an uneventful recovery. The Canadian Tumour Registry reported the lesion as a "malignant or invasive hydatidiform mole." She was last examined on April 9, 1954, one year and seven months after the operation. She felt well and had no complaints of any kind. On bimanual examination, however, there was a soft, rather tender mass on the right side of the pelvis. The left adnexa felt normal. The Aschheim-Zondek test was negative, as was a chest radiograph.

Case 2

On February 2, 1953, G.L., a 31-year-old, para 3, gravida 5, was admitted because of vaginal hemorrhage. According to the time of her last normal period she should have been 12 weeks pregnant. However, there was a soft, boggy tumor in the lower abdomen about the size of a 20 weeks' gestation. The patient had felt no movement, the fetal heart was not heard and a radiograph showed no fetal parts. An Aschheim-Zondek test was reported as positive. The patient continued to bleed, but there was no evidence of mole tissue being passed. The cervix was firm, thick and not dilated. In spite of the bleeding, urine received 3,000 c.c. of blood, her hemoglobin level was only 9.15 g.m., and her red cell count 2,940,000. A diagnosis of hydatidiform mole was made and, because of the anemia and uremia cervix, it was decided that a hysterotomy was the safest method to remove the uterus. At operation on February 19, 1953, large bilateral cystic ovaries were found. The uterus was emptied of a considerable amount of mole tissue, care being taken to prevent spill into the abdominal cavity. The patient made an uneventful recovery and was re-examined on March 30, 1953. The bleeding was not considered to be significant, and the patient was discharged. The radiograph was done and the patient was readmitted on April 9, 1954.

Case 3

On February 2, 1951, this 22-year-old, para 2, gravida 3 was admitted at 24 weeks' gestation because of vaginal bleeding of three weeks' duration. She felt no movement and the uterus was only the size of a 16 weeks' pregnancy. A diagnosis of missed abortion was made and medical induction was carried out. Three days later she developed uterine cramps and passed large clots and placenta-like tissue. She was considered to have had a complete abortion and was discharged. However, she continued to spot and have a brown discharge for seven weeks. She was readmitted on April 3, 1951, following a moderate hemorrhage. A dilatation and curettage was done and the pathologist reported "degenerate decidua." About seven weeks later, on June 1, 1951, she was readmitted because of a persistence of the intermittent spotting and bleeding. Dilatation and curettage was repeated. This time the pathologist found evidence of chorionic villi as well as degenerate decidua.

On August 21, 1951, 11½ weeks after the last dilatation and curettage, she was again admitted with a history of continued bleeding, which had become rather profuse in amount just before admission. The fundus was palpable 3-4 cm. above the symphysis pubis. The cervix was soft and closed. The uterus was boggy and estimated to be the size of a 9-10 weeks' gestation. An Aschheim-Zondek test on the urine was reported positive in dilutions of 1 in 50 and 1 in 100, while an Aschheim-Zondek test on the spinal fluid was reported negative. There was some question whether this was a new pregnancy or a continued complication of the abortion.

Finally on August 31, 1951, another dilatation and curettage was performed. The pathologist suspected chorio-epithelioma from the material obtained, but could not be definite. Then more material was obtained with a repeat curettage, and a diagnosis of chorio-epithelioma was made. On September 30, 1951, a total hysterectomy and bilateral salpingo-oophorectomy was done. The patient made an uneventful recovery. A diagnosis of chorio-epithelioma was made by our pathologist, Dr. A. R. Rainborough, and was confirmed by all the consultants of the Canadian Tumour Registry and by Dr. Emil Novak, chairman of the Mathieu Memorial Registry of Chorion-epithelioma, American Association of Obstetricians, Gynecologists and Abdominal Surgeons. A complete examination on April 3, 1954, two and one-half years after the hysterectomy, showed no clinical, radiological or biological evidence of recurrence or metastasis. The patient appeared healthy and seemed very well adjusted. She had required no ß-estradiol replacement therapy. She had noted a definite increase in libido and claimed to always have an orgasm on coitus—something that had only happened once or twice before the hysterectomy.

The first of these cases is interesting because of the development of the complication of uterine perforation and intraabdominal hemorrhage, which is as a rule the cause of death in chorioadenoma destruens. There is also the problem of the soft tender mass in the right side of the pelvis, which at the time of the last examination was causing no signs or symptoms.

In the second case it is interesting to note that the patient had a normal menstrual period about four weeks after the hysterotomy. She then developed abnormal uterine bleeding within only ten days of a negative Aschheim-Zondek test, done 5½ weeks after the hysterotomy.

The last patient is fortunate to be alive and well after two and one-half years, particularly with a history of abnormal bleeding for nearly eight months between the abortion and the hysterectomy. It makes one wonder as to the correctness of the diagnosis. However, I see no other reason to doubt it, particularly when it was confirmed by such well-recognized authorities.

It is also interesting to note the increase in libido. Granted that the removal of the uterus relieved her of the fear of pregnancy, nevertheless...
less it does indicate that the ovaries are not essential for a normal sexual life in a young person.

**SUMMARY**

This has been a brief review of chorioepithelioma. A comparative summary has been developed to help lessen the confusion as to the difference between chorio-adenoma destruens and chorio-carcinoma. Three cases have been presented, two with a diagnosis of chorio-adenoma destruens and the third with a diagnosis of chorio-carcinoma. All patients are alive and well at the present time.

I acknowledge my thanks to Dr. A. R. Bainborough for his help in preparing the material and to Drs. E. R. Poulsen and F. L. Johnson in permitting me to report their cases.

**REFERENCES**


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**THE PRESENT STATUS OF THE FENESTRATION OPERATION**

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**THE FENESTRATION OPERATION** for deafness is not new. It was first attempted in 1896 by Passow. Jenkins and Bárány also experimented with this procedure. These early workers were discouraged by infection of the labyrinth which often produced a labyrinthitis and sometimes fatal meningitis. This difficulty disappeared with the advent of chemotherapy and improved techniques. Another cause of failure in the early days was that most of the windows closed over with new bone. Holmgren, who first started to work on the problem in 1916 and was the first to produce successful hearing improvement, stated in 1938 that the fistulas remained open only occasionally. Sourdille, working with Holmgren, first used a microscope for the operation, developed the idea of sealing off the cavity with a skin flap attached to the drum, and first brought the operation to America. In 1938 Lempert devised his one-stage endaural operation which made the procedure more practical, but closure of the window still remained a big problem. Since that time research by Shambaugh, Lempert, Sullivan, Lindsay and others, using the monkey, has disclosed the main factors influencing osteogenesis after fenestration. Shambaugh lists these six factors as follows:

1. Careful removal of all bone dust by continuous irrigation and suction when making the window.
2. Wide exposure of the enchondral layer of bone surrounding the window.
3. Fitting the skin flap to the edges of the window tightly, as epithelium has an inhibitory effect on osteogenesis.
4. Avoiding any injury or stripping of the endosteum at the edge of the window.
5. The prevention of fibrosis in the window. This is accomplished by care in handling the flap, hemostasis and avoidance of infection.
6. Polishing the margins of the window, as a polished surface grows new bone less readily than an unpolished surface.

By careful attention to these conditions, closure of the window is no longer frequent.

A third cause of failure is postoperative serous labyrinthitis. This is a sterile inflammatory reaction of the inner ear, which is extremely sensitive to trauma or irritation. It can be produced by traumatic inflammation of the covering skin flap, with exudation of blood and serum into the labyrinth. Any infection in the postoperative cavity, while it cannot invade the sealed-off labyrinth, can accentuate the sterile reaction. By careful handling of the skin flap and attention to hemostasis and antiseptic technique, this reaction can be minimized, and its effect is transient. If the reaction is more severe, it will cause some permanent change and the result will be disappointing. This is the cause of most of the failures occurring at the present time. The development of anaesthetic techniques that mini-