HYDATIDIFORM MOLE

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The stimulus for the writing of this paper was a case observed at the University of Wisconsin Hospitals in the Department of Obstetrics and Gynecology. The case is as follows.

On 22 February 1957, a 20-year-old white single woman Gravida I, Para 0 was admitted as an emergency to the Obstetrics Service of the University Hospital.

Her menses had been normal but had ceased in September of 1956 and the patient stated she may have been pregnant. Subsequent to the menstrual period in September she had nausea and vomiting to a rather severe degree and her weight had dropped from a usual 120 pounds to 104 pounds on 13 February 1957 at which time she was admitted to Richland Center Hospital because the preceding day she had had hemoptysis and nose bleeds. She also complained of painful respiration, weakness and vomiting. At this time her blood pressure ranged from 108/80 to 184/100, she had a normal temperature but had a pulse rate of 104, was hyperventilating and had a foul dark brownish vaginal discharge and uterine enlargement to the size of a 6 to 7 month pregnancy. She had a positive frog test but had felt no fetal motion and no fetal heart tones were audible. She had a hemoglobin of 6.15 grams on admission so was given 3 units of blood which raised her hemoglobin level to 7.6 grams. Diagnosis at the time of admission was "six to seven month pregnancy with hyperemesis gravidarium and severe secondary anemia". She also had albuminuria and a total serum protein of 5.6 grams percent.

She was not responding to conservative management so on 22 February 1957 she was transferred to the University of Wisconsin Hospitals where when on admission she was in acute distress - on the day prior to admission she had begun to have cramping lower abdominal pain which had become more severe, also vaginal bleeding but no passage of fluid or tissue per vagina. She complained of severe abdominal pain and dyspnea while lying down to be examined and felt more comfortable sitting up. She was hyperventillating, had a tachycardia of 150 beats per minute and a blood pressure of 190/110. The uterus was seven months size, actively contracting, and was tense and exquisitely tender on palpation. No fetal heart tones were heard. Impressionsat this time were hydatidiform mole, associated toxemia of pregnancy and abruption of mole. A flat plate of the abdomen showed no fetal skeleton; a chest x-ray revealed a mottled density in the left upper lung field felt by the radiologist to be bronchopneumonia. (It cleared on a subsequent chest x-ray.)

Her hemoglobin on admission was 8.3 grams so blood was typed, cross matched and started. On vaginal examination the cervix was 1 cm. dilated, admitting the tip of the finger. Profuse hemorrhage was initiated and the patient was immediately transferred to the surgical ward where a laporotomy was performed and by means of a hysterotomy a large hydatidiform mole was removed. Bilateral lutein cysts of the ovaries were present and were left intact. General supportive measures were administered including five pints of whole blood, intranasal oxygen, and

antibiotics. She recovered well and at the time of discharge on 12 March 1957 her blood pressure had returned to 136/68, her hemoglobin was 11.2 grams and she was placed on a high protein, high calorie diet. Advice to avoid the possibility of future pregnancy was given. The report of the pathologist was hydatid mole.

She was seen in the Gynecology Outpatient Department on 15 April 1957, at which time she stated she had had two episodes of vaginal bleeding - one in mid March and another in early April, both episodes being less than a normal menses. Examination revealed the corpus uteri to be enlarged to an eight weeks size gestation and a palpable left ovary approximately twice normal size, though the right ovary was not enlarged. The serum was positive for chorionic gonadotrophin in 0.1 cc, serum per 10 grams of frog weight. A like reading was obtained from the serum on 26 April 1957.

On 10 May 1957 she noted a sensation of pressure in the lower abdomen and subsequently had vaginal bleeding and went immediately to Richland Center Hospital where a curettage was performed. Her hemoglobin at this time was 10.15 grams. The slides of the curettage were interpreted as a benign mole.

She re-entered University of Wisconsin Hospitals on 16 May 1957 for re-evaluation. She had remained quite weak and her weight was still 103 pounds. She denied any specific cardiorespiratory, gastrointestional, genito-urinary or neuro-psychiatic complaints except a dull constant supraorbital headache relieved by aspirin. Her blood

pressure was 90/20 and except for the generalized muscular weakness, systolic murmers at the apex and the secondary aortic area and a uterine enlargement of eight weeks gestational size without adnexal masses the physical examination was within normal limits. Her hemoglobin on admission was 8.7 grams however. The day after admission the patient noted lower abdominal discomfort and subsequent pain in the left shoulder which was worse on deep inspiration; there was also a drop in hemoglobin to 6.9 grams though her blood pressure, pulse and temperature remained normal. This clinical picture suggested intraperitoneal bleeding suspected to be due to a ruptured ovarian cyst or chorioadenoma destruens but a culdoparacentasis was performed without obtaining any blood.

A chest x-ray taken on admission was read as showing evidence of metastatic disease in the lungs and in view of the rest of the clinical and laboratory data on 20 May 1957 a total abdominal hysterectomy and bilateral salpingo-oophorectomy was carried out and numerous small tumors were removed from the peritoneum and omentum. She recovered uneventfully from the surgery and her hemoglobin was 15.4 grams on the second postoperative day after having received multiple transfusions prior to and during surgery.

The microscopic examination of the tissue removed at the time of surgery was interpreted as choriocarcinoma of the cervix, omentum and peritoneum; retained molar fragments were seen within the body of the uterus.

She is being treated with amethyopterin.

SUMMARY OF CASE

A case of a 20-year-old Gravida I, Para 0 with quite typical findings of a molar pregnancy including vaginal bleeding, abdominal pain, a uterus slightly larger than the expected size, anemia, pulmonary infection, hyperemesis and a rather severe pre-eclampsia is presented.

Her subsequent course is very interesting in that approximately three months after the diagnosis of mole evidence of pulmonary metastases were found and a chorioepithelioma with peritoneal implants was found at the time of hysterectomy.

It is interesting that the lutein cysts disappeared in spite of the development of the chorioepithelioma; that the gonadotrophin titer fell in spite of the development of the chorioepithelioma and that the mole persisted in the uterus with the chorioepithelioma in the wall of the uterus.

INTRODUCTION

One must be thoroughly familiar with normal pregnancy - its effects on maternal physiology, the hormonal changes, and the histological changes at the site of placental development, and the variations thereof - before one can properly understand the hydatidiform mole, hereafter referred to as mole.

The egg, after having been fertilized, descends via the Fallopian tube to the uterine cavity and implants, usually high on the anterior or posterior aspect of the uterine cavity. Development has advanced to the blastocyst stage at which time the outer layers of the spherical mass (the trophoblast) proliferate and there is further differentiation into the cytotrophoblast (Layer of Langhans) and the syncytiotrophoblast which are able to erode the uterine lining - destroying maternal cells and making them available for the nutrition of the embryo. They also penetrate uterine blood vessels allowing local escape of blood which further nourishes the developing embryo. By three weeks solid buds of trophoblast become vascularized and thus form secondary villi essential for continued support of the metabolism of the embryo. Early these villi completely cover the blastodermic vesicle but as further development occurs the villi of the chorion laeve degenerate while those of the chorion frondosum continue to proliferate and in conjunction with the decidua basalis form the placenta.

At the site of placental formation it is normal that the villi are able to invade maternal blood vessels, and thus trophoblastic cells, even whole villi, may break off and become blood borne to other parts of the body, most frequently to the lungs. Also trophoblastic cells in the

chorion frondosum often deeply invade the uterine musculature - a phenomena which is most marked at the site of implantation.[19] These cells are called "wandering trophoblastic cells". Thus normal trophoblastic cells possess, in their ability to invade blood vessels and tissue, the properties of malignant cells though normally the maternal organism is resistant to such "malignant invasion".

Trophoblastic proliferation and invasiveness normally are maximal through the second month of pregnancy - a phenomena rather constant in time and degree; after this time, i.e. two months, growth activity declines gradually during the subsequent course of pregnancy.[22]

The normal placenta produces estrogens, progestrone, ACTH, and corticoids in addition to chorionic gonadotrophin - the latter being of particular interest in this presentation. Chorionic gonadotrophin is produced by the Langhan's cells (cytotrophoblast) of the villi and has as its prime function the maintenance of the post-ovulatory corpus luteum and the transformation of this into the corpus luteum of pregnancy.[28]

The Langhan's cells being the site of chorionic gonadotrophin production, titers of this hormone in the serum of the mother parallel the rise and decline of the Langhan's layer, thus these titers are maximal at the end of the second month of pregnancy and then decline gradually to the end of pregnancy when they are at very low levels. (Note there is a virtual absence of Langhan's cells in the "older" placenta.[11])

INCIDENCE AND ETIOLOGY

Hydatidiform mole is an abnormality in the development of the fetal membranes, probably a type of neoplastic proliferation of the trophoblast, which occurs in approximately 1 in 2000 to 2500 pregnancies[11, 18]

though in certain geographical areas in the Orient, especially China, the Philippines, and Malaya, the reported incidence is much greater - estimated at 1 in 200 to 300;[21] the reason for this is unknown.

There is a great divergence in the reported incidence by age and parity but it is universally accepted that it occurs in the reproductive period.

Novak and Seah[21] give the following statistics from a series of 119 cases of mole.

Age Incidence	<20	20-30	30-40	40-50	>50
Number of Cases	20	71	19	7	2

Parity	0	1	2	3	4	5	6	7	8
Number of Cases	38	27	24	4	4	5	5	3	3

Though it was formerly thought that mole was most frequent in elderly women of high parity, from these statistics it would seem that the great majority of cases occur in women below the age of 30 and of nulliparity or of low parity. Cibelli[7] in a recent article also agrees with these conclusions.

The etiological factors involved in the production of mole are unknown but current feeling seems to indicate that the primary defect is in the ovum.[11] A theory advanced by Gordon[12] is that because of the defect in the ovum and a resultant failure of the embryo to develop in the third and fourth week of pregnancy, at which time the villi normally become vascularized, there is no stimulus for blood vessel penetration of the villi. Without blood vessels there is an accumulation of the secretory products leading to distention of the villi and hydropic degeneration of the stroma of the villi. This distention is thought to stimulate growth of the

trophoblastic cells which remain viable independently of the presence of the embryo or of vascular development of the villous stroma[22] and proliferate especially when in contact with maternal tissue having a good blood supply.

Recently Huber et al.[15] in a study of aborted specimens found that 20.2% of 188 specimens showed molar change on microscopic examination (no attention directed at the fetus); also that there were no specimens having unquestionable molar change having a normal fetus - all were pathological conceptus. (In fact only 24% of 90 complete intact specimens had a normal fetus.) These findings would seem to support Gordon's theory.[12] Huber et al. conclude their paper by stating that more than one-half of patients having spontaneous abortions have abnormal conceptus and further feel that were it possible to prevent abortion in this group of patients the frequency of molar pregnancy would be increased many times.

PATHOLOGY

A typical hydatidiform mole consists of a mass of grossly recognizable cystic villi of various sizes occurring joined in strings, in groups with no reference to previous villous pattern, or as detached isolated cysts[13] involving all or part of the chorionic villi and usually associated with an absent or abnormal embryo. However, molar change in association with a normal fetus and even extensive mole with a full term viable infant have been reported.[3, 5] Hydatid changes are not only found in association with molar pregnancy but are frequently found in the villi of a normal placenta at term.[5]

The microscopic characteristics of mole are well known and include avascular or relatively avascular villi; edema of the stroma with or without increase in size of the villi and the development of cystic spaces within the stroma which tend to coalesce, felt by most investigators[11,18] to represent hydropic degeneration of the stroma; and proliferation of the trophoblastic cells (either or both types - Langhan's and syncytial cells) in varying degree but in excess of the usual two-cell layer of the normal villi.[15]

Of greatest importance pathologically is the differential between mole and chorioepithelioma; as the latter is an occasional sequela of the former and is a highly malignant, almost universally fatal, rapidly growing tumor, it is all the more important to recognize each. However, microscopically this differential is exceedingly difficult. Many criteria of microscopic diagnosis have been advanced from a complex, somewhat vague, system of Hertig and Sheldon[14] which classifies tumor of the trophoblast as benign, probably benign, possibly benign, possibly malignant, probably malignant and malignant, depending upon the amount of hyperplasia and/or anaplasia present, to a relatively simple differential by Novak[19] which has only two groups - benign trophoblast and malignant chorioepithelioma. In the former, trophoblastic cells infiltrate along tissue spaces singly and exert no destructive or lytic effect upon the uterine musculature as does chorioepithelioma; also in mole both the infiltrating cells and the uterine musculature stain sharply and clearly. Chorioepithelioma, however, is characterized by large columns or masses of trophoblast advancing into

the uterine musculature killing the tissue as it advances and resulting in coagulation necrosis and hemorrhage which are universally seen with chorioepithelioma. Anaplastic changes in individual cells are frequently seen but the other findings mentioned above are more diagnostic. The presence of well formed villi tend to lead one away from the diagnosis of chorioepithelioma.

The criteria of Novak for differential diagnosis seems more logical than that of Hertig and Sheldon, yet there has been repeated stress by most authors[11,14,19] that there is little relation of histology to malignant potentiality and subsequent follow up of the patient's course with clinical and laboratory facts is the only way to differentiate the two conditions.

Chorioadenoma destruens, frequently referred to in literature about mole and chorioepithelioma, too is a tumor of the trophoblast which has microscopic features of mole except that there is more marked trophoblastic proliferation and intravascular invasion. Novak[19] feels that it is no different from the benign mole; both mole and chorioadenoma destruens maintain the ability to locally invade the myometrium; both are hormonally active so there is an elevated gonadotrophin titer. Chorioadenoma destruens is uncommon but when found there is usually extensive myometrial invasion with uterine enlargement. There is considerable risk of uterine perforation[16] and subsequent intraperitoneal hemorrhage so hysterectomy is generally indicated.

Transitional mole, an abortus in which various portions of the ovum - the chorion, villi, amnion, or embryo - can still be identified but there is grossly recognizable hydatid change, is a variant of the typical mole.[13]

Syncytial endometritis - another term found in the literature on mole - represents residual trophoblast in the decidua or myometrium, underlying the site of placental attachment and usually found in association with inflammatory infiltration of the decidua is merely the normal invasion of the myometrium by "wandering trophoblastic cells" but frequently is misdiagnosed as chorioepithelioma.[19]

Associated with mole in from 25 to 60%[11,12,20] of cases are multiple lutein cysts of the ovaries, though histologically they occur in almost every case. The cysts are felt to be a pathological response of the ovary to elevated chorionic gonadotrophin titer.[12] There seems to be a relationship between the character and degree of ovarian change and the stage of the intrauterine lesion but the relationship is not chronologically parallel.[20] (There usually is extensive cyst formation in association with larger moles and with longer periods of stimulation.)

The ovaries are large and have a more or less lobulated surface but there is a tendency to preserve the ovoid ovarian contour; the individual cysts vary in size, usually have thin smooth walls often with a yellowish tinge, and contain fluid varying in color from clear to yellow to bloody. The stroma of the ovaries is usually edematous.

The ovaries may become so large that they lead to pressure symptoms; they may be found on pelvic examination prior to realization of the underlying mole and may give a clue to the diagnosis; they may become twisted on their pedicle and signs of an acute abdomen may be the presenting complaint of a woman with mole.[17]

Microscopically the cysts are lined by large polyhedral cells resembling those of the developing corpus luteum. There is luteinization of both the granulosa cells and the theca cells.

After removal of the lesion producing the excess gonadotrophin there is spontaneous regression and disappearance of the cysts so no therapy for them is indicated, unless there is a complication of a twisted pedicle of the ovary.[12]

ENDOCRINE ASPECTS

The assay of chorionic gonadotrophin in pregnancy serves as an excellent index of fetal growth and development and when done quantitively it is of prognostic value[11] for values outside of the normal range, either higher or lower, are of significance. Delfs has done much research on chorionic gonadotrophin and his method of determination of serum levels of chorionic gonadotrophin (hereafter referring to gonadotrophin) is recommended.[8,10]

There is a normal pattern of serum gonadotrophin levels at various stages of pregnancy[9,10] which most observers feel very closely parallels the amount of secreting trophoblastic tissue present in the placenta. In mole where there is marked proliferation of the trophoblast, there, too, is characteristically marked elevation in serum gonadotrophin titers which, when viewed against normal values and correlated with significant clinical data, is often of great diagnostic significance.

The peak in gonadotrophin titer is approximately 60 days after the onset of the last menstrual period and may persist for 20 days; thereafter it decreases to remain at relatively low levels throughout

the rest of pregnancy. Thus attempts to diagnose mole by means of bioassay of serum gonadotrophin within 80 to 100 days (or before) of the last menstrual period is not possible because of the normally high values during this time. After 100 days, however, when the serum values normally fall off rapidly, a persistently high or increasing gonadotrophin titer indicates abnormality and should be repeated in a week to follow the titer.

Though the gonadotrophin titer is of definite diagnostic value, diagnostic difficulty may arise with irregular menstrual data. The pregnancy may be younger than the dates suggest in which case the uterus would be smaller than expected and the gonadotrophin titer would be that of a younger pregnancy; if a normal pregnancy is older than the dates suggest the uterus would be larger than would be expected and the gonadotrophin titer lower so in neither case should this be confused with a mole - of course the gonadotrophin titer needs to be correlated with the rest of the clinical picture.

Multiple pregnancy where the uterus is larger than expected for the duration of pregnancy and the gonadotrophin levels elevated somewhat (making for clinical suspicion of mole) is a real diagnostic problem. In multiple pregnancy, though data is scant, there is a maintenance of the peak gonadotrophin levels and a more gradual decline in titer[3] than with a normal single intrauterine pregnancy. Here again repeated assays of gonadotrophin will demonstrate whether the levels follow roughly the shape of the normal curve though not with its bounds

in which case a multiple pregnancy is likely or whether the levels become pregressively more elevated giving stronger support to the diagnosis of mole.[9]

By means of gonadotrophin levels within normal limits a negative diagnosis to rule out a mole, where there are suggestive clinical findings, is of great help to the clinician. (It is of interest that with markedly subnormal levels of gonadotrophin for the stage of pregnancy, abortion can often be anticipated.)

There is in the literature frequent mention of the use of cerebrospinal fluid for determination of gonadotrophin titer. Delfs[9] gives quantitive data comparing serum and spinal fluid levels of gonadotrophin which demonstrate that gonadotrophin does not readily pass into the cerebrospinal fluid even when the serum levels are markedly elevated, also that spinal fluid titers are very low when compared to serum values. He concludes that spinal fluid has no diagnostic usefulness for it gives no information that a serum assay would not give; furthermore it is much more difficult to obtain.

In molar pregnancy gonadotrophin levels are dependent upon the total size of the mass of the mole, the differing cellular constituents, varying degrees of necrosis or degeneration within the mole, or separation of the mole and so are variable due to variations in these characteristics. Upon evacuation of the mole gonadotrophin titers should revert to normal. High levels may persist in the first few days after delivery of the mole but after 10 days there is a rather marked decrease in the percentage of patients who maintain significant levels of gonadotrophin and at 60 days

only 23.5%[9] maintain a significant gonadotrophin titer. Those patients who were negative within 60 days continued to be negative and remained clinically well. If the level persists a repeat curettage is indicated and follow up must be evaluated on an individual basis by careful examination and evaluation of clinical, pathologic and endocrinologic data.[9]

CLINICAL ASPECTS

A detailed history is of utmost importance in the diagnosis of a mole for all of the characteristic symptoms of pregnancy may be present in an exaggerated state in mole.[27]

Vaginal bleeding following a period of amenorrhea is present in virtually all cases[16] - one-half of proven cases of mole begin bleeding in the first or second month and subsequently bleed from one day to 4½ months with no particular pattern to the bleeding; it is continuous in 69% of patients and intermittent in the remaining 31%. The bleeding varies from a brownish, prune-juice colored discharge to actual and profuse bleeding.[7] Commonly (in 58% of patients with mole) the hemoglobin level falls below 10.9 grams.[25]

Abdominal pain is also a common symptom (36% of patients in one series[16]) and in most cases it appears to be associated with undue distention of the uterus - frequently there is subsequent evidence of hemorrhage into the uterine cavity. The pain is significant too in that it often, as in cases of threatened or inevitable abortion, precedes passage of the mole by hours or days.

As in normal pregnancy where 50-75% of patients have nausea and vomiting (1/3 of which require some type of therapy), in mole a comparable number of patients have these symptoms but more severely and over a longer period.[11,25]

Toxemia without a mole is very rare in the first trimester of pregnancy so the sudden onset of toxemia with hypertension, fluid retention, and albuminuria occurring early in pregnancy is very suggestive of mole.[27] Some investigators feel that mole actually predisposes to pre-eclampsia and eclampsia. Though there does not seem to be any correlation between the duration of amenorrhea and the onset of eclampsia, the size of the uterus seems directly involved for most cases of mole do not manifest hypertension until the uterus is of such size and bulk that the fundus is at or above the umbilicus; it is postulated that the increase in intraabdominal pressure and the distention of the uterus with ischemia are contributing factors. This toxemia responds to the delivery of the mole as does eclampsia of pregnancy respond to delivery of the infant.[2] The reported incidence of toxemia in association with molar pregnancies is 10-40%. However, in patients whose amenorrhea has been greater than 4 months or with the uterus at or above the level of the umbilicus, the incidence rises to 71%.[2,6]

A discrepancy between the period of amenorrhea and uterine size is often present. The uterus is larger than would be expected in about 50% of cases and smaller than expected in 25% of cases; the remaining 25% have a size consistent with the period of amenorrhea. At

times there may be a 1 to 4 month size increase from what would be expected. Frequently the height of the uterus is prodigious and may change 3 to 5 centimeters over a period of one week.[16,25]

Polycystic changes in the ovaries as described above are present in from 16 to 60% of cases and may be of some aid in diagnosis if they are palpable.[25]

Acosta-Sison[1] stresses that frequently on vaginal examination the lower uterine segment in whole or in part is soft and full due to the soft molar contents - a condition not present in normal pregnancy until near term. He also describes the use of a uterine sound in the diagnosis of mole, however this technique should be done with extreme gentleness, if at all, under strictly aseptic conditions in an operating room or a delivery room where immediate evacuation of the uterus (per vagina or by abdominal hysterectomy) can be accomplished if necessary and intravenous fluids and blood are immediately available as this procedure may initiate bleeding which can be controlled only by immediate evacuation of the molar contents. If a mole is present the uterine sound penetrates far beyond the lower uterine segment and no amniotic fluid returns.

In disputed cases where the biologic test is positive fetal electrocardiography may be of aid in establishing the presence of a fetus. Blondheim[4] after describing the technique used for fetal electrocardiography gives the following figures of positive tracings according to lunar months.

Lunar Month	3	4	5	6	7	8	9	10
Percent Positive	0	14.3	71.9	90.6	75.0	64.9	92.2	96.7
No. of Cases Tested	16	35	89	64	52	57	77	92

Thus, it is not until the sixth lunar month that this method can be used with any degree of assurance.

Though there have been cases reported of mole in association with a fetus[26] and even occasional cases where a viable infant[3,5] has been born in the presence of massive molar tissue, there is usually no fetus present by palpation, no audible fetal heart tones, and no fetal movement perceived by the mother when a molar pregnancy is present.[1]

A flat film of the abdomen may be of assistance in diagnosis but may show only a large soft tissue mass without evidence of a fetal skeleton. Occasionally no fetal skeleton will be visible by x-ray at 20 weeks of gestation but it should be regularly present in approximately 6 months in the normal pregnancy.[11]

The differential diagnosis of mole includes threatened abortion, missed abortion, fibromyoma, multiple pregnancy, hydramnios, distended bladder with retroverted gravid uterus, ovarian neoplasm and ectopic pregnancy in which there is a spontaneous performation of the uterus and subsequent intraperitoneal hemorrhage.[12]

The mole having been diagnosed, clinical management of it has two phases - the early evacuation of the uterus and the subsequent follow-up of the patient whether symptomatic or asymptomatic by means of serum gonadotrophin titer.[11] This latter phase is directed primarily at the early detection of complications or sequela as retained mole which may

become invasive then called chorioadenoma destruens, continued trophoblastic proliferation or chorioepithelioma should they occur.

Frequently spontaneous evacuation of the uterus by abortion is either imminent or in process when the diagnosis of mole is made so treatment in these cases is directed at completion of evacuation - either by dilitation of the cervix to the point where digital separation of the mole can be accomplished as far as possible and completed with sponge holding forceps or by an intravenous pitocin drip or both. The intravenous pitocin drip not only helps to empty the uterus but also aids in decreasing blood loss and in decreasing the risk of injury to the soft atonic uterine wall. This latter fact - the consistency of the uterine wall - is, because of the possibility of uterine perforation, a contraindication to the use of a sharp curette in mole; also the mole may be of the locally infiltrative type further thinning the uterine wall and predisposing to perforation. King[16] reports that 55 of 64 (86%) of his cases of mole either delivered spontaneously or were delivered by dilitation of the cervix and evacuation of the uterus from below.

Important to remember is that there has been blood loss - often sufficient to produce a rather severe degree of anemia - and also vomiting which may produce alkalosis and dehydration which should be treated prior to and during evacuation as indicated[12] by the administration of blood, fluids, and electrolytes.

In a very small percentage of molar pregnancies (3 of 64 of King's cases[16]) because of any or all of the following - uterine enlargement greater than a 5 month pregnancy with no signs of impending spontaneous

abortion, sudden massive bleeding or a tense, tender, painful uterus probably signifying hemorrhage into the molar tissue[24] - immediate evacuation of the uterus is indicated and a hysterectomy should be performed.

In the above methods of management of mole, a thorough uterine curettage should be carried out early in the puerperium when the uterus is firm,[9] however in the presence of uterine infection, curettage should be delayed until the infection is controlled. This curettage removes fragments of trophoblastic tissue which may lead to confusion in the follow-up by causing bleeding and/or elevated gonadotrophin titers which may be interpreted as neoplasia.[11]

Special care in the early puerperium to guard against intrauterine infection is necessary. Because the mole is a mass of poorly vascularized tissue, often with old blood clots and necrotic decidua which is an excellent culture media for bacteria, there is a strong predisposition to intrauterine infection and peritonitis.[12] The accompanying anemia - due primarily to uterine bleeding but occasionally much greater than can be accounted for by obvious blood loss - too is common and predisposes to infection so any signs of infection, intrauterine or elsewhere, should be recognized and the patient treated with appropriate antibiotics.

Occasionally without prior uterine evacuation and sometimes secondarily after uterine evacuation, hysterectomy is done as therapy for mole or its complications. King[16] gives the following indications for hysterectomy: in a patient of greater age and parity, for there is an increasing risk of malignant change with increasing age;[23] in the presence

of an infiltrating or invasive mole where there is continued bleeding after evacuation and a persistently elevated titer of gonadotrophin.

Delfs[9] in his excellent article summarizing the present concepts of chorionic gonadotrophin outlines a method of follow-up on patients having a molar pregnancy. Reliable contraceptive advice should be given so hormonal follow-up will not be confused by another pregnancy[11] and quantitive serum gonadotrophin titers should be done at two week intervals until negative, then once per month. Normal menstrual function may be resumed any time after gonadotrophin disappears. (Menstrual bleeding is differentiated from pathological bleeding in that the former is cyclic and that it occurs after gonadotrophin has disappeared.)

If serum gonadotrophin titers remain elevated or increase in the follow-up period, if there is bleeding or subinvolution or a combination of these factors, Delfs feels that a repeat curettage is indicated and a chest x-ray should be taken as a baseline for future follow-up. Again serum gonadotrophin titers should be obtained and if they continue to be elevated or increase, hysterectomy is indicated (though this must be individualized) and monthly gonadotrophin titers again obtained.

If after hysterectomy gonadotrophin levels continue to be elevated, follow-up examinations should be continued (including chest x-ray) and complications should be treated as they arise.

Approximately 80% of patients with a molar pregnancy have no complications after evacuation of the mole; approximately 8% develop an invasive mole[16] - chorioadenoma destruens - usually requiring hysterectomy;

the remainder of cases show varying degrees of neoplasia, the extreme of which is the chorioepithelioma - one of the most malignant of all tumors in humans - which is a complication of mole in possibly 1 to 10% of cases[11] though there is considerable discussion as to the causative relationship between mole and chorioepithelioma. (Park and Lees state that 50-60% of chorioepithelioma cases are not preceded by mole and further that 90-99% of cases of mole are not followed by chorioepithelioma.[23]) Again serum gonadotrophin titers is the earliest and most reliable prognostic indicator in a patient who has been treated for a complication of mole.[9]

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