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Hydatidiform mole

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TABLE OF CONTENTS

Hydatidiform mole, a complication of pregnancy, is characterized by the progressive swelling of the stroma of the chorionic villi, associated with the disappearance of the fetal vascular system and accompanied by a variable amount of trophoblastic proliferation. (15) The common pathogenic factor in such swelling is absence or early death of the embryo during the first three or four weeks of development, with consequent disappearance of fetal vessels. The process of swelling is due to functional trophoblast on villi deprived of a functional fetal circulation.

Hydatidiform swelling, which is, therefore, not a degeneration, occurs in three principal situations:

1. The chorionic villi of the majority of "blighted" ova which constitute about one-half of all spontaneous abortions or nearly 5% of all pregnancies.
2. Focally throughout otherwise normally developing placentas whose fetuses are alive and whose chorionic circulation functions except in those focal areas.
3. The margin of normally developing placentas where the chorionic villi are alive, but the fetal circulation is becoming embarrassed by the development of the chorion laeve.

A true hydatidiform mole is a temporarily missed abortion of a "blighted" ovum whose microscopic hydatid swelling has become macroscopic during the additional weeks it has been retained in utero.

As a consequence of trophoblastic activity there may be (1) invasion of the uterine wall by one or more hydatidiform molar villi, (2) malignant neoplasia of the trophoblast, resulting in choriocarcinoma, or (3) rarely, "metastasis" of intact hydatidiform villi to the parametrium, local pelvic structures, lungs, or elsewhere in the body.

Grossly, the grape-like vesicles of a hydatidiform mole are characteristically discrete rounded, and translucent, and vary in size from bare visibility up to 10 mm. in diameter. The chorionic sac, usually empty or containing a small defective, macerated embryo, can be identified unless the sac has been traumatically ruptured.

Microscopically, the hydatidiform villus shows striking variation in the degree of trophoblastic proliferation. The cytotrophoblast may be present as an orderly Langhans epithelium, but more often it has proliferated as irregular masses whose pleomorphism and mitotic activity vary from specimen to specimen and from area to area within the same specimen. The syncytiotrophoblast also varies in appearance, from normal epithelium to an irregularly festooned mass containing lacunae, representing the primitive intervillous space. Primitive syncytiotrophoblast may also

be mixed with primitive cytotrophoblast, and indeed the cells may be so pleomorphic and anaplastic that it is difficult to distinguish cell types. (16)

The amount of trophoblastic proliferation and its degree of undifferentiation are, in general, proportional to the tendency of the hydatidiform mole to become locally invasive (chorioadenoma destruens) or to become truly neoplastic (choriocarcinoma). Nevertheless, it is impossible from microscopic examination of the individual mole to predict what will be the ultimate clinical outcome. Curettings are more important, although not absolutely diagnostic in evaluating potential malignancy, as they represent the trophoblast actually in juxtaposition to the endometrium.

Characteristics highly suggestive of mole include the following: uterine bleeding, varying in amount and color, and being more or less continuous during the second, third and fourth months after the last menstruation; increase in uterine size above the level expected for the suspected stage of gestation, the uterus presenting as a uniformly consistent, solid, boggy mass, which was soft when relaxed, but firm when contracted; absence of amniotic fluid, and absent history of fetal movements: negative results on

palpation for a ballotable or irregular mass during vaginal examination, there being in most patients instead, a fullness or part or all of the lower uterine segment; a closed or slightly open cervix on vaginal examination. (4)

Kurtz recommends transabdominal paracentesis of the uterus as a diagnostic aid in Hydatidiform Mole. When no amniotic fluid is obtained after puncture, mole should be expected. He recommends the use of a spinal needle for this purpose to minimize trauma, and, of course, the bladder should be catheterized prior to puncture. (19)

Serum gonadotropins in the normal pregnancy, after reaching a peak at about sixty days after the last menstrual period, progressively decreases so that after one hundred days, the titer is rarely above 20,000 I.U. per liter. At least two assays one week or more apart should be made before the diagnosis of Hydatidiform Mole is given. Difficulty may arise with irregular menstrual history, but the size of the uterus may be helpful. Multiple pregnancies may lead to suspicion of mole and human chorionic gonadotropins may be elevated because of a larger trophoblast. A diagnosis ruling out mole is made much more often than a positive diagnosis. (11)

The amount of chorionic gonadotropin excreted by women is extremely variable and a single dilution test is of little value in differentiation. During normal pregnancy, the excretion of chorionic gonadotropin rises to a normal of 450,000 I.U. per liter, and falls to 30,000 I.U. per liter. The only time a single estimation might be of value is when the excretion is over 600,000 I.U. during the first four months of pregnancy, higher than 300,000 I.U. between the fifth and final months of pregnancy. If there are clinical reasons for suspecting hydatidiform mole, such a high level of chorionic gonadotropin should be considered confirmatory evidence. The peak excretion of chorionic gonadotropin in normal pregnancy usually occurs between the sixth and fourteenth weeks. After this, the level falls rapidly to 3,000-30,000 I.U. per liter, and is maintained at this value until the end of pregnancy. If chorionic hormone excretion after the sixteenth week does not fall or increases, it implies that mole may be present. Assays on specimens sent for a week or so are more useful than those obtained from a single specimen. A low level of chorionic gonadotropin excretion or even a negative result does not rule out presence of mole tissue. A biologic test becomes negative within four weeks after removal of all tissue

producing human chorionic gonadotropin. A negative Hogben test was obtained with urine from sixty-two women within four weeks of removal of the mole and in forty-two within two weeks.

Possibly, if complete removal is accomplished, the test would always be negative after the latter interval. Unless the gonadotropin test is negative within four weeks of removal or abortion of the mole, prolonged excretion of HGG can be due only to retained chorionic tissue, This indicates the need for systematic followup, since choriocarcinoma develops more often from a molar pregancy than another type. (17)

In followup of hydatidiform mole, repeat hormonal assays should be made and correlated with clinical findings. A thorough re-curratage is advisable in every case seven days after expulsion to remove any residual proliferative molar tissue and to ascess later findings more accurately. A quantitative biological test should be performed four weeks after evacuation of molar tissue. This is usually negative and will remain so, but the test should be repeated monthly for six months, bimonthly for another six months, and at longer intervals for two years.

If the test becomes positive, it is due to another pregnancy, an invasive mole, or a choriocarcinoma. To

avoid this confusion the patient should not become pregnant for at least one year. If the first qualitative test is positive, quantitative determinations should be done weekly to determine whether hormone levels are rising or falling. (9)

A followup bioassay study for one to eight years was made on ninety cases of mole. Of eighty-one cases who had evacuation of the mole, seventy-three (ninety per cent) retained their uteri and were well. Eight had hysterectomy with the diagnosis of invasive mole in five, and chorionepithelioma in three. One had vaginal metastases which were excised locally at the time of hysterectomy. According to this study, a rising titer or persistent HCG level about 20,000 I.U. more than thirty days after evacuation of a mole indicates trouble, and after ninety days, a positive gonadotropin test warrants expecially close observation. (11)

Acosta-Sison followed 210 cases of mole. The instance of malignant development in these cases was 16.19% including destruens and 7.6% choriocarcinoma. The percentage of malignancy was 5.56 in women age 15-19; 10.85 in age 20-29; 12.96 age 30-39; 19.23 in age 40-44; and 5% in age 45-49. (2)

A further aid in diagnosis of hydatidiform mole

is determination of the serum glutamic oxaloacetic transaminase level. At times even after the use of the quantatitive pregnancy tests and consideration of the size of the uterus, the diagnosis of hydatidiform mole may still be in doubt. Tobin compared levels of SGOT in hydatidiform mole with normal pregnancy levels and levels in abortion. He found that the SGOT level is within normal limits in normal pregnancies, incomplete abortions and threatened abortion. The SGOT level was elevated in four out of five cases of hydatidiform mole. (A normal level of SGOT may occur in four out of five cases of hydatidiform mole, where minimal necrosis is present.) Necrosis and destruction of cells of certain tissues releases intracellular enzymes, of which glutamic oxaloacetic transaminase is one, into the serum in large quantities. Normal levels are between five and forty units. In certain other conditions such as hepatic disease or coronary thrombosis, elevated amounts are found. There are high levels of glutamic acid present in normal chorionic tissue intracellularly, and therefore high levels of glutamic acid transaminase. As long as the integrety of the cell structure of chorionic tissue is maintained, one finds normal levels of SGOT. Trophoblastic proliferation in moles is more active histologically and chemically than normal

chorionic tissue, and therefore, increased amounts of glutamic acid transaminase is present. If necrosis and destruction of this tissue occurs, increased levels of SGOT will be present. If mole occurs in which minimal destruction and necrosis is present, SGOT levels may remain within normal limits. (24)

Acosta-Sison believes it is possible to diagnose hydatidiform mole within ten to fifteen minutes without x-ray film of the abdomen or determination of chorionic gonadotropin. Her method is practical only in patients with unduly enlarged uteri. First, the gravid uterus of 10-14 weeks must reach at least one centimeter below or up to or above the level of the umbilicus, but other symptoms of hydatidiform mole must be present. A bivalve speculum is gently introduced into the uterus along the axis of the cervical canal. In the presence of a mole, the sound will penetrate easily more than ten centimeters. After the sound has been removed, a uterine forceps is introduced, and when it has passed the terminal os, a small piece of tissue is pinched off with its tip. Invariably molar cysts are thereby removed, giving a definite diagnosis. This rapid method has been successful in 163 out of 318 cases (51.3%). (3)

Lutein ovarian cysts were present in 41 of 176

women with mole examined by palpation or hysterectomy. (17) In the series at King George V Memorial Hospital, ovarian cysts, usually bilateral, were noted in 17 out of 64 cases (27%).

In Great Britain between 1940 and 1959, of 365 cases of hydatidiform mole, 118 (32%) were diagnosed by macroscopic evidence, including 16 cases of ectopic gestation. Of 15 patients with hydatidiform mole and associated fetus, 12 had macroscopic evidence of hydatidiform mole with typical vesicular appearance of placenta. In the other three patients, diagnosis was by histologic examination. The average period of gestation at delivery was 21.3 weeks. Diagnosis may be difficult unless molar tissue has spontaneously appeared per vaginam. When hydatidiform mole and fetus coexist the x-ray not only fails to provide diagnostic assistance, but leads to clinical confusion. The presence of fetal skeleton persuades one against the diagnosis of hydatidiform mole, especially as excess uterine enlargement is radiographically indistinguishable from hydramnios. (13) Hydatidiform mole with coexistent fetus is quite uncommon, the incidence being one out of 14,000 pregnancies.

In a study at Sloane Hospital for Women, preoperative diagnosis was made in 30 cases, 11, by

passage of vesicles, 15 by clinical signs.(10) In the study at Sloane Hospital for Women, the presenting complaint was bleeding in all 68 cases. In a clinical and pathologic study by Logan and Motzloff of 72 cases of hydatidiform mole, vaginal bleeding or spotting was the outstanding symptom in the cases reviewed. Uteri were larger than normally expected for the stage of gestation in only eight cases. (20)

Among 93, 148 live births at Sloane Hospital from 1921 to 1958, there were 79 cases of chorionic disease; 68 hydatidiform moles, 6 destruens, and 5 choriocarcinomas. (10)

The incidence of hydatidiform mole varies considerably according to geographic location. In the United States the incidence is about 1:2,000, in Brazil 1:1,000, in Hong Kong 1:530, and in Japan 1:232. In the Phillippines from 1955 to 1957, Acosta-Sison found the incidence to be 1:200 (ten times that in the United States). She feels that the cause of mole is inadequate intake of high class protein found in meat, eggs ad dairy products. In the Philippines, the patients subsist mostly on rice, fish and fruits and vegetables. This deficiency in high

class protein is common also to the bulk of the population of other Oriental countries. That the cause is not racial is shown by the fact that a high incidence of hydatidiform mole occurs only among poor Filipinos and not among the well-to-do private patients. (4)

In one series of 210 cases of mole followed by Acosta-Sison, the incidence of molar pregnancies in the second, third, fourth, fifth, and sixth decades was respectively 0.39, 0.44, 0.99, 2.38, and 12.5%. (2)

Divack and Janovski reported an increased incidence in the aged. From 1950 to 1958, there were 1,152 live births to women over 50 years of age in the United States, representing 0.0032% of all deliveries. During this period, three cases of hydatidiform mole in the same group were reported, an incidence of 1:384, thus demonstrating an increased tendency in aged pregnant women for degeneration of placental tissue. (12)

Reports of a series from King George V Memorial Hospital in Sydney showed 64 cases of hydatidiform mole among 52,452 pregnancies (1:820). The age range was 15-50. Forty-eight per cent were primagravidas.

Ojanen found distinct hydatidiform degeneration in 38% of 74 cases of tubal pregnancy. This figure agrees with that generally reported in connection with

spontaneous abortion. On this basis it seems that pathologic development of ovum is not a factor in the origin of tubal pregnancy. On the other hand the development of ovum in unfavorable environment does seem to increase the tendency to hydatidiform degeneration. (22)

A predisposing cause of pre-eclampsia or eclampsia is hydatidiform mole. Of 85 patients with hydatidiform mole, 54 had normal blood pressure (63.5%) and urinalysis, and 31 had increased blood pressure. Nine out of 54 without increased blood pressure had fundus uteri at or above the umbilicus, whereas all 31 had the fundus at this level. Of the 31, 10 had albuminuria, and five of the ten had casts and red blood cells in the urine. Hydatidiform mole per se does not cause hypertension until it is of such size and bulk that the fundus reaches the umbilicus. In most instances of pregnancies with fetus, complicated by pre-eclampsia, blood pressure does not rise until the eighth or ninth month unless the pregnancy is multiple. In over 45% of patients with mole and hypertension, the height of the fundus was at the level of a six month normal pregnancy. Hypertension in hydatidiform mole probably results from the high titer of HCG and increased abdominal pressure of a large mole, which

distends the uterus and may induce uterine ischemia. Of patients with hypertensive disease who have hydatidiform mole, hypertension becomes aggravated before the fundus reaches the unbilicus, and toxemia symptoms appear early. A high titer of HCG apparently aggravates hypertension, along with the other phenomenon of toxemia. (5)

Of 214 women with molar pregnancies studied by Hobson, 101 aborted spontaneously after gestation period averaging 130 ± 40 days. (17) In the study at King George V Hospital in Sydney, spontaneous expulsion of hydatidiform mole occurred in 32 of 64 cases. In only five of 28 cases with subsequent dilation and curretage (usually within twenty-four hours) was residual molar tissue lacking. Vaginal evacuation, which has proved safe and effective, was used in all but three of the other 32 cases. Abdominal hysterectomy was necessary in only two. Total abdominal hysterectomy was performed in one patient, age 50, with associated uterine fibromyomata. No deaths occurred in this series. (9)

If the material obtained with curettage is histologically suggestive of invasive mole, hysterectomy is indicated. This operation is also indicated when, with suspicious clinical and hormonal findings,

curettage reveals many fresh vesicles on macroscopic examination. (9)

There is general agreement that the treatment of choice for chorioadenoma destruens is hysterectomy, leaving the ovaries. The treatment of choice in chorionepithelioma is primarily surgical, whether the process seems to be confined to the uterus or whether metastases have been demonstrated. Simple hysterectomy should be done in all cases. Removal of the primary tumor apparently has favorable effects on distant metastases. It is unlikely that removal of the paracervical and paravaginal lymphatics or veins as well as regional nodes will improve the prognosis.

Metastases whether local or distant should be removed if accessible. Local lesions on the vulva or vagina can usually be easily excised. If solitary lesions are present in the lungs or kidneys, they may be successfully removed by lobectomy, or pneumonectomy or nephrectomy. (28)

There is some debate as to whether the ovaries should be removed also. Ovarian enlargement usually regresses following removal of the primary tumor. There is some evidence that the ovary exerts a protective action through estrin on the

growth of chorionic hormone-producing cells. Therefore, some feel the ovaries should be left if they are not involved in the primary disease process.

Because estrin may have a favorable effect on distant metastases, some feel daily exogenous estrin should be administered. There are well documented cases of falling titers of chorionic gonadotropin and of dimunition of lung metastases by x-ray following administration of large doses of oral estrogen.(29)

Radiation therapy has been tried. However, none of the radiation media by itself, such as x-ray, radium or radioactive substances, have had any consistently beneficial effect upon chorionepithelioma, either locally or in the metastases.

X-ray treatment combined with nitrogen mustard therapy has been used in hopes that one would supplement the other. The patient seems to feel better, gain weight and appetite, but a sufficient number of cases showing a consistent favorable response is not available to evaluate the treatment properly.(27)

Methotrexate has recently produced excellent remissions and apparently cures in documented cases of chorionepithelioma. Hysterectomy must still be carried out along with Methotrexate. This form of treatment appears to be the most promising.(26)

desire for children. Every patient with hydatidiform mole should be examined for metastases in vulva, vagina, and lungs. In the presence of metastasis, total hysterectomy with the mole in place should be performed. Pulmonary metastasis should be treated with deep roentgen therapy. (10)

Although hydatidiform mole is not an infrequent disease, its repetition in the same individual is extremely rare. After a thorough search for case reports of repeat moles, Chesley, Cosgrove and Preece were able to collect 43 cases from the literature as of 1946. (8) Acosta-Sison reports four cases of repeat hydatidiform mole. Three were complicated by chorionic malignancy, two of which were choriocarcinoma. One of these died. Of 155 patients with hydatidiform mole admitted to Philippine General Hospital from 1955 to 1958, 2.57% (four cases) had repeat moles. (1) Hsu, Lai, and Changchun report seven additional cases from Taipei during the period from 1951 to 1963. (18) The repetition of moles can be classified into two main patterns, i.e., interspersion of molar pregnancies between normal pregnancies and successive repetitions of molar pregnancies. Interspersion of molar pregnancies between normal

pregnancies is unusual according to Chesley, Cosgrove and Preece. They were able to collect only five cases of women who had a normal pregnancy occurring between moles. (8) Five out of the seven patients in the report by Hsu, Lai, Changchun had interspersion of molar pregnancies between normal pregnancies. (18)

Reiner and Dougherty reviewed 66 cases of hydatidiform mole and found that 30 women became pregnant subsequently to molar gestation and had a total of 66 living babies. Incidence of development of invasive mole and choriocarcinoma together was 11%. Mortality rate was 4.5%. Of the patients with recurrent bleeding, 31% had invasive mole. (23)

In the series reported in the Proceedings of the Royal Society of Medicine, in 43 patients the biologic test became negative within five to twenty days after evacuation of the mole. In 23 of the 42 who retained their uteri, 29 normal pregnancies occurred subsequently. (25)

The early trophoblast of early pregnancy exhibits certain characteristics quite like those of cancer. It infiltrates and destroys maternal tissue, and it even exhibits a physiologic type of metastasis in the form of villous and trophoblastic deportation to the lungs. On the other hand, unlike cancer, the normal

restitution of trophoblastic inroads into the uterus and the regression of deported trophoblast can be explained only on the assumption of a local and probably also a systemic defense mechanism, though nothing is known of its nature. Such a defense mechanism, however, may well explain some of the vagaries of choriomatous tumors, such as the regression and cure which has occurred in a small proportion of cases of choriocarcinoma of accepted authenticity.

Trophoblastic invasion of the uterine wall and of the decidua is seen in both normal pregnancy and with benign hydatidiform mole, though it varies greatly in degree. Where trophoblastic proliferation is excessive or where there is marked intravascular penetrative tendency, the diagnosis of invasive or destructive mole (chorioadenoma destruens) may be justified if one wishes to indicate an intermediate group. However, the morphologic characteristics in this group often differ in no noteworthy respect from those of the benign group. Moles of this type do not metastasise, although they may occasionally invade the vagina or parametrium, and they can ordinarily be cured by hysterectomy so they should not be placed in the malignant group. (21)

No true correlation was found between the histologic pattern of mole and its malignant tendency. In 31

of the 64 cases reviewed by Logan and Motzloff in which curettage was done, there was no histologic evidence of trophoblastic proliferation or invasion, yet in one of this benign-appearing group, choriocarcinoma developed five weeks later. In two of fourteen cases of an intermediate group, with minimal or localized trophoblastic proliferation, diagnosis was made one, and four months, respectively, after curettage. In nineteen cases in which histologic study showed excessive trophoblastic proliferation with infiltration tendencies, only five moles proved to be malignant.

Eight patients (11%) had rising titers of HCG after removal of the mole. Repeated curettage disclosed extensive trophoblastic proliferation in three, chorioadenoma destruens in two, and no evidence of chorionic elements in three. Pathologic diagnosis at hysterectomy on the three patients with extensive trophoblastic proliferation was chorioadenoma destruens. Thus the final diagnosis in their eight cases was chorioadenoma destruens in five, choriocarcinoma in one and metastatic moles in the lungs in two. No deaths or recurrences occurred in this particular series.

The author noted that curettage has limitations as a diagnostic proceedure. Negative histologic findings with rising titer of HCG indicate that chorionic

elements may be lodged deep in myometrium beyond the reach of the curette, or may have metastasis to distant organs such as the lungs. Positive x-ray findings with negative histological examination should be considered inconclusive evidence of malignant metastases unless substantiated by rising titer of HCG. HCG determinations are the most sensitive and accurate indicator of entopic or ectopic chorionepithelioma. (20)

Hydatidiform mole can occasionally metastasize to a distant site. Apparently such transports of hydropic villi or their trophoblasts may subsequently regress.

Duration and height of levels of HCG vary in a post-molar patient. This hormone has been shown to act through the corpus luteum, since castrated patients with induced secretory endometrium fail toform decidua or to delay menstruation. The rates of excretion are important, and factors such as the amount of chorionic tissue present, the degree of anatomic and physiologic differentiation and the rate of its regression as it occurs normally and pathologically determine the variation in different patients.

Fourteen cases with pathologic features observed in one author's study were reported. The pathologic

process began with hydatidiform mole, was followed for possible pulmonary metastases, and terminated by healing. The mechanism involved in regression of trophoblast is unknown. When benign, the chorionic tissue ages rapidly within a few months, though many of its characteristics initially simulate features of other tissue malignancies. While the tissue is malignant, some of its elements, in situ or metastatic, may become well differentiated, behaving probably like normal trophoblast and therefore susceptible to regression. Differentiation of trophoblast is perhaps its pathway to regression or transformation into fibroblast. The mechanism of regression of the trophoblast carries in itself the intricacies and complexities of cellular death and the presence of an antagonistic factor (or the absence of stimulating factor), which governs this biologic phenomenon. (6)

S.C. is a 21 year old para 1-1-0-1 who was admitted to University Hospital on 4-17-63. Her last baby was born on 9-22-62 and died neonatally. Her first child was born in 1961 after seven months gestation. Her last normal menstrual period prior to admission was December 15, 1962. She experienced one to two hour bleeding episodes in January and February. She had no period in March. The last history of coitus was in January 1963. Bleeding began two weeks prior to admission, with large clots being passed. Seventy-two hours prior to admission, she had noticed a slight increase in abdominal cramping. On admission she was hyperpyrexic and nauseated. She was normotensive, and urinalysis was normal. On physical examination there was a lower midline abdominal mass 13 cm. above the pubis which was mildly tender. No fetal heart tones were heard. The cervical os was closed with moderate mucous and blood extruding therefrom. Cervical movements caused movement of the mass. No adnexal masses were present. There was right lower quadrant direct and rebound tenderness. Hemoglobin was 8.4 grams %. She was given 500 cc. of whole blood and intravenous penicillin and streptomycin. On 4-18-63 pregnancy test was positive. After being given pitocin, the patient passed small fragments of material with hydropic

changes. Dilation and evacuation of the uterus was then carried out. Pathologic examination of the uterine material revealed clusters of clear translucent cystic structures. There were markedly dilated chorionic villi showing extensive hydropic degeneration. Upon the surface of these villi prominent trophoblastic proliferation is noted. These villi were avascular and had an histologic appearance consistent with hydatidiform mole. The segment of myometrium showed no extension of the molar tissue into surrounding smooth muscle. The patient was dismissed in satisfactory condition on 4-20-63.

Followup pregnancy tests on 5-3-63 were negative. Fundus uteri at this time was normal in size, but there was a question of a right cystic ovary. The patient was seen on 6-8-63 in the emergency room with a complaint of bleeding of eight days duration. The first three days were "normal flow", but then the bleeding became profuse. The patient was at this time admitted. On examination the vagina was filled with clots, the cervix was dilated one centimeter, and the uterus was one and one-half times enlarged. There were cystic ovaries bilaterally measuring approximately three to four centimeters. Pregnancy tests on 6-10-63 were positive. Dilation and curettage at this time revealed

no evidence of molar tissue. Pregnancy tests on 6-12-63 were negative. Chest xrays were negative. From the microscopic examination of the curetted material the pathologists were unable to differentiate with any certainty whether the trophoblastic tissue identified was a residual of the previously identified hydatidiform mole or represented trophoblastic tissue from an early implantation of a subsequent pregnancy. The patient was then dismissed to be followed with pregnancy tests and intramuscular provera for contraception. Pregnancy tests on June 13, 17, and 19 were negative. On 12-17-63 quantitative HCG levels were 20,000 I.U. per liter. She was hospitalized with heavy bleeding. She was discharged without further treatment, but continued to spot. She was readmitted on 12-31-63 at which time the uterus was neither palpable nor tender. Blood clots were passed, but no tissue. She was given pitocin, and a dilation and evacuation of the uterus was carried out. There was no gross suggestion of molar degeneration.

Microscopic examination of the curettings revealed large amounts of necrotic debris and fibrin. In addition, there were sheets and large clumps of trophoblastic cells. Both syncytial and cytotrophoblastic cells were present. In the sheets of cytotrophoblastic

cells there was considerable nuclear variation, and the nuclei contained considerable chromatin. Groups of cytotrophoblastic cells were surrounded by syntrophoblastic cells, forming the so-called plexiform pattern. In one of the sections there was myometrial tissue and trophoblastic cells were seen within the myometrium. No endometrial tissue with villi was identified. Diagnosis was choriocarcinoma. The patient was given a total hysterectomy, and is presently being followed with pregnancy tests and xray surveys.

C.M. is a 46 year old para 7-2-0-7 who was admitted to University Hospital with a chief complaint of bleeding. Her LMP was 10-11-61, and EDC was 7-18-62. The next bleeding episode began on 12-4-61 and continued until admission, which was on 1-11-61. Her menstrual periods had previously been regular with thirty day cycles and four to five days flow. On admission her blood pressure was 186/104. There was a smooth 12 x 15 cm. suprapubic mass confluent with the cervix. Adnexa were not felt. Pregnancy tests were positive. On 1-14-61 the patient began profuse bleeding, followed by passage of "molar-appearing tissue." Shock ensued, and the patient was given two units of blood and a dilation and curettage. Pathologic examination of the evacuated material revealed large hydropic avascular placental villi with moderate trophoblastic prolifer-

ative activity. Pregnancy tests on 1-16-62 and 1-18-62 were positive. The patient was febrile at this time and was treated with penicillin, streptomycin and chloromycetin, and dismissed. She was next admitted on 2-9-62 because she had continued to spot until this time, when the bleeding became heavy. The uterus at this time was anteflexed and twice normal size and non-tender. No adnexal masses were felt. Blood pressure was 160/84. In view of the patient's age and pathological diagnosis, abdominal hysterectomy was done. Pregnancy tests were negative on 2-10-62, positive four days after the operation, and then negative again on 2-28-62.

Pathologic examination showed that within the body of the uterus, projecting from the posterior wall, a mass of grape-like, cystic and watery fluid-filled structures. This mass appeared hemorrhagic on the surface. Transection of the uterus revealed the area beneath the mass to be soft and cystic in appearance and appeared somewhat necrotic. Up to 0.8 cm. of myometrium was present between this cystic mass and the serosal surface of the uterus. Examination of the ovaries revealed corpus luteum cysts on the right ovary. Films of the chest and abdomen revealed no abnormality.

J.B. is a 19 year old para 1-0-1-0 who was admitted to Clarkson Hospital on 11-8-62 because of passing clots and tissue per vaginam. Her LMP was 7-14-62 and EDC was 4-21-63. She had been treated with depoprovera on 10-27-62 and 11-3-62 because of the diagnosis of threatened abortion. On admission the fundal height was 20 cm., and she had bled to 9.2 gms. % hemoglobin. A dilation and curettage was then carried out after the patient had been given two units of whole blood. Pathologic examination revealed gross placental tissue composed of hydatid structures varying in size from 5 to 25 cm. The clear cysts were characteristic of hydatidiform mole. The chorionic villi were large and edematous. They tended to be covered by syncytial trophoblast cells which were often proliferating. The diagnosis was hydatidiform mole. Followup frog pregnancy tests on 12-11-62 and 3-11-63 were negative. It was reported that on 12-12-62 the patient demonstrated left ovarian enlargement approximately twice normal size. A subsequent pregnancy ended in abortion on 4-7-63. Pregnancy tests on 5-9-63 and 8-10-63 were negative.

B.M. is an 18 year old primagravida who came to the University Hospital emergency room with a complaint of intermittent suprapubic pain and bloody

spotting. Her LMP was 10-3-59 with an EDC of 7-10-60. Fundal height was 20 cm. above the pubis. On the day following admission, the patient passed what was described as a complete mole. Serum pregnancy tests at this time were positive at 1:100 dilution and negative at 1:1000 dilution. Dilation and curettage produced large amounts of tissue. On 3-15-59 serum pregnancy tests were negative. Pathologic report on the curetted material stated that there were multiple fragments of grape-like structures which were filled with clear fluid. Microscopic examination revealed large avascular villi, the central portion of which had undergone hydropic degeneration. Associated with the villi was a moderate amount of fibrin and blood clot. The diagnosis was hydatidiform mole. Serum pregnancy tests on 5-18-60, 6-15-60, and 12-29-60 were negative. On 3-13-61 the pregnancy tests became positive. Chest xray at this time showed a probable healed primary complex. The patient came to the emergency room on 7-1-61 with a chief complaint of vaginal bleeding and lower abdominal pain. Her LMP was 1-7-61. She had a bleeding episode on 2-9-61. She had bled for eight days prior to this admission. At this time the fundal height was compatible with a 16-18 week pregnancy. No adnexa were pal-

pated, and no fetal heart tones or fetal parts were detected. She was febrile and intravenous penicillin and streptomycin, as well as pitocin, were administered. Her blood pressure at this time was 140/80. That same day the patient passed placental tissue and molar tissue. The pathologic report stated the chorionic villi were considerably larger than usual. The stroma of the villi in many places was composed of very course fibrous tissue and in many areas there was considerable edema. Capillaries were not identified in those villi. There was moderate trophoblastic proliferation. The diagnosis was hydatidiform mole. On 7-7-61 quantitative urine and blood HCG titers were positive undiluted and negative at dilutions of 1:100. On 7-12-61 and 7-21-61 the pregnancy tests were negative. On November 4, 1962, the patient delivered a normal, vertex, living infant, having had a normal pre- and postpartum courses.

K.R. is a 35 year old para 2-1-0-3 who was admitted to Clarkson Hospital with a tenative diagnosis of an ovarian cyst. Her LMP was 10-6-62 with an EDC of 7-13-63. The patient reported persistent spotting since December. She had previously been treated for excessively heavy periods. The obstetrician reported hearing fetal heart tones, and the patient had felt

movement sometime prior to admission. On admission the patient was having severe right lower quadrant pain. The fundus was palpable at the umbilicus. No fetal heart tones were heard. The frog test on the patient's urine was positive. Abdominal xray revealed a 19 x 24 cm. homogeneous soft tissue density arising from the central portion of the pelvis and extending to the level of the third lumbar segment. No calcification of fetal parts was seen. The possibility of a large ovarian cyst was entertained at this time. A laparotomy revealed bilateral ovarian cysts, and a left oophorectomy and right partial oophorectomy were done. The uterus was found to be the size of a five month gravid uterus. A pathologic diagnosis of multiple theca lutein cysts of both ovaries was made. There were hydatid cysts of Morgagni on the left ovary. On the day following the operation, she began passing bright red blood per vaginam, and having two to four minute contractions. She was given ergot and later passed large amounts of gelatinous material. Curettage was done, and a diagnosis of hydatidiform mole was rendered. Frog tests were negative on 4-12-63, 5-10-63,7-6-63, 8-1-63, 9-27-63, 1-21-64, and 4-2-64.

D.Z. is a 26 year old para 1-0-0-1 who was ad-

mitted to Methodist Hospital on 6-1-60 because of bleeding and passing clots per vaginam. Her LMP and EDC were not recorded. A dilation and curettage was done. The chorionic villi were hydropic, and necrotic decidual tissue was present. The markedly dilated chorionic villi had a loose, relatively cellular stroma which had undergone myxomatous degeneration. Blood vessels were absent from the stroma. Villi were covered by both syncytial and cytotrophoblasts, which were markedly hyperplastic. Dark staining variable nuclei with prominent nucleoli were demonstrated. The diagnosis was a potentially malignant hydatidiform mole. Followup pregnancy tests on this patient were not done. However, she delivered a full term living infant by Caeserean section on 5-16-61.

D.P. is a 35 year old woman who was admitted to Clarkson Hospital on 3-30-60 because of persistent vaginal spotting. The uterus on admission was three to four times normal size. She spontaneously passed tissue and was dilated and curettaged. The chorionic tissue appeared to be undergoing hydropic change. The fragments of decidua were degenerating and tended to be dense and hyalinized. There was moderate distention of the chorionic villi. No mitotic figures were identified. The villi were covered by syncytial trophoblasts which were mildly

hyperplastic. There was a fetus of approximately six weeks gestation. The diagnosis was early hydatidiform mole. Rabbit pregnancy tests were positive on 4-13-60 and positive on 5-3-60.

P.D. is a 31 year old para 4-1-0-4 who entered Methodist Hospital on 1-24-63 because of continuous vaginal spotting and cramping in the lower abdomen for several weeks prior to admission. No fetal heart tones were ever heard. Her LMP was 7-22-62, and EDC was 4-29-63. The fundal height was three fingerbreadths above the pubis. On 1-25-63 the patient passed grape-like tissue spontaneously. The specimen consisted of multiple fragments of small grape-like cysts mixed with necrotic decidual tissue. There were large edematous villi. The stroma showed hydropic degeneration, and there were no remaining blood vessels. There were scattered areas of trophoblastic proliferation. The diagnosis was hydatidiform mole. Pregnancy tests on 5-8-63 were negative. She is presently pregnant, her EDC being in early May, 1965. Fetal heart tones have been heard, and the pregnancy is progressing normally.

P.M. is a 23 year old para 2-0-0-2 whose admission to Methodist Hospital was because of abnormal vaginal bleeding. Her LMP was 9-13-61, and her

EDC was 6-20-62. Chest xray was normal. The uterine height was compatible with 22 weeks of gestation. Frog tests on 12-19-61 were positive. The patient had 2.9 million rbc's, a hemoglobin of 8.2 gms. %, and a hematocrit of 25%. At this time she was using seven pads per day. She then began having irregular uterine contractions. The cervix was not dilated. On 12-24-61 the patient spontaneously passed molar tissue. The uterus at this time was described as being at the level of three-fourths of the way to the umbilicus. The pathological specimen obtained by curettage was reported as being portions of placenta showing large numbers of grape-like cystic clusters. The diagnosis was hydatidiform mole. Frog tests on 2-1-62 and 7-20-62 were negative. Since the mole the patient has had normal chest xrays twice yearly. She delivered a full term living infant on 1-25-64.

B.E. is a 19 year old primagravida who was admitted to Clarkson Hospital on 12-9-63 because of uterine bleeding. Her LMP was 6-1-63, and her EDC was 3-8-64. The rabbit test on the patient's serum was positive. She was given pitocin and passed a specimen on the following day. The specimen consisted of multiple large fragments of dark brown necrotic ma-

terial upon which were numerous clusters of vesicles filled with clear serous fluid. Markedly hydropic villi were covered by syncytial and trophoblasts which varied markedly in their degree of differentiation. In some areas there were anaplastic nuclei. These changes included marked enlargement of the nuclei, with thickening of the nuclear membrane and clumping of the chromatin material. The nucleoli tended to be enlarged. The cytoplasm of the cytotrophoblasts were often vesiculated and filled with proteinaceous fluid. The diagnosis was potentially malignant hydatidiform mole. The patient was followed elsewhere.

A.K. is a 32 year old woman who was admitted to Clarkson Hospital on 7-17-63. Her first pregnancy resulted in a living infant delivered by Caeserean section. Her second, third and fourth pregnancies ended in abortion. Her fifth pregnancy, also delivered by section, resulted in an infant which died neonatally due to hyalin membrane disease. Her sixth pregnancy resulted in a living infant also delivered by section. Her seventh pregnancy was in progress when she was admitted in July, 1963. Her LMP was in January, 1963, and her EDC was in October, 1964. In June, 1963, the patient began bleeding.

There was further uterine growth, but bleeding continued until admission. She began having lower abdominal cramping twelve days prior to admission. She had previously taken thyroid extract after a thyroidectomy because of nodules. On examination the uterus was below the pubis. Chest film was negative. A hysterotomy was performed, and a tubal ligation was also done. Necrotic placental tissue was retrieved. The villi had undergone marked hydropic degeneration. However, viable stromal tissue cells remained in most of the villi. Scattered blood vessels were seen within the stroma. The villi were covered with both syncyto- and cytotrophoblasts which were only mildly hyperplastic. The diagnosis was hydatidiform mole. Frog pregnancy tests on the patient's serum were negative on 6-14, 6-28, 7-10, 7-13, 7-17, 7-27, 9-12, and 12-23-63.

B.H. is a 31 year old para 5-0-0-5 who was hospitalized at Clarkson on 8-21-59 because of vaginal bleeding, and an initial diagnosis of "inevitable abortion at two months" was made. Her LMP was 6-1-59, and her EDC was 3-8-60. On the day following admission, the patient bled heavily and passed tissue. A dilation and curettage was done. Placental tissues without identifiable fetal parts were seen. There

were sheets of decidual cells, fragments of endometrial tissue and numerous chorionic villi. These villi tended to have a myxomatous basophilic stroma, and in numerous instances there was proliferation of the trophoblastic cells. The pattern was that of a hydatidiform mole with moderate trophoblastic hyperplasia. The patient had no pregnancy test followup. She had a subsequent pregnancy, delivering a viable infant on 7-15-60. On 4-30-63 she delivered a premature living infant.

M.J. is a 28 year old para 2-0-0-2 who was admitted to Clarkson Hospital because of passing clots and cramping pain in the lower abdomen. Her LMP was 12-25-58, and her EDC was 10-2-59. In 1956 the patient had a partial ovarian resection. On admission the uterus was 4.5 cm. above the pubis and tender to palpation. Following admission she passed tissue per vaginam. Dilation and evacuation for incomplete abortion was then done. The specimen consisted of several large irregular pieces of placental tissue. Umbilical cord was present, but no fetal parts were observed. There were numerous chorionic villi which tended to have an edematous cytoplasm containing only a few blood vessels. The villi were covered by both syncytial and Langhans cells. Occasional small areas

of trophoblastic hyperplasia were seen. The villi were large. The diagnosis was benign hydatidiform mole.

N.F. is a 27 year old para 2-0-0-2 who was admitted to Clarkson Hospital on 5-7-60 with a chief complaint of vaginal bleeding with clots for the past three months. She was reportedly three months pregnant. On examination she had tenderness on palpation of the lower abdomen. Pelvic examination revealed clots in the vaginal vault, and the cervix was dilated approximately two centimeters. She stated she thought she might have passed a fetus. She was subsequently curettaged, and molar tissue was obtained. Pathological examination showed the chorionic villi tending to be large and having loose edematous to myxomatous stroma which was avascular. There was moderate proliferation of cytotrophoblasts. The diagnosis was hydatidiform mole. The patient was transient in town, and no followup is known.

J.B. is a 30 year old para 2-0-0-2 who was admitted to Clarkson Hospital on 3-13-59 because of menorrhagia for three weeks prior to admission. Her LMP was 1-16-59, and her EDC was 10-23-59. She had passed no tissue, but the feeling was that she had a missed abortion. Therefore, dilation and curettage

was performed. Examination of the curetted material showed there were large sheets of decidual cells, some of which were undergoing necrosis. There were infiltrates of neutrophils, lymphocytes and occasional decidual giant cells. Numerous chorionic villi were undergoing hydropic degeneration. The stroma was loose and edematous. Moderate trophoblastic hyperplasia was evident. The diagnosis was hydatidiform mole. The patient began menstruating on 4-25-59. Frog tests on 3-23-59 and 6-15-59 and 9-20-59 were negative. In September, 1960, the patient delivered a healthy living infant. She is presently pregnant, her EDC being 5-20-65.

C.B. is a 25 year old para 2-0-0-2 who was admitted to Clarkson Hospital on 6-9-63 with a chief complaint of spotting since early May with no passage of tissue. Her LMP was 11-1-63, and her EDC was 8-15-63. On examination the fundal height was 17 cm. There were no adnexal masses. No fetal heart tones were heard. It was noted that there had been no increase in uterine size since March, 1963. She was given pitocin on admission, and on 6-11-63 she passed tissue. A dilation and curettage was then done. Fragments of membrane were retrieved, but no fetal tissue. The patient continued to bleed for two days

following the initial curettage, so a repeat curettage was done. Pathologic examination showed a few chorionic villi, which, although their stroma was free of hydatidiform swelling, had a moderate degree of hyperplasia of both syncytial and cytotrophoblast. Their nuclei were moderately variable and tended to be hyperchromic. There were also a few fragments of degenerated decidua and a large amount of blood clot.

M.K. is a 32 year old para 3-0-0-2, who lost one child neonatally, was admitted to Methodist Hospital because of cramping in the lower abdomen and vaginal spotting. Her LMP was 7-11-61, and her EDC was 4-19-62. Since her last menstrual period, there was uterine enlargement for three months consistent with pregnancy. Then there was regression of uterine size, accompanied by the onset of irregular spotting and occasional cramping for one to two days at a time for three months at monthly intervals. There had never been any fetal movements reported, and no tissue was passed prior to admission. On admission examination, there was slight left lower quadrant pain. There was also a midline mass two fingerbreadths above the pubis. Pitocin was given during the dilation and curettage. Retrieved was irregular friable pink-tan tissue fragments and clotted blood. En-

trapped within the tissue fragments were several dilated cystic vesicles. The diagnosis was hydatidiform mole. Frog tests were negative following the evacuation of the uterus, and on 8-29-62 and 10-10-62. On 11-16-62 the pregnancy test was positive. On 1-7-64 the patient aborted. There was no report of mole at this time. In June 1964, the patient was operated on for an ectopic pregnancy.

C.B. is a 27 year old para 1-0-0-1 who was admitted to Methodist Hospital on 8-16-61 because of heavy vaginal bleeding. Her LMP was 3-12-61, and her EDC was 12-19-61. On admission she had 2.9 million rbc's, a hemoglobin of 7.9 gms. % and a hematocrit of 22%. She was given two units of blood and pitocin intravenously. She spontaneously delivered a mole. A dilation and curettage followed. There were friable tissue fragments and portions of clotted blood. There were clusters of grape-like, clear fluid filled cysts. The diagnosis was hydatidiform mole.

M.P. is a 24 year old primagravida who was admitted to Clarkson Hospital on 2-25-62 because of intermittent vaginal bleeding since 11-1-61. Her LMP was 9-2-61, and her EDC was 6-9-62. Fundal height on admission was 13 cm. Pregnancy tests were positive on 12-30-61 and 1-31-61. She was given pito-

cin, and on the following day passed what was described as being molar tissue. The specimen consisted of partly necrotic endometrial tissue to which were attached thin-walled vesicles , which were filled with clear serous fluid and occasional dark brown, thick fluid. The large hydropic villi had an edematous stroma which was filled with partly inspissated proteinaceous material. The villi did not contain any blood vessels. The trophoblasts surrounding these villi were fairly well differentiated. The diagnosis of hydatidiform mole was made. Pregnancy tests on 3-2-61 and 6-12-61 were negative. Approximately one year following the mole the patient delivered a full term living infant.

D.R. is a 24 year old para 1-0-0-1 who was admitted to Methodist with a chief complaint of "possible pregnancy--vaginal bleeding--decrease in fundal height and no fetal heart tones." Her LMP was 12-28-60, and her EDC was 10-3-61. The patient had persistent vaginal spotting and brownish discharge vaginally since her last menstrual period. She also lost 14 pounds since then. Fundal height increased until 5-15-61 and then remained stationary until admission on 5-31-61. At this time it was noted that there was a decrease in fundal height. Fetal heart

tones were never heard. Breasts were no longer increasing in size, but were regressing. The patient had been followed with gonadotropins "without diagnostic help." Fundal height on admission was 15 cm. A dilation and evacuation was done without the patient ever having passed tissue. There was soft friable pink-tan tissue in which were embedded numerous cyst-like structures. Cut section across the cysts revealed edematous, gelatinous appearing semi-translucent gray-tan tissue. The diagnosis was reported as hydatidiform mole. Chest xray on 6-3-61 was normal. Frog tests were negative on 6-18-61 and 7-22-61. On 1-11-64 the patient delivered a full term living infant.

A.R. is a 42 year old para 2-0-0-2 who was admitted to Methodist Hospital on 1-17-63 because of continuous vaginal spotting, using one pad per day, since late December. Her LMP was 10-25-62, and her EDC was 8-1-63. On admission the uterus was palpated above the umbilicus without fetal parts or fetal heart tones being detected. She also had a grade II/IV systolic heart murmur. Xray of the abdomen showed a large soft tissue density in the abdomen the size of a five to six month pregnant uterus. There were no demonstrable fetal bones or areas

of calcification. Chest xray showed a probable healed primary complex. She had 2.9 million rbc's, a hemoglobin of 8.3 gms. %, and a hematocrit of 24%. She had received five units of whole blood in the past four weeks before admission. Serum gonadotropin levels at this time were 10,000,000 units per liter. Due to the patient's age and procidentia, it was decided to do a total abdominal hysterectomy. The entire uterine cavity was filled with multiple large cystically dilated grape-like structures. There was apparent invasion of the endometrium by the mole. The diagnosis was hydatidiform mole with invasion. She was followed in Minneapolis.

J.A. is a 23 year old para 1-0-0-1 who was admitted to Methodist Hospital on 1-30-62 with a chief complaint of persistent vaginal bleeding throughout her pregnancy. Her LMP was 10-15-62, and her EDC was 7-22-63. She had an onset of very heavy bleeding a fews hours before admission with the passage of large clots and lower abdominal cramping. On examination the placenta was presenting at the cervical os. It was then manually removed. A dilation and curettage followed. Pathological examination showed irregular flattened portions of soft, gray-tan tissue with blood clots. The diagnosis was hy-

datidiform mole. Frog tests on 3-6-62, 4-23-62, and 8-2-64 were negative.

J.B. is a 22 year old para 1-0-0-1 who entered Methodist Hospital on 10-18-61 with a chief complaint of vaginal bleeding intermittently for the past month. Her LMP was 5-18-61, and her EDC was 3-26-62. On admission she was having moderately heavy bleeding and low abdominal cramping. Her blood pressure was 142/90, and she had a grade II/VI systolic murmur. The uterus was the size of a three month pregnant uterus and was somewhat tender to palpation. She was given pitocin and the following day passed spontaneously placenta, a fetus, and a mole. Examination of the uterine contents showed many of the chorionic villi of the placenta to be hydropic and filled with viscid fluid. Edematous stroma and degenerative changes were present. No trophoblastic hyperplasia was noted. Pregnancy tests on 10-17-61 prior to passage of the mole were negative. She also had a negative pregnancy test in December, 1961. On 7-29-63 the patient delivered a full term living infant.

R.B. is a 17 year old girl who was admitted to Methodist Hospital on 8-11-63 because of "miscarriage one week ago." She had previously delivered three viable infants by Caeserean section. Her LMP

was 5-10-63, and her EDC was 2-17-64. On 8-2-63 she began having lower abdominal cramping and vaginal spotting. One week prior to admission she passed grayish tissue, after nine days of filling three pads per day. She had been taking thyroid extract. Dilation and curettage was then done. Pathological examination showed irregular portions of friable yellowish-tan tissue and multiple grape-like clear vesicles. The diagnosis was hydatidiform mole. The frog test on 9-12-63 was negative. No further followup was carried out.

V.H. is a 42 year old para 8-1-1-7 who was admitted to Methodist Hospital because of vaginal bleeding since the second month of pregnancy. She had no cramping, but passed clots and tissue just prior to admission. She was given pitocin followed by a dilation and evacuation. The specimen was friable gray-tan tissue and clotted blood within which were interspersed thin fluid-filled cysts. No saccular structures of fetus were grossly identified. There was hyperplasia of the cytotrophoblastic elements. The diagnosis was hydatidiform mole. The patient was followed in another city.

J.T. is a 37 year old woman who was first admitted to Clarkson hospital with a diagnosis of

chronic nephritis. Her second admission was on 2-5-60 with a diagnosis of threatened abortion. On her third admission on 2-26-60 the pregnancy test was positive in dilutions of 1:500 and negative at 1:1000. Chest xray showed atelectasis of the base of the left lung. A biopsy of the lower uterine segment and its contents proved a mole to be present. A dilation and evacuation was then performed. Large hydropic avascular villi were present. In many areas there was marked proliferation of both the syncytial and cytotrophoblast. Marked nuclear variation was present. Clumps of cytotrophoblastic cells were seen in which the giant nuclei were prominent, and the chromatin was extremely coarse. Occasional syntrophoblastic cells tended to form villous-like structures. It was felt that the trophoblastic anaplasia present in this tissue, and the subsequent biopsy of the uterus, would put this specimen in the potentially malignant group of hydatidiform moles. The patient continued to bleed. On 3-8-60 it was decided, in view of the pathological diagnosis of potentially malignant mole and the patient't age, to do a total abdominal hysterectomy and bilateral oophorectomy. At operation the uterus was three times normal size, and the ovar-

ies were polycystic. The diagnosis of choriocarcinoma was made. She presently is living and well. No xray studies or gonadotropin titers have been done.

P.G. is a 21 year old para 2-0-0-2 who in January, 1959, was hospitalized by her local doctor because at an estimated three months of gestation, her uterine size was compatible with a six to seventh month pregnancy. After a dilation and curettage in April, 1959, at which time the diagnosis of hydatidiform mole was made, she was told there was remaining tumor tissue. Therefore, she was admitted to Methodist Hospital for a repeat curettage. Following this curettage, her pregnancy tests remained positive two weeks later and one month later. On 5-21-59 the patient was admitted to University Hospital. Quantitative frog tests showed positive results to a 1:5 dilution. Chest xray at this time showed a spherical one centimeter density in the left subapical region and a similar finding in the right lower lung field. In view of the lung findings and serum chorionic gonadotropin titers, it was decided to remove the uterus. A total abdominal hysterectomy and left oophorectomy and right partial oophorectomy was carried out. At the superior pole of the uterus was a fungating mass which was

approximately five centimeters in diameter. The mass was necrotic and pedunculated. It appeared to be invading the muscle tissue. Sections of the uterus revealed a portion of uterus scattered through which were several chorionic villi. There was a moderate amount of trophoblastic tissue extending into the myometrium. The cells lining these structures were bizarre in nature. The nuclei were hyperchromatic and varied in size and shape. Some Langhans giant cells were seen. The diagnosis was chorioadenoma destruens. She was dismissed on 6-1-59. On 6-18-59 and 6-23-59 the pregnancy tests on the urine were positive, but negative on the serum. On 6-25, 8-3, 9-30, 12-1-59, 2-11-60, 6-1, 8-3, 9-5-60, 6-1-61, 11-2-61, 3-28-62, 6-7-62, 2-19-63, 8-5-63, 2-4-64, and 8-18-64 the pregnancy tests were negative. Chest films on 6-18-59 showed the one centimeter densities to be still present with essentially no change from the previous xray. On 7-9-59 these lesions were barely discernible. On 8-31-59 they were no longer visible by xray. Chest xrays for followup were normal essentially on 11-3-59, 1-7-60, 6-1-60, 11-2-60, 2-28-61, 6-7-61, 9-5-61, 3-6-62, 9-4-62, 8-6-63, 2-4-64, and 8-18-64. The patient is now well, and is still being follow at the Clinics.

AGE	NUMBER
17	1
18	1
19	2
21	2
22	1
23	2
24	2
25	1
26	1
27	2
28	1
30	1
31	2
32	2
35	2
42	2
46	1

Table I. Age of patient.

PARITY	NUMBER
Primagravida	3
1	5
2	9
3	1
4	1
5	1
6	1
7	1
8	1

Table II. Parity of patient.

WEEKS	NUMBER
5-6	1
6-7	1
9-10	1
10-11	4
12-13	3
14-15	1
15-16	1
19-20	2
22-23	3
24-25	3
25-26	1

Table III. Stage of gestation at delivery of mole.

STAGE OF GESTATION	FUNDAL HEIGHT
15-16	16-17
12-13	18-19
14-15	25-26
22-23	25-26
24-25	16-18
19-20	20-21
24-25	7-8
12-13	22-23
25-26	7-8
5-6	5-6
23-24	16-17
19-20	19-20
10-11	20-21
10-11	12-13

Table IV. Comparison of weeks of gestation as determined by LMP with expected weeks of gestation from fundal height.

Twenty-seven patients with hydatidiform mole were reviewed. The average stage of gestation at delivery of the mole was 16-17 weeks. The presenting complaint in every instance was abnormal vaginal bleeding. In addition to this complaint, eight of the patients also complained of lower abdominal pain or cramping.

Eight patients passed molar tissue spontaneously. Nine patients were given pitocin and subsequent curettages. In four patients dilation and curettage was the only treatment. Two patients had no curettage, but had an immediate hysterectomy. One patient was treated first by curettage followed by a hysterectomy. One patient had a laparotomy followed by a dilation and curettage. One patient was treated by hysterotomy and tubal ligation.

Two patients had had abortions prior to their moles. One patient had an abortion following her mole. Another patient had an abortion prior to passing the mole, and a subsequent pregnancy ending in abortion in which no evidence of mole was found. One patient had a mole which was followed by a pregnancy which also resulted in mole. Following these two moles, she went on to deliver a normal living infant. Eight patients had subsequent pregnancies with normal living infants.

One patient developed chorioadenoma destruens

following a mole. She was treated by hysterectomy. This was the only patient in which there were any significant lung findings, which were due to the chorioadenoma destruens. These lung lesions eventually regressed. Two patients developed choriocarcinoma.

It was specifically reported in six patients that the ovaries were cystic in association with the mole. Three patients had hypertension, but in no case was toxemia specifically mentioned or treated.

In only two cases of mole was there reported to be fetal parts identified. In another case the pathologist identified umbilical cord, but no fetal parts. In yet another case the obstetrician had previously reported hearing fetal heart tones, and the patient stated that she had felt movement. However, at pathological examination of the uterine contents, no fetal parts were reported being present.

SUMMARY

Hydatidiform mole is a complication of pregnancy which is characterized by progressive swelling of the chorionic villi, associated with the disappearance of the fetal vascular system, and accompanied by a variable amount of trophoblastic proliferation. A true hydatidiform mole is a temporarily missed abortion of a "blighted" ovum whose microscopic hydatid swelling had become macroscopic during the additional weeks it has been retained in utero. As a consequence of trophoblastic activity, there may be (1) invasion of the uterine wall by one or more hydatidiform molar villi, (2) malignant neoplasia of the trophoblast, resulting in choriocarcinoma, or (3) rarely, "metastasis" of intact hydatidiform villi to the parametrium, local pelvic structures, or lungs.

The syncytial and cytotrophoblastic cells proliferate excessively to some degree, the amount of proliferation being, in general, proportional to the tendency of the hydatidiform mole to become locally invasive, (chorioadenoma destruens); or to become truly neoplastic (choriocarcinoma).

Characteristics highly suggestive of mole include the following: uterine bleeding, varying in amount and color, being more or less continuous during the second, third, and fourth months after

the last menstrual period; increase in uterine size above the level expected for the suspected stage of gestation; absence of amniotic fluid; absent history of fetal movements and heart tones. Diagnosis is aided by the finding of absent amniotic fluid following transabdominal paracentesis. Serum gonadotropins in the normal pregnancy reach a peak at about 60 days after the last menstrual period, and then progressively decline so that after 100 days, the titer is rarely above 20,000 I.U. per liter. Multiple pregnancy may cause a rise in serum gonadotropins similar to that found in mole. Serial determinations of serum gonadotropins are helpful in diagnosis of moles.

Often in hydatidiform moles, especially with excessive necrosis of molar tissue, SGOT titers are elevated beyond the normal range. This may aid in diagnosis.

Acosta-Sison of the Philippines uses sounding of the uterus and biopsy to determine if molar tissue is present in the uterus.

Normally, when a mole is completely removed, tests for serum and urine gonadotropins are negative, usually after two weeks. Continued gonadotropin levels after this interval arouse the suspicion of re-

tained molar tissue, chorioadenoma destruens, or choriocarcinoma. To avoid confusion the patient should not become pregnant for one year after the delivery of a mole so that accurate followup of gonadotropins can be carried out. Followup of patients who have had moles should include examination for metastasis in the vulva, vagina, and lungs. Gonadotropin titers should be determined four weeks following delivery of the mole, and then monthly for six months, bimonthly for another six months.

Lutein ovarian cysts accompany moles in 25-30%. Hydatidiform mole with coexistent fetus is quite uncommon, the indidence being approximately 1:14,000 pregnancies. The incidence of moles varies according to geographical location, it being 1;2000 in the United States. There is a higher incidence of moles in aged women who become pregnant.

Hydatidiform is a predisposing cause of preeclampsia and eclampsia. Hypertension in hydatidiform mole is probably a result of the higher titer of HCG and increased abdominal pressure of a large mole, which may induce increased intrauterine ischemia. Toxemia symptoms appear considerably earlier in molar pregnancies than in normal pregnancies.

Hysterectomy is the treatment of choice when

curettings are histologically suggestive of invasive mole, or clinical and hormonal evidence is suspicious of the complications of hydatidiform mole. Acosta-Sison feels that all women with moles should have hysterectomies with the mole in situ. However, it is known that immediate hysterectomy after diagnosis of mole does not protect the patient against choriocarcinoma or chorioadenoma destruens in all cases. The incidence of these diseases is less than 15% of all moles. Over half of the people who have moles achieve subsequent normal pregnancies. In light of this evidence, I agree with other authors who feel that hydatidiform moles in themselves are not justification for hysterectomy unless the age of the patient, lack of desire for further pregnancies, or other concurrent complications are present. Hysterectomy should be carried out with "metastasis" of intact villi, chorioadenoma destruens, and even advanced cases of choriocarcinoma, since documented cases of regression of the metastatic lesions have occurred after removal of the primary lesion by hysterectomy.

Repeat moles and moles interspersed between normal pregnancies occur, but only very rarely.

Twenty-seven patients from the Clarkson, Methodist, and University Hospitals with a diagnosis of hydatidiform mole were reviewed. Average stage of gestation at delivery of the mole was 16-17 weeks. Presenting complaint in each instance was abnormal vaginal bleeding, and in addition, 30% complained of cramping.

About one third of the patients passed moles spontaneously. Another one third were given pitocin and then curettaged. Seven per cent had hysterectomies with the mole in situ. One patient was treated by a curettage and subsequent hysterectomy; one by curettage following laparotomy; and one by hysterotomy.

Four patients aborted either prior to or after delivery of their mole. One patient had a repeat mole followed by a normal pregnancy. Thirty per cent of the patients had normal pregnancies subsequent to their moles. One patient developed chorioadenoma destruens with lung metastasis, which regressed after hysterectomy. Two patients had hysterectomies with a diagnosis of choriocarcinoma.

Twenty-two per cent of the patients were reported to have cystic ovaries associated with their moles. Only 3.7% were reported to have coexistent fetus.

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