HYDATIDIFORM MOLE.*

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THE following points in that still baffling complication of pregnancy, hydatidiform mole, have been extracted from 37 cases treated in the Royal Maternity Hospital and the Gynecological Wards of the Royal Infirmary, to the physicians of which institutions I am indebted for permission to examine records.

The investigations throw no light on the essential cause of the disease, but on one occasion the condition was noted in one ovum of a twin pregnancy; this combination being the main support for the general belief that the primary process originates in the ovum.

The disease has been variously estimated as occurring in from 1 in 2400 (Williamson) to 1 in 20,000 pregnancies (Madame Boivin), while Meyer, who believes it to be much more common, states that of 348 specimens of abortion examined by him 100 showed evidence of the condition—an observation accepted with reserve by Whitridge Williams.

There have been 18 cases at the Royal Maternity Hospital between 1922 and 1926, and during the same period a total delivery including abortions of almost 8000 patients; giving an incidence of 1 in 450. This increased frequency is probably mainly explained by the large percentage of abnormal cases admitted to a hospital of this type.

Of the 18 cases recorded it is of noteworthy interest that in 1922 there were 2 cases; in 1923 there was 1 case; in 1924 there was 1 case; in 1925 there were 6 cases; in 1926 there were 8 cases. The figures for 1927 will help in deciding whether this is simply a periodicity fluctuation, or a true increased frequency.

The age period shows a marked predominance of cases in the earlier years of reproductive life—

70	per cent.	occurring	between	20 to 30	years of age.
22	„	„		30 to 40	„ „
8	„	„		40 to 50	„ „

Roughly 70 per cent. of the total cases occurred in multiparæ, 30 per cent. in primigravidæ, the latter figure showing a somewhat higher proportion of cases in primigravidæ than is generally supposed, and suggesting that previous abortions have but little bearing on the development of the disease. It

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has to be admitted, however, that of the 22 multiparous patients from whom the sexual history had been obtained, 7, or 32 per cent., had had an abortion previously, and in some cases more than one, while in 2 of these 7 cases the previous pregnancy had been complicated by the development of hydatidiform mole.

A definite statement cannot be made regarding the incidence of gynecological disease in relation to mole formation.

The degenerative process usually commences early in pregnancy, and it is found that the mole was expelled or removed between the twelfth and the eighteenth week in 72 per cent. of the cases, of which the majority were about the fourteenth week.

From the point of view of extremes, it was expelled as early as the sixth week in one case and removed as late as the thirty-fifth week in another.

As a general rule the patients were not seriously ill on admission but almost invariably there was a history of intermittent hæmorrhage, of which the average duration was about one month.

It was noticed that the term "brownish discharge" was frequently used when describing the hæmorrhage, and also in cases in which the symptoms had extended over several months, the brown discharge occurred at those times when normal menstruation should have taken place.

The size of the uterus compared with the duration of pregnancy revealed wide differences. In the majority of cases it was definitely enlarged compared with the duration of the pregnancy, but in the case previously referred to, where the mole was removed at the thirty-fifth week, the uterus was only the size of a three and a half months' pregnancy.

In two patients the fundus had risen to approximately one inch below the ensiform cartilage in pregnancies of less than four months' duration.

In one case, terminated at the sixth month, in which the abdomen was almost the size of a pregnancy at term, a large mass of placental tissue was felt on vaginal examination, leading to an original diagnosis of central placenta prævia.

Severe vomiting was a symptom frequently recorded.

In no instance was the Wassermann reaction recorded as positive, while albuminuria was present in 50 per cent. of the patients in whom the urine was examined.

Of the total series of 37 cases, 4 died, 2 from sepsis, 1 from severe uncontrollable hæmorrhage, and 1 from shock after vaginal hysterotomy in a patient who had gross kidney lesions revealed at post-mortem.

This represents a mortality rate of 11 per cent., a figure coinciding with those of other schools.

After-History.—The development of chorionepithelioma after hydatidiform mole is rare.

In an endeavour to obtain the after-history of patients, by personal interview with those resident in Edinburgh, and by communicating with the doctors of the remainder, it was possible to trace only 19 cases.

Regarding the development of chorionepithelioma after the disease, De Lee states that of 20 cases with hydatid mole treated by him, none developed chorionepithelioma, while of 122 cases studied by Sunde, only 5 per cent. were followed by the malignant growth.

In only one of the patients under review, so far as information is available, did the condition occur.

As further evidence of the rarity of chorionepithelioma, reference to the pathological records shows but 4 cases in the last six years at the Royal College of Physicians' Laboratory, 2 cases during the last eleven years in the University Midwifery and Gynecological Laboratory, and no case in the Pathology Department of the Royal Infirmary since 1904.

It is evident that hydatid mole, in itself, has little influence in preventing the occurrence of future normal pregnancies, for, in a fair proportion of the cases followed up, there has been the subsequent birth of a healthy child.

Treatment.—The most inferential method of summarising the results of treatment has been found to be the grouping of cases shown in tabulated form.

	Cases.	Morbid Puerperium.	Deaths and Cause.
Spontaneous	2	...	...
Spontaneous and curettage . .	14	7 (50%)	1 sepsis
Emptied manually and curettage	13	6 (46%)	2 { 1 sepsis, 1 hæmorrhage
Abdominal hysterotomy . .	1	1	...
Supra-vaginal hysterectomy .	2	2	...
Vaginal hysterotomy . . .	5	1	1 shock. Nephritis
Total	37	17 (46%)	4 (11%)

In this scheme the B.M.A. standard for morbid puerperium, *i.e.*, a temperature of 100° F. on two occasions during the first eight days after evacuation of the uterus has been taken.

The post-evacuation period in each case has been termed the puerperium for purposes of conciseness, although it will be appreciated that post-operative course would be a more strictly accurate term for those cases curetted some days after expulsion of the mole.

It will be observed that all recognised methods of treatment have been employed, of which by far the commonest were curettage after spontaneous expulsion, and manual removal followed by curettage.

The most outstanding figure on the chart is that of morbid puerperium, the total cases showing the alarming morbidity figure of 46 per cent., the average puerperal morbidity in pregnancy being about 9 per cent.

This incidence of septic infection predominates in all the various forms of treatment, with the exception of spontaneous expulsion without subsequent interference, and to a less extent, vaginal hysterotomy.

In endeavouring to find an explanation of this morbidity and the possibility of preventing its occurrence, examination of the cases grouped spontaneous expulsion and curettage, shows that they are divisible into two groups.

	Cases.	Morbid Puerperium.	Death.
Spontaneous and immediate curette, *i.e.*, within 24 hours . . .	6	5 (83%)	1 sepsis
Spontaneous and late curette . .	8	2 (25%)	...

These figures, while small, suggest that cases in which exploration of the uterus immediately after expulsion of the mole is done, are more apt to be followed by infection than those in which the procedure is delayed for twenty-four hours or more.

Moreover, neither of the two cases left alone after expulsion developed a septic infection, and incidentally, one has since had a normal pregnancy.

The risks of sepsis following the exploration of a uterus, from which an hydatidiform mole has just been expelled, are

rather *more* than those attending the operation for completion of an incomplete abortion, though probably *less* than those incurred in the removal of a retained placenta.

The intermittent hæmorrhage and severe vomiting very often associated with the condition are factors which so reduce the powers of resistance to infection that one is justified in regarding these cases as "Prospective puerperal septicæmias."

Severe hæmorrhage such as to endanger life at the time of evacuation was noted in only 8 per cent. of cases.

No case of perforation of the uterus, either spontaneous or artificial, has to be recorded.

Thus it has been noted that those cases curetted immediately after expulsion of the mole are most liable to infection, and also that severe hæmorrhage either from retained portions or from gross damage to uterine musculature is not a common complication.

It has also been shown and is generally acknowledged that chorionepithelioma is a rare sequel.

The risks therefore in their order of frequency would appear to be sepsis, hæmorrhage, the development of chorionepithelioma, perforation of the uterus.

With these facts in view, it seems reasonable to suggest that, in the absence of a definite indication such as severe hæmorrhage, little is gained, and unnecessary risks are taken, by the immediate exploration of a uterus from which a mole has just been expelled.

If the expulsion of the mole is followed by slight intermittent hæmorrhage, in excess of or of longer duration than normal lochia, a late curettage may be done. This operation is less liable to give rise to sepsis, can be done more thoroughly at this stage, and probably provides an equal protection against the development of chorionepithelioma.

Many of the cases treated in the gynecological wards are of this type.

Examining the cases in which the condition was diagnosed, or suspected, while the mole was still in utero, it is found that an attempt to induce labour was the most frequent line of treatment.

The method generally employed was that of packing the cervical canal and the vagina, an operation definitely increasing the risk of subsequent sepsis. Spontaneous expulsion following

this procedure was not common, and in most cases the uterus had to be emptied manually.

Vaginal hysterotomy was employed on five occasions, with satisfactory results. The single mortality in this group cannot, with fairness, be cited as a contra-indication, the patient being a bad operative risk.

Abdominal hysterotomy has been strongly advocated. Schumann, emphasising that the mole can be inspected *in situ* and if there is evidence of invasion of the uterine musculature, supra-vaginal hysterectomy should be performed.

In the single case in this group treated by abdominal hysterotomy, the mole was removed with little difficulty, the uterine wall being uninvolved and contracting well.

The morbidity of the puerperium in this instance was probably due to a previous unsuccessful attempt to induce labour by packing the cervix and vagina. This was the case previously referred to in which central placenta prævia had been diagnosed.

Supra-vaginal hysterectomy was done on two of the cases, in one of which there had been very severe hæmorrhage resulting in a red count of less than two millions, with the expulsion of only a very small part of the mole. The indication in the other case was indefinite.

This form of treatment has received some support, in that it is an almost certain method of preventing the development of chorionepithelioma.

The rarity of this complication however, and the occurrence of a fairly large percentage of cases of hydatid mole in primigravidæ, are points against its usefulness as a routine method of treatment. Severe uncontrollable hæmorrhage is probably the main indication for its employment.

In only one of the three cases in which the abdomen was opened was the presence of lutein cell ovarian cystomata commented upon.

While percentages are frequently fallacious and deductions are not easy when dealing with comparatively small numbers, the investigations suggest the following outstanding **conclusions**:—

(1) Most cases occur in the earlier years of reproductive life, *i.e.*, twenty to thirty years of age, and the disease appears to be more common in primigravidæ than is generally thought.

(2) The main dangers in their order of frequency are sepsis, hæmorrhage, development of chorion epithelioma, perforation

of the uterus. These facts should be considered in deciding the treatment to be adopted.

(3) As a routine, exploration of the uterus immediately following the spontaneous expulsion of an hydatid mole is of doubtful value.

(4) Vaginal and abdominal hysterotomy are lines of treatment deserving of more consideration.

(5) Observation for one year—as generally advised—should be insisted upon from the point of view of patients and statistical records, patients being communicated with if they fail to report.

I express my sincere thanks to those who have allowed me to use their records in gathering these few points.

REFERENCES.—Boivin, Madame, *La mole vésiculaire*, Paris, 1827. De Lee, *Surg. Gyn. and Obst.*, 1923, xxxvii., p. 238. Meyer, *Am. J. Obst.*, 1918, lxxvii., 641-668. Schumann, *Trans. Am. Gyn. Soc.*, 1922, xlvii., 193-201. Sunde, *Acta Gyn. Scandinavica*, 1921, i., 16-60. Williams, *Text-book: Obstetrics*, New York, 1924, xxvii. Williamson, *Trans. London Obst. Soc.*, 1900, xli., 303-338.

DISCUSSION.

Dr Fordyce said he was interested to hear that Dr Lodge had found a larger proportion of cases of hydatidiform mole occurring in early life than later on, as he had always thought that hydatidiform mole was a disease peculiar to the later part of child-bearing life. He agreed that chorionepithelioma was a rare complication of the disease. He wondered how soon after hydatidiform mole chorion epithelioma did occur. He had had a patient sent from Fife a few days after the expulsion of a mole and she died on the tenth day after delivery. Post-mortem examination showed a definite chorion-epithelioma in the broad ligament and there were well-marked deposits in both lungs. He had understood that chorionepithelioma was a comparatively late development, but the two conditions must have been almost coincident in this case.

Dr Haig Ferguson was struck by the fact that Dr Lodge had found hydatidiform mole in so many young women, this being contrary to his own experience. He had had two cases of hydatidiform mole, both with severe hæmorrhage and closed os, each of them the size of a full-time pregnancy: in both cases he removed the uterus by supra-vaginal hysterectomy with good results. He had seen ten cases of chorionepithelioma and only two of them had followed upon

hydatidiform mole. He agreed with Dr Lodge and was glad that Dr Lodge had emphasised the fact that chorionepithelioma was as likely to occur after an ordinary abortion as after a hydatidiform mole.

Dr Farquhar Murray advised exploration of the uterus after the passage of a hydatid mole.

Dr Douglas Miller said with reference to the date of onset of chorionepithelioma, that light was thrown on this question by a paper which Professor James Millar had read before the Society some three years ago. In the case which was then recorded the patient had died with the hydatidiform mole still unexpelled but metastatic deposits were already present in the lungs and other organs of the body as shown by autopsy. Dr Miller referred to the classification of hydatidiform mole which Professor James Millar had suggested at that time, the classification being based on the varying degrees of malignancy found in different forms of this growth.

Dr Haultain said that he thought Dr Lodge's statistics with regard to the age of women suffering from the disease agreed with those generally given, the only discrepancy being the small proportion of cases in women over 40 in Dr Lodge's statistics.

With regard to Dr Farquhar Murray's question regarding the abdominal hysterotomy a young married woman aged 19 had come under his care who had been sent in with a provisional diagnosis of placenta prævia. The fundus of the uterus was right up to the ensiform. After trying to dilate the os with packing nothing happened, and it was decided that the best thing for her was to have the mole removed abdominally. He was surprised with the ease with which the mole could be removed by this means. In this case two large basins full of vesicles were removed. The question of lutein cysts associated with chorionepithelioma had always interested him. In the one case, he had seen the large size of the lutein cysts both at operation for the mole, and also their uninterrupted increase in size for the next month or six weeks following, when further bleeding occurred, was very noteworthy.

The President said that he was struck with Dr Lodge's figures but thought that the number of cases quoted was too small to enable any dogmatic deduction being drawn. He reminded the Society that some years ago Professor F. J. Browne read a paper in which he sought to establish that the presence of Langhans' cells in an active state were histological proof of the potential malignancy of any hydatidiform mole. With regard to the question of supra-vaginal hysterectomy as a method of treatment, he had first seen it done by Dr Fordyce and had assisted him at the operation. The patient was

so exsanguine that she could not possibly have stood the loss of blood inevitably associated with evacuation in the ordinary way. The operation of supra-vaginal hysterectomy on that occasion occupied only a very few minutes and he thought that the patient did not lose more than a teaspoonful of blood. Subsequently she made a perfect recovery. In another case some years later with an almost equal degree of anæmia, he had again performed the same operation with complete success. At the same time it was a method of treatment to be confined only to exceptional cases and not to be advocated in the ordinary type of case.

Dr Lodge (in reply) referred to Dr Farquhar Murray's remarks about curettage after spontaneous expulsion. Dr Haig Ferguson had had ten cases of chorionepithelioma of which only two were after hydatidiform mole; this also showed that chorionepithelioma was rare after a hydatidiform mole and it seemed to him that immediate curettage was contra-indicated in view of the increased incidence of subsequent sepsis, as shown by his figures in these cases.