The Value of Abderhalden's Test for Pregnancy.¹

By HERBERT WILLIAMSON.

From the Obstetrical and Chemical Pathology Departments of
St. Bartholomew's Hospital.

WHEN I first read Abderhalden's papers it seemed to me a matter of importance to test the correctness of his observations. If it be true that the blood of a pregnant or recently delivered woman contains a ferment specific to placental albumen, if this ferment is constantly present and can be easily demonstrated, if the sources of error are few and can be readily avoided, the test possesses great value in both clinical and forensic medicine. It is obvious that such an investigation can be carried out only by one possessing a wide knowledge of pathological chemistry, and I therefore asked Mr. Mackenzie-Wallis to undertake the matter. The results of his admirable work have been placed before you in the paper just read, and it remains for me to add a few remarks upon the clinical aspect of these observations. In the first place, they support strongly the theory of a ferment specific to placental albumen present in the blood of women from the 8th week of pregnancy until ten days after delivery. The ferment is not formed in the placenta, but is elaborated in the maternal organism for the purpose of reducing into simpler molecules the masses of chorionic albumen which constantly pass into the mother's blood-stream.

The intra-vascular injection of a foreign albumen leads to the production of specific ferments and a similar result follows the injection of other substances as, for example, cane-sugar.

It is obvious therefore that the test is capable of wide application and may be used for the detection of carcinoma and other forms of new growth. It has been used for this purpose in a number of cases under my care, but I propose to confine my remarks to the diagnosis of pregnancy.

For experimental purposes the test was applied to fifty patients. Of these, twenty women were either in the last three months of pregnancy or had recently been delivered. In each case the result was positive. Thirty women were not pregnant, in all thirty the reaction was negative. This series demonstrates the importance of further investigating the test, and I propose to describe briefly the

1. A paper read before the Obstetrical Section of the Royal Society of Medicine, October 9, 1913.

clinical features of sixteen cases in which it was applied for diagnostic purposes. I have fortunately been able to follow the history of all the patients; in twelve the deduction drawn from the test proved correct, in two it proved wrong, and in two the result still remains in doubt.

The cases are as follows:—

Suspected ectopic gestation	...	...	...	...	...	...	...	3
Pelvic and abdominal tumours where it was suspected that the whole or part of the tumour might be the pregnant uterus	...	...	...	...	...	...	...	5
Suspected chorion-epithelioma	...	...	...	...	...	...	...	2
Chorea in a woman of 21	...	...	...	...	...	...	...	1
Heart disease with amenorrhœa	...	...	...	...	...	...	...	1
Nephritis with exacerbation of symptoms and amenor- rhœa	...	...	...	...	...	...	...	2
Late puerperal sepsis	...	...	...	...	...	...	...	2
								—
								16
								—

1. *Cases of suspected ectopic gestation.*

The first case was that of a woman who had previously borne two children, the last two years ago. She stated that her periods had been perfectly regular in both time and duration and that the last had ceased on June 3 1913. On June 5 she suddenly lost four or five ounces of blood, and from that time there was a small daily loss up to the date of her admission on June 27. On June 8 she suffered an acute attack of abdominal pain lasting $1\frac{1}{2}$ hours, and similar, though less severe, attacks were experienced on June 10 and 17. There had been no nausea or vomiting and no secretion could be expressed from the breasts.

Above the left Poupart's ligament was a tender indefinite swelling; the uterus, of natural size, was situated in the mid-line behind the symphysis pubis. Clinically the diagnosis lay between an inflammatory mass and an ectopic gestation. Abderhalden's test gave a positive result. Operation revealed a gestation sac in the left Fallopian tube with a broad ligament hæmatoma.

CASE II was that of a patient admitted into a surgical ward under the care of Mr. Wilson. After six weeks' amenorrhœa in a woman whose periods had for some time been irregular a sudden attack of abdominal pain associated with vomiting and collapse led to her admission to hospital. The breasts were inactive, and pelvic examination revealed nothing abnormal. Abderhalden's test gave a negative result. Within two days the patient appeared quite well and has remained so since. I examined her a month later and found no evidence of any pelvic lesion.

Williamson : Abderhalden's Test for Pregnancy 213

CASE III was that of a woman who had been married nine years and had never been pregnant. On June 19 she was seized with acute abdominal pain associated with retching and vomiting, and within two hours commenced to lose blood per vaginam. The breasts were inactive, the uterus, of normal size, lay behind the right pubic ramus, and a tender, indefinite swelling occupied the left posterior quarter of the pelvis. Abderhalden's test gave a negative result. At operation I found a hydrosalpinx of the left tube with torsion of the pedicle.

In the light of these cases I think Abderhalden's test is of value in the diagnosis of doubtful cases of ectopic gestation, but it must be remembered that in the event of rupture and death of the ovum within the first six weeks a negative result would probably be obtained.

2. *Abdominal and pelvic tumours of doubtful nature.*

This group includes five cases:—

CASE I. A woman, aged 37, who had been married for 13 years, and had never been pregnant, came to hospital complaining of a swelling in the abdomen. There was a history of menorrhagia for five years, but for the last seven weeks there had been amenorrhœa. On examination a tumour was discovered rising from the pelvis and reaching to the level of the umbilicus. The greater part of the tumour was clearly a uterine fibromyoma, but in view of the history of amenorrhœa, although I could detect no signs of activity in the breasts or softening of the cervix, I suspected that she had probably become pregnant. Abderhalden's test proved positive. I saw the patient six weeks later and then the signs and symptoms of pregnancy were clearly marked.

CASE II. A patient, aged 35, was admitted into hospital on account of an acute attack of abdominal pain. On examination two tumours were discovered, the one a thin-walled ovarian cyst, the other the uterus enlarged to the size of three months' gestation. Menstruation had been regular and no signs of pregnancy were detected. Abderhalden's test gave a negative result. At operation the uterine tumour proved to be a soft fibro-myoma.

In CASE III the test gave a misleading result. This was probably due to an error in technique, for when repeated it proved negative. The patient was admitted under the care of Dr. Griffith on June 27 1913. The menstrual periods were regular until February 1913, and from this date were absent until May 6, when there was slight bleeding for four days; after this there was again amenorrhœa up to the time of admission. On June 17 she felt ill and suffered severe pain over the right iliac fossa; the pain gradually diminished, but had never entirely ceased. On examination the right breast contained clear secretion, and a cystic mass was detected rising out of

the pelvis and reaching to the level of the umbilicus, situated mainly to the right of the middle line. Abderhalden's test gave a positive result. At operation the mass was found to consist of a uterine fibromyoma, a suppurating ovarian cyst and a pyosalpinx.

CASE IV. A woman, aged 36, sought advice because she had not seen her periods for three months. She had previously borne two children, but did not think that she had again become pregnant because there had been no morning sickness and she had noticed no changes in the breasts. On examination a fluid tumour was discovered rising out of the pelvis and reaching to $1\frac{1}{2}$ inches above the navel. The uterus could not be definitely identified apart from the tumour, and the diagnosis lay between hydramnios and an ovarian cyst. Abderhalden's test was negative. At operation the tumour proved to be an ovarian cyst.

CASE V was the second of the two in which the test gave an erroneous result. The patient, a girl of 19, was admitted into a medical ward under the care of Dr. Howard Tooth. Menstruation had been irregular, periods of rather profuse bleeding alternating with periods of amenorrhœa. She gave a history of several attacks of severe abdominal pain. The temperature was raised, sometimes reaching 102° F. at night; and the girl was obviously very ill. The abdomen was distended and a centrally-situated mass of irregular outline was felt rising out of the pelvis. Vaginal and abdominal examination was extremely difficult on account of tenderness. The case appeared to me to be one of tuberculous pyosalpinx, but Abderhalden's test was tried, and, to my great surprise, proved positive. At operation I found bilateral tuberculous pyosalpinx.

It is interesting to note that the two cases in which the test proved fallacious were cases of suppuration within the abdominal cavity; this suggested the advisability of ascertaining whether a similar result was common in suppurating cases, but the controls we have made do not support this view.

3. *Chorion-epithelioma.*

CASE I. A patient, aged 39, was admitted into hospital on August 2 1913. She had previously borne two children, and on February 1 1912 was delivered of a hydatidiform mole. In March 1912 a pelvic abscess was opened per vaginam, and the patient made a rapid recovery. Menstruation was re-established in April 1912, and the periods were perfectly regular until April 1913; from that time until her admission into hospital there had been amenorrhœa. In July 1913 she commenced to suffer from pain in the abdomen, which gradually increased in severity, and on two occasions there was hæmoptysis. On admission she was deeply jaundiced, the movements of the chest were restricted, the air-entry was poor and scattered râles were heard. The liver was enlarged. The lower abdomen was

distended by a centrally-situated elastic tumour rising from the pelvis and reaching to within an inch of the umbilicus, dumb on auscultation and non-contractile. The cervix uteri was high in the pelvis and behind it was an elastic mass occupying the pouch of Douglas.

The case was apparently one of malignant pelvic growth with metastatic deposits in the lungs and liver, but seeing that seventeen months had elapsed between the expulsion of the mole and the onset of symptoms I did not feel certain that the growth was a chorion-epithelioma. Abderhalden's test proved positive. At post mortem examination a chorion-epithelioma of the uterus with secondary growths in the lungs, liver and intestine was discovered.

This case suggested to me the importance of subjecting at regular intervals to Abderhalden's test all patients who have borne a hydatidiform mole. Should a chorion-epithelioma develop the test ought to remain positive instead of becoming negative, as after a normal pregnancy; in this way we may obtain evidence of the development of the malignant growth before it can be recognized clinically. We are adopting this procedure in the following case:—

A lady was delivered of a hydatidiform mole on February 11 1913 after four months' amenorrhœa. I was asked to see her on March 26, and found the uterus well involuted and the cervix closed. Behind the uterus was a tender irregular body rather larger than a tangerine orange, partly cystic and partly solid; probably a lutein cyst of the ovary. Abderhalden's test was positive. I am feeling some anxiety about this patient, and feel doubtful whether I ought not to advise immediate exploration of the cervix.

Note. The test has been repeated with a negative result. The positive result first obtained was probably due to the presence of diffusible substances in the blood, for the control was also positive, and we have since discovered that a meal had been eaten one hour before the blood was taken. When the test was repeated with proper precautions the result was negative. It is interesting to note that the optical test was negative on both occasions.

4. *Chronic Nephritis with exacerbation of symptoms.*

Two such cases have been tested; there was no doubt whatever from clinical evidence that both women were pregnant, so that the application of the test was for the purpose of control rather than of diagnosis. The result in both cases was positive. On clinical grounds, chiefly because of the development of a marked acidosis, I regarded both cases as instances of the grafting of a pregnancy toxæmia upon an old nephritic lesion. We must, I think, be prepared to recognize that the discovery of ferments specific to

placental albumen in the blood of pregnant women opens a new chapter in the pathology of pregnancy toxæmia, but how far the lesions may be attributed to a failure of production or to an undue abundance or activity of ferments are questions which have yet to be investigated.

5. *Late puerperal sepsis.*

The test may prove of value in cases of late puerperal sepsis when it is uncertain whether the uterus still contains placental remains. We have employed the test in two such cases:—

CASE I was that of a patient admitted twenty-one days after labour. The temperature was 100·2°F., and the uterus was bulky, although the cervical canal was closed. Abderhalden's test proved positive. The uterus was explored and a portion of placenta removed.

CASE II. A patient was admitted on August 20 who had been delivered 15 days previously. The temperature had risen to 100°F. on the eighth day, and from that time had run an irregular course, occasionally reaching 102°F. at night. The lochia had ceased on the eighth day, and before that had been a little offensive. On admission the uterus appeared to be well nourished, but the cervical canal admitted the finger. Abderhalden's test was positive. The uterus was explored; it contained a considerable quantity of decomposing blood-clot, but no tissue which could be identified definitely as placenta.

The remaining two cases call for very little comment. The first was a woman, aged 21, who, after a fright, suddenly developed choreaform movements. Abderhalden's test was positive. I have seen this patient again; the signs and symptoms of pregnancy are now unmistakable.

The second was a patient under the care of Dr. Hamill at the Hospital for Diseases of the Heart. When seen she complained, amongst other symptoms, of six weeks' amenorrhœa. Dr. Hamill suspected pregnancy, but the patient did not think this possible, and further stated that her periods had always been irregular and scanty. Abderhalden's test gave a negative result. Dr. Hamill has not examined the patient again, but she states that she has no doubt of her condition and has felt foetal movements.

It is probable that the test was applied too early in this case; and we were anxious to repeat it at a later stage of gestation; indeed the patient came to St. Bartholomew's for this purpose, but felt unwell and left before the blood was taken.

In reviewing these cases I draw the following conclusions:—

1. It is established that the serum of pregnant women contains a ferment specific to placental albumen.

2. This ferment can be demonstrated from the 8th week of pregnancy until ten days after delivery.

3. That its presence may be demonstrated by the polarimeter or dialysis.

4. That the former method is the more reliable in that the sources of error are fewer.

5. That the accuracy of the test depends upon the most scrupulous care in details, and it is only in the hands of an expert that the results can be relied upon.

6. That the ferment is found only when chorionic tissue is present in the body.

7. It is probable that under other conditions the colour reactions and optical effects produced by the test may be simulated.

8. That we have already detected most of the common sources of error, and that in the near future the test may be expected to give reliable results.