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Vaginal Cytology in Obstetric practice

by

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Introduction

It was Favarger in 1913 who first described the changes that took place in the vaginal epithelium during pregnancy. In 1925 Papanicolaou described the characteristic navicular cells of pregnancy in the vaginal smear. Then the vaginal smear was developed and used to detect malignant cells from the female genital tract. In 1951 Pundel and Ven Meensel began to study the cytological changes in pregnancy and since then interest in this aspect of vaginal cytology was revived. The following account of vaginal cytology in obstetric practice is a short review of how the cytological method can assist the obstetrician in the care of his patient.

The use of vaginal cytology in obstetric practice can be considered under two main headings.

A. The identification of cell types as an aid to diagnosis

B. The recognition of cell patterns as they reflect hormonal changes in pregnancy.

Under the general heading of the identification of cell types as an aid to diagnosis, we have the following:-

1. The diagnosis of intra-epithelial carcinoma of the cervix in pregnancy and the puerperium

An important result of ante-natal care of pregnant women is the benefit conferred on them as a result of a thorough medical examination. This is exemplified in the detection of otherwise symptomless organic heart disease and pulmonary tuberculosis. Patients who attend for ante-natal care and post-natal examination afford an excellent opportunity for cytological screening to detect intra-epithelial carcinoma of the cervix. The taking of a Pap smear can be incorporated as part of the routine examination of the patient. This would obviate any cancerophobic tendency in those prone to this. As malignant cells from the cervix remain unchanged in pregnancy they can be as easily diagnosed as in the non-pregnant patient. The cytological screening of obstetrical patients for intra-epithelial carcinoma of the cervix by various investigators show the following results.

TABLE I

Intra-Epithelial Carcinoma Cervix in Obstetrical Patients

Authors	No. of cases	No. of intraepithelial carcinomas
McLaren (1961)	5,000	9 (1·8/1000)
Parker et al (1960)	10,053	64 (6/1000)
Schmitz et al (1960)	10,369	13 (1·2/1000)
Wright (1961)	3,295	9 (2·7/1000)

Experience in the Teaching Unit of the Kandang Kerbau Hospital for the 5½ months from May to October 1965 have revealed the following findings. I am indebted to Prof. Tow for these figures from the department. Three hundred obstetrical patients over the age of 30 years had a Pap smear taken when they first attended the ante-natal clinic. Of these, 3 smears were reported as having suspicious cells for carcinoma of the cervix. In the case of one of them, J.K., a 37 year old para 7 Malay woman, a repeat smear taken 10 weeks after delivery was reported as having malignant cells. A punch biopsy taken at the same time as the repeat smear revealed carcinoma-in-situ. She has been admitted for a cone biopsy of the cervix after which definitive treatment will be instituted. The other two patients have not delivered yet and are being closely followed up by repeat smears and biopsy if necessary. The important point to note from this patient who has at least carci-

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endometrial cells seems to be limited to a few instances only.

3. The cytological diagnosis of ruptured membrances

Premature rupture of membranes is a common obstetrical problem. In many instances the diagnosis can be easily confirmed by physical examination. However, there is a small proportion of cases where clinical examination is inconclusive and a simple reliable test would be useful.

Philipp and Williams (1929) first described the presence of lanugo hairs in the vaginal secretion of patients with ruptured membranes. The finding of lanugo hairs is time consuming and impracticable as only a few hairs are shed. The identification of vernix caseosa cells is also diagnostic of ruptured membranes. However, this requires the services of an experienced cytologist and false positive results can be obtained if there is contamination by squamous cells from the patient's vulva. Recently Brosens and Gordon (1965) at the Hammersmith Hospital, London, evaluated the Nile Blue Sulphate Test first carried out by Kittrich in 1963. Vaginal secretion is obtained by aspiration from the posterior fornix using a sterile pipette. A smear of the secretion is then made on a clean slide. No fixative is required and the preparation may be stained wet or dry. A solution containing 0·1 per cent of Nile Blue sulphate is used as a stain. The foetal cells will be seen as orange staining anucleate cells derived probably from the sebaceous glands of the foetus. The accuracy of this test is high after the 32nd week of gestation when these cells are more readily shed.

The usefulness of the Nile Blue Sulphate Test is its simplicity. It can be performed in 5 to 10 minutes and the identification of the stained foetal cells require no prior cytological experience. This test merits to be more extensively carried out so that its usefulness can be further evaluated.

Variations of Cytological Smear Patterns in Pregnancy

The epithelium of the upper vagina responds to the interaction of multiple hormones during pregnancy. Oestrogen stimulates growth and maturation of the squamous epithelium and the individual cell becomes increasingly superficial, has more affinity for eosin-like stains, and has a less pronounced nucleus. The last two features are the basis for the Eosinophilic and Karyopyknotic indices (E.I. and K.I.). Progesterone stimulates proliferation and desquamation of the intermediate layer. Thus, in normal pregnancy due to the progesterone opposition, the pure oestrogen stimulated maturation of the cell is never achieved. The majority of the cells are from the intermediate layer and show little eosinophilia or pyknosis. Thus it seems that the typical pattern of normal pregnancy is dependant on a normal oestrogen-progesterone balance. Vaginal smears for hormonal cytology are usually collected by either scrapping lightly the upper lateral vaginal wall or aspirating cells from the posterior fornix. Pundel and Lichtfus have classified the different smear types in pregnancy as follows:-

1. Cytology of the first trimester

The smear pattern reflects the activity of the corpus luteum and is composed of intermediate and superficial cells. The pre-menstrual smear pattern is carried on for 1—2 weeks of the pregnancy, then navicular cells appear. The C.I. (Cornification Index) is under 10 and the K.I. (Karyopyknotic Index) is under 12. The smear pattern gradually changes to that of the last 2 trimesters.

2. Cytology of the last two trimesters.

There are 3 smear patterns described. They reflect the activity of the placenta

a) "Pregnancy prior to Term" smear

From the 12th to the 38th week the smear in a normal pregnancy is characterised by a constant and uniform pattern of thick clusters of navicular cells with a C.I. of under 6, and a K.I. of under 10.

b) "Pregnancy at Term" smear

In the last two weeks of pregnancy the vaginal smear changes its pattern. There is a marked diminution of cell clusters, the appearance of an increasing number of isolated and flattened cells and a rise of the C.I. and K.I.

c) "Postpartum" smear

This type of smear can occur in a patient at term. The cell clusters disappear completely so that nearly all the cells are single. The C.I. and K.I. continue to rise. Appearance of parabasal cells of the postpartum type occurs.

The Cytolytic Smear

In some cases the smears throughout the whole pregnancy present a specific pattern. They are composed mostly of free nuclei which are all from the same vesicular type of intermediate cell, surrounded by a massive flora of Bacillus Doderlein. Intact cells are few in number. These cytolytic smears cannot be classified into any of the types enumerated above because of the destruction of the cytoplasm of many of the cells.

Under the second general heading of the recognition of cell patterns during pregnancy, the following are some of the clinical applications.

1. Abortion—prognosis and treatment

Hassan (1965) in Edinburgh studied the smear pattern in 66 patients with clinically threatened abortion. Thirty had a good pregnancy smear and among these 24 (80 per cent) continued to term with delivery of normal living infants. Thirty-four had abnormal smears and only 2 (5·8 per cent) carried the pregnancy past the 28th week; all the rest aborted. Vaginal cytology can thus be seen to give an accurate prognosis of the outcome of threatened abortion. That this is so is also supported by the work of Fayad and Yousef in Cairo University. Hochstaedt, Lange and Spira (1960) in Haifa, Israel, investigated 140 pregnant patients who were habitual aborters. Smears were collected from the previously untouched anterior part of the upper vaginal wall and stained by the Shorr stain. In 118 patients a diagnosis of progesterone deficiency was made as they all had a C.I. of more than 15. Of these 118 patients, 89 were treated with progesterone until the smears became normal and 69 (78 per cent) had normal, deliveries. Of the remaining 29 progesterone deficient pregnant women who were not treated only 7 (24 per cent) had normal deliveries. This study revealed that six out of seven habitual aborters had progesterone deficiency in pregnancy as diagnosed by the vaginal smear. When treated 4 out of 5 had successful pregnancies. In those who were not treated, 3 out of 4 aborted. However, it must be recognised that 1 in 5 of habitual aborters did not show hormone deficiency, and in a fifth of those with hormone deficiency, pregnancy continued successfully.

More recently, McLennan and McLennan (1965) from the Stanford University School of Medicine made a prospective study of vaginal smears in 1,000 ante-natal patients before the 20th week of pregnancy. The smears were collected from the upper lateral vaginal wall and stained by the Papanicalaou method. They found that the single reliable index of hormonal balance was the K.I. which should be less than 10 per cent. In those with a K.I. of more than 10 per cent there was a progressive increase of the abortion rate which reached 24·4 per cent if the K.I. was more than 25 per cent. They also found that the K.I. remained fairly constant in the first 20 weeks and therefore single smears for each patient sufficed for diagnosis of the hormonal status in early pregnancy. They recommend that at the first ante-natal visit a lateral vaginal smear should be taken for assessment of hormonal status. Those who have progesterone deficiency would be detected and treated.

From the results of the 3 series above one can come to the following conclusions:-

In early pregnancy when the smear pattern is abnormal whether the patient is threatening to abort or not, there is in each case a greater likelihood to abort. When progesterone is given to the hormone-deficient patients a significantly large proportion of these patients continue the pregnancy normally. There are patients who abort with normal smear patterns showing that in these causes other than hormone-deficiency operate.

2. Toxaemias pf pregnancy

Wood, Osmond-Clarke and Murray (1961) at the Queen Charlotte's Hospital, London, investigated the vaginal smear pattern of 30 patients with pre-eclampsia and 12 with essential hypertension. Eleven of these had abnormal smears and among these there were 4 peri-natal deaths and an increased incidence of foetal distress and extensive placental infarction. Where the smears were normal, there was no perinatal deaths. Abnormal smears occurred

more commonly when the pre-eclampsia was severe and prolonged. In two patients with intra-uterine deaths, the smears became abnormal half a week and 2 weeks before the death occurred. These findings suggest that abnormal smears reflect placental insufficiency in toxaemias of pregnancy. There is also an indication that a change to an abnormal smear pattern may indicate impending foetal death. The vaginal smear would seem to be of great value in the prognosis and management of patients with conditions that pre-dispose to placental insufficiency.

3. The diagnosis of biological "Term"

Lichtfus studied the vaginal smear patterns of 713 patients near term. He found that when the smear pattern changed to the "Pregnancy at Term" type smear, spontaneous onset of labour within 5 days occurred in 97 per cent of the patients.

The diagnosis of "biological term" by the vaginal smear pattern is especially helpful when due to uncertain dates the duration of pregnancy is unknown. Based on the above findings, Leeton (1963) has used the "Pregnancy at term" type smear as a sensitivity test in 60 patients having surgical induction of labour. He found that in patients with the "At term" smear as opposed to those with "Prior to term" smear more had shorter induction-delivery intervals, induction-labour intervals of less that 24 hours and did not have longer than 24 hours labour.

The usefulness of the vaginal smear patterns with surgical induction of labour is that one may expect a more difficult outcome if the smear is of the "Prior to term" type and not the "At Term" type.

TABLE II

Relation of the Vaginal Smear at term to the time of onset of Spontaneous Labour in Normal Pregnancy

Assessment of Smear	Time of Onset of Labour			
	Within 5 days		More than 5 days	
	No. of Cases	Per Cent	No. of Cases	Per Cent
Prior to term	10	3	305	96
At term	359	92	31	8

4. The diagnosis of postmaturity

Lichtfus had 8 patients at term whose vaginal smears revealed the "Postpartum" type. Although immediate delivery was effected, all the babies had clinical signs of postmaturity and 4 of them ended in neo-natal deaths. He emphasised that the "Postpartum" type smear indicates that the foetus is in jeopardy and must be delivered immediately. On the other hand, no harm came to any of the babies born many days after the expected date of delivery provided the smear remained the "Prior to term" type smear.

Pundel has instituted the taking of weekly vaginal smears on all ante-natal patients from the 36th week onwards. No induction of labour needed to be done for post-maturity if the smear remains "Prior to term" type. Induction is performed if spontaneous delivery does not occur 5 days after the smears become the "At term" type. If the "Postpartum" type smear is seen labour must be immediately induced. To

TABLE III

Results of Surgical Induction of 60 patients

Assessment of Smear	I - D - I		Not in labour 24 hrs. after induction	Labour more than 24 hrs. after induction
	Less than 12 hrs.	More than 12 hrs.		
Prior to term	6	31	10	5
At term	10	2	0	0

quote the words of Lichtfus and Pundel, "With an accuracy obtained by no other technique, the vaginal smear permits one to determine whether or not a pregnancy is at its biological term and how long it can continue without risk for the baby. The practical results of the general use of the vaginal smear in obstetric practice are, therefore, a reduction of induction of labour to a minimum and a sensible reduction of foetal mortality. If the vaginal smear could be applied systematically to every pregnant patient during the last month of pregnancy, it would be possible that no baby should die from post-maturity or from needless induction of labour". With these words the symposium on "Hormonal cytology in Pregnancy" held in 1959 was concluded. However, several authors including Wachtel and Frampton (1964) at the Hammersmith Hospital were not able to reproduce consistent findings of a change to the "At Term" smear before labour or the "Postpartum" smear of postmaturity described by Pundel and Lichtfus.

Apart from general agreement on changes in smear pattern in the hormone-deficient early pregnancy, conclusions by different authors on the cytological pattern of placental insufficiency or postmaturity have either been inadequately studied or contradictory. Since there are ample examples to indicate that the cytological evaluation of placental function can assist the obstetrician in the care of the pregnant patient, further investigations should be performed. To obtain results which are comparable, agreement should be reached as regards the method of smear collection. One staining technique should preferably be employed and the criteria for assessing smears should be uniform.

Table 4 summarises the use of cytology in obstetric practice today. Its use to screen for early carcinoma of the cervix is undisputed and will remain. The detection of ruptured membranes by the Nile Blue Sulphate method and the microscopical evidence of inevitable abortion is of limited application. While the cytological diagnosis of progestorone deficiency in early pregnancy is generally agreed to by many, the diagnosis of "biological term" is not established The detection of placental insufficiency seems worthy of further investigation and we may yet find the solution to a placental function test in the vaginal smear.

TABLE IV

The Use of Vaginal Cytology in Obstetric Practice

By identification of cell types	By recognition of patterns
1. Cancer detection	1. Prognosis and management of hormone deficient abortions
2. Diagnosis of ruptured membranes	2. Diagnosis of biological "term"
3. Diagnosis of inevitable abortion	3. Diagnosis of placental insufficiency

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