The Journal of
Obstetrics and Gynaecology of the British Empire

VOL. LXIV, No. 6 NEW SERIES DECEMBER 1957

# COLPOSCOPY

## The Results of Its Routine Employment in 1,000 Gynaecological Patients

BY

ABDEL FATTAH YOUSSEF, M.B., M.Ch., D.G.O.

*From the Department of Obstetrics and Gynaecology, Kasr-el-Aini Hospital, Cairo University, Egypt*

THE gynaecologist who has the opportunity of studying or working both in Continental and in British clinics will no doubt be impressed by the extensive use of colposcopy in the former as contrasted with its almost complete disregard in the latter. Some British and American standard works on gynaecology refer to colposcopy without giving any description of the method. Wilfred Shaw (1952) wrote that "The technique should be regarded as one of the most important advances in clinical gynaecology". MacLeod and Read (1955) stated that "for detailed inspection of the cervix, especially in cases suspected of early malignant change, the use of the colposcope has become popular". Meigs (1954) maintained that "the use of Schiller's test and the colposcope are extremely important in demonstrating to the examiner the area in the cervical epithelium which is abnormal and which should be biopsied". Yet, to my knowledge, no paper has so far been published in Britain on the use of colposcopy and, since the articles published by Martzloff (1934, 1938), the American literature on the subject has also been a complete blank until the recent appearance of two papers by Scheffey *et al.* (1955). In discussing the latter paper Novak (1955) remarked that "perhaps the chief value of Scheffey's paper may be to impel us to ask ourselves whether we have too completely disregarded what may possibly be a worthwhile part of the armamentarium in cancer detection. It is really a curious phenomenon to note the sharp difference of opinion and practice as regards colposcopy which exists between the clinics of our Anglo-Saxon countries and those of Europe and, in recent years, those of South America."

In our University Hospital in Cairo, the practice was similar to that in British and North American hospitals in that colposcopy was almost completely ignored. It appeared that if the method could be introduced and regularly practised for some time an unprejudiced opinion could be formed by comparing the results before and after the use of colposcopy.

### MATERIAL AND METHOD

Since my return from Europe in September, 1954, I started to examine routinely by the colposcope every patient admitted to Professor A. Shaaban's gynaecological section at Kasr-el-Aini Hospital. Some pregnant and puerperal women from the obstetric service were also colposcoped, as well as several patients referred from other wards and from the out-patient department. One thousand gynaecological patients have so far been examined not including the obstetric cases nor the cases in whom carcinoma of the cervix was clinically evident.

Several important improvements of the original apparatus as invented by Hinselmann (1927) have resulted in the development of the modern colposcope. The one we now use is

illustrated in Figure 1 and is essentially an apparatus which allows binocular examination of the vulva, vagina and cervix under magnification of 10 to 20 times. A source of ultraviolet light is included and a camera attachment can be added which allows making black and white or coloured colpophotographs as desired.

In order to disturb the parts as little as possible, it is our practice to colposcope the patient before doing the vaginal examination. After examining the external genitals and the urethral meatus a Cusco's bivalvular speculum is introduced into the vagina and the cervix is first inspected by the naked eye and then examined by the colposcope without wiping. Any mucus, discharge or blood is then wiped off by a dry piece of gauze and the cervix is re-examined. In multiparous women the lower part of the cervical canal can very often be visualized. The cervix is examined again first after applying 2 per cent acetic acid and then after applying Lugol's iodine solution. In some cases 3 per cent silver nitrate solution or ½ per cent alcoholic salicylic acid solution may also be used. If a detailed examination of the blood vessels is considered necessary ultraviolet light colposcopy is indicated. While withdrawing the speculum the vaginal walls are carefully examined. If a biopsy has to be made from a localized area in the cervix, vagina or vulva this can be done under direct colposcopic vision by the punch instrument shown in Figure 2.

## Results

The colposcopic findings will be described under the following 3 headings:

I. Typical (Non-suspicious) Appearances.

II. Atypical or Suspicious Appearances.

III. Miscellaneous Conditions.

### I. Typical (Non-suspicious) Cervical Appearances

These indicate the presence of typical (non-suspicious) epithelium.

#### (1) *The Original Mucous Membrane*

This is the typical squamous epithelium which is and has been originally present in this region. The squamous epithelium ends at the external os and is sharply limited from the columnar epithelium of the cervical canal. The mucous membrane appears pink and smooth all round the external os (Fig. 3) and lacks the characteristic features that distinguish the other colposcopic pictures. This is the ideal but not the commonest finding. It was present in 122 of our 1,000 cases (12·2 per cent).

#### (2) *The Ectopia*

If an area of columnar epithelium is present outside the external os it is considered ectopic for normally columnar epithelium is limited to the inside of the cervical canal. Ectopia may be congenital but is more often acquired. It may first appear during or after pregnancy or it may be due to chronic inflammatory or to endocrine factors. The ectopia has a very characteristic colposcopic appearance (Fig. 4). It shows the picture of grapes of variable size which swell and give a very impressive picture when 2 per cent acetic acid solution is applied to the cervix. The ectopic area may be small or large. Of our 1,000 cases 137 (13·7 per cent) showed the picture of ectopia. Since the columnar epithelium is very delicate and may bleed easily on examination early carcinoma may be suspected on naked eye examination and if colposcopy is not used an unnecessary biopsy may be made.

#### (3) *The Transformation Zone*

In cases of ectopia the columnar epithelium is usually replaced, sooner or later, by squamous epithelium which draws itself in tongue-like form over the ectopic area. The term "transformation zone" indicates an area of columnar epithelium transformed into squamous epithelium. This secondary squamous epithelium can be easily differentiated from original squamous epithelium by the colposcope, for the transformation zone shows very characteristic appearances. The growing squamous epithelium usually closes the orifices of the glands present in the columnar epithelium and the presence of these closed glands, which are always covered by regularly branching blood vessels, is a well-known colposcopic feature of the transformation

zone (Fig. 5). If the epithelium covering the glands gives way under the pressure of retained secretion they will appear as small holes with a sharp epithelial edge exuding a clear mucoid secretion. These so-called "open glands" are another feature of the transformation zone. Still another characteristic feature of the transformation zone is the presence of "ectopic islands" which simply indicate that some areas of columnar epithelium have not been replaced by squamous epithelium. The blood vessels in the transformation zone almost always show a regular tree-like branching appearance (Fig. 5) which helps to differentiate this condition from suspicious and malignant appearances. Sometimes a highly vascular transformation zone may bleed on examination and here also colposcopy, by establishing its benign nature, may obviate making an unnecessary biopsy. The transformation zone is by far the commonest colposcopic finding seen in the cervix and was, in its typical picture, present in 619 (61·9 per cent) of our 1,000 cases.

The transformation zone may show evidence of active infection in which case it appears abnormally vascular, lymph follicles are found in abundance and the open glands exude muco-pus instead of clear mucus. The lymph follicles appear as elevated yellow spots surrounded by enlarged but regularly arranged blood vessels. They are easily distinguished from Nabothian follicles for the latter are much bigger and are always themselves covered by blood vessels while the lymph follicles are not. If a transformation zone shows evidence of active infection, cauterization of the cervix is indicated. The uninfected transformation zone, as a rule, spontaneously undergoes complete epithelialization, causes no symptoms and requires no treatment. The decision as to the presence or absence of infection cannot generally be made by the naked eye.

It will be seen that in 878 of our 1,000 cases (87·8 per cent), colposcopic examination of the cervix sufficed to establish the presence of typical or non-suspicious epithelium (Table I) although in some of them the cervix had, on simple inspection and palpation, appeared to be "eroded", "unhealthy" or even suspicious of malignancy.

TABLE I

*Typical (Non-suspicious) Colposcopic Findings among 1,000 Gynaecological Patients*
(Cases of Clinically Manifest Cancer excluded)

| Colposcopic Findings | Number | Per cent |
|---|---|---|
| Original mucous membrane .. | 122 | 12·2 |
| Ectopia .. .. .. .. | 137 | 13·7 |
| Transformation zone .. .. | 619 | 61·9 |
| Total .. .. .. | 878 | 87·8 |

## II. Atypical or Suspicious Cervical Appearances

### *A. Atypical Epithelium*

Pathologists have for a long time used the term "atypical epithelium" to describe changes in the cervical epithelium which, through the peculiar appearances of the cells and their nuclei in regard to shape, staining properties, mitoses and growth tendencies, go far beyond the usual proliferative changes met with, for example, in regenerative processes and inflammatory conditions. Considerable interest has been aroused in this subject in recent years by the extensive use of vaginal cytology and the great attention paid to the problem of carcinoma *in situ*. The studies of Hinselmann and his pupils have shown that atypical changes in the cervical epithelium give rise to characteristic colposcopic appearances which can be recognized without difficulty by the experienced observer (Wespi, 1946; Limburg, 1952; Ganse, 1953; Mestwerdt, 1953; Hinselmann, 1954; Menken, 1955; Cramer, 1956a). It is even possible to differentiate "simple" deviations which microscopically usually show minor degrees of epithelial hyperactivity from "intensified" deviations which histologically reveal the more pronounced degrees of epithelial hyperplasia up to the presence of actual pre-invasive or even early invasive carcinoma. The colposcopic pictures denoting the presence of atypical epithelium will now be briefly described.

(1) *Leucoplakia.* Leucoplakia of the cervix may very occasionally be seen with the naked eye (Von Franqué, 1907). Before the introduction of colposcopy it was believed to be a very rare condition. The widespread use of

colposcopy has revealed that this lesion is by no means uncommon and that it invariably denotes the presence of atypical epithelium. Leucoplakia of the cervix appears as a white patch or patches sharply demarcated from the surrounding epithelium (Fig. 6) and always negative to the Schiller's iodine test. If the white patches are thin and relatively smooth they indicate the presence of simple atypia. If they are thick, rough, irregular and elevated above the surface they usually indicate the presence of intensified atypical epithelium (Fig. 6).

(2) *The Leucoplakic Ground.* The cornified layers covering a leucoplakic patch may fall off spontaneously or through mechanical influences. Even if the leucoplakia was apparent clinically nothing will now be visible to the naked eye. Such an area, however, always shows unmistakable colposcopic appearances which immediately differentiate it as a "leucoplakic ground". It is sharply demarcated from the rest of the epithelium and is always negative to the Schiller's iodine test. It may be smooth, even and regular and show very fine red spotting (Fig. 9). The red spots are tiny capillary vessels at the tips of very fine papillae. This is known as "simple ground" and it indicates the presence of simple atypical epithelium. Sometimes the ground area is elevated and irregular and the papillae are much coarser and appear as warty-like elevations in a glassy yellowish area with recognizable capillary loops at their tips which may be corkscrew-like. This is known as "papillary ground" and it indicates the presence of intensified atypical epithelium.

(3) *The Mosaic.* This is one of the most impressive colposcopic appearances of atypical epithelium. The mucous membrane of the cervix shows a mosaic of small fields whitish or yellowish in colour and separated from each other by very fine red lines. The fields are formed through block-like growth of the atypical epithelium whereby between the individual blocks narrow thin epithelial areas remain whose blood vessels shine through the thin epithelium. The mosaic often surrounds the external os in a circular fashion (Fig. 7). The individual fields may be big or small, square, rhomboid or irregular in shape and may be cornified or not cornified. If the fields are regular, lie on the level of the mucous membrane and show little or no cornification, they generally indicate the presence of simple atypical epithelium. If, on the other hand, they are very irregular, elevated above the surface, show marked cornification or are glassy-yellow in colour they are, as a rule, formed by the growth of intensified atypical epithelium. The mosaic areas are always negative to the Schiller's iodine test (Fig. 8).

It is not at all uncommon to find a combination of different appearances of atypical epithelium in one and the same case. In our material atypical epithelium in its different appearances was found in 109 cases (10·9 per cent) (Table II). In 36 cases the atypical epithelium was of the intensified type and in each of these biopsy was made. Microscopic examination revealed 9 cases of carcinoma *in situ*, 2 cases of early invasive carcinoma and 5 cases of bilharziasis of the cervix. The remainder showed varying degrees

TABLE II

*Atypical (Suspicious) Colposcopic Findings Among 1,000 Gynaecological Patients*
(Cases of Clinically Manifest Cancer excluded)

| Colposcopic Findings | | | Microscopic Findings | | |
|---|---|---|---|---|---|
| | | | Invasive Cancer | Cancer *in situ* | Bilharziasis |
| Atypical epithelium (109 cases) | Intensified atypical epithelium | 36 | 2 | 9 | 5 |
| | Simple atypical epithelium | 73 | – | 1 | 1 |
| Microcarcinoma | | 4 | 4 | – | – |
| Atypical transformation zone | | 9 | – | 1 | – |
| Total | | 122 (per cent 12·2) | 6 | 11 | 6 |

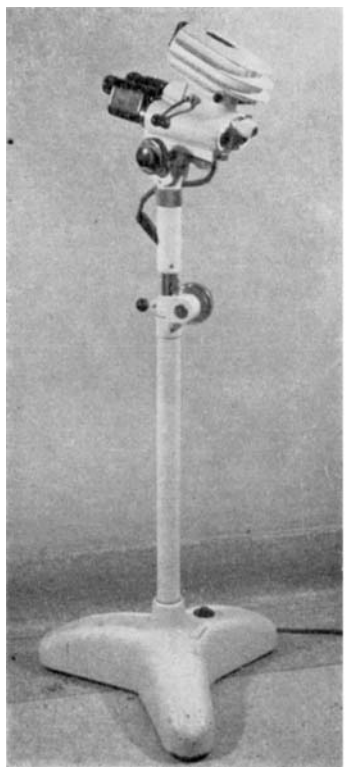


FIG. 1

The Colposcope (Moeller and Co., Hamburg).

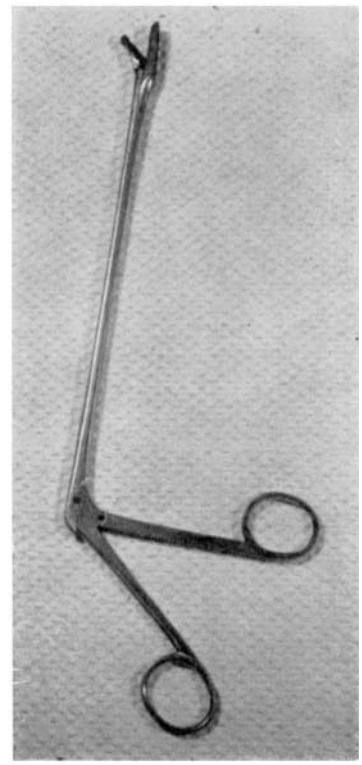
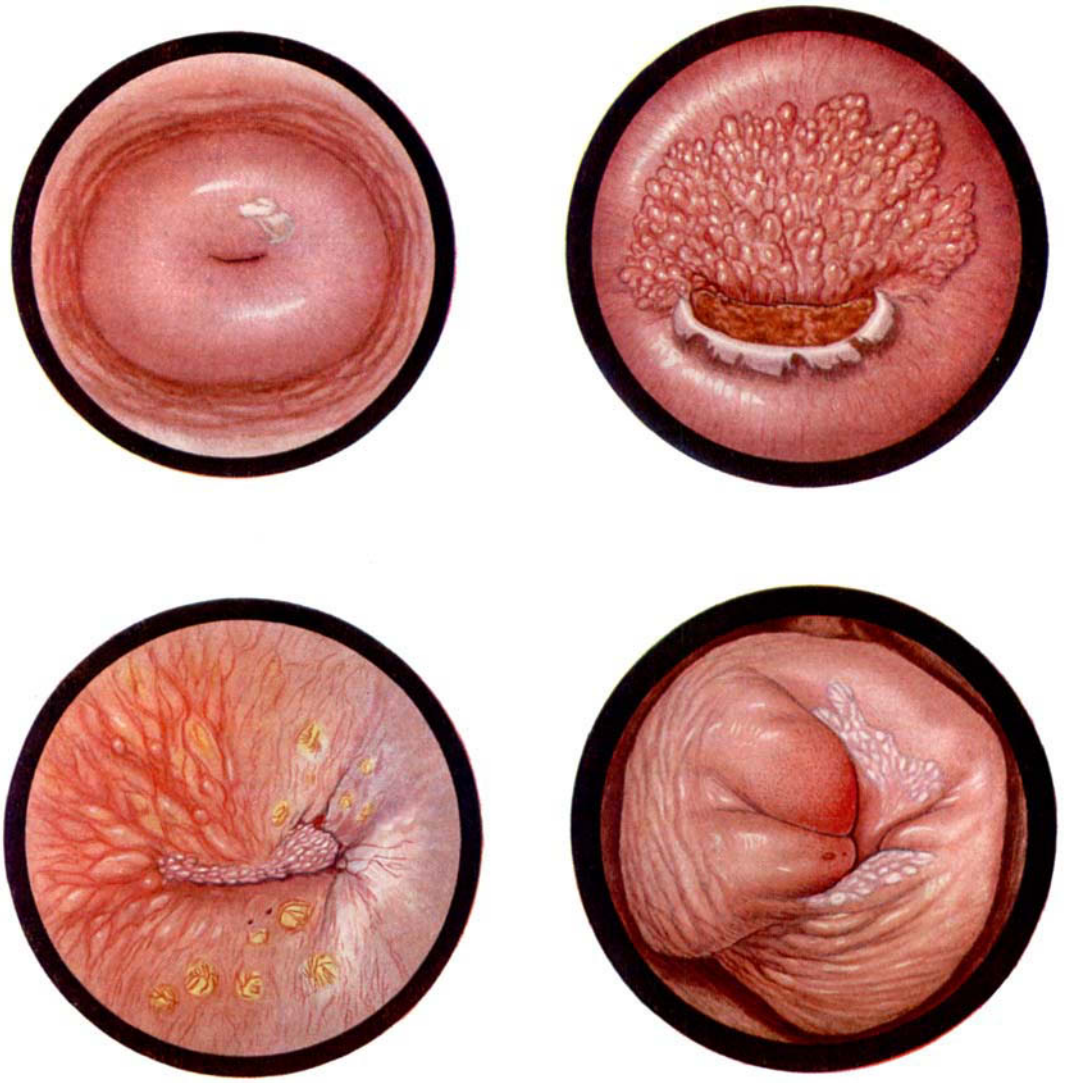


FIG. 2

The punch biopsy forceps.



(*Top left*) FIG. 3

Original mucous membrane. Drop of cervical mucus on anterior lip of cervix.

(*Top right*) FIG. 4

Ectopia on anterior lip of cervix (after application of 2 per cent acetic acid). *Erosio vera* inside original mucous membrane on posterior lip. Note the raw area uncovered by epithelium. The latter is heaped up at the edge of the true erosion.

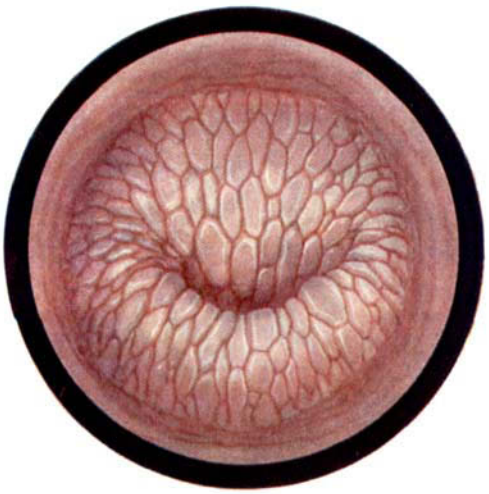
(*Bottom left*) FIG. 5

Transformation zone. Ectopic island on anterior lip. Many small closed glands covered by blood vessels on both cervical lips. All blood vessels show regular tree-like branching pattern.

(*Bottom right*) FIG. 6

Leucoplakia. The two leucoplakic patches are thickened, irregular and elevated indicating the presence of intensified atypical epithelium. This is confirmed by the presence of comma-shaped blood vessels.

A.F.Y.



(*Top left*) FIG. 7

Mosaic surrounding the external os in circular fashion. The fields are regular in size and shape and are not raised above the surface indicating the presence of simple atypical epithelium.

(*Top right*) FIG. 8

Same case as shown in Figure 7 after applying Lugol's iodine solution. The fields did not take the stain.

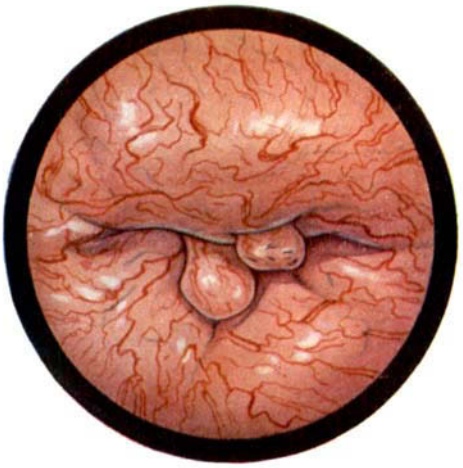
(*Bottom left*) FIG. 9

Two circumscribed areas of leucoplakic ground on anterior and posterior lips of cervix. Big *erosio vera* surrounding the external os. Blood vessels irregular in size and shape, many of them showing characteristic comma-shaped and corkscrew-like patterns.

(*Bottom right*) FIG. 10

Microcarcinoma. Irregular bossy elevations some of which appear glassy-yellow in colour. Blood vessels irregular in size and shape. Elevated leucoplakic patches can be seen on the anterior lip.

A.F.Y.



(*Left*) FIG. 11

Senile vaginitis. The cervical mucosa has a pale rose colour. The blood vessels are seen shining through the atrophic epithelium. Two areas of subepithelial haemorrhage on posterior lip.

(*Right*) FIG. 12

Small benign polypi of the cervix. Note the typical epithelial covering and the regular arrangement of the blood vessels.

of epithelial hyperplasia. In 73 of the 109 cases only simple atypical epithelium was found. In 47 of these which were biopsied microscopic examination revealed one case of carcinoma *in situ* and one case of cervical bilharziasis. The remainder showed minor degrees of epithelial hyperplasia or hyperkeratinization.

*B. Microcarcinoma*

Mestwerdt (1953) introduced the term "microcarcinoma" to describe invasive carcinomata which are still very limited locally and possess a size that can be approximately measured under the microscope. They are, as a rule, symptomless and cannot be recognized by palpation or naked eye inspection but can be detected by colposcopy followed by biopsy and microscopic examination of serial sections. Microcarcinoma may be found on the surface of the portio or in the visible portion of the cervical canal. Atypical epithelium is almost always present in the neighbourhood of microcarcinoma and it is often the detection of the former which puts the observer on the look out for the latter. Microcarcinoma is considered as a transitional stage between intensified atypical epithelium from which it has obviously originated and manifest carcinoma into which it develops. It appears on colposcopic examination as small irregular glassy-yellowish elevations. There is marked capillary proliferation and the vessels do not show the tree-like branching pattern but are characteristically irregular in shape and size and are very often corkscrew-like or comma-shaped. Loss of the epithelial surface (*erosio vera*) may also be noticed. The presence of a true erosion inside an area of typical epithelium need give rise to no concern (Fig. 4) but if a true erosion is detected in an area of atypical epithelium one should suspect the presence of early carcinoma (Fig. 9).

Among our 1,000 cases examined by the colposcope 4 cases were diagnosed as microcarcinoma and in all of them the colposcopic diagnosis was confirmed by biopsy and microscopic examination (Table II). Two of these are illustrated in Figures 9 and 10.

The colposcopic picture shown in Figure 9 is that of a woman 35 years old who was complaining of secondary sterility. On speculum examination a so-called "erosion" of the cervix was found for which diathermy cauterization was going to be performed. On colposcopic examination, which is routinely carried out in our section before any treatment is applied to the cervix, the circumscribed areas of leucoplakic ground present on both the anterior and posterior lips of the cervix immediately attracted our attention to the presence of atypical epithelium. In addition, the corkscrew-like pattern of the blood vessels was apparent. The presence of an *erosio vera* aroused the suspicion that an early carcinoma was already present. Biopsy and microscopic examination showed the presence of an early invasive undifferentiated squamous cell carcinoma.

The colposcopic picture shown in Figure 10 is that of a patient who had a fibrosarcoma of the shoulder region and also complained of uterine bleeding because of which she was referred for gynaecological examination. On palpation the uterus was bulky and on speculum examination an "erosion" of the cervix was seen. A diagnosis of dysfunctional uterine bleeding and erosion of the cervix was made. Colposcopic examination performed 2 days later showed multiple bossy elevations some of which were characteristically glassy-yellow in colour. Leucoplakic patches could also be seen on the anterior lip of the cervix and the vessels showed an irregular corkscrew-like pattern. The diagnosis of microcarcinoma was confirmed by biopsy and microscopic examination.

*C. Atypical Transformation Zone*

Occasionally a transformation zone may be extremely vascular and its blood vessels show irregularity in size and shape, some of them being corkscrew-like or comma-shaped without any evidence of the presence of atypical epithelium or microcarcinoma. Cramer (1956b) attaches great importance to such atypical transformation zones. We have encountered this condition in only 9 of our 1,000 cases. Biopsy was made from each of them and in one case microscopic examination revealed the presence of pre-invasive carcinoma (Table II).

It will be seen from Table II that among our 1,000 gynaecological patients routine colposcopic examination showed the presence of

atypical or suspicious appearances in 122 cases (12·2 per cent). Removal of the suspicious area or areas under colposcopic vision and subsequent microscopic examination has led to the detection of 6 cases of very early (clinically unrecognizable) invasive carcinoma, 11 cases of carcinoma *in situ* and 6 cases of bilharziasis of the cervix. In many of the other cases the cervical epithelium showed marked hyperplasia and hyperactivity so that, as will be discussed later, its removal is believed to have been useful from the point of view of prophylaxis of carcinoma of the cervix.

### III. Miscellaneous Conditions

(1) *Inflammations*

In patients complaining of vaginal discharge we found it, as a rule, possible by means of colposcopy to determine if this originated from the vagina, the exocervix, the cervical canal or from within the uterus. If the discharge comes from the uterine cavity it is expelled intermittently into the cervical canal through the contractions of the uterus in the form of small balls of pus which do not mix with the cervical secretion but remain suspended in it. Discharge from the cervical canal itself does not come out in rhythmic pulsations because the cervix is much less contractile than the body of the uterus.

Some varieties of inflammation give rise to characteristic colposcopic pictures which make them easy to diagnose. In senile vaginitis the atrophic vaginal and cervical mucosa is seen by the colposcope to have a pale rose colour that lacks the red brightness of the epithelium in the childbearing age. The blood vessels shine through the thin atrophic epithelium (Fig. 11). Sub-epithelial haemorrhages are common and appear in a spotty or a diffuse form. In several patients complaining of post-menopausal bleeding in whom the presence of malignancy was clinically suspected, a single glance by the colposcope was sufficient to reveal the true cause of the bleeding and the discharge. Similar colposcopic appearances were observed in some long-standing cases of amenorrhoea and this usually indicated almost complete failure of ovarian function.

In *Trichomonas* vaginitis colposcopic examination reveals the presence of numerous small lymph follicles surrounded by blood vessels arranged in a spiderweb-like form. This arrangement of lymph follicles and blood vessels sometimes gives rise to a characteristic strawberry-like appearance.

Specific infections (syphilis and tuberculosis) of the cervix and vagina may give colposcopic appearances indistinguishable from early carcinoma. Biopsy is in such cases essential for differential diagnosis.

(2) *Bilharziasis of the Cervix*

This was considered a very rare disease even in countries where bilharzial infestation is quite prevalent. Thus, only 16 cases of cervical bilharziasis were detected by the South African Institute of Medical Research in the period from 1911 to 1948 (Charlewood, Shippel and Renton, 1949). The diagnosis was made when an ulcer or a papilloma was found from which biopsy showed the presence of bilharzia ova.

Since we began routine colposcopic examination it became apparent that this lesion, in its early and otherwise unrecognizable stages, is not so uncommon. It causes the appearance of the pictures of atypical epithelium which have already been described. Among our 1,000 patients 6 cases of bilharziasis of the cervix have been detected. The diagnosis was made by biopsy taken because of the presence of suspicious atypical epithelium. The subject of the detection of early bilharziasis of the cervix by means of colposcopy was discussed in detail in a previous communication (Youssef, 1957).

(3) *The External Genitals*

In one of our cases early leucoplakia of the vulva which was not recognized by the naked eye was readily detected by the colposcope. In another case, colposcopic examination of a manifest leucoplakia revealed the presence of tiny otherwise invisible ulcers from which biopsy showed the presence of early invasive carcinoma. Leucoplakia of the vulva is a well-known pre-cancerous condition and colposcopy not only helps in its diagnosis but also indicates the suspicious area or areas from which biopsy should be made. If no malignancy is found

simple vulvectomy is carried out; if carcinoma is detected radical vulvectomy with lymphadenectomy is indicated.

Colposcopy is also useful in differentiating benign from malignant conditions in the region of the external urethral meatus.

We have lately used the colposcope in the examination of the hymen in a number of cases. The 20-times magnification seems to be particularly helpful in differentiating congenital notches from scars and lacerations. This may prove to be of medicolegal importance.

(4) *Pregnancy and the Puerperium*

In addition to our 1,000 gynaecological patients we have examined by the colposcope some 150 women during different phases of gestation and for varying periods after labour. Our studies in this interesting and little investigated field continue. In pregnancy the mucous membrane of the cervix appears succulent and bluish red in colour. The capillary vessels are increased in number and in calibre but they retain the regular tree-like branching pattern and are uniform in size and shape. Such changes may, however, be brought about by other causes of pelvic congestion and, unlike some previous observers, we do not believe that colposcopy can be used for the diagnosis of pregnancy although on a few occasions we first suspected early gestation on colposcopic examination.

During pregnancy the columnar epithelium often grows outside the cervical canal, probably under endocrine influences, so that the appearance of ectopia is quite common. This columnar epithelium may shortly become replaced by squamous epithelium or this replacement may not occur even for a considerable time after delivery. The growth and replacement of columnar epithelium may take place several times in the course of one pregnancy. The resulting transformation zones are similar to those observed in non-pregnant women but are usually more succulent and more vascular. Whether a so-called erosion is or is not seen by the naked eye in the postnatal examination depends on the extent of growth and thickness of the squamous epithelium and on the degree of vascularity and is of little or no practical significance. What is important is to determine which cases show evidence of active infection or of the presence of atypical epithelium (*vide supra*) for these are the cases that require appropriate treatment even if no "erosion" is clinically apparent. We now feel strongly against routine cauterization of postnatal "erosions" and have often followed up the complete spontaneous healing of very large "erosions", sometimes in a surprisingly short time.

Colposcopy is useful and should be used for examining all patients complaining of bleeding in early or late pregnancy. In some cases in whom a threatened abortion or a mild degree of placenta praevia had been suspected we were able to find out by colposcopy that the bleeding did not come from within the uterus but from engorged vessels in the cervix or vagina, a swollen ectopia, a vascular transformation zone or a true erosion which not uncommonly occurs in the swollen and sodden epithelium during pregnancy. In most of these cases the source of bleeding could not be detected by the naked eye. In one case early carcinoma of the cervix had been suspected but on colposcopic examination the benign nature of the condition was established and unnecessary biopsy, which is particularly undesirable during pregnancy, was avoided.

## Discussion

In discussing the subject of the non-malignant unhealthy cervix at the 14th British Congress of Obstetrics and Gynaecology in 1955 no reference to colposcopy was made but it appeared that a gap in the knowledge of the subject was felt by many of the speakers. Read, for example, said that "recent work has shown that even the clinically innocent looking cervix can be the site of early malignant metaplasia. The use of cervical and vaginal smears may be useful but inflammatory and endocrine factors often make them inconclusive. In addition 5 per cent of cervical malignant lesions do not exfoliate and in consequence a false negative smear may prove highly misleading." McLaren said: "We have therefore omitted from the clinical definition of the unhealthy cervix conditions which may lead to invasive cancer for the simple reason that short of biopsy or cytological studies there is no way to recognize

them . . . a cervix may look nasty without necessarily being diseased . . . the fact that we have to guess reveals a large gap in our knowledge of the cervical syndrome." Dodek stated "that inspection or palpation of the female genital organs is not sufficient evidence upon which to decide the non-cancerous status of those organs nor is it considered consistent with good medical practice to do major surgery or other definite treatment for cancer on a smear report alone". And in summing up Read stated that "as a result of all the investigations of cytology and cervical inspection I believe we have got to the stage where we hardly know whether the cervix is simple or malignant".

After only 3 years of experience with colposcopy we feel that the method has definitely contributed to filling what McLaren aptly called the large gap in our knowledge of the cervical syndrome.

*I. The Early Diagnosis of Cervical Cancer*

Four methods of examination, apart from colposcopy, may help in the early diagnosis of cervical cancer, namely inspection and palpation, the Schiller's test, the vaginal smear method and biopsy. We shall now briefly outline the shortcomings of these methods and how they may with advantage be supplemented by colposcopy. It must be clearly understood that colposcopy is not meant to replace the other means of diagnosis and is not to be considered as a rival but as a complementary method.

(a) *Inspection and Palpation.* There is no doubt that these are inadequate for early diagnosis since, as mentioned before, the clinically innocent cervix can be the site of early malignant metaplasia while the cervix may look suspicious without necessarily being diseased.

The relatively high incidence of clinically undiagnosed cervical cancer in uteri removed by total hysterectomy for benign conditions has recently been stressed by Narducci (1954) and by McDuff, Martin and Waterman (1956). Biopsy taken from clinically benign "erosions" has revealed an incidence of unsuspected invasive carcinoma ranging from 1·99 per cent (Schrimpf, 1954) to 11·8 per cent (Seki, 1955).

The term "erosion" applied to any red area on the cervix is one of the most misleading terms used in modern gynaecology. McLaren (1955) has pointed out that the incidence of cervical erosion exceeds 20 per cent and that it is thus not practicable to cauterize every erosion seen. He, therefore, does not treat the asymptomatic erosion and does not inform the patient of its presence. While we agree that many so-called erosions require no treatment we definitely believe that some asymptomatic erosions can be more dangerous and require more active treatment than some erosions which cause symptoms. While he advised the same policy for postnatal erosions and found that the majority of these disappeared spontaneously, Fisher (1955) strongly disagreed and advised routine cauterization. Among gynaecologists who employ colposcopy such a difference of opinion cannot exist for to them what to the naked eye appears as an erosion can prove on colposcopic examination to be an *erosio vera*, an ectopia, a transformation zone with or without active inflammation, an area of simple or intensified atypical epithelium, or even an early carcinoma (Fig. 10). Should colposcopy be widely adopted in Britain and in America, the term "erosion" will undoubtedly disappear from the Anglo-American literature, as it has from the German and the French, etc., to be replaced by more accurate scientific terms.

In some cases when inspection and palpation strongly point to the possibility of malignancy, colposcopy may suffice to establish the benign nature of the condition. The patient whose colposcopic picture is shown in Figure 12 complained of bleeding on coitus and on douching. Speculum examination revealed the presence of two small nodules within the external os which bled on touch and made the examiner suspect the presence of early carcinoma. Colposcopic examination showed that these were two very small polypi, the benign nature of which was apparent from the typical epithelium covering and surrounding them and from the normal regular appearance of the blood vessels. Biopsy confirmed the absence of malignancy.

Not only does colposcopy differentiate between cervical appearances that are indistinguishable by inspection and palpation but

the gynaecologist who practises routine colposcopy will soon find out that he can see more in the cervix and vagina even by the naked eye than he used to see. In our section, registrars and house surgeons are now showing much keener interest in the examination of the cervix and vagina as is evidenced by the increasing number of cases referred for colposcopy.

(b) *The Schiller's Iodine Test.* If used alone this test may be highly misleading and may result in a large number of biopsies being made unnecessarily. This is because many benign conditions of the cervix do not take the Lugol's iodine stain, for example, the ectopia, the simple *erosio vera* and the recent transformation zone. On the other hand, areas of atypical epithelium or even of early carcinoma may, though very rarely, take the Schiller's stain. Recent cyto-chemical studies by Foraker and Marino (1956) have shown that variable degrees of glycogen staining were demonstrable in 13 of 21 examples of invasive squamous cell carcinoma of the cervix.

Used in conjunction with colposcopic examination the Schiller's test has proved to be of value. Occasionally it will draw the observer's attention to an area of atypical epithelium which he may have overlooked. Sometimes it will confirm his suspicion that a certain doubtful appearance is really caused by the presence of atypical epithelium.

(c) *The Vaginal Smear Method.* This method has undoubtedly proved useful in the early detection of carcinoma of the cervix but it also has its drawbacks and its limitations.

The great effort and expenditure involved have been stressed by almost every worker on the subject (Novak, 1949; Younge, Hertig and Armstrong, 1949; Lombard *et al.*, 1952; Martin *et al.*, 1955; McLaren, Taylor and Attwood, 1956; Spriggs, 1956). The cost of detecting one case of pre-invasive cancer by routine cytology has been estimated as 500 dollars by Younge *et al.* (1949) and as 1,700 dollars by Lombard *et al.* (1952). The latter authors, who were among the early exponents of the method, concluded after many years of study that "it seems impracticable to consider the use of the vaginal smear as a routine screening procedure". Bourne and Williams (1953) have estimated that over 1,000 technicians working whole time would be required to screen twice annually the Greater London female population in the cancer age. Novak (1949) has calculated that some 500 hours of work are required to reveal one carcinoma while McLaren *et al.* (1956) have pointed out that there is also a considerable amount of work involved apart from microscopy and concluded that Novak's calculation was without doubt a low estimate.

Errors of interpretation are not uncommon even in the hands of very expert cytologists. The problem of the false positive smear has been discussed by Fennel and Graham (1955) and by Graham and McGraw (1950) who stressed the point that a positive smear is not a green light for radical treatment. The false negative smear is an even more serious problem because of its frequency and the false sense of security which it gives. Kjellgren (1955) in a recent study of 3,000 vaginal smears in Sweden has found that false negative results were obtained in 24 per cent of endocervical carcinomata and in 38 per cent of all adenocarcinomata of the cervix. Younge *et al.* (1949) have found that the vaginal smear was positive in only 53 per cent of cases of cancer *in situ* with only surface involvement. Rakoff (1948) has calculated that almost 30 per cent of cases of cancer are missed by a single smear taken routinely. The frequency of the "suspect" smear and how it may be misleading has been discussed by Stoll, Riehm and Back (1955). Martzloff (1948) has emphasized that a positive smear is not diagnostic of cancer and that a negative smear does not exclude cancer. He stated his belief that in most reports concerning the reliability of the smear method the bulk of the material comes from clinically evident cases. If such errors of interpretation are now often made by experienced cytologists in specialized institutes it is evident, as pointed out by Spriggs (1956), that if the method becomes widely used and consequently adopted by persons with little interest or insufficient training the results would probably be poor. In fact, one of the chief limitations to the usefulness of the smear method is the paucity of expert cytologists as emphasized by Lock and Caldwell (1949) and by Pundel and Schwachtgen (1956)

who concluded that "the difficulties of interpretation and the small number of expert cytologists available make it a method only to be used in large centres".

The number of clinically unsuspected cases of cancer detected by routine cytology is very small in proportion to this vast expenditure of time and effort. McLaren *et al.* (1956) have found that in 2,250 patients examined cytology was responsible for the diagnosis of only one case of corpus carcinoma, one case of invasive cervical carcinoma and 8 cases of cervical cancer *in situ*. Hedberg (1954) of Stockholm has reported that among 6,000 gynaecological patients cytologically examined, only 0·37 per cent were found to have cervical cancer *in situ* and only one case of occult invasive carcinoma of the cervix was detected. Brudenell (1956) examined 2 smears from each of 1,055 gynaecological patients above 30 years of age at King's College Hospital, London and found that only 3 surprise positive smears were detected (2 *in situ* and 1 invasive).

It is interesting to note that in France and in Switzerland, where colposcopy and cytology have both been extensively employed, most gynaecologists who have had experience with both methods now regard colposcopy as far the less tedious, less expensive and more efficient method for the early detection of cervical cancer. Moricard (1955) of Paris has gone so far as to say that while colposcopy in good hands may be very useful, the use of the vaginal smear, in his experience, is completely useless for the early diagnosis of cervical cancer because it is frequently so difficult to interpret. Béclère (1951) of Paris has expressed himself strongly in favour of colposcopy. Held (1953, 1954) of Zurich has concluded that colposcopy supplemented by biopsy is the procedure of choice in a gynaecological clinic and that the results of combining colposcopy with routine cytology are not superior to the results obtained by routine colposcopy alone.

In Germany and Austria, on the other hand, the trend is to make use of both methods (Cramer, 1952; Limburg, 1954; Navratil, 1954; Schubert and Schmermund, 1954; Waschke, 1954; Burghardt and Bajardi, 1954). This is also now the practice in most South American clinics (De Moraes *et al.*, 1954).

In British and North American clinics, where cytology is now used alone, colposcopy may, we believe, be introduced with advantage to supplement the vaginal smear method. If cytology is used as a screening method, the use of colposcopy will help to pick up the suspicious cases from which a smear should be taken and examined. Way (1956) has emphasized the pressing need at the present moment for research directed along lines which would reveal how best to use the smear method economically since it is clearly impossible to take smears from everyone. Greenhill (1952) has expressed the same opinion. There is, in our opinion, no better means for this selection than the use of colposcopy. In clinics where the smear method is only used for the investigation of in-patients, the combination of colposcopy with cytology will help to solve the problems of the false positive, the false negative and the suspect smears.

We have started this year routine cytologic examination of our in-patients. The interpretation of the smears is undertaken by a colleague who was trained in Papanicolaou's laboratory. We look forward to discovering whether the use of cytology will improve the results that were obtained by the use of colposcopy alone.

(d) *Biopsy*. Whichever method may be used for the early detection of carcinoma of the cervix, the ultimate diagnosis and treatment must be based on biopsy and microscopic examination. One of the major disadvantages of using the smear technique alone is that the best site from which biopsy should be taken cannot be defined. Rogers, Ayre and Millar (1955) have pointed out that single biopsies are inadequate to confirm a pre-clinical lesion. In spite of making multiple blocks and serial sections there was quite a variance between cytological and histological findings. Cytologists have described different techniques for taking multiple or extensive biopsies from the cervix or even for removing the whole portio. Harris and Peterson (1955) found that even the four quadrant biopsy technique was misleading in 45·5 per cent of the cases and recommended the use of the cold knife cone biopsy procedure. Scott and Reagan (1956) also use this technique. Ullery (1956) has devised a new conizing and biopsy knife for the

uterine cervix. Thomas (1955) described his multiple biopsy technique by means of which up to 30 pieces of tissue may be removed from the cervix. These mutilating procedures often require hospitalization and anaesthesia and must not infrequently be complicated by haemorrhage, sepsis, cervical stenosis and repeated abortion. An extensive amount of work is required in the pathological laboratory to examine the large amount of cervical tissue removed by means of serial sections and, needless to say, in many cases nothing abnormal is found out for the lesion for which biopsy was made may have been perfectly benign.

The use of colposcopy will not only obviate the need for biopsy in a large number of cases which appear suspicious to the naked eye (*vide supra*), but also when biopsy is indicated the suspicious area, i.e., the site of atypical epithelium or possibly microcarcinoma, can be accurately defined and removed under colposcopic vision for microscopic examination.

*II. The Prophylaxis of Cervical Cancer*

The extensive experience of workers on colposcopy has clearly shown that cervical carcinoma does not originate in a healthy mucous membrane but only from areas of atypical epithelium. If such areas can be detected in time and removed the formation of cervical carcinoma would be exceedingly rare.

The relationship of intensified atypical epithelium to the formation of pre-invasive and invasive carcinoma of the cervix has been established beyond reasonable doubt (Wespi, 1946; Ganse, 1953; Mestwerdt, 1953; Glatthaar and Funck-Bretano, 1954; Hinselmann, 1954). In our own material, among the 36 cases of intensified atypical epithelium which were colposcopically detected and biopsied, apart from the 9 cases of cancer *in situ* and the 2 cases of invasive cancer which were revealed (Table II), the histological examination in almost all the other cases showed a marked degree of hyperplasia of the cervical epithelium. In some cases this was described as basal cell hyperplasia while in others hyperplasia and hyperkeratinization were also present in the superficial layers and in still others the hyperplastic epithelium was described as dipping into the sub-epithelial connective tissue layer or into the glands but the pathologist did not find that the picture justified a diagnosis of pre-invasive or invasive cancer. In some of these cases we amputated the cervix while in others it was felt that the whole area of atypical epithelium was removed by the original biopsy and the patients were instructed to come at regular intervals for colposcopic follow-up. We consider this result of our work to be significant from the point of view of prophylaxis of cervical cancer and believe that it is not less important than our detection of some cases of pre-invasive and of early invasive carcinoma. Our finding in this group of 5 cases of bilharziasis of the cervix is also important in this direction for this has been definitely shown to be a pre-cancerous condition (Coutinto and Coelho, 1940; Afifi, 1948; Charlewood *et al.*, 1949).

There is less agreement on the significance of the finding of simple atypical epithelium in the cervix. While some observers (Treite, 1942; Limburg, 1952; Cramer, 1956b) believe that simple atypical epithelium usually retrogresses and has therefore little relation to carcinoma, most authorities (Wespi, 1946; Glatthaar, 1950; Mestwerdt, 1953; Ganse, 1953; Hinselmann, 1954) maintain that simple atypical epithelium may undergo further de-differentiation processes and may proceed to the formation of intensified atypical epithelium which is the predecessor of carcinoma. During the first year of our investigation areas of simple atypical epithelium were not biopsied but the patients were instructed to attend at 3- to 6-monthly intervals for re-examination (Youssef, 1956). However, most of our patients of the hospital class are uneducated and many did not show up for repeated observation. We have therefore lately decided to remove all areas of simple atypical epithelium by the punch biopsy method and send them over for microscopic examination. Among 47 cases so treated, only one case of bilharziasis of the cervix and one case of carcinoma *in situ* have been detected but in several others the cervical epithelium has shown variable though usually minor degrees of hyperplasia. Many of these changes may be reversible but we believe that the presence of simple atypical epithelium should not be ignored. If, however, the patient can be

trusted to come for repeated observation, we think that immediate biopsy is usually unnecessary.

The recent widespread use of vaginal cytology has revived interest in the different grades of hyperplasia of the cervical epithelium and their relationship to pre-invasive and invasive carcinoma. Galvin, Jones and TeLinde (1955) have described three degrees of basal cell hyperactivity and stated that evaluation of a selected group of cases seemed to indicate that basal cell hyperactivity may actually progress to carcinoma *in situ*. Stern and Menoher (1954) emphasized the existence of a stage in cervical carcinogenesis intermediate between benign epithelial hyperplasia and squamous carcinoma. Bungeler (1955) observed patients with atypical cervical epithelium for a considerable period of time. Of 34 untreated cases, 5 (14·6 per cent) subsequently developed invasive carcinoma. Vetter (1952) maintained that cytological variations in the epithelium, similar to those observed in actual carcinoma, were observed as early as 10 to 20 years before the development of demonstrable malignancy. Petersen (1956) has followed up, for periods varying from 3 to 10 years, 127 cases who had shown varying degrees of epithelial hyperplasia of the cervix and received no treatment and found that 34 of them subsequently developed cervical carcinoma.

Since hyperplastic changes in the cervical epithelium are fully symptomless and cannot be discovered by inspection or palpation colposcopy or cytology or both must be used for their detection. Colposcopy has the advantage that the area of atypical epithelium can be accurately defined and removed without performing wholesale cervical amputation or hysterectomy which methods are usually reserved for cases in which the diagnosis of carcinoma *in situ* is microscopically established.

Careful colposcopic examination of the cervix is of special importance when subtotal hysterectomy is contemplated. We are strongly in favour of the total operation but some surgeons still not infrequently perform subtotal hysterectomy. If colposcopic examination shows atypical or suspicious appearances in the cervix it should never be left behind.

*III. Other Uses of Colposcopy*

The use of colposcopy in the differential diagnosis of inflammations of the cervix and vagina, in determining which cases of cervical "erosions" are associated with infection and require cauterization, in the post-natal examination of the cervix, in detecting local causes of bleeding in early and late pregnancy and in the examination of the external genitals and hymen, has already been discussed.

## Summary

(1) A description of the technique of colposcopic examination and of the normal and abnormal colposcopic appearances is given. It is hoped that this may prove useful as a guide to gynaecologists who may wish to start self-training in colposcopy.

(2) The results of routine colposcopic examination of 1,000 gynaecological patients, excluding cases of manifest carcinoma of the cervix, in a clinic where colposcopy had not been used before are discussed.

(3) The method has proved of definite value in the early detection and in the prophylaxis of cervical cancer. The important role it can play in supplementing the conventional methods in these directions is outlined.

(4) Colposcopy has also been found useful in certain other aspects of clinical gynaecology.

(5) Colposcopic examination of a number of pregnant and puerperal women has yielded some interesting information.

(6) The technique is simple and can be learnt without difficulty. With increasing experience it has been found that the short time spent in colposcopic examination (5 to 7 minutes for every patient) is rewarded by the results obtained.

(7) The results of this experimental study in the use of colposcopy support Wilfred Shaw's contention that the technique should be regarded as one of the most important advances in clinical gynaecology.

I wish to thank Mr. N. Strekalovsky who has meticulously drawn the coloured pictures from our cases at Kasr-el-Aini Hospital. I am also

grateful to Professor Ali H. Shaaban whose enthusiastic support has made it possible to undertake this study.

## References


Afifi, M. A. (1948): *Bilharzial Cancer*. Lewis, London.

Béclère, C. (1951): *Gynéc. prat.*, **2,** 175.

Bourne, A., and Williams, L. (1953): *Recent advances in obstetrics and gynaecology*. 8th edition. Churchill, London.

Brudenell, J. M. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63,** 380.

Bungeler, W. (1955): *Strahlentherapie*, **96,** 296.

Burghardt, E., and Bajardi, F. (1956): *Arch. Gynäk.*, **187,** 621.

Charlewood, G. P., Shippel, S., and Renton, H. (1949): *J. Obstet. Gynaec. Brit. Emp.*, **56,** 367.

Coutinto, B., and Coelho, B. (1940): *Mem. Inst. Oswaldo Cruz*, **35,** 231.

Cramer, H. (1952): *Geburtsh. u. Frauenheilk.*, **12,** 76.

Cramer, H. (1956a): *Die Kolposkopie in der Praxis*. Thieme, Stuttgart.

Cramer, H. (1956b): *Dtsch. med. Wschr.*, **81,** 1553.

De Moraes, A., Rieper, J. P., Stoltz, H., and Gebara, D. (1954): *Rev. brasil. Cir.*, **28,** 5.

Dodek, S. M. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62,** 805.

Fennel, R. H., and Graham, R. M. (1955): *Cancer*, **8,** 310.

Fisher, H. M. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62,** 807.

Foraker, A. G., and Marino, G. (1956): *Amer. J. Obstet. Gynec.*, **72,** 400.

von Franqué, V. O. (1907): *Z. Geburtsh. Gynäk.*, **60,** 237.

Galvin, G. A., Jones, H. W., and TeLinde, R. W. (1955): *Amer. J. Obstet. Gynec.*, **70,** 808.

Ganse, R. (1953): *Kolpofotogramme zur Einführung in die Kolposkopie. Band I and II Ergänzung der Kolposkopie bei der Prophylaxe des Portiokarzinoms durch das Kolpofot*. Akademie Verl, Berlin.

Glatthaar, E. (1950): *Studien über die Morphogenese des Plattenepithelcarcinoms der Portio vaginalis uteri*. Karger, Basel.

Glatthaar, E., and Funck-Brentano, P. (1954): *Rev. franç. Gynéc.*, **49,** 320.

Graham, R. M., and McGraw, J. (1950): *Surg. Gynec. Obstet.*, **90,** 221.

Greenhill, J. P. (1952): *Yearb. Obstet. Gynec.*, p. 445.

Harris, J. H., and Peterson, P. (1955): *Amer. J. Obstet. Gynec.*, **70,** 1092.

Hedberg, G. T. (1954): *Nord. Med.*, **52,** 1439.

Held, E. (1953): *Gynéc. Obstét.*, **52,** 233.

Held, E. (1954): *Schweiz. med. Wschr.*, **84,** 856.

Hinselmann, H. (1927): *Zbl. Gynäk.*, **51,** 901.

Hinselmann, H. (1954): *Die Kolposkopie*. Girardet, Wuppertal-Elberfeld.

Kjellgren, O. (1955): *Acta obstet. gynec. scand.*, **34,** 249.

Limburg, H. (1952): *Die Fruhdiagnose des Uteruscarcinoms*. 2nd edition. Thieme, Stuttgart.

Limburg, H. (1954): *Proc. int. Congr. Obstet. Gynec., Geneva*, p. 175.

Lock, F. R., and Caldwell, J. B. (1949): *Amer. J. Obstet. Gynec.*, **57,** 1133.

Lombard, H. L., Middleton, N., Shields, W., and Gates, O. (1952): *New Engl. J. Med.*, **246,** 523.

McDuff, H. C., Martin, R. E., and Waterman, G. W. (1956): *Amer. J. Obstet. Gynec.*, **71,** 407.

McLaren, H. C. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62,** 801.

McLaren, H. C., Taylor, C. W., and Attwood, M. E. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63,** 801.

MacLeod, D. H., and Read, C. D. (1955): *Eden and Lockyer's Gynaecology*. 5th edition. Churchill, London.

Martin, O. P. L., Higgins, L. W., Slate, J. A., and De Santo, D. (1955): *West. J. Surg. Obstet. Gynec.*, **63,** 223.

Martzloff, K. H. (1934): *Int. Clinics*, **4,** 179.

Martzloff, K. H. (1938): *J. Amer. med. Ass.*, **111,** 1921.

Martzloff, K. H. (1948): *J. Amer. med. Ass.*, **136,** 516.

Meigs, J. V. (1954): *Surgical treatment of cancer of the cervix*. Grune and Stratton, New York.

Menken, F. (1955): *Photokolposkopie und Photodouglasskopie*. Girardet, Wuppertal-Elberfeld.

Mestwerdt, G. (1953): *Atlas der Kolposkopie*. 2nd edition. Fischer, Jena.

Moricard, R. (1955): *Gynéc. Obstét.*, **54,** 294.

Narducci, U. (1954): *Minerva ginec.*, **6,** 767.

Navratil, E. (1954): *Gynéc. prat.*, **5,** 197.

Novak, E. (1949): *Amer. J. Obstet. Gynec.*, **58,** 851.

Novak, E. (1955): *Amer. J. Obstet. Gynec.*, **70,** 887.

Peterson, O. (1956): *Amer. J. Obstet. Gynec.*, **72,** 1063.

Pundel, J. P., and Schwachtgen, F. (1956): *Gynéc. prat.*, **7,** 7.

Rakoff, A. E. (1948): *Radiology*, **50,** 190.

Read, C. D. (1955): *J. Obstet. Gynaec. Brit. Emp.*, **62,** 796.

Rogers, W. S., Ayre, J. E., and Millar, B. (1955): *Obstet. Gynec.*, **6,** 487.

Scheffey, L. C., Bolten, K. A., and Lang, W. R. (1955): *Obstet. Gynec.*, **5,** 294.

Scheffey, L. C., Warren, K. L., and Tatarian, G. (1955): *Amer. J. Obstet. Gynec.*, **70,** 876.

Schrimpf, H. (1954): *Arch. Geburtsh. Forsch.*, **6,** 333.

Schubert, G., and Schmermund, H. J. (1954): *Krebsarzt.*, **9,** 142.

Scott, R. B., and Reagan, J. W. (1956): *J. Amer. med. Ass.*, **160,** 343.

Seki, S. (1955): *Nagasaki Igakkai Zassi*, **30,** 250.

Shaw, W. (1952): *Textbook of gynaecology*. 6th edition. Churchill, London.

Spriggs, A. I. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63,** 444.

Stern, E., and Menoher, N. P. (1954): *J. Amer. med. Women's Ass.*, **9,** 343.

Stoll, P., Riehm, L., and Back, H. G. (1955): *Gynaecologia, Basel*, **139,** 39.

Thomas, H. H. (1955): *Obstet. Gynec.*, **6**, 599.
Treite, P. (1942): *Zbl. Gynäk.*, **66**, 1570.
Ullery, J. C. (1956): *Amer. J. Obstet. Gynec.*, **71**, 440.
Vetter, H. (1952): *Gynaecologia, Basel*, **134**, 154.
Waschke, G. (1954): *Arztl. Wschr.*, **9**, 398.
Way, S. (1956): *J. Obstet. Gynaec. Brit. Emp.*, **63**, 446.
Wespi, H. J. (1946): *Entstehung und Früherfassung des Portiocarcinoms*. Schwabe, Basel.
Younge, P. A., Hertig, A. T., and Armstrong, D. (1949): *Amer. J. Obstet. Gynec.*, **58**, 867.
Youssef, A. F. (1956): *J. Egypt. med. Ass.*, **39**, 142.
Youssef, A. F. (1957): *Geburtsh. u. Frauenheilk.*, **17**, 445.