Distinguished Expert Series

Terminologia colposcopica: a personal perspective

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Introduction

According to the definitions of medical dictionaries [1, 2].

– terminology is a) science dealing with construction, investigation and arrangement of terms; b) vocabulary of a science or art;

– term is a word or combination of words commonly used to designate a specific entity;

– nomenclature is a classified system of terms and/or names of a specific field of science or organisms etc., e.g. binominal nomenclature (scientific classification of living organisms).

The anatomical nomenclature (nomina anatomica) is a classification formerly applied to anatomical terms but it has been superseded by terminologia anatomica; also called International Anatomical Terminology.

The mission of the Nomenclature Committee of the International Federation of Cervical Pathology and Colposcopy (IFCPC), as its name implies, is to classify colposcopic terms. The Nomenclature Committee has published the International Terminology of Colposcopy several times, with slight modifications in each. However, this terminology consists of not only the arrangements (classification) of colposcopic terms (nomenclature of colposcopy), but their definition and interpretation (terminology of colposcopy) as well as, i.e., its objectives are the same as that of the International Anatomical Terminology. Therefore one may wonder if the International Terminology of Colposcopy might be called "Terminologia Colposcopica".

The aim of the terminologia colposcopica is to guide physicians in integrating colposcopy in identifying, screening, grading and managing lesions of the uterine cervix and vagina, and occasionally those of the vulva.

Definition of colposcopy

The colposcope is a binocular instrument used to study human tissue in vivo with magnification ranging from x5 to x25. This allows recognition of tissue changes not visible to the naked eye. The colposcope was devised by Hinselmann in Germany as an instrument applicable for vaginal examination, hence the name (colpos-vagina), to improve the visualisation of the vulva, vagina and uterine cervix [3]. Colposcopy per se is the recognition of colposcopic features, i.e., colposcopic patterns, signs (see below) and thereby detecting mucosal abnormalities.

Objectives of colposcopy

– To identify and reassure women with normal epithelium;
– to detect lesions (HPV infection, precancer, etc.);
– to be an important triage tool in the assessment of cervical abnormalities and/or high-risk HPV infections;
– to indicate and tailor biopsy or excision procedures;
– to exclude invasive cancer;
– to follow-up women treated for cervical and vaginal disease.

The objectives differ whether the colposcope is used in a triage setting (referral colposcopy) or routinely (integrated in the gynaecological exam), which is called routine colposcopy. In the former, the role of colposcopy is to serve as a guide for histological biopsy or to assess the severity of the lesion in the 'see and treat' policy [4]. In the latter, colposcopy is used to detect epithelial abnormalities with the potential of using colposcopy as a screening tool [5]. The screening potential of colposcopy is reflected in the concept of cervicography. Whichever the objective is, it is essential to understand the low sensitivity of colposcopy in distinguishing a) low-grade precursors from squamous cell metaplasia or HPV infection, b) CIN1 from CIN2 or small CIN3. Some colposcopic features (coarse patterns and signs), however, are highly suggestive of high-grade lesions or cancer (see below).

Referral colposcopy mostly includes biopsy tailored by the colposcope (colposcopically directed biopsy), but by definition, colposcopy per se does not involve biopsy.

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Assessment of colposcopy examination

Colposcopic examination can be:
– *satisfactory:* assessment of the cervix and the full transformation zone (TZ) is complete;
– *limited:* the cervix is assessable but the TZ is visualised only in part;
– *unsatisfactory:* the cervix is not visible, or severe inflammation, trauma, etc. precludes a full assessment of the uterine cervix.

Terms 'adequate' and 'inadequate' instead of satisfactory/unsatisfactory are also used in the literature, having the same meaning. However, the latter (old terms) might be preferred because a) they are widely used and familiar to clinicians, and b) they are included in the latest IFCPC terminology.

Colposcopy does have clinical implications even when the entire TZ cannot be assessed (limited colposcopy), particularly in routine colposcopy [6, 7]. The most important perhaps is reduction of the false-negative rate of cytology: the association of high-grade colposcopic features on the assessable part of the ectocervix with negative cytology is highly suggestive of false-negative cytology and invariably requires histology, i.e., cone biopsy or loop excision. In contrast, when negative cytology is associated with normal colposcopic findings even if the TZ is only partially visible, the risk of false-negative cytology is negligible and the woman can be ensured confidently. In the presence of high-grade cytological findings (triage setting), colposcopically directed biopsy (punch biopsy) is not satisfactory unless the entire TZ is assessable. In this setting, if the TZ is not fully visible, one of the excision techniques (loop, cone biopsy) is indicated, which is tailored by the colposcopic finding, e.g., if there is no abnormality on the assessable TZ, high cone biopsy is needed as the lesion is in the endocervical canal and vice versa.

Specifying terms such as 'limited colposcopy with normal ectocervix' or 'limited colposcopy with abnormal findings (with details)' might be useful in reporting the results of colposcopic examination in such cases.

Colposcopic Glossary

(Definitions of colposcopic terms)

Acetowhitening

Whitening following application of 3-5% acetic acid is a common phenomenon but its intensity, appearance and duration are different. The acetowhitening is mainly due to transient denaturation of cellular proteins (nucleoproteins, cytokeratins) by the acetic acid (a non-coagulant fixative) [8, 9], which cross-links protein molecules and transiently converts the cytoplasm into an insoluble gel (transient dehydration), with preservation of the cell organelles [10, 11]. Following fixation of their nucleoproteins, cells become opaque. When rehydration of the cytoplasm occurs, nucleoproteins revert to their normal state [10].

This acetowhitening depends on the number of epithelial cells and the amount of their cytoplasm and nuclear proteins (nuclear-to-cytoplasmic ratio). However, it is mostly proportioned to the amount of the nucleoproteins (nuclear density) precipitated by the acetic acid. The larger the amount of these nucleoproteins (e.g., numerous cells with large nuclei and small cytoplasm in the upper layers of the epithelium), the less the distance that the light penetrates the epithelium and the more intense is the whitening, which is also faster in appearance and lasts longer [11]. An increased amount of nucleoproteins is found in cancer, its precursors and immature squamous cells (metaplasia) as well as in the presence of viral DNA in the cells. In high-grade CIN, not only the number of cells with large nuclei and a small amount of cytoplasm is increased (high nuclear-cytoplasm ratio, high nuclear density) but there are extra proteins in the nuclei (polyploidy, aneuploidy), explaining the intense acetowhitening. Whitening may also occur in inflammation but it is not characteristic.

The acetic acid causes intra- and extracellular changes throughout the epithelium and even to a minor extent, also in the stroma of normal squamous epithelium. However, the cells remain relatively transparent, allowing visualisation of the vessels in the stroma, hence the pink colour (MacLean). The single-layer columnar epithelium remains transparent and therefore pink-red after acetic acid application. In atrophic epithelium (postmenopausal women), the whitening following acetic acid application is not substantial, if any → atrophic epithelium.

The extent of light penetration in CIN3 is only in the superficial third of the dysplastic epithelium from where the light is reflected without reaching the stroma; consequently, the pink color changes to white (MacLean). The distance that the light penetrates the epithelium in CIN1 is longer than in CIN3, which also explains why the acetowhitening is slower to appear, less intense and fades rapidly in low-grade lesions. Unlike CIN1, the whitening is more prominent in high-grade precursors as compared to metaplasia. The difference in whitening between CIN2 and CIN3 is indistinct.

Parameters of acetowhite changes include:
– intensity (pale, moderate, intense) and uniformity (homo- or heterogenous);
– rapidity of maximum white changing (slow [may require frequent application of acetic acid], quick);
– the length of time the epithelium retains its white appearance (short in duration, requires several applications to maintain colour change, moderate, long lasting).

Acetowhite epithelium

Acetowhite epithelium is a common term for tissues, which appear white following acetic acid application → acetowhitening.

Atrophic epithelium

Atrophic epithelium is thin and consists mainly of parabasal cells (small cells with larger nuclei) with few intermediate cells and a single basal cell layer. Subepithelial vascularity is decreased. Due to its relatively higher nuclear density, more light is reflected than from the mature squamous epithelium, and because of its poor vascularity, the atrophic epithelium is less pink or rather gray, and its colour does not change following acetic acid application. As the parabasal cells contain less glycogen, the atrophic epithelium is usually iodine negative. The vessels are near the surface (thin epithelium), hence they are vulnerable and bleed easily.

Atypical vessels

Intrusion of the cancer cells into the stroma is invariably associated with accelerated cell proliferation and continuous unregulated production of angiogenic factors, resulting in an influx of more vessels to sustain cancer growth and expansion [12]. This in turn leads to irregular and forced vascular growth with newly formed vessels that have lost their consistent branching pattern because they are not capable of keeping up with the cell proliferation. These abnormally developed, non-branching vessels are called atypical vessels. Unlike normal vessels (finely branching capillaries), atypical vessels can paradoxically increase in size when they divide [13, 14], have abrupt or interrupted branching, and they may appear and disappear abruptly, i.e., they are irregular in width, shape and course. Their appearances vary considerably: commas, noodle-like, root-like, corkscrew, glyphs (like a pictogram), etc.

Border shape

Borders, margins, and edges are all synonyms that are used alternatively in the literature. Border shape depicts the border (interface) between two different tissues, and appears as a line (borderline or line of demarcation) through the colposcope. The borders can be inconspicuous (ill-defined, almost imperceptible – indistinct); distinct (easily recognisable – markedly distinct, well-defined); sharp; rolled (rolled edge); irregular (geographic); line-like (distinct and regular like a line around the lesion); sharp or strait. Inconspicuous margins, which are mostly geographic, usually but not invariably indicate minor changes, whereas line-like, sharp margins are suggestive of major changes. A marked rolled edge is characteristic of endophytic cancer and ulcer. A border may also appear within a lesion, which is called inner border, and most often occurs between high- and low-grade cervical intraepithelial neoplasia in the TZ.

Cervicalisation

The term cervicalisation implies the process of eversion of the endocervical lining canal onto the ectocervix. This term occurred in the old literature – it is no longer in use and has been replaced by ectopy → ectopy.

Cervicography

Pictures of the cervix (cervicograms) taken following acetic acid application by e.g., trained nurses (non-colposcopists) with a special camera (cerviscope) developed by Stafl in 1981 [15]. Cervicograms are sent for evaluation to expert colposcopists with feedback reports, including recommendations. Cervicography utilises the same principles as colposcopy and is used for screening cervical carcinoma. Its terminology is slightly different from that of colposcopy.

Cleft (crypt) openings → openings

Colour tone sign

Colour tone sign depicts the colour of a colposcopic pattern and colour changes after acetic acid and Lugol solution application. Normal tissue patterns are pink, red with variation in tone, while the atrophic epithelium may be greyish. A red colour may also be due to haemorrhage. White lesions (leukoplakia) are mostly caused by hyperkeratosis. A dull oyster gray colour may result from microinvasion, while a yellow appearance commonly indicates necrosis. As for colour changing, see: acetowhitening, acetowhite epithelium, iodine staining.

Colposcopic features

These are characteristic, special colposcopic findings important in practising colposcopy, i.e., in distinguishing normal and abnormal tissues to diagnose, screen, grade and localise lesions. Colposcopic features consist of colposcopic patterns (→) and signs (→) and comprise two tissue elements: a) the epithelium (thickness, architecture and density [content of nuclei]), b) composition and growth of the stroma (vessel formation, etc.). Each colposcopic feature is the summation and configuration of these morphological elements (Table 1).

Colposcopic findings

These are actually what are seen through the colposcope.

Colposcopic grading

Colposcopic grading implies grading the colposcopic patterns and signs, which has nothing to do with grading of the underlying lesion. However, with grading of colposcopic findings, one can suspect but not definitely diagnose the degree of abnormality → colposcopic indices.

Colposcopic indices

Colposcopic indices are scoring systems, assigning points to the variable colposcopic patterns and signs to overcome the subjective nature of colposcopy by standardising the colposcopic findings (e.g., Reid's colposcopic index/colposcopic score). Related expressions: quantification of colposcopic images and grading of abnormal colposcopic findings.

Colposcopic patterns

These are characteristic individual colposcopic features, having special tissue basis (Table 1).

Colposcopic signs

These are common colposcopic features occurring in all colposcopic patterns (Table 1), i.e., they are not individual colposcopic features, rather part of them. Colposcopic signs are important additional features to colposcopic patterns in decision making.

Colposcopic variables

Less commonly used term for colposcopic features.

Congenital transformation zone (CTZ)

The CTZ is deviant squamous metaplasia histologically characterised by irregular epithelial projections into the stroma (dentate epithelial-stromal margin) with occasional keratinisation [16]. Its origin is obscure; it might be due to disordered squamous metaplastic maturation during late foetal life, with full or even excessive maturation in the surface and arrested maturation (immature metaplastic epithelium) in the deeper layers [16]. Slight keratosis or parakeratosis may occur (leukoplakia). CTZ is mostly seen in young women, indicating that full squamous cell maturation will finally take place later in life.

Colposcopically, CTZ presents with the same features as low-grade cervical intraepithelial neoplasia (acetowhite, punctation, mosaic, etc.) and is characteristically localised around the active TZ, occasionally extending to the vagina. Whether it is around the TZ or forms the distal circular part of it, is a matter of consideration. Interestingly, although it may be more intensely acetowhite than high-grade CIN, the maximum white change after acetic acid develops slowly. However, the whiteness is retained for a longer time as compared to high-grade CIN, i.e., CTZ may still be white when the CIN is fading [17]. Unlike CIN, it might also stain weakly with Lugol's solution due to the incompletely glycogenated metaplastic cells, albeit the CTZ is iodine-negative in most cases.

Crypt openings → openings

Cuff (abnormal) openings → openings

Deciduosis

Deciduosis is "the presence of decidual tissue or of tissue resembling the endometrium of pregnancy in an ectopic site" [1]. In colposcopy, the term deciduosis comprises the changes of the uterine cervix (and vagina) during pregnancy. The most significant changes are:

– increased vascularity and interstitial fluid retention, resulting in cervical enlargement and softening;

– stromal (fibroblast) decidualisation, which is mostly focal and may appear as a plaque or pseudopolyp on the surface [18];

– enlargement and eversion of the glandular epithelium with increased mucus production and hypertrophy of villi, leading to an irregular surface;

– active (marked) squamous metaplasia, which mostly becomes apparent from the end of the first trimester [19].

Colposcopic findings include:

– enlarged TZ with irregular surface (course texture and deep in-foldings), polypoid appearance, decidual polyps and prominent gland openings (doughnut rims);

– accentuated capillary vessel patterns;

– acetowhitening of squamous metaplasia;

– adherent mucus, making colposcopic examination difficult;

– plush, purplish ectocervix, with dense iodine uptake [17];
– gaping of the external os.

Due to progressive eversion of the endocervical mucosa, the new squamoculumnar junction moves downwards towards the ectocervix during pregnancy. As a result, type 2, or even type 3 transformation zone may become type 1 in the third trimester → transformation zone.

Ectopy

Ectopy is defined as columnar epithelium extending onto the ectocervix (synonyms: ectopia, cervical ectropion, cervicalisation → transformation zone, squamocolumnar junction (SCJ).

Erosion and ulceration

Erosion is epithelial surface distraction whereby the underlying normal stroma (connective tissue) becomes visible. An ulcer is a local defect or excavation of the surface epithelium and the underlying stroma. Ulceration is the process of developing an ulcer.

In the past, the term erosion was used to denote ectopic columnar epithelium on the cervical surface. This is erroneous and superseded by the term of TZ → transformation zone.

Erythroplakia

Erythroplakia is an out-of-date term formerly used for the TZ → transformation zone.

Eversion

Eversion is the process of turning outward of the columnar epithelium onto the cervical surface mostly due to hormonal changes → ectopy.

Extension (localisation)

Extension depicts the localisation of any lesion including various forms of HPV infection, etc. On the uterine cervix, the lesion can be within or outside the TZ, can overgrow the TZ and/or extend to the vagina. High-grade lesions tend to locate next to the neo-squamocolumnar junction. In the vagina, the lesion can reside on the anterior, posterior, or lateral wall, in the upper or lower half of the vagina, or sub-urethra.

Glandular (gland) openings → openings

Hyperkeratosis → keratosis

Inner border

This a border between two abnormalities within one lesion → border shape.

Intercapillary distance

The distance between the punctuated dots in punctation → punctation.

Iodine staining (iodine negativity)

The application of Lugol's solution/Lugol's iodine is the iodine test, also called Schiller's test. Only the cells rich in glycogen will take up iodine and stain deep brown. After Lugol's iodine application, the squamous epithelium is dark brown in contrast to metaplasia that stains pale or partially depending on its maturation state; the more mature metaplasia stains the browner it becomes (partial iodine-positivity). It may have a speckled appearance. Columnar cells and epithelial abnormalities (precursor lesions, cancer) lack glycogen and remain unstained (iodine-negative). Atrophic epithelium takes up iodine and stains poorly.

Iodine negativity is a colposcopic term – part of the colour tone sign – which indicates no or minimal staining with Lugol's iodine.

Keratosis

In the normal squamous epithelium covering the cervix and vagina, there are no keratinised cells in the superficial layer, but this epithelium has the potential of developing keratinised cells as a protective mechanism under chronic stimulation, e.g., uterine prolapse, chronic infection, etc. This is an abnormal differentiation of the covering epithelium and because normally this stratified squamous epithelium lacks keratinised cells, it is called hyperkeratosis regardless of thickness of keratinized cell layers. By definition, however, hyperkeratosis implies excessive formation of keratin (i.e., heavily keratinised squamous cells, squames, devoid of nuclei) covering the superficial epithelial layers. Hyperkeratosis

is usually associated with increasing thickness of the epithelium (acanthosis), which is another protective mechanism. Parakeratosis is also a protective reaction of the stratified squamous epithelium and is defined by the presence of layers of small keratinised squamous cells with small, pyknotic and hyperchromatic nuclei on the top of the superficial squamous cells. Albeit both hyper- and parakeratosis are protective phenomena associated with differentiation of the normal mature epithelium, it is not unusual that such epithelium covers abnormal lesions, including cancer.

Lesion size

The lesions may be small, moderate or large. Metric measurement for size does not seem appropriate as the lesion's size is always proportional to the size of the uterine cervix. For this reason, a measure as percentage (< 25%, 25-50%, > 50%) of the visible cervical surface has been proposed. Large lesions usually cover multiple quadrants of the cervix, however, small lesions around the cervical os may also occupy even four quadrants, making measurement in quadrants inappropriate. Vaginal/vulvar lesions can be measured in centimetres.

Leukoplakia

Leukoplakia is defined as a dense white, elevated area (plaque) of the mucosal surface visible by the naked eye without magnification or acetic acid accentuation. It is often called hyperkeratosis. Acetic acid does not alter its appearance and it does not stain with Lugol's iodine. Its surface can be smooth and glossy, rough or irregular. Leukoplakia is due to pronounced keratosis (hyper- and/or parakeratosis) which precludes visualisation of the underlying tissue. Leukoplakia can be caused by neoplastic changes, chronic irritation and reactive changes of the overlying normal epithelium, e.g., uterine prolapse → keratosis.

Location of the lesions → extension (localisation)

Lugol'solution/iodine → iodine staining (iodine negativity)

Metaplasia

In colposcopy, metaplasia is the process of replacement of the columnar cells by metaplastic cells, which differentiate into mature squamous cells (squamous metaplasia) in the TZ during adolescence, reproductive age and frequently the late foetal life. The process is relatively quick – mostly measured in days [12]. This is the most common protective mechanism of endocervical mucosa, physiologically initiated and promoted by the stimuli of the hostile vaginal environment (high acidity) to the columnar epithelium outside the cervical os. Other chronic stimuli (chemical, inflammation, hormonal, etc.) and destructive treatment (electrocautery, etc.) can also induce metaplasia [20]. The process is irreversible, and the evolving metaplastic epithelium cannot revert to columnar cells.

Squamous metaplasia starts from the proliferating reserve cells beneath the columnar epithelium (known as reserve cell hyperplasia [several layers of reserve cells]), tending to commence at the neo-SCJ junction. Reserve cell hyperplasia progresses to immature metaplasia and gradually with continuous maturation, end up with a mature squamous epithelium. The maturation of metaplastic squamous epithelium can be divided into three stages (pallor, attachment and fusion of the villi; stage 1-3) [21], but this distinction has no clinical significance. The process can be and mostly is arrested at any stage. Because of this, the colposcopic appearance of various stages is visible at the same time, and the maturation may resume at any time [20]. Metaplasia mostly takes place on the surface of the villi but in the crypts as well → metaplastic epithelium, columnar epithelium.

Metaplastic epithelium

Metaplastic epithelium constitutes a range from immature to mature squamous cells, normally situated exclusively in the TZ. These metaplastic cells have larger nuclei than columnar or mature squamous epithelial cells and their nuclei are uniform. The immature epithelium comprises few cell layers, which grow over time. At colposcopy, the surface of the metaplastic epithelium is smooth. Acetic acid application causes slight whitening, varying with the maturation of the metaplastic epithelium. The least mature epithelium demonstrates the most prominent whitening, mostly at the neo-SCJ, resulting in a distinct margin between columnar and metaplastic epithelium. However, the colouration is still weak and usually requires several acetic acid applications to become visualised [12]. The whitening of metaplasia is translucent, flocculent or snow white. Metaplastic epithelium stains either negative or only partially positive with Lugol's iodine, and the colouration parallels its maturation state; the more mature being more brown → iodine staining (iodine negativity).

Feeding vessels supplying epithelial maturation occasionally grow from the stroma into metaplastic epithelium to maintain the blood supply of the proliferating cells. These capillary loops may appear as fine, uniform punctation at colposcopy. Some of the fine vessel loops may branch or grow laterally, causing fine mosaic patterns.

Mosaic

Mosaic is a vascular (colposcopic) pattern resulting from increased vessel formation with arborisation and/or laterally growing vessels that coalesce, surrounding and isolating surface epithelial cells into individual nests in a mosaic-like fashion (rectangular pattern). This is a progression from punctation due to further cell proliferation and production of angiogenic factors (→ punctation) [12]. Consequently, mosaic is commonly seen together with punctation, dots being adjacent to or within the mosaic area.

Mosaic patterns are categorised as fine and coarse. Fine mosaic is characterised by small, more or less regular nests with uniform surrounding vessels, smooth surface and inconspicuous border. In coarse mosaic, the nests are large and irregular in size and shape with non-uniform surrounding vessels. The surface is usually uneven with sharp borders. Mosaic lesions become aetowhite following acetic acid application, but, as with punctation, fine vascular changes are mainly transient, fading quickly (→ punctation). Fine mosaic occurs in metaplastic epithelium and in low-grade precursors but it is a nonspecific pattern, in contrast to coarse mosaic which is suggestive of a high-grade lesion.

In the literature, the term mosaicism is also commonly used to refer to mosaic vascular patterns. However, the term mosaic defined as "a pattern made up of numerous small pieces fitted together" [1] apparently is a better description. The term mosaicism is usually referred to in genetics, e.g., individuals with two distinct karyotypic cell lines.

Nabothian cyst

A Nabothian cyst (Nabothian follicle, Naboth's ovula) is a grape-like retention cyst resulting from continuous mucus secretion of a cervical crypt with an occluded opening by squamous metaplastic epithelium. In its thin wall, branching vessels are clearly visible.

Openings

Openings are small apertures of the remaining crypts of the endocervical mucosa in mature metaplastic epithelium. Two forms can be distinguished: 1. Openings of mucosal invagination covered by columnar cells that might be partly visible with a colposcope. They are called crypt or cleft openings (synonym: gland or glandular openings) and are a normal component of the TZ. The orifice is smooth surrounded by a narrow acetowhite ring with a slightly raised surface; 2. Cuff (abnormal) openings develop in the presence of high-grade lesions in the crypts. Cuff openings are thick, more raised, dense acetowhite and frequently have a doughnut ring appearance.

Original columnar epithelium

The original columnar epithelium lines the endocervical canal, it is built up by single-layer, mucous-producing cells with small nuclei and a moderate amount of cytoplasm, mixed with a few ciliated cells. The endocervical lining has papillary projections (villi) separated by crypts (infolding columnar cell layer). Each villus has a core connective tissue with a loop of capillaries. The crypts are elongated and form a labyrinth extending deep (up to 1 cm) in the cervical stroma. They are often termed glands, but strictly speaking they are not glands as they have neither ducts nor acini. The vascularity is directly underneath the columnar cells (lamina propria), producing its red (pink-red) color. After menopause, the villi decrease in size or may disappear and columnar cells become atrophic. Close to the columnar cells occasionally another cell type, the reserve cells appear, which are very small with round nuclei and scarce cytoplasm.

Colposcopically, the columnar epithelium is red and has a characteristic grape-like or villous appearance, representing the papillary projections (villi) and crypts, with no white change after acetic acid application. Since glycogen is absent in the columnar cells, they do not stain with Lugol's solution either (pale yellow, iodine negative). Sometimes, there are two or three subdivisions on the lips, appearing as cushions and called rugae that are an extension of the endocervical palmate folds or arbour vitae [22].

Original squamous epithelium

The original squamous epithelium (also called: native portio epithelium) covers the ectocervix and has multiple cell layers (basal, parabasal, intermediate and superficial) that vary in size depending on the effect of estrogens and progesterone [20]. Development of the superficial cells requires dominant estrogens effect. The basal and parabasal cells are immature with a relatively high nuclear-to-cytoplasmic ratio. With cell differentiation, the nuclei will decrease in size and the cytoplasm will become more abundant. The intermediate cells are of moderate size with round nuclei, while the superficial cells are the largest, having small (mostly pyknotic) nuclei. Both cell types have abundant cytoplasm rich in glycogen. In contrast to basal and to a certain extent to parabasal cells, intermediate and superficial cells do not undergo mitosis. Blood vessels are beneath the basement membrane supplying the dividing basal and parabasal cells. Not infrequently, however, these vessels can grow into the epithelium, but not up to the surface. The original squamous epithelium is non-keratinizing, i.e., devoid of a keratin layer on its surface, it is continuous with the stratified vaginal

epithelium, and is continuously remodelled by the sequence of proliferation-maturation-desquamation in the period [20] → keratosis.

Colposcopically, the original squamous epithelium is pink without any feature (no cleft openings, Nabothian cysts, remnants of columnar epithelium) and has a smooth surface. It does not stain white following acetic acid application but will stain mahogany brown with Lugol's iodine (iodine-positive).

Parakeratosis → keratosis

Punctation

Punctation is a vascular (colposcopic) pattern in which the capillary loops are seen on end as punctate dots (stippled pattern). It is the result of increased capillary formation with capillary loops growing into the epithelium and approaching or reaching the upermost epithelial layer. These loops may even extend above the epithelial surface (floating dots). As vascular growth continues, capillary loops become larger and irregular in size (irregularly sized surface dots) [12]. Along with the cell proliferation laterally, the distance between the loops (intercapillary distance) increases and they become irregularly spaced [13]. This is enhanced by the accelerated cell proliferation that tends to compress the small loops [14].

The increased capillary formation is due to high cell proliferation with production of angiogenetic factors stimulating feeding vessels to grow and intrude into the epithelium. High cell proliferation and turnover occurs in premalignant and frankly neoplastic lesions, but also during metaplastic and (rarely) in the healing process. Thus, albeit most common, punctation is not specific for neoplastic processes.

Fine and coarse punctations are distinguished depending on the size of and the space between the punctate dots. The fine punctation pattern is characterised by small, almost equally spaced, uniform dots with a short intercapillary distance, smooth surface and inconspicuous border. The vessels are fine. In coarse punctuation, the dots are large, irregular in size and unevenly spaced, occasionally appearing above the epithelial surface, and the intercapillary distance is increased. The vessels are coarse. The surface of the lesion is usually rough with a distinct border. Following acetic acid application, acetowhitening is commonly seen in both lesions. As compared with the saline application, the precipitated nuclear material by acetic acid may compress small capillary loops resulting in a lesser degree of punctation.

Ridge sign → surface contour [23]

Ruga (pl. rugae) → original columnar epithelium

Saline colposcopy

Prior to acetic acid application, the cervix is cleaned and moistened with a saline-soaked cotton ball, which allows better assessment of vascular patterns, particularly with the use of a green filter.

Schiller test → iodine staining (iodine negativity)

Squamocolumnar junction (SCJ)

There are two squamocolumnar junctions: the original and the neo (new) squamocolumnar junction. The original is the junction between original squamous epithelium and columnar epithelium, while the neo (new) is the junction between metaplastic squamous and the columnar epithelium (→ transformation zone). In colposcopic practice, the term SCJ usually refers to the neo-SCJ. In the early intrauterine period, the original SCJ separates the columnar and squamous epithelium at the external cervical os, hence its name. Due to hormone (mostly estrogens) response, however, it moves onto the ectocervix (eversion of the columnar epithelium → ectropion) during late foetal life, in adolescence and during the reproductive age. After menopause, SCJ may be high up in the endocervical canal, precluding visualisation of the full TZ.

Surface contour

The surface contour depicts the surface appearance of a colposcopic pattern. The surface can be smooth, soft or coarse (rough) and irregular resulting from uneven cell proliferation. A coarse and irregular surface may have various appearances depending on the type and grade of the lesions: slightly uneven; micropapillary or papillary; raised, raised and papillary (e.g., low-grade lesions), raised and nodular; thick; thick, raised and glossy (leukoplakia); exophytic (e.g., condyloma acuminatum); cauliflower appearance (e.g., adenocarcinoma, adherent condylomas); raised and irregular like a mountain range (caused by stromal invasion and accelerated cell proliferation), raised with ridges (ridge sign – suggestive of high-grade lesions [23]), cerebroid (brain-like), and depressed (due to erosion and ulceration). The surface of the columnar epithelium is grapelike (villous) often with rugae. The surface (the lesion) can be homogenous or complex.

Transformation zone (TZ)

The TZ is the area of the ectopic columnar epithelium on the cervix, which as a rule is replaced by squamous metaplasia and is demarcated by the two (neo and original) SCJs, i.e., the area is situated between the original columnar (endocervical) and the original squamous (ectocervical) epithelium (→ squamocolumnar junctions) Components of the normal TZ include columnar and metaplastic epithelium, the latter in different stages of maturation, as well as cleft openings and Nabothian cysts.

There are three types of the TZ (types 1-3) [24]. Type 1 is completely ectocervical and fully visible, type 2 has an endocervical component but is fully assessable, while type 3 has an endocervical component and cannot be assessed entirely. All may be small or large. The TZ may extend onto the upper vagina.

The old terms: cervical ectopy, ectopia, and erythroplakia, formerly used interchangeably to denote TZ, are no longer used in modern colposcopic terminology.

The term atypical TZ denotes TZ with abnormal colposcopic findings as opposed to physiological TZ with physiological squamous metaplasia. The concept of the congenital transformation zone (→) is discussed separately.

Vaginal adenosis

Vaginal adenosis is the presence of columnar cells in the vagina. In women exposed to diethylstilbestrol (DES) in utero, not only the entire cervix but partly the upper vagina is covered by columnar epithelium due to premature arrest of the migration of the squamous epithelium. As a result, the original SCJ is located in the vagina. This is often associated with other abnormalities (multiple sulci, cock's comb and pseudopolyps), collectively called cervicovaginal deformities. It should be remembered, however, that vaginal adenosis can occur with DES exposure. This condition is benign and undergoes spontaneous resolution in almost all women, mostly by the time of puberty. The colposcopic appearance resembles that of columnar and metaplastic epithelium and is frequently associated with circular sulci, pseudopolyps on the ectocervix and occasionally cervical protuberance of the cervix bulging into the vagina (cock's comb) → sqamocolumnar junction.

Vulvoscopy

Colposcopy of the vulva.

Colposcopic classification

Traditionally, colposcopic classification by IFCPC is focused on the colposcopic findings of the uterine cervix and vagina, i.e., mucosal tissues of the lower genitalia. The colposcopic findings of the vulva have not been covered. In addition, evaluation of the colposcopic examination, whether it is satisfactory or unsatisfactory, has been included. The latest IFCPC classification made a distinction between normal and abnormal colposcopic findings. However, colposcopic features suggestive of invasive cancer and miscellaneous findings were not included in the latter group in spite of the fact that all findings are not considered normal are abnormal. The use of terms 'typical' and 'atypical' colposcopic findings, substituting the 'normal' and 'abnormal' adjunctive is less common and not preferred.

Colposcopic findings may be classified either according to the types (patterns and signs) of colposcopic features, or based on the interpretation of the colposcopic findings. Colposcopic features comprise colposcopic patterns and signs (for definitions of colposcopic features, patterns and signs see Glossary).

1. The classification of colposcopic features (Table 1).

The main objective of this classification is to aid in learning the recognition of colposcopic features, i.e., colposcopic patterns and colposcopic signs. Colposcopically, all diseases of the uterine cervix and vagina are invariably made up by some of these colposcopic patterns and signs.

Table 1. — *Classification of cervical and vaginal (mucosal) colposcopic features (patterns and signs).*

Colposcopic patterns
Original squamous epithelium
Atrophic squamous epithelium
Original columnar epithelium
Metaplastic squamous epithelium
Openings
Nabothian cyst
Deciduosis
Punctation (fine, coarse)
Mosaic (fine, coarse)
Atypical vessels
Acetowhite epithelium
Leukoplakia
Erosion, ulcer
Colposcopic signs
Colour tone sign
Border shape
Surface contour
Extension (localisation) and size

2. Colposcopic classification (Table 2).

Table 2. — *Colposcopic classification*.

Interpretation of colposcopic exam	Satisfactory (the transformation zone is fully assessable)
	Limited (the transformation zone is partially assessable only)
	Unsatisfactory (colposcopic assessment is precluded)
Normal colposcopic findings	Original squamous epithelium
	Original columnar epithelium
	Transformation zone (type 1-3) (cervix only)
	columnar epithelium
	metaplastic epithelium
	crypt openings
	nabothian cysts
	Atrophic epithelium
	Deciduosis
Non-specific colposcopic features	Fine acetowhitening
	Fine punctation
	Fine mosaic
	Leukoplakia (hyperkeratosis)
	Iodine negativity
	Erosion, ulceration
	Geographic border
Colposcopic features suggestive of high-grade lesions (high-grade colposcopic features)	Dense acetowhitening (oyster white)
	Dense punctation
	Dense mosaic
	Sharp, strait outer border
	Sharp inner border
Colposcopic features suggestive of cancer	Atypical vessels
	Additional features of frankly invasive cancer
	large lesion (> 50% of the visible uterine cervix)
	irregular surface (exophytic or endophytic growth)
	grey colour tone
	marked, rolled edge
	necrosis
	friable vessels (contact bleeding, haemorrhage)
	features of high-grade lesions
Miscellaneous colposcopic findings	Congenital transformation zone
	Healing tissue
	Abnormal granulation
	Condyloma acuminatum
	Subtle and flat HPV infection(26)
	Endometriosis
	Common cervical and vaginal infections (candida, trichomonas etc.)
	Polyps
	Radiotherapy reactions
	Cyst and adenosis (vagina only)
	etc.
Location of cervical lesions	Within the transformation zone
	Outside the transformation zone
	Overgrowing the transformation zone
	Extending to the vagina
	Upper lip, lower lip, upper and lower lip
Location of vaginal lesions	Anterior, posterior, right or left vaginal wall
	Upper half, lower half
	Vaginal fornix
	Sub-urethral

Colposcopic classification is more complex as compared to sorting colposcopic features (Table 1). In addition to the classification of colposcopic findings based on their interpretation, it also includes assessment of the colposcopic examination per se, of the type of the TZ and the extension (location) of the abnormal lesions. Normal colposcopic findings result from tissue variants occurring physiologically at some point in a woman's life. Doubtfully interpretable features,

called non-specific colposcopic features, include colposcopic patterns and signs that can be due to two or more different tissue changes, therefore their clinical implication is uncertain. In contrast, high-grade colposcopic features do suggest a high-grade precancer lesion or cancer but are by no means diagnostic. For diagnosis in such cases, biopsy and histopathology are mandatory. Miscellaneous colposcopic findings include colposcopic features of cervical and vaginal diseases other than precursors or invasive cancer. Some of the miscellaneous colposcopic findings are characteristic enough to be used as the basis of treatment decisions, e.g., polyps, condyloma acuminatum.

The major points of consideration in making colposcopic classifications as defined by IFCPC are the following:

– "the classification should be descriptive to allow colposcopists throughout the world to be able to describe lesions to each other and to undertake important collaborative research;

– nomenclature should be written in such a way that it can guide a colposcopist in training and aid the established colposcopist during the diagnostic process;

– the terminology should be pragmatic (...)" [25, 26].

These principles have not changed, and are equally valid today. Indeed, classifications are made for clinicians to speak the same language in talking to each other, in colposcopy reports and research, and to share ideas.

Colposcopy of vulvar diseases (vulvoscopy)

Colposcopy of the vulva is often called vulvoscopy. By definition, "vulvoscopy consists of careful observation and the possible use of a 5% acetic acid solution to the entire vulvar area to facilitate examination of the vulva by the colposcope" [27]. Theoretically, it may be beneficial in a) identifying subclinical lesions (i.e., lesions not visible to the naked eye), particularly after acetic acid application; b) delineating clinically evident diseases; and c) recognising details not evident clinically. In practice, however, unlike the vagina and the cervix, colposcopy of the vulva does not add much to the naked-eye examination. (28). In addition, acetic acid application may be painful, colouration with toluidine blue is unreliable and observation of the colposcopic features is mostly obscured by the dermal tissues. Moreover, biopsy remains the gold standard in diagnosing vulvar disease, irrespective of the colposcopic findings. Regarding colposcopic features of vulvar lesions, the same patterns and signs are applied as for the vagina and cervix,

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Conflict of interest statement

The author may have the following conflicts of interest: he is member of the Nomenclature Committee of the International Federation of Cervical Pathology and Colposcopy.

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