

# Inflammatory lesions of the cervix

This chapter describes the colposcopic appearances of a variety of common inflammatory conditions but is not a substitute for a full description of lower genital tract infection.

The interested reader is referred to Hicks (2002) for a fuller description of the investigation and management of gynaecological infections.

Inflammatory conditions are extremely common in many parts of the Southern Hemisphere and in particular for socioeconomically disadvantaged women. They are usually, but not always, caused by infection, which may be viral, bacterial, or protozoal.

Non-infective causes of inflammation include a foreign body (tampon, IUCD), trauma, or chemical irritation in the form of gels, creams,

and other non-proprietary formulations that have been prescribed for symptomatic reasons. Table 9.1 lists the common infections responsible for cervicovaginitis. Lower genital tract infections are usually symptomatic and should always be treated.

Pruritus and vaginal discharge, which is often offensive, and dysuria and introital dyspareunia are additional burdens for affected women. They should always be treated.

The more common infections are trichomoniasis (caused by *Trichomonas vaginalis*), candidiasis, bacterial vaginosis, chlamydia, gonorrhoea, and herpes simplex.

Less common infections that occur in the cervicovaginal epithelium are tuberculosis, amoebiasis, schistosomiasis, *Haemophilus ducreyi*, *Mycoplasma hominis*, and *Escherichia coli*.

## 9.1 Wet preparation, cytological, and histological appearances of infection

The infective organism responsible for cervicovaginitis is most accurately identified in the laboratory. At a tissue level, inflammatory changes in the epithelium are characterized by vascular hypertrophy and intraepithelial cellular damage and denudation. Cellular layers may be denuded through the full spectrum of desquamation, from fewer epithelial layers to frank ulceration. In the deeper layers, the cells may be enlarged and swollen with a neutrophilic infiltration. There is an associated collection of cellular debris and fluid as discharge on the epithelial surface.

Gram staining or even cytological examination of infection is diagnostically specific.

**Table 9.1. Treatment of reproductive tract infections**

| Reproductive tract infection                  | Treatment guidelines   |  |
|---|--|--|
|   | Non-pregnant women   | Pregnant women   |
| <i>Trichomonas vaginalis</i> (trichomoniasis) | Metronidazole 400–500 mg orally, 2 times daily for 7 days <u>or</u> a single dose of metronidazole 2 g orally <u>or</u> a single dose of tinidazole 2 g orally.  | Metronidazole 400–500 mg orally, 2 times daily for 7 days. High-dose treatment not recommended. Safety of tinidazole not well evaluated.   |
| Candidiasis                                   | Clotrimazole pessary 500 mg immediately or clotrimazole pessary 200 mg for 3 nights <u>or</u> a single dose of fluconazole 150 mg orally. All topical and oral azoles are effective.   | Clotrimazole pessary 200 mg for 3 nights <u>or</u> clotrimazole pessary 100 mg for 6 nights. Oral treatment contraindicated.   |
| Bacterial vaginosis                           | Metronidazole 400 mg orally, 2 times daily for 5–7 days <u>or</u> metronidazole 2 g immediately <u>or</u> intravaginal metronidazole gel (0.75%) once daily for 5 days <u>or</u> intravaginal clindamycin cream (2%) once daily for 7 days.  | Metronidazole 400 mg orally, 2 times daily for 5–7 days <u>or</u> intravaginal metronidazole gel (0.75%) once daily for 5 days <u>or</u> intravaginal clindamycin cream (2%) once daily for 7 days.  |
| Chlamydial infection                          | Doxycycline 100 mg orally, 2 times daily for 7 days <u>or</u> a single dose of azithromycin 1 g orally.  | A single dose of azithromycin 1 g orally <u>or</u> erythromycin 500 mg orally, 4 times daily for 7 days <u>or</u> amoxicillin 500 mg orally, 3 times daily for 7 days. Pregnant women require a test of cure.  |
| Gonococcal infection                          | <b>Refer to local sensitivity data.</b><br>A single dose of intramuscular ceftriaxone 500 mg plus a single dose of oral azithromycin 2 g. Alternatives include a single dose of intramuscular ceftriaxone 500 mg <u>or</u> a single dose of intramuscular spectinomycin 2 g plus a single dose of oral azithromycin 2 g <u>or</u> other regimens as guided by sensitivities. | <b>Refer to local sensitivity data.</b><br>A single dose of intramuscular ceftriaxone 500 mg plus a single dose of oral azithromycin 1 g. Alternatives include a single dose of intramuscular ceftriaxone 500 mg <u>or</u> a single dose of intramuscular spectinomycin 2 g plus a single dose of oral azithromycin 1 g <u>or</u> other regimens as guided by sensitivities. |
| Syphilis                                      | Early syphilis: A single dose of intramuscular benzathine penicillin 2.4 MU <u>or</u> doxycycline 100 mg, 2 times daily for 14 days.<br>Late syphilis: Intramuscular benzathine penicillin 2.4 MU weekly for 3 doses <u>or</u> doxycycline 100 mg, 2 times daily for 28 days.<br>Neurosyphilis: Seek specialist advice.  | Early syphilis: A single dose of intramuscular benzathine penicillin 2.4 MU <u>or</u> intramuscular ceftriaxone 500 mg, once daily for 10 days.<br>Late syphilis: Intramuscular benzathine penicillin 2.4 MU weekly for 3 doses.<br>Neurosyphilis: Seek specialist advice.   |
| Lymphogranuloma venereum                      | Doxycycline 100 mg orally, 2 times daily for 21 days <u>or</u> erythromycin 500 mg orally, 4 times daily for 21 days.  | Erythromycin 500 mg orally, 4 times daily for 21 days.   |
| Chancroid                                     | Ciprofloxacin 500 mg orally, 2 times daily for 3 days <u>or</u> a single dose of azithromycin 1 g orally <u>or</u> erythromycin 500 mg orally, 4 times daily for 7 days.   | A single dose of azithromycin 1 g orally <u>or</u> erythromycin 500 mg orally, 4 times daily for 7 days.   |
| Granuloma inguinale                           | Azithromycin 1 g orally, weekly <u>or</u> ciprofloxacin 500 mg, 2 times daily <u>or</u> doxycycline 100 mg, 2 times daily. All treatment should be for a minimum of 3 weeks or until lesions have healed.  | Erythromycin 500 mg, 4 times daily for 3 weeks or until ulcers have healed.  |
| Genital herpes                                | Acyclovir 400 mg orally, 3 times daily for 5 days <u>or</u> famciclovir 250 mg, 3 times daily for 5 days.  | Acyclovir 400 mg orally, 3 times daily. Seek specialist advice.  |
| Pelvic inflammatory disease                   | A single dose of intramuscular ceftriaxone 500 mg plus a single dose of azithromycin 1 g orally plus doxycycline 100 mg, 2 times daily and metronidazole 400 mg, 2 times daily for 14 days.  | A single dose of intramuscular ceftriaxone 500 mg plus a single dose of azithromycin 1 g orally plus erythromycin 500 mg orally, 4 times daily for 14 days. Poor evidence available.   |

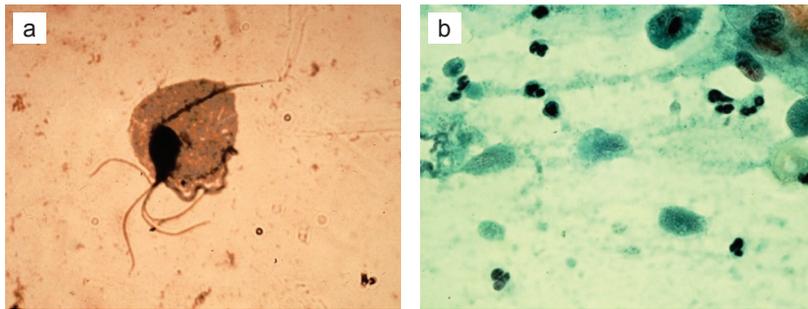
Figs. 9.1–9.9 show examples of specific infections recognized at either Gram staining or cytological examination. Cytology is not the best method of detecting cervico-vaginal infections but will sometimes incidentally recognize them and can alert the clinician to an unsuspected infection.

## 9.2 Colposcopic appearance of cervicovaginitis

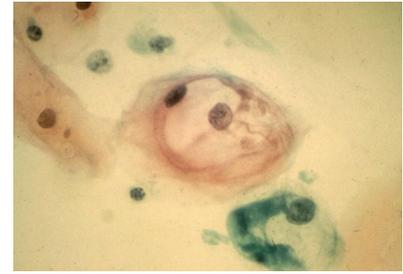
The epithelium of a mild infection may be minimally altered, but by the time it presents to a gynaecologist the appearances are usually very abnormal. Typically, there is a vascular response as well as evidence of

epithelial damage. The inflammatory response does not usually reflect the infecting organism. The vascular response includes redness, punctation (often grouped in a distribution commonly known as “strawberry appearance”), and a diffuse, fluffy acetowhitiness not dissimilar to LSIL but distributed non-specifically and

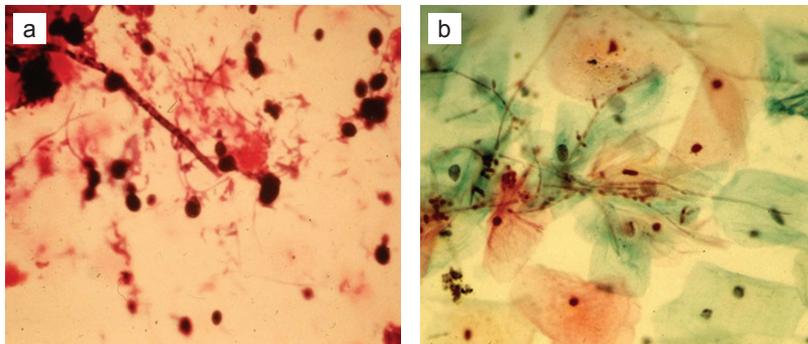
**Fig. 9.1.** (a) A Gram stain view of a trichomonad. (b) A cytology preparation revealing trichomoniasis.



**Fig. 9.2.** A cytology preparation showing a typical cytoplasmic halo, characteristic of HPV infection.



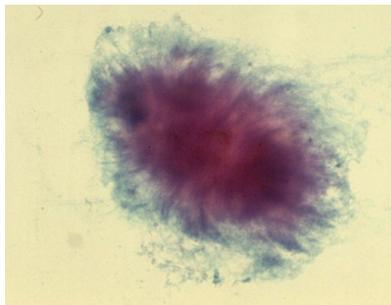
**Fig. 9.3.** (a) A Gram stain preparation of candidiasis. (b) A cytology slide showing candidiasis.



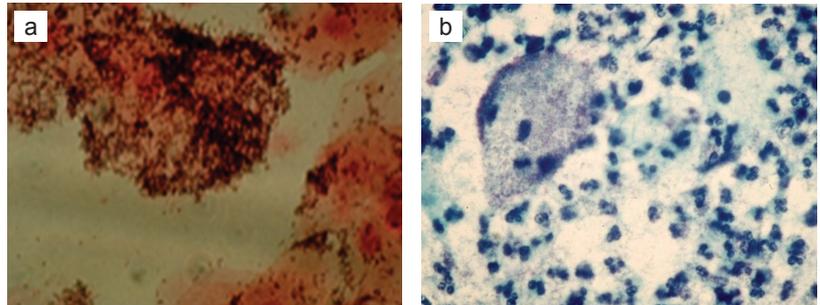
**Fig. 9.4.** A cytology preparation showing a case of herpes simplex.



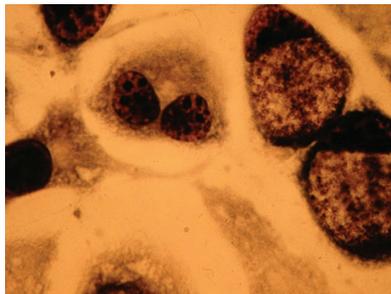
**Fig. 9.5.** A cytology preparation showing a case of actinomycosis.



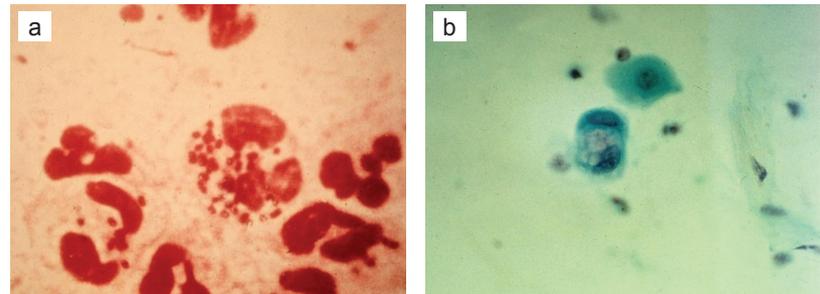
**Fig. 9.6.** (a) A Gram stain revealing bacterial vaginosis. (b) A cytology slide showing a case of bacterial vaginosis.



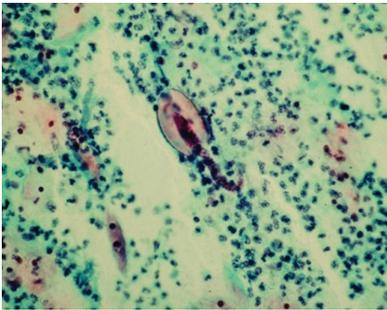
**Fig. 9.7.** A tissue culture slide showing a case of chlamydia.



**Fig. 9.8.** (a) A Gram stain showing an (intracellular) gonococcus infection. (b) A cytology preparation showing an (intracellular) gonococcus infection.



**Fig. 9.9.** A cytology preparation showing threadworm (*Enterobius vermicularis*), which is actually hatching in this image.



very widely, both inside and outside the TZ. Terminal capillaries may become hypertrophied, i.e. they may appear coiled, duplicated, or simply dilated. Vertical capillary loops in the epithelium may become hyperaemic and, again a little like mild squamous intraepithelial lesion (SIL) changes, may have a punctate appearance, sometimes in specific clumps, creating the strawberry appearance referred to above. When the infection has produced these appearances, there will almost always be an associated vaginal discharge and it is usually pruritic.

### 9.3 Colposcopic examination

#### 9.3.1 Before application of acetic acid

An examination in the presence of infection is usually more uncomfortable for the patient. Swabs for culture should be taken before any fluids have been applied. Examination, before the application of acetic acid, may reveal moderate to severe cervical and vaginal secretions, and these may sometimes suggest the nature of underlying infection. Bacterial infections are associated with thin, liquid, seropurulent discharge. The secretion may be foul-smelling in the case of anaerobic bacterial overgrowth, bacterial vaginosis,

and *Trichomonas* infection. Gonorrhoea results in a purulent vaginal discharge and cervical tenderness. Excoriation marks may be present with trichomoniasis, moniliasis, and mixed bacterial infections. Foul-smelling, dark-coloured mucopurulent discharges are associated with inflammatory states due to foreign bodies, for example a retained tampon.

A large coalesced ulcer due to herpes, or other inflammatory conditions, may mimic the appearance of invasive cancer. Chronic inflammation may cause recurrent ulceration and healing of the cervix, resulting in distortion of the cervix due to healing by fibrosis. There may be associated necrotic areas as well. When there is any doubt, a biopsy should be taken. Rare and uncommon cervical infections, due to protozoal infections (schistosomiasis and amoebiasis) or tuberculosis, cause extensive ulceration and necrosis of the cervix with symptoms and signs that mimic invasive cancer; again, a biopsy will discriminate.

If the infectious process is accompanied by marked ulceration (with or without necrosis), the ulcerated area may be covered with purulent exudate, with marked differences in the surface level of the cervix. There may be exudation of serous droplets.

Long-standing bacterial, fungal, or protozoal infection and inflammation may lead to fibrosis, which appears white or pink, depending on the degree of fibrosis. The epithelium covering the connective tissue is fragile, leading to ulceration and bleeding. Appearances after the application of acetic acid and iodine are variable, depending on the integrity of the surface epithelium.

In the case of cervicitis, the columnar epithelium is intensely red and bleeds on contact, and an opaque purulent discharge may be

present. The columnar villous or grape-like appearance may be lost because of flattening of the villi, because of repeated inflammation, and because there are no clearly defined papillae (Fig. 9.10). Extensive areas of the cervix and infected vaginal mucosa appear red because of congestion of the underlying connective tissue.

#### 9.3.2 After application of acetic acid

The liberal application of acetic acid clears the cervix and vagina of secretions but may cause pain or discomfort. Cervicovaginitis is associated with oedema, capillary dilatation, enlargement of the stromal papillae (which contain the vascular bundles), and infiltration of the stroma with inflammatory cells. The chronically inflamed cervix may appear reddish, with ill-defined, patchy acetowhite areas scattered in the cervix, not restricted to the TZ, and it may bleed on contact. The enlarged stromal papillae appear as red spots (red punctation) on a pinkish-white background, usually in the case of *T. vaginalis* infection, after the application of acetic acid.

An inexperienced colposcopist may confuse the inflammatory punctations with those seen in CIN. However, one can differentiate using the

**Fig. 9.10.** An inflamed cervix; non-specific infection.



**Fig. 9.11.** Strawberry appearance in an inflamed cervix, with multiple red spots (labelled a).



following criteria. Inflammatory punctations are fine, with extremely minimal intercapillary distances, and are diffusely distributed (not restricted to the TZ), and they involve the original squamous epithelium and vagina. As the inflammation persists and becomes chronic, it results in large, focal red punctations due to large collections of capillaries grouped together, which appear as several red spots of different sizes visible on a pinkish-white background, producing the so-called strawberry spots (Fig. 9.11). Colposcopically, a chronically inflamed cervix may sometimes resemble invasive cervical cancer.

### 9.3.3 After application of Lugol's iodine

The test outcome after the application of Lugol's iodine depends on the desquamation and loss of cell layers

**Fig. 9.12.** Stippled appearance (labelled a) after the application of Lugol's iodine in a case of trichomoniasis.

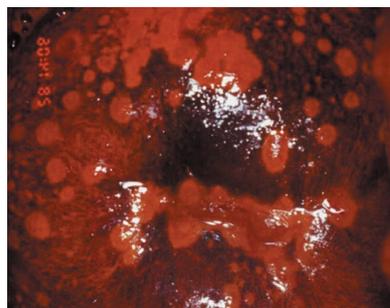


containing glycogen. If desquamation is limited to the summit of the stromal papillae, where the squamous epithelium is thinnest, a series of thin yellow spots are seen on a mahogany-brown background, giving a stippled appearance (Fig. 9.12). When the inflammation persists and the infection becomes chronic, the small desquamated areas become confluent to form large desquamated areas, leading to the so-called leopard-skin appearance (Fig. 9.13). These features are often found with *Trichomonas* infection but also may be seen with fungal and bacterial infections. If there is marked desquamation, the cervix appears yellowish-red, with involvement of the vagina. Again, the application of Lugol's iodine can be intensely uncomfortable in the presence of infection.

### 9.3.4 Summary

Inflammatory conditions of the cervix are associated with excessive, usually malodorous, mucopurulent, seropurulent, or whitish discharge, red punctations, ulceration, and healing by fibrosis. The secretion is frothy with bubbles in the case of trichomoniasis, and sticky and cheese-white in candidiasis. Inflammatory lesions of the cervix may be differentiated from CIN by their large, diffuse involvement of the cervix, extension

**Fig. 9.13.** Leopard-skin appearance of vaginitis associated with a trichomoniasis infection.



to the vagina, red colour tone, and associated symptoms such as discharge and pruritus.

## 9.4 Specific infections

### 9.4.1 Candidiasis

Infection with *Candida albicans* is extremely common and, with low-grade chronic infection, may be entirely asymptomatic. It is sometimes called a thrush infection, because the breast of the common thrush bird has the speckled grey-white appearance once thought typical of candidal pharyngitis. When it flourishes, it nearly always becomes symptomatic, producing a thick cheese-like discharge and pruritus of the vulva and vagina. There may be a concurrent vulvitis. The appearances are more specific than for most cervicovaginal infections and do not usually require laboratory confirmation, but where simple treatment does not work, the usual workup for candidal vulvovaginitis should be implemented. Fig. 9.14 depicts candidal cervicitis and vaginitis seen through the colposcope.

### 9.4.2 Trichomoniasis

This extremely common infection causes serious discomfort by way of an intensely pruritic and offensive discharge often described as fishy

**Fig. 9.14.** Typical candidiasis seen at high-power examination of the cervix.



in odour. The discharge is frothy, sometimes almost green, and quite profuse, sometimes even requiring a sanitary towel to prevent staining of underclothes. It produces the classic strawberry appearance more commonly than other infections, but not exclusively, and may be present in association with other pathology (cancer, polyps, a foreign body, and/or surgical intervention). Colposcopically, the epithelial inflammatory response is non-specific. The colposcopic appearance of trichomoniasis is shown in Figs. 9.12, 9.13, and 9.15.

### 9.4.3 Herpes simplex

Small vesicles filled with serous fluid may be observed in the cervix and vaginal epithelia in the early vesicular phase of herpes simplex viral infection. Herpetic infections are associated with episodes of painful vulvar, vaginal, and cervical ulceration lasting for up to 2 weeks. The ulceration that accompanies some herpetic

infection can be so pronounced and the associated epithelial inflammatory response so severe as to render the colposcopic appearances very similar to those of cancer. A biopsy will sometimes be necessary to discriminate between them. Fig. 9.16 shows typical appearances of a herpetic infection on the cervix and vulva.

### 9.4.4 Bacterial vaginosis

The classic sign of bacterial vaginosis is the relative lack of inflammatory response in the epithelium despite the presence of significant symptoms and a profuse grey-white fluid discharge (Fig. 9.17). When mixed with potassium hydroxide, the discharge also has a fishy smell (Fig. 9.18).

### 9.4.5 Syphilis

Syphilis is not often symptomatic. Also, a primary cervical ulcer is not usually the sole site of a syphilitic

lesion. Any ulcer can and does mimic invasive cancer, and it is often necessary to take a biopsy to rule out cancer. Table 9.2 lists the differential diagnosis of a cervical ulcer.

### 9.4.6 Chlamydia and gonorrhoea

The clinical presentation of chlamydia and gonorrhoea, both sexually transmitted infections, is not disease-specific. In other words,

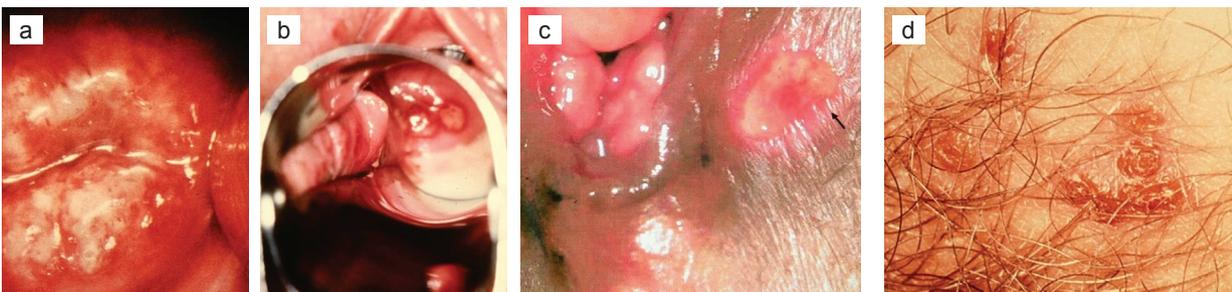
**Table 9.2.** Differential diagnosis of a suspicious cervical ulcer

| Condition                             |
|---------------------------------------|
| Cervical cancer                       |
| Syphilis                              |
| Herpes simplex                        |
| Chancroid                             |
| Tuberculosis (or protozoal infection) |
| Lymphogranuloma venereum              |
| Behçet disease                        |

**Fig. 9.15.** Three examples of colposcopic appearance of typical trichomoniasis.



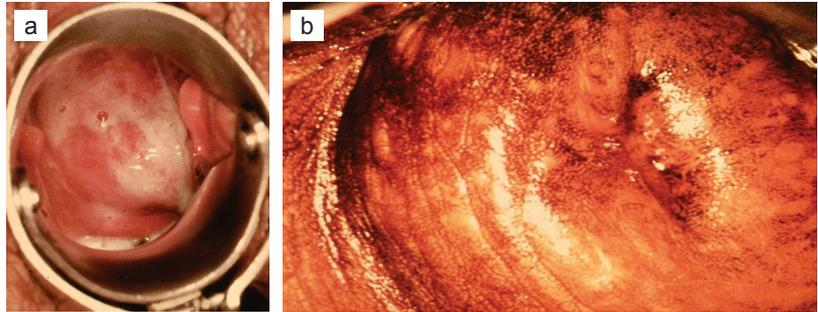
**Fig. 9.16.** Colposcopic appearance of cervical and vulvar herpes simplex, representing the (a) blistering, (b) ulcerating, (c) healing (arrow indicates healing vulvar ulcer), and (d) scabbing phases of the condition.



**Fig. 9.17.** Greyish discharge suggestive of bacterial vaginosis.



**Fig. 9.18.** Bacterial vaginosis (BV) before (a) and after (b) the application of Lugol's iodine. Note the nondescript discharge in (a). The BV infection has produced relatively little inflammatory response and shows the thick, adherent nature of the discharge associated with BV.

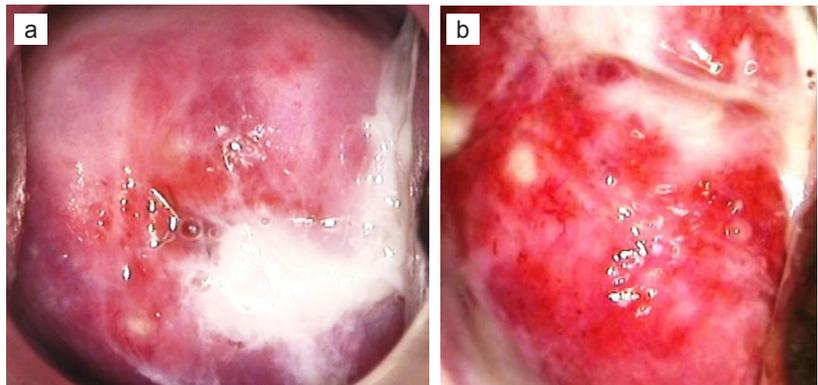


chlamydia and gonorrhoea may present in completely asymptomatic women or they may present with cervicitis of a varying degree. To confirm or rule out the suspicion of either requires a laboratory diagnosis from swabs taken from the endocervical canal. This will often cause contact bleeding. These infections are both intracellular infections. Gonorrhoea is an obligate human pathogen. It is a gram-negative diplococcus. The bacterial parasite chlamydia is also an intracellular organism. When symptomatic, chlamydia does produce a relatively specific cervical folliculitis, but this is not in all cases, and it may infect the upper genital tract with significant organ function damage without any lower genital tract symptoms or signs. The interested reader is referred to Faro (2006) for a fuller description of both gonorrhoeal and chlamydial cervicitis (Fig. 9.19).

#### 9.4.7 Other infections

Tuberculosis, schistosomiasis, and amoebiasis may all produce such

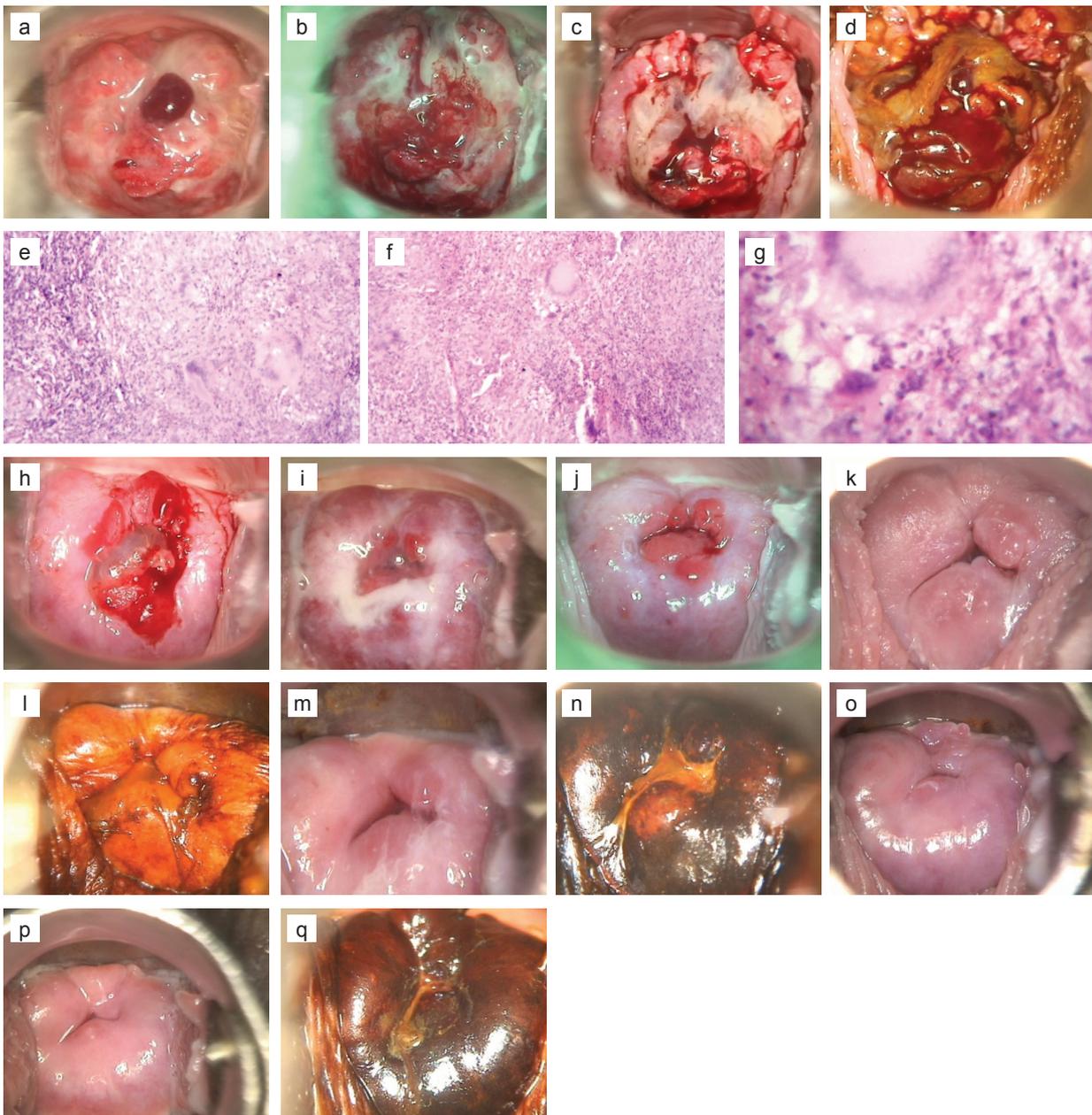
**Fig. 9.19.** (a) Cervical discharge suggestive of cervicitis. (b) Beefy-red cervix with discharge suggestive of cervicitis.



a profound inflammatory response that they are indistinguishable from cancer and a biopsy is required for diagnosis. Fig. 9.20a–q follows the chronology of a case of cervical tuberculosis. The case is typical in that it was difficult to recognize and responded completely to appropriate therapy. The patient, a 26-year-old nulliparous and married woman, presented after many years of postcoital bleeding, serosanguinous vaginal discharge, and, eventually, almost continuous per vaginal bleeding.

She was seen for colposcopic evaluation 7 years after symptoms began, and at examination, contact bleeding was immediate. The series of images reveals the cervical appearance over 6 years from before diagnosis to post-treatment follow-up. The diagnosis was made at histological examination of a colposcopically directed biopsy. A cytology smear was persistently reported as normal over 6 years after treatment with antituberculous therapy.

**Fig. 9.20.** (a) First colposcopic assessment before acetic acid application. (b) Green-filter low-power view. Pap smear contact produced immediate brisk bleeding. (c) Appearance after acetic acid application. (d) Appearance after iodine application. (e) A granuloma seen at histological examination of a biopsy taken at the first colposcopic assessment visit. (f) Langhans giant cell reaction seen at low-power magnification. (g) Langhans giant cell reaction seen at high-power magnification. (h) Colposcopic appearance 4 weeks after beginning antituberculous therapy. (i) Colposcopic appearance before saline application, 8 weeks after treatment. (j) Colposcopic appearance after saline washing of the epithelium, 8 weeks after treatment. (k) Colposcopic appearance after saline washing of the epithelium, 6 months after treatment. (l) Colposcopic appearance after Lugol's iodine application, 6 months after treatment. (m) Colposcopic appearance at low-power magnification after saline application, 2 years after antituberculous therapy. (n) Colposcopic appearance after Lugol's iodine application, 2 years after antituberculous therapy. (o) Colposcopic appearance after saline washing, 3 years after antituberculous therapy. (p) Colposcopic appearance after saline washing, 4 years after antituberculous therapy. (q) Colposcopic appearance after Lugol's iodine application, 4 years after antituberculous therapy.



## Key points

- Inflammatory lesions of the cervix are most commonly caused by specific infections and will produce a non-specific inflammatory response, which typically includes redness, discharge, vascular abnormalities, and varying degrees of epithelial desquamation.
- Inflammatory lesions are not confined to the transformation zone.
- Cervical infections may mimic intraepithelial lesions or cancer. A biopsy will sometimes be necessary to discriminate between infection and squamous intraepithelial lesion or cancer.
- Colposcopy and cytology are not methods to be relied upon in diagnosing sexually transmitted infection.
- A delay in treating a significant sexually transmitted infection can be the cause of more morbidity than delay in treating squamous intraepithelial lesion, particularly low-grade (e.g. gonorrhoea or chlamydia).