




Screen-and-Treat Cervical Cancer Prevention Programmes

in Resource-Constrained Environments


A Manual for Physicians, Nurse Practitioners, and Managers

Custom Publication of the African Centre of Excellence for Women's Cancer Control

Edited by:
Groesbeck P. Parham, MD
Mulindi Mwanahamuntu, MH, MBBS, MMed
Michael L. Hicks, MD

Abridged Version, Second Edition

Over 300 full colour images and basic text designed for newcomers to the cervical cancer specialty

Screen-and-Treat Cervical Cancer Prevention Programmes in Resource-Constrained Environments

Printed in Zambia.

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Chapter 1 Summary 

Abbreviations and Acronyms

ACCP	Alliance for Cervical Cancer Prevention
ACEWCC	African Centre of Excellence for Women's Cancer Control
AIDS	Acquired Immunodeficiency Syndrome
AIN	Anal Intraepithelial Neoplasia
ART	Antiretroviral Therapy
ARVs	Antiretrovirals
BID	Twice-per-day
CIN	Cervical Intraepithelial Neoplasia
CIS	Carcinoma In Situ
CO_2	Carbon Dioxide
DC	Digital Cervicography
DNA	Deoxyribonucleic Acid
FIGO	International Federation of Obstetrics and Gynaecology
GAVI	No longer an acronym; formerly Global Alliance for Vaccines Initiative
GYN	Gynaecology
HAART	Highly Active Antiretroviral Therapy

HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HSIL	High-Grade Squamous Intraepithelial Lesions
HSV	Herpes Simplex Virus
IARC	International Agency for Research on Cancer
ICC	Invasive Cervical Cancer
IM	Intramuscular
LEEP	Loop Electrosurgical Excision Procedure
LGV	Lymphogranuloma Venereum
LSIL	Low-Grade Squamous Intraepithelial Lesions
N_2O	Nitrous Oxide
PATH	Program for Appropriate Technologies in Health
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PID	Pelvic Inflammatory Disease
RHO	Reproductive Health Outlook
SEARO	Regional Office for South-East Asia
STI	Sexually Transmitted Infection
VIA	Visual Inspection with Acetic Acid
VILI	Visual Inspection with Lugol's Iodine
WHO	World Health Organization

Acknowledgements

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The African Centre of Excellence for Women's Cancer Control is funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Centers for Disease Control and Prevention, and represents a collaborative effort involving the Zambian Ministry of Health, the Ministry of Community Development, Mother and Child Health, University Teaching Hospital, Cancer Diseases Hospital, the Centre for Infectious Disease Research in Zambia (CIDRZ), Centers for Disease Control Zambia, and Pink Ribbon Red Ribbon.

This manual was written, designed and typeset by Lisa Grossman. Medical illustrations by Caitlin Hartmann.

Foreword

Cancer, the world's leading cause of death, is projected to increase at a staggering rate in developing countries over the next two decades. Developing countries face a perfect storm of high population growth and aging, increased prevalence of risk factors associated with economic transition, and low detection and treatment coverage. Africa, particularly its women, will be hardest hit by the unprecedented rise in cancer incidence. By 2030, cancer will kill a million Africans a year. Among women in Africa, cervical cancer is the most common malignancy and has the highest cancer-related mortality rates.

The time to act is now, and that there is a unique opportunity to build on the health system improvements created by local governments and international efforts and partnerships, such as PEPFAR (U.S. President's Emergency Plan for AIDS Relief) and Pink Ribbon Red Ribbon, to rapidly scale up access to cervical cancer detection and treatment in Africa.

As PEPFAR's flagship cervical cancer prevention implementing partner, the African Centre of Excellence for Women's Cancer Control (ACEWCC) has been able to scale up cervical cancer screening because it:

- incorporates a strong community awareness component;
- uses a simple low-cost prevention approach;
- is nurse-led at the point-of-care;
- links screening with immediate treatment (screen-and-treat) or referral;
- achieves efficiencies in quality control and provider retraining;
- facilitates rapid distance communication between providers and experts, when needed, using an appropriate technological matrix.

This manual is designed to help healthcare providers develop and manage cervical cancer prevention programmes in their own resource-constrained settings. Topics range from cervical cancer epidemiology and clinical procedures to programme management. Over 300 images accompany easy-to-read, comprehensive text for newcomers to the cervical cancer prevention specialty.

We recognize that book learning, while valuable, cannot replace practical experience. We therefore encourage all trainees to obtain clinical skills during the practicum offered at our facilities. Only qualified providers with practical training should offer clinical care.

In this new era of prevention, no woman should die from cervical cancer. Join us as we work to realize the dream of a world free from cancer.

Dr. Groesbeck Parham
Founder, African Centre of Excellence for Women's Cancer Control

Foreword

The Cervical Cancer Prevention Program in Zambia (CCPPZ) was conceptualized in 2003 when two American gynecologic oncologists, Dr. Groesbeck Parham and Dr. Michael Hicks, visited Zambia in response to an invitation from Dr. Jeffrey Stringer, Former CEO of the Centre for Infectious Disease Research in Zambia (CIDRZ). I met Drs. Parham and Hicks during this visit. At the time, the need for a national cervical cancer prevention effort in Zambia was more than apparent. At the University Teaching Hospital (UTH) in Lusaka, 80% of beds in the gynaecology unit were occupied by cervical cancer patients, most of whom had advanced-stage disease and were HIV-infected. To further substantiate the need for cervical cancer screening, Dr. Parham and I, in collaboration with Dr. Vikrant Sahasrabuddhe, conducted a study of HIV-infected Zambian women (2006). The study revealed that greater than 50% of the women had evidence of either severe precancer or cancer.

Because of the strong demonstrated association between cervical cancer and HIV, PEPFAR (U.S. President's Emergency Plan for AIDS Relief) supported our efforts to establish cervical cancer screening and treatment in Zambia, with support through the Centers for Disease Control (CDC). In January 2006, the Cervical Cancer Prevention Programme in Zambia (CCPPZ) was born. In 2012, CCPPZ became a unit of the African Centre of Excellence for Women's Cancer Control. Since inception, CCPPZ has screened over 150,000 women and trained hundreds of healthcare providers.

As a consequence of indisputable evidence that cervical cancer is highly preventable, scientists have perfected a myriad of tools to detect cervical precancer, including visual inspection with acetic acid (VIA). Even more screening tools will emerge as HPV testing is adapted to low-resource settings. Despite the plethora of screening tools, the status quo in disease prevalence and mortality has hardly changed, primarily because far less emphasis has been placed on utilizing these tools than on developing them. A lack of systems, not science, prevents us from achieving a world without cervical cancer.

This manual uses the experience acquired from CCPPZ to present a systematic approach to secondary prevention of cervical cancer in low-resource settings. The suggested system recognizes the logistical problems of low numbers of medical personnel, lack of resources to fund expensive equipment, and the low personal resources among those who seek care. It is a system that promotes population-based use of "screen-and-treat."

We hope this manual will be a resource to all those developing cervical cancer screening programmes in their own settings. To newcomers in the field of cervical cancer prevention, I congratulate you on joining a community of activists dedicated to improving the lives of women and families through the eradication of cervical cancer from the globe.

Dr. Mulindi Mwanahamuntu
Co-Director, African Centre of Excellence
for Women's Cancer Control

Foreword

Africa has greater potential to reduce cervical cancer rates than ever before. For the first time, the GAVI Alliance will subsidize HPV vaccination for the world's low income countries, targeting young adolescent girls. There is now global acceptance of more sensitive and less expensive alternatives to conventional Pap smear screening for adult women, such as "visual inspection with acetic acid," or VIA. New, more "field-friendly" HPV DNA tests will soon be available as well.

Every woman and girl has the right to access these cervical cancer prevention services. Recognizing and facilitating women's rights is critical to preserving human dignity and autonomy, acheiving the millenium development goals, and keeping the African continent's commitment to economic development. Cervical cancer strikes women primarily during their reproductive years, between the ages of 25 and 45. The deaths of these women have an enormous impact on their families, especially their children, and on the local economy.

The HIV epidemic has compounded the global cervical cancer crisis. More than 15 million women over the age of 15 are living with HIV. These women are much more likely to develop a persistent HPV infection and subsequently develop cervical cancer. HIV-positive women also develop cervical cancer at much younger ages. However, cervical cancer prevention programmes are generally extremely limited in areas with a high HIV prevalence.

In light of new screening techniques, the recent global emphasis on women's rights, and the HIV epidemic, more and more countries are implementing cervical cancer prevention programmes. We recognize the need to strengthen the relationships between providers, government, donors, traditional leaders, religious leaders, and civil society to ensure country effective and efficient readiness for such programmes. We also recognize the need to build capacity for cervical cancer prevention by training healthcare providers in the necessary techniques.

This manual is intended to meet both these needs. Although primarily written for healthcare providers, anyone interested in cervical cancer prevention will benefit from the information contained here. It is essential that not only our doctors and nurses be well-informed, but that our governments, donors, and leaders understand the basics necessary to make critical decisions about cervical cancer policies and country reforms.

We have made great strides globally in the control and eradication of major communicable and non-communicable diseases and the same could be achieved for cervical cancer. Every woman has the right to live a life free from cervical cancer.

Dr. Sharon Kapambwe
Co-Director, African Centre of Excellence
for Women's Cancer Control

Chapter

1

Anatomy and Physiology of the Cervix

After this section, the reader will be able to...

- State the name and function of basic female reproductive structures.
- Diagram the structures of the cervix.
- Understand squamous metaplasia.
- Identify the squamocolumnar junction and transformation zone.
- Understand and identify cervical abnormalities including ectopy, polyps, and Nabothian cysts.

1.1 The Female Reproductive System

The term "**female reproductive system**" refers to all the parts of the body which allow women to get pregnant, nourish the foetus, and give birth. Three important parts of the female reproductive system are the uterus, the cervix, and the vagina (Figure 1.1).

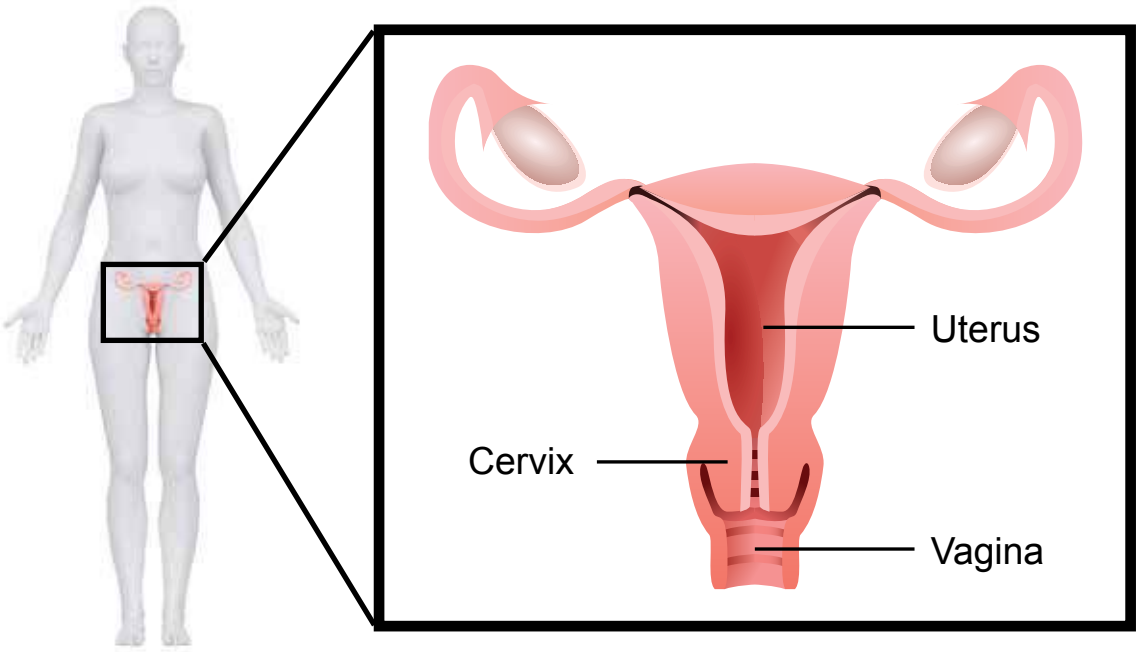


Figure 1.1 The female reproductive system.

The **uterus** is also called the womb. During pregnancy, the uterus expands to hold the baby. The **cervix** is the lower part of the uterus. Sometimes, people call the cervix the "uterine cervix" or the "mouth of the womb." The cervix connects the main body of the uterus to the vagina. The **vagina**, also called the birth canal, connects the uterus and cervix to the outside of the body. The baby passes through the vagina during birth.

Female Reproductive Terminology

When the baby passes through the vagina during birth as normal, the birth is called **vaginal birth**. When a healthcare provider uses a surgical procedure called a caesarian section to deliver the baby, the birth is called **caesarian birth**. **Menstruation** refers to a woman's monthly bleeding from the vagina. **Menopause** occurs when an older woman, usually around age 50, stops bleeding each month and can no longer get pregnant. If a woman has undergone menopause, she is postmenopausal.

1.2 The Structures of the Cervix

Endocervix and Ectocervix

The part of the cervix next to the main body of the uterus is called the **endocervix**. The part next to the vagina is called the **ectocervix** (or the exocervix).

Endocervical Canal

The passageway through the cervix from the vagina to the uterus is called the **endocervical canal** (or the cervical canal).

Internal Os and External Os

The opening of the endocervical canal into the uterus is called the **internal os**. The opening of the endocervical canal into the vagina is called the **external os**. The size and shape of the external os depends on whether a woman has given birth vaginally. If a woman has given birth vaginally, the external os is large and slit-like. If a woman has not, it is small and circular.

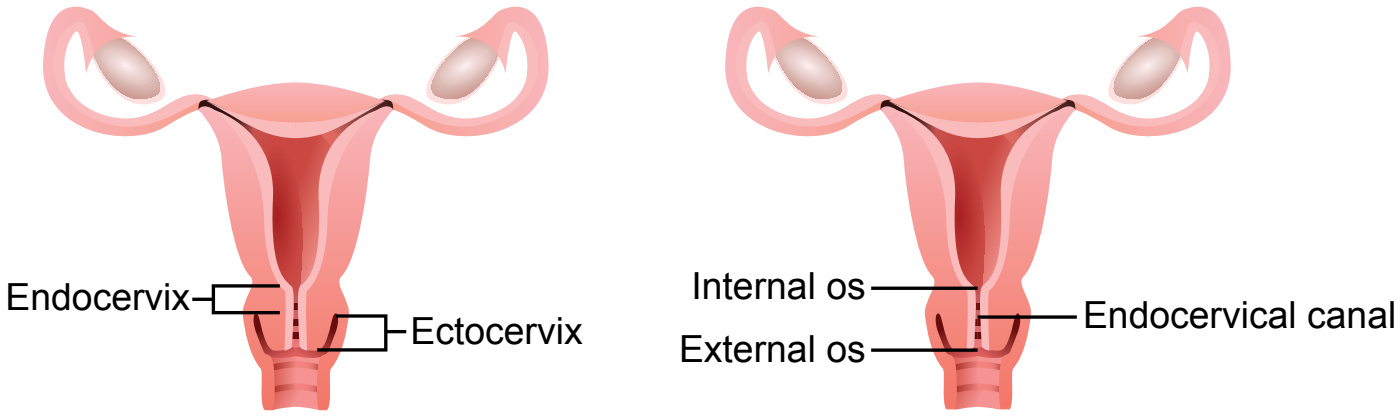


Figure 1.2 The structures of the cervix.

1.3 Visualizing the Cervix

Step 1: The provider asks the woman to lie on her back with her legs spread apart (Figure 1.4a).

Step 2: The provider inserts a speculum into the vagina to hold it open, so the ectocervix can be seen (Figure 1.4b).

Step 3: If desired, the provider can take pictures of the ectocervix (Figure 1.4c).

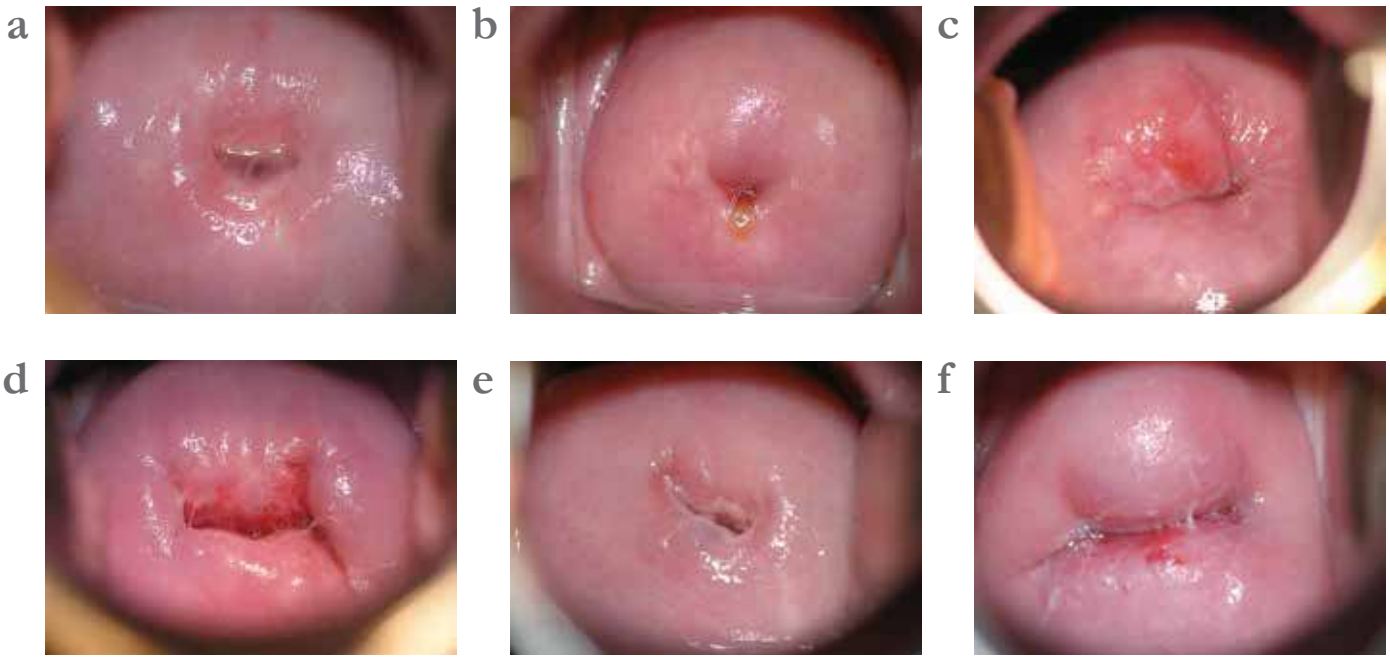


Figure 1.3a-f Photographs of the cervix from the provider's perspective. The ectocervix, external os, and a small portion of the endocervical canal can be seen.

a

b

c

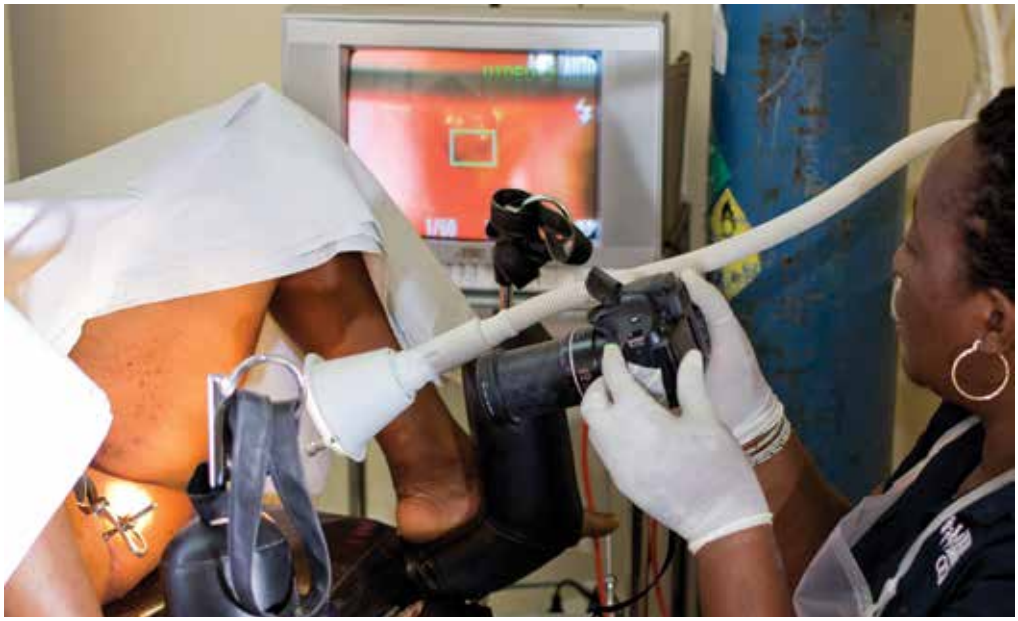


Figure 1.4a-c The steps in visualizing the cervix.

1.4 What is the Transformation Zone?

Cells called **epithelial cells** cover all surfaces of the body. Examples of epithelial cells include the skin and the linings of the intestines, mouth, and lungs. Two main types of epithelial cells cover the cervix, called **columnar cells** (or glandular cells) and **squamous cells**. Columnar cells cover the endocervix, while squamous cells cover the ectocervix. The layer of columnar cells covering the endocervix is called the **columnar epithelium** and the layers of squamous cells covering the ectocervix are called the **squamous epithelium**.

Squamous Metaplasia

Metaplasia occurs when one type of adult tissue replaces another type. As a woman ages, the squamous epithelium on her cervix gradually replaces the columnar epithelium. This gradual replacement is called **squamous metaplasia**.

The Squamocolumnar Junction (SCJ)

The place where the squamous epithelium meets the columnar epithelium is called the **squamocolumnar junction (SCJ)**. Because squamous epithelium slowly replaces columnar epithelium on the cervix, the junction changes location over time. During a woman's early adult years, the junction can be seen on the ectocervix (Figure 1.6b). As she ages, the junction moves into the canal and cannot be seen (Figure 1.6b).

The Transformation Zone

The **transformation zone** is the area between the old SCJ and the current SCJ. Squamous metaplasia occurs within the transformation zone. The old SCJ often cannot be seen with the naked eye. The transformation zone is usually a pale pinkish-white colour and may be seen.

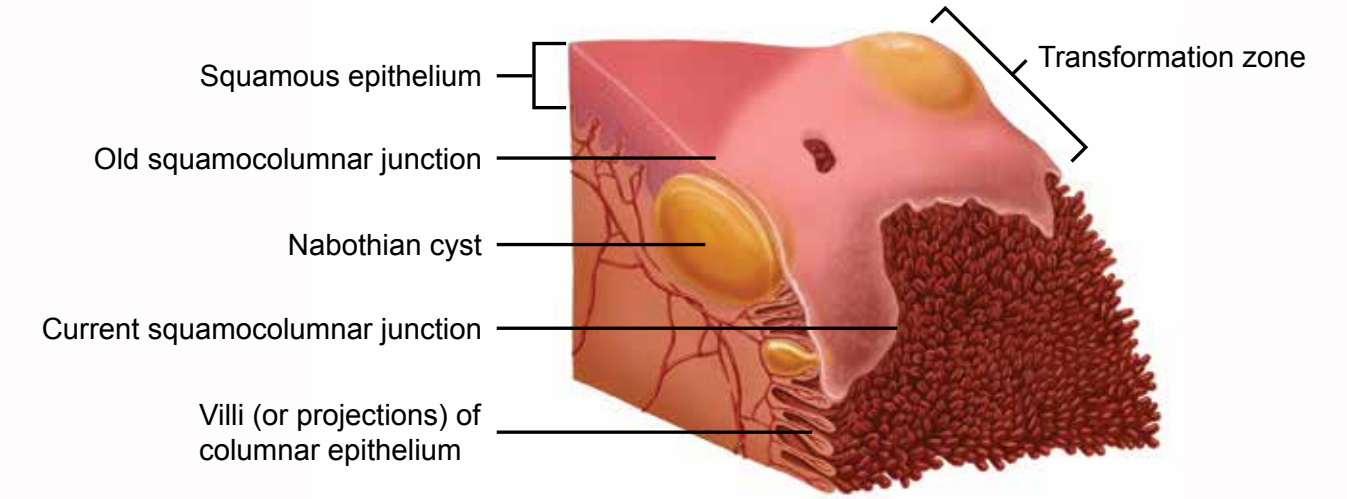


Figure 1.5 Illustration of a cross section of the cervix, depicting the columnar epithelium, squamous epithelium, and squamocolumnar junction at the histological (tissue) level. Nabothian cysts will be discussed in section 1.5.

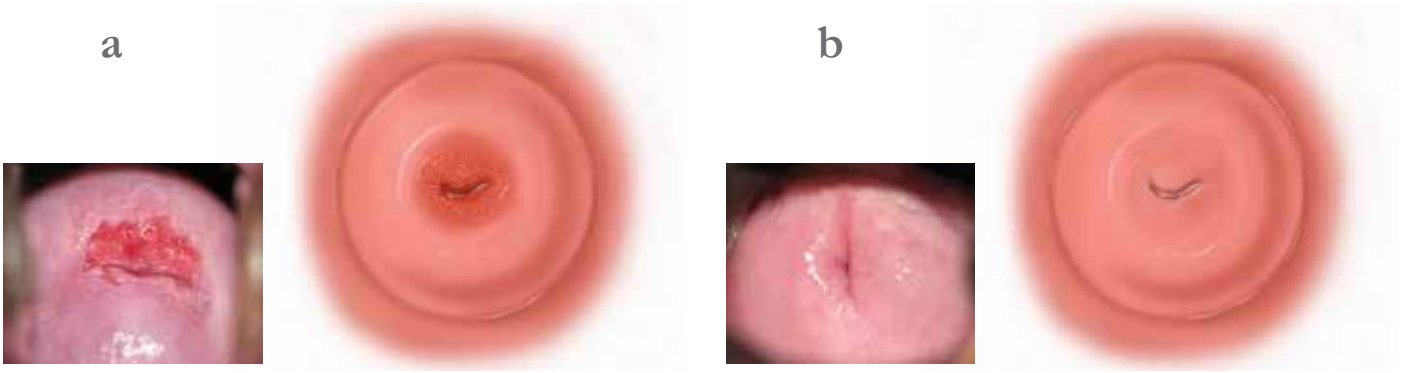


Figure 1.6a Illustration and photograph of the cervix of young adult woman at age 30.
Figure 1.6b Illustration and photograph of the cervix of a postmenopausal woman at age 65.

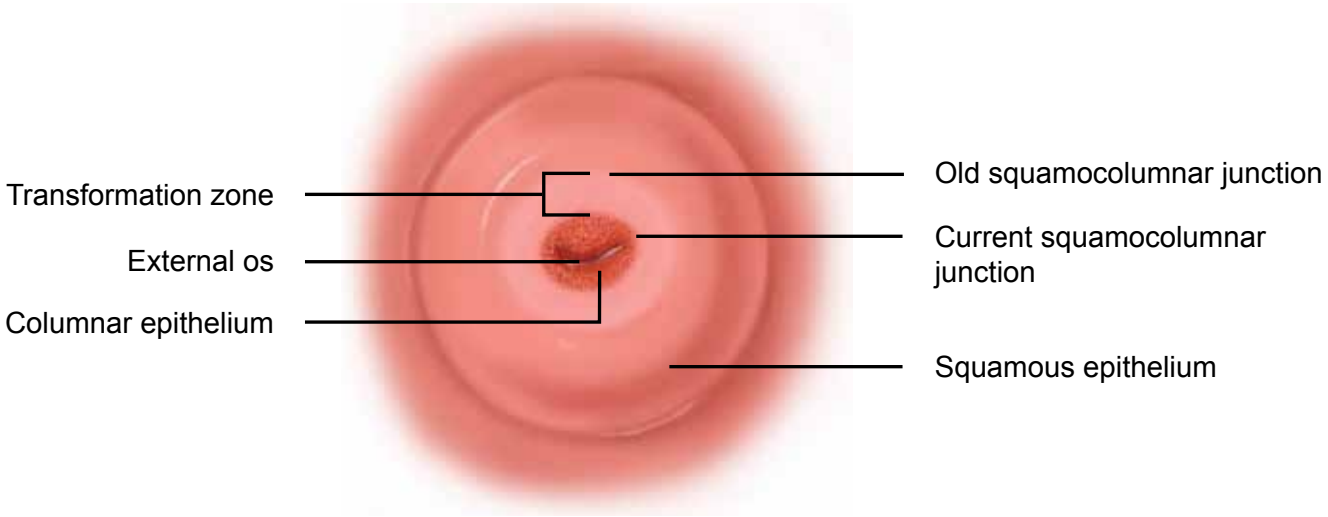


Figure 1.7 Illustration of the cervix with structures labelled.

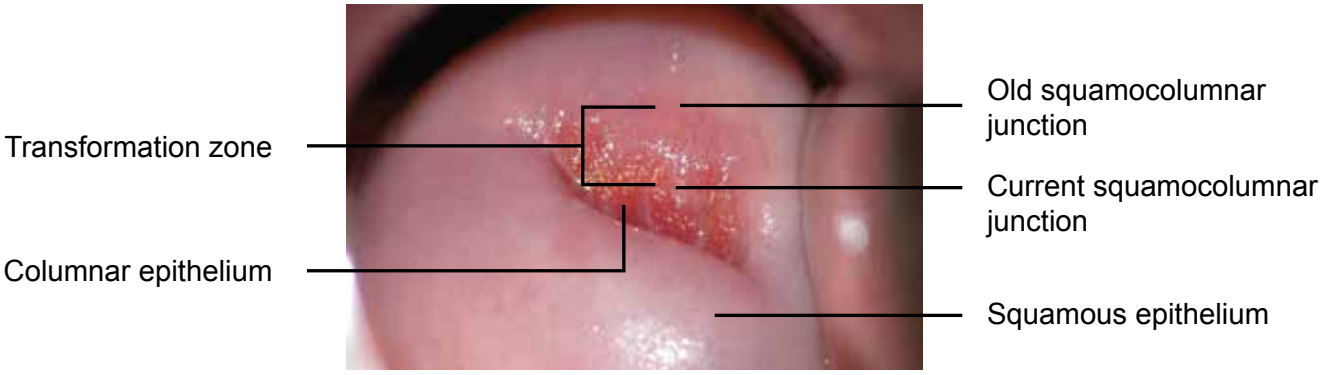
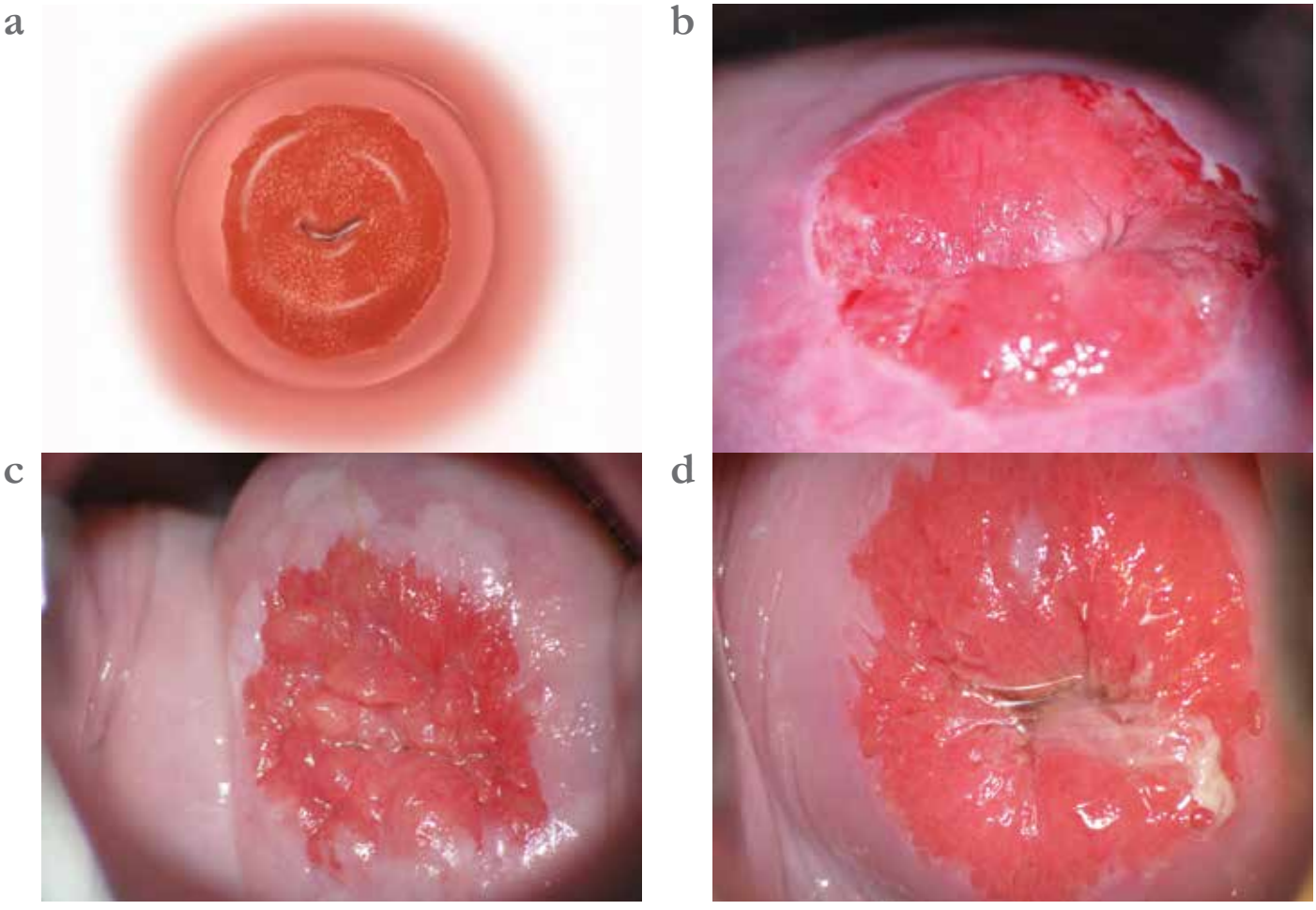


Figure 1.8 Photograph of the cervix with structures labelled.

1.5 Cervical Abnormalities: Cervical Ectopy, Polyps, and Nabothian Cysts

Cervical Ectopy

Usually, primarily squamous cells cover the ectocervix. **Cervical ectopy** is a condition where the ectocervix contains columnar cells. Squamous cells which cover the cervix are multiple layers thick. However, columnar cells are only one layer thick, meaning that the blood vessels underneath columnar cells are closer to the surface. Studies suggest that women with ectopy more often get sexually transmitted infections and HIV because the blood vessels are closer to the surface.[3,4]



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(Images of cervical ectopy, continued)

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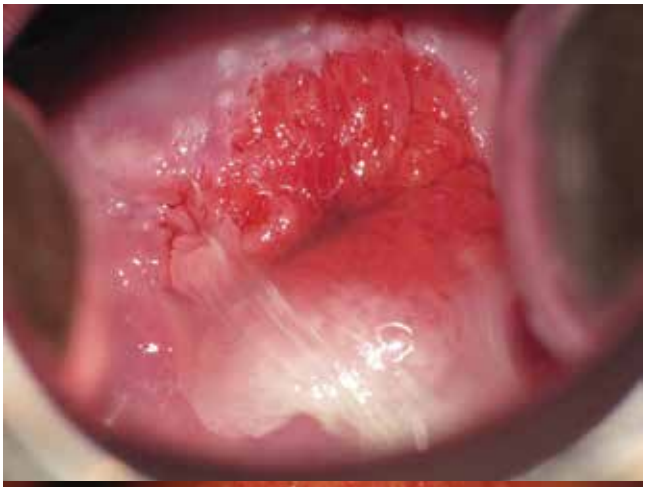

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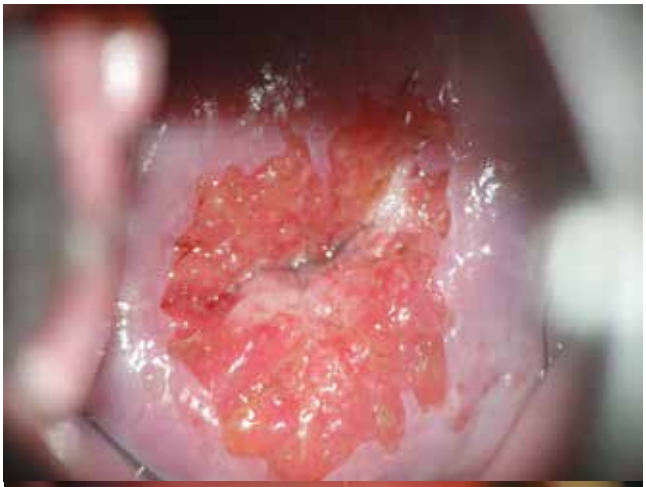

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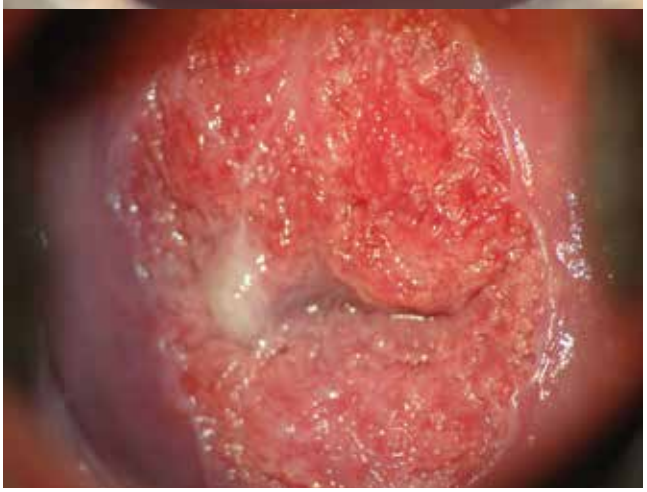

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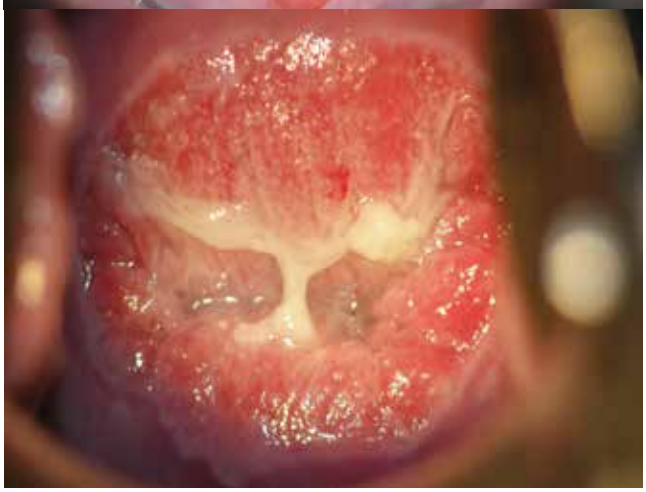


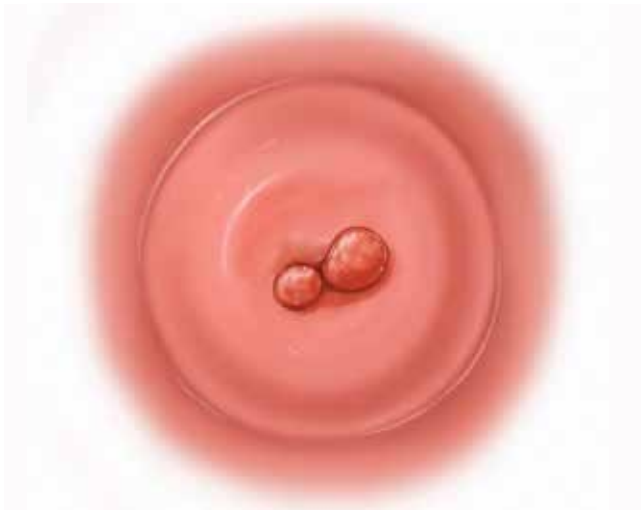
Figure 1.9a Illustration of a cervix with ectopy.
Figure 1.9b-h Photographs of cervixes with ectopy.

Cervical Polyps

Cervical polyps are growths on the ectocervix or endocervix. They vary in size and often have the shape of a raindrop or grape. Most polyps are small, between 2 and 30 mm in length.

The causes of cervical polyps are not well understood, however, most are associated with previous infection or inflammation of the cervix.

a



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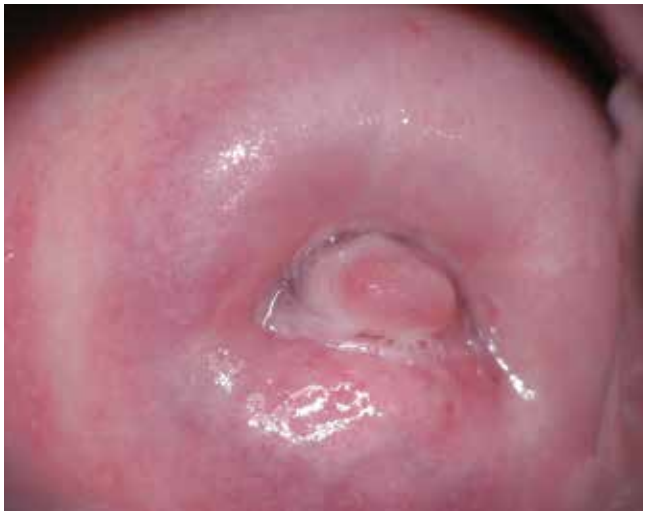

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(Images of cervical polyps, continued)

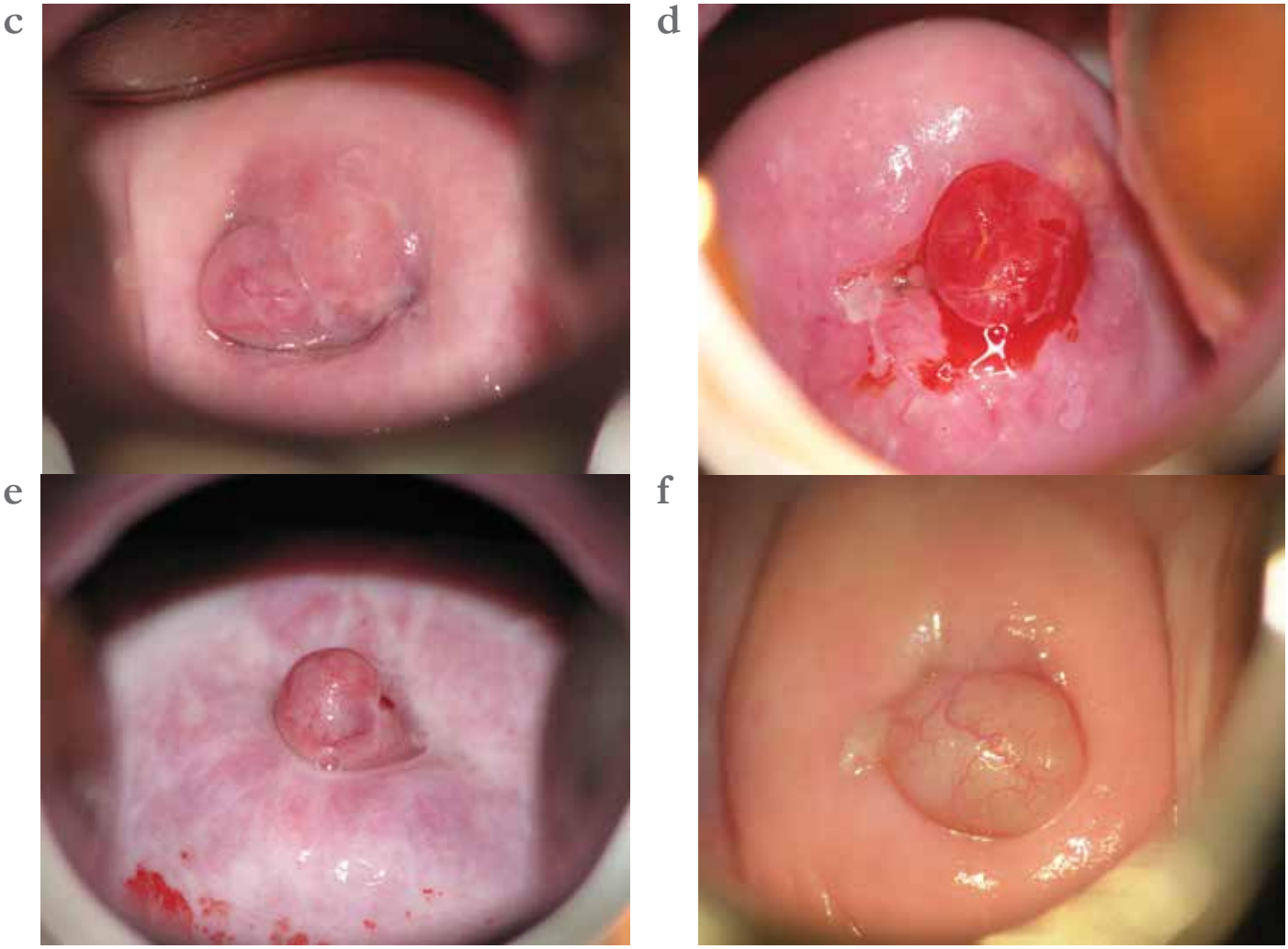

Figure 1.10a Illustration of a cervix with endocervical polyps.
Figure 1.10b-f Photographs of cervixes with endocervical polyps.

Cervical polyps are common and occur in 2-5% of adult women. Endocervical polyps are much more common than ectocervical polyps. Most women who have polyps are older, between 40 and 65 years.[5]

Polyps may be associated with abnormal vaginal bleeding and discharge.[1,5] However, in most cases, polyps are non-threatening and asymptomatic. The chance of a polyp developing into cancer is small, less than 1.5%.[5]

Nabothian Cysts

Nabothian cysts are mucus-filled lumps on the surface of the cervix. They look like yellowish balls beneath the surface of the cervix, pushing outward. Usually, Nabothian cysts are only a few millimetres in diameter. However, the cysts can become as large as 3 or 4 cm in diameter.

Nabothian cysts form when squamous epithelium grows on top of columnar epithelium during squamous metaplasia. The new squamous epithelium covers and blocks the openings of glands in the columnar epithelium, trapping mucus. Sometimes, the mucus secretions push blood vessels outward such that blood vessels become visible on the surface of Nabothian cysts.

Often, Nabothian cysts form after vaginal birth. Less often, cysts form in response to chronic inflammation as occurs from chronic cervicitis, a long-term infection of the cervix.

Nabothian cysts are common and almost always nonthreatening.[2] The cysts nearest the vagina may mark the original squamocolumnar junction.

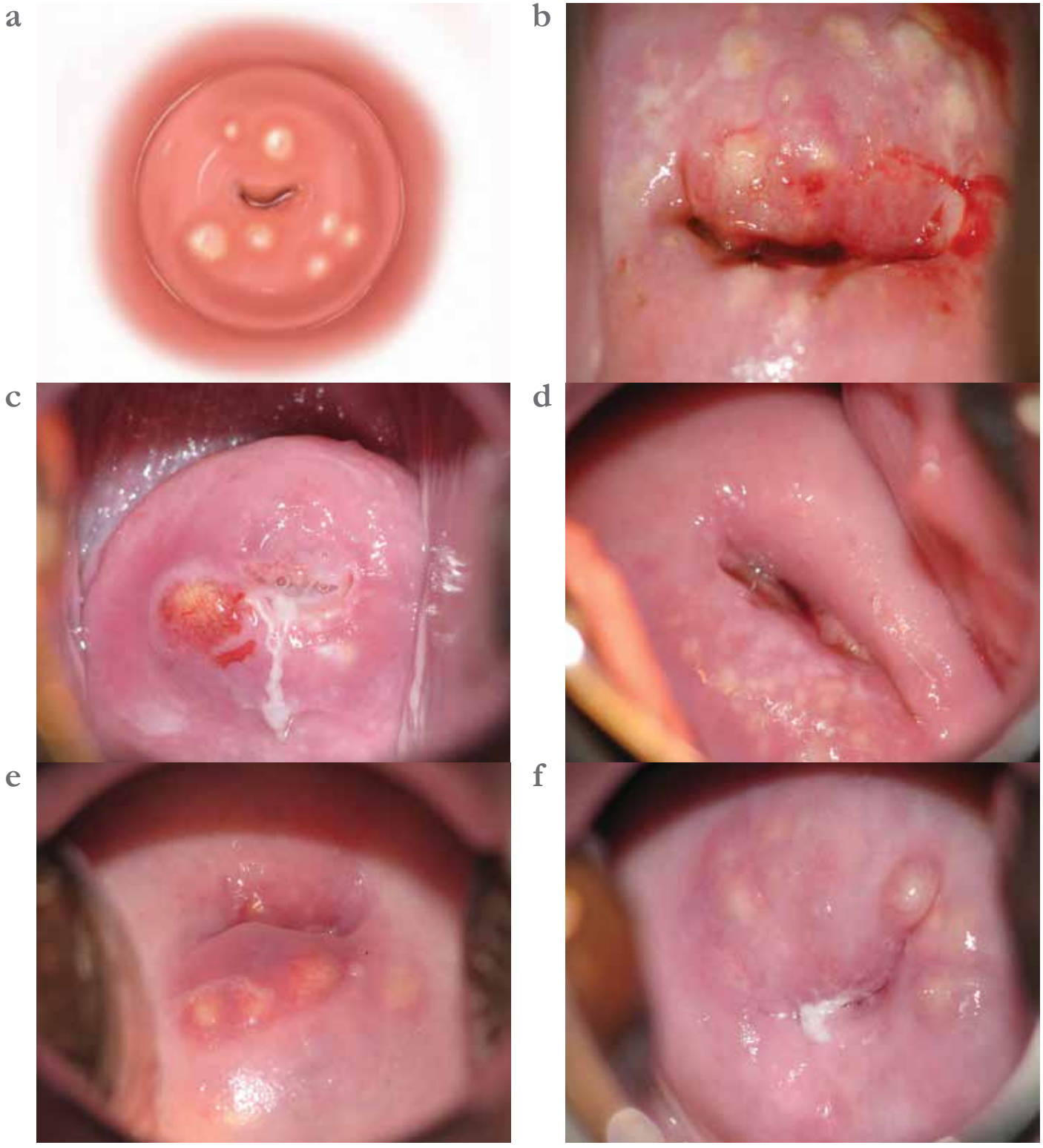

Figure 1.11a Illustration of a cervix with Nabothian cysts.
Figure 1.11b-f Photographs of cervixes with Nabothian cysts.

Chapter 1 Summary

- The **cervix** is the lower part of the uterus, or womb.
- The part of the cervix closest to the main body of the uterus is called the **endocervix**. The part closest to the vagina is called the **ectocervix**.
- The opening of the ectocervix into the vagina is called the e**xternal os**. The opening of the endocervix into the uterus is called the **internal os**.
- **Squamous metaplasia** occurs when squamous epithelium on the cervix grows over and replaces columnar epithelium. Squamous metaplasia takes place gradually as a woman ages.
- The **squamocolumnar junction** is the location where the squamous epithelium on the ectocervix meets the columnar epithelium.
- The **transformation zone** is the area between the old squamocolumnar junction and the current squamocolumnar junction.
- **Cervical ectopy** is when the ectocervix contains columnar cells, **polyps** are growths on the endocervix or ectocervix, and **Nabothian cysts** are mucus-filled lumps on the ectocervix.
- Ectopy, polyps, and Nabothian cysts are almost always benign.

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Chapter

2

Epidemiology and Natural History of Cervical Cancer

After this section, the reader will be able to...

- Differentiate between prevalence and incidence.
- Discuss the incidence and prevalence of cervical cancer in different regions of the world.
- Understand basic information about human papillomavirus (HPV).
- Diagram the process by which HPV causes cervical cancer.
- Understand the stages of cervical cancer and the terminology surrounding cervical lesions and precancer.
- Discuss the signs and symptoms of cervical cancer.
- Differentiate between primary, secondary, and tertiary prevention of cervical cancer.
- Recognize the risk factors for HPV infection and cervical cancer.

2.1 Understanding Prevalence and Incidence

Prevalence is the number of existing cases of a disease at a given time. **Incidence** is the number of new cases of a disease which develop over a period of time. Here are two examples:

- On December 31, 2011, an estimated 34 million people were living with HIV worldwide.
- Worldwide, an estimated 2.5 million people become infected with HIV each year.[45]

The first statement is an example of prevalence, because it states the existing cases of HIV at a given time. The second statement is an example of incidence, because it states the new cases of HIV which developed over a period of time.

2.2 What is Cervical Cancer?

Cervical cancer, or cancer of the cervix, is a serious disease which can cause death. However, if recognized and treated early, it can be easily prevented. A virus called human papillomavirus (HPV) causes virtually all cases of cervical cancer.[8,32]

2.3 The Prevalence and Incidence of Cervical Cancer

Cervical cancer is the second most common cancer in women worldwide. Each year, approximately 500,000 new cases occur. In 2012, the cancer killed 266,000 women.[16]

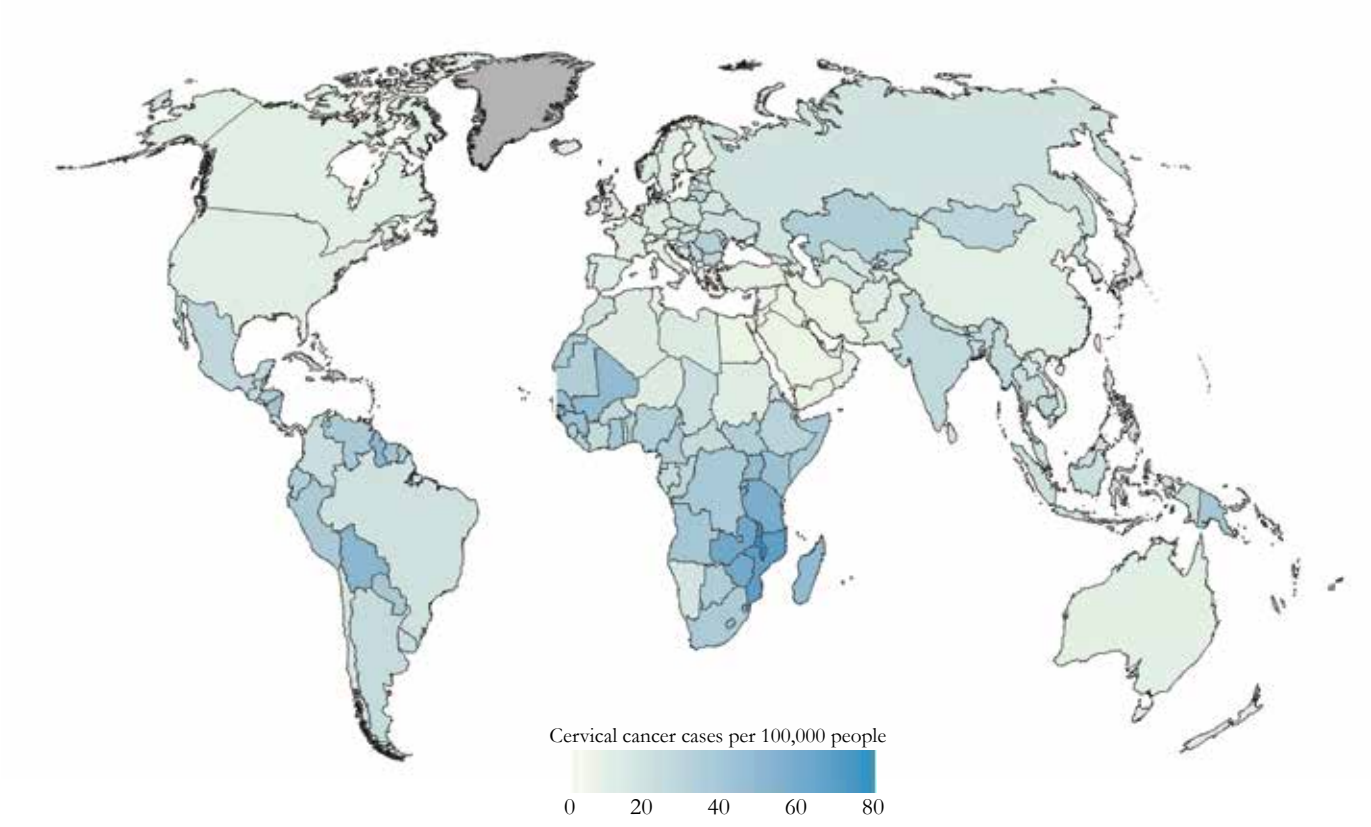


Figure 2.1 Estimated cervical cancer incidence in 2012 by country *(Source: Globocan 2012).*[16]

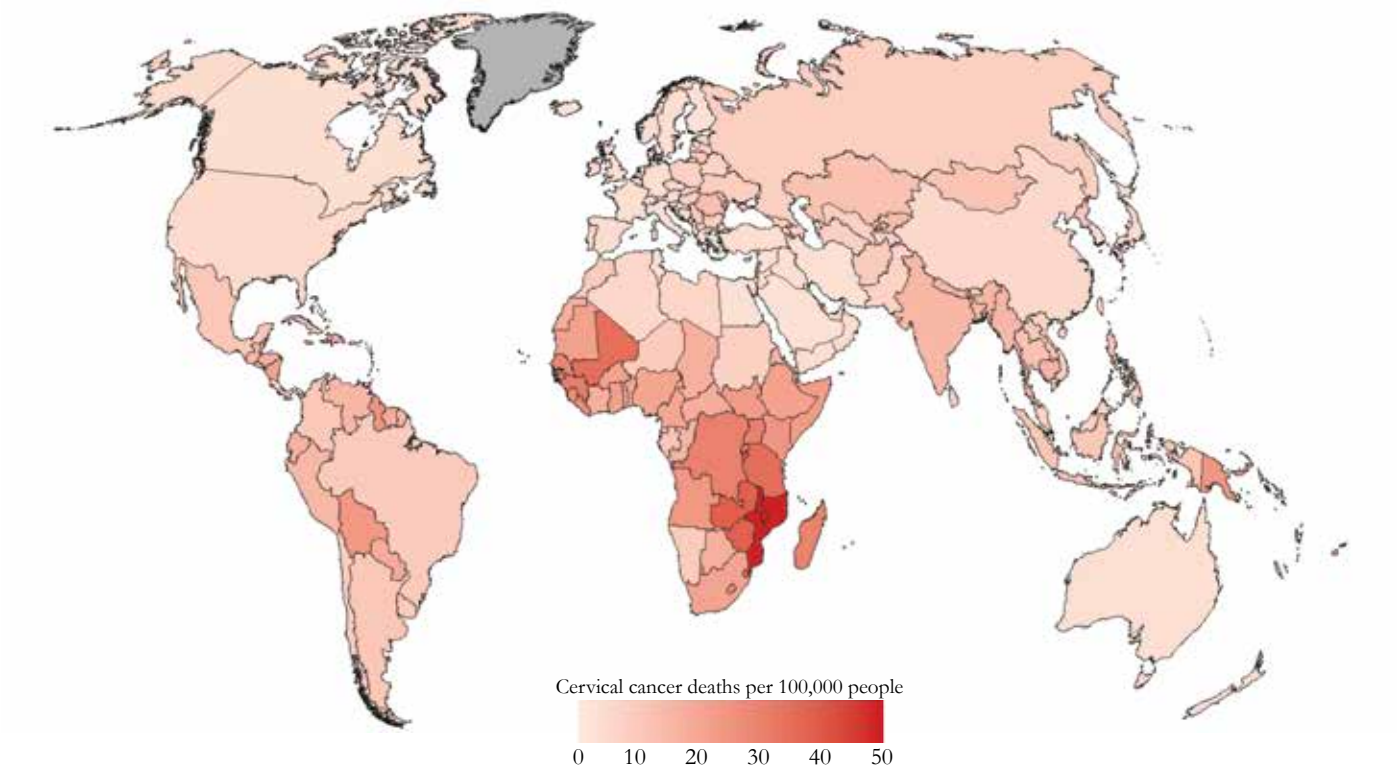


Figure 2.2 Estimated cervical cancer mortality in 2012 by country *(Source: Globocan 2012).*[16]

Cervical cancer disproportionately affects developing nations. Around 85% of all cervical cancers and 87% of cervical cancer deaths occur among women who live in developing nations. In many developing nations, it is the most common cancer in women.[16]

The Impact of Large-Scale Screening on Cervical Cancer Mortality

In several countries in North America and Western Europe, cervical cancer mortality fell dramatically when screening became widely available in the 1950s, 1960s and 1970s.[9,25,36] For instance, between 1952 and 2006, cervical cancer mortality decreased 83% in Canada following the gradual introduction of free screening.[9,10] In England, a re-launch of the cervical cancer screening programme in 1988 reduced cervical cancer mortality over 60% in women younger than 55.[38] In countries without large-scale cervical cancer screening, cervical cancer incidence remains mostly unchanged over the past century.[23]

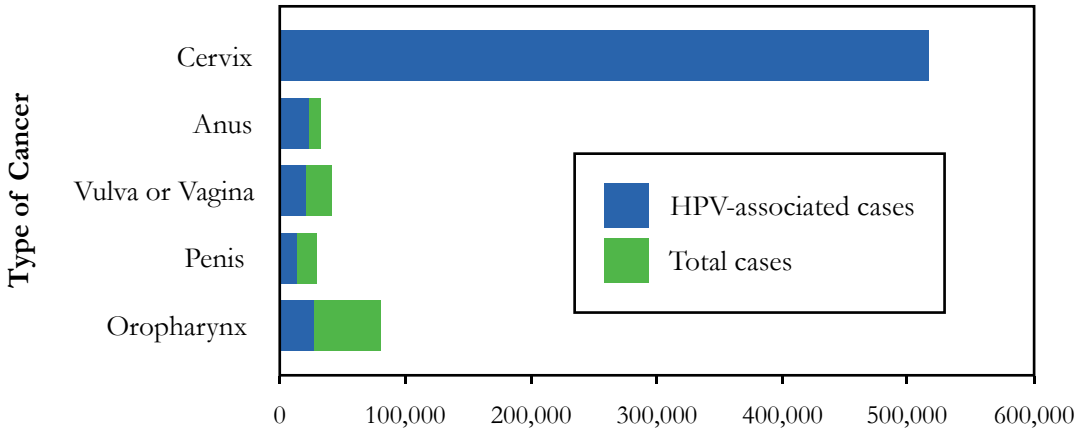
2.4 The Principal Cause of Cervical Cancer: Human Papillomavirus (HPV)

A virus called **human papillomavirus** (HPV) causes nearly all cervical cancers (over 99%).[8,32,48] HPV can infect both men and women. HPV is very common; over 75% of men and women get HPV at some point in their lives and some may be repeatedly infected.[28] Most people with HPV do not have any signs or symptoms and are unaware of the infection.[29]

HPV is a sexually transmitted infection (STI). A person can get the virus through any kind of genital contact with someone who has HPV.[50]

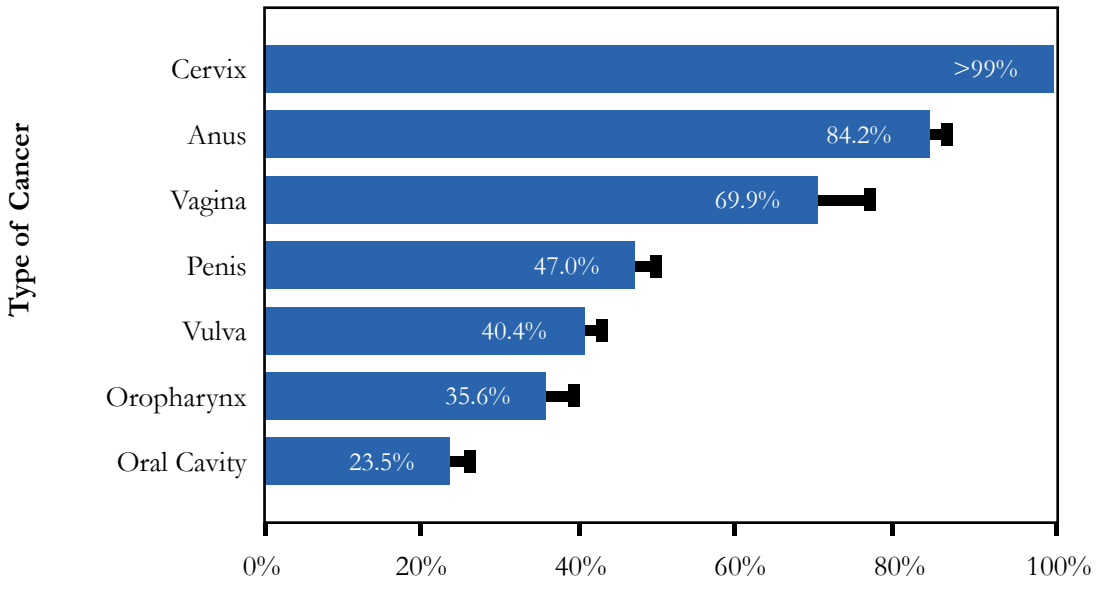
In both men and women, HPV causes almost all cases of **genital warts** and can cause cancers of the anus, oral cavity (mouth), and oropharynx (throat).[26,32] HPV can also cause cancers of the vagina, vulva and penis.[32] These cancers are much less common than cervical cancer.[33]

Graph 2.1 Prevalence of Different HPV-Associated Cancers



Adapted from Schiller and Lowy, 2012.[40]

Graph 2.2 Estimated HPV Contribution to Different Cancers



Adapted from de Martel et al., 2012.[9]

2.5 Understanding Cervical Cancer Development

Most HPV infections of the cervix go away on their own within one or two years and do not cause cancer. However, about 10% of HPV infections persist beyond two years.[31] Persistent HPV infections can cause changes which lead to precancer and then cancer (Figure 2.3).[39]

The Development of Cervical Cancer

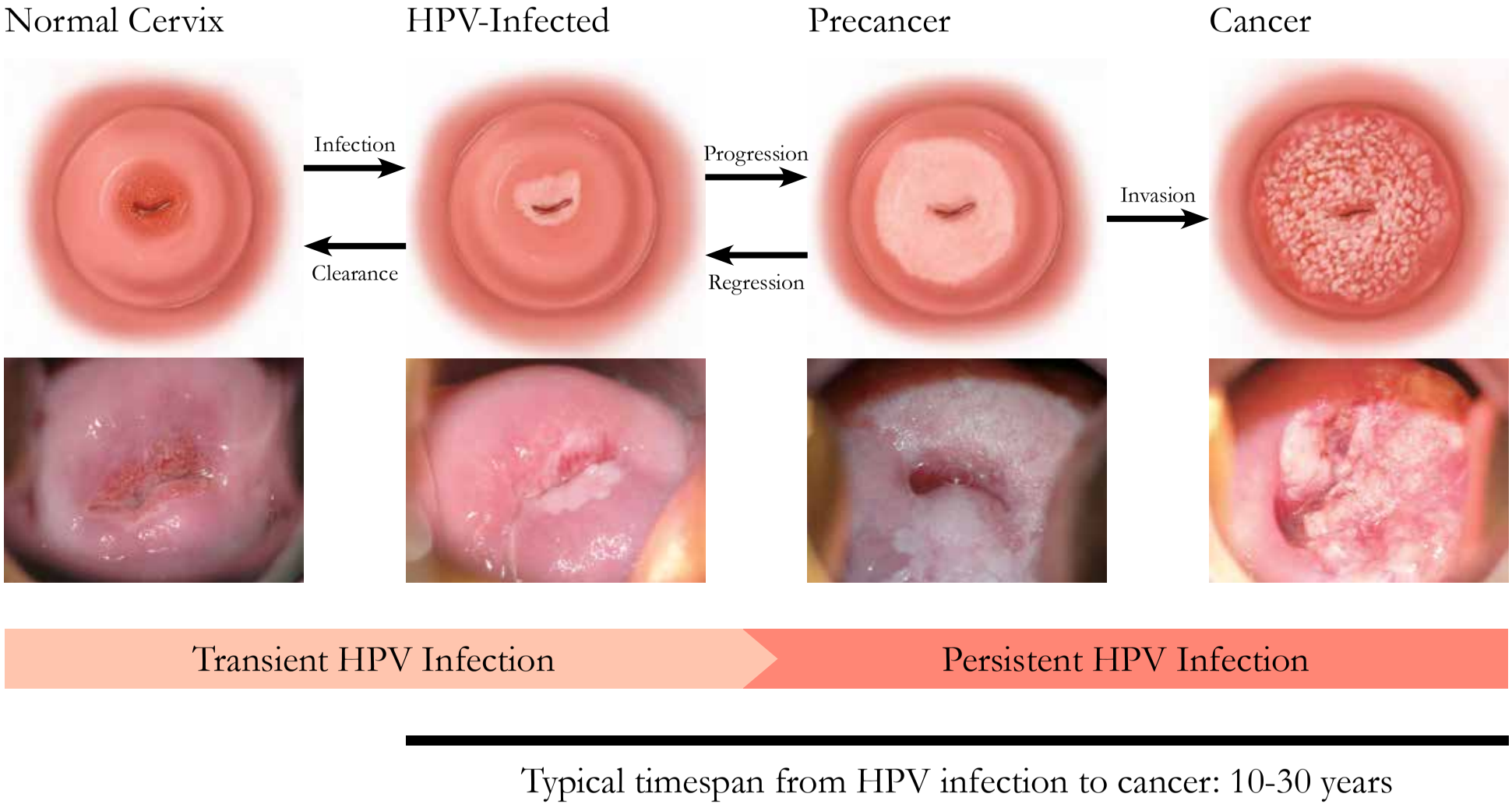
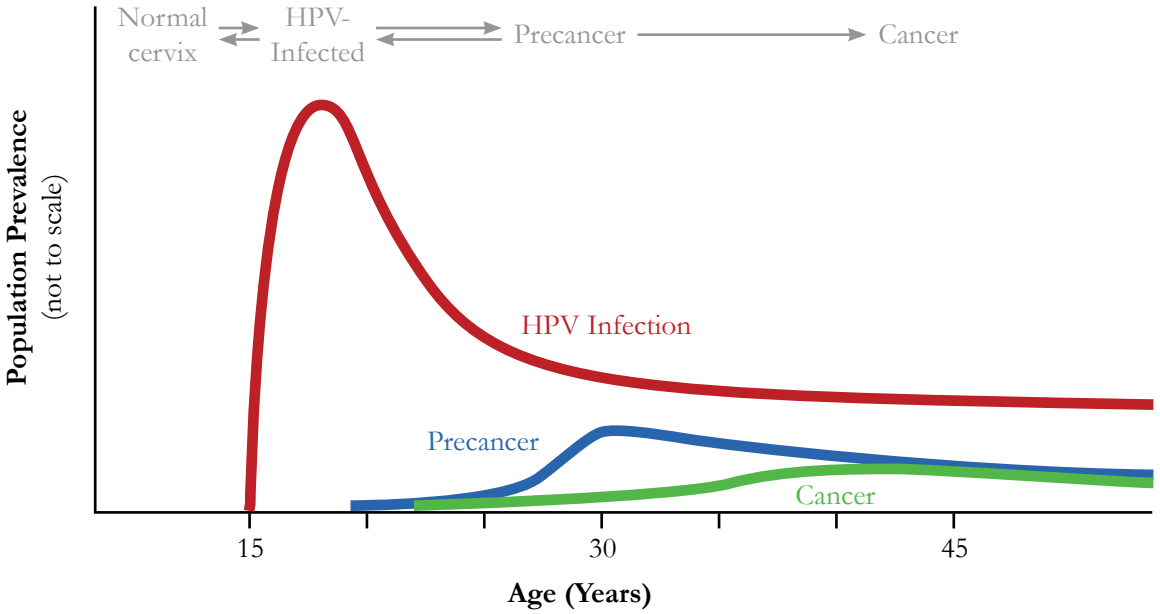


Figure 2.3 The development of cervical cancer. Cervical cancer develops according to the following steps: (1) infection with a cancer-causing HPV type; (2) HPV persistence instead of clearance, (3) development of precancer; (4) development of invasive cancer.[39]

Cervical cancer takes ten or more years to develop from the time of initial HPV infection.[31,39] Most women become infected with HPV at or soon after their first sexual encounter, between ages 15 to 25. Most cervical precancers occur in women ages 25 to 45 and most cervical cancers occur in women ages 35 to 55 (Graph 2.3).[18,39,54] In populations with a high HIV prevalence, however, cervical cancer more often strikes younger women.[15,30]

Graph 2.3 Prevalence of HPV Infection, Cervical Precancer, and Cervical Cancer by Age



Adapted from the WHO monitoring manual on cervical cancer, 2013.[53]

2.6 The Grades of Cervical Precancer

Cervical precancer is the extensive multiplication of abnormal cells in the cervical epithelium prior to and usually leading to the development of cancer. Potential cervical precancer is classified into grades depending on the severity of the disease.[11]

Terminology Surrounding Cervical Precancer

A **cervical lesion** is an area of abnormal cells on the cervix. The cervical intraepithelial neoplasia (CIN) terminology uses an internationally agreed-upon criterion to divide potentially precancerous cervical lesions into three grades: CIN 1, CIN 2, and CIN 3.[35] The grading depends on how many layers of the epithelium are involved.

CIN 1: the abnormal cells are confined to the bottom third of the cervical epithelium.
CIN 2: the bottom and middle third of the cervical epithelium contain abnormal cells.
CIN 3: all three layers (bottom, middle, and upper) of the epithelial layer contain abnormal cells.[39]

In 1969, the World Health Organization began using mild, moderate, and severe dysplasia and carcinoma in situ (CIS) to describe the severity of precancerous cervical lesions.[52] Dysplasia is when cells become abnormal and change in size, shape, or organization. Dysplasia should not be confused with metaplasia, described on page 4. Carcinoma in situ (CIS) occurs

when dysplastic cells occupy the entire thickness of the cervical epithelium (all three layers).[19] CIS used to be called "stage 0" cervical cancer, but that terminology is no longer used.[47] Most healthcare professionals no longer use mild, moderate, and severe dysplasia and CIS to describe lesions.[19]

Severe dysplasia and CIS are now known to have equivalent biological significances and both are precancerous. The CIN system does not differentiate between severe dysplasia and CIS.[19] CIN 1 corresponds to mild dysplasia, CIN 2 corresponds to moderate dysplasia, and CIN 3 corresponds to both severe dysplasia and CIS.[11]

In 1998, a US National Cancer Institute workshop created the Bethesda System for Reporting Cervical Cytology, later revised in 2001.[42] The Bethesda system classifies potentially precancerous squamous cervical epithelial cells into the following categories according to appearance.

1. Atypical squamous cells (ASC).
2. Low-grade squamous intraepithelial lesions (LSIL or LGSIL).
3. High-grade squamous intraepithelial lesions (HSIL or HGSIL).

Atypical squamous cells (ASC) do not have a normal appearance but are not clearly precancerous. ASC can be further divided into atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells cannot exclude HSIL (ASC-H). **LSIL** cells appear slightly precancerous and **HSIL** cells appear highly precancerous. Generally, LSIL corresponds to CIN 1, while HSIL corresponds to CIN 2/CIN 3. The Bethesda system is widely used.[11,12,27]

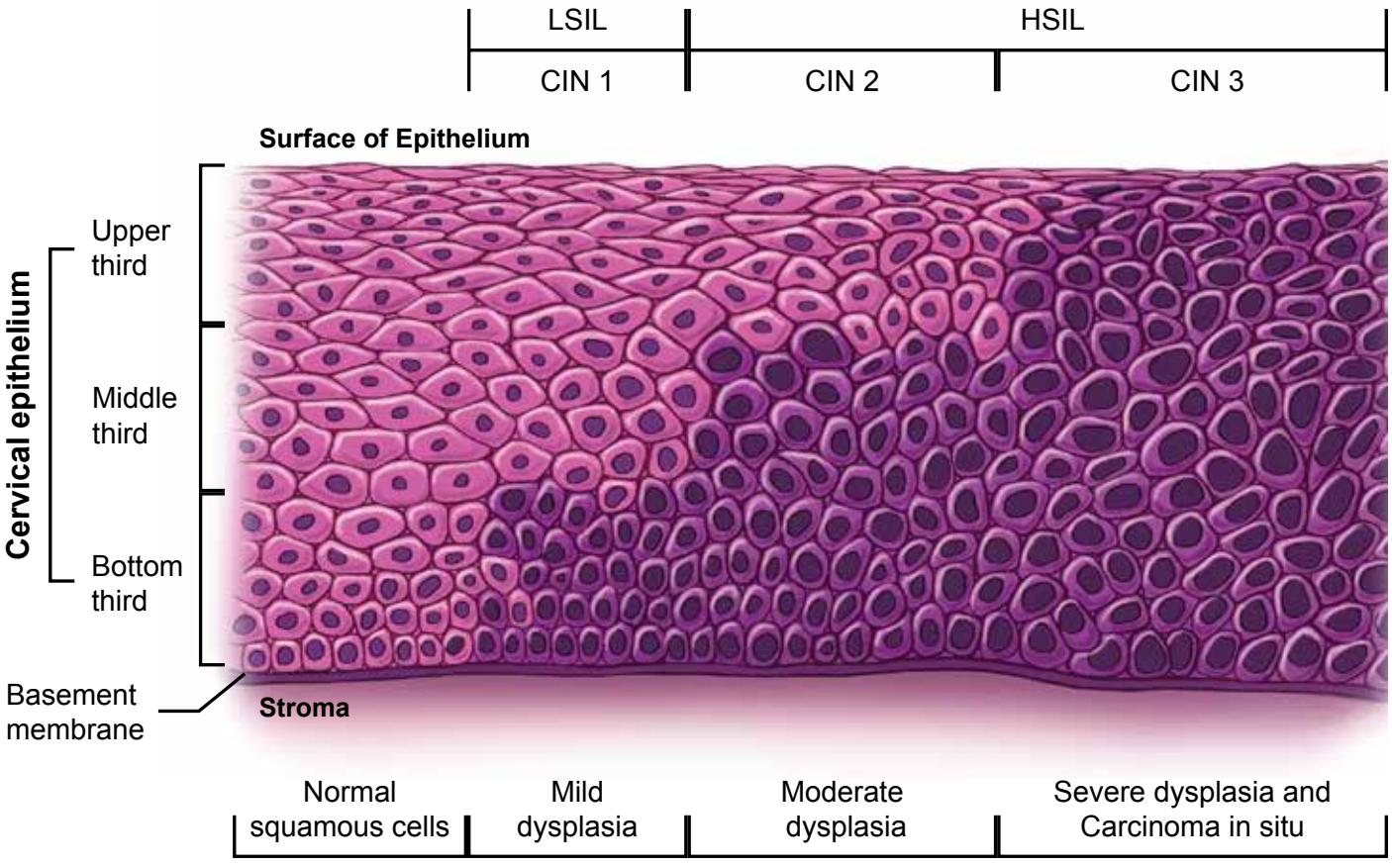


Figure 2.4 The grades of cervical precancer. Abnormal cells are darker purple.

Appropriate Use of the Term "Cervical Precancer"

The term "cervical precancer" generally refers to HSIL. Because LSIL lesions usually clear without treatment, LSIL is not considered cervical precancer.[5,39] Notably, the natural history of LSIL lesions have not been adequately studied in women immunosuppressed from HIV, malnutrition, or other causes.

2.7 The Stages of Cervical Cancer

The Stages of Cervical Cancer

Cervical precancer becomes cancer when the abnormal cells spread below the epithelial layer down into the deeper tissues (**stroma**) of the cervix, a process called **invasion**. Cervical cancer is classified into stages, according to the International Federation of Obstetrics and Gynaecology (FIGO) classification system.[47]

Stage 1A: The cancer remains confined to the cervix and can only be seen when looking at the tissue under a microscope because when examining the client, the cervix looks normal to the naked eye.

Stage 1A can be divided into sub-stages 1A1 and 1A2. In stage 1A1, the cancer has grown 3 mm or less down into the stroma and extends up to 7 mm in width (Figure 2.5a). In stage 1A2, the cancer has grown more than 3 mm but no more than 5 mm into the stroma and extends up to 7 mm in width (Figure 2.5b).

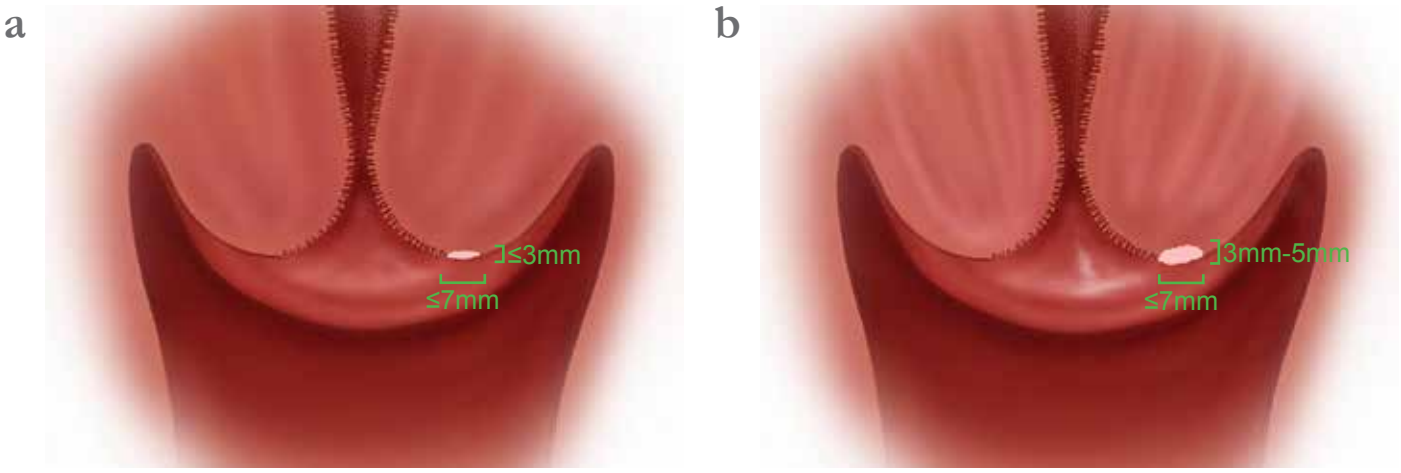


Figure 2.5a Stage 1A1 cervical cancer. Cancer is depicted in white.
Figure 2.5b Stage 1A2 cervical cancer.

Stage 1B: The cancer is visible to the naked eye during clinical examination. Stage 1B can be divided into sub-stages 1B1 and 1B2. In stage 1B1, the cancer is more than 5 mm deep or 7 mm in width, and has grown up to or equal to 4 cm in size (Figure 2.6a). In stage 1B2, it has grown more than 4 cm in size (Figure 2.6b).

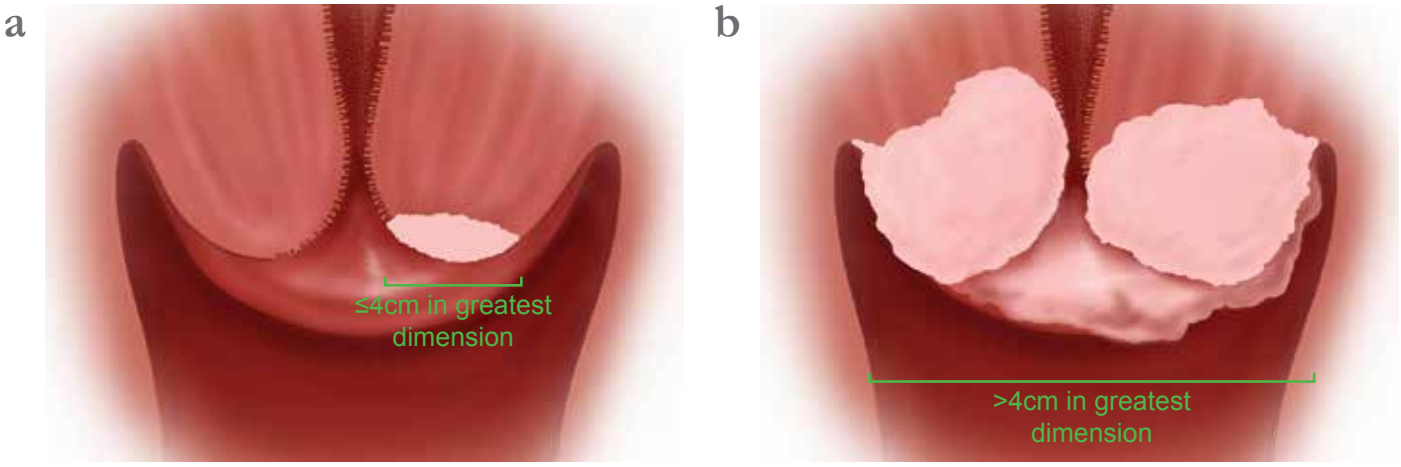


Figure 2.6a Stage 1B1 cervical cancer.
Figure 2.6b Stage 1B2 cervical cancer.

Stage 2A: The cancer has spread beyond the cervix down along the vagina, but not to the lower third of the vagina. Stage 2A can be divided into sub-stages 2A1 and 2A2. In stage 2A1, the cancer is 4 cm or less in size (Figure 2.7a). In stage 2A2, the cancer is more than 4 cm in size (Figure 2.7b).

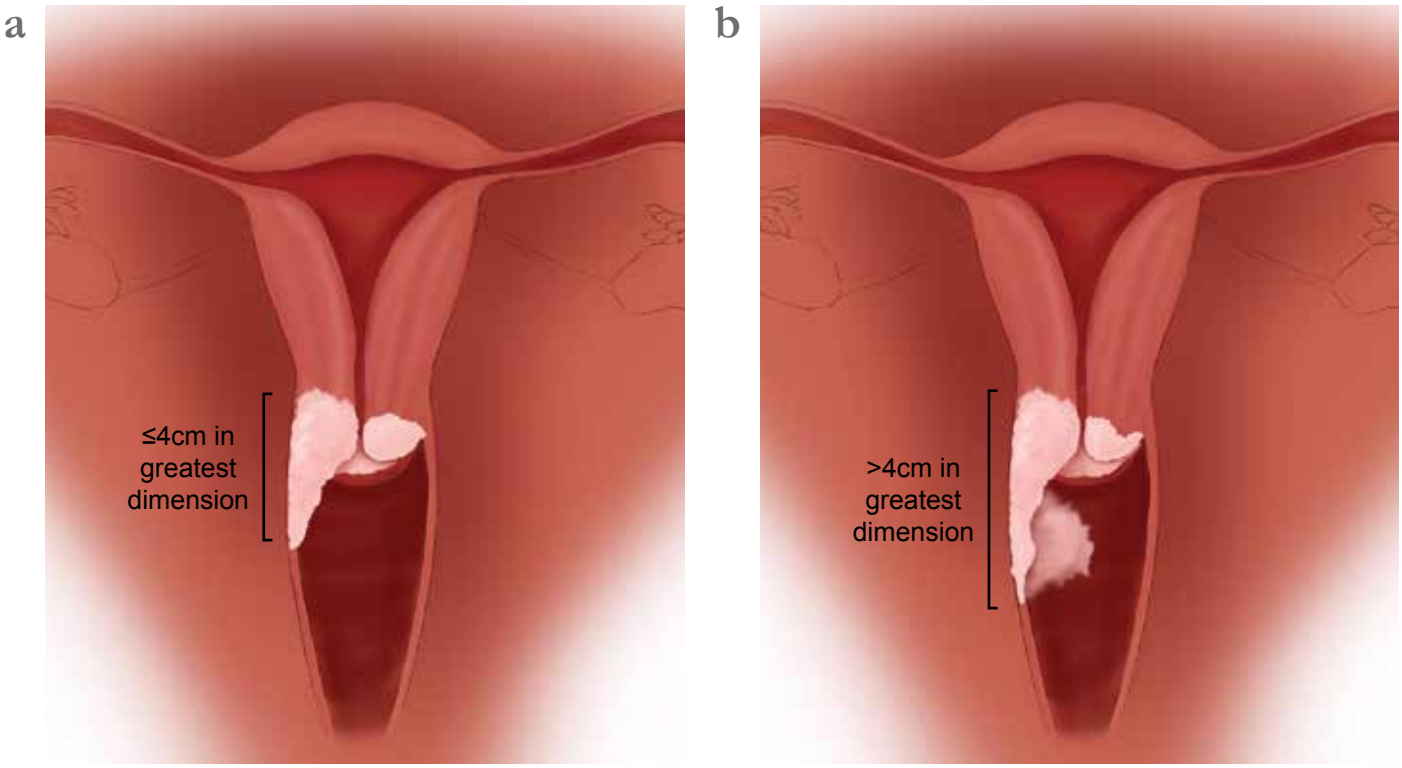


Figure 2.7a Stage 2A1 cervical cancer.
Figure 2.7b Stage 2A2 cervical cancer.

Stage 2B: The cancer has spread into the tissues surrounding the cervix, called the parametrium (Figure 2.8).

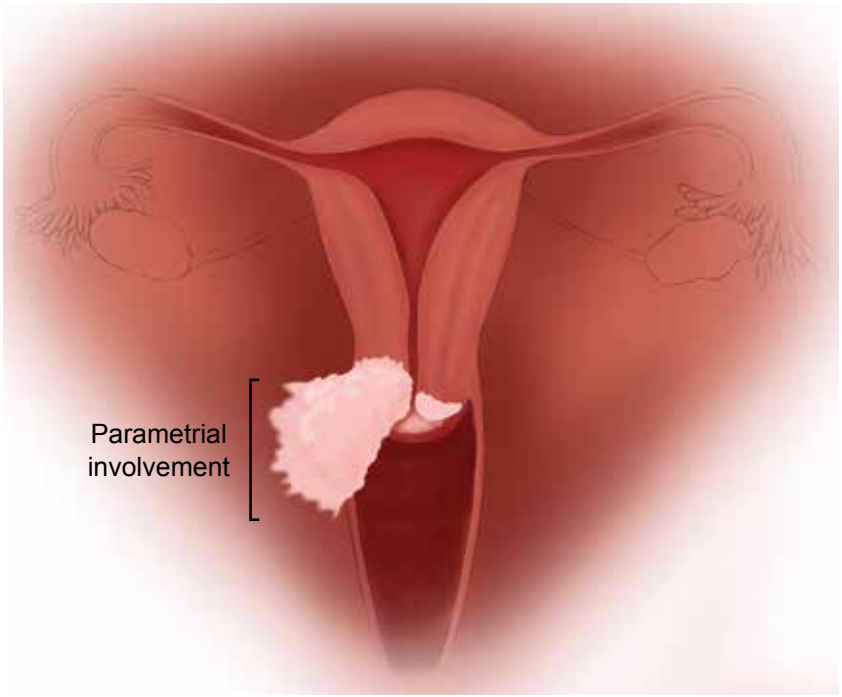


Figure 2.8 Stage 2B cervical cancer.

Stage 3A: The cancer has spread into the lower third of the vagina (Figure 2.9).

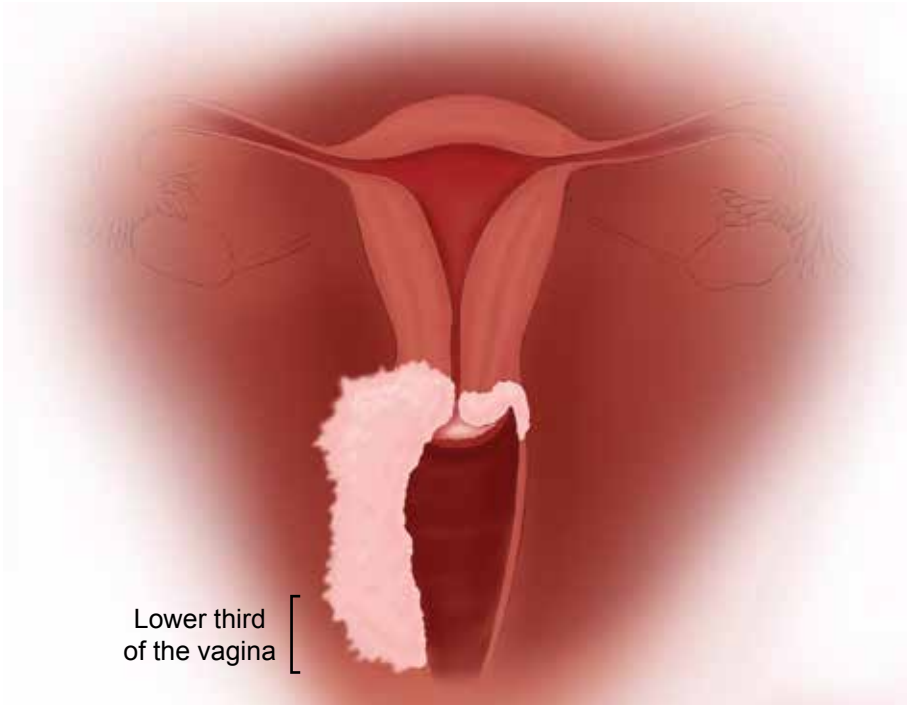


Figure 2.9 Stage 3A cervical cancer.

Stage 3B: The cancer has either spread out to the pelvic wall or is blocking one or both of the tubes (ureters) that drain the kidneys (Figure 2.10).

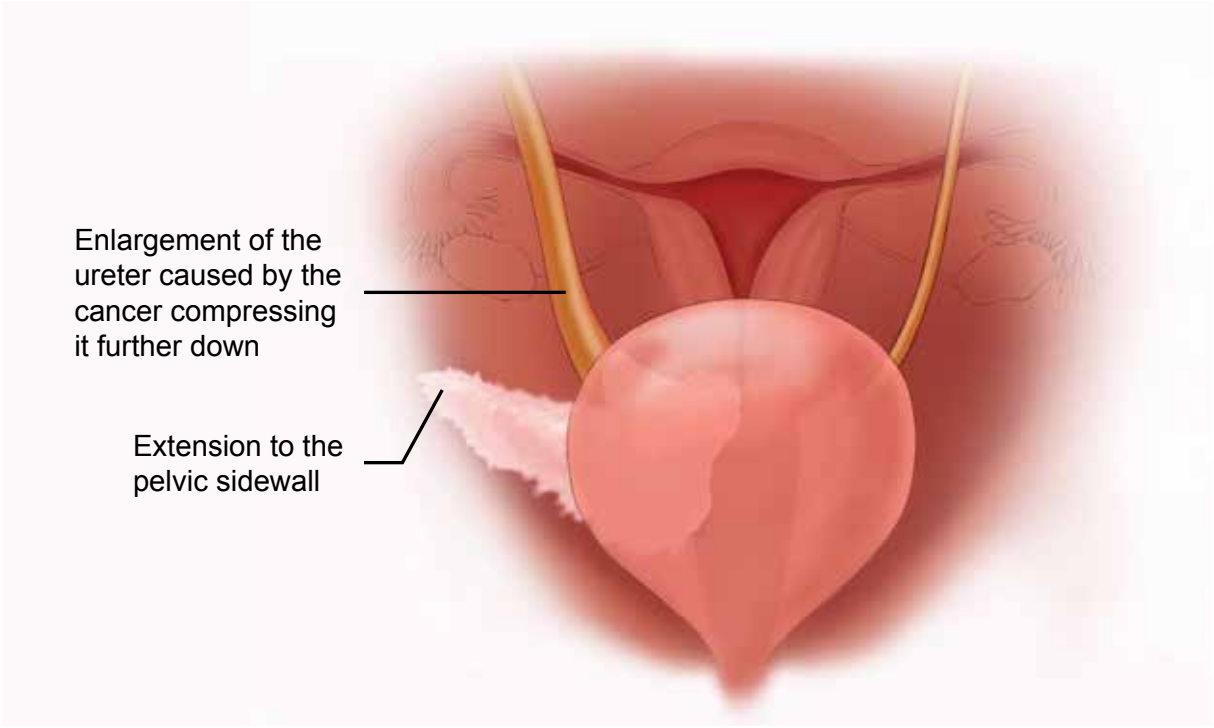


Figure 2.10 Stage 3B cervical cancer.

Stage 4A: The cancer has spread to nearby organs such as the bladder or rectum (Figure 2.11).

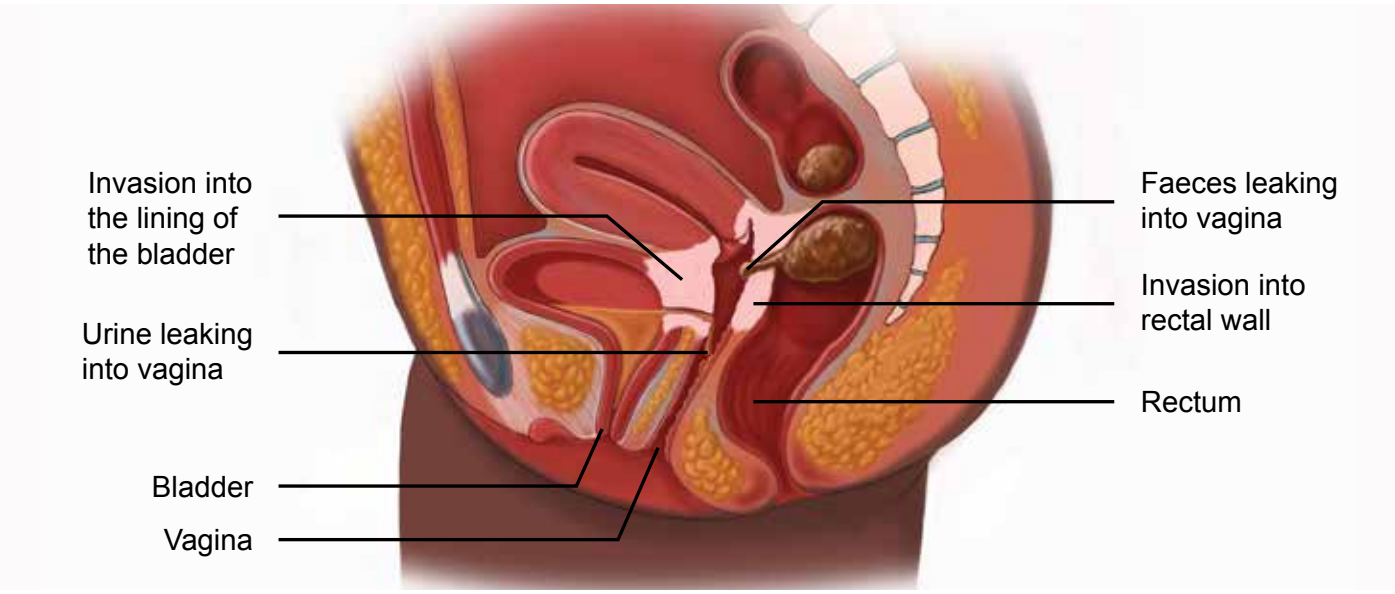


Figure 2.11 Stage 4A cervical cancer.

Stage 4B: The cancer has spread to faraway organs, such as the lungs (Figure 2.12).

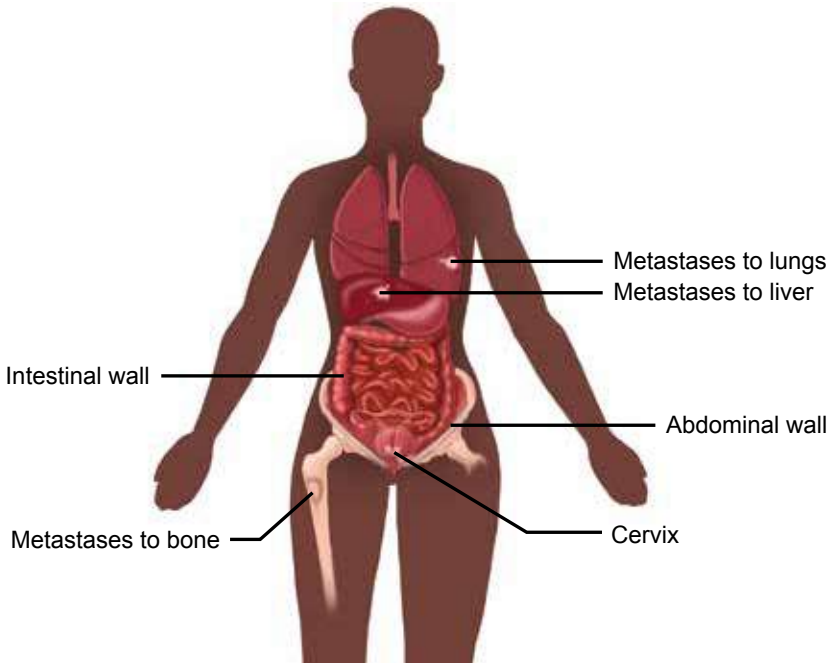


Figure 2.12 Stage 4B cervical cancer.

Using the Terms "Invasive" and "Microinvasive"

Invasive means the abnormal cells have spread from the epithelium into the stroma and become cancerous. In the past, healthcare professionals used the term "invasive cervical cancer" (ICC) to refer to stages 1A through 4B, excluding stage 0. Nowadays, stage 0 is considered precancerous and does not exist as a stage of cancer, making the terms "invasive cervical cancer" and "cervical cancer" interchangeable.

According to FIGO, **microinvasive** means the cancerous cells have spread less than 5 mm into the stroma. The term "microinvasive cervical cancer" refers to stage 1A.

2.8 The Signs and Symptoms of Cervical Cancer

Abnormal vaginal bleeding: Including bleeding after having sex, postmenopausal bleeding, and heavy bleeding in between periods.

Abnormal vaginal discharge: Every woman normally releases some discharge (fluid or mucus) from the vagina. Discharge which is different than normal, foul-smelling, pale, watery, pink, brown, or bloody can be a sign of cervical cancer.

Discomfort in back, leg, pelvis, abdomen, or after having sex[51]

2.9 Understanding Primary, Secondary, and Tertiary Prevention

Cervical cancer prevention can be divided into three categories: primary prevention, secondary prevention, and tertiary prevention. Because primary prevention cannot always prevent cervical cancer, all cervical cancer prevention programmes must incorporate secondary and tertiary prevention.[54]

Primary prevention means preventing HPV infection. The most effective and reliable primary prevention technique is vaccination against HPV. The vaccine is discussed further in chapter 3. Another primary prevention technique is living a lifestyle that minimizes the risk factors for HPV infection and cervical cancer.

Secondary prevention means preventing cervical cancer from developing. The most effective secondary prevention technique is cervical cancer screening and the treatment of cervical precancers.

Tertiary prevention means the diagnosis and treatment of cervical cancer.[17,28]

2.10 Risk Factors for HPV Infection and Cervical Cancer

Presence of HIV and Other Sexually Transmitted Infections (STIs): Infection with HIV and other STIs can weaken the immune system, leaving the body susceptible to persistent HPV infection.[20,32,46] See chapter 4 for more on HIV and cervical cancer.

Having Multiple Sexual Partners: Men and women with multiple partners are more likely to acquire HPV.[4,43] Unfortunately, because HPV infection often has no symptoms, a person cannot always tell whether or not their sexual partner has HPV.[29]

Not Using Condoms: Condom use can reduce the spread of HPV between partners. However, because HPV can infect areas not covered by the condom, condoms do not provide 100% protection from HPV infection.[41,49] However, condoms do provide significant protection against HIV and other STIs.

Smoking: Smoking is associated with a significantly increased risk of cervical cancer. Researchers believe smoking increases the risk of persistent HPV infection because it weakens the immune system.[2,13,24,44]

Low Intake of Fresh Fruits and Vegetables: Research indicates that a diet high in fruits and vegetables protects against cervical cancer.[14,34] Fresh fruits and vegetables contain nutrients which strengthen the body's immune system.[7] To stay healthy, men and women should eat five or more servings of locally available fresh fruits and vegetables each day.[3]

Having Multiple Pregnancies: Women who carry three or more full-term pregnancies have a higher risk of developing cervical cancer.[6] The reason why is uncertain.[32]

Long-Term Oral Contraceptive Use: Using oral contraceptives ("the pill") for five or more years is associated with about a doubling in the risk of cervical cancer. The risk of cervical cancer declines rapidly after stopping oral contraceptives and returns to normal within ten years of stopping.[1] Most providers agree that the benefits of oral contraceptives outweigh these risks.[37]

Young Age at First Sexual Intercourse: Several studies report that being an adolescent at sexual debut increases the risk of HPV infection and persistence. Adolescent women have immature cervixes with increased ectopy and which produce less protective mucus. Immature cervixes are thought to be more susceptible to HPV.[21]

Chapter 2 Summary

- **Prevalence** is the number of people with a disease at a given time. **Incidence** is the number of people who develop a disease during a given period of time.
- **Cervical cancer** is a deadly disease of the cervix that can be easily treated and cured if found early.
- Cervical cancer is the most common cancer among women in developing nations. Over 85% of deaths from cervical cancer occur among women living in developing nations.
- A common, sexually transmitted virus called **human papillomavirus** (HPV) causes almost all cervical cancers (over 99%).
- Most HPV infections go away on their own within 1-2 years and do not cause cancer. Only a few HPV infections persist beyond 1-2 years.
- Persistent HPV infections can cause changes to the cervix which promote cervical precancer and then cervical cancer. Persistent HPV infections take ten years or more to develop into cervical cancer.
- Usually, early-stage cervical cancer does not have symptoms. Symptoms only appear in the later stages.
- Cervical cancer prevention programmes must incorporate **primary, secondary, and tertiary prevention** strategies.

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Chapter

3

Human Papillomavirus (HPV) and the Vaccine Against It

After this section, the reader will be able to...

- Recognize the difference between low-risk and high-risk HPV.
- Understand basic information about HPV vaccination and how the vaccine prevents cervical cancer.
- Discuss the lessons learned from HPV vaccination programmes around the world.
- Identify factors which do and do not influence HPV vaccine efficacy.
- Recognize that cervical cancer screening programmes should accompany HPV vaccination programmes.

3.1 The Types of HPV: High-Risk and Low-Risk

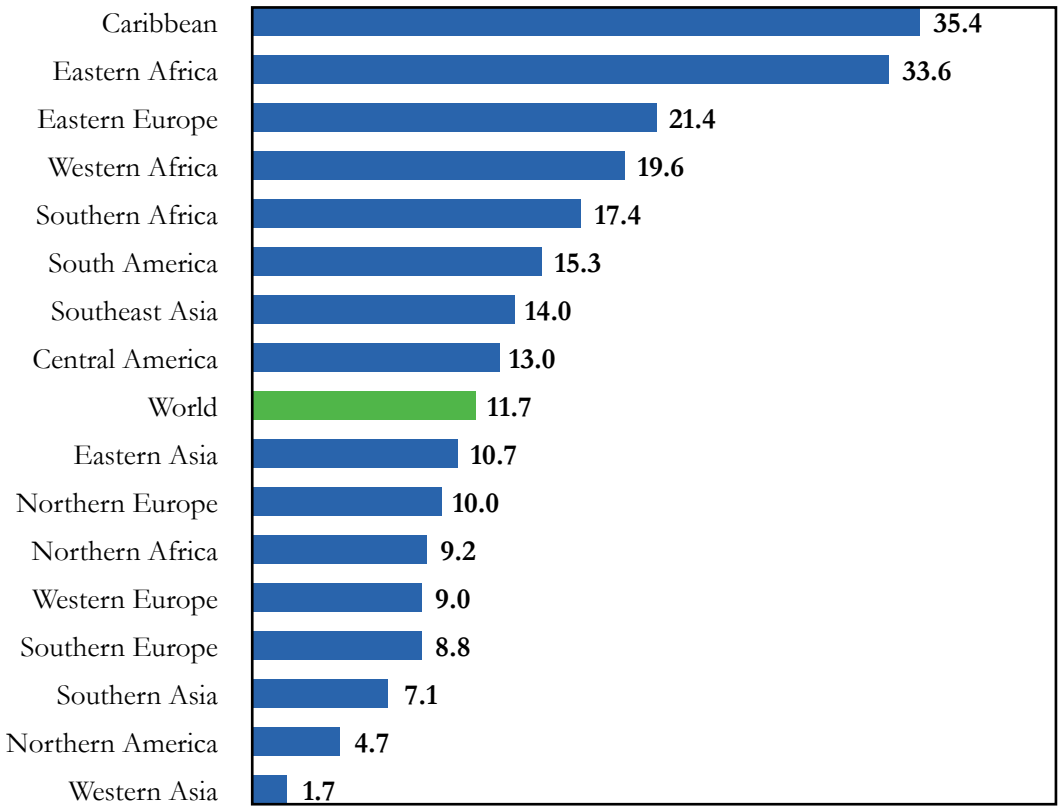
More than 100 types of human papillomavirus (HPV) exist. Only approximately 40 types of HPV can infect the genital area, including the cervix.[25] Some types of HPV can infect the oral cavity (mouth). A man or woman can be infected with multiple types of HPV at once. Often, when professionals discuss HPV without specifying, they refer to genital HPV.[12]

Scientists classify HPV types as low-risk or high-risk. **Low-risk** types do not cause cancer, but can cause genital warts. **High-risk** types are oncogenic, or cancer-causing. The two most common low-risk types associated with genital warts are HPV 6 and 11. The two most common high-risk types are HPV 16 and 18. In fact, HPV 16 and 18 alone cause over 70% of all cervical cancers.[32] Fifteen different high-risk types exist overall: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82.[1,24]

The prevalence of each type varies by region.[33] However, HPV 16 and 18 are the two most prevalent types worldwide.[5,32]

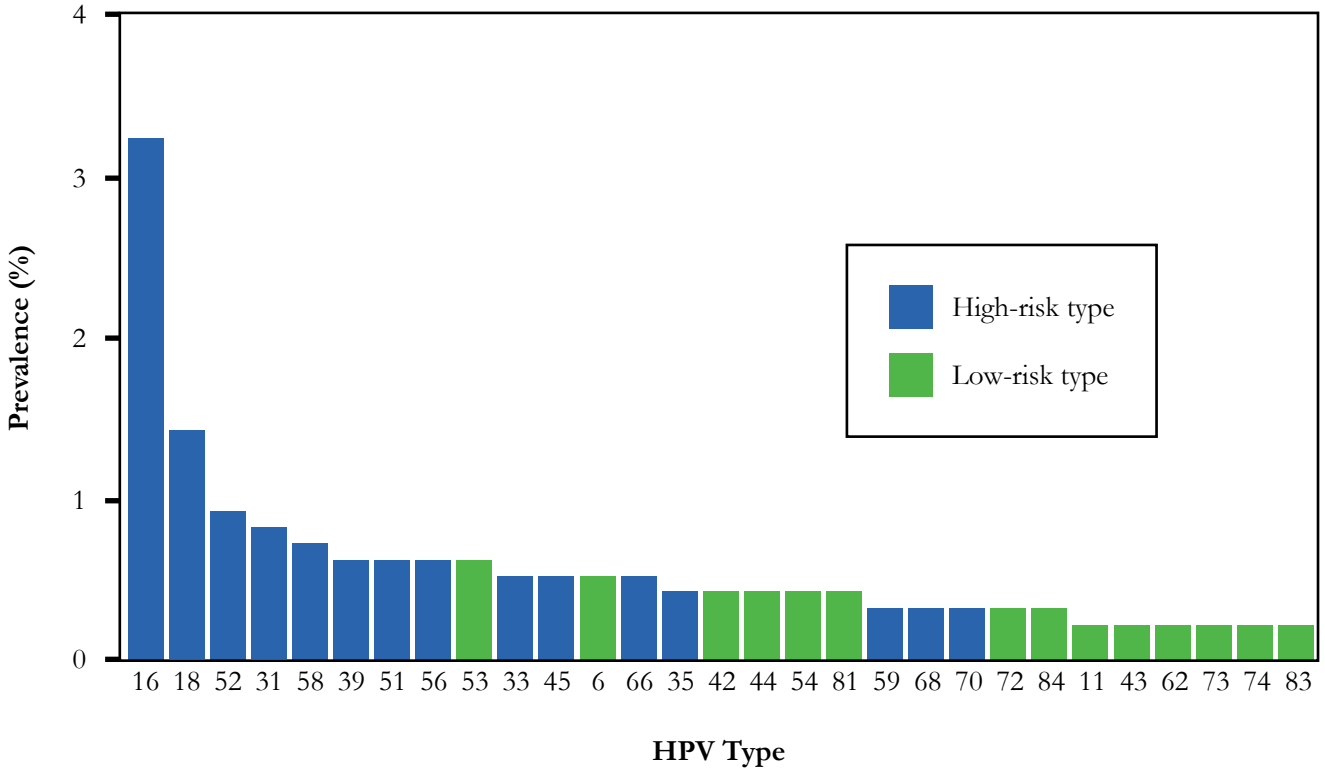
The prevalence of different high-risk types among women with cervical cancer also varies by region. HPV 16 and 18 cause 74-77% of cervical cancers in Europe, North America and Australia, but only 65-70% of cervical cancers in Africa, Asia, and South/Central America.[32] In Sub-Saharan Africa, HPV 16, 18, 45, and 35 are the most common types associated with cervical cancer, respectively.[6] In Latin America, HPV 16, 18, 31, and 58 are the most common types associated with cervical cancer.[4]

Graph 3.1 HPV Prevalence (%) in Different Regions of the World



HPV prevalence from females with normal cytology; that is, without cervical precancer or cervical cancer. Based on results from over one million women. Adapted from Bruni et al, 2010.[2]

Graph 3.2 Worldwide HPV Prevalence by Type



HPV prevalence from females with normal cytology; that is, without cervical precancer or cervical cancer. Adapted from Bruni et al, 2010.[2]

3.2 The HPV Vaccine: Essential Facts

Currently, two different HPV vaccines are licensed for use in most countries: Gardasil™ (manufactured by Merck) and Cervarix® (manufactured by GlaxoSmithKline). Gardasil™ protects against HPV 6, 11, 16, and 18, while Cervarix® protects against HPV 16 and 18.[15] Gardasil™ therefore protects against genital warts as well as cervical cancer.

To prevent HPV infection, the vaccine must be given before exposure to HPV.[13,30,34] Most girls are exposed at or soon after their first sexual encounter.[10,20] The World Health Organization (WHO) recommends administering the vaccine to girls 9-13 years of age, before the girls have sex. HIV-infected girls can be vaccinated. The vaccine does not treat existing HPV infections, precancers, or cancers.[13,30] The vaccine is given as an injection in the upper arm. For a girl to be fully protected, she should receive three doses of the HPV vaccine.[17]

GARDASIL™
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

Cervarix®
Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant

Figure 3.1 Logos for the Gardasil™ and Cervarix® HPV vaccines.

Table 3.1 Dose Schedule for HPV Vaccine

	Gardasil™	Cervarix®
First dose	0 months	0 months
Second dose	2 months	1 months
Third dose	6 months	6 months

The HPV vaccine has been tested in thousands of men and women around the world. Serious side effects are rare.[8,23,29] Occasional mild side effects include pain at the injection site, headache, fever, nausea, and fainting. Sitting or lying down for fifteen minutes after vaccination can help prevent fainting.[22]

Gardasil™ and Cervarix® are made from particles of the outer coating of the virus, referred to as virus-like particles (VLPs). The vaccines do not contain live virus and cannot cause HPV infection.[15]

3.3 HPV Vaccination Programmes Around the World: Lessons Learned

Currently, national HPV vaccination programmes exist in 61 countries and pilot HPV vaccination programmes exist in 38 countries.[3] The programmes use a variety of delivery strategies, including school-based vaccination, delivery through health centres, and delivery alongside other existing community-based programmes. The WHO encourages countries to conduct pilot programmes to determine the best delivery strategy prior to implementing national programmes.[34] Rigorous evaluations of HPV vaccination pilots conducted globally have resulted in some common lessons learned.

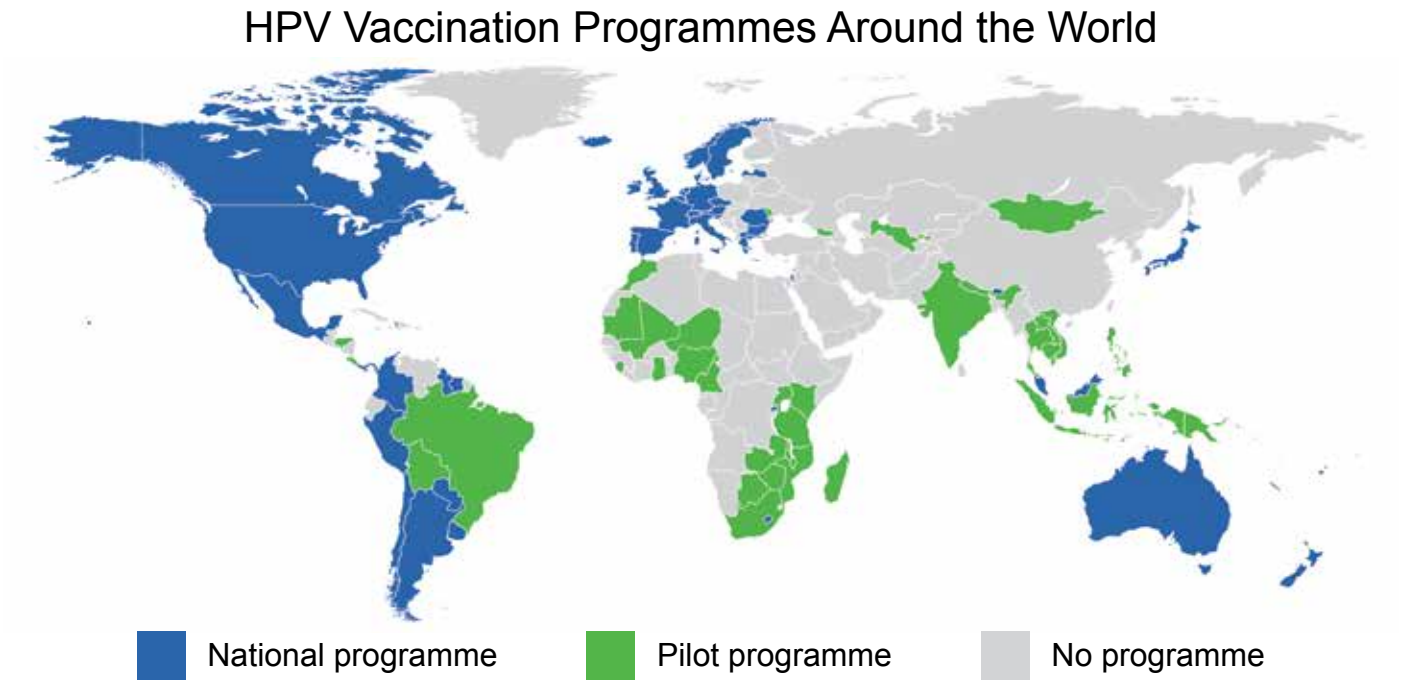


Figure 3.2 Map adapted from Cervical Cancer Action.[3]

Delivery Strategy

School-based vaccination programmes have been highly successful, especially in areas with high school enrolment.[31] School-based vaccination requires careful micro-planning and coordination to ensure vaccine delivery does not disrupt school activities and does not occur during holidays. Different approaches are needed to reach girls who are not attending school and may be especially at risk.

Health Messaging

HPV vaccination programmes have required visible government endorsement to be successful. As with any vaccination programme, rumours can quickly undermine an HPV vaccination programme.

Vaccination Costs

Managers must evaluate both the vaccine costs and operational costs before starting a programme. Support from GAVI alliance and the vaccine manufacturing industry can reduce vaccine costs in low-resource environments.[34]

For more information about lessoned learned from HPV vaccination pilots, visit the RHO Cervical Cancer website at http://www.rho.org/.

3.4 How Effective is the HPV Vaccine?

The HPV vaccine is remarkably effective.[17] In clinical trials supported by Merck, GlaxoSmithKline, and the US National Cancer Institute, both Gardasil™ and Cervarix® prevented 100% of HPV 16- and 18-associated CIN 3 in young women who had received at least one dose four years previously and who had no evidence of genital HPV infection at enrolment.[19,26] Gardasil™ conferred >95% protection against genital warts in women.[26,31]

In 2011, clinical trials found Gardasil™ highly effective at preventing anal HPV infection, genital warts, and anal precancers in young men who had no evidence of HPV 16 or 18 infection at enrolment.[11,27] In developed countries, where screening has dramatically reduced the rate of cervical cancer, a greater fraction of HPV-mediated cancers occur in men. As such, several countries now offer or recommend the HPV vaccine for men.[7] In most developing countries, however, HPV vaccination programmes only target women due to limited resources for vaccination and the high prevalence of cervical cancer.[16]

Table 3.2 Efficacy of Gardasil™ and Cervarix®

Protection Against	Sex	Age	Vaccine	Trial Requirement	Efficacy (95% confidence interval)
CIN 3	Female	15-25	Cervarix®	ITT-naive**	100% (90.5-100)
CIN 3	Female	15-26	Gardasil™	ITT-naive	100% (85.5-100)
Genital warts	Female	15-26	Gardasil™	ITT-naive	96.4% (91.4-98.9)
AIN*	Male	16-26	Gardasil™	PPE***	77.5% (39.6-93.3)
Genital warts	Male	16-26	Gardasil™	PPE	89.4% (65.5-97.9)

Adapted from Schiller and Lowy, 2012.[31]
**AIN stands for anal intraepithelial neoplasia, a precursor to anal cancer.*
***ITT-naive means participants received at least one dose of the vaccine four years previously and had no evidence of genital HPV infection at enrolment.*
****PPE means participants received three doses of the vaccine and had no evidence of genital HPV infection until after the vaccination schedule was completed.*

Evidence exists that Gardasil™ and Cervarix® provide some protection against HPV 31 and 45, types closely related to HPV 16 and 18.[9,21] Unfortunately, Gardasil™ and Cervarix® do not provide protection against any other cancer-causing HPV types. A new vaccine which protects against nine HPV types (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58) is currently in clinical trials under Merck.[28]

Although the WHO primarily recommends HPV vaccination for girls ages 9-13, the vaccine is effective in older adolescent girls and young women who have not been exposed to HPV.[20,31] The WHO recommends HPV vaccination programmes for older adolescent girls and young women only if:

- feasible, affordable, and cost-effective;
- the programme does not divert resources from vaccinating girls ages 9-13 or screening;
- a significant proportion of older adolescent girls and young women have not been exposed.[14]

Even in developed countries, failure to complete all three doses remains a barrier to HPV vaccination programmes. However, two doses may confer the same protection as three. For example, an analysis of the 2009 Costa Rica Vaccine Trial demonstrated that two doses of the HPV vaccine provided equal protection.[18] Research to confirm this is ongoing.

The HPV vaccine does not appear to be less effective in populations with a high HIV prevalence (discussed on page 37).

3.5 Integrating HPV Vaccination with Other Programmes

Importantly, HPV vaccination does not replace the need for cervical cancer screening and treatment. The vaccine does not protect against all cancer-causing HPV types. Screening and treatment options should be available to women who cannot or have not benefited from the vaccine. Prior to introducing the HPV vaccine, countries must have a strong screening programme.

HPV vaccination programmes can raise awareness of cervical cancer to governments. Increased awareness can motivate governments develop more comprehensive approaches to cervical cancer prevention and treatment.

HPV vaccination programmes offer an excellent gateway to deliver other health interventions to pre-teen girls. HPV vaccination programmes have been combined with interventions on topics such as nutrition, exercise, smoking, and sexual health.[34]

Chapter 3 Summary

- Over 100 types of HPV exist. Only about 40 HPV types can infected the genital area, including the cervix.
- HPV types can be classified as low-risk or high-risk. **High-risk** types can cause cancer. **Low-risk** types do not cause cancer but may cause genital warts.
- Two vaccines against HPV exist, called Cervarix® and Gardasil™. Both vaccines protect against HPV types 16 and 18, which cause 70% of cervical cancers. Gardasil™ also protects against HPV types 6 and 11, which cause 90% of genital warts.
- Both vaccines work best if administered prior to HPV exposure. The vaccine cannot treat or cure existing HPV infections, cervical precancer, or cervical cancer.
- Most girls get the HPV infection at or soon after their first sexual encounter. Therefore, the WHO recommends vaccinating young girls ages 9-13.
- HIV-positive boys and girls can be vaccinated.
- The vaccines can also prevent cancers and genital warts in men and women older than 13 years who have not been exposed to HPV.
- The vaccine is being used in over 90 countries worldwide and is extremely safe.
- The HPV vaccine is given as three doses over 6 months.
- HPV vaccination does NOT replace the need for cervical cancer screening, treatment, and palliative care.
- Other health interventions for pre-teen girls can be delivered alongside HPV vaccination programmes.

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Chapter

4

The Interaction between HIV and Cervical Cancer

After this section, the reader will be able to...

- Articulate why HIV-positive women are at greater risk for cervical cancer.
- Discuss the benefits of developing cervical cancer screening programmes alongside ART programmes.
- Recognize the potential benefits and limitations of HPV vaccination in populations with high HIV prevalence.

Before the introduction of antiretroviral therapy (ART), HIV-positive women died from opportunistic infections like pneumonia and tuberculosis long before chronic disease could develop. Now, with access to ART and treatments for opportunistic infections, HIV-positive women can live much longer. The paradox of this success is that many HIV-positive women now live long enough to develop chronic diseases like cervical cancer.[6] As such, cervical cancer prevention services are critical for HIV-positive women, especially in conjunction with ART. Unfortunately, cervical cancer screening rates are often lowest in areas with the highest HIV prevalence.

4.1 HIV Prevalence, Testing, and Treatment

Human immunodeficiency virus (HIV) suppresses the immune system, leaving people vulnerable to disease and causing mild illness to become deadly.[16] In 2011, an estimated 34 million people were living with HIV. The virus causes about 1.7 million deaths and infects 2.5 million new people each year.[40]

Drugs called **antiretrovirals (ARVs)** reduce the amount of HIV in the blood. In 1997, clinicians began using combinations of three different ARVs to suppress HIV and prevent the infection from progressing.[31] This approach is called **highly active antiretroviral therapy (HAART)**. HIV-infected clients who start HAART early and adhere closely have near-normal

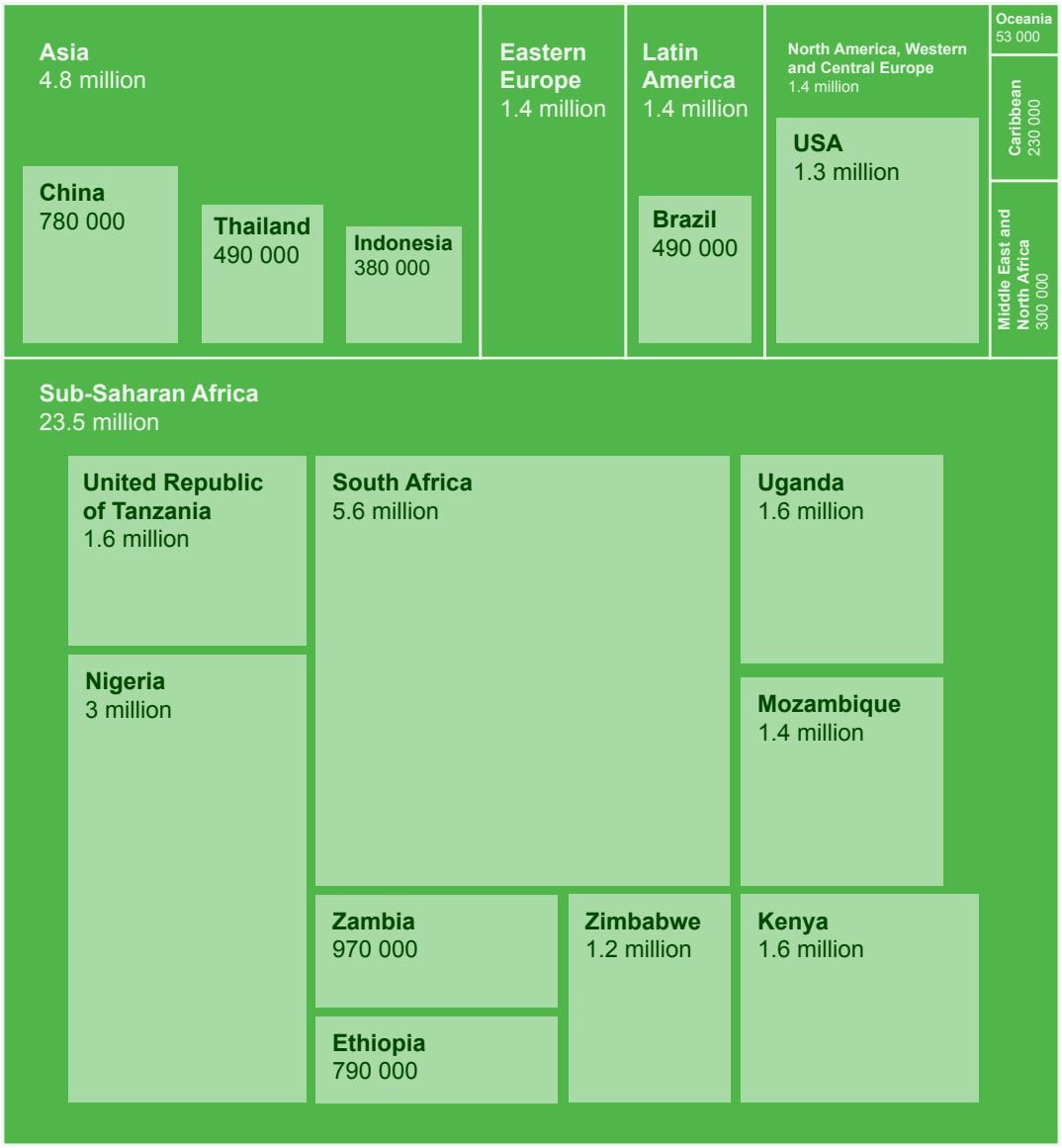


Figure 4.1 Number of people living with HIV by region in 2011. Adapted from the UNAIDS World AIDS Day Report 2012.[40]

life expectancy and immune systems.[16,24] ARVs and HAART cannot cure HIV.[9,35,37] No known cure for HIV exists at this time, but research to find a cure is ongoing.[32]

Rapid, point-of-care HIV tests take ten to twenty minutes to determine if a person is HIV-positive. Healthcare providers monitor the progression of infection in HIV-positive clients using:

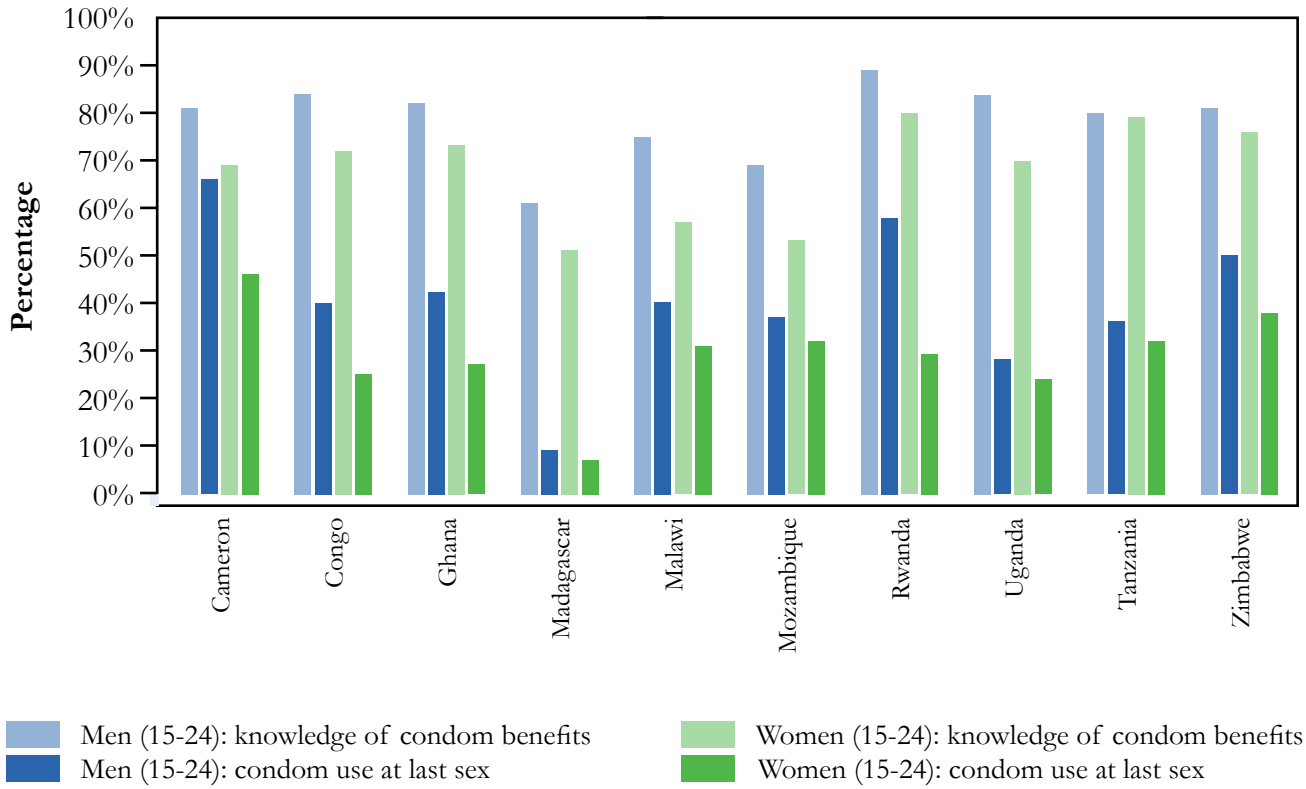
- **Viral load tests**. The HIV viral load test measures the amount of HIV in the blood. The higher the viral load, the more severe the infection.
- **CD4 cell counts**. A CD4 cell count measures the strength of the immune system. The lower the CD4 count, the weaker the immune system.

4.2 HIV in Women and Girls

HIV profoundly affects women and girls from all regions. In Sub-Saharan Africa, the region with the most HIV infections, women account for 60% of people living with HIV. Women account for over 70% of people ages 15-24 living with HIV in Sub-Saharan Africa.[40]

Gender inequalities, economic instability, war, and domestic violence decrease women's ability to consent to sex, negotiate condom use, access HIV treatment and education, and otherwise protect themselves from HIV. Fear of violence, abandonment, or discrimination if found to be HIV-positive may lead women to avoid HIV testing and treatment services.[40]

Graph 4.1 Knowledge about condoms and reported condom use at last sex (select countries in Sub-Saharan Africa)



Among men and women with more than one sexual partner in the last year. Adapted from the UNAIDS Global Report, 2012.[40]

Fortunately, the recent efforts of leaders have successfully reduced HIV transmission rates and improved access to ARVs among women in various communities. Addressing gender inequality is now a central feature of most global and national policies concerning HIV. However, much work remains to be done to universally reduce women's vulnerability to HIV and associated diseases.[12]

4.3 The Influence of HIV on HPV Infection

Compared to HIV-negative (HIV-) women, HIV-positive (HIV+) women have:

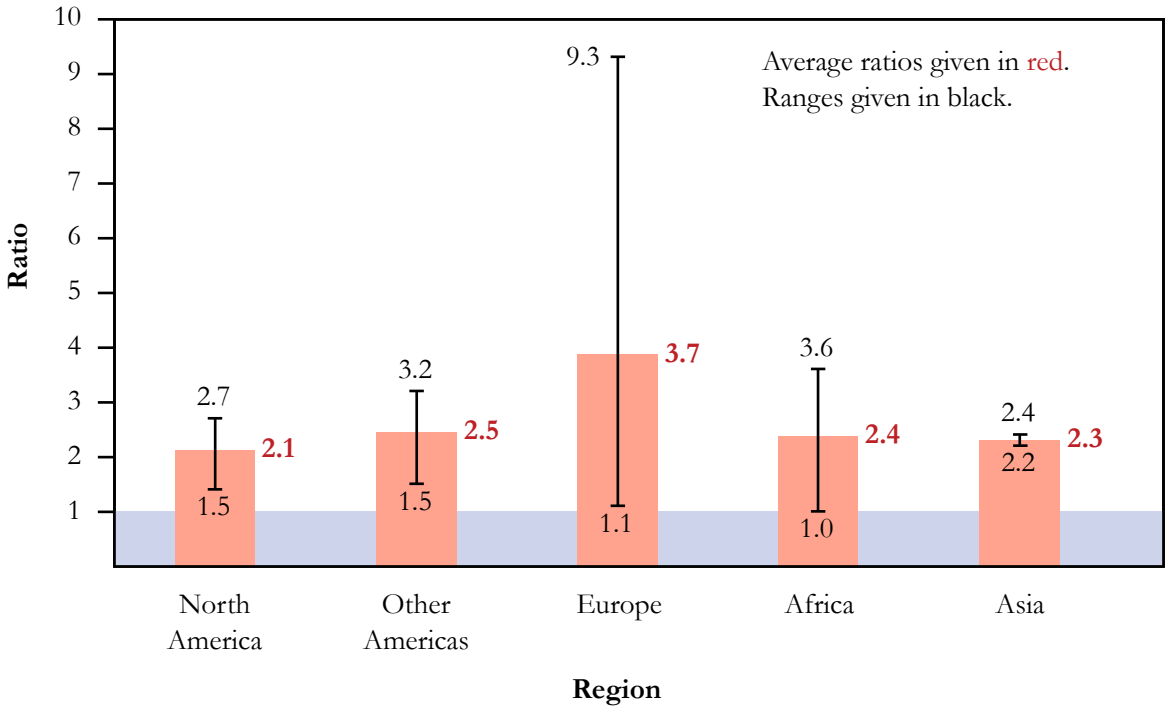
- higher rates of persistent HPV infection;[2,6,41]
- higher incidence of HPV infection;[3,25,36,38,39]
- higher prevalence of HPV;[6]
- higher likelihood of infection with multiple HPV types at once.[4,41]

HPV persists in HIV +ve women because their weakened immune systems have more difficulty clearing the infection. The weaker the immune system (lower CD4 count and higher viral load), the more likely persistence is.[41]

The reason why HPV incidence is higher in HIV +ve women is debated. One theory is that weakened immune systems make HIV +ve women more susceptible to HPV infection.[6,41]

HPV prevalence is higher because the incidence and persistence of HPV infection is higher. Whether infection with multiple HPV types increases the risk of cervical lesions is unknown.[6]

Graph 4.2 Ratio of HPV Prevalence in HIV +ve Women to HPV Prevalence in HIV -ve Women



Compiled from data from De Vuyst et al, 2008.[6]

HIV +ve women on HAART appear to have the same incidence, prevalence, and persistence of HPV infection as HIV +ve women not on HAART. This is unexpected because HAART restores the immune system to near-normal function. Further research on HPV infection in HIV +ve women on HAART is ongoing.[6]

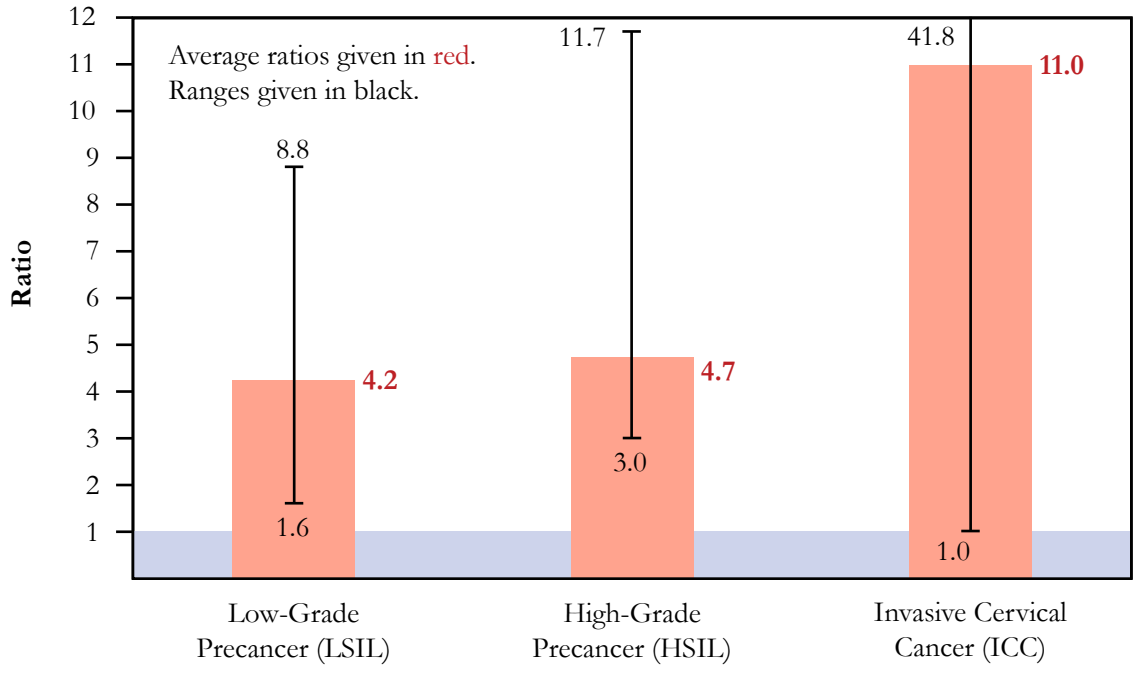
4.4 HPV Vaccination in Populations with a High HIV Prevalence

Recent studies demonstrated that HPV 16 and 18 cause the same percentage of cervical cancers in HIV +ve women as in HIV -ve women.[5,6,28,33] Therefore, the HPV vaccine is thought to be equally effective in HIV +ve and HIV -ve women, and recent research supports this.[17] Still, more research is needed to determine the vaccine's effectiveness in populations with a high HIV prevalence.[8]

Evidence exists that HPV infection increases the risk of HIV in men and women. If so, HPV vaccination may decrease HIV incidence. The potential effect of HPV vaccination on the HIV epidemic requires further study.[15]

4.5 The Influence of HIV on Cervical Cancer Development

Graph 4.3 Ratio of Cervical Lesion Prevalence in HIV +ve Women to Cervical Lesion Prevalence in HIV -ve Women



Compiled from data from De Vuyst et al, 2008.[6]

Compared to HIV -ve women, HIV +ve women have:

- higher incidence and prevalence of cervical precancer and cancer;[6,10,23]
- more rapid progression from HPV infection to cervical precancer and cervical cancer;[6]
- higher recurrence of cervical precancer and cancer after treatment.[20,21]

Persistent HPV infection significantly increases the risk of cervical precancer.[18] HIV +ve women have higher rates of cervical precancer because of higher rates of persistence.[13,38,42]

Because HPV infection rapidly progresses to cervical cancer in HIV +ve women, HIV +ve women may get cervical cancer at a much younger age.[11,26] One study reported finding a 16-year-old HIV +ve girl with stage 3B cervical cancer.[22]

Cervical precancer and cancer recurs not only more often, but more quickly in HIV +ve women.[20,21] In one study, low-grade CIN recurred in 48% of HIV +ve women compared to 1% of HIV -ve women.[21] Close post-treatment follow-up and aggressive re-treatment of recurrent precancers is needed to successfully prevent cervical cancer in HIV +ve women.[19]

The effect of HAART on cervical lesions in HIV +ve women is debated. Some studies found that HAART promotes regression of cervical lesions, while other studies did not.[1,6,41]

HAART does not appear to reduce the risk of cervical cancer in HIV +ve women. This is expected because although HAART restores the immune system to near-normal function, HAART allows HIV +ve women to live long enough to develop cervical cancer.[30,34]

Notably, HIV +ve men and women have a higher incidence and prevalence of all HPV-associated cancers, not just cervical cancer.[8,14,29] New data imply the incidence of HPV-related cancers will not decline among HIV +ve men and women on HAART.[29]

4.6 Integrating HIV Care and Cervical Cancer Prevention Services

Integrating HIV care and cervical cancer prevention services in a resource-limited setting can:

- facilitate the rapid scale-up of cervical cancer screening;
- address high rates of cervical cancer among HIV +ve women.

Potential Benefits of Integration

- Providing both services in one clinic allows HIV +ve women to access both services in one visit, reducing follow-up efforts and maximizing the client's time.
- Integrating the two services allows optimization of resources. The services can share utilities, maintenance and toxic waste disposal services, and other medical or pharmacy services.
- Placing newly-implemented cervical cancer prevention programmes within pre-existing HIV care infrastructure ensures sustainability and allows implementers to learn from the HIV care programmes.

Potential Challenges of Integration

- Stigma of cervical cancer as an "HIV-only" disease.
- Staff with competing priorities focus less on screening.
- Increased time spent in the clinic for clients.
- High level of planning and organization required.

For more information regarding the benefits and challenges of integrating HIV care and cervical cancer prevention services, access the article "Implementation of 'see-and-treat' cervical cancer prevention services linked to HIV care in Zambia" by Mwanahamuntu et al.[27]

Chapter 4 Summary

- **Human immunodeficiency virus (HIV)** suppresses the immune system, increasing susceptibility to disease.
- **Highly active antiretroviral therapy (HAART)** restores the immune system and lifespan of HIV-infected people to near-normal.
- HIV +ve women have a higher incidence, prevalence, and persistence of HPV infection.
- Unexpectedly, HIV +ve women on HAART appear to have the same incidence, prevalence, and persistence of HPV infection as HIV +ve women not on HAART.
- The HPV vaccine appears to be equally effective in populations with high or low HIV prevalence.
- HIV +ve women have a higher incidence and prevalence of cervical precancer, cancer, and all other HPV-associated cancers.
- The high incidence and prevalence of cervical cancer in HIV +ve women is thought to be due in part to HAART allowing HIV +ve women to live long enough to develop cervical cancer.
- Whether HAART promotes regression of cervical precancer in HIV +ve women is debated.
- HIV +ve women are more likely to get cervical cancer at a younger age because cervical cancer develops more quickly in HIV +ve women.
- In HIV +ve women, cervical precancer and cancer recurs more often and within a shorter time period.
- Integrating HIV care and cervical cancer prevention services confers numerous benefits.

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Chapter

5

Choosing a Cervical Cancer Screening Method

After this section, the reader will be able to...

- Conceptualize sensitivity and specificity.
- Understand what cervical cancer screening is.
- Assess the potential of a screening programme to reduce cervical cancer deaths and improve the lives of women.
- Broadly understand VIA, VILI, Pap smears, digital cervicography, and HPV testing.
- Identify why resource-limited settings use VIA and digital cervicography for cervical cancer care.
- Discuss the benefits and limitations of the screen-and-treat approach.

5.1 Understanding Sensitivity and Specificity

Sensitivity and specificity measure the accuracy of a diagnostic test. **Sensitivity** is the ability of the test to identify people with the disease as having the disease. **Specificity** is the ability of the test to identify people without the disease as not having the disease.

Calculating Sensitivity and Specificity

There are 100 healthy people. Suddenly, ten out of the 100 people become sick with a disease. A provider tests each of the 100 people for the disease.

	Test Positive	Test Negative	Total
Disease	8	2	10
No Disease	5	85	90

$$\text{Sensitivity} = \frac{\text{Test positive}}{\text{People with disease}} = \frac{8}{10} = 80\% \qquad \text{Specificity} = \frac{\text{Test negative}}{\text{People with no disease}} = \frac{85}{90} = 94\%$$

Table 5.1 Using Sensitivity and Specificity to Make Clinical Decisions

Test Characteristic	Meaning...
High Sensitivity	Almost all clients who have the disease will test positive. Therefore, we can assume that any client who tests negative does not have the disease.
Low Sensitivity	Some clients who have the disease may test negative. The provider should retest clients every few months or years to confirm that any clients who test negative do not have the disease.
High Specificity	Almost all clients who do not have the disease will test negative. Therefore, we can assume that any client who tests positive has the disease.
Low Specificity	Some clients who do not have the disease may test falsely positive. The provider should confirm that a client who tests positive actually has the disease before beginning treatment.

5.2 What is Cervical Cancer Screening?

Screening is the detection of early forms of disease in an otherwise healthy population. **Cervical cancer screening** is the detection of precancerous cervical lesions in otherwise healthy women before the lesions develop into cancer. Unlike cancer,

precancerous lesions can be easily treated and removed. The removal of precancerous lesions stops cervical cancer from developing. Because precancerous lesions take years to develop into cervical cancer,[22] even infrequent screening can detect almost all lesions before they progress to cancer.

5.3 Why Cervical Cancer Screening is Necessary

Each year, 500,000 new cases of cervical cancer occur. Around 85% of the cases occur in developing countries.[17] Screening can predict and prevent the majority of cervical cancers, even in developing settings.

Cervical cancer can have serious consequences if not found and treated early. Cervical cancer is the biggest single cause of years of life lost from cancer in the developing world, with an estimated 2.7 million years of life lost in 2000 alone.[39] Cervical cancer commonly affects women in the reproductive age group (15-49 years old), decreasing the quality and length of their lives.[27] The deaths of young women from cervical cancer has an immeasurable impact on their families, especially their children, and on the local economy. When a mother dies, her children are three to ten times more likely to die.[38]

Most cervical cancers in countries without screening programmes present at an advanced stage.[27] Unfortunately, many developing countries lack the resources to treat advanced-staged cervical cancer with radiation therapy and chemotherapy. Even when available, radiation therapy is extremely costly and often palliative rather than curative, depending on the stage of the cancer and the available medical resources. Chemotherapy, if available, may cause severe side effects including nausea and vomiting, diarrhoea, fatigue, leukopenia (low white blood cell count), anaemia, and hair loss. Cervical cancer screening can identify cervical lesions at a stage when treatment is easier and less risky to the client.

In developed countries where screening occurs on a wide scale, cervical cancer incidence has decreased over 50%.[19] In developing countries, the "screen-and-treat" method has been shown to significantly decrease cervical cancer incidence and mortality.[10,14] Screening tests like visual inspection with acetic acid (VIA) are extremely low-cost and have been shown to be acceptable in developing settings.[14] In Zambia, screening prevents one death for every 46 HIV-positive women screened.[25]

5.4 Screening in Developed Countries: The Pap Smear

Cervical cytology is the study of the cells on the cervix using **the Papanicolaou (Pap) smear**. To perform a Pap smear, the surface of the cervix is scraped with a spatula or brush to obtain cells. The cells are studied under a microscope for signs of HPV infection and precancerous or cancerous changes.[12]

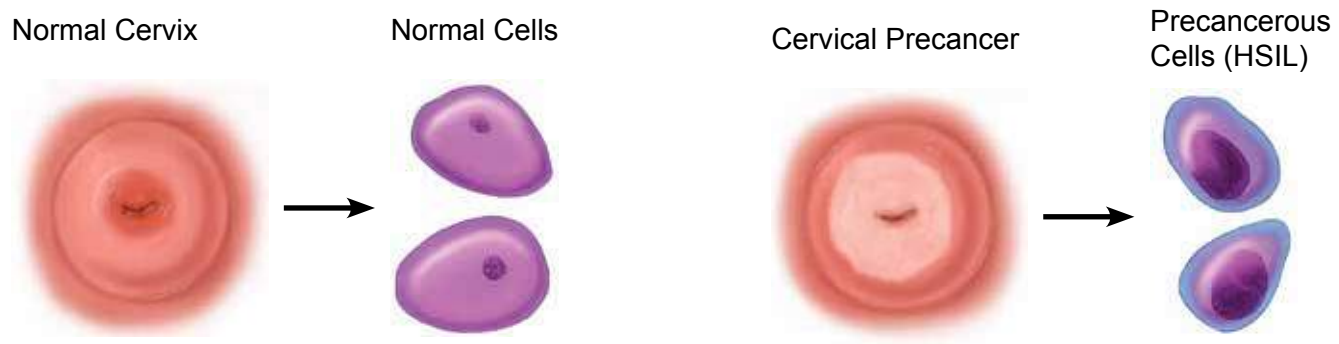

Figure 5.1 Illustration of cells taken from a normal cervix and a cervix with precancer as seen through a microscope during a Pap smear. Normal cells have small nuclei compared to the overall cell size, while precancerous cells have extremely large nuclei.

Conventional Pap smears have a moderate to low sensitivity (mean, 58%; range, 44-78%)[33] for detecting CIN 2 and above.[13,24] Therefore, the provider must re-screen women frequently to identify those lesions missed on first screening.[19] Recommendations on the frequency of screening vary by country, although many call for a Pap smear every three years in reproductive-age women.[25,28,36] Intervals may be increased if HPV testing is coupled with the Pap.[36] HIV-positive women should get Pap smears more often. In contrast with the moderate to low sensitivity, Pap smears have a high specificity (mean, 95%; range, 91-96%).[11,33]

Following-Up on Abnormal Pap Smears

A woman with an abnormal Pap smear may require **colposcopy** to confirm the presence of a cervical lesion. During colposcopy, a **colposcope** (magnifying or photographic instrument) is used to observe the cervix in detail.

At the time of colposcopy, **endocervical curettage** and a **biopsy** may be done to characterize any lesions. During endocervical curettage, the provider removes potentially cancerous tissue from the endocervix using a narrow instrument called a curette. During a biopsy, the provider uses a biopsy forceps to remove a small piece of tissue from the cervix. The tissue samples are analysed for the presence of precancer or invasive cancer.

If a precancerous lesion is found, it is generally removed using **loop electrosurgical excision procedure (LEEP)**. Cervical cancer prevention programmes do not use colposcopy for screening because:

- the instrument is expensive;
- the procedure is time consuming and less reproducible than the Pap;
- the procedure requires a highly-trained colposcopist.[11]

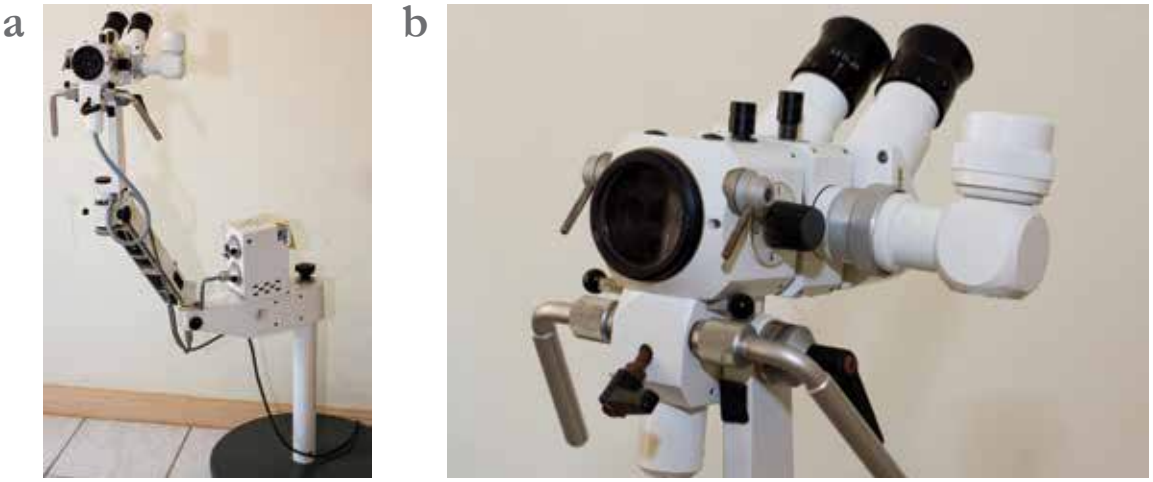

Figure 5.2a-b A colposcope.

5.5 Screening in Developing Countries: VIA, VILI, and Digital Cervicography

Barriers to Screening in Developing Countries

Considerable barriers exist to implementing screening in developing countries. Competing healthcare priorities like HIV/AIDS, maternal mortality, malaria, and tuberculosis leave few resources for cervical cancer screening programmes. Gender inequalities mean women lack access to education and healthcare services. The shortage of trained medical professionals, political instability, war, and poor healthcare infrastructures may make acquiring necessary resources difficult.[18,29]

Most screening programmes in developed countries use cytology to identify cervical lesions. Unfortunately, many developing countries lack the financial resources and capacity to implement cytology-based screening. Cytology and colposcopy require high-quality laboratories, highly-trained medical professionals, and the ability to obtain, store, and transport smears. Under

less-than-ideal conditions in resource-constrained environments, the sensitivity of the Pap smear may be significantly lower.[6,7,11] Because Pap smears are not point-of-care, problems with follow-up can occur.[11] In developing countries, one-third or more of women do not return for their Pap smear results.[6,7,8]

Visual Inspection with Acetic Acid (VIA)

In the early 2000s, researchers began evaluating **visual inspection with acetic acid (VIA)** as an alternative screening method to cytology in developing settings. To perform VIA, the provider soaks the cervix in dilute acetic acid (table vinegar) for one minute. The application of acetic acid causes cervical lesions to appear white in the presence of a bright light, so the provider can see them.[11] If a precancerous lesion is found during VIA, the lesion is treated and removed using **cryotherapy**, **cold coagulation**, **loop electrosurgical excision procedure (LEEP)**, or another method.

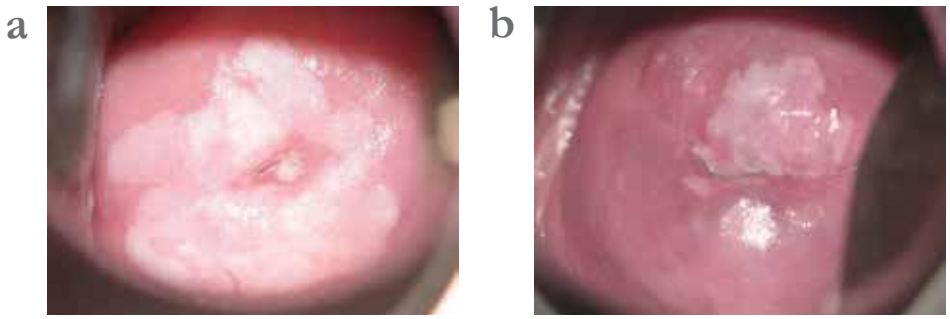

Figure 5.3a-b Cervixes with precancerous lesions after the application of dilute acetic acid (vinegar). The lesions are white, while the squamous epithelium remains pink.

For detecting CIN 2 and above in developing countries, VIA has a higher sensitivity (mean, 74%; range, 67-79%)[33] than the conventional Pap smear.[11,32] The high sensitivity and low cost makes VIA ideal for screening in low-resource settings, where frequent re-screening is less likely. VIA has a lower specificity (mean 73%; range 49-86%)[33] than the conventional Pap smear. Notably, pooled estimates of specificity for VIA range from 77-84% after adjusting for verification bias.[11] The lower specificity of VIA may cause **overtreatment**, defined as mistaken or excessive treatment.[32] Some experts feel the overtreatment is acceptable given high mortality rates of cervical cancer, the effectiveness of treatment, and the low rate of complications associated with treatment.

VIA solves many of the problems with cytology-based screening in low-resource settings. VIA does not require sophisticated laboratories, uses less equipment and money than other screening methods, and can be easily learned and performed by non-physician providers. Because VIA is point-of-care, cervical lesions can be diagnosed and treated in the same visit using the "screen-and-treat" method.[11]

Visual Inspection with Lugol's Iodine (VILI)

Like VIA, **visual inspection with Lugol's iodine (VILI)** was evaluated as an alternative to cytology in the early 2000s. VILI uses Lugol's iodine instead of acetic acid to identify cervical lesions. When the provider applies Lugol's iodine to the cervix, the cervical lesions turn a mustard-yellow colour and can be seen.[11]

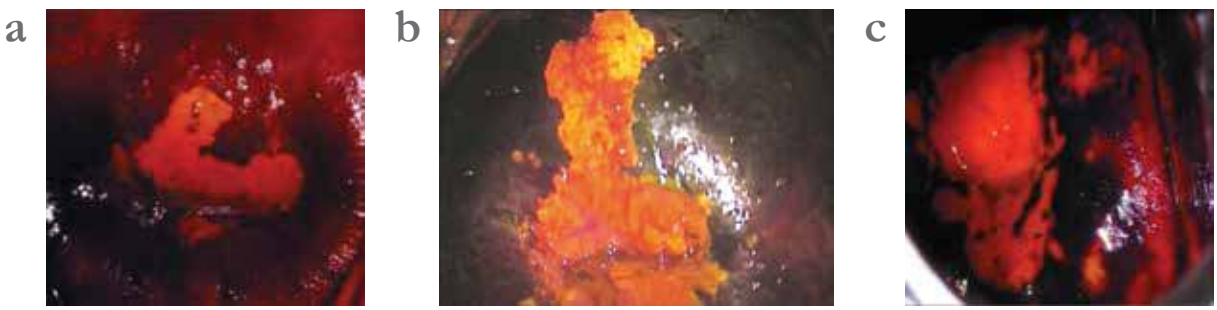

Figure 5.4a-c Cervixes with precancerous lesions after the application of Lugol's iodine. The lesions are mustard yellow and the squamous epithelium is dark brown. Adapted from various sources.[21,34]

Some data indicate VILI has a slightly higher sensitivity than VIA.[5,33] However, using VILI by itself for cervical cancer screening is not recommended, because VILI is less well-studied than and not as widely taught as VIA.[9,11] VILI can be used to confirm the results of VIA.[20,23]

Digital Cervicography (DC)

VIA can be combined with **digital cervicography (DC)**, a substitute for colposcopy in low-resource environments. During DC, the provider takes a picture of the cervix after the application of acetic acid using a high-magnification camera. DC allows the provider to magnify the cervix (up to 50 times) and see blood vessel abnormalities that cannot be seen with the naked eye. Because DC increases the sensitivity and specificity of VIA, DC is a highly useful addition to VIA in resource-constrained settings.[3] Notably, lower-level magnification of the cervix (2X to 4X) does not increase VIA performance.[35]

Figure 5.5 A digital camera with magnifying lens and lens adapter used for digital cervicography.

5.6 The Screen-and-Treat Approach to Cervical Cancer Prevention

The **screen-and-treat approach** uses a point-of-care screening test (such as VIA) to identify cervical lesions. The provider ablates less advanced lesions during the same visit using cryotherapy or cold coagulation. The provider refers more advanced lesions for loop electrosurgical excision procedure (LEEP) or cancer diagnosis and treatment.

Screen-and-treat programmes do not require sophisticated laboratories, expensive equipment, highly-trained doctors, or extensive client follow-up systems, removing some of the barriers to the development of large-scale cervical cancer prevention initiatives in resource-constrained settings.[28] The remaining chapters in this manual focus on the clinical and management aspects of screen-and-treat cervical cancer prevention programmes in low-resource settings.

5.7 HPV Testing and Cervical Cancer Screening

HPV testing detects high-risk HPV infection on the cervix. At a young age (15-29 years), HPV is common and a high-risk infection does not necessarily indicate a high-grade lesion. However, at an older age (30 years or older), a high-risk infection usually indicates HPV persistence and the presence of a high-grade lesion.[2] Therefore, HPV testing may be used to identify lesions in women aged 30 years or older. Although recommendations call for routine HPV testing and Pap smears concurrently,[36] some studies support the potential use of HPV testing as the sole primary screening test in women 30 years or older.[9]

Most HPV tests work by detecting the DNA of high-risk HPV types. Current data indicate HPV DNA tests have a much higher sensitivity (mean, 88%; range, 76-95%)[14] and somewhat lower specificity (mean: 88%; range, 82-95%) than the Pap smear for identifying high-grade lesions in women 30 or 35 years and older. In studies of varying age groups (18-70 years old, 35-45 years old, 20-45 years old, etc.), sensitivities range from 66-100% and specificities range from 61-96%.[11,14] The sensitivity of HPV DNA tests in resource-constrained settings may be slightly lower.[2]

Table 5.2 Sensitivity and Specificity of Cervical Cancer Screening Methods for High-Grade Lesions

	Sensitivity	Specificity
Conventional Pap Smear	Low to moderate (58%; range: 44-78%)[32]	High (95%; range: 91-96%)[32]
VIA (without DC)	Moderate (74%; range: 67-79%)[32]	Moderate (range: 77-84%)[11]
HPV DNA Testing*	Moderate to high (88%; range: 76-95%)[14]	Moderate to high (88%; range: 82-95%)[14]

**In women 30 or 35 years and older*

Because of the high sensitivity for lesions, many providers have high hopes for HPV DNA testing. In 2012, the American Cancer Society recommended routine HPV testing for women ages 30-65, alongside routine Pap smears.[36] As of October 2013, five countries have incorporated HPV testing into their national screening programmes. Twelve other countries are piloting HPV testing.[4] Because of the lower specificity, programmes use HPV DNA tests alongside Pap smears to reduce the number of false positives.

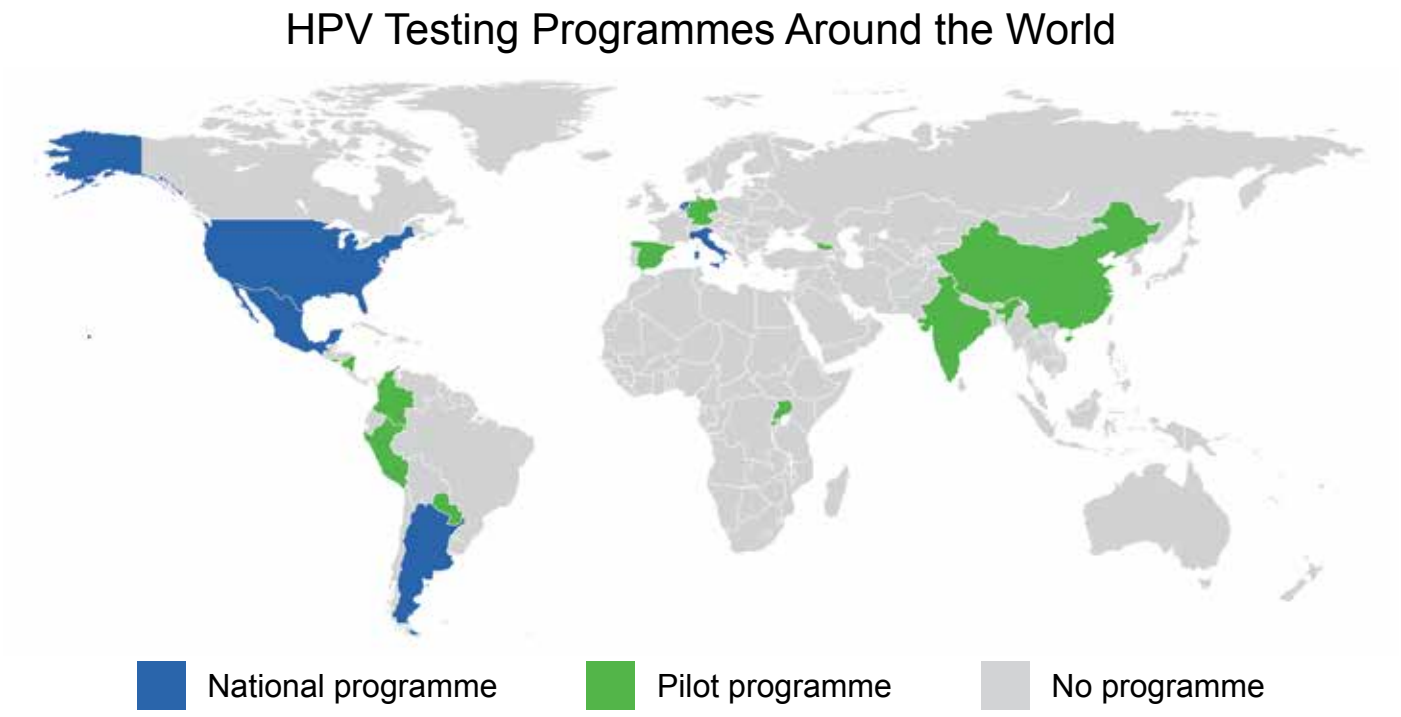

Figure 5.6 Map adapted from Cervical Cancer Action.[4]

HPV Testing in Low-Resource Settings

Current HPV tests require a high-quality laboratory, making them difficult or impossible to perform in low-resource environments. To make HPV testing more widely available, PATH recently led the development of two new HPV tests specifically for use in low-resource areas. The first, **CareHPV**, is an HPV DNA test produced by Qiagen. The second, **OncoE6**, detects the E6 proteins of three high-risk HPV types and is produced by Arbor Vita Corporation.

Both CareHPV and OncoE6:

- require minimal laboratory equipment and training;
- do not require refrigeration or running water;
- are portable and easy-to-use;
- give results in 2.5 hours.[1,30]

Unfortunately, neither CareHPV or OncoE6 are truly point-of-care, meaning the screen-and-treat method cannot be used. CareHPV is somewhat less cost-effective than VIA.[37]

CareHPV may be done with or without a speculum exam, meaning the client herself may collect the sample. Self-sampling may allow screening programmes to reach larger populations more easily.[30] A notable concern about self-sampling is the difficulty of follow-up with treatment for test-positive clients.[16]

CareHPV will be commercially available in China beginning November 2012, to be followed by India and Brazil. At the time of writing, OncoE6 is not yet commercially available.[1,30]

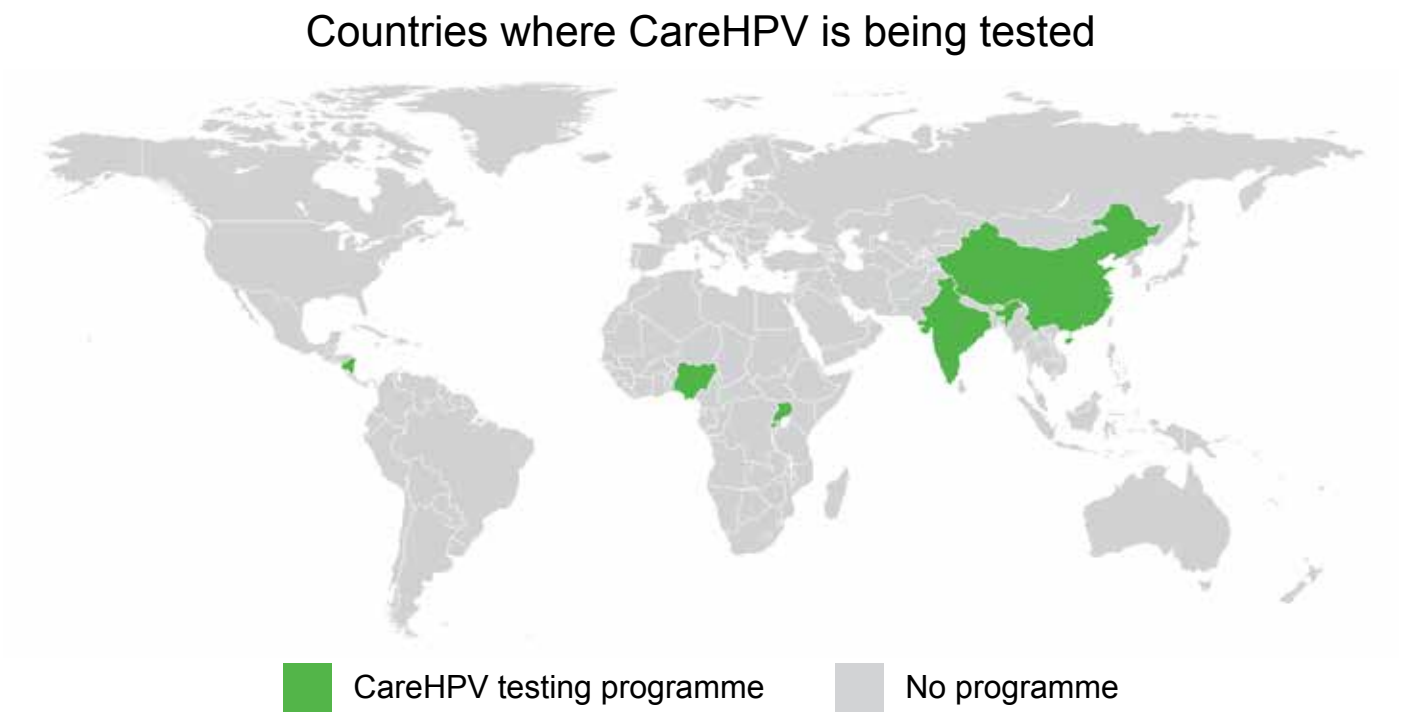

Figure 5.7 Map adapted from Qiagen.

Chapter 5 Summary

- The **sensitivity** and **specificity** of a diagnostic test indicate how accurate the test is. Sensitivity is the percentage of people with the disease who test positive. Specificity is the percentage of people without the disease who test negative.
- **Cervical cancer screening** detects precancerous cervical lesions in otherwise healthy women, so the lesions can be removed before they progress to cancer.
- In countries where cervical cancer screening occurs on a wide scale, cervical cancer incidence has decreased over 50%.
- Most screening programmes in developed countries use **Pap smears** to identify cervical lesions.
- Most developing countries cannot implement Pap-smear-based screening because Pap smears require sophisticated laboratories, expensive equipment, highly-trained doctors, and extensive follow-up.
- New methods such as visual inspection with acetic acid (VIA) and screen-and-treat make cervical cancer screening and prevention in developing countries feasible, affordable, and essential.
- **VIA** uses acetic acid (vinegar) to identify cervical lesions.
- The **screen-and-treat method** can identify and treat precancerous cervical lesions in a single visit.

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Chapter

6

Conducting Visual Inspection with Acetic Acid (VIA) and Digital Cervicography (DC)

After this section, the reader will be able to...

- Understand how VIA works.
- Discuss who, how often, and when to screen for cervical cancer.
- Know how to perform VIA and DC.
- Recognize the benefits and challenges of using DC as an adjunct to VIA.
- State the steps in a client's screening visit.
- Understand in detail pre-screening counselling, infection prevention, and informed consent.
- Discuss incorporating HIV testing and counselling into cervical cancer screening visits.

6.1 How Does VIA Work?

Several layers of cells called epithelial cells cover the surface of the ectocervix. Normally, when a provider looks at the surface of the cervix, it appears pink. The pink colour results from the blood that flows through the deeper tissues of the cervix (stroma).

When the provider applies vinegar (3-5% dilute acetic acid) to the surface of the cervix, the proteins inside the epithelial cells clump together. Under normal conditions, the cells in the top layer of the epithelium contain little protein, and the cervix still looks pink after the application of vinegar.

Abnormal epithelial cells on the cervix contain high levels of protein due to increased metabolic activity. When the provider applies vinegar to the surface of a cervix containing abnormal cells, large amounts of protein clump together, causing light to reflect into the eyes of the examiner. As a result, the abnormal epithelium appears white and stands out from the normal-looking pink tissue. The whitening of abnormal cells using acetic acid is called **acetowhitening**.[6]

The more severe a cervical abnormality, the quicker and more pronounced the acetowhitening effect. High-grade precancerous lesions in particular turn a dense white colour after exposure to acetic acid and have well-defined edges.

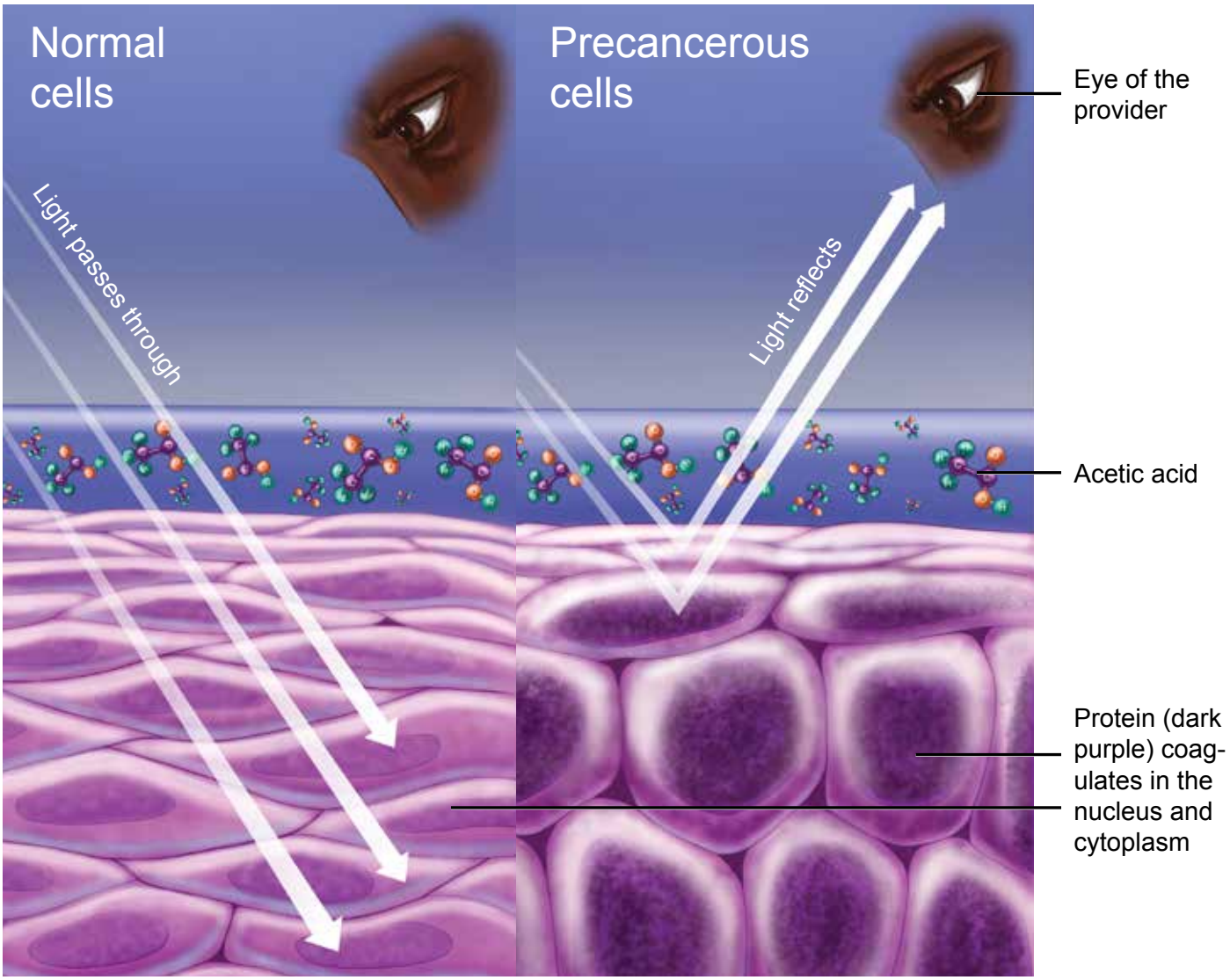

Figure 6.1 Illustration depicting the acetowhitening of normal and precancerous cells on a molecular level. Light reflects off the large clumps of protein in precancerous cells, but passes through the normal cells, which have less protein.

Low-grade precancerous lesions appear whiter than the surrounding tissue, but usually not as white as high grade lesions. However, high-grade lesions can occasionally appear less white than low-grade lesions.

The Importance of the Transformation Zone

Abnormal (precancerous and cancerous) lesions generally arise in the transformation zone of the cervix.[4] During VIA and DC, the provider should make sure the entire transformation zone can be seen. Lesions can occur outside the transformation zone, called **satellite lesions**. Usually, satellite lesions result from low-risk HPV infection and do not cause cancer.[5]

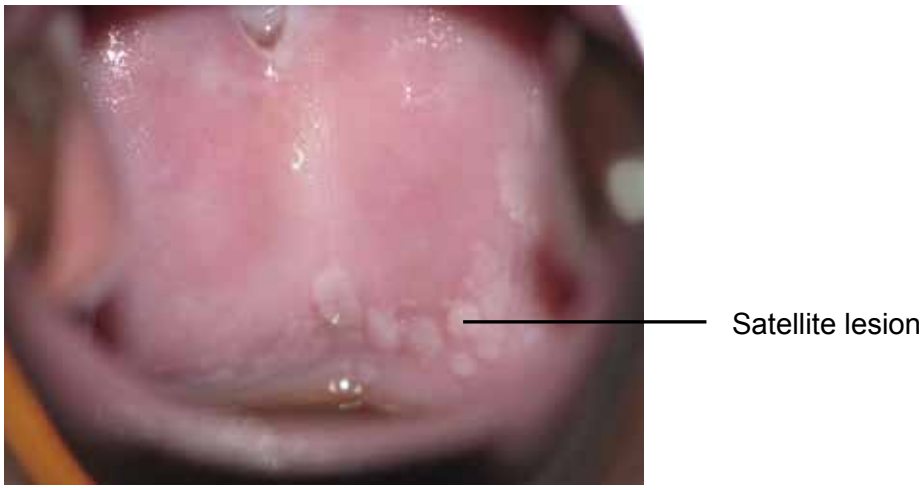

Figure 6.2 A cervix with satellite lesions.

6.2 Using DC as an Adjunct to VIA

In digital cervicography (DC), the provider photographs the cervix after VIA using a high-magnification camera. The photograph is called a **cervigram**. DC is a substitute for colposcopy in low-resource settings.

The Benefits of Using DC

- **Enhanced visualization of cervical lesions**. Photographing the cervix up-close allows the provider to see surface characteristics and abnormal blood vessels not generally visible to the naked eye. Using a high-powered, commercially-available digital camera, the cervigram can be magnified 30 or even 50 times for detailed inspection of lesions. Therefore, DC can increase the sensitivity and specificity of VIA.[2]

- **Client education**. The provider can use the cervigram to educate the client on what the cervix is, show her why her cervix is normal or abnormal, and explain why she needs treatment.

- **Portable, relatively cheap equipment.** One high-quality camera costs much less than a colposcope ($300-500 vs. $10,000-15,000). Unlike a colposcope, a camera is portable and easier to store.

- **Distance consultation**. If the provider cannot determine the results of VIA, he or she can send the cervigram to an expert over the internet. The expert can provide immediate feedback before the client leaves the clinic.

- **Quality improvement**. At our programme in Zambia, providers present their cervigrams and clinical decisions each week for review and discussion with a team of peers and gynaecologic consultants.

- **Additional medical records**. When a client returns for a follow-up visit, the provider can refer to her old cervigrams if necessary.

6.3 Who and How Often to Screen

At minimum, the WHO recommends cervical cancer screening for every women aged 30-49 at least once in a lifetime. If resources permit, women should be screened more frequently, but not more frequently than every 5 years. Programmes should also consider screening women older than 49 if resources permit.[8]

In areas with high HIV prevalence, the WHO recommends more frequent screening and the screening of women younger than 30.[7,8] In Zambia, 40% of cervical cancers are diagnosed in women younger than 35. These women have four times the rate of HIV than older women with cervical cancer. Our policy at the present time is to encourage all women who have ever had sex to be screened. We re-screen all clients every three years regardless of HIV status. A client is considered HIV status unknown if she has never been tested or her last HIV test was more than six months previously.

When deciding who and how often to screen, consider both the local HIV prevalence and your programme's resources and expertise. Prioritize widespread screening over closer management of fewer clients.

6.4 When to Screen

Screening can be performed at any point in the menstrual cycle.[6] However, if the woman is bleeding heavily, the provider may not be able to see the cervix. In this case, the provider should reschedule the woman for screening after her menstrual cycle ends.

Screening should be performed on women with HIV/AIDS or sexually transmitted infections. If the woman has a severe infection or obvious cervical cancer, discharge may obscure the cervix. If obvious cervical cancer is not present and the cervix cannot be properly seen, the provider should reschedule the woman for screening after antibiotic treatment.

Recent sexual intercourse does not affect screening.[6] Even if a woman is sexually active, she can and should be screened. Screening can be performed during post-partum or post-abortion visits.

Advanced pregnancy can cause bleeding and increased vascularity (blood vessels) on the cervix. Increased vascularity and bleeding due to pregnancy can be confused with cervical cancer. Any woman more than 20 weeks pregnant should return for screening 6-8 weeks after delivery, unless cervical cancer is suspected. If cervical cancer is suspected, perform a speculum exam and refer the client for further evaluation if the findings are suspicious.

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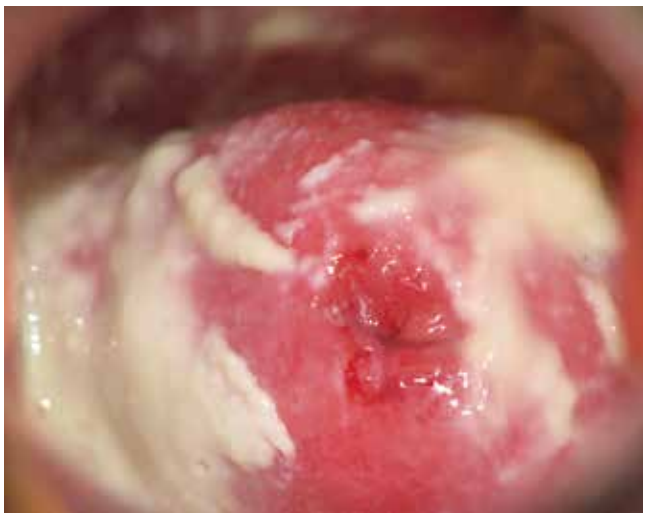

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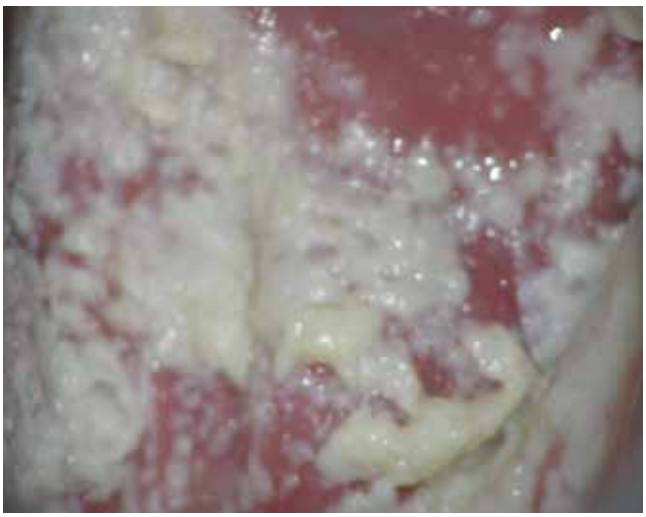


Figure 6.3a-b Cervixes obsured by discharge from infection.

6.5 Materials for VIA, DC, and Infection Prevention

Materials for VIA

- Examination table, preferably with stirrups and a plastic cover.
- Stool (for provider to sit on while examining).
- A bright light which does not give off much heat; preferably a halogen lamp. Sunlight or ceiling lights do not adequately illuminate the cervix and should not be used. A halogen torch may be used instead of a lamp. Make sure to purchase extra light bulbs or batteries.
- Instrument tray with the following:
  - sterile bivalved speculums, large and medium;
  - clean disposable examination gloves;
  - clean cotton swabs;
  - sterile ring forceps or pickup forceps;
  - small, sterile metal dish (gallipot);
  - table vinegar or 3-5% dilute acetic acid.
- Watch or clock.
- Prescription paper (to write prescriptions on for treating infection) or antibiotic supply.
- Designated examination room (to preserve privacy during the procedure).

Optional Items:

- Large cloth or blanket (to preserve privacy during the procedure).
- Large screen (to preserve privacy during the procedure).
- HIV testing kit.
- A small stool to help the client step up on the examination table.
- Disposable wooden spatulas (to position the cervix and vaginal walls).
- Machine oil (to prevent rusting of speculums).

Choosing an Appropriate Speculum

The speculum must be bivalved; the Simms speculum is not recommended because it requires an assistant to hold it open. Disposable speculums may be used as an alternative to non-disposable speculums.

Extra Cloth, Speculums, Gallipots and Forceps

Have enough autoclave cloths, speculums, gallipots, and forceps for the maximum number of clients the clinic expects to see in one day. Our programme's clinics have at least fifteen of each.

Figure 6.4 The materials found on the instrument tray.

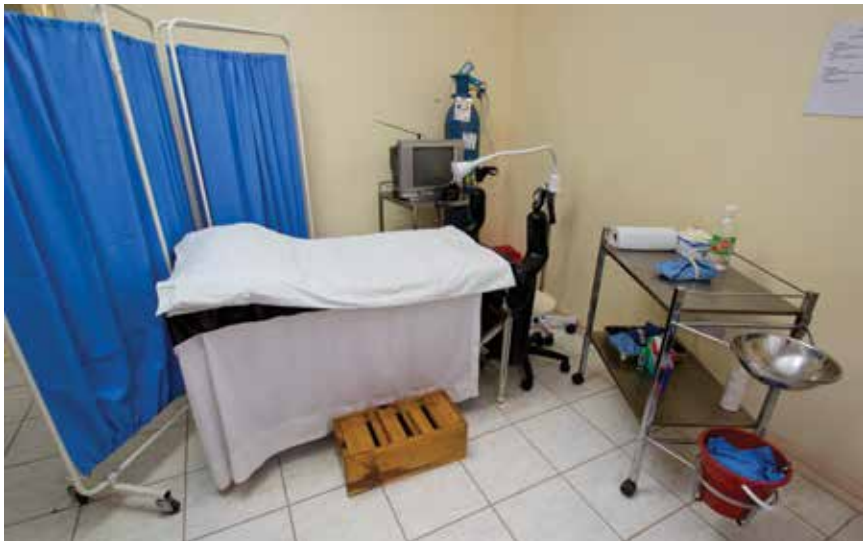


Figure 6.5 The screening room, containing an exam table with stirrups, instrument tray, large screen, and halogen lamp.

Protocol: Making 5% Dilute Acetic Acid

Ingredients:

- Glacial acetic acid: 5 mL.
- Distilled water: 95 mL.

Preparation:

- Carefully add 5 mL of glacial acetic acid into 95 mL of distilled water and mix thoroughly.
- Put the mixture into a container and label it "5% dilute acetic acid."
- Unused dilute acetic acid not in the container should be discarded at the end of the day rather than put back into the container and stored.

STOP

Warning: remember to dilute the acetic acid, because the undiluted strength causes a severe chemical burn if applied to the cervix.

Figure 6.6 Poster on making 5% dilute acetic acid for the clinic.

Finding 5% Dilute Acetic Acid

White kitchen vinegar for VIA can be purchased in the store. Check to make sure the strength of the acetic acid in the vinegar is 3%-5%. In countries where vinegar is not available, 5% dilute acetic acid can be prepared as a substitute using the above protocol.

Materials for DC

- A digital camera with an optical zoom and automatic flash. Our programme currently uses the Canon SX50.
- A macroconverter magnifying lens and lens adapter. Despite the magnification of the camera, this lens is absolutely necessary to decrease the focal length and obtain a clear picture of the cervix. Our programme uses the Canon 58 mm 500D close-up lens and the lensmate SX50 filter adapter 58 mm.
- Memory card(s) appropriate for the camera, 2 GB (gigabytes) or greater.

- Camera charger or extra batteries. Our programme uses rechargeable AA batteries and the energizer rechargeable compact charger 2500 (NiMH/NiCd).

Optional Items:

- Extension cords and surge protectors.
- Television or computer with external mouse and keyboard (to show the client the cervigram). Our programme uses an analogue 14 inch colour TV.
- Power cord for the television or computer.
- Power source (electrical outlet or generator) for the television or computer.
- Cable for connecting camera to television or computer (AV cables).
- Internet source to share images and data electronically.

Materials for Infection Prevention

- Autoclave machine with 3 or 4 sterilizing drums.
- Cloth (about 40 cm by 40 cm), permanent marker, and autoclave tape (to package equipment to be autoclaved).
- Sterile, covered tray (to store autoclaved instrument packets).
- Water source (to make solutions, wash instruments, and wash hands with).
- Bar soap (to wash hands with) and paper towels (to dry hands with).
- Distilled water for autoclave machine.
- Wash rags or mutton cloth (to clean the examination table).
- 10 L plastic container with soapy water (to hold used speculums).
- Detergent powder (to make soapy water).
- 10 L plastic container with 0.5% chlorine solution (to decontaminate the examination table and instruments).
- Chlorine granules or bleach (to make 0.5% chlorine solution).
- Scrub brush (to clean the instruments).
- Vinyl reusable or plastic disposable aprons (to protect the nurse and clinic assistants).
- A normal waste basket and waste bags (to dispose of paper waste).
- Hazardous waste bags and basket (to dispose of used gloves and cotton swabs).
- Two pairs of heavy-duty rubber cleaning gloves (to protect hands from the chlorine solution).
- Additional cleaning supplies, such as a mop, broom, dustpan, window cleaner, desk polish, and floor cleaner.

6.6 Pre-Screening Counselling and Informed Consent

Key Messages

- "The cervix is the mouth of the womb. Today, I will perform at test to see if your cervix is healthy. I will give you treatment if the cervix is not healthy. I want to make sure you understand and agree to the test and treatment."

- "Let me tell you how the test is done.
  First, you will need to remove your clothes and lie on the examination table.
  I will place an instrument in your vagina so I can see the cervix.
  Your cervix will be washed with vinegar. You may feel a slight burning sensation.
  The vinegar is used to see if there is a sore on the cervix.
  After the test, I will show you a picture of your cervix."

- "After I finish the test, I will discuss the findings with you (explain the different possible findings and show pictures of a healthy cervix and a cervix with precancer. Emphasize that a positive test does not always mean cancer is present, but means that the cervix has unhealthy changes which could become cancer in the future)."

- "If your cervix is unhealthy, I will either perform treatment or send you to another clinic to see a doctor. Let me tell you how the treatment is done (discuss key messages for cryotherapy or cold coagulation, found on page 105 and page 118, respectively)."

- "You don't have to have the test or treatment if you don't want to. Please feel free to leave. None of your regular health care will be affected by your decision to leave. If you decide to have the test or treatment, you may decide at any time to stop. You may come back later for the test or treatment if you want."

- "Most of the time, the test and treatment work well. At this time, this is the best test and treatment available. The test and treatment is very safe and is used in many countries around the world. Problems may occur, but only very rarely."

- "Please let me know if you have any questions (pause to allow time for questions)."

- "Thank you for listening."

Test for Comprehension

Ask the client to explain the importance of screening and what will occur during the examination. If she cannot tell you correctly, repeat the messages and show pictures until she understands.

The Consent Form

After the client understands, ask her to sign a consent form indicating she understands the procedure and potential complications and wishes to undergo treatment. If she cannot write her name, she can place a thumbprint to signify her consent. In some settings, verbal consent may be acceptable.

Proper Counselling Behaviour

How you conduct yourself during counselling can impact how well the client understands and reacts to the results. NEVER be rude, judgemental, or critical. ALWAYS:

- welcome the client into the room;
- introduce yourself by name;
- greet the client in her preferred language;
- create an environment where she feels comfortable by being calm and reassuring;
- encourage the client to ask questions;
- help the client make her own decision regarding her care;
- allow her to express her concerns without interrupting;
- gently correct any misunderstandings;
- use simple language;
- avoid medical terms;
- answer all questions to the best of your ability;
- dress nicely and act professional.

Quality Improvement

Quality improvement activities can improve providers' counselling skills and ensure respect of clients' rights to information.

6.7 A Step-by-Step Approach to VIA

The following protocol describes the steps of a typical VIA screen-and-treat screening visit in detail.[5,6] For a checklist version of the VIA protocol, see figure 6.15.

Step 1: Prepare for the Client's Arrival

Before beginning, prepare the instrument tray and ensure all necessary equipment is available and sterile (including cryotherapy or cold coagulation equipment). Clean the examination table and bright light using a wash rag soaked in 0.5% chlorine solution or bleach. All persons who will be present in the room during screening should put on an apron, except the client.

Step 2: Welcome the Client and Obtain Informed Consent

Make sure the client empties her bladder, as the cervix may be difficult to see when the bladder is full. Counsel the client on the test and treatment, and obtain consent. Whenever possible, offer HIV testing and counselling to all clients. If not possible, refer clients who wish to be tested for HIV testing and counselling. Record any necessary information which has not been recorded prior to the client entering the screening room.

a

b

Figure 6.7a The provider cleans the examination table with 0.5% chlorine in preparation for the client's arrival.
Figure 6.7b The provider counsels the client as discussed in section 6.6.

Step 3: Position the Client on the Examination Table

Ask the client to undress from the waist down and lie on her back on the examination table. Ask the client to place her feet in the stirrups and move down until her buttocks reaches the edge of the table. If the examination table lacks stirrups, she can place the bottoms of her feet on the end of the table. If possible, place a large cloth or blanket across her waist and thighs to preserve privacy.

a

b

Figure 6.8a-b The client correctly positioned on an examination table.

Step 4: Perform the Bimanual and External Genitalia Exams

Conduct the exams as discussed on page 73. After palpating the abdomen, make sure to wash your hands thoroughly with soap and water, dry them, and put on clean exam gloves.

Step 5: Insert the Speculum

Pour vinegar (3%–5% acetic acid solution) into the small, sterile metal dish. Choose a larger speculum for older women, women who have had multiple children, and larger women. Dip the speculum in vinegar to lubricate it. Clean warm water, antibacterial soap, or water-soluble lubrication gel can also be used to lubricate the speculum.

Inform the client you are inserting the speculum. Carefully separate the outer folds of the vagina (labia) with the fingers of the non-dominant hand and slowly insert the speculum diagonally with the dominant hand, using a slight downward pressure to avoid touching the urethra. Insert the speculum slowly or until resistance is felt. Slowly open the speculum until the cervix comes into view. Open the speculum as widely as possible without making her uncomfortable.

You should see the entire cervix and the upper part of the vagina. If necessary, use a cotton swab or wooden spatula to push the walls of the vagina outwards or move the cervix up and down for a better view. Dispose of any used cotton swabs or wooden spatulas in the hazardous waste basket. Fix the speculum blades in the open position.

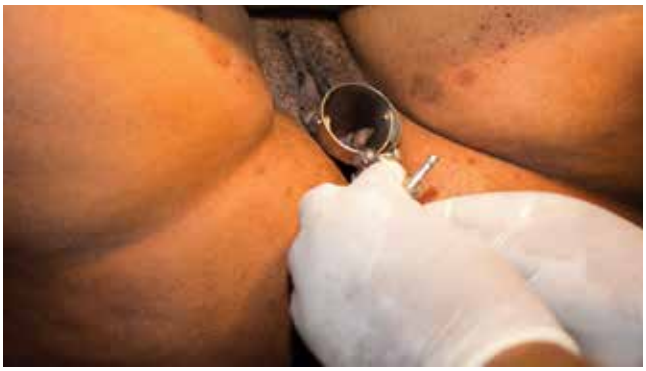
a  b 

Figure 6.9a-b The speculum before and after insertion, respectively.

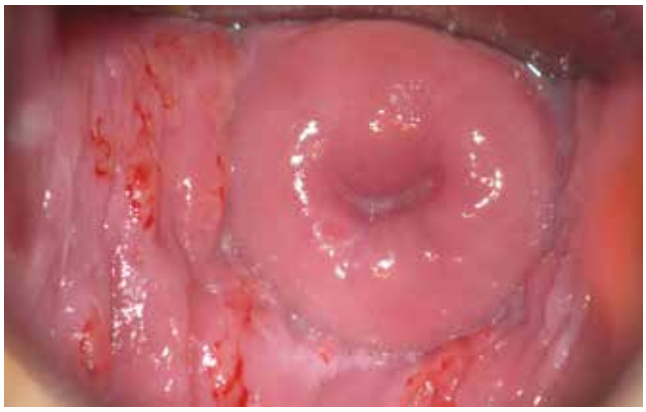
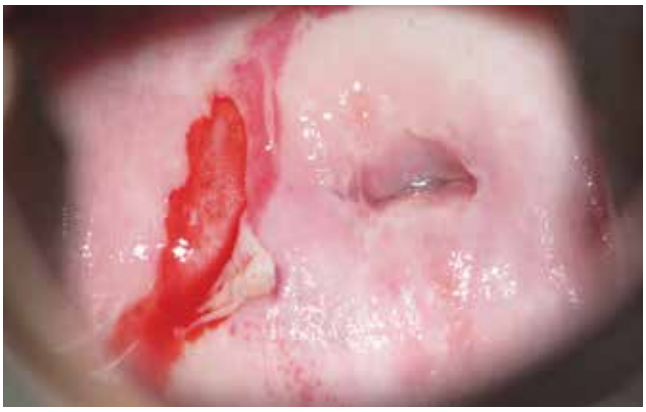
a  b 

Figure 6.10a-b It is important to lubricate the speculum and insert it gently, otherwise the woman may experience trauma from the insertion as shown.

Step 6: Perform the Speculum Exam

Position the bright light so the cervix can be easily seen. Identify the columnar epithelium, the squamous epithelium, the squamocolumnar junction, and the transformation zone. Identify any atypical vessels (discussed on page 72). Conduct the exam as discussed on page 75.

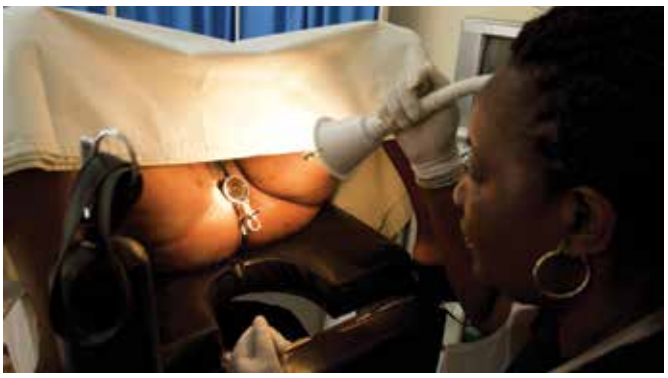


Figure 6.11 The provider identifies the transformation zone.

Step 7: Perform VIA

If necessary, use a cotton swab to wipe away excess blood, mucus, or discharge from the cervix. If the cervix still cannot be seen due to discharge caused by infection or heavy menstrual bleeding, ask the client to return for screening later.

Using the forceps, pick up a clean cotton swab, thoroughly soak it in vinegar and place it on the cervix. Make sure the vinegar is applied to the entire transformation zone. Wait at least three full minutes, using a watch or clock to keep track of the time. If possible, cover the client with a large cloth or blanket to preserve privacy while waiting. Then, remove the cotton swab from the cervix and put it into the hazardous waste basket.

Position the bright light so the cervix can be easily seen. Carefully check the transformation zone for distinct, opaque (dense) acetowhite lesions with sharp borders. DC can be performed in addition to examining the cervix with the naked eye. Discuss the results with the client and show the client her cervix if possible. Wait to tell the woman the result until the result is certain. Do not make comments during the speculum exam or screening procedure such as "your cervix looks healthy" because you may find a problem later.

a

b

c

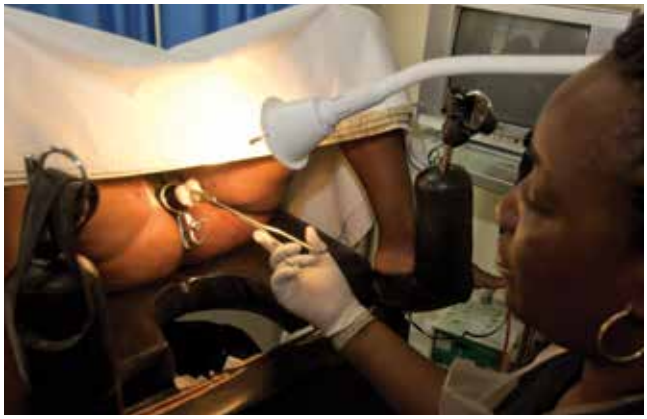
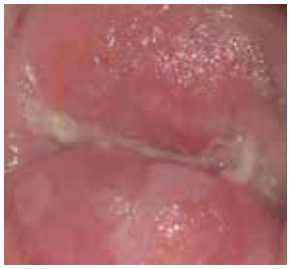


Figure 6.12a-b
The provider pours vinegar into the gallipot and soaks the cotton swab in it.

Figure 6.12c
The provider places the cotton swab on the cervix.

a



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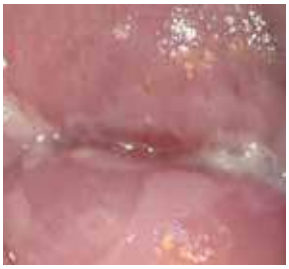

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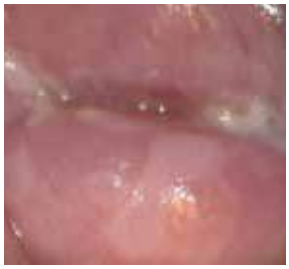

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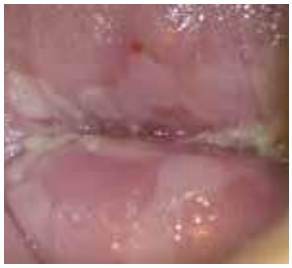

Figure 6.13a-d The same cervix with no vinegar (a), after a one minute application of vinegar (b), after a two minute application of vinegar (c), and after a three minute application of vinegar (d). The lesion becomes whiter and easier to see the longer the vinegar is applied.

Step 8: Give Treatment (if necessary)

Perform cryotherapy or cold coagulation if the lesion meets the appropriate criteria discussed in chapters 8 and 9.

Step 9: Finish the Exam and Thank the Client

Inform the client you are removing the speculum and gently remove it. Place the speculum in the plastic container with soapy water. The speculums will be decontaminated at the end of the day using 0.5% chlorine solution.

Ask the client to stand up and get dressed. If possible, have paper towels ready so the client can dry the outside of her vagina. Remove your gloves and put them into the hazardous waste basket. Wash your hands with soap and water. Record the results of VIA and the bimanual, external genitalia, and speculum exams.

Once the client has dressed, prescribe medication for any infections and ask her to provide feedback on the screening process. If the client requires referral for LEEP or another reason, make an appointment for her before she leaves the clinic. Thank her for her visit and remind her of the date of her next screening visit or follow-up visit.

6.8 A Step-by-Step Approach to DC

Step 1: Photograph the Cervix

ALWAYS use new, unsoiled gloves to pick up the camera. This protects the camera from contact with body fluids and acetic acid. A possible strategy is to wear two pairs of gloves at the beginning of the procedure (double glove), then remove the top pair prior to picking up the camera.

Turn on the camera. Make sure the flash is on and the batteries are strong. Hold the camera steady and zoom in so only the cervix can be seen. Tilt the camera forward or backward and move the camera up and down until the cervix occupies the centre of the picture. Hold the shutter release button halfway down to focus the camera. Press the shutter release button all the way down to take the picture. Make sure the cervix is not shadowed in the photograph.

If possible, the provider should connect the camera to a television or computer screen. The TV or computer screen enlarges the image and allows the client to watch as the provider photographs the cervix. In this way, the provider can show the client her cervix and explain cervical health issues. Position the television so both client and examiner can see the cervix on screen.

a 

b 

Figure 6.14a The provider photographs the cervix.
Figure 6.14b The provider discusses the client's cervigram with her.

Step 2: Interpret the Results

View the cervigram on the camera, computer, or television screen. Carefully check the transformation zone for distinct, opaque acetowhite lesions with sharp borders. Zoom in on any suspicious areas to look for abnormal blood vessels.

Step 3: Discuss the Results with the Client

Show and explain the cervical image to the client. If necessary, show the client other cervigrams and compare her cervix to cervigrams of healthy and unhealthy cervixes. Perform cryotherapy or cold coagulation if necessary.

Step 4 (Optional): Save the Cervigram as a Medical Record

At the end of the day, transfer the images from the camera to the computer. Be sure to name the photos according to the client's number for easy identification.

Visual Inspection with Acetic Acid and Digital Cervicography

Before client arrives, ensure:

- ☑ Vinegar, gloves, and instrument packet are on instrument tray.
- ☑ Exam table is clean.
- ☑ Treatment equipment is available.
- ☑ Apron is on.

After palpating the abdomen and before beginning the exam, ensure:

- ☑ Client has given informed consent.
- ☑ Client is properly positioned on the exam table.
- ☑ Hands are washed and gloves are on.

Before discussing results with the client, ensure:

- ☑ The speculum, bimanual, and external genitalia exams are done.
- ☑ Vinegar was applied for three full minutes.
- ☑ The cervix was photographed and fully inspected for lesions and abnormal blood vessels.

If treatment will be given, ensure:

- ☑ The cryotherapy or cold coagulation checklist is completed.

Before the client leaves, ensure:

- ☑ Your hands are washed.
- ☑ Necessary medications are prescribed.
- ☑ Necessary referrals are made.
- ☑ The client knows the date of her next visit.
- ☑ All equipment is properly decontaminated or disposed of.

Figure 6.15 Work with your screening provider(s) to develop a reminder poster for the VIA and DC procedures. Print and place one in each examination room. Above is a sample reminder poster.

6.9 Infection Prevention

Good infection prevention:

- stops the spread of HIV and other diseases from one client to another;
- helps clients trust the medical instruments a clinic uses;
- helps staff feel the work environment is clean, effective, and safe;
- prevents rumours about uncleanliness that could negatively impact the programme.

Hand Washing

The importance of hand washing cannot be overstated. Improper hand washing causes the majority of infections contracted in health facilities. The provider must wash his or her hands with soap and water before and after putting on gloves.

Aprons and Gloves

The provider must wear an apron and gloves to protect against contact with the client's blood and body fluids. Except the client, all persons present in the room during screening should wear an apron.

Cleaning the Examination Table

Wipe down the examination table between every client using a wash rag soaked in 0.5% chlorine solution or bleach. Additionally, wipe down all surfaces (table tops, examination lights, etc.) that may have contacted body fluids. Ethyl or isopropyl alcohol (60-90%) can be used if 0.5% chlorine solution or bleach is unavailable.

Cleaning the Clinic Facility

Cleaning the clinic facility both prevents infection and ensures presentability. The facility should be cleaned at the beginning and end of each day. Sweep at least once daily to keep the floor free of debris and dirt. After any blood or body fluid spills and at the end of each day, disinfect the floor with 0.5% chlorine solution. There should not be any carpet or other bacteria-harbouring flooring in the examination room.

Protocol: Making 0.5% Chlorine Solution

From shelf liquid bleach or other chlorine solution:

- Determine the concentration (% concentrate) of the chlorine solution you are using.
- Determine the "number of parts water" using the following formula:
  number of parts water = (% concentrate – 0.5%) divided by 0.5%.
- Mix one part concentrated chlorine solution with the calculated number of parts water.

Example: making 0.5% chlorine solution from shelf liquid bleach.
The concentration of standard shelf liquid bleach is 3.5%.
Number of parts water = (3.5% - 0.5%) divided by 0.5% = (3.0%) divided by 0.5% = 6.
Add one part shelf liquid bleach to six parts water to make 0.5% chlorine solution.

From dry chlorine:

- Add 50 litres of water to 200 grams dry granules of chlorine.
- To reduce corrosive action of chlorine, add a tablespoon of washing powder.

STOP

Warning: metal instruments should not be left in 0.5% chlorine solution for more than ten minutes because the chlorine can corrode the metal.

STOP

Warning: wear heavy-duty rubber gloves at all times while handling chlorine solution to protect your hands, wrists, and forearms.

Figure 6.16 Poster on making 0.5% chlorine solution for the clinic.

Decontamination of Instruments

After every use, speculums, forceps, and gallipots must be washed in soapy water and soaked in 0.5% chlorine solution to remove biological matter prior to autoclaving.

Step 1: Washing Instruments with Soapy Water

Use a scrub brush to scrub the instruments free of biological matter.

Step 2: Cleaning Instruments Using 0.5% Chlorine Solution

Submerge all used instruments in 0.5% chlorine solution for ten minutes. Wear heavy-duty gloves to protect your hands. Make sure to submerge the instruments for exactly ten minutes by the clock. If you do not submerge them for long enough you may not completely decontaminate them. However, if you submerge them longer than ten minutes they will be ruined by corrosion.

Immediately after removing metal instruments from chlorine solution wash them with soapy water and then rinse in clean water. This prevents corrosion of the instruments by removing excess chlorine solution prior to autoclaving.

Step 3: Autoclaving Instruments

Our programme autoclaves instruments and cotton swabs in "packets." The nurses uses one equipment packet per client, minimizing the chances of cross-contamination. Each packet to be autoclaved should consist of:

- one gallipot;
- several cotton swabs;
- one speculum;
- one forceps.

Wrap the packet in a cloth and secure with autoclave tape. Write the date of autoclaving on the tape in permanent marker. After autoclaving, allow time for drying and cooling of instruments prior to examination of clients. In general, it is best to autoclave equipment at the end of each day to allow for drying and cooling overnight.

Please follow the manufacturer's protocol provided with your autoclave machine regarding the duration of autoclaving and drying cycles and water requirements.

Figure 6.17 Preparation of the autoclave packet.

Storage of Instruments

Store instruments in a covered, sterilized tray. Store for no more than 21 days; otherwise repeat autoclaving.

Chemical Sterilization

High-level chemical sterilization can be used as an alternative to autoclaving in mobile settings or in case of power outages. Our programme uses Cidexplus. Please see chapter 14 of the IARC online colposcopy manual for more information, found at http://screening.iarc.fr/colpochap.php?lang=1&chap=14.

Hazardous Waste

Appropriate procedures for the demarcation and disposal of hazardous waste must be followed. If appropriate structures for disposal of hazardous waste do not exist, hazardous waste must be decontaminated with 0.5% chlorine solution prior to disposal.

Figure 6.18a The clinic assistant submerges the metal instruments in 0.5% chlorine solution while wearing heavy-duty gloves.
Figure 6.18b The assistant immediately rinses the instrument in water after washing with chlorine.
Figure 6.18c The assistant places the autoclave packets in the autoclave and tightens the lid.
Figure 6.18d Sterilized packets after autoclaving.

What to do in case of exposure to blood or body fluids

Wash the affected area with soap and water. If punctured or cut, allow the wound to bleed and rinse it with soap and water. Take antiretroviral prophylaxis and undergo HIV testing after six weeks if:

- the injury is deep;
- there is visible blood on the object that caused the injury;
- the injury was caused by an object placed in the client's vein or artery.

Vaccination Against Hepatitis B

Because healthcare workers may come in contact with blood during screening and treatment, especially LEEP providers, vaccinate all healthcare workers against hepatitis B as a precaution when possible.

Cryotherapy, Cold Coagulation, and LEEP

Specific infection prevention information for cryotherapy and cold coagulation is discussed on page 109 and page 122, respectively.

Quality Improvement

Implement strategies to ensure healthcare workers comply with infection prevention guidelines, such as clinical checklists.

Daily Preparation

Before the first client arrives each day, prepare the containers of 0.5% chlorine solution and soapy water. The individual packets of autoclaved equipment should remain closed to prevent exposure to dust and bacteria. Clean the examination table. The hazardous waste basket and container with soapy water should be placed within easy reach of the examiner.

6.10 Integrating HIV Testing and Counselling

Just as ART programmes can refer women for cervical cancer screening, screening programmes can refer women for HIV testing and counselling.

Here is an example:
In 2010, a new cervical cancer screening programme began in Zambézia province, Mozambique. During the first year of the program, nurses screened 4651 women. Forty-eight per cent (2206 women) did not know their HIV status. Of the 48%, 12% accepted referral for HIV testing and counselling, of whom 23% were positive.[1,3]

Mozambique demonstrates how screening offers the opportunity to identify HIV-positive women for treatment. Our programme in Zambia offers HIV testing and counselling during the screening visit for all women.

Potential benefits of offering HIV services during screening include:

- more women benefit from HIV testing and counselling than otherwise;
- women can access testing and counselling in the same visit, maximizing their time.

Potential challenges include:

- women might not want to come for screening if it integrates HIV testing (due to stigma);
- HIV testing and counselling increases the length of the screening visit;
- providing HIV services requires additional training and supplies.

Resources for Training Providers in HIV Counselling and Testing

- Family Health International (2004): Voluntary Counselling and Testing (VCT) Toolkit, Voluntary Counselling and Testing: Skills Training Curriculum (Participant' Manual). To access, visit http://pdf.usaid.gov/pdf_docs/Pnadc072.pdf.

- Commonwealth Regional Health Community Secretariat for East, Central and Southern Africa (2002): HIV/AIDS Voluntary Counselling and Testing: Review of Policies, Programmes and Guidelines in East, Central and Southern Africa. To access, visit http://www.who.int/hiv/topics/vct/toolkit/components/policy/review_of_policies_programmes_and_guidelines.pdf.

Chapter 6 Summary

- Dilute acetic acid (vinegar) turns abnormal epithelium white, so it can be identified using a bright light.
- The whitening of abnormal epithelium with vinegar is called **acetowhitening.**
- Cervical cancer almost always occurs in the transformation zone of the cervix. The provider should make sure the entire transformation zone can be seen during VIA.
- DC is a substitute for colposcopy in low-resource environments.
- The photograph of the cervix taken during DC is called a **cervigram**.
- DC can facilitate correct diagnoses, enable distance consultation, help educate clients, enhance quality improvement activities, and improve medical records.
- The WHO recommends screening women ages 30-49 at least once in a lifetime and older women if possible. The interval between screenings should not be less than 5 years.
- In areas with high HIV prevalence, women should be screened more frequently and at younger ages. In Zambia, we encourage all women who have had sex to be screened.
- During the screening visit, the provider should:
  prepare for the client's arrival;
  welcome the client, fully explain the test and treatment, and obtain informed consent;
  position the client on the examination table;
  perform the external genital exam;
  insert the speculum;
  perform the speculum exam;
  perform VIA and DC;
  give cryotherapy or cold coagulation if necessary;
  finish the exam and thank the client.
- Infection prevention at the clinic is extremely important. Every provider must understand and practice all the measures described in section 6.9.
- HIV testing and counselling can be offered during the screening visit for all women who do not know their status.

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7. Spitzer, M. (1999). Lower genital tract intraepithelial neoplasia in HIV-infected women: guidelines for evaluation and management. [Review]. *Obstet Gynecol Surv, 54*(2), 131-137.
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Chapter

7

Interpreting Visual Inspection with Acetic Acid (VIA) and Digital Cervicography (DC)

After this section, the reader will be able to...

- Identify abnormal blood vessels on the cervix.
- Conduct the external genitalia, bimanual, and speculum exams.
- Diagnose clients as VIA-negative, VIA-positive, or suspicious of cervical cancer.
- Conduct counselling for VIA-negative clients, VIA-positive clients, and clients suspicious for cancer.

7.1 An Overview of Abnormal Blood Vessels

Abnormal blood vessels on the cervix may indicate high-grade precancer, microinvasive cancer, or invasive cancer. Importantly, the abnormal vessels are only significant when associated with acetowhite areas, because pregnancy and infection can also cause abnormal vessels.

Mosaicism and Punctation

Mosaicism is when blood vessels appear as a network of red lines criss-crossing the surface of the acetowhite lesion, similar to tiles on a floor (Figure 7.1). **Punctation** is when blood vessels appear as red dots on the lesion's surface (Figure 7.2).

The thicker and larger the mosaicism or punctation, the more severe the lesion. Mosaicism and punctation tends to occur in high-grade precancerous lesions.[2,17]

Illustration and Images of Mosaicism

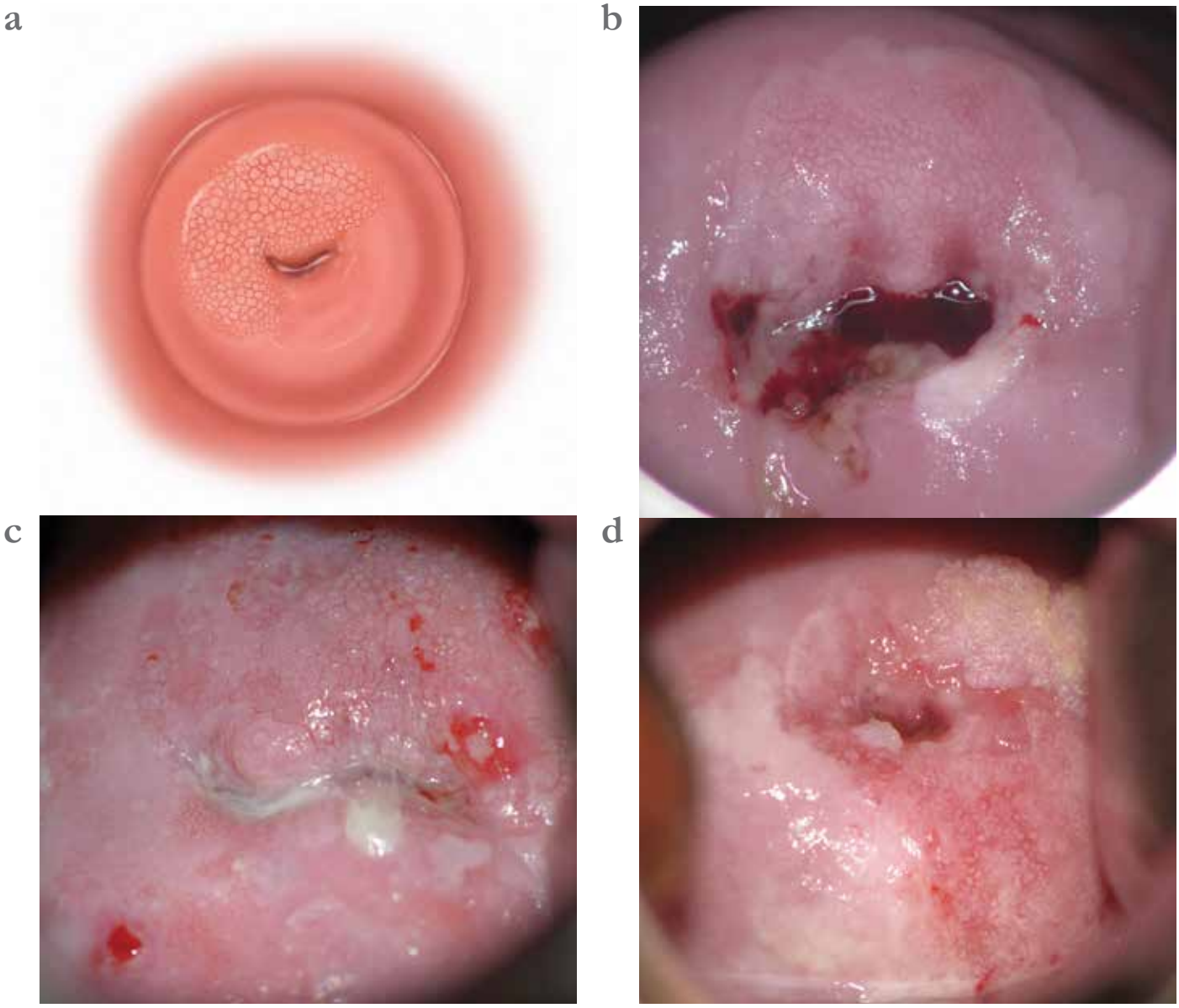

Figure 7.1a Illustration of a cervix with mosaicism.
Figure 7.1b-d Photographs of cervixes with mosaicism.

Illustration and Images of Punctation

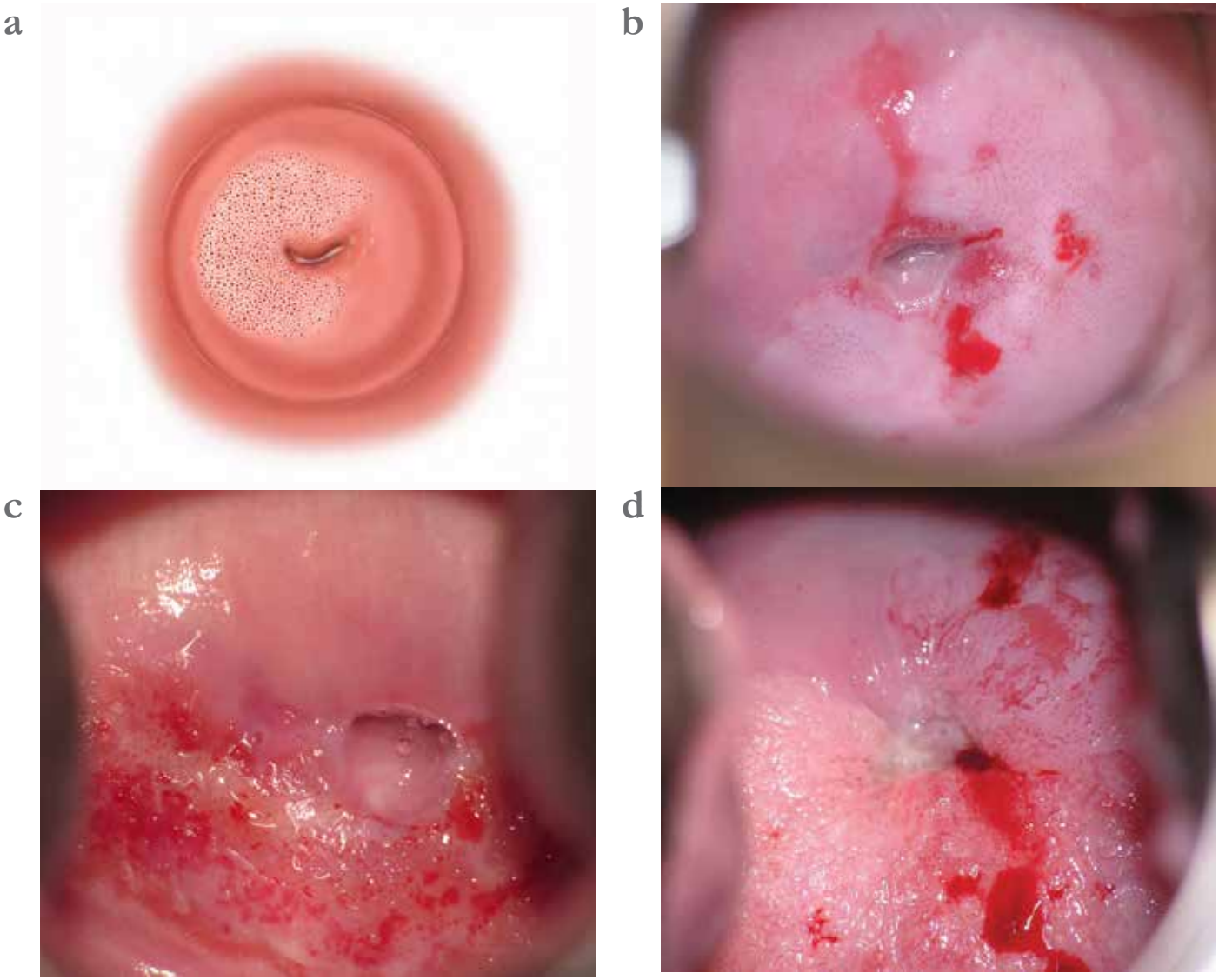

Figure 7.2a Illustration of a cervix with punctation.
Figure 7.2b-d Photographs of cervixes with punctation.

Mosaicism at the Histological (Tissue) Level

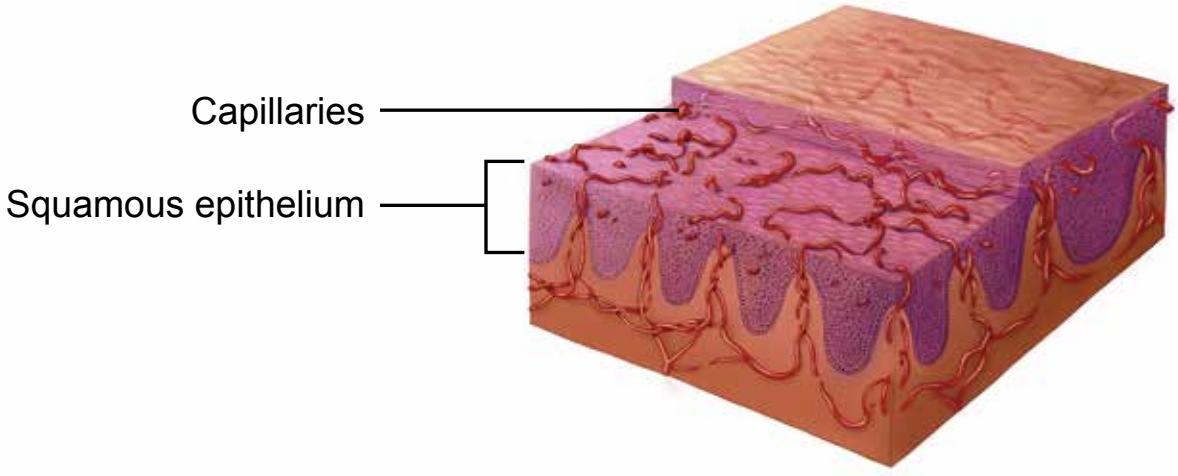

Figure 7.3 Illustration of mosaicism at the histological level.

Punctation at the Histological (Tissue) Level

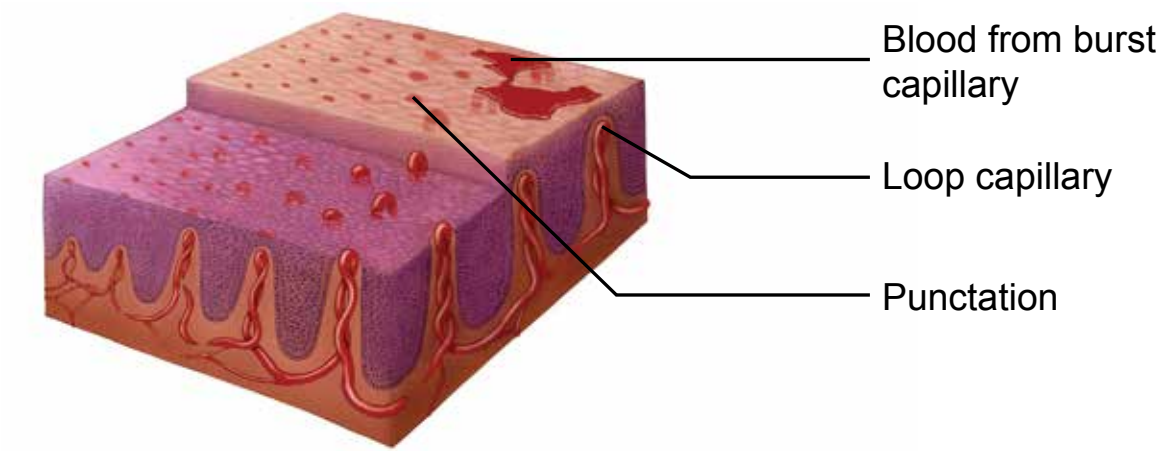

Figure 7.4 Illustration of punctation at the histological level.

Atypical Vessels

Normal or typical blood vessels appear smooth, with smaller vessels branching off larger ones. **Atypical vessels** appear chaotic and jagged, with blood vessels of every size going in different directions. Atypical vessels may not even appear branched. Features of atypical vessels include "commas" (pools of blood) and "apostrophes" (curves or loops). Highly atypical vessels tend to occur in invasive cervical cancer (Figure 7.5).[2,17] The cervix should always be inspect with the naked eye prior to VIA to identify abnormal vessels that may have resulted from precancer or cancer.

Illustration and Images of Atypical Vessels

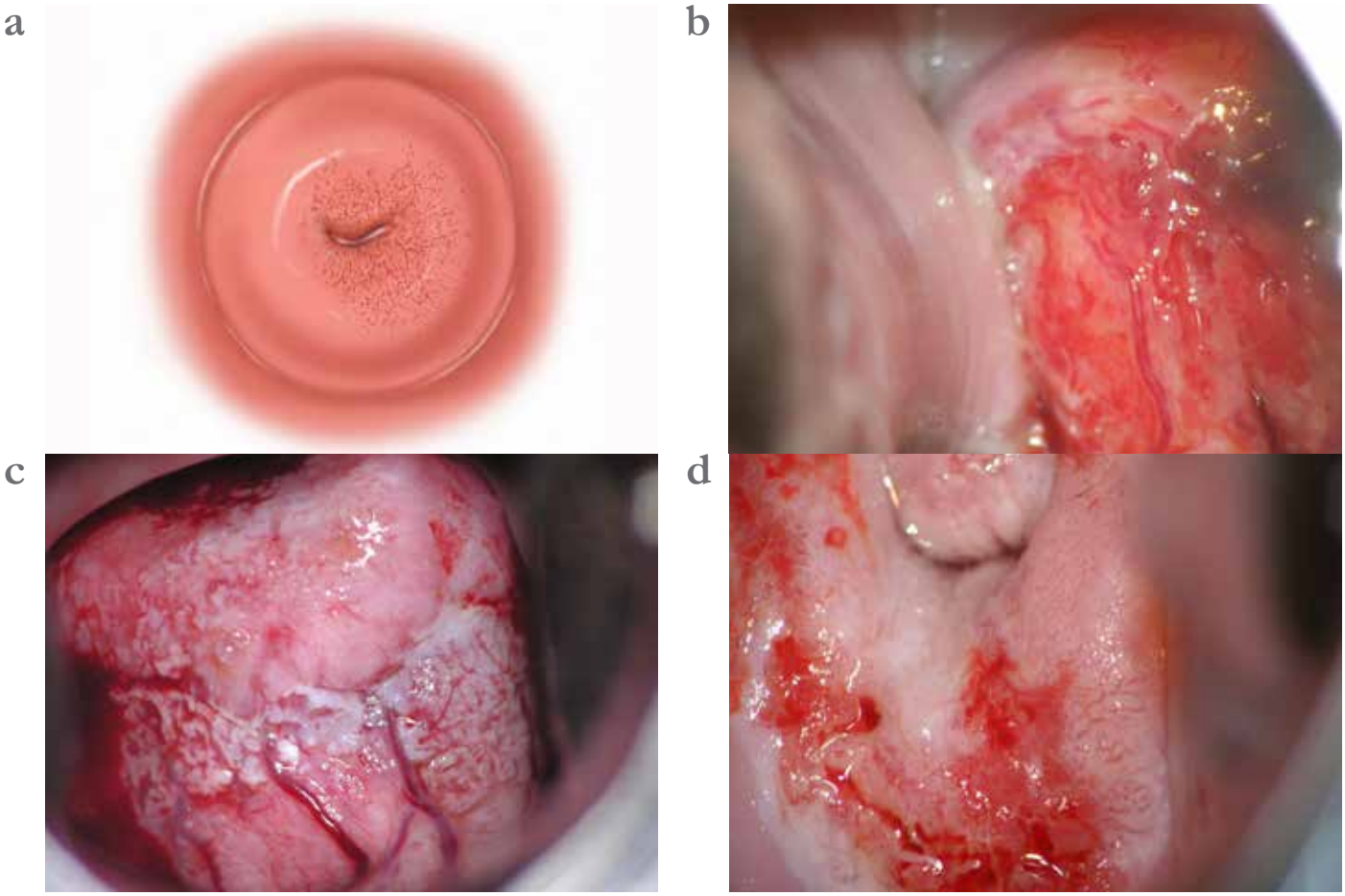

Figure 7.5a-d Illustration and photographs of a cervix with atypical vessels.

Images of Punctation and Mosaicism Together

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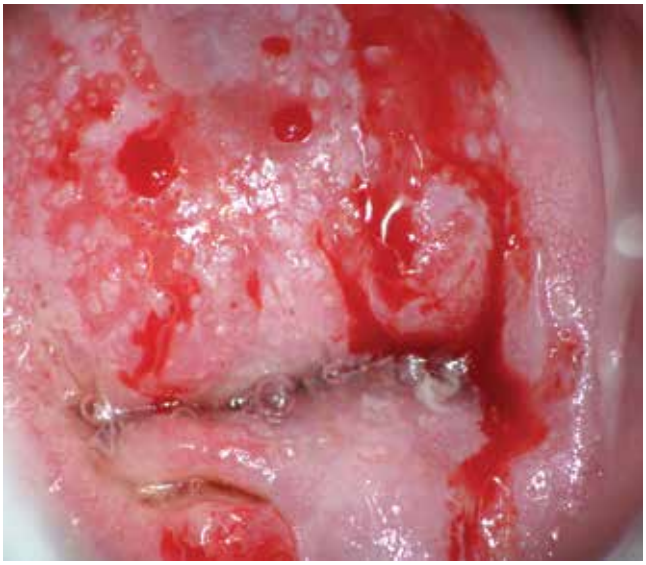

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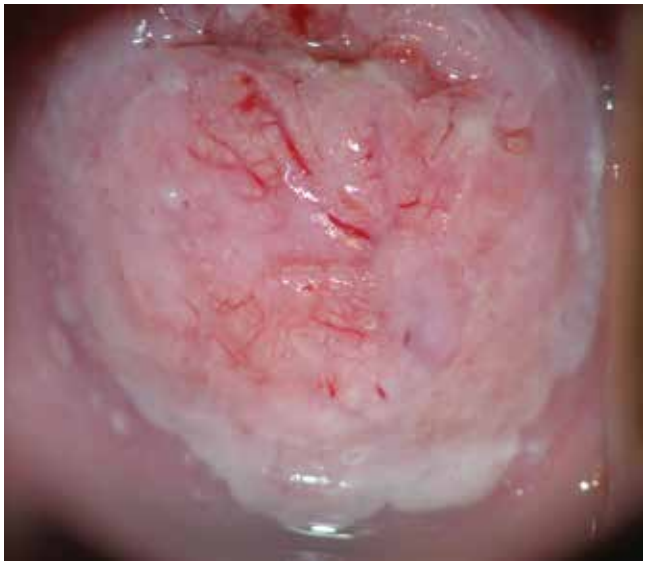

Figure 7.6a-b Cervixes with both punctation and mosaicism. The first displays the bleeding typical of cervixes with punctation or mosaicism.

7.2 Interpreting the Results of the Bimanual and External Genitalia Exams

This section provides a brief overview of the bimanual and external genitalia exams. For more detailed information on conducting and interpreting the results of these exams, please consult the book *Fast Facts about the Gynecological Exam for Nurse Practitioners: Conducting the GYN Exam in a Nutshell.*[20]

Performing the Bimanual and External Genitalia Exams

Do not underestimate the importance of being gentle during the exam. A rough examination may cause the client to become uncomfortable and tense, making the discovery of abnormalities more difficult. Always inform the client you are going to touch her before doing so.

First, gently palpate the abdomen for masses and pain. Wash your hands thoroughly with soap and water, dry them, and put on clean exam gloves. Then, perform the bimanual exam. To perform the bimanual exam, place two gloved, lubricated fingers in the vagina until you feel the cervix. Place your other hand on the abdomen below the belly button and push down towards the two fingers in the vagina. Feel the entire uterus for masses, pain, tenderness, and distension. Finally, carefully inspect the external genitalia for vulvar lesions, lichen sclerosus, and infectious disorders.

Pregnancy or Abdominal Abnormalities

Masses, pain, tenderness, and distension in the abdomen or uterus may indicate:

- pregnancy, especially if the client has recently missed menses and the walls of the uterus feel soft and smooth;
- cervical, uterine, vaginal, or ovarian cancers, especially if the client complains of abnormal vaginal bleeding;
- ectopic pregnancy or appendicitis;
- pelvic inflammatory disease (PID).[3]

Refer clients who report missed menses and may be pregnant for antenatal care. Treat lower abdominal pain and masses as described on page 137.

Surgery Scars

Scars may indicate a previous surgery or hysterectomy. Ask the client about any previous surgeries if scars exist. If the client has undergone a radical hysterectomy, total hysterectomy, or trachelectomy, the client does not have a cervix and should not be screened. If the client has undergone a partial hysterectomy, she has a cervix and should be screened.

Vulvar Lesions and Cancer

Vulvar cancer is rare compared to cervical cancer. Although vulvar cancer occurs primarily among elderly women around age 70, vulvar cancer can occur among much younger women.[26] HPV causes approximately 40.4% of all vulvar cancers.[18] Vulvar lesions and cancer occur more commonly in HIV-positive women.[22]

Any lump or mass on the vulva may indicate vulvar cancer. On physical examination, vulvar lesions usually appear raised and may be fleshy, warty, or ulcerous.[4] Vulvar lesions may appear similar to lichen sclerosus or a rash. Refer clients with possible vulvar lesions or cancer to a physician for a biopsy. Treatment for vulvar cancer usually involves surgery and radiation therapy or chemotherapy.[28]

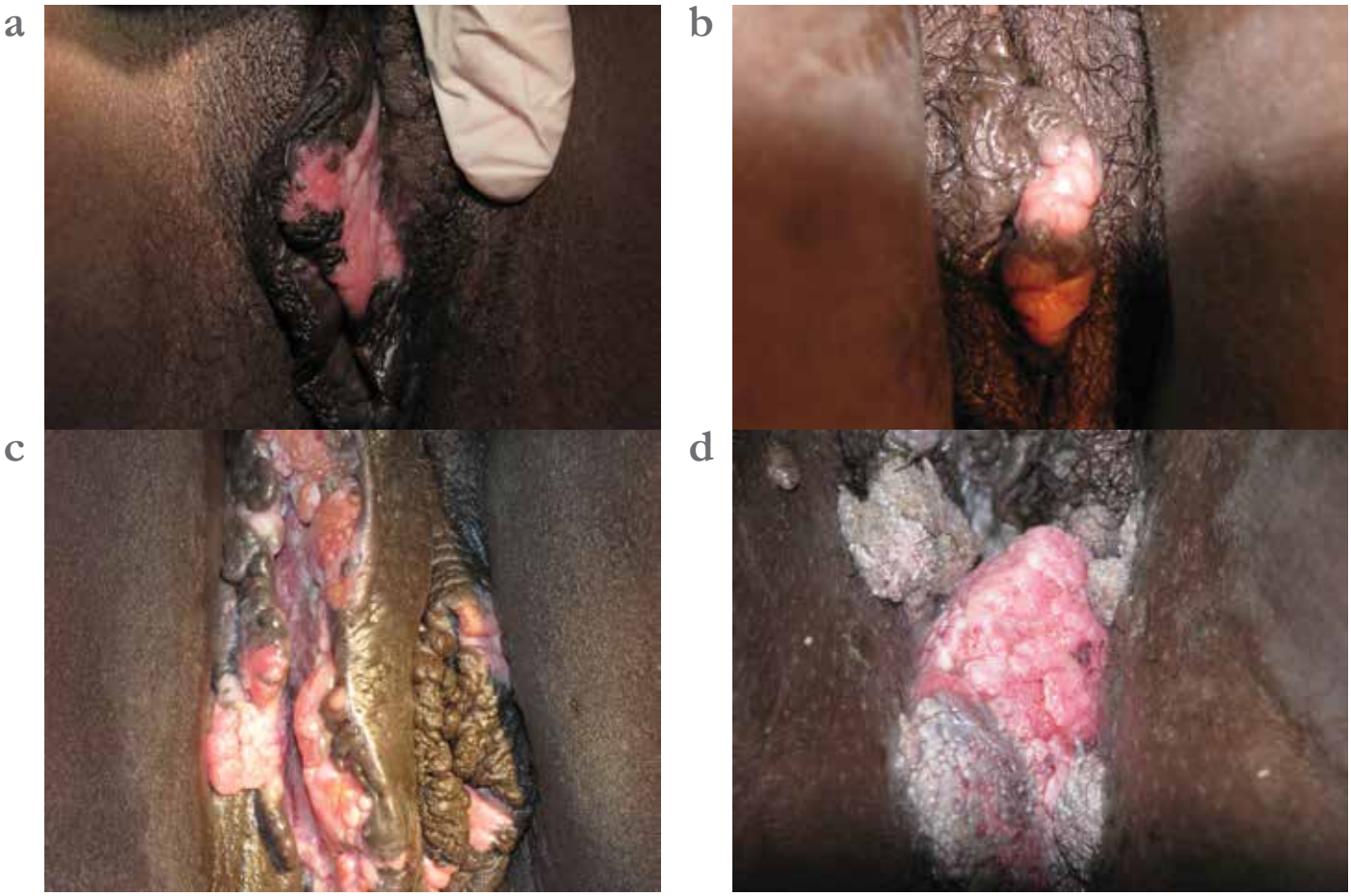

Figure 7.7a-b The vulva with precancer. Similar to cervical cancer, potentially precancerous lesions are classified into grades of vulvar intraepithelial neoplasia (VIN).

Figure 7.7c-d The vulva with cancer.

Lichen Sclerosus

Lichen sclerosus is a skin disease commonly found in the genital area. Lichen sclerosus usually affects adult postmenopausal women. However, women who have not undergone menopause, men, and children can also be affected. The underlying cause and exact prevalence of lichen sclerosus is unknown.

Common symptoms of lichen sclerosus include severe itching and soreness. Common signs include small white spots on the external genitalia. As the disease progresses, the spots grow into bigger patches and become thin and wrinkled. Bruising, bleeding, and scarring can occur, including severe scarring which may require surgery.

Treat lichen sclerosus clients with a potent topical corticosteroid ointment (e.g. clobetasol proprionate 0.05%) twice daily for 2-3 months. Then, decrease the dose gradually to zero and resume only when necessary. Check with your local pharmacy to see what lichen sclerosus treatment ointments may be available.

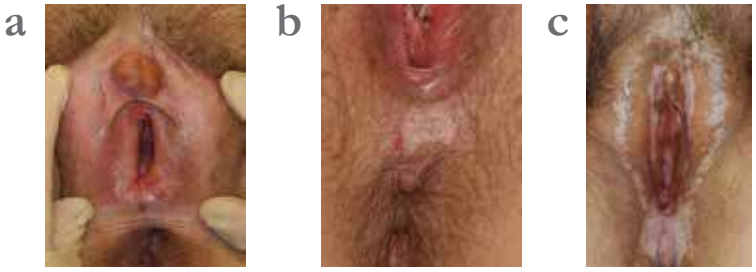

Figure 7.8a-c Lichen sclerosus.[7]

Vulvar cancer is more common in clients with lichen sclerosus. Carefully observe every client with lichen sclerosus and with raised or warty lesions that do not heal after treatment as they may represent vulvar cancer. All clients with lichen sclerosus should be informed that it is associated with vulvar cancer and monitored over the subsequent years.[16,27]

Infectious Disorders

Infectious disorders such as genital ulcers should be diagnosed and treated if necessary (discussed in chapter 10).

7.3 Interpreting the Results of the Speculum Exam

This section provides a brief overview of the speculum exam. For more detailed information on conducting and interpreting the results of the speculum exam, please consult the book *Fast Facts about the Gynecological Exam for Nurse Practitioners: Conducting the GYN Exam in a Nutshell.*[20]

No woman enjoys a speculum exam, but with a comforting attitude, the provider can make the speculum exam less anxiety-inducing. Always lubricate the speculum before inserting it and always tell the client before touching her. Notably, a history of sexual abuse or trauma can cause special anxiety prior to the speculum exam. Let the client know exactly what to expect, and if the client does not wish to be examined that day, schedule the exam for another day.

The Transformation Zone

Right after inserting the speculum, identify the columnar epithelium, the squamous epithelium, the squamocolumnar junction, and the transformation zone. The provider should make sure the entire transformation zone can be seen, so he or she does not miss any lesions during VIA. If the entire transformation zone cannot be seen gently adjust the speculum or push back the walls of the vagina.

Cervical Abnormalities: Ectopy, Polyps, and Nabothian Cysts

Although ectopy does not cause cancer, ectopy increases the risk of sexually transmitted infections such as HIV.[12] Providers should inform clients with ectopy of the associated risks.

Nabothian cysts do not cause problems except in extremely rare cases when they become extremely large.[13,24] Except for educational purposes, it is not necessary to inform clients of Nabothian cysts.

Our programme in Zambia does not routinely remove cervical polyps because of the low probability of a polyp developing into cancer and the cost of treatment.[23] However, most studies recommend the routine removal of cervical polyps, especially in clients with abnormal cytology, although the removal is not considered mandatory.[6,8] Large polyps require surgery under general anaesthesia for removal, but small polyps can be removed as an office procedure by twisting them off. Once removed, polyps typically do not recur.[1]

Evidence of Cleaning or Foreign Body Inside the Vagina

A healthy vagina has acidic mucus which prevents infection.[5] When a woman cleans her vagina, she washes away the mucus and increases her risk of infection.[11,19,29] Women should not clean the inside of the vagina with fingers, a cloth, or anything

else, even after sex. However, women should wash the outside of the vagina with soap and water to prevent infection and stay clean. Placing foreign objects such as herbs or chemical substances in the vagina to promote dry sex may damage the cervix (Figure 7.9).[10]

Infection, healed lacerations, or unhealed lacerations on the vagina and cervix may indicate unhealthy vaginal practices. If lacerations or infection exists, the provider should consider counselling the client on the risks of unhealthy vaginal practices.

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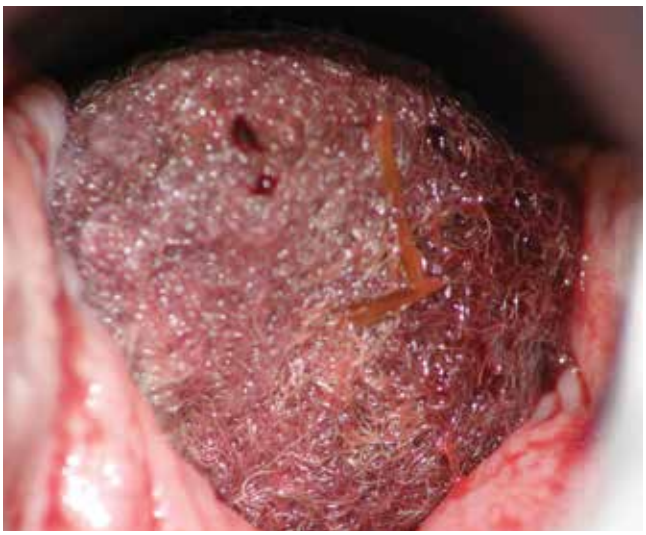

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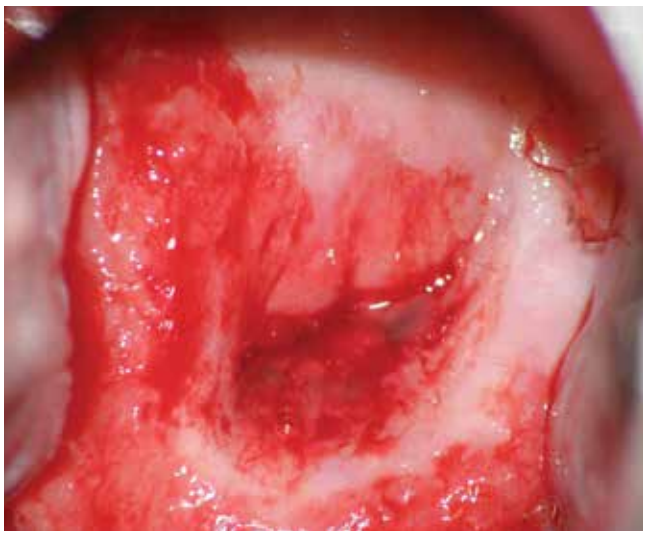

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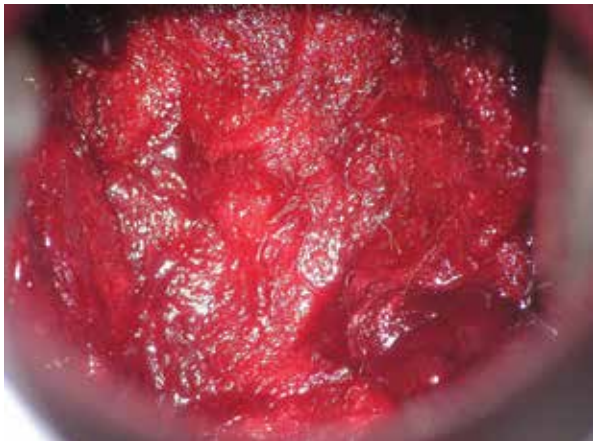

Figure 7.9a
A cervix covered by dry herbs.

Figure 7.9b
The same cervix after removal of the dry herbs.

Figure 7.9c
A cervix with bleeding due to the presence of a foreign body.

Leukoplakia (Keratosis)

Leukoplakia is a thick white patch. The provider should look for leukoplakia patches on the cervix prior to VIA.[25] Though usually benign, leukoplakia may cover a cervical lesion.[9] Therefore, our programme recommends treating leukoplakia like an acetowhite lesion.

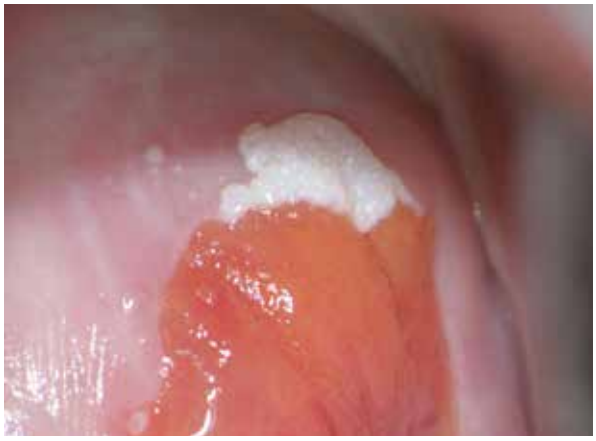

Figure 7.10 Close-up of a leukoplakia patch on the cervix.

Sexually Transmitted Infections (STIs)

STIs should be diagnosed and treated during the speculum exam as discussed in chapter 10.

Follow-Up and Referral

During the external genitalia, bimanual, or speculum exams, it may become apparent that follow-up is needed. Agree on a follow-up plan with the client and schedule any referrals before she leaves the clinic.

7.4 Interpreting the Results of VIA and DC

There are four possible results for VIA and DC:

- VIA-negative;
- VIA-positive;
- suspicious for cancer;
- indeterminate.

VIA-Negative

A VIA-negative result means no acetowhite lesions or faint acetowhite areas without distinct borders.

Nabothian cysts, polyps, and ectopy are considered VIA-negative findings. Take care not to mistake Nabothian cysts, cervical mucus, or infection for an acetowhite lesion.

When performing digital cervicography, the camera flash may generate a white glare on the cervix in the photograph. Take care not to mistake the camera glare for an acetowhite lesion.

White dot-like areas on the cervix may exist due to acetowhitening around the openings of normal glands. This phenomenon is called "cuffing." Cuffing is a VIA-negative result.

After the provider applies acetic acid, a thin translucent white veil or patchy acetowhite areas may cover the transformation zone near the squamocolumnar junction. The veil appears because normal cells undergoing squamous metaplasia (benign metaplastic epithelium) have more protein than other normal cells. The veil is not abnormal. Inflammation and regenerating epithelium may also cause pale, translucent, patchy acetowhitening with ill-defined margins not restricted to the transformation zone.

The columnar epithelium may react slightly to the dilute acetic acid and become slightly whitened. Slight whitening of the columnar epithelium is not abnormal.

In older women who have undergone menopause, the cervical epithelium may become atrophied, or slightly degenerated. Atrophic epithelium will appear white and fibrous after the application of dilute acetic acid. Atrophic epithelium can be distinguished from an acetowhite lesion because it covers the entire cervix and lacks a distinct, raised border.

VIA-Positive

A VIA-positive result means thick, opaque white lesions with distinct borders located in the transformation zone of the cervix. The provider should treat the lesion with cryotherapy or cold coagulation depending on the specific criteria discussed on page 98 and page 117, or refer for LEEP.

Lesions due to low-risk HPV infection, such as satellite lesions and cervical warts (Figure 7.22 and 7.23), may occur and rarely progress to cervical cancer.[17,21] However, lesions due to low-risk HPV infection may cover a more serious lesion. Therefore, our programme recommends treating all satellite lesions and cervical warts as VIA-positive. Notably, researchers lack an understanding of the severity of satellite lesions in HIV-positive women. Further research is necessary to characterize satellite and low-grade lesions in HIV-positive women.

Consider the following four characteristics of any possible lesion.

- **Colour.** Is the lesion an opaque white colour?
- **Borders.** Are the borders of the lesion distinct?
- **Location.** Is the lesion located in the transformation zone?
- **Thickness.** Is the lesion raised above the surrounding tissue?

If the lesion has these characteristics, it is VIA-positive.

Suspicious for cancer

Clients with lesions suspicious for cancer should be referred for further assessment and management. Lesions with the following characteristics may be cancerous:

- visible ulcers;
- acetowhite cauliflower-like growths;
- rough or irregular surface;
- bleeds easily when touched;
- highly atypical vessels.

Indeterminate

If you cannot determine whether a lesion is VIA-negative, VIA-positive, or suspicious for cancer, use distance consultation to help determine the result. If distance consultation is not available, gently repeat VIA once or twice without causing bleeding. Tell the client what you are doing. If doubt still exists, consider classifying the result as positive and treating according to protocol.

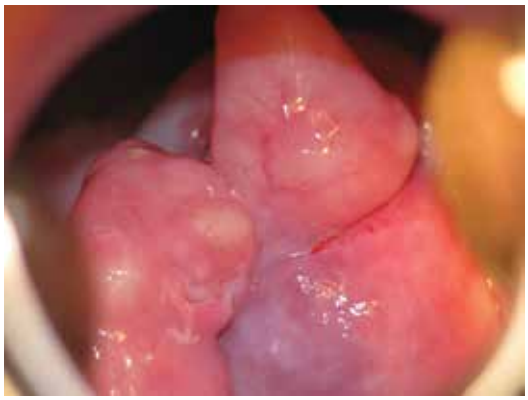

Figure 7.11 This cervix is VIA indeterminate because the presence of large ectocervical polyps prevents the provider from seeing the entire cervix. Repeat VIA after removal of the polyps.

7.5 VIA-Negative Cervical Images

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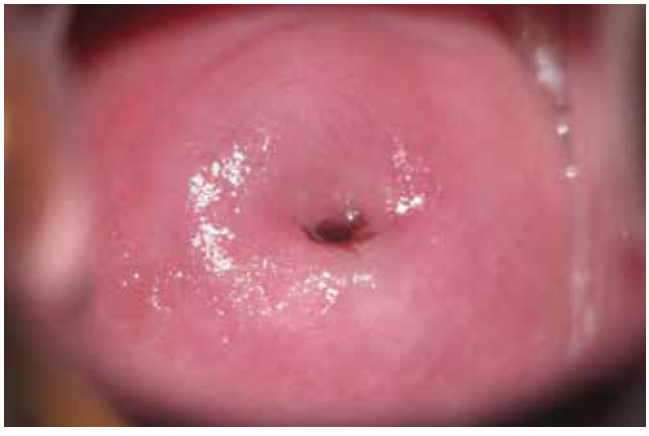

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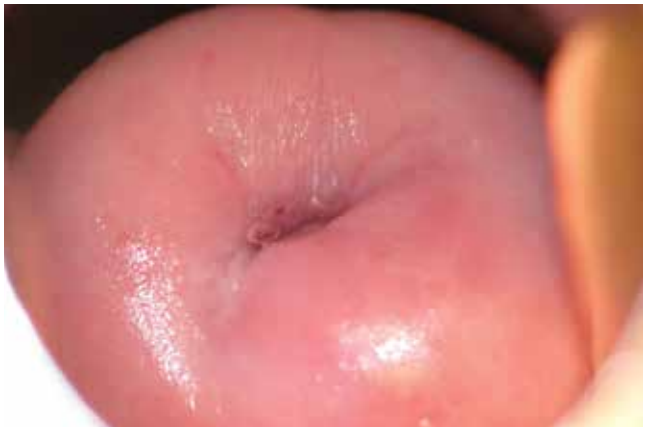

(Continued on next page)

(VIA-negative cervical images, continued)

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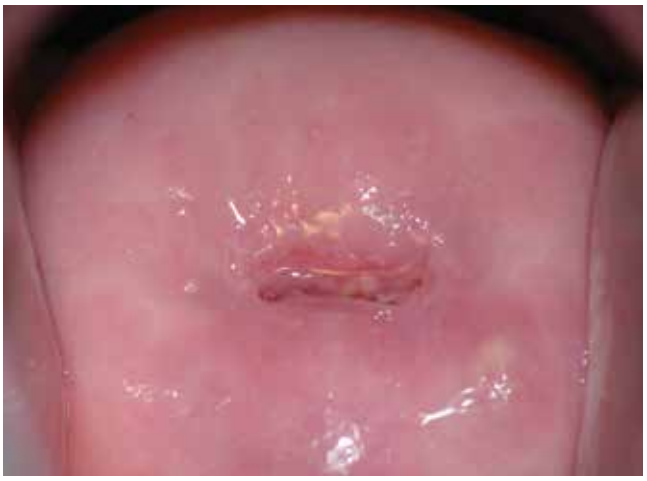

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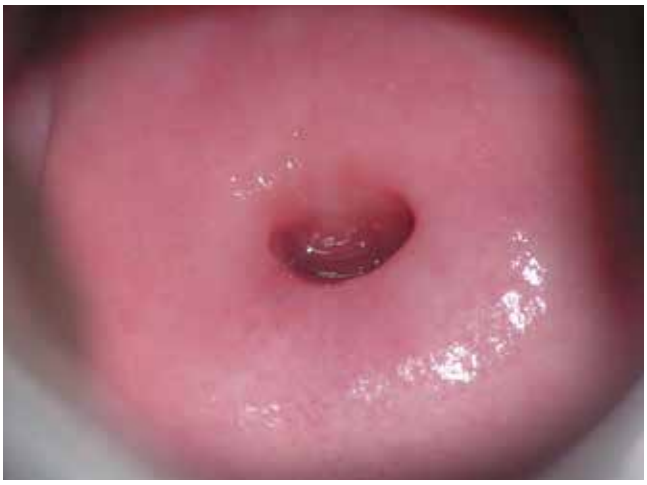
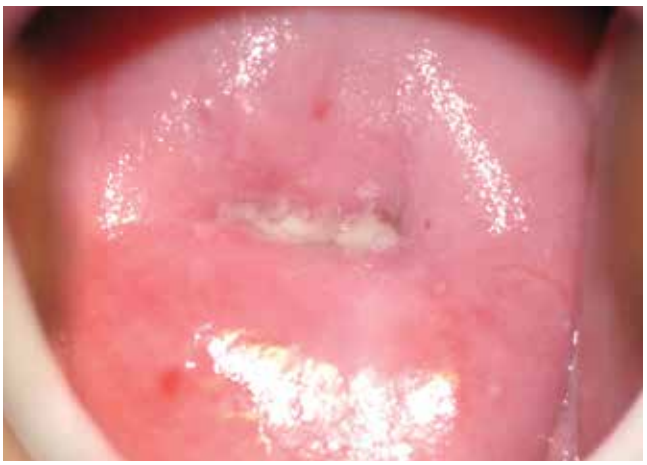


Figure 7.12a-d VIA-negative cervical images.

Camera Glare

a



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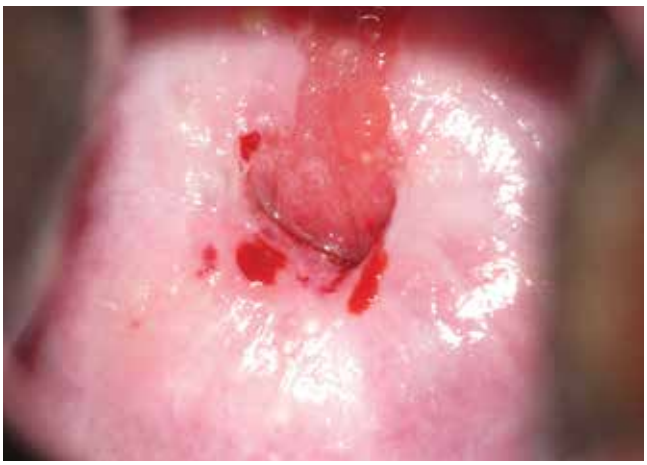

Figure 7.13a-b VIA-negative cervical images with camera glare. Take care not to confuse the bright light reflecting off the cervix with an acetowhite lesion.

Intrauterine Device (IUD)

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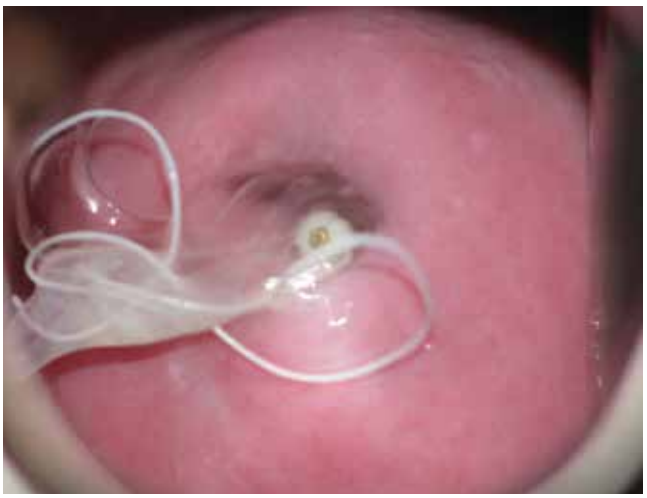

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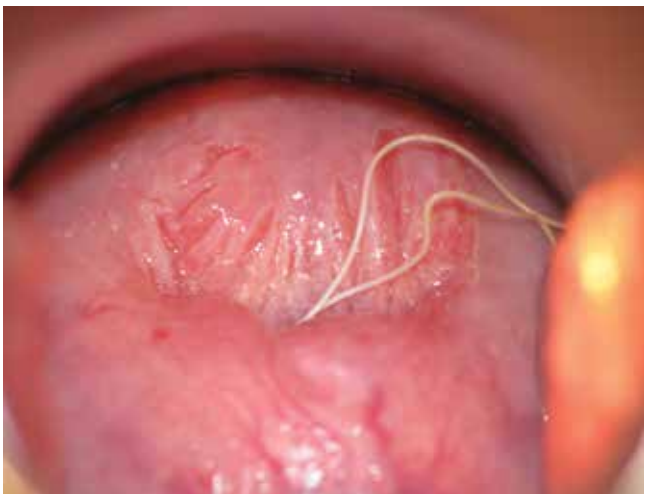


Figure 7.14a-b VIA-negative cervical images with an intrauterine device (IUD) present. An IUD is a common family planning tool.

Mucus

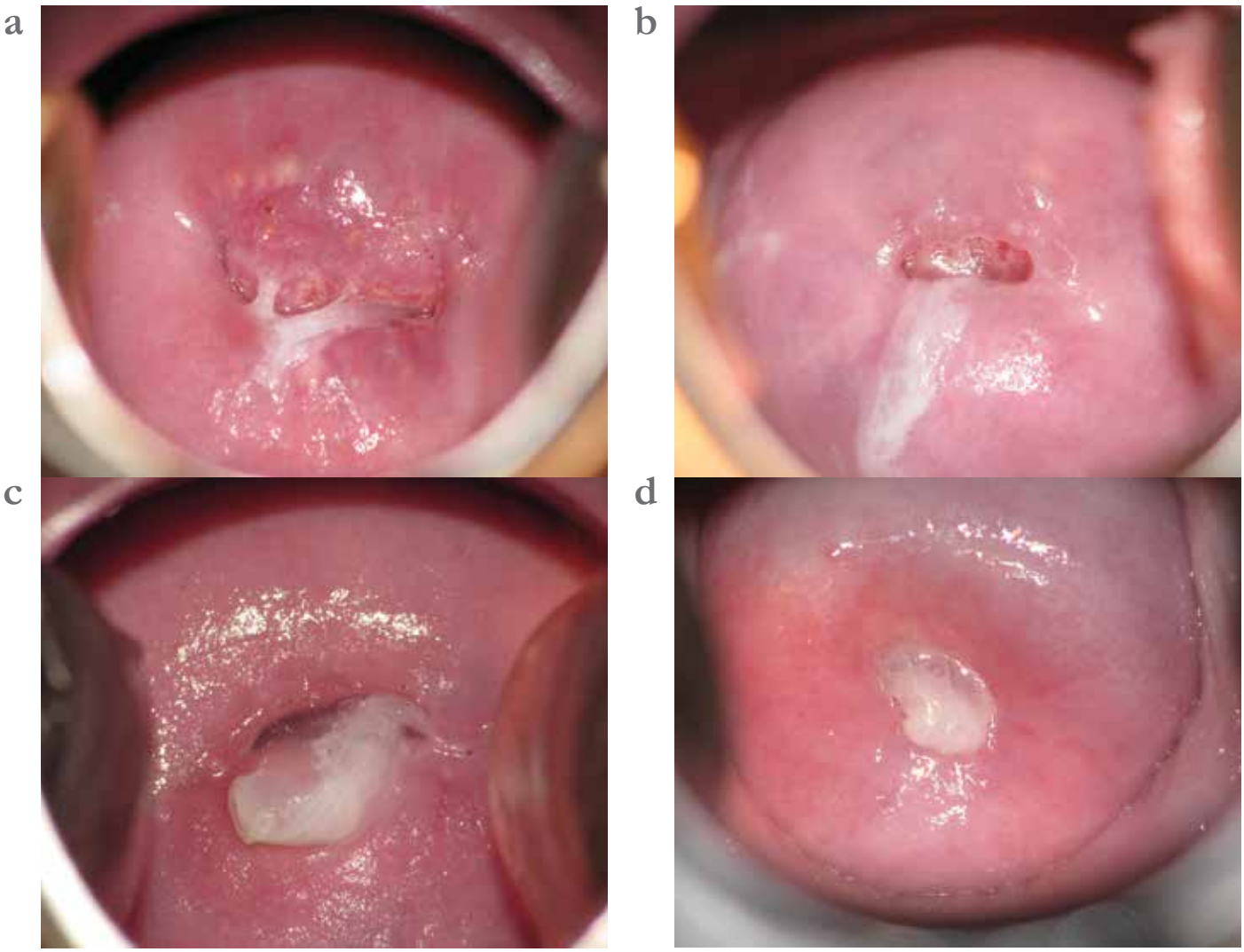


Figure 7.15a-d VIA-negative cervical images with cervical mucus coming from the endocervical canal. Take care not to confuse the mucus for an acetowhite lesion.

Recent Menstruation

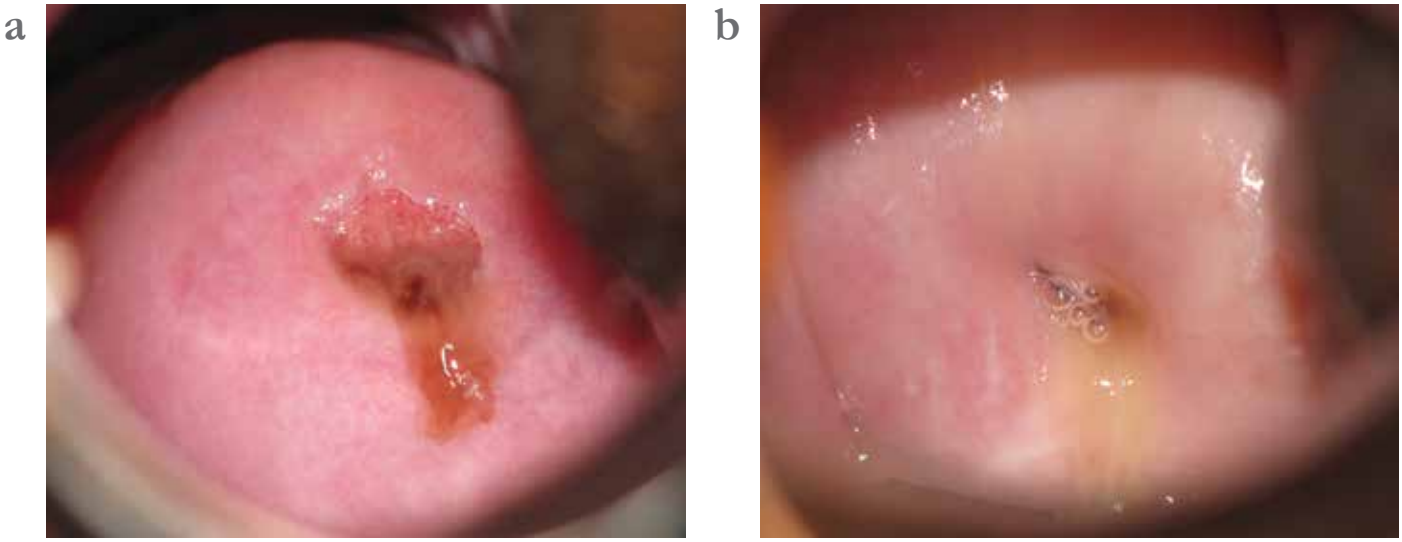


Figure 7.16a-b VIA-negative cervical images with bloody discharge due to recent menstruation.

Atrophic Epithelium

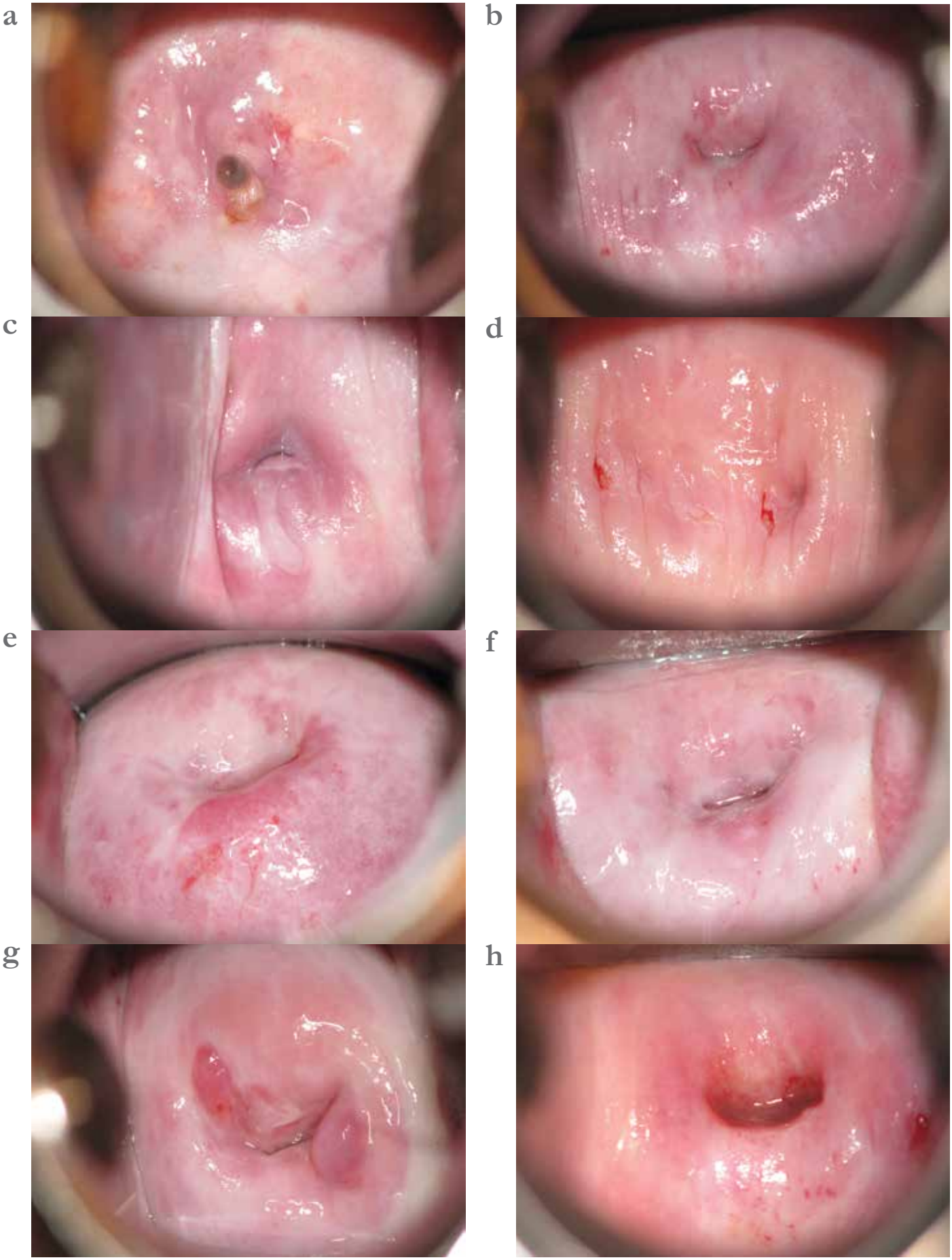


Figure 7.17a-h VIA-negative cervical images with atrophic epithelium.

Reactive Columnar Epithelium

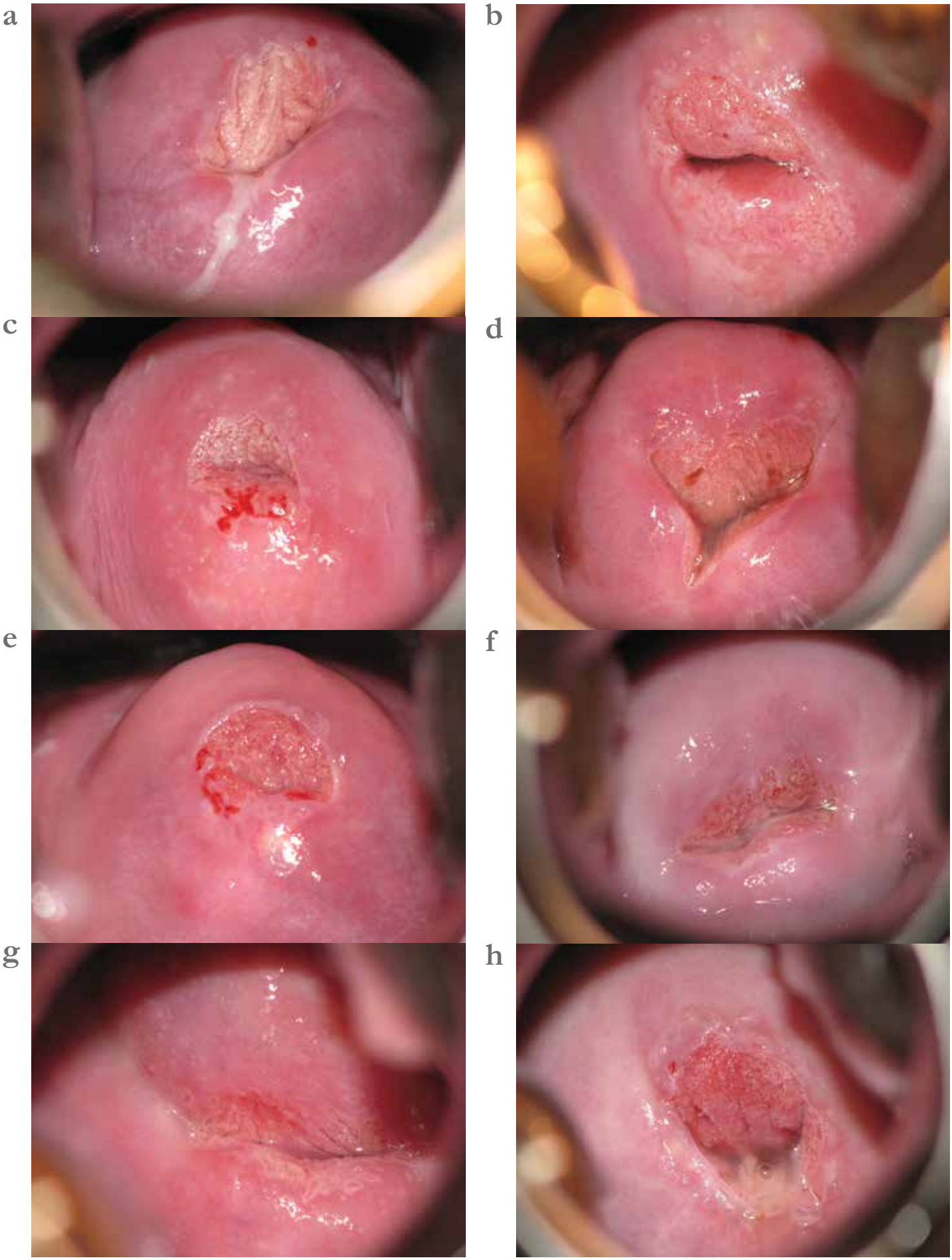
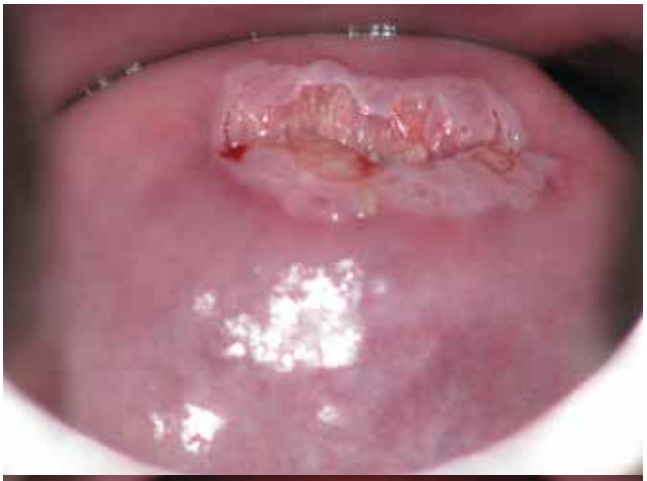


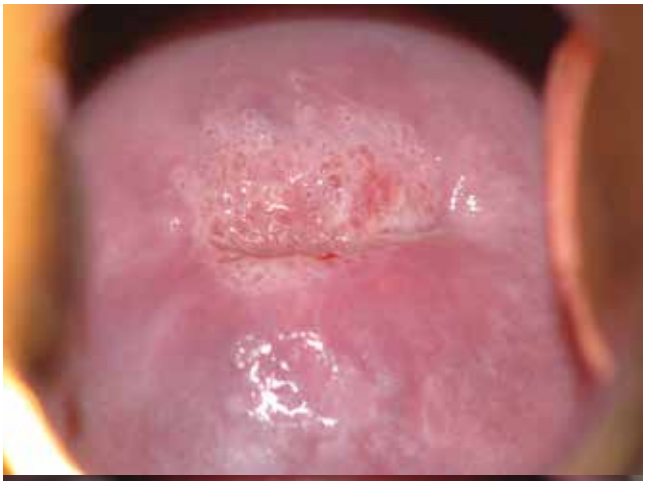
Figure 7.18a-h VIA-negative cervical images with slightly acetowhite columnar epithelium.

Cuffing Around Glands and/or Benign Metaplastic Epithelium

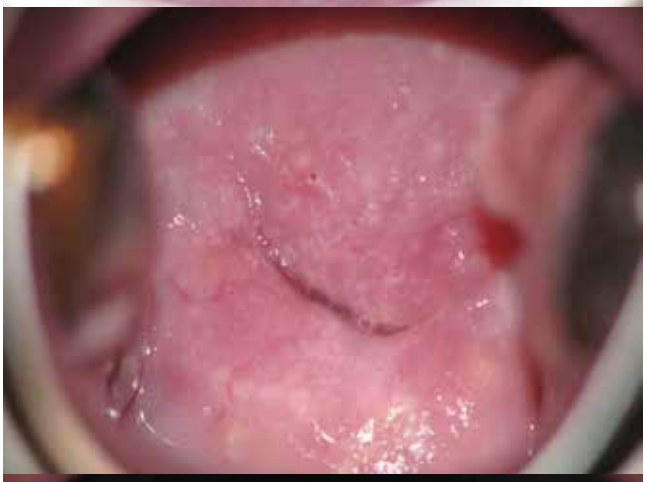
a



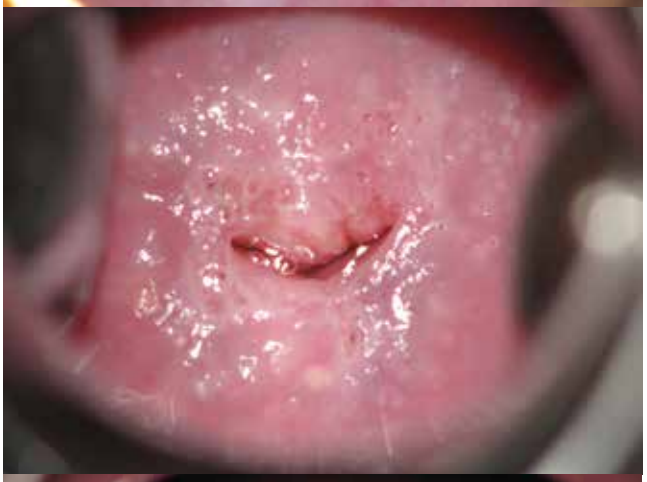
b



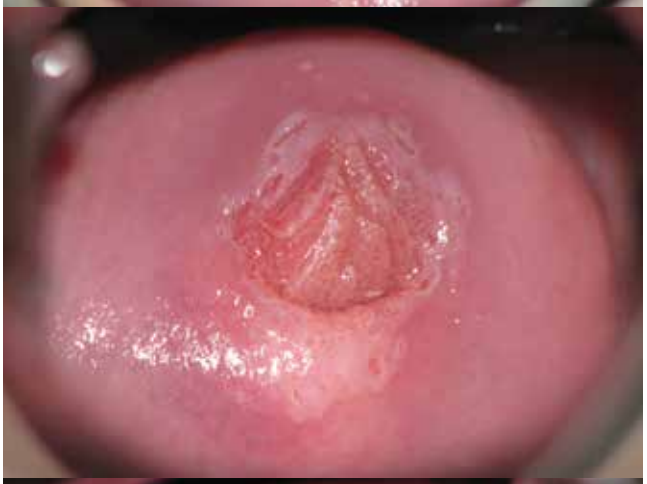
c



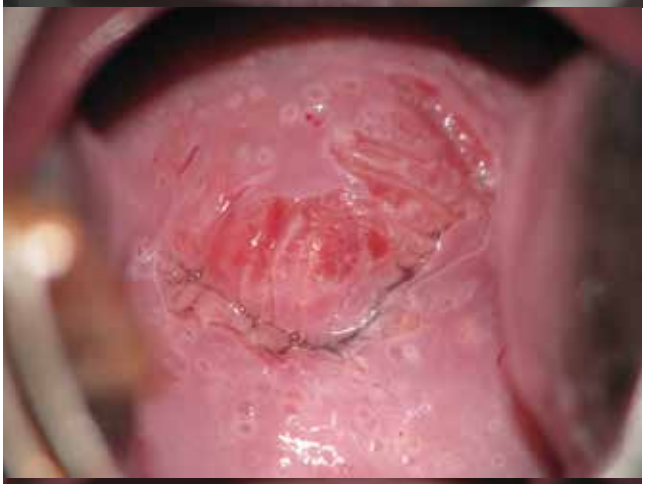
d



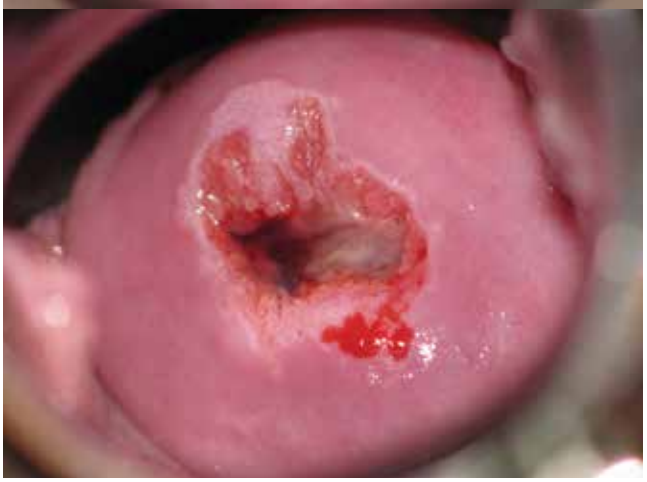
e



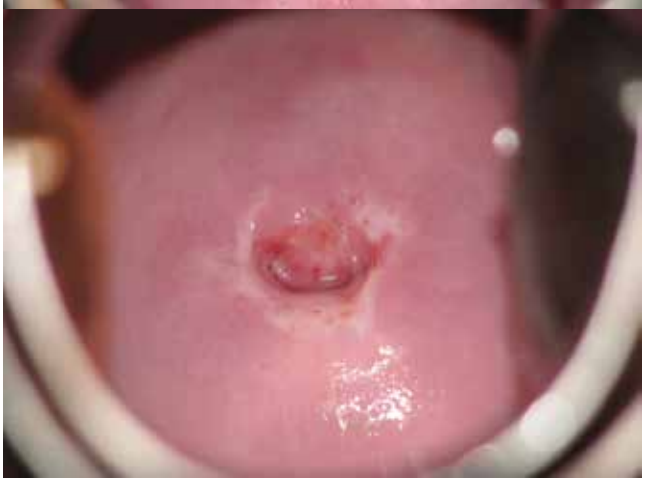
f



g



h



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(Cuffing and/or benign metaplastic epithelium, continued)

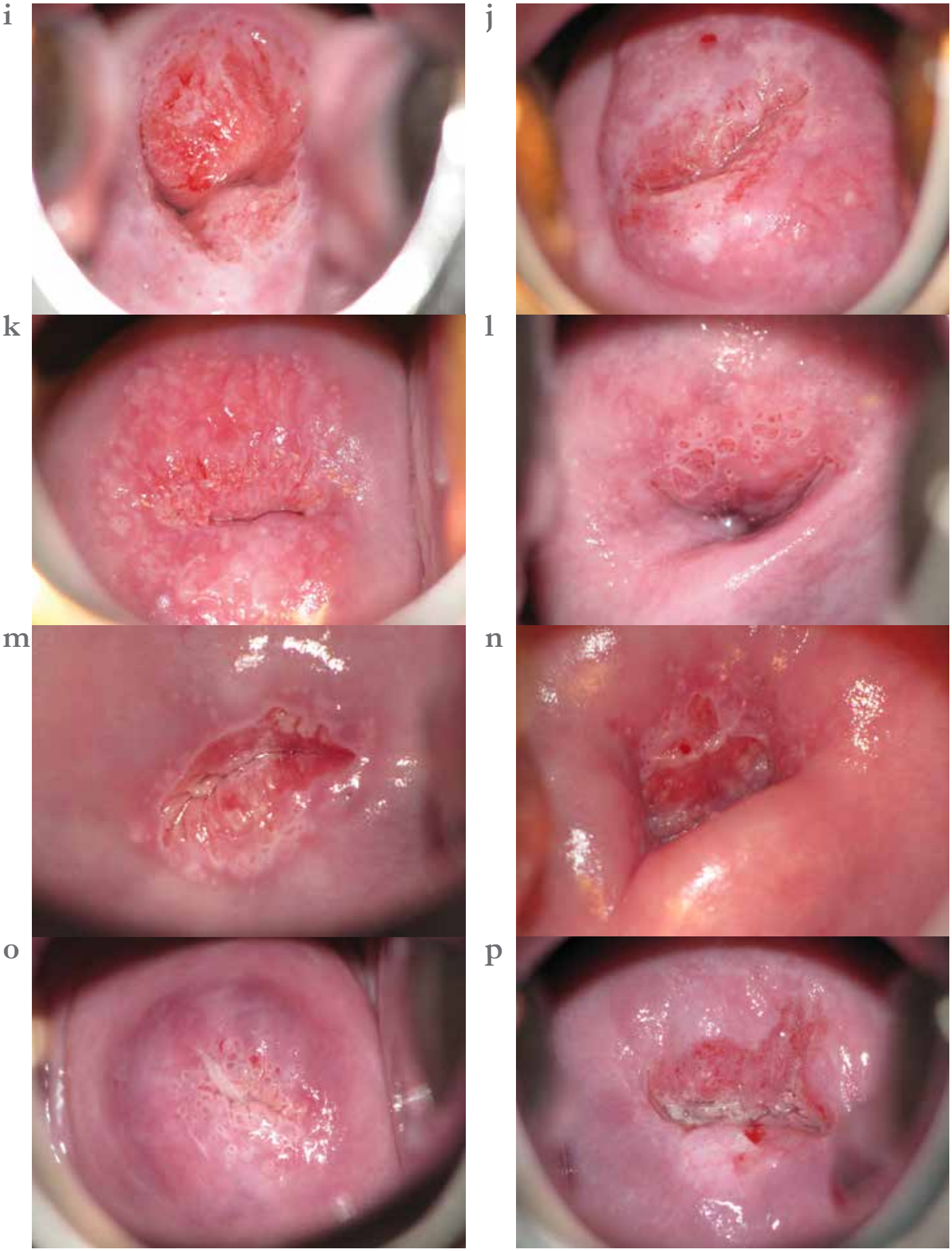


Figure 7.19a-p VIA-negative cervical images with cuffing due to acetowhitening around glands and/or benign metaplastic epithelium causing a thin white veil in the transformation zone.

7.6 VIA-Positive Cervical Images

For more VIA-positive images, see page 99.

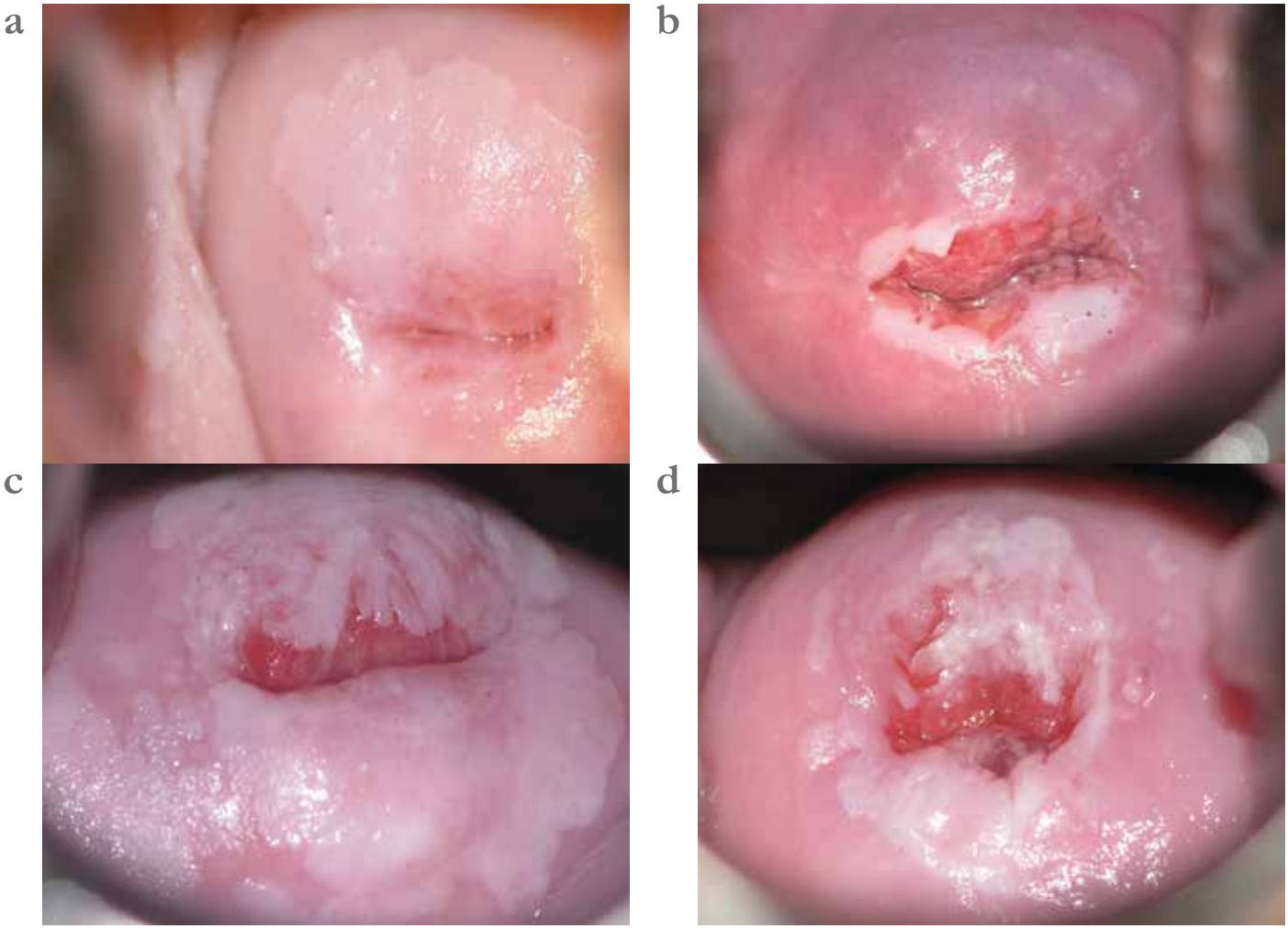


Figure 7.20a-d VIA-positive cervical images.

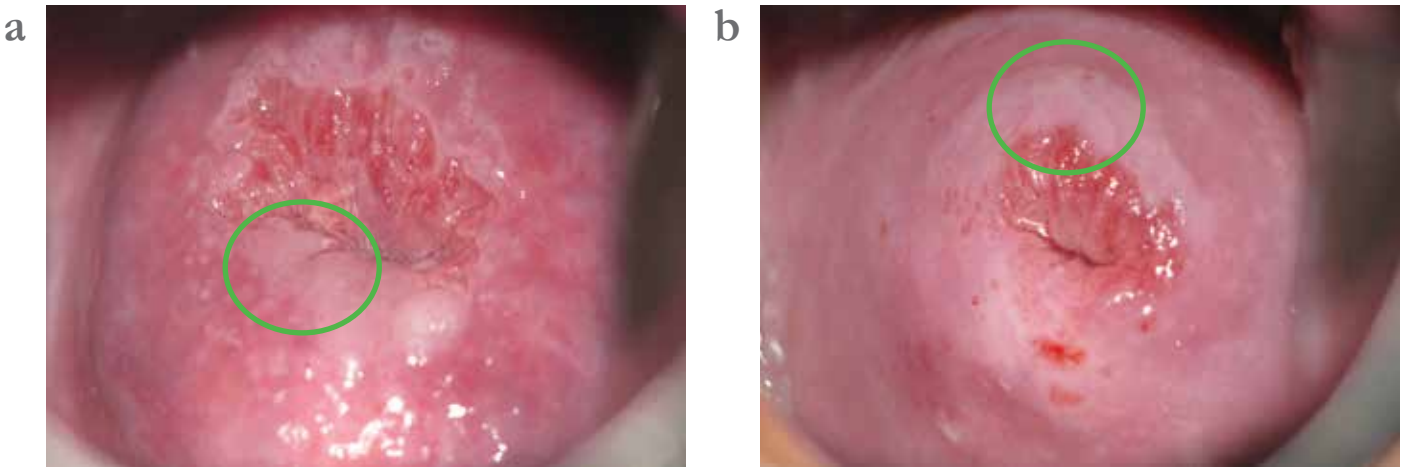


Figure 7.21a-b Borderline VIA-positive cervical images, with areas of concern circled in green. Shown as examples of a difficult VIA diagnosis.

Satellite Lesions

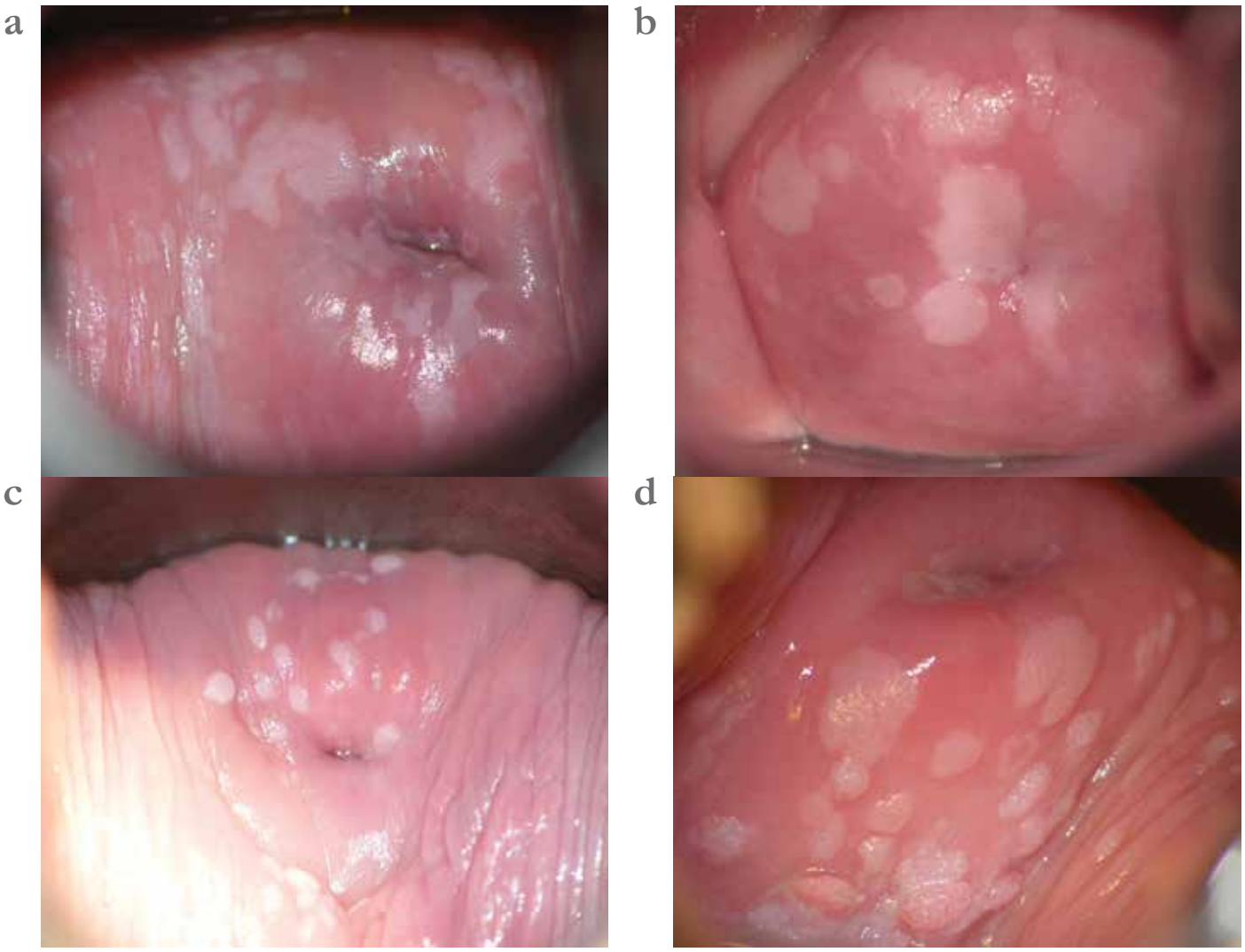


Figure 7.22a-d Cervical images with satellite lesions.

Cervical Warts

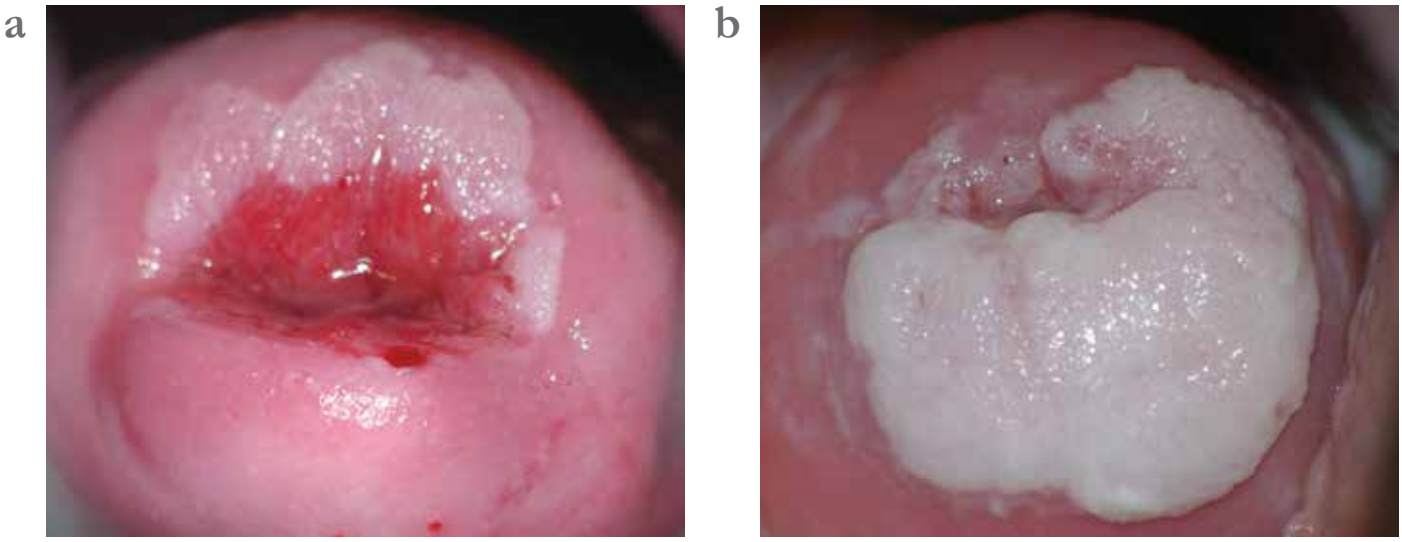
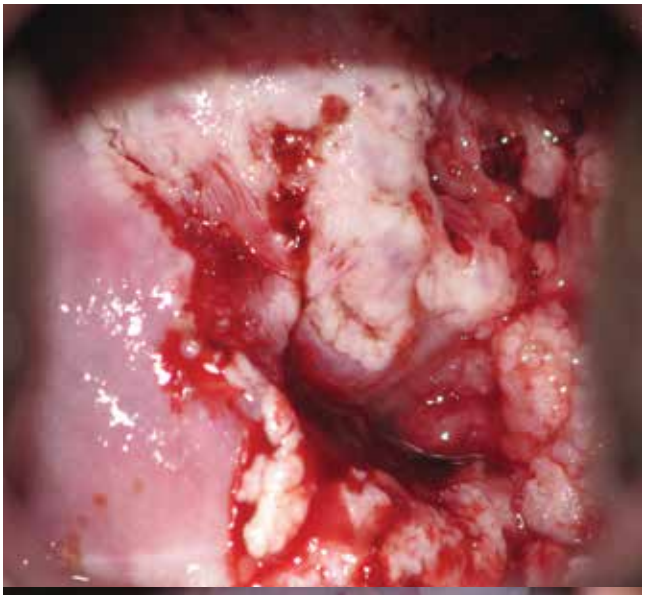


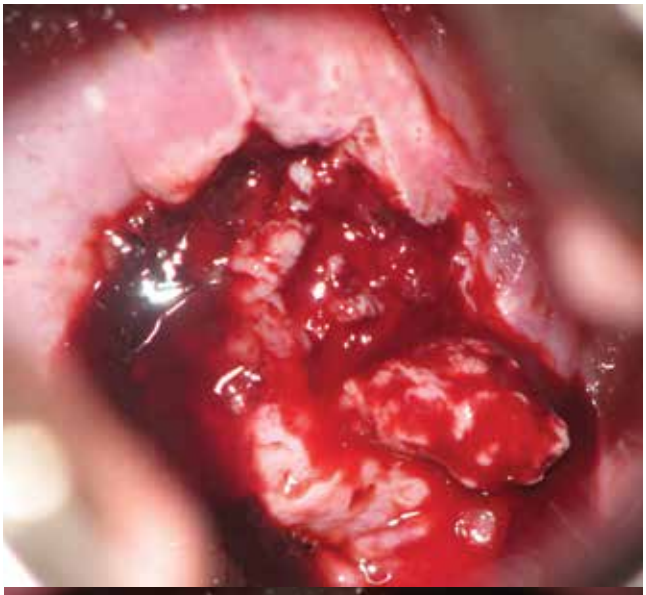
Figure 7.23a-b Warts due to low-risk HPV infection. A thick lesion with a cornflower-like texture is usually a wart. Warts may mask a high-grade lesion and should be treated.

7.7 Cervical Images Suspicious for Cancer

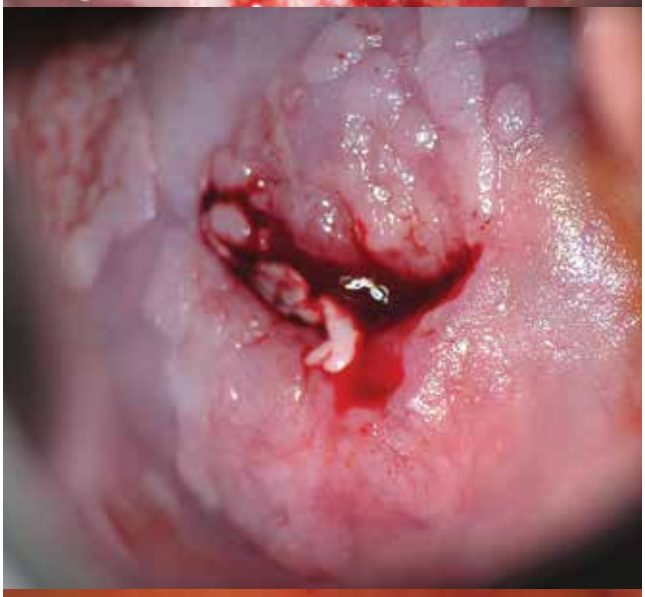
a



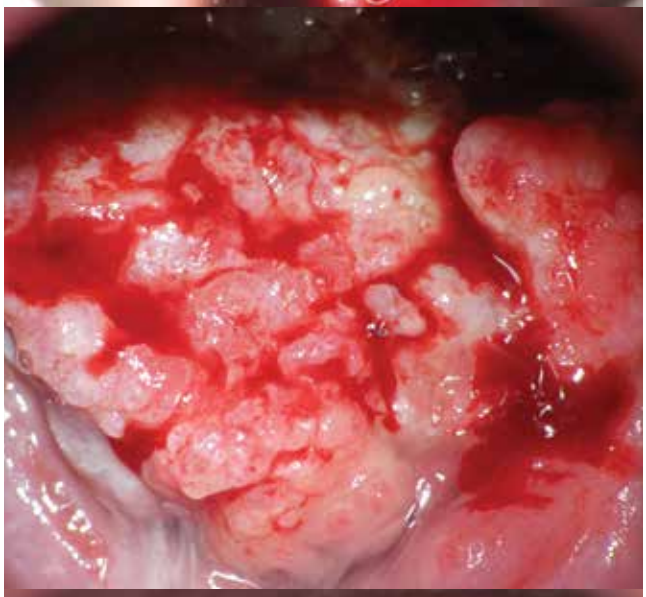
b



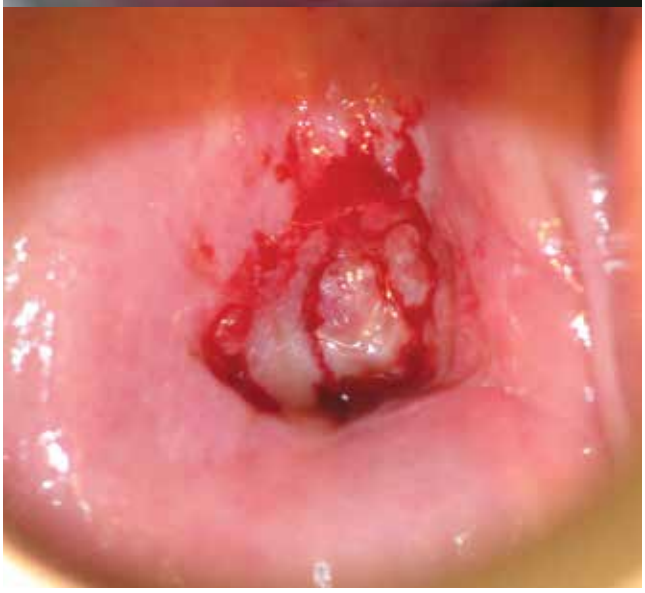
c



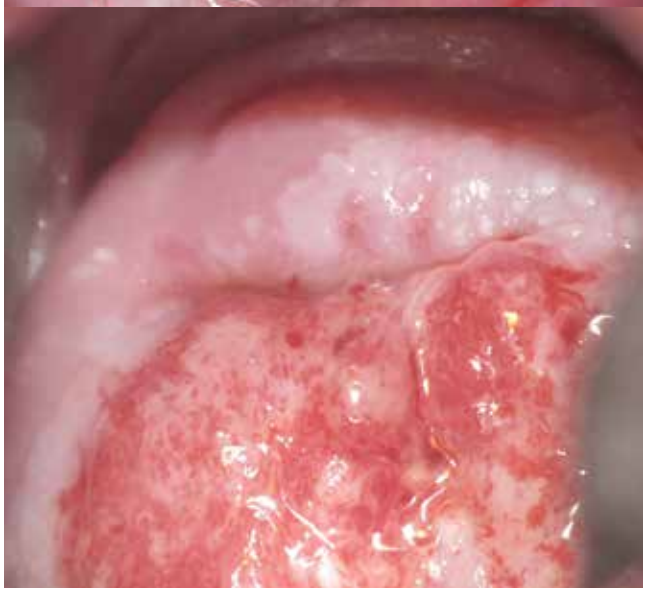
d



e



f



(Continued on next page)

(Cervical images suspicious of cancer, continued)

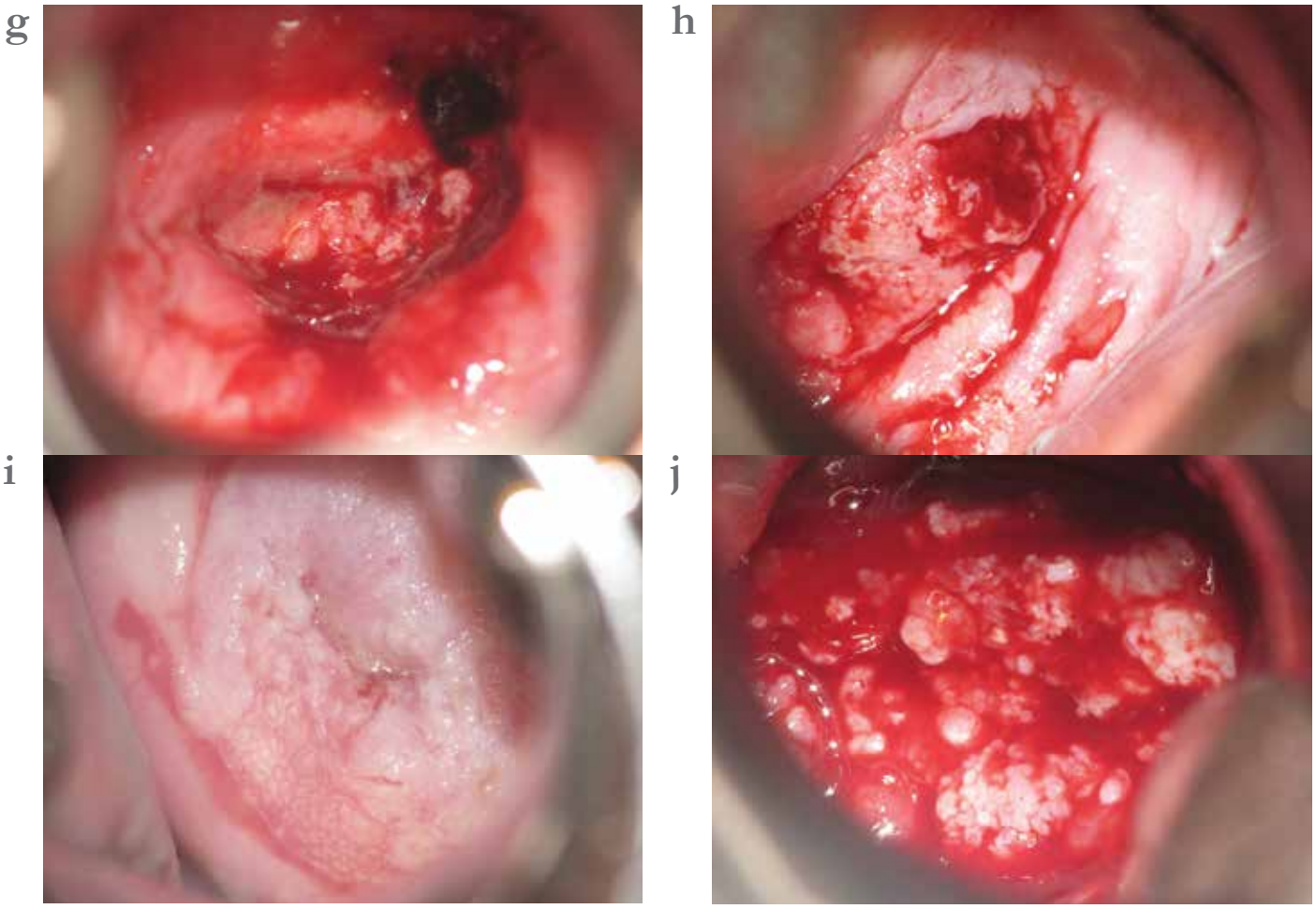


Figure 7.24a-j Cervical images suspicious of cancer.

7.8 Differentiating Between Lookalikes

Cancer vs. Ectopy

Take care not to confuse cancer and ectopy. Cancer takes many forms but is usually irregular in its growth patterns and causes distortions in the shape and size of the cervix.

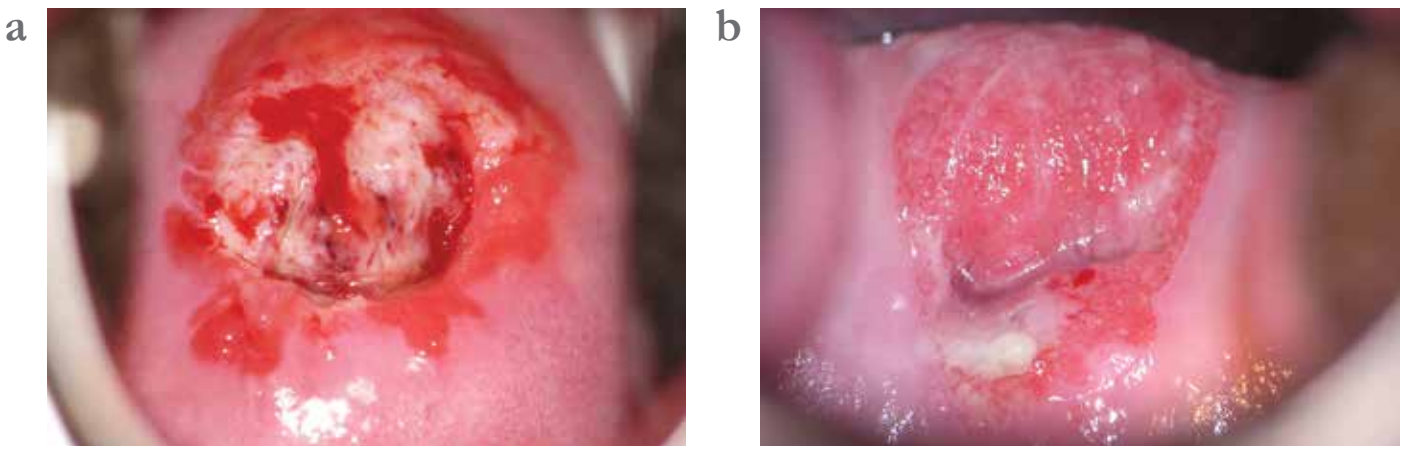
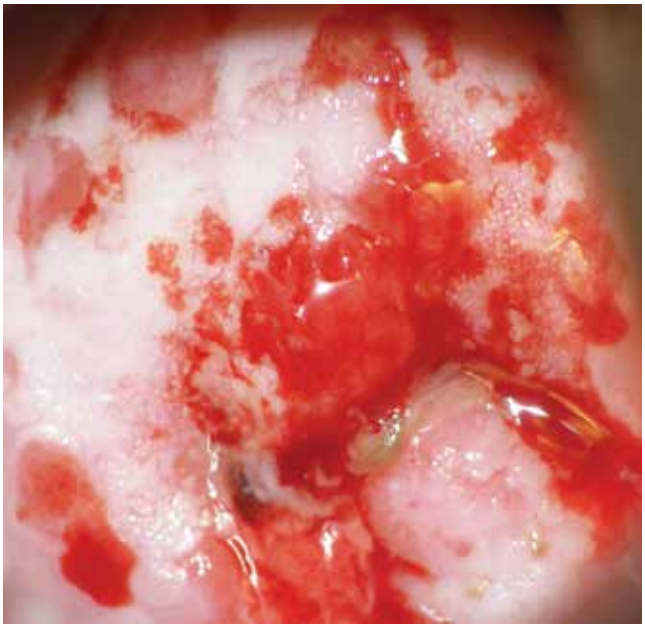


Figure 7.25a-b Cancer (a) and ectopy (b).

Cancer vs. Cervicitis

Cervicitis may be easily confused with cancer, particularly when the cancer becomes infected or the cervicitis causes ulcers. Cervicitis should be treated with antibiotics, whereas possible cancer should be referred for a diagnostic biopsy. Notably, VIA alone cannot be used to diagnose cancer. VIA can only be used to identify possible cancers. Cervicitis is discussed in chapter 10.

a



b

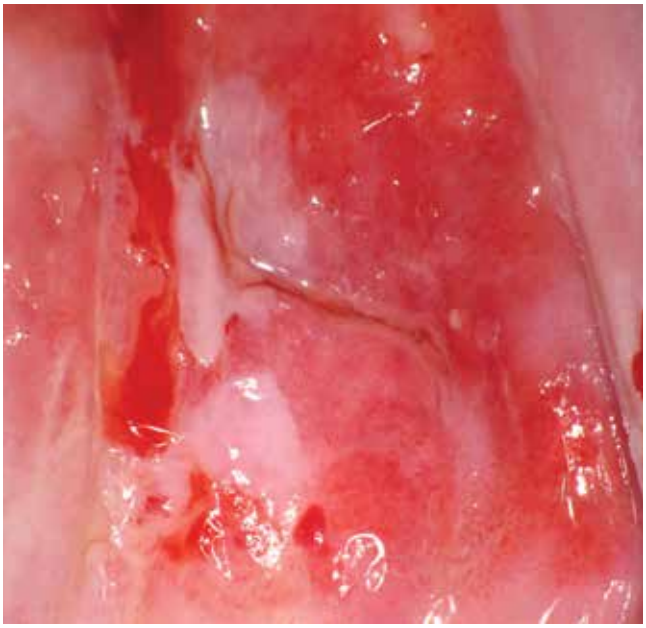
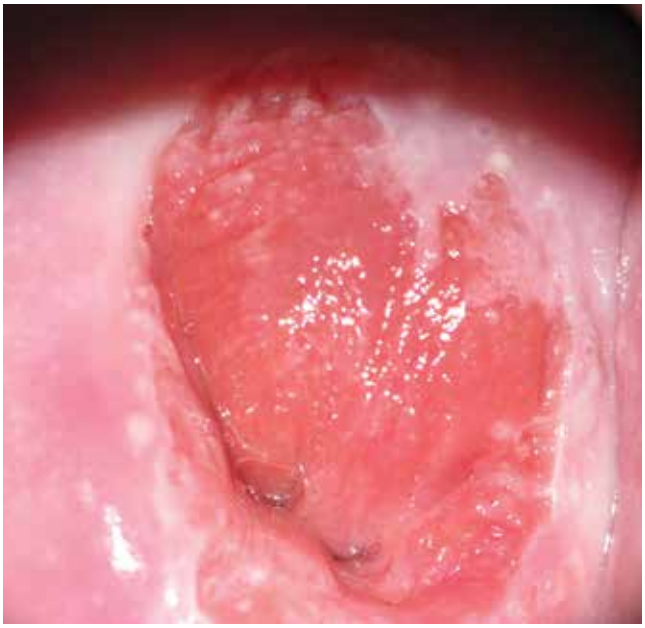


Figure 7.26a-b Cancer (a) and cervicitis (b). Note the presence of mosaicism on (a).

Ectopy vs. Cervicitis

Ectopy has distinct borders, is localized to the central portion of the cervix, and sometimes bleeds when touched. Ectopy may become more red in colour when infected. Cervicitis can involve all portions of the cervix and can be associated with bleeding and discharge.

a



b

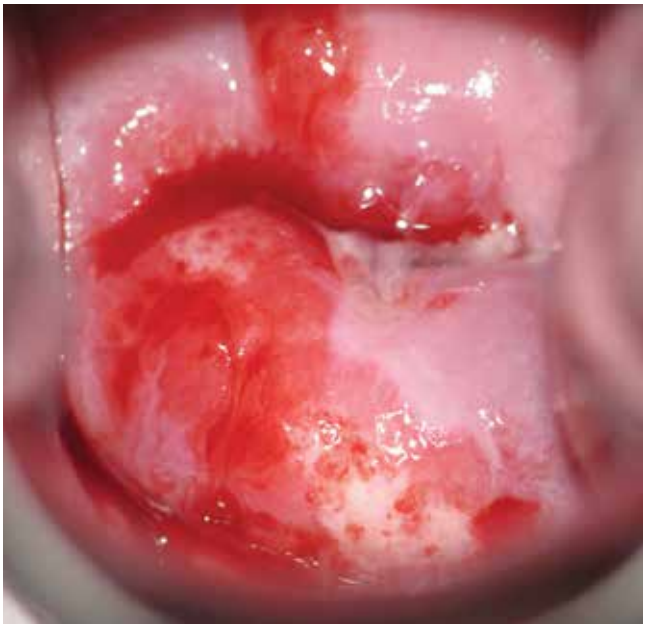


Figure 7.27a-b Ectopy (a) and cervicitis (b).

Punctation vs. Cuffing

Punctations are blood vessels that have reached the surface of the cervix. Punctations which occur within areas of acetowhite epithelium are evidence of cervical precancer or cancer. Cuffing is when the openings of glands on the surface of the cervix are surrounded by rings of acetowhite tissue. Cuffing is normal.

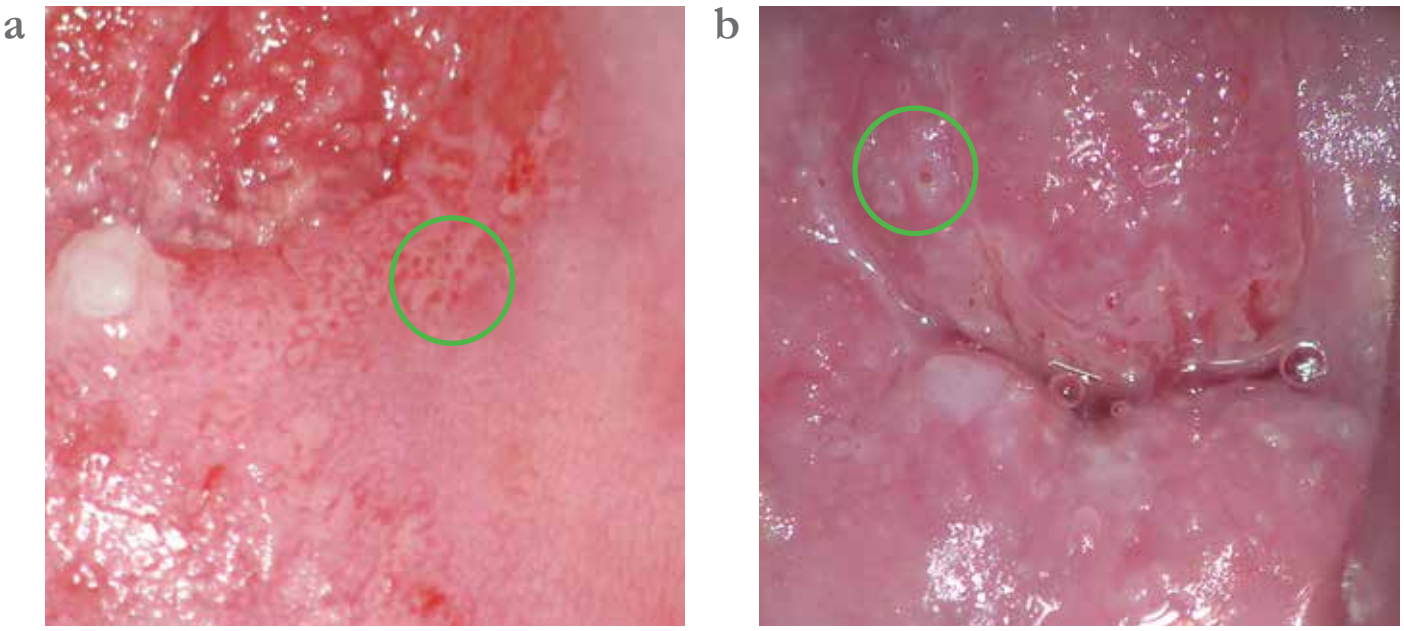


Figure 7.28a-b Punctation (a) and cuffing (b). Examples of punctation or cuffing circled in green.

Mosaicism vs. Warts

Mosaicism is when islands of acetowhite tissue are surrounded by blood vessels. Mosaicism is evidence of cervical precancer or cancer. Warts occur when the tissue is infected with low-risk HPV. Warts may have a cornflower-like pattern.

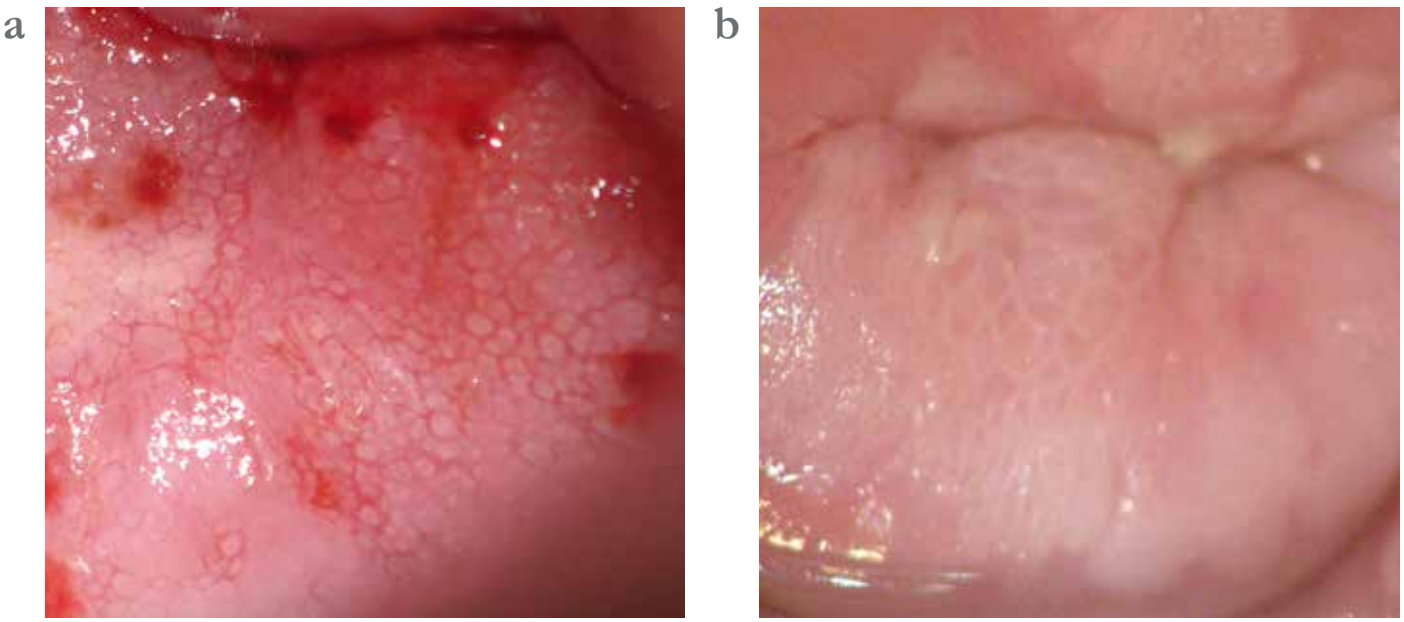
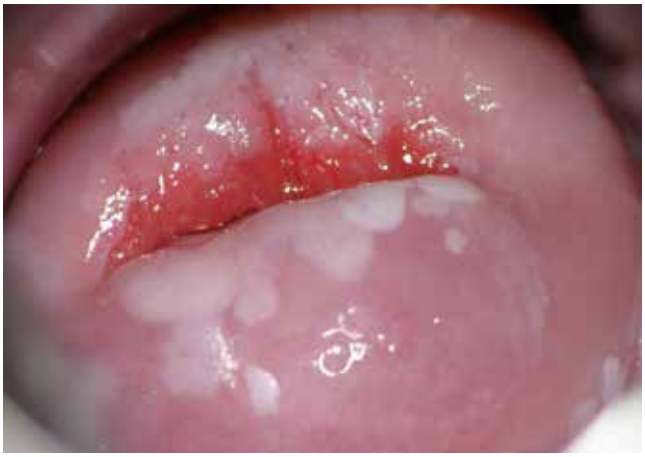


Figure 7.29a-b Mosaicism (a) and warts (b).

VIA-Positive Lesion vs. Benign Metaplastic Epithelium

VIA-positive lesions have sharp, distinct borders. Epithelial cells undergoing squamous metaplasia (benign metaplastic epithelium) usually appear as a thin white veil with feathery, indistinct borders after the application of vinegar.

a



b

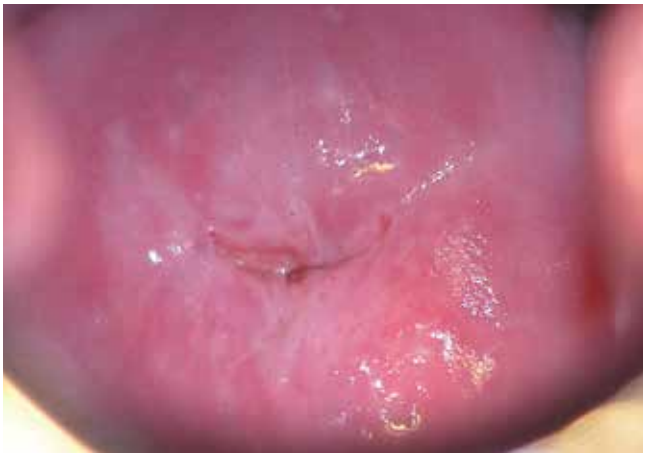
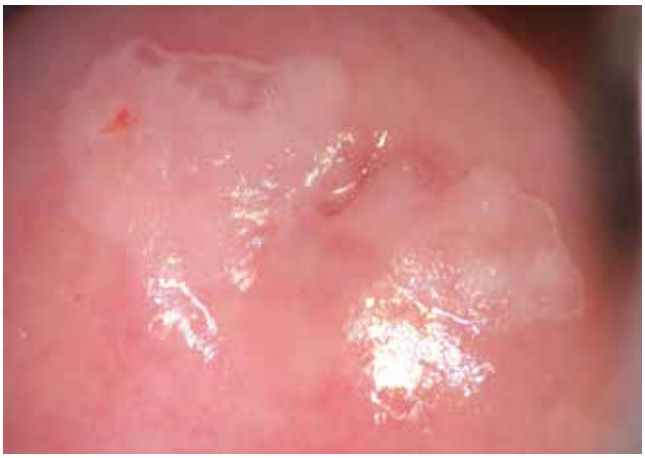


Figure 7.30a-b VIA-positive lesion (a) and benign metaplastic epithelium (b).

VIA-Positive Lesion vs. Nabothian Cyst

Nabothian cysts are yellowish in colour, raised, and commonly have blood vessels in their centres.

a



b

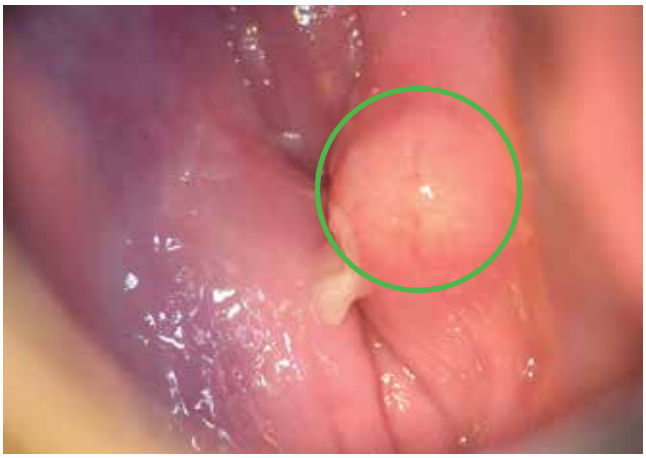
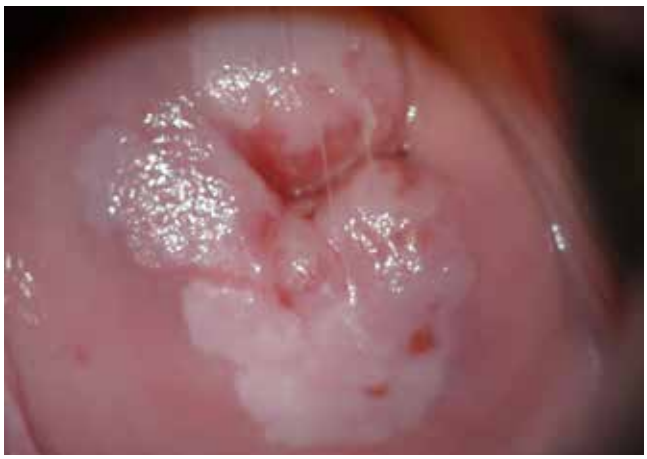


Figure 7.31a-b VIA-positive lesion (a) and a Nabothian cyst circled in green (b).

VIA-Positive Lesion vs. Atrophic Epithelium

Atrophic epithelium has a diffuse white appearance with focal collections of blood vessels that can be seen on the surface. VIA-positive lesions have sharp, distinct borders.

a



b

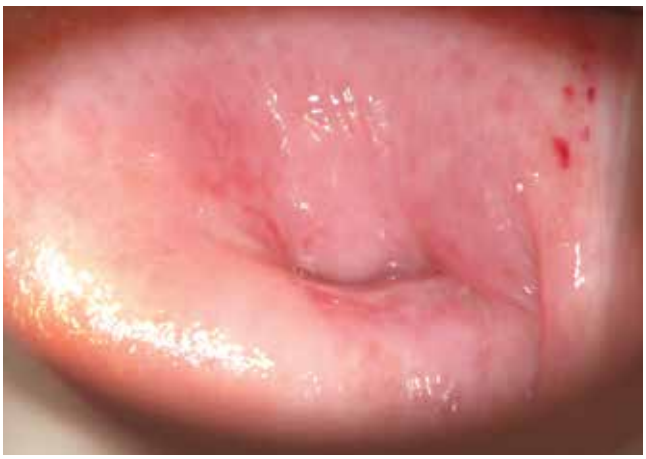
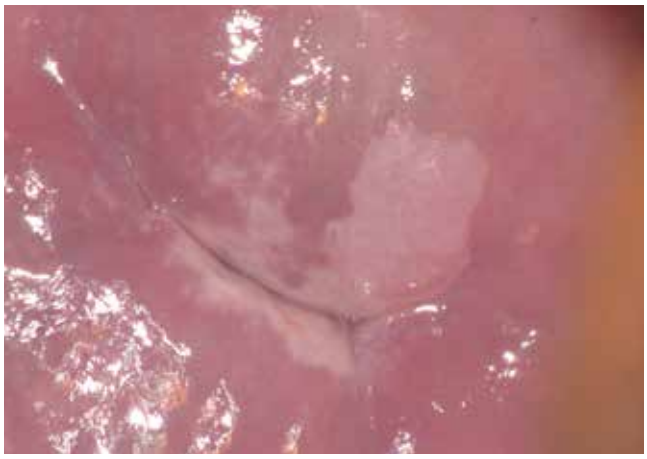


Figure 7.32a-b VIA-positive lesion (a) and atrophic epithelium (b).

VIA-Positive Lesion vs. Mucus

Mucus may appear glob-like, stringy, and yellowish, while a lesion will not. When in doubt, use a cotton ball to wipe away any potential mucus.

a



b

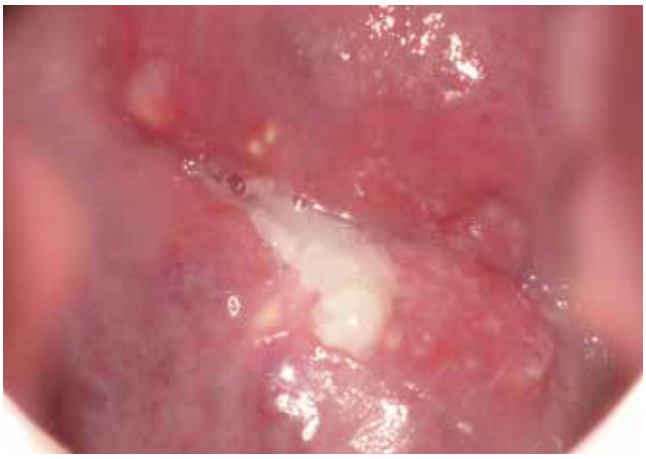
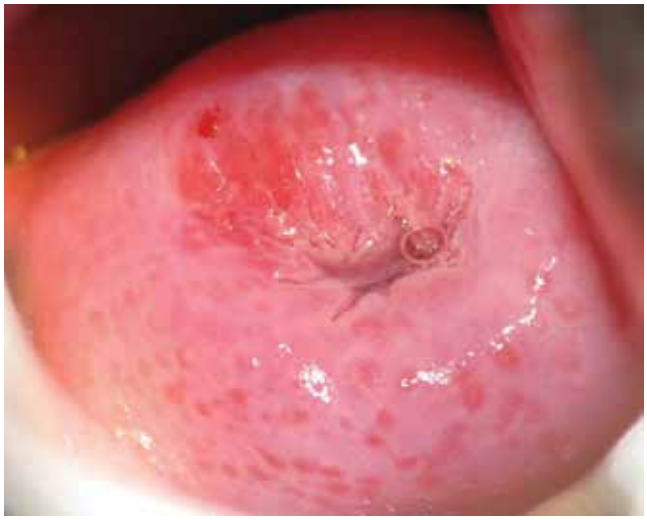


Figure 7.33a-b VIA-positive lesion (a) and mucus (b).

Trichomoniasis vs. Cervical Herpes

Trichomoniasis is usually associated with collections of blood vessels grouped together against the pinkish-white background of the cervix. The collections of blood vessels give the cervix the appearance of a strawberry, and may be called "strawberry spots." Herpes is associated with fluid-filled lumps called vesicles. Herpes and trichomoniasis may occur together. Herpes and trichomoniasis are discussed in chapter 10.

a



b

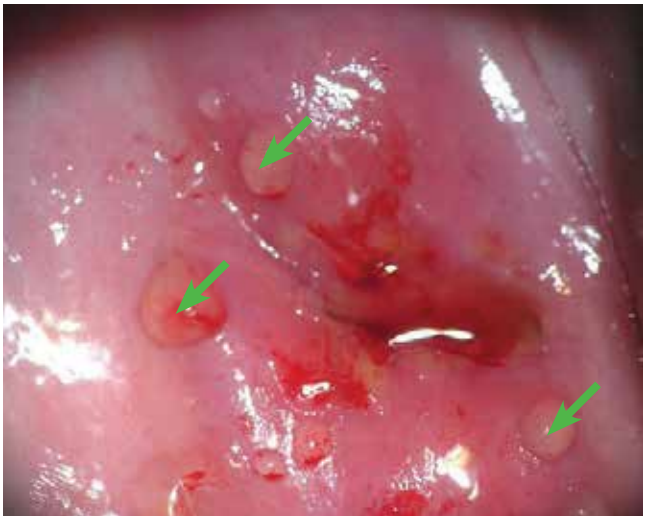


Figure 7.34a-b Trichomoniasis (a) and cervical herpes (b). Green arrows indicate vesicles.

7.9 Post-Screening Counselling

VIA-Negative Clients

If possible, show the woman her cervigram and explain why the cervix looks healthy. Discuss the importance of additional screening visits and let the woman know when she should return for her next screening visit according to your country's guidelines. Help her think of ways to remember to return.

VIA-Positive Clients

After identifying a VIA-positive lesion, show the woman her cervigram and the VIA-positive lesion. Make sure she understands that you believe it is NOT cervical cancer but precancer, which can become cancer in the future. If possible, proceed to treatment with cryotherapy or cold coagulation during the same visit. If the client needs to travel to another clinic for LEEP, schedule her appointment immediately. Consider re-offering HIV testing and counselling if the client previously declined to be tested.

Clients Suspicious of Cervical Cancer

Telling a client she may have cervical cancer can cause uncertainty, denial, stress, and depression. Providing as much information as possible about the diagnostic, treatment, and care options available can help the client manage her emotions and make the best decisions about her health.[14]

Encourage the client to ask questions. Answer all questions honestly and thoroughly, and do not answer any questions to which you do not know the answer. Give your full attention to the client while providing information. Avoid negative talk such as "cervical cancer at this stage cannot be cured." At the same time, do not tell the client her cancer can be cured. The provider cannot truly know whether or not a cancer can be cured until after treatment.[15] At the end of the visit, refer the client for testing to confirm the diagnosis, further counselling, and possible treatment.

Chapter 7 Summary

- Abnormal blood vessel patterns associated with acetowhite areas on the cervix may indicate high-grade precancer or cervical cancer.
- During the external genitalia and bimanual exams, the providers should look for pregnancy, abdominal abnormalities, lichen sclerosus, vulvar lesions, and infectious disorders such as genital warts.
- During the speculum exam, the provider should identify the transformation zone and look for polyps, ectopy, leukoplakia, infection, and evidence of cleaning inside the vagina.
- VIA-negative clients have no acetowhite lesions or only faint acetowhite areas without distinct borders.
- VIA-positive clients have thick, opaque white lesions with distinct borders located in the transformation zone of the cervix.
- Lesions which bleed easily or have ulcers, acetowhite cauliflower-like growths, or a rough and irregular surface may be cancerous.
- Make sure the client understands the VIA-positive lesion is NOT cervical cancer but precancer, which can become cancer in the future.
- Counsel women with possible cancer carefully, as the news can cause uncertainty, denial, stress, and depression.

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Chapter

8

Conducting Cryotherapy

After this section, the reader will be able to...

- Define ablative and excisional treatment.
- Understand in detail how to perform cryotherapy.
- Describe the parts of the cryotherapy unit.
- Name ALL the criteria for treatment with cryotherapy.
- Troubleshoot problems with the cryotherapy unit.
- Counsel clients on cryotherapy.
- Conduct post-cryotherapy follow-up care.
- Recognize the possible complications of cryotherapy.

8.1 Ablative and Excisional Treatment for Cervical Lesions

The ability to offer safe, effective, inexpensive, and simple treatment for precancerous lesions is a critical component of every cervical cancer prevention programme.[8] Lesions can be treated using either excisional or ablative methods.

Excisional treatment such as loop electrosurgical excision procedure (LEEP) removes the lesion from the cervix.

Ablative treatment, including cryotherapy and cold coagulation, destroys the lesion.

8.2 An Overview of Cryotherapy

Cryotherapy uses pressurized gas, either carbon dioxide (CO_2) or nitrous oxide (N_2O), to freeze and destroy abnormal areas on the cervix. Pressurized CO_2 can freeze tissues up to 3 mm deep. Pressurized N_2O produces colder temperatures and can freeze tissues up to 5 mm deep.

To produce pressurized CO_2 or N_2O, a manufacturing company compresses gaseous CO_2 or N_2O until it becomes liquid. The manufacturer bottles the liquid CO_2 or N_2O in high-pressure gas tanks or gas cylinders for transportation to the clinic. The CO_2 or N_2O produces extremely cold temperatures upon release from the cylinder and return to gaseous form.

8.3 Advantages and Disadvantages of Cryotherapy

Advantages

- High cure rate for small and medium-sized lesions.
- Very low complication rates.
- Serious complications requiring medical intervention are extremely rare.
- Temporary side effects such as vaginal discharge and cramping are well-tolerated.
- Can be performed by a wide range of healthcare workers, including doctors, nurses, nurse assistants, clinical officers, and midwives.
- Does not require electricity or anaesthesia.
- Relatively inexpensive compared to other procedures.

Disadvantages

- Cannot treat large lesions or lesions extending into the endocervical canal.
- Associated with temporary side effects such as vaginal discharge and cramping.
- Requires a continuous supply of gas.[9]

8.4 The Cryotherapy Unit

The term "**cryotherapy unit**" refers to the equipment which conducts gas from the cylinder to the cervix.

Key Features of the Cryotherapy Unit

- **Cryotip (or tip)**: covers the surface of the cervix and induces freezing.
- **Cryoshaft (or shaft)**: attaches the cryotip to the cryogun. Together, the cryotip and cryoshaft are sometimes called the cryoprobe.
- **Cryogun**: controls the flow of gas into the cryoprobe. The cryogun has a fibreglass handle grip, a freeze trigger, and an unfreeze trigger.
- **Gas-conveying tube (or hose)**: connects the cryogun to the pressure gauge apparatus. The hose conducts gas to cryogun and back to the exhaust port to be vented.
- **Exhaust port**: allows gas to leave the cryotherapy unit.
- **Pressure gauge**: monitors the pressure at which gas leaves the cylinder. Most pressure gauges have a yellow, green and red colour zone. The needle should point to the green zone when the cylinder is open. If the needle points to the yellow zone, the pressure is too low for adequate cryotherapy and the cylinder should be replaced. If the needle points to the red zone, the pressure is too high and the operator should release the excess pressure.
- **Gas cylinder connector (or connector)**: attaches the cryotherapy unit to the cylinder. The gas flows from the cylinder through the connector and pressure gauge apparatus to the hose. Multiple types of connectors are available and may vary by country.

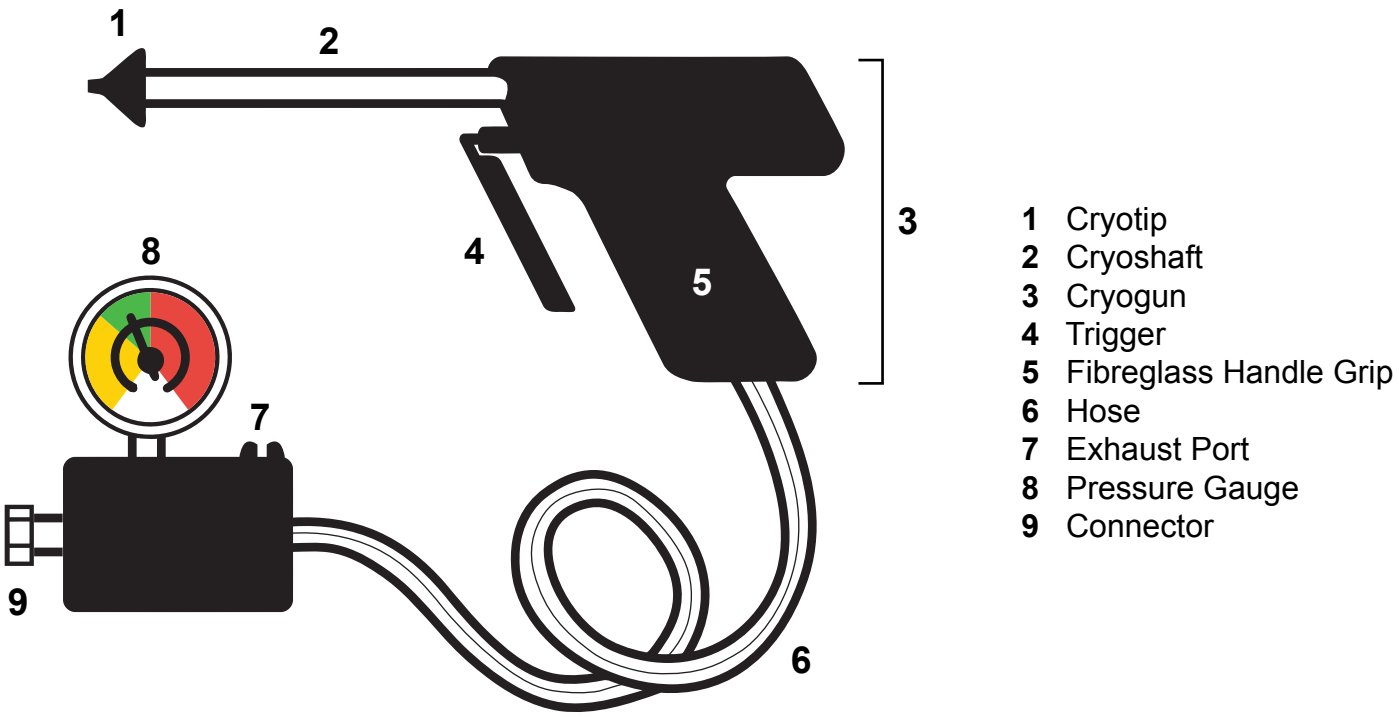


Figure 8.1 Illustration of the cryotherapy unit with features labeled.[16]

For more information, see the WHO technical specifications document entitled "Cryosurgical equipment for the treatment of precancerous cervical lesions and prevention of cervical cancer."

The connector may vary by country or depending on the type of gas tank. Always talk with your gas supplier prior to purchasing and setting up any cryotherapy unit.

8.5 Criteria for Cryotherapy

The provider can treat a VIA-positive lesion with cryotherapy if ALL the criteria listed on the following page are met.

If any of the first six criteria are not met, refer the client for LEEP. If the woman is pregnant, reschedule her for cryotherapy six weeks after delivery and refer her for antenatal care.

Do not perform cryotherapy on women with severe cervicitis because the infection may worsen after the procedure. Reschedule the client for cryotherapy after the infection is treated.[12,14] Cervicitis is discussed on page 132.

The provider can perform cryotherapy on menstruating women as long as the menstrual flow does not obscure the lesion.[8]

Notably, cryotherapy can only treat lesions up to 3 mm deep (for CO_2) or 5 mm deep (for N_2O), meaning it may not be appropriate for treatment of extremely raised or warty lesions. The provider should consider referring such lesions for LEEP or closer follow-up.

Criteria for Cryotherapy

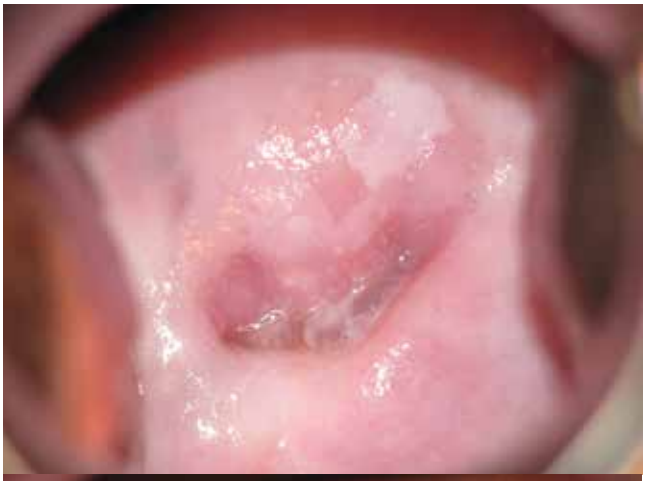
- ☑ The lesion occupies less than 75% of the transformation zone.
- ☑ All of the lesion can be seen.
- ☑ The cryotip can completely cover the lesion.
- ☑ The lesion is not suspicious for cancer.
- ☑ No abnormal blood vessels can be seen.
- ☑ There are no polyps or scarring that prevent full contact between the cervix and cryotip.
- ☑ The woman is not pregnant.
- ☑ The woman does not have severe cervicitis.

Figure 8.2 Poster on criteria for cryotherapy for the clinic.[15]

Figure 8.3a This lesion is cryotherapy-eligible.
Figure 8.3b This lesion is cryotherapy-ineligible because it extends into the os and cannot be entirely seen. Refer for LEEP.
Figure 8.3c This lesion is cryotherapy-ineligible because it occupies greater than 75% of the transformation zone. Refer for LEEP.

VIA-Positive, Cryotherapy-Eligible Lesions

a



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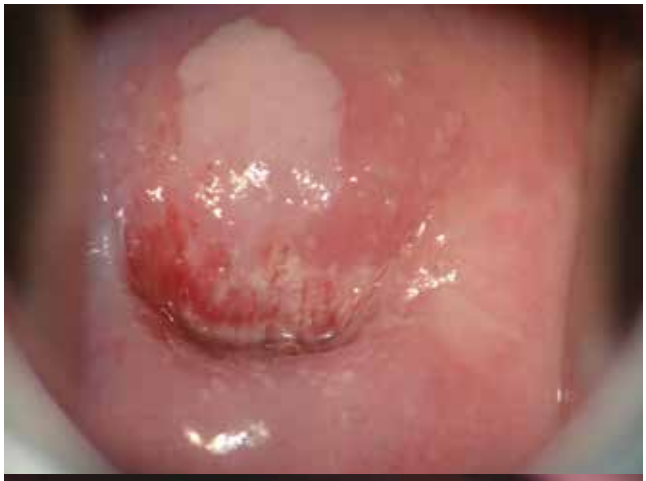

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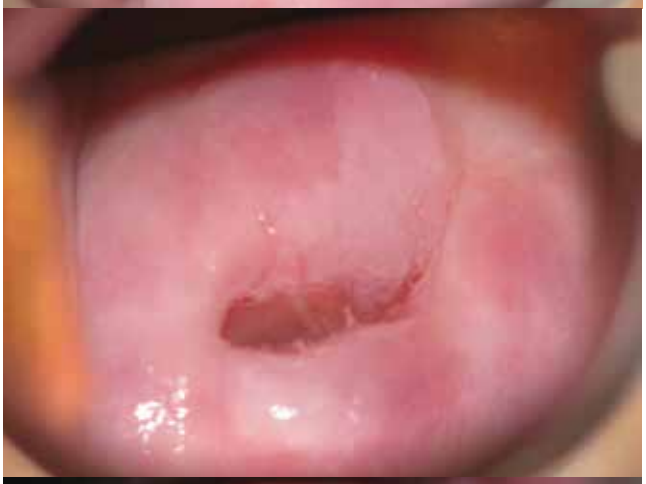

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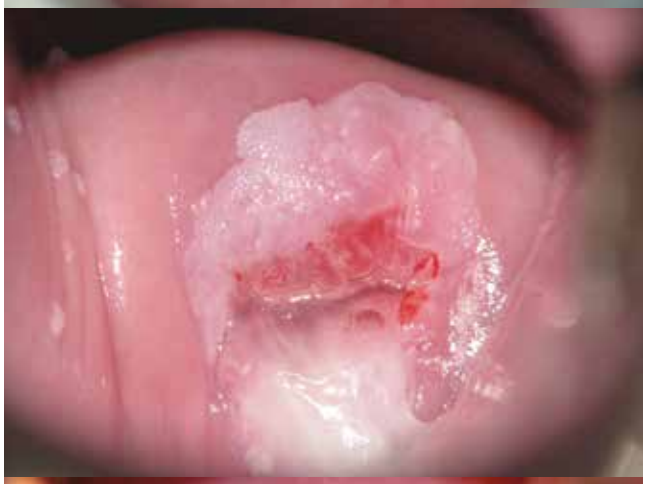

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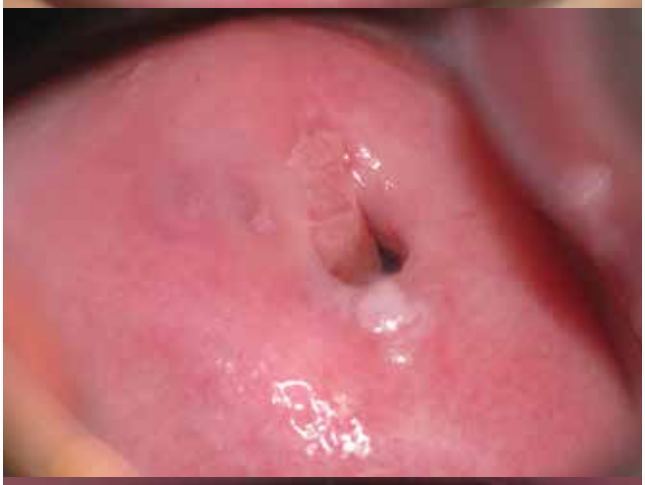

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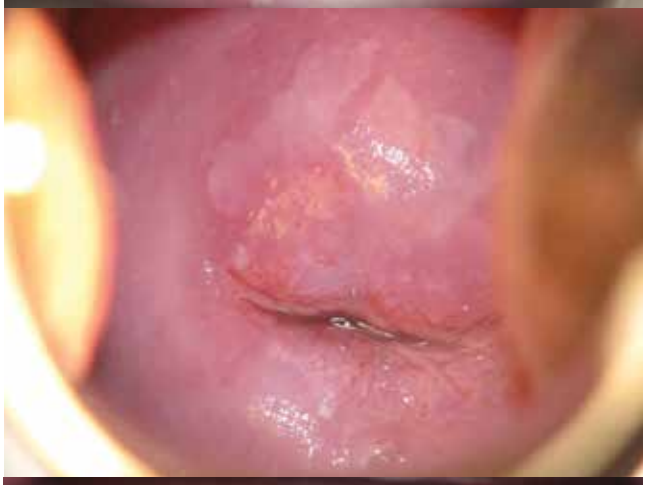

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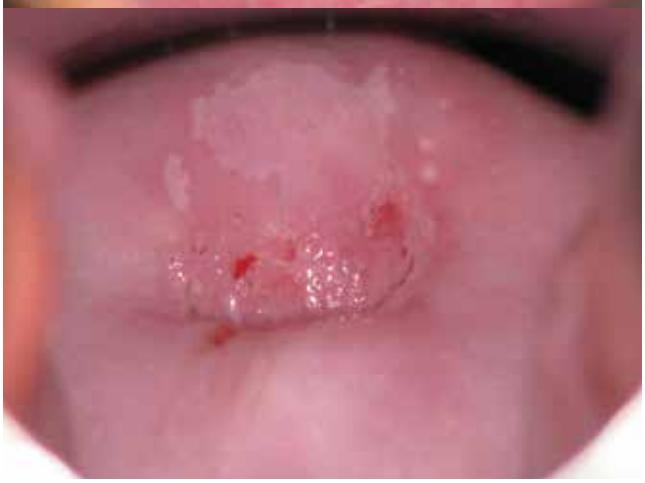

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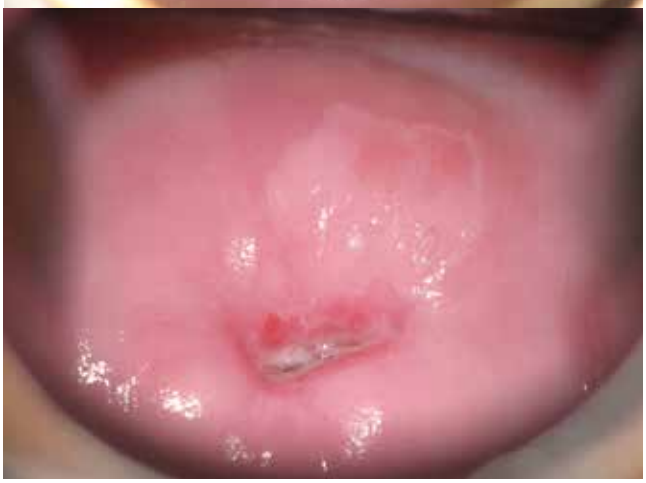

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(VIA-positive cryotherapy-eligible lesions, continued)

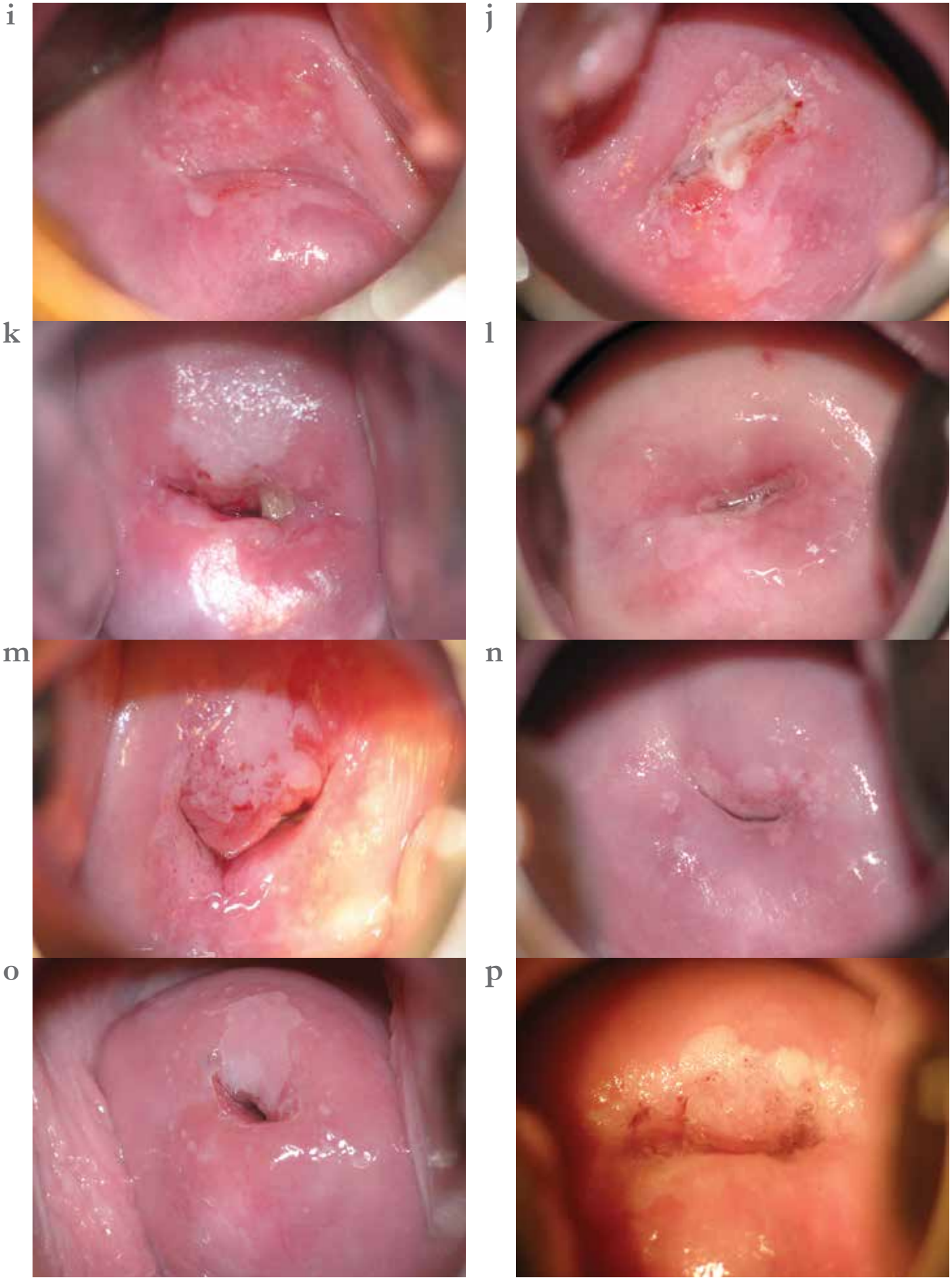
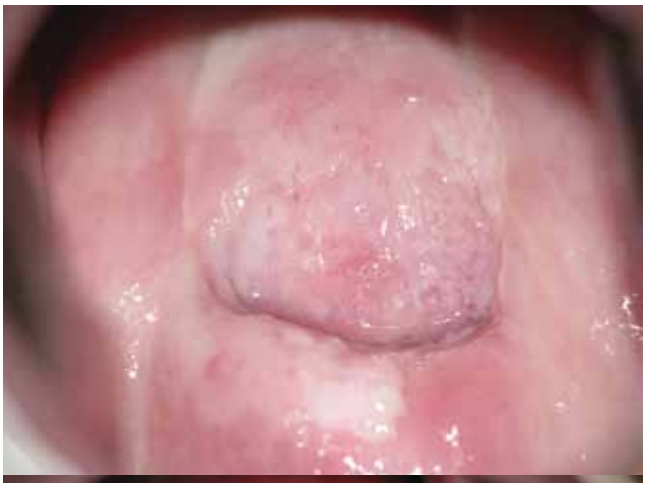


Figure 8.4a-p Cervical images of VIA-positive cryotherapy-eligible lesions.

VIA-Positive, Cryotherapy-Ineligible Lesions (Too Large)

a



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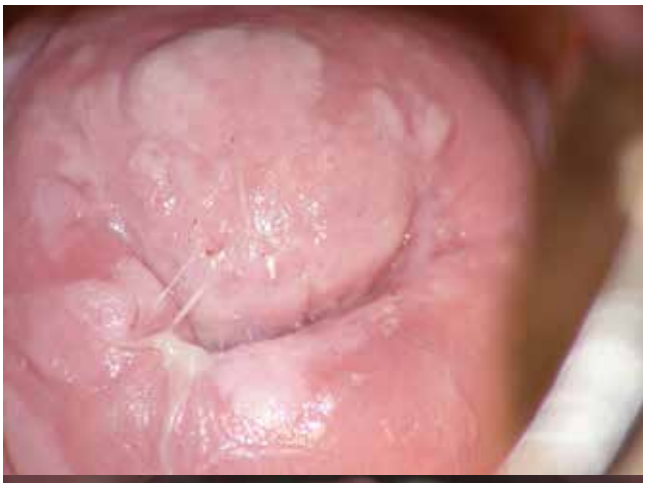

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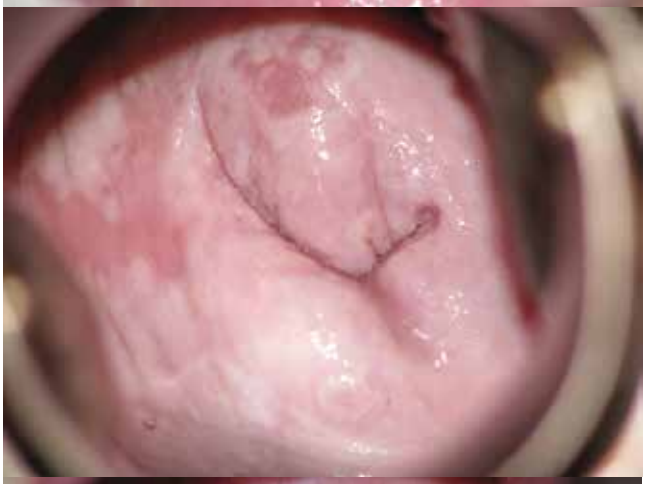

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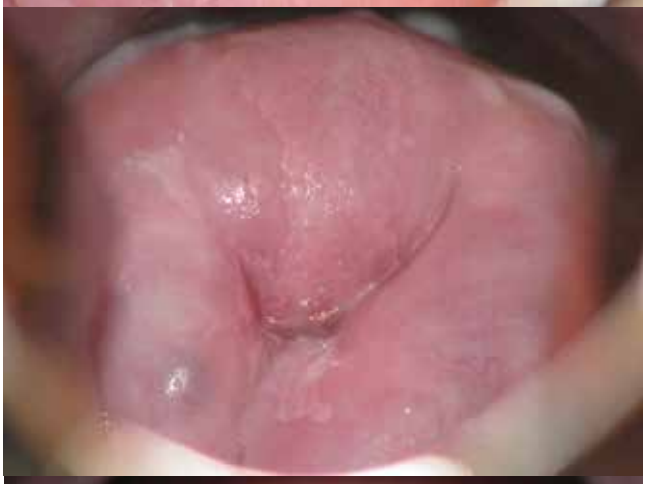

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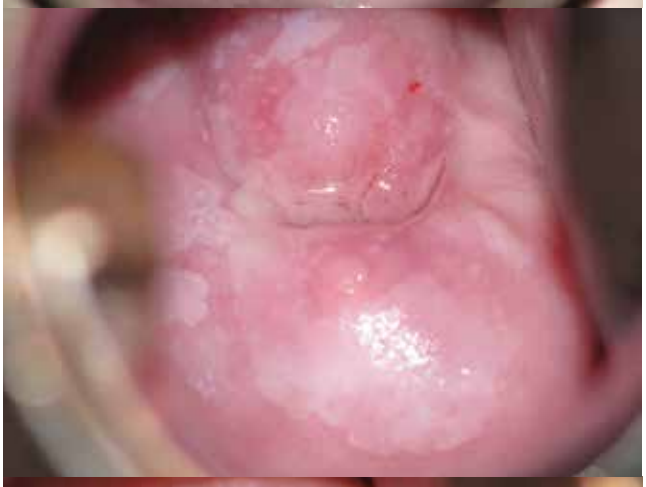

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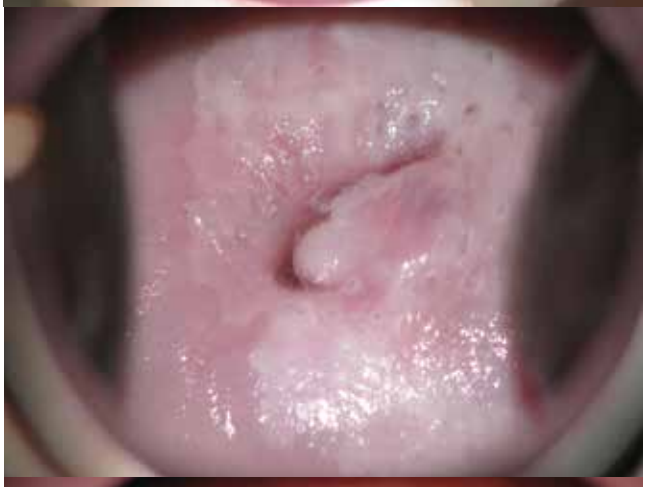

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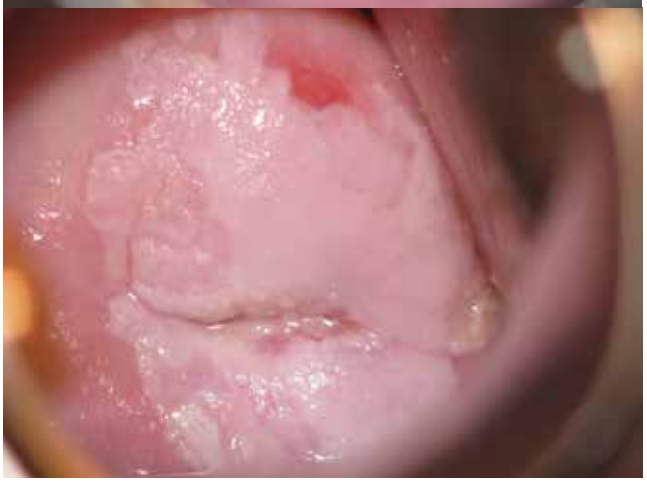

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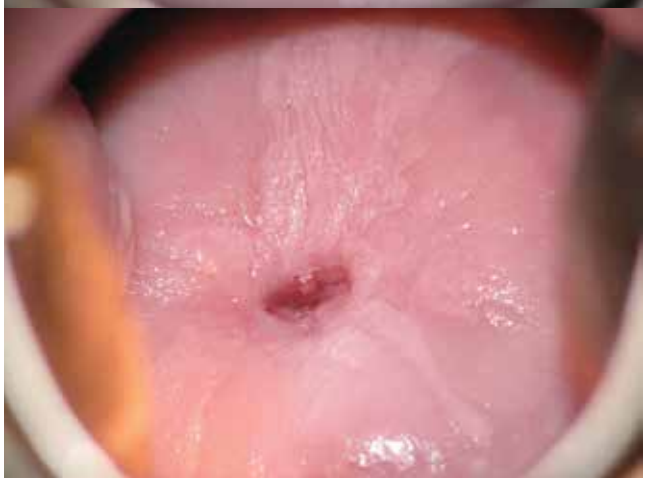

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(VIA-positive cryotherapy-ineligible lesions, too large, continued)

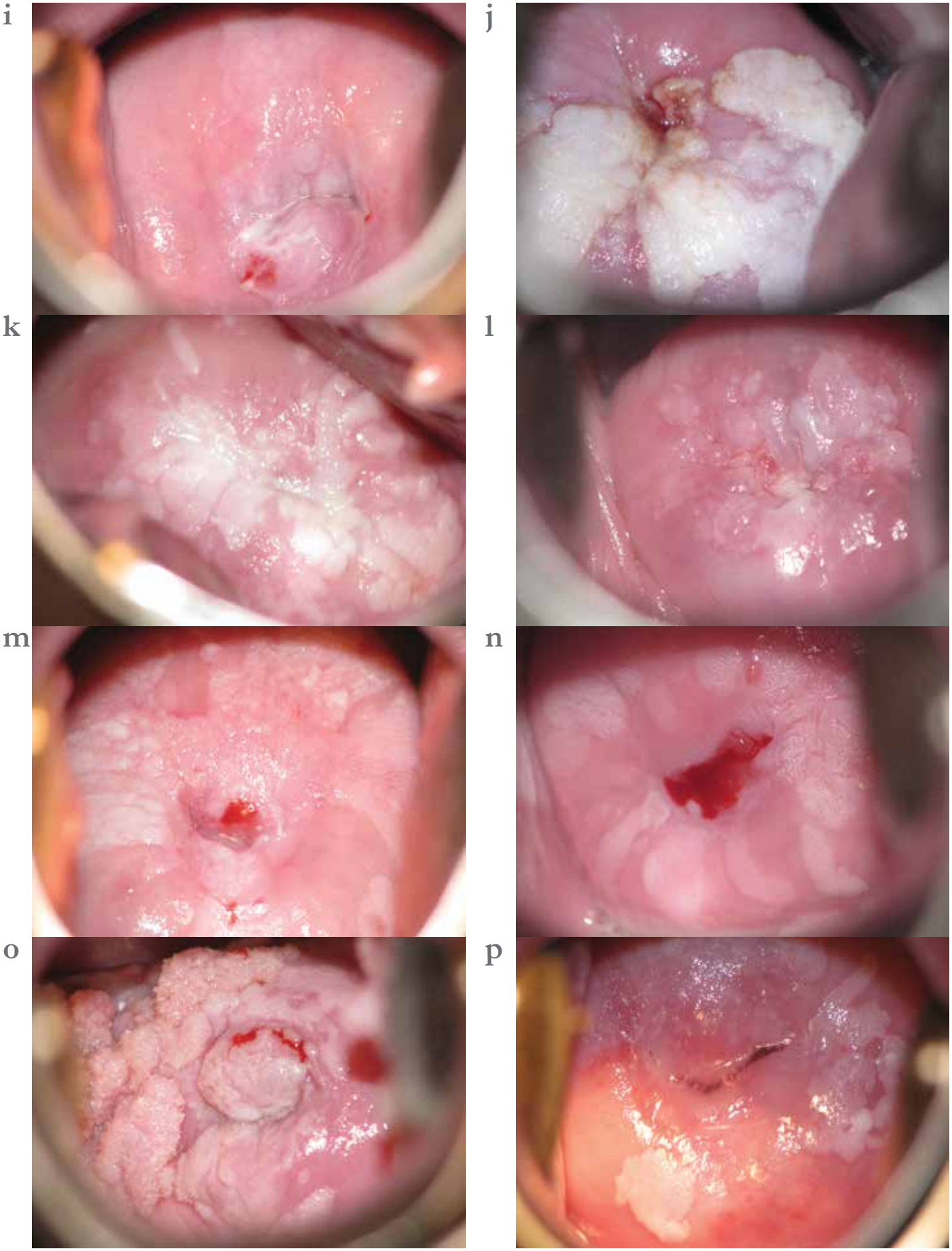
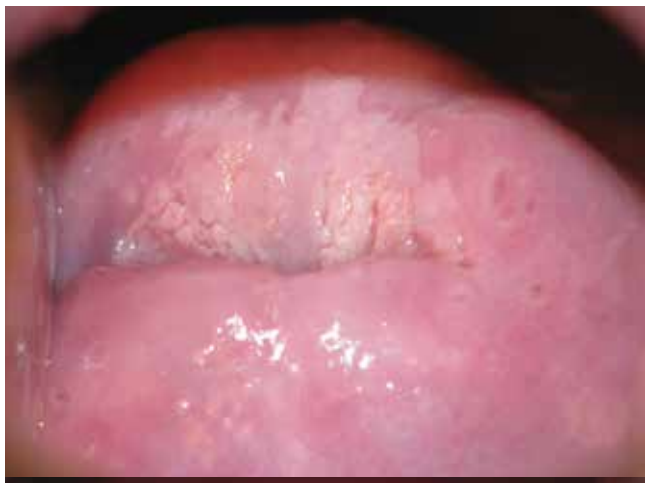


Figure 8.5a-p Cervical images of VIA-positive, cryotherapy-ineligible lesions. The lesions are ineligible because they occupy over 75% of the transformation zone and/or cannot be covered by the cryotip. Some extend into the os as well.

VIA-Positive, Cryotherapy-Ineligible Lesions (Extends Into Os)

a



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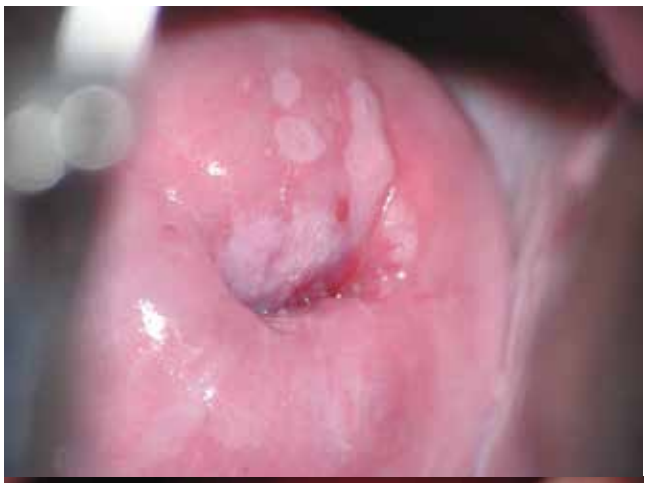

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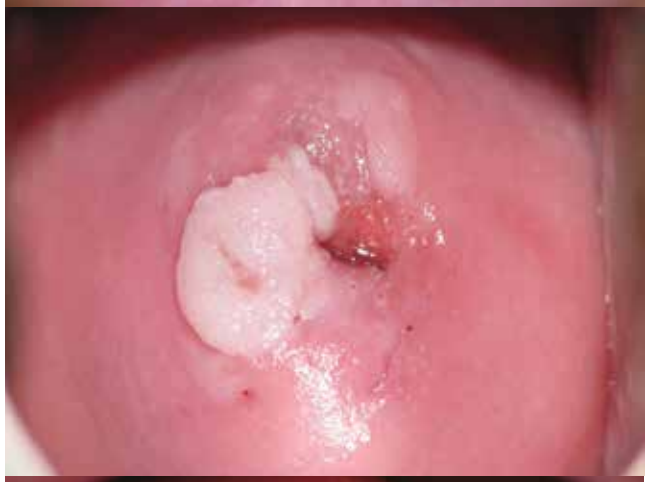

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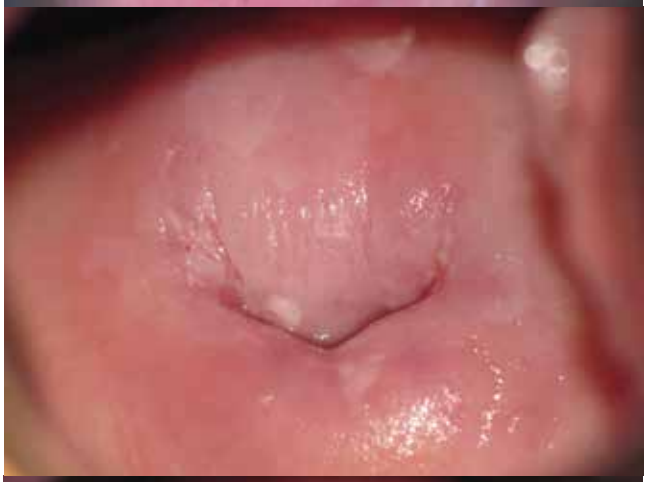

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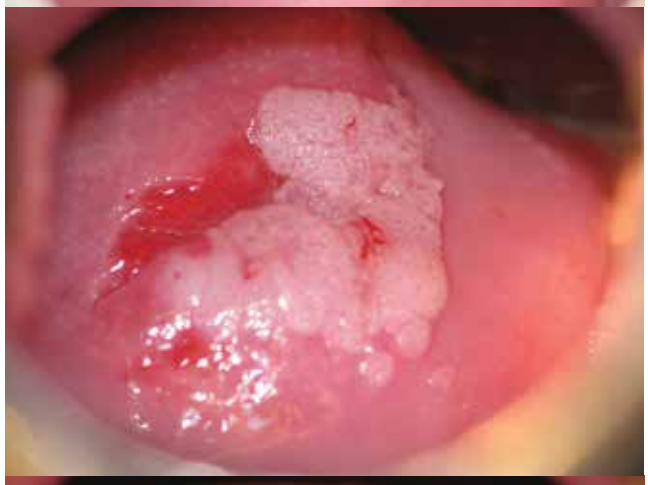

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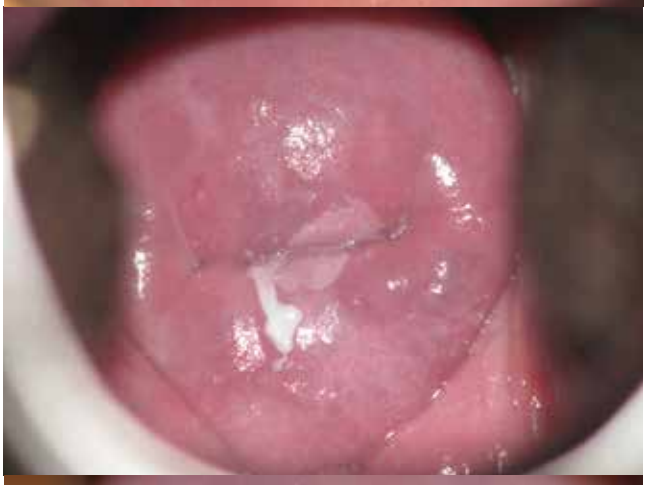

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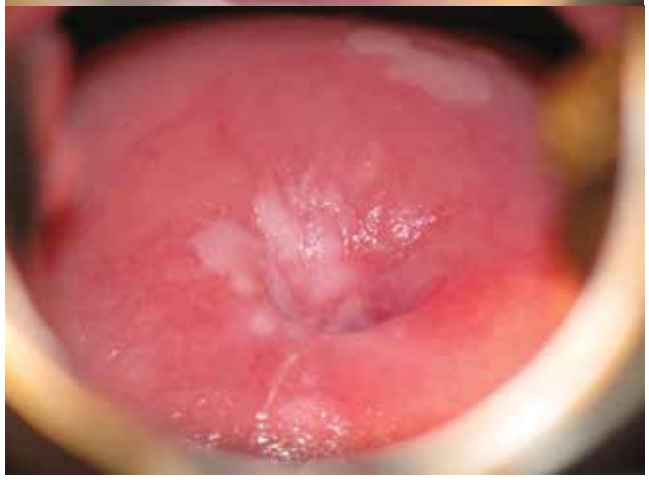

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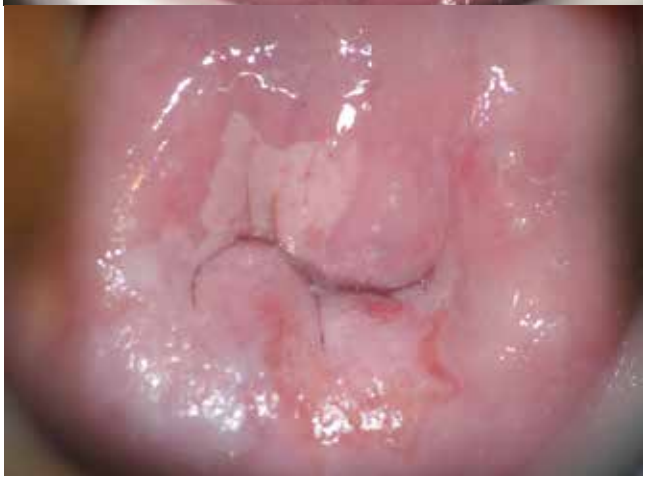

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(VIA-positive cryotherapy-ineligible lesions, extends into os, continued)

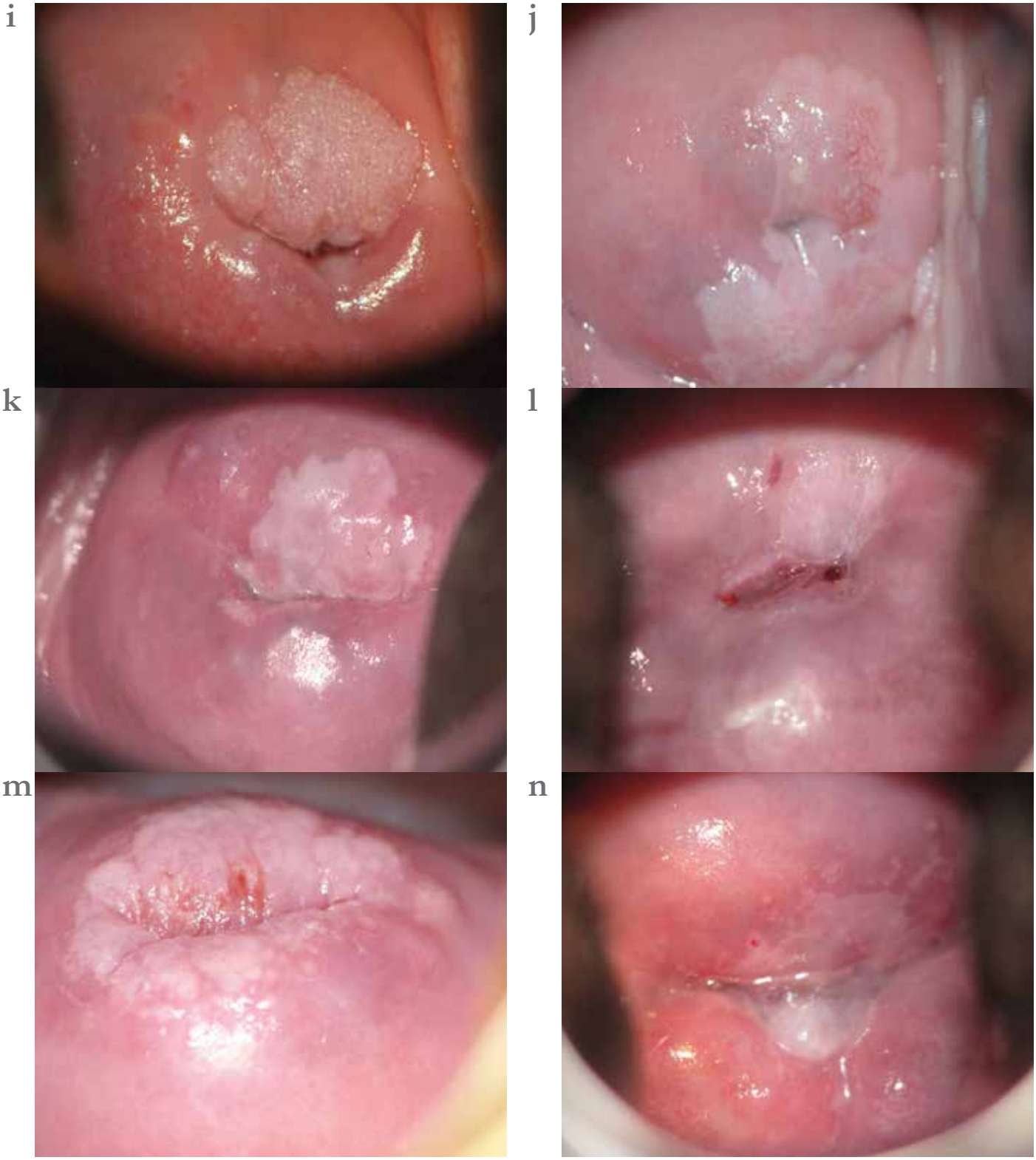


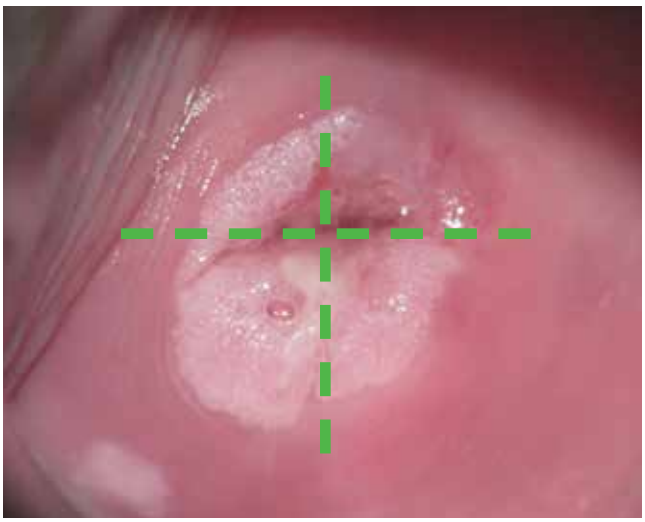
Figure 8.6a-n Cervical images of VIA-positive, cryotherapy-ineligible lesions. The lesions are ineligible because they extend into the cervical os and cannot be entirely seen.

The "Quadrants" Method

One method of determining whether the lesion occupies greater than 75% of the transformation zone is to roughly divide the cervix into four quadrants (Figure 8.7). If the lesion occupies more than three quadrants, refer the client.

Generally, occupation of greater than 75% of the transformation zone indicates the lesion is more advanced. This is why such lesions should be referred.

a



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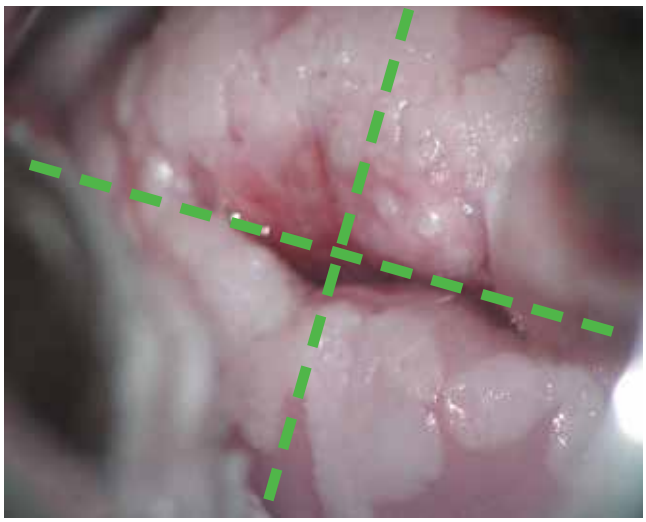

Figure 8.7a-b Cervical images of VIA-positive, cryotherapy-ineligible lesions. Quadrants shown in green. These lesions occupy more than 75% of the transformation zone.

8.6 Counselling on Cryotherapy

Key Messages

The messages given on the following page are in addition to the messages discussed previously on page 57. Reinforcement of key messages is extremely important for cryotherapy clients. If possible, provide written materials detailing post-cryotherapy instructions. In low-literacy areas, the materials may need appropriate illustrations.

- "Cervical precancer can become cervical cancer in the future if not treated. Cryotherapy uses ice-cold gas to freeze the precancer, which destroys the precancer."
- "You may feel some abdominal or lower back pain, similar to menstrual cramps, during the treatment or shortly after the treatment."
- "After cryotherapy, a watery discharge from the vagina is normal. You can use sanitary pads or cotton wool pads to manage the discharge. The discharge should stop about four weeks after cryotherapy. A little bleeding and discomfort is also normal."
- "If you have any concerns after cryotherapy, please return to the clinic immediately. Concerns may include:
  Vaginal discharge that smells extremely bad;
  Bleeding heavier than a menstrual cycle;
  Fever with or without chills;
  Severe lower abdominal pain."
- "For four weeks after cryotherapy, do not have sex. If you cannot abstain, PLEASE make sure your partner uses a condom to protect your cervix. Also, do not clean your vagina or put any objects in your vagina, including your fingers, tampons, or herbs. If you do, you may hurt your cervix."
- "You must return to the clinic for a follow-up exam (provide the date, time, and place)."

Additional Considerations

Cryotherapy clients may more easily transmit and contract infections, including HIV, after the procedure and before the cervix heals. Research has not yet confirmed this. However, until proven otherwise, our programme recommends counselling clients on the possibility of increased transmission and contraction of infection after cryotherapy.[5,8]

CIDRZ

Post-Cryotherapy Instructions

What you are required to do after treatment of the cervix

You received treatment today because the provider found a bad spot on your cervix. At this clinic, we removed the bad spot with a freezing treatment called cryotherapy. This treatment should make the cervix healthy again.

After treatment, certain symptoms might occur.

These symptoms disappear within two to four weeks. Do not let these symptoms worry you.

- Your vagina will probably have some watery discharge.
- You may feel pain similar to the pain that is felt during your monthly period.
- You may have a little bleeding, but not as much as you have during your monthly period.

Do not have sex for one month after the treatment.

If you do, your cervix could be injured or get infected while it is healing. If you cannot abstain for one month, then ask your partner to use a condom. However, it is good to wait until you heal. Do not put anything, even medicine or herbs, into your vagina for one month.

Return to the clinic if you have ANY of the following:

- Discharge from the vagina that smells extremely bad.
- Bleeding more than you have during your monthly period.
- Fever or chills.
- Extremely bad pain in the stomach worse than during you monthly period.

This treatment is very safe and is used in many countries. Problems may occur, but only very rarely.

Please return to _____ clinic at _____ hours on

_____ to make sure your cervix is healthy.

Figure 8.8 Sample post-cryotherapy instructions.

8.7 Materials for Cryotherapy

In addition to the materials required for VIA, cryotherapy requires the following.

- A cryotherapy unit.
- At least two different cryotips (to treat lesions of different sizes). The Alliance for Cervical Cancer Prevention (ACCP) recommends having 20 mm and 25 mm diameter cryotips.[8] According to the WHO, the cryotips must be circular in shape and 19±2 mm in diameter. The surface that contacts the tissue must be either flat or with a nipple-shaped cone extrusion not exceeding 5 mm in height.[16]
- High-pressure cylinder with pressurized nitrous oxide or pressurized medical-grade carbon dioxide. A 31.3 kg cylinder can treat around 40-45 women. The clinic should have 2-3 full cylinders at all times to avoid the possibility of exhausting the gas supply.
- Sanitary pads or cotton wool (to help the client manage discharge).
- 60-90% ethyl or isopropyl alcohol (to clean cryotherapy unit).
- Materials to disinfect the cryotip and cryoshaft.

Optional Items:

- Heavy-duty gloves (to protect the provider's hands from cold temperatures).
- Condoms (to give to clients).
- Ibuprofen or other mild pain reliever (to help the client manage discomfort and cramping).

Figure 8.9 Illustration of the cryotips recommended for the treatment of precancerous lesions. Adapted from the WHO technical specifications, 2012.[16]

8.8 A Step-by-Step Approach to Cryotherapy

The following protocol may not apply to every cryotherapy unit. Operate units according to the manufacturer's instructions. Always check the instructions prior to using any unit.

The following protocol describes the steps of cryotherapy, assuming:

- cryotherapy will be performed in the same visit as VIA;
- the woman was counselled on the cryotherapy procedure and gave informed consent for cryotherapy before VIA;
- the provider ensured all cryotherapy materials were available and sterile before the screen-and-treat visit began;
- cryotherapy will be performed using the double-freeze technique rather than the single freeze technique. The WHO recommends the double-freeze technique.[15]

Notably, the speculum does not need to be removed and reinserted between VIA and cryotherapy.

Step 1: Check Criteria

Ensure all the criteria for cryotherapy are met. Importantly, if the client is pregnant, do not perform cryotherapy.

Step 2: Prepare for the Procedure

Select a clean, sterile cryotip of the appropriate size to completely cover the lesion. Do not select a cryotip much larger than necessary to cover the lesion. If you do not have a cryotip large enough to cover the lesion, refer the client for LEEP.

Attach the cryotip to the cryoshaft and double check it is properly attached. Attach the cryoshaft to the cryogun if necessary. Briefly open the gas cylinder and check the pressure gauge to ensure the gas is flowing. The needle on the pressure gauge should register in the green area (above 40 mmHg). Otherwise, freezing and treatment will be inadequate. If the pressure gauge indicates inadequate pressure, change the cylinder or use the troubleshooting advice in section 8.10 to find the problem.

Figure 8.10 The provider checks the pressure gauge to ensure the needle registers in the green zone.

Press the freeze trigger on the cryotherapy gun to see if the cryotip freezes. If the cryotip does not freeze, use the troubleshooting advice in the next section to solve the problem. If the cryotip freezes, press the unfreeze trigger until the tip thaws.

Step 3: Freeze the Lesion

If necessary, use a cotton swab to wipe away excess blood, mucus, or discharge from the cervix. Seated in a comfortable position, place the cryotip on the ectocervix with gentle pressure. The nipple should be placed over the external os. Importantly, the tip should cover the entire lesion and make full contact with the cervical epithelium. Putting clean water on the tip before placing it on the cervix can improve contact.

Tell the client you are beginning the treatment and that she will hear noise from the machine. Squeeze the freeze trigger to begin freezing. Begin timing using a watch or clock when an ice ball forms on the cervical tissue beyond the edges of the cryotip. Freeze for 3 minutes, then press the unfreeze trigger until the cryotip can be removed from the cervix gently.

If the tip does not separate from the frozen cervix at first, be patient and continue pressing the unfreeze trigger. Do not pull on the tip to separate it from the cervix. If necessary, rotate the tip gently clockwise and counter-clockwise to separate it from the cervix. Take care not to touch the tip or cryoshaft to the vaginal walls.

Step 4: Refreeze the Lesion

Wait for five minutes and then freeze the lesion again for 3 minutes. As before, only begin timing when an ice ball forms on the cervical tissue beyond the edges of the cryotip. Increase the freezing time to 5 minutes if the ice ball does not extend more than 2 mm past the cryotip's edges.

Step 5: Finish the Exam and Thank the Client

Finish the exam as described on page 62 in chapter 6. After cryotherapy, the speculum may ice over and adhere to the vagina. If the speculum adheres, allow time for thawing before removing it.

Once the speculum is removed, remind the client of post-cryotherapy care instructions and key messages. Provide a sanitary pad or cotton wool to help the client manage discharge. Some programmes recommend keeping the client under observation for fifteen minutes after the procedure in case of possible cramping, bleeding, or fainting.

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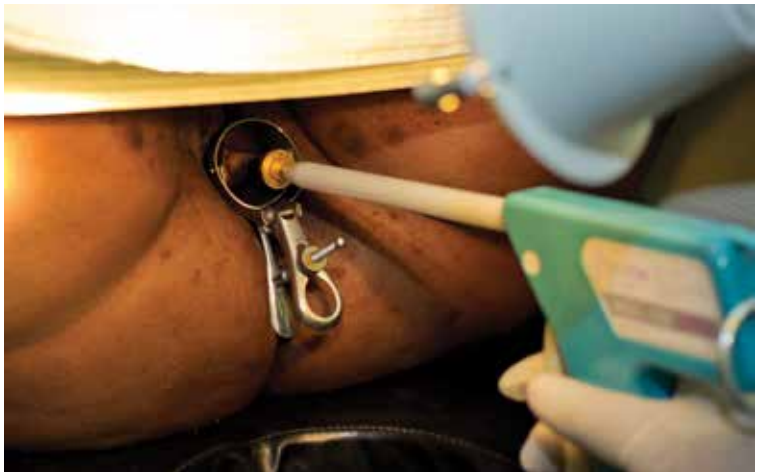

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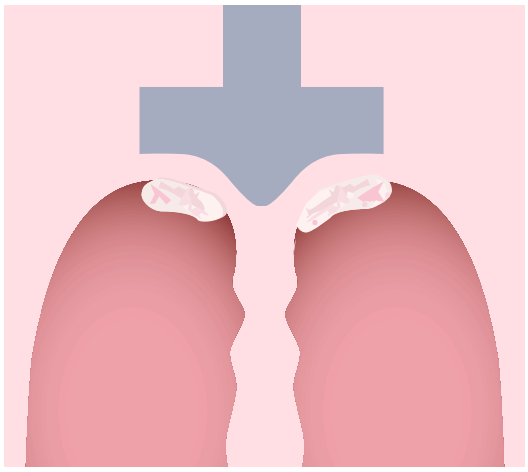

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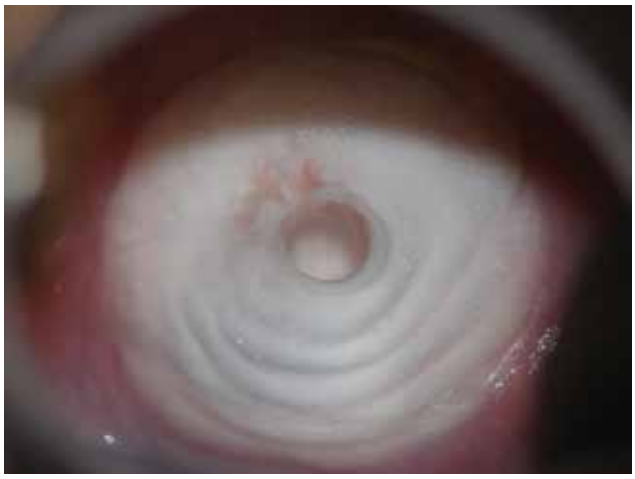

Figure 8.11a The provider prepares to place the cryotip on the ectocervix.
Figure 8.11b Illustration depicting the proper placement of the cryotip.
Figure 8.11c The provider freezes the precancerous lesion.
Figure 8.11d The cervix after freezing and removal of the cryotip.

8.9 Infection Prevention and Cryotherapy

STOP

The following recommendations may not apply to every cryotherapy unit. Clean units according to the manufacturer's instructions. Always check the instructions prior to cleaning any unit.

STOP

Do not clean the cryotip or cryoshaft with 0.5% chlorine solution.

Cryotips must be properly disinfected after every cryotherapy session using high-level disinfection. High-level disinfection is the complete elimination of all microorganisms except possible bacteria spores. High-level disinfection must be used because intermediate-level is inadequate for instruments potentially contaminated with HIV or hepatitis virus.[11]

The World Health Organization recommends using one of the two possible high-level disinfection procedures below.[16]

- Boil instruments for at least 20 minutes in plain tap water, which is changed at least daily. Make sure that instruments are fully covered by the water, and start timing after the water with the instruments is fully boiling. Do not add anything to the pot once you have started to time.

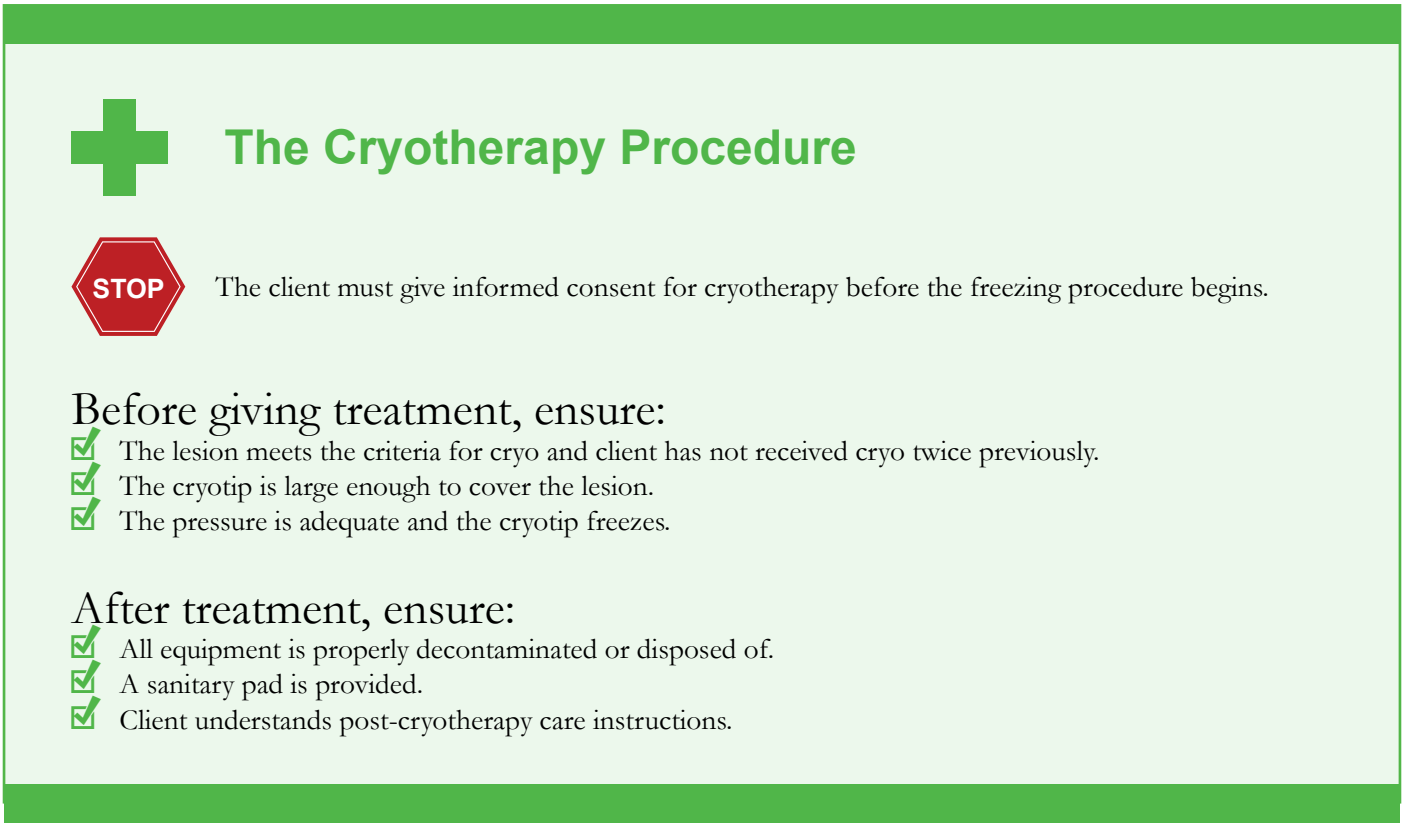

Figure 8.12 Poster on cryotherapy for the clinic.

- Soak instruments in 0.1% chlorine or 2% glutaraldehyde solution for 20 minutes, or 6% hydrogen peroxide for 30 minutes. Rinse thoroughly in boiled water, air-dry and store in a sterile cloth. These chemicals may be corrosive and can reduce the useful life of instruments that are repeatedly disinfected with them. To prevent unnecessary corrosion, take care not to sterilize instruments longer than recommended.

To extend the life of the cryotip, our programme recommends closing off the open ends with silicone plugs prior to disinfection with chemical sterilization. Similar to the cryotip, the cryoshaft must be disinfected after every session. Some designs allow the cryoshaft to be detached for sterilization, while others do not. Follow the manufacturer's instruction for disinfection. Do not use 0.5% chlorine solution because it corrodes the cryotip and shaft and severely limits their lifespans.

In addition to disinfection, the cryotip and shaft may be autoclaved at the end of each day to kill possible bacterial spores. The remainder of the cryotherapy unit can be cleaned with a cloth soaked in ethyl or isopropyl alcohol (60-90%).

8.10 Troubleshooting Cryotherapy

During cryotherapy, the hose may become extremely cold and ice crystals may develop. As long as the connector and pressure gauge are not freezing and the cryotip is freezing, the client will receive proper treatment. If the cryotip is not freezing, one or more of the following problems may be present.

Blockage of Gas Flow

One of the most common problems is an ice blockage in the hose that interrupts the flow of gas. To clear the blockage, the provider should "flush the tube," or press the unfreeze trigger until the tube clears If flushing the tube does not work, the provider should use the "freeze-flush-freeze" method. Press the freeze trigger for 15 seconds, then the unfreeze trigger for 1 second or less. Repeat the "15 seconds freeze, 1 second unfreeze" cycle for 3 minutes.

Poor Gas Quality

The clinic must use medical-grade CO_2 gas. Impurities in non-medical-grade (industrial or commercial) CO_2 gas can deteriorate the hose and other parts of the cryotherapy unit.

Leakage

During cryotherapy, the gas passing through the exhaust port makes a hissing sound. A louder hissing sound than usual may indicate a gas leak where the connector attaches to the cylinder. Check to ensure proper alignment of the connector and cylinder. If no source of leakage can be determined but there is a variation in the number of clients that can be treated with each cylinder, check the pressure on each new cylinder you receive to ensure they are being completely filled at the plant where you purchase your gas.

Misfit

The cryotherapy unit may be incompatible with the cylinder. For example, a cryotherapy unit manufactured in the United States of America may be incompatible with a gas cylinder produced in Britain or South Africa. Consult a local machinist to solve the problem or purchase a connector from MedGyn.

Other Problems

Consult the manufacturer's instructions.

8.11 Following-Up on Cryotherapy

Cervical lesions persist or recur in 5-10% of HIV-negative cryotherapy clients.[6,12] Repeat VIA one year after cryotherapy to assess the persistence or recurrence of lesions. The Alliance for Cervical Cancer Prevention (ACCP) recommends annual follow-up visits for five years after cryotherapy to assess the persistence or recurrence of lesions.[8]

Treat persistent or recurrent lesions with cryotherapy, cold coagulation, or LEEP as appropriate. If the lesion does not resolve after two cryotherapy sessions consider biopsy or LEEP for histologic evaluation.

Cryotherapy treatment fails more often in HIV-positive women than HIV-negative women.[7,13] One study reported that lesions persist or recur in 40.5% of HIV-positive women.[2] Our programme recommends closer follow-up of HIV-positive cryotherapy clients.

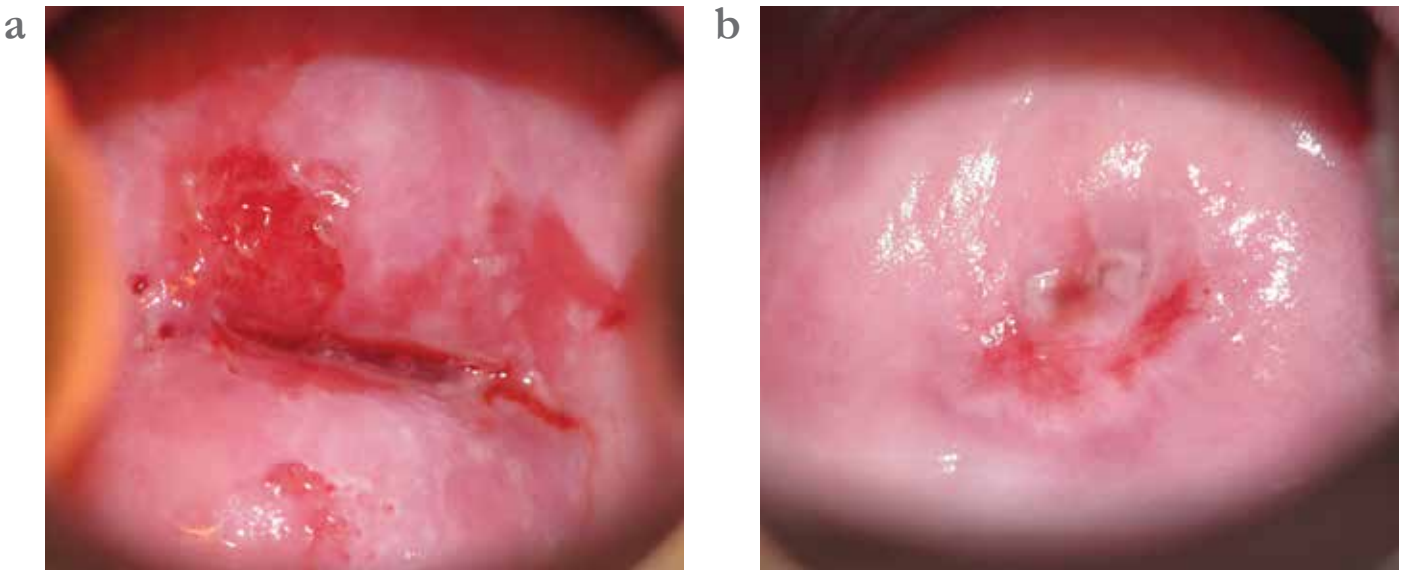

Figure 8.13a-b Cervixes four months after cryotherapy. These cervixes are still healing.

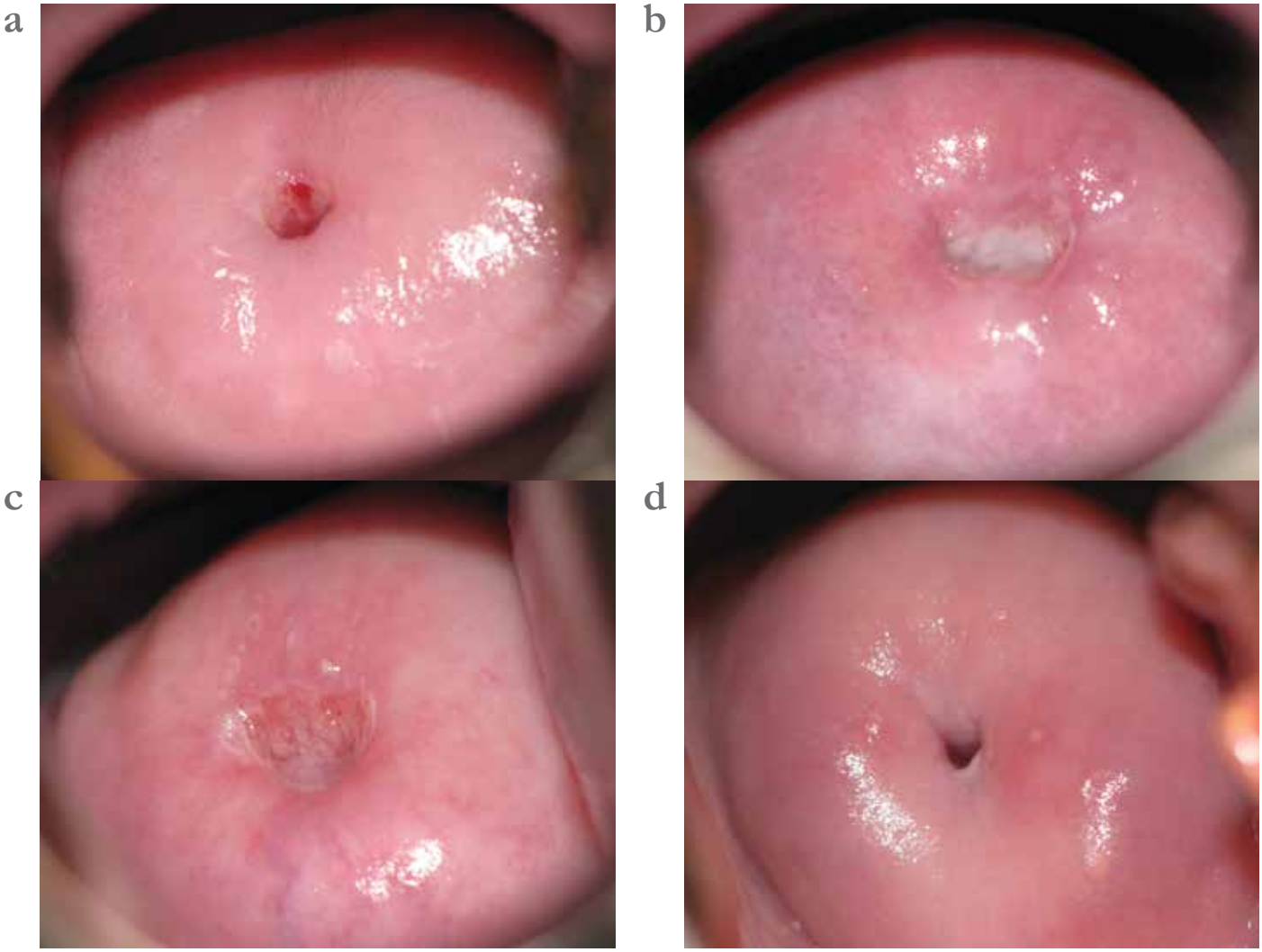

Figure 8.14a-d Cervixes six months to one year after cryotherapy which have completely healed.

8.12 Possible Complications of Cryotherapy

The cryotherapy procedure rarely causes pain. However, some women may experience lower abdominal discomfort and cramps. If cramping continues more than 5-10 minutes past the procedure, give a mild pain reliever such as ibuprofen. Rarely, clients may feel faint or experience bleeding during the procedure.[8,12] Apply direct pressure to the cervix to stop the bleeding.

During the first 4-5 weeks following cryotherapy, women commonly experience a pink, yellow, or white discharge from the vagina. The yellow or pink colour comes from blood mixing with the discharge. The discharge may develop a slightly foul odour. Light bleeding from the vagina may occur and the client may experience mild pain.[4,14]

Severe complications requiring hospitalization, such as heavy bleeding or pelvic inflammatory disease, occur in approximately 0.03% of clients.[8] Any woman with the following symptoms may have a severe complication and should be treated immediately:

- extremely foul-smelling vaginal discharge;
- bleeding heavier than a menstrual cycle;
- fever with or without chills;
- severe lower abdominal pain.

The provider must emphasize the importance of returning to the clinic if such symptoms occur.

Several studies found women may experience severe pain or cramping after cryotherapy, referred to as **necrotic plug syndrome**. Necrotic plug syndrome results from **cervical stenosis**, or narrowing of the endocervical canal. The canal narrows because of tissue destruction in the canal from cryotips with long nipple-shaped cone extrusions. This is why the WHO recommends the nipple-shaped cone extrusion not exceed 5 mm in height. Refer all clients with necrotic plug syndrome to a physician for the removal of necrotic tissue blocking the canal.[8]

Mild infections develop in less than 10% of cryotherapy clients.[10] Some programmes in developing countries place all post-cryotherapy clients on antibiotics to prevent infection. However, the WHO does not recommend this.[15] Consider post-cryotherapy antibiotics if your country's guidelines recommend presumptive treatment of sexually transmitted infections.[8] Possible post-cryotherapy antibiotic regimens include metronidazole (400 mg three times daily for 7 days) or doxycycline (100 mg twice daily for 7 days). Do not give doxycycline to pregnant women.[12]

Some studies suggest that cryotherapy complications occur more frequently in HIV-positive women, but insufficient evidence exists overall.[3]

Cryotherapy does not affect pregnancy outcomes, and no evidence indicates that cryotherapy affects fertility.[1,8] Regardless, our programme does not recommend cryotherapy in pregnant women because of potential liability concerns. Specifically, if a client associated a birth defect or miscarriage with cryotherapy, the misconception could negatively impact the programme.

Chapter 8 Summary

- **Ablative treatment** for cervical precancer destroys the lesion, while **excisional treatment** removes it.
- **Cryotherapy** uses pressurized gas to freeze and destroy the cervical lesion.
- Do not perform cryotherapy unless all the following criteria are met:
  - the lesion occupies less than 75% of transformation zone;
  - all of the lesion can be seen;
  - the cryotip can completely cover the lesion;
  - the lesion is not suspicious for cancer;
  - there are no polyps or scarring that prevents full contact between the cervix and cryotip;
  - the woman is not pregnant;
  - the woman does not have severe cervicitis.
- The provider must counsel the woman with all the key messages in section 8.6 prior to performing VIA.
- The cryotip and cryotherapy unit must be properly disinfected after each cryotherapy session.
- Repeat VIA one year after cryotherapy to assess the persistence or recurrence of lesions.
- After cryotherapy, a little discharge, pain, and bleeding is normal. Severe complications are rare and may include pelvic inflammatory disease and heavy bleeding. The client must return the clinic immediately if the following symptoms occur:
  - vaginal discharge that smells extremely bad;
  - bleeding heavier than a menstrual cycle;
  - fever with or without chills;
  - severe lower abdominal pain.

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Chapter

9

Conducting Cold Coagulation

After this section, the reader will be able to...

- Understand in detail how to perform cold coagulation.
- Discuss the advantages and disadvantages of cold coagulation compared to cryotherapy.
- Name ALL the criteria for treatment with cold coagulation.
- Counsel clients on cold coagulation.
- Conduct follow-up care after cold coagulation.
- Recognize the possible complications of cold coagulation.

9.1 An Overview of Cold Coagulation

Cold coagulation uses a heated metal probe to destroy abnormal areas on the cervix. The heated probe can destroy tissues up to 4 mm deep in 30 seconds and 7 mm deep in 45 seconds. The probe is connected to a machine called a **Semm cold coagulator**, which uses electricity to heat the probe.

9.2 Advantages and Disadvantages of Cold Coagulation

A relatively new procedure compared to cryotherapy, fewer data exist on cold coagulation. However, published data indicates that cold coagulation treats cervical lesions as well or better than cryotherapy.[2,3,5,6,7] Like cryotherapy, cold coagulation does not require anaesthesia and can be performed by a wide range of healthcare providers.

Cold coagulation offers several advantages over cryotherapy. The procedure incorporates automatic sterilization and takes less time than cryotherapy. The portability of the Semm cold coagulator makes it ideal for rural settings.[5] Although the Semm cold coagulator is more expensive than a cryotherapy unit, cold coagulation is less expensive than cryotherapy overall because it does not require a continuous gas supply.

However, unlike cryotherapy, cold coagulation requires an energy source such as electricity, batteries, or solar power.[6]

9.3 The Semm Cold Coagulator

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b

Figure 9.1a-b The Semm cold coagulator.

The Semm cold coagulator weighs only about 2kg. The machine's display indicates the temperature of the metallic probe. Generally, the provider heats the probe to 100˚C for cold coagulation. A knob on the front of the machine controls the temperature of the probe. Turning the knob left or right increases or decreases the temperature.

9.4 Criteria for Cold Coagulation

The provider can treat a VIA-positive lesion with cold coagulation if ALL the following criteria are met.

If the first five criteria are not met, the provider should refer the client for LEEP. Reschedule pregnant women for cold coagulation twelve weeks after delivery and refer them for antenatal care.[4]

Performing cold coagulation on women with severe cervicitis may cause the infection to worsen. Until proven otherwise, our programme recommends rescheduling the client for cold coagulation after the infection is treated. One can perform cold coagulation on menstruating women as long as the menstrual flow does not obscure the lesion.

Criteria for Cold Coagulation

- ☑ The lesion occupies less than 75% of the transformation zone.
- ☑ All of the lesion can be seen.
- ☑ The lesion is not suspicious for cancer.
- ☑ No abnormal blood vessels can be seen.
- ☑ There are no polyps or scarring that prevent full contact between the cervix and probe.
- ☑ The woman is not pregnant.
- ☑ The woman does not have severe cervicitis.

Figure 9.2 Poster on criteria for cold coagulation for the clinic.[1,4]

VIA-Positive, Cold-Coagulation-Eligible, Cryotherapy-Ineligible Lesions

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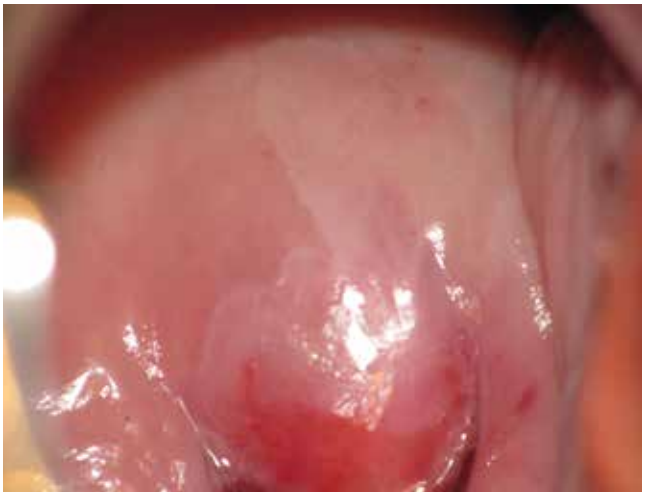

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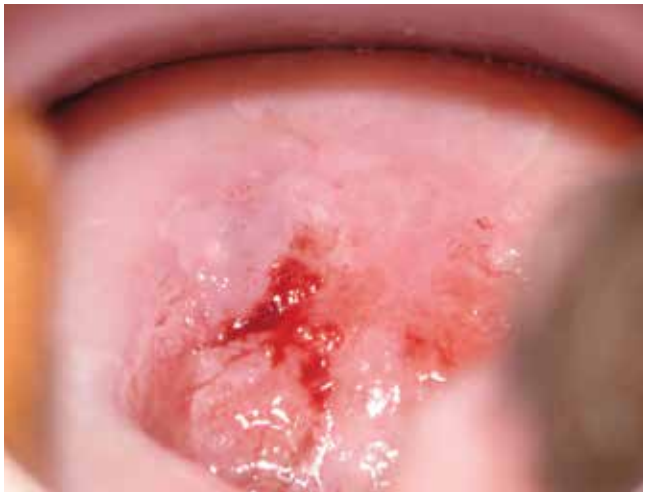

Figure 9.3a-b These lesions are cryotherapy-ineligible because they cannot be covered by the cryotip. However, they may be treated with multiple applications of the cold coagulation probe.

Notably, cold coagulation can only treat lesions up to 7 mm deep, meaning it may not be appropriate for treatment of extremely raised or warty lesions. The provider should consider referring such lesions for LEEP or closer follow-up.

The "Quadrants" Method

One method of determining whether the lesion occupies greater than 75% of the transformation zone is to roughly divide the cervix into four quadrants (Figure 9.4). If the lesion occupies more than three quadrants, refer the client.

Generally, occupation of greater than 75% of the transformation zone indicates the lesion is more advanced. This is why such lesions should be referred.

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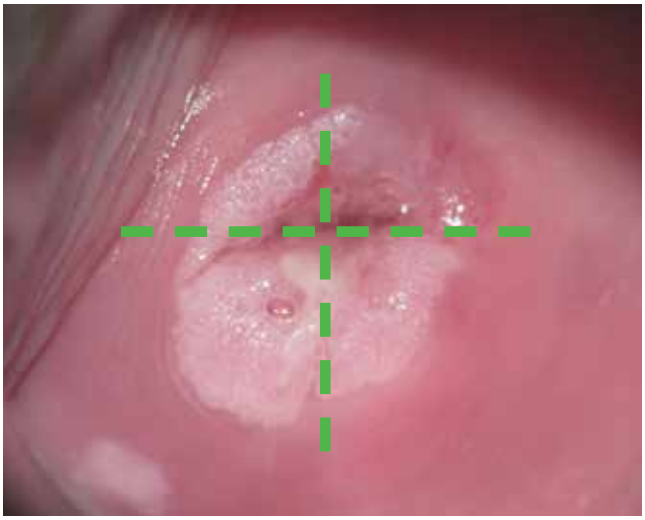

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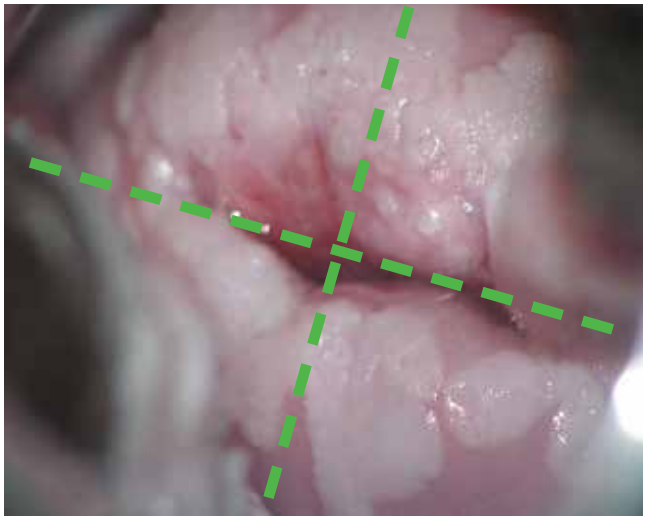

Figure 9.4a-b Cervical images of VIA-positive, cold-coagulation-ineligible lesions. Quadrants shown in green. These lesions occupy more than 75% of the transformation zone.

9.5 Counselling on Cold Coagulation

Key Messages

These messages are in addition to the messages discussed on page 57. As with cryotherapy, always reinforce key messages to cold coagulation clients. Provide written instructions if possible.

- "Cervical precancer can become cervical cancer in the future if not treated. Cold coagulation uses heated metal to destroy the precancer."
- "You may feel some abdominal or lower back pain, similar to menstrual cramps, during the treatment or shortly after the treatment."
- "After cold coagulation, a watery discharge from the vagina is normal. You can use sanitary pads or cotton wool pads to manage the discharge. The discharge should stop about four weeks after cold coagulation. A little bleeding and discomfort is also normal."
- "If you have any concerns after cold coagulation, please return to the clinic immediately. Concerns may include:
  Vaginal discharge that smells extremely bad;
  Bleeding heavier than a menstrual cycle;
  Fever with or without chills;
  Severe lower abdominal pain."

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Post-Cold Coagulation Instructions

What you are required to do after treatment of the cervix

You received treatment today because the provider found a bad spot on your cervix. At this clinic, we removed the bad spot with a heat treatment called cold coagulation This treatment should make the cervix healthy again.

After treatment, certain symptoms might occur.

These symptoms disappear within two to four weeks. Do not let these symptoms worry you.

- Your vagina will probably have some watery discharge.
- You may feel pain similar to the pain that is felt during your monthly period.
- You may have a little bleeding, but not as much as you have during your monthly period.

Do not have sex for one month after the treatment.

If you do, your cervix could be injured or get infected while it is healing. If you cannot abstain for one month, then ask your partner to use a condom. However, it is good to wait until you heal. Do not put anything, even medicine or herbs, into your vagina for one month.

Return to the clinic if you have ANY of the following:

- Discharge from the vagina that smells extremely bad.
- Bleeding more than you have during your monthly period.
- Fever or chills.
- Extremely bad pain in the stomach worse than during you monthly period.

This treatment is very safe and is used in many countries. Problems may occur, but only very rarely.

Please return to _____ clinic at _____ hours on

_____ to make sure your cervix is healthy.

Figure 9.5 Sample post-cold-coagulation instructions.

- "For four weeks after cold coagulation, do not have sex. If you cannot abstain, PLEASE make sure your partner uses a condom to protect your cervix. Also, do not clean your vagina or put any objects in your vagina, including your fingers, tampons, or herbs. If you do, you may hurt your cervix."

- "You must return to the clinic for a follow-up exam (provide the date, time, and place)." [1,5]

Additional Considerations

Similar to cryotherapy, clients may more easily transmit and contract infections, including HIV, after the cold coagulation. Our programme recommends counselling clients about this possible risk.

9.6 Materials for Cold Coagulation

In addition to the materials required for VIA, cold coagulation requires the following.

- Semm cold coagulator.
- Step-down unit, current regulator, or surge protector (to convert high-voltage power to low-voltage power if necessary and protect the cold coagulator from power surges).
- Metallic cervical probe.
- Wire (to connect the probe to the Semm cold coagulator).
- Sanitary pads or cotton wool (to help the client manage discharge).
- Optional: condoms (to give to clients); mild pain reliever (to help the client manage cramping).

9.7 A Step-by-Step Approach to Cold Coagulation

The following protocol may not apply to every cold coagulator. Cold coagulators should be operated according to the manufacturer's instructions. Always check the manufacturer's instructions prior to using any cold coagulator.

The following protocol describes the steps of cold coagulation, assuming:

- cold coagulation will be performed in the same visit as VIA;
- the woman was counselled on the cold coagulation procedure and gave informed consent for cold coagulation before VIA;
- the provider ensured all cold coagulation materials were available and sterile before the screening visit began.

Notably, the speculum does not need to be removed and reinserted between VIA and cold coagulation.

Step 1: Check Criteria

Ensure the lesion meets all the requirements of a cold-coagulation-eligible lesion. Only perform cold coagulation on clients with eligible lesions. Do not perform it on pregnant women. Cold coagulation does not require anaesthesia.

Step 2: Prepare for the Procedure

Turn on the cold coagulator and set the temperature to 100˚C. Wait 45 seconds for the probe to heat up.

Step 3: Heat the Lesion

Apply the probe to the lesion and heat the lesion for exactly 45 seconds, using a watch or clock to keep time. Take care not to touch any tissues except the cervix with the probe to avoid unnecessary burns.

If the probe cannot cover the entire lesion, apply the probe to the remaining acetowhite areas for an additional 45 seconds, making sure the applications overlap one another. The provider can apply the probe to the cervix up to 5 times, although over 90% of cervical lesions require only one or two applications.

Step 4: Finish the Exam and Thank the Client

Finish the exam as discussed on page 62 in chapter 6. Remind the client of post-cold-coagulation instructions and key messages. Provide a sanitary pad or cotton wool to help the client manage discharge.[5]

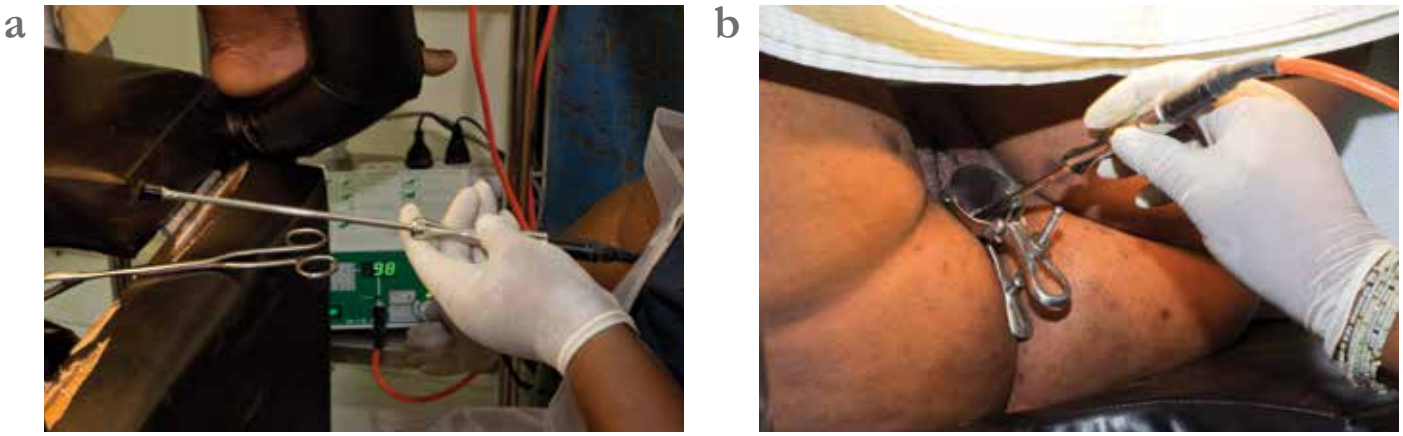

Figure 9.6a The provider turns on the cold coagulator while carefully keeping the probe from touching other objects.
Figure 9.6b The provider places the probe on the lesion.

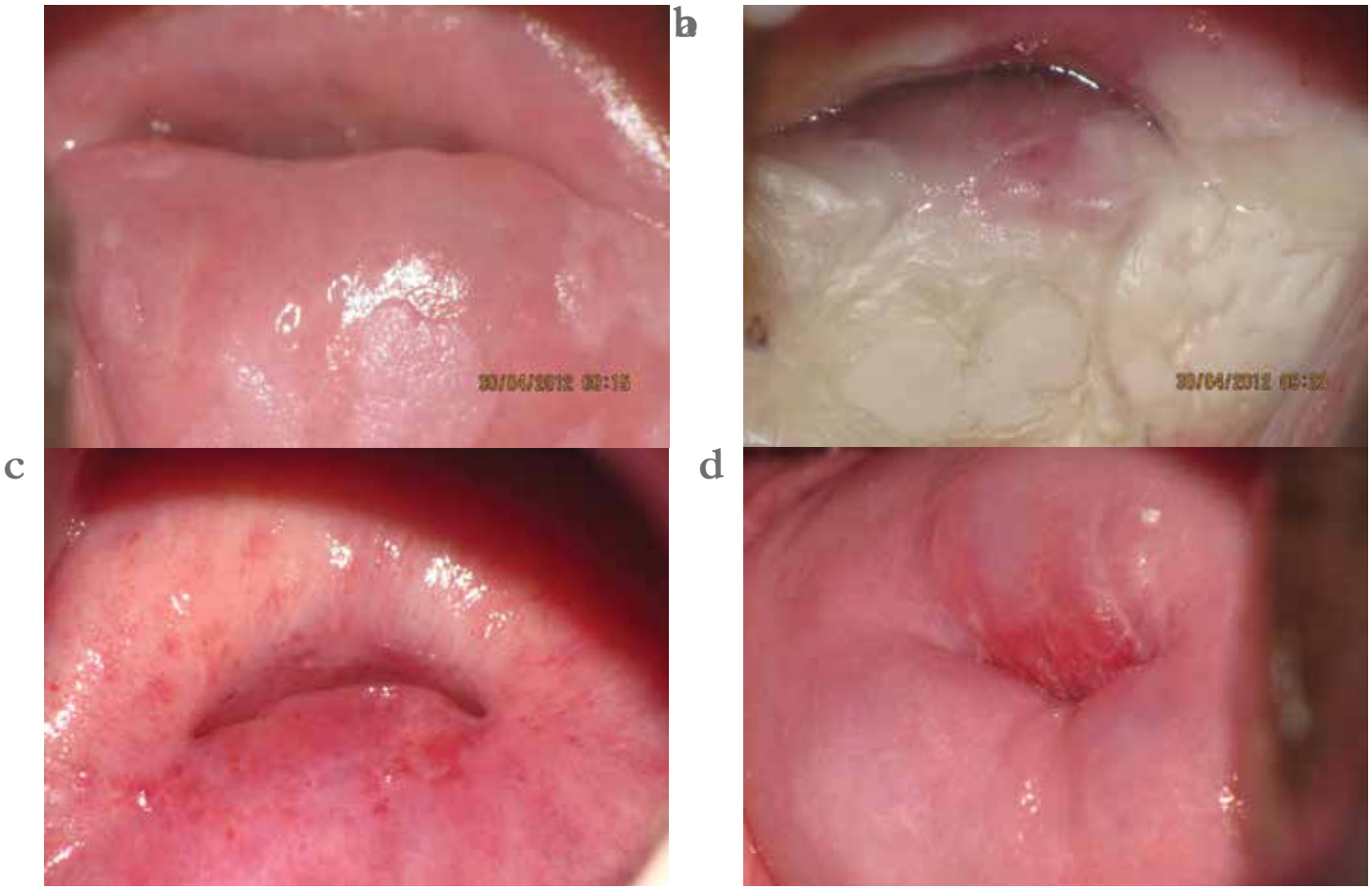

Figure 9.7a A cervix prior to cold coagulation.
Figure 9.7b The same cervix directly after cold coagulation.
Figure 9.7c The same cervix six months after cold coagulation.
Figure 9.7d The same cervix one year after cold coagulation.

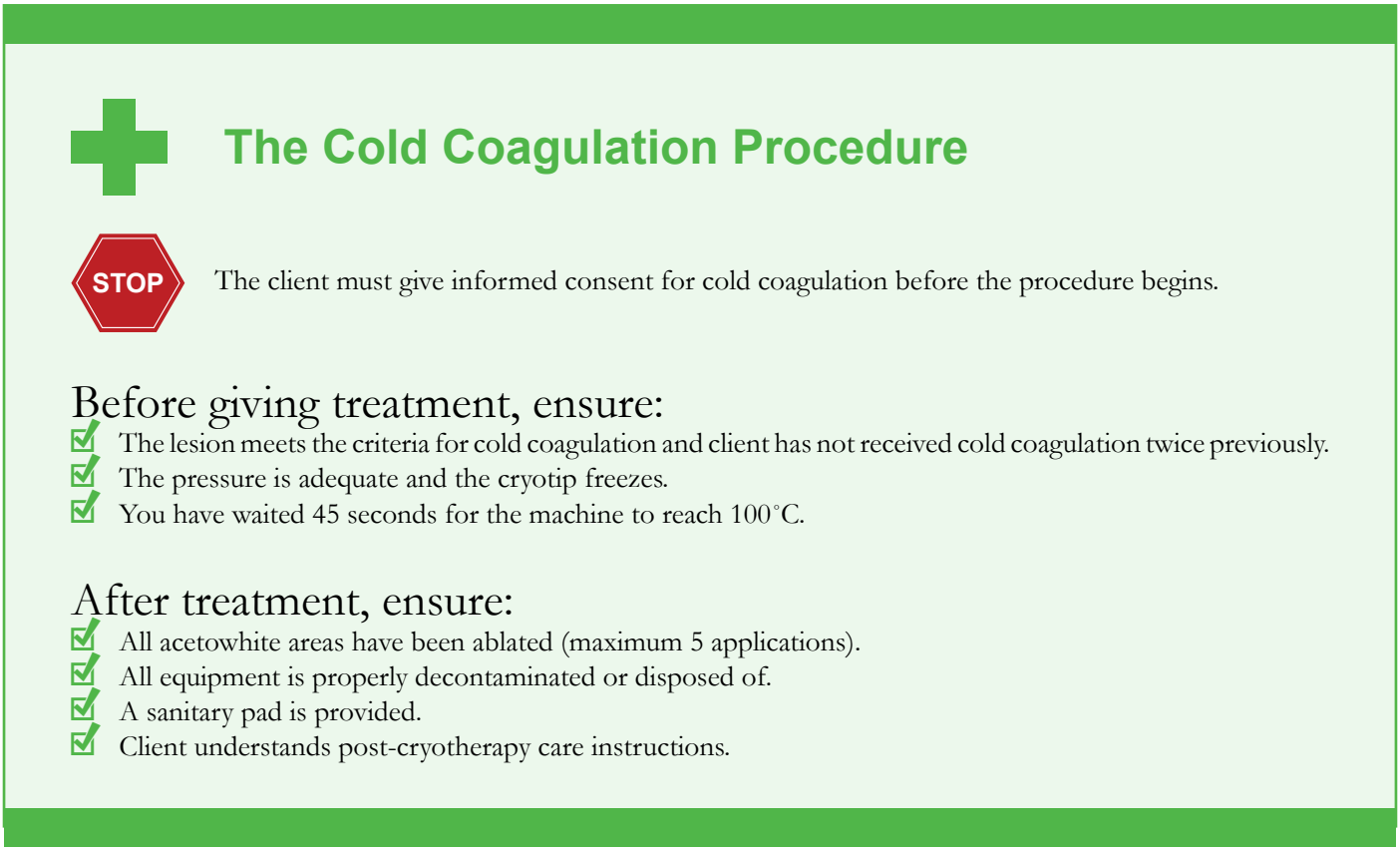

Figure 9.8 Poster on cold coagulation for the clinic.

9.8 Infection Prevention and Cold Coagulation

This sterilization procedure may not apply to every probe. The provider should sterilize the probe according to the manufacturer's instructions.

The cold coagulator incorporates automatic self-sterilization and should be sterilized after every use.

To sterilize the probe, first dip the probe in clean water and scrub away any visible matter with a cotton swab. Then, set the machine to 120°C. When the temperature reaches 120°C, wait 45 seconds for the probe to self-sterilize.

9.9 Following-Up on Cold Coagulation

Follow-up on cold coagulation in the same manner as cryotherapy.[5] Retreat persistent and recurrent lesions with cold coagulation or other methods as appropriate.

The limited data available indicate that lesions persist and recur with a similar frequency after cold coagulation as cryotherapy.[6]

Similar to cryotherapy, lesions may persist or recur more frequently in HIV-positive than HIV-negative women. Our programme recommends close follow-up of HIV-positive clients after cold coagulation.

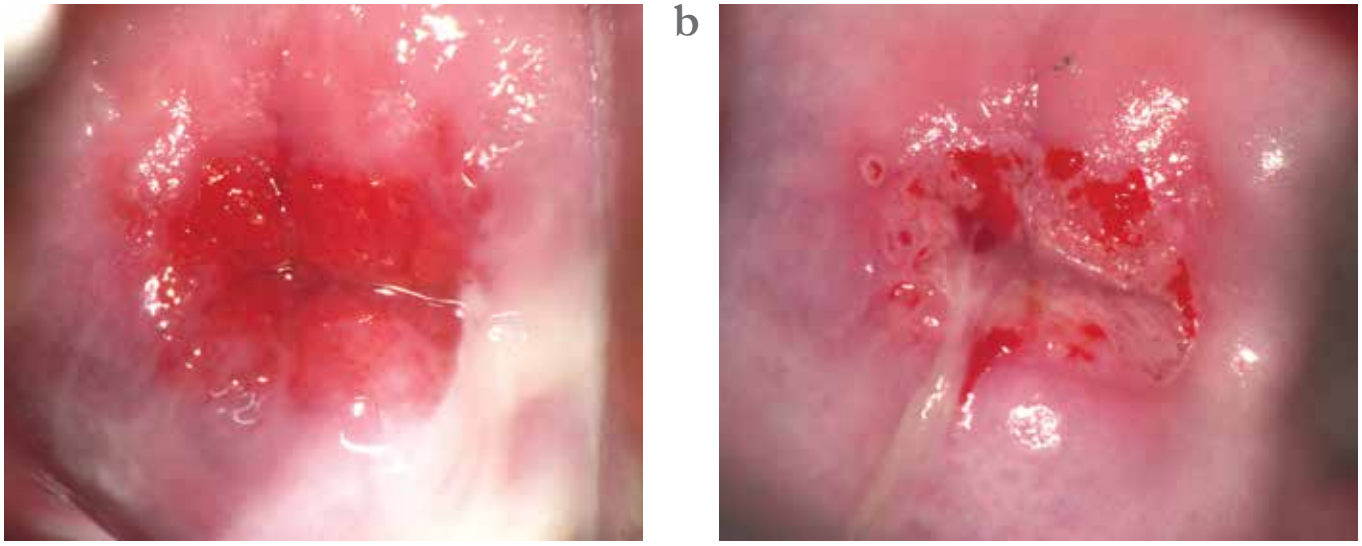

Figure 9.9a A cervix six weeks after cold coagulation.
Figure 9.9b The same cervix six months after cold coagulation.

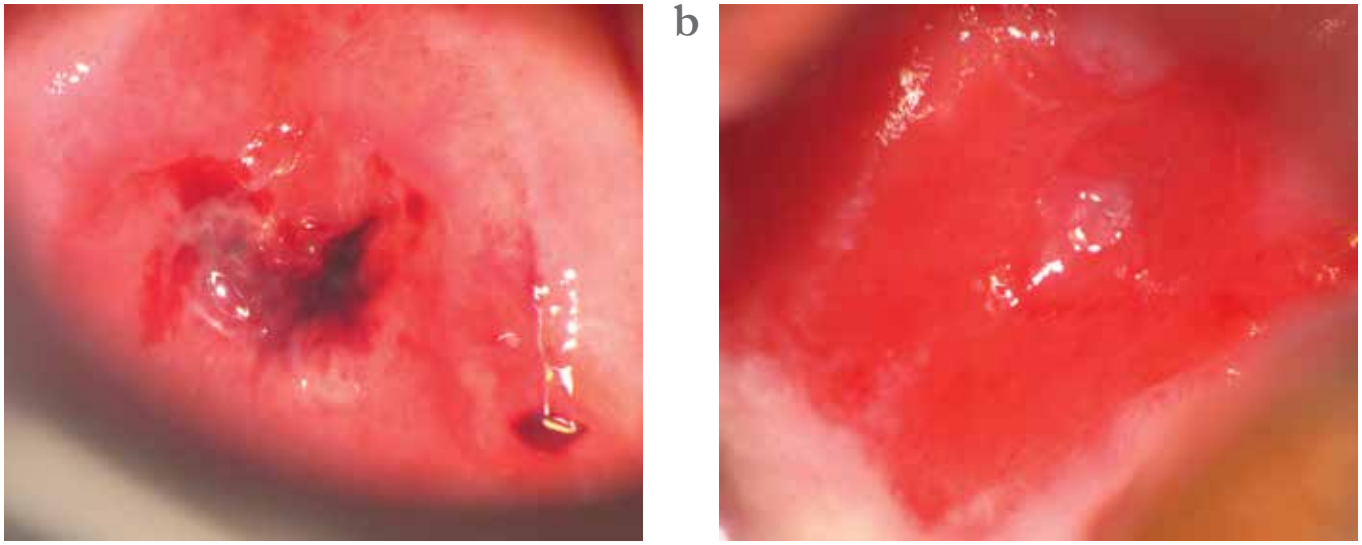

Figure 9.10a-b Cervixes six weeks after cold coagulation.

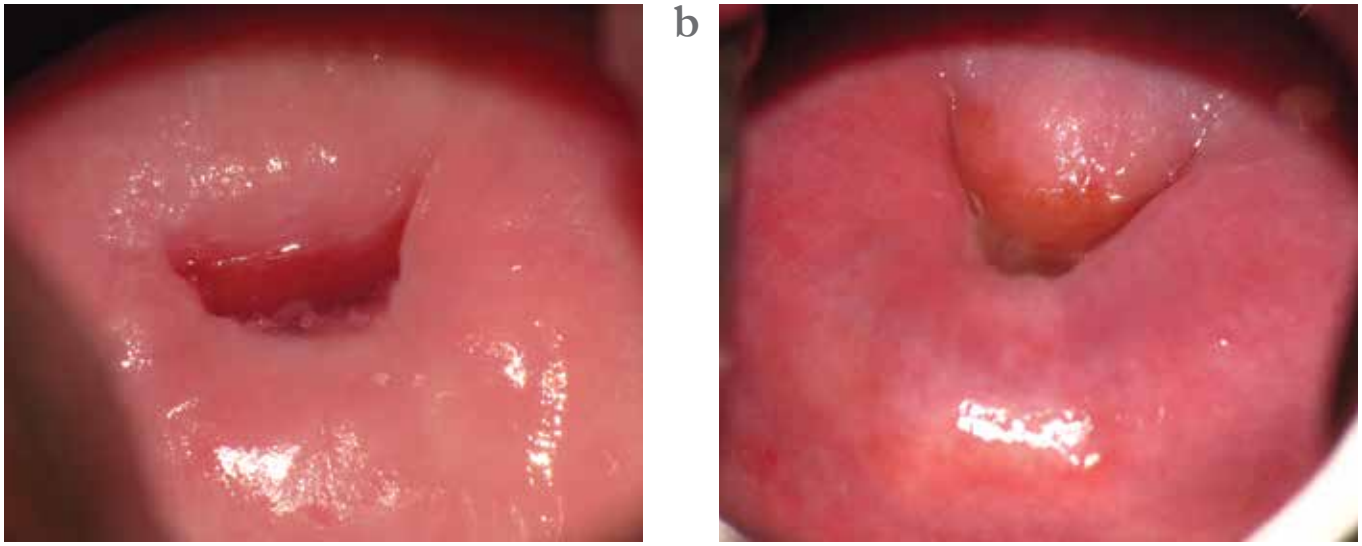

Figure 9.11a-b Cervixes one year after cold coagulation.

9.10 Possible Complications of Cold Coagulation

Cold coagulation has the same complications as cryotherapy. The woman may experience cramps, feel faint, or bleed slightly during the procedure. After cold coagulation, the woman will have a white or blood-stained discharge from the vagina and may experience mild pain.[1] Severe complications such as heavy bleeding, infection, and cervical stenosis may occur.[1,5] Any woman with extremely foul-smelling vaginal discharge, heavy bleeding, fever, chills, or severe lower abdominal pain may have a severe complication and should be treated immediately.[5] No data suggest that cold coagulation negatively impacts pregnancy outcomes or fertility.[1]

Chapter 9 Summary

- **Cold coagulation** uses a heated metal probe destroy the cervical lesion.
- Do not perform cold coagulation unless all the following criteria are met:
  - all of the lesion can be seen (i.e. the lesion does not extend into the endocervical canal);
  - the lesion is not suspicious for cancer;
  - there are no polyps or scarring that prevents full contact between the cervix and probe;
  - the woman is not pregnant;
  - the woman does not have severe cervicitis.
- The provider must counsel the woman with all the key messages in section 9.5 prior to performing VIA.
- Sterilize the probe according to the manufacturer's instructions after every cold coagulation session.
- Follow-up on cold coagulation in the same manner as cryotherapy.
- After cold coagulation, a little discharge, pain, and bleeding is normal. However, the client must return the clinic immediately if the following symptoms occur:
  - vaginal discharge that smells extremely bad;
  - bleeding heavier than a menstrual cycle;
  - fever with or without chills;
  - severe lower abdominal pain.

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4. Sankaranarayanan, R. (2010). *Screencast - Cold coagulation.* International Agency for Research on Cancer. Available: http://screening.iarc.fr/talks/coldcoagulator/en/ColdCoagulation.html. Accessed 17 June 2013
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7. Williams, O. E., Bodha, M., & Alawattegama, A. B. (1993). Outcome of cold coagulation for the treatment of cervical intraepithelial neoplasia in a department of genitourinary medicine. *Genitourin Med, 69*(1), 63-65.

Chapter

10

Recognizing and Treating Sexually Transmitted Infections (STIs) in Women

After this section, the reader will be able to...

- State the name and function of female reproductive organs and nearby structures.
- Recognize and treat major STIs using the WHO syndromic approach.
- Discuss partner management and referral.

10.1 The WHO Syndromic Approach to STI Treatment

Unlike traditional diagnostic approaches, the World Health Organization (WHO) syndromic approach does not focus on identifying the underlying causes of disease. Instead, the provider prescribes treatment based on the presence of certain signs and symptoms. The syndromic approach does not require laboratory equipment, expensive tests, or highly-trained personnel, making it ideal for resource-constrained environments.[25]

The WHO developed the syndromic approach in 1991.[26] Since then, it has been promoted and used in both developed and developing countries. Over the past two decades, STI management programmes that use the approach have contributed to dramatic declines in STI prevalence and incidence.[10,12,17,19,23]

The syndromic approach has two notable limitations. Because it does not rely on highly-specific laboratory tests, overdiagnosis and overtreatment may occur. Additionally, the approach cannot identify disease in asymptomatic individuals.[16]

This chapter provides basic information on the syndromic approach to STI treatment. Importantly, the approach may vary according to the prevalence of certain STIs in a region. Adapt the approach to your region according to your country's guidelines. For more information, the WHO offers a training programme on the syndromic management of STIs, accessible at: http://www.who.int/reproductivehealth/publications/rtis/9789241593407index/en/.

10.2 Writing Prescriptions

Know the contraindications for and possible side effects of every medication you prescribe. Notably, some medications cannot be given to pregnant women.

When prescribing a medication, warn the client of any common side effects.

Some medications may not be available or may be prohibitively expensive for your clients. Discuss the availability and cost of different medications with your local pharmacy.

Be advised that the STI treatment recommendations in this manual may change frequently according to new research.

Table 10.1 Terms for Writing Prescriptions

Term	Meaning
BID	Twice a day
IM	Intramuscular (regarding an injection)
Orally	Medication is taken by mouth
Pessary	Medication is placed into the vagina

10.3 Anatomy of the Female Reproductive System

Key Terms and Definitions

- **Uterus**. The pear-shaped, thick-walled organ consisting of the uterine corpus and uterine cervix. Commonly known as the womb.
- **Uterine corpus**. The upper part and main body of the uterus. The uterine corpus holds and nourishes the baby during pregnancy.
- **Uterine cervix (cervix)**. The lower part of the uterus that opens into the vagina.
- **Vagina (birth canal)**. Connects the uterus to the outside of the body.
- **Ova (eggs)**. Female reproductive cells that can develop into a baby after fertilization.
- **Ovaries**. Organ that produces eggs. Every woman has two ovaries.
- **Fallopian tubes**. Connects the ovaries and uterus; allow eggs to travel from the ovaries to the uterus.
- **Internal genitalia**. The internal reproductive organs, including the uterus, cervix, vagina, fallopian tubes, and ovaries.
- **Vulva (external genitalia)**. The external reproductive organs, including the labia, clitoris, and perineum.
- **Labia**. The external folds of the vagina, consisting of the labia majora (larger outer folds) and the labia minora (smaller inner folds).
- **Inguinal regions**. The regions directly to the left and right of the genitals. The legs join the body at the inguinal regions.
- **Inguinal nodes**. The lymph nodes in the inguinal region. Lymph nodes are oval-shaped organs of the immune system.
- **Bartholin's glands**. Two small glands on either side of the opening of the vagina. Bartholin's glands produce mucus to lubricate the vagina during sex.
- **Clitoris**. A sensitive organ which is the primary source of female sexual pleasure.
- **Urethra**. The canal that transports urine from the bladder to the outside of the body.
- **Perineum**. The area between the anus and vulva.
- **Anus**. The opening through which people defecate.
- **Rectum**. The final section of the intestine leading up to the anus.
- **Colon**. The section of the intestine prior to the rectum.
- **Anogenital region**. The region containing and surrounding the external genitals and anus.
- **Lower genital tract**. The cervix, vagina, and vulva.
- **Upper genital tract**. The reproductive organs above the cervix, including the uterine corpus, ovaries, and fallopian tubes.

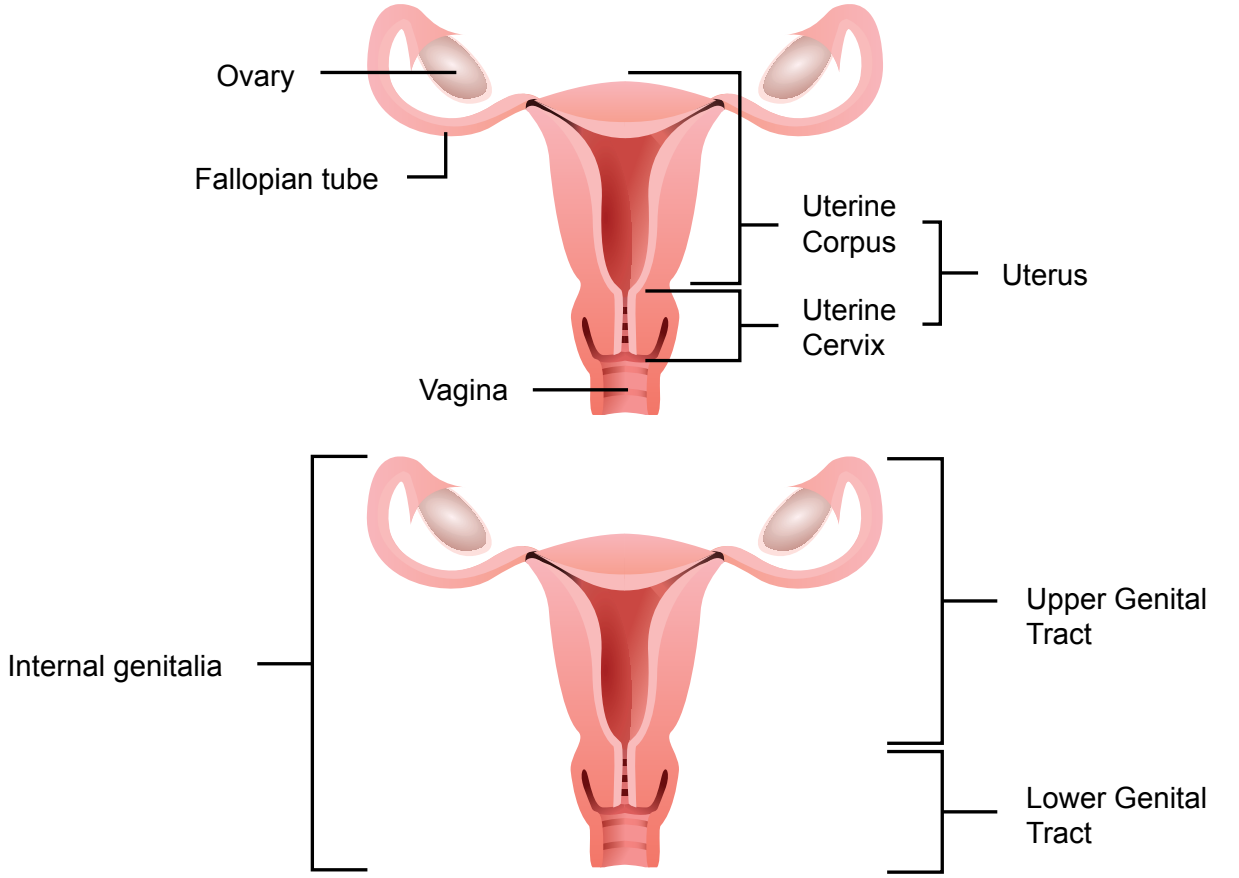


Figure 10.1 Illustrations of the female reproductive system with structures labelled.

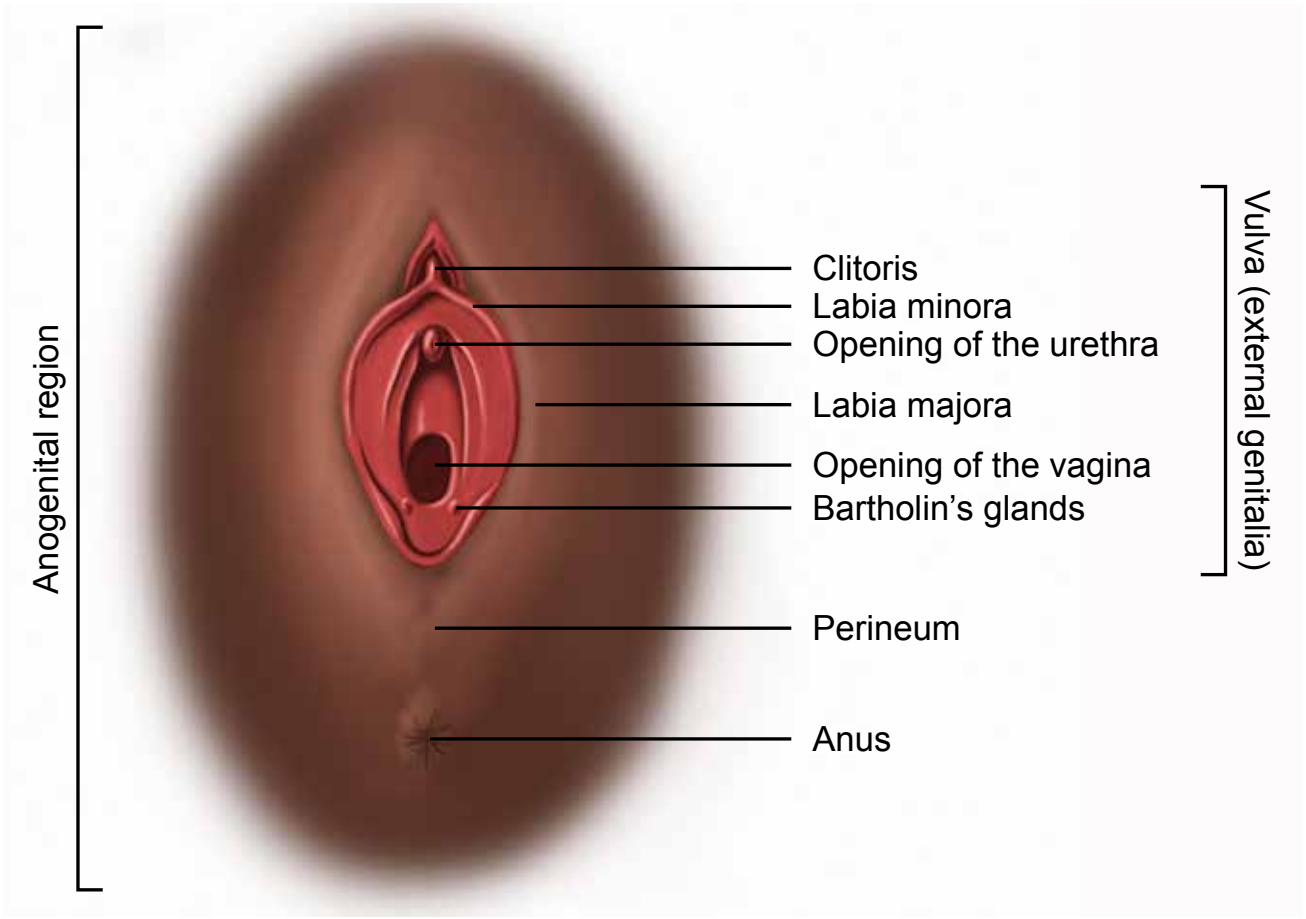


Figure 10.2 Illustration of the female anogenital region.

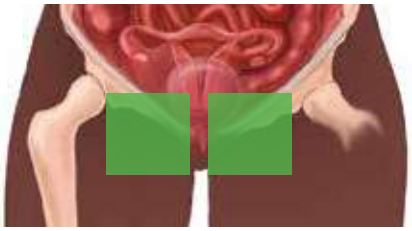


Figure 10.3 The inguinal region (shown in green).

10.4 Vaginitis

Vaginitis is inflammation of the vagina from irritation or infection. The three major causes of vaginitis are bacterial vaginosis, candidiasis, and trichomoniasis.[9] Usually, abnormal vaginal discharge is the first symptom of vaginitis. Vaginal discharge becomes abnormal when:

- The volume of discharge increases;
- A foul-smelling odour develops;
- The colour or consistency changes.

Bacterial Vaginosis

Many different types of bacteria can cause bacterial vaginosis, the most common vaginal infection. Approximately half of all infected women do not have symptoms.

Symptoms:

- Homogeneous, grey-white vaginal discharge.
- A fish-like smell.[9]

Candidiasis (Yeast Infection)

An estimated 75% of women get candidiasis at least once in a lifetime. A yeast-like fungus called Candida albicans causes candidiasis in 90% of cases. As such, candidiasis is commonly known as a yeast infection.

Symptoms:

- Extreme itching.
- Burning pain following urination (dysuria).
- White, curd-like, cheesy vaginal discharge.
- Red spots on the vulva (vulvar erythema).[9]

Trichomoniasis

The common parasite Trichomonas vaginalis causes trichomoniasis.

Symptoms:

- Profuse, extremely frothy, yellowish or greenish vaginal discharge (possibly foul-smelling).
- Possible itching and burning with urination.
- Red spots on the cervix (strawberry cervix).
- Red spots inside the vagina (vaginal erythema).[9]

Strawberry Cervix

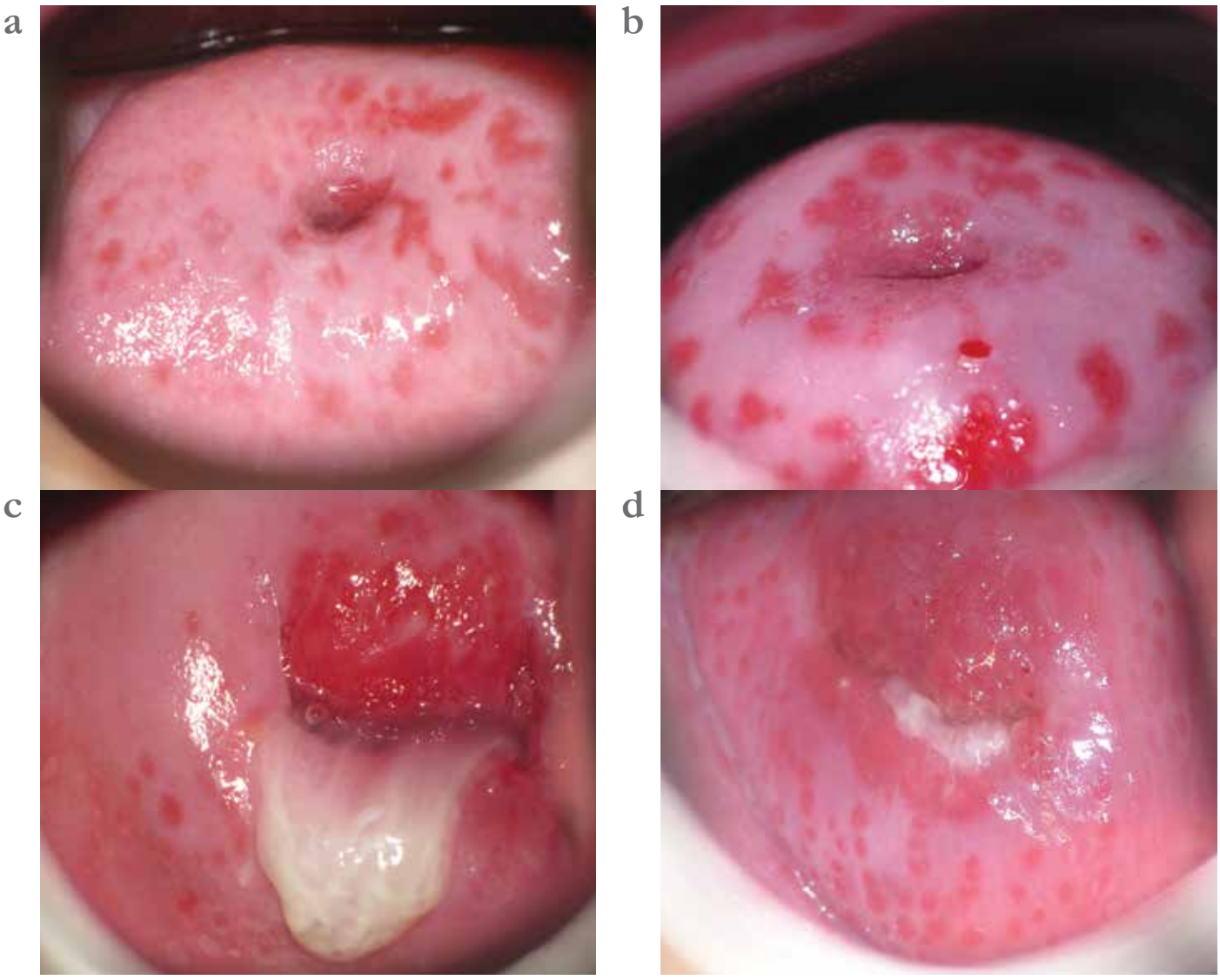
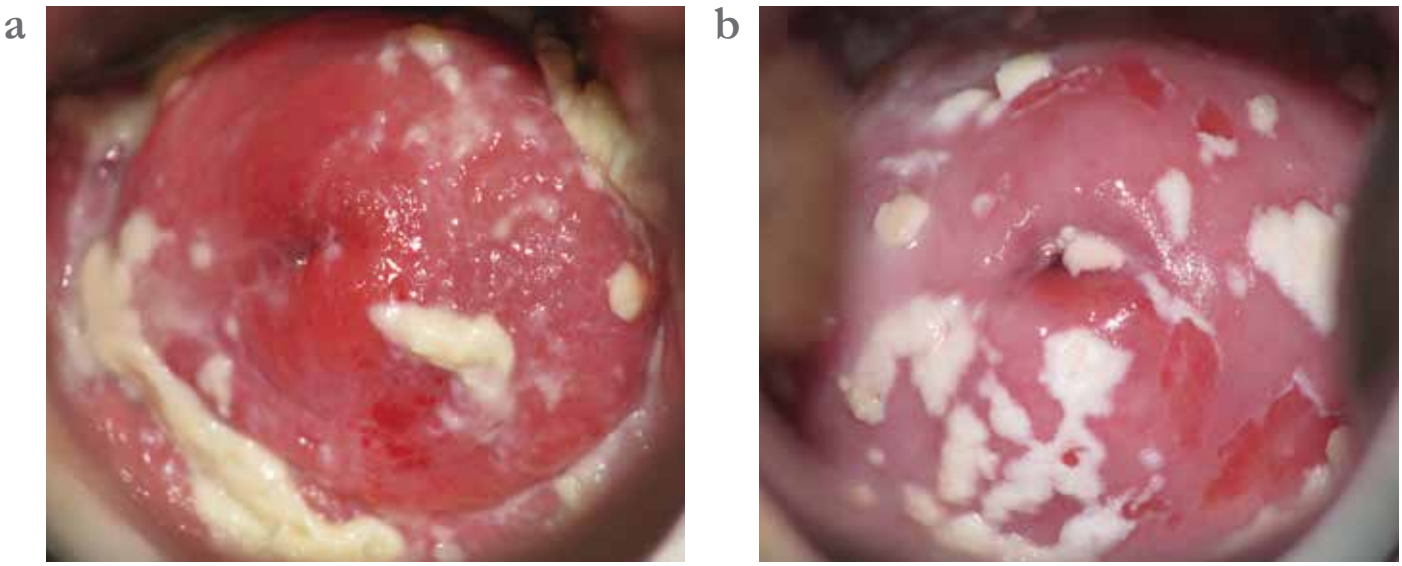


Figure 10.4a-d Strawberry cervix, a key sign of trichomoniasis.

Candidiasis



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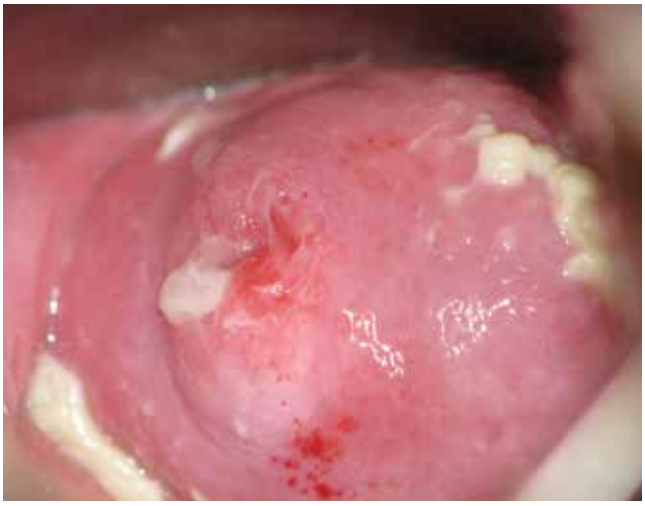

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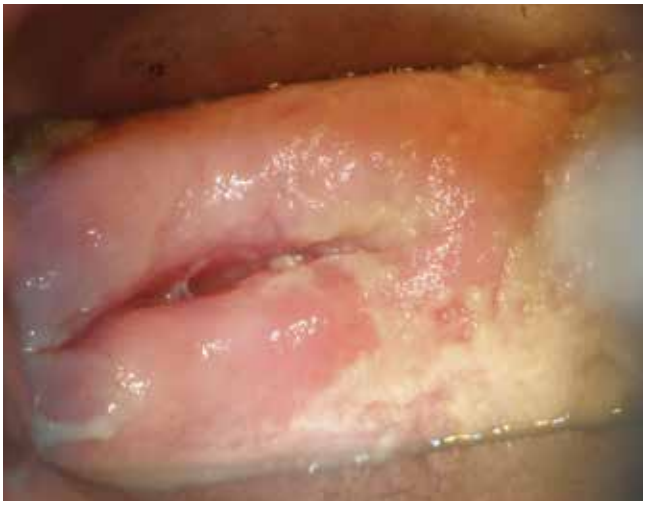


Figure 10.5a-d Candidiasis. Note the white, curd-like, cheesy discharge.

Treating Vaginitis

Our programme treats all clients with abnormal vaginal discharge for either: (1) bacteria vaginosis and trichomoniasis, or (2) candidiasis, depending on symptoms. Others may treat for bacterial vaginosis, candidiasis, and trichomoniasis regardless of symptoms. Provide and promote condoms at the time of diagnosis.[27]

Recommend Treatment for Bacterial Vaginosis and Trichomoniasis

- Metronidazole 2 g orally single dose under supervision, **or**
- Metronidazole 500 mg orally BID for 7 days.

Figure 10.6 Poster on treatment for bacterial vaginosis and trichomoniasis.[9]

Recommend Treatment for Candidiasis

- Fluconazole 150 mg orally single dose under supervision, **or**
- Clotrimazole 500 mg pessary single dose, **or**
- Clotrimazole 100 mg pessary BID for 3 days, **or**
- Miconazole 200 mg pessary once a day for 3 days.

Figure 10.7 Poster on treatment for candidiasis.[9]

Table 10.2 Distinguishing Bacterial Vaginosis, Trichomoniasis, and Candidiasis

Infection	Discharge	Itching	Red Spots on Vulva	Foul Odour
Bacteria Vaginosis	Grey-white, homogeneous	No	No	Yes
Trichomoniasis	Yellowish, frothy	Maybe	No	Yes
Candidiasis	White, cheesy	Yes	Yes	No

10.5 Cervicitis

Cervicitis is inflammation of the cervix from irritation or infection. The two major causes of cervicitis are chlamydia and gonorrhoea.[9]

Gonorrhoea

The bacteria Neissaria gonorrhoeae causes gonorrhoea. The majority of women with gonorrhoea do not have symptoms.[14]

Chlamydia

Chlamydia trachomatis is one of the most common sexually transmitted infections in women.[7] Chlamydia has similar symptoms to gonorrhoea, and the two infections often coexist. Approximately 20% of men and 42% of women with gonorrhoea also have chlamydia.[18] As with gonorrhoea, the majority of women with chlamydia do not have symptoms.[14,18]

Symptoms:

- Copious yellow vaginal and cervical discharge containing mucus or pus.
- Inflammation, itching, or burning of the vulva, vagina, cervix, or urethra.
- Burning pain following urination (dysuria).
- Change in frequency of urination.
- Inflammation and swelling of Bartholin's duct and gland (bartholinitis).

Gonorrhoea clients may develop conjunctivitis, bleeding, systemic infection, and inflammation of the pharynx, rectum, and anus.[9]

Treating Cervicitis

Abnormal vaginal discharge is highly predictive of vaginitis but poorly predictive of cervicitis. The WHO recommends treating clients with abnormal vaginal discharge for both vaginitis and cervicitis only if the client presents with visible cervicitis and reports one of the following risk factors:

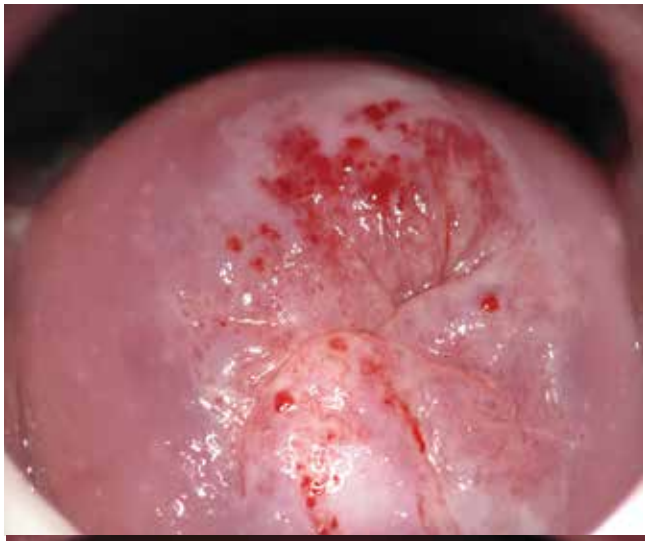
- recent new sexual partner;
- partner with the symptoms of chlamydia or gonorrhoea;
- multiple partners;
- spouse who returned after a long stay away from home;
- younger than 21 years of age or unmarried.[27]

Otherwise, treat only for vaginitis.[25] Provide and promote condoms at the time of diagnosis. Offer HIV testing and counselling if possible.

The risk factors for chlamydia and gonorrhoea vary from one region to another. The risk factors listed above may not apply to your setting. Consult an expert to see what risk factors apply in your area. Notably, some countries may use criteria other than risk factors to determine when to treat for cervicitis.

Images of Cervicitis

a



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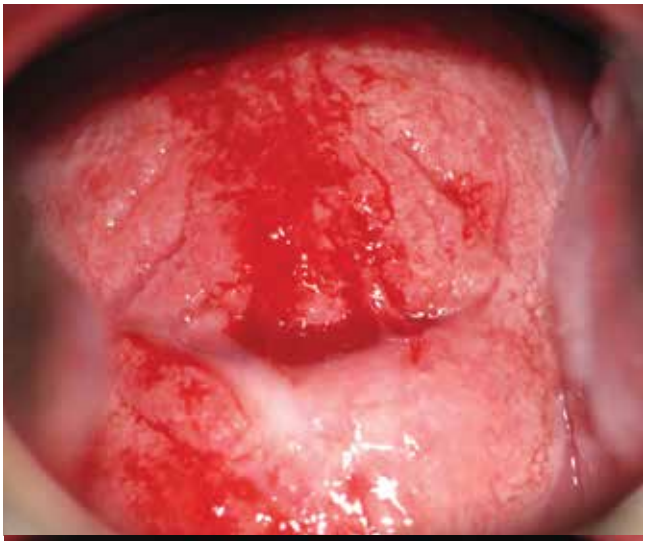

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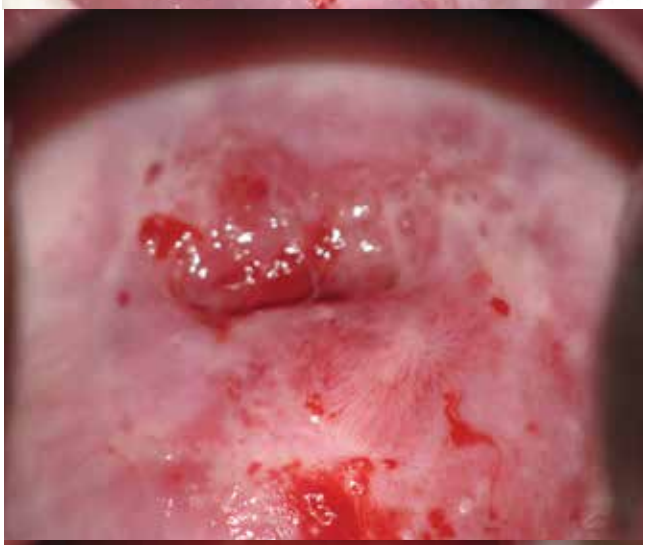

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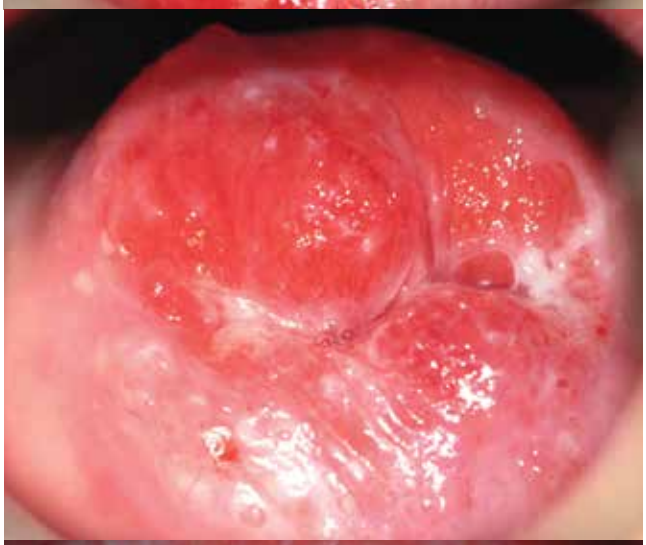

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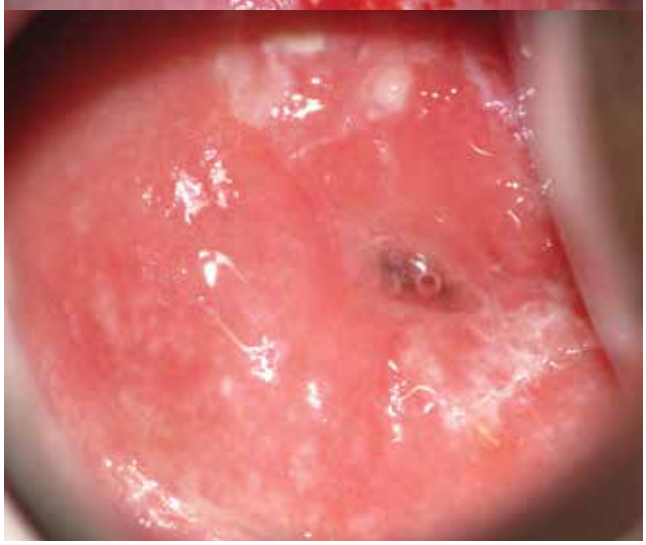

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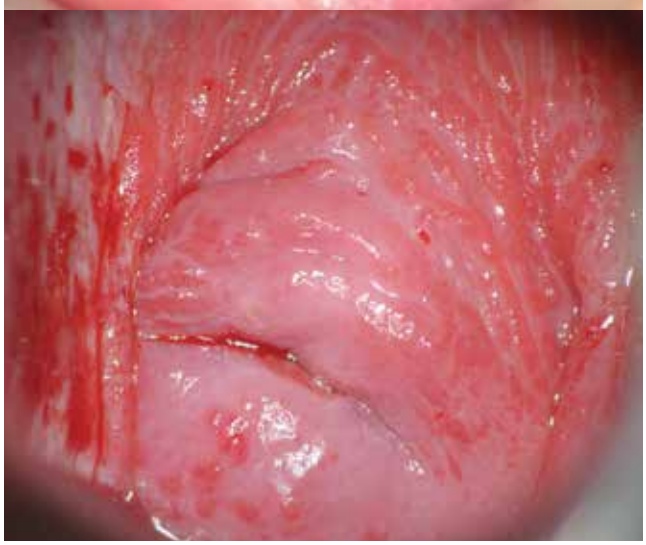

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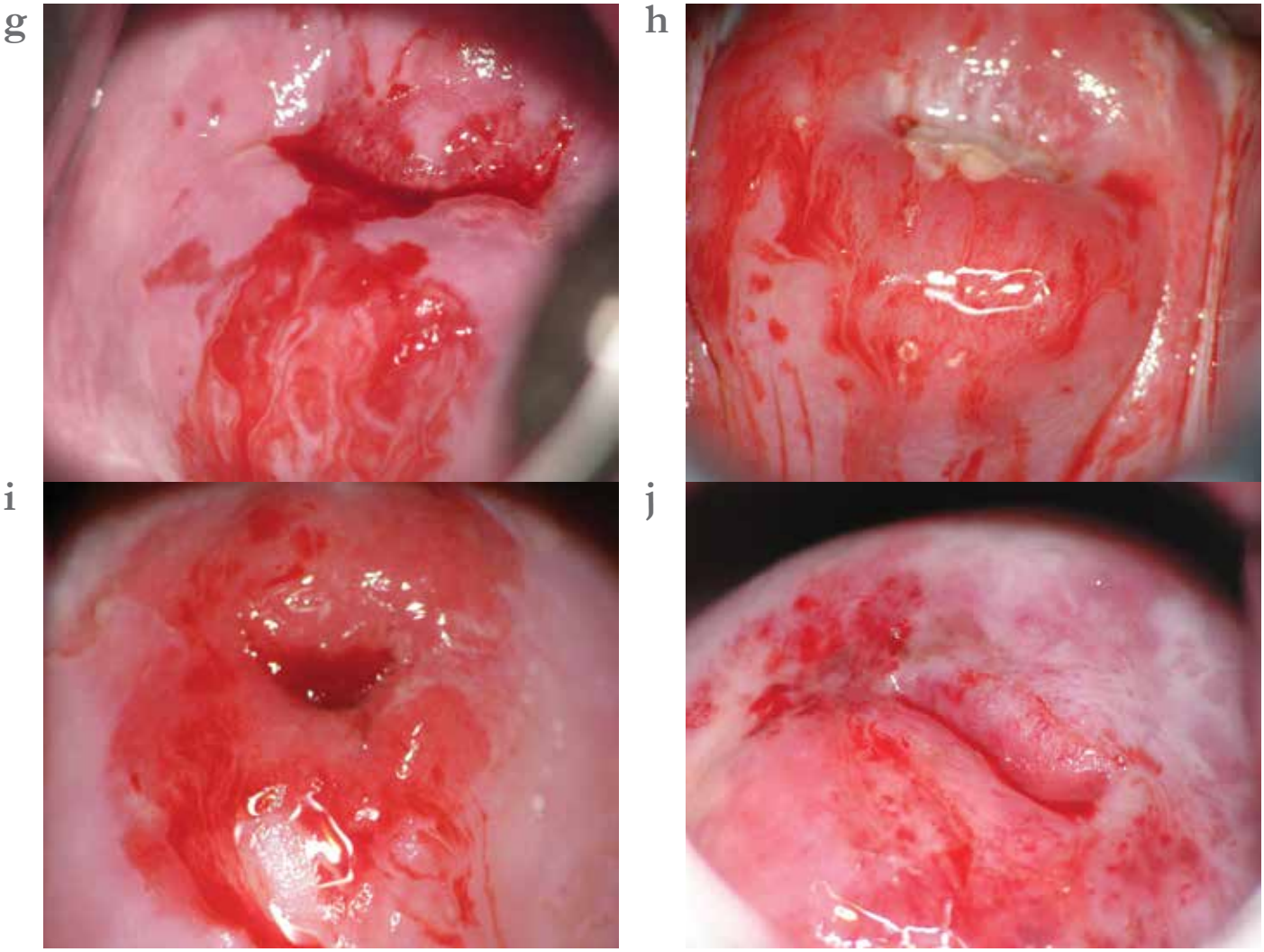

Figure 10.8a-j Cervicitis.

Recommend Treatment for Cervicitis

Treatment for gonorrhoea:

- Ceftriaxone 250 mg IM single dose.

Combined with treatment for chlamydia:

- Azithromycin 1 g orally single dose under supervision, **or**
- Doxycycline 100 mg orally BID for 7 days.

STOP

Do not give doxycycline to pregnant women. Negative gastrointestinal side effects and cost make azithromycin impractical in some developing settings. Cefixime is not recommended based on evidence of limited effectiveness in Asia, the Pacific, and the United States.

Figure 10.9 Poster on treatment for cervicitis.[2,3,4,9]

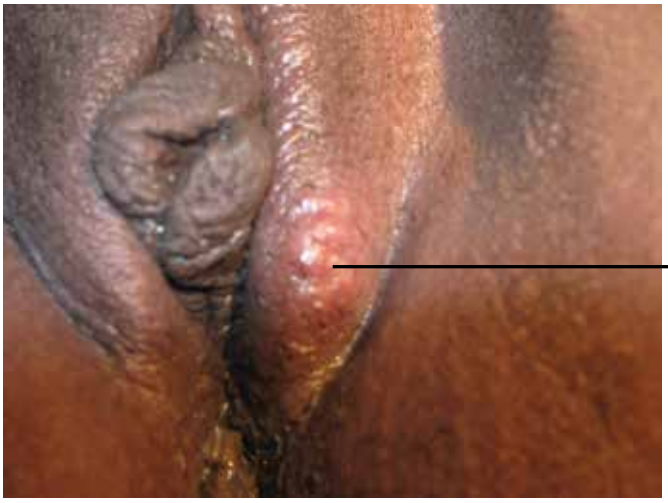

Figure 10.10 Bartholinitis.

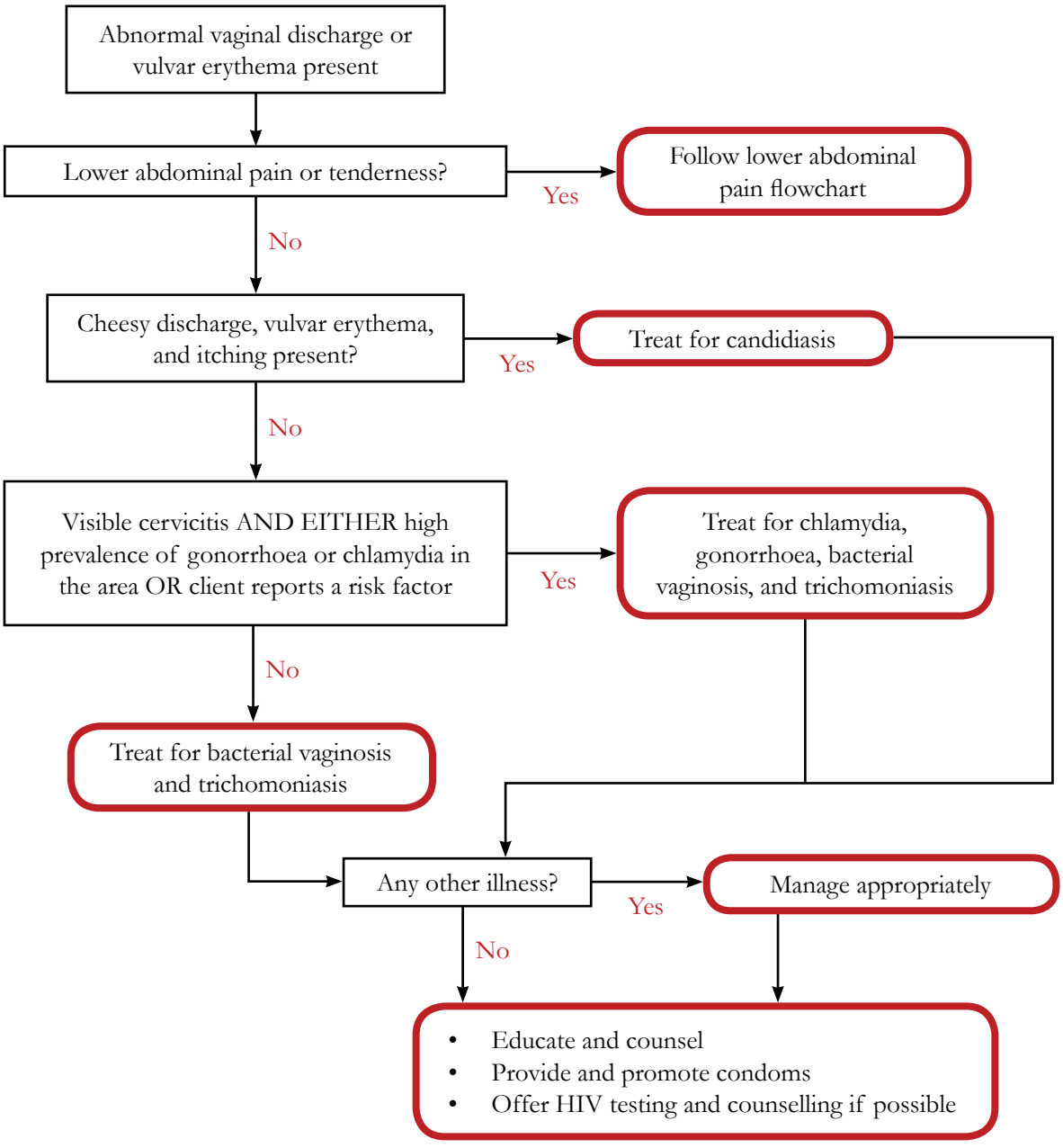

Figure 10.11 Flowchart on the management of vaginal discharge. Revise as necessary for your setting. Adapted from the WHO Training Modules for the Syndromic Management of STIs.[27]

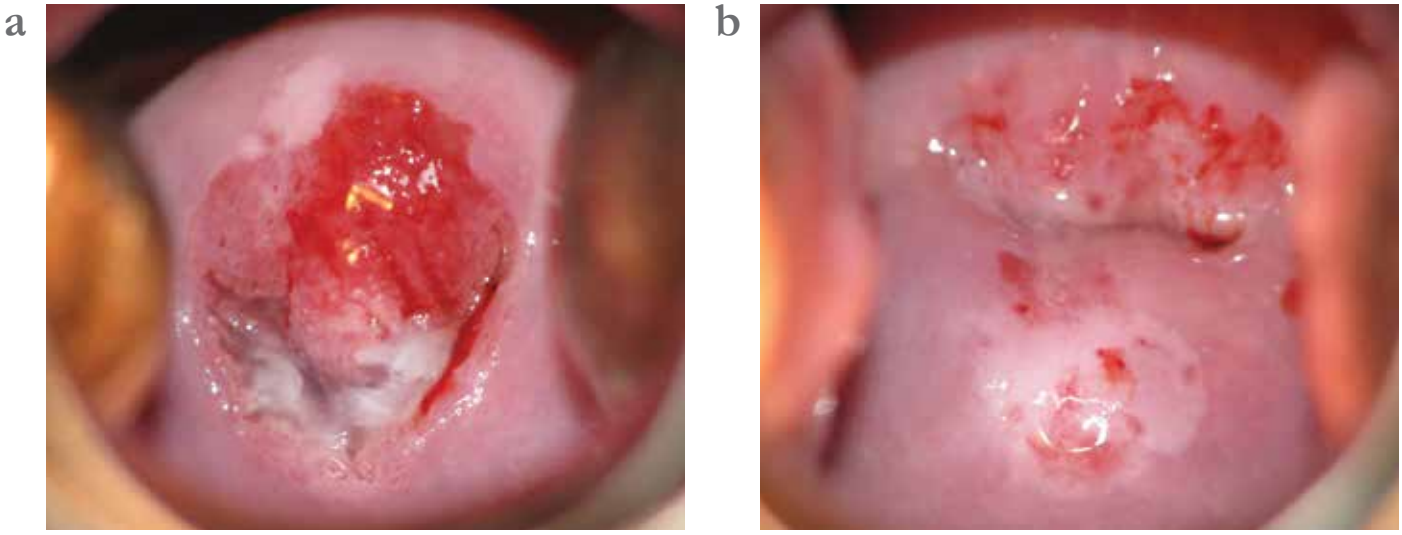

Figure 10.12a-b VIA-positive and cervicitis.

Partner Management

Men and women with chlamydia or gonorrhoea frequently transmit the infection to their sexual partners. An estimated 20-50% of men and 60-90% of women become infected with gonorrhoea after exposure to an infected partner.[9] One study found 70% of people with chlamydia infect their sexual partners.[22]

Providers must treat the sexual partners of women with chlamydia or gonorrhoea to prevent the spread of these STIs. The WHO recommends treating the partner even if he or she lacks symptoms.[27]

The client can refer her sexual partners for treatment using:

- **Direct discussion.** The client discusses the infection and the need for treatment with her partners.
- **Referral cards.** The provider gives the woman one card for each of her sexual partners. The card asks the partner to visit the clinic without specifying why. The card uses a "diagnostic code" or number to inform the provider what infection to treat the partner for. Referral cards work well for women who feel uncomfortable discussing their infections with their partners.

Card #: _____

Date of Issue: _____

Diagnostic Code: _____

Partner's Name and Details:

_____

Clinic:

_____

Card #: _____ Date of Issue: _____

Clinic: _____

Name: _____

Please visit
_____ clinic
and bring this card with you

Diagnostic code: _____

Figure 10.13 Sample referral card number one. After recording the details, the provider cuts the card in half and gives the right side to the client to pass on to the partner. The provider retains the left side for clinic records. Adapted from the WHO Training Modules for the Syndromic Management of STIs.[27]

Figure 10.14 Sample referral card number two. The provider writes the date and circles the code – A, B, or C – for the original client's syndrome. The advantages of this card include:

- it does not look like a referral card;
- it gives no details about the client or partner;
- the code does not reveal the diagnosis.

Adapted from the WHO Training Modules for the Syndromic Management of STIs.[27]

Never force a client to refer her partners. During the referral visit, always check the partner for other STIs. For more information on partner referral and treatment, access the WHO training module on partner management at: http://whqlibdoc.who.int/publications/2007/9241593407_mod6_eng.pdf.

10.6 Lower Abdominal Pain

Pelvic Inflammatory Disease (PID)

Lower abdominal pain may indicate **pelvic inflammatory disease (PID)**. PID is an infection and inflammation of the upper female genital tract and surrounding tissues. PID is common and may have serious consequences.[2,27]

Chlamydia, gonorrhoea, and some bacteria cause PID. Without therapy, 10-17% of women with gonorrhoea and up to 40% of women with chlamydia develop PID.[9,15]

Salpingitis can block one or both fallopian tubes, leading to decreased fertility or total infertility. Total infertility occurs in estimated 20% of clients with PID, and PID increases the risk of ectopic pregnancy tenfold.

Notably, some women with PID may not complain of lower abdominal pain.[2]

Symptoms:

- Lower abdominal pain.
- A history of abnormal vaginal discharge.
- Salpingitis (infection and inflammation of the fallopian tubes).
- Foul-smelling odour.
- Abnormal vaginal bleeding.
- Stomach upset.
- Pain during sex.
- Pain during urination.
- (Rarely) fever, nausea, or vomiting.[2,28]

Treating Lower Abdominal Pain

Immediately hospitalize any woman with extreme lower abdominal pain for immediate follow-up as ectopic pregnancy and appendicitis cannot be excluded.

Refer clients who report missed menses and may be pregnant for further gynaecologic assessment and/or antenatal care.

Refer the woman for further gynaecological assessment if she reports:

- a recent abortion, delivery, or miscarriage;
- abnormal vaginal bleeding;
- abnormal abdominal masses;
- abdominal tenderness without a history of abnormal vaginal discharge.

Treat for PID if the woman complains of lower abdominal pain and abnormal vaginal discharge. Follow-up three days later and if the client has not improved, refer her for further assessment or hospitalization.

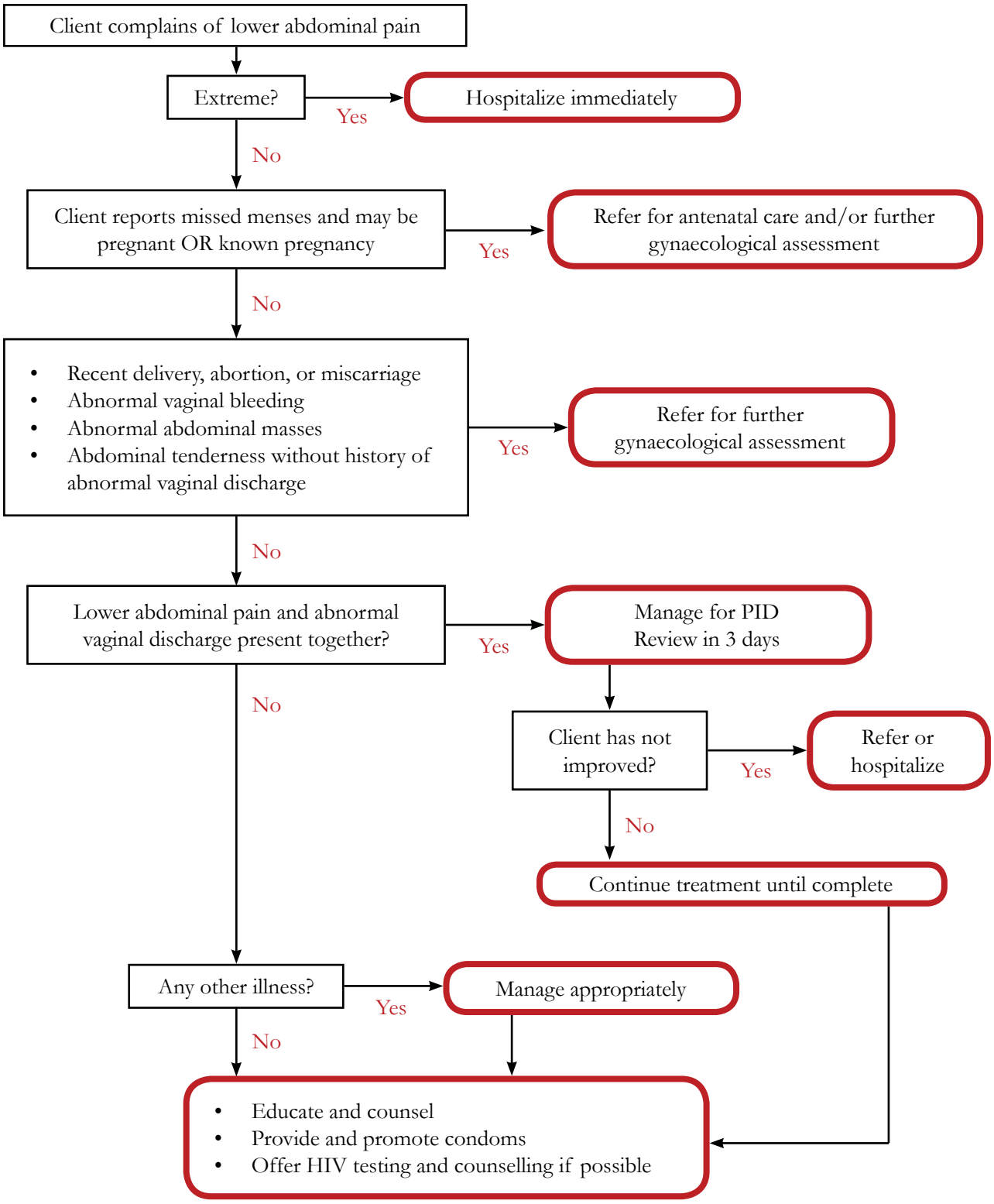

Figure 10.15 Flowchart on the management of lower abdominal pain. Revise as necessary for your setting. Adapted from the WHO Training Modules for the Syndromic Management of STIs.[27]

Seriously consider hospitalizing clients with PID when:

- the diagnosis is uncertain;
- surgical emergencies such as ectopic pregnancy and appendicitis cannot be excluded;
- a pelvic abscess is suspected;
- severe illness precludes management on an outpatient basis;
- the client is pregnant;
- the client is unable to follow or tolerate an outpatient regimen;
- the client has failed to respond to outpatient therapy.[27]

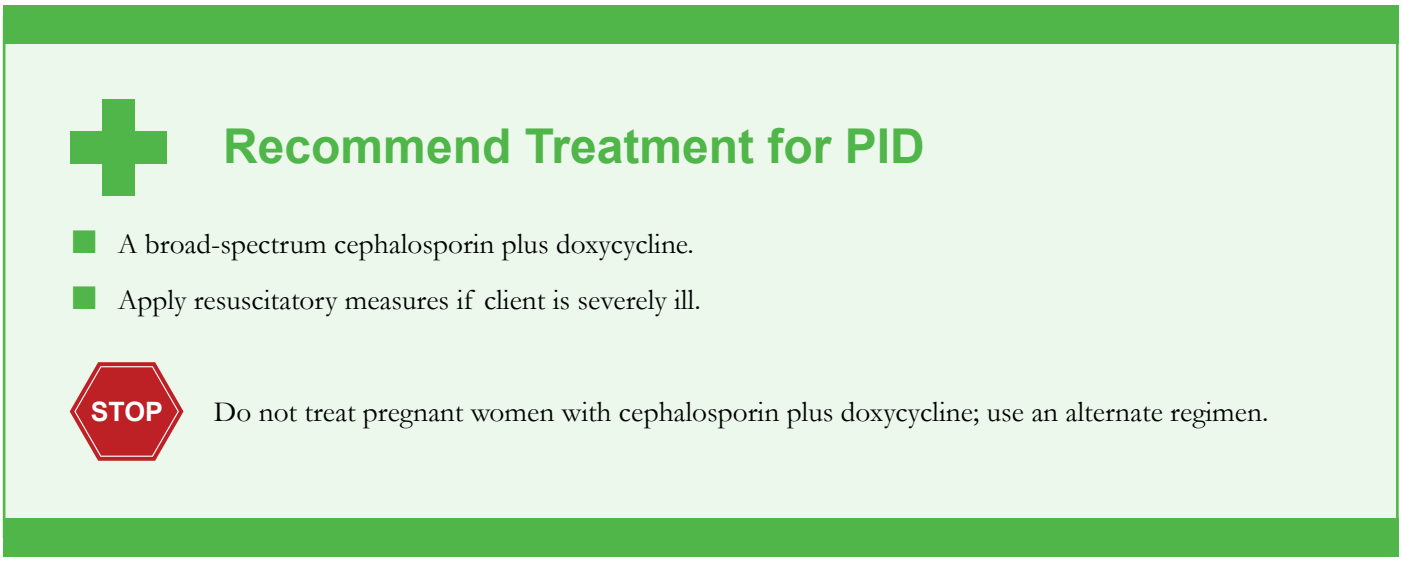

Figure 10.16 Poster on treatment for pelvic inflammatory disease (PID).

10.7 Genital Ulcers

Genital ulcers are open sores on the external or internal genitalia. Causes of genital ulcers include genital herpes, syphilis, chancroid, granuloma inguinale, and lymphogranuloma venereum.

Syphilis

Over 90% of syphilis cases occur in developing countries.[11] The bacteria Treponema pallidum causes syphilis and usually enters the body through small cuts in the skin. Syphilis usually has two stages, a primary stage and a secondary stage. Rarely, a severe tertiary stage may occur.

In the primary stage, T. pallidum causes painless, red, round, firm ulcers approximately 1 cm in size with raised edges. Ulcers develop near the site of infection and most often occur on the vulva, vagina, cervix, anus, nipples, or lips. The glands near the ulcer may enlarge.

One to three months after the primary stage ends, the secondary stage begins. A maculopapular rash or moist papules appear on the skin, usually on the palms of the hands and soles of the feet. A maculopapular rash is a red area covered with small bumps. Moist papules are small, moist, raised red bumps. Meningitis (inflammation of the meninges), nephritis (inflammation of the kidneys), or hepatitis (inflammation of the liver) may occur. Usually, the secondary stage resolves spontaneously, and the infection enters a dormant phase that can last for years.[2]

Syphilis can profoundly negatively impact pregnancy outcomes. The earlier the foetus is exposed, the more severe the foetal infection, birth defects, and tissue damage, and the greater the risk of pre-term birth or stillbirth.[9]

Genital Herpes

Herpes simplex virus (HSV) causes genital herpes. Although some women with genital herpes present with painful genital ulcers, others lack symptoms entirely. Initial infection causes flu-like symptoms, including malaise, muscle tenderness, fever, nausea, and diarrhoea. Vulvar burning and itching usually precedes the development of fluid-filled lumps which burst to become painful genital ulcers. The ulcers usually heal 10-22 days later. The ulcers may recur as frequently as six times per year.

Pregnant women with ulcers should deliver via caesarean section, because herpes can cause death and other extremely serious problems in newborns.[2,5]

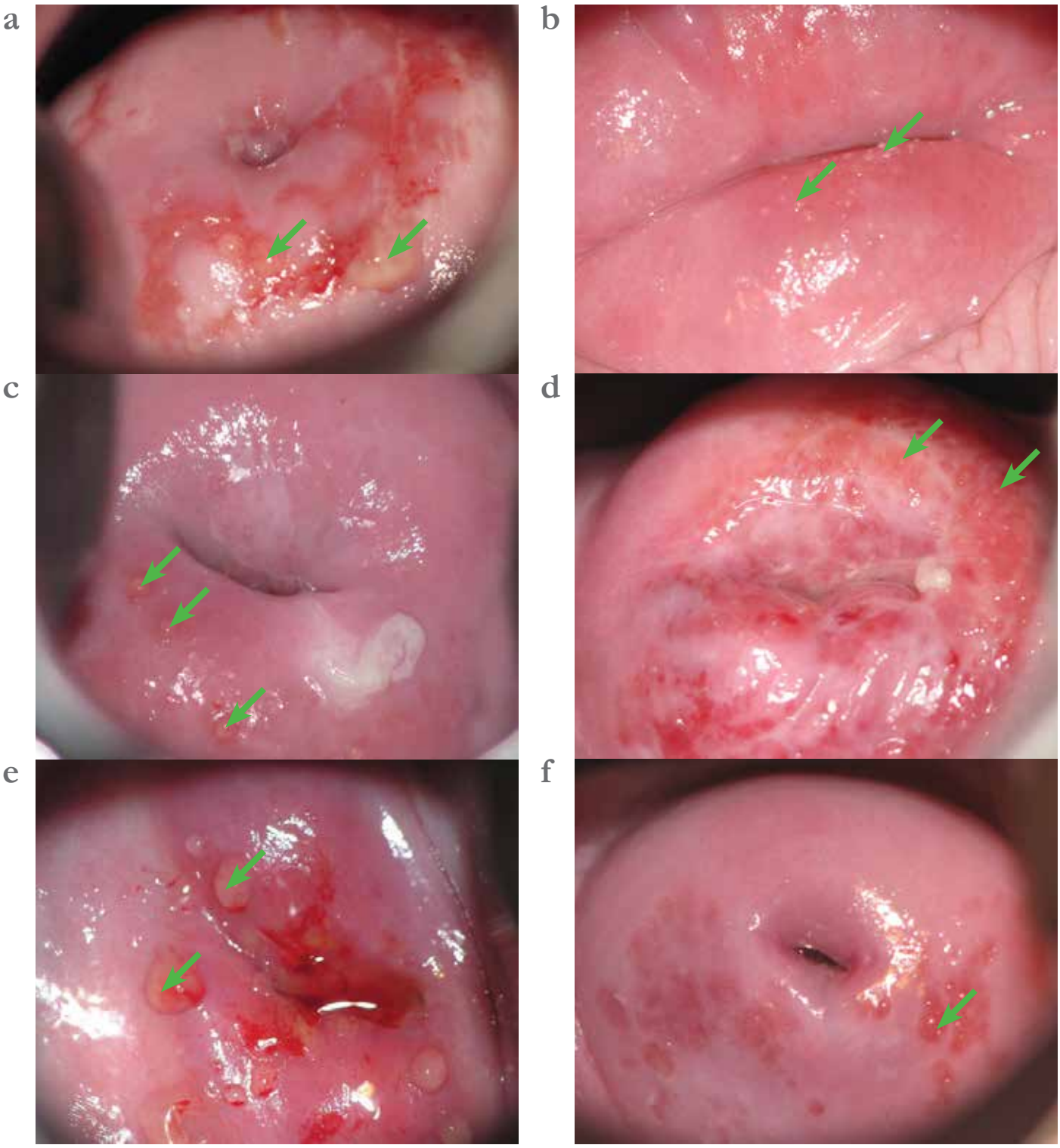

Figure 10.17a-e Cervical herpes. Note the presence of fluid-filled lumps.
Figure 10.17f Cervical herpes and trichomoniasis.

Chancroid

The bacteria Haemophilus ducreyi causes chancroid. Chancroid manifests as a painful, hard, well-defined ulcer on the anogenital region. Usually just one ulcer exists, although multiple ulcers may occur. Painful inflammation and swelling of the inguinal nodes may occur.[2]

Granuloma Inguinale

Granuloma inguinale, a bacterial disease, occurs in some areas of India, Brazil, the Caribbean, the South Pacific, Australia, China, and Africa. Symptoms include a foul-smelling discharge and red, well-defined ulcers which heal extremely slowly. Although the ulcers generally occur on the vulva and inguinal region, ulcers can occur on the cervix, uterus, mouth, and ovaries. Rarely, granuloma inguinale ulcers on the cervix may mimic cervical cancer.[2,9]

Lymphogranuloma Venereum

Some aggressive types of chlamydia can cause lymphogranuloma venereum (LGV). LGV has a primary, secondary, and tertiary stage.

Recommended Treatment for Bacteria-Mediated Genital Ulcers

Syphilis:

- Benzathine penicillin G 2.4 million units IM single dose.

Chancroid:

- Azithromycin 1 g orally single dose under supervision, **or**
- Ceftriaxone 250 mg IM single dose, **or**
- Erythromycin 500 mg orally 3 times daily for 7 days, **or**
- Ciprofloxacin 500 mg orally BID for 3 days.

STOP — Do not give ciprofloxacin to pregnant or lactating women and women younger than 17 years old.

Granuloma Inguinale:

- Doxycycline 100 mg orally BID for at least 21 days and until ulcers have healed.
- Alternatively for pregnant women, erythromycin base 500 mg orally 4 times a day for at least 21 days and until ulcers have healed.

Lymphogranuloma Venereum:

- Doxycycline 100 mg orally BID for 21 days.
- Alternatively for pregnant women, erythromycin base 500 mg orally 4 times a day for 21 days.

STOP — Do not give doxycycline to pregnant women.

Figure 10.18 Poster on treatment for bacteria-mediated genital ulcers.[2,3,9]

Primary stage LGV manifests as papules or shallow ulcers on the vulva. Secondary stage LGV, also called inguinal syndrome, manifests as painful inflammation and swelling of the inguinal nodes. Fever and headaches may occur. Tertiary stage LGV, also called anogenital syndrome, manifests as:

- proctocolitis (inflammation of the rectum and colon);
- rectal stricture (narrowing of the rectum making defecation difficult or impossible);
- rectovaginal fistula (abnormal passageway between the rectum and vagina);
- hardening or thickening of the skin on the external genitalia.[2]

Genital Ulcers and HIV Infection

Genital ulcers increase the risk of HIV infection and transmission.[13,21,24,27] Conversely, HIV infection increases the risk of herpes and may increase the risk of syphilis.[6,29]

HIV-positive clients with syphilis present with aggressive secondary syphilis more often.[13] In regions with high HIV prevalence, herpes may cause a higher percentage of genital ulcers. HIV-positive individuals with herpes may present with multiple persistent ulcers that heal slowly.[27] HIV-positive individuals with chancroid get multiple ulcers more frequently and can get fever or chills.[27]

Inform all clients with genital ulcers of the increased risk of HIV infection. Follow all HIV-positive clients with genital ulcers closely to ensure adequate treatment.[9]

Treating Genital Ulcers

Treat clients with genital ulcers or sores for chancroid and syphilis. Treat for lymphogranuloma venereum, HSV, or granuloma inguinale according to local recommendations.

The WHO recommends treating all women with genital ulcers for herpes if the prevalence of HSV in clients with genital ulcers exceeds 30%.[27]

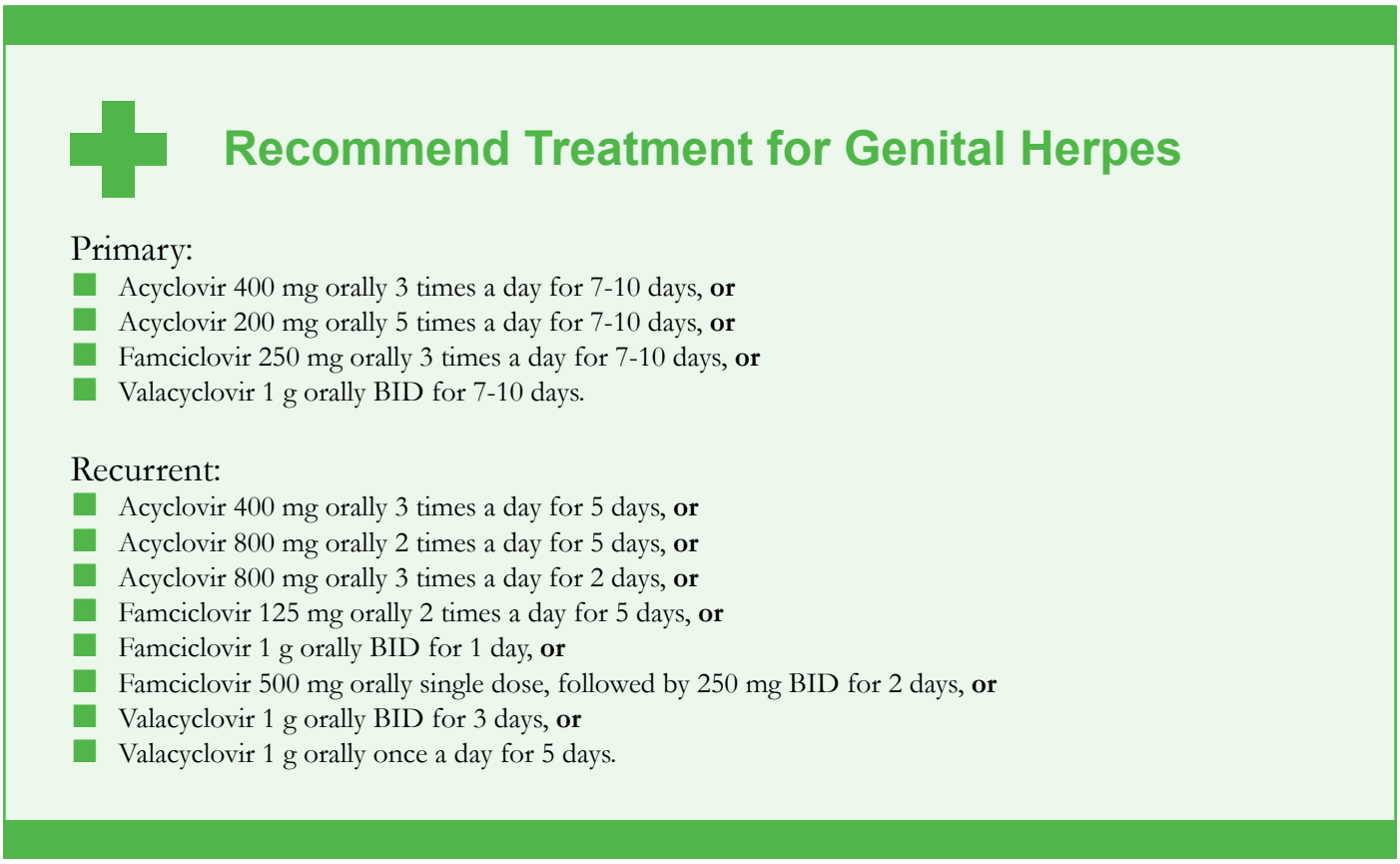

Figure 10.19 Poster on treatment for genital herpes.[3,9]

If no genital ulcers are present, but vesicles (fluid-filled lumps) are, treat for syphilis if the client hasn't been treated for syphilis recently or has a positive syphilis test. In addition, treat for HSV if locally recommended.

Notably, the treatment of genital ulcers in HIV-infected individuals may differ from the recommended treatments.

Provide and promote condoms at the time of diagnosis. Offer HIV testing and counselling if possible.

As with cervicitis, the sexual partners of women with genital ulcers should be referred for treatment.[27]

Although antibiotics can cure syphilis and chancroid, no cure for HSV exists. At best, treatment for HSV eases or prevents symptoms. Treatment depends on whether the client has a new (primary) infection or a recurrent infection.

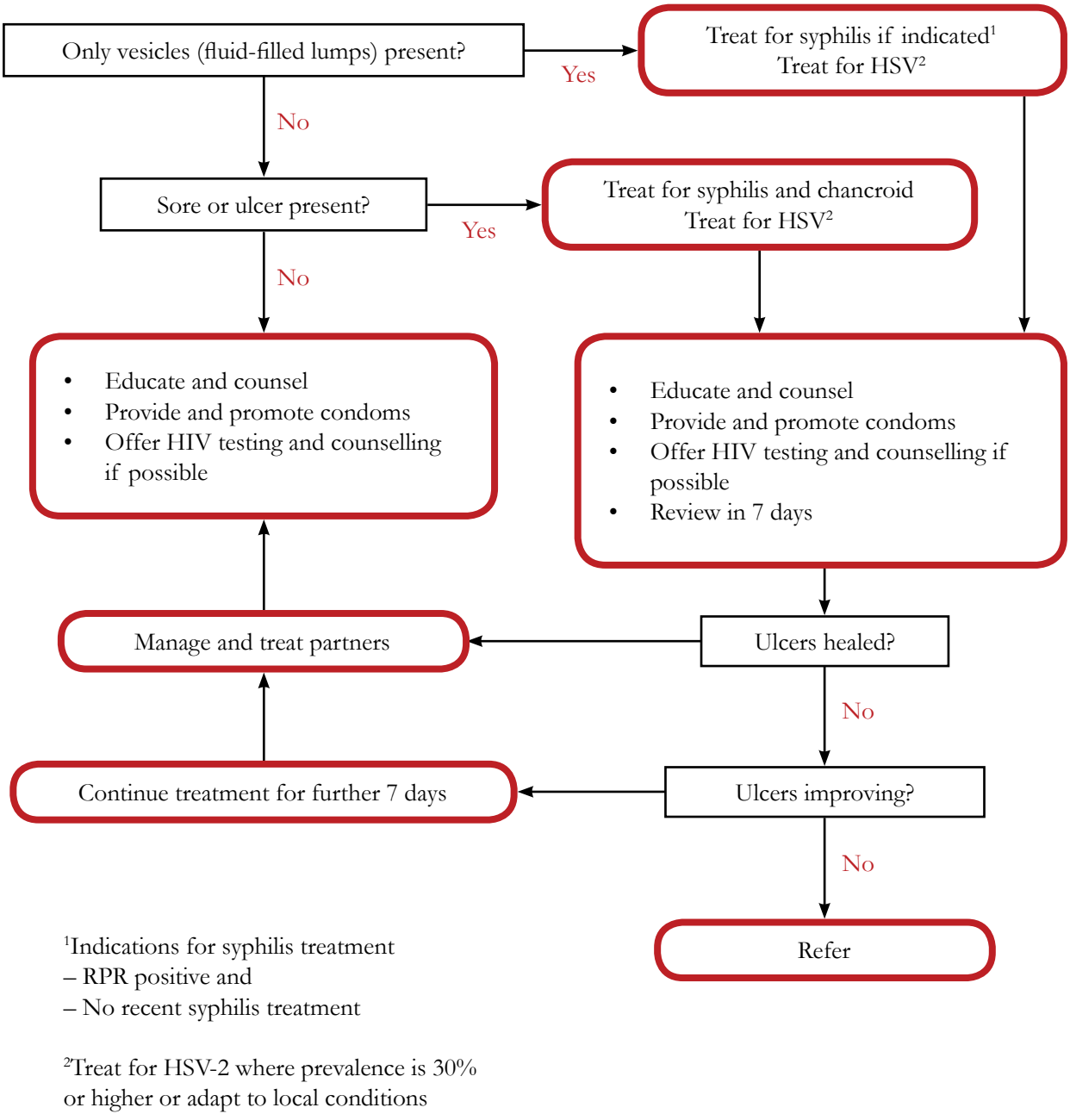

Figure 10.20 Flowchart on the management of genital ulcers. Revise as necessary for your setting. Adapted from the WHO Training Modules for the Syndromic Management of STIs.[27]

10.8 Genital Warts

Human papillomavirus (HPV) infection causes 90% of **genital warts** (condyloma acuminata).[28] Genital warts usually occur on the vulva and anogenital region, but can also occur inside the vagina, rectum, and on the cervix.[2] Although small at first, genital warts can combine to form large cauliflower-like masses. Genital warts may grow more rapidly during pregnancy and require special management.[9]

Worldwide, approximately one in every 600 people has genital warts.[20] This high prevalence places genital warts among the most common sexually transmitted diseases. Genital warts often coexist with other STIs or cervical lesions.[9]

Genital warts may undergo spontaneous regression without treatment. Approximately 30% of warts regress within four months of infection.[28] Genital warts do not cause cancer and usually do not require treatment. However, the stigma associated with genital warts may lead women to seek treatment. Treatment involves covering the wart in acid or medication every week until the wart no longer exists. Cryotherapy or excision can also remove genital warts.[9] Unfortunately, treatment does not cure the HPV infection and genital warts often recur after treatment.[1,28] Genital warts recur more frequently in HIV-positive clients.[8]

Genital Warts

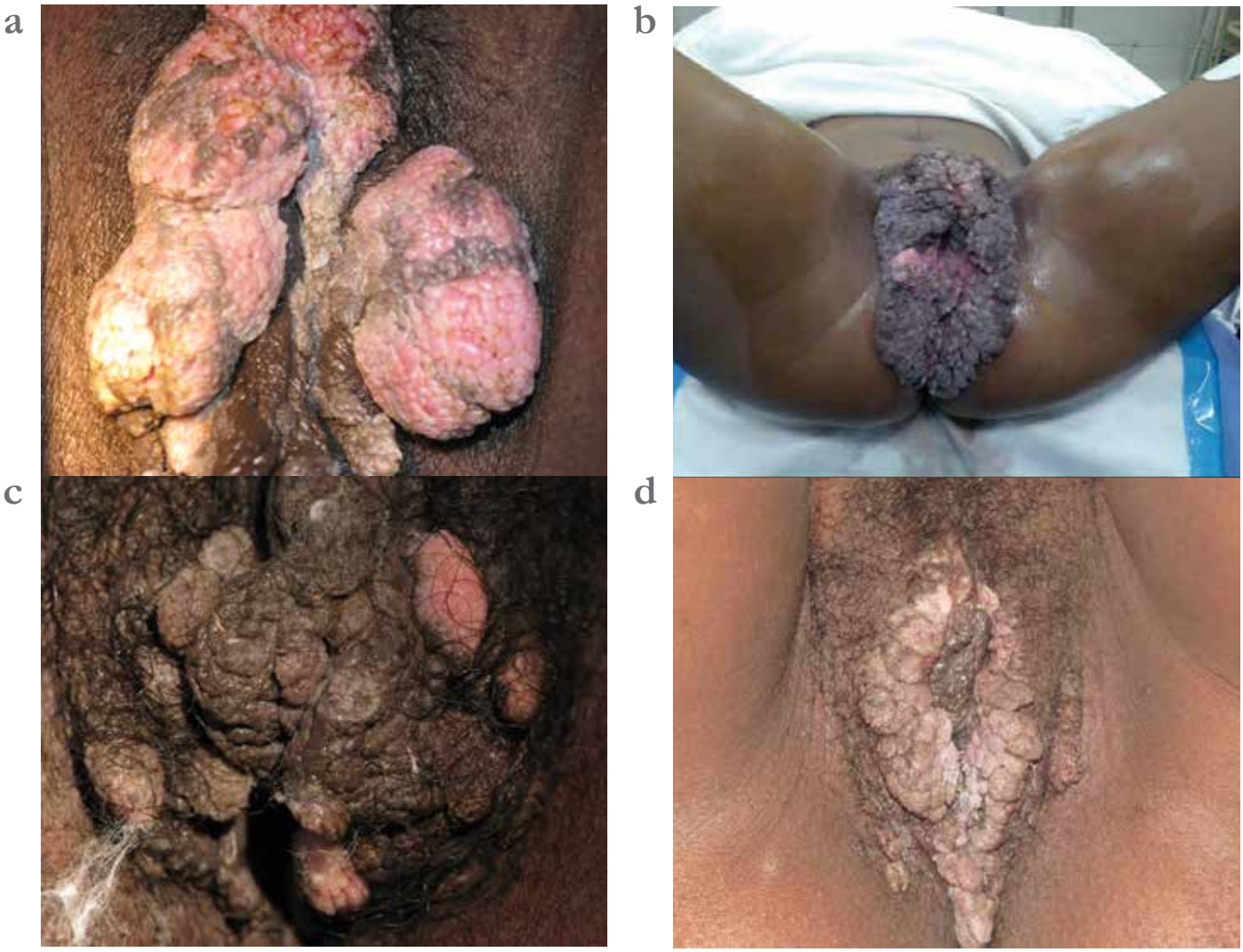

Figure 10.21a-d Genital warts on the vulva.

Genital Warts and Vulvar Precancer or Cancer

a

b

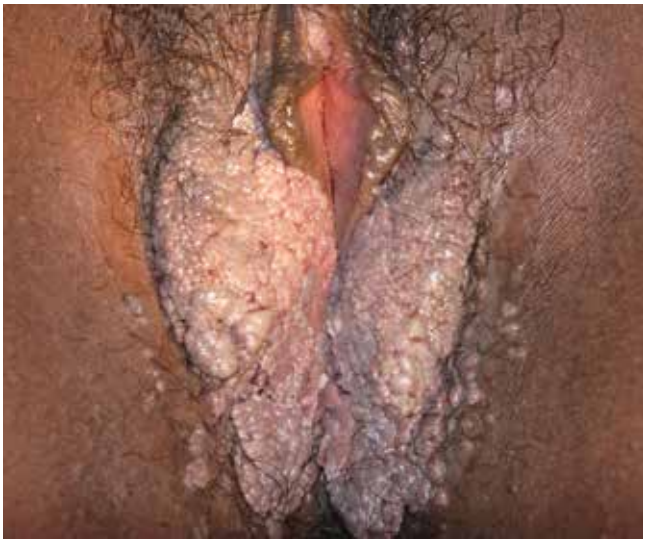

Figure 10.22a Genital warts and VIN (vulvar intraepithelial neoplasia), a precancerous lesion.
Figure 10.22b Genital warts and microinvasive vulvar cancer.

Chapter 10 Summary

- The syndromic approach means treating the symptoms of sexually transmitted infections based on the diseases most likely responsible for the symptom.
- Before prescribing a medication, check with your local pharmacy to ensure the medication is available.
- Know the cost, contraindications for, and side effects of every medication you prescribe.
- Treat all clients with abnormal vaginal discharge for vaginitis.
- Treat clients with abnormal vaginal discharge for cervicitis only if the client reports certain risk factors. Alternatively, treat cervicitis according to your country's guidelines.
- Treat clients with genital ulcers for syphilis, chancroid, and possibly genital herpes, granuloma inguinale, and lymphogranuloma venereum depending on your country's guidelines.
- Genital ulcers can increase the risk of HIV acquisition and transmission.
- Refer the sexual partners of women with cervicitis and genital ulcers for treatment.
- Genital warts do not require treatment but can be treated to prevent stigma.

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