UniFOA

Mestrado Profissional em Ensino em Ciências da Saúde e do Meio Ambiente - MECSMA

VIRTUAL CLASSROOM

WITH A FOCUS ON HPV-ASSOCIATED CERVICAL CANCER

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TEACHING RECOMMENDATIONS FOR IMPLEMENTING THE VIRTUAL CLASSROOM WITH A FOCUS ON HPV-ASSOCIATED CERVICAL CANCER

a) Structure and guidelines for the VIRTUAL CLASSROOM WITH A FOCUS ON HPV-ASSOCIATED CERVICAL CANCER PROVIDED with the educational product (EP).
b) In-person classes using a data projector.
c) Remote classes conducted in a virtual classroom.
d) Flipped classroom approach, where the teacher shares the EP via a link and provides step-by-step guidance, encouraging students to engage in more autonomous activities.
e) Reinforcement of theoretical classes, where the teacher also shares the EP via a link, assigning activities about the female reproductive system with a focus on cervical cancer.
f) Dynamic workshops, in which different groups analyze specific phases of the virtual classroom, developing interactive learning tools, such as student-led educational games based on the 20 questions included in the EP.
g) Workshops at academic conferences, with virtual presentations showing the different phases of the EP, correlated with three-dimensional teaching models that may be developed by the students themselves.

- The content is designed to be flexible, covering topics from the normal female reproductive system to HPV-related pathologies. Educators can choose to use specific sections as needed to align with their curriculum.
- According to Rizzatti et al. (2020, p. 2), “teachers have the autonomy to refuse (choose not to use), revise (adapt, modify, translate), remix (combine multiple materials), redistribute (share), and retain (keep their own copy) the various groups of students”.

VIRTUAL CLASSROOM WITH A FOCUS ON HPV-ASSOCIATED CERVICAL CANCER

Nice to meet you, I’m Hela!
We are going to learn about
HPV-associated cervical cancer
in this virtual classroom.

FEMALE REPRODUCTIVE SYSTEM

Door A gives access to the female reproductive system.
Let’s review this topic, shall we?

Click on door
A

HPV-ASSOCIATED CERVICAL CANCER

Click on door **B**

Door B gives access to HPV-associated cervical cancer. Let's learn about it!

These are the phases of the path about the female reproductive system.

1 - Vulva	4 - Útero
2 - Vagina	5 - Ovário
3- Colo do Útero	6 - Trompa

6

5

4

3

2

1

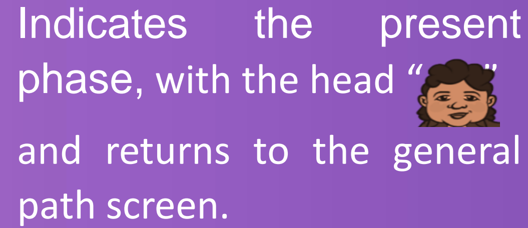
Understand the layout used in all phases before you get started.
Click here

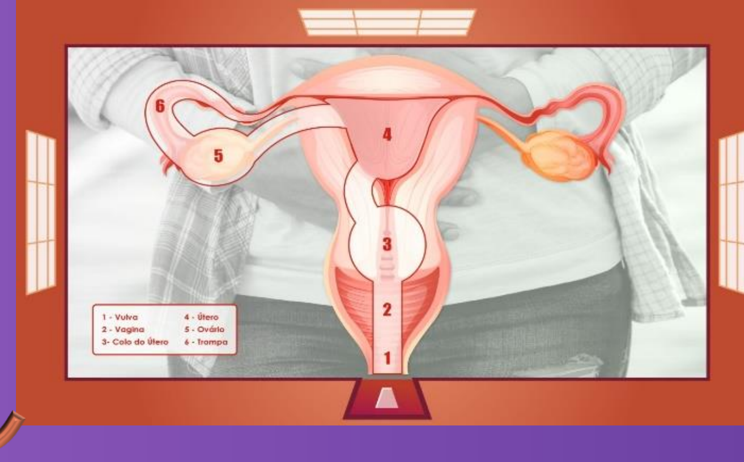
1- Vulva	4- Útero
2- Vagina	5- Ovário
3- Colo do útero	6- Trompa

The name of each selected phase is shown in the top right corner, next to the "path" button, which takes you back to the general path screen at any time.

Here are the action icons that direct your studies, as explained in the captions.

Phase name

Indicates the present phase, with the head "" and returns to the general path screen.



Presents the main video of the phase - **Video**

Shows the image gallery of the stage - **Image**

Provides access to the theoretical explanation of the content - **Theoretical Basis**

Shows the clinical case presented in the text - **Clinical Case**

Gives access to the audio - **Podcast**

Continue or **return** - directs you to the next of previous phase

Return

Continue

Tube

6

Ovary

5

Uterus

4

Cervix

3

Vagina

2

Vulva

1

1- Vulva	4- Útero
2- Vagina	5- Ovário
3- Colo do útero	6- Trompa

Let's start the path of the female reproductive system.

Tube

6

Uterus

4

Ovary

5

Cervix

3

Vagina

2

Vulva

1

Select the phase of female reproductive system.

1- Vulva	4- Útero
2- Vagina	5- Ovário
3- Colo do útero	6- Trompa

Female reproductive system

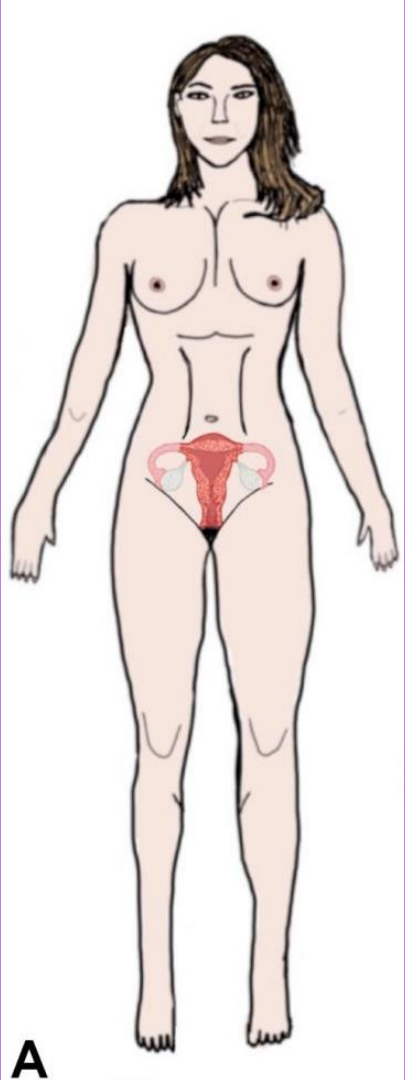
The female reproductive system is divided into external and internal.

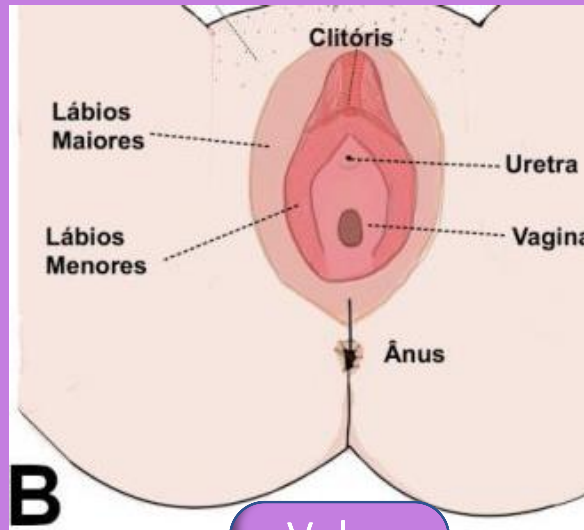
It is located in the lower part of the abdominal cavity and is protected by the pelvic bones.

The external genitalia is called vulva.

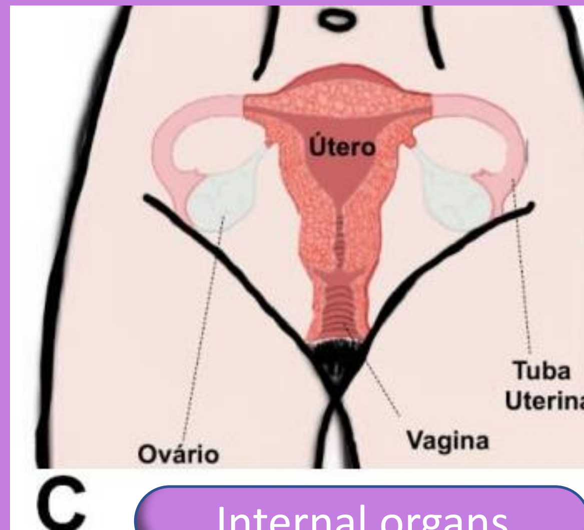
Return Continue

Female reproductive system

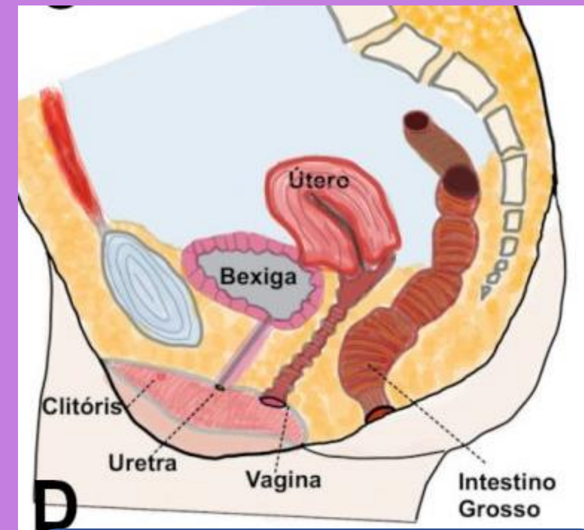




Vulva



Internal organs



Lateral view of internal organs

Source: Adapted from histologiatextoeatlssufpr.com.br.

Tube

6

Uterus

4

Ovary

5

Cervix

3

Click here to access the general path.

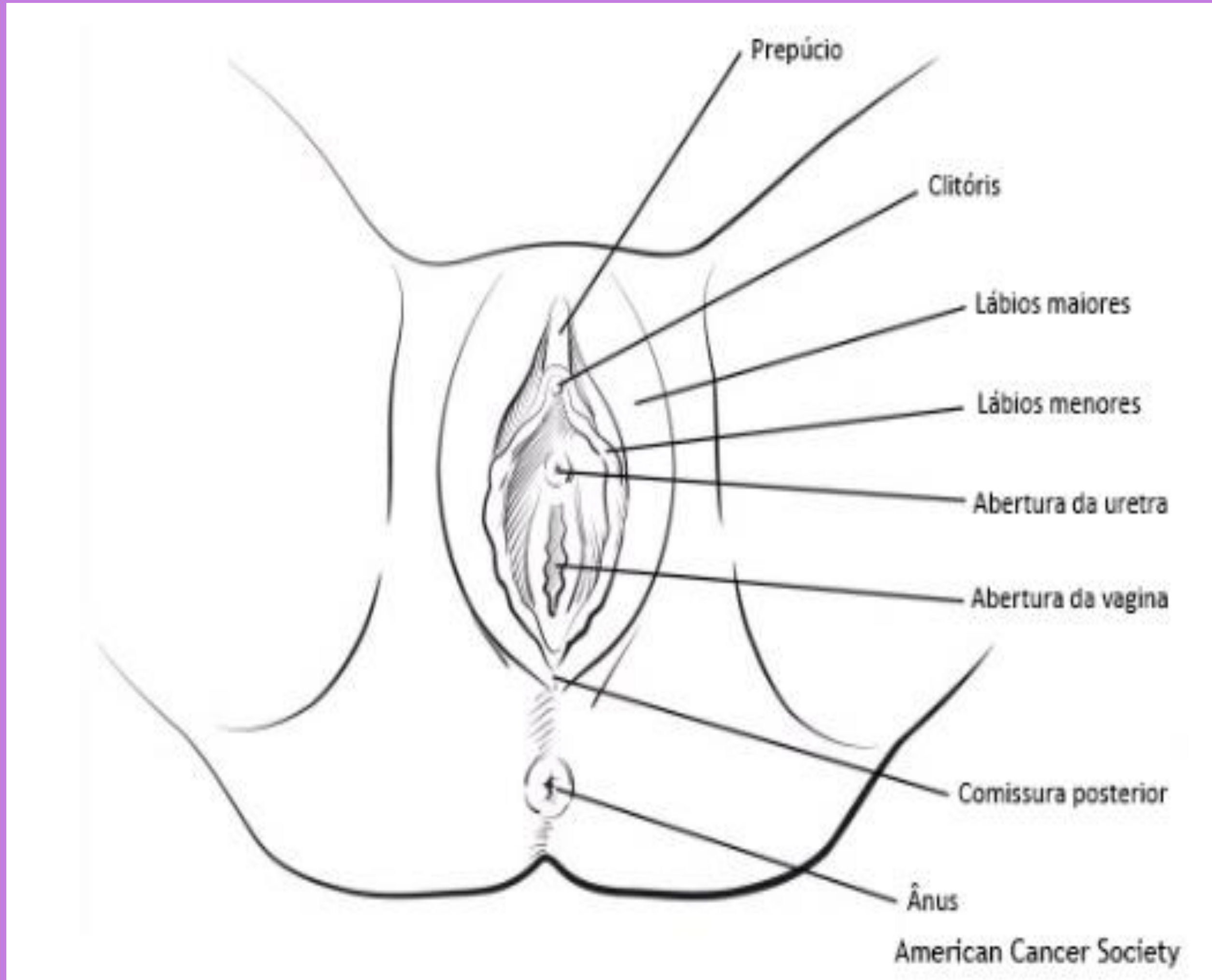
Vagina

2

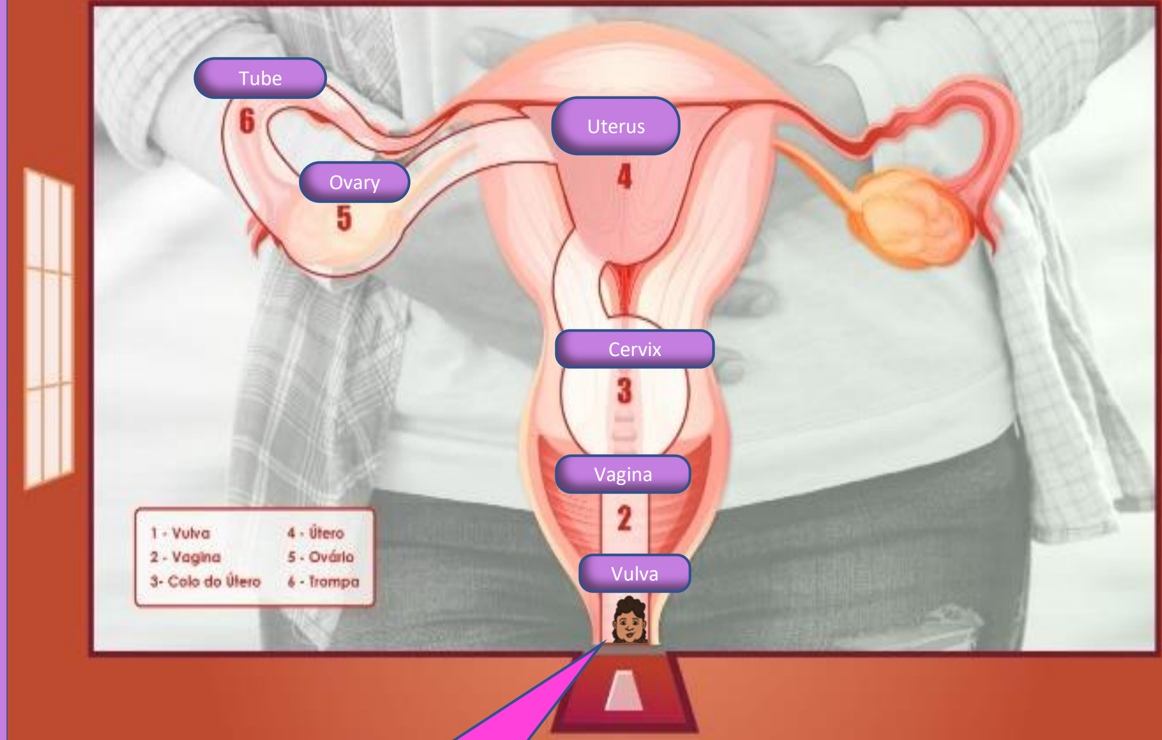
1 - Vulva
2 - Vagina
3- Colo do Útero
4 - Útero
5 - Ovário
6 - Trompa

Vulva

Vulva



Source: American Cancer Society.



Click here to access the general path.

Return

Continue

External genitalia

The external genitalia includes:

a) the mons pubis,

b) the labia majora,

c) the labia minora, and

d) the clitoris

Return

Continue

Functions of the external genitalia

It has three main functions:

a) fertilization through sexual intercourse, allowing the entry of sperm,

b) protection of the internal reproductive system against infectious organisms, and

c) lubrication.

Return

Continue

External genitalia

MONS PUBIS

PUBIC HAIR

Clitoris

Urethra

Vagina

Perineum

Anus

Labia majora

Labia minora

Bartholin's gland

Source: adapted from Programa-ato.

Vulva

It constitutes the external and visible region of the female genitals, with structures that cover the superficial and deep perineal compartments.

Return

Continue

Vulva

The figure below shows some of the different types of normal vulvas.

The Vulva Galery
@the.vulva.gallery

The Vulva Galery
@the.vulva.gallery

Source: The Vulva Gallery, 2022.

Mons pubis

The mons pubis is a rounded mass of fatty tissue, covered by skin and pubic hair, that lies over the pubic bones and extends to the junction with the abdominal wall (BEREK & NOVAK, 2021).

Return Continue

Mons pubis

Labia majora

The labia majora are two folds of fibroadipose skin that extend from the mons pubis downward and backward to merge in the midline to form the posterior furcula in front of the anus (BEREK & NOVAK, 2021). They are laterally covered with sparse hair and rich in sebaceous, apocrine, and eccrine glands (Berek & E Novak, 2021).

Return

Continue

Labia minora

The labia minora are two folds of skin made up of connective tissue. They have less adipose tissue than the labia majora. They merge anteriorly to form the prepuce of the clitoris, and posteriorly at the vaginal opening. This merge forms the posterior commissure, called perineum (American Cancer Society).

Return

Continue

Clitoris

The name clitoris is derived from the Greek word *Kleitoris*, which means “small hill”. It was first described in 1998 by Australian urologist Helen O’Connell, who analyzed the relationship between this organ and adjacent structures such as the vagina, urethra, and vestibular glands. The clitoris glans is covered by the foreskin.

Return Continue

Female urethral bulb

It is visible below the clitoris and in front of the vaginal opening, in the vaginal vestibule. The female urethra is an extension of the bladder that passes through the pelvic floor and opens through the urethral bulb.

Return

Continue

Female urethra

Óstio do ureter
Trígono da bexiga
Colo da bexiga
Músculo detrusor da bexiga
Músculo esfíncter interno da uretra
Músculo levantador do ânus e
Extensão fibromuscular
Uretra
Músculo esfíncter externo da uretra
Membrana do períneo
Bulbo do vestíbulo
Músculo bulboesponjoso e fáscia superficial do períneo (de Gallaudet)
Ligamento redondo do útero (parte terminal)
Tela subcutânea do períneo (de Colles) (camada membranácea)
Lábio maior do pudendo
Lábio menor do pudendo
Lacunas e óstios das glândulas uretrais
Óstios dos ductos parauretrais (de Skene)

Source: Netter (2016).

Vulvar histology

Histologically, the vulva presents specific characteristics. The labia majora consist of skin folds containing a considerable amount of adipose tissue and a small amount of smooth muscle, with an external surface covered with thick, wavy hair. Internally, it has a similar structure to the labia minora, with many sebaceous and sweat glands outside and inside. The clitoris is histologically and embryonically similar to the penis. The larger vestibular glands are known as Bartholin's glands. They produce mucus and are located on the sides of the vestibule. Smaller glands, called Skene's glands, can be found around the urethra and clitoris.

Return

Continue

Internal genitalia

It comprises the internal sexual organs:

a) vagina,

b) uterus,

c) ovaries, and

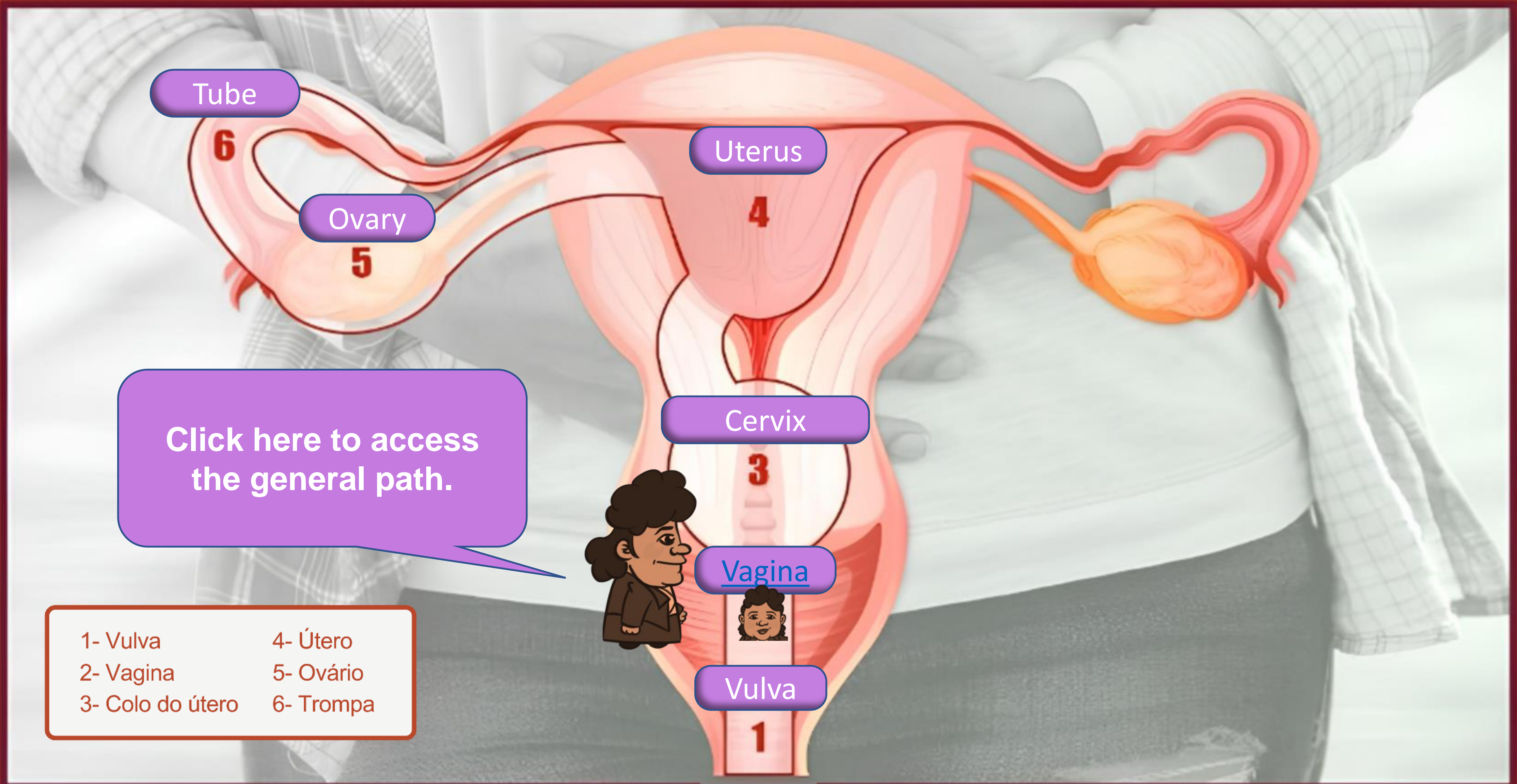
d) uterine tubes.

Return

Continue

Internal genitalia

Tube
Uterus
Ovary
Vagina



Tube
6
Uterus
4
Ovary
5
Click here to access the general path.
Cervix
3
Vagina
Vulva
1
1- Vulva
2- Vagina
3- Colo do útero
4- Útero
5- Ovário
6- Trompa

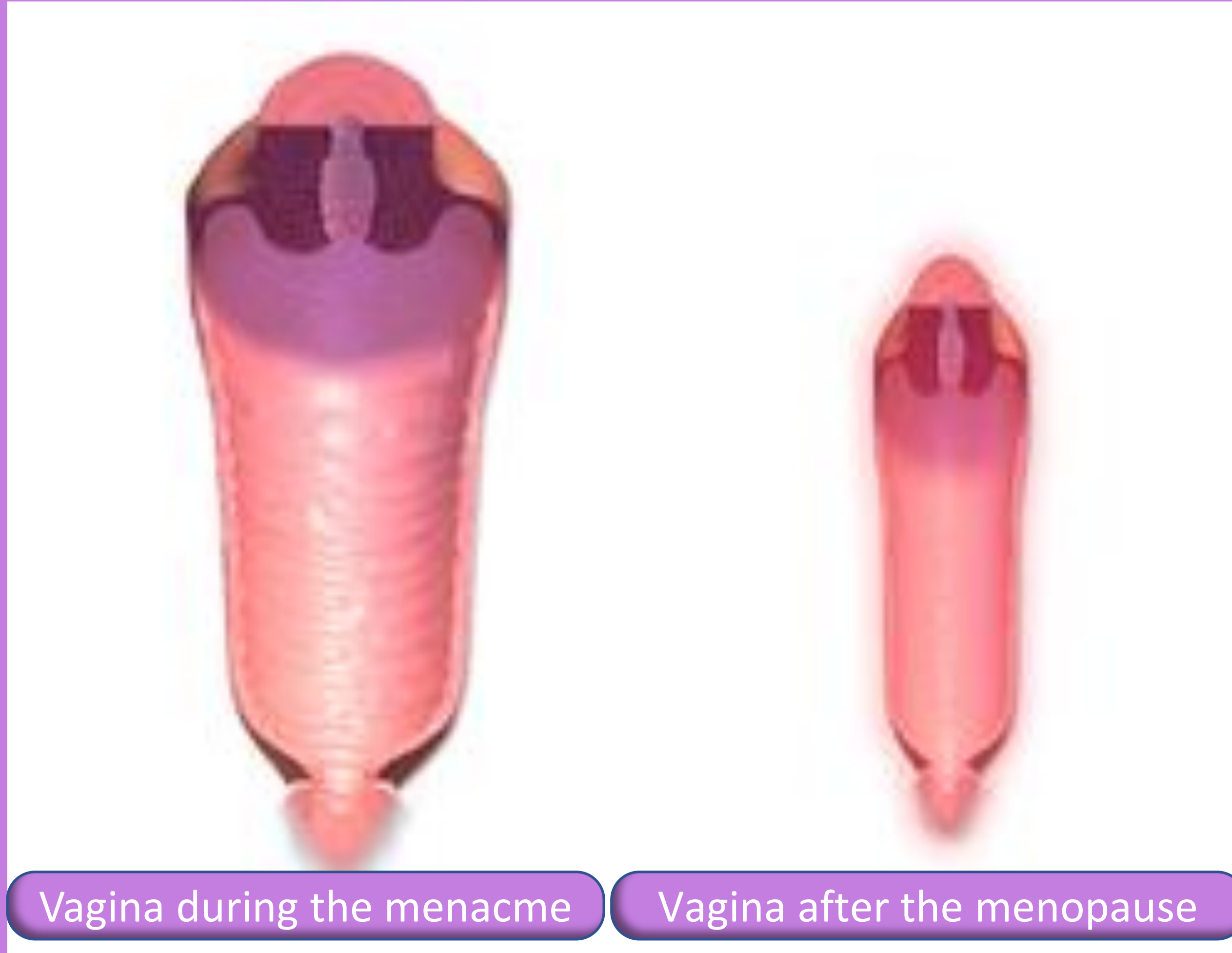
Vagina

The vagina is an internal organ of the female reproductive system. It extends from the opening in the vulva to the cervix, measuring 10 to 15 centimeters in length. This organ has great dilation capacity and a structure similar to a tubular canal that is commonly collapsed. The vagina has its own microbiota, which includes *Lactobacillus* sp., *Candida albicans*, and *Mycoplasma hominids*.

Return

Continue

Vagina

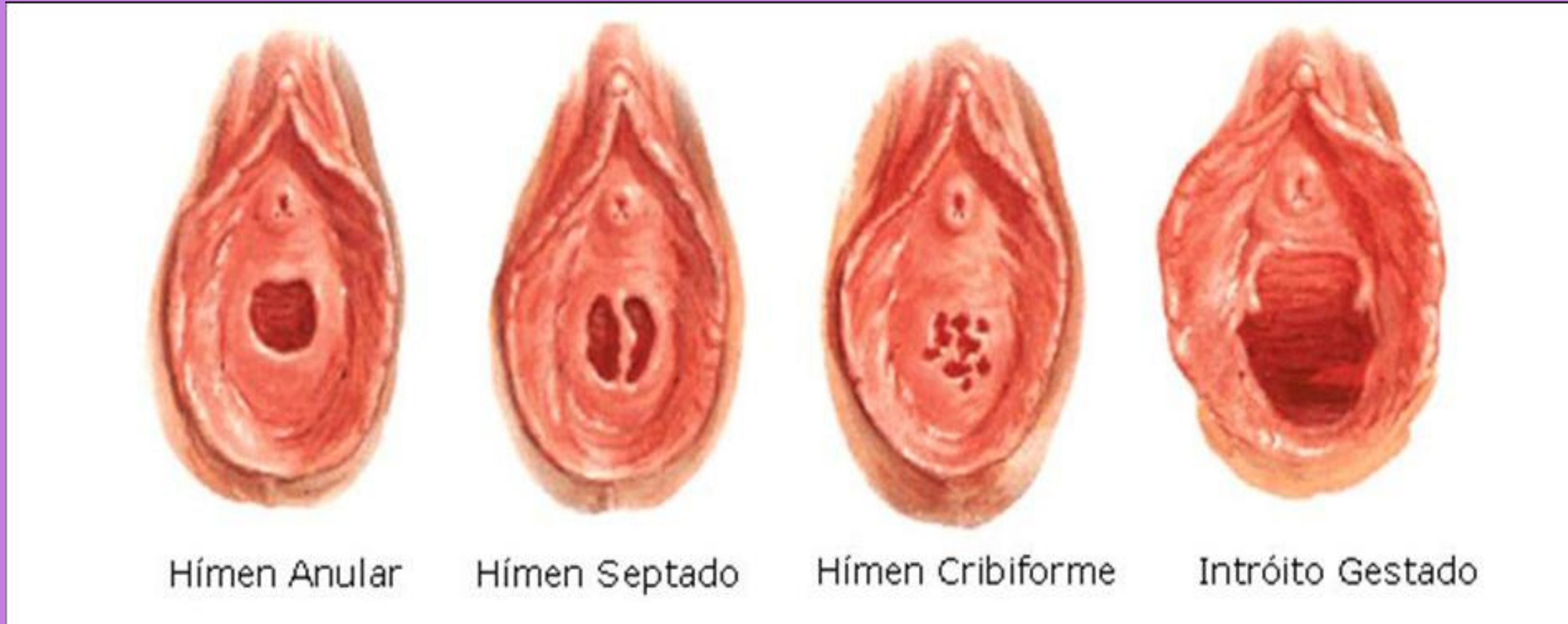


Vaginal ostium

It is the transversely flattened portion of the vagina, which is externalized into the vulva. Virgin women have a delicate, vascularized membrane partially obstructing this ostium, the hymen. Between the vaginal opening and the anus there is a space called the perineum.

Return Continue

Hymen variations



Source: Netter (2016).

Vaginal anatomy

The vagina extends from the uterus to the vulva, functioning as an internal genital organ that connects to the external environment. Its functions include sexual intercourse, release of menstrual flow and, together with the cervix, the formation of the normal birth canal. It is positioned behind the bladder and the urethra and in front of the rectum. At the superior part, it connects to the cervix, forming the vaginal fornix (anterior, posterior, and lateral). In the lower part, the vaginal opening is located in the vaginal vestibule, just behind the urethral orifice, and may be partially covered by the hymen.

Return

Continue

Vaginal histology

Histologically, the vagina is formed by three layers: the mucosa, the muscularis, and the adventitia. The mucosa is composed of stratified squamous epithelium containing cells with a reduced amount of keratin. The presence of estrogen induces this epithelium to produce and store glycogen, which is released when the cells desquamate and is excreted along with these cells into the vaginal lumen. Then, the vaginal bacteria use this glycogen to produce lactic acid, helping maintain the vaginal pH at acidic levels to protect the vagina against pathogenic microorganisms.

Return

Continue

Vaginal histology

Plano
Transversal
Vagina

Lúmen Vaginal

MUCOSA:
Tecido epitélio
escamoso
estratificado
não queratinizado

Lamina Própria

CAMADA MUSCULAR:
Camada
circular
externa

CAMADA MUSCULAR:
Camada
longitudinal
interna

Adventícia

Source: Adapted from Farmacologia - Galeria de Biologia Forum (biology-forums.com).

Vaginal embryology

Embryologically, the vagina develops in the third month of embryological life, originating from the primitive mesoderm and endoderm. The embryonic urinary system can induce this development process.

Return

Continue

Embryology of the female reproductive system

Membrana peritoneal
Ligamento largo
Seio urogenital primitivo
Ductos paramesonéfricos fundidos
Tubérculo sinusal
A
Canal genital
Bulbo sinovaginal
B
Cisto de Gartner
C
Himen
Ovário
Ureter
Bexiga
Útero
Tubas uterinas
Vagina
Cisto de Gartner (remanescente do ducto mesonéfrico)

Source: BEREK & NOVAK, 2020.

Tube

6

Ovary

5

Uterus

4

Click here to access the general path.

Cervix

Vagina

2

Vulva

1

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Cervix

It is a cylindrical organ composed of few smooth muscle fibers and predominantly formed by dense connective tissue. The cervix extends from the internal cervical os, which connects to the body of the uterus, to the external cervical os. The approximate distance between the internal and external openings varies from 2.5 to 3 cm.

Return

Continue

Cervix

Internal os

External os

Cervix

Source: Adapted from BEREK & NOVAK, 2020.

Cervical histology

Histologically, the cervix consists of the endocervix and the ectocervix. The endocervix consists of a simple columnar epithelium composed of glandular cells that produce mucus.

The ectocervix, which is connected to the vagina, consists of stratified squamous cell epithelium.

Return

Continue

Cervical histology

Útero
Canal endocervical
Junção escamo-colunar
Ectocérvice
Células colunares altas
Vagina
Células epiteliais escamosas

Source: Atlas de Citopatologia Ginecológica.

Squamocolumnar junction (SCJ)

The squamocolumnar junction (SCJ) is a transitional area between the stratified epithelium and the simple columnar epithelium.

Return

Continue

Squamocolumnar junction (SCJ)

Original SCJ

Transformation zone

Active SCJ

Columnar epithelium

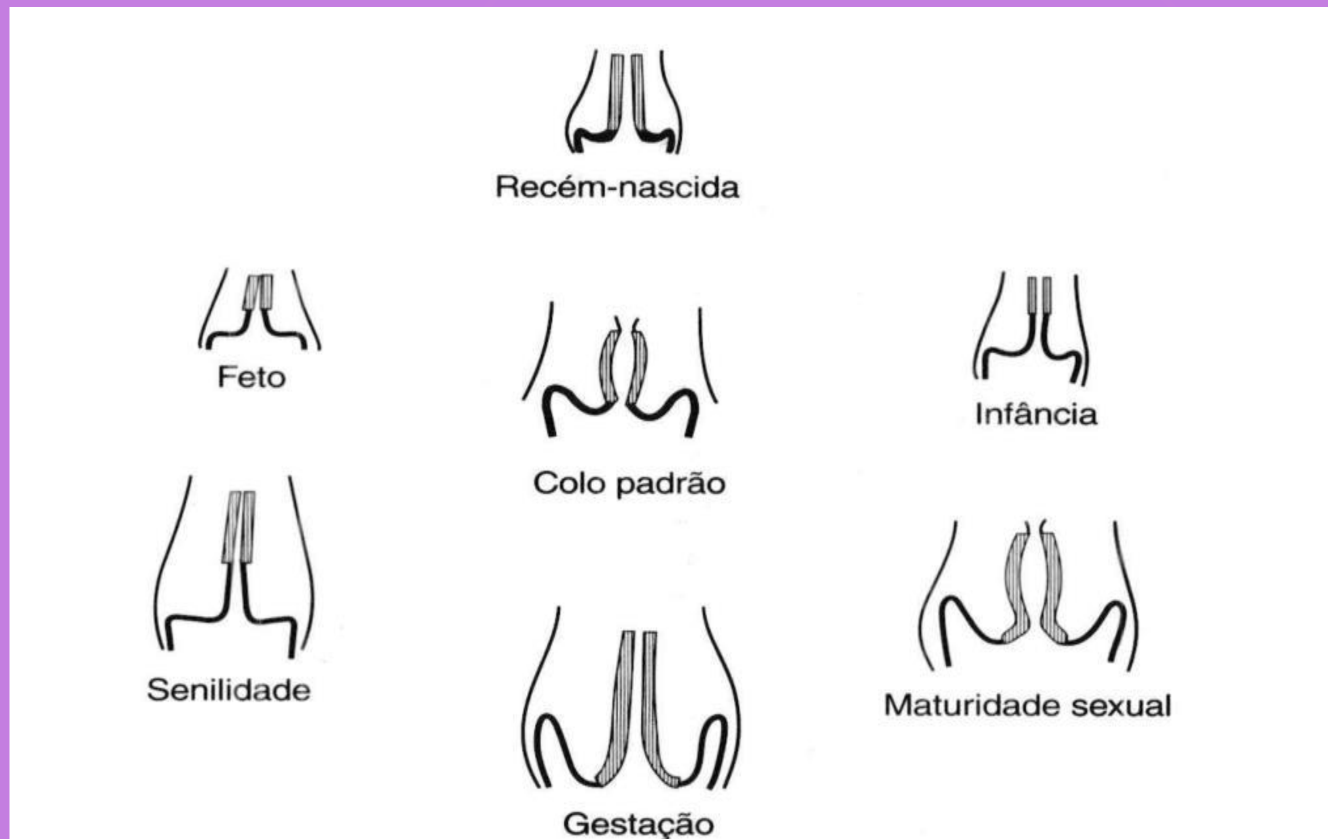
External os

Opening of the endocervical crypt (glandular os)

Source: Adapted from BEREK & NOVAK, 2020.

JEC variations by age group

The SCJ is a transition area between the stratified epithelium and the simple columnar epithelium, changing dynamically with hormonal stimuli in the different phases of female life (BEREK & NOVAK, 2020).



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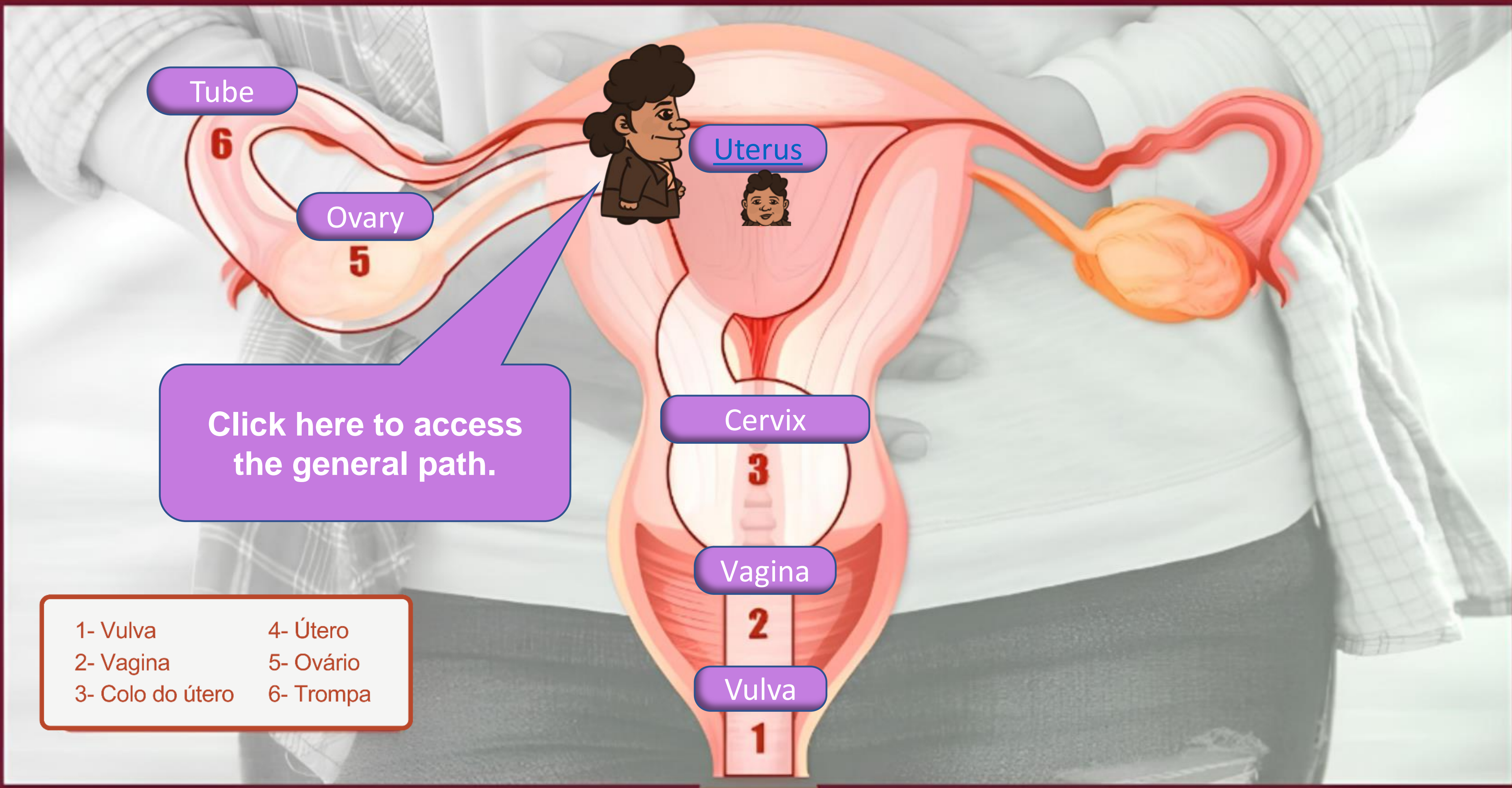
Tube
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6- Trompa

Uterus

It is a single, hollow, medial, and symmetrical organ located in the posterior pelvic cavity. Its lower continuity is through the vagina. In front of the uterus we find the bladder, and behind, the rectum.

Return

Continue

Anatomy of the uterus and ligaments

Escavação vesicouterina
Útero através do peritônio que o reveste
Ureter (retroperitoneal)
Ligamento suspensor do ovário contém vasos ováricos
Ovário direito
Ligamento útero-ovárico (próprio do ovário)
Tuba uterina direita (de Falópio)
Prega vesical transversa
Vasos epigástricos inferiores
Prega umbilical mediall e ligamento (parte oclusa da artéria umbilical)
Ligamento inguinal
Vasos ilíacos externos
Ligamento umbilical mediano (remanescente do úraco)
Ligamento redondo do útero
Bexiga urinária
Sínfise púbica
Prepúcio do clitóris
Ramo do clitóris (*cortado*)
Lábios menores do pudendo
Músculo bulboesponjoso
Uretra
Tuba uterina (*cortada*) e ovário esquerdos
Prega retouterina ("uterossacral") direita
Colo sigmoide
Tuba uterina (de Falópio) (*cortada*)
Artéria ilíaca interna
Ligamento útero-ovárico (próprio do ovário) (*cortado*)
Artéria uterina
Ligamento redondo do útero (*cortado*)
Escavação retouterina (de Douglas)
Parte posterior do fórnice da vagina
Ureter e artéria vaginal esquerdos
Colo do útero
Parte anterior do fórnice da vagina
Reto
Óstios uretéricos
Trígono da bexiga urinária
Vagina

C. Machado M.D.

Ligamentos Pélvicos
Prancha 357
Útero, Vagina e Estruturas de Sustentação

Uterine divisions

The uterus is composed of three parts: the body, the isthmus, and the cervix (AMERICAN CANCER SOCIETY, 2016). At the top and sides of the uterine body are the uterine horns, from which the uterine tubes (fallopian tubes) extend (CUNNINGHAM; GILSTRAP, 2019).

Return

Continue

Uterine divisions

Fundus

Body

Isthmus

Cervix

Source: Adapted from BEREK & NOVAK, 2020.

Uterine histology

The uterus is histologically composed of three layers: the mucosa, the muscularis, and the serosa.

- The mucosa (endometrium) is formed by an epithelium and a lamina propria, with cells organized in a simple columnar epithelium that includes ciliated and secretory cells. The endometrium is divided into the basal and the functional layers. The basal layer is the deepest and remains unchanged throughout the menstrual cycle, while the functional layer undergoes significant changes at each cycle.

Return

Continue

Uterine histology (continued)

- The muscularis (myometrium) is composed of layers of smooth muscle interspersed with connective tissue. These muscle fibers undergo hyperplasia and hypertrophy during pregnancy.
- The serosa (perimetrium) covers most of the uterus, while the anterior part of the uterus has an adventitia comprised of connective tissue (JUNQUEIRA, CARNEIRO, 2017).

Return Continue

Uterine histology

Endométrio

Miométrio

Perimétrio

Source: Sistema Reprodutor Feminino – Histologia de Órgãos e Sistemas (histologiatextoeatlasufpr.com.br)

Uterine anomalies

Source: IPGO

Septate uterus: uterus whose cavity is divided by a septum that may extend to the cervix.

Bicornuate uterus: the result of a partial fusion of the two Müllerian ducts.

Didelphys uterus: the result of a non-fusion of the Müllerian ducts.

Unicornuate uterus: uterus whose only one half developed.

Return

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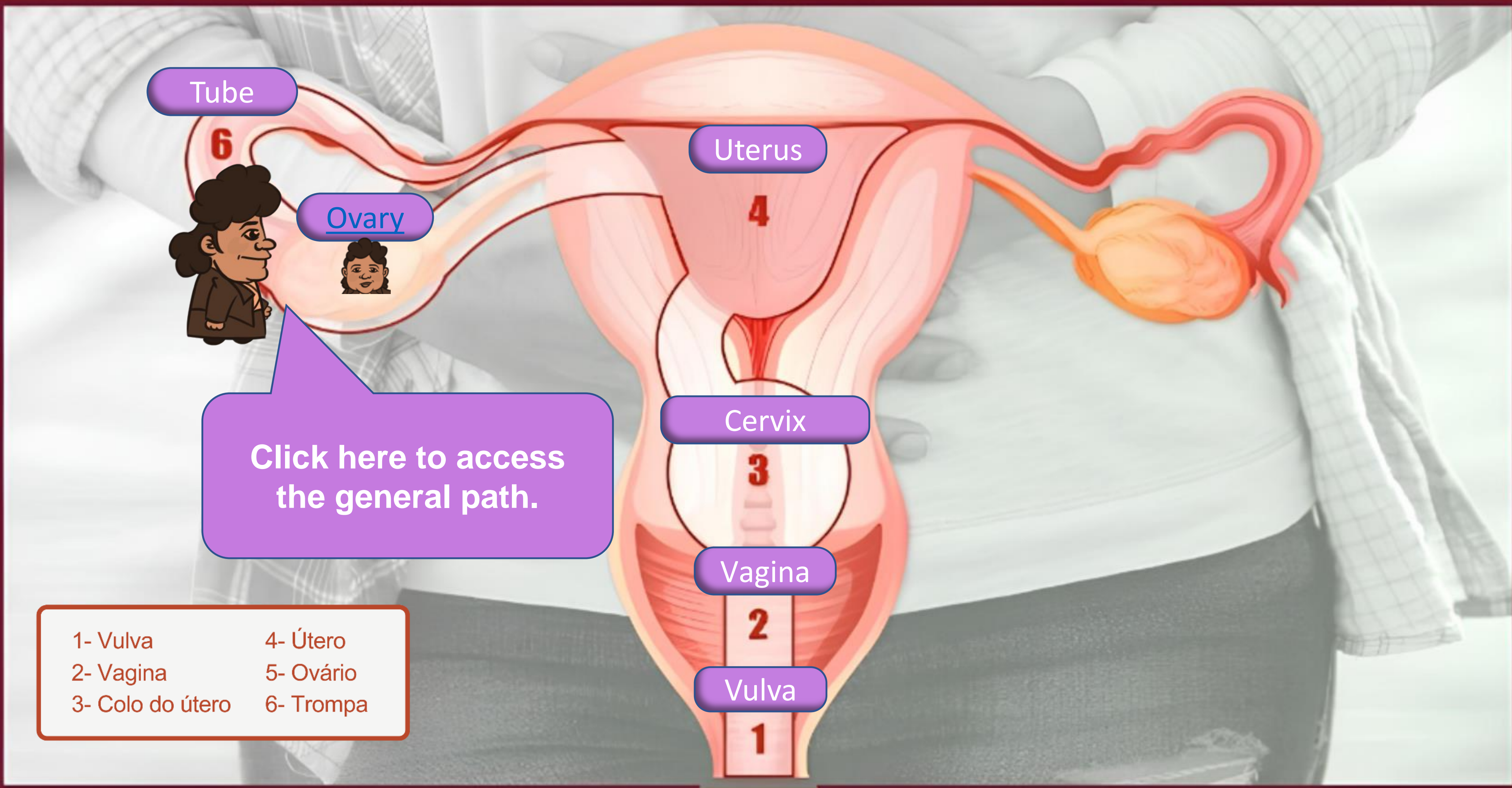

Tube
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Ovary
Uterus
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Cervix
3
Vagina
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Ovaries

The ovaries are ovoid and measure approximately three centimeters in length and one and a half centimeters in width. They are the female gonads, located in the pelvic wall and connected to the uterus bilaterally by infundibulopelvic ligaments and medially by the utero-ovarian ligament. The lower part of the hilar region is connected to the broad ligament through the mesentery (BEREK & NOVAK, 2020, p. 73).

Return

Continue

Ovarian anatomy

Ovário

Rede vasculonervosa do Ovário

Córtex do Ovário

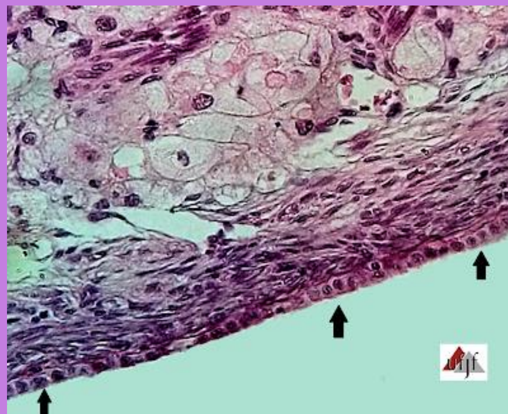
Ovócitos

Source: The ovaries (adapted from Santos and Taoufik)

Ovarian histology

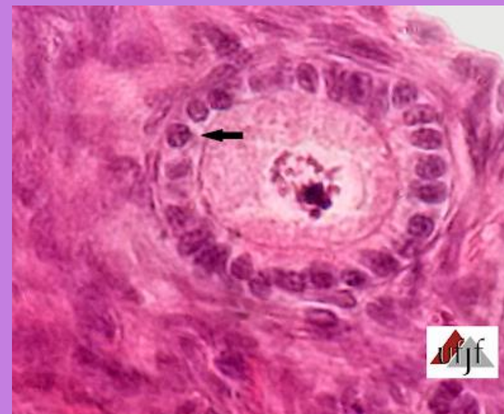
- The ovaries are covered by a single layer of germinal epithelium.
- In young women, this layer is formed by cuboidal cells, which become flatter over time.
- The connective tissue present in the ovaries is known as stroma, where it is possible to find spindle cells and an intercellular substance.

Outer lining of the ovary - greater magnification.



Atlas Histológico Online®, slide 38.

Developing ovarian follicle - greater magnification.
Arrow - simple cuboidal lining epithelium.



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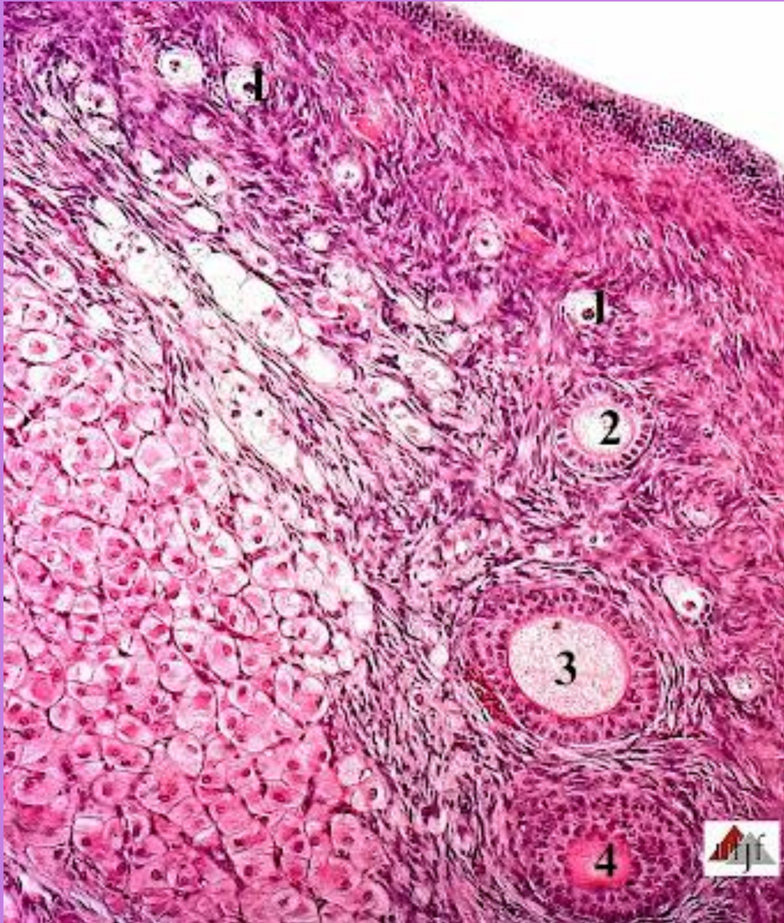
Ovarian histology



Source: Atlas Histológico Online®, slide 38.

1- Primordial or immature ovarian follicle - simple squamous lining epithelium.

2- Growing or developing ovarian follicle - simple cuboidal lining epithelium.

3- Developing ovarian follicle - stratified cuboidal lining epithelium.

4- Corpus luteum.

Return

Continue

Ovarian physiology

Physiologically, the ovaries are responsible for the synthesis and secretion of sexual steroid hormones, including estrogens, androgens and progesterone, being affected by the gonadotropins produced by the pituitary gland: the follicle stimulating hormone (FSH) and the luteinizing hormone (LH).

Some of the main products secreted by these organs are the estradiol and progesterone, in addition to estrone, androstenedione, and 17a-hydroprogesterone.

In addition to their hormonal functions, they also play a crucial role in gametogenesis and steroidogenesis.

Return

Continue

Ovarian physiology: gametogenesis

Female gametogenesis, also known as oogenesis, begins in the seventh week of pregnancy of a female embryo. During this period, oogonia are formed from germ cells through mitosis, which results in cell division. The oogonia then begin meiosis, which stops at prophase I at birth, becoming primary oocytes (oocytes I). These oocytes remain surrounded by the follicle, awaiting the beginning of female reproductive life, which occurs with menarche and ends with menopause.

Return

Continue

Ovarian physiology: gametogenesis

OVOGÊNESE

Célula germinativa

2n

MITOSE

MITOSE

Ovogônias

2n

2n

MITOSE

MITOSE

MITOSE

MITOSE

Ovogônias

2n

2n

2n

2n

CRESCIMENTO SEM DIVISÃO CELULAR

Ovócitos I

2n

MEIOSE I

Ovócitos II

n

Glóbulo polar

n

MEIOSE II

Óvulo

n

n

Glóbulo polar

n

n

Glóbulos polares

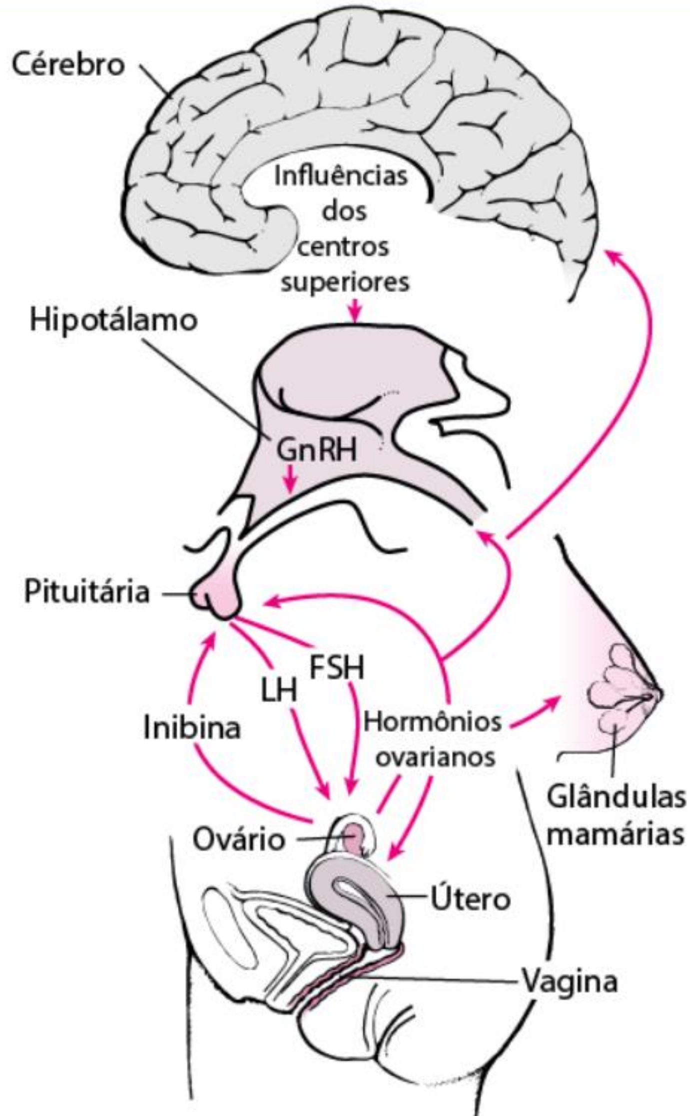
PERÍODO GERMINRTIVO

PERÍODO DE CRESCIMENTO

PERÍODO DE MATURAÇÃO

Source: The author, 2023.

Ovaries and the menstrual cycle



Source: Adapted from Manual MSD, 2022.

The menstrual cycle is regulated by the hypothalamic-pituitary axis. The ovaries act as the gonads responsible for producing the hormones that start this cycle, and the uterus is the organ that reflects each woman's specific rhythm every month from menarche onwards.

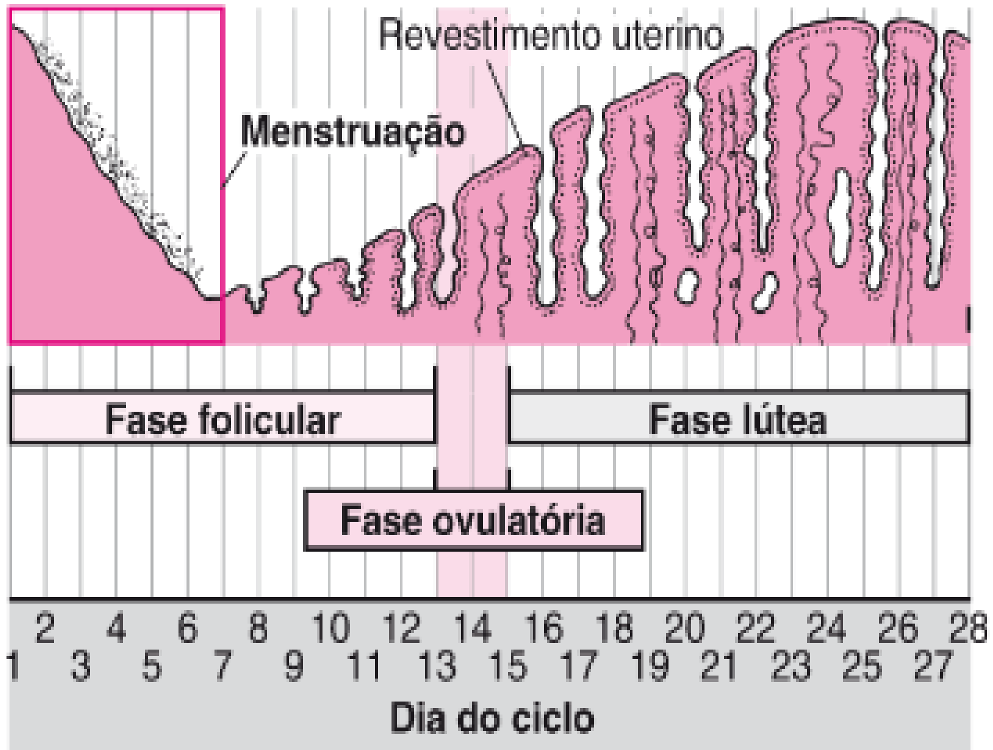
The menstrual cycle is regulated by a complex interaction between the luteinizing, follicle-stimulating, and female sex hormones, as well as estrogen and progesterone.

FSH = follicle stimulating hormone
GnRH = gonadotropin-releasing hormone
LH = luteinizing hormone

Return

Continue

The menstrual cycle



Source: Adapted from Manual MSD, 2022.

The menstrual cycle begins with menstrual bleeding (menstruation), which marks the first day of the follicular phase.

The three phases of the menstrual cycle are:

- Follicular phase (before the egg is released).
- Ovulatory phase (when the egg is released).
- Luteal phase (after the egg is released).

1- Vulva
2- Vagina
3- Colo do útero
4- Útero
5- Ovário
6- Trompa

Uterine tubes

The uterine tubes are two muscular funnel-shaped structures measuring about 12 centimeters each. They are divided into three parts: the isthmus (which connects to the uterus), the ampulla, and the infundibulum (where the fimbriae that capture the released egg are located). Fertilization occurs in the middle third of these tubes, and the movement of smooth muscle, together with the ciliated cells of the epithelium present in the tubes, helps transport the fertilized egg (zygote) to the uterine body (SOUZA, 2021).

Return

Division of the uterine tubes

Source: Netter, 2022.

Cervical cancer (CC)

According to Berek and Novak (2020), infection by the human papillomavirus (HPV) causes cytological changes in the SCJ. This pathology was recognized in 1956, being initially called koilocytosis. The importance of this viral infection in the pathophysiology of CC was only confirmed in 1976, being classified by Alexander Meisels as cervical intraepithelial neoplasia (CIN).

In the absence of treatment, cellular changes progress gradually from CIN1 (mild) to CIN3 (severe).

Cervical cancer (CC)

Normal

CIN 1

CIN 2

CIN 3

Source: www.msdmanuals.com

Epidemiology

The National Cancer Institute (INCA, 2023) estimates a CC incidence of approximately 17 thousand (4.7%) new cases per 100 thousand women per year in Brazil for 2023-2025, with an expected mortality of 6,385 per 100 thousand women per year. These estimates show CC as the third type of cancer that kills the most Brazilian women, ranking second in regions with the lowest human development index (HDI).

Return

Continue

Epidemiology

CC is the third most common female cancer according to estimates for 2023 (INCA, 2022).

Distribuição proporcional dos dez tipos de câncer mais incidentes estimados para 2023 por sexo, exceto pele não melanoma*

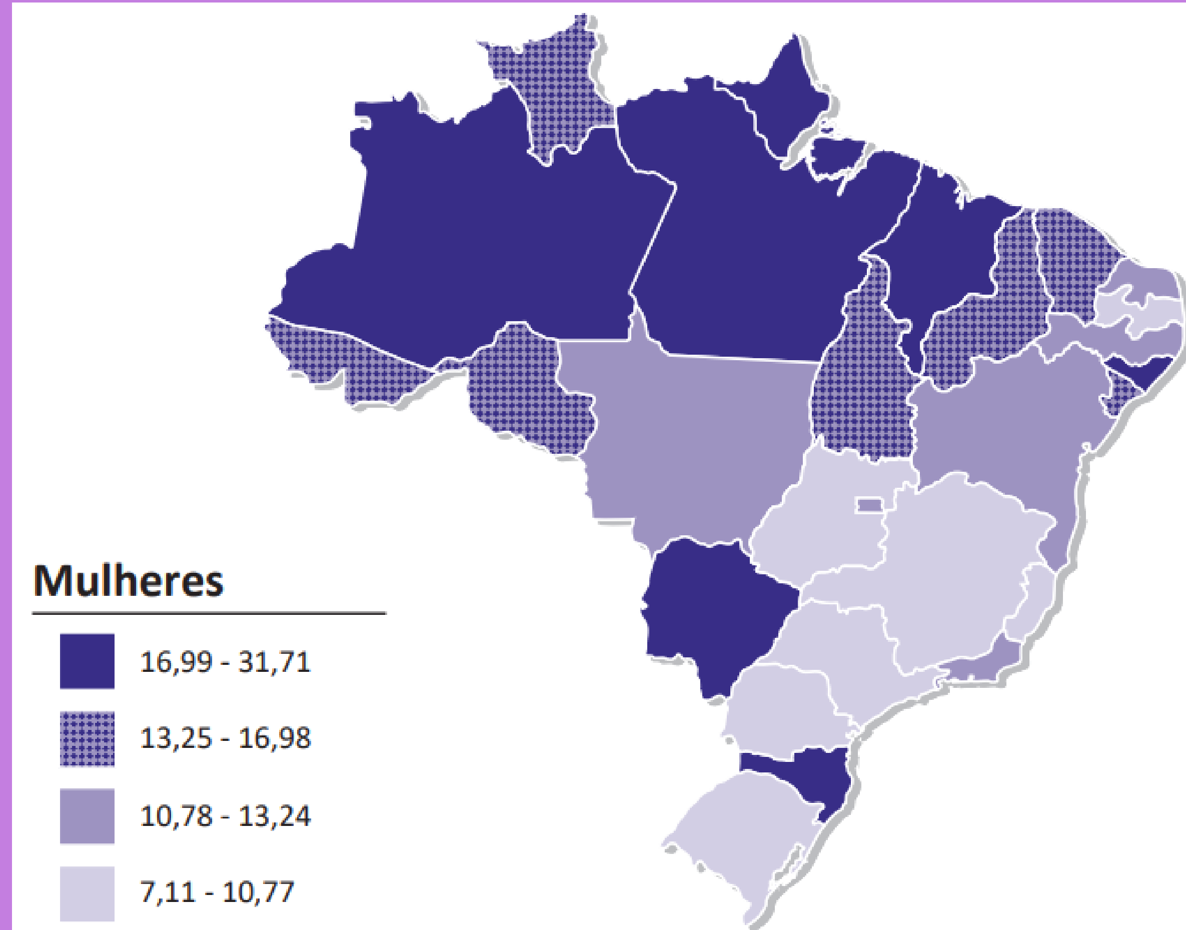
Localização Primária	Casos	%	Homens	Mulheres	Localização Primária	Casos	%
Próstata	71.730	30,0%			Mama feminina	73.610	30,1%
Cólon e reto	21.970	9,2%			Cólon e reto	23.660	9,7%
Traqueia, brônquio e pulmão	18.020	7,5%			Colo do útero	17.010	7,0%
Estômago	13.340	5,6%			Traqueia, brônquio e pulmão	14.540	6,0%
Cavidade oral	10.900	4,6%			Glândula tireoide	14.160	5,8%
Esôfago	8.200	3,4%			Estômago	8.140	3,3%
Bexiga	7.870	3,3%			Corpo do útero	7.840	3,2%
Laringe	6.570	2,7%			Ovário	7.310	3,0%
Linfoma não Hodgkin	6.420	2,7%			Pâncreas	5.690	2,3%
Fígado	6.390	2,7%			Linfoma não Hodgkin	5.620	2,3%

*Números arredondados para múltiplos de 10.

Source: INCA, 2022.

Epidemiology

Spatial representation of adjusted incidence rates per 100,000 women, estimated for 2023 by Brazilian states.



Source: INCA, 2022.

Return

Continue

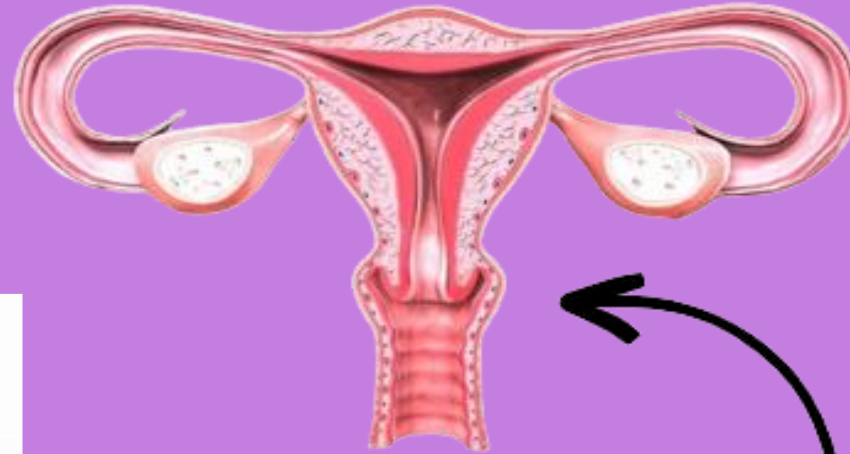
Etiology

Human papillomavirus (HPV) is the etiological agent of CC. The types with the greatest oncogenic potential are HPV-16 (53%) and HPV-18 (15%), which correspond to approximately 70% of cases. The types described in smaller proportions are: HPV-31 (6%), HPV-33 (3%), HPV-45 (9%). HPV-52 and HPV-58 can also cause the disease (INCA, 2021).

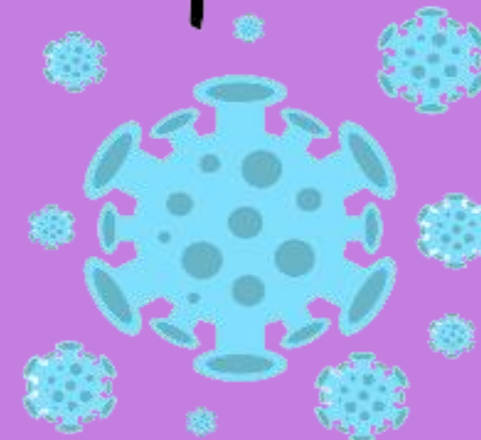
Return

Continue

Etiology



Source: MANA, Medical.



HPV

Source: The author, 2023.

Prevention

In the Brazilian Unified Health System (SUS), CC is primarily prevented with vaccination, available free of charge to girls and women aged 9 to 26 and boys aged 9 to 14. Additionally, immunosuppressed men and women and individuals with cancer between the ages of 9 and 45 can also receive the vaccine.

Return

Continue

Prevention

The Technical Note 41/2024 of the National Immunization Program (PNI, 2024) recommends a single dose of the vaccine to girls and boys aged 9 to 14, and three doses to immunocompromised individuals and victims of sexual violence. The vaccine protects against virus types 16 and 18, which are potentially oncogenic, and types 6 and 11, which cause genital warts (PNI, 2024).

Return

Continue

WHO strategy for CC prevention

To accelerate the eradication of CC, the World Health Organization (WHO) has developed a strategy with targets to be achieved by 2030.

90%

das garotas de até 15 anos totalmente vacinadas contra o HPV.[16]

70%

das mulheres devem realizar um teste de alto desempenho aos 35 anos e, novamente, aos 45 anos.[16]

90%

das mulheres que tenham a doença cervica identificada devem receber tratamento.[16]

Source: MSD, 2023.

Prevention with condoms

Considering the relationship between CC and the transmission of persistent HPV infection during sexual intercourse, promoting prevention with the routine use of condoms (male and female), provided free of charge in SUS units, aims to reduce infection between infected and uninfected people (INCA, 2022).

Return

Continue

Prevention

Dia Mundial do Câncer

4 de fevereiro

Desde o pré-carnaval,
USE PRESERVATIVO!

Esta atitude previne contra o HPV e reduz o risco de câncer de colo uterino, vagina, vulva, pênis, ânus, boca e garganta em homens e mulheres.

Source: Brazilian Society of Oncological Surgery.

Secondary prevention

Secondary prevention of CC includes oncotic colpocytology, a test called Pap smear, which screens women between 25 and 64 years with active sexual life.

Return

Continue

Preventive exam

Source: Pap smear collection.

Early detection

CC screening is the first phase of the early detection strategy, which aims to identify the disease in its preclinical phase, that is, through precursor lesions that do not yet present signs or symptoms. The second phase of early detection is early diagnosis, when cancer is detected in the initial phase but already presenting signs and symptoms (WORLD HEALTH ORGANIZATION, 2020).

Return

Continue

Early detection strategies based on disease progression

Início dos sintomas

Células saudáveis ↔ Células anormais ↔ Câncer pré-invasivo → Câncer invasivo → Câncer avançado (metástase) → MORTE

Rastreamento

Diagnóstico precoce

Source: Adapted from World Health Organization, 2020, p. 73.

CC site

The most frequent site of CC is in the SCJ, with 90% of cases occurring in the transformation zone, where the columnar epithelium is replaced by metaplastic squamous epithelium. The columnar epithelium is endocervical, being located within the cervical canal. When this epithelium is externalized for physiological reasons, it modifies into metaplastic squamous epithelium.

Return Continue

CC site

Epitélio escamoso

JEC

Epitélio colunar

Epitélio escamoso original (nativo)

Junção escamocolunar

Epítélio escamoso metaplásico

Epitélio colunar

Orifício cervical externo

Nova junção escamocolunar

Zona de transformação

Source: Colposcopia e tratamento da neoplasia intraepitelial cervical: Manual para principiantes, J.W. Sellers & R. Sankaranarayanan.

CC histological types

There are two main types of CC.

a) Squamous cell carcinoma: attacks the squamous epithelium, represents 80–85% of reported cases.

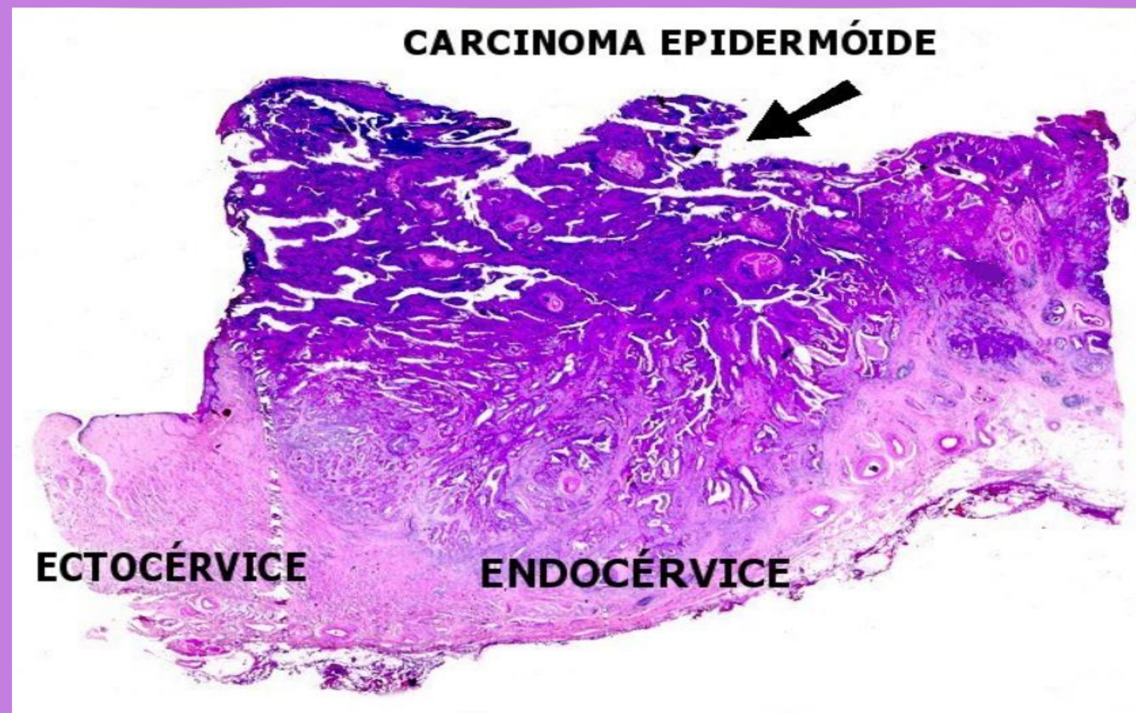
b) Adenocarcinoma: attacks the glandular epithelium, represents 10–25% of reported cases and is considered rarer (WILD; WEIDERPASS; STEWART, 2020). Adenocarcinoma is also rare in the endometrium, with persistent mucorrhea and metrorrhagia as primary symptoms.

Return

Continue

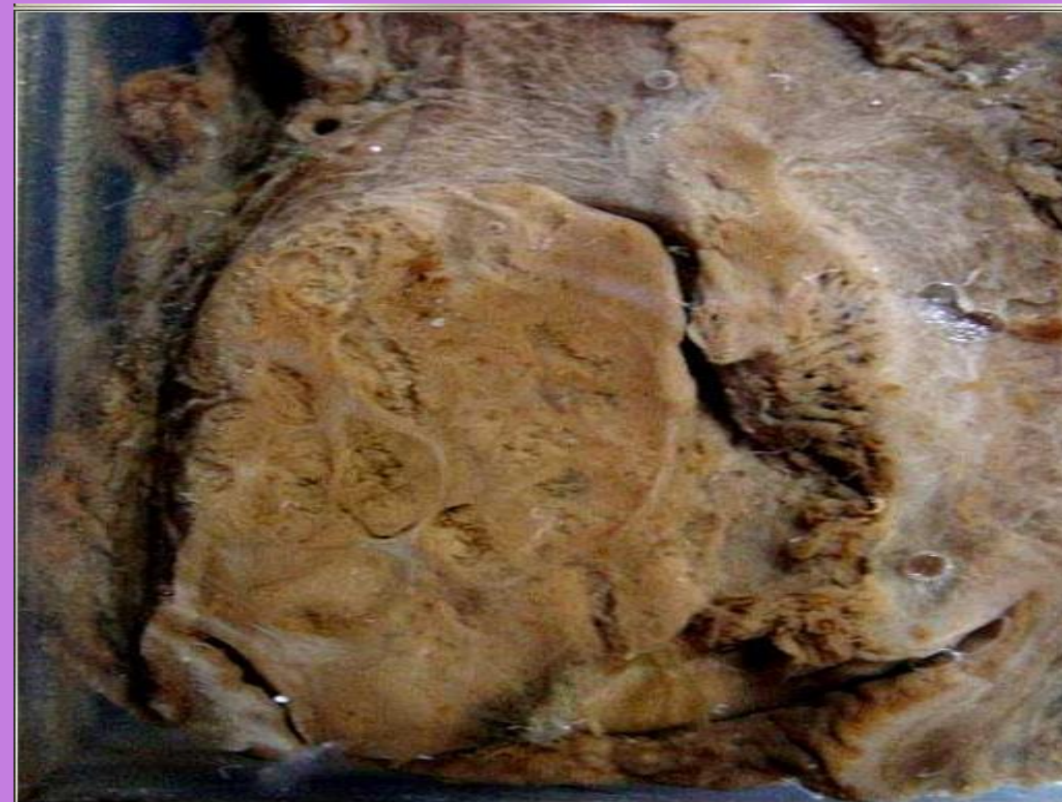
CC histological types

SQUAMOUS CELL CARCINOMA



Source: Anatpat-UNICAMP

ADENOMACARCINOMA



Source: Anatpat-UNICAMP

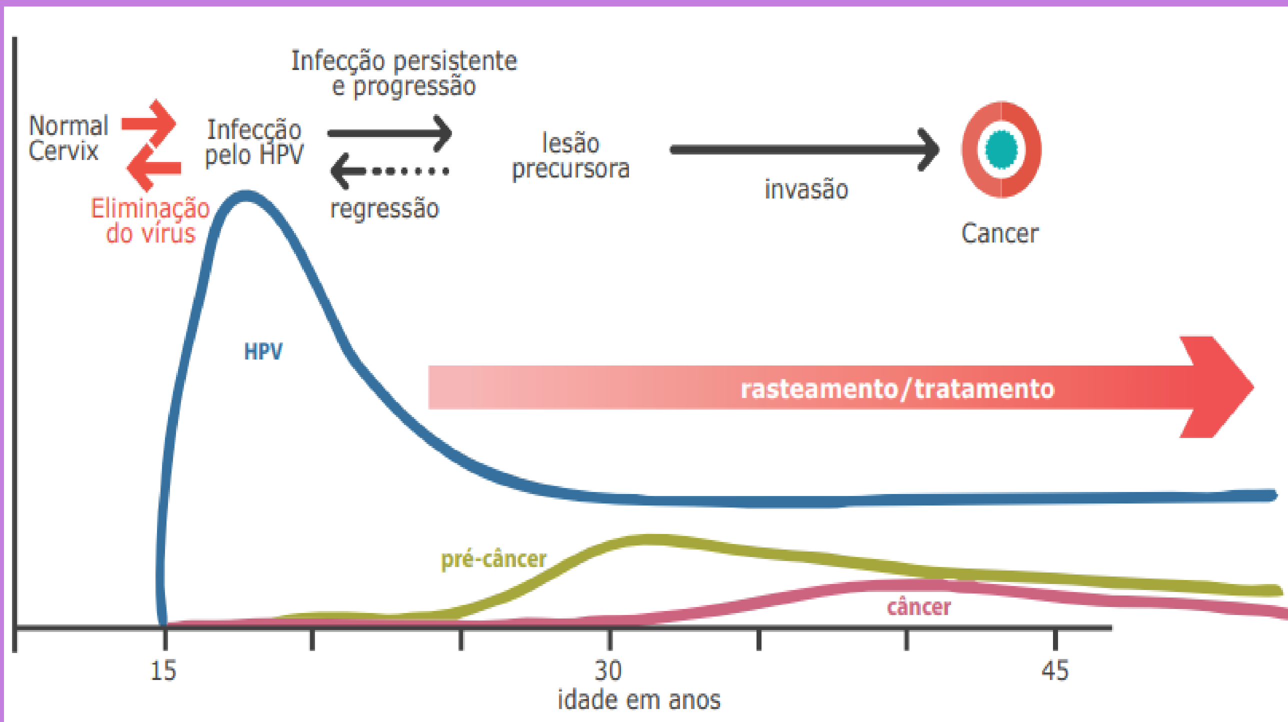
Stages of CC progression

CC has a slow progression and can last from 10 to 20 years. Low-grade lesions can easily regress. Precursor lesions, detectable by screening, are high grade and may progress to CC. Early diagnosis and timely treatment result in a high cure rate (WILD; WEIDERPASS; STEWART, 2020).

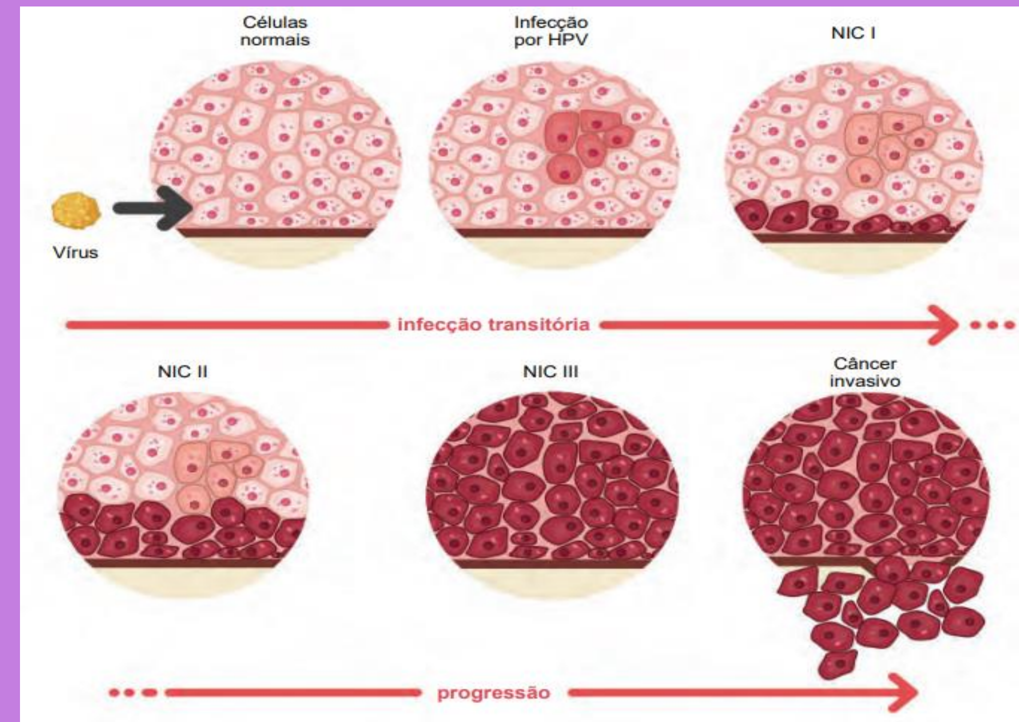
Return

Continue

Stages of CC progression by age group



Source: NEAD/INCA Team.



Source: NEAD/INCA Team.

Risk factors

- Persistent HPV infection may be related to the immune status and/or genetics of the affected patient (WILD; WEIDERPASS; STEWART, 2020).
- HPV infection is most common after age 30.
- Smoking may facilitate viral infections, contributing to carcinogenesis (INTERNATIONAL COLLABORATIONS OF EPIDEMIOLOGICAL STUDIES OF CERVICAL CANCER, 2006).
- The use of oral contraceptives for more than five years may slightly increase the risk of CC (SASIENI, 2007).

Return

Continue

CC risk factors

História familiar

Fumo

HPV

Início precoce da vida sexual

Comprometimento da imunidade

Maior número de parceiros sexuais

Condições de higiene inadequadas

Source: Instituto Vencer o Câncer, 2023.

Signs and symptoms

CC often has no specific symptoms in the initial phase—period of undetected precursor lesions not timely treated. As the disease progresses, clearer signs and symptoms begin to appear:

- Spontaneous bleeding after physical activities or sexual intercourse.
- Vaginal discharge, with or without an unpleasant odor.
- Pelvic pain.
- In more advanced stages, patients may report symptoms such as pain, with or without urinary and/or intestinal complaints, and weight loss.

Return

Continue

Signs and symptoms

Corrimento vaginal anormal

Sangramento vaginal anormal

Ciclo menstrual mais longo

Desconforto ao urinar

Perda do controle da bexiga

Dor durante a relação sexual

Cansaço constante

Dor pélvica (no "pé da barriga")

Perda de peso sem explicação

Dores nas pernas

instituto Oncoguia

Source: Instituto Oncoguia, 2018.

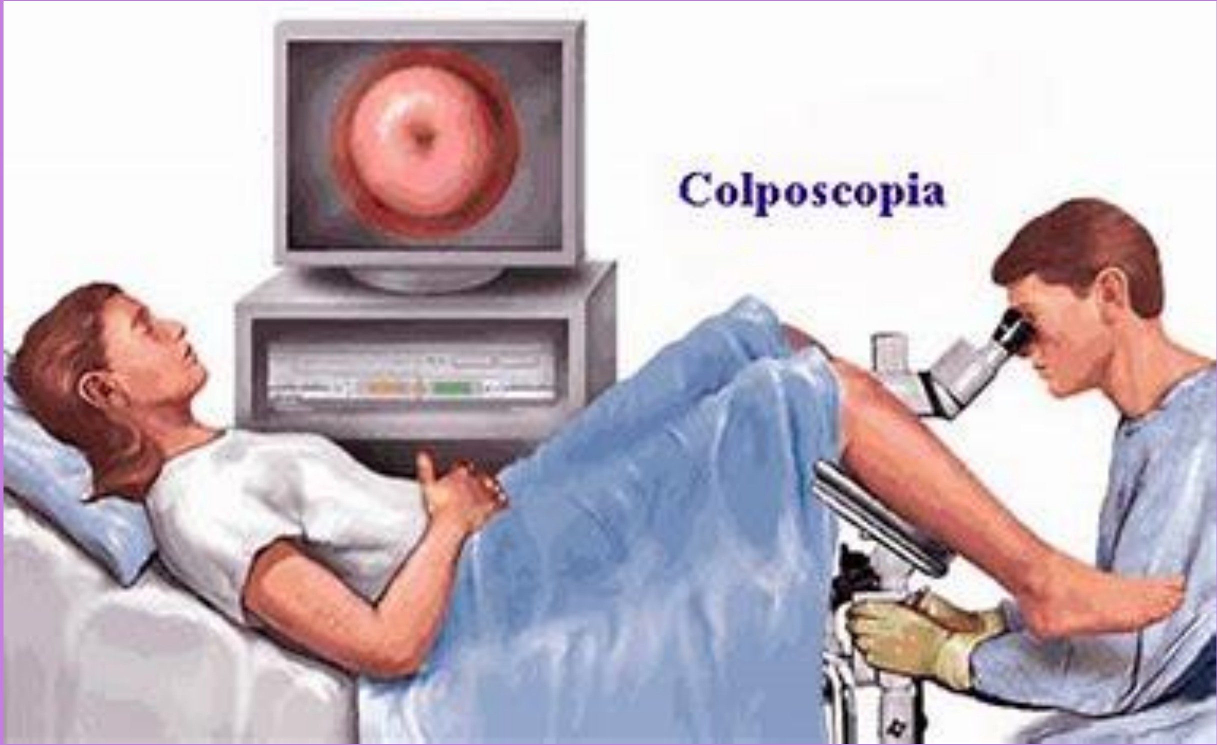
Colposcopy

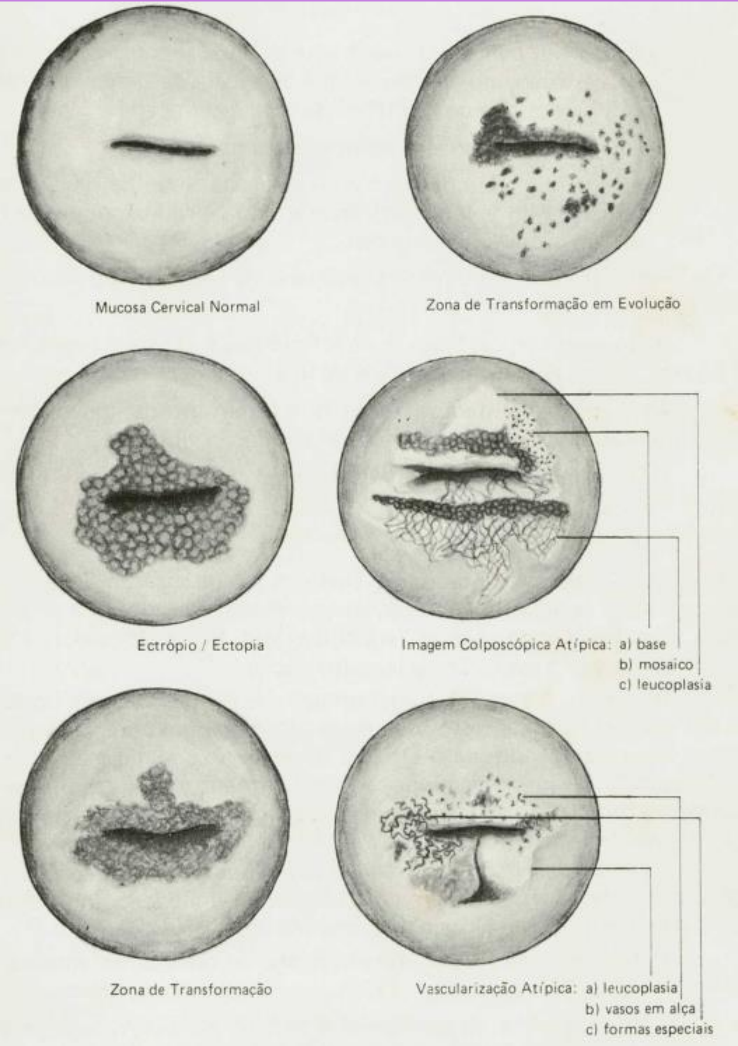
The Brazilian Guidelines for CC screening recommend colposcopic investigation of all women whose Pap smear shows: atypical squamous cells of undetermined significance (ASC-US), when it is not possible to rule out the presence of a high-grade squamous intraepithelial lesion (HSIL); atypical glandular cells (AGC); atypical cells of undetermined origin; high-grade squamous intraepithelial lesion (HSIL); invasive adenocarcinoma in situ; and squamous cell carcinoma.

Return

Continue

Colposcopy





Source: Ministério da Saúde, 1977.

Indications for colposcopy

- Abnormal cytopathological diagnosis.
- Clinical suspicion of invasive carcinoma.
- Postoperative follow-up after large-loop excision of the transformation zone (LLETZ), with control every 6 months until 2 years after the procedure was performed.

Return Continue

Cervical biopsy

A biopsy is recommended to confirm the diagnosis in cases with abnormal cytology results and is performed during colposcopy.

Return

Continue

Colposcopy and biopsy

FIGURA 13.8: Excisão de uma lesão ectocervical que se estende para o canal endocervical por meio de método de excisão de duas camadas; (a) aspecto de lesão NIC 3 após aplicação de ácido acético a 5%; (b) aspecto após aplicação de solução de Lugol; (c) excisão de lesão ectocervical em progressão; (d) incisão ectocervical completa; (e) incisão endocervical completa e amostra no lugar (setas finas); (f) amostra endocervical retirada e pontos hemorrágicos no assoalho da cratera que passaram por fulguração para hemostasia

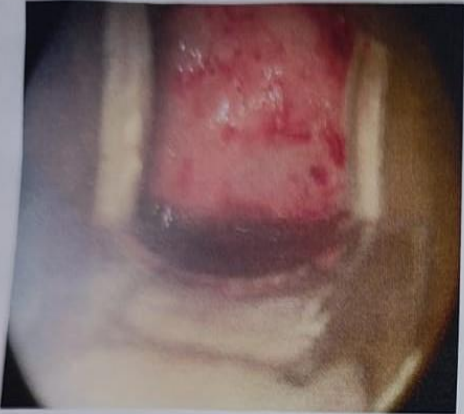
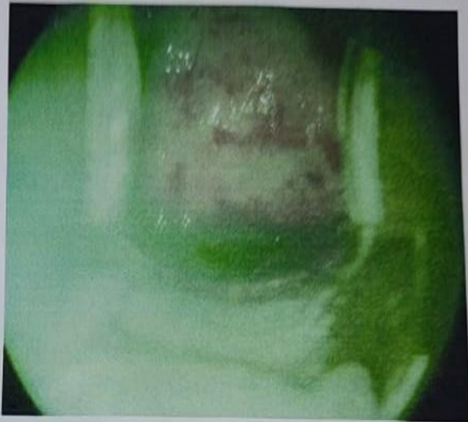
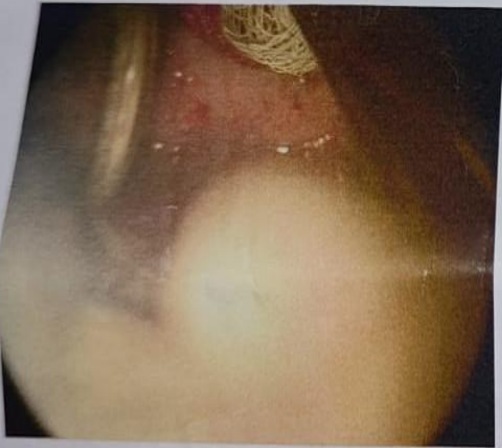
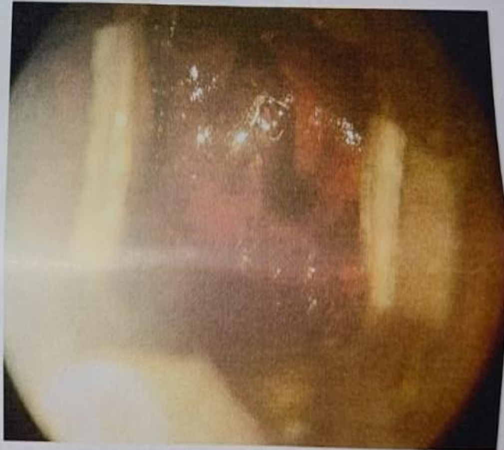
Clinical case

Patient: CSM, 33 years old, divorced, housewife, Catholic.
Major complaint: pelvic pain, discharge with odor.
History of present illness (HPI): The patient reports intense pain in the lower abdomen progressing for six months and the feeling that her menstrual cycle never ends. She present a serosanguineous secretion with a foul odor. She never underwent the preventive exam. GII, PII, and A0. She had normal deliveries at ages 17 and 22 with the same man, who was her only sexual partner. She has been divorced for 5 years due to his infidelities.
Past medical history (PMH): She denies previous illnesses, allergies, or surgeries.
Family history (FH): Healthy children, parents alive and without diseases, no family history of cancer, no siblings.
Life history (LH): Smoker of 2 packs of cigarettes a day since the age of 15, social drinker, never used drugs. The patients has a healthy diet (3x/day) and goes to work by bicycle.
No findings on physical examination; on bimanual gynecological examination, pelvic pain and hardened cervix. On speculum examination, the cervix was centrally positioned, friable when manipulated with the Ayres spatula, and showing difficulty in brush penetration.
Pap smear report indicated ASC-US. Due to her clinical presentation, colposcopy was requested.

Return

Continue

Clinical case (continued)

Source: Author's collection, 2023.

Colposcopy report:

- Cervical description: the examination was deemed unsatisfactory due to tumor-related distortion of the transformation zone. The procedure was performed with significant technical difficulty due to the extent of the lesion.
- Colposcopy findings: presence of a tumor mass involving the entire cervix, with a hardened and irregular appearance, extending to the posterior and right fornixes.
- Positive Schiller test.
- Suspected invasion, with diffuse hemorrhagic suffusion through the external os. Signs of necrosis and associated ulceration.
- Normal vulvoscopy.
- Conclusion: INVASIVE CERVIX ADENOCARCINOMA.
- A biopsy was performed.

Return

Continue

Clinical case - biopsy

Pathological examination:

- Material: two cervix fragments.
- Macroscopy: brown and elastic cervix fragments measuring 1.4 x 0.5 cm.
- Microscopy: histopathology compatible with squamous cell carcinoma.

Return

Continue

Clinical case management

- The patient is medicated with painkillers.
- Referral and counter-referral forms are sent to the Department of Health of the municipality of residence.
- At the Secretariat, the patient presents her ID, SUS card, proof of residence, and the referral and counter-referral forms.
- The patient is included into the State Regulation System (SER) and waits for her oncology appointment to start disease staging and treatment.

Return

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage I: neoplastic cells grow from the cervical surface into deeper layers, but the tumor does not involve lymph nodes or other organs. Subdivisions:

- IA: small tumor that has not spread to other organs or lymph nodes.

  IA1: tumor visible only under a microscope, with a depth of less than 3 mm.

  IA2: tumor visible only under a microscope, with a depth of 3 to 5 mm.

Return

Continue

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

- IB: clinically visible tumor confined to the cervix or a microscopic lesion larger than IA1 and IA2. It covers all visible macroscopic lesions, including those with superficial invasion.

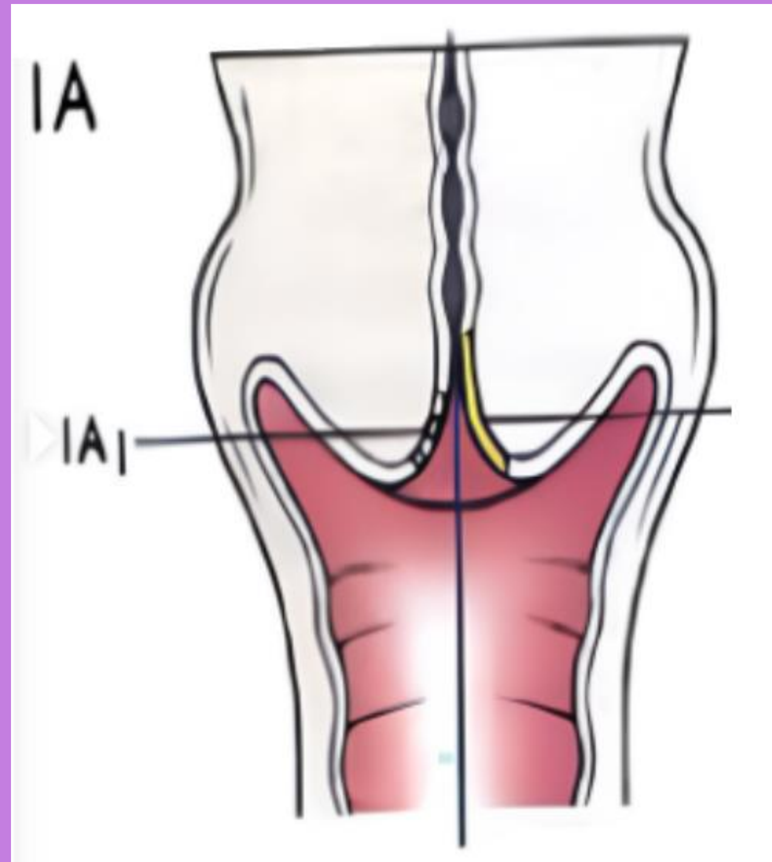
    IB1: clinically visible tumor measuring ≤ 4 cm.

    IB2: clinically visible tumor measuring > 4 cm.

Return

Continue

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)



Source: FIGO

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

In stage I, neoplastic cells originate from the cervical surface and extend into deeper layers, but the tumor does not invade lymph nodes or other organs.

The figure illustrates the progression of stage I, including IA, IB1, and IB2.

Return

Continue

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage I:
IA_1, IA_2, IB_1, and IB_2.

IA
IA1
IA2
IB1
IB2
≤ 4 cm
> 4 cm

Source: FIGO

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage II:

- IIA: the tumor extends beyond the cervix but does not invade adjacent tissues, such as the parametrium or lymph nodes, and is smaller than 4 cm.
- IIB: The tumor extends beyond the cervix, affecting adjacent tissues such as the parametrium, but does not invade other tissues or lymph nodes.

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage II:
IIA and IIB.

IIA

IIB

Source: FIGO

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage III:

- IIIA: the tumor spreads beyond the cervix, reaching the lower third of the vagina without involving the pelvic wall, organs, or lymph nodes.
- IIIB: the tumor extends beyond the cervix, affecting the pelvic walls and potentially obstructing the ureters, but without invading other tissues or lymph nodes.

Return

Continue

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage III:
IIIA and IIIB.

IIIA

IIIB

Source: FIGO

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage IV:

- IVA: the tumor extends beyond the cervix, reaching the bladder and rectum, potentially affecting pelvic organs.
- IVB: the tumor spreads beyond the cervix to the bladder and rectum, with possible involvement of pelvic organs and lymph nodes.

Return

Continue

FIGO staging of CC
(International Federation of Gynecology and Obstetrics)

Stage IV:
IVA and IVB.

IVA

IVB

Source: FIGO

Treatment

According to CC staging, treatment will be conducted in accordance with the patient's decision regarding preserving fertility. In addition, the treatment will also consider tumor location and cell type (squamous cell or adenocarcinoma) (AMERICAN CANCER SOCIETY, 2020).

Return

Continue

Treatment

External radiotherapy

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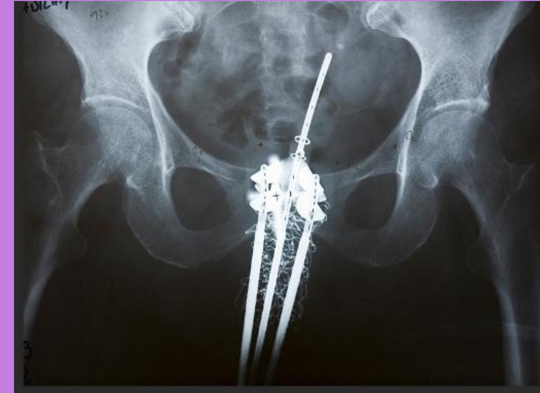

Brachytherapy

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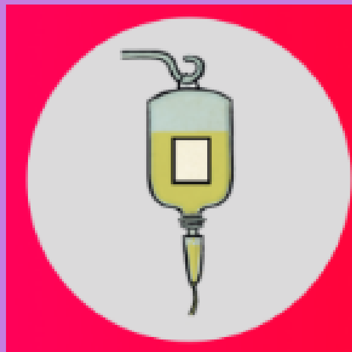


Chemotherapy

+

Source: The author, 2024.

Surgical treatment

Surgical procedures depending on staging and may be useful for:

a) diagnosing CC,

b) assessing the extent of CC spread, and

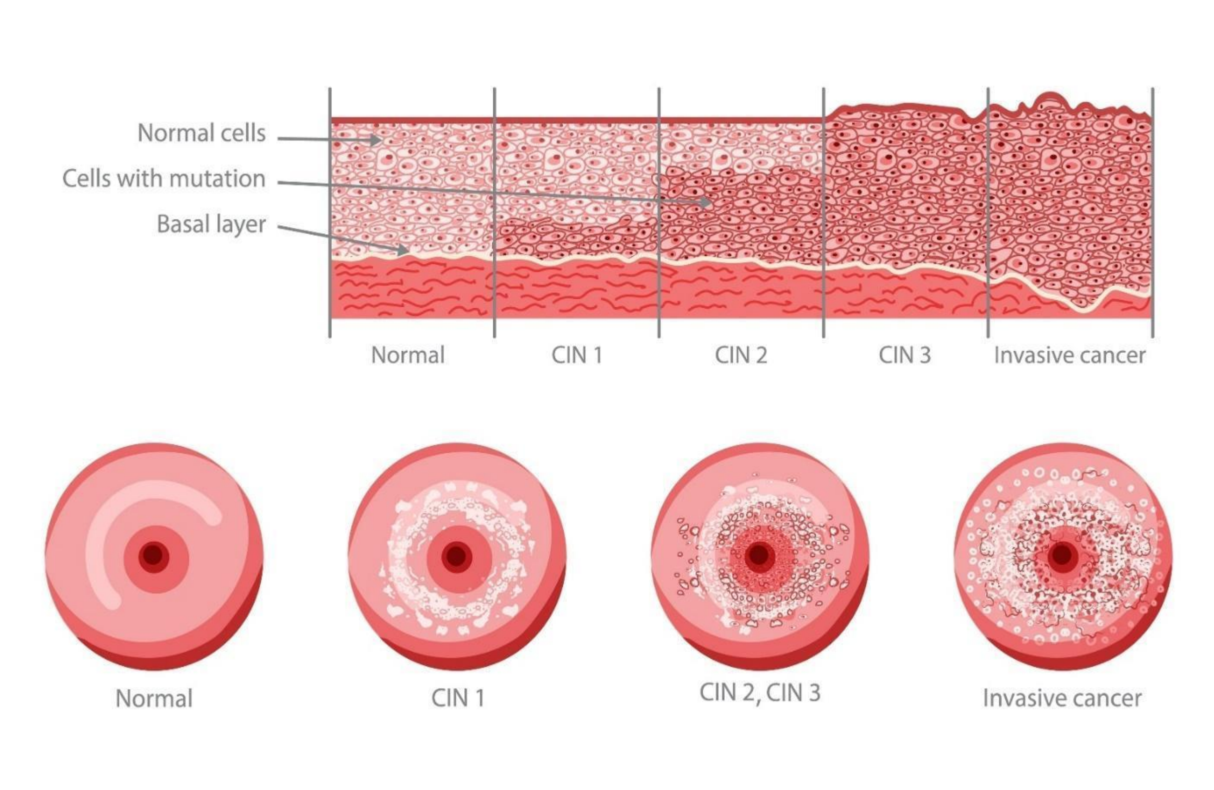
c) treating CC (especially in early stages).

Return

Continue

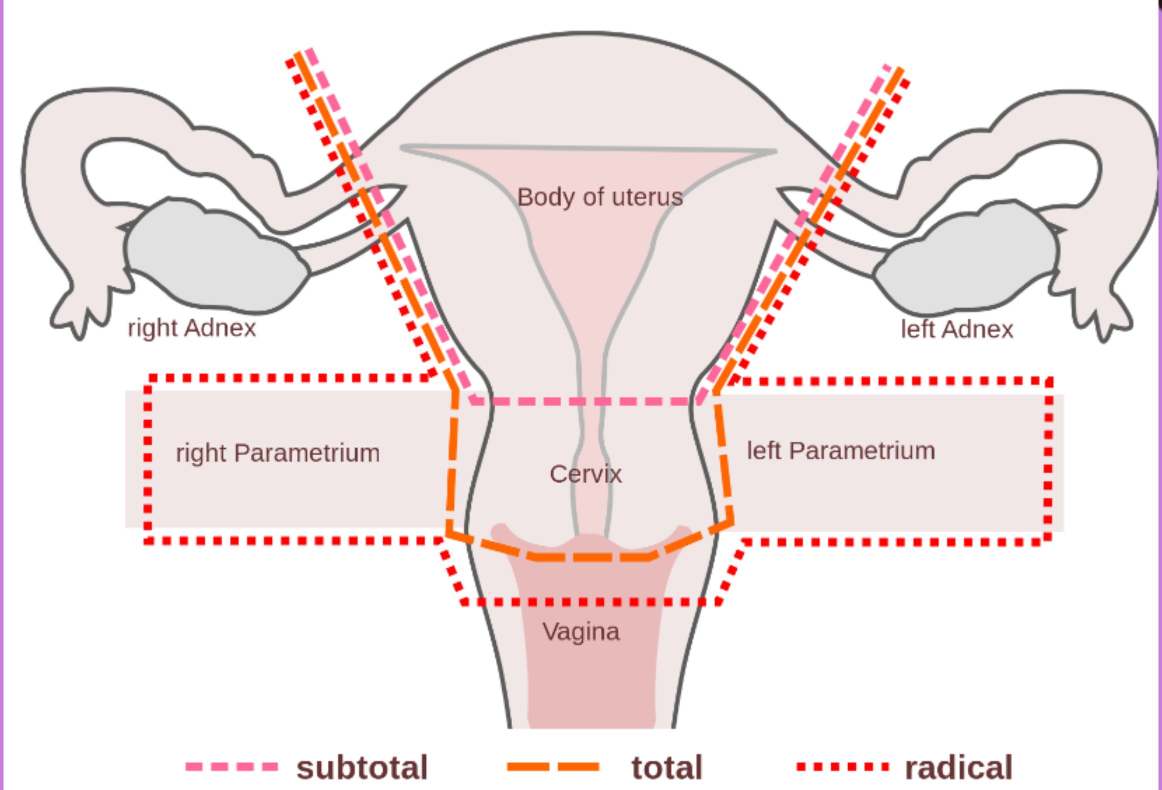
Surgical treatment

Conization



Source: Instituto vencer o câncer, 2024.

Hysterectomy



Source: Instituto vencer o câncer, 2024.

Radiotherapy

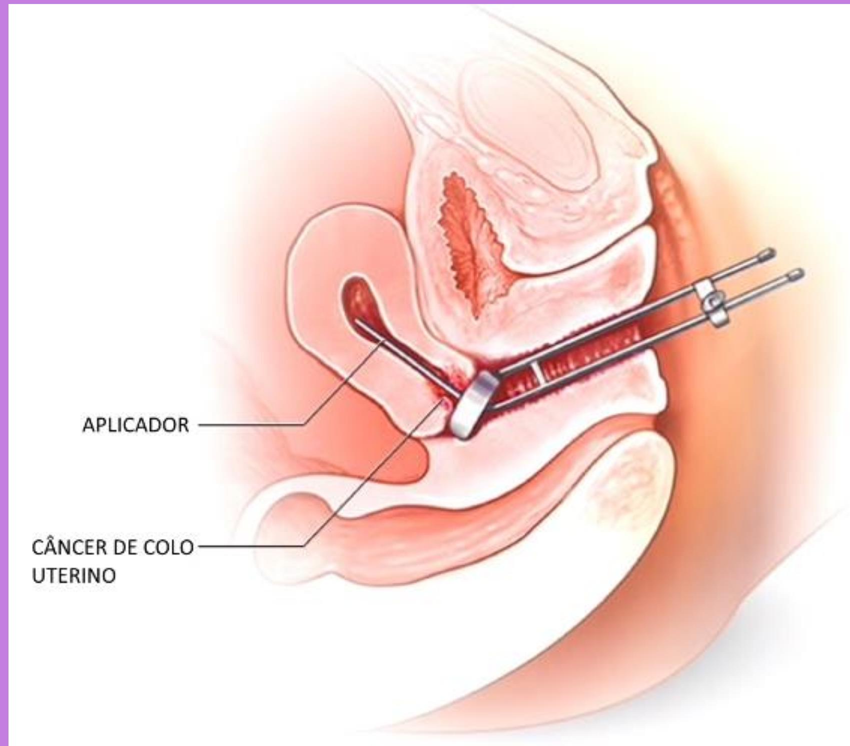
Radiotherapy can be used at all stages of CC, either postoperatively to eliminate any remaining cancer or combined with chemotherapy. Although it does not cause pain, radiation therapy can result in side effects, which can be treated or managed. Most side effects disappear after the end of treatment.

Return

Continue

Radiotherapy

Brachytherapy applicator: probe and ring placed inside the patient's vagina (sagittal view).



Source: dricarocarvalho.com.br, 2021.

Source: dricarocarvalho.com.br, 2021.

Chemotherapy

Chemotherapy includes drugs capable of eliminating tumor cells, often combined with radiotherapy. In case of metastasis to other organs, chemotherapy may be administered alone.

Return

Continue

Chemotherapy

Source: revista.abrale.org.br, 2021.

Consulted bibliography:

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REVISE!

Resposta inadequada Prossiga na sua aprendizagem

Evaluation

A 23-year-old patient, who began her sexual life at the age of 18, is treated at the Family Health Unit by a general practitioner. Regarding the Pap smear, the most appropriate approach is:

a) It must be conducted annually.

b) It is an unnecessary procedure.

c) It may be done biannually, as long as the two previous tests were negative.

d) There may be a three-year interval, as long as the two previous tests were negative and the patient is older than 21.

e) I don’t know/I don’t want to answer.

Continue

Evaluation

PARABÉNS!

Resposta adequada Prossiga na sua aprendizagem

For patients with a high-grade lesion detected on Pap smear, the physician should do the following:

a) Repeat the Pap smear immediately.

b) Repeat the Pap smear after three months.

c) Colposcopy and directed biopsy.

d) Conization.

e) I don’t know/I don’t want to answer.

Continue

Evaluation

PARABÉNS!

Resposta adequada Prossiga na sua aprendizagem

Anatomically, the uterus can be divided into three parts:

a) Fundus, middle, and cervix.

b) Uterine body, isthmus, and cervix.

c) Fundus, uterine body, and myometrium.

d) Uterine body, cervix, and vagina.

e) I don’t know/I don’t want to answer.

Return

Continue

Evaluation

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

Regarding the following statements: *

I. The uterus is formed by fibromuscular tissue and has three layers: externally, it is covered by the peritoneum and has the parametrium; in the medial part, it is composed of smooth muscle fibers of varying thicknesses that intertwine (myometrium); and internally, it is lined by the endometrium.

II. In the upper and lateral part of the uterine body, the uterine horns are located, from which the uterine tubes (fallopian tubes) project.

Indicate the CORRECT option:

a) Both statements are true.
b) Statement I is true, but II is false.
c) Statement II is true, but I is false.
d) Both statements are false.
e) I don’t know/I don’t want to answer.

Continue

Evaluation

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

Regarding laboratory results of the analysis of vaginal secretion, the physician informs the patient that the microorganisms listed below are considered part of the healthy vaginal microflora:

a) *Mycoplasma hominis, Chlamydia trachomatis,* and *Candida albicans.*

b) *Chlamydia trachomatis, Gardnerella vaginalis*, and human papillomavirus (HPV).

c) *Candida albicans,* lactobacilli, and *Chlamydia trachomatis*.

d) *Lactobacillus* sp., *Candida albicans,* and *Mycoplasma hominis.*

e) I don’t know/I don’t want to answer.

Return

Continue

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

Evaluation

Research over the years has demonstrated a correlation between HPV and CC. Among the different types of HPV, it is clear that some types have a greater correlation with cervical neoplasia or greater oncogenic potential. These are the types:

a) 6 and 11.

b) 16 and 18.

c) 31 and 33.

d) 43 and 44.

e) I don’t know/I don’t want to answer.

Continue

Evaluation

According to INCA guidelines for CC screening, when Pap smear results are satisfactory and indicate high-grade lesion, showing significant and fully visible abnormalities restricted to the cervix that extend up to a maximum of 1 cm above the internal cervical os, the recommended approach is:

a) Repeat the Pap smear immediately.
b) Repeat the Pap smear after 6 months.
c) Perform a biopsy.
d) Perform a large loop excision of the transformation zone.
e) I don’t know/I don’t want to answer.

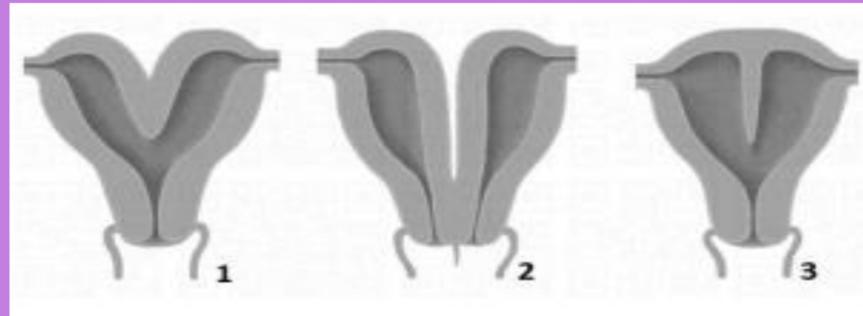
Continue

Evaluation

REVISE!

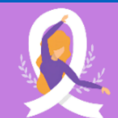
Resposta inadequada Prossiga na sua aprendizagem

Analyze the numbered illustrations below. Select the alternative that indicates the correct name of uterine abnormalities:*



a) 1. Arcuate, 2. double, 3. septate.
b) 1. Bicornuate, 2. didelphis, 3. septate.
c) 1. Didelphis, 2. double, 3. divided.
d) 1. Didelphis, 2. bicornuate, 3. dysmorphic.
e) I don’t know/I don’t want to answer.

Continue



Evaluation

Regarding the CCU, which statement is correct?*

a) Smoking is not a risk factor, as it has been recently discovered that it is caused by HPV infection.
b) CC can spread by contiguity, by continuity via the lymphatic system, and via the hematogenous system.
c) The most common histological type is mucinous adenocarcinoma.
d) In situ and invasive carcinoma can only be differentiated by colposcopy and cervical biopsy.
e) I don't know/I don't want to answer.

Continue

Evaluation

Regarding CC screening using the Pap smear:*
I. The Pap smear is a complementary action in CC prevention.
II. The vaccine protects against all types of HPV potentially causing neoplasia, thus eliminating the need for Pap smear in vaccinated individuals.
III. The test is easy to perform and recommended for individuals in the age group of 25 to 64 years, living with a uterus, and having active sexual life.
Which statements are correct?*

a) Only statement I is true.
b) Statements I and II are true, but III is false.
c) Statements II and III are true, but I is false.
d) Only statement II is false.
e) I don’t know/I don’t want to answer.

Continue

Evaluation

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

A 28-year-old woman was diagnosed with stage IA1 CC and reports her desire to maintain fertility. What therapeutic approach is the most appropriate?*

a) Cervical chemoradiation.
b) Cervical radiation.
c) Cervical chemotherapy.
d) Cervical conization or trachelectomy.
e) I don’t know/I don’t want to answer.

Continue

Evaluation

A 60-year-old woman was diagnosed with CC stage IVB. What therapeutic approach is the most appropriate?*

a) Chemoradiation, aimed at curing the cancer.
b) Chemotherapy associated or not with radiation, aimed at reducing tumor size.
c) Cervical conization or trachelectomy to remove the tumor, aiming at curing the cancer.
d) No further treatment options are available.
e) I don’t know/I don’t want to answer.

Continue

Evaluation

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

RCP, a 38-year-old woman who has been sexually active since the age of 13, reports multiple partners, rare use of condoms, and post-coitus bleeding progressing for 6 months. Regarding this clinical case, we can state that the risk factors for the development of CC include:*

I. HPV infection, which always causes CC.

II. HPV infection, which can cause CC when associated with other risk factors.

III. Early initiation of sexual activity without using condoms, which is not always associated with HPV, can be a risk factor for CC.

We can affirm that:

a) Statement I is true, but II and III are false.

b) Statement II is true, but I and III are false.

c) Statement III is true, but I and II are false.

d) Statements I and II are true, but III is false.

e) I don't know/I don't want to answer.

Continue

Evaluation

Regarding endometrial cancer, it is correct to state that when the diagnosis is made in the initial phase, the patient may present:*

a) Persistent mucorrhea or metrorrhagia, and the cancer is an adenocarcinoma.

b) Persistent mucorrhea or metrorrhagia, and the cancer is a leiomyosarcoma.

c) Persistent mucorrhea or metrorrhagia, and the cancer is a sarcoma.

d) Persistent mucorrhea or metrorrhagia, and the cancer is an adenomyoma.

e) I don’t know/I don’t want to answer.

Continue

Evaluation

Brazilian authorities have approved the quadrivalent vaccine for the prevention of pre-cancerous cervical, vulvar, and vaginal lesions; CC in women; and HPV-related genital warts in women and men.*

I. In 2014, the Ministry of Health implemented free HPV immunization with the quadrivalent vaccine in the SUS for girls between 9–13 years.

II. In 2017, vaccination was expanded to include girls and adolescents between 9–14, and introduced to the male population between 11–14 or 9–26 living with HIV/AIDS, as well as individuals undergoing solid organ/bone marrow transplants and cancer patients.

III. In 2021, immunosuppressed women between 26–45 years were also included.

IV. Vaccination is available through the SUS for all immunocompetent population over 14 years of age.

It is correct to state that:

a) Statements I and IV are correct, but II and III are false.
b) Statements I, II, and IV are correct, but III is false.
c) Statements II, III, and IV are correct, but I is false.
d) Statements I, II, and III are correct, but IV is false.
e) I don't know/I don't want to answer.

Continue

Evaluation

REVISE!

Resposta inadequada Prossiga na sua aprendizagem

Mark T for true and F for false:*

( ) HPV infection is difficult to prevent, as it depends on contact between diseased skin and healthy skin and does not depend on ejaculation.

( ) A condom must be used throughout sexual intercourse.

( ) Having numerous sexual partners can also help reduce the risk of HPV infection.

( ) Vaccinated women require no preventive exams.

Now select the correct option:

a) F, T, T, F.
b) T, F, F, T.
c) T, F, T, F.
d) T, T, F, F.
e) I don't know/I don't want to answer.

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REVISE!

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Resposta inadequada
Prossiga na sua aprendizagem

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Return

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