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Common sexually transmitted diseases(STD) in tropical regions

It is estimated that the incidence of chlamydia, gonorrhea, syphilis, and trichomoniasis alone is 500 million per year. Of these infections, about 75% occur in tropical countries in Latin America, Sub-Saharan Africa, and South and Southeast Asia. These bacterial infections, the chancroid, the lymphogranuloma venereum (LGV), and the granuloma inguinale (GI, donovanosis), are known as tropical STIs. These mainly occur in tropical countries, i.e., areas between the equator and the northern and southern 23.5° latitudes, which are characterized by a hot and humid climate, and by poverty and underdevelopment. The three diseases are primarily associated with ulcers on the skin, so their presence poses an increased risk for transmission of HIV and other sexually transmitted diseases. Like all sexually transmitted diseases, it is important to avoid dangerous sexual practices and use condoms to minimize the risk of STD-related tropical infection. [1]

Due to the high incidence in this area, I would like to share the 3 most important STDs such as **chancroid, lymphogranuloma venereum, and granuloma inguinale**. However, it is also very important to be aware of sexually transmitted diseases or sexually transmitted infections that are passed from one person to another through sexual contact. This contact is usually through vaginal, oral, or anal intercourse. But sometimes they can also be transmitted through intimate physical contact. After all, some sexually transmitted diseases, such as herpes and human papillomavirus (HPV), are transmitted through skin-to-skin contact. On the other hand, gonorrhea, acquired immunodeficiency syndrome, and syphilis are very common worldwide, regardless of geographic location.

The Chancroid

This is caused by the bacterium Haemophilus ducreyi and manifests clinically as painful, superficial ulcers, often with regional lymphadenopathy. Chancroid is an important cofactor for HIV transmission and is found in Asia, Africa, and the Caribbean. The genital ulcer in the chancroid is painful, tender, and noninflamed. The symptoms usually appear 4-10 days after exposure. Lesions at the site of infection are initially pustules that break open and form a painful, soft ulcer with a necrotic base and irregular margins and the chancroid is painful, tender, and not inflamed. Frequently, multiple lesions and adenopathy of the groin develop. If the lymph nodes are also concerned, there may be fever, chills, and malaise. Additional symptoms of chancroid include painful urination, vaginal discharge, rectal bleeding, pain during bowel movements, and dyspareunia.

Figure 1: Author: Vanessa Ngan, Staff Writer, 2003. Updated by Dr.Natalie Renaud, Registrar, Sexual Health Services, Waikato District Health Board, Hamilton, New Zealand. DermNet NZ Editor in Chief: Adjunct A/Prof. Amanda Oakley, Dermatologist, Hamilton, New Zealand. April 2018.

How is Chancroid treated?

The treatment for Chancroid is antibiotics. The antibiotics of choice are azithromycin, ciprofloxacin, ceftriaxone, or erythromycin.

There have been reports of resistance to trimethoprim-sulfamethoxazole and tetracycline. In pregnancy and lactation, ciprofloxacin is not recommended. A single-dose regimen is preferable to increase treatment compliance (except in immunocompromised individuals). Evaluation of the risk of QT prolongation is required when erythromycin is prescribed.

Since most chancroid diagnoses are based on clinical criteria and patients may have duplicate infections, empiric therapy includes treatment for herpes simplex and syphilis.

The follow-up should be continued until signs and symptoms have completely resolved. Antibiotics result in improvement within 3 to 4 days, and reepithelialisation should be evident by the seventh day. Time to complete healing depends on the area of skin affected, the presence of blisters, and the immune status of the infected person. If healing is delayed beyond 7 days: Empty fluctuating blisters by needle aspiration; this may need to be repeated.

Consider the possibility of treatment failure, poor treatment adherence, antimicrobial resistance, underlying HIV infection, or another diagnosis.

An individual with Chancroid should not resume sexual activity until all lesions are completely healed. Any sexual contacts must be notified and treated immediately, even if they have no signs or symptoms, particularly if the contact occurred within 10 days before the onset of Chancroid ulcers.

The importance of patients with Chancroid undergoing a complete work-up for other sexually transmitted infections; the workup should be repeated several weeks later.

Lymphogranuloma venereum

Lymphogranuloma venereum infectious (LGV) is caused by three subtypes of C. trachomatis: Serovars L1, L2, or L3. It most commonly occurs in tropical areas of Asia, Africa, South America, and the Caribbean. Signs appear 3-30 days after infection and usually take the form of a painless ulcer or papule at the site of inoculation. Both inguinal and femoral lymphadenopathy may also occur. Rectal exposure may result in mucoid or hemorrhagic rectal discharge, anal bowel movements, and constipation. Later manifestations include rectal and perirectal inflammation, which may lead to rectal strictures and rectovaginal and perianal fistulas. Constitutional symptoms such as fever may also occur. [2]

Figure 2: Lymphogranuloma venereum on the penis of an HIV-infected patient. Ulceration on the coronal sulcus and lymphedema of the prepuce.

https://www.actasdermo.org/es-lymphogranuloma-venereum-in-public-health-articulo-S1578219020302869

How is lymphogranuloma venereum(LGV) treated?

Tetracycline or erythromycin or possibly drainage of blisters to relieve symptoms. Doxycycline 100 mg orally twice daily for 21 days is the preferred treatment. As an alternative, erythromycin 500 mg orally 4 times daily for 21 days may be used. Another alternative is azithromycin 1 g orally once a week for 3 weeks.

The swelling of the damaged tissues in later stages may not go down despite the elimination of the bacteria. Vesicles can be drained with a needle or surgically to relieve symptoms, but most patients respond quickly to antibiotics. Vesicles and sinuses may require surgical intervention, but rectal strictures can usually be dilated.

If people had sexual contact with someone who has lymphogranuloma venereum in the 60 days before the onset of symptoms, depending on the site of exposure, they should be screened and tested for urethral, cervical, or rectal chlamydial infection. It should be treated presumptively (with a single dose of azithromycin 1 g orally or doxycycline 100 mg orally twice daily for 7 days), regardless of whether there is evidence of LGV.

Granuloma Inguinale (Donovanosis)

Infiltrating granuloma (donovanosis) is a genital ulcerative disease caused by the intracellular gram-negative bacterium Klebsielgranulomatoustis (formerly known as Calymmatobacterium granulomatis). It is widely present in the countries such as India, South Africa, and South America. It is characterized clinically by painless, slowly progressive ulcerative lesions on the genitalia or perineum without regional lymphadenopathy; some subcutaneous granulomas (pseudobulbs) may also occur. Lesions are highly vascular (i.e., fleshy red) and may bleed. Extra-genital infection may occur, in which the infection spreads to the pelvis, or it may spread to intra-abdominal organs, bones, or the mouth. Lessons may also develop a secondary bacterial infection and coexist with other sexually transmitted pathogens.

Figure 3: Granuloma inguinal

Source. Image courtesy of Dr. Shahbaz A. Janjua, https://dermnetnz.org/topics/granuloma-inguinale

How is granuloma inguinale (donovanosis) treated?

There are many oral antibiotics that kill the bacteria, but tetracyclines, macrolides, and trimethoprim/sulfamethoxazole (TMP/SMX) are most effective, to be followed by ceftriaxone, aminoglycosides, fluoroquinolones, and chloramphenicol.

Recommended oral therapy is azithromycin 1g once a week or 500 mg per day for at least 3 weeks and continued until all lesions are completely healed.

Alternative oral therapies should be continued until all lesions are completely healed and include

- The doxycycline 100 mg twice daily for a period of at least 3 weeks or
- The TMP/SMX 160/800 mg twice daily for a period of at least 3 weeks, or
- ERYTHROME 500 mg four times daily for a period of at least 3 weeks.
- IV or IM antibiotics (e.g., ceftriaxone) are an alternative.

Treatment response should begin within 7 days, but recovery from the extensive disease may be slow and lesions may recur, requiring longer treatment. HIV-infected patients may also require longer or more intensive treatment. Follow-up should be continued for 6 months after apparently successful treatment. Cave Current sexual partners should be screened and, if infected, treated. [3]

Common cancers in tropical regions

For World Cancer Day on February 4, 2020, the WHO reminded us that cancer is responsible for one in six deaths worldwide, but up to 50% of all cancers can be prevented. The theme of the day was cervical cancer, from which more than 310,000 women die each year, and this figure is expected to reach 460,000 deaths per year by 2040, without preventive measures. Immunization against human papillomavirus (HPV) is a safe, efficacious, and essential measure in the fight against cervical cancer.

The WHO recorded 18.1 million new cancer cases worldwide in 2018 and expects the number to reach between 29 and 37 million cases by 2040. By 2040, WHO estimates that cancer cases will increase by 81% in low- and middle-income countries due to insufficient resources for prevention. The WHO presented a range of interventions to prevent new cancer cases, such as tobacco control, which is responsible for 25% of cancer deaths. Furthermore WHO presented a range of interventions to prevent new cancer cases, such as tobacco control, which accounts for 25% of cancer deaths, hepatitis B vaccination to prevent liver cancer, and cervical cancer elimination through HPV vaccination.

High-income countries have adopted prevention, earlier diagnosis, and detection programs that, combined with improved treatment, have contributed to a 20% reduction in premature mortality between 2000 and 2015. In lower-income countries, the reduction was only 5%. But African countries, such as Kenya, have begun to provide cancer care as part of national efforts to achieve universal coverage. [4;5]

Every year, there are two million cancers of infectious origin in the world. Most of them are cancers of the liver, cervix, or stomach. Most of these cancers are liver, cervical, or stomach

cancers. These cancers could be avoided: indeed, against these cancers, there are means of prevention and sometimes treatments that are all the more effective if they are implemented early.

The fact that cancers in developing countries have an infectious origin is one of the original features of the disease. Thus, in Africa, 26% of cancer cases have an infectious origin. As cancers of infectious origin are more frequent in vulnerable tropical countries, I will be writing about forms of cancer such as hepatocellular carcinoma and hepatitis viruses, Cervical cancer, human papillomavirus, AND Kaposi's disease, and the human herpes virus type 8. [6;7]

Hepatocellular carcinoma and the hepatitis viruses

In Africa, hepatocellular carcinoma (HCC) is the second leading cause of cancer in men and the third leading cause in women. The prevalence of HCC is increasing worldwide, with a likely increase of 35% between 2005 and 2030. Over 50% of HCC worldwide is diagnosed at a locally advanced stage, with vascular invasion, which has a poor prognosis, with a survival time of between 2 and 5 months. The main causes of HCC in sub-Saharan Africa are chronic infection with the hepatitis B virus (HBV) or hepatitis C virus (HCV). The most common cause is hepatitis B virus (HBV), with chronic active hepatitis B virus → cirrhosis → HCC. The young age of patients (20-40 years) with HCC is due to vertical transmission from mother to child at the end of pregnancy and at the time of delivery and through close contact during infancy. The risk of chronic carriage is 90% in newborns infected by their mothers during the viral replication phase (HBsAg and HBeAg positive). The chronic HBsAg prevalence rate is over 8% in sub-Saharan Africa. The treatment of HCC includes liver transplantation, liver resection, radiofrequency tumor destruction, hepatic intra-arterial chemoembolization, and percutaneous alcohol injection. Transplantation of the liver is limited to a single tumor less than 5 cm or up to three lesions, none of which exceeds 3 cm in diameter, and in the absence of thrombosis of the trunk or a lobar branch of the portal system (Milan criteria). The resection is discussed if the liver function allows it and if the necessary liver resection is not too large. An alternative to surgery is percutaneous destruction, which is simple and usually well tolerated and has the advantage of preserving non-tumorous parenchyma. In the case of HCC with vascular invasion, anticancer drugs, including sorafenib (Naxavar®) have shown limited therapeutic efficacy. Anticancer drugs are too expensive for countries with limited health budgets. For instance, the monoclonal antibody trastuzumab (Ogivri®), a leading breast cancer drug, benefited only 3% of patients in Botswana, while consuming 43% of the cancer drug budget. The curative treatment of HCC in practice is surgical. After curative treatment of HCC due to the hepatitis C virus, antiviral therapy with direct-acting antivirals is associated with a significant reduction in the risk of death. It is necessary to :

- Screen patients for hepatocellular carcinoma (HCC) every six months screening for HCC in patients with chronic active hepatitis or cirrhosis by ultrasound,

- Treating chronic active hepatitis in order to stop viral multiplication. A mass vaccination program against HBV should be developed from birth.

  The efficacy of the HBV vaccine has been widely demonstrated. However, the introduction of this vaccine in the EPI in Africa is relatively recent: dating from 2000, it will therefore take until 2020 for the prevalence of HCC in Africa to decrease. No vaccine is available for hepatitis C. But the treatment of HCV has been

revolutionized by direct-acting antivirals (DAAs), which are very effective drugs that prevent the progression to cirrhosis and HCC. Today, a rapid diagnostic test can easily identify those in need of treatment, allowing for early treatment. [8;9;10]

Cervical cancer and human papillomavirus (HPV)

HPV is the second leading cause of cancer death among women in developing countries and the leading cause of cancer death among African women, causing 300,000 deaths per year, of which 80% occur in developing countries. The high-risk HPV 16 and 18 infections cause cervical cancer as a late consequence of infection. Testing for cervical cancer is based on colposcopy, a cytological study of smears or biopsies of lesions, and/or HPV testing, which uses molecular biology to detect the presence of the virus in cervical cells. This test can detect lesions at an earlier stage than a Pap smear. Because effective screening is rarely available in Africa, the focus should be on prevention through vaccination. Vaccination as a means of prevention.

There are three vaccines available:

- A quadrivalent vaccine (Gardasil®), HPV types 16 and 18 and types 6 and 11, a bivalent vaccine (Gardasil®), HPV types 6 and 11. types 6 and 11
- A bivalent vaccine (Cervarix®), HPV 16 and 18
- A nonavalent vaccine (Gardasil 9®), HPV types 16 and 18. (Gardasil 9®), HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58. [11;12;13;14]

Kaposi's disease and the human herpes virus type 8 (HHV8)

The AIDS-related Kaposi's disease (or Kaposi's sarcoma) has become the leading cause of death among men in Africa and the fourth leading cause of death among women. The disease accounts for 20-50% of all cancers diagnosed in some regions. It involves a mesenchymal proliferative process involving cells of the blood and lymphatic systems, induced by viral growth factors, including HHV8 interleukin 6. It has been identified as the etiological agent of Kaposi's disease, but also of cavity lymphoma or primary serous lymphoma (PSL). The mainstay of treatment for AIDS-related Kaposi's disease is antiretroviral therapy. [15;16;17]

Conclusion

STD:

- Sexually transmitted diseases are transmitted to a person through sexual contact.
- Sexually transmitted diseases are difficult to control because it is hard to determine who has an STD.
- People or travelers in tropical countries are more prone to STDS.

Cancers:

- The global incidence of cancer is steadily increasing, regardless of geographic location.
- There are multiple response cascades between cancer infection and inflammation.
- Unfortunately, due to the increased risk of infection, infectiously caused cancers are becoming more common in tropical countries.

References

1. Bendick C. (2018). Sexuell übertragbare Infektionen in den Tropen [Sexually Transmitted Infections in the Tropics]. *Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und verwandte Gebiete*, *69*(11), 945–959. https://doi.org/10.1007/s00105-018-4275-6.

2. Repiso-Jiménez, J. B., Millán-Cayetano, J. F., Salas-Márquez, C., Correa-Ruiz, A., & Rivas-Ruiz, F. (2020). Lymphogranuloma Venereum in a Public Health Service Hospital in Southern Spain: A Clinical and Epidemiologic Study. Estudio clínico y epidemiológico del linfogranuloma venéreo en un hospital público del sur de España. *Actas dermo-sifiliograficas*, *111*(9), 743–751. https://doi.org/10.1016/j.ad.2020.02.006

3. Centers for Disease Control and Prevention, 2022, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Global Migration and Quarantine (DGMQ) viewed 5 February 2023 <https://www.cdc.gov/ncezid/dgmq/index.html>

4. Ly, A. Cancer et environnement en Afrique. *Oncologie* **9**, 370–379 (2007). https://doi.org/10.1007/s10269-007-0636-y

5. Bray, F., Ferlay, J., Laversanne, M., Brewster, D. H., Gombe Mbalawa, C., Kohler, B., Piñeros, M., Steliarova-Foucher, E., Swaminathan, R., Antoni, S., Soerjomataram, I., & Forman, D. (2015). Cancer Incidence in Five Continents: Inclusion criteria, highlights from Volume X and the global status of cancer registration. *International journal of cancer*, *137*(9), 2060–2071. https://doi.org/10.1002/ijc.29670

6. http://dspace.univ-jijel.dz:8080/xmlui/bitstream/handle/123456789/11181/M-Bc.02-21.pdf?sequence=1&isAllowed=y

7. Dr. Bernard-Alex Gaüzère, Pierre Aubry 2012, *Médecine Tropicale*, Université Bordeaux Segalen, viewed 5 February 2023 <http://medecinetropicale.free.fr/>

8. Yang, J. D., Hainaut, P., Gores, G. J., Amadou, A., Plymoth, A., & Roberts, L. R. (2019). A global view of hepatocellular carcinoma: trends, risk, prevention and management. *Nature reviews. Gastroenterology & hepatology*, *16*(10), 589–604. https://doi.org/10.1038/s41575-019-0186-y

9. Chidambaranathan-Reghupaty, S., Fisher, P. B., & Sarkar, D. (2021). Hepatocellular carcinoma (HCC): Epidemiology, etiology and molecular classification. *Advances in cancer research*, *149*, 1–61. https://doi.org/10.1016/bs.acr.2020.10.001

10. Nyagabona, S. K., Mushi, B. P., Selekwa, M., Philipo, G. S., Haddadi, S., Kadhim, E. F., Breithaupt, L., Maongezi, S., Mwaiselage, J., Balandya, E., Leyna, G. H., Van Loon, K., & Mmbaga, E. J. (2021). A mixed methods needs assessment and gap analysis for establishment of a cancer research training program in East Africa. *Journal of global health reports*, *5*, e2021028. https://doi.org/10.29392/001c.22120

11. Hessel L. (2009). Introduction de la vaccination contre les papillomavirus humains dans les pays en développement: bilan et perspectives [Introduction of vaccination against human papillomavirus in developing countries: update and perspectives]. *Medecine tropicale : revue du Corps de sante colonial*, *69*(4), 323–326.

12. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

13. Stelzle D, Tanaka LF, Lee KK, Ibrahim Khalil A, Baussano I, Shah ASV, et al. Estimates of the global burden of cervical cancer associated with HIV *Lancet Glob Health*, Published online 17 November 2020; https://doi.org/10.1016/S2214-109X(20)30459-9

14. Lei, J., Ploner, A., Elfström, K. M., Wang, J., Roth, A., Fang, F., Sundström, K., Dillner, J., & Sparén, P. (2020). HPV Vaccination and the Risk of Invasive Cervical Cancer. *The New England journal of medicine*, *383*(14), 1340–1348. https://doi.org/10.1056/NEJMoa1917338

15. Mesri, E. A., Cesarman, E., & Boshoff, C. (2010). Kaposi's sarcoma and its associated herpesvirus. *Nature reviews. Cancer*, *10*(10), 707–719. https://doi.org/10.1038/nrc2888

16. Ablashi, D. V., Chatlynne, L. G., Whitman, J. E., Jr, & Cesarman, E. (2002). Spectrum of Kaposi's sarcoma-associated herpesvirus, or human herpesvirus 8, diseases. *Clinical microbiology reviews*, *15*(3), 439–464. https://doi.org/10.1128/CMR.15.3.439-464.2002

17. Kaplan, J. E., Benson, C., Holmes, K. K., Brooks, J. T., Pau, A., Masur, H., Centers for Disease Control and Prevention (CDC), National Institutes of Health, & HIV Medicine Association of the Infectious Diseases Society of America (2009). Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR. Recommendations and reports: Morbidity and mortality weekly report. Recommendations and reports*, *58*(RR-4), 1–CE4.