

Cancer Association of South Africa (CANSA)



CANSA Fact Sheet on Paget's Disease of the Scrotum

Introduction

The male genital system consists of both external and internal parts. The external male genitalia include the penis, urethra, and scrotum. The internal male genitalia include the seminal vesicle, testes, vas deferens, epididymis, prostate, bulbourethral gland, and ejaculatory duct.

[Picture Credit: Genitalia]



The penis is the main part of external male genitalia, which has both sexual and bodily functions. It is able to ejaculate semen (containing sperm) during sexual intercourse and to relieve the body of urine. The urethra transports the urine from the bladder, out of the male body. Semen also travels through the urethra.

Each male has two scrotal pouches, which house certain parts of the internal male genitalia (epididymis, testes, and lower spermatic cords). The testes are the most important part of internal male genitalia because they make and store sperm, as well as supply the male body with hormones, which control the development of male characteristics and reproductive organs.

The epididymis stores, matures, and transports sperm between the testes and the vas deferens, which channels sperm toward the urethra. The seminal vesicles are adjacent to the urethra and secrete a milky fluid that is ultimately discharged through the ejaculatory duct. The bulbourethral glands also assist in the discharge of semen.

Paget's Disease of the Scrotum

Paget's disease of the scrotum is classified as extramammary Paget's disease (EMPD). It is often confused with jock itch. Afrikaans men will refer to "jock itch" as onderbroekjeuk.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

Page 1

Paget's Disease of the scrotum is an intra-epidermal malignant neoplasm that arises in areas rich in apocrine glands. Common sites of occurrence include the vulva, perianal region, perineum, and scrotum. The lesion may be accompanied by an invasive adenocarcinoma or adenocarcinoma *in situ* of the apocrine glands. Generally, the prognosis is poor.

[Picture Credit: Paget's Disease of Scrotum]



Dauendorffer, J.N., Herms, F., Baroudjian, B., Basset-Seguin, N., Cavelier-Balloy, B., Fouéré, S., Bagot, M. & Lebbé, C. 2021.

“Paget's disease (PD) denotes an initially intra-epidermal adenocarcinoma that can later invade the dermis and metastasise. Among the extramammary forms of PD (EMPD), penoscrotal presentations are rarer than the vulvar and perianal forms. Once diagnosis has been confirmed by histopathological examination, a search for associated neoplasia must be conducted, although penoscrotal EMPD is less frequently associated with underlying neoplasia than mammary PD (MPD). The associated cancer most often involves a neighbouring organ, with prostate cancer being the most common, or in some cases consists of underlying cutaneous adnexal tumours. First-line therapy consists of surgical excision. Alternatives to surgery (imiquimod, CO₂ laser vaporisation, dynamic phototherapy) may be considered in certain cases.”

Ishizuki, S. & Nakamura, Y. 2021.

“Extramammary Paget's disease (EMPD) is a rare neoplasm that usually develops in apocrine gland-bearing areas, such as the vulva, scrotum, and penis. EMPD may present with a focal, multifocal, or an ectopic lesion. Clinically, EMPD lesions often exhibit infiltrative erythema, which is sometimes similar to other skin disorders such as eczema. While primary EMPD arises as intraepithelial neoplasm of the epidermis, EMPD-like lesions may occur from epidermotropic spread of malignant cells or direct extension from an underlying internal neoplasm, known as secondary EMPD. Because treatment strategies differ for primary EMPD and secondary EMPD, accurate diagnosis based on detailed histopathological evaluation is required. In the early stages, EMPD usually shows indolent growth, and most cases are diagnosed as carcinoma *in situ*. However, invasive lesions may result in metastases, and deep invasion is associated with high incidence of metastases. Conventional chemotherapies have been used for EMPD treatment in patients with distant metastases, but the efficacy is not satisfactory, and the prognosis for such patients remains poor. Recent studies have provided various insights into the molecular pathogenesis of the development and advancement of EMPD, which may lead to novel treatment approaches for metastatic EMPD. This review addresses the diagnosis, pathogenesis, and treatment of EMPD with focus on recent progress in understanding this disease.”

Zhao, D., Wen, B.P. & Xu, S.Y. 2021.

“Extramammary Paget's disease (EMPD) is an uncommon intraepithelial malignancy that is rarely found in the male. Currently, there is very little knowledge pertaining to EMPD imaging, particularly in cases that involve the scrotum. Here, a 67-year-old man with lichenification on his left scrotum confirmed to be EMPD was reviewed. Bloodwork did not return a positive result, but syphilis-specific antibodies were found. Conventional high-frequency ultrasound (US) and contrast-enhanced ultrasound (CEUS) imaging were utilized to determine the lesion size and blood perfusion. In the

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

Page 2

present case, the lesion's size and involvement were vividly depicted by CEUS, while results obtained by conventional US were grossly underestimated. Consequently, multimodal imaging assessment is likely to provide more accurate diagnoses for uncommon diseases, such as EMPD, and to aid in clinical decision-making.”

Incidence of Paget’s Disease of the Scrotum in South Africa

The outdated National Cancer Registry (2019) does not provide any information on the incidence of Paget’s Disease of the Scrotum in South Africa.

Risk Factors for Paget’s Disease of the Scrotum

Risk factors associated with Paget’s Disease of the Scrotum are:

- Advanced age
- Exposure to radiation
- Obesity
- Alcohol Consumption
- Smoking
- Race: being Caucasian

Having a risk factor does not mean that one will get the condition. A risk factor increases ones chances of getting a condition compared to an individual without the risk factors.

Also, not having a risk factor does not mean that an individual will not get the condition. It is always important to discuss the effect of risk factors with one’s healthcare provider.

Diagnosis of Paget’s Disease of the Scrotum

Symptoms are not specific - most patients report itching, burning, and soreness. A small subset of patients may be asymptomatic. Presence of pain, bleeding, and tumour formation are reported to be more common in patients affected by invasive disease. Signs and symptoms are skin lesions, often mistaken as eczema, that may be itchy or painful.

Extramammary Paget’s Disease (EMPD) typically presents in elderly white patients as a pruritic (itchy) white or red patch in the area of distribution of apocrine glands. Typically it affects a single site. However, Japanese investigators have documented triple lesions involving the anogenital regions and axilla simultaneously

Excision biopsy will confirm the diagnosis.

Reducing the Risk for Paget’s Disease of the Scrotum

Since the exact cause of Paget’s Disease of the Scrotum is not known, no preventive methods have thus far been reported for this condition. Nevertheless, maintaining a healthy lifestyle could help one avoid/delay the onset of disease.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

The following tips might be helpful:

- Maintaining healthy lifestyle habits
- Leading an active life
- Eating a healthy diet
- Limiting alcohol and smoking

Management of Paget's Disease of the Scrotum

Extramammary Paget's Disease (EMPD) is associated with concurrent visceral malignancy in 12% to 50% of cases. The frequency and site of associated malignancies differ in various anatomic locations. The location of the EMPD predicts the underlying malignancy.

Vulvar and scrotal Paget's disease are often associated with gastrointestinal malignancies, especially of the colon and rectum. This strong correlation between the presence of EMPD and underlying malignancy warrants lifelong endoscopic and radiographic evaluation to exclude this possibility.

EMPD that has well-defined margins with or without underlying adenocarcinoma is treated with wide local excision. Recurrence rates of 15% to 50% have been described, depending upon the site and type of resection.

[Picture Credit: Surgery for Scrotal Paget's Disease]



Newer primary and adjuvant strategies for preventing recurrences are MMS, radiation, chemotherapy, CO₂ laser ablation and photodynamic therapy. Although local wide excision, MMS or chemoradiation are effective when used alone for the treatment of noninvasive, well-defined unicentric lesions, none of these used alone is well suited for invasive, poorly defined, multicentric EMPD.

Noninvasive EMPD usually responds well to primary and adjuvant radiation therapy, whereas the invasive type is poorly controlled with radiation therapy alone, with a 50% recurrence. As adjuvant therapy, radiation was effective in both types of lesions.

Chemotherapy remains controversial. Topical 5-FU application was effective for patients with scrotal and penile EMPD. Systemic chemotherapy using carboplatin, calcium folate and 5-FU has been found to be effective in patients with perineal EMPD.

Besides adjuvant therapy, other methods of obtaining better control rates include perioperative tumour mapping. The method involves using photodynamic substances such as fluorescein, which is taken up by EMPD cells preferentially to normal tissue. Besides ensuring completeness of excision, this method allows for conservation of uninvolved tissue leading to an optimal reconstructive result. (Chandawakar, *et al.*, 2003).

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The *South African National Clinical Trials Register* provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

Wang, D., Wang, P., Li, C., Zhou, Z., Zhang, L., Zhang, G. & Wang, X. 2022.

Background: Extramammary Paget's Disease (EMPD) is an intraepithelial cancer that is prone to recurrence and sometimes refractory to therapy. A few EMPD cases have been treated with Photodynamic therapy (PDT), which reported high complete remission (CR) rates and low recurrence with hematoporphyrin derivatives (HpD) The aim of this study was to further explore the efficacy and safety of HpD-PDT for EMPD patients.

Methods: Open-label, single arm, pilot study was designed to investigate the role of HpD-PDT in EMPD. The HpD sensitizer was given intravenously at a dose of 3 or 5 mg/kg 48 h before light irradiation with a laser 630 nm red light at a dose level of 150-200 J/cm². Clinical parameters involving gender, age, disease course, previous treatment, tumor thickness, long diameter of lesion, TNM staging, EMPD staging, HpD dosage, Visual Analogue Scale (VAS) score, 1st month visit result, subsequent treatment, follow up period and endpoint outcomes were collected to evaluate efficacy and safety of the intervention.

Results: Eleven patients with pathologic confirmed EMPD were treated with HpD-PDT. The thickness of skin lesions which were located in vulva, penis, scrotum, and perianal area is 0.8~6.7 mm (mean thickness 2.9 mm). All patients were followed up for an average of 17.4 months (12~27 months). Complete remission (CR) rate and partial remission (PR) rate at the 1st month were 90.1% (10/11) and 9.1% (1/11) respectively. At the end of follow-up, 72.7% of the subjects (8/11) showed CR. Pain, infection, photosensitivity and uroschisis are recorded as adverse events (AEs) in this population, and no event of hepatic impairment was reported. After treatment, all the eleven patients showed different degrees of scar in the treatment site, but none of them had any structural or functional abnormalities.

Conclusions: According to our study, HpD-PDT in EMPD is able to offer acceptable disease outcomes including relatively high CR rate, with good cosmetic and functional outcomes, and could be considered a potential recommended therapy for patients with EMPD.

Trial registration: Chinese Clinical Trial Register (ChiCTR-1900024965).

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst CANSA has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

International Support Group for Paget's Disease of the Scrotum

An international support group can be contacted at the following URL:

<https://www.myempd.com/contact/>



Sources and References Consulted or Utilised

Al-Obaidy, K.I., Kao, C.S. & Idrees, M.T. 2018. P16 Expression in Extramammary Paget's Disease of the Vulva and Scrotum Is Not Human Papillomavirus Related. *Int J Surg Pathol.* 2018 Oct;26(7):617-620. doi: 10.1177/1066896918775513. Epub 2018 May 10.

Barth, P., Dulaimi, Al-Saleem, E., Edwards, K.W., Millis, S.Z., Wong, Y.N. & Geynisman, D.M. 2015. Metastatic Extramammary Paget's Disease of Scrotum Responds Completely to Single Agent Trastuzumab in a Hemodialysis Patient: Case Report, Molecular Profiling and Brief Review of the Literature. *Case Rep Oncol Med.* 2015;2015:895151. doi: 10.1155/2015/895151. Epub 2015 Jan 27.

Chandawakar, R.Y., Ricchuiti, D., Amjad, I., Maarsico, R.E. (Jn), & Wells, M.D. 2003. Extramammary Paget's disease of the perineum: avoiding pitfalls in diagnosis and management. *Can J Plast Surg.* 2003 Winter, 11(4):205-208.

Chen, Q., Chen, B.Y., Wang, Z., Cai, Z.K., Peng, Y.B., Zheng, C.D., Ma, L.M., Yao, H.J. & Zhou, J. 2013. Penoscrotal extramammary Paget's disease: surgical techniques and follow-up experiences with thirty patients. *Asian J Androl.* 2013 Jul;15(4):508-12. doi: 10.1038/aja.2013.27. Epub 2013 May 20.

Chung, P.H., Leong, J.Y. & Voelzke, B.B. 2019. Surgical experience with genital and perineal extramammary Paget's disease. *Urology.* 2019 Jun;128:90-95. doi: 10.1016/j.urology.2019.03.006. Epub 2019 Mar 19.

Dauendorffer, J.N., Herms, F., Baroudjian, B., Basset-Seguin, N., Cavalier-Balloy, B., Fouéré, S., Bagot, M. & Lebbé, C. 2021. Penoscrotal Paget's disease. *Ann Dermatol Venerol.* 2021 Jan 15;S0151-9638(20)31154-6.

DoveMed

<http://www.dovemed.com/diseases-conditions/pagets-disease-scrotum/>

Genitalia

<https://www.quora.com/What-is-the-use-of-underwear>

Guerr, R. & Misra, S. 2013. Management of Extramammary Paget's Disease: A Case Report and Review of the Literature. *Case Rep Dermatol Med.* 2013;2013:436390. doi: 10.1155/2013/436390. Epub 2013 Nov 14.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

Han, H., Niu, Y.N., Lei, H.E., Zhang, X.D., Zhou, X.G. & Tian L. 2020. The surgical treatment of male perineum Paget's disease. *Zhonghua Yi Xue Za Zhi*. 2020 Jun 9;100(22):1711-1714.

Healthline

<https://www.healthline.com/human-body-maps/male-genitalia>

Hu, J., Ge, W., Mao, S., Ding, Q., Hu, M. & Jiang, H. 2020. First time versus recurrent penoscrotal extramammary Paget's disease: clinicopathological characteristics and risk factors in 164 Chinese male patients. *Indian J Dermatol Venereol Leprol*. 2020 Mar-Apr;86(2):134-140. doi: 10.4103/ijdvl.IJDVL_382_18.

Ishizuki, S. & Nakamura, Y. 2021. Extramammary Paget's Disease: Diagnosis, Pathogenesis, and Treatment with Focus on Recent Developments. *Curr Oncol*. 2021 Aug 5;28(4):2969-2986.

Juel, J., Røge, R., Petersen, A., Langkilde, N.C. & Kloster, B.O. 2014. Scrotal Paget's disease. *Ugeskr Laeger*. 2014 Apr 7;176(15). pii: V12130714.

Kang, Z., Zhang, Q., Zhang, Q., Li X., Hu, T., Xu, X., Wu, Z., Zhang, X., Wang, H., Xu, J., Xu, F. & Guan, M. 2015. Clinical and pathological characteristics of extramammary Paget's disease: report of 246 Chinese male patients. *Int J Clin Exp Pathol*. 2015 Oct 1;8(10):13233-40. eCollection 2015.

Kruse, C., Day, D. & Lang, C. 2019. Extramammary Paget's disease can easily be overlooked. *Ugeskr Laeger*. 2019 May 27;181(22):V01190035.

Lee, G.C., Kunitake, H., Stafford, C., Bordeianou, L.G. Francome, T.D. & Ricciardi, R. 2019. High risk of proximal and local neoplasms in 2206 patients with anogenital extramammary Paget's disease. *Dis Colon Rectum*. 2019 Nov;62(11):1283-1293. doi: 10.1097/DCR.0000000000001487.

Lopes Eilho, L.L., Lopes, I.M., Lopes, L.R., Enokihara, M.M., Michalany, A.O. & Matsunaga, N. 2015. Mammary and extramammary Paget's disease. *An Bras Dermatol*. 2015 Mar-Apr;90(2):225-31. doi: 10.1590/abd1806-4841.20153189.

Meng, F., Py, Y., Chen, Z., Cen, Y. & Chen, J. 2017. Comparison of wide local excision and radical excision for Paget's disease involving the penis and scrotum. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi*. 2017 Jun 1;31(6):714-717. doi: 10.7507/1002-1892.201701070.

Paget's Disease of the Scrotum

<http://www.pathologyoutlines.com/topic/penscrotumpagets.html>

Pathology Outlines

<http://www.pathologyoutlines.com/topic/penscrotumpagets.html>

Phyo, A.K., Mun, K-S., Kwan, K.C., Ann, C.C. & Kuppusamy, S. 2020. Genitourinary extramammary Paget's disease: review and outcome in a multidisciplinary setting. *Int J Clin Exp Pathol*. 2020 Sep 1;13(9):2369-2376. eCollection 2020.

Piras, A., Sanfratello, A., Boldrini, L., La Vecchia, M., Venuti, V., Amari, M.L., Orlando, M., Zichichi, L., Angileri, T. & Daidone, A. 2020. Paget's disease of scrotum and penis case report of a re-irradiation and review of the literature. *Dermatol Ther*. 2020 Nov;33(6):e13890.

ScienceDirect

<http://www.sciencedirect.com/science/article/pii/S1726490111001638>

Surgery for Scrotal Paget's Disease

<http://www.sciencedirect.com/science/article/pii/S0090429508004822>

Wang, D., Wang, P., Li, C., Zhou, Z., Zhang, L., Zhang, G. & Wang, X. 2022. Efficacy and safety of HpD-PDT for Extramammary Paget's Disease refractory to conventional therapy: A prospective, open-label and single arm pilot study. *Photodiagnosis Photodyn Ther*. 2022 Mar;37:102670.

Wikipedia

https://en.wikipedia.org/wiki/Extramammary_Paget%27s_disease

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

Page 7

Zhang, J., Zhang, J., Zhang, J., Xiao, X., Su, Z., Liu, M. & Liang, W. 2020. Experiences with Surgical Reconstruction of Penoscrotal Extramammary Paget's Disease: A review of 21 cases. *J Plast Reconstr Aesthet Surg.* 2020 Sep;73(9):1700-1705.

Zhao, D., Wen, B.P. & Xu, S.Y. 2021. Extramammary Paget's Disease in the Genital Area of a Male: A Case Report and Review of the Literature. *Front Oncol.* 2021 Nov 4;11:713786.

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

April 2022

Page 8