Review article

Neurobiology and neuroplasticity of the prepuce

Neurobiología y neuroplasticidad del prepucio

Martín Donnet Oloarte-Flores,[1] José Manuel Viveros-Elías,[2] Yolanda Cruz-Gómez.[1*]

Abstract

The male prepuce is the skin that covers and protects the glans. This structure has been underestimated, stigmatized and even ablated for non-medical reasons. The main aim of this review is to summarize existing literature on male prepuce neurobiology and secondary to it, to discuss the potential effect of circumcision and the associated axotomy on neuroplasticity and male urogenital physiology. It was found that the prepuce ontogeny and innervation include prenatal and postnatal development. Since its separation from the glans penis is androgen dependent, the physiological phimosis at birth is resolved during childhood and adolescence. In contrast to the glans penis, the prepuce is innervated by a dense network of corpuscular sensory receptors, specialized nerve endings that are essential for the perception of various tactile sensations, including light touch, pressure, vibration, and stretch. Thus, the foreskin is a specialized sensory tissue, with potential roles in sexual perception and modulation of genital reflexes. Its ablation may induce peripheral and central neural reorganization, but little is known about the neuroplasticity associated with genital nerve axotomy. Preclinical research will allow elucidating the mechanisms and their long-term implications, understanding these aspects is essential for interpreting clinical findings.

Keywords:
Circumcision, foreskin, prepuce innervation, foreskin physiology, neuroplasticity

Citation: Oloarte-Flores M. D., Viveros-Elías J. M., Cruz-Gómez Y. *Neurobiology and neuroplasticity of the prepuce. Rev Mex Urol. 2026;86(4)*:1-15.

Corresponding author:
*Yolanda Cruz Gómez.
Address: Carretera Federal Tlaxcala-Puebla Km 1.5, C.P. 90070, Tlaxcala, México. Email: cruzgomezy@yahoo.com.mx

[1.] Universidad Autónoma de Tlaxcala, Tlaxcala, México.
[2.] Urología Integral, La Paz, Baja California Sur, México.

Recived: January 29, 2026
Accepted: July 29, 2026

Resumen

El prepucio masculino es la piel que cubre y protege al glande. Esta estructura ha sido subestimada, estigmatizada e incluso extirpada por razones no médicas. El objetivo principal de esta revisión es resumir la literatura actual sobre la neurobiología del prepucio, y de manera secundaria discutir el efecto potencial de la circuncisión y la axotomía asociada sobre la neuroplasticidad y la fisiología urogenital masculina. La ontogenia e inervación del prepucio incluyen desarrollo prenatal y posnatal, con fimosis fisiológica al nacimiento. La separación del glande es dependiente de andrógenos y ocurre durante la infancia y la adolescencia. A diferencia del glande, el prepucio está inervado por una densa red de receptores sensoriales corpusculares, terminaciones nerviosas especializadas esenciales para la percepción de diversas sensaciones táctiles, como el tacto ligero, la presión, la vibración y el estiramiento. Por lo tanto, el prepucio es un tejido sensorial especializado, con posibles funciones en la percepción sexual y la modulación de reflejos genitales. Su ablación puede inducir una reorganización neural periférica y central, pero poco se sabe sobre la neuroplasticidad asociada a la axotomía de nervios genitales. Investigaciones preclínicas permitirán dilucidar los mecanismos neuroplásticos y sus implicaciones a largo plazo, así como interpretar los hallazgos clínicos.

Palabras clave: Circuncisión, inervación del prepucio, fisiología del prepucio, neuroplasticidad

Introduction

During sexual intercourse, the penis reaches the vaginocervical tract and ejaculates semen. While this physiological process is crucial for human reproduction, this event is mostly driven due to the associated rewarding pleasure resulting from it, especially during orgasm.[1]

Male sexual pleasure relies on an intricate neural network of peripheral nerves, spinal neurons and supraspinal pathways; sensory innervation of the penis is crucial.[1] However, there is little information in the literature about sensory innervation and contribution of one component of the penis, the prepuce. This structure that has been underestimated and even ablated for non-medical reasons.

The main aim of this review is to summarize existing literature on male prepuce neurobiology and secondary to it, to discuss the potential effect of circumcision and the associated axotomy on neuroplasticity and male sexual and urinary physiology.

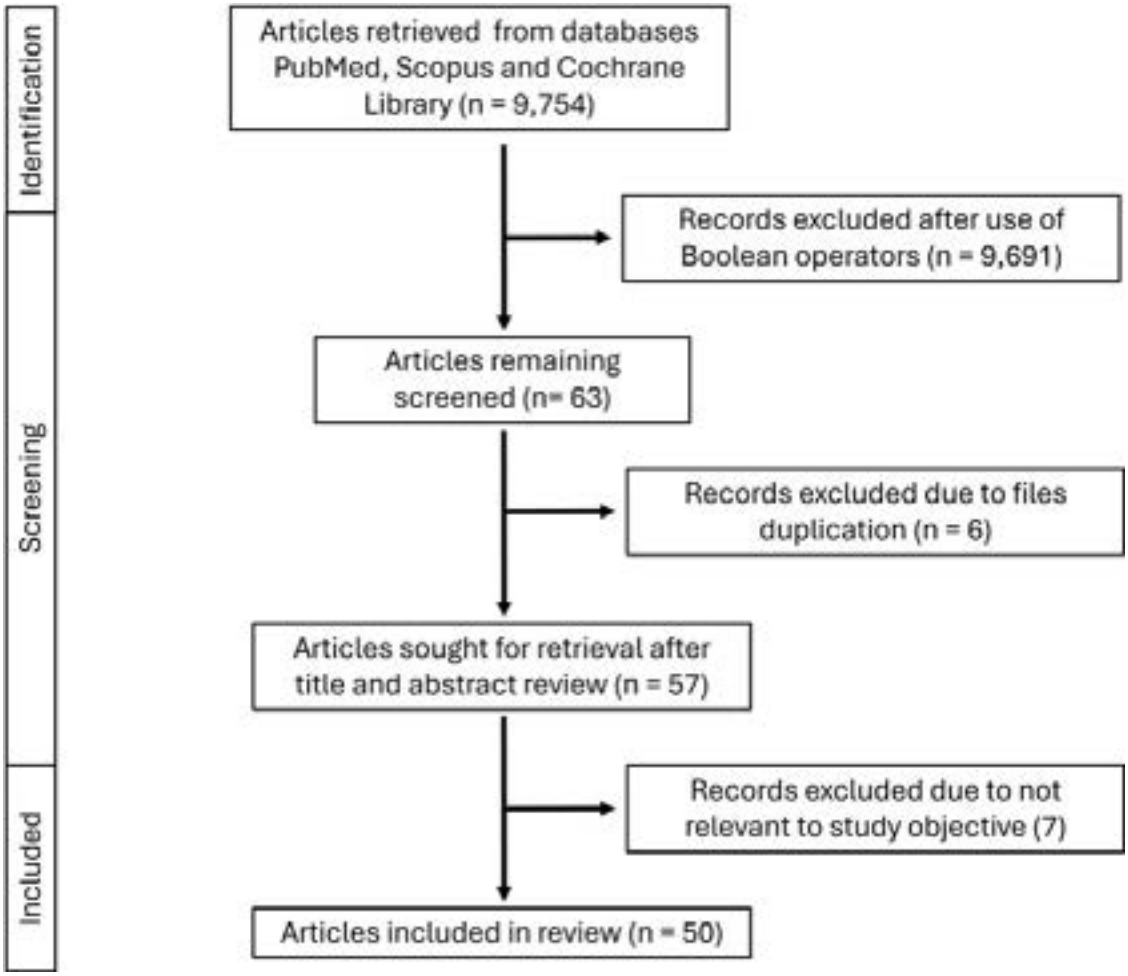
Search strategy and selection criteria

A literature review was conducted using the electronic databases PubMed, Scopus and Cochrane Library. The search included publications available from the first records indexed in each database up to December 2025. The initial search was broad and combined synonymous terms related to the structure of interest: “Human male prepuce” OR “human male foreskin”. Subsequently, advanced search was performed by adding the Boolean operator AND to refine the results according to specific thematic areas (neurobiology, embryology, anatomy, histology, physiology, sexual function, sensory innervation, neuroplasticity or circumcision). Additionally, animal models of male prepuce or male foreskin reflexes, development and mechanisms of neuroplasticity associated to sensory nerve axotomy were reviewed.

Inclusion and exclusion

Studies in both humans and experimental animals providing relevant evidence for understanding the structure and/or function of the foreskin were included. Eligibility criteria included original research articles and review articles published in peer-reviewed journals, available in English or Spanish, directly related to the aims of this review. Publications focused exclusively on surgical techniques, studies addressing unrelated urogenital structures, conference abstracts, editorials, letters to the editor, duplicate records, and manuscripts lacking sufficient methodological information were excluded. Titles and abstracts were initially reviewed for relevance, followed by a full-text evaluation of potentially eligible studies (Figure 1).

Figure 1. PRISMA flow diagram for the review detailing the database searches, the number of articles screened and the full texts retrieved



Anatomy and development

In adult mammals, the prepuce is a continuation of the skin of the penile stem, is a retractable skin that covers the glans and urinary meatus when the penis is in the flaccid state.[2] In humans, it is a double layered fold of skin, with a rigged band of mucous membrane lining the tip of the prepuce, when it is not retracted. The ridged band merges into the frenulum penis.[2] The frenulum is found underside of the penis, where the prepuce intersects with the glans.[2]

The prepuce is made up of five tissular layers: an inner mucosal epithelium, a vascular lamina propria, the dartos muscle, a collagen-rich dermis, and an outer glabrous epidermis.[3]

The inner squamous mucosal epithelium is in direct contact with the glans. It presents as a variably keratinized squamous surface that is histologically continuous with the glans epithelium and lacks structures such as hair follicles, sweat glands, or sebaceous glands.[3]

The lamina propria is composed of loose connective tissue rich in capillaries and small vessels, a structural arrangement that provides mucosal mobility and meets the metabolic demands of the epithelium.[3]

The dartos muscle consists of a specialized sheet of smooth muscle fibers. This contributes to penile thermoregulation and volumetric adjustments during erection.[3]

The dermis layer is next to the dartos muscle, forming a compartment of connective tissue rich in collagen and elastin with larger blood vessels, nerve bundles, and mechanoreceptors, including Meissner's corpuscles and Pacinian corpuscles.[3]

The outer surface (epidermis) is covered by keratinized glabrous epithelium containing melanocytes, Langerhans cells, and Merkel cells, typical features of skin tissue.[3]

Prepuce formation is directly related to the formation of the glans and penile urethra. Prepuce ontogeny includes prenatal development and postnatal maturation and separation.[4] Human embryonic development starts at 11-12 weeks and ends around 18 weeks. At the 12th week post-conception, the prepuce extends over the coronal sulcus and the base of the penis. At this stage, the frenulum has not yet formed, leaving the urethral lumen partially exposed. During the 16th week post-conception, the foreskin almost completely covers the glans, and a nascent frenulum is visible. Between the 18th and 19th weeks post-conception, the foreskin is fully developed; the preputial folds have completely fused along the ventral surface of the penis, enveloping the urethra and forming the definitive frenulum.[4]

Physiological phimosis

Normal foreskin development implies *physiological phimosis*. At birth the glans penis and the inner preputial mucosa remain fused, sharing a common epithelial layer (physiological phimosis). Prepuce separation occurs progressively, by accumulation of smegma, epithelial desquamation, keratin pearl formation, and mechanical factors, such as intermittent erections.[5] This is resolved during childhood and often completed by puberty. Thus, preputial separation from the glans increases with age, progressing rapidly in adolescence.[6] Normally, the foreskin can be completely retracted in around 70 % of ten-year-old boys, 84 % of 13-years old boy and 99 % of 17-year-olds. When complete prepuce separation does not occur at puberty

the *phimosis is considered* pathological (secondary phimosis).[7]

It is proposed that prepuce separation is gonadal hormone dependent.[2] The theory that gonadal hormones play a role in the separation of the glans and foreskin is supported in preclinical studies.[8] In rats, preputial separation occurs at 39-45 postnatal days, when circulating androgen levels increase significantly, and is blocked by castration.[8]

Pathological phimosis is described as a non-retractable foreskin that can arise due to acquired lack of elasticity of the foreskin, secondary to forceful retractions, chronic inflammation and subsequent scarring, as well as due to balanitis xerotica obliterans.[7] It is a chronic and progressive inflammatory disease presented as a white, scaly, hyperkeratosis atrophic plaque or patch on the glans or foreskin.[7] When secondary phimosis occurs, topical steroids with gentle foreskin retraction may be applied or, in persistent cases, circumcision.[2]

Neural pathways

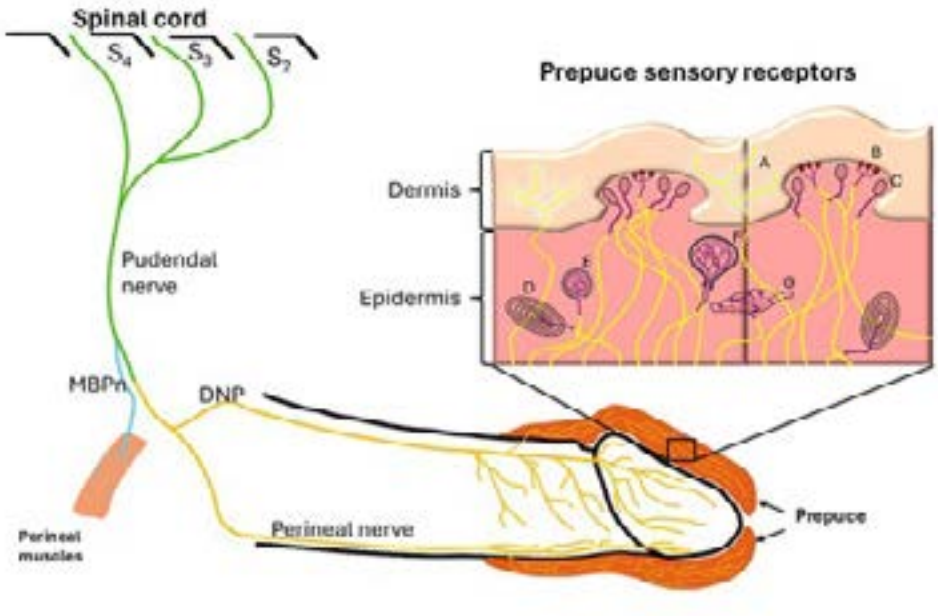
Penile and prepuce innervation is identifiable as early as gestational week.[9] Neural fibers of the dorsal nerve of the penis enter the proximal glans and progressively extend distally over the following weeks, reaching the distal glans and prepuce between gestational weeks 14 and 16.[9]

Postnatal maturation of preputial innervation is age dependent. In general, the number of nerves, vessels, and collagen fibers increase with age.[10] In children under three years old, the neurovascular bundles remain loosely organized within the deep dermis and run parallel to the epidermal basement membrane.[10] Compared to children 6 to 11 years old, prepuce innervation under 3 years old is characterized by markedly reduced sensory innervation, including free nerve endings and few corpuscular receptors (Meissner's and Pacini's corpuscles, Ruffini endings), and small diameter blood vessels.[10] In adulthood, prepuce has a lot of Meissner corpuscles which are regularly distributed in the dermal papillae, reflecting the progressive maturation of the preputial innervation.[11,12] The mechanosensory innervation of the human foreskin reaches its maximum value around the age of 20, remains stable during adulthood and decreases with maturity.[13]

Sensory receptors

In adults, the prepuce is highly innervated and presents different sensory receptors at the dermal and epidermal levels such as free nerve endings and specialized capsulated mechanoreceptors (Meissner's corpuscles, Pacinian corpuscles, Ruffini endings and Merkel cells) (Figura 2).[12]

Figure 2. Drawing of the innervation of the human prepuce



A sagittal view of the penis is shown. Amplification of the black square illustrates encapsulated sensory receptors (A, free nerve endings; B Merkel disk; C, Meisner corpuscular; D, Pacini corpuscular; E bulbs of Krause; F, Genital receptor and G, Ruffini receptor) within the skin layers. Note that the pudendal nerve carries sensory (yellow) and motor components (blue). S_2, S_3, S_4, sacral spinal nerves; MBPn, motor branch of the pudendal nerve; DNP; dorsal nerve of the penis.

These receptors transduce physical stimuli into electrical signals to bring sensory information to central nervous system through sensory neurons.[12,13] General anatomical and physiological characteristics of sensory receptors are as follows:

Free nerve endings are simple axon terminals. Sensory axons progressively lose their myelin sheath as they approach the epithelium and branch into numerous short varicose fibers that terminate as flattened or slightly expanded discs between epithelial cells, forming the anatomical substrate for nociception and thermal sensitivity.[14]

Merkel cell endings mediate slowly adapting fine touch discrimination. They are in the basal epidermis forming "tactile domes", each one innervated by single or several myelinated afferent fibers that branch before ending.[15] The terminal axon forms a biconvex tactile disc situated between two or more semilunar sustentacular cells, all enclosed within a connective capsule continuous with the Henle sheath.[14]

Meissner's corpuscles are oval-shaped encapsulated structures situated at the apex of dermal papillae in glabrous and mucocutaneous skin. These receptors are rapidly adapting mechanoreceptors for low frequency dynamic touch. Meissner's corpuscles contain intertwined and unmyelinated branches running through stacks of lamellar Schwann derived cells which maintain close membrane associations with the axon endings.[16]

Pacinian corpuscles detect high-frequency vibrations and are in the deep dermis or subcutaneous tissue. They consist of a central axon terminal surrounded by numerous concentric lamellae that form an onion-shaped capsule, allowing for rapid adaptation and transmission of vibratory stimuli. Handler and Ginty highlight the unique three-dimensional lamellar architecture, essential for its frequency-dependent responsiveness, and emphasize that the mechanotransduction mechanisms within these lamellae remain partially unresolved.[14–16]

Ruffini endings are slowly adapting mechanoreceptors specialized in detecting skin stretches and lateral tension. They are elongated, spindle-shaped structures located in the dermis, composed of a collagen-rich capsule through which the terminal branches of the axon intertwine.[15]

Although the prepuce contains all the above-described sensory receptors, Meissner's corpuscles are the most abundant in all layers, except the outer epithelium, where Merkel cells predominate.[12]

Nerves

Axons of prepuce primary afferent neurons are carried out by branches of the pudendal nerve, which originates from S2-S4,[17] primarily by branches of the dorsal nerve of the penis (DNP) along with the perineal nerve. The latter supplies the frenular and distal ventral foreskin.[2]

Prepuce dual somatic input indicates an intricate innervation that has implications for neurophysiological interpretation and perioperative anesthesia[18]. Thus, effective anesthesia of the penis requires injection of at least three regions: base, dorsal and ventral regions.[18]

In humans and rodents, the sensory fibers are distributed throughout the superficial and deep layers of the prepuce.[19,20] In men, the DNP fibers are asymmetrically distributed, with increased nerve density near the frenulum, ventral and around the dorsal coronal sulcus.[21] At the ridged band, a high concentration of Meissner's corpuscles and nerve fibers has been described, making this region one of the most specialized sensory zones of the male genitalia[11]. This pattern of innervation aligns with the high sensitivity reported at the mucocutaneous junction and the ridged band and positive fibers to peptides such as substance P (SP) and calcitonin gene-related peptide (CGRP).[22,23] These peptides play an important role in regulation of penile erection, pain and touch sensitive, as well as in processing tactile and nociceptive stimuli.[23]

Dorsal root ganglia

In humans, the primary sensory neurons project prepuce information to sacral spinal segments. Spinal and supraspinal neural pathways of the prepuce have not been unveiled.[24]

In rodents, afferent innervation to the prepuce is supplied by the sensory branch of the pudendal nerve (SBPdn), mechanical stimulation evoked robust afferent discharges in this nerve.[20] Action potentials travel through the pudendal nerve, which emerges from L6-S1 spinal segments. Blue Evans staining method suggests that L3, L4 and L5 also give some sensory fibers.[25] However, these results need to be corroborated by electrophysiological techniques.

The sensory information of rodent prepuce projects to the medulla oblongata, and from

there to the gracile nucleus.[26] Mechanical stimulation of the penis recruit neurons of this nucleus. Interestingly, 47 % of the neurons responding to penile stimulation also responded to preputial stimulation, indicating penis-prepuce central sensory convergence, and a possible role in the coding of genital pleasure.[26]

Physiology of the prepuce

In many anatomical textbooks the prepuce is minimized, often described merely as a fold of skin with covering functions; protecting the glans physically from irritative fluids such as urine (neonates and babies) and other chemicals of physical injuries.

In addition to the physical function, the prepuce dense innervation and richness in encapsulated receptors, especially at the ridged bands of the prepuce, indicate that the foreskin executes neurophysiological function as specialized tactile sensory tissue.[22,27] The presence in the prepuce of mechanoreceptors such as Meissner's, Pacinian, and Ruffini corpuscles indicate an active role in fine touch, nociceptive, and potentially erotic perception.[12] Considering that the prepuce is not a homogeneous sensory tissue, its regions with different sensory thresholds may be relevant but especially the most sensitive region, the ridged band and mucosal region, a zone densely populated by Meissner's corpuscles and free nerve endings.[22]

Prepuce sensory information may be highly relevant in erogenous perception during sexual intercourse, especially considering that its pattern of innervation contrasts sharply with the protophatic innervation of the glans penis, which is characterized of high free terminal endings with few corpuscular receptors, this enables the skin to discriminate relatively coarse stimuli as heat cold, and pain but is insensitive to fine touch.[27]

The prepuce and penis also participate in triggering somato-somatic pudendal reflexes such as contraction of perineal muscles (bulbospongiosus or ischiocavernosus), in response to brisk compression of the glans penis. Elicitation of this reflex is reduced in circumcised men.[28] In rats, preputial mechanical stimulation also induces reflex activity of the external urethral sphincter.[29] Reflex activity of these muscles may contribute to expelling urine or semen during micturition and ejaculation, respectively.

Another function of the prepuce is as an immunological defense barrier. Preputial mucosal surface provides substances such as lysozyme, chymotrypsin, neutrophil elastase, cytokines, histone B and androstenedione.[30] These secretions are part of the natural composition of the preputial microenvironment and contribute to the local immune response and lubrication of the glans. Epithelial Langerhans cells, a component of the immune system, are also present in the prepuce, being more abundant in the outer surface of neonatal prepuce comparable with adult skin.[31]

Circumcision and its potential effect on sexual function

Circumcision is the action of removing the foreskin for therapeutic or non-therapeutic reasons. It may be performed for medical reasons, in condition such as pathological phimosis, severe balanoposthitis, recurrent paraphimosis, congenital urological abnormalities, traumatic foreskin injury, persistent or recurrent urologi-

cal infections and as a treatment for a pre-malignant or malignant condition confined to the prepuce.[32]

Non-therapeutic, or elective circumcision refers to the surgical removal of part of or all the foreskin, in healthy males (babies, children and adults), where there is no medical condition requiring surgery. But this practice is still controversial.[33]

Some authors refer that elective circumcision has shown a decrease in the incidence of penile cancer, urinary tract infections in newborns, a decrease in the incidence of some sexually transmitted disease diseases, heterosexual HIV infection, as well as preventing future complications (phimosis, paraphimosis etc.). It has been shown that 98 % of men diagnosed with penile cancers are uncircumcised, and urinary tract infections occurred in the first year mostly in uncircumcised infants.[34] It has also been indicated that it is more expensive to treat UTI's than to perform elective circumcision in neonates.[35,36] Thus, the American Academy of Pediatrics (APP) has issued an official policy statement reading: "*Evaluation of current evidence indicates that the health benefits of newborn male circumcision outweigh the risks; furthermore, the benefits of newborn male circumcision justify access to this procedure for families who choose it*".[33] But it is important to highlight the small risks of elective circumcision and their prevalence (0.2-5 %,).[37,38] The most common complications are bleeding, infection and penile injury in the immediate postoperative period, and meatal stenosis, penile entrapment, excess or shortage of skin, penile curvature, torsion or inclusion cysts, in the later postoperative period.[37,38]

On the other side, some authors indicate that neonatal circumcision immediately compromises the immune system, making the circumcised male neonate vulnerable to infection, often with avoidable harm and even occasional deaths.[38] The AAP acknowledges in its technical report: "*The true incidence of complications after newborn circumcision is unknown*".[38] In addition, resection of the prepuce neither inhibits risky sexual behavior nor confers immunity after exposure to pathogens and there has not been shown a significant positive association between *infant* circumcision and a lower risk of heterosexually transmitted HIV.[38] In several countries circumcised men had a significantly higher prevalence of HIV than men who were not circumcised, and responsible use of condoms, regardless of circumcision status, will provide close to 100 % reduction in risk for any STD".[38] The Royal Dutch Medical Association, the Danish Medical Association and the Canadian Pediatric Society consider that the benefits, compared to the alternatives and potential risks of the procedure, do not show enough weight to consider it as a preventive measure in newborns due to a balanced benefit-risk ratio.[33,38] For example, since the risk of developing a urinary tract infection in newborns and infants is 0.5-1 % in the first year, it has been estimated that 111 healthy males need to be circumcised to prevent 1 UTI.[39] Thus, some authors conclude that, based on UTI prevention, neonatal circumcision cannot be justified, except for male infants with recurrent UTI and high-grade vesico-ureteric reflux, in which the circumcisions-needed-to-prevent urinary infections are 11 and 4, respectively.[39]

Sexual dysfunction?

The fact that the prepuce is a densely innervated structure,[40] with richness in encapsulated receptors, especially in the ridged band, brings the question about the effect of its on sexual function. Histological evidence indicates that circumcised men exhibit a reduction in penile skin area, loss of sensory receptors, surgical scarring and keratinization of the glans secondary to its permanent exposure.[41] These neuroanatomical modifications suggest consequences on erogenous perception during sexual intercourse.[2,41] However, since most circumcisions are performed during childhood, it is not possible to compare intrasubject changes in sexual perception associated with the circumcision, and functional alterations remain a matter of debate. Neurophysiological studies of fine-touch pressure thresholds of the adult penis in circumcised and uncircumcised men reveled that the glans of the uncircumcised men had significantly lower pressure thresholds than that of the circumcised men.[22] The authors concluded that the glans of the circumcised penis is less sensitive to fine touch than the glans of the uncircumcised penis.[22] Increased threshold of the penis cavernous reflex and reduced genital sensitivity, orgasmic intensity and sexual pleasure have also been reported.[28] Regarding sexual function and sensory perception, while some studies report adverse effects on sensitivity and sexual performance other finds no significant differences between circumcised and uncircumcised men.[33,41] One possible explanation for these contrasting findings is the ability of the nervous system to undergo plasticity. As occurs following others forms of peripheral axotomy, the loss of sensory afferents may trigger receptive field reorganization and synaptic remodeling at peripheral, spinal and cortical levels. Such compensatory mechanisms could attenuate or modify the subjective perception of anatomical changes, thereby generating considerable inter-individual variability in sensory and sexual outcomes following circumcision.

Neuroplasticity

The prepuce is innervated by two pudendal branches, DNP and perineal nerves, which carry primary sensory neurons that relay sensory information from prepuce tissue to the spinal cord.[21] These nerves are transected during circumcision. What neuroanatomical and neurophysiological neuroplasticity could result from this injury?

In animal models, neuroplasticity has been demonstrated after a peripheral nerve injury.[42]The specific mechanisms depend on the site of lesion.[43] Axotomy close to dorsal root ganglia results in chromatolysis, Wallerian degeneration and neuronal death, with loss of the receptive field of the primary afferent, and denervation of the target.[43] Over time, reinnervation of the denervated structure may occur through afferent neurons innervating close to the denervated site.[44] If the axotomy occurs close to the target, Wallerian degeneration is initiated, followed by regenerative processes. The initial response is a sealing of the cut ends of the axons, followed by orderly degenerative and phagocytic events in the segments lying distal and proximal to the lesion.[45] The cell body responds with morphological, physiological, and biochemical properties of the neuron to prepare the neuron for synthesizing proteins needed for formation of growth cones and regeneration of the axon.[44,45] Although recovery of

receptive field is guaranteed, unspecific or maladaptive reinnervation may occur, resulting in dysfunctional and painful sensation, as occur in phantom limb pain.[46,47] Neuropathic pain may also result from alteration in the physiology of dorsal root ganglia, neurons or glial cells,[48] in response to nerve injury. Satellite glial cells are glial cells that form an envelope surrounding each sensory neuron soma. These cells proliferate and enlarge in response to nerve injury,[49] changes that may contribute to chronic pain by augmenting neuronal activity. Additional changes occur at cortical levels; cortical topography changes have been described following deafferentation or limb amputation. [50]

Concluding remarks

The prepuce ontogeny and innervation include prenatal and postnatal development. In contrast to the glans penis, the prepuce is innervated by a dense network of corpuscular sensory receptors, specialized nerve endings that are essential for the perception of various tactile sensations, including light touch, pressure, vibration, and stretch. Thus, the foreskin represents a specialized sensory tissue, with potential roles in sexual perception and modulation of genital reflexes. Its ablation may induce peripheral and central neural reorganization, but little is known about the neuroplasticity associated with genital nerve axotomy. Preclinical research is needed to elucidate the underlying mechanisms and their long-term implications. Understanding these aspects is essential for interpreting clinical findings and guiding surgical decisions.

CRediT taxonomy

Martín Donnet Oloarte Flores: Search of literature, data curation, visualization and writing the draft.

José Manuel Viveros-Elías: Search of literature and writing, especially for the pathologies section, and revision and edition of the manuscript.

Yolanda Cruz Gómez: Conceptualization, search of literature, data curation, visualization, writing, revision and editing of the manuscript.

Aknowledgments

Posgrado en Ciencias Biológicas del Centro Tlaxcala de Biología de la Conducta (CTBC), Universidad Autónoma de Tlaxcala, México.

Conflict of interest

None.

Funding

Support from SECIHTI PhD scholarship 840356 (to MDOF).

References

1. **Azadzoi KM, Yang J, Siroky MB.** Neural regulation of sexual function in men. *World journal of clinical urology*. 2013;2(3): 32–41. https://doi.org/10.5410/wjcu.v2.i3.32.
2. **Cold CJ, Taylor JR. The prepuce.** *BJU international*.1999;83Suppl1:34–44.https://doi.org/10.1046/j.1464-410x.1999.0830s1034.x.

3. Fahmy MAB. *Normal and Abnormal Prepuce*. Cham: Springer International Publishing; 2020. https://doi.org/10.1007/978-3-030-37621-5. [Accessed 5th August 2026].
4. Favorito LA, Balassiano CM, Costa WS, Sampaio FJB. Development of the human foreskin during the fetal period. *Histology and Histopathology*. 2012;27(8): 1041–1045. https://doi.org/10.14670/HH-27.1041.
5. Kayaba H, Tamura H, Kitajima S, Fujiwara Y, Kato T, Kato T. Analysis of shape and retractability of the prepuce in 603 Japanese boys. *The Journal of Urology*. 1996;156(5): 1813–1815.
6. Ko MC, Liu CK, Lee WK, Jeng HS, Chiang HS, Li CY. Age-specific prevalence rates of phimosis and circumcision in Taiwanese boys. *Journal of the Formosan Medical Association = Taiwan Yi Zhi*. 2007;106(4): 302–307. https://doi.org/10.1016/S0929-6646(09)60256-4.
7. Clouston D, Hall A, Lawrentschuk N. Penile lichen sclerosus (balanitis xerotica obliterans). *BJU international*. 2011;108 Suppl 2: 14–19. https://doi.org/10.1111/j.1464-410X.2011.10699.x.
8. Korenbrot CC, Huhtaniemi IT, Weiner RI. Preputial separation as an external sign of pubertal development in the male rat. *Biology of Reproduction*. 1977;17(2): 298–303. https://doi.org/10.1095/biolreprod17.2.298.
9. Cunha GR, Sinclair A, Cao M, Baskin LS. Development of the human prepuce and its innervation. *Differentiation; Research in Biological Diversity*. 2020;111: 22–40. https://doi.org/10.1016/j.diff.2019.10.002.
10. Özdemir-Sancı T, Sancı A, Nakkaş H. Foreskin neurovascular structure: A histological analysis comparing 0–3 years and 6–11 years children. *Journal of Pediatric Urology*. 2024;20(4): 704.e1-704.e7. https://doi.org/10.1016/j.jpurol.2024.03.016.
11. Taylor JR, Lockwood AP, Taylor AJ. The prepuce: specialized mucosa of the penis and its loss to circumcision. *British Journal of Urology*. 1996;77(2): 291–295. https://doi.org/10.1046/j.1464-410x.1996.85023.x.
12. García-Mesa Y, García-Piqueras J, Cobo R, Martín-Cruces J, Suazo I, García-Suárez O, et al. Sensory innervation of the human male prepuce: Meissner's corpuscles predominate. *Journal of Anatomy*. 2021;239(4): 892–902. https://doi.org/10.1111/joa.13481.
13. Vega JA, Aiello V, Martín-Cruces J, Suazo I, Jones R, Musa W, et al. Sexual Mechanosensitivity: Age-Related Changes in the Innervation of the Human Prepuce. *Journal of Clinical Medicine*. 2025;14(13): 4730. https://doi.org/10.3390/jcm14134730.
14. Ramón y Cajal S. Terminaciones de la expansión periférica de las células ganglionares raquídeas. In: *Histología del Sistema Nervioso del Hombre y de los Vertebrados*. Boletín Oficial del Estado; 2012.
15. Willis WD, Coggeshall RE. *Sensory Mechanisms of the Spinal Cord: Volume 1: Primary Afferent Neurons and the Spinal Dorsal Horn Volume 2: Ascending Sensory Tracts and their Descending Control*. Boston, MA: Springer US; 2004. https://doi.org/10.1007/978-1-4615-0035-3. [Accessed 5th August 2026].
16. Handler A, Ginty DD. The mechanosensory neurons of touch and their mechanisms of activation. *Nature Reviews. Neuroscience*. 2021;22(9): 521–537. https://doi.org/10.1038/s41583-021-00489-x.
17. Shafik A, el-Sherif M, Youssef A, Olfat ES. Surgical anatomy of the pudendal nerve and its clinical implications. *Clinical Anatomy*. 1995;8(2): 110–115. https://doi.org/10.1002/ca.980080205.

18. **Long RM, McCartan D, Cullen I, Harmon D, Flood HD.** A preliminary study of the sensory distribution of the penile dorsal and ventral nerves: implications for effective penile block for circumcision. *BJU international*. 2010;105(11): 1576–1578. https://doi.org/10.1111/j.1464-410X.2009.09044.x.
19. **Winkelmann RK.** The cutaneous innervation of human newborn prepuce. *The Journal of Investigative Dermatology*. 1956;26(1): 53–67. https://doi.org/10.1038/jid.1956.5.
20. **Pastelín CF, Zempoalteca R, Pacheco P, Downie JW, Cruz Y.** Sensory and somatomotor components of the 'sensory branch' of the pudendal nerve in the male rat. *Brain Research*. 2008;1222: 149–155. https://doi.org/10.1016/j.brainres.2008.05.012.
21. **Yucel S, Baskin LS.** Identification of communicating branches among the dorsal, perineal and cavernous nerves of the penis. *The Journal of Urology*. 2003;170(1): 153–158. https://doi.org/10.1097/01.ju.0000072061.84121.7d.
22. **Sorrells ML, Snyder JL, Reiss MD, Eden C, Milos MF, Wilcox N, et al.** Fine-touch pressure thresholds in the adult penis. *BJU international*. 2007;99(4): 864–869. https://doi.org/10.1111/j.1464-410X.2006.06685.x.
23. **Wu ZM, Chen YF, Qiu PN, Ling SC.** Correlation between the distribution of SP and CGRP immunopositive neurons in dorsal root ganglia and the afferent sensation of preputial frenulum. *Anatomical Record*. 2011;294(3): 479–486. https://doi.org/10.1002/ar.21327.
24. **Weech D, Ameer MA, Ashurst JV.** Anatomy, Abdomen and Pelvis, Penis Dorsal Nerve. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2026. http://www.ncbi.nlm.nih.gov/books/NBK525966/ [Accessed 5th August 2026].
25. **Fang Y, Han S, Li X, Xie Y, Zhu B, Gao X, et al.** Cutaneous Hypersensitivity as an Indicator of Visceral Inflammation via C-Nociceptor Axon Bifurcation. *Neuroscience Bulletin*. 2020;37(1): 45–54. https://doi.org/10.1007/s12264-020-00577-5.
26. **Cothron KJ, Massey JM, Onifer SM, Hubscher CH.** Identification of penile inputs to the rat gracile nucleus. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*. 2008;294(3): R1015-1023. https://doi.org/10.1152/ajpregu.00656.2007.
27. **Cold CJ, McGrath KA.** Anatomy and Histology of the Penile and Clitoral Prepuce in Primates. In: Denniston GC, Hodges FM, Milos MF (eds) *Male and Female Circumcision*. Boston, MA: Springer US; 1999. p. 19–29. https://doi.org/10.1007/978-0-585-39937-9_3. [Accessed 5th August 2026].
28. **Podnar S. Clinical elicitation of the penilo-cavernosus reflex in circumcised men.** *BJU international*. 2012;109(4): 582–585. https://doi.org/10.1111/j.1464-410X.2011.10364.x.
29. **Juárez R, Zempoalteca R, Pacheco P, Lucio RA, Medel A, Cruz Y.** Activity of the external urethral sphincter evoked by genital stimulation in male rats. *Neurourology and Urodynamics*. 2016;35(8): 914–919. https://doi.org/10.1002/nau.22850.
30. **Fleiss PM, Hodges FM, Van Howe RS.** Immunological functions of the human prepuce. *Sexually Transmitted Infections*. 1998;74(5): 364–367. https://doi.org/10.1136/sti.74.5.364.
31. **Weiss GN, Sanders M, Westbrook KC.** The distribution and density of Langerhans cells in the human prepuce: site of a diminished immune response? *Israel Journal of Medical Sciences*. 1993;29(1): 42–43.
32. **Offenbacher J, Barbera A.** Penile Emergencies. *Emergency Medicine Clinics of North*

America. 2019;37(4): 583–592. https://doi.org/10.1016/j.emc.2019.07.001.

33. **Moreton S, Cox G, Sheldon M, Bailis SA, Klausner JD, Morris BJ.** Comments by opponents on the British Medical Association's guidance on non-therapeutic male circumcision of children seem one-sided and may undermine public health. *World Journal of Clinical Pediatrics*. 2023;12(5): 244–262. https://doi.org/10.5409/wjcp.v12.i5.244.
34. **Hayashi Y, Kojima Y, Mizuno K, Kohri K.** Prepuce: phimosis, paraphimosis, and circumcision. *TheScientificWorldJournal*. 2011;11: 289–301. https://doi.org/10.1100/tsw.2011.31.
35. **Schoen EJ, Colby CJ, Ray GT.** Newborn circumcision decreases incidence and costs of urinary tract infections during the first year of life. *Pediatrics*. 2000;105(4 Pt 1): 789–793. https://doi.org/10.1542/peds.105.4.789.
36. **TASK FORCE ON CIRCUMCISION, Blank S, Brady M, Buerk E, Carlo W, Diekema D, et al.** Male Circumcision. *Pediatrics*. 2012;130(3): e756–e785. https://doi.org/10.1542/peds.2012-1990.
37. **Ben Chaim J, Livne PM, Binyamini J, Hardak B, Ben-Meir D, Mor Y.** Complications of circumcision in Israel: a one year multicenter survey. *The Israel Medical Association journal: IMAJ*. 2005;7(6): 368–370.
38. **Svoboda JS, Adler PW, Howe RSV.** Circumcision Is Unethical and Unlawful. *Journal of Law, Medicine & Ethics*. 2016;44(2): 263–282. https://doi.org/10.1177/1073110516654120.
39. **Singh-Grewal D, Macdessi J, Craig J.** Circumcision for the prevention of urinary tract infection in boys: a systematic review of randomised trials and observational studies. *Archives of Disease in Childhood*. 2005;90(8): 853–858. https://doi.org/10.1136/adc.2004.049353.
40. **Malkoc E, Ates F, Tekeli H, Kurt B, Turker T, Basal S.** Free nerve ending density on skin extracted by circumcision and its relation to premature ejaculation. *Journal of Andrology*. 2012;33(6): 1263–1267. https://doi.org/10.2164/jandrol.112.016709.
41. **Bronselaer GA, Schober JM, Meyer-Bahlburg HFL, T'Sjoen G, Vlietinck R, Hoebeke PB.** Male circumcision decreases penile sensitivity as measured in a large cohort. *BJU international*. 2013;111(5): 820–827. https://doi.org/10.1111/j.1464-410X.2012.11761.x.
42. **Wang Z, Zhang D, Yi XZ, Zhao Y, Yu A.** Effects of regenerative peripheral nerve interface on dorsal root ganglia neurons following peripheral axotomy. *Frontiers in Neuroscience*. 2022;16. https://doi.org/10.3389/fnins.2022.914344.
43. **Gordon T.** Peripheral Nerve Regeneration and Muscle Reinnervation. *International Journal of Molecular Sciences*. 2020;21(22): 8652. https://doi.org/10.3390/ijms21228652.
44. **Bishop B.** Neural Plasticity. *Physical Therapy*. 1982;62(9): 1275–1282. https://doi.org/10.1093/ptj/62.9.1275.
45. **Navarro X.** Functional evaluation of peripheral nerve regeneration and target reinnervation in animal models: a critical overview. *The European Journal of Neuroscience*. 2016;43(3): 271–286. https://doi.org/10.1111/ejn.13033.
46. **Gangadharan V, Zheng H, Taberner FJ, Landry J, Nees TA, Pistolic J, et al.** Neuropathic pain caused by miswiring and abnormal end organ targeting. *Nature*. 2022;606(7912): 137–145. https://doi.org/10.1038/s41586-022-04777-z.
47. **Jang K, Garraway SM.** A review of dorsal root ganglia and primary sensory neuron plasticity mediating inflammatory and chronic neuropathic pain. *Neurobiology of Pain*. 2024;15: 100151. https://doi.org/10.1016/j.ynpai.2024.100151.

48. **Konnova EA, Deftu AF, Chu Sin Chung P, Pertin M, Kirschmann G, Decosterd I, et al**. Characterisation of GFAP-Expressing Glial Cells in the Dorsal Root Ganglion after Spared Nerve Injury. *International Journal of Molecular Sciences*. 2023;24(21): 15559. https://doi.org/10.3390/ijms242115559.

49. Ramachandran VS, Hirstein W. The perception of phantom limbs. The D. O. Hebb lecture. *Brain: A Journal of Neurology*. 1998;121 (Pt 9): 1603–1630. https://doi.org/10.1093/brain/121.9.1603.

50. Makin TR, Flor H. Brain (re)organisation following amputation: Implications for phantom limb pain. *Neuroimage*. 2020;218:116943. https://doi.org/10.1016/j.neuroimage.2020.116943