

Fordyce Spot Symptoms and Treatment: An Updated Review

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ABSTRACT

Fordyce granules occur frequently, and most people consider their quality to be a typical variation of the oral mucosa. The multiple yellow granules that primarily show up in the lower lip are a clear sign of Fordyce granules, a type of benign ectopic sebaceous gland. Most often, it affects adult males. Although it has been proven that such glands have been there since the time you were born, their tubes flow directly onto the skin's surface. When they develop as a consequence of steroid hormones released by the gonadal and adrenal glands, they are not visible until pubescence. Around 70 to 80% of the population are adults. A comprehensive analysis of the literature search was conducted. A number of databases have been searched using the common terms "sebaceous glands," "oral mucosa", "Fordyce patches", "Fordyce granules," "Fordyce spots," and "Fordyce glands" using Science Direct, Springer PubMed and Google Scholar as search engines. We have focused on the reviews and research papers published between 2001 and 2024. Although they are a common occurrence in the body, they are not connected to any disease or condition and are not contagious. They can be treated with isotretinoin, picrolimus, 5-aminolaevulinic acid, CO2 laser therapy, and micropuncture therapy. Hormonal fluctuations, greasy sebaceous glands, and hyperlipidemia bring on Fordyce spots. This is a rare but serious condition that causes lesions on the skin's surface along with pain and discomfort in the affected part of the body.

Keywords: Sebaceous glands, Oral mucosa, Fordyce patches, Fordyce granules, Fordyce spots, Fordyce glands.

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INTRODUCTION

Fordyce spots are normally 1 to 3 mm long, whitish-yellow lumps that most frequently develop in skin regions devoid of hair follicles. Fordyce spots, which are located where the lips and face skin meet, most frequently show up symmetrically around the inner cheeks and the vermilion line of the lips. Less frequently, Fordyce spots can develop on the labia majora, labia minora, scrotum, and/or penis.

These spots tend to be either purple or reddish in color. Fordyce spots can manifest as single spots, dispersed patterns, or areas on the skin that may consist of 50 to 100 spots in a group.^{1,2} Fordyce lesions are benign variations on the skin that are entirely normal. They could be viewed as a cosmetic issue by some people who don't experience any bodily issues. Fordyce spots are thought to be unattractive in certain situations, causing some people to experience worry, despair, or other emotional effects. Those people may need reassurance and counseling.

The Fordyce patches on the genitalia may also bleed after or during sexual activity if they are present. Fordyce spots are thought to be caused by an assortment of environmental and biological variables, but the specific reason is yet unknown.

Several investigations have linked hormonal changes and/or elements of embryonic development to the proliferation of the ectopic glands that produce sebum, which is a common cause of Fordyce spots.³ Fordyce spots are frequently linked to a number of risk factors, including skin that is oily, postpubertal age, gender identity at birth, dyslipidemia, rheumatic conditions, and colorectal malignancies. A healthcare expert will frequently diagnose Fordyce spots after a visual examination. People who are bothered by their Fordyce spots, are exhibiting any symptoms associated with them, like bleeding, sadness, or anxiety, or are worried regarding other diseases might want medical advice and assistance from a healthcare provider for diagnosis or treatment.

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Because of their widespread distribution in the mouth cavity and frequent consideration of dermal adnexal tissues, these sebaceous glands are generally referred to as “ectopic” sebaceous glands.⁴ These sebaceous glands, which are also known as the exocrine (holocrine) glands, reduce the water penetration of hair, skin, and eyelids while also assisting in lubrication. mostly consists of triglycerides, wax esters, and squalene and secretes an oily or waxy material known as sebum or fat that forms a covering of lipids and repels water in cooler conditions.

They naturally work to prevent dehydration in hot weather. Additionally, they contain sapienic acid, a free fatty acid that promotes the growth of acne.⁵⁻⁸ These lesions, which were invisible during childhood, became more common as people aged and are found in the buccal mucosa in 75% of adults. Fordyce granules become more abundant and prevalent with age in adults (70–80%) compared to youngsters (because of hormonal causes and puberty increasing their formation).⁹ These normally asymptomatic lesions exhibit a 2:1 preference for females.¹⁰

Most usually found on the area of cheek mucosa opposing the cheek mucosa, but also occasionally on the tongue, gingiva, palate, and frenum. It is also occasionally found on the innermost layer of the lips. Clinically, they present as tiny, painful red or white patches around the size of a pinhead.¹¹

Epidemiology

Fordyce spots, or Fordyce glands, are more prevalent in adults compared to children, and their frequency rises with age.¹² Adult prevalence ranges from 70 to 80%. The ratio of men to women is roughly 2:1.¹³

Pathogenesis

A Fordyce spot is an enlargement of a sebaceous gland that can appear on the surface of the oral mucosa, penis, or labia. Fordyce spots, according to some authors, are ectopic or heterotopic sebaceous glands. Other writers contend that while it is typical to have small or undetectable glands that produce sebum on the lips, the lesions may not necessarily be ectopic or heterotopic.^{14,15} In one study, between 80 and 95% of adults had healthy sebaceous glands on the vermilion line of their lips.

Fordyce spots have ducts that open freely onto the epidermal surface but lack a connection with hair follicles.¹⁶ Despite being present from birth, these glands that produce sebum are not readily apparent until adolescence, when they increase in response to androgenic hormones produced by the adrenal and gonadal glands, as depicted in Figure 1, showing Sebaceous gland enlargement makes them apparent throughout the underlying epithelium.¹⁷

Clinical Manifestations

Clinically, Fordyce spots present as asymptomatic, distinct, tiny (pinhead-sized), creamy yellow papules that can be found alone or in groups. The papules might occasionally develop into plaques or lobules. On the lips, oral mucosa, and less frequently around the genital area, scrotum, and labia, they appear most frequently and prominently.

Typically, the lesions are symmetrical and bilateral. These papules on the genital shaft are more noticeable when the foreskin has been stretched or when the penile is erected. Squeezing the lesion may occasionally result in the expression of a thick, chalky, or cheesy substance.¹⁸

Complications

Fordyce patches can be ugly on the surface. Penile lesions may infrequently produce discomfort during sexual activity.¹⁹ They typically have no clinical importance and are unrelated to systemic illness. According to a recent study, those with elevated lipid profiles frequently have more Fordyce spots on their mouths.²⁰

Diagnosis

Skin biopsy

Only a few cases necessitate a skin biopsy, and most Fordyce spots are identified with clinical examination. According to a histological investigation, a developed sebum gland located beneath the mucosal membrane rises directly to the outermost layer and is devoid of a hair follicle. In order to properly diagnose other conditions that may resemble them, it is crucial to distinguish these expanded pores from Fordyce patches. Fordyce spots can indicate a number of sexually transmitted diseases (STIs); therefore, it's important to have your doctor make an accurate diagnosis. As soon as possible after discovery, STIs should be treated.^{21,22}

Differential diagnosis

It is important to distinguish milia and sebaceous hyperplasia from Fordyce patches. Small, dome-shaped, white, noninvasive keratinocyte cysts are known as milia. On histological inspection, they show up as tiny infundibular cysts surrounded by squamous epithelial cells with a coarse cell layer. Keratin layers are piled inside the cyst. Primary milia, which can be benign in both children and adults, can present at birth (derived primary milia) or emerge later in life (adolescent primary milia). Regardless of gender, 40% of all neonates have congenital primary milia. Although benign primary milia damage the eyelids, hereditary primary milia damage the nose in both children and adults. Secondary milia may develop as a result of trauma, medication, or illness.

Milia typically breaks down and heals on its own. The most prevalent clinical symptoms of sebaceous hypertrophy are numerous, recognizable, yellow, or flesh-colored glass dome papules that are left untreated. Lesions can range in size from 2 to 5 mm in width, yet they may also grow considerably bigger. The areas of the face most frequently affected include the nose, cheeks, and forehead. People in their forties and fifties are most commonly affected by the illness. Syringas, granulomatous contagiosum, fungal nitidus, closed comedones, epidermal myxomas, and calcinosis cutis are further differential diagnoses.²³

Treatments

Fordyce granules are usually benign exogenous sebaceous organs that are most commonly present on the surface of

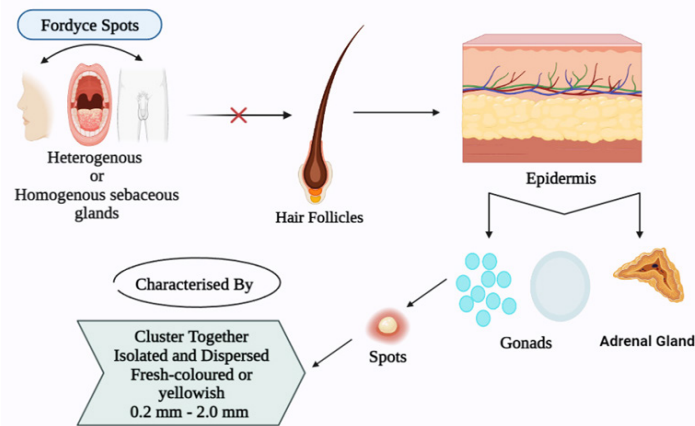


Figure 1: Pathogenesis of fordyce spots

the oral mucosa, crimson borders, and radicular area. Their abundance of yellow granules distinguishes them. Some studies claim that while they are more prevalent in boys today, they were more prevalent in girls in the fourth as well as fifth centuries. Although they are a common occurrence in the body, they are not connected to any medical condition or disease and are not contagious. As shown in Figure 2 there are numerous therapies available for Fordyce spots.

CO₂ laser

The CO₂ laser operates at a frequency of 10,600 nm, which is in the infrared band's inaccessible region. It has been used for over 30 years in meticulous dermatology due to its skill in tearing and chopping tissues as well as in establishing strong intraoperative hemostasis. With acceptable results, this type of laser can be used to treat a variety of skin lesions. The designers acknowledge that the laser is thought to be an excellent alternative due to the restoration of Fordyce granules, taking into account its direct use and the accuracy it provides when the sores are removed.

Primary milia can also be inborn (inherent primary milia) or progressively develop in both children and adults (generic essential milia). In general, essential milia are found in about 40% of neonates who do not have an affinity for sex. In contrast to the nose, which is favored with intrinsically required milia, both children's and adults' eyelids have been favored with benign essential milia. Injury, drugs, or disease can all lead to secondary milia. Milia resolves fast and sheds frequently. Medically, sebaceous hyperplasia often presents as a number of discrete, asymptomatic dome papules that are yellow or fresh-colored. Many of the lesions will have localized umbilication. Solitary sores might be larger than their typical 5 mm width. Your forehead, cheeks, and nose are the most often impacted locations.^{24,25}

Picrolimus

Skin-specific clindamycin, corticosteroids, retinoids, benzaldehyde oxidants, oral retinoids, ultraviolet light, electrocoagulation, copper fumes, laser, and liposuction-related curettage are among the available treatments. Utilizing tretinoin ensures that future damage is avoided. The most

recent instance similarly responded well and improved after a three-month course of picrolimus medication.²⁶ Mild to moderate atopic dermatitis-related inflammatory reactions are treated with it. It is an ascomycin derivative that also aims to inhibit the intracellular receptor-ligand FK 506 protein.

This complex blocks the biologically active calcineurin phosphorylation of the nuclear factor in an active T-cell's cytoplasm. As a result, there is limited information about many inflammatory cytokines. This category of proinflammatory cytokines contains IL-2, IFN γ , IL-4, and IL-10. Different cytokines, including interleukin-5 and tumor necrosis factor, are reduced in a partially subservient way.

Additionally, picrolimus prevents serotonin from entering the center and b-hexosaminidase from combining with all the cytokine mediators produced and combined in pole cells. Studies on the pharmacokinetics of picrolimus show that, following effective delivery, there is little fundamental assimilation. Picrolimus is a typically safe, straightforward substitute. Therefore, it is highly recommended and might be employed as the initial therapy for Fordyce's disease. Picrolimus may aid in reducing inflammation brought on by Fordyce's disease's apocrine gland channels rupture.²⁷

Photodynamic treatment using 5-aminolaevulinic Acid

5-Aminolaevulinic acid can be used in photodynamic treatment to treat Fordyce spots.²⁶ A photosensitizer precursor as well as light, are infused in a certain order as part of the photodynamic therapy (PDT) method. Recently, it was discovered that protoporphyrin IX preferentially accumulates in malignant cells as well as sebaceous glands, which are also target tissues in 5-aminolaevulinic acid (ALA)-PDT. This provides a theoretical framework for researching the use of ALA-PDT to identify various pilosebaceous unit disorders. Recent clinical trials employing ALA-PDT have been successful in treating sebaceous hyperplasia and vulgaris.²⁸

Micro-punch surgery/technique

Fordyce spots and small portions of the tissue underneath are removed during this treatment using a small marking device and local freezing. It's a really touchy strategy, this one. During this procedure, the doctor uses a tool resembling



Figure 2: Various treatments of Fordyce spots

a pen to “punch” the skin in Fordyce spot-affected areas. The use of anesthesia is common because operations can be painful. Fordyce spots have been successfully treated using micro punch surgery after producing positive results in studies conducted on males.²⁹

Not everyone should choose one of these options, though. For instance, carbon dioxide (CO₂) laser resurfacing may leave scars, and isotretinoin has a short-lived therapeutic window. To decide what course of action is best for you, it is essential to examine your Fordyce spot treatment options with a doctor. To rapidly and effectively remove multiple spots from the face or genital area, your doctor could do micro-punch surgery. Before performing it, they administer a topical anesthetic to make you feel less uncomfortable. Then, any extra tissue is removed by poking the area with a little device resembling a pen.³⁰

Isotretinoin

Fordyce’s spots are frequently treated with isotretinoin, a type of retinol that was initially made from vitamin A.³¹ Due to its vital anti-inflammatory qualities, it is beneficial for scars and other skin issues, including.

Fordyce spots. Isotretinoin is typically administered orally, but when used excessively or under unfavorable circumstances, it may have undesirable effects. Isotretinoin pills may be useful in some situations, particularly when paired with laser therapy. However, these drugs cannot be taken for an extended period of time.³²

CONCLUSION

Hormonal fluctuations, greasy sebaceous glands, and hyperlipidemia.³³ bring on Fordyce spots. This is a rare yet serious condition that causes lesions on the skin’s surface along with pain and discomfort in the affected area of the body.³⁴ It frequently affects the mucosae of the oral, vaginal, laryngeal, and esophageal parts of the body. Leukoedema, white sponge nevi, gingival pigmentation, fissured tongue, white and black hairy tongue, eruption cysts, etc., are some of the mucosal issues it encompasses. Skin biopsies and other differential diagnosis techniques can be used to diagnose it, and isotretinoin, CO₂ laser therapy, picrolimus, 5-aminolaevulinic acid, and micropuncture therapy can all be used to treat it.

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