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# Fox-Fordyce Disease

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Updated: Jan 12, 2007

# Introduction

## Background

Fox-Fordyce disease is an infrequently occurring chronic pruritic papular eruption that localizes to areas where apocrine glands are found. The etiology is currently unknown. The eponym is based on the 1902 report by G. Fox and J. Fordyce.

## Pathophysiology

Fox-Fordyce disease is a disease of the skin alone. In 1956, Shelley and Levy proposed apocrine miliaria as the cause. The observed pathophysiology is a keratin plug in the hair follicle infundibulum obstructing the apocrine acrosyringium and producing an apocrine anhidrosis. Histologically, a rupture of the apocrine excretory duct occurs, and spongiotic inflammation results. Extravasation of sweat and inflammation is postulated to cause the intense itching. Ranalletta et al found that the acrosyringium of the eccrine glands was similarly involved.

In 2003, Kamada et al published a histopathologic analysis from which they concluded that the 2 types of this disease are (1) an apocrine (follicular) type and (2) an apocrine (nonfollicular) type.

## Frequency

### United States

Fox-Fordyce disease is an infrequent condition. Geographic influence is not evident. Many case reports mention heat, humidity, and stress as exacerbating factors.

### International

Reports from the United States are the most common; however, a geographic limitation is not evident.

## Mortality/Morbidity

This disease has no risk of loss of life or limb. Patients often experience severe pruritus. Therefore, the patient's quality of life may be adversely affected.

## Race

No racial predilection is evident.

## Sex

A distinct predilection for women exists; the female-to-male ratio is 9:1.

## Age

Fox-Fordyce disease is most common in women aged 13-35 years; it is rare before or after this age.

# Clinical

## History

- This condition frequently appears under conditions of heat, humidity, and friction, often appearing suddenly.
- Many patients present after decades of symptoms.
- Few patients are asymptomatic.
- Most patients relate pruritus that disturbs sleep.
- Changing antiperspirants has not been reported to help.
- Some patients report diminution of sweating after the onset of symptoms.

## Physical

- The apocrine glands are the site of Fox-Fordyce disease.
- Lesions are most often found in the axillae, where they tend to be bilateral.
- Lesions may also affect the periareolar, inframammary, and pubic areas.
- The primary lesion is a flesh-colored to reddish, smooth, dome-shaped, discrete, and follicular or perifollicular papule.
- Affected areas usually have many papules. The papules usually appear to affect every follicle in a given area.
- Excoriations and lichenification may be seen as a consequence of scratching.
- Sweating is often absent in the affected area.

## Causes

- The definite increased prevalence in woalvato da Windows Internet Explorer 8> Subject: Fox-Fordyce Disease: [Print] - eMedicine Dermatology Date: Fri, 4 Sep 2009 00:57:19 +0200 MIME-Version: 1.0 Content-Type: multipart/related; type="text/html"; boundary="----=_NextPart_000_02BA_01CA2CFA.A7300A30" X-MimeOLE: Produced By Microsoft MimeOLE V6.00.2900.5579 This is a multi-part message in MIME format. ------=_NextPart_000_02BA_01CA2CFA.A7300A30 Content-Type: text/html; charset="Windows-1252" Content-Transfer-Encoding: quoted-printable Content-Location: http://emedicine.medscape.com/article/1070560-print

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- Sweating is often absent in the affected area.

## Causes

- The definite increased prevalence in women has led to an unproved theory of hormonal influences. Reports of cases in prepubertal girls are evidence against the hormonal theory. The exact pathophysiology is still unknown.
- A number of factors, including (1) emotional and/or hormonal influences and (2) alterations in sweat components, have been implicated.

# Differential Diagnoses

Folliculitis

Milia

Miliaria

## Other Problems to Be Considered

Pseudofolliculitis of the axillae

# Workup

## Laboratory Studies

- Histopathologic diagnosis may be very difficult with conventional sectioning. Stashower et al proposed transverse histologic sectioning as the most effective way to demonstrate diagnostic features.
- Diagnosis is usually made on clinical/historical grounds. Laboratory or even histopathologic tests are seldom necessary for clinicians familiar with this condition.

## Procedures

- In 2002, Chae et al described axillary Fox-Fordyce disease treated with liposuction-assisted curettage.

## Histologic Findings

The proposed apocrine origin was based on the finding of a keratin plug in the follicular infundibulum that occluded the apocrine acrosyringium. Reports also include a rupture of the apocrine duct and a resulting spongiotic inflammation. Plasma cells may be noted, and the deeper apocrine duct may be dilated with sialomucin. The dermis may show fibrosis and chronic inflammation. These latter findings depend on the condition's chronicity.

# Treatment

## Medical Care

Based on the observations of follicular occlusion, Shelley proposed topical tretinoin cream as therapy in 1972. Reports of success with topical retinoids followed, along with reports of success with topical steroids, antibiotics, clindamycin in alcoholic propylene glycol solution, hormonal therapy in women, ultraviolet light, dermabrasion, and surgical excision. Usually, these therapies were not curative and were often complicated by intolerable irritation. In 1994, Effendy et al reported the short-term success of isotretinoin when given for 4 months in a daily oral dose of 15-30 mg; the condition returned 3 months after cessation of therapy.

## Surgical Care

Surgical excision of affected areas in the axilla has been performed in the past, but it is seldom recommended.

## Consultations

Consultation with a dermatologist is usually recommended.

## Activity

Activity that leads to sweating is counterproductive. Swimming is the preferred form of exercise.

# Medication

Medical therapy has been complicated by the irritant potential of the topical medications. Topical steroids have not been useful. Topical retinoids have been irritating, which has limited their long-term use. In 1979, Giacobeti reported success with topical 0.1% tretinoin cream. In 1990, Casani reported treatment with topical 0.5% tretinoin cream. In 1995, Miller et al reported treatment of Fox-Fordyce disease with topical clindamycin solution.

Hormonal therapy with high-estrogen oral contraceptives, estrogen creams, and testosterone creams has been reported, sometimes with success but often with failure.

In 2006, Pock et al reported effective therapy, with no adverse effects, using pimecrolimus in 3 young female patients. The response was deemed "very impressive." Based on this report, the DOC could be this class of drug, which includes tacrolimus.

## Retinoids

Based on follicular infundibular occlusion, the retinoids (first tretinoin, later isotretinoin) have been used with reported short-term success. Consider therapy with alternative retinoids as they become available. Based on the success of tretinoin, oral retinoids have also been used with reported success.

## Tretinoin (Avita, Retin-A)

Since 1972, therapy with topical retinoids has the most support in the literature. Several reports exist on the efficacy of topical tretinoin. Severe irritation may occur when used in the axillae. The 0.025% cream, or even a dilution to a milder form or short contact therapy, would be prudent to begin therapy.
Increasing both the time and the amount gradually as tolerated is a safe way to avoid irritation.

## Dosing

### Adult

Begin with lowest tretinoin formulation and increase as tolerated; apply hs or qod; lower frequency of application if irritation develops

### Pediatric

<12 years: Not established
>12 years: Apply as in adults

## Interactions

Toxicity increases with coadministration of benzoyl peroxide, salicylic acid, and resorcinol; avoid topical sulfur, resorcinol, salicylic acid, other keratolytics, abrasives, astringents, spices, and lime

## Contraindications

Documented hypersensitivity; open wounds; lacerations

## Precautions

### Pregnancy

C - Safety for use during pregnancy has not been established.

### Precautions

May take several wk for skin to adapt to irritative effect; by starting application qwk and slowly increasing to qhs, noncompliance from warmth and redness is decreased; avoid contact with eyes and mucous membranes; minimize exposure to sun and UV light

# Isotretinoin (Accutane)

By analogy, because isotretinoin worked topically, it was predicted that oral retinoids would be effective. Low doses of isotretinoin have been efficacious. Although symptoms were relieved at relatively low doses, the condition returned in a few months after cessation of therapy.

## Dosing

### Adult

10-30 mg/d PO; lower doses may be effective (therapy may need to be continued for long periods)

### Pediatric

Not established

## Interactions

Toxicity may occur with vitamin A coadministration; pseudotumor cerebri or papilledema may occur when coadministered with tetracyclines; acitretin may reduce plasma levels of carbamazepine

## Contraindications

Documented hypersensitivity; possibility of pregnancy; pregnancy

## Precautions

### Pregnancy

X - Contraindicated in pregnancy

### Precautions

May decrease night vision; inflammatory bowel disease may occur; may be associated with development of hepatitis; occasional exaggerated healing response of acne lesions (excessive granulation with crusting) may occur; patients with diabetes may experience problems in controlling their blood sugar level while on isotretinoin; avoid exposure to UV light or sunlight until tolerance achieved; discontinue treatment if rectal bleeding, abdominal pain, or severe diarrhea occur

# Antibiotics

Topical clindamycin in propylene glycol was first reported to help patients with Fox-Fordyce disease in 1992. Confirmation of this study was reported in 1995. Topical erythromycin should also be helpful.

## Clindamycin (Cleocin-T)

Lincosamide for treatment of serious skin and soft tissue staphylococcal infections. Also effective against aerobic and anaerobic streptococci (except enterococci). Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes causing RNA-dependent protein synthesis to arrest.

## Dosing

### Adult

Apply topically bid

### Pediatric

Apply as in adults

## Interactions

None reported

## Contraindications

Documented hypersensitivity; regional enteritis; ulcerative colitis; hepatic impairment; antibiotic-associated colitis

## Precautions

### Pregnancy

B - Usually safe but benefits must outweigh the risks.

### Precautions

Superinfections may occur with prolonged or repeated antibiotic therapy

## Erythromycin (A/T/S, Erycette, Staticin, T-Stat)

Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes, causing RNA-dependent protein synthesis to arrest. Used in the treatment of staphylococcal and streptococcal infections.

## Dosing

### Adult

Apply topically bid

### Pediatric

Apply as in adults

## Interactions

Topical erythromycin is inactivated in the presence of acids due to hydrolysis; activity of erythromycin is also reduced in the presence of sodium alginate, pectin, bentonite, calamine, silica, and polysorbate 80

## Contraindications

Documented hypersensitivity

## Precautions

### Pregnancy

B - Usually safe but benefits must outweigh the risks.

### Precautions

For external use only; avoid eyes, mouth, and other mucous membranes; adverse reactions include dryness, tenderness, pruritus, desquamation, erythema, and burning sensation; concomitant topical therapy should be used with caution because cumulative irritancy may occur; prolonged use may be associated with overgrowth of antibiotic-resistant organisms

# Immunosuppressants

Used because of inflammatory and hyperkeratinization character of the disease.

## Pimecrolimus (Elidel) cream or tacrolimus (Protopic) ointment

Because of the rapidity of response, effectiveness of therapy, and lack of adverse effects, this could be current DOC. Both are in immunomodulating macrolactam (neuraminidase inhibitors) class of drugs and have significant anti-inflammatory activity and a highly favorable adverse effect profile in at least the short range. Both are especially safe to use in the axilla, periareolar, and groin areas.

# Dosing

## Adult

Pimecrolimus: 1% cream topically bid until relief, then 1-2 times/wk over prolonged period

Tacrolimus: 0.1% ointment topically bid until relief, then 1-2 times/wk over prolonged period

## Pediatric

>2 to <12 years: 0.03% tacrolimus; administer as in adults

# Interactions

Topical tacrolimus is minimally absorbed; however, levels may increase with diltiazem, nicardipine, clotrimazole, verapamil, erythromycin, ketoconazole, itraconazole, fluconazole, bromocriptine, grapefruit juice, metoclopramide, methylprednisolone, danazol, cyclosporine, cimetidine, or clarithromycin; levels may reduce with rifabutin, rifampin, phenobarbital, phenytoin, and carbamazepine

# Contraindications

Documented hypersensitivity

# Precautions

## Pregnancy

C - Safety for use during pregnancy has not been established.

## Precautions

Do not use with occlusive dress