Cutaneous Mycology: A New Perspective on Tinea Versicolor, Tinea Pedis, and Seborrheic Dermatitis

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Abstract

We here in demonstrate the effect of three common microbes (M. furfur/ovale, T. rubrum, M. oleosa) in three common diseases: tinea versicolor, tinea pedis, and seborrheic dermatitis. We show how the Malassezia furfur/ovale yeast in tinea versicolor behaves in such a way (biofilm formation) that it causes only scaling and color change while leading to a chronic state. The biofilm resides amongst the corneocytes in the stratum corneum and does not encounter living cells; thus, it does not upregulate the innate immune system. In the presentation of T. pedis and seborrheic dermatitis, the microbes (T. rubrum and M. oleosa) behave in similar fashion to the gene (filaggrin or other) in the genetic side of the “double-hit” phenomenon seen in eczema. The gene contributes to a faulty stratum corneum; by their presence within the stratum corneum and the resultant disruption of the normal activity of the corneocytes, the microbes fill a similar role to the gene. The environmental side in T. pedis and seborrheic dermatitis is the same as found in eczema. These three microbes in these three diseases do not adhere to the paradigm that other organisms follow in many chronic diseases; namely, microbes make biofilms that activate the immune system, and the immune system creates tissue damage.

Keywords

Biofilms; Tinea Versicolor; Tinea Pedis; Seborrheic Dermatitis

We have recently demonstrated a paradigm that appears to be operative in many chronic diseases: microbes make biofilms which activate the innate immune system and cause tissue damage. This has been shown with atopic dermatitis (eczema), psoriasis, acne, leprosy, and others [1-4]. In eczema, normal flora Staphylococci make biofilms and occlude sweat ducts which initiates the immunologic cascade [1]. In acne, the Propionobacterium acnes creates biofilms within the cutaneous hair follicles; and, in psoriasis, Streptococci make biofilms inside and outside tonsillar epithelial cells leading to activation of both the innate and the adaptive arms of the immune system [2, 3]. In leprosy, the biofilms made by Mycobacterium leprae have been found in the skin (“globi” in lepromatous leprosy) and in the liver, spleen, and kidney. Those in the internal organs form the amyloid that is present in “amyloidosis” seen with chronic disease [4].

In this paper, we will discuss the chronic diseases tinea versicolor (caused by Malassezia furfur/ovale), tinea pedis (most commonly associated with Trichophyton rubrum) and seborrheic dermatitis (recently associated
with *Malassezia oleosa*) and show how the microbes affect the disease [1]. It will become apparent that these diseases do not follow the paradigm seen with other cutaneous disorders.

**Tinea Versicolor**

Tinea Versicolor (TV) is a chronic disease of the skin characterized by superficial scaling and peeling like that seen after a sunburn. Color change, generally hypopigmentation, arises not from shielding of the ultraviolet by the microbes, but is considered to be due to the elaboration of azelaic acid by the yeast.5 *M furfur/ovale* is part of the normal flora in nearly all individuals and becomes active with sweating and other factors [5]. The yeast has been shown to make biofilms in vitro (Figure 1) and in vivo [6]. These biofilms form in the stratum corneum of the skin and do not occlude eccrine ducts like staphylococcal biofilms in eczema. The reason for this is the yeast is too large. The duct is 30 µ in diameter, and the yeast is 3-6µ; inasmuch as biofilms form when there is a minimum of 10 microbes in any direction, the resultant community of these microbes is too large [6]. Without the duct occlusion (by the biofilm) and/or the involvement of living cells, there is no activation of the innate immune system molecule Toll-like receptor 2 (TLR2). Thus, all the yeast does is cause disruption of the stratum corneum by its presence. The involvement of the immune system, as in the paradigm for other organisms, is not present in TV. Moreover, because of the absent immune response, most patients do not have any itching or other symptoms. In its own way, the yeast and its biofilm act as a control for eczema which causes symptoms arising from the ductal occlusion upregulating TLR2. TV is a biofilm-related mycological disease that causes no (or very few) symptoms.

Current treatments for TV include periodic washing with selenium sulfide lotion/shampoo and/or topical azoles. It is of interest that both compounds (selenium and azoles) are biofilm dispersers [7] while selenium is also sporicidal [8].

**Tinea pedis**

Tinea pedis, “athlete’s foot,” has been considered a fungal infection, and it is, but it only becomes symptomatic (with considerable pruritus) when it is accompanied by the staphylococcal biofilm-occluded sweat ducts of eczema [9, 10]. Skin biopsies show the exact same changes as are seen in eczema save for the filamentous hyphae in the stratum corneum. Microbial analysis shows the *Staphylococci* to be the same as are found in eczema, and genetic analysis shows all the *Staphylococci* carry the icaD gene for biofilm formation. The colorimetric XTT assay also shows all to be biofilm formers [9].

We have proposed that the role of the fungi (*T. rubrum* and *T. mentagrophytes* primarily) in *Tinea pedis* is to disrupt the function of the stratum corneum [1]. As such, it behaves like the “filaggrin” gene in eczema which is present in up to 50% of cases) [1]. We have shown that other genes (steroid sulfatase, transglutaminase, and others) cause a “faulty” stratum corneum are also associated with eczema[1].
It is somewhat surprising that the symptoms disappear nearly four times more rapidly when treated with ceramide-containing moisturizing cream as compared to the antifungal azole creams. Consequently, treating the “genetic” side of \textit{T.pedis} affords more symptom relief than does treating with anti-fungals [10].

**Seborrheic dermatitis**

Seborrheic dermatitis has long been considered an inflammatory disease of unknown origin. Sulzberger, however, in his landmark paper in 1947, commented it had the same occluded eccrine sweat ducts that he saw in eczema [11]. His observations lay dormant for six decades, until we observed similar findings and evaluated them with many more probes than were available to him [1].

We have observed staphylococcal biofilm-occluded eccrine ducts on pathology and upregulation of TLR2 on immunopathology in seborrheic dermatitis similar to eczema. The biofilms have all been shown to be made by normal flora staphylococci, all of which had the \textit{icaA} gene for biofilm formation [1]. This was exactly the same pathology and microbiology as in eczema.

**Figure 3:** Biopsy of Seborrhoeic Dermatitis showing Numerous yeast Blastospores in Stratum Corneum. PAS 40X

In the presentation of seborrheic dermatitis, \textit{Malassezia} yeasts (likely “oleosa”) are responsible for the disruption in the stratum corneum like the fungi in \textit{T. pedis}. And, Like the dermatophytes, they behave like the gene in the double-hit phenomenon in eczema [1].

Treatment either with topical corticoids or with topical azoles is effective. The efficacy of the topical azoles was first noted in the seborrhoeic dermatitis seen in HIV patients. Since then it has been proven effective for all patients [1]. This is true even for pediatric patients who lack the yeast. They instead have the “filaggrin” gene the impact of which is markedly improved using any topical cream which behaves as a moisturizer (even though it is used as an anti-fungal). Ordinary eczema is markedly improved by moisturizing and decreasing the use of soap in bathing [1]. This is important for the prevention of eczema over time, and it obviously is addressing the genetic side of the disease. The fact that azoles act as biofilm dispersers, as noted previously, cannot be anything but beneficial in the treatment regimen.

We have shown in this work how three common diseases are affected by yeasts and fungi. In TV, the \textit{M. furfur/ovale} yeasts form biofilms which are related to the chronicity of the disease. In \textit{T. pedis}, the presence of dermatophytes disrupts the stratum corneum, and their presence acts similarly as the gene in eczema. The environmental component in eczema is staphylococcal biofilms which occlude eccrine sweat ducts and upregulate the innate immune system. In similar fashion, the \textit{Malassezia} yeasts present in seborrhoeic dermatitis, impact the stratum corneum and also behave like the gene in eczema. In none of these diseases, does the offending organism cause tissue destruction via biofilm formation leading to the activation of TLR2. In the cases of seborrhoeic dermatitis and \textit{T. pedis}, that is carried out by staphylococcal biofilms occluding the ducts and in the case of TV there is no tissue destruction.

**Conclusion**

We have shown the mechanism of disease production in three common yeast/fungal diseases, namely TV, \textit{T. pedis}, and seborrhoeic dermatitis. The latter two are similar in that the microbe in each disrupts the stratum corneum, and the symptomatic disease is actually produced by staphylococcal biofilm-occluded sweat ducts. This is the same mechanism as seen in eczema except the microbes are giving rise to an ineffective stratum corneum instead of a gene (filaggrin in many cases) providing that alteration. TV produces minimal symptomology except for color change and scaling. Treatment for these diseases is currently effective and does not need to be altered. However, it would likely be of considerable benefit if a moisturizer were to be added to the protocol for \textit{T. pedis}.

**References**


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