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REVIEW ON SCIENTIFIC INSIGHT OF DANDRUFF/SEBORRHEIC DERMATITIS: A COMMON SKIN DISORDER

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ABSTRACT

Dandruff is a mild form of seborrheic dermatitis, which is chronic, relapsing scalp condition and negatively generates the socio-economic impact. It is associated with an imbalance in the proportion of bacterial and fungal populations colonizing the scalp. Statistics show that 50% of the postpubertal population across the globe, irrespective of ethnicity and gender suffered with dandruff. The review article discuss in detail, the prevalence, pathophysiology, three etiologic facets of dandruff formation and its implications on the corneocynte. Despite, recent advances in the field of molecular and biochemical tools, particularly with genetic-based detection methods has greatly increased our understanding of the organisms, mechanisms, and therapeutic treatment of dandruff and seborrheic dermatitis. This article highlights the importance of research needed to understand the lack of correlation between *Malassezia* (formerly *Pityrosporum ovale*) number and the individual susceptibility on severity of dandruff. It also discusses other unexplored factors of dandruff formation.

KEY WORDS: **Dandruff, Malassezia, Individual Susceptibility, Corneocyte**

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INTRODUCTION

The word dandruff (dandriff, dandriffe) is of Anglo-Saxon origin, a combination of *tan* meaning "tetter" and *drof* meaning"dirty".[1] Thus, dandruff is 'itch-dirt'. It can be perceived by an individual with excessive desquamation of flakes on the scalp, in the hair, sometimes shed on the cloth. In medical terminology, this skin disorder often referred as *pityriasis simplex* and *pityriasis capitis.*[2] Regardless of ethnicity and gender, the most common problem of dandruff is confined to the scalp, and it is experienced by about half of the postpubertal population. Dandruff is a widespread skin disorder and the precise understanding of dandruff has been controversial owing to multiple variables. However, it represents a persistent aesthetical disturbance, psychological trauma, exhibiting the loss of self-esteem and provokes negative socio-economic impact.[3] Nonetheless, upon regular use of anti-dandruff shampoo represents a proven therapeutic strategy to improve the most common symptom of flakes and itch.[3] This paper avoids dealing with the therapeutic efficacy and its treatment of dandruff, which in itself a large subject.[4]

GLOBAL PRESENCE OF DANDRUFF

Dandruff is a universal scalp disorder, had estimated 15-20% of sufferers of the global population and in particular more than 50% of adult population.[5] The severity of dandruff varies with season as it often worsens in winter for poor personal hygiene, and may moderate in summer. For instance, a survey of dandruff carried out in different ethnic groups in the U.S.A. and China, it had been documented that the scalp flaking was much commoner. The dandruff occurrence rate of African-Americans is 81-95%, whereas for Caucasians is 66-82%, and 30-42% in the Chinese.[5] Furthermore, there are more studies of the occurrence of seborrhoeic dermatitis in specific groups such as the immunosuppressed. It has been recorded to have a prevalence of 31% in HIV-positive patients, and 9.5% in renal transplant recipients.Annually, in USA nearly $ 300 million spent on various anti- dandruff products.[5,6]Another interesting study correlates the occurrence of dandruff and blood group.[7] The study reveals that blood group 'O' subjects may be the most susceptible, followed by 'AB' group. It is assumed to be fungal glycoprotein can cross react with the human isoantigens of different blood group and the cross reactivity may help the organism to skip the immune surveillance of the host's defense mechanism. Albeit, very limited studies are available and still leaves some doubts why some subjects in a given population develop dandruff while others not.

DANDRUFF AND SEBORRHEIC DERMATITIS

The spectrum bands of dandruff and seborrheic dermatitis are difficult to pinpoint because it blurs with each other. Nevertheless, dandruff is the mildest form of clinical presentations of seborrheic dermatitis. It is characterised by minimal inflammation and remains subclinical. It is recognised by the presence of scattered lymphoid cells and 'squirting capillaries' in the papillary dermis with hints of spongiosis and focal parakeratosis. Conversely, seborrheic dermatitis is highly inflammatory often extending outside the limits of the scalp. It is characterised by a spongiotic dermatitis in which mounds of parakeratosis and scale crusts form at lips of Infundibular ostia.The key variation between the dandruff and seborrheic dermatitis are visible redness or erythema and the presence of flakes beyond the scalp.[7] The defined pathogenetic mechanisms involved in both dandruff and seborrhoeic dermatitis are unclear. Although, it appears that common root cause for both the dandruff and Seborrheic dermatitis are the gene *Malassezia* produce different irritants or metabolites. However, the presence of HIV may intensify this pathway. For seborrheic dermatitis, therapeutic treatment is often required to cure the disease; however it was report that some cosmeceuticals may show efficacy.[8]

COMPOSITION OF DANDRUFF

Dandruff is an improper collation of corneocytes, which are gathered large degree of cohesion with one another. Collectively, it detached at the surface of the stratum corneum in a scattered manner and can be visually perceived by an individual. The

magnitude of size and abundance of dandruff scales are non-similar from one site to another and over period. The numbers and visual appealing of dead flaking cells on scalp are linked to the severity of the clinical manifestations, which may also be influenced by seborrhoea dermatitis.[8, 9]

SCALP -A PLAYGROUND FOR FUNGI

The human scalp provides a favorable atmosphere for the growth of a number of microorganisms. It flourishes the micro-organism which is lipophilic, kerartinolytic and saccharolytic. Scalp skin is physiologically very similar to non-palmoplantar skin of rest of the body. The scalp environment is covered by a thick fabric of hair. There are nearly 250 hair fibers per cm^2. For instance, in a typical individual, the hair surface area of 50,000 cm^2 relative to the scalp surface area of 600 cm^2. Altogether, it appears to be relative inaccessibility of the scalp surface to targeted delivery of actives.[10] However, this protected environment of scalp with bunches of hair is an intrinsic challenge to achieving therapeutic benefits (anti-dandruff) with minimal application time.

THREE ETIOLOGICAL FACETS OF DANDRUFF

Based on recent technology, the aetiology of dandruff and seborrheic dermatitis are dependent upon three main factors: Fungi (*Malassezia*), Sebum, and Individualsusceptibility.[11]

MALASSEZIA - A FUNGI

The existence of the fungi has been known since 1800 when Eichstedt described the occurrence of yeast when a patient with Pityriasis Versicolor.[11] The term 'Pityriasis' used to describe skin conditions in which the skin scale is similar to bran. The multiple colours arising in the disorder give rise to the second part of the name, 'Versicolor'. It is a common skin complaint in which flaky discoloured patches appear mainly on the chest and back. In 1873, Rivolta brought another dimension into the context that he suggested that yeasts were also present in dandruff.[12] A French scientist Malassez subsequently described both oval and round spores in scalp scales from patients with dandruff.[13] His break through discovery of the genus named *Malassezia* was described in 1889 *Malassezia furfur* was the name given to the organism seen in pityriasis versicolor.[14] Sabouraud believed that there was a distinct difference between the yeasts that caused pityriasis versicolor and scaly scalps, largely because of the presence of hyphae in the former; although he had accepted that the yeast forms were morphologically similar.[15] He then named the cause of scalp scaling *Pityrosporum malassezii*. For many years, the nomenclature of these fungus assumed that *Pityrosporum* was the correct term for the genus. As the day progressed, invention of two species of *Pityrosporum* were recognized, a round yeast form, *P. orbiculare*, and an oval form, *P. ovale* by Burkein 1961.[16-19] Some investigators, notably Midgle, recognized that there were probably more than two species in this complex, by detailed study of their morphology and antigenicity. With the application of molecular genetic techniques also came the realisation that there were more species than originally suspected. The apparent conflict between the two different names of the genera, *Malassezia* and *Pityrosporum*, has only been resolved with the application of molecular genetic techniques.[20] *Malassezia,* being the earlier name for the genus, was therefore the genus assigned to these organisms. Today, it was classified as lipid dependent and non-lipid dependent species, where the non-lipid dependent species is primarily on animal whereas former is present on human. The lipid dependent species are M*. furfur, M. sympodialis, M. globosa, M. obtusa, M. slooffiae, M. restricta, M. Japonica, and M. Nana* and non-lipid dependent species is *M. pachydermatis*. It may not be wonder that the list may go long. However, many species are occasionally found in nature. Recently the complete genomes of two *Malassezia* species, *M. globosa* and *M. restricta*, have been sequenced. *Malassezia globosa* is the root cause and it can produce short hyphae, both in culture and in skin affected by pityriasis versicolor.[21,22] It can also grow as round yeast and found responsible for sebum metabolites leads to dandruff. The relative abundance of fungus and the cause of dandruff are not answerable till date. The specific reason why *Malassezia globosa* is the major causative responsible for the cause, besides being

bunches of other fungus in the harbour of scalp.

SEBUM- FOOD FOR FUNGI

Human sebum is a multifaceted mixture of triglycerides, fatty acids, squalene, and esters of wax, sterol and cholesterol.[23] The functional attributes of sebum are epidermal development, barrier maintenance, transporting antioxidants, and generation of pheromones.[24] It is directly involved in epidermal differentiation, and also acts as defence from ultraviolet (UV) pollution.[25,26] When it is secreted and broken down by microbes, sebum consists of esters and triglycerides which are converted into diglycerides, monoglycerides, and free fatty acids. The free fatty acids, for instance oleic acid, plays major role in instigation of the irritant response, which is involved in scalp hyperproliferation, then leads to excessive desquamation of scalp scales. The influence of excessive androgens in the blood irrigating the scalp as this is one of the important consideration of dandruff after puberty in young men and women, and in women experiencing a decrease in oestrogen either through the natural or artificial menopause. Hence therefore, it is unavoidable that the role of sebaceous secretion also impacts the dandruff incidence and severity.[27-30]

INDIVIDUAL SUSCEPTIBILITY

It had been reported[31] that the fatty acid metabolite of *Malassezia*, releases oleic acid, induces flaking in dandruff-susceptible patients, but not in non-susceptible patients.[31] It is noteworthy to mention that, conducted the study and applied a fatty acid *Malassezia* metabolite, oleic acid, to the scalp of human volunteers who were clinically assessed as dandruff or non-dandruff.[32,33] Oleic acids initiate a flaking response which was indistinguishable from dandruff by visual observation or electron microscopy. However, it was observed that dandruff for susceptible individuals but not in non-susceptible patients.[34-36]The turning point in understanding of fatty acid metabolites of *Malassezia* leads to itching and irritation, suggests an underlying the root cause of dandruff and shows the difference amongst individuals, that steering infurther development of dandruff or seborrheic dermatitis. The fine line of difference between dandruff susceptible and non-susceptible individuals remains perplex and yet to understand in depth. This may be due to the characteristic differences in stratum corneum barrier function, skin permeability, and immune response to free fatty acids or proteins and polysaccharides from *Malassezia*. [37-40]

SCORING OF DANDRUFF

The subjective observation and optical scoring is widely practiced to evaluate the harshness of dandruff. During the anti-dandruff *in-vivo* efficacy studies, the inspection of entire scalp is advisable rather than defined specific area.[41] Typically, trained volunteers are involved in scoring the dandruff for the studies. Bioinstrumental quantitative methods like squamometry and photography are often employed in some places.[42-44]

CORNEOCYTE IMPLICATIONS OF DANDRUFF

The population of *Malassezia* is uneven throughout the scalp surface and inside the stratum corneum. Clumpy adherence of the yeast is seen in some corneocytes; conversely, corneocytes in the neighbourhood region harbour few of this yeast. It seems to be perhaps the *Malassezia* binding site may differ in corneocytes. Another hypothesize is the natural antifungal peptides of the inborn immunity to the above cause. The colonization of the yeast boosts the expression of *β–defensin-2* (known as skin-antimicrobial peptide 1 (SAP1) is a peptide that in humans is encoded by the *DEFB4)* by keratinocytes.[45,46] In dandruff, their expression of *β–defensin-2* could be reduced at some sites where the abundance of *Malassezia* is more. In spite of everything, dandruff doesn't alter the immune response. The *Malassezia* corneocyte hypothesis still leaves some doubt. Despite dandruff being resolved, it does not explain with low parakeratotic index persists and *Malassezia* largely removed. It is hypothesized that the antifungal agents may not be able to remove deep-seated yeasts allowing a minimal inflammatory reaction to be maintained or the anti-inflammatory activity claimed in the antidandruff agents is not effective enough in vivo.The adverse reaction such as irritant dermatitis or contact allergic

dermatitis may be triggered by the treatment agents.

INFLUENCE OF HAIR SHEDDING AND ULTRASTRUCTURAL MODIFICATION OF SC

On a two-day survey, it was reported that nearly 100-300 numbers of hairs were shed in dandruff sufferers instead of 50-100 in normal subjects. In some cases of dandruff, hair shedding may be a result of alterations in the teloptosis process (exogen phase) and hair eclipse phenomenon. Another study shows that Transmission electron microscope (TEM) of scalp tape trips indicates that dandruff scalp possess abnormal stratum corneum (SC) and ultrastructural alterations and decrease in desmosomes.[46] Again very limited studies are available, the detailed understanding of Hair Shedding and the dandruff yet to be studied.[47] The schematic representation of dandruff formation is shown in fig1.

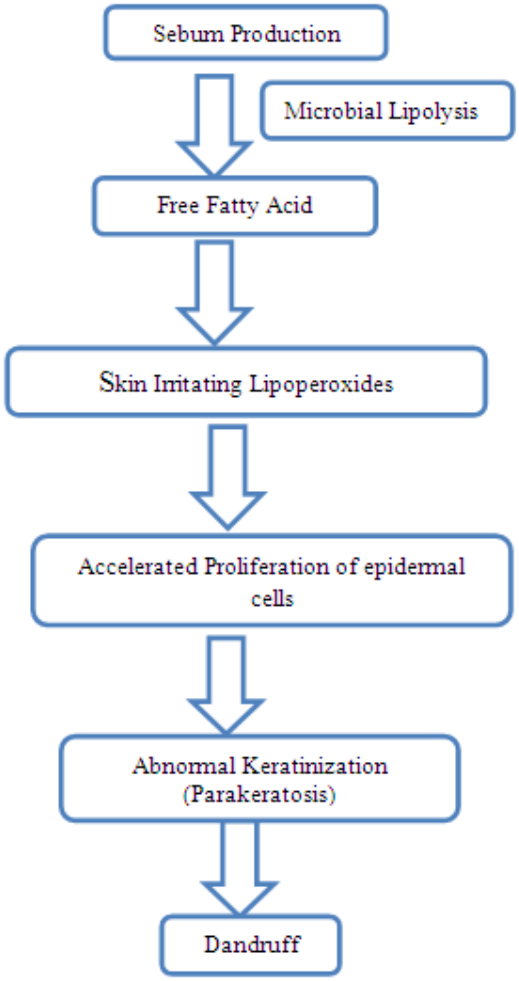

Figure 1
Pathogenesis of Dandruff

CONCLUSION

Dandruff is a day-to-day problem and is reactive response of the epidermis of the scalp to various stimuli. The above discussions, provides the convergent set of physiopathology supports that the role of *Malassezia spp*. as the main contributing agent. There are other non-microbial factors such as UV rays and airborne irritant agents which must not be overlooked. Extended research will be necessary for precise finding

on sebum metabolites for both the susceptible and non-susceptible individuals. It will be necessary to understand the fundamental interaction between *Malassezia* biology with human skin. The sequencing of these genomes, in accordance with the already sequenced human genome, will allow a detailed investigation of the metabolic interactions between human skin and *Malassezia*. The new break through research will enable the development of new technologies to interrupt dandruff, which may or may not compliment to the existing antidandruff treatments. Besides, hair is not only an aesthetic appealing but also protects the skin from wounds, bites, heat, cold, and UV radiation. Nevertheless, protecting and maintaining the existing hair is another challenging task from various skin disorders. Hence, more scientific work needed for the influence of hair shedding during dandruff and plausible reason for its recurrence. Hopefully, these basic investigations of dandruff will ease the formulators to develop the effective therapeutic dandruff products.

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