PROPIONIBACTERIUM ACNES AND THE SKIN DISEASE OF ACNE VULGARIS

PROPIONIBACTERIUM ACNES ȘI IMPLICAREA LUI ÎN ACNEEA VULGĂRĂ

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Abstract

The human skin encompasses a vast variety of microorganisms which construct the structure of skin microflora. Bacteria and yeasts may be the pioneers of the human skin normal flora. The anatomical situations and physicochemical conditions determine the demography of the microbial populations. Among different types of microbial populations, Propionibacterium acnes is the predominant member in the skin areas of back, face and chest. Although this bacterium is part of the normal flora, Propionibacterium acnes contributes to the disease of acne vulgaris. By the progression of scientific disciplines such as Microbiology, Genetics, and Molecular Biology, it is going to be clear that some strains of Propionibacterium acnes are useful and good bacteria and some strains are harmful and bad bacteria. Therefore, in this review, the authors have a look on different characteristics of P.acnes and the related skin disease of acne vulgaris.

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Propionibacterium acnes, or former Corynebacterium parvum, is an important bacterial agent which acts as a multifunctional microorganism. This bacterium is seen in different parts of the human body, from the conjunctivae, oral cavity, and nares to intestinal and respiratory tracts. The biochemical properties of P. acnes are related to the bacterial functions and activities. This bacterium is a slow growing Gram +ive, anaerobic and microaerophilic bacillus which is able to produce propionic acid as a fermentative microbial product. P. acnes populations cover 50% of the human skin normal flora; however, the number of populations differs in different parts of the body. It ranges from <10 cells/cm² on the nose to 10⁷ cells/cm² on the human facial skin. On the other hand, this bacterium may act as a skin pathogenic microorganism, which may lead to different types of skin diseases like acne vulgaris. According to previous studies, there are many factors, comprising nourishment program and skin hygiene that determine the number of bacterial populations of P. acnes as an opportunistic microbial agent causing acne vulgaris. Dekio et al. have indicated that P. acnes encompasses several strains and the highest strain diversity has been observed on the facial skin. Among different bacterial strains of P. acnes, ST6 has a high tendency to dryness and rigid conditions (1-7).

P. acnes is an interesting opportunistic bacterium which plays a significant role in both health and infection of human hosts. In addition to acne vulgaris, the ubiquitous bacterial agent of P. acnes has a bold contribution to different types of infections associated with indwelling medical devices and prostheses. Despite the vast activity regarding infectious diseases, the presence of P. acnes as an important skin microbiota prevents colonization of dangerous pathogenic microorganisms. In this review, the authors have a look on different characteristics of P. acnes and the related skin disease of acne vulgaris (7-9).

Skin is recognized as the largest outer organ in the human body which protects the inner system from outsiders and foreigners. Indeed, skin acts as the first natural barrier against microorganisms as a part of the innate immune system. Human skin involves a wide range of microflora, significantly including Acinetobacter, Candida, Corynebacterium, Malassezia, Micrococcus, Propionibacterium, Saccharomyces, Staphylococcus (10-15).

Among aforementioned microorganisms, the populations of Propionibacterium are predominant bacterial microorganisms on sebum rich zones (such as chest, back, and head) and pilosebaceous follicles. In accordance with several investigations, there is a considerable variety among Propionibacterium species which comprises P. avidium, P. acnes, P. lymphophilum, P. granulosum and P. propionicum (12,15,16).

Furthermore, the physicochemical conditions of the skin including glands (their size, number and functions), follicles (their size, number and functions), the density of secreted discharges like sweat, sebum, antimicrobial secretions such as defensins and dermicidin, nutrition, temperature, oxygen, pH, microbial products and their antagonistic and synergistic effects determine the residue of cutaneous normal flora populations. The ability of enzyme secretions in microorganisms is another factor in their colonization of the skin, because the presence of microbial extracellular enzymes in the human skin makes a wide range of nutrition accessible for microorganisms (12,17).

Acne vulgaris is a chronic skin condition, originating from hair follicles and the related sebaceous glands, classified as inflammatory/non-inflammatory or alternation of both. However, minor populations of patients have severe forms of acne vulgaris. There are many factors which may lead to the occurrence of acne vulgaris. One of the most im-
portant factors regarding the appearance of acne vulgaris is genetic predisposition, accompanied by deep hormonal changes. The prevalence of acne vulgaris in Dark skinned people, the Mediterranean region people, the Caspian Sea region and the Persian Gulf region people is higher than other parts of the world. Moreover, young boys (male teenagers) are more frequently affected by severe, nodulo-cystic forms of acne, while in women the disease is lasting longer, reaching adulthood or, in some cases, appears for the first time into the 3rd or 4th decade of life. Acne pathology comprises 4 steps including blockage of the follicle via abnormal keratinization of follicular units, overwhelmed sebum production and storage, hyperactivity of resident normal flora populations of P.acnes and the appearance of inflammation\(^{(18-23)}\).

In patients with acne vulgaris, comedones and swollen, erythematous, painful papules, pustules and nodules are seen mostly on facial skin area, back and chest (particularly on the upper chest zone). Comedones are made by abnormal secretion of lipids resulting in follicular keratinization. Simultaneously, the resident populations of P.acnes begin to proliferate within the accumulated sebum and keratinized follicle. A closed whitehead comedone consists of dead cell debris, P.acnes and the related bacterial secretions (such as hyaluronidase, neuraminidase, protease etc.), and sebum. These materials provide the proper environment for the comedones to become inflamed and breached. Among these compounds, the bacterial extracellular enzymes secreted by P.acnes cells raises up the rate of breakage of the closed comedones. The activity and proliferation of P.acnes’ bacterial cells stimulate the innate immune system with different types of chemokines and cytokines\(^{(1,24-26)}\).

### Genomics and Biofilm formation of Propionibacterium acnes

The complete genome of some strains belonging to P.acnes has been determined and published. The study of complete genome sequences shows a diversity of virulence factors such as adhesins, inflammatory factors and weakening host cell factors (in particular, extracellular enzymes like protease, lipase, hydrolase etc.). The major differences between bacterial strains of P.acnes are recognized in island-like regions (ILRs) which play a key role in the expression of virulence factor genes\(^{(27-29)}\).

The diphtheroid-like bacterium of P.acnes has a predominant ability to form stable biofilms. This characteristic helps P.acnes colonies to reside on host’s skin surface, which has a protective property for the host. Simultaneously, the property of biofilm formation can be recognized as an important virulence factor for pathogenic bacterial strains. So, the ability of biofilm formation in P.acnes can be considered beneficial for useful strains and harmful for pathogenic strains. The biofilm structure is composed of bacterial polysaccharides which embeds the bacterial cells of P.acnes within itself. Indeed, the polysaccharide acts as a biocement. The main characteristic of biofilm is to prevent the penetration of outsider microorganisms, immune cells, and antibiotics. Thus, the biofilm structures of P.acnes strains relating to normal flora populations are good and the biofilms of invasive and infectious strains of P.acnes may be life-threatening and deathful. A considerable factor which helps P.acnes to dominate other microorganisms which reside on the surface of human skin is the ability of secretion of extracellular enzyme of lipase. That is why, the bacterium of P.acnes are isolated from the fatty portion of the skin like face, back, and chest\(^{(1,20-33)}\).

### Propionibacterium acnes and host’s immune system

The immunologic investigations have revealed that opportunistic pathogenic strains of P.acnes trigger the pattern recognition receptor (PRR) molecules within the host immune system. The PRRs have different types of members like Toll-Like Receptors (TLRs). Secretion of extracellular enzymes by P.acnes makes some injuries in host skin tissues. The damaged skin tissue stimulates TLRs (TLR-2 and TLR-4) on keratinocytes which may lead to secretion of chemokines and cytokines comprising Interleukin (IL)-1a, IL-8, and Tumor Necrosis Factor (TNF)-α. TLR-2 has a key role in association with inflammation of comedones on the host skin\(^{11,9,34-36}\).

### Treatment

Treatment must address all the factors implicated in acne pathogenesis and has to be tailored to disease severity. The simultaneous use of topical retinoids and antibiotics is the best choice for a definite treatment of acne vulgaris caused by P.acnes. The use of antibiotics, especially in the form of oral consumption, is recommended for moderate to severe acne vulgaris. However, there are several reports regarding drug resistant strains against metronidazole and some members of aminoglycosides. The use of benzoyl peroxide is recommended for all forms of acne vulgaris. The use of retinoids in the form of oral consumption is the best choice for severe forms of acne vulgaris. Furthermore, hormonal therapy may be used as the second choice when hormonal disturbances or polycystic ovary syndrome have been documented\(^{19,20,37,38}\).

### Conclusion

Acne vulgaris is a multifactorial condition. Genetic predisposition, hormonal changes, race, geographic situation, sex and bacterial strains have direct effects on the occurrence of acne vulgaris in patients. So, no single factor may be able to arise the disease of acne vulgaris. The role of P.acnes in acne pathogenesis has
been a matter of dispute over the years; therefore, future studies are mandatory in order to conclude this subject. Recent data suggests that this interesting Gram positive bacillus has the ability to act both as a skin commensal with protective action in people without acne and as a skin pathogen, by promoting follicular inflammation and hyperkeratinization in patients with acne. Its ability to form stable biofilms can be regarded as a protective phenomenon in healthy skin as well as a dangerous mechanism for the development of antibiotic resistant strains in acne affected skin. 

Bibliography