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The Complex Role of Microbial Parasites in Human Health: Their Benefits, Risks, And Impact on the Body And Genes: Areview

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Annotation: Microbial parasites play a complex role in human health, with effects ranging from beneficial to harmful. Some cause severe diseases, while others support the immune system or help maintain microbiome balance. These parasites can influence gene expression, contributing to varied immune responses. The Demodex mite is a notable example, naturally residing in hair follicles and sebaceous glands, aiding in the removal of oils and dead skin cells. However, excessive proliferation can lead to skin issues, such as blepharitis or associations with rosacea. The interaction between this parasite and the immune system may result in genetic changes in immune expression, explaining its varied effects on individuals. Studying this relationship offers deeper insights into human health and potential treatments for skin and immune-related disorders.

Keywords: Microbial parasites, Demodex, genetic identification, immune expression, hu.

Introduction

protozoa, and mites, interact with the human body in diverse ways, ranging from beneficial to harmful. While some parasites are well-known for causing severe diseases and infections, others play subtle but essential roles in maintaining human health. They can regulate immune system function, contribute to microbiome stability, and influence genetic expression, shaping how our bodies respond to various environmental challenges. This delicate balance between symbiosis and pathology highlights the complexity of microbial parasites' role in human health.(Ristori et al., 2024)

A compelling example of this dynamic relationship is Demodex, a genus of microscopic mites that naturally reside in humans' hair follicles and sebaceous glands. Demodex mites, particularly Demodex folliculorum and Demodex brevis, are generally considered harmless and may even provide certain benefits, such as helping to remove dead skin cells and excess sebum. However, when their populations grow excessively or when the immune system reacts abnormally to their presence, they can contribute to various dermatological conditions, such as rosacea, blepharitis, and other inflammatory skin disorders. Moreover, the interaction between Demodex and the immune system may trigger changes in gene expression, leading to unique responses in different individuals.(Kairey et al., 2023)

By examining the complex interplay between human biology and microbial parasites like Demodex specifically Demodex folliculorum and Demodex brevis, we can gain deeper insights into their dual roles as both potential allies and adversaries. This understanding is crucial for developing targeted treatments for parasitic-related disorders while preserving their beneficial contributions to our overall health.(Murillo Rojas, 2019)

Biological Characteristics

Demodex mites are among the smallest arthropods, measuring approximately 0.3-0.4 mm in length for D. folliculorum and 0.15-0.2 mm for D. brevis. They have elongated bodies, eight legs, and are primarily active at night. These mites feed on sebum and epithelial cells, and their life cycle lasts about 14 days, during which they reproduce within the hair follicles.(Izri et al., 2025)

Genetic Identification and Characteristics of Demodex Mites

Two genetically identified species of Demodex mites commonly inhabit human skin:

Demodex folliculorum

Typically resides in the hair follicles near the skin surface. Genetic analysis has verified it as a distinct species from D. brevis.Exhibits a novel mitochondrial gene order that differs substantially from the ancestral chelicerate pattern.Possesses extremely truncated tRNA genes in its mitochondrial genome, with several lacking the sequence to code for both D- and T-arms(Alsaeedi, 2020)

Demodex brevis

Generally found deeper in the sebaceous glands compared to D. folliculorum.Genetic studies using mitochondrial and nuclear markers have confirmed it as a distinct species from D. folliculorum.Shares the same novel mitochondrial gene order and truncated tRNA genes as D. folliculorum.The high level of sequence divergence between D. folliculorum and D. brevis suggests they last shared a common ancestor no more recently than about 87 million years ago.

While only two species have been genetically identified on humans, there are over 140 described Demodex species or subspecies that infest various mammals. The genus Demodex is considered highly host-specific, with estimates suggesting there may be as many as 10,000 Demodex species across mammalian hosts. However, the true diversity and evolutionary history of this genus remains poorly explored.(Anderson, 2023)

Molecular Techniques for Identifying Demodex Species

1. PCR Amplification of rRNA Genes

18S rRNA Gene: This gene is commonly targeted for species identification due to its conserved nature across different mite species. Primers designed for the 18S rRNA gene can amplify DNA from various Demodex species, allowing for differentiation based on sequence analysis. This method has shown high sensitivity and specificity in detecting Demodex mites in various samples, including skin and hair follicles.16S rRNA Gene: Similar to the 18S rRNA gene, the 16S rRNA gene is another target for PCR amplification. It has been used to identify Demodex species, particularly in studies focusing on phylogenetic relationships. Specific primers can amplify regions unique to Demodex, aiding in species differentiation.

2. Mitochondrial DNA Analysis

Mitochondrial 12S rRNA Gene: This gene has been highlighted as particularly effective for the molecular identification of Demodex species. Studies have shown that the mitochondrial 12S rRNA gene provides a reliable marker for distinguishing between species such as Demodex folliculorum and Demodex brevis. The amplification of this gene has proven useful in both clinical and research settings for accurately identifying Demodex mites.

3. DNA Sequencing

Following PCR amplification, sequencing of the amplified products is crucial for accurate species identification. The sequences obtained can be compared to existing databases like GenBank to confirm species identity. This method allows for the detection of genetic variations and the establishment of phylogenetic relationships among different Demodex species.

4. Cloning Techniques

In some studies, cloning of PCR products has been employed to isolate and sequence individual copies of rRNA genes. This approach helps in understanding the diversity of Demodex species present in a sample and can reveal intra-species variations.(Hamamci and Acikgoz, 2019)

Effect on the skin

Commonality: Demodex mites are found on nearly all adults, with estimates suggesting that between 23% and 100% of healthy individuals harbor them without any symptoms.

Role in Skin Health: In small numbers, these mites help maintain skin health by consuming dead skin cells and excess oils, contributing to the skin's natural balance.

- **Problems Associated with Overpopulation**

When the population of Demodex mites increases excessively, typically due to factors such as immunosuppression, poor skin hygiene, or certain skin conditions, they can cause several dermatological issues:

Demodicosis: This condition arises when the mite population becomes uncontrolled, leading to symptoms such as: Itchy, irritated skin, Redness and inflammation, Acne-like blemishes, Rough or scaly skin, Eye irritation, particularly in cases affecting the eyelids (blepharitis) and potentially leading to loss of eyelashes.

Rosacea: There is a notable association between high densities of Demodex mites and rosacea, a chronic inflammatory skin condition characterized by facial redness, flushing, and visible blood vessels. The exact relationship is unclear; it may be that the mites exacerbate rosacea symptoms or vice versa.

Other Conditions: Increased Demodex populations have also been linked to non-specific dermatitis, which can manifest as dryness, itching, and acne-like lesions.

Risk Factors for Complications

Certain individuals are more susceptible to demodicosis, including:Those with weakened immune systems (e.g., individuals with HIV/AIDS, cancer, or liver disease),Older adults and children under five,People using immunosuppressive medications.(Honey et al., 2025)

Relationship between Demodex Mites and Sebaceous Glands

Demodex mites thrive within the sebaceous glands, where they feed on sebum, a lipid-rich secretion produced by these glands. Sebum consists of triglycerides, wax esters, squalene, and free fatty acids, which provide essential nutrients for the mites. Demodex mites rely on the lipids and cellular debris found in sebaceous secretions. Their enzymatic activity, including lipase secretion, can damage glandular and epithelial cells, further increasing nutrient availability as they break down these cells. Demodex mites break down triglycerides into free fatty acids, which serve as a primary energy source. Excessive triglyceride production can therefore promote Demodex proliferation. Squalene and wax esters contribute to the structural integrity of sebum and the skin barrier. Higher levels of squalene are associated with enhanced Demodex growth due to its nutritional value. The pH of sebum can affect Demodex survival. A slightly acidic environment, typical of healthy skin, may regulate mite populations. However, deviations in pH, often due to skin conditions, can create conditions that favor overgrowth (Demirdağ et al., 2016; Turan et al., 2017).

Impact of Sebum Composition on Demodex Density

Sebum Production and Mite Density:

The density of Demodex mites is influenced by the composition and quantity of sebum. Higher sebum production, often linked to hormonal changes or skin conditions like acne, creates a favorable environment for mite proliferation. Conversely, reduced sebum production may limit mite growth, although some species of Demodex can survive in low-sebum environments by utilizing minimal resources effectively (Demirdağ et al., 2016; Vanderwolf et al., 2023).

Hormonal Fluctuations and Sebum Composition:

Hormonal changes, such as those occurring during puberty or pregnancy, increase sebum production and alter its composition, often resulting in higher Demodex densities. These changes are frequently associated with conditions like acne and rosacea. In contrast, aging typically decreases sebaceous gland activity, but older adults may still exhibit higher Demodex densities due to alterations in lipid composition or immune function (Turan et al., 2017; Vanderwolf et al., 2023).

Sebaceous Gland Activity and Skin Health

Sebaceous glands play a vital role in maintaining skin health by regulating moisture and providing a protective barrier. Increased activity of these glands, due to hormonal changes, skin conditions, or age, can create an environment conducive to Demodex mite growth. For instance, rosacea is associated with higher sebaceous gland activity, which in turn correlates with increased Demodex populations (Botsali & Yürekli, 2022).

Skin Conditions Associated with Demodex Proliferation:

Increased sebum production, as seen in acne and hormonal fluctuations, supports higher mite populations. This can lead to conditions like rosacea, seborrheic dermatitis, and acne vulgaris, where the mites exacerbate inflammation and damage the skin barrier (Paichitrojjana, 2022; Vanderwolf et al., 2023).

Demodex and Sebum-Mediated Skin Conditions

Enzymatic Activity and Skin Conditions:

When Demodex populations increase, their enzymatic activity, such as the secretion of lipases, can disrupt sebaceous gland function. This disruption leads to the release of inflammatory molecules, worsening skin conditions such as acne, rosacea, and demodicosis (Chioveanu et al., 2024).

Cycle of Inflammation and Mite Proliferation:

The interaction between Demodex mites and altered sebum composition creates a cycle of inflammation, glandular damage, and further mite proliferation. Additionally, Demodex mites can influence sebum composition by carrying bacteria that alter the local skin environment, contributing to dysbiosis and the pathogenesis of inflammatory skin disorders (Schaller et al., 2002; Aktaş & Aksu Çerman, 2020).

The Role of Demodex Mites in Immune System Modulation:

Demodex folliculorum and Demodex brevis are typically harmless skin commensals residing in hair follicles and sebaceous glands. However, under certain conditions, they can provoke pathological responses by modulating immune pathways, including Toll-like receptor (TLR) signaling and the secretion of pro-inflammatory cytokines, such as interleukin-8 (IL-8). These interactions between Demodex mites and the human immune system play a significant role in both dermatological health and disease (Rhee et al., 2023).

Interaction with Toll-like Receptor (TLR) Pathways:

Toll-like Receptors (TLRs) and Immune Response:

TLRs are crucial in recognizing pathogens and initiating immune responses. Demodex mites interact with TLRs in the following ways:

Initial Immunosuppression:

Demodex mites downregulate TLR signaling, particularly in sebocytes, through the release of protease inhibitors. This immunosuppressive effect allows the mites to thrive in sebaceous glands without triggering an immediate inflammatory response (Akkaş et al., 2022; Kumari et al., 2018).

Prolonged Exposure and Immune Activation:

Over time, the presence of Demodex mites leads to the upregulation of TLR2, shifting the immune response to one of inflammation. This results in the secretion of pro-inflammatory molecules and the recruitment of immune cells, contributing to symptoms like skin redness, irritation, and inflammation (Lacey et al., 2018).

Cytokine Secretion and Inflammatory Response

Interleukin-8 (IL-8) and Other Cytokines:

The presence of Demodex mites induces cytokine activity, which is central to the inflammatory response:

IL-8 Secretion:

IL-8 is crucial in the inflammatory cascade, recruiting neutrophils to the site of infestation. This leads to clinical manifestations such as papules, pustules, and redness, common in conditions like rosacea. In addition to IL-8, the mites also contribute to the increased expression of other pro-inflammatory cytokines, such as IL-1β and TNF-α, which amplify local inflammation and disrupt the skin barrier (Akilov et al., 2004; Kim et al., 2011; Rhee et al., 2023).

Immunosuppression and Chronic Inflammation:

Immunosuppressive Mechanism:

Demodex mites secrete protease inhibitors that create a localized immunotolerant environment. This suppression allows the mites to proliferate without triggering significant immune responses. However, prolonged modulation can lead to chronic, ineffective inflammation, characterized by T-cell exhaustion. This results in an ongoing inflammatory response without resolving the underlying infestation (Reithofer & Jahn-Schmid, 2017; Marquardt-Feszler et al., 2022).

Immune System Influence on Demodex

Factors Promoting Demodex Growth:

Several factors influence the growth of Demodex mites, particularly in compromised or altered immune environments:

Immunosuppression:

Conditions like HIV, cancer, and the use of immunosuppressive medications allow unchecked growth of Demodex mites by weakening immune surveillance (Marquardt-Feszler et al., 2022).

Genetic Predispositions:

Variations in immune system genes can affect an individual's susceptibility to Demodex-related inflammation and influence the ability to regulate mite populations effectively (Paichitrojjana,2022).

Hormonal and Age-Related Factors:

Increased sebum production during hormonal fluctuations (e.g., puberty, pregnancy) or a reduced immune response with aging creates favorable conditions for Demodex proliferation, particularly in individuals with acne or rosacea (Akilov et al., 2004; Gazi et al., 2019; Akkaş et al., 2022).

Modulation of TLR Signaling and Immune Response:

TLR Modulation in Sebocytes:

Demodex mites can modulate TLR2 expression in sebocytes, which plays a critical role in recognizing pathogens and initiating immune responses. Initially, mites may suppress certain immune genes, but prolonged exposure leads to the upregulation of pro-inflammatory responses, contributing to inflammation and immune activation (Chen et al., 2023).

Interaction with the Skin Microbiome:

Bacterial Antigens and Immune Modulation:

Demodex mites can act as vectors for bacteria like Bacillus oleronius, which produce bacterial antigens that stimulate immune responses. This interaction can exacerbate inflammation, especially in individuals with rosacea, where there is a significant correlation between Demodex density and immune reactivity to bacterial antigens (Zhu et al., 2028; Pyzia, et al., 2024).

Antigen Expression:

Demodex mites express specific antigens, such as the Thomsen-Friedenreich (Tn) antigen, which may induce immunotolerance and contribute to chronic inflammatory states. These antigens interact with dendritic cells, potentially leading to T-cell exhaustion and a tolerogenic immune environment, allowing the mites to persist in the skin (Forton, 2020).

Bioactive Molecules Secreted by Demodex Mites (Jarmuda et al., 2012; Lacey et al., 2018)**:**

Lipases and Cytotoxic Effects:

Demodex mites secrete lipases that break down sebum into cytotoxic components. These components irritate the skin, leading to inflammation and exacerbating skin conditions by damaging the follicular epithelium and promoting perifollicular inflammation.

Pro-inflammatory Cytokine Secretion:

In addition to lipases, Demodex mites induce the secretion of pro-inflammatory cytokines, such as IL-8, contributing to the inflammatory response and the progression of conditions like rosacea.

Demodex as a Vector for Bacteria

Demodex mites are believed to act as vectors for several bacteria, including *Bacillus oleronius*, *Staphylococcus aureus*, and coagulase-negative staphylococci. These bacteria can reside on the surface of the mites or within their bodies, potentially contributing to skin conditions when

the mite population increases beyond normal levels. The presence of bacteria associated with Demodex mites may exacerbate inflammatory skin conditions. For instance, *B. oleronius* is thought to play a role in the inflammatory processes seen in rosacea, as it can induce neutrophil activation and contribute to the immune response. This relationship suggests that Demodex mites may not only be bystanders but could actively participate in the pathogenesis of certain skin disorders. The overpopulation of Demodex mites can lead to conditions such as demodicosis, which may present with symptoms similar to skin disorders like folliculitis and rosacea. In these cases, the interaction between the mites and the bacteria they carry can complicate the clinical picture, making diagnosis and treatment more challenging. The interaction between Demodex mites and skin bacteria is also part of the broader human skin microbiome. Changes in the skin environment, such as increased sebum production or altered immune responses, can influence Demodex populations and the bacterial communities present, potentially leading to dysbiosis and associated skin problems.(Li et al., 2025)

Unique Interactions with Bacteria

Demodex mites can act as vectors for bacteria like Bacillus oleronius, which may function as co-pathogens in rosacea by interacting with the immune system.The relationship between Demodex and bacteria is not well-documented for other mite species, suggesting a potentially unique interaction.

Unique Properties of Bioactive Molecules Secreted by Demodex Mites

Demodex mites can modulate the Toll-like receptor (TLR) signaling pathway in sebocytes. They initially downregulate TLR-related genes but can switch to upregulating them after prolonged exposure, indicating a dynamic interaction with the host immune system. High densities of Demodex mites lead to increased secretion of pro-inflammatory cytokines, such as interleukin-8 (IL-8), from sebocytes. This response is dose-dependent, with higher mite populations correlating with greater inflammatory activity.When Demodex mites die, they release chitinous exoskeletons and internal contents, which can trigger inflammatory responses and increase TLR-2 expression in the skin. This process activates immune responses, including neutrophil and macrophage activation. The mites secrete lipases that digest sebum, which not only provides nutrients for the mites but also contributes to the degradation of the follicular epithelium. This enzymatic activity can lead to tissue damage and inflammation, exacerbating skin conditions like rosacea and demodicosis.Demodex mites can carry bacteria such as Bacillus oleronius, which may act as co-pathogens in inflammatory skin conditions. This relationship enhances the inflammatory response and complicates the clinical picture of skin disorders. Interestingly, the immune-reactive lipases produced by Demodex mites may also help protect against pathogenic bacteria by producing free fatty acids from sebum triglycerides, which can inhibit the growth of harmful microbes like Staphylococcus aureus and Streptococcus pyogenes.(Leonard, 2024)

The Role of Demodex Mites in Skin Health and Disease:

Demodex mites, particularly Demodex folliculorum, play a significant role in both skin health and disease. These mites, which are naturally found in the hair follicles and sebaceous glands, can carry bacteria such as Bacillus oleronius, which is believed to act as a co-pathogen in conditions like rosacea (Wei et al., 2024). The presence of this bacterium may provoke an inflammatory response, contributing to increased skin inflammation and the exacerbation of conditions associated with Demodex overgrowth. The relationship between Demodex and bacteria may result in an altered immune response, where bacterial presence can inhibit the host's immune function, facilitating both mite and bacterial proliferation (Gueniche et al., 2022).

When Demodex populations increase, they can mechanically block hair follicles and sebaceous glands, disrupting the skin barrier and increasing susceptibility to infections. The mites release chitinous exoskeletons and other internal components upon death, triggering immune responses. This can activate Toll-like receptor (TLR-2) signaling pathways and recruit immune cells such as

neutrophils and macrophages, further complicating the skin condition. Interestingly, Demodex mites may also offer protection against certain pathogens, such as Staphylococcus aureus and Streptococcus pyogenes, through immune-reactive lipase enzymes that maintain a balanced skin microbiome (Zhang et al., 2024).

Skin Conditions Associated with Demodex Mites

Demodex overpopulation has been linked to several dermatological conditions (Kaddu et al., 2001; Jacob et al., 2019; Aktas et al., 2020):

Seborrheic Dermatitis:

Demodex mites are found in higher densities in patients with seborrheic dermatitis. While the exact causal relationship is debated, the mites may contribute to the inflammation characteristic of this condition.

Perioral Dermatitis:

Increased mite density is observed in individuals with perioral dermatitis, which is marked by inflammatory papules and pustules around the mouth.

Chalazion:

Chalazion, a blockage of the meibomian glands in the eyelids, has been associated with Demodex infestation. The mites may exacerbate inflammation and gland blockage.

Demodicosis:

This refers to an infestation of Demodex mites, which can lead to various skin manifestations. It can occur as a primary condition or as a secondary effect related to immunosuppression.

Acne Vulgaris:

Some studies suggest a link between Demodex mites and acne vulgaris. Mites may exacerbate inflammation and contribute to the development of acne lesions.

Eosinophilic Folliculitis:

Demodex mites have been implicated in eosinophilic folliculitis, characterized by itchy papules on the face and upper body. The exact relationship between mite density and the severity of this condition is still under study.

Pityriasis Folliculorum:

This condition, marked by follicular papules, may also be associated with Demodex infestation, though the mechanisms are not fully understood.

Grover’s Disease:

Grover’s disease, also known as transient acantholytic dermatosis, has been linked to Demodex mites, although the nature of this association requires further research.

The Influence of Hormonal Changes and Acne on Demodex Mite Populations

Demodex populations fluctuate based on internal and external factors, particularly hormonal changes and skin conditions like acne. These factors alter sebum production and composition, creating an environment that can either promote or inhibit mite growth, thereby influencing skin health.

Hormonal Changes and Their Impact on Demodex Populations

Puberty:

During puberty, hormonal surges—especially in androgens like testosterone—stimulate sebaceous gland activity, resulting in increased sebum production. This nutrient-rich environment promotes

Demodex proliferation, which is often accompanied by acne, further complicating the skin's microbiome balance (Elston & Elston, 2014).

Pregnancy:

Hormonal fluctuations during pregnancy, including increases in progesterone and estrogen, can alter sebum production. Some individuals may experience an increase in oily skin, creating a favorable habitat for Demodex, while others may see a reduction in sebum, limiting mite growth. This variability in hormonal effects explains the inconsistent impact of pregnancy on Demodex populations (Keskin et al., 2014).

Menopause and Aging:

As hormonal activity declines with age, sebum production decreases. However, older individuals often exhibit higher Demodex densities, likely due to changes in lipid composition, decreased skin renewal rates, and weakened immune responses, which favor mite survival and proliferation (Chudzicka-Strugała et al., 2023; Pagac et al., 2024).

Hormonal Imbalances:

Conditions such as polycystic ovary syndrome (PCOS) or other endocrine disorders that elevate androgen levels can result in excessive sebum production, often correlating with increased Demodex populations and exacerbating related skin conditions (Eser et al., 2017).

Acne and Its Relationship with Demodex

Acne, characterized by clogged pores, inflammation, and bacterial overgrowth, is closely linked to Demodex proliferation. Acne-prone skin often exhibits hyperactive sebaceous glands, producing an excess of sebum. This abundance not only fuels bacterial growth but also provides an ideal environment for Demodex mites, whose populations tend to rise in acne-affected areas Inflammatory processes in acne can disrupt the skin microbiome balance, allowing Demodex to thrive (Zhao et al., 2012).

Impact of Demodex on Acne:

The mites contribute to inflammation by releasing lipases and other enzymes, which damage the follicular epithelium. Additionally, Demodex mites act as vectors, carrying Propionibacterium acnes deeper into the hair follicles, further amplifying skin inflammation. This interaction may lead to the development of pustules and nodules (Abdel-Aal et al., 2022).

Post-Acne and Residual Mite Populations:

After the resolution of active acne, altered sebaceous activity and scarring may create microenvironments that support persistent Demodex populations. These residual mite densities can contribute to chronic inflammation or conditions like rosacea. The interplay of hormonal changes and acne increases Demodex density, particularly in areas with high sebaceous gland activity such as the face, chest, and back (Paichitrojjana & Chalermchai, 2024).

Potential Inhibitors and Management Strategies

Essential Oils:

Tea Tree Oil: This is one of the most commonly cited treatments for Demodex-related conditions, particularly blepharitis and rosacea. Tea tree oil has antimicrobial and anti-inflammatory properties, which may help inhibit the activity of Demodex mites and the bacteria they carry. While its effectiveness is noted, there is no strong consensus on its efficacy against the bioactive molecules specifically secreted by the mites.

Ivermectin:

Ivermectin is an antiparasitic agent that has shown effectiveness in reducing Demodex populations. It may help mitigate the inflammatory response associated with high mite densities, although its

direct inhibitory effects on the bioactive molecules are not well-documented.

Doxycycline:

Doxycycline, an antibiotic with anti-inflammatory properties, has been used in the treatment of rosacea and may indirectly inhibit the inflammatory responses triggered by Demodex mites and their secretions. It can reduce the levels of pro-inflammatory cytokines, such as interleukin-8 (IL-8), which are influenced by Demodex activity.(Leonard, 2024)

Other Anti-inflammatory Agents:

Research is ongoing into various anti-inflammatory agents that could potentially inhibit the immune-modulating effects of Demodex secretions. These include compounds that target the Toll-like receptor (TLR) signaling pathways, which are affected by the presence of Demodex mites.

Alternative Therapies:

There is ongoing research into alternative treatments, including herbal extracts and other natural products that may possess anti-Demodex activity or modulate the immune response to mitigate the effects of the bioactive molecules secreted by the mites.(Yosipovitch and Frost, 2024)

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