

Inflamed Feelings: The Psychological Effects of *Inflammatory Disorders*



Data suggest that children and adults suffering from chronic inflammatory skin diseases, such as eczema and psoriasis, are at higher risk for depression, anxiety, and other psychiatric illnesses.

By Diane Hanna, MSN, ARNP-C and Lucinda Arnold Whitney, RN, MSN, ARNP

For many patients, a dermatologic condition affects more than just skin. Perhaps due to the visual nature of dermatology, skin disease can also impact a patient's functioning and psychosocial state. This may explain why depression in the dermatology patient population occurs more frequently than in the general population. Dermatologists should not be surprised to learn that the incidence of psychiatric disorders in the dermatological patient

population has been estimated to be between 30 and 60 percent, nearly tenfold that of the general population.¹ The most common disorders are mood disorders, depressive disorders, suicidal ideation, anxiety disorders, obsessive disorders and delusional disorders.² Importantly, there is considerable evidence suggesting that those with inflammatory skin diseases are at higher risk of physiological morbidity, which is often undetected, undiagnosed, and undertreated.³ Therefore, it is essen-

tial that dermatologists and dermatology providers work to broaden their knowledge of these psychological disorders and how they may affect patients. Ahead, we will review research in the psychology and psychiatry literature and lay out strategies for identifying psychodermatoses.

Inflammatory Links

Determining the etiological factors of inflammatory skin disorders and psychological disorders is not easy. In a recent cross-sectional study, patients were recruited from both dermatology specialists and general dermatology practices, and assessed for disease severity of AD, psoriasis, and acne. In addition, patients completed three psychological assessment screening tools. Data revealed confounding effects in the association between skin disease and psychological morbidity.³ In the past decade, a better understanding for the pathophysiology of inflammatory diseases such as atopic dermatitis and psoriasis has resulted in more selective therapies and a continued research emphasis. Current research is exploring the role of the over expression of proinflammatory cytokines and their manifestation in skin disease. It is well understood that the pathophysiology of both AD and psoriasis is multi-factorial, however, the current understanding of immune dyscrasias focuses on both adaptive and cell-mediated immunity; specifically, the imbalance of the CD4 helper cells, Th1/Th2 and their mediators.

Immunopathogenesis of atopic dermatitis is theorized to center on hyperstimulation of Th2 cells mediated by IL-4, IL-5 and IL-13. Furthermore, IL-4 regulates B cell differentiation into plasma cells and then to antibodies.⁴ This initial acute inflammatory response then leads to chronic inflammation with an influx

of cytokines including TNF- α and IFN- γ . TNF- α also plays a role in the pathophysiology of psoriasis. The increased levels of TNF- α are strongly considered to be linked to physiological comorbidities.⁵ These pro-inflammatory mediators have long been thought to play a role in brain function and mood regulation. Through this inflammatory pathway, patients with psoriasis are at greater risk for depression, poorer quality of life, and a loss of productivity. In addition, evidence is emerging of comorbidities: cardiovascular disease, metabolic syndrome, obesity, and dyslipidemia.

Miller, Maletic, and Raison⁶ published data further supporting the notion that inflammation has been extended to neuropsychiatric disorders such as major depression. The study found that patients had increased peripheral biomarkers that included inflammatory cytokines. These cytokines are able to access the brain and influence and elicit interactions that have been identified in the pathophysiology of depression. Patients with elevated inflammatory biomarkers who were initiated on antidepressant therapy were associated with a decreased inflammatory response. Inhibition of pro-inflammatory cytokines and their pathways may play a role in improving depressed mood.⁷

Psychiatric research demonstrates that stress is an inducer of an inflammatory cascade. The activation of the hypothalamic-pituitary-adrenal axis stimulates corticotrophin-releasing factor (CRF), which in turn leads to an elevated plasma cortisol and catecholamines. In tandem, CRF is released peripherally and acts as a catalyst for activation of pro-inflammatory cytokines mainly, IL-1, IL-6 and TNF- α .⁸ Pro-inflammatory cytokines have been demonstrated to have strong effects on the brain and mood. In one study, patients that received interferon-alpha treatment

Tips for Patient Assessment

To understand the dermatology care provider's role in assessing the psychological burden of a disorder, it may be useful to envision a patient scenario.

First, it's important for physicians to note that they are treating more than a skin condition when treating many inflammatory dermatoses, so it is crucial to assess a patient's psychological state when evaluating their skin. This includes letting patients know that you are there to help, surveying their response and behavioral state, and asking questions about how their condition affects their lives.

Questions pertaining to everyday activities and social interaction are critical toward understanding the extent to which the patient's condition is affecting their quality of life. Patients' willingness to take their clothes off to show you the condition may also give you an indication as to their psychosocial state.

For adults, you may ask what has motivated them to seek treatment. In the case of children, asking simple, direct questions will often yield honest answers. These questions also serve to queue up the parents, who can likely provide insight into the psychological state of the child. Parents, too, may be depressed and exhausted if their child is suffering from atopic dermatitis. Therefore, parents would benefit from knowing what to look for. Asking about their child's performance in school, changes in sleep and eating patterns, and social interaction with friends is essential.

Finally, just letting parents and patients know you care could have positive implications for their willingness to comply with treatment regimens and relieve some stress. If physicians lack comfort or time to address these matters, nurses can be knowledgeable and helpful resources.

Inflammatory Disorders

Medications for Depression^{1,17}

The following is a dosing guideline for SRI's:

Fluoxetine (Prozac, Eli Lilly) (20-80mg): Initially 20mg in the morning. Prozac can be helpful when a patient has low energy

Sertraline (Zoloft, Pfizer) (50-200mg): Initially 50mg for depression. 25mg for anxiety

Paroxetine (Paxil, Glaxo SmithKline) (20-50mg) Paxil CR (25-62.5mg): Initially 20 or 25mg

Fluvoxamine (Luvox, Jazz) (100-200mg): Initially 50mg

Citalopram (Celexa, Forest) (20-60mg): Initially 20mg

Escitalopram (Lexapro, Forest) (10-20mg): Initially 10mg

Duloxetine (Eli Lilly) Cymbalta (40-60mg): Initially 40mg in single or divided dose

Venlafaxine (Effexor & Effexor XR, Wyeth) (75-225mg): Initially 25-50 mg divided into BID or TID dosing or XR 37.5mg

Children:

Fluoxetine (10-40mg): 10mg for children over seven years & 20mg for adolescents

reported experiencing anhedonia, anorexia, social withdrawal, fatigue, anxiety and depressed mood.⁹ In vitro studies demonstrated that several classes of anti-depressants reduce pro-inflammatory cytokine production in animal models. In addition, researchers have hypothesized that proinflammatory cytokines suppress the production of serotonin, the neurochemical link to anxiety and depression.¹⁰

Depression and Dermatology

Now that we have laid out a review of recent literature on the role of inflammation and its correlation to psychiatric disorders, we will examine a psycho-dermatologic approach to assessing and treating depression and anxiety in this patient population. As already discussed, patients seeking treatment from a dermatologist or related healthcare provider are at a high risk for depression and psychiatric illness. In addition to assessing and treating the presenting skin disorder, an evaluation of mood, anxiety, preoccupations, stress levels and expectations during treatment are part and parcel of increasing compliance and patient outcomes. Ohya, et al.¹¹ asserted that the assessment of a patient's experience beyond the skin disorder strengthens the doctor-patient relationship, which has been shown to be an integral part of adherence to the management of atopic dermatitis. Additionally, antidepressants have shown favorable benefit in treating pruritis, urticaria, and pain.¹² The burden of skin disease is multifaceted, and there is a clear relationship between distress, depression, dermatologic symptoms, and dissatisfaction with treatment.¹³

The basis of assessment begins with a willingness to listen to a patient's subjective report of their dermatological and psycho-

logical experience. Multiple assessment tools are readily available for assessing depression and anxiety in both children and adults. Symptoms of depression include changes in: mood, energy, concentration, social/family involvement, appetite, sleep, and feelings of hopelessness or helplessness. It's worth noting that women are twice as likely to report depression or anxiety as are their male counterparts. Rating scales also aid in identifying patients with psychiatric illness that might otherwise go unnoticed.¹⁴ A rating tool can elucidate psychiatric symptoms but does not quantify illness. Thus, it may be necessary to refer to a psychiatrist. For general purposes, a patient self-rating assessment tool is the easiest to incorporate into daily practice.

The Zung Self-Rating Depression Scale is a self-administered screening tool for depression and can be used for adults and adolescents. The State Trait Anxiety Inventory (STAI) is a screening tool for adults.

Assessment tools for children include the Children's Depression Rating Scale (CDRS), State Trait Anxiety Inventory for Children (STAIC), and Screen for Child Anxiety Related Disorders (SCARED). These tools are free online, have well documented psychometrics, and are intended for data collection; they are not substitutes for psychiatric evaluation. Once a patient with depression or anxiety has been identified, the psychiatrist or health care provider must decide whether to initiate treatment or refer to a collaborating colleague for psychiatric evaluation. A clinician may choose to initiate a psychiatric medication and refer in an effort to not delay treatment as patients are often reluctant to see a mental health provider.

Antidepressants, specifically serotonin re-uptake inhibitors (SRI's), are an eclectic group of medications that share a similar

mechanism of action, but are diverse in their secondary receptor profiles. The SRI's are fluoxetine (Prozac, Eli Lilly), sertraline (Zoloft, Pfizer), paroxetine (Paxil, GlaxoSmithKline), fluvoxamine (Luvox, Jazz), citalopram (Celexa, Forest), and escitalopram (Lexapro, Forest), while duloxetine (Cymbalta, Eli Lilly) and venlafaxine (Effexor, Wyeth) are serotonin and norepinephrine reuptake inhibitors. All of these agents are approved by the FDA for use in adults with major depression. Paroxetine and venlafaxine are approved for Generalized Anxiety Disorder while paroxetine, venlafaxine, and sertraline are approved for Social Anxiety Disorder. Panic disorder has been successfully treated with fluoxetine, sertraline, and paroxetine.

For children, fluoxetine is the only SRI that is FDA approved to treat depression in patients over age seven and adolescents. Fluoxetine, sertraline, and fluvoxamine have approval to treat obsessive compulsive disorder. The remaining SRI's are off-label for children, and all SRI's carry a black box warning for pediatrics. The FDA offers clear guidelines on how to initiate and monitor antidepressant therapy in children along with helpful parent education sheets that addresses the black box warnings. Children may be under-diagnosed and go untreated as the initiation of a psychopharmacological agent can be intimidating. This is the perfect scenario for collaboration with a mental health provider.

It is important to remember that when treating a child you are also treating the family. The heritability of depression and anxiety is well understood, and without question children only fare as well as their parents or primary support system. Fought, Bierl, and Kemp¹⁵ support this in their report that high levels of stress in children and family systems was strongly associated with severe eczema. To improve the overall outcomes for children, it is important to also assess, consider treating, and refer family members for counseling and/or medication evaluation. If you are unsure where to start, consider referring the parent to their work based Employee Assistant Program. These programs are confidential.

As with all medications, there are potential drug-to-drug interactions to consider when prescribing SRIs. SRIs can both inhibit and induce the Cytochrome P-450 isoenzyme system (CYP). The CYP system is actively involved in rendering lipid solid drugs into water-soluble molecules for excretion through the kidneys.¹⁶ The primary enzymes are 1A2, 2D6, 2C9/10, 2C19, and 3A4. Interestingly, cigarettes are a potent inducer of the CYP system.² The newer antidepressants, particularly selective serotonin reuptake inhibitors, have a well-established track record for safety and efficacy when prescribed and monitored appropriately. It is clear that emotional distress is a risk factor for negative outcomes in patients with inflammatory skin disease.

A Multidisciplinary Approach

Dermatologists have a unique opportunity to assess patients for psychosocial stressors and levels of emotional distress.

Employing a multidisciplinary approach with collaboration between dermatology and psychiatry, physicians can significantly improve a patient's sense of well-being and decrease the burden of disease. Our hope is that dermatologists and dermatology care providers will talk actively and openly with their patients about their emotional health and develop interventions to reduce emotional distress and psychosocial dysfunction in the service of improving patient outcomes. ■

The authors have no relevant disclosures.

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