

Attention-Deficit/Hyperactivity Disorder in Atopic Dermatitis: An Appraisal of the Current Literature

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Atopic dermatitis (AD) is a chronic inflammatory skin disease with hallmark characteristics in terms of pruritus, psychological stress, and sleep disturbance, all possibly associated with an increased risk of attention-deficit/hyperactivity disorder (ADHD). Epidemiological data indicate that AD and ADHD exhibit a parallel rise in global prevalence, and several cross-sectional studies have indicated co-occurrence of the 2 conditions. Furthermore, recent cohort studies have reported a temporal association between AD and later development of ADHD. However, underlying pathophysiological mechanisms of this association are insufficiently explored. The aim of the present review was to provide any clinician encountering AD an update on the most recent studies examining the possible AD-ADHD association. In turn, this could aid counseling of patients and parents. This review may encourage healthcare providers to refer AD patients and families to psychiatric specialists when ADHD is suspected.

Keywords: atopic dermatitis, atopic eczema, attention-deficit/hyperactivity disorder (ADHD), pediatric dermatology

Introduction

ATOPIC DERMATITIS (AD) is a very common, chronic or relapsing, pruritic inflammatory disorder of the skin that has reached endemic proportions in large parts of the world. In the past decades there has been an increase in the prevalence, and about 10%–25% of children and 1%–6% of adults are affected¹; hence, AD has become the commonest inflammatory skin disease in the pediatric population. There is an eagerness to explain the global rise in the prevalence of AD as data imply that developing countries may soon display a picture that resembles that of affluent nations.²

Presentation and consequences of AD

In most patients, AD presents in infancy or early childhood, but it may also develop in adolescents and even adults. Several diagnostic criteria exist for AD—the one by Hanifin and Rajka still being the gold standard (Table 1).³ Since approximately one-fourth does not clear the disease before adulthood, many carry the burden of AD throughout life.⁴ In severe cases AD is a debilitating condition with a burdensome socioeconomic impact and a need for systemic treatment.^{5,6} Patients often experience accompanying morbidity from pruritus like chronic scratching, restlessness,

and disturbed sleep.^{5,7} A childhood impeded by AD may cause significant problems in the daily life of these patients.⁸

Psychiatric comorbidities in AD

It is established that rates of depression, stress-related disorders, and anxiety are significantly increased in the AD population.^{9,10} However, as recent data indicate, AD also may lead to psychiatric morbidities. The most extensively described so far being attention-deficit/hyperactivity disorder (ADHD).¹¹ A lead on this possible association is the global rise of atopic disease being paralleled by rising prevalence of mental health problems, including depression and ADHD.

ADHD is the most common behavioral disorder in children and adolescents worldwide, affecting 5%–8% in this group.^{12–14} ADHD is according to DSM-5 a persistent pattern of inattention and/or hyperactivity–impulsivity that interferes with functioning or development. ADHD can, according to clinical presentation, be divided in to the inattentive, the hyperactive/impulsive, or the combined disorder according to the dominant symptoms (Table 2).¹⁵ The consequences of ADHD are difficult for both the patients and their families. Children experience sleeping disorders, impaired learning abilities at school, reduced social capability leading to social isolation, and a significantly reduced quality of life.¹⁶ Later in

TABLE 1. HANIFIN AND RAJKA DIAGNOSTIC CRITERIA OF ATOPIC DERMATITIS

Major criteria (must have 3 or more)
• Pruritus • Typical morphology and distribution • Chronic or chronically relapsing dermatitis • Personal or family history of atopy (asthma, allergic rhinitis, AD)
Minor criteria (should have 3 or more)
• Xerosis • Ichthyosis, palmar hyperlinearity, or keratosis pilaris • Immediate (type 1) skin test reactivity • Raised serum IgE • Early age of onset • Tendency toward cutaneous infections (especially <i>S. aureus</i> and herpes simplex) • Tendency toward nonspecific hand or foot dermatitis • Nipple eczema • Cheilitis • Recurrent conjunctivitis • Dennie–Morgan infraorbital fold • Keratoconus • Anterior subcapsular cataracts • Orbital darkening • Facial pallor or facial erythema • Pityriasis alba • Anterior neck folds • Itch when sweating • Intolerance to wool and lipid solvents • Perifollicular accentuation • Food intolerance • Course influenced by environmental or emotional factors • White dermographism or delayed blanch

AD, atopic dermatitis; IgE, immunoglobulin E.

life, ADHD may lead to depression and anxiety as well as antisocial and addictive behavior.¹⁷

Do AD and ADHD share pathophysiological pathways?

The possible connection between AD and ADHD has been a subject of ongoing discussion since the 1980s, as it was hypothesized that immunological changes from atopic disease could explain an increased coexistence of the 2 entities.^{18–20} However, underlying psychoendocrine and psychoneuroimmunological mechanisms remain unclear. Granting this, reports suggest that the manifestation and chronification of AD in infancy or early childhood increase the risk for ADHD. Others have hypothesized that the development of ADHD-related symptoms opts the child more susceptible to develop AD. Finally, AD and ADHD patients may share one or more risk factors that increase the vulnerability for both diseases.²¹ However, the explanatory mechanisms are unclear.

Identifying the mechanisms and understanding the association between AD and ADHD are of great interest from a socioeconomic healthcare provider and especially patient point-of-view, as it could potentially lead to better targeted treatments and preventive measures.

In this review, we present an appraisal of studies and data investigating the link between AD and ADHD.

Atopic disease as risk factor for ADHD

The first studies on the association between atopic diseases and ADHD were performed in the early 1990s.^{19,22,23} They were encouraged by the hypothesis put forward by Geschwind and Behan²⁴ that immune diseases are associated with learning disorders, a hypothesis that was tested and contested. Biederman et al. did not find any statistically significant association between asthma and ADHD²³ and neither did McGee et al.,²² whereas Roth et al. did find a correlation.¹⁹ In 2009, Schmitt et al.²⁵ performed a cross-sectional study on children and adolescents in a German Health Care Database with information from 2003 to 2004, showing a significant correlation between ADHD and AD as well as other behavioral disorders. The difference between the findings of Biederman et al. and Schmidt et al. may be found in the definition of atopy. Atopic disease requires that immunoglobulin E (IgEs) against environmental allergens is involved in the pathogenesis,²⁶ although this is not necessarily the case for AD.²⁷ This is also apparent in the comprehensive review by Schmitt et al. from 2010, in which they systematically review 20 articles on atopic diseases, defined as eczema, asthma, and rhinitis without considering the IgE level, and ADHD, where they disclosed that ADHD is not associated with atopy as such, but rather to the specific entity AD (eczema).¹¹

AD as risk factor for ADHD

The association between AD and ADHD. Several studies have now shown the association between AD and ADHD (Table 3). The first study published was a cross-sectional study from Germany showing an increased risk of having ADHD when diagnosed with AD.²⁵ Large cross-sectional studies from Germany,²⁸ Taiwan,^{29,30} and the United States^{9,31} have also shown a significant association between AD and ADHD. One German cross-sectional study on the mental health in children with early-onset AD, including 2,916 infants, showed a significant risk of conduct problems, including hyperactivity/inattention³² supporting the association. A study from Korea using a Korean version of the Child Behavior Checklist also showed an increased prevalence of attention problems in children treated for AD within the last 12 months compared to children who were not.³³

The association of AD and ADHD has also been studied in 3 Taiwanese studies, 1 cross-sectional, and 2 case–control studies of patients diagnosed with ADHD.^{34–36} They all showed a significant association between ADHD and AD. One study showed that having ADHD and Tic disorder increased the risk of having AD.³⁴

A German prospective birth cohort was studied over a span of 12 years by Genuneit et al. in 2014.³⁷ They used questionnaires from both parents and treating physicians and showed a statistically significant association between early AD and ADHD (higher among the parental reported symptoms) and a nonsignificant association between late AD and late ADHD. However, they did not find any association between early AD and late ADHD. Chen et al. carried out a case–control study from 1997 to 2010 on patients born between 1997 and 2000, showing an increased risk of developing ADHD among children with atopic diseases, including AD. They did not show the risk for AD alone, but they showed that the risk of ADHD increased with increased number of atopic diseases.³⁸

TABLE 2. DIAGNOSTIC CRITERIA FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN DSM-5

Symptoms of inattention

- Fails to give attention to details or make careless mistakes in schoolwork, at work, or during other activities
- Difficulty in sustaining attention to tasks or play activities
- Does not seem to listen when spoken to
- Does not follow through on instructions and fails to finish tasks
- Difficulties in organizing tasks and activities
- Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort
- Loses things necessary for tasks or activities
- Easily distracted by extraneous stimuli
- Forgetful in daily activities

Symptoms of hyperactivity

- Fidgets with or taps hands or feet, squirms in seat
- Leaves seat when remaining is expected
- Runs about or climbs in situations where it is inappropriate
- Unable to play or engage in leisure activities quietly
- Acts as driven by a motor
- Talks excessively

Symptoms of impulsivity

- Blurts out answer before a question has been completed
- Difficulty waiting for his/her turn
- Interrupts or intrudes on others

Additional required diagnostic features

- The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions
- Symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic or occupational activities
- Several symptoms were present before the age of 12 and in 2 or more settings
- There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning
- The symptoms do not happen only during the course of schizophrenia or another psychotic disorders. The symptoms are not better explained by another mental disorder

Liao et al. showed an increased risk of developing ADHD among infants suffering from AD before the age of 2 years when studying a Taiwanese cohort of 387,262 through the National Health Insurance Program from 2000 to 2010.³⁹ Riis et al. also studied the temporal association between AD and ADHD through national registries, using admission/outpatient diagnoses of ADHD or ADHD medication prescription, as outcome. This showed a substantially increased risk for ADHD diagnoses in patients with AD compared with the general population [hazard ratio (HR) of 1.3 (1.2–1.5)] as well as for redeeming ADHD medication prescriptions [HR of 1.3 (1.1–1.5)].

Sleep disturbances as confounder. Factors affecting the association between AD and ADHD have also been examined, and the strongest factor is reported to be sleep disturbance. In the study by Romanos et al., a subanalysis of 6,484 children showed that in those with concurrent sleeping problems there was a strong association between AD and ADHD [odds ratio (OR)=2.67; 95% CI: 1.51–4.71], whereas in the group of children without sleeping problems there was no association (OR=1.24; 95% CI: 0.83–1.84).²⁸ The association between sleep quality and AD is thoroughly examined by Yaghmaie et al.⁹ and Strom et al.,³¹ partially based on the same data from the national Survey of Children's Health. In the study by Strom et al., they found a strong association between eczema and ADHD, which is increased when stratified for 0–3 “Nights of adequate sleep” per week (OR=2.82; 95% CI: 2.05–3.86) when compared to 4–7 “Nights of adequate sleep” per week (OR=1.32; 95% CI: 1.12–1.56). Inadequate sleep and

ADHD were also associated in the group of children without eczema, however, not as strong (OR 1.78; 95% CI: 1.51–2.09).

The risk of developing ADHD when suffering from severe eczema and adequate sleep in only 0–3 nights per week, compared to children without eczema and adequate sleep, was high and significantly increased (OR=16.83; 95% CI: 7.02–40.33), whereas the risk when having severe AD but adequate sleep (4–7 nights) was still increased but not to the same degree (OR=3.05; 95% CI: 1.62–5.74). These results support the data reported in a study from 2013 by Yaghmaie et al.⁹

Other atopic diseases' effect on the association between AD and ADHD. Other atopic diseases such as bronchial asthma, allergic rhinitis, and conjunctivitis have also been implicated as risk factors for the development of ADHD, reviewed by Schmitt et al.¹¹ Almost all studies, including these diseases, show an association with ADHD increasing the risk when coexisting with AD, although not as strong as sleeping problems.^{29–31,34–36,39} Only one study did not find this association.²⁵ Taken together, other atopic diseases also seem to affect the risk of having ADHD.

Discussion

Key findings

Seven out of 8 newer cross-sectional and case-control studies show statistically significant ORs around 1.5 for the coexistence of AD and ADHD. These data are supported by 2 larger cohort studies revealing HRs of 1.15 and 1.3 (both $P<0.001$). As most studies in this review are cross sectional, with no incident exposure included, these provide no

TABLE 3. STUDIES ON ATOPIC DERMATITIS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

<i>Reference</i>	<i>Study period</i>	<i>Country</i>	<i>Study design</i>	<i>Setting</i>	<i>Result</i>	<i>Study population</i>	<i>Covariates</i>
Schmitt et al. ²⁵	2003–2004	Germany	Cross sectional	Register study	OR = 1.47 (1.01–2.15)	1,436 AD patients, 1,436 age- and sex-matched general population controls	BA and AR not increased
Romanos et al. ²⁸	2003–2006	Germany	Cross sectional	Register study	OR = 1.54 (1.24–1.93)	13,318 children and adolescents	Sleeping problems
Shyu et al. ²⁹	2005	Taiwan	Cross sectional	Register study	OR = 0.73 (0.48–1.09)	10,620 AD patients, 178,093 general population controls, without allergy diagnoses	BA and AR increased the risk of ADHD. AD in combination with BA and AR also increased the risk
Chen et al. ³⁴	1996–2010	Taiwan	Case–control	Register study	OR = 1.64 (1.54–1.75)	5,811 patients with ADHD age-/gender-matched controls (1:4)	BA, AR, CO all increased in the ADHD group
Chang et al. ³³	2013	Korea	Cross sectional	Questionnaire, response rate 73%	Increased mean ADHD scale score in individuals in AD treatment	84 individuals in AD treatment compared with 472 responders without AD treatment	AR, BA, Urticaria, Ankylosing spondylitis, Ulcerative colitis, Autoimmune thyroid disease.
Yaghmaie et al. ⁹	2007	US	Cross sectional	Survey, 51% response rate	OR = 1.62 (1.35–1.93)	10,401 responders with AD and 69,266 without AD	Sleep quality
Tsai et al. ³⁶	2002–2009	Taiwan	Case–control	Register study	OR = 1.80 (1.58–2.05)	4,692 ADHD cases and 18,768 age- and gender-matched non-ADHD controls	AR, BA, CO.
Genuneit et al. ³⁷	2000/2001–2011/2012	Germany	Cohort	Survey/physician report. Twenty-nine percent lost to follow-up.	RR = 5.17 (2.18–12.28)	200 responders with AD, 570 responders without AD	Physicians report included (RR = 2.58 (1.11–5.99). Late AD/late ADHD see text.
Liao et al. ³⁹	2000–2010	Taiwan	Cohort	Register study	HR = 1.15 (1.12–1.18)	387,262 patients with AD and 387,262 controls without AD	AD before the age of 2 years. Atopic respiratory diseases increase HR.
Lin et al. ³⁰	2010	Taiwan	Cross sectional	Survey, response rate 87%	OR = 1.66 (1.23–2.25)	251 responders with AD and 2,645 responders without AD	BA, AR, Depression, Stress, Sleep quality
Riis et al. ⁷¹	1995–2010	Denmark	Cohort	Register study	HR = 1.3 (1.2–1.5)	11,877 patients with AD and 118,770 birth year- and gender-matched controls	ADHD medication requirement
Strom et al. ³¹	1997–2013	US	Cross sectional	Survey (pooled data from 19 surveys)	OR = 1.14 (1.03–1.26)	354,416 children/34,613 adults.	Severe AD, Quality of sleep, BA, Anemia, BMI.

ADHD, attention-deficit/hyperactivity disorder; AR, allergic rhinitis; BA, bronchial asthma; BMI, body mass index; CO, allergic conjunctivitis; HR, hazard ratio; OR, odds ratio; RR, risk ratio.

insight regarding causality or temporal aspects, although they justify the assumption that AD increased the risk for concurrent ADHD by ~ 1.5 -fold, which is in line with the conclusion from the only systematic review on the topic from 2010.¹¹ This review, in comparison, presents 3 cohort studies assessing the temporal and causal relationship between AD and the risk of subsequent ADHD (Table 3). All significantly support an increased risk of developing ADHD when diagnosed with AD. This temporal aspect is additionally augmented by the simple fact that AD is usually diagnosed within the first 2 years of life and in many cases fade before puberty,² while ADHD displays a diagnostic peak incidence around the early school years.¹² As highlighted above, the risk of AD and concomitant ADHD or impending development of ADHD is strongly supported. The studies presented have to a varying degree accounted for covariates like lifestyle factors and environmental exposures, for example, family history of AD, concurrent atopic diseases, number of siblings, and pattern of early life nutrition, thus the question arises—what primary modulatory mechanisms could rationalize this relationship?

Explanatory mechanisms

Buske-Kirschbaum et al. discussed 3 possible explanatory mechanisms behind the AD–ADHD relationship.²¹

One explanatory mechanism is (1) the release of inflammatory cytokines caused by augmented Th2 inflammatory pathways and/or increased levels of emotional stress from chronic diseases that interfere with the development of mature prefrontal cortex (PFC) regions and neurotransmitter systems directly involved in the ADHD pathology. As it is impossible to separate the individual components of this explanatory mechanism, one has to simplify it by examining the impact from AD-related immunomodulation and elevated stress on brain maturation and development in its entirety.

The second explanatory mechanism could be that (2) increased psychological stress levels in ADHD patients may prompt AD through neuroimmunological mechanisms.

The last explanatory mechanism (3), consider AD and ADHD as 2 separate conditions with communal risk factors like genetics, prenatal stress, and various environmental exposures that increase the predisposition for both AD and ADHD, explaining the co-occurrence of these disorders. It is important to mention that neither of these explanatory mechanisms is mutually exclusive. It seems reasonable, however, in the light of the 3 cohort studies published after the systematic review by Schmitt et al. in 2010 and the one by Buske-Kirschbaum et al. in 2012 to focus primarily on the first conception of causality comprising elevated stress levels from a chronic pruritic disease and the increased levels of modulatory cytokines. These factors may together hamper maturation of the PFC and interfere with ADHD-related neurotransmitter systems.

Cytokines and neuromodulation

Several well-described immune abnormalities have been characterized in AD. The changes include (1) increased quantities of Th2-typical cytokines, for example, interleukin (IL)-4, IL-5, IL-13, IL-31, and furthermore, thymic stromal lymphopoietin, IL-25, IL-33, and high mobility group box 1 protein^{40–45} and (2) elevated numbers of Th2 cells, particu-

larly CD4⁺ cells and an augmented expression of the high-affinity IgE receptor on dendritic, Langerhans, and eosinophil cells.^{46,47} Acute disease and flare-ups are mainly dominated by epidermal dendritic cells and Th2 cells producing IL-4, IL-5, and IL-13,^{48,49} while chronic AD demonstrates a cellular infiltrate with both Th2 and Th1 cells, and far less Th17 cells and Th22 cells. Th1 cells are characterized by interferon (IFN)- γ , TNF (tumor necrosis factor)- β , and IL-2 production, while the Th17 and Th22 subsets are sources of IL17A and IL22, respectively. In the systemic immune regulation, hallmark modifications include sensitization to allergens and increased allergen-specific IgE antibodies and furthermore Th2 polarization of circulating T cells.⁵⁰ In parallel with the more localized immune response, the acute phase of AD is generally considered a Th2-mediated disease with high circulating and intradermal levels of Th2-typical cytokines such as IL-4, IL-5, IL-13, IL-31, IL-33, and thymic stromal lymphopoietin.^{51,52} Th1-associated cytokines such as IFN γ , TNF- β , and IL-2 are mainly important in the recruitment and activation of other immune active cells in AD and are considered associates in crime with the other implicated cells in the AD immune response. Finally, a variety of serologic changes in AD are well known, including elevated serum concentrations of total IgE, thymus and activation-regulated chemokine, macrophage-derived chemokine, cutaneous T-cell-attracting chemokine, and IL-31, all of which have immunological implications and exhibit correlation with disease severity.⁵³

These data clearly suggest both acute and chronic AD expose affected individuals to significantly elevated levels of inflammatory cytokines. Interestingly, evidence support that these cytokines can activate neuroimmunological pathways involving behaviorally and emotionally relevant cognitive systems.

In several animal models, allergen-induced reactions and elevated IgE levels resulted in limbic brain stimulation and consequently avoidance behavior, anxiety, or impeded social behavior.^{54–56} Human studies have shown altered neuronal activity of the PFC when a chronic allergic response was observed using functional magnetic resonance.⁵⁷ As the PFC facilitates executive cognitive functions, including planned behavior, decision-making, motivation, and attention, any operational alterations in PFC regions have been linked to various cognitive disturbances like reduced attention control, disturbed decision-making, and inexpedient motor output, all main characteristics of ADHD.⁵⁸

How the inflammatory cytokines elevated in AD affect the PFC and higher cognitive functions is not directly answered, although it is reasonable to consider several mechanisms. It could be directly through passage of the blood–brain barrier or facilitated by cytokine-specific transporters in the blood–brain barrier, or it could be indirectly through novel production of cytokines/neurotransmitters from endothelial cells in the blood barrier or from microglia.⁵⁹ Finally, it is possible that circulating cytokines may indirectly affect CNS function and structure by activation of afferent fibers.⁶⁰

Besides the above-mentioned plausible causes of effect, it is demonstrated that inflammatory cytokines alter the metabolism of pivotal neurotransmitters, most importantly dopamine and norepinephrine, both critically involved in ADHD pathophysiology.⁶¹ Changes first studied experimentally in animal models revealed comparable deviations later described in patients with ADHD, in part due to increased levels of

glucocorticoids (GCs), as elevated levels of stress-induced GCs weaken cognitive flexibility, which require PFC function.⁶² In summary, the elevated levels of inflammatory cytokines in AD patients may directly or indirectly influence ADHD-relevant brain regions like the PFC. The altered neurotransmitter regulation may disturb behavior and motor regulation and emotional control—effects that might be calamitous with an onset of AD in early life while the brain is immature and vulnerable.

Psychological stress

The AD-dependent toil and stress experienced by patient and family and derived reduction of life quality are well documented. Many negative effects are linked to the tormenting pruritus and altered physical appearances, for example, psychological stress, dysfunctional sleep, altered mood, and impaired cognitive and social performance. Furthermore, stigmatization and discrimination may lead to aggravated stress levels and feelings of hopelessness. Other effects are related to an at times dysfunctional parent—child relationship prompting anxiety and lessened support.^{63–66} Studies in both animal models and humans have revealed that the brain is especially sensitive to stress in infancy and childhood, possibly due to the profound developing alterations in this period in life. Again the GCs play a pivotal part as maternal separation or obstructed feeding in studies of rodents and monkeys increases GC levels that reduce PFC functions and moreover increases central GC-receptor density and induces long-term changes in key neurotransmitter pathways.^{67,68} Finally, evidence of early life stress-related changes of ADHD-related neurotransmitter pathways has been identified. Maltreated girls displayed increased levels of catecholamine positively correlating with the length of the mistreatment.⁶⁹ Pruessner et al. reported raised dopamine synthesis under stressful conditions in children with poor parental bonding, suggesting that a dysfunctional parent—child relationship may impact normal development of the brain.⁷⁰

In summary, literature supports the hypothesis that prolonged periods of stress in early life as a result of a chronic disease condition may provide causality concerning AD and concurrent or future ADHD. Increased levels of GCs in the child suffering from AD may interfere with the development and maturation of ADHD-related parts of the brain, most importantly the PFC and the hypothalamus–pituitary–adrenal axis. It is likely that changes of functional and structural nature in those regions could lead to impaired cognition and consequently ADHD.

Conclusion

The high prevalence of AD implies that dermatologists and general practitioners frequently encounter this disease. AD is caused by a complex interaction of both an inborn and an acquired barrier and immune dysfunction. However, a novel focus is directed toward the possibility that this chronic pruritic disease might directly or indirectly lead to an increased risk of psychiatric comorbidities, ADHD included. This concept of prolonged psychoendocrine and psychoneuroimmunological effects from elevated inflammatory cytokine levels, continuous sensory stimuli, disturbed sleep, and increased stress is, however, poorly elucidated. In conclusion, data support that children with

AD have an ~1.5-fold increased risk for ADHD symptoms and that the ascribed population risk for ADHD explained by AD is roughly 9%.¹¹ This review presents a range of epidemiologic studies heavily supporting an increased incidence of the psychiatric entity ADHD in AD patients and furthermore argues that AD likely is one of several risk factors for ADHD.^{31,71} Taken together, these data emphasize the importance of future studies examining underlying mechanisms and relevant preventive measures in this complex multimorbid pediatric population. We trust that a brighter future is in store for all AD patients because basic research discoveries accelerate the development of impending new drugs that in conjunction with an effort toward the identification of psychiatric comorbidities, psychotherapy, and relevant treatment altogether could relieve patients of both the dermatological condition and secondary psychiatric comorbidity.

Author Contributions

All authors have participated sufficiently in the work to take public responsibility in its contents as stated at www.publicationethics.org.uk.

Author Disclosure Statement

M.D. is an investigator, speaker, and/or an advisor for AbbVie A/S, MSD, Pierre Fabre Dermo-cosmétique, Meda Pharma, Leo Pharma, Sanofi, and Regeneron. C.V. is an investigator for AbbVie A/S, Pierre Fabre Dermo-Cosmétique. He has served on advisory boards for Astellas Pharma and has been a speaker for Leo-Pharma, Astellas, MSD, AbbVie, Novartis, and Pfizer.

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