Medical Marijuana Program

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Petition to Add a Medical Condition, Medical Treatment or Disease to the List of Debilitating Conditions

INSTRUCTIONS: Please complete each section of this Petition and attach all supportive documents. All attachments must include a title referencing the Section letter to which it responds. Any Petition that is not fully or properly completed will not be submitted to the Board of Physicians.

Please Note: Any individually identifiable health information contained in a Petition shall be confidential and shall not be subject to disclosure under the Freedom of Information Act, as defined in section 1-200, Connecticut General Statutes.

Section A: Petitioner's Information

Name (First, Middle, Last): [redacted]		
Home Address (including Apartment or Suite #): [redacted]		
City: [redacted]	State: CT	Zip Code: [redacted]
Telephone Number: [redacted]	E-mail Address: [redacted]	

Section B: Medical Condition, Medical Treatment or Disease

Please specify the medical condition, medical treatment or disease that you are seeking to add to the list of debilitating medical conditions under the Act. Be as precise as possible in identifying the condition, treatment or disease.

Atopic dermatitis, Eczema

Section C: Background

Provide information evidencing the extent to which the condition, treatment or disease is generally accepted by the medical community and other experts as a valid, existing medical condition, medical treatment or disease.

- Attach a comprehensive definition from a recognized medical source.
- Attach additional pages as needed.

Please see attached.

Section D: Negative Effects of Current Treatment

If you claim a treatment, that has been prescribed for your condition causes you to suffer (i.e. severe or chronic pain, spasticity, etc.), provide information regarding the extent to which such treatment is generally accepted by the medical community and other experts as a valid treatment for your debilitating condition.

- Attach additional pages as necessary.
- If not applicable, please indicate N/A.

The symptoms of condition cause suffering. Phototherapy sometimes worsens conditions by drying out skin and causing increased itching and flaking. Please see attached.

Section E: Negative Effects of Condition or Treatment

Provide information regarding the extent to which the condition or the treatments thereof cause severe or chronic pain, severe nausea, spasticity or otherwise substantially limits one or more major life activities.

- Attach additional pages as necessary.

The itchy and sore skin associated with chronic eczema limits daily activities. The condition causes constant discomfort which can affect bathing, sleeping, and moving around. Please see attached.

Section F: Conventional Therapies

Provide information regarding the availability of conventional medical therapies, other than those that cause suffering, to alleviate suffering caused by the condition or the treatment thereof.

- Attach additional pages as necessary.

Compared to psoriasis, eczema therapies are limited. All of which may cause discomfort. Please see attached.

Section G: General Evidence of Support for Medical Marijuana Treatment

Provide evidence, generally accepted among the medical community and other experts, that supports a finding that the use of marijuana alleviates suffering caused by the condition or the treatment thereof.

- Attach additional pages as necessary.

Section H: Scientific Evidence of Support for Medical Marijuana Treatment

Provide any information or studies regarding any beneficial or adverse effects from the use of marijuana in patients with the condition, treatment or disease that is the subject of the petition.

- Supporting evidence needs to be from professionally recognized sources such as peer reviewed articles or professional journals.
- Attach complete copies of any article or reference, not abstracts.

Please see attached.

Section I: Professional Recommendations for Medical Marijuana Treatment

Attach letters in support of your petition from physicians or other licensed health care professionals knowledgeable about the condition, treatment or disease at issue.

N/A

Section J: Submission of Petition

In the event you are unable to answer or provide the required documentation to any of the Sections above (excluding Section D); provide a detailed explanation indicating what you believe is "good cause" for not doing so.

- Attach additional pages as necessary.

Eczema and psoriasis are very similar in symptoms and treatment methods. The anti-inflammatory and pain relieving effects that marijuana has on psoriasis may also be beneficial to eczema. According to recent articles marijuana may even be effective for skin disorders in topical form.

I hereby certify that the above information is correct and complete.

My signature below attests that the information provided in this petition is true and that the attached documents are authentic. I formally request that the commissioner present my petition and all supporting evidence to the Board of Physicians for consideration.

Signature: [redacted]	Date Signed: 10/11/2016

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Review Article

Atopic Dermatitis: Natural History, Diagnosis, and Treatment

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Atopic dermatitis is an inflammatory skin disease with early onset and with a lifetime prevalence of approximately 20%. The aetiology of atopic dermatitis is unknown, but the recent discovery of filaggrin mutations holds promise that the progression of atopic dermatitis to asthma in later childhood may be halted. Atopic dermatitis is not always easily manageable and every physician should be familiar with the fundamental aspects of treatment. This paper gives an overview of the natural history, clinical features, and treatment of atopic dermatitis.

1. Definition

Atopic dermatitis is a common, chronic, relapsing, inflammatory skin disease that primarily affects young children. *Atopy* is defined as an inherited tendency to produce immunoglobulin E (IgE) antibodies in response to minute amounts of common environmental proteins such as pollen, house dust mites, and food allergens. Dermatitis derives from the Greek "derma," which means *skin,* and "itis," which means *inflammation*. Dermatitis and *eczema* are often used synonymously, although the term eczema is sometimes reserved for the acute manifestation of the disease (from Greek, ekzema, *to boil over*); here, no distinction is made. Over the years, many other names have been proposed for the disease, for instance, prurigo Besnier (*Besnier's itch*), named after the French dermatologist Ernest Besnier (1831–1909). Allergic sensitization and elevated immunoglobulin E (IgE) are present in only about half of all patients with the disease, and therefore *atopic dermatitis* is not a definitive term.

2. Epidemiology

Atopic dermatitis affects about one-fifth of all individuals during their lifetime, but the prevalence of the disease varies greatly throughout the world [1]. In several so-called industrialised countries, the prevalence increased substantially between 1950 and 2000 so much that many refer to as the "allergic epidemic." However, current indications point to eczema symptoms having levelled off or even having decreased in some countries with a formerly very high prevalence, such as the United Kingdom and New Zealand. This indicates that the allergic disease epidemic is not increasing continually worldwide. Nevertheless, atopic dermatitis remains a serious health concern, and in many countries, particularly in the developing world, the disease is still very much on the rise.

2.1. Natural History. Around 50% of all those with atopic dermatitis develop symptoms within their first year of life, and probably as many as 95% experience an onset below five years of age [2]. Around 75% with childhood onset of the disease have a spontaneous remission before adolescence, whereas the remaining 25% continue to have eczema into adulthood or experience a relapse of symptoms after some symptom-free years. Many with adult-onset atopic dermatitis or atopic dermatitis relapsing in adulthood develop hand eczema as the main manifestation. In some patients, this constitutes a serious concern as it may affect their choice of career or employment and in some cases it may even lead to an early exit from the labour market.

Around 50–75% of all children with early-onset atopic dermatitis are sensitized to one or more allergens, such as food allergens, house dust mites, or pets, whereas those with late-onset atopic dermatitis are less often sensitized [3]. However, intake of foods or exposure to airborne allergens is rarely the cause of exacerbations in atopic dermatitis; many

patients with the disease are sensitized to foods without this playing a role in eczema activity. Atopic dermatitis, particularly severe disease, in a child heralds other atopic diseases. A child with moderate to severe atopic dermatitis may have as much as 50% risk of developing asthma and 75% risk of developing hay fever [4].

2.2. Risk Factors. The risk of developing atopic dermatitis is much higher in those whose family members are affected. For example, the concordance rate of atopic dermatitis in monozygotic twins is around 75%, meaning that the risk of the disease in the twin sibling is 75% if the cotwin is affected [5]. In contrast, the risk in dizygotic twins is only 30%. This shows that genetic factors play a role in the susceptibility to atopic dermatitis. However, as there is not complete concordance between monozygotic twins, who share all their genes, environmental and developmental factors must play a role too. As such, atopic dermatitis is a complex genetic disease arising from several gene-gene and gene-environment interactions.

2.2.1. Genetics. Many genes have been associated with atopic dermatitis, particularly genes encoding epidermal structural proteins and genes encoding key elements of the immune system. A recent and interesting genetic discovery is the documented strong association between atopic dermatitis and mutations in the *filaggrin* gene, positioned on chromosome 1 [6]. The *filaggrin* gene is the strongest known genetic risk factor for atopic dermatitis. Around 10% of people from western populations carry mutations in the *filaggrin* gene, whereas around 50% of all patients with atopic dermatitis carry such mutations. *Filaggrin* gene mutations give rise to functional impairments in the filaggrin protein and thereby disrupt the skin barrier. The clinical expression of such impairments is dry skin with fissures and a higher risk of eczema. Not all patients with atopic dermatitis have these mutations and other genetic variants have also been incriminated [7]. It is the combined action of all these genetic variants along with environmental and developmental risk factors that cause atopic dermatitis.

2.2.2. Environment. Although many different environmental risk factors have been considered potentially causative for atopic dermatitis, only a few are consistently accepted. For example, there is substantial evidence that our western lifestyle leads to some of the reported increase in eczema occurrence over the past years although this has not pointed to specific environmental risk factors or has translated directly into functional preventive measures [8]. Many advocate the *hygiene hypothesis* when explaining the rapid increase in eczema prevalence [9]. This hypothesis states that the decrease in early childhood exposure to *prototypical* infections, such as hepatitis A and tuberculosis, has increased susceptibility to atopic diseases [10]. The hypothesis is supported by the observations that the youngest among siblings has the lowest risk of atopic dermatitis and that children who grow up in a traditional farming environment where they are exposed to a variety of microflora, for instance, from unpasteurized cow's milk, livestock, and livestock quarters, are protected to some extent against developing the disease and against allergic diseases in general [11]. In contrast, disease development is probably positively correlated with duration of breastfeeding [12], whereas several studies have linked a high social position of the parents to an increased risk of atopic dermatitis in the child [13]. Although such observations are not easy to interpret, they may also lend support to the hygiene hypothesis or at least to the generally accepted theory that eczema occurs in genetically susceptible individuals who are exposed to a certain disadvantageous environment.

3. Pathophysiology

Two main hypotheses have been proposed to explain the inflammatory lesions in atopic dermatitis. The first hypothesis concerns an imbalance of the adaptive immune system; the second hypothesis concerns a defective skin barrier. Although these two hypotheses are not thought to be mutually exclusive, they may complement each other.

3.1. Immunological Hypothesis. The theory of immunological imbalance argues that atopic dermatitis results from an imbalance of T cells, particularly T helper cell types 1, 2, 17, and 22 and also regulatory T cells [14]. In the allergic (atopic dermatitis) state—particularly in acute eczema—the Th2 differentiation of naive CD4+ T cells predominates. This causes an increased production of interleukins, primarily IL-4, IL-5, and IL-13, which then leads to an increased level of IgE, and the Th1 differentiation is correspondingly inhibited.

3.2. The Skin Barrier Hypothesis. The theory of skin barrier defects is more recent and has its origin in the observation that individuals with mutations in the *filaggrin* gene are at increased risk of developing atopic dermatitis [6]. The *filaggrin* gene encodes structural proteins in the stratum corneum and stratum granulosum that help bind the keratinocytes together. This maintains the intact skin barrier and the hydrated stratum corneum. With gene defects, less filaggrin is produced, leading to skin barrier dysfunction and transepidermal water loss, which causes eczema. There is evidence to suggest that the impaired skin barrier, which results in dry skin, leads to increased penetration of allergens into the skin, resulting in allergic sensitization, asthma, and hay fever [15]. Preventing dry skin and active eczema early in life via application of emollients may constitute a target of primary prevention of progression of eczema into allergic airways disease.

4. Histopathology

A skin biopsy taken from a site with acute atopic eczema is characterised by intercellular oedema, perivascular infiltrates primarily of lymphocytes, and retention of the nuclei of the keratinocytes as they ascend into the stratum corneum—so-called parakeratosis. Chronic eczema is dominated by a thickened stratum corneum, so-called hyperkeratosis, a thickened stratum spinosum (acanthosis), but sparse lymphocytic infiltrates.

Table 1: Diagnostic criteria for atopic dermatitis.

Essential features
Itch
Eczema with typical morphology and age-specific pattern
Important features
Early age of onset
Atopy (personal or family history)
Dry skin
Associated features
Atypical vascular response (i.e., facial pallor, white dermographism)
Keratosis pilaris, palmar hyperlinearity, ichthyosis
Ocular and periorbital changes
Other regional findings (e.g., perioral and periauricular lesions)
Perifollicular accentuation, lichenification, and excoriations

Modified from American Academy of Dermatology [16].

Table 2: Therapeutic approaches to atopic dermatitis.

Topical treatments
Corticosteroids
Calcineurin inhibitors
Phototherapy
Ultraviolet light A (UVA)
Ultraviolet light B (UVB)
Ultraviolet light A + Psoralene (PUVA)
Systemic treatments
Oral corticosteroids
Azathioprine
Cyclosporine A
Methotrexate

5. Diagnosis and Clinical Presentation

The appearance of the individual skin lesion in atopic dermatitis does not differ from other eczemas such as contact eczema. In its acute form, eczema is characterised by a lively red infiltrate with oedema, vesicles, oozing, and crusting; lichenification, excoriations, papules, and nodules dominate the subacute and chronic form. Accordingly, the diagnostic approach builds upon other characteristics such as the distribution of the eczema as well as associated features of the patient. The typical patient with atopic dermatitis is a person with:

> *an early onset of itchy eczema localised at typical sites such as the flexures of the elbows and knees in an atopic patient or in a person with a familial predisposition to atopic disease.*

The most widely used diagnostic criteria for atopic dermatitis were developed by Hanifin and Rajka in 1980 and were later revised by the American Academy of Dermatology (Table 1) [16].

This set of criteria is primarily useful in clinical practice; another set of diagnostic questions widely used in epidemiological research was developed by the UK Working Party in 1994 (Table 2) [17].

The severity of eczema can be graded according to several scoring systems such as SCORAD [18] and EASI [19].

5.1. Typical Manifestations. Although this description fits many with the disease, the clinical presentation of atopic dermatitis is often more elaborate with a large variation in the morphology and distribution of the eczema combined with various other features. However, many patients with atopic dermatitis have a general tendency to present with dry skin (xerosis) due to the low water content and an excessive water loss through the epidermis. The skin is pale because of increased tension in the dermal capillaries and the ability to sweat is reduced. There is an increased cholinergic response to scratch, so-called white dermographism or *skin-writing,* resulting in hives at the affected site. The palms of the hands and feet may show hyperlinearity, and the individuals' hair is dry and fragile. Often, there is a double skinfold underneath the inferior eyelid (Dennie-Morgan fold) that becomes exaggerated in times of increased disease activity. The eye surroundings may be darkened due to postinflammatory hyperpigmentation.

Atopic dermatitis can be grouped into three clinical stages, although these may be difficult to reproduce in the individual patient [2].

5.1.1. Atopic Dermatitis of Infancy. Infants experience eczema that is often localised to the face, scalp, and extensor aspects of the arms and legs, but it can also be widespread. The lesions are characterised by erythema, papules, vesicles, excoriations, oozing, and formation of crusts.

5.1.2. Atopic Dermatitis of Childhood. In toddlers and older children, the eczema lesions tend to shift location so that they are often confined to the flexures of the elbows and knees as well as the wrists and ankles, although it can occur at any site. In general, the eczema becomes drier and lichenified with excoriations, papules, and nodules.

5.1.3. Atopic Dermatitis of Adolescence and Adulthood. In adult patients, the lesions frequently localise to the face and neck, *head-and-neck dermatitis*, and a considerable portion of patients, around 30%, develop atopic hand eczema, which may interfere with workplace activities.

5.2. Special Manifestations. Some patients may present with several other common, benign skin conditions, for example, *pityriasis alba*, which is a condition characterised by dry, pale patches on the face and upper arms, and *keratosis pilaris*,

which manifests as small, rough keratotic papules particularly on the upper arms and thighs. Atopic winter feet—*dermatitis plantaris sicca*—a condition usually seen in school-aged children is characterised by symmetric eczema on the weight bearing areas of the soles of the feet. Earlobe eczema, eczema of the nipple, and eczema around the margins of the mouth (cheilitis) can be particularly troublesome and often involve infection with staphylococci. Keratoconus and cataracts sometimes complicate atopic dermatitis.

5.3. Aggravating Factors. In many patients, atopic dermatitis takes a chronic, relapsing course when it is not possible to predict periods of activity or pinpoint aggravating factors. However, several exposures are well known for aggravating eczema and should be avoided. A large number of patients are sensitive to woollen clothing, which aggravates itching and discomfort. Hot water may also exacerbate itching, and long baths should be avoided. Several infections, notably staphylococci, are frequent causes of exacerbations as various foods are, particularly in cases where a patient is sensitized to the food. Food avoidance should be advocated only if a patient has documented allergy to a suspected food and not on the basis of asymptomatic sensitization alone. Another phenomenon that can lead to the eczema worsening is contact urticaria, which is a reaction following skin exposure to a food, for example, citrus fruits or tomatoes. The skin around the mouth is often the site of such a reaction. Lastly, many patients report that stressful living aggravates their eczema.

5.4. Differential Diagnoses. Several diseases present with a skin rash that resembles atopic dermatitis. However, careful evaluation of the morphology and localization of the rash combined with information about the individual patient usually leads to a diagnosis. Diseases that sometimes resemble atopic dermatitis are scabies, seborrheic dermatitis, and contact dermatitis.

5.5. Complications. Several microorganisms, such as bacteria, viruses, and fungi, can complicate the eczema (causing superinfections). The skin of the patient with atopic dermatitis is often colonised with *Staphylococcus aureus*, particularly when the eczema is not well controlled. The mere presence of such bacteria does not require antibiotic treatment. However, if staphylococci become invasive, oozing crusted lesions—*impetigo*—can be the result, which indicates the need for topical or, preferably, oral antibiotics [20]. Some advocate skin washing with antiseptic remedies, such as chlorhexidine, as this lowers the number of bacteria on the skin; however, chlorhexidine can lead to secondary sensitization. Due to deficiencies in the production of antimicrobial peptides in the skin, patients with atopic dermatitis also have a greater risk of several viral infections, for example, molluscum contagiosum, caused by a pox virus, which gives small, umbilicated, dome-shaped, pearly coloured papules. Another typical superinfection of the skin in atopic dermatitis patients is herpes virus. If such a herpes infection spreads, it can cause *eczema herpeticum*, which is a widespread vesicular eruption, typically localised to the face, scalp, and upper chest. Eczema herpeticum requires systemic antiviral treatment.

6. Treatment

Atopic dermatitis is not curable, and many patients will experience a chronic course of the disease. Accordingly, the treatment of atopic dermatitis aims to [21]

(1) minimise the number of exacerbations of the disease, so-called *flares*,

(2) reduce the duration and degree of the flare, if flare occurs.

The first aim relates primarily to prevention; the second aim relates to treatment. Prevention is best attained by trying to reduce the dryness of the skin, primarily via daily use of skin moisturising creams or *emollients* along with avoidance of specific and unspecific irritants such as allergens and noncotton clothing. When dryness is reduced, the desire to scratch will lessen and the risk of skin infection will decrease. Avoiding long, hot baths further prevents skin dryness, but when a bath is taken, an emollient should be applied directly after it to secure a moist epidermis and augment the skin barrier function. Reducing the flare is warranted when actual eczema occurs or when mild intermittent eczema worsens. Management of an eczema exacerbation requires medical treatment often in the form of corticosteroid creams. In addition to topical treatment, severe acute or chronic eczema often requires systemic immunosuppressant drugs or phototherapy (ultraviolet, UV light).

6.1. Emollients: Maintaining an Intact Skin Barrier. The use of emollients in the management of atopic dermatitis is pivotal. They should be applied several times a day, and a systematic use has been shown to reduce the need for corticosteroid creams [22, 23]. The main reason for intensive use of an emollient is its ability to increase the hydration of the epidermis, mainly by reducing the evaporation, as it acts as an occlusive layer on the top of the skin. As such, emollients have no direct effect on the course of the eczema. However, the appearance of the skin is enhanced and itching is reduced. Other moisturizers have more complex modes of action as they act by restoring the structural (lipid) components of the outer skin layers, thereby reducing cracks and fissures. Others act by attracting water molecules from the air in order to moisturize the skin. The choice of emollient depends on the individual patient. It is generally recommended that a thick (with a high fat content) cream or ointment is used for the driest skin, whereas creams and lotions with a higher water content are used only for very mild eczema. Such creams must be applied several times a day because of their rapid absorption into the skin. It is important to recommend an emollient without perfume or other potential allergens as they may provoke secondary allergic sensitization. Those with chronic, dry eczema benefit from tar preparations in the form of creams and occlusive bandages.

6.2. Topical Corticosteroids. Topical corticosteroids are the mainstay of the treatment for moderate to severe atopic dermatitis, both in children and adults. Corticosteroids are hierarchically grouped into different classes based on their

Table 3: Topical corticosteroids.

Mild (Class I)
Hydrocortisone
Moderate (Class II)
Hydrocortison-17-butyrate
Clobetason-17-butyrate
Strong (Class III)
Betamethason-17-valerate
Fluticasone propionate
Betamethasone
Mometasonfuroate
Desoximethasone
Fluocinonide
Fluocinolonacetonide
Very strong (Class IV)
Clobetasol propionate

Table 4: Fingertip unit.

Area that needs treatment	FTUs (adults)	FTUs (children 1-2 years)
Face and neck	2.5	1.5
One hand and fingers	1	0.5
One arm, hand, and fingers	4	1.5
Chest and abdomen	7	2
Back and buttocks	7	3
One leg and foot	8	2

vasoconstrictory abilities. For ease, four classes are considered: mild, moderate, strong, and very strong preparations (Table 3).

6.2.1. How Should Corticosteroids Be Applied? Most patients benefit from treatment with mild to moderate corticosteroid preparations, whereas only a small subset—those with severe disease—needs potent preparations; very strong preparations are rarely needed. Mild and moderate corticosteroid creams are reserved for children, while adults can be treated with stronger preparations. Mild and moderate corticosteroids should be used chiefly for treating eczema on body sites where the skin is thin, notably in the face, axillae, groins, and anogenital area, whereas strong corticosteroids should be used for treating eczema on the rest of the body. Unlike medications used for treating asthma and allergic rhinitis, creams for atopic dermatitis are not prepared with a fixed amount of drug release per round of usage. Instead, the "rule of the fingertip unit (FTU)" must be applied. A fingertip unit is the amount of cream or ointment squeezed from a standard tube along an adult's fingertip—a fingertip is from the very end of the finger to the distal crease in the finger. One FTU is sufficient to treat an area of skin twice the size of the flat of an adult hand with the fingers together (Table 4).

As one FTU equals roughly 0.5 g cream, the amount needed to adequately treat an entire adult body surface once is 20 g, whereas a 1-2-year-old child, for instance, requires about 7 g.

6.2.2. Proactive and Reactive Treatment. Corticosteroid creams are used both for treating acute flares of atopic dermatitis and for maintenance therapy; that is, prevention of disease relapses when the acute flare is under control. For treating acute flares, one daily application is recommended of the cream with the lowest potency deemed sufficient to clear the eczema within 1-2 weeks [24]. When the eczema flare is well controlled, that is, when the rash is quiescent and particularly when the itch has subsided substantially, use of the corticosteroid cream should be tapered off to two to three weekly applications for an additional 1-2 weeks. Another tapering approach is to use a lower potency cream daily for 1-2 weeks. However, patients may find this approach slightly more difficult to manage. In theory, treatment could be discontinued at the end of the tapering period if the flare is sufficiently under control, but in many patients the eczema relapses, and an additional round of treatment is required. If this is the case, it is preferable to continue the maintenance treatment, applying the corticosteroid cream two to three times weekly on those sites—for instance, the elbow creases—likely to become active again if treatment is discontinued. This strategy is called the *proactive* treatment strategy, as compared with the *reactive* strategy, which recommends intermittent use of the corticosteroid preparation according to the activity of the eczema. The proactive treatment strategy is being increasingly advocated because the overall quantity of corticosteroid cream used is smaller than that used with the reactive treatment strategy; additionally, the risk of an exacerbation of the eczema is smaller when using the proactive treatment strategy.

6.2.3. Side Effects. Patients and physicians alike fear the cutaneous and systemic side effects from using topical corticosteroids. However, although topical corticosteroids can cause thinning of the skin, teleangiectasies, and stretch marks, when used properly, the risk of side effects is very small. It is essential that physicians try to reassure parents of atopic children and the patients themselves and explain that this fear of side effects should not inhibit the use of corticosteroids since insufficient use can cause worsening of the eczema. Including the patient (and the parents) in the treatment plan is paramount. Rather than dictating what is best for the child, physicians should discuss the parents' concerns in order to avoid disrupting the physician-patient-parent relationship, which would ultimately lead to complications for the child.

6.3. Calcineurin Inhibitors. Pimecrolimus cream and tacrolimus ointment—also termed topical calcineurin inhibitors—are newer formulations used both for the treatment of acute flares and for maintenance therapy of atopic dermatitis [25]. Pimecrolimus has the potency of a mild corticosteroid cream, whereas tacrolimus corresponds to a moderate to strong topical corticosteroid. The side effects of corticosteroids, such

as thinning of the skin, are not seen with topical calcineurin inhibitors, and this allows daily treatment for longer periods. Topical calcineurin inhibitors can also be used in the proactive treatment strategy.

6.4. Phototherapy. Widespread eczema benefits from treatment with UV light. Narrowband UVB light is particularly suitable for treating adults with recalcitrant eczema. Broadband UVA light and a combination of UVA light and the photosensitizing drug *psoralene* can also be used to treat severe recalcitrant eczema. Difficult-to-treat atopic dermatitis often clears with 1-2 months' phototherapy three to five times a week, preferably combined with topical corticosteroids. Nevertheless, as phototherapy causes premature aging of the skin and increases the risk of skin cancer in the long run, it should be prescribed with caution.

6.5. Systemic Immunosuppressant Treatments. Short-term tapered treatment with oral corticosteroids is recommended for acute flares of severe, widespread atopic dermatitis, preferably in combination with topical corticosteroids. As *Staphylococcus* infections often trigger such flares, oral antibiotics should be prescribed simultaneously. Due to the risk of side effects, continuing treatment with oral corticosteroids is not recommended. Instead, tapering should be done while introducing a second immunosuppressant drug, for example, azathioprine, methotrexate, or cyclosporine A, for very severe, chronic, relapsing atopic dermatitis [26]. Such treatment should be administered from specialised clinics or, preferably, from hospital dermatology departments.

6.6. Other Medications. Specific immunotherapy in patients with atopic dermatitis mainly has an effect on upper airway symptoms if the patient has concomitant allergic rhinitis, whereas the effect on the activity of the eczema is negligible.

Oral antihistamines are recommended for itching but have no effect on the activity of the eczema. Nonsedating antihistamines should be used, but when night-time itching interferes with sleep, sedating antihistamines are recommended.

Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this paper.

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Phototherapy to treat eczema

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Phototherapy or light therapy refers to the use of ultraviolet (UV) light to treat moderate to severe eczema in adults (and sometimes in school-aged children) in cases where topical therapies alone have not been effective. Phototherapy is a second-line treatment option that is usually only available at a specialist clinic or hospital.

To be considered for phototherapy treatment, you first need to be referred to a consultant dermatologist who may prescribe a course of phototherapy. Your phototherapy treatment will then be supervised by a trained healthcare professional (a dermatology nurse or occasionally a physiotherapist).

WHAT IS PHOTOTHERAPY?

During phototherapy treatment, the patient stands inside a specially designed cabinet (or uses smaller hand and foot cabinets) containing fluorescent tubes that administer UV light to the skin.

In nature, UV radiation is part of the electromagnetic (light) spectrum that reaches the earth from the sun. UV wavelengths are classified as UVA, UVB or UVC. The latter has the shortest rays, and is mostly absorbed by the ozone layer, so does not reach the earth. However, both UVA and UVB penetrate the atmosphere (90% UVA and 10% UVB). UV light is important for health (vitamin D production) and is responsible for tanning, but over-exposure causes premature skin aging. Excessive UV radiation causes skin cell damage that can lead to skin cancer.

HOW DOES PHOTOTHERAPY WORK?

Natural sunlight can help reduce symptoms in eczema for some people. For others, symptoms may become worse. Both UVA and UVB light are used as treatments in phototherapy.

Although phototherapy treatment can be beneficial in the treatment of eczema, with improved symptoms and a reduction in the need for topical steroids, eczema symptoms can recur for some patients once phototherapy is stopped.

UV light in eczema appears to have an effect on the immune system. In particular, it seems to reduce the number of white cells (T-cells) in the skin. They are responsible for causing inflammation and are known to play an important part in the eczematous process, making your skin red, itchy and sore. A reduced number of white cells results in less inflammation and an associated improvement in any areas of eczema.

Improvement with phototherapy happens gradually after several weeks of regular treatments. There is a reduction of itching and the eczema slowly clears as treatments continue. Once there is absence of itching and clearance of most, if not all, of the active eczema, a controlled period of reducing the frequency of treatments is often used successfully to 'wean the patient off', thereby reducing any likelihood of an early flare, and inducing remission. It is important to attend treatment sessions regularly in order to optimise the chances of success.

WHAT ARE THE DIFFERENT TYPES OF PHOTOTHERAPY?

There are three types of phototherapy used in the treatment of atopic eczema – broadband UVB, narrowband UVB and UVA. Sometimes other wavelengths of light, known as UVA1, or combined treatment with UVA and UVB may be used, but these are less commonly available.

Broadband UVB (type B UV light) phototherapy

This is the original phototherapy treatment and has been used for 80 years. The length of treatment increases at each visit unless the skin becomes pink. Broadband UVB is not very effective at clearing skin conditions such as eczema and has now largely been replaced with a different type of UVB called narrowband UVB (often called TL0-1).

Narrowband UVB (TL-01) phototherapy

In narrowband phototherapy, the light tubes produce a narrow part of the UVB spectrum – two wavelengths between 311 and 313 nm (nanometres) – which penetrates more effectively into the skin than the older broadband sources and is able to reduce inflammation and itching and improve the

flare of eczema. The dose of UV given at each treatment is also higher compared to the broadband dose because many of the unwanted wavelengths that cause burning are excluded. Once clearance is achieved, narrowband UVB can often induce a longer period of clear skin. A course of treatment to clear eczema involves two or three appointments per week (a total of 20–40 treatments, depending on response). The time spent in the machine at the beginning is very short and gradually increases at each visit.

UVA phototherapy

This treatment uses longwave UVA light in conjunction with a photosensitising medicine called psoralen – a combination known as PUVA. Psoralen can be taken in tablet form 2–3 hours prior to each treatment, or added as a liquid to a bath of warm water in which the person soaks for 15 minutes. Alternatively, psoralen can be applied directly to small areas of skin as a gel. PUVA treatment is administered to the whole body in a stand-up cabin or can be given to localised areas such as the hands and feet with smaller, compact machines.

HOW LONG AND WHAT DOSAGE IS A COURSE OF PHOTOTHERAPY TREATMENT?

Phototherapy treatment courses are usually given 2–3 times a week for UVB and twice a week for PUVA. Both UVB and PUVA courses last on average around 3 months – maybe longer for severe cases. Shorter courses may also be given. Sometimes, weekly 'maintenance courses' are recommended for a short period after clearance. It is important that you are able to commit to a course of phototherapy as it may take some weeks before you see the benefits of treatment.

UVA and narrowband UVB treatment sessions are administered with a dose of light called Joules. A Joule is a unit of light energy. Your dose (J/cm^2) is individual and will depend on the colour of your skin (or skin type) or – more accurately – by a baseline series of six to ten small test doses of UV to your skin. This skin patch test is called a minimal erythema dose (MED) for UVB and minimal phototoxic dose (MPD) for PUVA. Generally, the dose at which clearance is achieved is up to 5J/cm^2 of UVB and up to 15J/cm^2 for tablet PUVA. However, dosage depends on your skin type, as phototherapy needs to be tailored to the individual and very carefully administered and monitored.

WHEN IS PHOTOTHERAPY USED?

Phototherapy may be used for adults and older children with moderate to severe eczema that is not responding to conventional treatment with topical steroids and emollients. Phototherapy is not usually used in individuals who have UV-sensitive dermatitis/eczema or any other photo-allergic disorder. Patients with these types of eczema are best treated in specialist units.

Narrowband UVB may be helpful for patients with moderate to severe eczema requiring long-term topical steroid use, whereas PUVA is usually more effective for more severe disease that has not responded well to narrowband UVB.

It is important to remember that the total amount of lifetime treatments that can be given is limited because long-term phototherapy poses an increased risk of skin cancer. PUVA should not be used during pregnancy or breastfeeding because of the risk of damage secondary to the psoralen. However, broadband UVB and narrowband UVB can be used in both pregnancy and when breastfeeding.

WHAT ARE THE SIDE EFFECTS?

UVB light treatment is usually well tolerated. However, some patients may experience redness or itching of the skin after treatment. It is important to report any side effects to phototherapy staff so that adjustments can be made to the doses.

Sometimes psoralen tablets can cause nausea – again, adjustments can be made in relation to the type of psoralen tablet to try to prevent this side effect of treatment.

In order to prevent UVA wavelengths entering the eyes and possibly increasing the risk of cataracts in the long term, protective goggles will be provided by the dermatology department to be worn during the actual treatment, and glasses with UV protection need to be worn for 12–24 hours after oral PUVA, though not usually with bath PUVA. (Bath PUVA does cause systemic absorption but it is short term, whereas PUVA tablets mean the whole skin is sensitised to light for 24 hours – hence the need to wear glasses afterwards. Some units ask bath PUVA patients to wear glasses for a short time after treatment, but this is unusual. Since only a small area of the body is made light sensitive with gel PUVA, there is no need to wear glasses after this type of treatment.) The treatment clinic should be able to give advice on the type of sunglasses that are suitable. Clear UV-coatings for non-tinted spectacles are also available.

Despite efforts to prevent burning – by testing the skin's sensitivity to light using controlled incremental doses for each treatment, careful skin assessments and asking about any side effects each visit – occasionally sunburn-type reactions may occur with all types of phototherapy. If this happens, it is important to contact the hospital for appropriate advice.

Phototherapy to treat eczema

Occasionally, eczema may flare at the beginning of a course of phototherapy. This can usually be managed by making adjustments to doses and using topical steroids and emollients to settle the flare. In patients prone to *eczema herpeticum* (eczema infected with the cold-sore virus), phototherapy can sometimes trigger reactivation of the infection, which needs treatment with antiviral tablets (e.g. aciclovir). Patients with a history of cold sores triggered by sunlight should routinely wear sunblock in the phototherapy machine during treatments to prevent any reoccurrence.

As with exposure to natural sunlight, long-term use of UV light therapy can result in accelerated aging of the skin (e.g. freckles and wrinkles). More importantly, there is a potential risk of developing skin cancers. There is a greater long-term risk of developing skin cancer with PUVA compared to UVB, which is why UVB is considered safer in the long term and PUVA is used less frequently.

Men usually cover their genitals with a close-fitting pouch/jock strap unless this area needs treatment. This is because skin in the male genital area is much thinner and sensitive to light and has an increased risk of some skin cancers if exposed to UV light. It is important to cover the same area for each treatment to prevent burning.

After starting a course of treatment, care should be taken to avoid further exposure to UV light. Therefore, it is important not to sunbathe – you should wear sun protection (25 SPF, applied every 2–3 hours) when outside and wear a sunhat on a sunny day. Sun beds are prohibited during a course of phototherapy treatment as they would increase the UV dose and could cause severe burning.

In fact, sun beds should never be used in a tanning salon or bought for home use by people with eczema. They are not an alternative to phototherapy as you are not carefully monitored and there are no controls over the dose of UV light. Sunbeds generally use UVA light but recently the World Health Organisation (WHO) has identified sun beds that produce higher levels of UVB to speed the tanning process. It is important to note that, because of the increased risk of developing skin cancer, the WHO does not recommend the use of sun beds by anyone for cosmetic purposes and only endorses medically supervised light treatment for skin conditions.

DO I STILL USE MY EMOLLIENTS AND TOPICAL TREATMENTS?

You should continue to use emollients during a course of phototherapy. However, you should check with the doctor or nurse that your emollient is suitable as some emollients can block UV light. You may need to use more copious amounts of emollients, especially after treatment, as the skin will be dry. Some people with eczema find phototherapy makes them more itchy, so using emollients for washing and bathing will help. Some phototherapy departments even advise patients to apply emollients at least 30–60 minutes prior to phototherapy treatment, particularly if the skin is dry and uncomfortable.

You may be advised to continue to use topical steroids during a course of phototherapy because of the risk of irritation and flare. If the eczema is improving, the potency of topical corticosteroids will be reduced (as flare management) and the amount or frequency may be reduced depending on the individual and their flare pattern. Topical steroids can be stopped if all eczema has cleared (though the patient will continue using emollients.)

Occasionally, small, localised areas of eczema remain – e.g. on the ankles or wrists – after a course of phototherapy and will require continued treatment with topical steroids.

Topical calcineurin inhibitors (TCIs) – e.g. Elidel and Protopic – are not used on phototherapy days, as they make the skin more sensitive to light, which may increase the risk of burning. Patients may be advised to continue with TCIs on non-treatment days.

It is important to avoid perfumes, deodorants, aftershave lotions and other cosmetics before UV treatment, as some of these products may make you more sensitive to UV light and cause patchy discolouration of the skin, which may take months to fade.

CONCLUSION

Phototherapy is an additional treatment option for people with moderate to severe atopic eczema who have discussed this option at length with their dermatologist, who will prescribe the phototherapy course. In children, the NICE guidelines recommend that phototherapy be used with caution and only for children with severe eczema, where other treatment options have failed and there is a severe negative impact of eczema on quality of life. These children are best managed in a unit where staff are experienced in the treatment of children.

There has been very little clinical research on light therapy as a treatment for eczema and it seems to work better for some people than for others. In those patients who report benefits – although long-term remission is not achieved – phototherapy does give relief of symptoms and induce a period of remission.

FURTHER INFORMATION

The British Association of Dermatologists (BAD) Phototherapy patient information leaflet. Available from: **www.bad.org.uk/site/1223/Default.aspx**

Sleep Disturbances in Adults with Eczema Are Associated with Impaired Overall Health: A US Population-Based Study

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Sleep disturbances are associated with poor health outcomes in adults. However, little is known about the sleep disturbances that occur in adult eczema. We studied the association between adult eczema and sleep disturbance and their impact on overall health and health care utilization. We used the 2012 National Health Interview Survey, a cross-sectional questionnaire of 34,613 adults. Eczema was associated with higher odds of fatigue (odds ratio (95% confidence interval): 2.97 (2.65–3.34)), regular daytime sleepiness (2.66 (2.34–3.01)), and regular insomnia (2.36 (2.11–2.64)), even after controlling for sleep duration, history of allergic disease, sociodemographics, and body mass index. There were significant interactions between eczema and fatigue, sleepiness, and insomnia as predictors of poorer overall health status, number of sick days, and doctor visits, such that eczema and each of the sleep symptoms were associated with higher odds of poorer outcomes than either eczema or sleep symptoms alone. Latent class analysis was used and identified five classes of fatigue, sleep disturbances, and allergic disorders. Two classes had high probabilities of eczema: one with high probabilities of asthma, hay fever, food allergy, and multiple sleep symptoms and the other with intermediate probability of insomnia alone. Future studies are warranted to better characterize sleep loss in eczema and develop strategies for treatment and prevention.

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INTRODUCTION

Sleep disorders are associated with poor performance in school and work, impaired overall health and safety, and considerable economic burden (Skaer and Sclar, 2010). Eczema is a common inflammatory skin condition that causes significant morbidity secondary to severe itch, sleep impairment, social embarrassment, and psychological distress (Carroll *et al.*, 2005). Sleep disturbance is attributed to the intense pruritus; it results in functional impairment (daytime fatigue, irritability, disturbed cognition, and decreased motor performance) and profoundly worsens the quality of life (QOL) in eczema patients (Bender *et al.*, 2003; Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007; Beikert *et al.*, 2014). Having eczema and concurrent sleep disturbance also significantly increases the risk of psychological disorders (Romanos *et al.*, 2010; Schmitt *et al.*, 2011), motor vehicle accidents, and workplace injury (Young *et al.*, 1997; Akerstedt *et al.*, 2002; Gander *et al.*, 2005).

Previous studies have demonstrated significantly worsened sleep quality in childhood eczema with less sleep, more frequent and prolonged awakening, and overall lower sleep efficiency (Monti *et al.*, 1989; Dahl *et al.*, 1995; Stores *et al.*, 1998; Chamlin *et al.*, 2005; Hon *et al.*, 2008; Camfferman *et al.*, 2010; Anuntaseree *et al.*, 2012; Camfferman *et al.*, 2013; Chang *et al.*, 2013). However, few studies have addressed the quality of sleep in the adult eczema population. Further, little is known about how different patterns of sleep disturbance affect the overall health in affected adults. Better understanding of the impact of adult eczema on sleep patterns could lead to new treatment and improve QOL. We hypothesized that adult eczema in the United States is associated with fatigue and disturbance of sleep patterns, which worsen overall health, independent of allergic airway disease.

RESULTS

Prevalence of eczema and other atopic disorders

Data were collected on 34,613 adults, representing all age, gender, and racial/ethnic groups. The US prevalence (95%

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The results of this study were presented in part at the 2014 Society of Investigative Dermatology meeting in Albuquerque, New Mexico, USA

Abbreviations: AD, atopic dermatitis; aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio

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confidence intervals (CIs)) of eczema in adults was 7.2% (6.9–7.6%). Eight percent (7.6–8.4%) currently had asthma, 7.5% (7.1–7.9%) had hay fever, 11.2% (10.8–11.7%) had respiratory allergies, and 3.9% (3.6–4.2%) had food or digestive allergies.

Prevalence of eczema was significantly associated with female sex (survey logistic regression; crude odds ratio (OR) (95% CIs): 1.52 (1.36–1.70)) and post-high school education (1.37 (1.13–1.66)) but inversely associated with African-American race (0.82 (0.70–0.96)), Hispanic origin (0.73 (0.62–0.85)), household income of $75,000–99,999 (0.76 (0.61–0.95)), families with children and either a single parent (0.79 (0.67–0.94)) or both parents living in the household (0.76 (0.65–0.89)) compared with those that had no children, and birthplace outside the United States (0.63 (0.54–0.73)). Prevalence was not associated with age (Table 1). Class II and III obesity, as defined by body mass index (BMI) of 35–39 and ⩾40, respectively, was also associated with eczema (class II: 1.31 (1.04–1.64); class III: 1.49 (1.18–1.88)).

Prevalence of fatigue and sleep disturbances

The 1-year prevalence of self-reported fatigue or lack of energy for more than 3 days was 15.8% (15.0–16.0%). Frequent excessive daytime sleepiness was described in 12.8% (12.3–13.2%), and 19.3% (18.8–19.9%) reported regularly having insomnia or trouble sleeping. Among adults who reported having regular insomnia, 43.6% (42.1–45.1%) also reported fatigue, and 36.8% (35.3–38.2%) had daytime sleepiness.

Prevalence of having more than 3 days of fatigue, regular daytime sleepiness, and/or insomnia was associated with age 50–69 (1.42 (1.29–1.55)) and ⩾70 years (1.59 (1.43–1.76)), female sex (1.67 (1.57–1.78)), and lower household income ($0–34,999: 2.15 (1.95–2.36); $35,000–74,999: 1.55 (1.40–1.71); $75,000–99,999: 1.19 (1.05–1.36)) and inversely associated with African–American (0.80 (0.74–0.87)) and Asian race (0.52 (0.45–0.60)), Hispanic origin (0.80 (0.74–0.87)), single (0.81 (0.74–0.89)) or multiple (0.67 (0.62–0.73)) children in the household, post-high school education (0.84 (0.76–0.92)), families that had children and either a single parent (0.83 (0.76–0.90)) or both parents in the household (0.60 (0.55–0.66)), and birthplace outside the United States (0.62 (0.57–0.67)). There was a U-shaped distribution of fatigue, daytime sleepiness, and/or insomnia associated with BMI, such that both, being underweight (1.57 (1.24–1.98)) and being obese (class I: 1.30 (1.19–1.42); class II: 1.90 (1.69–2.15); class III: 2.59 (2.25–2.99)), were associated with a higher prevalence of fatigue and sleep disturbance.

Association between eczema and sleep duration

History of eczema in the past year was associated with significantly higher odds of both short (1.35 (1.20–1.51)) and long (1.44 (1.19–1.74)) sleep duration (Table 2). These associations remained significant in multivariate models that controlled for the history of asthma, hay fever, respiratory allergy, food or digestive allergy, age, sex, race, Spanish origin, household income, level of education, US birthplace, number of children in the home, family structure, and BMI.

Association between eczema, fatigue, and sleep disturbance

Adults with eczema had a higher 1-year prevalence of fatigue (5,580,472 people or 32.8% (30.4–35.2%)), regular daytime sleepiness (4,430,186 people or 26.0% (23.8–28.3%)), and insomnia (5,847,404 people or 34.4% (32.0–36.8%)) compared with those without eczema (27.5% (26.9–28.1%); Table 2). In particular, eczema was associated with higher odds of fatigue (OR (95% CIs): 2.97 (2.65–3.34)), regular daytime sleepiness (OR (95% CIs): 2.66 (2.34–3.01)), and regular insomnia (OR (95% CIs): 2.36 (2.11–2.64)). These associations remained significant in multivariate models that included the above-mentioned atopic disorders, sociodemographics, and BMI, as well as sleep duration (Table 2).

Significant two-way interactions were found between symptoms of insomnia and fatigue/daytime sleepiness and between insomnia and sleep duration. Therefore, contrast statements were used to generate estimates for OR and 95% CIs at each level of combination. Odds of eczema were higher in subjects with either fatigue/daytime sleepiness (2.67 (2.28–3.13)) or insomnia (1.96 (1.65–2.34)) and highest with both fatigue/daytime sleepiness and insomnia (3.61 (3.15–4.12); Table 2). Adults with insomnia had higher odds of eczema for all sleep durations (3–6 hours: 2.38 (2.05–2.76); 7–8 hours: 2.40 (2.02–2.85); 9–14 hours: 3.72 (2.73–5.05)). These interactions remained significant in multivariate models. In contrast, adults without insomnia did not have significant interactions with sleep duration as predictors of eczema.

There were no significant differences of association between eczema, asthma and/or hay fever, and sleep disturbance in obese (class I–III) versus normal weight adults (data not shown).

Association between eczema, fatigue, sleep disturbance, and overall health status

In univariate models, eczema (OR (95% CIs): 1.98 (1.74–2.26)), fatigue (6.21 (5.70–6.76)), daytime sleepiness (4.71 (4.29–5.16)), and insomnia (3.99 (3.68–4.33)) were all significant predictors of having only fair/poor overall health. However, there were significant two-way interactions between eczema and fatigue and sleep disturbances. In models of interaction between eczema and fatigue, eczema alone was associated with fair/poor health (OR (95% CIs): 1.29 (1.07–1.56)), whereas fatigue without eczema was associated with higher odds of fair/poor health (OR (95% CIs): 5.93 (5.42–6.50)); those with both eczema and fatigue had even higher odds of fair/poor health (OR (95% CIs): 8.63 (7.15–10.43); Table 3).

Similarly, in models of interaction between eczema and regular daytime sleepiness or insomnia, eczema alone was consistently associated with fair/poor health; regular daytime sleepiness or insomnia without eczema had even higher odds of fair/poor health; and both regular daytime sleepiness or insomnia and eczema had the highest odds of fair/poor health.

Associations between eczema, sleep disturbances, and number of sick days and doctor visits

Significant two-way interactions were found between eczema and sleep disturbances as predictors of the number of missed

Table 1. Determinants of eczema and sleep problems in adults ($n = 34,613$)

Variable—no. (%)	Eczema			Fatigue, daytime sleepiness, or insomnia		
	% Prev (95% CI)	Crude OR (95% CI)	*P*-value	% Prev (95% CI)	Crude OR (95% CI)	*P*-value
Age (years)						
18–29	6.6 (5.8–7.4)	1.00	—	25.6 (24.1–27.0)	1.00	—
30–49	7.4 (6.7–8.0)	1.12 (0.96–1.31)	0.14	26.2 (25.2–27.2)	1.03 (0.94–1.14)	0.47
50–69	7.6 (7.0–8.3)	1.17 (1.00–1.37)	0.05	32.7 (31.6–33.8)	1.42 (1.29–1.55)	<0.0001
⩾70	6.9 (6.0–7.8)	1.05 (0.87–1.27)	0.59	35.3 (33.6–37.0)	1.59 (1.43–1.76)	<0.0001
Sex						
Male	5.8 (5.3–6.3)	1.00	—	23.8 (22.9–24.6)	1.00	—
Female	8.6 (8.0–9.1)	1.52 (1.36–1.70)	<0.0001	34.3 (33.4–35.2)	1.67 (1.57–1.78)	<0.0001
Race						
Caucasian	7.4 (7.0–7.8)	1.00	—	30.4 (29.7–31.1)	1.00	—
African American	6.1 (5.3–7.0)	0.82 (0.70–0.96)	0.01	25.9 (24.4–27.4)	0.80 (0.74–0.87)	<0.0001
American Indian	8.2 (5.0–11.4)	1.12 (0.73–1.72)	0.59	34.3 (28.3–40.2)	1.20 (0.92–1.56)	0.19
Asian	6.6 (5.3–8.0)	0.89 (0.71–1.11)	0.31	18.4 (16.3–20.5)	0.52 (0.45–0.60)	<0.0001
Multiracial/other	13.3 (6.7–20.0)	1.93 (1.08–3.44)	0.03	29.3 (20.7–37.9)	0.95 (0.63–1.44)	0.81
Hispanic origin						
No	7.5 (7.1–7.9)	1.00	—	29.9 (29.2–30.6)	1.00	—
Yes	5.6 (4.8–6.3)	0.73 (0.62–0.85)	<0.0001	25.5 (24.0–26.9)	0.80 (0.74–0.87)	<0.0001
Household income (× $1,000)						
0–34	7.3 (6.8–7.9)	0.97 (0.83–1.12)	0.65	36.8 (35.8–37.8)	2.15 (1.95–2.36)	<0.0001
35–74	7.8 (7.1–8.5)	1.03 (0.88–1.21)	0.72	29.6 (28.4–30.7)	1.55 (1.40–1.71)	<0.0001
75–99	5.9 (4.9–6.8)	0.76 (0.61–0.95)	0.01	24.5 (22.6–26.3)	1.19 (1.05–1.36)	0.008
⩾100	7.6 (6.7–8.5)	1.00	—	21.4 (20.0–22.7)	1.00	—
Children in household						
None	7.8 (7.3–8.2)	1.00	—	31.4 (30.7–32.2)	1.00	—
Single	6.3 (5.4–7.2)	0.80 (0.68–0.94)	0.008	27.2 (25.5–28.9)	0.81 (0.74–0.89)	<0.0001
Multiple	6.1 (5.4–6.9)	0.78 (0.67–0.90)	0.0009	23.5 (22.2–24.8)	0.67 (0.62–0.73)	<0.0001
Highest level of household education						
<High school	5.8 (4.8–6.7)	1.00	—	33.1 (31.2–35.0)	1.00	—
High school or GED	5.7 (5.0–6.3)	0.98 (0.79–1.22)	0.85	31.4 (30.0–32.7)	0.92 (0.83–1.03)	0.15
>High school	7.7 (7.2–8.2)	1.37 (1.13–1.66)	0.001	29.2 (28.4–30.1)	0.84 (0.76–0.92)	0.0002
Family structure						
No children	7.8 (7.3–8.2)	1.00	—	31.4 (30.7–32.2)	1.00	—
Both parents	6.3 (5.4–7.2)	0.76 (0.65–0.89)	0.0004	21.6 (20.3–23.0)	0.60 (0.55–0.66)	<0.0001
Single parent	7.5 (4.6–10.4)	0.79 (0.67–0.94)	0.007	27.5 (25.8–29.1)	0.83 (0.76–0.90)	<0.0001
Other adult, no parents	6.0 (5.2–6.8)	0.96 (0.63–1.46)	0.84	34.7 (29.4–40.0)	1.16 (0.92–1.47)	0.22
Birthplace in the United States						
No	5.0 (4.3–5.6)	0.63 (0.54–0.73)	<0.0001	21.6 (20.3–22.8)	0.62 (0.57–0.67)	<0.0001
Yes	7.7 (7.3–8.1)	1.00	—	30.8 (30.1–31.5)	1.00	—
Body mass index						
<18.5	7.8 (4.9–10.6)	1.11 (0.74–1.67)	0.62	35.6 (30.4–40.9)	1.57 (1.24–1.98)	0.0002
18.5–24.9	7.1 (6.5–7.7)	1.00	—	26.1 (25.1–27.1)	1.00	—
25–29.9	6.6 (6.0–7.2)	0.93 (0.81–1.06)	0.29	26.2 (25.2–27.3)	1.01 (0.93–1.09)	0.87
30–34.9	7.3 (6.4–8.2)	1.04 (0.89–1.22)	0.63	31.4 (29.9–32.9)	1.30 (1.19–1.42)	<0.0001
35–39.9	9.0 (7.3–10.7)	1.31 (1.04–1.64)	0.02	40.2 (37.6–42.8)	1.90 (1.69–2.15)	<0.0001
⩾40	10.1 (8.2–12.1)	1.49 (1.18–1.88)	0.0009	47.8 (44.5–51.1)	2.59 (2.25–2.99)	<0.0001

Abbreviations: CI, confidence interval; GED, graduate equivalent degree; OR, odds ratio; Prev, prevalence.
Refusal to answer a particular question or response of ''don't know'' occurred for the questions pertaining to eczema in 25 (0.07%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

Table 2. Eczema as a predictor of sleep duration, fatigue, daytime sleepiness, and insomnia in adults ($n = 34,613$)

Variable		No eczema	Eczema				
		% Prev (95% CI)[1]	% Prev (95% CI)[2]	OR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Sleep duration (h)							
Short: 3–6		28.9 (28.2–29.5)	34.3 (31.9–36.7)	1.35 (1.20–1.51)	<0.0001	1.30 (1.14–1.79)	0.0001
Average: 7–8		62.8 (62.1–63.5)	55.2 (52.6–57.7)	1.00 (ref)	—	1.00 (ref)	—
Long: 9–14		8.3 (7.9–8.7)	10.5 (8.8–12.2)	1.44 (1.19–1.74)	0.0002	1.43 (1.14–1.79)	0.002
Fatigue							
No		85.9 (85.4–86.4)	67.2 (64.8–69.6)	1.00	—	1.00	—
Yes		14.1 (13.6–14.6)	32.8 (30.4–35.2)	2.97 (2.65–3.34)	<0.0001	2.23 (1.93–2.58)	<0.0001
Daytime sleepiness							
No		88.3 (87.8–88.7)	74.0 (71.7–76.2)	1.00	—	1.00	—
Yes		11.7 (11.3–12.2)	26.0 (23.8–28.3)	2.66 (2.34–3.01)	<0.0001	2.04 (1.75–2.38)	<0.0001
Insomnia overall							
No		81.8 (81.3–82.4)	65.6 (63.2–68.0)	1.00	—	1.00	—
Yes		18.2 (17.6–18.7)	34.4 (32.0–36.8)	2.36 (2.11–2.64)	<0.0001	1.83 (1.59–2.12)	<0.0001
Insomnia	*Fatigue*						
No	No	75.3 (74.7–75.9)	52.7 (50.1–55.3)	1.00	—	1.00	—
No	Yes	6.6 (6.2–6.9)	12.9 (11.1–14.7)	2.80 (2.34–3.35)	<0.0001	2.22 (1.80–2.74)	<0.0001
Yes	No	10.6 (10.2–11.0)	14.5 (12.7–16.3)	1.94 (1.66–2.28)	<0.0001	1.65 (1.35–2.00)	<0.0001
Yes	Yes	7.5 (7.1–7.9)	19.9 (17.9–21.9)	3.78 (3.28–4.35)	<0.0001	2.74 (2.28–3.29)	<0.0001
Insomnia	*Daytime sleepiness*						
No	No	76.5 (76.0–77.1)	55.5 (53.0–58.1)	1.00	—	1.00	—
No	Yes	5.3 (5.0–5.6)	10.1 (8.5–11.8)	2.63 (2.16–3.21)	<0.0001	2.22 (1.77–2.78)	<0.0001
Yes	No	11.7 (11.3–12.2)	18.4 (16.5–20.4)	2.17 (1.88–2.50)	<0.0001	1.78 (1.48–2.13)	<0.0001
Yes	Yes	6.4 (6.1–6.8)	15.9 (14.2–17.7)	3.42 (2.95–3.98)	<0.0001	2.47 (2.04–2.99)	<0.0001
Insomnia	*Sleep duration (h)*						
No	3–6	23.3 (22.6–24.0)	25.1 (22.4–27.9)	1.14 (0.97–1.32)	0.11	1.18 (0.98–1.41)	0.07
No	7–8	68.2 (67.5–68.9)	64.9 (61.8–68.0)	1.00	—	1.00	—
No	9–14	8.5 (8.1–9.0)	10.0 (8.0–12.0)	1.23 (0.97–1.56)	0.08	1.30 (0.99–1.71)	0.06
Yes	3–6	54.5 (52.9–56.1)	51.9 (47.6–56.1)	2.38 (2.05–2.76)	<0.0001	1.94 (1.63–2.32)	<0.0001
Yes	7–8	38.1 (36.5–39.7)	36.6 (32.5–40.8)	2.40 (2.02–2.85)	<0.0001	1.93 (1.57–2.37)	<0.0001
Yes	9–14	7.4 (6.5–8.3)	11.5 (8.6–14.4)	3.86 (2.83–5.26)	<0.0001	3.07 (2.08–4.51)	<0.0001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; Prev, prevalence.

Binary survey logistic regression models were constructed with sleep duration (3–6, 7–8, and 9–14 hours) and 1-year history of more than 3 days with fatigue or tiredness and regular daytime sleepiness and insomnia as the independent variables and 1-year history of eczema as the dependent variable. OR and 95% CIs were estimated. Multivariate logistic regression models were constructed that included current asthma, hay fever, respiratory and digestive allergies, age, race, Hispanic/Spanish origin, household income, highest level of education in the household, US birthplace, number of children in home, family structure, and body mass index. Models of fatigue, daytime sleepiness, and insomnia also included sleep duration as a covariate. A significant two-way interaction was found between insomnia and fatigue, daytime sleepiness, and sleep duration ($P<0.0001$). Contrast statements were used to estimate various combinations of insomnia, fatigue, daytime sleepiness, and sleep duration.

Refusal to answer a particular question or response of ''don't know'' occurred for the questions pertaining to eczema in 25 (0.07%), sleep duration in 497 (1.3%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

[1]Data are presented as the percent prevalence of sleep duration and/or disturbance in subjects with no history of eczema.

[2]Data are presented as the percent prevalence of sleep duration and/or disturbance in subjects with a history of eczema.

Table 3. Association between eczema and overall health status is related to sleep disturbance in adults ($n = 34,613$)

Variable	Eczema	Poor/fair vs. excellent/very good/good health				
		% Poor/fair (95% CI)	OR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Fatigue						
No	No	8.5 (8.1–8.9)	1.00	—	1.00	—
No	Yes	10.7 (9.0–12.5)	1.29 (1.07–1.56)	0.009	1.41 (1.13–1.76)	0.002
Yes	No	35.6 (33.8–37.3)	5.93 (5.42–6.50)	<0.0001	5.23 (4.68–5.85)	<0.0001
Yes	Yes	44.5 (40.0–49.0)	8.63 (7.15–10.43)	<0.0001	7.53 (5.97–9.49)	<0.0001
Sleepiness						
No	No	9.6 (9.2–10.0)	1.00	—	1.00	—
No	Yes	14.7 (12.7–16.8)	1.62 (1.37–1.92)	<0.0001	1.71 (1.40–2.09)	<0.0001
Yes	No	32.7 (30.8–34.6)	4.57 (4.15–5.05)	<0.0001	4.00 (3.55–4.50)	<0.0001
Yes	Yes	41.9 (36.9–46.9)	6.78 (5.49–8.36)	<0.0001	5.23 (4.08–6.71)	<0.0001
Insomnia						
No	No	9.0 (8.6–9.4)	1.00	—	1.00	—
No	Yes	12.9 (10.6–15.2)	1.50 (1.21–1.85)	0.0002	1.58 (1.26–1.99)	<0.0001
Yes	No	27.4 (25.9–28.0)	3.81 (3.49–4.16)	<0.0001	3.27 (2.95–3.62)	<0.0001
Yes	Yes	38.8 (34.8–42.9)	6.43 (5.37–7.68)	<0.0001	5.18 (4.12–6.51)	<0.0001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.
Binary survey logistic regression models were constructed with overall health status as the dependent variable (fair/poor vs. excellent/very/good) and 1-year history of eczema and fatigue, daytime sleepiness, and/or insomnia as the independent variable. Significant interactions found between history of eczema and sleep disturbances. Contrast statements were used to estimate OR and 95% CIs at each level of interaction. Multivariate logistic regression models were constructed that included current asthma, hay fever, respiratory and digestive allergies, age, race, Hispanic/Spanish origin, household income, highest level of education in the household, US birthplace, number of children in home, family structure, body mass index, and sleep duration.
Refusal to answer a particular question or response of "don't know" occurred for the questions pertaining to eczema in 25 (0.07%), sleep duration in 497 (1.3%), fatigue in 20 (0.05%), daytime sleepiness in 14 (0.04%), insomnia in 9 (0.02%), overall health in 0 (0.0%), current asthma in 37 (0.1%), hay fever in 25 (0.07%), respiratory allergies in 48 (0.1%) and digestive allergies in 37 (0.1%), age in 0 (0.0%), sex in 0 (0.0%), race in 0 (0.0%), Hispanic/Spanish origin in 0 (0.0%), household income in 1,928 (5.6%), highest level of education in the household in 69 (0.2%), US birthplace in 10 (0.03%), number of children in home in 0 (0.0%), family structure in 4 (0.01%), and body mass index in 1,361 (3.9%), respectively.

workdays, days in bed, and doctor visits. Adults who had eczema as well as fatigue, daytime sleepiness, and/or insomnia had even higher numbers of missed workdays and days in bed than those with either eczema or fatigue/sleep disturbances (general linear models, $P<0.0001$ for all; Figure 1a–f). In contrast, adults with eczema and insomnia had a higher number of doctor visits than those with either eczema or insomnia ($P<0.0001$), but a similar number to those with fatigue or daytime sleepiness and no eczema ($P\geqslant0.66$; Figure 1g–i). Similar results were also found with the Wilcoxon rank sum test and Poisson regression models (data not shown).

We tested whether the association between eczema and overall health status is mediated by fatigue and/or sleep disturbance using three different approaches. All approaches indicated there was significant mediation (the Sobel test (95% CIs): 0.042 (0.038–0.046), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.10 (1.09–1.11)), although only partial mediation ($\beta(yx,m)=0.02$, $P=0.003$; $R^2=0.002$). Similarly, partial mediation was found for the number of missed workdays (the Sobel test (95% CIs): 0.02 (0.015–0.027), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.05 (1.03–1.07); $\beta(yx,m)=0.06$, $P=0.01$; $R^2=0.0003$) and doctor visits (the Sobel test (95% CIs): 0.28 (0.23–0.33), $P<0.0001$; bootstrapping approach, indirect effects OR (95% CIs): 1.92 (1.70–2.19); $\beta(yx,m)=1.02$, $P<0.0001$; $R^2=0.003$).

Latent class analysis of fatigue, sleep disturbance, and allergic disorders

LCA was used to identify patterns of fatigue, sleep disturbances, and allergic disorders. The best-fit model had five classes based on minimal Bayesian information criteria, corrected Akaike information criteria, and adjusted Bayesian information criteria (Supplementary Table 2 online). Conditional probabilities of having fatigue, sleep disturbance, or allergic disease in each class are plotted in Figure 2. Two classes had high probabilities of sleep disturbance (classes 3 and 4). Class 4 had high probabilities of eczema, asthma, hay fever, and food allergy, whereas class 3 had low probabilities of these disorders. Class 1 had an intermediate probability of insomnia but not fatigue or sleepiness; this group also had an intermediate probability of eczema. Class 2 included those with a high probability of hay fever and respiratory allergies but low probability of fatigue and sleep disturbances. Finally, class 5 included those with a low probability of fatigue, sleep disturbance, and allergic disease.

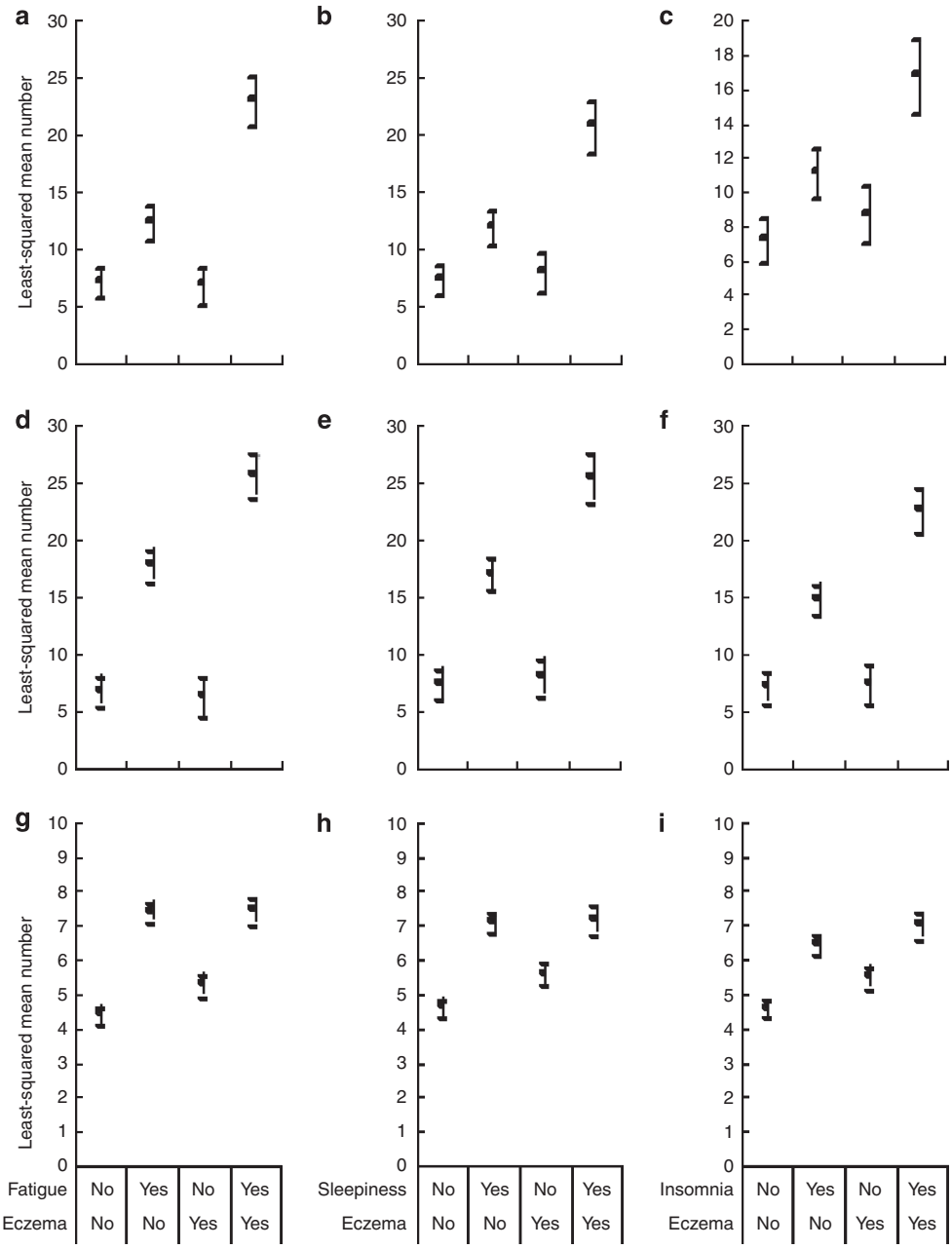

Figure 1. Association between eczema, sleep disturbance, and number of sick days, days in bed, and doctor visits. General linear models were constructed with number of sick days (**a**–**c**), days in bed (**d**–**f**), and doctor visits (**g**–**i**) as the dependent variables using a normal link function. The dependent variables were eczema, as well as fatigue (left column), daytime sleepiness (middle column), or insomnia (right column), and a two-way interaction term between them. *Post hoc* analyses were conducted of differences among the levels of one factor at a fixed level of the other factor. Least-square means (95% confidence intervals (CIs)) are plotted for each combination of factors included in the interaction effects. In addition, β values (95% CIs) for comparisons between each group and those without eczema or sleep disturbance are presented as text.

DISCUSSION

In the present study, we demonstrate that eczema in adults is associated with both short and long sleep durations. Short duration is likely due to difficulty falling asleep and premature awakening secondary to itch, whereas long duration is likely due to poor sleep efficiency, excessive fatigue, and sleepiness and perhaps the use of sedating antihistamines. Even after controlling for sleep duration, other atopic diseases, and sociodemographic factors, eczema was associated with fatigue, daytime sleepiness, and insomnia. In particular, adults with insomnia as well fatigue and/or daytime sleepiness had the highest odds of eczema. Adults with eczema were more likely to have fair/poor overall health, even without fatigue or sleep disturbances. However, the presence of fatigue or sleep

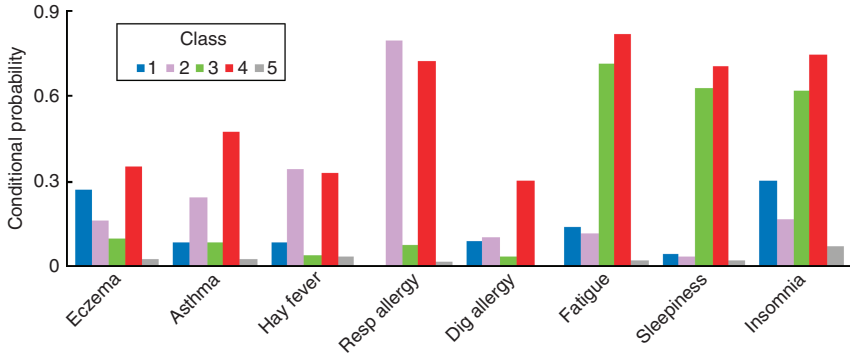

Figure 2. Conditional probability plot for sleep disturbance, eczema, and allergic disease within latent classes. Latent class analysis (LCA) was used to examine patterns of binary variables of sleep disturbance and the occurrence of eczema, asthma, hay fever, and respiratory and/or food (digestive (Dig)) allergy. LCA used the observed binary data to identify homogeneous patterns, i.e., $n=5$ latent classes. Conditional probabilities were estimated using maximum likelihood to characterize the latent classes. Conditional probability plots are presented, where probabilities closer to 0 or 1 indicate lower or higher chances, respectively.

disturbance and eczema led to significantly higher rates of self-reported fair/poor health, as well as higher numbers of missed workdays, days in bed, and doctor visits. The associations between eczema and poorer health outcomes were only partially mediated by fatigue and/or sleep disturbance, suggesting that there are additional factors at play. Finally, there were two distinct groups of subjects that had sleep disturbance with eczema: one with other allergic disease who had higher probabilities of insomnia, fatigue, and daytime sleepiness and the other with a higher probability of insomnia alone. Of note, there were other latent classes observed with similar probabilities of eczema and low probabilities of fatigue, insomnia, and/or sleepiness, indicating there are subsets of eczema without major sleep disturbances. Together, the results of this study suggest that adults with eczema have high rates of fatigue and sleep disturbances, which severely impact on overall health and increase health care utilization. With almost 9 million US adults with eczema reporting fatigue or sleep disturbance, our study demonstrates the considerable public health burden of eczema. A previous study of childhood atopic dermatitis (AD) found that having more severe disease was associated with increased health care utilization, including seeing a specialist and using more health-related services (Silverberg and Simpson, 2013). The results of the present study suggest that fatigue and sleep disturbances are major drivers of lost workdays and increased health care utilization and weigh heavily on the public health burden of eczema. It would therefore be prudent to improve our understanding of sleep disturbance in eczema and why some eczema patients are particularly affected by sleep problems, whereas others are not. Ultimately, this will lead to targeted interventions for prevention and treatment and improved care of eczema.

Previous smaller-scale studies also found high rates of sleep disturbances among adults with eczema (Bender *et al.*, 2003; Zuberbier *et al.*, 2006; Hanifin *et al.*, 2007; Bender *et al.*, 2008; Torrelo *et al.*, 2012). A case-control study of 14 eczema patients and 14 control patients without skin disease assessed sleep impairment using the Pittsburgh sleep quality index and actigraphy (Bender *et al.*, 2003). Questionnaires revealed lower sleep quality, more awakening, and daytime dysfunction among eczema patients. Similarly, actigraphic assessment revealed that eczema patients slept less, awoke more often, and spent more time awake during waking episodes, with resultant lower overall sleep efficiency (Bender *et al.*, 2003). Another study administered questionnaires, actigraphy, and polysomnography to 20 adult eczema patients and found that greater disease severity was associated with poorer sleep (Bender *et al.*, 2008). A multicenter questionnaire–based study from the International Study of Life with Atopic Eczema, including 1,098 adults, found that a typical AD flare disrupts the sleep of patients for an average of 8.4 nights per flare, which extrapolated to ~81 days per year per patient (Zuberbier *et al.*, 2006).

An important limitation of the above-mentioned studies is the lack of control for comorbid asthma and rhinoconjunctivitis, which are common confounding factors in adults with eczema (Silverberg and Hanifin, 2013) and can independently cause sleep disturbances. Approximately 40% of asthma patients experience night-time awakenings every night (Turner-Warwick, 1988), leading to shortened sleep duration and increased daytime sleepiness (Dales *et al.*, 1992; Fitzpatrick *et al.*, 1993; Janson *et al.*, 1996; Vir *et al.*, 1997; Craig *et al.*, 2004; Leger *et al.*, 2006; Mastronarde *et al.*, 2008). In addition, the prevalence of early morning awakenings and difficulty inducing sleep was twice as high, and the prevalence of daytime sleepiness 50% higher, in European asthmatic adults compared with non-asthmatics (Janson *et al.*, 1996). Similarly, allergic rhinitis sufferers experience interruption of the sleep cycle leading to increased daytime somnolence and decreased QOL, attributed to nasal obstruction and linked to increased night-time microarousals (Lavie *et al.*, 1981; Craig *et al.*, 2004; Leger *et al.*, 2006; Bender and Leung, 2005; Leger *et al.*, 2006). We now demonstrate an association between eczema, fatigue, and sleep disturbances, even after controlling for the history of respiratory allergies, as well as for food and digestive allergies and other potentially confounding sociodemographic factors. Moreover, LCA models revealed a

latent class of adults with eczema that had higher probability of insomnia even in the absence of other allergic disorders.

Allergic airway disorders that often accompany eczema, such as asthma and hay fever, are associated with obstructive sleep apnea (OSA) and its sequelae. A study of OSA syndrome found a higher risk of perennial allergic rhinitis (Canova *et al.*, 2004). Similarly, our study found significant associations between obesity and each of the sleep disturbances (consistent with OSA) in adults with asthma and hay fever. Yet, there were no such associations between obesity, sleep disturbances, and eczema, suggesting that the sleep disturbances in adult eczema patients were not due to OSA or comorbid airway disease. Rather, pruritus is likely the major contributor to sleep disturbance in eczema. Further studies are needed to identify the specific patterns of sleep disturbance in eczema and distinguish them from those found in atopic airway disorders.

Our results also confirm past observations in the United States (Karacan *et al.*, 1976) and Japan (Doi *et al.*, 2000) showing the association of sleep disturbance with female gender, older age, and lower household income. The lower prevalences of sleep disturbances among African-Americans, Asians, and Hispanics with eczema are consistent with previously described racial/ethnic differences in sleep disturbances regardless of eczema (Ruiter *et al.*, 2011; Ralls and Grigg-Damberger, 2012; Chapman *et al.*, 2013; Grandner *et al.*, 2013; Jackson *et al.*, 2013; Knutson, 2013; Pranathiageswaran *et al.*, 2013). They may be related to differential self-reporting and household income, and reflect socioeconomic differences of adult sleep patterns, including differences in sleep behavior and duration, social pressures and psychosocial stress, poor environmental conditions, noise, air, and light pollution, more nightshift work, etc. Future studies with objective measurements of sleep disturbance are needed to verify these associations.

Growing evidence suggests an association of eczema with obesity, including the results of our study. Obesity has previously been associated with increased prevalence and severity of eczema and higher prevalence of atopic asthma in 2,090 adults aged $\geqslant$19 (Silverberg *et al.*, 2012). Another study associated prolonged obesity ($>$2.5 years) in early childhood and increased odds and severity of eczema (Silverberg *et al.*, 2011), suggesting that obesity and its chronic pro-inflammatory effects (Jin and Flavell, 2013) may be a modifiable risk factor for eczema. In the present study, obesity was also associated with higher prevalence of eczema but not with greater sleep disturbances in eczema.

Eczema is known to have a significant and negative impact on health-related QOL (Bender *et al.*, 2003; Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007; Hon *et al.*, 2008; Beikert *et al.*, 2014), and our study supports this notion by demonstrating that sleep disturbance is a major driver of poor overall health status, lost workdays, and increased health care utilization. In 384 adult eczema patients, sleep disturbance was strongly associated with decreased QOL using Dermatology Life Quality Index (Beikert *et al.*, 2014). In childhood eczema, sleep disturbance was the second highest scoring item, alongside itching (Hon *et al.*, 2008). Other studies in children similarly demonstrate that sleep disturbance is among the top contributing factors to reduced QOL (Beattie and Lewis-Jones, 2006; Ricci *et al.*, 2007). Together, these studies suggest that interventions targeting sleep disturbance are of utmost importance and likely to improve the overall health and QOL of adults and children with eczema.

The present study found the 1-year prevalence of adult eczema to be 7.2%, which is lower than the 10.2% prevalence recently demonstrated by Silverberg and Hanifin (2013). There are a number of differences between the questions used to measure eczema prevalence in these studies. The question used in the study of Silverberg and Hanifin (a) did not specify health care diagnosis of eczema and (b) assessed for ''eczema, dermatitis, or red inflamed rash'', which is less specific but more sensitive than the question used in the present study. Of note, many adult eczema patients either underutilize or do not utilize health care for their eczema (data not shown). Thus, the health care-diagnosed eczema outcome used in the present study may introduce a selection bias toward those who have higher household income and greater access to health care and are more likely to utilize health care for their eczema. This may explain why the previously demonstrated inverse association between eczema prevalence and household income was not found in the present study. It is therefore possible that the present study actually underestimates the prevalence of sleep disturbances in US adults with eczema. Regardless, we believe that the eczema question used in this study is sufficiently sensitive and specific to examine the burden of sleep disturbances in adult eczema.

The mechanisms underlying the association between eczema and sleep disturbance are not fully understood. The itch-scratch cycle of eczema interferes with initiation and maintenance of sleep (Camfferman *et al.*, 2010). Actigraphy and infrared video evidence reveals fragmented sleep with increased scratch time and restless nocturnal movement in both adults and children with eczema (Camfferman *et al.*, 2010). In addition, evidence for circadian rhythm–induced modification of itch exists, as studies have shown greater transepidermal water loss at night time along with decreased cortisol secretion (Gupta and Gupta, 2013). Both processes may lead to increased night time itch and fragmented sleep. Inflammatory cytokines implicated in sleep regulation are also elevated in patients with allergy (Bender and Leung, 2005). However, patients with eczema, even when in clinical remission, exhibit more sleep impairment than do healthy patients (Reuveni *et al.*, 1999), suggesting a more complex etiology beyond itch and inflammatory pathway activation. In a study of five children with eczema, regular antihistamine use had no effect on sleep latency, total sleep time, or other sleep parameters, determined by polysomnography (Camfferman *et al.*, 2013). However, the role of learned abnormal sleeping patterns or medication use (e.g., antihistamines or corticosteroids, which may interfere with sleep-wake regulation) deserves exploration in larger-scale studies.

This study has several strengths, including having prospective data collection, US population-based, and having a very large, randomly sampled and diverse sample. In addition, the

study had sufficient numbers for subset analyses and was controlled for a large number of potential confounding factors using logistic regression. The use of latent class analysis (LCA) allowed for identification of two distinct patterns of sleep disturbance in adult eczema. The random sampling, large sample size across all states, with representation of a host of racial and ethnic groups and complex weighting indicate that the results are likely generalizable to the entire US population. However, this study has potential limitations. Eczema history was based on a self-report of health care diagnosis and neither assessed clinically nor verified with any diagnostic testing. The specific question used in this study has not been previously validated; however, self-report of eczema using other instruments has been validated and found to have good correlation with clinical exam (Susitaival *et al.*, 1995; Flohr *et al.*, 2009). Moreover, the waxing and waning course and more variable presentation of adult eczema argue in favor of a broader question related to the history of eczema in the past 12 months. Nevertheless, there may be more than one type of eczema in adults (Abuabara and Margolis, 2013) that are detected by the question used in this study, including irritant, allergic contact, and xerotic dermatitis. We do not consider this to be a limitation because adult eczema often has a variable phenotype compared with childhood eczema and may present with overlapping atopic, irritant, and/or allergic contact dermatitis, rather than flexural eczema alone (Katsarou and Armenaka, 2011; Silverberg, 2014). Previous studies found a strong correlation between self-report of fatigue and sleepiness and objective measures of sleep disturbance: i.e., actigraphy and polysomnography (Bender *et al.*, 2008; Braley *et al.*, 2012). Further, self-reported measures of sleep disturbance have been the mainstay of epidemiologic study of sleep in cardiovascular disease (Shankar *et al.*, 2010; Westerlund *et al.*, 2013), diabetes (Plantinga *et al.*, 2012), chronic kidney disease (Plantinga *et al.*, 2011), etc. Family history of eczema may be an important confounding factor but was not assessed in National health interview survey (NHIS). The accuracy of self-reported family history by adults with eczema has not previously been studied and, based on the authors' clinical experience, is likely not very reliable. Finally, the cross-sectional nature of the study does not allow for the determination of causality of the association between eczema and sleep. That is, eczema may cause sleep impairment or perhaps underlying sleep disorders trigger eczema in predisposed individuals. Future longitudinal studies with objective measures of sleep disturbance are needed to verify these associations.

In conclusion, adult eczema is associated with altered sleep duration, fatigue, and sleep disturbances, including daytime sleepiness and insomnia. Although adults with eczema were more likely to report fair/poor health, the presence of sleep disturbances in combination with eczema significantly increased the rates of fair/poor health. This study suggests that sleep disturbances weigh heavily on adults with eczema and that treatments targeting sleep loss are likely to improve the overall health of eczema patients. Future studies are warranted to better characterize sleep loss in eczema and develop strategies for treatment and prevention.

MATERIALS AND METHODS

National health interview survey

After approval by Northwestern University's institutional review board, data were assessed using 2012 NHIS, a database collected by the National Center for Health Statistics and the principal source of health information on US noninstitutionalized civilians. Waiver of informed consent was obtained by the National Center for Health Statistics, as the survey posed minimal risk and respondents were not identifiable by the recorded data. The survey included a separate questionnaire about adult health to estimate the prevalence of physical, emotional, and behavioral health issues. The survey was administered in-person to selected households by the Bureau of the Census using ~400 trained interviewers with computer-assisted personal interviewing in English and Spanish. Using data from the US Census Bureau, sample weights were created that factored age, sex, race, ethnicity, household size, and educational attainment of the most educated household member using a multi-stage area probability sampling design by NHIS. These sample weights are needed to provide nationally representative prevalence estimates for each state's population of noninstitutionalized adults. All frequency data are presented as raw values, whereas prevalence estimates presented reflect this complex weighting. Questions used in the survey pertaining to history of eczema, sleep problems, and overall health are listed in Supplementary Table 1 online.

All data processing and statistical analyses were performed in SAS version 9.3. Outlier detection was performed for sleep duration revealing that responses of $\geqslant$15 hours duration were outliers. Models that incorporated sleep duration were tested with and without the exclusion of outliers, and no significant differences were found. Therefore, we only present models that excluded outliers. Bivariate and multivariate analyses of survey responses were performed using SURVEY procedures. Bivariate associations were tested with Rao-Scott χ^2 tests. Multivariate logistic regression models were constructed for fatigue, daytime sleepiness, and insomnia (binary outcomes) using two different approaches. First, we included all significant predictors from bivariate analyses in the models. Two- and three-way interaction terms between other covariates were also tested. Our *a priori* hypothesis was that adult eczema is associated with specific patterns of insomnia with sleep duration, fatigue, and sleepiness. Therefore, models were constructed that tested interaction terms between insomnia and either sleep duration, fatigue, or daytime sleepiness. We used stepwise and backward selection for multivariate logistic regression models to determine whether eczema would be selected consistently as a predictor and identify other significant predictors of sleep problems. Adjusted ORs (aORs) and 95% CIs were determined.

Multivariate logistic regression models were also constructed with personal health status as the dependent variable. Personal health status was modeled as the binary dependent variable. This approach was used over ordinal logistic regressions because the data did not meet the proportional odds assumption (Score test, $P<0.01$). Our *a priori* hypothesis was that adults with eczema, fatigue, and sleep disturbances have worse overall health than those with eczema alone. Therefore, models were constructed that tested interaction terms between eczema and sleep problems. Significant predictors from bivariate analyses were also included in the models.

Number of sick days, days in bed, and doctor visits were modeled using generalized linear models with a normal (linear regression) and

log (poisson regression) link function in SAS PROC GLIMMIX. The independent variables were history of eczema, as well as fatigue, daytime sleepiness, or insomnia and a two-way interaction term between them. *Post hoc* analyses were conducted of differences among the levels of one factor at a fixed level of the other factor. Least-square means and aORs (95% CIs) were estimated for each combination of factors included in the interaction effects.

Two- and three-way interactions between other covariates were tested and included in the above models if *P*-value <0.01 and modification of estimates by $>20\%$. The best models were selected using the Bayesian information criterion, which penalizes for extra parameters and takes into account the large sample size. To test whether any associations between eczema and poor personal health status, lost workdays, and health care utilization were mediated by fatigue and/or sleep disturbance (composite binary variable), mediation was tested using the approaches of Baron and Kenny, the Sobel test, and the bootstrap method described by Preacher and Hayes ($n=5{,}000$ bootstrapping samples; Preacher and Hayes, 2008). Complete data analysis was performed, i.e., subjects with missing data were excluded.

LCA was performed in SAS as previously described (Yang *et al.*, 2012; Supplementary Methods online).

CONFLICT OF INTEREST

PCZ is a consultant for Merck, Jazz, Vanda, and Aptalis Pharmaceuticals and owns stock in Teva Pharmaceuticals. The remaining authors state no conflict of interest.

AUTHOR CONTRIBUTIONS

JIS had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. JIS, ASP, AF, and PCZ were responsible for study concept and design. JIS and NG were responsible for acquisition of data. JIS, NG, ASP, AF, and PCZ were responsible for analysis and interpretation of data. JIS, NG, ASP, AF, and PCZ were responsible for drafting of the manuscript. JIS, NG, ASP, AF, and PCZ were responsible for critical revision of the manuscript for important intellectual content. JIS and NG were responsible for statistical analysis.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/jid

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Skin Disorders and Quality of Life

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Introduction

Chronic skin disorders like psoriasis and atopic eczema have profound influence on patients' lives. More or less visible painful or itching symptoms affect patients' social life, their daily work and their personal relationships. Nevertheless, very often the influence of chronic skin diseases on the Quality of Life (QoL) might be underestimated in comparison with other more life threatening disorders like cancer or heart disease. Comparing health-related QoL of 317 patients with psoriasis and QoL of patients with 10 other diseases, Rapp et al. (1999) found that in patients with psoriasis the impaired physical and mental functioning was comparable to that seen in cancer, arthritis, hypertension, heart disease, diabetes, and depression. Chronic skin diseases do not only affect patients QoL, but also have impact on the patient`s family or their partner. Basra and Finlay propose the concept of the "Greater Patient" to describe the immediate close social group affected by the patient. They recommend seeing the patient as "the centre of a complex web of surrounding relationships", which makes it important to keep also in mind the QoL of the family and their partners (Basra and Finlay 2007).

Looking at the QoL of children with different chronic diseases noted that children with cerebral palsy showed the greatest impairment of QoL, followed by atopic dermatitis, renal diseases and cystic fibrosis. The QoL of children with psoriasis was more reduced than that of children with enuresis, diabetes and epilepsy (Beattie and Lewis-Jones 2006a). Beside problems in daily life and personal relationships the feelings of stigmatization, increased anxiety, depressive symptoms and following avoidance of social activities are very common in chronic skin disorders and should be kept in mind in the treatment of those patients. This article will focus on the frequent chronic skin disorders psoriasis and atopic eczema and their influence on QoL. Because stigmatisation is one of the most important psychological aspects of skin diseases it is highlighted in this article. The increasing acceptance of recognizing the value of QoL studies in psoriasis and atopic dermatitis treatment research supports the opinion that the somatopsychic view is the most important psychodermatological aspect. However, some recent psychoneuroimmunological studies suggest new psychosomatic connections in psoriasis and atopic dermatitis going beyond questions of conflict or personality specificity (e.g., Kiecolt-Glaser et al. 2002, Stephan et al. 2004, Buske-Kirschbaum et al. 2007, Schmid-Ott et al. 2009).

Defining Quality of Life (QoL) and Feelings of Stigmatization

In the last decades measuring of QoL in different diseases became more and more important in medical research. Beside physical well-being QoL contains also social, mental and emotional well-being and might be influenced not only by the specific disease, but also by different concomitant factors. Knowledge about the impact of disorders on the QoL becomes more and more important in the sense of a more holistic understanding of diseases. This may lead to more effective therapies. Keeping patient´s QoL in mind may also have an influence on the decision of treatment in the clinical routine and consecutive on patient´s compliance. The impact of disease-related QoL might be best estimated by the patients themselves. Multiple validated measuring instruments exist for medical research. Special measuring instruments have been configurated for skin disorders. Only three of them should be mentioned briefly, because of their frequent use in dermatological studies. The Dermatology Life Quality Index (DLQI) by Finlay and Khan (Finlay and Khan 1994, Basra et al. 2008) is a health quality of life scale comprised of 10 items which focus on 6 dimensions: ‘symptoms’, ‘daily activities’, ‘leisure’, ‘work’, ‘personal relationships’ and ‘treatment’. For estimating children’s QoL, the Children`s Dermatology Life Quality Index (CDLQI) - which is very similar to the DLQI - has been developed (Finlay and Khan 1994). The Psoriasis Disability Index (PDI) measures the impact of psoriasis on specific aspects of daily living consisting of 15 disease-specific items (Lewis-Jones and Finlay 1995, Finlay et al. 1990).

Skin diseases very often come along with symptoms which may be very discriminating. Patients with visible skin symptoms are often glared at or even avoided for fear of infection or for disgust. So, in speaking about the QoL of skin disorders the experience of stigmatization is an important factor which should not be neglected. Stigmatization - defined as a process in which skin appearance is negatively judged and persons who are affected experience absence of acceptance because of their visible symptoms – may have profound consequences in the life of patients, such as increased anxiety or social avoidance.

Quality of Life in Different Skin Diseases

Atopic dermatitis

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that presents itself often during early childhood and may persist in adulthood. Sometimes it even starts in adulthood. Over the last decades the prevalence has increased continuously up to a lifetime prevalence in children of 10-20% and 1-3% in adults (Leung and Bieber 2003). It is well known that AD has great impact on the Quality of Life (QoL) of patients and their families. There are several studies demonstrating this matter of fact. Comparing children with AD or other chronic diseases it has been found that AD has a greater impact on the QoL of children than for example diseases like epilepsy and diabetes (Beattie and Lewis-Jones 2006a).

Itching and scratching, as well as difficulties with falling asleep and problems with bathing, show very great impact on the QoL in affected children. However, in the

parents' emotional distress, sleep loss and tiredness/exhaustion are important influencing variables (Beattie and Lewis-Jones 2006a). Quality of life and disease severity in children may be correlated (Ben-Gashir et al. 2004). Atopic dermatitis may not only influence childhood but also the further life of those who are affected. Brenninkmeijer et al. (2009) found out that children with severe atopic dermatitis showed a significant delayed social development in their further course of life. Looking at adults with AD, higher anxiety levels could be found in comparison to a healthy control group (Linnet and Jemec 1999). A beautiful skin has great influence of the sexual attractiveness of a person, so it can be assumed that AD may even have impact on the sexual life of the patients and their partners. Misery at al. (2007) showed that 57.5% of patients with AD noted a decreased sexual desire and 36.7% of their partners reported that the appearance of eczema had an impact on their sexual life. A German study showed that the exchange of tenderness in patients with AD and psoriasis was significantly reduced. Although this issue may be very discriminating for the individual, 96% of the patients with AD indicate that their attending physician have never addressed that problem (Niemeier et al. 1997).

Psoriasis

Psoriasis is a chronic skin disease affecting even joints with a prevalence between 0.5% and 4.6% (Lebwohl 2003). Different studies suggest that psoriasis is associated with an increased cardiovascular risk and a higher prevalence of metabolic syndrome (Gisondi et al. 2007, Neimann et al. 2006). It is well known that psoriasis may affect the whole life of patients. The results of a National Psoriasis foundation patient-membership survey, which has been performed in the United States in 1998, showed that 79% of the patients with psoriasis felt impaired by their disease. It was noticed that elderly patients felt less impaired by the psychosocial consequences than younger people between 14 and 54 years. Young patients between 18 and 34 years especially stated a very high psychological burden in comparison with other ages (Krueger et al. 2001). Similar results have been found in a European study investigating patients with psoriasis in the Nordic countries. Married and older patients showed less impairment of QoL than younger patients and those living alone. The most important predictive factor of psoriasis-related QoL in this study was self-reported disease severity (Zachariae et al. 2002). Additionally, Sampogna et al. (2007) found that especially in elderly women with co-morbidity of depression and anxiety the influence of psoriasis on the QoL is very high.

A further large European study with 17,990 psoriasis patients investigating their disease-related QoL showed a high percentage of patients (77%) pointing out that they have problems or significant problems with their disease (Dubertret et al. 2006). Looking at the 3753 German participants of this study, 47% of them referred 'clothing', 44% 'more frequent bathing than normal' as a special problem, and 35% felt impaired in their sporting activities. 'Going to the hairdresser' causes problems for 29% of the participants and 'going to a public bath' is a problem for 21% of them. And last but not least, 23% of participants told of adverse affects of the psoriasis on their sexual life (Schmid-Ott et al. 2005b). Understandably, psoriasis affects also the lives of partners and family members concerning many different aspects of everyday life. In questioning 63 relatives and partners respectively of 33 patients with psoriasis, Eghlileb et al. (2007) found that only 8% of all did not notice any influence of their lives.

Co-morbidity of psychiatric disorders is common in dermatologic disorders. Approximately 30% of all dermatologic patients show psychiatric disturbances (Gupta and Gupta 1996), whereas major depressive disorders are the most frequent. A study screening 265 patients with psoriasis for depressive symptoms revealed a rate of 32% of patients with a positive screening for depression (Schmitt and Ford 2007). As it is known, depressive symptoms are often associated with suicidal tendency. So it is not surprising to find a prevalence of active suicidal tendation among psoriasis inpatients of 7.2%, which is higher than the 2.4 – 3.3% prevalence reported among general medical patients (Gupta and Gupta 1998). A similar prevalence of 10% of suicidal thoughts in patients with psoriasis has been found by Picardi et al. (2006). These findings show the need to take care of psychiatric co-morbidity in patients with psoriasis.

Vitiligo

Basra and Shahrukh (2009) report on the burden of vitiligo that approximately 75% of those concerned estimate their appearance as moderately to severely intolerable (Salzer and Schallreuter 1995). In addition some of them have low self-esteem, fear, anxiety, stress and a feeling of shame in social interactions (Van Moffaert 1992 , Porter et al. 1979, Porter et al. 1986, Ahmed et al. 2007). Female vitiligo patients show a more impaired QoL than men, which can be compared with the impairment experienced by psoriasis patients (Ongenae et al. 2005).

Skin Cancer

Cutaneous malignant melanoma (MM) is less common than the basal cell and squamous cell carcinomas; however, it has a much higher mortality. The most important contribution of the psychosomatic medicine in the treatment of MM patients is supporting their coping which is central for the QOL of the concerned (cf. Söllner et al. 1998). The review of Basra and Shahrukh (2009) summarizes the studies concerning QOL of skin cancer patients: patients with recent diagnosis of MM experience the same levels of psychic distress as other cancer patients (Fawzy et al. 1990). At 3 months after surgical intervention, around 20 % of MM patients showed clinically high levels of anxiety; however, depressive symptoms seem more often in patients with metastatic melanoma (Brandberg et al. 1992b). Women with the disease have higher levels of anxiety and depression (Brandberg et al. 1992a).

Squamous cell and basal cell carcinomas (i.e. nonmelanoma skin cancers [NMSCs]) of the skin are the most frequent malignant tumors in the Caucasian population (Joseph et al. 2001). The incidence of this kind of carcinomas increases and is 18-20-times greater than MM (Diepgen andMahler 2002) The location of NMSCs on visible areas, i.e. face, head or neck, suggests a higher probability of psychic or social consequences. In addition, most of the present treatments result in scars (cf. Bock 2006) mostly on visible areas and partly with a relevant disfigurement.

Urticaria

The review of Basra and Shahrukh (2009) summarizes that urticaria may have a relevant impact upon the QoL of the concerned. Increased anxiety and depression have been

observed in patients with chronic urticaria as well as restriction of clothing and footwear choices, mainly due to the pressure effect of tight-fitting wears aggravating the symptoms (Basra and Shahrukh 2009). Because exercise has been suggested to provoke urticaria in some of the concerned, many patients avoid exercise. In addition, affection of social life, mobility, sleep, and sexual relationships have been reported (O'Donnell et al. 1997).

Feelings of Stigmatization in Different Skin Diseases

Negative impact of psoriasis and AD on QoL can be influenced by feelings of stigmatization. Very often patients with psoriasis and AD experience rejection because of their visible symptoms. Strangers or even friends and relatives may show disgust or fear of infection. Social reclusiveness associated with anxiety, depressive symptoms or even alcoholism or other addictions can be the consequences. Patients may even feel disgust of their own body and suffer from a low self-confidence. And in a vicious circle these feelings may lead to an impairment of the skin disease and further stigmatization.

Schmid-Ott et al. (2003) investigated 463 patients with psoriasis and atopic eczema for their experience of stigmatization and the influence on QoL. Correlations have been found between stigmatization and QoL in terms of a negative influence of stigmatization on the QoL. Comparing patients with psoriasis with those who have an atopic dermatitis no significant differences could be found concerning their experience of stigmatization and their self-reported QoL. In contrast, Vardy et al. (2002) found in comparing psoriasis with other chronic skin disorders (acne vulgaris, atopic dermatitis, viral and fungal infection, sun-damaged skin and different types of eczema) patients with psoriasis suffer more from experiences of stigmatization than a control group consisting of patients with mixed different other dermatologic diseases . A study with 125 patients with atopic dermatitis revealed similar results. Perceptions of stigma were significantly associated with quality of life and an association was found between perceived stigma and disease severity (Wittkowski et al 2004). But even if the severity of psoriasis is not very distinct, lesions on invisible parts of the body can already cause serious adverse impairment (Schmid-Ott et al. 2007b).

Vitiligo

Schmid-Ott et al. (2007a) examined the extent of stigmatization experienced by 363 vitiligo patients considering the visibility of the lesions. The patients were assessed using the Experience with Skin Complaints (QES), Adjustment to Chronic Skin Disorders (ASC), and Sense of Coherence (SOC) questionnaires. Out of the total patients group two representative samples with 52 patients each were identified with comparable characteristics of age, gender, and duration of the skin disease; the first with visible and the second with invisible lesions. Data indicate a significant negative correlation between the QES dimensions, except for 'Composure', and between coping scales with sense of coherence withstanding. The 'visible lesions' group scored higher compared to the 'invisible lesions' group on the two QES scales 'Self-Esteem' and 'Refusal', i.e., patients with visible lesions experienced a higher level of stigmatization.

Strategies to Improve Quality of Life and Reduce Stigmatization in Skin Disorders

Today we know good therapies do not only focus on the organic symptoms of a disease, but are aimed also at the improvement of QoL and the prevention of secondary psychiatric diseases like depression or anxiety caused by the chronicity of the disorder. Especially in chronic diseases, coping with the disease is very important as a motivational factor for undergoing long and restrictive therapies.

Medical research allows for these aspects and a lot of studies not only investigate the medical effects of different therapies but also their consequences on the QoL of the patients (Kawashima and Harada 2007, Drake et al. 2001, Van de Kerkhof 2004). Surely, a phase adapted dermatological therapy of chronic skin disorders like psoriasis and AD is indispensable. Certainly, healing of visible and distracting skin symptoms lead to an improvement of QoL. But beside essential dermatologic therapies, further supporting measures may be helpful. Very often dermatologic therapies take a lot of time and frequently, success may be only seen with delay. Unfortunately, relapses occur regularly and may have negative impact on the motivation for therapy. A good physician-patient relationship can be very helpful in preventing this problem. The attending physician should not only be able to prescribe the right medication, but also to motivate his patient in phases of insufficient success. He should although take time to speak with his patient about the consequences of the skin disorder on his daily life.

Symptoms of anxiety and depression should be addressed in evaluating if further psychotherapeutic measures should be considered. Different psychological approaches are available and for some of them supporting effects could be demonstrated. A meta-analysis of the effects of eight different psychological interventions (aromatherapy, autogenic training, brief dynamic psychotherapy, cognitive-behavioural therapy, dermatological education, habit reversal behavioural therapy, a stress management program, and structured educational programs) on atopic dermatitis achieved by Chida et al. in 2007 revealed significant ameliorating effects on eczema severity, itching intensity and scratching, but a definite conclusion about the effectiveness of those therapies could not be drawn.

Recently, Idriss et al. (2009) examined the role of online support communities for patients with psoriasis and his study revealed, that the intensity of participation in online support was associated with improved quality of life. Psoriasis virtual communities are found to be a valuable educational resource and a source of psychological and social support. Finally, a 1-year follow-up of the illness and its psychosocial consequences in psoriatic men and women showed a moderate but significant relevance of skin state for feeling of stigmatization over time only in men, thus suggesting a considerable influence of other psychic variables, probably coping skills, especially in women (Schmid-Ott et al. 2005a).

Patient associations like the National Psoriasis Foundation in the U.S.A. or the German Psoriasis Association offer the possibility of getting information about the disease and are a platform to get in contact with other attended patients. Not every patient with psoriasis

or atopic dermatitis needs a specific psychotherapy, but if a patient prefers to cope actively with his disease, educational outpatient programs might be a good opportunity. Good results are available especially with parents of young children with atopic dermatitis. In an Italian program improving knowledge of the disease produced lower anxiety levels in parents (Ricci et al. 2009). A German multicentre, randomised controlled trial of age related, structured educational programs for the management of atopic dermatitis in children and adolescents revealed significant improvements in severity of eczema and subjective severity in all intervention groups after the program. Even the QoL of the parents was improved after undergoing those educational programs (Staab et al. 2006).

Conclusion

Chronic skin disorders like psoriasis and atopic eczema have profound influence on the patient's QoL. Patient's daily life and their relationships can be significantly impaired and social avoidance, depressive symptoms and anxiety might be negative consequences. A very important factor, especially in skin disorders, is experience of stigmatization due to visible and even hidden skin lesions, which are only relevant in personal relationships. More and more, medical studies focus on these problems and therapies should not only treat the skin lesions, but should be aimed on an improvement of QoL.

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