



# An update on diaper dermatitis

Christopher Klunk, BS<sup>a</sup>, Erik Domingues, MD<sup>b</sup>, Karen Wiss, MD<sup>c,\*</sup>

<sup>a</sup>University of Massachusetts Medical School, Worcester, MA

<sup>b</sup>Division of Dermatology, University of Massachusetts Medical School, Worcester, MA

<sup>c</sup>Division of Dermatology, University of Massachusetts Medical School, 281 Lincoln Street, Worcester, MA 01605

**Abstract** Diaper dermatitis leads to approximately 20% of all childhood dermatology visits. There have been several technologic advances in diaper design the last several years; however, due to the unique environment of the diaper area, many children continue to suffer from a variety of dermatologic conditions of this region. Common causes include allergic contact dermatitis, irritant contact dermatitis, infection, and psoriasis. Treatments include allergen avoidance, barrier protection, parent education, and topical therapies.

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## Introduction

Diaper dermatitis is a term used by clinicians to describe any of the various cutaneous eruptions appearing in the diaper area; however, it is important to determine the exact cause of a rash in this region because it may provide clues to the diagnosis of a more significant systemic disease or local infection. While most rashes in the diaper area are simple cases of irritant contact dermatitis responsive to topical treatments and parental education on proper diapering practices, it is important to recognize that rashes of the diaper area may be the direct result of diaper use, reflect exacerbation of a more diffuse dermatologic condition by the diaper, or be related to a condition that has coincidentally manifested in the diaper area but is otherwise unrelated. This paper is intended to provide an update on some diaper dermatoses and an in-depth look at diagnosis and treatment of the most common conditions rather than a comprehensive review. Table 1 lists conditions that could be considered in the differential diagnosis for diaper dermatitis.

## Epidemiology

The conglomerate of dermatologic conditions labeled as diaper dermatitis is thought to account for nearly 20% of childhood dermatology visits.<sup>1</sup> The overall prevalence of diaper dermatitis has been difficult to accurately assess as many studies do not differentiate between the various causes of rashes in the diaper area, but old estimates in Western countries ranged from 7% to 35%.<sup>2,3</sup> Variations in the incidence of diaper dermatitis throughout the world may be tied to any number of factors influencing the diapering and hygiene practices of parents in a given region as evidenced by incidence rates of 15.2%, 7%, and 4% in Italy, Nigeria, and Kuwait, respectively.<sup>4–6</sup> The incidence of diaper dermatitis has been shown to peak between the ages of 9 and 12 months<sup>7</sup> but a study of 12,103 singleton infants in the United Kingdom identified the incidence of “nappy rash” to be 25% during the first 4 weeks of life<sup>8</sup>; however, it is a condition that may affect patients of any age that require the use of diapers for treatment of incontinence.

## Diaper design

Many years ago, diapers were crude pieces of cloth wrapped around babies’ bottoms. Today, they are technologically advanced devices containing highly absorptive

\* Corresponding author. Tel.: +1 508 334 5979; fax: +1 508 334 5981.  
E-mail address: Karen.wiss@umassmemorial.org (K. Wiss).

polymers and multiple layers of various materials optimally suited to perform their chosen roles. Cotton diapers have also continued to evolve and only loosely resemble the diapers of fifty years ago when diaper laundering services were only available in a few major cities. Modern diaper design has adapted to take into account the pathophysiology of diaper irritant contact dermatitis.

The first layer of a modern diaper is in contact with the wearer's skin and is responsible for allowing passage of the fluid "insult" while preventing rewetting. This layer is referred to as the top sheet and frequently consists of hydrophobic polypropylene fibers or an apertured film that has been treated with hydrophilic surfactant. Capillary action and surfactant draw fluids through the top sheet and rewetting is prevented by the hydrophilic qualities of the material and/or the one-way valve effect of the apertures. The next layer of the modern diaper is referred to as the surge layer and was developed largely to address the slow rate of absorption in many superabsorbent polymers. Before the development of superabsorbent polymers, wood pulp was the most frequently used material in the core of diapers and while it had a fraction of the absorptive capacity of modern polymers, it had a significantly greater rate of absorption. As a result, a porous hydrophilic layer that serves to rapidly absorb and distribute the insult as it passes through the top sheet was added. Fluid disperses throughout the surge layer allowing for maximal contact with the inner absorbent core. Rewetting is prevented by acting as a reservoir for fluid while it is more slowly absorbed by the superabsorbent polymer of the core. The innermost layer, the absorbent core, usually consists of a cross linked polymer able to absorb many times its weight in fluid allowing for the lighter weight and greatly reduced bulk of modern diapers.<sup>9</sup> Modern

disposable diapers often incorporate various dyes for aesthetic purposes and recently these have been identified as a source of allergic contact diaper dermatitis.<sup>10</sup>

Beyond the absorptive capabilities of modern disposable diapers, significant effort has been invested into improving comfort and convenience. Folded cuffs and elastic bands around the leg openings provide a more snug fit and add a degree of third dimensionality to the diaper, further preventing undesired leaks. Adjustable fastening tabs and spiral glued elastic bands in ease comfort and reduce excess pressure that may cause skin irritation around the waistline and leg openings.<sup>9</sup> Diaper manufacturers continue working to improve diaper design under the close scrutiny of parents, environmental groups, and dermatologists around the world.

## Diapers, the environment, and politics

Parents frequently find themselves with well-meaning, but frequently, contradictory advice as to proper diapering practices. A debate over the environmental and health impacts of disposable and cloth diapers has been ongoing for many years and has drawn the attention of organizations, such as the National Resources Defense Council and Environmental Protection Agency (EPA) in the United States and the Environment Agency of England and Wales. A report from the EPA estimated that 1.5% of the municipal solid waste entering landfills in 2010 consisted of disposable diapers, amounting to 3.7 million tons.<sup>11</sup> While some manufacturers have reported that standard disposable diapers may be upwards of 80% biodegradable it is important to note that studies of biodegradability may be carried out under conditions similar to those created by composting processes rather than actual landfills.<sup>12</sup> Due to the poor ability of material to biodegrade in the conditions created by a landfill it is difficult to know if there is any benefit to products claiming to be 100% biodegradable. Despite these data, careful analysis of the environmental impact of disposable diapers in comparison to cloth diapers by the NRDC, Environment Agency, and the EPA has not been able to show a clear advantage to either design.<sup>13–15</sup> Suboptimal use of cloth diapers appears to exact a greater toll on the environment than disposable diapers due to energy consumption and waste water production secondary to laundering practices.<sup>13,14</sup> The use of laundering services results in less environmental impact than home laundering. In Table 2, the Environmental Agency outlines the steps for parents wanting to be more environmentally conscious.<sup>14</sup>

## Allergic contact dermatitis

Previously thought rare, allergic contact dermatitis as a cause of diaper dermatitis, has recently come to the forefront

**Table 1** Potential diaper (napkin) dermatoses

| Diagnosis                           | Psoriasis                     |
|-------------------------------------|-------------------------------|
| Irritant Contact Dermatitis         | Seborrheic Dermatitis         |
| Tidewater (tidemark)                | Langerhans Cell Histiocytosis |
| Granuloma gluteale infantum         | Hyper IgE Syndrome            |
| Jacquet's erosive diaper dermatitis | Baboon Syndrome               |
| Candidal dermatitis                 | Nutritional Deficiency        |
| Allergic Contact Dermatitis         | Acrodermatitis Enteropathica  |
|                                     | Biotinidase Deficiency        |
| Lucky Luke's (cowboy holster)       | Cystic Fibrosis               |
| Bacterial                           | Scabies                       |
| Cellulitis                          | Human Immunodeficiency Virus  |
| Impetigo (Bullous impetigo)         | Congenital Syphilis           |
| Necrotizing Fasciitis               | Tinea Corporis                |
| (Fournier's Gangrene)               |                               |
| Folliculitis                        | Perianal Pseudoverrucous      |
|                                     | Papules                       |
| Miliaria                            | Child abuse                   |
| Intertrigo                          |                               |
| Atopic Dermatitis                   |                               |

**Table 2** Cloth nappy users can reduce their environmental impacts by:

- Line drying outside whenever possible
- Tumble drying as little as possible
- When replacing appliances, choosing more energy efficient appliances (A + rated machines are preferred)
- Not washing above 60 °C.
- Washing fuller loads.
- Reusing nappies on other children.

(Copied with permission from Reference <sup>14</sup>.)

with the identification of diaper dyes as a source of sensitization<sup>10</sup> (Fig. 1). Additionally, a class action lawsuit against a major diaper manufacturer over a specific diaper product culminated in a multimillion dollar lawsuit,<sup>16–18</sup> drawing further attention to the possibility of allergic contact dermatitis to diaper additives.

The National Ambulatory Medical Care Survey estimated that there were 6.9 million outpatient visits for “contact dermatitis and other eczema” in both 1995 and 1996 and a large cohort study of eighth grade schoolchildren followed for fifteen years that identified the incidence rate of allergic contact dermatitis to be 7% to 8% in Denmark<sup>19,20</sup>; however, no studies to date have looked at the prevalence of allergic contact dermatitis in infants despite the growing number of case reports in the literature and relatively high percentage (55.8% to 77%) of clinically relevant positive results seen in retrospective reviews of patch testing.<sup>21,22</sup>

Cases of allergic contact dermatitis supported by positive patch testing and treated by allergen avoidance in response to mercaptocompounds in the elastic portions of diapers<sup>23</sup> and colored dyes, found in many diapers, have been reported.<sup>10</sup> “Lucky Luke” dermatitis refers to a particular distribution of allergic contact dermatitis thought to resemble the shape of a cowboy’s holster on the buttocks and hips of affected children. It has been attributed to substances potentially found in modern



**Fig. 1** Scaly pink papules coalescing into plaques that correspond with the green dye in the diapers. These findings are suggestive of allergic contact dermatitis from the diaper dye.

disposable diapers, such as the rubber additives mercaptoben-zothiazole and cyclohexylthiophthalimide and the glue resin p-tert-butyl-phenol-formaldehyde.<sup>24–26</sup>

A review of patch test results published in 2003 looked at 667 children with suspected allergic contact dermatitis and 431 children with atopic dermatitis undergoing testing for sensitization to seven commonly used disperse dyes. Of the children tested 4.6% were found sensitive to at least one dye, the three most frequent being disperse yellow 3, disperse orange 3, and disperse blue 124.<sup>27</sup> Disperse dyes are used on a variety of synthetic fabrics and are well known to be loosely adherent and frequently leech from clothing onto skin in areas of increased moisture or friction.<sup>28</sup> Sensitization to disperse dyes is common, and therefore, recommendations have surfaced to include these substances as standard components of screening for suspected textile dye dermatitis.<sup>29</sup> Even though allergic contact dermatitis to diaper dyes has only recently been reported and the actual prevalence is unknown, a large review of studies addressing the prevalence of textile dye allergic contact dermatitis found that patients sent for routine patch testing including disperse dyes were found to have positive results 1.4% to 5.8% of the time. When patients with suspected textile dye allergic contact dermatitis were tested the prevalence reached 17.1%.<sup>30</sup> Data addressing which color dyes are the most frequent culprits in cases of allergic contact dermatitis may not be helpful because dyes are often mixed to form the desired color; therefore, it may not be readily apparent that a particular garment contains a given dye on visual inspection.<sup>31</sup>

The issue of allergic contact dermatitis to substances within diapers has spread beyond the medical community and reached the headlines within recent years as a legal battle between Proctor & Gamble and a group of parents on the social networking website Facebook. In late 2009, parents gathered with complaints of “chemical burns” and “burn marks,” as well as reports of frequent emergency department visits for severely painful diaper rashes caused by a change in the design of Pampers® diapers. Proctor & Gamble eventually disclosed that Dry Max® technology, utilizing an absorbent gel core, had been introduced into the market over the last year and a class action lawsuit began.<sup>16</sup> In the end, a review by the Consumer Products Safety Commission found no connection between Dry Max diapers and the reported cutaneous eruptions,<sup>18</sup> but Proctor & Gamble still agreed to settle out of court for upwards of three million dollars, a portion of which was to be dedicated to the education of pediatric residents about proper skin care.<sup>32</sup> This case is presented here to highlight the increasing awareness of the general public that components utilized in the construction of diapers may be responsible for their child’s dermatologic conditions. Many parents may experience significant emotional distress at the sight of, what may appear to the trained eye to be, a relatively benign diaper rash.

Beyond the components within the diaper itself, there have been numerous case reports of allergic contact dermatitis and/or positive patch tests in response to

**Table 3** Substances potentially appearing in the diaper-area found to cause sensitization<sup>27,33,34,38,39,125,126</sup>

| <i>Allergen</i>                                                                                                       | <i>Common locations</i>                                                                           |
|-----------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Bacitracin                                                                                                            | OTC topical antibiotic                                                                            |
| Benzalkonium chloride                                                                                                 | Baby moisturizers, creams, body wipes                                                             |
| Benzophenone-3                                                                                                        | Soaps, sunscreens                                                                                 |
| Benzoyl peroxide                                                                                                      | Topical preparations (also an irritant that may mimic allergy)                                    |
| Bronopol (Formaldehyde releaser)                                                                                      | Baby wipes, shampoos, soaps                                                                       |
| Bufexamac                                                                                                             | Antiinflammatory ointments and creams                                                             |
| Carba mix (diphenylguanidine, Zincdiethylthiocarbamate, zincdiethylthiocarbamate)                                     | Rubber additive, soaps, shampoos, adhesives, clothing                                             |
| Cobalt                                                                                                                | Buttons, zippers, snaps, buckles                                                                  |
| Cocamidopropyl betaine (CAPB)                                                                                         | Surfactant in baby shampoos and washes                                                            |
| Colophony                                                                                                             | Adhesive bandages                                                                                 |
| Compositae mix (sesquiterpene lactone mix)                                                                            | "Natural" soaps, shampoos, plant-based oils                                                       |
| Corticosteroids (Tixocortol pivalate, budesonide, triamcnolone acetone)                                               | Many frequently prescribed topical preparations                                                   |
| Cyclohexlthiophthalimide                                                                                              | Rubber additive                                                                                   |
| Diaminodiphenylmethane                                                                                                | Rubber, dye, and adhesive additive                                                                |
| Diazolidinyl urea                                                                                                     | Lotions, soaps, shampoos, conditioners                                                            |
| Disperse dyes                                                                                                         | Dye in synthetic fabrics                                                                          |
| DL-alpha tocopherol                                                                                                   | Baby wipes, creams, lotions, emollients, shampoos, conditioners, soaps, sunscreens                |
| DMDM hydantoin                                                                                                        | Emollients, shampoos, conditioners, soaps                                                         |
| Ethylenediamine                                                                                                       | Cross-reacts with hydroxyzine and cetirizine                                                      |
| Formaldehyde                                                                                                          | Emollients                                                                                        |
| Fragrances (including balsam of Peru/myroxylon pereirae)                                                              | Any scented product (can be flavoring or mimicked by tomato)                                      |
| Geraniol                                                                                                              | Soaps, shampoos, lotions, perfumes                                                                |
| Imidazolidinyl urea                                                                                                   | Lotions, creams, soaps, conditioners                                                              |
| Iodopropylcarbamate                                                                                                   | Baby wipe ingredient                                                                              |
| Isopropyl myristate                                                                                                   | Hand sanitizer, topical corticosteroid preparations, emollients                                   |
| Lanolin/Amerchol L-101 (wool alcohol, stearyl and cetyl alcohol)                                                      | Emollients, lotions, ointments, creams, topical corticosteroid preparations                       |
| Mercapto mix (n-cyclohexyl-benzothiazole sulfenamide, dibenzothiazide sulfite, and morpholinyl mercaptobenzothiazole) | Rubber additive                                                                                   |
| Mercaptobenzothiazole (MBT)                                                                                           | Rubber additive                                                                                   |
| Methylchloroisothiazolinone (Kathon CG)                                                                               | Lotions, shampoos, conditioners, body wash                                                        |
| Methyldibromoglutaronitrile phenoxyethanol (Euxyl K400)                                                               | Shampoos, conditioners, soaps                                                                     |
| Methylisothiazolone                                                                                                   | Shampoos, conditioners, soaps                                                                     |
| Neomycin                                                                                                              | OTC topical antibiotics                                                                           |
| Nickel                                                                                                                | Buttons, zippers, snaps, buckles                                                                  |
| N-isopropyl-N'-phenyl-p-phenylenediamine (IPPD)                                                                       | Rubber additive                                                                                   |
| Octyl gallate                                                                                                         | Shampoos, soaps, lotions                                                                          |
| PABA                                                                                                                  | Sunscreens                                                                                        |
| Paraben mix                                                                                                           | Topical corticosteroid preparations, diaper balms, lotions, creams, soaps, shampoos, conditioners |
| Potassium dichromate                                                                                                  | Dark green dye and cosmetics                                                                      |
| Propolis                                                                                                              | "Natural" emollients and cosmetics                                                                |
| Propylene glycol                                                                                                      | Soaps and emollients                                                                              |
| p-tert-butyl-phenol-formaldehyde (PTBF)                                                                               | Glue additive                                                                                     |
| Quaternium-15                                                                                                         | Baby oils, baby bath, shampoos, soaps, lotions                                                    |
| Sodium benzoate                                                                                                       | Shampoos, conditioners, soaps, body wipes                                                         |
| Sorbitan sesquioleate                                                                                                 | Topical ointments, creams, and lotions                                                            |
| Span 20                                                                                                               | Baby bath, baby shampoo, baby wipes, antibacterial wipes, shampoos, conditioners, soaps           |
| Thiuram                                                                                                               | Rubber additive                                                                                   |

ingredients found in baby wipes, topical creams, lotions, and ointments, as well as fragrances used in many soaps and shampoos, all of which may come in contact with the diaper

area and contribute to a diaper rash.<sup>21,22,33–40</sup> For example, the emulsifier sorbitan sesquioleate, found in products, such as Desitin Diaper Rash Ointment® (Pfizer Inc., New York,

NY, US), Baby Magic Creamy Baby Oil® (Playtex Products, Streetsboro, OH, US), Cutivate Cream® (GlaxoSmithKline, Brentford, Middlesex, UK), and Cutemol Emollient Skin Cream® (Summers Laboratories Inc., Collegeville, PA, US), has been identified as the responsible agent in case reports of allergic contact dermatitis.<sup>33,36</sup> Interestingly, sorbitan sesquiolate is also found in many topical corticosteroid preparations and one retrospective review of 112 dermatitis patients undergoing patch testing identified a positive response in 10% of patients, several of whom had been using topical corticosteroid preparations containing this substance.<sup>35</sup> Table 3 lists many of the agents reported in the literature that may play a role in the development of allergic contact dermatitis of the diaper area.

When evaluating potential cases of allergic contact dermatitis it is important to remember that the exposure may have occurred at a site distant to the diaper area. One example of such a situation is baboon syndrome, where a systemic contact dermatitis occurs after exposure to an allergen that the patient has previously been sensitized to. The dermatologic manifestations of baboon syndrome include upper inner thigh and buttocks erythema, mimicking a baboon's bottom. Baboon syndrome was originally reported in response to ampicillin, nickel, and mercury; however, numerous reports of baboon syndrome in response to different allergens exist in the literature.<sup>41</sup>

### Current therapy for common diaper-area dermatoses

As previously mentioned, the differential diagnosis for cutaneous eruptions appearing in the diaper area is broad, but "diaper rash" is most frequently an irritant contact dermatitis caused by a number of factors. Included on the spectrum of irritant contact dermatitis are the more severe conditions, such as Jacquet's erosive diaper dermatitis, granuloma gluteal infantum, and pseudoverrucous papules and nodules. The Berg model of diaper dermatitis formation outlined in 1988<sup>42</sup> has served as the framework for our current understanding of the pathophysiology of irritant contact dermatitis in the diaper area. Increased moisture in the diaper area is created by a combination of the occlusive effect of the diaper combined with the presence of fecal and urinary waste. Increased moisture leading to maceration of the skin and disruption of the stratum corneum increases susceptibility of the skin to damaging frictional forces created within the numerous skin folds of this area, as well as the diaper itself. Proteases and lipases found within feces increase in activity in the high pH environment of the diaper and begin to cause skin irritation. This pH imbalance disrupts maintenance of normal skin flora making the skin more susceptible to infection by organisms commonly found on the skin, such as staphylococcus and streptococcus species, as well as organisms found in the stool such as *Candida*.<sup>43-45</sup> The shift in pH is thought to be caused by one of two major

mechanisms. First, urease in stool breaks down urea as urine and feces mix increasing skin pH. Second, as several studies have shown, bathing products can cause a shift in the microbiologic flora of the skin by raising the pH.<sup>46,47</sup> This second observation prompted recommendations to use cleansing products with synthetic detergents (syndets) that have pH values closer to that of normal skin. Berg concluded that the diaper environment was perfectly suited to cause skin irritation and the goal should be to make the conditions for diapered skin similar to those on nondiapered skin.<sup>42,48</sup>

### Basics of treating irritant contact diaper dermatitis

A substantial amount of evidence exists supporting many current practices in the treatment of irritant contact dermatitis in the diaper area. The backbone of such treatment can easily be remembered by the mnemonic ABCDE: Air, barrier, cleansing, diaper, and education.<sup>49</sup>

Air refers to the safest, most basic, time-honored, and often most efficacious therapeutic intervention: removing the diaper. The diaper environment is well-suited to causing skin irritation and allowing the infant time outside of the diaper provides an opportunity for the skin to dry and respite from the constant frictional forces of the diaper and the irritants in urine and feces. While it is often difficult for parents to incorporate diaper holidays into their schedule, this diaper-free time will not only improve the infant's skin but may even encourage earlier development of gross motor skills, such as walking, which has been shown to be impaired by the presence of bulky diapers between an infant's legs.<sup>50</sup> In some developing countries, diapers are a luxury and many forego their use, but this may be beneficial. Parents in Thailand have been reported to begin toilet training infants as early as 4 months old, often with success within twelve months.<sup>51</sup> Whether or not such early toilet training has any long term developmental benefits for the child is unknown, but the economic and environmental burden avoided is likely to be substantial.

Barrier creams, ointments, and pastes are often the first line treatments used by parents and physicians since diaper use is largely unavoidable.<sup>49,52</sup> There are many products on the market or products used as popular home remedies for years despite minimal or complete absence of data supporting their use.<sup>53</sup> Burow's solution, a mixture of aluminum acetate in water, is an astringent found in some commonly used products such as 1-2-3 Paste (petrolatum, zinc oxide, and aluminum acetate compounded by a pharmacy) that seems to never have been studied for use in irritant contact dermatitis of the diaper area. Maalox® (Novartis Consumer Health, Inc., Parsippany, NJ), a mixture of aluminum hydroxide and magnesium hydroxide marketed as an oral antacid, has gained popularity as a topical therapy for "diaper rash" despite a lack of studies addressing the safety or efficacy of such use. Topical diphenhydramine has gained

momentum as a treatment for “diaper rash,” but there have not been any studies of safety or efficacy in this setting. Topical diphenhydramine may result in systemic absorption and resultant severe toxicity and therefore, should be avoided.<sup>54–56</sup> Lastly, a 2005 Cochrane review by Davies et al. did not find sufficient evidence to support or refute the use of topical vitamin A in the treatment of irritant contact dermatitis, but the author acknowledged that only a single small randomized controlled trial had been performed.<sup>57</sup>

Better studied topical therapies include zinc oxide, lanolin, petrolatum, and vitamin A&D ointment® (containing the active ingredients lanolin and petrolatum).<sup>52,58–60</sup> A 2001 study showed benefits of continuous topical administration of zinc oxide and petrolatum by a specially-designed diaper.<sup>61</sup> A single study of oral zinc supplementation conducted in 89 normal newborn infants in 1989 found a significant reduction in the incidence of diaper dermatitis.<sup>62</sup> Products containing these substances have been available for many years and are frequently employed as first line therapy considering the available data and substantial experience many clinicians and parents have with them.

Recent data has emerged showing the potential benefits of several novel therapies. Dexpanthenol, a pantothenic acid analog, was recently compared to zinc oxide in a prospective block randomized investigator-blinded trial of 46 children with irritant diaper dermatitis from diarrhea and was found to have a similar ability to reduce transepidermal water loss thereby improving stratum corneum hydration.<sup>63,64</sup> An observational study of 309 children aged 27 days to 11 years in Germany found the benefits of Hamamelis (witch hazel) to be comparable to those of dexpanthenol in the treatment of several dermatologic conditions including “diaper dermatitis.”<sup>65</sup> Successful treatment of irritant diaper dermatitis in the setting of diarrhea and high-output stomas with the use of topical cholestyramine has been reported and compounded preparations of cholestyramine and petrolatum ointment are in use at some institutions.<sup>66–68</sup> Studies have shown the successful use of topical eosin<sup>69</sup> and bufexamac<sup>70</sup> for irritant diaper dermatitis, though neither of these treatments is frequently employed in the United States. Most recently, potato-derived proteases were shown to have a benefit in the treatment of protease-induced skin irritation in four infants following colon resection for Hirschsprung’s disease.<sup>71</sup> Guaiazulene, a naturally occurring substance used as a cosmetics dye in the United States, has been used to treat diaper dermatitis in NICU patients possibly via previously shown antioxidant effects.<sup>72,73</sup> A single randomized comparative trial of topical aloe vera and *Calendula officinalis* in Iranian children found both to be effective for treatment of diaper dermatitis.<sup>74</sup> This study did not include a control group or a group treated with one of the current standards, such as zinc oxide or petrolatum. Lastly, topical sucalfate has been used successfully in the treatment of recalcitrant irritant diaper dermatitis in an incontinent nonambulatory adult with severe erosive disease.<sup>75</sup>

Experts have advised parents to apply topical barrier products thickly and not attempt to completely remove the product before each new application as the necessary rubbing may cause further irritation.<sup>76,77</sup> A layer of petrolatum may be applied over the barrier paste or ointment to prevent the diaper from sticking to the thicker and more adherent product.<sup>78</sup>

As previously mentioned, cleaning of the diaper area should involve the use of cleansing products with near-physiologic pH values and the avoidance of harsh scrubbing. Some authors have recommended continued use of an old-fashioned damp cloth with water for cleaning of the diaper area in hopes of avoiding potential allergens and irritants.<sup>78,79</sup> Other authors support the use of baby wipes demonstrating their mildness on the skin, as well as the potential for more effective pH buffering capabilities compared to water and cloth.<sup>47,80,81</sup> Wipes containing benzalkonium chloride may result in allergic contact dermatitis and are a common cause of cutaneous eruptions in adults using wipes to cleanse the perineum (nonpublished evidence). Parents need to be warned not to over cleanse the area with wipes or a damp cloth because this can worsen the irritant effect.

While a 2006 Cochrane review failed to find sufficient evidence to support or refute the use of conventional disposable diapers in the treatment of diaper dermatitis,<sup>82</sup> several authors have identified benefits to using diapers containing super absorbent materials better capable of wicking moisture from the skin.<sup>76,83,84</sup> Frequent diaper changes, even as often as every two hours, are an important component of maintaining skin integrity by reducing exposure to irritants in stool and urine, as well as allowing the skin to contact the air and have an opportunity to dry.<sup>78,79</sup> A 2010 study in France was able to demonstrate improvements in irritant diaper dermatitis solely by implementing the use of diapers designed for enhanced breathability and maintenance of normal skin pH.<sup>85</sup>

The final strategy used in addressing irritant contact dermatitis is parent education. If parents are not given adequate instruction in proper care and information about which products are helpful, or even harmful, then the best intentions of physicians will never generate meaningful results and could even cause further morbidity. Examples of potentially harmful products include those containing baking soda (sodium bicarbonate), phenol, camphor, boric acid, benzocaine, and salicylates, all of which have been shown to carry the risk of systemic toxicity and/or methemoglobinemia.<sup>86–91</sup> Cornstarch and talc powders may have some benefit in treating irritant diaper dermatitis by reducing moisture and friction, but there is an associated risk of severe respiratory disease if inhaled and, therefore, should be avoided.<sup>91–93</sup> Combination creams such as Mycolog II® (triamcinolone/nystatin) and Lotrisone® (clotrimazole/beta-methasone) should also be avoided in the diaper as the steroids contained in these products are too potent for use on occluded diapered skin.<sup>94,95</sup> There have been numerous case reports of

**Table 4** Outline of irritant contact diaper dermatitis treatment NNABCDEs)<sup>49</sup>

Air—Diaper-free time.

Barrier—Zinc oxide, lanolin, and/or petrolatum. Instruct caretaker to not completely wipe off residue with each change and to reapply liberally. Petrolatum may be placed over other pastes and ointments to prevent sticking to the diaper. The barriers can also be placed over topical antifungals and topical steroids when necessary.

Clean—Damp cloth or baby wipes. Preference is for products with near to physiologic pH values. Warn parents not to over cleanse the area as this further irritates the skin. Cleansing should only be for stool and not for urine.

Diaper—The type of diaper may not be as important as frequent changes, up to as often as every 2 hours, to maintain dryness.

Education—The treatment plan must be clearly explained to caregivers to ensure adherence.

Others—Low potency non-fluorinated topical corticosteroids, mycostatin, topical azole antifungals, mupirocin and oral amoxicillin clavulanate, clindamycin, and cephalexin form the backbone of most treatment plans for recalcitrant or complicated irritant diaper dermatitis.

Cushing's syndrome resulting from the inappropriate use of potent topical corticosteroids in the diaper area.<sup>96,97,98</sup> Despite recommendations to avoid these products, there are still a significant number of physicians promoting their use.<sup>95</sup>

## Treating recalcitrant irritant contact diaper dermatitis

Recalcitrant diaper dermatitis that has not responded to the above treatments may warrant the use of topical corticosteroids or further evaluation for other common causes of irritation in this area, such as allergic contact dermatitis and fungal or bacterial infection. Allergen avoidance is the optimal treatment for allergic contact dermatitis in the diaper area. If necessary, low potency nonfluorinated topical corticosteroids, such as desonide 0.05% and hydrocortisone valerate 0.2% ointments, are known to be safe and effective in the diaper area and can be combined with barrier ointments/pastes, antimicrobial agents, and antifungals. Useful topical antifungal agents for the diaper area in cases of suspected or confirmed candidal dermatitis include mycostatin, clotrimazole, ketoconazole, miconazole, econazole, tioconazole, and ciclopirox.<sup>99–101</sup> While parents may try over-the-counter topical antibiotics, such as bacitracin for suspected bacterial infection, these products are not recommended. Topical antibiotics are not as effective as other treatments and often contain bacitracin or neomycin, which are common topical allergens.<sup>33,53</sup> In cases of mild localized staphylococcal infection, mupirocin applied twice daily has been used effectively, but more severe infections warrant the use of oral antibiotics, such as amoxicillin clavulanate, clindamycin, cephalexin, or trimeth-

oprim-sulfamethoxazole in sufficiently old infants.<sup>102–104</sup> Though not commonly used, especially in the United States, there exists evidence that topical fusidic acid and retapamulin are effective in the treatment of superficial staphylococcal infections.<sup>105,106</sup> One randomized double-blind study comparing the efficacy of hydrogen peroxide cream and fusidic acid for the treatment of impetigo found both treatments to be similarly efficacious in the 73% to 85% range.<sup>107</sup>

There are many safe and effective strategies and therapies for the treatment of the most common causes of diaper dermatitis. The ABCDEs for treatment of irritant diaper dermatitis combined with any of the numerous evidence-supported products currently available for cases of particularly severe disease or in cases of fungal or bacterial infection will provide safe and effective treatment in a majority of cases (Table 4). The effective use of patch testing and parental education to identify and avoid allergens is the most effective means of treating allergic contact dermatitis of the diaper area. Parents must understand proper diaper area care and which products are helpful, harmful, or unknown.

## Streptococcal infection and psoriasis

The association between streptococcal infection and the development of plaque-type, guttate, and pustular psoriasis has been well-described in the literature although the exact mechanism by which this occurs is incompletely understood. It has been postulated that psoriasis may develop as the result of a superantigen exotoxin and/or molecular mimicry with the well-studied M protein.<sup>108–110</sup> In 1991, McFadden et al. compared the amino acid sequence of protein M6 to 4721 ubiquitous peptides identifying 50-kDa keratin type 1 as the closest human homolog.<sup>108</sup> Since psoriasis is a T-cell mediated immune response<sup>111</sup> it is thought that exposure to streptococcal M protein may cause activation of T-cells that attack bacteria and have a proliferative effect on keratinocytes. Interestingly, acute rheumatic fever and acute post-streptococcal glomerulonephritis, both complications of immune dysfunction following streptococcal infection, have never been reported to occur concomitantly in a patient with acute guttate psoriasis according to a 2010 review of the literature by Krishnamurthy et al.<sup>112</sup>

Some authors suggest the lack of concomitant disease may be because psoriasis is an external manifestation of an evolutionary adaptation to rheumatic fever, similar to sickle cell anemia and its evolutionary response to malaria.<sup>113</sup> This is largely based on the above observation that psoriasis, acute rheumatic fever, and acute poststreptococcal glomerulonephritis do not appear in the same patients, despite considerable geographic overlap. The existence of particular HLA subtypes known to be associated with psoriasis may provide further support of this evolutionary hypothesis. A difference in subtype prevalence between populations known to have suffered significantly from rheumatic fever in the



**Fig. 2** Bright erythema in the perianal region due to beta hemolytic *Streptococci* that led to a flare of psoriasis in this infant.

past and populations known to have had minimal exposure to rheumatic fever would be of great interest as it might indicate a degree of natural selection for protection from rheumatic fever.<sup>112</sup> The unfortunate downside to this protection may have been increased susceptibility to psoriasis, a condition with much lower mortality.

Perianal streptococcal dermatitis (Fig. 2) and streptococcal pharyngitis have both been associated with the development of psoriasis. The association with pharyngitis has prompted the use of tonsillectomy as a treatment for recalcitrant skin disease despite a lack of evidence supporting its use.<sup>114</sup> Older data identified a benefit to the use of penicillin or erythromycin with or without the addition of rifampin in patients with streptococcal-associated psoriasis.<sup>115</sup> More recent evidence, including a placebo controlled randomized trial comparing penicillin or erythromycin to placebo, found no benefit in using antibiotics for psoriasis control.<sup>116,117</sup> Treating streptococcal infection is beneficial when considering the significant discomfort caused by perianal dermatitis and pharyngitis and the possible long-term sequelae; however, there does not appear to be any information demonstrating a benefit to treating psoriatic patients without an active infection.

While some authors have stated there have not been any documented cases of group-A beta hemolytic streptococcus resistant to penicillins,<sup>112</sup> there have been reports of erythromycin resistant streptococcus<sup>118</sup> and recurrence rates of 38.1% for perianal streptococcal infection treated with penicillin or amoxicillin.<sup>119</sup> As a result, some authors recommend the use of beta-lactamase resistant penicillins or cefuroxime with courses ranging from 10 to 21 days.<sup>119,120</sup> Some authors recommend combination therapy primarily with oral antibiotics and topical therapies such as antiseptics (polyhexanide, chlorhexidine, or clioquinol) or antibiotics (mupirocin, fusidic acid, erythromycin, or bacitracin).<sup>121</sup>

It has recently been observed that the microbiologic content of perianal bacterial dermatitis may not always be group A beta hemolytic streptococcus as previously observed. A report from New York found that staphylococcus aureus was isolated more frequently than streptococcus from patients aged 5 months to 12 years with anal erythema



**Fig. 3** Well-demarcated bright red erythema in the diaper area due to inverse psoriasis.

or recurrent buttock dermatitis.<sup>122</sup> Additionally, a German study published in 2012 found that group B beta-hemolytic streptococcus, rather than group A, is the most common culprit in perianal streptococcal dermatitis in adults.<sup>123,124</sup>

Our understanding of perianal streptococcus, its association with psoriasis, and their potential evolutionary connection has grown significantly in recent years. At this time there does not appear to be sufficient evidence to support the use of antibiotics in the treatment of psoriasis and the risk of developing additional long term sequelae of streptococcal infection appears minimal.<sup>112,114</sup> It is important that clinicians recognize the association between these conditions and although current data are not available to support the treatment of streptococcus carrier status in individuals with recalcitrant psoriasis, significant anecdotal evidence indicates that patient's often see a noticeable improvement in their skin condition.

## Inverse psoriasis

One final consideration in regards to psoriasis is the clinical entity inverse psoriasis. This refers to well-demarcated, shiny red plaques of psoriasis involving the intertriginous areas, such as the perineal, genital, and inguinal regions within the diaper (Fig. 3). The clinician should look for signs of psoriasis elsewhere including the scalp, umbilicus, external auditory canals, periauricular region, and nails. This fairly common presentation for psoriasis in infants and toddlers may often be misdiagnosed as candidiasis or irritant contact dermatitis.

## Conclusions

It is important to determine the etiology of cutaneous eruptions in the diaper area because multiple entities may result in diaper dermatitis. Although irritant contact

dermatitis is the most common cause, others include infections, allergic contact dermatitis, psoriasis, nutritional deficiency, and immunodeficiency syndromes as listed in Table 1. Technologic advances in diaper design have led to increased absorption, decreased rewetting, and increased comfort for children; however, with these advances, have also come increased cases of allergic contact dermatitis to substances found in diapers including disperse dyes, glue resin, and rubber additives. Irritant contact dermatitis results from increased moisture leading to skin maceration and pH imbalance from feces and urine making the skin more susceptible to infection. The ABCDE's of irritant dermatitis treatment include incorporating "diaper holidays," using barrier creams and ointments such as zinc oxide, petrolatum, and new more advanced treatments such as dexpanthenol, topical cholestyramine, and topical sucalfate. Over-cleansing and harsh scrubbing need to be avoided and only cleansing products with near-physiologic pH values should be used. Use of superabsorbent diapers and frequent diaper changes may also be effective. Educating parents on which products to use and which to avoid is helpful in treating irritant contact dermatitis and avoiding side effects from unjustified therapy, such as methemoglobinemia and Cushing's syndrome. Physicians must be able to recognize perianal dermatitis secondary to streptococcal infection and its role in the development of psoriasis. Inverse psoriasis in the diaper area must be considered in children with well demarcated shiny red plaques so that an accurate diagnosis is made and the correct treatments recommended.

## References

- Verbov JL. Skin problems in children. *Practitioner*. 1976;217:403-415.
- Pratt AG. Perianal dermatitis of the newborn. *Am J Dis Child*. 1951;82:429-432.
- Tanino J, Steiner M, Benjamin B. The relationship of perianal dermatitis to fecal pH. *J Pediatr*. 1959;54:793-800.
- Longhi F, Carlucci G, Bellucci R, et al. Diaper dermatitis: a study of contributing factors. *Contact Dermatitis*. 1992;26:248-252.
- Oduko OM, Onayemi O, Oyedeji GA. A prevalence survey of skin diseases in Nigerian children. *Niger J Med*. 2001;10:64-67.
- Nanda A, Al-Hasawi F, Alsaleh QA. A prospective survey of pediatric dermatology clinic patients in Kuwait: an analysis of 10,000 cases. *Pediatr Dermatol*. 1999;16:6-11.
- Jordan WE, Lawson KD, Berg RW, et al. Diaper dermatitis: frequency and severity among a general infant population. *Pediatr Dermatol*. 1986;3:198-207.
- Philipp R, Hughes A, Golding J. Getting to the bottom of nappy rash. ALSPAC Survey Team. Avon Longitudinal Study of Pregnancy and Childhood. *Br J Gen Pract*. 1997;47:493-497.
- Ratnapandian S, Warner SB. Modern diaper technology. *Tappi J*. 1996;79:173-177.
- Alberta L, Sweeney SM, Wiss K. Diaper dye dermatitis. *Pediatrics*. 2005;116:450-452.
- U.S. Environmental Protection Agency. Municipal Solid Waste Generation, Recycling, and Disposal in the United States Tables and Figures for 2010. Pittsburgh, PA: U.S. Government Printing Office. 2011.
- Soil Control Lab. Analysis of material by aerobic biodegradation using ASTM Method D5338. Available at <http://www.gdiapers.com/assets/files/pdf/gDiapers-ASTM-test.pdf> 2009. [accessed 1/5/13].
- Hershkovitz A. Q&A. TLC "truly loving care for our kids and our planet." 1; 1989. p. 2.
- Aumonier S, Collins M, Garrett P. An Updated Lifecycle Assessment Study for Disposable and Reusable Nappies. Almondsbury, Bristol: Environment Agency. 2008.
- U.S. Environmental Protection Agency. Study of Environmental Impacts of Selected Disposable Versus Reusable Products with Health Considerations. Pittsburgh, PA: U.S. Government Printing Office. 1978.
- Gilllin P. Attack of the Customers: The Pampers Dry Max Crisis. Available at <http://gilllin.com/blog/2012/08/attack-of-the-customers-the-pampers-dry-max-crisis> 2012. [accessed 12/17/12].
- Jacob SE, Herro EM, Guide S, et al. Allergic contact dermatitis to Pampers Drymax. *Pediatr Dermatol*. 2012;29:672-674.
- U.S. Consumer Product Safety Commission. No Specific Cause Found Yet Linking Dry Max Diapers to Diaper Rash. U.S. Consumer Product Safety Commission. 2010. 10-331. Available at <http://www.cpsc.gov/en/Newsroom/News-Releases/2010/No-Specific-Cause-Found-Yet-Linking-Dry-Max-Diapers-to-Diaper-Rash/>.
- Mortz CG, Bindslev-Jensen C, Andersen KE. Prevalence, incidence rates and persistence of contact allergy and allergic contact dermatitis in The Odense Adolescence Cohort Study: a 15-year follow-up. *Br J Dermatol*. 2013;168:318-325.
- U.S. Department of Health and Human Services. National Ambulatory Medical Care Survey: 1995-1996 Summary. *Vital Health Stat*. 1999;13:41.
- Hogeling M, Pratt M. Allergic contact dermatitis in children: the Ottawa hospital patch-testing clinic experience, 1996 to 2006. *Dermatitis*. 2008;19:86-89.
- Jacob SE, Brod B, Crawford GH. Clinically relevant patch test reactions in children: a United States based study. *Pediatr Dermatol*. 2008;25:520-527.
- Onken AT, Baumstark J, Belloni B, et al. Atypical diaper dermatitis: contact allergy to mercapto compounds. *Pediatr Dermatol*. 2011;28:739-741.
- Belhadjali H, Giordano-Labadie F, Rance F, et al. "Lucky Luke" contact dermatitis from diapers: a new allergen? *Contact Dermatitis*. 2001;44:248.
- Di Landro A, Greco V, Valsecchi R. "Lucky Luke" contact dermatitis from diapers with negative patch tests. *Contact Dermatitis*. 2002;46:48-49.
- Roul S, Ducombs G, Leaute-Labreze C, et al. "Lucky Luke" contact dermatitis due to rubber components of diapers. *Contact Dermatitis*. 1998;38:363-364.
- Giusti F, Massone F, Bertoni L, et al. Contact sensitization to disperse dyes in children. *Pediatr Dermatol*. 2003;20:393-397.
- Storrs F. Dermatitis from clothing and shoes. In: Fischer A, ed. *Contact Dermatitis*. Philadelphia: Lea & Febiger; 1986. p. 283-337.
- Pratt M, Taraska V. Disperse blue dyes 106 and 124 are common causes of textile dermatitis and should serve as screening allergens for this condition. *Am J Contact Dermatitis*. 2000;11:30-41.
- Hatch KL, Maibach HI. Textile dye allergic contact dermatitis prevalence. *Contact Dermatitis*. 2000;42:187-195.
- Cronin E. Studies in contact dermatitis. 18. Dyes in clothing. *Trans St Johns Hosp Dermatol Soc*. 1968;54:156-164.
- Sarko L, Ireland D. Case: 1:10-cv-00301-TSB Doc #: 54-2 Filed: 05/27/11. Available at <http://www.diaperclassactionsettlement.com/docs/sa.pdf> 2011. [accessed 12/17/12].
- Jacob SE, Burk CJ, Connelly EA. Patch testing: another steroid-sparing agent to consider in children. *Pediatr Dermatol*. 2008;25:81-87.
- Smith WJ, Jacob SE. The role of allergic contact dermatitis in diaper dermatitis. *Pediatr Dermatol*. 2009;26:369-370.
- Asarch A, Scheinman PL. Sorbitan sesquiolate, a common emulsifier in topical corticosteroids, is an important contact allergen. *Dermatitis*. 2008;19:323-327.

36. Castaneda-Tardan MP, Jacob SE. Allergic contact dermatitis to sorbitan sesquioleate in children. *Contact Dermatitis*. 2008;58:171-172.
37. Seidenari S, Giusti F, Pepe P, et al. Contact sensitization in 1094 children undergoing patch testing over a 7-year period. *Pediatr Dermatol*. 2005;22:1-5.
38. Heine G, Schnuch A, Uter W, et al. Frequency of contact allergy in German children and adolescents patch tested between 1995 and 2002: results from the Information Network of Departments of Dermatology and the German Contact Dermatitis Research Group. *Contact Dermatitis*. 2004;51:111-117.
39. Roul S, Ducombs G, Taieb A. Usefulness of the European standard series for patch testing in children. A 3-year single-centre study of 337 patients. *Contact Dermatitis*. 1999;40:232-235.
40. Beattie PE, Green C, Lowe G, et al. Which children should we patch test? *Clin Exp Dermatol*. 2007;32:6-11.
41. Andersen KE, Hjorth N, Menne T. The baboon syndrome: systemically-induced allergic contact dermatitis. *Contact Dermatitis*. 1984;10:97-100.
42. Berg RW. Etiology and pathophysiology of diaper dermatitis. *Adv Dermatol*. 1988;3:75-98.
43. Rebora A, Leyden JJ. Napkin (diaper) dermatitis and gastrointestinal carriage of *Candida albicans*. *Br J Dermatol*. 1981;105:551-555.
44. Benjamin L. Clinical correlates with diaper dermatitis. *Pediatrician*. 1987;14:21-26.
45. Gokalp AS, Aldirmaz C, Oguz A, et al. Relation between the intestinal flora and diaper dermatitis in infancy. *Trop Geogr Med*. 1990;42:238-240.
46. Korting HC, Braun-Falco O. The effect of detergents on skin pH and its consequences. *Clin Dermatol*. 1996;14:23-27.
47. Adam R, Schnetz B, Mathey P, et al. Clinical demonstration of skin mildness and suitability for sensitive infant skin of a new baby wipe. *Pediatr Dermatol*. 2009;26:506-513.
48. Berg RW, Milligan MC, Sarbaugh FC. Association of skin wetness and pH with diaper dermatitis. *Pediatr Dermatol*. 1994;11:18-20.
49. Boiko S. Treatment of diaper dermatitis. *Dermatol Clin*. 1999;17:235-240.
50. Cole WG, Lingeman JM, Adolph KE. Go naked: diapers affect infant walking. *Dev Sci*. 2012;15:783-790.
51. Benjasuwantep B, Ruangdaraganon N. Infant toilet training in Thailand: starting and completion age and factors determining them. *J Med Assoc Thai*. 2011;94:1441-1446.
52. Humphrey S, Bergman JN, Au S. Practical management strategies for diaper dermatitis. *Skin Therapy Lett*. 2006;11:1-6.
53. Beeckman D, Schoonhoven L, Verhaeghe S, et al. Prevention and treatment of incontinence-associated dermatitis: literature review. *J Adv Nurs*. 2009;65:1141-1154.
54. Filloux F. Toxic encephalopathy caused by topically applied diphenhydramine. *J Pediatr*. 1986;108:1018-1020.
55. Huston RL, Cypcar D, Cheng GS, et al. Toxicity from topical administration of diphenhydramine in children. *Clin Pediatr*. 1990;29:542-545.
56. Turner JW. Death of a child from topical diphenhydramine. *Am J Forensic Med Pathol*. 2009;30:380-381.
57. Davies MW, Dore AJ, Perissinotto KL. Topical vitamin A, or its derivatives, for treating and preventing napkin dermatitis in infants. *Cochrane Database Syst Rev*. 2005(4):CD004300.
58. Wigger-Alberti W, Elsner P. Petrolatum prevents irritation in a human cumulative exposure model *in vivo*. *Dermatology*. 1997;194:247-250.
59. Xhaufaire-Uhoda E, Henry F, Pierard-Franchimont C, et al. Electrometric assessment of the effect of a zinc oxide paste in diaper dermatitis. *Int J Cosmet Sci*. 2009;31:369-374.
60. Zhai H, Willard P, Maibach HI. Evaluating skin-protective materials against contact irritants and allergens. An *in vivo* screening human model. *Contact Dermatitis*. 1998;38:155-158.
61. Baldwin S, Odio MR, Haines SL, et al. Skin benefits from continuous topical administration of a zinc oxide/petrolatum formulation by a novel disposable diaper. *J Eur Acad Dermatol Venereol*. 2001;15:5-11.
62. Collipp PJ. Effect of oral zinc supplements on diaper rash in normal infants. *J Med Assoc Ga*. 1989;78:621-623.
63. Gehring W, Gloor M. Effect of topically applied dexpanthenol on epidermal barrier function and stratum corneum hydration. Results of a human *in vivo* study. *Arzneimittelforschung*. 2000;50:659-663.
64. Wananukul S, Limpongsanuruk W, Singalavanija S, et al. Comparison of dexpanthenol and zinc oxide ointment with ointment base in the treatment of irritant diaper dermatitis from diarrhea: a multicenter study. *J Med Assoc Thai*. 2006;89:1654-1658.
65. Wolff HH, Kieser M. Hamamelis in children with skin disorders and skin injuries: results of an observational study. *Eur J Pediatr*. 2007;166:943-948.
66. Moller P, Lohmann M, Bryniz S. Cholestyramine ointment in the treatment of perianal skin irritation following ileoanal anastomosis. *Dis Colon Rectum*. 1987;30:106-107.
67. Rodriguez JT, Huang TL, Ferry GD, et al. Treatment of skin irritation around enterostomies with cholestyramine ointment. *J Pediatr*. 1976;88:659-661.
68. White CM, Gailey RA, Lippe S. Cholestyramine ointment to treat buttocks rash and anal excoriation in an infant. *Ann Pharmacother*. 1996;30:954-956.
69. Arad A, Mimouni D, Ben-Amitai D, et al. Efficacy of topical application of eosin compared with zinc oxide paste and corticosteroid cream for diaper dermatitis. *Dermatology*. 1999;199:319-322.
70. Lube G. Treatment of diaper rash with Parfenac lipid ointment (bufexamac). A study by Austrian pediatricians. *Pediatr Padol*. 1989;24:227-236.
71. Berger S, Rufener J, Klimek P, et al. Effects of potato-derived protease inhibitors on perianal dermatitis after colon resection for long-segment Hirschsprung's disease. *World J Pediatr*. 2012;8:173-176.
72. Gunes T, Akin MA, Sarici D, et al. Guaiazulene: a new treatment option for recalcitrant diaper dermatitis in NICU patients. *J Matern Fetal Neonatal Med*. 2013;26:197-200.
73. Kourounakis AP, Rekka EA, Kourounakis PN. Antioxidant activity of guaiazulene and protection against paracetamol hepatotoxicity in rats. *J Pharm Pharmacol*. 1997;49:938-942.
74. Panahi Y, Sharif MR, Sharif A, et al. A randomized comparative trial on the therapeutic efficacy of topical aloe vera and *Calendula officinalis* on diaper dermatitis in children. *Sci World J*. 2012;8:102-134.
75. Markham T, Kennedy F, Collins P. Topical sucralfate for erosive irritant diaper dermatitis. *Arch Dermatol*. 2000;136:1199-1200.
76. Lund C, Kuller J, Lane A, et al. Neonatal skin care: the scientific basis for practice. *J Obstet Gynecol Neonatal Nurs*. 1999;28:241-254.
77. Taquino LT. Promoting wound healing in the neonatal setting: process versus protocol. *J Perinat Neonatal Nurs*. 2000;14:104-118.
78. Borkowski S. Diaper rash care and management. *Pediatr Nurs*. 2004;30:467-470.
79. Lund CH, Osborne JW, Kuller J, et al. Neonatal skin care: clinical outcomes of the AWHONN/NANN evidence-based clinical practice guideline. Association of Women's Health, Obstetric and Neonatal Nurses and the National Association of Neonatal Nurses. *J Obstet Gynecol Neonatal Nurs*. 2001;30:41-51.
80. Adam R. Skin care of the diaper area. *Pediatr Dermatol*. 2008;25:427-433.
81. Ehretsmann C, Schaefer P, Adam R. Cutaneous tolerance of baby wipes by infants with atopic dermatitis, and comparison of the mildness of baby wipe and water in infant skin. *J Eur Acad Dermatol Venereol*. 2001;15:16-21.
82. Baer EL, Davies MW, Easterbrook KJ. Disposable nappies for preventing napkin dermatitis in infants. *Cochrane Database Syst Rev*. 2006(3):CD004262.
83. Nield LS, Kamat D. Prevention, diagnosis, and management of diaper dermatitis. *Clin Pediatr*. 2007;46:480-486.
84. Scheinfeld N. Diaper dermatitis: a review and brief survey of eruptions of the diaper area. *Am J Clin Dermatol*. 2005;6:273-281.
85. Beguin AM, Malaquin-Pavan E, Guihaire C, et al. Improving diaper design to address incontinence associated dermatitis. *BMC Geriatr*. 2010;10:86.

86. Ferraro-Borgida MJ, Mulhern SA, DeMeo MO, et al. Methemoglobinemia from perineal application of an anesthetic cream. *Ann Emerg Med.* 1996;27:785-788.
87. Guilbert J, Flamant C, Hallalel F, et al. Anti-flatulence treatment and status epilepticus: a case of camphor intoxication. *Emerg Med J.* 2007;24:859-860.
88. Jensen JP. Transcutaneous absorption of boron from a baby ointment used prophylactically against diaper dermatitis. *Nord Med.* 1971;86:1425-1429.
89. Morra P, Bartle WR, Walker SE, et al. Serum concentrations of salicylic acid following topically applied salicylate derivatives. *Ann Pharmacother.* 1996;30:935-940.
90. Tush GM, Kuhn RJ. Methemoglobinemia induced by an over-the-counter medication. *Ann Pharmacother.* 1996;30:1251-1254.
91. Samuel D. Deadly diapers. *Br Med J.* 1970;2:314.
92. Gonzalez J, Hogg RJ. Metabolic alkalosis secondary to baking soda treatment of a diaper rash. *Pediatrics.* 1981;67:820-822.
93. Pairaudeau PW, Wilson RG, Hall MA, et al. Inhalation of baby powder: an unappreciated hazard. *BMJ.* 1991;302:1200-1201.
94. Greenberg HL, Shwayder TA, Bieszk N, et al. Clotrimazole/betamethasone dipropionate: a review of costs and complications in the treatment of common cutaneous fungal infections. *Pediatr Dermatol.* 2002;19:78-81.
95. Tempark T, Phatarakijnurud V, Chatproedprai S, et al. Exogenous Cushing's syndrome due to topical corticosteroid application: case report and review literature. *Endocrine.* 2010;38:328-334.
96. Guven A, Gulumser O, Ozgen T. Cushing's syndrome and adrenocortical insufficiency caused by topical steroids: misuse or abuse? *J Pediatr Endocrinol Metab.* 2007;20:1173-1182.
97. Semiz S, Balci YI, Ergin S, et al. Two cases of Cushing's syndrome due to overuse of topical steroid in the diaper area. *Pediatr Dermatol.* 2008;25:544-547.
98. Siklar Z, Bostanci I, Atli O, et al. An infantile Cushing syndrome due to misuse of topical steroid. *Pediatr Dermatol.* 2004;21:561-563.
99. Balkrishnan R, Cook JM, Shaffer MP, et al. Analysis of factors associated with prescription of a potentially inappropriate combination dermatologic medication among US outpatient physicians. *Pharmacoepidemiol Drug Saf.* 2004;13:133-138.
100. Gallup E, Plott T, Ciclopirox TS Investigators. A multicenter, open-label study to assess the safety and efficacy of ciclopirox topical suspension 0.77% in the treatment of diaper dermatitis due to *Candida albicans*. *J Drugs Dermatol.* 2005;4:29-34.
101. Gibbs DL, Kashin P, Jevons S. Comparative and non-comparative studies of the efficacy and tolerance of tioconazole cream 1% versus another imidazole and/or placebo in neonates and infants with candidal diaper rash and/or impetigo. *J Int Med Res.* 1987;15:23-31.
102. Spraker MK, Gisoldi EM, Siegfried EC, et al. Topical miconazole nitrate ointment in the treatment of diaper dermatitis complicated by candidiasis. *Cutis.* 2006;77:113-120.
103. Bass JW, Chan DS, Creamer KM, et al. Comparison of oral cephalixin, topical mupirocin and topical bacitracin for treatment of impetigo. *Pediatr Infect Dis J.* 1997;16:708-710.
104. Fortunov RM, Hulten KG, Hammerman WA, et al. Evaluation and treatment of community-acquired *Staphylococcus aureus* infections in term and late-preterm previously healthy neonates. *Pediatrics.* 2007;120:937-945.
105. Koning S, Verhagen AP, van Suijlekom-Smit LW, et al. Interventions for impetigo. *Cochrane Database Syst Rev.* 2004(2):CD003261.
106. Koning S, van der Sande R, Verhagen AP, et al. Interventions for impetigo. *Cochrane Database Syst Rev.* 2012;1:CD003261.
107. George A, Rubin G. A systematic review and meta-analysis of treatments for impetigo. *Br J Gen Pract.* 2003;53:480-487.
108. Christensen OB, Anehus S. Hydrogen peroxide cream: an alternative to topical antibiotics in the treatment of impetigo contagiosa. *Acta Derm Venereol.* 1994;74:460-462.
109. McFadden J, Valdimarsson H, Fry L. Cross-reactivity between streptococcal M surface antigen and human skin. *Br J Dermatol.* 1991;125:443-447.
110. Valdimarsson H, Baker BS, Jonsdottir I, et al. Psoriasis: a T-cell-mediated autoimmune disease induced by streptococcal superantigens? *Immunol Today.* 1995;16:145-149.
111. Valdimarsson H, Sigmundsdottir H, Jonsdottir I. Is psoriasis induced by streptococcal superantigens and maintained by M-protein-specific T cells that cross-react with keratin? *Clin Exp Immunol.* 1997;107:21-24.
112. Nickoloff BJ. The immunologic and genetic basis of psoriasis. *Arch Dermatol.* 1999;135:1104-1110.
113. Krishnamurthy K, Walker A, Gropper CA, et al. To treat or not to treat? Management of guttate psoriasis and pityriasis rosea in patients with evidence of group A Streptococcal infection. *J Drugs Dermatol.* 2010;9:241-250.
114. McFadden JP. Hypothesis—the natural selection of psoriasis. *Clin Exp Dermatol.* 1990;15:39-43.
115. Owen CM, Chalmers RJ, O'Sullivan T, et al. Antistreptococcal interventions for guttate and chronic plaque psoriasis. *Cochrane Database Syst Rev.* 2000(2):CD001976.
116. Rosenberg EW, Noah PW, Zanolli MD, et al. Use of rifampin with penicillin and erythromycin in the treatment of psoriasis. Preliminary report. *J Am Acad Dermatol.* 1986;14:761-764.
117. Vincent F, Ross JB, Dalton M, et al. A therapeutic trial of the use of penicillin V or erythromycin with or without rifampin in the treatment of psoriasis. *J Am Acad Dermatol.* 1992;26:458-461.
118. Dogan B, Karabudak O, Harmanyeri Y. Antistreptococcal treatment of guttate psoriasis: a controlled study. *Int J Dermatol.* 2008;47:950-952.
119. Martin JM, Green M, Barbadora KA, et al. Erythromycin-resistant group A streptococci in schoolchildren in Pittsburgh. *N Engl J Med.* 2002;346:1200-1206.
120. Olson D, Edmonson MB. Outcomes in children treated for perineal group A beta-hemolytic streptococcal dermatitis. *Pediatr Infect Dis J.* 2011;30:933-936.
121. Meury SN, Erb T, Schaad UB, et al. Randomized, comparative efficacy trial of oral penicillin versus cefuroxime for perianal streptococcal dermatitis in children. *J Pediatr.* 2008;153:799-802.
122. Jongen J, Eberstein A, Peleikis HG, et al. Perianal streptococcal dermatitis: an important differential diagnosis in pediatric patients. *Dis Colon Rectum.* 2008;51:584-587.
123. Heath C, Desai N, Silverberg NB. Recent microbiological shifts in perianal bacterial dermatitis: *Staphylococcus aureus* predominance. *Pediatr Dermatol.* 2009;26:696-700.
124. Kahlke V, Jongen J, Peleikis HG, et al. Perianal streptococcal dermatitis in adults: its association with pruritic anorectal diseases is mainly caused by group B streptococci. *Colorectal Dis.* 2013;15:602-607.
125. Fortina AB, Piaserico S, Larese F, et al. Diaminodiphenylmethane (DDM): frequency of sensitization, clinical relevance and concomitant positive reactions. *Contact Dermatitis.* 2001;44:283-288.
126. U.S. Department of Health and Human Services. Household Products Database. Available at <http://householdproducts.nlm.nih.gov/> 2013. [accessed 12/20/13].