CURRENT MEDICAL RESEARCH and Opinion®

Reprinted from
Curr Med Res Opin 2004; 20(5): 645-649

A review of the pathophysiology, prevention and treatment of irritant diaper dermatitis

David J. Atherton

www.cmrojournal.com

Current Medical Research and Opinion® (now in its 32nd year and indexed by MEDLINE and most other major databases) is a peer-reviewed international journal for the rapid publication of original research on new and existing drugs, medical devices and therapies. Contributions based on Phase I–IV studies, and on pharmaco-economic, outcomes and QoL trials, are especially encouraged. The journal publishes full-length original research papers, brief reports, review and commentary articles. Utra-rapid publication of priority publications is effected by online, electronic publication. Publication of all papers is first carried out electronically on the ***Fast*Track** section of **CMRO Online** (at www.cmrojournal.com) followed by print publication in one of the 12 print issues per year.

Print and Online Publication: Accepted manuscripts are published online in 4–6 weeks (2–3 weeks for priority ***Fast*Track** manuscripts) and in print publication in a further 4–8 weeks (monthly). Full-text archival versions of all papers are published electronically on the CMRO Online site (hosted by Ingenta Select and augmented by CrossRef citation links).

Distribution and Abstracting/Indexing: Over 5000 copies per issue of CMRO are physically distributed worldwide, including more than 3000 to medical libraries and selected physicians, pharmacists and other healthcare professionals. Online hosting via Medscape (from *Web*MD) provides full text papers to over 2.4 million physicians and healthcare professionals. Indexing in MEDLINE/*Index Medicus* and EMBASE/*Excerpta Medica*, listed in *Current Contents/Clinical Medicine*, and cited in ISI's Science Citation Index (2002 ISI impact factor 1.92). It is also indexed and abstracted by several other major data-retrieval, abstracting and bibliographic services, including: Adis Clinical Trials Insight, CA Search/CAS Online, CAB Abstracts, CancerLit, CINAHL, Derwent Drug File, International Pharmaceutical Abstracts, NLM Gateway, PubMed, Pascal, Pharm-line, SciSearch and TOXFILE/Toxline.

Subscriptions/Claims: *Current Medical Research and Opinion* (Print ISSN: 0300–7995) is published by LibraPharm Limited. In 2004 one volume will be published – Volume 20 – which will have 12 regular issues published on a monthly basis; supplementary issues may be also published on an occasional basis.

Subscription prices:

UK and Europe:	£235/€375
USA and Rest of World:	£270/$475

Paid subscriptions include postage by air or accelerated surface post, supplements and online, full text access.

Subscriptions run on a volume basis, no cancellations. There is a three-months claim period: all replacement copies must be paid at the single issue rate of UK: £27/US & ROW: $50.

US Postmaster: Send address changes to World Net Shipping, c/o *Current Medical Research & Opinion*, 133 Doughty Blvd, Inwood, New York 11096.

Online Access for Libraries and Individuals: The journal is electronically published in full-text format, hosted by Ingenta Select (Electronic ISSN: 1473–4877). Access to the online, electronic service is provided free of charge to those libraries and subscribers who already receive the printed version of the journal. Instructions for doing this are provided on our website at: www.cmrojournal.com/subscribe. Other institutions and individuals may download full-text articles on a pay-per-view basis.

Publisher: LibraPharm Limited, 29–34 Venture West, New Greenham Park, Newbury, Berkshire RG19 6HX, UK.

Publishing Staff: *Group Publisher:* Peter L. Clarke, MA, PhD; *Publisher:* Stan Heimberger, PhD, MBA; *Managing Editor:* Piers R. Allen; *Editorial Coordinator:* Penny Bass; *Editorial and Production Manager:* Richard M. Powell; *Marketing Manager:* Jane F. Anthony; *Business Development Manager:* Adrian Reinhold; *Subscriptions and Distribution Manager:* Mary Jordan; *Administration/Website:* Liz Jones

Editorial Offices/Contributions: Editorial correspondence and manuscripts should be addressed to the most convenient *Editorial Office* as given below. For full details on how to prepare material for submission (including e-submissions), please refer to the latest published *Instructions for Authors* in the journal, consult the website at www.cmrojournal.com or contact:

Europe/ROW: Piers Allen, Managing Editor CMRO, LibraPharm Limited, 29–34 Venture West, New Greenham Park, Newbury, Berkshire RG19 6HX, UK (Tel: +44 (0)1635–522651; Fax: +44 (0) 1635–36294; email: pallen@cmrojournal.com)

North America: Stan Heimberger PhD, Publisher CMRO, 959 Dogwood Trail, Franklin Lakes, NJ 07417-1605, USA (Tel: +1 (201) 651 7601; Fax: +1 (201) 651 7602; email: sheimberger@cmrojournal.com)

CURRENT MEDICAL RESEARCH AND OPINION®
VOL. 20, NO. 5, 2004, 645–649

0300-7995
doi:10.1185/030079904125003575

BRIEF REVIEW

A review of the pathophysiology, prevention and treatment of irritant diaper dermatitis

David J. Atherton

Department of Paediatric Dermatology, Great Ormond Street Hospital for Children, London WC1N 3JH, UK

Address for correspondence: Dr David J. Atherton, Consultant and Honorary Senior Lecturer in Paediatric Dermatology, Great Ormond Street Hospital for Children, London WC1N 3JH, UK. Tel.: +44-20-7405-9200; Fax: +44-20-7813-8274; email: AtherD@gosh.nhs.uk

Key words: Baby – Barrier – Emollients – Irritant diaper dermatitis – Moisturisers – Nappy rash – Skin – Skin care – Stratum corneum

SUMMARY

Irritant diaper dermatitis (IDD) is a form of contact dermatitis occurring in the diaper area as a consequence of disruption of the barrier function of the skin through prolonged contact with faeces and urine. Despite advances in diaper technology, it is a condition that still occurs regularly in young children. To combat this, barrier preparations can be used to protect the skin by coating the surface of the skin and/or by supplying lipids that can penetrate the intercellular spaces of the stratum corneum. In this review, the pathophysiology of IDD is outlined and its prevention and treatment are discussed, with particular reference to the role of emollients.

Introduction

Although the introduction of absorbent gels in diapers has been associated with a marked reduction in the severity of irritant diaper dermatitis (IDD), this condition is still common, with a 1 in 4 likelihood of diagnosis in the at-risk age range of the paediatric population[1,2]. IDD does not usually develop immediately after birth; onset is generally between 3 weeks and 2 years of age, with prevalence highest between 9 and 12 months[3,4].

Pathophysiology of IDD

Irritant diaper dermatitis is a form of irritant contact dermatitis. It is the consequence of an interaction of several factors, not a reaction to a single irritant. The single most important factor in the provocation of IDD is prolonged contact of the skin with a mixture of urine and faeces.

The wearing of diapers causes a significant increase in skin wetness and pH[5]. Prolonged wetness leads to maceration (softening) of the stratum corneum, the outer, protective layer of the skin, which is associated with extensive disruption of intercellular lipid lamellae[6]. Weakening of its physical integrity makes the stratum corneum more susceptible to damage by (1) friction from the surface of the diaper, and (2) local irritants. The main irritants in this situation are faecal proteases and lipases[7], whose activity is increased greatly by elevated pH. An acidic skin surface is also essential for the maintenance of the normal microflora, which provide innate anti-microbial protection against invasion by pathogenic bacteria and yeasts[8,9]. Faecal lipase and protease activity is also greatly increased by acceleration of gastrointestinal transit; this is the reason for the high incidence of IDD observed in babies who have had diarrhoea in the previous 48 h[4].

The factors described above are now known to be critical in the development of IDD. Conversely, it has been established that other factors previously thought to be key to the development of IDD, such as ammonia, have lesser roles than were popularly assumed. *Candida albicans* can only be isolated from a minority of IDD cases[10]; in many cases this is a reflection of antibiotic therapy[11]. It has also been established that bacterial infection does not play a substantial part in the development of IDD[12].

The role of emollient formulations in the care of the diaper area

It is logical to assume that skincare routines are of fundamental importance in the prevention of IDD. There is, however, a dearth of controlled trial data to support any particular practice, and therefore the principles guiding good practice must be based mainly on a rational analysis of what we know of its aetiology.

A study in the early 1990s demonstrated that regular application of a water-in-oil emollient was associated with significantly less dermatitis in neonates, changing established perceptions regarding the prevention of IDD[13]. In the US, the Association of Women's Health, Obstetric and Neonatal Nurses and the National Association of Neonatal Nurses have developed guidelines for routine skincare. These recommend that babies should be bathed without soap and that a barrier ointment should be applied daily[14]. A subsequent study showed that when the guidelines were integrated into the skincare routines for babies in intensive care and special care, increased use of emollients and reduced use of soap led to a significant improvement in skin condition reflected by less visible dryness, redness and skin surface damage[15].

There is therefore an increasing recognition that gentle cleansing, good diaper practice and the regular application of a protective barrier are all essential elements in the prevention of IDD[8,16].

Emollients and Cleansing

It is clear that faeces should be removed from the skin as soon as possible after the diaper has been soiled. Since soap or lipid solvents will remove lipid from the stratum corneum, it seems logical to use water alone in this situation. The best of the fragrance- and alcohol-free modern baby wipes are also highly satisfactory for this purpose, having the additional advantage of very soft fabric to minimise friction.

It is generally believed to be beneficial, in addition, to bath babies once daily in water, using a water-dispersible cream as if it were soap. Suitable preparations include Aqueous cream BP, or proprietary creams such as Diprobase (Schering-Plough Ltd, UK) or Cetraben (Sankyo Pharma, UK).

Choice of Diaper

Ideally, good quality super-absorbent disposable diapers should be used. Compared with washable cloth diapers, these have been shown to be associated with a reduced incidence and decreased severity of IDD[3,17]. This benefit is likely to be attributable to urine being quickly absorbed into the diaper core, away from the skin, reducing both wetting of the skin and mixing of urine with faeces. There is a risk that this type of diaper will be left in place for too long. The diaper should be changed immediately following defaecation, and at reasonably frequent intervals in any case, depending on the age of the baby (and therefore the volume of urine passed at micturition).

Emollient and Barrier Formulations

The practice of applying barrier preparations in the diaper area has been established for many years. The purpose of such applications is to reduce friction, wetting and contact with urine and faeces.

It is now clear that the barrier function of the skin is provided by the stratum corneum, and that production of the stratum corneum is the main purpose of the epidermis[18]. The healthy stratum corneum is elastic and pliable; its foremost function is to minimise water loss and prevent the ingress of toxic substances and micro-organisms. Therefore, the principal functional effects of damage to the stratum corneum will be, firstly, an increase in the outward permeation of water, known as transepidermal water loss (TEWL), and secondly, an increase in the inward permeation of a wide variety of potentially harmful molecules and microbes.

'Barrier' preparations work in two ways, either by providing a lipid film over the surface of the skin and/or by providing lipids that can penetrate into the stratum corneum, simulating the effects of normal intercellular lipids[19]. Ideally, a barrier preparation will contain lipids that are similar to those naturally present in the stratum corneum, such as cholesterol, free fatty acids and ceramides[20]. A barrier preparation may be used either to reinforce normal skin whose stratum corneum is under stress from outside and is, therefore, at risk of damage, or in an attempt to restore the function of an already damaged stratum corneum.

It follows that the ideal barrier preparation will form a durable and long-lasting lipid shield which protects the skin from irritants and micro-organisms while preventing excessive water loss. While fulfilling these functions, it is important that optimal moisture levels within the

epidermis and stratum corneum are not exceeded. As discussed above, excessive water retention causes maceration, which makes the stratum corneum vulnerable to mechanical trauma. Furthermore, it has been demonstrated that, following barrier perturbation, complete occlusion can prevent the synthesis of epidermal lipids[21]. Therefore, formulation of barrier preparations must aim to maintain TEWL as near to normal as possible.

Treatment of Established IDD

Once IDD has developed, there are two goals of treatment: (1) to facilitate the repair of damaged skin and (2) to prevent recurrence. Prevention and treatment comprise essentially the same actions[22]. Good routine skincare should be implemented, with frequent diaper changes, gentle cleansing and regular use of a barrier preparation. It has been shown that the application of a barrier ointment at every diaper change is a valuable component of IDD therapy[16]. Topical steroid therapy is generally effective, but caution is required as babies percutaneously absorb proportionately greater quantities of topical medication than adults[23]. It should, therefore, be reserved for use where the condition is of a more severe degree and, in any case, nothing stronger than 1% hydrocortisone should be used. Antifungal therapy should not be used routinely, only when *Candida* infection is established or suspected. Similarly, antibacterial agents should not be used, as it is known that bacterial infection does not have a role in IDD, and the normal microflora should be preserved[12].

Selecting a barrier preparation for IDD management

In many countries, pastes have been a popular class of formulation for IDD, containing a high proportion (at least 10%) of finely powdered material such as zinc oxide or titanium dioxide, suspended in a water-in-oil (lipophilic) or an oil-in-water (hydrophilic) vehicle. Whereas all pastes were traditionally believed to be able to dry the skin, it is now known that lipophilic pastes cannot absorb water, and are in practice highly occlusive[24]. Conversely, hydrophilic pastes are able to take up certain amounts of water[24], but will not be as effective as a barrier[19]. In general, water-in-oil formulations, with a lipid content ≥ 50%, provide a superior moisture barrier than lighter oil-in-water products[19]. For this reason, ointments are generally more effective than creams and lotions[25].

When considering what would constitute the ideal everyday barrier preparation, one needs to consider the relevance, tolerability and safety of constituents other than the lipids alone. Every ingredient should have a rationale for its inclusion. Thus, antifungal and antibacterial agents should not be included due to the absence of data establishing the need for them. There should be no ingredient that is known to be toxic or that does not have a documented safety record. This concern has been voiced by US paediatric specialists, owing to the lack of regulations governing the disclosure of information about topical products[20,25]. If possible, a preservative should not be included; the greater the lipid content, the less likely a preservative will be required. Thus, a preservative is always required in creams and lotions, but not in ointments.

Healthcare professionals have indicated unease over the widespread use of manufactured baby skincare products which are promoted as especially suitable for babies' skin, but actually include ingredients that are potentially allergenic[26]. For this reason, non-essential ingredients such as perfumes should be omitted, since they are strongly associated with allergic contact sensitization[27]. Also, ideally, the safety and effectiveness of a barrier preparation in IDD should be clinically proven.

Currently, a wide range of products is available to prevent and treat IDD, yet few fulfil all the criteria proposed above. Zinc or titanium oxide-containing preparations are commonly used to prevent and treat IDD. However, as we have discussed, hydrophilic paste formulations do not provide a very effective barrier and are generally unsuitable for daily use in a preventive role. On the other hand, lipophilic formulations containing zinc or titanium oxides will be reasonable barriers, but are very difficult to remove; this can result in frictional damage to the skin when attempts to remove them are over-vigorous.

Talcum powder offers no protection to the skin, since it does not form a continuous lipid barrier layer over the skin. It is also extremely abrasive, and its routine use in the skincare of infants may be hazardous[28].

White soft paraffin BP is regularly used by healthcare professionals to protect the skin. It is, however, exceptionally occlusive when compared with other emollients and is, therefore, less than ideal for continuous use[29], since complete occlusion can prevent the recovery of damaged stratum corneum[21]. However, the regular use of white soft paraffin on babies' skin for the prevention and treatment of IDD has not been evaluated.

Some commercially available barrier preparations that are promoted for use in preventing and treating IDD contain an antiseptic, which is not necessary or desirable. These preparations often also contain cosmetic ingredients such as fragrance and colouring, which have no therapeutic or prophylactic value. It has been suggested that, in practice, products are often chosen by the consumer with less regard for efficacy than for the way they are marketed[30]. This is perhaps unsurprising in view of the paucity of clinical data for most IDD products. Similarly, there are no clinical trial

data to support the use of a variety of other commercial preparations for the prevention and treatment of IDD, including several branded products.

Clinical data are available for some barrier emollients that can be used to prevent and treat IDD. The adoption of a skincare regimen in which there was increased use of emollients has been shown to improve skin condition[15]. Furthermore, in premature infants (who demonstrate increased TEWL compared with full-term babies), topical ointment therapy significantly improved skin condition scores[31].

A clinical study has shown that, compared with vehicle control, topical application of dexpanthenol significantly decreases TEWL and increases the hydration of the stratum corneum[32]. It has been demonstrated in two clinical trials that an ointment containing dexpanthenol, Bepanthen Ointment (Roche Consumer Health, UK), can help prevent and treat IDD[16]. This formulation also contains lanolin, which is one of the most physiological emollient constituents currently available, containing many of the lipid groups present in the human stratum corneum, and having the advantage of permitting water exchange[33]. This product, which has been in use for many years in other European countries, has recently become available in the UK.

Conclusions

Positive action should be taken to prevent IDD. This should comprise gentle cleansing, careful diaper selection, changing the diaper as soon as possible after defaecation, and application of a barrier preparation at every change. The barrier preparation should mimic the skin's natural function by forming a long-lasting barrier to increase protection against irritants and micro-organisms, and to maintain optimum moisture levels within the stratum corneum. Ideally, the promotion and use of such products should be supported by evaluation in appropriately controlled clinical trials. Treatment of IDD comprises essentially the same elements as prevention, with topical steroids and antifungal therapies used for more severe cases which have proven refractory to simpler treatment approaches. It is hoped that, by improving routine skincare of the diaper area in hospitals and at home, the incidence and severity of IDD will be reduced.

Acknowledgements

The author acknowledges Dr Linda Landells for editorial assistance and Roche Consumer Health for support in the preparation of this manuscript.

References

1. Odio M, Friedlander SF, Railan D, et al. Diaper dermatitis and advances in diaper technology. Curr Opin Pediatr 2000;12(4):342-6
2. Ward DB, Fleischer Jr. AB, Feldman SR, Krowchuk DP. Characterization of diaper dermatitis in the United States. Arch Pediatr Adolesc Med 2000;154(9):943-6
3. Jordan WE, Lawson KD, Berg RW, Franxman JJ, Marrer AM. Diaper dermatitis: frequency and severity among a general infant population. Pediatr Dermatol 1986;3(3):198-207
4. Benjamin L. Clinical correlates with diaper dermatitis. Pediatrician 1987;14(Suppl 1):21-6
5. Berg RW, Milligan MC, Sarbaugh FC. Association of skin wetness and pH with diaper dermatitis. Pediatr Dermatol 1994;11(8):18-20
6. Warner RR, Stone KJ, Boissy YL. Hydration disrupts stratum corneum ultrastructure. J Invest Dermatol 2003;120(2):275-84
7. Berg RW, Buckingham KW, Stewart RL. Etiologic factors in diaper dermatitis: the role of urine. Pediatr Dermatol 1986;3(2):102-6
8. Lund C, Kuller J, Lane A, Lott JW, Raines DA. Neonatal skin care: the scientific basis for practice. J Obstet Gynecol Neonatal Nurs 1999;28(3):241-54
9. Fluhr JW, Elias PM. Stratum corneum pH: formation and function of the 'acid mantle'. Exog Dermatol 2002;1:163-75
10. Concannon P, Gisoldi E, Phillips S, Grossman R. Diaper dermatitis: a therapeutic dilemma. Results of a double-blind placebo controlled trial of miconazole nitrate 0.25%. Pediatr Dermatol 2001;18(2):149-55
11. Honig PJ, Gribetz B, Leyden JJ, McGinley KJ, Burke LA. Amoxicillin and diaper dermatitis. J Am Acad Dermatol 1988;19(2 Pt 1):275-9
12. Lund C. Prevention and management of infant skin breakdown. Nurs Clin North Am 1999;34(4):907-20, vii
13. Lane AT, Drost SS. Effects of repeated application of emollient cream to premature neonates' skin. Pediatrics 1993;92(3):415-9
14. Lund CH, Kuller J, Lane AT, Lott JW, Raines DA, Thomas KK. Neonatal skin care: evaluation of the AWHONN/NANN research-based practice project on knowledge and skin care practices. [Association of Women's Health, Obstetric and Neonatal Nurses/National Association of Neonatal Nurses]. J Obstet Gynecol Neonatal Nurs 2001;30(1):30-40
15. Lund CH, Osborne JW, Kuller J, Lane AT, Lott JW, Raines DA. 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(1):41-51
16. Putet G, Guy B, Andres P, Sirvent A, De Bony R, Girard F. Effect of Bepanthen ointment in the prevention and treatment of diaper rash on premature and full-term babies. Réalités Pédiatriques 2001;63:33-8
17. Lane AT, Rehder PA, Helm K. Evaluations of diapers containing absorbent gelling material with conventional disposable diapers in newborn infants. Am J Dis Child 1990;144(3):315-8
18. Madison KC. Barrier function of the skin: 'la raison d'être' of the epidermis. J Invest Dermatol 2003;121:231-41
19. Clark C, Hoare C. Making the most of emollients. Pharm J 2001;266:227-9
20. Darmstadt GL, Dinulos JG. Neonatal skin care. Pediatr Clin North Am 2000;47(4):757-82
21. Grubauer G, Elias PM, Feingold KR. Transepidermal water loss: the signal for recovery of barrier structure and function. J Lipid Res 1989;30:323-33
22. Atherton DJ. The aetiology and management of irritant diaper dermatitis. J Eur Acad Dermatol Venereol 2001;15(Suppl 1):1-4
23. West DP, Worobec S, Solomon LM. Pharmacology and toxicology of infant skin. J Invest Dermatol 1981;76(3):147-50
24. Juch RD, Rufli T, Surber C. Pastes: what do they contain? How do they work? Dermatology 1994;189:373-7
25. Siegfried EC. Neonatal skin care and toxicology. In: Eichenfield LF, Frieden IJ, Esterly NB, editors. Textbook of neonatal dermatology. Pennsylvania: W.B. Saunders Company; 2001. p. 62-71
26. Trotter S. Skincare for the newborn: exploring the potential harm of manufactured products. RCM Midwives J 2002;5(11):376-8

27. de Groot AC, Frosch PJ. Adverse reactions to fragrances. A clinical review. Contact Dermatitis 1997;36(2):57-86
28. Reynolds JEF, editor. Dermatological agents. In: Martindale. The extra pharmacopoeia, 31st ed. London: Royal Pharmaceutical Society; 1996. p. 1096
29. Morrison DS. Petrolatum. In: Loden M, Maibach HI, editors. Dry skin and moisturizers. Boca Raton: CRC Press; 2000. p. 251-7
30. Siegfried EC, Shah PY. Skin care practices in the neonatal nursery: a clinical survey. J Perinatol 1999;19(1):31-9
31. Nopper AJ, Horii KA, Sookdeo-Drost S, Wang TH, Mancini AJ, Lane AT. Topical ointment therapy benefits premature infants. J Pediatr 1996;128(5 Pt 1):660-9
32. 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(7):659-63
33. Orr S. A brief guide to lanolin technology and applications. Lipid Technol 1998;10(1):10-4

CrossRef links are available in the online published version of this paper:
http://www.cmrojournal.com
Paper CMRO-2503, *Accepted for publication*: 04 March 2004
Published Online: 22 March 2004
doi:10.1185/030079904125003575

CURRENT
MEDICAL RESEARCH
and Opinion®

LibraPharm

094-004J_2503_Atherton_NN