Sri Lanka College of Dermatologists (SLCD) Oration – 2009

Current management strategies of atopic dermatitis in children

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It is a great honour and a privilege to deliver the oration of the Sri Lanka College of Dermatologists this year and I thank the president and council for according me the honour.

It is now nearly 24 years since I entered the folds of dermatology. I am honoured by the presence of my first teacher of dermatology Dr. W. D. H. Perera in the audience this evening.

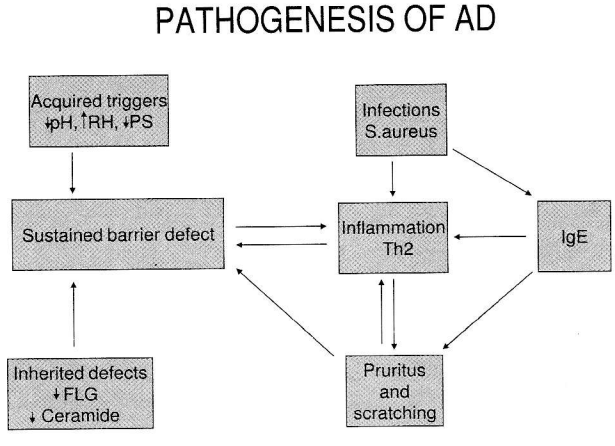
Since my Board certification as a specialist in 1992, I have mainly worked in rural Sri Lanka. Thanks to the untiring efforts of Dr. D. N. Atukorale, a full time post of a paediatric dermatologist was advertised in the year 2001 at the Lady Ridgeway Hospital for Children.

It is with gratitude I note his presence in the audience today. This is the largest children's hospital in the world with more than one thousand beds and is also a tertiary referral center for general paediatrics and its specialties. Initially I was reluctant to apply for the new post, as my experience in paediatrics was limited. However I took up the challenge and time will prove the wisdom of this decision. Dermatology clinics are held daily and on average 200 children attend the clinic. After I assumed duties, among the multitude of issues, I had to deal with atopic dermatitis, which was one of the most demanding and challenging problems. This made me develop a special interest in the subject.

The word atopy is derived from the Greek word '*atopos*' meaning 'strange'. One might argue that the meaning is applicable even today, as there are many unresolved issues pertaining to this condition. In developed countries, the incidence and prevalence of the disease is increasing. In Sri Lanka too, there appears to be an increase in the incidence especially in the urban sector. A recent study done by us revealed atopic dermatitis to be the commonest cause of clinic attendance at the Children's Hospital.

The presenting features of the illness depend on the age of the child and the duration of the illness. I will now briefly present my experiences of cutaneous manifestations of atopic dermatitis in children, depicting the usual features, the unusual features and the rare associations. This strange illness often starts from the face in early infancy and localizes to the flexures as the child grows. Follicular lesions are often seen in the Indian subcontinent and lichenification denotes chronicity. Unusual presentations include inflammation of the salmon patch, photolocalisation and linear lesions. Atopic dermatitis is a known presentation of many primary immunodeficiency syndromes.

These include Wiskott Aldrich syndrome, hyper IgE syndrome chronic granulomatous disease of childhood and ataxia telangiectasia. Over the years these are some of the issues that I had to face during my work at the Children's Hospital. Even more daunting was their management. This made me realize the importance of and the need for a scientific, evidence based approach, the basis of which I feel, should be the pathogenesis.



It is this evidence based approach along with my experiences that I wish to share with you in the next half an hour or so.

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Atopic dermatitis was known to be an inflammatory disease for a long time. As the condition was topical steroid responsive there was proliferation and over utilization of these products driven by the marketing efforts of the pharmaceutical industry. Pruritus is a major diagnostic feature and a troublesome aspect of the disease.

A tendency to develop secondary infections is also known. Raised levels of immunoglobulin E contribute to the inflammation by mast cell activation. Recent work indicates that the primary defect is in the stratum corneum permeability barrier.

This is made worse by environmental triggers such as alkalinity and low humidity. Known inherited abnormalities include ceramide deficiency and reduced filaggrin expression. As you would now realize, permeability barrier depends on stratum corneum hydration, which in turn depends mainly on the ceramides and fillagrin expression.

It has been shown that both ceramide deficiency and reduced fillaggrin expression contribute to the barrier defect in atopic dermatitis. The barrier defect in atopic dermatitis leads to the entry of antigens and also activates the cytokine cascade, initiating inflammation. The dermal inflammation in turn worsens the barrier defect. Thus, a sustained barrier defect leads to an ever worsening state of inflammation. This is the current "outside-inside-outside" hypothesis of atopic dermatitis. The evidence for a barrier defect in atopic dermatitis is overwhelming. The extent of barrier defect runs parallel to the severity of clinical disease. The ordinary emollients, which temporarily correct the barrier abnormality, are known effective forms of therapy. Specific repair therapy is claimed to be extremely effective, although I claim no experience with this treatment.

Let me now discuss the principles of management I use, and relate them to the underlying the pathogenesis. If the primary event in atopic dermatitis is a barrier defect, then it is rational to protect the existing barrier and if possible to improve its function and perhaps repair it therapeutically. The other pathogenic mechanisms such as, inflammation, pruritus and secondary infections should also be addressed in a similar manner. Childhood is a state of growth and development. In dealing with a chronic catabolic state like atopic dermatitis in children, it is crucial to maintain adequate nutrition. To suit individual patients and to overcome practical problems these principles can be used as different strategies.

In implementing them, approaches should be adopted to achieve adherence and compliance. Next, I will address each strategy giving the details of the practical application in patient care. The first strategy is barrier related. Barrier related management strategies are based on barrier protection, enhancement and repair. Over the years I have realized the value of simple measures like bathing, avoidance of triggers and use of emollients, to mention a few. Bathing at least once a day with 1% cetrimide lotion as shampoo and aqueous cream as soap is often adequate. Bathing a child with atopic dermatitis has many benefits.

Personally, I feel bathing to be a continuation of the aqueous environment in which the foetal skin developed. It is my view that that when this is disrupted in the setting of inherited defects of the barrier function, repeated external barrier insults possibly lead to a barrier failure and to the onset of atopic dermatitis in early infancy. In a recent study of hundred patients with atopic dermatitis, we found it to affect mainly urban children, with an average age of onset of 3 months and a strong family history of atopy. Analysis of the bathing patterns revealed that a delay in having the first bath was linked to an earlier onset of the disease.

On follow up it was found that not bathing even for a day was linked to an acute flare of the disease. The majority of mothers could give no particular reason for not bathing the baby after birth. It was surprising that I was unable to find a single publication or previous work on the bathing patterns in atopic dermatitis. Emollients are accepted as a safe form of therapy for atopic dermatitis, with many benefits. Aqueous cream is less greasy and well accepted and is my personal emollient of choice. Research too has shown that increased doses of emollients have lead to a dramatic decline in the severity of atopic dermatitis. It is my experience that many an item of clothing can act as a trigger. I advise parents to use loose fitting cotton clothes and to avoid detergents when washing clothes.

Barrier repair strategies using a combination of physiologic stratum corneum lipids are a novel rational therapeutic approach. A ceramide dominant barrier repair cream was recently approved by the FDA for atopic dermatitis. My personal experience of its use is very limited.

Now I come to the inflammation related management strategies. Before the discovery of a barrier defect in atopic dermatitis, use of potent topical steroids led to the development of systemic side effects. The possible explanation for this is the systemic absorption of the drug through the breached barrier more so than through intact skin. The use of barrier

related management strategies has partly helped me to overcome this problem. As shown by research topical steroids are known to delay barrier recovery. This made me adopt a new strategy in the use of topical steroids.

Based on this I now use them intermittently along with barrier based strategies. The potency of the topical steroid is determined by the age of the child, site of treatment and severity of the condition. In infants with moderately severe atopic dermatitis, my personal choice is fluticasone cream as it has been properly evaluated. Topical immunomodulators, such as calcineurin inhibitors are an accepted form of anti inflammatory therapy. I do not find them to be superior to topical steroids in efficacy. They are expensive, promote infections and their long term safety in children is not known. However, I prefer to use them when the eyelids are involved.

Under my care is a small group of growing children with severe atopic dermatitis, requiring systemic therapy. Some of them have sought alternative forms of medical therapy earlier on without any success. Any form of systemic therapy, I must admit, is bound to cause side effects. Systemic steroids are not recommended for long term use. Cyclosporin is my choice of systemic therapy. Used as short courses it is extremely effective, however I am yet to see their long term consequences.

Now I come to pruritus related management strategies. Itching is a devastating aspect of this strange illness. I have seen infants as young as two months attempting to scratch. In grown up children itching is often severe. They seem to be itch sensitized. Psychological stress is another cause for severe itching which disrupts the quality of life in the child and the family. Prolonged nocturnal pruritus is also linked to other psychological and medical problems. My approach to management of itching is to achieve disease control as soon as possible. For the majority of children, barrier based strategies, a topical steroid and a sedative antihistamine is often adequate. For infants bathing appears to be helpful.

Let me now address the management strategies for acute flares. Atopic dermatitis is, I would say, an unpredictable disease. Often children in whom we have gained good control turn up suddenly with an acute exacerbation. Presence of pus, pain, swelling or fever indicates active staphylococcal infection. Such patients require an oral anti-staphylococcal antibiotic. Antibiotic sensitivity pattern is essential in view of the emergence of community acquired methicillin resistant strains of *Staphylococus aureus*.

Often these children need hospitalization. When used fresh and in correct dilution, condys compresses are of use in infection related exacerbations. Sudden worsening with fever and a widespread monomorphic vesicular eruption often heralds the onset of eczema herpeticum. Such patients require oral aciclovir therapy. However, I have often failed to identify the primary source of infection.

Once the acute flare is controlled in mild to moderate atopic dermatitis, the aim is to maintain them disease free. This can be achieved by barrier based therapies and an occasional application of a topical steroid. The alternative strategy is to use topical calcineurin inhibitors with barrier repair therapy. This form of therapy is expensive.

Management of severe atopic dermatitis in children often requires a multidisciplinary approach.

Next is nutrition related management strategies. Normal childhood is a period of rapid growth. Atopic dermatitis on the other hand is a severe catabolic state. Dietary management in atopic dermatitis is to me one of the most controversial aspects of disease management.

Diet is not the cause of the disease. However a food item can be a known trigger. In my experience many a food item containing a good quality protein is avoided as 'heaty'. Often breast feeding mothers are not allowed to eat them. I have not observed a significant improvement of the disease in such circumstances.

Over the years, I had to manage a number of severely malnourished infants with severe atopic dermatitis. Their illness was characterized by early onset, severe disease, fair hair, fair complexion, peripheral oedema and hypoalbuminaemia. These infants were only breast fed and were managed with the greatest difficulty. It is my personal observation that the early use of fresh frozen plasma is life saving. I am happy to say that we managed to save most of them. However, the case fatality rate was 10%.

A study of 20 such patients was published in the *Sri Lanka Journal of Dermatology* by us in 2007. Managing these children, made me rethink the overall nutritional management of children with atopic dermatitis. An attempt should be made to maintain normal requirements whilst replacing the calorie and protein losses. Identifiable triggers can be removed and replaced with suitable alternatives.

My last management strategy is regarding parental education and compliance. In my experience the burden of managing a child with AD falls on a mother who has many other commitments. I find written

instructions to yield better compliance and patient outcomes than verbal instructions alone. In a study conducted by us I was happy to note some form of improvement in this aspect of management.

Ladies and gentleman, what I have presented so far is the approach, progress and development of what I practice today in managing children with atopic dermatitis. You will realize that some of the strategies are a direct application of knowledge from bench to bedside.

If I may summarize what I have presented so far, I would say modern management of atopic dermatitis in children should be based on its pathogenesis. Barrier related management strategies should play a vital role in all patients. For majority of patients' topical steroids are effective and safe in controlling inflammation when properly used.

Nutritional management is of vital importance in countries like Sri Lanka. When dealing with severe atopic dermatitis in children, a multidisciplinary approach should be adopted.

Over the years I have realized the benefits of early intervention in preventing the progression of disease, especially in infants. Too little too late is inadequate.

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