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# Atopic Dermatitis and Essential Fatty Acids: a Biochemical Basis for Atopy?

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The effects of dietary supplementation with evening primrose oil (Efamol®) in 99 patients with atopic dermatitis were investigated in a double blind, controlled crossover study. Simultaneously, plasma phospholipid essential fatty acid status was determined in 50 of these patients before and after treatment. In a separate study, lymphocyte subsets and mitogen responses were investigated in 15 atopic patients before and after treatment. The conclusion is that evening primrose oil improves atopic dermatitis; an abnormality of the enzyme delta-6-desaturase is proposed to explain the biochemical findings. Finally, it is concluded that the therapeutic effect of evening primrose oil is unlikely to be mediated through a primarily immunological mechanism. *Key words: Atopic dermatitis; Essential fatty acids; Evening primrose oil; Delta-6-desaturase; T lymphocytes.*

The possibility of exerting a therapeutic effect on atopic dermatitis (AD) through means of manipulation of the diet is a subject of increasing interest. Alteration of dietary lipid intake was considered by most investigators to be of definite therapeutic value (1–5) although investigation of this approach largely ceased with the introduction of topical corticosteroids. Equally, the potential therapeutic and/or prophylactic benefit of breast feeding in infants at risk of developing atopic dermatitis has been discussed at length, with the overall conclusion that breast feeding probably is of benefit in delaying the onset of the condition (6, 7). Hence the finding that oil pressed from the seeds of the evening primrose plant yields substantial quantities of an essential fatty acid otherwise found only in breast milk prompted us to investigate the therapeutic possibilities of dietary essential fatty acid (EFA) supplements again. The possible mode of action has also been investigated, and we here present our findings.

## CLINICAL INVESTIGATION

In the first two studies, 99 patients (60 adults, 39 children) with atopic eczema, as defined by the criteria of Hanifin & Rajka (8) were admitted to a double blind placebo controlled crossover study of the effects of different doses of evening primrose oil.

Clinical assessment of the condition was carried out at three–weekly intervals by patient and investigator (S. W.) on a 0–10 cm visual analogue scale for the symptoms of redness, scaling, pruritus and the overall impression of severity.

Evening primrose oil was administered in the form of Efamol®, which contains 8–9 % of gammalinolenic acid (18 : 3n6).

Adult patients were divided into three dose groups, receiving 2 g, 4 g or 6 g of evening primrose oil daily, while the two children groups received 1 or 2 g daily. Treatment and placebo periods were each twelve weeks.

Results for the two higher dose adult groups and the higher dose children group showed that evening primrose oil was significantly better than placebo for all symptoms except for

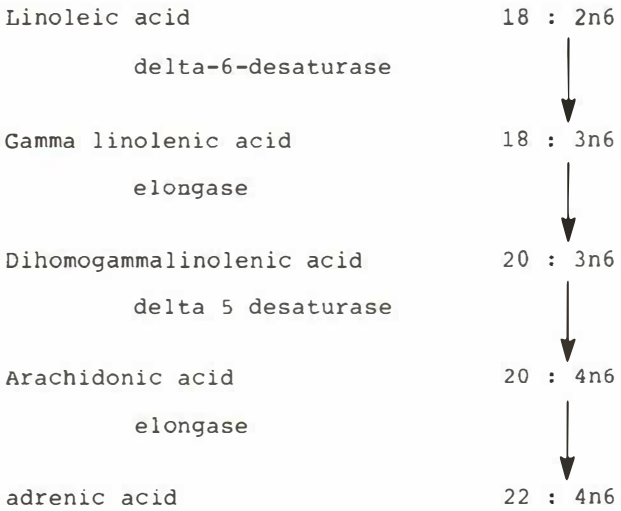


*Fig. 1.* The pathways of metabolism of the n6 essential fatty acids.

itch in the children group (9). There were no unwanted effects and all biochemical and haematological parameters measured throughout the trial remained normal.

The conclusion is that evening primrose oil in high dosage improves atopic dermatitis (9).

## BIOCHEMICAL INVESTIGATIONS

Paired sets of blood samples from the adult patients were available for the analysis of plasma phospholipid EFAs, in 50 patients. Analysis was by gas chromatography of the methyl-esters of the fatty acids and is described in detail elsewhere (10). Results show patients with AD to have high levels of linoleic acid (18 : 2n6) and low levels of its metabolites, dihomogammalinolenic acid (20 : 3n6) and arachidonic acid (20 : 4n6). These abnormalities were partially corrected by evening primrose oil. The conclusion is that patients with AD have defective function of the enzyme responsible for de-saturating linoleic acid, delta-6-desaturase (see Fig. 1).

Table I. *Absolute numbers and percentage of T lymphocytes and T lymphocyte subpopulations in patients with atopic eczema*

| | Before EPO | | After EPO | | Control | |
|---|---|---|---|---|---|---|
| | Absolute number (x $10^9$/titre) | Percentage | Absolute number (x $10^9$/titre) | Percentage | Absolute number | Percentage |
| OKT3 | 1.54±0.46 | 76.7±6.5 | 1.55±0.5 | 77.0±5.7 | 1.49±0.6 | 71.8±6.8 |
| OKT4 | 1.08±0.28 | 53.8±9.3[a] | 1.07±0.4 | 52.4±7.6 | 1.0±0.4 | 47.7±7.3 |
| OKT8 | 0.45±0.19 | 22.5±8.3 | 0.46±0.1 | 23.7±5.0 | 0.49±0.2 | 24.5±5.0 |
| OKT4 OKT8 | | 2.93±1.5 | | 2.35±0.7[b] | | 2.1±0.6 |
| B cells | 0.07±0.05[a] | 3.4±1.7 | 0.08±0.04 | 4.07±1.7 | 0.18±0.07 | 7±2.2 |

[a] Different from control, $p<0.05$.
[b] Different from before treatment, $p<0.05$.

## IMMUNOLOGICAL INVESTIGATIONS

The T cell subpopulations and proliferative responses to phytohaemagglutinin were investigated in 15 patients with AD before and after 6 weeks treatment with evening primrose oil. Mitogen responses were assessed using a microculture technique in inverted Terasaki plates described elsewhere (11) and T cell subsets assessed using the OKT series of monoclonal antibodies. Results are shown in Fig. 2. Overall, the helper/suppressor ratio fell as a result both of a rise in suppressor cells and a fall in helper cells. Mitogen responses showed no change overall, but could be divided into two groups, one of which showed falling responses with a falling helper/suppressor ratio, while the other showed rising responses with a rising helper/suppressor ratio. There was no relationship between changes in immune status and clinical response, the latter being almost uniformly good.

## DISCUSSION

Essential fatty acids have two main physiological roles. The first is as precursors of prostaglandin formation, where arachidonic acid is the substrate for the formation of Prostaglandin $E_2$ and dihomogammalinolenic acid acts as the substrate for Prostaglandin $E_1$ formation. Both of these may have profound effects on cellular interactions. Secondly, essential fatty acids are of major structural importance in cell membranes, being largely responsible for the maintenance of normal membrane fluidity, and also for the normal function of membrane bound enzymes. Our demonstration of an abnormal plasma phospholipid essential fatty acid profile suggests that either of these mechanisms could be involved, although our immunological work makes it unlikely that evening primrose oil exerts its therapeutic effect through a primarily immunological mechanism. Further studies on the essential fatty acid status of patients with atopic dermatitis are currently under way, but our proposal of defective function of the enzyme delta-6-desaturase suggests a biochemical basis to some of the clinical manifestations of atopic dermatitis.

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