

N-3 polyunsaturated fatty acids and allergic disease

Current Opinion in Clinical Nutrition and Metabolic Care

Volume 7(2) March 2004 pp 123-129

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Abbreviations

DHA: docosahexaenoic acid

EPA: eicosapentaenoic acid

PGE2: prostaglandin E2

PUFA: polyunsaturated fatty

Th: T helper

FROM ABSTRACT:

Purpose of review:

With escalating rates of allergic disease, it is vital to explore novel causal pathways.

This review examines the evidence for a potential role of changing dietary intake of n-3 polyunsaturated fatty acids in the development, treatment and prevention of allergic diseases.

Recent findings:

Although it is difficult to determine the contribution of altered (decreased) dietary intake of n-3 polyunsaturated fatty acids to the recent rise in the incidence of allergic disease, there is growing evidence that these nutrients have antiinflammatory properties and may modulate immune responses.

These fatty acids have few side effects, and may be of some benefit in established allergic diseases (such as asthma and atopic dermatitis), although these effects are not strong.

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Because of this limited efficacy in established disease, the focus has shifted to the potential benefits of these immune modulators in earlier life for disease prevention.

Two recent preliminary reports in infants suggest that dietary n-3 polyunsaturated fatty acid supplements in pregnancy or in the early postnatal period could have immunomodulatory properties and associated clinical effects.

Summary:

Dietary factors are important but still under-explored candidates in the search for environmental strategies to reduce the enormous impact of allergic diseases in modernized societies.

There is an ongoing need for further research into the role of n-3 polyunsaturated fatty acids in allergic disease, particularly in early life before atopy is established.

THESE AUTHORS ALSO NOTE:

³While the growing burden of allergic diseases (asthma, allergic rhinitis, food allergies, atopic dermatitis) has been apparent in Westernized countries for the last few decades, there is now mounting concern that billions of people will be affected as developing countries begin to show the same trends.² [WOW!]

³Environmental changes must be responsible for the recent epidemic rise in allergic disease with progressive Westernization.²

³Environmental factors may also provide feasible and relatively noninvasive avenues for modifying or preventing the processes that lead to allergic disease.²

Allergy prevention strategies that have focused on allergen avoidance in early life and have been particularly disappointing. [IMPORTANT]

Allergens are not responsible for the general increase in allergic propensity either at the individual or the society level.

³This suggests that other environmental changes are involved.²

³Modern diets differ in many respects from more traditional diets, with more complex, processed and synthetic foods and less fresh fish, fruits and

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vegetables.²

³One change that has been identified is increased consumption of n-6 polyunsaturated fatty acids (n-6 PUFAs) and decreased consumption of n-3 PUFAs (n-3 PUFAs).²

The interest in n-3 PUFAs is because there is an epidemiological decline in intakes of n-3 PUFAs and because n-3 PUFAs are anti-inflammatory.

IgE-mediated allergic diseases are inflammatory conditions.

It is clear that the initiating events that establish allergic disease occur early immune development.

Established allergic disease is the result of excessive and inappropriate type 2 T helper cell (Th2) responses to allergens.

Recent studies suggest that allergy affected individuals are more generally responsive to allergens with increases in both Th1 and Th2 responses.

The antiinflammatory n-3 fatty acids appear to be associated with suppression of both Th1 and Th2 cytokine responses.

³Dietary n-3 PUFAs have well documented immunoregulatory effects.²

³Previous attempts to explain the immunological effects of n-3 PUFAs have largely focused on the ability of these fatty acids to suppress the production of the inflammatory prostaglandin E2 (PGE2).²

³PGE2 is produced from the n-6 PUFA arachidonic acid by the action of cyclooxygenase-2.²

³When its intake is increased, the n-3 PUFA eicosapentaenoic acid (EPA) partly replaces arachidonic acid in the membranes of inflammatory cells. This means that less arachidonic acid is available for PGE2 production.²

³Furthermore, EPA and docosahexaenoic acid (DHA) inhibit cyclooxygenase-2 activity and decrease expression of the cyclooxygenase-2 gene. Thus, n-3 PUFAs decrease the production of PGE2 by inflammatory cells.²

PGE2 to suppress Th1 activity and increases Th2 activity, promoting IgE switching.

Therefore, n-3 PUFAs may counter the adverse Th1-Th2 balance in individuals with an allergic predisposition.

PGE2 also has some immunosuppressive effects.

³In addition to effects on production of prostaglandins, n-3 PUFAs can regulate T-cell function directly through effects on cell membrane fluidity and consequent cell signalling and gene transcription.² [IMPORTANT]

³The major dietary source of long-chain n-3 PUFAs is oily fish.²

³Over the last few decades there has been a relative decline in the consumption of these fatty acids and an increase in the consumption of the potentially more proinflammatory¹ n-6 PUFAs.²

³Associations between dietary exposures and immune development are of greatest interest in childhood when immune responses are developing.² [IMPORTANT]

One study showed that children who regularly consumed oily fish were 74% less likely to develop asthma. [Hodge L, Salome CM, Peat JK, et al. Consumption of oily fish and childhood asthma risk. Med J Aust 1996; 164:137-140].

³Allergic disease in childhood has also been associated with higher consumption of n-6 PUFAs (more margarine and less butter).²

Supplementation of the diet with fish oil results in decreased generation of inflammatory mediators.

Studies show that fish oil supplementation is associated with improved asthma symptom scores and reduced medication usage.

³It is possible that the immunomodulatory benefits of n-3 PUFAs may be greater during critical stages of early immune development before allergic

responses are established.²

Omega-3 PUFAs in pregnancy (3.7 g n-3 PUFAs/day from 20 weeks' gestation until delivery) have important positive effects on neonatal immune function.

Infants in the fish oil group were consistently less likely to develop clinical features including food allergy, recurrent wheeze, persistent cough, diagnosed asthma, angioedema, or anaphylaxis, compared with the control group.²

Earlier interventions (in utero v. starting at 6 months) could be more effective in preventing early sensitization (and possibly the processes which lead on to allergen sensitivity).

CONCLUSIONS

³The well described immunomodulatory effects of n-3 PUFAs (both in vitro and in vivo) highlight the potential role of these dietary factors in preventing and treating allergic disease.²

³These fatty acids can modify developing immune responses and disease expression in early life.²

KEY POINTS

- 1) Allergic disease rates are escalating in all countries that became Westernized, affecting billions of people.
- 2) Environmental changes are responsible the epidemic rise in allergic disease with progressive Westernization.
- 3) Omega-3 polyunsaturated fatty acids are anti-inflammatory.
- 4) Dietary n-3 PUFAs have important immunoregulatory effects.
- 5) The initiating events that establish allergic disease occur early immune development.
- 6) In utero and early postnatal exposure to n-3 polyunsaturated fatty acids have the greatest immunomodulatory effects and ability to reduce allergic diseases.
- 7) Allergy prevention by the avoidance allergens does not work because allergens are not responsible for the increase in allergic

propensity.

8) Modern diets contain increased n-6 polyunsaturated fatty acids and decreased n-3 PUFAs.

9) Established allergic disease is the result of excessive and inappropriate Th2 responses over the Th1 response (switching).

10) Omega-3 PUFAs can regulate T-cell function directly through effects on cell membrane fluidity, altering cytokine genetic expression.

11) The major dietary source of long-chain n-3 PUFAs is oily fish.

12) Allergic disease in childhood is associated with higher consumption of n-6 PUFAs (more margarine and less butter).

THIS MECHANISM IS PROPOSED:

A) PGE2 is produced from the n-6 PUFA arachidonic acid by the action of cyclooxygenase-2.

B) PGE2 to suppress Th1 activity and increases Th2 activity, which promotes IgE switching.

C) The n-3 PUFA eicosapentaenoic acid (EPA) partly replaces arachidonic acid in the membranes of inflammatory cells. This reduces the arachidonic acid available for PGE2 production.

D) Both EPA and docosahexaenoic acid (DHA) inhibit cyclooxygenase-2 activity and decrease expression of the cyclooxygenase-2 gene, decreasing the production of PGE2 by inflammatory cells.