

A LACK OF ESSENTIAL FATTY ACIDS AS A POSSIBLE CAUSE OF HYPERACTIVITY
IN CHILDREN

Irene Colquhoun and Sally Bunday, Hyperactive Children's Support Group,
59 Meadowside, Angmering, West Sussex, England.

ABSTRACT

The Hyperactive Children's Support Group (HCSG) is an organisation with over 70 branches in Britain devoted to helping such children and their families. We have carried out a detailed survey of the characteristics of many of our children and their families and have studied the literature in detail. We have come to the conclusion that many of these children have a deficiency of essential fatty acids (EFAs) either because they cannot metabolise linoleic acid normally, or because they cannot absorb EFAs normally from the gut, or because their EFA requirements are higher than normal. The main pieces of evidence are: 1. Most of the food constituents which cause trouble in these children are weak inhibitors of the conversion of EFAs to prostaglandins (PGs). 2. Boys are much more commonly affected than girls and males are known to have much higher requirements for EFAs than females. 3. A high proportion of our children have abnormal thirst and thirst is one of the cardinal signs of EFA deficiency. 4. Many of our children have eczema, allergies and asthma which some reports suggest can be alleviated by EFAs. 5. Many of our children are deficient in zinc which is required for conversion of EFAs to PGs. 6. Some of our children are badly affected by wheat and milk which are known to give rise to exorphins in the gut which can block conversion of EFAs to PGE1. A preliminary study of EFA supplementation in a number of our children has given promising results. We hope that others with better facilities will be encouraged to test out this hypothesis.

INTRODUCTION

Hyperactivity is a major problem. It goes under several names including hyperkinesis, minimal brain dysfunction and attention deficit disorder. We became interested in it because of family contact with a hyperactive child and we founded the support group (HCSG) in 1977. It has grown rapidly and now has over 70 groups in Britain. The Group is mainly made up of parents and other relatives of hyperactive children and enjoys the cooperation of many interested professionals. Our main functions are to provide information and support to families with hyperactive children and to look for the causes of and solutions to the problem.

We ourselves and many of our members have obtained dramatic benefit for our children by adherence to the diet developed by Dr Ben Feingold (1,2). However this is obviously not a complete answer and there are a number of problems associated with its use:

1. Normal children are not affected by the food additives and natural salicylates discussed by Feingold. This has been shown in uncontrolled studies (1) and also in a placebo-controlled challenge study (3). This must mean that the hyperactive children are different in some way from most children even before they are challenged by the additives and salicylates. Removal of the additives will not correct this underlying abnormality and we want to find out what the problem is.

2. Many children do not seem to be helped even by strict adherence to the diet or are helped only partially. We would like to be able to offer something other than drug therapy to these children. We suspect that some children may have the same sort of underlying abnormality as those who do respond to the Feingold regime but that it is even more severe and is obvious even without precipitation by additives or salicylates.

3. It is not easy to be totally consistent in sticking to the diet especially as a child gets older. Since even minor indiscretions can cause problems we would like to find some way of making hyperactive children less likely to be upset by occasional deviations from the diet such as are likely to occur at parties and on school outings.

We have therefore actively encouraged different lines of research and have carried out an in depth survey of all the characteristics of 214 of the children with whom we are in contact.

RESULTS OF THE HCSG SURVEY

The following are the most important findings:

1. At least half our children have shown a good response to the diet and more have shown a partial response. Like others we have found that foods containing synthetic colouring material such as tartrazine preservatives such as butylated hydroxytoluene and butylated hydroxyanisole (BHT and BHA), and foods containing natural salicylates are the main offenders.

2. Also like others we have found that many more boys than girls are affected. Of our 214 children, 161 were boys.

3. A range of minor and sometimes major health problems repeatedly recurred in about four fifths of our children. They included infantile colic, eczema, asthma, rhinitis and repeated chest and ear infections.

4. We took hair samples from 31 boys and 15 girls and had them analysed by Dr PJ Barlow of the Department of Environmental Health, University of Aston, Birmingham. 24 of 31 boys and 7 of 15 girls had zinc values below the normal range.

5. About four fifths of our children were consistently thirsty. This was particularly striking in families which contained normal children as well as a hyperactive one.

6. Some of our children who had not responded or who had responded only partially to the Feingold diet did respond to a regime which eliminated all milk and wheat products.

7. There was a striking preponderance of fair and ginger-haired children in the group.

Salicylates are known to block the formation of substances called prostaglandins (PGs) and Mrs Nim Barnes of Foresight suggested that we should show our findings to Dr David Horrobin in Montreal who had done work on PGs and mental illness (4,5). He pointed out that many of our observations were consistent with the idea that hyperactive children might be deficient in PGs, notably PGE1 which is formed from the EFA dihomogammalinolenic acid (DGLA).

COULD HYPERACTIVITY BE A PGE1 DEFICIENCY?

The evidence that there might be a deficiency of PGs and especially of PGE1 in hyperactive children is as follows:

1. The salicylates are known inhibitors of formation of PGs from EFAs. BHT and BHA although they do not appear to have been tested themselves are chemically closely related to substances which are known to block PG formation. Some years ago in work never published Dr Horrobin's research group happened to have studied the effects of two dyes, tartrazine and ponceau R, on PG formation. They found that they had a weak effect which was clear if only very small amounts of the EFA precursor were present but which was not apparent in the presence of large amounts of EFAs. Since normal children do not seem to be affected by additives this raises the possibility that normal children have adequate amounts of EFAs but that hyperactives are susceptible because their EFA levels are low.

2. Males require about three times as much EFA as females for normal development (6). This means that if the level of EFA in the body is marginal, a male is much more likely than a female to suffer adverse consequences. This could explain the sex difference in the risk of developing hyperactivity.

3. PGE1 seems important in the functioning of cells known as T lymphocytes which are important in resisting infections and in the maintenance of a normal immune system (7,8). T lymphocytes seem to be defective in patients with asthma and eczema. EFAs may be of value in the treatment of eczema in children (9). A lack of PGE1 might lead to problems in the immune system and to the recurrent infections, asthma and eczema which seem so common in our children.

4. Zinc seems important in the formation of PGs and in particular of PGE1 (10-12). A lack of zinc could thus lead to a lack of PGs because of a failure to metabolise normally the main dietary EFA, linoleic acid (12). Other factors known to be important in PG formation from EFAs are pyridoxine (vitamin B6), magnesium, niacin (vitamin B3) and ascorbic acid (7,8).

5. Gluten of wheat and alpha-casein of milk can both give rise to opioid-like peptides (exorphins) in the intestines (13). These exorphins can have effects similar to those of narcotic drugs. In most people they are rapidly digested and do not enter the body. However in people who are sensitive to wheat and milk it seems possible that part of the problem may be related to the entry of these exorphins into the blood (13). Opioids and opiates have been shown to block PGE1 formation from DGLA (8,14).

WHERE MIGHT THE DEFECT BE?

Since it is not uncommon for there to be only one hyperactive child in a family all eating much the same food. it seems unlikely that the main prob-

lem is a simple deficiency of dietary EFAs. There are at least three possible explanations:

1. Hyperactive children could have difficulty in absorbing EFAs from the intestine. A recent large scale study from the New York Institute for Child Development has indicated that hyperactive children may be unable to absorb carbohydrates normally (15). A problem in fat absorption would not therefore be surprising. A 1932 description of behaviour in children with coeliac disease who have a fat absorption problem could be one of the earlier descriptions of hyperactivity (16). "The behavior characteristics of these patients furnish a most interesting, if somewhat exasperating, subject for study...In their periods of improvement the subjects of coeliac disease are most attractive, although perhaps more easily moved to tears than a normal child, and usually somewhat spoiled; but in their diarrheal periods they are moody, irritable and passionate, and their tempers are as capricious as their appetites. Nothing pleases them and their misery reaches such a degree that they become a trial to those who have charge of them; one would not suppose them to be the same children who were previously so fascinating. When they are good, they are very good; but when they are bad, they are horrid. One writer said: Taken as a whole the coeliac child is an introspective, hysterical and unhappy child until proper treatment is adopted. In every way that a little child can become a source of misery to itself and to all round it, the coeliac child excels. It is so hysterical that no one knows if its complaints are true or false; it is so ill-humoured that it tries the most loving parent; it is so timid that it is a horror to its doctor; and yet withal it has well marked the bullying attributes of the invalid." Since an EFA deficiency itself leads to a defect in fat absorption which will exaggerate the deficiency (17), a vicious circle could result.

2. Hyperactive children might have some genetically based difference in metabolism which meant that they required much higher levels of EFAs than normal.

3. Hyperactive children might have some defect in EFA metabolism. Almost all the EFA in the diet is in the form of cis-linoleic acid. This must be converted first to gamma-linolenic acid (GLA) and then to DGLA before it reaches PGE1. The first step in this sequence, catalysed by the enzyme delta-6-desaturase seems to be vulnerable to blockade (18,19). In animals it matures after birth and if this were also true in humans, it is possible that the enzyme could mature in different children at different rates leading to problems in forming adequate amounts of GLA in some children but not in others. Human milk contains surprisingly large amounts of DGLA (20), so by-passing the potentially weak step and suggesting that this may indeed be a problem in humans. In children with eczema (which sometimes follows a switch from breast feeding to bottle feeding), evening primrose oil which contains GLA itself has recently been found effective (9). GLA is very rapidly converted to DGLA and 1g of the primrose oil contains an amount of GLA approximately equivalent to the DGLA consumed by a breast fed human infant in one day. The delta-6-desaturase seems to require zinc, magnesium and possibly pyridoxine for normal function (18,19,7,12). Moreover trans fatty acids which are produced during the processing of vegetable oils and which are abundant in foods of various sorts (21), including most "junk" foods, and in margerine (21) block the formation of GLA from linoleic acid. If hyperactive children had a genetic variation in the delta-6-desaturase which made it more susceptible to blockade, there are many features of a modern diet which might be associated with ineffective function of the enzyme.

PRELIMINARY HUMAN STUDIES

We decided to test the idea that EFA supplementation might help hyperactive children. We chose to give the children evening primrose oil (Efamol) because it is a uniquely rich source of EFAs and because it is the only readily available source of GLA. We gave 2 or 3g per day (half in the morning and half in the evening). In some children this was given by mouth and in some by rubbing it into the skin (EFAs are very rapidly absorbed from normal skin, particularly from soft areas such as the insides of the forearms, the thighs and the abdomen. About 25 children have now been tested and at least half have responded. In some, challenge with previously offending substances has produced no behavioural change. We recognise that this evidence is anecdotal but we are not in a position to carry out a formal trial. We hope that the evidence we have presented and the initial clinical results will lead to full scale controlled studies. Some case histories are presented below:

1. Steven R. A 6 year old boy with a characteristic history of hyperactivity, severely disturbed sleep and disruptive behaviour at home and at school. He had never been tried on a Feingold diet and his parents were at a loss as to what to do. The crisis came when he was threatened with expulsion from school because of impossible behaviour. His parents were given two weeks to improve matters. Desperate they contacted someone familiar with our work and primrose oil was suggested. Three capsules (1.5g) were cut open and the oil rubbed into the skin morning and evening. The school was unaware of this but after five days the teacher telephoned the mother and said that never in 30 years teaching had she seen such a dramatic change in a child's behaviour. After three weeks the evening primrose oil was stopped and one week later the school again complained. The oil was then reintroduced with good effect.

2. Donald J. A 6 year old boy who from childhood had had a disturbed sleep pattern. He was continually restless and had repeated stomach upsets. His concentration and speech were poor and he was abnormally thirsty. We was found to be sensitive to wheat products and on removing wheat from the diet he became a changed child with normal sleep, behaviour and speech. On trial introduction of wheat products he rapidly deteriorated, his pulse rate rose rapidly and his speech became almost incomprehensible. He was given each morning and evening by mouth 3 capsules of primrose oil and 3 tablets of a combined zinc, vitamin C, pyridoxine and niacin tablet (Efavit). After two weeks on this regime he was challenged with wheat and no behavioural reaction or change in pulse rate occurred. Over the next four weeks he was gradually introduced to a normal wheat-containing diet with no evidence of the previous abnormal reactions.

3. Charles B. An 11 year old boy with eczema, disordered sleep and severely disruptive behaviour which led to his expulsion from school. He responded moderately well to a Feingold diet together with a low dose of dexamphetamine. However he still had bouts of disruptive behaviour when he became unmanageable both at school and at home. He was given three capsules of primrose oil by mouth each morning and evening. His eczema improved and over a period of eight weeks he had no episodes of hyperactivity. This was particularly surprising since over Christmas he ate a number of normally "forbidden" foods without a reaction.

4. David K. A 20 year old boy with a history of disturbed sleep and behavi-

our right from birth. He developed eczema and asthma during childhood. He was given dexedrine and phenergan from ages 8 to 14. he had very serious problems in school between 14 and 16. At 16 he began to take a modified Feingold diet and progressively improved. He was given three capsules of evening primrose oil and three of Efavit morning and evening. His parents noted a rapid positive change with a more relaxed attitude to people and situations and more self-confidence.

5. Keith F. A 10 year old boy who was partially deaf from birth possibly due to rubella. He had a poor attention span, rocked himself to sleep, was impulsive, aggressive and uncooperative. He was attending a special school for the deaf and substantially improved on the Feingold diet. However he was still markedly hyperactive and rapidly deteriorated following even minor dietary indiscretions. He was given three capsules of evening primrose oil morning and evening, plus one multivitamin and one Efavit tablet each evening. His mother reported "his behaviour and attitude have shown tremendous improvement and he has been promoted to the top academic group in the school. This seems to be due to his vastly improved behaviour, his better attitude to his work and his newly acquired ability to concentrate to a far greater extent than previously."

These five children, each with a somewhat different problem, all seem to have responded well and are representative of the others. None have experienced any side effects due to the primrose oil although some have flushed following the niacin-containing tablets. On the other hand we must emphasise that some children do not appear to have responded and this approach can in no sense be regarded as a cure. However it does seem to be soundly based and to offer a completely new and safe approach to the problem. We believe that these children should continue to be managed using a Feingold type diet and we in no way condone the indiscriminate use of food additives, especially ones with "cosmetic" value only. However the EFAs may help children to withstand indiscretions and may help them to avoid the use of drugs. We hope that others will test this for themselves.

ACKNOWLEDGEMENTS

We thank Efamol Ltd, 40 Warton Road, London E15 2JU, England and Primrose Research Inc, Suite 10, 245 Victoria, Montreal H3Z 2M6, Canada for the supplies of Efamol and Efavit.

REFERENCES

1. Feingold BF. Why Your Child Is Hyperactive. Random House, New York, 1975.
2. Feingold BF. Dietary management of nystagmus. J Neural Transm 45: 107-115, 1979.
3. Swanson JM, Kinsbourne M. Food dyes impair performance of hyperactive children on a laboratory learning test. Science 207: 1485-7, 1980.
4. Horrobin DF. Schizophrenia: reconciliation of the dopamine, prostaglandin and opioid concepts and the role of the pineal. Lancet 1: 529-31, 1979.
5. Horrobin DF, Manku MS. Possible role of prostaglandin E1 in the affective disorders and in alcoholism. Br Med J 1: 1363-6, 1980.
6. Pudlakewicz C, Seufert J, Holman RT. Requirements of the female rat for

- linoleic and linolenic acids. *J Nutr* 64: 138, 1968.
7. Horrobin DF, Manku MS, Oka M et al. The nutritional regulation of T lymphocyte function. *Med Hypotheses* 5: 969-85, 1979.
 8. Horrobin DF. The regulation of prostaglandin biosynthesis: negative feedback mechanisms and the selective control of the formation of 1 and 2 series prostaglandins: relevance to inflammation and immunity. *Med Hypotheses* 6: 687-709, 1980.
 9. Lovell CR, Burton JL, Horrobin DF. Treatment of atopic eczema with evening primrose oil. *Lancet* 1: 278, 1981.
 10. Bettger WJ, Reeves PG, Moscatelli EA et al. Interaction of zinc and essential fatty acids in the rat. *J Nutr* 109: 480-8, 1979.
 11. Manku MS, Horrobin DF, Karmazyn M, Cunnane SC. Prolactin and zinc effects on rat vascular reactivity: possible relationship to dihomogammalinolenic acid and to prostaglandin synthesis. *Endocrinology* 104: 774-9, 1979.
 12. Horrobin DF, Cunnane SC. Interactions between zinc, essential fatty acids and prostaglandins: relevance to acrodermatitis enteropathica, total parenteral nutrition, the glucagonoma syndrome, diabetes, anorexia nervosa and sickle cell anaemia. *Med Hypotheses* 6: 277-96, 1980.
 13. Zioudrou C, Streaty RA, Klee WA. Opioid peptides derived from food proteins: the exorphins. *J Biol Chem* 254: 2446-9, 1979.
 14. Horrobin DF. Possible roles of prostaglandins in mediating opioid actions. In NS Shah and AG Donald (eds) *Endorphins*. New York, Plenum Press, in press.
 15. Langseth L, Dowd J. Glucose tolerance and hyperkinesis. *Food Cosmet Toxicol* 16: 129-33, 1978.
 16. Parsons LG. Celiac disease. *Am J Dis Child* 43: 1293-1346, 1932.
 17. Clark SB, Ekkers TE, Singh A et al. Fat absorption in essential fatty acid deficiency: a model experimental approach to studies of the mechanism of fat malabsorption of unknown etiology. *J Lipid Res* 14: 581-8, 1973.
 18. Brenner RR. Metabolism of endogenous substrates by microsomes. *Drug Metab Rev* 6: 155-212, 1977.
 19. Brenner RR. Nutritional and hormonal factors influencing desaturation of essential fatty acids. Golden Jubilee Congress on Essential Fatty Acids and Prostaglandins, Minneapolis, May 1980. *Progress Lipid Res* in press.
 20. Jensen RG, Clark RM, Ferris AM. Composition of the lipids in human milk: a review. *Lipids* 15: 345-355, 1980.
 21. Kummerow FA. Nutrition imbalance and angiotoxins as dietary risk factors in coronary heart disease. *Am J Clin Nutr* 32: 58-83, 1979.