The Management with a Low Oxalate Diet of Abdominal Migraine in Children

WITH A NOTE ON OXALATE METABOLISM

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SUMMARY

Thirty-one cases of abdominal migraine have been successfully managed on a low oxalate diet.

A suggestion has been put forward to account for some of the symptoms based on an enzyme deficiency of hereditary origin.

Further studies are necessary to decide whether ketosis does in fact precede the onset of vomiting and other symptoms, and whether there is a genetically-determined enzymatic fault.

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There is a contradiction in terms in naming this syndrome abdominal migraine in children, (also called cyclical vomiting, recurrent acidosis and the periodic syndrome), but the association with cephalic migraine in a parent is so strong that it suggests a dominant inheritance, and this was also the opinion of authors as far back as 1925.[1] In this series every patient had a parent with migraine, and there seems no reason to disagree with Graham[2] and Sacks[3] that the syndrome is migrainous.

On the other hand, the syndrome has been regarded as an epileptic equivalent,[4] and attention has been drawn to the role of tyramine in causing headaches.[5]

Down the years a dietetic cause has been suggested for the syndrome of migraine, both cephalic and abdominal. Success has been claimed for the abstraction of certain foods from the diet, for example, milk and chocolate, or even whole groups of foodstuffs, such as fats. However, the results have been conflicting, and the aetiology has not been determined.

In this article success is claimed for the management of 31 cases of abdominal migraine, with a low oxalate diet, and there is a note in addition on the management of 27 cases by treatment of the symptoms, and 9 cases of treatment on a low citrate diet, without consistent improvement. This makes 67 cases in all. Only 31 successfully treated cases will be dealt with in detail. This diet (Table I) has been based on the food tables in Geigy's Scientific Tables (6th ed., 1962, as modified in the 7th ed.,

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1970), and other tables.[6] Because of uncertainty as to the oxalate content of foods, there may be more prohibited items than necessary. However, with more facts available today, the diet in Table II is to be preferred, even though this may be incomplete.

TABLE I. DIET USED IN THIS SERIES

Section A. Fruit and foods in no circumstances to be taken, whether fresh, canned, or in jam, syrup, or beverage*

Apricots	Dandelion leaves	Chicory and endives
Blackberries	Parsley	Onions
Blueberries	Rhubarb	Peppers
Currants	Turnip tops	Spinach
Oranges	Gooseberries	Chocolate
Celery	Carrots	Cocoa
Beetroot	Plums	Tea

Section B. Fruit and foods which may be taken in small quantities†

Bananas	Potatoes	Brussel sprouts
Pears	Kohlrabi	Lettuce
Asparagus	Peaches	Tomatoes
Cabbage	Pineapples	

Section C. Ordinary foods to be taken freely

Meat	Cereals	Apples
Fish	Honey	Grapes
Eggs	Golden syrup	Bread
Milk—less than 500 ml daily	Peanuts	Sugar
Cheese	Lemons	Coffee

* Foods containing more than 10 mg oxalate/100 g.
† Foods cantaining less than 10 mg oxalate/100 g.

TABLE II. DIET AMENDED TO INCLUDE ALTERATIONS ARISING SINCE 1963

Section A. Fruit and foods in no circumstances to be taken, whether fresh, canned, or in jam, syrup, or beverage*

Raspberries	Carrots	Endives
Strawberries	Celery	Kale
Whortleberries	Rhubarb	Peppers
Blackberries	Parsley	Tea
Currants (red or white)	Spinach	Cocoa
Oranges	Cucumber	Coffee (Instant)
Beans	Turnip tops	Ovaltine
Beetroot	Sweet potatoes	
	Dandelion leaves	

Section B. Foods which may be taken in small quantities†

Tomatoes	Asparagus
Cake	Lettuce
Cornflakes	Maize
Bananas	Parsnips
Pineapples	Potatoes
Plums	

Section C. Ordinary foods to be taken freely

Meat	Cereals	Apples
Fish	Honey	Grapes
Eggs	Golden syrup	Bread
Milk—less than 500 ml daily	Peanuts	Sugar
Cheese	Lemons	Coffee

* Foods containing more than 10 mg oxalate/100 g.
† Foods containing 5 - 10 mg oxalate/100 g.

SELECTION OF CASES

The criteria for diagnosis in this series are those adopted by previous writers.[4,7-9]

In particular, Wyllie and Schlesinger[7] reported 80 cases, saying that the syndrome consists of attacks of headaches, vomiting, fever and abdominal pain. These attacks are repeated at irregular intervals and not all the symptoms are present in every case. They note also the presence of an aura of lassitude and malaise. Ketosis is also remarked upon as a feature, and they note that it is said to precede the vomiting. It has not been possible to confirm this in the present series, but Professor Ford[10] agrees that this is the case.

They note also the presence of a family history of migraine, which is more common on the mother's side. All the cases in this series have a history of migraine in a parent. In 19 cases it was the mother, in 10 the father, and in 2 cases both parents were affected.

To the symptomatic aurae which they observed, can be added pallor and dark rings under the eyes. In young children it is not easy to determine whether fortification spectra are seen, but 4 cases had photophobia with their attacks.

The attacks in this series usually occurred irregularly at 4- to 12-week intervals, between which the child was said to be quite well, although this aspect will be commented upon in considering the results of treatment.

CASES AND SYMPTOMS

Sex

There were 18 girls and 13 boys.

Age

The average age of onset in each group was 6 years, with a scatter of $2\frac{1}{2}$ - 8 years for the girls and $2\frac{1}{2}$ - 9 years for the boys.

Symptoms

The incidence of symptoms is recorded in Table III. No patient had abnormal physical signs. A few had, or had had, asthma, eczema, or other signs of allergy.

TABLE III. SYMPTOMS IN 31 CASES (18 GIRLS AND 13 BOYS)

	Girls	Boys
Vomiting	16	10
Abdominal pain	15	12
Headache	10	5
Fever	8	6
Photophobia	3	1

Nineteen children had mothers with migraine; 10 children had fathers with migraine; and 2 children had both parents with migraine.

RESULTS OF DIETETIC TREATMENT

The diet is recorded in Table II and was given to the parents when the diagnosis was made. It is never easy to determine whether in fact a diet is being adhered to, but it has been most encouraging to hear that the children are particularly careful in sticking to it. More than one parent reported that the children would correct them when they were about to introduce a forbidden item.

Three weeks after the initial consultation all patients were reviewed. This was too early to assess the effect of the diet on attacks, but all parents reported a marked change for the better in temperament and activity. It appears, therefore, that the symptomatic good health between attacks is relative, and the child is not completely well. It is also interesting to speculate on this psychological improvement in the light of the possible toxic effects of oxalate intolerance.

The effect of the diet on the attacks themselves was the same. The attacks were abolished or, if they occurred, were the result of eating a forbidden item of food.

The cases were reviewed again after 6 weeks and the items in Section B of the diet in Table I were restored. Thereafter items in Section A were restored individually, and after 3 months it was usually possible to restore the diet practically to normal, the usual exceptions being chocolate and oranges. Follow-up questionnaires were answered by parents, and it appears that the original complaints had not recurred.

CHRONOLOGY OF RESEARCH

From 1956 - 1962, 27 cases of this syndrome were seen. Treatment varied and included chlorpromazine, glucose, miscellaneous dietetic restrictions, including citrus, pork, and chocolate. No particular success could be claimed.

From 1962 - 1963 a report of benefit from the deletion of citrus from the diet led to the construction of a low-citrate diet. Oranges were particularly implicated. Nine cases were so treated with variable results, and finally a serum citrate curve was constructed for a control and an affected subject without any difference (Fig. 1). From 1964 onwards the present diet (Table I) was developed with the results recorded above.

COMMENT

It will be seen from Table I that the high-oxalate foods are either expensive, or not usually eaten by children,

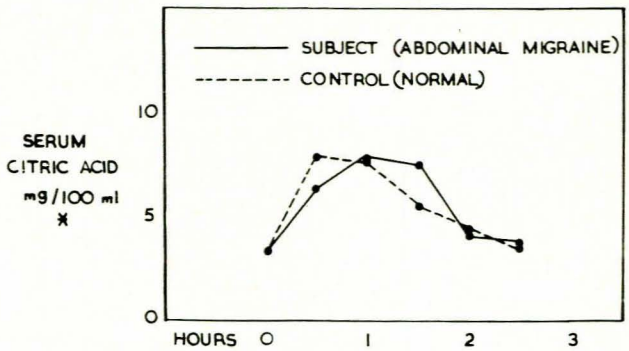

Fig. 1. Citrate tolerance test in 10-year-old males, given sodium citrate 0,5 g/kg body weight, after first blood samples.

which may account for the absence of the syndrome in low-income groups.[11]

OXALATE POISONING

Apart from the corrosive action of oxalic acid, the toxic effects of oxalate poisoning arise from the combination of oxalate with calcium and lead to tetany, weakness, and gastro-intestinal symptoms.[12] In industrial poisoning, renal injury may also occur.[13] To this may be added excruciating headaches and repeated spells of vomiting when oxalic acid is carried by steam.[14]

OXALOSIS

Oxalosis is a rare autosomal recessive disorder characterised by the excessive excretion of calcium oxalate leading to nephrolithiasis, nephrocalcinosis, anaemia, and deposits in the myocardium, with death at an early age if left untreated. It appears to be a defect of glycine metabolism rather than an excessive intake of oxalates.

NORMAL METABOLISM OF OXALATES

Studies made of normal subjects[15] on a fixed diet showed that 2% of the daily intake of oxalate was excreted in the urine. When sodium oxalate was given in a dose of 2,0 g daily, 2,3 - 4,5% of the total dose administered was excreted, and this returned promptly to basic levels when discontinued. These findings have been repeated in a study on myself (Fig. 2 and Table IV). Apart from malaise and a marked diuresis, no untoward symptoms were noted. No ketosis occurred.

VITAMINS

Seventy per cent of ascorbic acid, if given to man as carbon-labelled L-ascorbic acid, is excreted as oxalate.[16]

Experimentally-produced pyridoxine and pantothenic acid deficiency in man leads to oxaluria which may be aggravated by giving tryptophane.[17] In 1 case, epigastric pain, nausea and anorexia occurred.

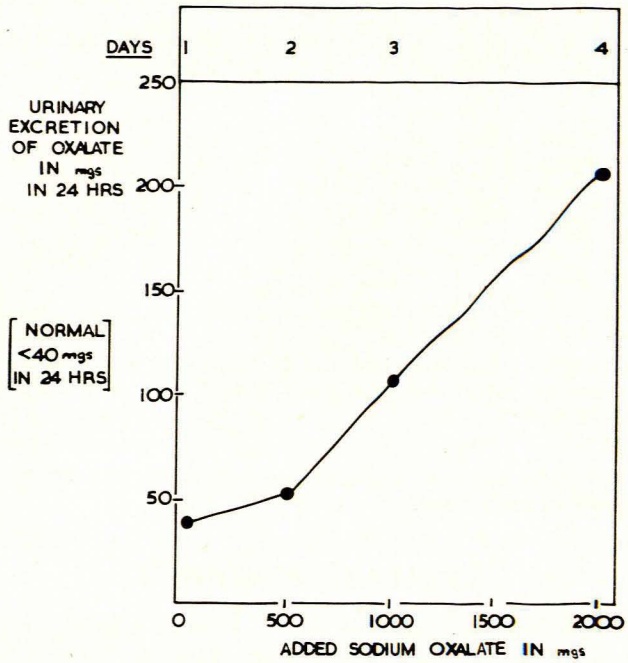

Fig. 2. Supplements of sodium oxalate given to a non-migrainous 85 kg male volunteer on low oxalate diet.

TABLE IV. NON-MIGRAINOUS 85 kg MALE VOLUNTEER ON LOW OXALATE DIET

	Sodium oxalate			
Day	Intake (mg)	24-hour urine output (mg)	Urine volume (ml)	Ketonuria
1	**10**	**37,7**	**1 300**	**Nil**
2	**500**	**51,8**	**2 300**	**Nil**
3	**1 000**	**114,4**	**2 300**	**Nil**
4	**2 000**	**211,6**	**2 300**	**Nil**

HYPOTHESIS

The syndrome described appears to have an hereditary basis in that one parent (occasionally both) suffers from cephalic migraine. However, it is unusual to find a sibling so affected. Raine[18] does not include migraine in his list of inherited metabolic diseases.

Professor H. A. Krebs writes as follows:[19]

'Theoretically, it is feasible that oxalate causes ketosis by inhibiting succinate dehydrogenase in the liver. This would prevent the re-formation of oxaloacetate, and hence acetyl CoA gives ketone bodies instead of entering the cycle. In model experiments with liver homogenates one can, in fact, demonstrate this kind of ketogenic effect of oxalate. I doubt, however, whether this occurs *in vivo*. The quantities of oxalate required would be rather large. Nevertheless, it may be worth while carrying out animal experiments, and to test whether feeding oxalate in amounts that can be tolerated causes a rise in the ketone body concentration of the blood. The enzymatic methods now available for the determination of the ketone bodies make such experiments rather easy'.

However, if there were to be a genetically-determined shortage of succinate dehydrogenase or if the enzyme were to be altered so as to be unduly sensitive to oxalate, then relatively low doses of oxalate might produce a ketosis. That ketosis precedes the vomiting and other symptoms,[7,10] has already been mentioned. Varying degrees of genetically-determined enzyme deficiencies are not unknown.

The metabolism of oxalates has been discussed and it appears that ketosis in non-migrainous people does not follow the administration of oxalates in the doses recorded.

The question arises as to whether ketosis alone can produce the syndrome. The consequences of ketosis are noted[19] to be nausea and consequent emesis, with depression of the central nervous system. Ketones do not appear to be exceptionally toxic materials when injected intravenously into experimental animals. Nor do Johnson *et al.*[21] in their paper on ketosis after exercise record any unusual symptoms.

Whereas, therefore, the cyclical vomiting may be explained as a sequel to ketosis, it is not clear whether the headache and abdominal pain can be so explained. However, headache and vomiting are striking features of oxalic acid steam poisoning,[14] and it may be that metabolism in brain cells is disturbed in like manner when there is undue sensitivity to oxalates.

The periodicity of the syndrome is reminiscent of paroxysmal luetic cold haemoglobinuria, in which temporary exhaustion of complement nullifies the effect of cooling in producing haemoglobinuria. May this be an exhaustion of a co-enzyme system inhibiting the toxic action of oxalates in abdominal migraine?

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