yoga group to the regular practice of yoga. The considerable reduction in their drug treatment score in contrast with a non-significant increase in intake of drugs in the control group strengthens this view, as do the significant differences between the groups in the number of attacks per week and peak flow rate.

McFadden clearly showed that the responsiveness of airways is noticeably increased in patients with asthma, who develop bronchoconstriction in response to smaller quantities of physical, chemical, and pharmacological stimuli than healthy subjects.[10] A complex interplay of several factors—namely, an inherent responsiveness of the smooth muscle to stimuli, an abnormality in autonomic nervous control, and a breakdown in airway defences—may promote bronchial hyper-reactivity. Thus reducing the responsiveness of the tracheobronchial tree could benefit these patients considerably.

Abundant objective data now exist indicating that pyschological factors can interact with the asthmatic diathesis to worsen or improve the course of the disease. The mechanisms of these interactions are complex and not well understood, but psychological factors may affect about half of all patients. Modification of vagal efferent activity seems to affect the calibre of airways. It has been shown that suggestion can actually decrease or increase the effects of pharmacological stimuli on the airways. The role of the psychic factor in inducing or prolonging attacks in acute exacerbations may vary from patient to patient and in individual patients from episode to episode.

Goyeche *et al* claimed that the psychosomatic imbalance is present in many, if not all patients with asthma.[1] Suppressed emotion, anxiety, dependence, and extreme self consciousness may all be accompanied by generalised and localised muscle tension, including that of the voluntary respiratory musculature. This increased muscle tension may be a precipitating or concomitant factor that perpetuates and aggravates the asthmatic syndrome.

Yoga seems to stabilise and reduce the excitability of the nervous system. Transcendental meditation (a traditional yogic meditation technique) and Savasana have been clearly shown to be associated with reduced metabolic rate.[11] Crisan showed a significant reduction in the level of anxiety after the practice of Pranayama, as evidenced by increased skin resistance and a reduction in pulse rate, urinary catecholamine concentration, urinary cholinesterase activity, and anxiety scores.[12] Several workers have found an increase in alpha synchrony in electroencephalograms taken during transcendental meditation, which points to its stabilising effect on the nervous system. Yoga clearly relaxes the muscles, and this deep physical and mental relaxation associated with the physiological changes seen in our patients after daily yoga seems to have a stabilising effect on bronchial reactivity, thus making the vagal efferents less excitable.

In conclusion, the reduction in psychological hyper-reactivity and emotional instability achieved by yoga can reduce efferent vagal reactivity, which has been recognised as the mediator of the psychosomatic factor in asthma.

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Treatment of homozygous familial hypercholesterolaemia: an informative sibship

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Abstract

In a family in which both parents had the heterozygous form of familial hypercholesterolaemia four of the children had the homozygous form. The three oldest homozygous children, two of whom did not receive any treatment and in one of whom treatment did not lower the plasma cholesterol concentration, developed xanthomas in early childhood and died aged 3, 9, and 10 years. The fourth homozygous child was treated with diet and drugs from the age of 1 and at the age of 15 had no xanthomas, no clinical evidence of heart disease, and a virtually normal coronary angiogram. His plasma cholesterol concentration was reduced by about 30% but remained considerably raised.

It is concluded that treatment, if started before atherosclerosis develops, can delay the onset of atheroma and coronary heart disease even though normal plasma cholesterol concentrations are not achieved.

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Introduction

Familial hypercholesterolaemia is dominantly inherited, and heterozygotes have an increased risk of coronary heart disease in adult life. Homozygotes have extremely high plasma cholesterol concentrations and die of coronary heart disease in childhood or early adult life.[1] Treatment of homozygotes is difficult. Normal cholesterol concentrations are unlikely to be achieved, and uncertainty exists over whether coronary atherosclerosis can be prevented.[2,3]

We report on a family containing four siblings homozygous for the disease. The progress of the youngest contrasted with that of the other affected siblings, suggesting that prevention of atherosclerosis is possible.

Family history

PARENTS

Both parents were Asian and came from east Africa to live in England after the deaths of their first three children. At the age of 38 the father was asymptomatic and his plasma cholesterol concentration was 9·3 mmol/l (359 mg/100 ml). He was given only dietary advice. He had a myocardial infarction at the age of 54 and died two weeks later. The mother had a plasma cholesterol concentration of 8·8 mmol/l (339 mg/100 ml) at the age of 31. At age 48 it was 8·4 mmol/l (324 mg/100 ml) and treatment with cholestyramine was started. She remained asymptomatic.

THREE OLDEST CHILDREN

By the age of 3 the first child, a boy, had developed xanthomas (proved by biopsy) of skin and tendons, which became more extensive. By the age of 9 he had exertional dyspnoea, and at the age of 10 he suffered central chest pain of sudden onset and died one week later.

The second child, a girl, developed xanthomas at the age of 2. Investigation in Kampala when she was 9 showed extensive xanthomas, aortic stenosis, and enlargement of the left ventricle. Plasma cholesterol concentration was above 15 mmol/l (579 mg/100 ml), and she died shortly afterwards of left ventricular failure.

The third child, another girl, was brought to the United Kingdom for investigation at the age of 2. She had pronounced skin xanthomas but no other abnormalities. Plasma cholesterol concentration was over 23 mmol/l (888 mg/100 ml). Treatment with a diet low in saturated fats and with dextrothyroxine 3 mg daily was started, and subsequently triparanol was added, but there was no effect on plasma cholesterol concentration or the xanthomas. When she was 3 she died suddenly, just after returning to east Africa. Death was presumed to have been due to coronary heart disease, but necropsy was not performed.

FOURTH AFFECTED CHILD

Because of the family history we saw the fourth affected child, a boy, when he was 11 months old. He had no clinical abnormalities, but his plasma cholesterol concentration was 24·4 mmol /l (942 mg/100 ml) (low density lipoprotein cholesterol 21·6 mmol/l (834 mg/100 ml)). Treatment was started with a diet low in fats, cholestyramine 32 g daily, clofibrate 25-30 mg/kg/day, and iron and vitamin supplements. Plasma cholesterol concentration after eight weeks was 23·2 mmol/l (895 mg/100 ml) so nicotinic acid was added in increasing dosage up to 100 mg/kg/day. Plasma cholesterol concentration gradually fell and after five months of treatment was 16·6 mmol/l (641 mg/100 ml) (low density lipoprotein cholesterol 14·6 mmol/l (563 mg/100 ml)).

The family returned to Africa for 10 months before settling in the United Kingdom. During this interruption of treatment small xanthomas of the skin developed behind his knees and in the natal cleft and the plasma cholesterol concentration rose to 24·7 mmol/l (954 mg/100 ml). From the age of 2 years 4 months he received treatment with diet, cholestyramine, clofibrate, and nicotinic acid. He was reviewed regularly, and compliance with treatment was good. The xanthomas resolved, and no new lesions or corneal arcus developed. Plasma cholesterol concentrations fluctuated between 12·9 and 20·9 mmol/l (498 and 807 mg/100 ml); mean concentrations over the periods 2-5, 6-10, and 11-15 years were 17·0, 16·3, and 17·6 mmol/l (656, 629, and 680 mg/100 ml), representing reductions of 30%, 33%, and 28%, respectively.

This child's growth and pubertal development were normal; he was athletic and played competitive sports. At the age of 15 his heart was clinically, radiographically, and electrocardiographically normal. Coronary angiography showed a normal left ventricle (end diastolic pressure 8 mm Hg) and aortic root. The right coronary artery was normal. The left had a short main stem; there was minor irregularity at the origin of the left anterior descending artery, but the appearances were otherwise normal.

Discussion

The deaths during the first decade of the first three children homozygous for familial hypercholesterolaemia showed the potential lethality of the disorder in this family. In the first two children there was evidence of coronary heart disease, but the cardiac state of the third is speculative. The first two children were untreated, and treatment of the third child did not lower plasma cholesterol concentration.

The progress of the remaining homozygous child contrasted noticeably with that of his similarly afflicted siblings. At 15 he had no xanthomas, no clinical coronary heart disease, and a virtually normal coronary angiogram. He was treated with diet and drugs to lower his plasma cholesterol and low density liproprotein cholesterol concentrations from the age of 1, and although values remained high, they represented a reduction of about 30% from the concentrations before treatment. This reduction, which was maintained from the age of 1, was almost certainly responsible for delaying the development of atheroma in this boy, indicating that starting preventive treatment early is probably very important.

Our experience with this family leads us to conclude that though treatment in familial hypercholesterolaemia may not achieve normal plasma cholesterol concentrations, any reduction may be beneficial, particularly if treatment is started before the development of atherosclerosis. We see no reason why these conclusions should not be equally applicable to the more common heterozygous form of familial hypercholesterolaemia.

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100 YEARS AGO

A lamentable example of this misadventure was once more recorded at an inquest held on December 1st, at Brompton, near Northallerton, before Mr. Walton, touching the death of Mary Ramshaw. The deceased, whilst crossing the street, had been knocked down and injured by a passing conveyance. She was brought home, and medical aid called in, when it was found she had received a fracture of the right thigh. She was ordered a mixture to take, as well as an embrocation. The deceased being in great pain, her daughter gave her a dose of medicine, when she instantly became convulsed, and in the course of about ten minutes died. The daughter, as soon as she had administered the dose, perceived that she had taken it from the wrong bottle, the two standing on the same table. Mr. Lumley, surgeon, said he attended the deceased, and supplied the bottles referred to, the embrocation containing a very strong preparation of belladonna, and he had no doubt the woman died from the effects of that poison. Although the embrocation was poisonous, he did not think it necessary to place any label on the bottle to that effect to warn the persons of its nature. The bottles were of the same shape, and the one containing the embrocation was graduated in tablespoonful doses, the same as that in which the mixture was. It had on it a label, "The embrocation to be used twice or three times a day." After a lengthened inquiry, the jury recorded as their verdict that the deceased was poisoned by belladonna, administered to her by mistake, and that the medical attendant was not free of blame in the matter. They considered that great care should be used in sending out such poisonous compounds, and that in this case there ought to have been something about the bottle to indicate the dangerous nature of the contents. The recurrence of these terrible tragedies recalls once and again the vast importance of dispensing poisonous mixtures and all external liniments in roughened or fluted bottles, which give mechanical warning of danger; at the same time that the obvious precaution in labelling is adopted. Such a domestic calamity leaves a wound which can never heal. (*British Medical Journal* 1885;ii:1126.)