mm line. The degree of pruritus was recorded by the patient on a visual analogue scale ranging from "no itching" to "intense itching" on a 100 mm line.

Patients were included in the trial only if at least one wheal other than that induced by histamine was larger than 4 mm in diameter. Coded creams of identical appearance, one containing 2% mepyramine maleate and a control cream consisting of the same base without the active drug, were applied in a randomised double blind fashion, one to the right arm and the other to the left. Wheal size, erythema, and itching were reassessed 10 minutes afterwards.

Analysis of covariance was performed on the difference between the initial values and those found on reassessment.

The table shows that there was no significant difference between the initial values for erythema, wheal size, and pruritus on the two arms or between the effects of active and placebo creams in suppressing pruritus and reducing erythema and wheal size.

Differences in reactions to skin prick tests before and after application of active and placebo creams

Reaction	Type of cream	Before cream	After cream	Difference	p
Pruritus*	Active	45	30	−15	0·92
	Placebo	43	31	−12	
Wheal size (mm)	Active	8	9	+1	0·20
	Placebo	8	9	+1	
Erythema*	Active	35	38	+3	0·80
	Placebo	34	37	+3	

* Assessed on visual analogue scale of 0-100.

Comment

Topical mepyramine cream is no better than placebo cream in reducing wheal size, erythema, and pruritus when used after allergen skin testing. This is not unexpected as antihistamine drugs are competitive antagonists and would not have an effect when mediators have already been released into the tissues and are bound to receptors. Both active and placebo creams, however, reduced pruritus despite an increase in erythema and wheal size. After the results of skin tests have been recorded a simple soothing cream may therefore be applied to provide symptomatic relief.

We thank May and Baker for supplying the active and placebo creams and for help with statistical evaluation.

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An unusual cluster of babies with Down's syndrome born to former pupils of an Irish boarding school

Clustering in time and space of cases of Down's syndrome has attracted attention. Collmann and Stoller suggested an infective cause.[1] We report an unusual cluster of babies with Down's syndrome born to six young mothers whose only common feature was that they attended school together in Dundalk, an eastern coastal town in the Republic of Ireland, during the 1950s. An outbreak of illness similar to influenza occurred in the school in October 1957.

Patients, methods, and results

A child with Down's syndrome was examined by one of us in 1974, and the mother mentioned that babies with Down's syndrome had also been born to some of her school friends. All 213 pupils who had attended the school in the 1950s were contacted, and details of their obstetric and other personal histories were sought. This revealed that six babies with Down's syndrome had been born to six former pupils (table). Because of the influenza epidemic in 1957 sera from the six mothers of babies with Down's syndrome and from 128 controls, who included 55 other former pupils of the "affected" school, were tested for influenza and other possible teratogenic agents.

Six school companions who had babies with Down's syndrome

Mothers		Babies	
Date of birth	Dates at school	Normal	Down's syndrome (year of birth)
10 Nov 1943	1956-62	6	F (1970)
25 Feb 1944	1954-9	2	F (1963)
4 Sept 1938	1955-7	2	M (1964)
7 July 1939	1952-7	3	F (1966)
11 June 1941	1955-9	6	M (1972)
13 April 1946	1951-60	2	F (1972)

The sera from all 134 mothers were examined for antibody titres to several influenza strains and also to rubella, cytomegalovirus, hepatitis B, and to the protozoan *Toxoplasma gondii*. None of the results was significant. Karyotyping of the six babies with Down's syndrome showed that all were simple trisomy 21. In each case both the parents had normal chromosomes. All have since had only normal children in a total of 26 pregnancies (table). Fetal wastage was compared in all groups but results showed no statistical significance.

In the control group one baby with Down's syndrome was born as a result of a fifth pregnancy to a 40 year old mother from another school. Two controls had also spent their teens in Dundalk though not at the same school. None of the 134 used contraceptives, fertility pills, or drugs. None of the six mothers of babies with Down's syndrome smoked. Only one had been exposed to *x* rays during pregnancy and she had had a single dental *x* ray examination.

Comment

The number of affected children was far too high to be the result of chance alone. The incidence of six babies with Down's syndrome in a total of 26 pregnancies (table) is significantly higher than the accepted overall incidence of one in 600.

Trisomic clustering in space and time has been reported many times.[2] This unique cluster is related to neither space nor time; the babies were born in different locations. The only common factor is that their mothers lived in close association during their teenage years and had an illness similar to influenza in October 1957.

Another possible time related causative factor was the nuclear accident at Windscale 10 October 1957. Irish meteorological reports are consistent with radioactive fallout having reached Ireland at a time of heavy rainfall in the Dundalk area. Radioactive iodine (^{131}I) and Polonium 210 are transmitted via cows' milk and the food chain.[3] Milk supplies were not monitored for radioactivity in Ireland at that time so no figures are available. We suggest that the levels of exposure to radiation in Dundalk were probably similar to those of the average population in southern England. Estimates of dosage are well below those that would be expected to give rise to demonstrable consequences unless perhaps some other unknown interacting factor, such as a virus infection, had been present.

An increased incidence of Down's syndrome along the east coast of Ireland with a peak in 1974 has been reported.[4] There has also been an increase in the number of deaths from leukaemia and cancer along the east coast.

What happened to these young women when they were teenagers in school together? We are left with the nagging doubt that possible exposure to radiation associated with some infection had an adverse influence on the subsequent non-disjunction of chromosome 21 in their six babies.

We thank the staff of the Meteorological Office and Dr Eric Feeney, principal physicist, St Luke's Hospital, Dublin, for their help, and Mrs S Duffy for typing the manuscript.

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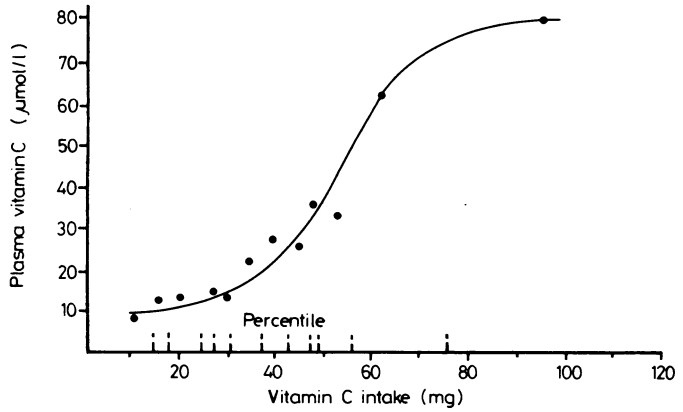
Relation between intake and plasma concentration of vitamin C in elderly women

The plasma concentration of vitamin C is relatively low in the elderly, particularly those in long stay hospitals,[1] but it is not clear to what extent these low concentrations are due to low intake. We examined the relation between intake and plasma concentrations of vitamin C in elderly women living at home and in long stay hospitals.

Patients, methods, and results

We studied 101 elderly women: 24 were healthy and living at home (mean age 74), and 77 were long stay patients (mean age 83) in two geriatric hospitals and one psychiatric hospital. Food intake was weighed and noted for five days in the case of the elderly women in hospital and for seven days in the case of those at home. Vitamin C intake was calculated from standard food tables except in the case of vegetables and potatoes delivered to the wards, which we analysed for vitamin C. Each subject's plasma concentration of vitamin C was measured at the end of the period during which intake of food was measured.[2]

The figure shows the relation between plasma concentration and intake of vitamin C. The relation was sigmoidal, not linear, the curve being constructed by plotting the median concentration of vitamin C at the median point for each decile of intake. First and last deciles were split again to give greater detail. When the intake of vitamin C was above 60 mg a day the median plasma concentration was 74 μmol/l (1·3 mg/100 ml), and all but one of the subjects had a plasma concentration above 20 μmol/l (0·35 mg/100 ml). There was a large decrease in the median plasma concentration of vitamin C as the median intake decreased from 60 to 30 mg a day, and most patients with an intake of less than 30 mg a day had a plasma concentration of less than 20 μmol/l (0·35 mg/100 ml).



Median plasma concentration of vitamin C at median point for each decile of daily intake of vitamin C (percentiles indicated by dotted lines on horizontal axis).

Conversion: SI to traditional units—Plasma vitamin C: 1 μmol/l ≈ 17·6 μg/100 ml.

Comment

The sigmoidal relation between intake and plasma concentration of vitamin C has not been reported before. Garry *et al*[3] showed that the relation was not linear, but their study did not include elderly people with low vitamin C intakes. We found that as intake increased from 10 to 30 mg a day the plasma concentration of vitamin C rose only slowly. The rapid change in plasma concentration as the intake increased from 30 to 60 mg a day suggested that a pathway of metabolic utilisation was being saturated. The much slower increase with intakes above 60 mg a day may have been due to a large loss of vitamin C in the urine when the renal threshold of a plasma vitamin C concentration of 51-57 μmol/l (0·9-1·0 mg/100 ml) was exceeded.[4] When we gave a similar group of elderly patients 1 g vitamin C a day for two months their mean plasma concentration reached only 78 μmol/l (1·37 mg/100 ml).[5]

Evidence shows that plasma concentrations of vitamin C should be maintained above 20 μmol/l (0·35 mg/100 ml) to ensure against impairment of health.[4] The results presented here suggest that this may be achieved, even in the elderly, if intake of vitamin C is kept above 60 mg a day.

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Protracted survival in patients with Down's syndrome

The life expectancy of patients with trisomy 21 remains less than that of the general population,[1] but there seems little doubt that it is steadily increasing.[2 3] We report on an old man who suffered from Down's syndrome, coeliac disease, and oesophageal carcinoma.

Case report

A 50 year old man with Down's syndrome presented in 1962 with a three year history of diarrhoea. Investigation showed megaloblastic anaemia, and a jejunal biopsy specimen showed villous atrophy. A gluten free diet was started, with excellent results. Haemoglobin concentrations returned to normal over the following weeks and diarrhoea stopped. Coeliac disease was diagnosed.

Down's syndrome was diagnosed on the clinical features, including handprint and footprint studies, and was confirmed by chromosome analysis of 40 fibroblasts cultured from a skin biopsy specimen. Trisomy 21 occurred in 39 of them, which made a diagnosis of mosaicism unlikely.

The patient lived at home with an older sister and remained well for a further 20 years. He presented again, when his sister could no longer look after him, with a six month history of weight loss and anorexia. Investigation showed almost complete obstruction of the oesophageal lumen by a 3 cm long annular squamous cell carcinoma. He died three weeks later. Repeat chromosome analysis had confirmed trisomy 21.