

Discussion

We have shown that the oral bioavailability of theophylline from a hydroalcoholic preparation and an alcohol-free preparation was similar. This was established in a carefully controlled trial, a specific and precise analytical technique to measure plasma theophylline concentrations. Interestingly, a non-specific ultraviolet assay⁹ used in earlier studies reported the enhancement of theophylline absorption by alcohol.^{1,2} The pitfalls in using the ultraviolet assay have since been documented.¹⁰

Our findings suggest that the non-alcoholic theophylline preparation could be substituted for the hydroalcoholic elixir in cases where ingestion of alcohol is inadvisable because of its sedative or gastrointestinal side effects.

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Vitamin C and the common cold

Using identical twins as controls

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ABSTRACT: We analysed self-reported cold data for 95 pairs of identical twins who took part in a double-blind trial of vitamin C tablets. One member of each twin pair took vitamin C and the other took a well

matched placebo each day for 100 days. Vitamin C had no significant effect except for shortening the average duration of cold episodes by 19%.

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THE EFFICACY of vitamin C in prevention and cure of the common cold is still widely believed in Australia despite the fact that most studies to date have failed to show any consistent effects. We summarise here the results of a study using the perfect matching of identical twins in age, sex and genetical constitution to compare the effect of vitamin C and placebo treatment on colds.^{1,2} A full description will be published elsewhere.

Subjects and Methods

One hundred and twenty-five pairs of monozygotic (MZ) twins born between 1916 and 1965 and living in the Sydney metropolitan area volunteered to begin the trial. Zygosity was checked by typing all twins with the following antisera (anti-A, A₁B, M, N, S, s, C, c, D, E, e, K, k, Fy^a, Jk^a) and none was excluded as a dizygotic pair. One twin of a pair was assigned at random to the treatment group; the other, to the control group. The experiment was "double-blind" in that neither subjects nor experimenters knew which group was which until the experiment and the analysis were completed.

The treatment group received 1.0 g of ascorbic acid per day in the form of Redoxon[®] tablets (Roche Products) and the control group received a placebo with the same ingredients in different proportions but the lactose substituted for ascorbic acid. The placebo and active tablets were well-matched in taste and appearance.

Twins were asked to take their 1.0 g tablet (active or placebo)

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and supplied multivitamin capsule at the same time each day, for 100 days beginning June 2, 1980. They were asked not to take any other vitamin preparations during the course of the trial and to note each day any cold symptoms present. The nine cold symptoms listed were: sore throat, sneezing, runny nose, blocked nose, cough, headache, feverish, tiredness and muscle ache. Subjects were asked to rate their symptoms on the following scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe.

We have analysed complete cold data for 95 of the 125 pairs of twins who began the trial. A cold episode was defined by the following criteria:

- A "cold" must have a total of at least five severity points for the cold symptoms sore throat, sneezing, runny nose, blocked nose, cough and feverish.
- One day could be defined as an episode if the sum of cold symptom ratings was greater than or equal to five.
- Otherwise a cold was defined as an illness episode of two or more days duration with at least two different cold symptoms (those listed in criterion 1) present together on at least two of the days, not necessarily consecutive.
- An episode begins following three days, each with cold symptom points less than or equal to one, and ends before the three days each with cold symptom ratings totalling no more than one.
- Cold episodes already present at the start of the trial were disregarded. Individuals were excluded from cold data analysis if the initial cold lasted for more than 14 days or if the total number of "cold" days was greater than 60.

Six main variables were computed from each individual's cold data.

Incidence: the number of defined cold episodes experienced over the trial period.

Total duration: the total number of "cold-days" experienced.

Average duration: the total duration divided by incidence.

Total severity: the total of all severity points within cold episodes reported by each individual.

Average severity: the total severity divided by the incidence of colds.

Intensity (the average severity per cold day): the total severity divided by the total duration.

The data were analysed by paired analysis of variance.²

TABLE 1: Treatment means of cold variables for males, females and total sample of MZ twins

	Males (38 pairs)		Females (57 pairs)		Total (95 pairs)	
	Active	Placebo	Active	Placebo	Active	Placebo
Incidence	1.26	1.26	1.81	1.63	1.58	1.48
Total duration	8.58	8.76	12.7	12.6	11.0	11.1
Average duration	4.37	5.08	5.72	7.26	5.18*	6.39
Total severity	34.4	37.8	56.7	53.3	47.8	47.1
Average severity	17.3	21.3	26.5	31.6	22.8	27.5
Intensity	2.73	3.12	3.68	3.95	3.30	3.62

* Active and Placebo means differ at 5% level.

Results

Cold data were analysed for 38 male pairs and 57 female pairs of twins. Females had significantly longer, more severe and more

intense colds than males. Several analyses suggest that the placebo was a good one and that the double-blind design of the experiment was not compromised.

The results of the paired analyses of variance between active and placebo groups for the six summary cold variables are shown in Table 1. There are no significant differences between active and placebo groups for any of the variables in either males or females considered separately. In the total sample, the vitamin C treatment has a significantly shorter average duration, but the reduction is only slight.

Our results are consistent with those of earlier trials¹ which, at best, only suggest a modest effect of a daily 1.0 g dose of vitamin C in preventing the common cold.

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MEDICAL PRACTICE

Clinical Review

Colorectal cancer

Francis T. McDermott, Adrian L. Polglase, Anthony J. Buzzard, Warren Johnson, Eric A. V. Pihl and Edward R. S. Hughes

A review of the present situation concerning the epidemiology, aetiology, clinical features and management of colorectal cancer.

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COLORECTAL CANCER is the second most common cause of death from malignancy in Australia, New Zealand, Britain and the United States of America. Its incidence varies more than tenfold among different regions of the world; it is more prevalent in "westernised" countries. In Australia its incidence has recently increased.¹

The colon is more frequently affected than the rectum. In 1978, the mortality rate attributed to colonic cancer in Victoria was 19.1 per 100 000 compared with 6.75 per 100 000 for rectal cancer. Whereas males are more likely to contract rectal cancer than females, the incidence of colonic carcinoma is similar for both sexes.

Recently, an increased incidence of proximal colonic carcinoma has been noted in the United States, but no similar trend is apparent in Australia.² Areas with higher incidence rates in the United States are reported to be deficient in the trace element selenium, which may have a protective effect.³

Aetiology

The major importance of environmental factors in the aetiology of colorectal cancer is supported by the finding that migrants

coming to the United States from Japan, where the incidence of colorectal cancer is low, acquire the higher rate of Americans within one generation. The incidence of colorectal cancer in migrants to Australia from Southern Europe and South-East Asia has also been found to reach the level of the local population.⁴

The evidence that dietary excess of fat and meat, especially beef, and low fibre intake are of aetiological importance is circumstantial and uncertain.⁵ International comparisons show high correlation between the incidence of colorectal cancer and these dietary factors but studies within individual countries and case control investigations have frequently failed to confirm the association. Other investigations suggest that carcinogens result from the action of intestinal bacteria on bile acids.

Correlation has been demonstrated in Australia, the United States and Western Germany between the consumption of alcohol, especially beer, and colorectal cancer.¹ The correlation is higher for

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