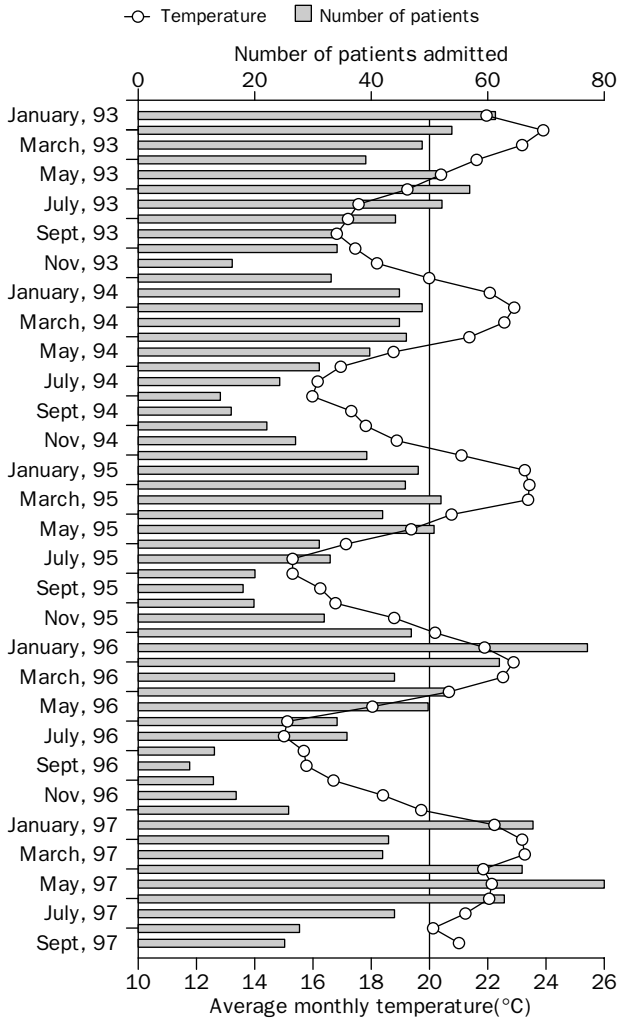

Variations in air temperature and number of patients with diarrhoea and dehydration admitted to the Rehydration Unit of Cayetano Heredia Hospital from 1993 to 1997

35% relative to the first trimester, in contrast to the 16% average decrease in the years 1993–96. During the third trimester of 1997, the number of cases of diarrhoea decreased, yet were still 25% above the figures seen in previous years for the same trimester.

In Peru and neighbouring countries affected by El Niño—Chile, Ecuador, and Colombia—we anticipate an outbreak of diarrhoea and dehydration in the coming summer months when the high seasonal temperatures will be exacerbated by the presence of El Niño. This outbreak will burden local health services treating infections and/or diseases for which temperature may be an important determinant. Should we prepare for another cholera outbreak? Over the past 2 years, few cases of cholera have been seen in Peru,[1] mainly, we think, because there was no susceptible population left after the huge 1991 and 1992 outbreaks. Children born after 1991 and 1992 who were neither infected nor exposed to *Vibrio cholerae* are the most susceptible population now. *V cholerae* can survive in a dormant stage in cool, brackish water, in association with plankton.[2] When the water temperature rises, plankton blooms, and the population of *V cholerae* increases. R Colwell[3] has suggested that remote satellite sensing of plankton beds might be used as an early warning system to help predict outbreaks of cholera.

Analysts have examined the agricultural and economic implications of El Niño.[4] Our data lead us to believe that it is equally imperative that we begin to examine El Niño's implications on health and health care.

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Melatonin in feverfew and other medicinal plants

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In 1995, the US magazine, *Newsweek*, named synthetic melatonin (N-acetyl-5-methoxytryptamine) the "Pill of the Year" for its potential health benefits. In the same year, there was a report associating chronic migraine headaches with lower circulating levels of melatonin.[1] Edible plant tissues contain melatonin and their consumption increases the circulating melatonin supply in mammals.[2] Commercial preparations of feverfew *(Tanacetum parthenium)*, St John's Wort *(Hypericum perforatum)*, and Huang-qin *(Scutellaria biacalensis)* leaves are recommended as a medicine for the treatment for ailments of the nervous system based on anecdotal and historical evidence. Feverfew preparations, taken prophylactically, can reduce the frequency and severity of migraine attacks in some patients.[3] The efficacy of feverfew has been attributed to a sesquiterpene lactone, parthenolide. However, a double-blind study indicated that parthenolide could not be the sole active ingredient in feverfew preparations.[4] St John's Wort has been called a "herbal tranquilliser" because a tea prepared from the flowers may benefit several neurological disorders but can also induce sensitivity to sunlight after long-term use. We questioned whether melatonin may be present in plants with historical medicinal value and pharmaceutical preparations of plant leaves.

Feverfew is known synonymously by four botanical names: *Chrysanthemum parthenium* (L) Bernh, *Matricaria parthenium* (L), *Pyrenthrum parthenium* (L) Sm, and *Tanacetum parthenium* (L) Schultz Bip. All plants were obtained from Richter's Greenhouses, Goodwood, Ontario, Canada, with the exception of St John's Wort which was collected from roadside populations. Tanacet (Ashbury Biologicals Inc, Toronto, Canada), a commercial preparation of feverfew, was purchased locally. Leaf samples of feverfews contained an average of 0·18% and 0·35% (green leaf and gold leaf) of parthenolide, and Tanacet contained no less than 0·2% parthenolide as required by Canadian standards (0·213% in our analyses). Duplicate samples from four feverfew plants were analysed for melatonin.[5] Average recovery was 68% and average percentage coefficient of variation was 18%.

Melatonin was identified in all the samples and the commercial preparation. Two varieties of feverfew were compared and melatonin was found at significantly higher levels in the green leaf variety regardless of the drying style (table). Tanacet also contained melatonin at 0·57 μg/g of leaf tissue or 0·143 μg/g of prepared tablet. An average Tanacet tablet contained 70–80 ng of melatonin and the packaging recommends 1–2 tablets per day over a period of months or years. Melatonin was found in relatively high concentration in two of the other medicinal plants, St John's Wort and

Sample	Melatonin (μg/g)*
Tanacetum parthenium (fresh green leaf)	2·45
Tanacetum parthenium (fresh golden leaf)	1·92
Tanacetum parthenium (freeze-dried green leaf)	2·19
Tanacetum parthenium (freeze-dried golden leaf)	1·61
Tanacetum parthenium (oven-dried green leaf)	1·69
Tanacetum parthenium (oven-dried golden leaf)	1·37
Hypericum perforatum (St John's Wort flowers)	4·39
Hypericum perforatum (St John's Wort leaves)	1·75
Scutellaria biacalensis (Huang-qin)	7·11
Scutellaria lateriflora (Scullcap)	0·09
Tanacet	0·57

*Per g of dried material.

Melatonin in feverfew and other medicinal plants

Huang-qin (table). The amount of melatonin found in feverfew, St John's Wort, and Huang-qin was higher than previously found in edible-plant products.[2]

Plant tissues are a complex mixture of biochemicals. Melatonin in plant tissues may explain anecdotal evidence of physiological effects but also emphasises the need for complete biochemical characterisation of medicinal herbs.

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Leukotriene C_4 synthase promoter polymorphism and risk of aspirin-induced asthma

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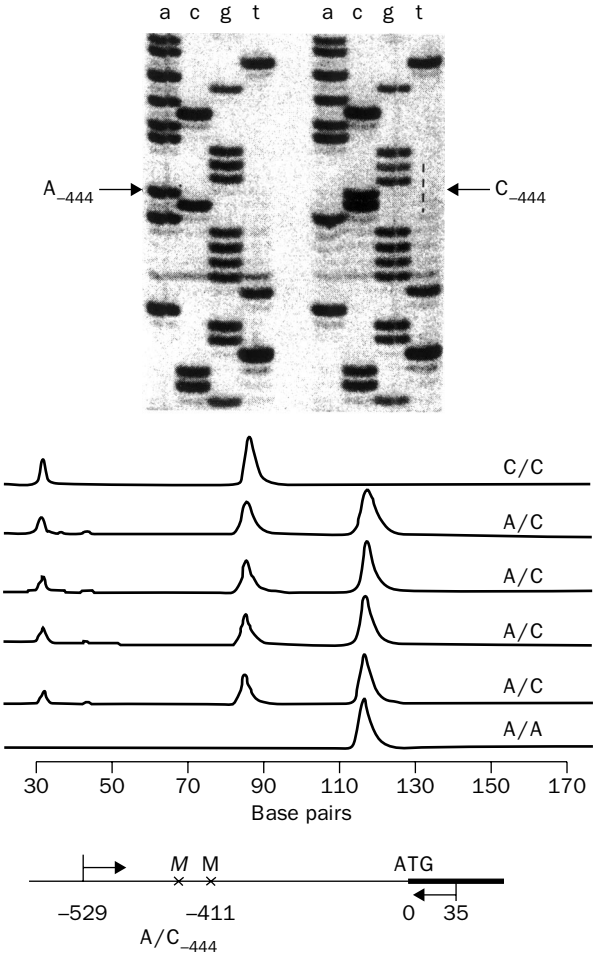
Aspirin-induced asthma (AIA) is a clear-cut clinical syndrome that affects about 10% of adult asthmatics.[1] In these patients, aspirin and other cyclo-oxygenase inhibitors release cysteine-leukotrienes (cys-LTs) into airways[2] and precipitate asthmatic attacks. Pretreatment with leukotriene-modifying drugs can attenuate these events.[1] In bronchial biopsy specimens of AIA patients there is a profound over-representation of LTC_4 synthase (LTC4S), the perinuclear membrane enzyme that forms LTC_4, compared with aspirin-tolerant asthmatics (ATA) or controls.[3] The increased numbers of cells expressing LTC_4 synthase in AIA bronchial biopsy specimens correlated with increased LTC_4 in bronchoalveolar lavage fluid and with bronchial hyperresponsiveness to inhaled lysine-aspirin. LTC_4S^+ cells were predominantly eosinophils and a small number were mast cells.[3] The gene for LTC_4 has been localised to the chromosome 5q35 region,[4] telomeric to other candidate asthma genes. Polymorphism directed to regulation of LTC_4 expression could predispose to this highly leukotriene-dependent asthma. We searched for genetic polymorphism in the *LTC4S* locus in our AIA patients.

The *LTC4S* gene was screened for by amplified-fragment single-strand conformation polymorphism (SSCP). A change of a single base pair, adenine to cytosine transversion, was found in the promoter region of the gene, 444 nucleotides upstream of the first codon (figure). The $A_{-444}C$ transversion creates a new *MspI* restriction site, which has been used for genotyping of patients by restriction-fragment length polymorphism (RFLP). The genotyping included 47 AIA patients (11 men, mean age 45·2 years, with diagnosis confirmed by aspirin provocation tests), 64 aspirin-tolerant asthmatics (ATA; 21 men, mean age 40·5), and 42 healthy individuals (18 men, mean age 38·5). Six AIA patients, but only one in the healthy group and one ATA patient, were homozygous for the less common allele (C_{-444}). The distribution of heterozygotes for the same allele and its frequencies were: 17 in healthy (q=0·226), 27 in ATA (q=0·227), and 29 in AIA. Thus, the frequency of C_{-444} transversion was doubled in AIA (q=0·436). No deviation from the Hardy-Weinberg equilibrium was observed in any examined group. Allele frequencies were different between AIA and controls (p=0·0024, Fisher's test, two sided), and AIA and ATA (p=0·0008). The relative risk of AIA associated with the C_{-444} allele was 3·89 (95% CI 1·57–8·98). Linkage disequilibrium between *LTC4S* alleles and AIA was significant within a wide interval of an assumed disease frequency (0·001–0·5) and penetrance (10–100%).

The promoter region of the *LTC4S* includes numerous



***LTC4S* promoter polymorphism**

Sequences (upper panel) of *LTC4S* alleles; adenine (–444) to cytosine transversion indicated by arrows, *MspI* restriction site in allele C_{-444} marked by dashed line. Fluoregram of RFLP fragments (middle panel). Genomic sequence (563 bp) amplified with primers 5'-TCC ATT CTG AAG CCA AAG GC and 5'-GTG ACA GCA GCC AGT AGA GC and digested with *MspI*. Allele A_{-4444} (A) corresponds to the 117 bp fragment, allele C_{-444} (C) separates as 32 and 85 bp fragments. Constant fragment (446 bp) is not shown. *MspI* restriction sites (M, lower panel) within the promoter of *LTC4S*.The prime sequences are indicated by arrows.