

diagnosis, type of diabetes, body mass index, mode of treatment) and the number of subjects screened for glucokinase defects in their Japanese population. In American black and caucasian NIDDM patients, structural mutations in the glucokinase gene are very rare (<2%).⁸

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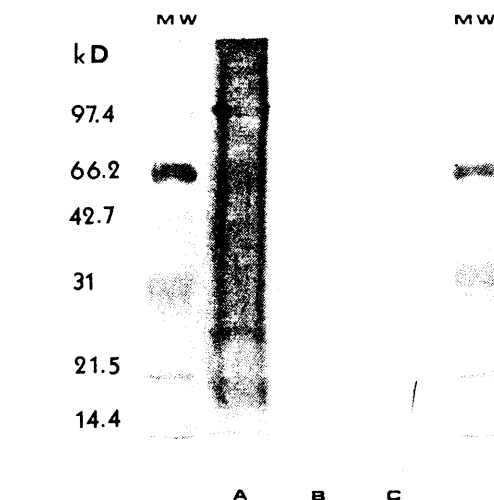
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Immunotherapy: what are we administering to the allergic patient?

SIR,—Since its introduction by Noon in 1911, the practice of attempting to cure patients with allergic diseases by subcutaneous administration of the offending pollen has been questioned.¹ A major difficulty, apart from possible serious adverse reactions,² is the absence of international standardised allergen extracts.^{1,3} Despite the position statements that most national allergy societies, including the Società Italiana di Allergologia ed Immunologia Clinica, have made,⁴ in which a clear indication for immunotherapy is restricted to those allergens for which placebo-controlled trials exist (eg, *Ambrosia*, *Olea europea*, *Dermatophagoides pteronyssinus*, *Alternaria tenuis*, *Cladosporium herbarum*), pharmaceutical companies continue to offer a wide range of pollen extracts for immunotherapy without any standardisation. We have studied *Cupressus sempervirens*.

The fresh cypress pollen extract has several protein bands ranging from 15 to 98 kDa on sodium-dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE), with a major allergen protein of about 36 kDa that is recognised by specific IgE present in almost all the sera of allergic patients despite the frequent negative reactions in conventional radioallergosorbent assay in 30% of cases.⁵ The cypress inflorescences usually appear in winter, from December to March, and generally cause a seasonal allergic rhinitis or oculorhinitis,⁶ often mistaken as being infectious or vasomotor. Because of this confusion, its occurrence is underestimated. The cypress-sensitive patients are usually monosensitive and complain of serious symptoms.

In our institute during the past 48 months, we observed some cases of cypress pollenosis, generally represented by monosensitive patients with winter oculorhinitis. The diagnosis was made on the basis of a significant agreement between the history and skin prick tests. We treated 10 cypress-sensitive patients for 3 years with conventional immunotherapy (Bayropharm, Milan) with poor or no clinical response. During the last year of immunotherapy we analysed randomly some of the concentrated commercial extracts (lots A1G10381 and A1H11367, 10 000 protein nitrogen units [PNU]/mL as stated by manufacturer) by SDS-PAGE and, surprisingly, were not able to demonstrate any protein substances (figure). After several months, we re-extracted our dried pollen and unfortunately were not able to find any significant protein content. The storage of the pollen at room temperature, even if protected



Silver-stained SDS-PAGE of crude cypress-tree pollen.

A = ammonium carbonate extraction compared with two commercially available extracts (B = lot A1G10381, C = lot A1H11367) used for immunotherapy in 2 of 10 patients. Silver-stain can detect protein to 1 ng/mL, sensitive enough to reveal protein content of pollen extract as declared by manufacturer (10 000 PNU/mL, about 620 µg of extractable nitrogen). MW = molecular weight standards.

from light, was unsuccessful because it allowed irreversible degradation of all protein substances.

Most, if not all, Italian pharmaceutical companies, are supplied with pollen extracts collected and probably stored for a long time by foreign manufacturers. Then, simplified extractions to keep costs down and long-term storage of pollens may alter the biological characteristics and compromise efficacy.

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"Keyhole" surgery inquest

SIR,—Whilst I am pleased to see that no criticism of my actions has been incorporated in the clarification (Jan 23, p 233) of the inquest account in your Jan 16 issue, I wish to point out that I was misreported as a "physician and cardiologist". My NHS appointment is as a cardiologist and I restrict my work to cardiology, both in the NHS and in the private sector. Nor did I secure the patient's admission to the Harley Street Clinic; I did agree to visit her after colleagues had already made arrangements.

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CORRECTION

HIV viraemia and seroconversion.—In this letter by Dr Lu and colleagues (Jan 9, p 113) the unit for concentration of free HIV-1 virion in the table should have been the number of virions per µL rather than per L.