

serological titre for syphilis, and the patient was discharged. Clinical findings and test results were compatible with the secondary stage.

Cardiovascular complications of secondary syphilis are rare. There is a report of a patient in whom ventricular tachycardia may have been caused by syphilitic myocarditis, but without histological evidence of *T pallidum* infection.² Another group described the development of cerebral syphilis in an AIDS patient about 4 months after he had developed the venereal infection.³ Our patient was negative for HIV and hepatitis B virus infection.

Although rare, syphilis should be borne in mind as a cause of myocarditis or ventricular aneurysm in young patients.

Masao Chino, Tomoyuki Minami, Kuni Nishikawa

Department of Cardiology, Ashikaga Red Cross Hospital, Ashikaga-city, Tochigi-ken, 326 Japan

- 1 Jackman JD, Radolf JD. Cardiovascular syphilis. *Am J Med* 1989; 87: 425-33.
- 2 Beecher P, Gursch D, Fischer J. Ventricular arrhythmia in secondary syphilis. *Lancet* 1987; 336: 382-83.
- 3 Johns DR, Maureen T, Felenstein D. Alteration in the natural history of neurosyphilis by concurrent infection with the human immunodeficiency virus. *N Engl J Med* 1987; 316: 1569-72.

Allele sharing on chromosome 11q13 in sibs with asthma and atopy

SIR—Cookson, Sandford, and their co-workers¹ reported genetic linkage between atopy underlying asthma and allergic rhinitis and chromosome 11q13 and suggested exclusively maternal inheritance of atopy as well as linkage between the supposed gene for atopy and the β -subunit of the high-affinity receptor for IgE (Fc ϵ RI- β) on 11q. Others have not been able to confirm these findings.^{2,3} We studied chromosome 11q13 in 26 nuclear families with 2 sibs with asthma and atopy by using affected sib-pair analysis. This method does not require assumptions about penetrance, gene frequency, or mode of inheritance.

Families were recruited from the outpatient department of pulmonology in a paediatric clinic. Inclusion criteria for affected sib-pairs were the presence of a positive score (two symptoms or more) on a modified Dutch version of the MRC/ECCS questionnaire on respiratory symptoms⁴ and positive IgE tests (specific IgE ≥ 0.35 PRU/mL; total serum IgE for children under 10 years of age as described,⁵ for older children > 100 U/mL). Genotyping was done for the pMS.51 probe (in 16 families), the PYGM marker (25 families) and a CA-repeat in the Fc ϵ RI- β gene (23 families).

The pMS.51 and PYGM results show increased sharing of alleles compared with the expected proportion of 0.5 (table). We found no significantly increased proportion of shared alleles at the Fc ϵ RI- β locus and no significant difference in the

proportion of maternal and paternal alleles shared at the other two loci. Our results confirm, however, the suggested linkage of atopy underlying asthma and chromosome 11q13 markers.

J M Collé, L P ten Kate

Department of Human Genetics, Free University, 1081 BT Amsterdam, Netherlands

H G de Vries, J W Kliphuis, K Bouman, H Scheffer

Department of Medical Genetics, University of Groningen

J Gerritsen

Department of Paediatric Pulmonology, Beatrix Children's Hospital, University of Groningen

- 1 Sandford AJ, Shirakawa T, Moffatt MF, et al. Localisation of atopy and β subunit of high-affinity IgE receptor (Fc ϵ RI) on chromosome 11q. *Lancet* 1993; 341: 332-34.
- 2 Hizawa N, Yamaguchi E, Ohe M, et al. Lack of linkage between atopy and locus 11q13. *Clin Exp Allergy* 1992; 22: 1065-69.
- 3 Rich SS, Rotman-Johnson B, Greenberg B, et al. Genetic analysis in three large kindreds: no evidence of linkage to D11S97. *Clin Exp Allergy* 1992; 22: 1070-76.
- 4 Amelung PJ, Panhuysen GJM, Postma DS, et al. Atopy and bronchial hyperresponsiveness: exclusion of linkage to markers on chromosomes 11q and 6p. *Clin Exp Allergy* 1992; 22: 1077-84.
- 5 Iympany P, Welsh KI, Cochran GM, et al. Genetic analysis of the linkage between chromosome 11q and atopy. *Clin Exp Allergy* 1992; 22: 1085-92.
- 6 Lende R van der, Orie NGM. The MRC-ECCS questionnaire on respiratory symptoms (use in epidemiology). *Scand J Respir Dis* 1972; 53: 218-26.
- 7 Kjellmann N-IM, Johansson SJO, Roth A. Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clin Allergy* 1976; 6: 51-59.

Caterpillar hairs as allergens

SIR—Anaphylactic reaction to insects (wasp or bee stings) are frequent and sometimes fatal.^{1,2} In Europe, pine processionary caterpillars (*Thaumetopoea pityocampa* S), oak processionary caterpillars (*T processionary* L), and brown-tail moths (*Euproctis chrysorrhoea* L) are the three major Lepidoptera that not only cause considerable damage to forests, but also are responsible for certain skin lesions, mainly contact urticaria, conjunctivitis, and rarely, respiratory signs in animals and people.³ The response is caused by the urticating hairs of these caterpillars. We have isolated the responsible urticating protein (thaumetopoein) from pine processionary hairs.⁴ The oak processionary caterpillar also produces a closely-related urticating protein. Urticating hairs of these caterpillars are detectable in air with an apparatus originally designed for the collection of airborne particles.⁵

Study of the mechanism leading to mast-cell degranulation has revealed a direct (non IgE-dependent) effect of thaumetopoein on mast cells.⁶ Nevertheless, an IgE-mediated mechanism that activates mast cells via an immediate hypersensitivity reaction can also be postulated. A few people who have been exposed to caterpillars develop severe illness despite moderate exposure.

The presence of IgE directed against pine processionary caterpillars was investigated in sera of 21 pine-forest workers who are repeatedly exposed to these caterpillars. Specific IgE antibodies directed against urticating-hair extracts of the three species, or directed against purified thaumetopoein, were assayed by enzyme-linked immunosorbent assay (ELISA). IgE directed against the pine-processionary extract were detected in 4 of the 21 samples. Similar results were obtained with the extract of oak-processionary hairs. For the brown-tail extract, all sera were negative. 3 of the 4 positive samples had significant levels of IgE directed against purified thaumetopoein.

In western blotting, each of the 4 sera had IgE reactive bands

with pine-processionary extract. The reactive bands were localised at the thaumetopoein band (18 000 kDa), and we also observed a strong band over 45 000 kDa. The strongest reaction with this second allergen was obtained with the serum of the subject in which IgE directed against purified thaumetopoein were not detected by ELISA.

We propose that thaumetopoea urticating hairs, especially those of *T pityocampa*, should be considered as important airborne insect-allergens.

J Werno, M Lamy

Laboratory of Neuroendocrinology, University of Bordeaux I, Talence

P Vincendeau

Laboratory of Parasitology, Bordeaux University Hospital, 3076 Bordeaux, France

- 1 Frankland AW. Allergy to insect and arachnids. In: Lessof MH, ed. Allergy: immunological and clinical aspects. Chichester: Wiley, 1984: 425-45.
- 2 Dib G, Ferguson RK, Sljivic V. Hypersensitivity to Samsum ant. *Lancet* 1992; 339: 552-53.
- 3 Ducombs G, Lamy M, Mollard S, Guillard JM, Maleville J. Contact dermatitis from processionary pine caterpillar (*Thaumetopoea pityocampa* Schiff Lepidoptera). *Contact Dermatitis* 1981; 7: 287.
- 4 Lamy M, Pastureau MH, Novak F et al. Thaumetopoein: an urticating protein from the hairs and integument of the pine processionary caterpillar (*Thaumetopoea pityocampa* Schiff). *Toxicol* 1986; 24: 347-56.
- 5 Hirst JM. An automatic volumetric spore trap. *Ann Appl Biol* 1952; 39: 257-65.
- 6 Lamy M, Vincendeau P, Ducombs G, Pastureau MH. Irritating substance extracted from the *Thaumetopoea pityocampa* Schiff caterpillar mechanism of action. *Experientia* 1983; 39: 299.

Human papillomavirus and cervical carcinoma in China and Taiwan

SIR—The presence of certain types of human papillomaviruses (HPV) are one of the major risk factors in the development of malignancies of the uterine cervix. However, factors other than HPV infections may also have important roles in cervical carcinogenesis.¹ To understand better the association between HPV and cervical carcinoma, we looked for HPV DNA sequences in cervical carcinomas in Chinese subjects living in two different geographic locations where the incidences of cervical carcinoma were low or high.

Tissue sections of cervical carcinoma were obtained from 61 Chinese patients living in Taiwan (incidence 23.7 per 100 000)² and from 49 Chinese patients living in LueYang county of Shanxi province, China (1026 per 100 000).³ HPV DNA sequences were examined: DNA was purified from these tissues by in-vitro amplification with consensus primers MY09 and MY11 (Perkin-Elmer Cetus). These primers can amplify DNA from the L1 open-reading frame of more than 40 types of genital and dermal HPV at a sensitivity of about 200 HPV genome equivalents.⁴

DNA sequences homologous to those of HPV were found in 54 (89%) specimens from Taiwan and in 28 (57%) specimens from LueYang. Although the distribution of all HPV types was not assessed, 46 of 54 HPV-positive specimens from Taiwan and 21 of 28 HPV-positive specimens from LueYang contained either type 16 or 18.

The reason for the low HPV prevalence in LueYang is not clear but may be related to the fact that almost all of the residents in LueYang lived all their lives in conservative farming communities with puritanical mores. We could not rule out the possibility of infections by HPV other than the types that could be detected by the primers we used. However, if this was the case, then these putative HPV(s) would have to infect as frequently, if not more so, as HPV 16 and 18 did in cervical carcinomas. So far, no HPV has been found anywhere

in cervical carcinomas more frequently than types 16 and 18.

Although the association between HPV as a sexually transmissible aetiological agent and the development of cervical carcinoma is strong,⁵ risk factors other than HPV appear to exist, especially in HPV-negative women. Our results suggest that HPV may not be the only factor that determines the development of cervical carcinoma, at least in certain geographic areas.

Chia C Pao, Shu-Min Kao, Gu-Chin Tang

Department of Biochemistry, Chang Gung Medical College, Taipei, Taiwan 33332

Kun Lee, Jingyi Si

Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, China

Shuxue Ruan

Institute of Cervical Cancer Research, LueYang County, Shanxi, China

- 1 Kjaer SK, de Giliers EM, Caglayan H, et al. Human papillomavirus, herpes simplex virus and other potential risk factors for cervical cancer in a high-risk area (Greenland) and a low-risk area (Denmark): a second look. *Br J Cancer* 1993; 67: 830-37.
- 2 Reported Cancer Incidence. In: Health statistics, volume 1: general health statistics. Taipei, Republic of China: Department of Health, 1988: 48-49.
- 3 Zhang JM, Ruan SX, Liu DK, et al. The distribution and characteristics of carcinoma of cervix uteri in LueYang county. *Chin J Epidemiol* 1986; 7: 343-45.
- 4 Bauer HM, Ting Y, Greer CE, et al. Genital human papillomavirus infection in female university students as determined by a PCR-based method. *JAMA* 1991; 265: 472-77.
- 5 Schiffman MH, Bauer HM, Hoover RN, et al. Epidemiologic evidence showing that human papillomavirus infection causes most cervical intraepithelial neoplasia. *J Natl Cancer Inst* 1993; 85: 958-64.

Thrombin generation after fast or prolonged regimens of tissue-type plasminogen activator

SIR—Genser et al reported that tissue-type plasminogen activator (tPA) administered over 3 h, but not streptokinase infused over 1 h or urokinase given in 10 min, induces thrombin generation in patients with acute myocardial infarction (AMI).¹ We investigated whether the duration and mode of thrombolytic therapy, rather than type of drug, may influence thrombin formation in AMI.

24 patients with AMI (16 men, 8 women, aged 36-71 years, mean 58) were randomised to receive, within 6 h from onset of chest pain, either 4 intravenous tPA boluses of 10 MU with 20 min intervals (12 patients), or a continuous tPA infusion of 40 MU over 90 min followed by 20 MU over 5 h (12 patients).² All patients received an intravenous heparin bolus of 5000 IU before the start of tPA, immediately followed by 1000 IU/h infused for 24 h, adjusted to a partial thromboplastin time of twice the control value. AMI was diagnosed according to WHO criteria. Coronary arteriography was done 90 min after the start of tPA. Blood samples were drawn before (time 0) and 1.5, 4, 8, and 24 h after the start of heparin and tPA. Plasma concentrations of thrombin-antithrombin III complex (TAT), an index of thrombin generation, were measured by enzyme immunoassay (Enzygnost TAT, Behring).

Patients receiving tPA in boluses, compared with infusion, differed significantly in age (mean 54 vs 63 years, $p < 0.01$) but not in sex, delay to treatment, location and 90 min patency of the infarct artery, or infarct size estimated by serial measurements of the creatine kinase MB isoenzyme. Plasma TAT at time 0 was not significantly different in the two groups. Thereafter, TAT values rose significantly and more than twofold only in the infusion-treated patients ($p < 0.04$, Wilcoxon signed-rank test). TAT values were significantly