Table 1 Distribution of *ACE* I/D and *ET-1* –3A/–4A, G2288T and Lys198Asn polymorphisms and their combinations in the HAPE-p and HAPE-r

Genotypes/ genotype combinations*	HAPE-p (n = 64)	HAPE-r (n = 53)	χ^2	p value	OR (95% CI)
<i>ACE</i>					
II	18 (28)	23 (43)			
ID	34 (53)	21 (40)			
DD	12 (19)	9 (17)	5.10	0.07	
ID+DD	46 (72)	30 (57)	4.91	0.03	1.94 (1.08 to 3.50)
<i>ET-1</i>					
Longer repeats†	17 (27)	19 (35)			
Shorter repeats†	47 (73)	34 (65)	1.15	0.28	1.46 (0.80 to 2.66)
–3A/–3A	44 (69)	35 (66)			
–3A/–4A	20 (31)	18 (34)	0.21	0.65	0.87 (0.48 to 1.58)
GG	15 (23)	23 (43)			
GT	37 (58)	22 (42)			
TT	12 (19)	8 (15)	9.09	0.01	
GT+TT	49 (77)	30 (57)	9.05	0.002	2.53 (1.37 to 4.65)
Lys198Lys	22 (34)	17 (31)			
Lys198Asn	32 (50)	27 (52)			
Asn198Asn					
Lys198Asn+	10 (16)	9 (17)	0.20	0.90	
Asn198Asn	42 (66)	36 (69)	0.65	0.76	0.87 (0.48 to 1.58)
<i>ACE+ET-1</i>					
II/Longer repeats	1 (1)	4 (8)			
Remaining combinations	63 (99)	49 (92)	5.70	0.02	0.12 (0.01 to 0.95)
II/–3A/–3A	13 (21)	15 (28)			
Remaining combinations	51 (79)	38 (72)	1.32	0.25	0.68 (0.36 to 1.31)
II/GG	5 (7)	12 (23)			
Remaining combinations	59 (93)	41 (77)	10.04	0.002	0.25 (0.10 to 0.62)
II/Lys198Lys	9 (14)	8 (16)			
Remaining combinations	55 (86)	45 (84)	0.15	0.69	0.85 (0.39 to 1.86)

HAPE-p, individuals with high altitude pulmonary oedema; HAPE-r, individuals resistant to high altitude pulmonary oedema.

The genotypes and genotype combinations are presented as number (%).

*Genotype combinations were grouped into wild-type genotype combinations and remaining combinations.

†(CT)_n-(CA)_n repeats were segregated and recognised as shorter (13–30) and longer (31–45).

Lys198Lys genotype combination within *ET-1* was significantly less in HAPE-p than in HAPE-r (1% v 9%, odds ratio 0.10 (95% CI 0.01 to 0.82), $p = 0.01$). Our findings support the hypothesis that *ACE* and *ET-1* polymorphisms have a role in the susceptibility to HAPE. The findings of the present study and earlier reports on adaptation to high altitude^{2,3} together indicate that *ACE* and *ET-1* genes are significant in high altitude physiology.

In conclusion, this study showed that *ACE* and *ET-1* variants have independent and interactive roles in the susceptibility to HAPE. Higher *ACE* activity and *ET-1* levels correlated with HAPE. The *ACE* I/D and *ET-1* G2288T polymorphisms emerged as noteworthy variants showing association with HAPE. Owing to the small sample size, the difference in representation of the polymorphisms and their correlation with biochemical parameters did not reach greater statistical significance; in particular, we consider our data on the genotype combinations between the polymorphisms of the two genes to be preliminary. Nevertheless, since HAPE samples are difficult to obtain, the findings of this study are important and warrant confirmation in a larger sample. The results of this study may find application in identifying individuals with a predisposition to HAPE.

Acknowledgements

The authors thank Ven Thubten Choegyal, Chairman, Ladakh Heart Foundation who helped with the collection of blood samples and Professor S K Brhamachari for his support and encouragement.

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doi: 10.1136/thx.2006.066019

This work was funded by the Council of Scientific and Industrial Research.

Competing interests: none.

Details of the primers and conditions for genotyping the five polymorphisms are shown in table S1 available on the Thorax website at <http://www.thoraxjnl.com/supplemental>.

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NSIP in a curry sauce factory worker

Curry powder and ground pepper are commonly used spices in many countries of the world. Although a case of bronchiolitis obliterans organising pneumonia has been reported in a worker who inhaled spice dust in a potato chip factory,¹ we report the first case of non-specific interstitial pneumonia (NSIP)² with bronchiolar lesions associated with curry powder and ground pepper.

A 50 year old male smoker (20 pack-years) developed a cough with sputum and shortness of breath on both working days and non-working days and was admitted to our hospital 1 month after developing the symptoms. He had worked in a factory that produced curry sauce for 13 years. His job was to carry sacks filled with curry powder (containing a mix of ground spices) and ground pepper on his shoulders and to empty them into a large curry sauce cooker without any equipment to protect against dust inhalation.

Physical examination on admission revealed inspiratory crackles in the bilateral lower lungs without digital clubbing. Serum markers for interstitial pneumonia, surfactant protein D (SP-D), and KL-6 were raised to 2410 ng/ml and 5570 U/ml, respectively. A high resolution computed tomographic (HRCT) scan of the chest revealed multiple irregular consolidations along with bronchovascular bundles and, in the subpleural lesions, trivial pleural effusion and cystic air spaces in the bilateral apex portions (fig 1A). Bronchoalveolar lavage was performed; the total cell count was 4.1×10^6 /ml with 23.8% macrophages, 70.4% lymphocytes, 0.2% neutrophils, 2.6% eosinophils, and 3.0% basophils. The CD4+/CD8+ lymphocyte ratio was 0.94 and pathogenic organisms were not detected.

Specimens obtained by video assisted thorascopic surgery from the right lung (S³ and S⁸) 2 months after the onset of disease revealed a cellular and fibrosing NSIP pattern with polypoid granulation tissues in a few respiratory bronchioles and alveolar ducts. The bronchioles showed reparative proliferation of the bronchiolar epithelium and infiltration of eosinophils, lymphocytes, and multinucleated giant cells, together with stenosis with intraepithelial infiltration of lymphocytes. These findings suggest an association between the patient's disease and the particles he inhaled while working.³

Four months after the onset of disease his serum SP-D and KL-6 levels had fallen and the consolidations seen on the HRCT scan had spontaneously resolved. Lymphocyte stimulation tests (LST) using the patient's peripheral blood lymphocytes were positive for the curry powder, ground black pepper, and ground

Figure 1 Radiological findings during the clinical course of lung disease in a patient who worked with curry powder and ground pepper. (A) HRCT scan at the onset of lung disease showing multiple peribronchovascular consolidations and pleural thickening. (B) After 14 months the consolidations in the lung fields had almost completely resolved, but the subpleural cystic air spaces had increased in size and number.

white pepper used in the factory, with stimulation indices of 311%, 244% and 245%, respectively. The LST were negative for curry powder and ground pepper used in another curry sauce factory. LST using blood samples from three healthy volunteers and the three substrates were negative. We therefore concluded that the patient's lung disease was associated with the spices used in his factory and we advised him not to return to work. Prednisolone and azathioprine were administered but both drugs were discontinued owing to the occurrence of bilateral pneumothoraces which were surgically treated. Although the consolidations on the HRCT scan did not recur after his isolation from the factory, the subpleural cystic lesions—thought to be caused by a check valve mechanism with bronchiolar constriction—increased in size and number and post-inflammatory pleural thickening progressed (fig 1B). Fourteen months after onset of the disease the patient died from ventilatory insufficiency with hypercapnia.

Although fungi or bacilli in the spices may have induced the lung disease⁴ and further investigation is needed to determine the exact elements responsible, we wish to draw attention to the possibility of this type of lung disease. Progressive pulmonary cysts and respiratory failure may happen even after avoidance of pathogenic antigens, as found in pigeon breeder's lung,⁵ and early diagnosis is necessary to improve its prognosis.

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doi: 10.1136/thx.2006.062182

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Critical care as part of respiratory medicine training in the UK

Intensive care in the UK has traditionally been delivered by intensivists within the physical boundaries of the intensive care or high dependency unit. The recent adoption of the term "critical care" reflects an increasing focus on the patient rather than the location or attending physician.^{1,2} The Joint Committee of Higher Medical Training curriculum in respiratory medicine identifies that experience in "intensive care medicine" is essential for respiratory trainees, and specifies that no less than 60 days should be spent in an intensive care unit recognised by the regional programme director. This is equivalent to 3 months full time training and should ideally be undertaken as a single full time allocation, but can be delivered as blocks of a minimum of 15 consecutive working days, ideally with trainees taking part in the intensive care medicine on-call rota.³

The recently formed Respiratory Critical Care Group (RCCG), a subcommittee of the Education and Training Committee of the British Thoracic Society (BTS), has identified that one of their primary goals is to focus on the interface between respiratory and critical care medicine. The group therefore undertook a survey of respiratory trainees (RTs) and programme directors (PDs) to establish whether the critical care experience prescribed in the curriculum was being delivered. The RCCG sent out questionnaires to all PDs and RTs registered with the BTS. The overall response rate was 55% (208/389 RT, 16/18 PD).

Reassuringly, 94% of PDs and 96% of RTs agreed that experience in critical care medicine was an essential part of respiratory training. Furthermore, 90% of RTs were allocated to 3 months training in a recognised unit. However, 41% of RTs also covered acute general

internal medicine and/or respiratory medicine during this period, and more than half the PDs attributed local limitations on training to a lack of available posts. Despite this, 85% of trainees reported that their regional training programme included sessions focusing on critical care topics. More interestingly, especially when considering future plans for respiratory and critical care training provision, a number of trainees expressed an intention to develop a specialist interest in intensive care medicine (19%), high dependency medicine (32%), non-invasive ventilation (57%), and weaning (13%).

Accepting the limitations of questionnaires, there are still some key messages that need to be highlighted. Firstly, there is broad agreement between RTs and PDs on the importance of experience in critical care as part of respiratory medicine training, and the majority of RTs have an opportunity to access it. However, 10% of trainees still have inadequate exposure to critical care, either in terms of length of experience or availability of dedicated training, and many trainees are potentially diluting their critical care experience by having to cross-cover for general internal medicine and/or respiratory medicine. Secondly, a significant number of trainees wish to be involved in the delivery of critical care outside the intensive care unit. However, is full accreditation in intensive care medicine necessary to provide this? Probably not, but a longer period of training in intensive care medicine combined with a period of anaesthetics training and experience in a recognised high dependency unit would be acceptable if a competency-based approach were applied.

The provision of critical care services is no longer the sole responsibility of intensivists. However, for RTs to manage critically ill patients effectively outside the intensive care unit, some adjustments may need to be made to training programmes. The obvious question raised is whether training for sub-speciality service provision in this area should be pursued by the BTS? Although this question goes beyond the limits of the current survey, the results do identify that there are a number of RTs dedicated to pursuing a career in the area. The aims of the RCCG will be to support those respiratory physicians practising in this emerging field.

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doi: 10.1136/thx.2006.064311

Competing interests: none.

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