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P53 INTRON 2 POLYMORPHISMS AND MUTATIONS IN NON-SMALL CELL LUNG CARCINOMA IN HONG KONG

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Background Lung cancer is the commonest cause of cancer death in Hong Kong. Gene mutations are involved in the multistage process of lung tumorigenesis. p53 gene mutations with ethnic differences have been reported. In our previous study of non-small cell lung carcinoma (NSCLC) patients, mutation of the hot spot exon 5-exon 8 was 0-6%. On the other hand, a polymorphism in p53 intron 2 (A1 and A2 alleles) and a 15% frequency of p53 intron 2 mutations were detected. In the present study, the significance of these polymorphisms and mutations was further studied.

Methods Triple specimens from the lung tumour, normal lung tissue and peripheral blood of 23 NSCLC patients were analysed for polymorphisms and mutations in p53 gene intron 2 by polymerase chain reaction - single strand conformation polymorphism and direct DNA-sequencing techniques.

Results All cell lines established from peripheral blood lymphocytes shared the same genotypes found in the normal lung tissue, but differed in 4 cases where mutations were detected in the tumours. Detected mutations in the tumour tissues resulted from an A2 to A1 conversion. The A1 allelic frequency appeared to be specifically and significantly increased in the adenocarcinoma tumour tissues as compared to normal tissues in these patients.

Conclusions (1) The p53 intron 2 polymorphic locus is a hot spot for mutations in Hong Kong NSCLC patients. (2) The Al allelic frequency appeared to be specifically increased in adenocarcinoma tumor tissues. (3) The mutations are probably somatic. Peripheral blood DNA may be used to analyse the normal genotype of this locus.

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EFFECTIVENESS OF AN ASTHMA EDUCATION PROGRAMME

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A structured asthma education programme was introduced in December 1996 with the aim of improving patient care. This study evaluates its effectiveness and factors that are associated with favourable outcomes. Knowledge of the above would enhance the effectiveness of the service.

Adult and paediatric patients were recruited into the programme on a voluntary basis. In addition to an intensive education programme to promote patients' knowledge of their disease, spirometry, symptoms, technique for using inhaler devices, treatment compliance were assessed on entry and at one year on exit of the programme. Complete data are available in 103 (40.1±14.3 yrs) adults and 77 (10.7±3.4 yrs) children. The results are summarised as follows:

	FEV_1 (% predicted)		Steroid (ug/d)		Symptom†		Technique†		Knowledge†	
	Entry	Exit	Entry	Exit	Entry	Exit	Entry	Exit	Entry	Exit
Adults (n=103)	**86.1**	**86.6**	**1304**	**1329**	**6.97**	**5.95***	**51.9**	**92.4***	**68.0**	**80.8***
Children (n=77)	**82.9**	**99.8***	**423**	**328***	**4.91**	**4.31***	**71.9**	**93.1***	**65.6**	**76.6***

† score; *indicates statistical significance for comparing data ascertained between entry and exit of study

FEV_1 at one year was associated with inhaler technique (p=0.03) and knowledge (p=0.04) score and inversely correlated with symptom score (p=0.02), daily steroid dose (p=0.0001) and age (p=0.0001) of the adult patients. No such association was found in the paediatric patients except for age (p=0.0001). Improvement in lung function in the children was associated with improvement in symptom score (p=0.04). On exit of the programme, old age was associated with higher symptom score (p=0.03), higher steroid dose (p=0.007), poorer inhaler technique (p=0.02) and poorer disease knowledge (p=0.0001) in the adults. On the contrary, age was positively correlated with knowledge score in the children (p=0.01).

Our study shows that this programme is effective in improving patients' disease outcomes. Differences in the outcomes between the adult and paediatric patients suggest that the natural history of the disease is different between the two age groups and that age plays an important part in delivering the programme. Older subjects in the paediatric age group and younger patients in the adult group are most likely to benefit from the current programme.