



<b>Title</b>	<b>The impact of aging on ciliary function and ultrastructure in human respiratory epithelium</b>
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## **G-RC-8**

### **THE IMPACT OF AGING ON CILIARY FUNCTION AND ULTRASTRUCTURE IN HUMAN RESPIRATORY EPITHELIUM**

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The elderly have increased susceptibility to lower respiratory tract infections which is partly attributed to concomitant respiratory diseases, gastro-oesophageal reflux, swallowing difficulties, and immobility. Although mucociliary clearance plays a crucial role in the defence against inhaled microbes, little is known on the effect of aging on respiratory ciliary function and ultrastructure. We have studied the ciliary beat frequency and ultrastructure of respiratory cilia on 100 volunteers (53 males; mean  $\pm$  S.D. age  $52.7 \pm 24$  yrs; range 11-90 yrs). Respiratory cilia were obtained from the inferior turbinate for measurement of ciliary beat frequency using an established photometric method. The mean  $\pm$  S.D. ciliary beat frequency were  $12.9 \pm 1.7$  Hz (range 9.1-17). Transmission electron microscopy (TEM) examination was performed on ultrathin sections using a morphometric protocol on all subjects. TEM examination revealed a significant increase in the frequency of microtubular disarrangement and presence of single tubules with aging ( $p=0.002$  and  $0.005$  respectively). The mean SD derived from the angles formed between the central microtubules of neighboring cilia was  $12.4^\circ (\pm 3.7^\circ)$ . Ciliary beat frequency negatively correlate with age ( $r=-0.45$ ,  $p<0.001$ ) but bore no gender difference ( $p>0.05$ ). Our finding of impaired ciliary function and the increased frequency of ciliary ultrastructural anomalies with aging could help explain the frequent occurrence of respiratory infections in the elderly.

## **G-RC-9**

### **CHEMORADIOTHERAPY IN ADVANCED LYMPHOEPITHELIOMA-LIKE CARCINOMA (LELC) OF LUNG**

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Lymphoepithelioma-like carcinoma (LELC) of the lung, an Epstein-Barr virus (EBV)-associated undifferentiated carcinoma, is a rare entity of pulmonary malignancy. It appears to show predilection for young non-smoking Asians and is often resectable. However, little is known on the treatment of the even rarer locally advanced or metastatic cases. We have conducted a prospective study on the use of combination chemotherapy (5-fluorouracil, leucovorin, and cisplatin) and radiotherapy in the treatment of locally advanced or metastatic LELC of lung. The inclusion criteria included age between 18 and 70 years, good performance state (WHO 0 or 1), histologically proven stage III or IV unresectable tumours, chemotherapy or radiotherapy naïve, and nasopharyngeal carcinoma ruled out by endoscopic biopsy and magnetic resonance imaging. Exclusion criteria included previous malignancies, major organ failure and active uncontrolled infections. In-situ hybridization (ISH) for EBV-encoded small nuclear RNA (EBER) was performed on the biopsy specimens. Serological tests for EBV viral capsid antigen were serially performed during chemotherapy. Chemotherapy constituted four 4-weekly cycles of 5-fluorouracil (5-FU,  $1000\text{mg}/\text{m}^2/\text{day}$  on day 1 to 4), leucovorin ( $200\text{mg}/\text{m}^2$  on day 1 to 4), and cisplatin ( $100\text{mg}/\text{m}^2$  on day 1). Sequential local radiotherapy to mediastinum, given as  $16 \times 2.5\text{Gy}/\text{fraction}$ , was included for locally advanced disease. Three cases (two females, mean age 42 years) of lung LELC were recruited between July 98 to June 99. Serum IgA titres to EBV were raised to the upper limit of detection of our laboratory at  $>1/640$  in all three cases. These remained at the same level throughout the course of chemotherapy. Two of the patients had adequate biopsy specimens for detection of EBER which were positive. The tumour response rate to chemotherapy was 67% (2/3) partial response and 33% (1/3) stable disease. The latter was given local radiotherapy with partial response. Severe toxicities (NCI grade 3 or 4) included grade 3 vomiting (1 case) and grade 3 stomatitis (1 case). *Our experience with the chemoradiotherapy helps in better understanding of the combined modality treatment in advanced or metastatic LELC of lung. This warrants future research in the treatment of this rather chemoradiosensitive malignancy.*