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# Cigarette Smoking is a Risk Factor for Bleomycin-induced Pulmonary Toxicity

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To ASSESS late pulmonary toxicity after bleomycin administration, we measured the vital capacity (VC), total lung capacity (TLC) and single breath diffusion capacity (KCO) on a single occasion in 71 patients who had completed treatment for testicular germ cell tumour.

All patients had a haemoglobin concentration (Hb) of > 11 g/dl and the 44 treated with bleomycin received a median dose of 360 mg (range 90–630 mg). Their median age at time of testing was 32 years (range 17–60) and the median time from treatment completion was 28 months. No patient had other evidence of pulmonary toxicity.

Multiple regression techniques were used to estimate the simultaneous effects of bleomycin dose, time since treatment, disease stage, smoking and anaesthesia on the various measures of lung function. The information obtained on current smoking, having ever smoked and average number of cigarettes smoked was highly correlated. Analysis of variance techniques were used to estimate the difference in lung function between those who never received bleomycin, those patients less than 2 years post-treatment and those more than 2 years post-treatment.

Bleomycin-treated smokers had significantly worse VC and TLC values than non-smokers ($P = 0.021$ and $P = 0.016$, respectively), and a significant improvement ($P = 0.049$) in VC occurred in those tested more than 2 years post-bleomycin. There was a suggestion that a slower recovery rate occurred in smokers ($P = 0.067$, test for interaction). When patients treated with bleomycin were compared with those not so treated (controls), the same pattern of improvement of lung function with time was seen and the poorer performance of smokers confirmed. Bleomycin-treated smokers also suffered a much greater drop in KCO compared with non-smokers within the first 2 years, but this difference in KCO disappeared for patients treated more than 2 years previously. None of the other patient characteristics examined had a significant effect on lung function measurements.

Impaired pulmonary function measurements in patients surviving overt bleomycin pneumonitis can be reversed completely in 2 years [1]. However, bleomycin-treated cigarette smokers have formed the majority of patients with persistent abnormalities of lung function in other studies of teratoma patients [2, 3, 4].

Alveolar macrophages from cigarette smokers release hydrogen peroxide both spontaneously and when incubated with bleomycin, a finding not seen in macrophages from non-smokers [5]. These findings may partly explain the association between smoking and impaired pulmonary function seen in this and other studies.

Our findings provide additional evidence that smoking is an important risk factor for bleomycin-induced pulmonary toxicity. The significance of this finding is increased by the absence of abnormalities in these tests of lung function in young cigarette smokers [6, 7].

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# Overcoming Tumour Radiation Resistance Resulting from Acute Hypoxia

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IN RESPONSE to our editorial entitled "Overcoming tumour radiation resistance resulting from acute hypoxia" [1], Senan writes that in our article we discuss the induction of acute hypoxia in tumours as a means of exploiting hypoxic cytotoxins,

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