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Letters to the Editor

Scar adenocarcinoma of the lung

I am confused about the purpose of the article by Edwards and Carlile.[1] On the one hand, they stated that the main purpose of their investigation was to define the cellular subtypes of adenocarcinoma in general and that little attention was paid to scar cancer as such; on the other hand, they described the ultrastructure of five selected cases of peripheral adenocarcinomas associated with a focus of scarring. A lot of their discussion was devoted to the morphology and histogenesis of scarring.

The authors observed that the central nidus of scarring consisted of elastic outlines of partly collapsed alveoli containing fine collagen fibrils. Only in one case was dense collagen seen.

These features are described in detail in another paper.[2] It is now quite clear that the so called central scar is, in fact, the collapsed elastic framework of alveoli. The fine collagen fibrils within alveolar spaces are most likely a result of organisation of exudate, which appears after collapse. This localised collapse also accounts for the pleural puckering. One needs to be very careful about not mistaking fibrous tissue between the opposing surfaces of the puckered pleura for pre-existing intrapulmonary fibrosis or desmoplastic reaction. The cause of the collapse is most probably tumour obstruction of a peripheral airway.

The term scar cancer should now be restricted to those in which definite pre-existing collagenous fibrosis, either diffuse or localised, is found.

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2 Kung ITM, Lui IOI, Loke SL, *et al*. Pulmonary scar cancer: a pathologic reappraisal. *Am J Surg Pathol* 1985;**9**:391–400.

Dr Edwards replies:

The confusion arises from an error which was overlooked at the proof stage. The second sentence of the second paragraph should have read: "The main purpose of these investigations ..." and not "the main purpose of our investigations ...". It refers to the ultrastructural studies by other authors mentioned in the preceding sentence.

It was not our intention to make a detailed study of scar formation in these tumours, but we felt it necessary to discuss possible mechanisms in the light of previous work. The paper by Dr Kung *et al*[1] reached us some time after our own paper had been accepted for publication. It is clearly an important contribution, and the conclusions are valid and reasonable. Nevertheless, it is difficult to rule out the possibility that a desmoplastic reaction is responsible for this appearance in some tumours, and the further possibility of malignant transformation around pre-existing scars cannot be ignored. The question still appears to be open. It may be that all three mechanisms play a part.

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Proposed classification of resistances to oral anticoagulant therapy

Resistance to oral anticoagulant therapy (OAT) is defined as the inability of OAT to bring the prothrombin time down to the adequate levels of anticoagulation when administered at a dose near or equivalent to the normally recommended doses. We retrospectively studied a series of 220 patients receiving OAT (acenocoumarol, tioclomarol, ethylbiscoumacetate, warfarin, phenindione): 10 resistances to OAT were found. Based on these and observations from other data, we propose a classification of different types of OAT resistance: (i) primary or secondary resistance according to the rapidity of occurrence (at the start of treatment or later); (ii) selective or generalised resistance according to the number of drugs taken (only one or several); (iii) absolute or relative resistance judged by the modification of the prothrombin time: absent effect (prothrombin time, 75%) or slight effect (prothrombin time between 50 and 75%).

The mechanisms of OAT resistance are various: absence of drug intake, excessive dietary vitamin K intake,[1] variations in the pharmacokinetics of oral anticoagulants (drug interaction),[2] oral anticoagulant malabsorption, enhanced metabolism,[3] and hereditary resistance. Serial measurements of the serum concentration permits estimation of the half life of oral anticoagulant[4] and provides information on the greatest part of the mechanisms of OAT resistance. Hereditary resistance is rare[5] and attributed to a changed hepatic receptor site for the oral anticoagulant. Diagnosis is difficult because a detailed genetic study is rarely possible. This sort of resistance is always primary.

When resistance is not overcome by progressive increase in doses of oral anticoagulant, change to another drug is necessary. But this change cannot be arbitrary. If a patient is resistant to ethylbiscoumacetate, he or she will probably also be resistant to phenindione. A change to acenocoumarol rather than warfarin is preferable (warfarin is associated (statistically) with the least resistance). Resistances to the drugs must be taken into consideration following any change in OAT.

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