FIBRE SIZE AND CHEMISTRY EFFECTS IN VITRO AND IN VIVO COMPARED

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INTRODUCTION

The biological activities of mineral fibres including their ability to cause disease are primarily related to their physical form. Fibres with widely different chemical compositions and composed of crystalline or amorphous materials can all cause the same biological effects if the fibres are within certain size ranges (Chamberlain & Brown, 1978, Stanton & Layard, 1978, Brown et al. 1978, Pott et al., 1987; Donaldson et al., 1989). However to cause disease such fibres must persist in situ in animals or man for a period probably related to life span and therefore shorter in animals than man. In in vitro systems with a time of exposure only rarely exceeding a few days even very soluble fibres can exert an effect even if that effect is still dependent on fibre dimension.

The chemical composition of the fibre is an obvious determinant of solubility but the role of chemistry as a further determinant of activity is far from certain. Throughout this volume the catalytic activities of some types of fibre are described but even so it is not obvious that such effects are primary determinants of pathogenesis. Although the composition of the fibres may contribute to the production of, for example, biologically damaging free radicals (see chapters by Aust, Pezerat, Yano etc. in this volume) it is not clear that such effects actually cause disease in vivo. The best evidence that a particular activity is responsible for pathogenesis is the absence of that activity in a closely related but harmless analogue or conversely the absence of pathogenicity in a material lacking the suspect short term activity.

If the composition of the fibre is important then it might be possible to create fibres with chemical compositions minimising pathogenicity. This possibility alone would make an examination of the effect of composition on activity worthwhile.

We have been studying the activities of mineral fibres and attempting to correlate these activities with both chemical composition and size. In particular we have been modifying the surface of fibres to obtain populations which differ in their apparent
chemical composition but retain similar size distributions. We have also been studying the activities of thermally degraded ceramic fibres in which partition of the components of the originally vitreous materials causes changes in both bulk and surface chemistry.

MATERIALS AND METHODS

Histopaque 1119 (sodium diatrizoate-Ficoll mixture (s.g. 1.119), poly-D-lysine and poly-L-lysine (molecular weight 130,000) and other biochemicals were obtained from Sigma, Poole, Dorset; the pentapeptide gly-arg-gly-asp-ser (GRGDS) was obtained from both Sigma and Boehringer, Lewes, Sussex. Octyldimethylchlorosilane and octadecyldimethylchlorosilane were obtained from The Aldrich chemical Co., Gillingham, Dorset.

Tissue culture medium, serum and sterile plastic-ware were from Flow Laboratories, Irvine, Scotland, and Gibco Europe, Paisley, Scotland. Fibronectin depleted serum, prepared by affinity chromatography on gelatin-sepharose, and rat plasma fibronectin were a kind gift from Dr R. Davies (MRC Toxicology Unit).

Figure 1. The time course of binding of amosite fibres to \(^3\)H-Thymidine labelled V79-4 cells, in Minimum Essential Medium (MEM) containing 10% fibronectin depleted serum or the same with the addition of 50 \(\mu\)g/ml human plasma fibronectin. The proportion of cells attached to the fibres was estimated by adding samples of cell suspension to density gradients 15 minutes after mixing cells and fibres. Upon centrifugation cells attached to fibres migrate to the bottom of the gradient.

Figure 2. The attachment of V79-4 cells to Standard grade ceramic fibres (squares) and the same fibres after exposure to 1200°C (triangles) and 1400°C (●) for two weeks. The proportion of cells bound to the fibres is estimated by totalling the proportion of radioactivity in the last 2 fractions on density gradients prepared as in figure 1.