Biological Foreign Particle Film Encapsulation

All foreign, biologically "inert" particles that are at least initially insoluble in biological fluids are enveloped by films composed of endogenous macromolecular and/or tissue surfactants. Marck *et al.*[1] reported that, under the conditions of their investigation, particles of different degrees of hydrophilicity showed different degrees of tissue interaction. They felt that their findings were relevant for bioadhesives, suture materials, and controlled drug release carriers[1]. It is our belief that the process of film formation has broad significance for the total field of the health sciences.

Ecanow[2,3] theorized that the presence of foreign particles, regardless of whether they are introduced as drug carriers, environmental pollutants, or whatever, can initiate pathological processes. Foreign particles are not "inert" in a physical–chemical sense[4]. The data developed in our studies of the relationship between pathology and particulate matter have resulted in a classification of inert particles similar to that of Marck *et al.*[1]

Class A particles are very hydrophobic and are wetted with great difficulty by tissue fluids. Such particulate matter is generally phagocytosed or walled off or floats on the tissue fluids as in the respiratory tract.

Class B particles sorb strongly onto cellular surfaces; these particles produce abnormal membrane-structuring effects. These effects, in turn, may initiate the process of uncontrolled cellular growth[3–5].

Class C particles are dissolved by the biological fluids after varying periods of time.

Particulate matter of Class A is the least biologically toxic. Particles of Class B are potentially the most pathogenic. Class C particulates are toxic only if they result in, among other responses, chemical or free radical reactions that may have a protein-denaturing effect.

Drugs and other therapeutic agents must be tested for their toxic potential. We wish to suggest that toxicity studies be expanded to include investigation of the possibility of encapsulation or partial film formation to determine the long-term biological effects. Aside from the pharmaceutical implications, films may contain significant etiological inferences. Thus, foreign inert particles, most of which are of Class A or C, are almost continuously present in the GI tract. Therefore, it is critical that no agent, *e.g.*, a surfactant, be introduced that will convert these particles to the Class B type.

If the matter of film formation is placed in the context of a lesion, its importance can be made explicit. In many respects, the lesion surface is similar to that of a foreign particle surface. In an ulcer, the crater edge contains fragments of denatured protein. If surfactants are introduced that can combine with these denatured particles and, in time, form a film matrix, then interference with normal healing of the ulcer may take place or a neoplasm might begin[3].

It is our belief that before any given substance is introduced into the body, there must be evidence that it does not initiate or promote adverse tissue reaction of the type discussed. Thus, products containing agents that conceivably bind inert particles to tissue membranes (*e.g.*, antacids that contain surfactants) should be studied to determine whether the surface-active components do initiate tissue changes and whether the surfactant involved adsorbs onto the surface of any lesion and, in the case of an ulcer, prevents normal healing. Failure to satisfy these requirements may cause patients an unacceptable risk.

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