

shown by SEM photomicrographs. In addition, touch to a smooth stainless steel sphere caused complete loss of endothelial cells in several areas. This type of damage induced by metal instruments will be examined further.

The acrylic polymer used for intraocular lenses has good optical and mechanical properties and has demonstrated a reasonable degree of bioacceptance during many years of ophthalmic application. It is a rigid, hydrophobic material and is not readily wet by physiological fluids or saline solution. Since the immediate tissue interactions are primarily biophysical and probably involve a hydrophobic interaction between the plastic and cell surfaces, our initial approach to interfering with adhesion was to apply a hydrophilic polymer (polyvinylpyrrolidone, PVP) solution in an attempt to produce an adhesion barrier-lubricant boundary layer (2). Both PVP and other hydrophilic polymer solutions completely eliminated adhesion damage to the endothelial cells.

The tissue-materials interface has been extensively studied from the standpoint of polymer biocompatibility for nonthrombogenic and tissue-compatible implants or prostheses (4). Short-term toxicology and thrombogenicity as well as long-term tissue acceptance have been major points of concern. However, except for attention to cell adhesion to plastic surfaces pertinent to tissue culture studies, cell binding to polymer surfaces from the standpoint of blood and tissue compatibility, and some studies related to surgical adhesives, dental restoratives, and the changes of the adhesive properties of cell surfaces accompanying tumor cell metastasis, there has been relatively little attention devoted to the fundamentals of short-term bioadhesion phenomena. The literature on protein and cell adhesion to hydrophobic polymer surfaces (5) does suggest that increasing surface hydrophilicity tends to reduce adhesion. Only a very qualitative understanding of the basis for improvement in what is loosely termed "biocompatibility" as a result of increased wettability or hydrophilicity of surfaces seems yet to exist.

Our research indicates that contact adhesion by hydrophobic or electrostatic surface interactions (or both) may be an important general phenomenon that occurs in many surgical procedures when foreign surfaces, such as plastic, rubber, metal, and glass, contact exposed tissue. Our finding that the elimination of such adherence is achieved by interposing a hydrophilic polymer at the interface suggests (i) a mechanism by which hydro-

phobic and electrostatic surface interactions can be masked and (ii) a role for the hydrophilic polymer as a lubricating boundary layer to minimize frictional shearing forces and so limit cell membrane damage.

We may be dealing with a phenomenon in surgery whose importance is not generally recognized because tissue damage of this type is not obvious and because postoperative complications are often complex in their origins. However, we believe that careful investigation of contacts with surgical gloves, surgical instruments, and catheter surfaces is likely to reveal tissue damage that is now unsuspected but that may significantly affect tissue healing and repair mechanisms. For example, abdominal adhesions may occur after contact with rubber gloves. Efforts have in fact been reported to minimize adhesions by intraperitoneal injection of hydrophilic polymer solutions. Although PVP and dextran appeared to produce significant improvements in animal experiments, the technique used for administering the antiadhesive polymer solution was not practical and unfortunately appears to have received little further attention (6).

In the case of vascular and urinary tract catheters, ample clinical evidence exists that tissue damage produces thrombosis, inflammatory reactions, phlebitis, and urinary tract infection, all of which may be lessened by hydrophilic coating (7, 8). We believe that such coatings are effective primarily because they produce a hydrophilic, nonadherent sur-

face with a low coefficient of friction so as to minimize the damage to the vascular endothelium or the urethral mucosa surfaces. Further studies in these areas are important because it may be relatively easy to favorably alter the surfaces that contact living cells to minimize tissue damage and so to avoid unnecessary surgical complications.

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Retinoyl Complexes in Batten Disease

A retinoyl complex was identified as the autofluorescent component of the neuronal storage material in Batten disease in a recent report by Wolfe *et al.* (1). Part of the evidence presented was based on their interpretation of the mass spectrum of lipid-free curvilinear bodies (CLB's). Prominent fragment ions included were those with a mass-to-charge ratio (m/e) of 255, 213, 185, 173, 159, 145, 133, 121, 119, 107, 105, 95, 93, 91, 81, 69, 55, 43, and 41. They compared these peaks with mass spectra of retinol, retinoic acid, and methyl retinoate obtained in our laboratory (2), as summarized by Elliott and Waller (3). The ions with m/e greater than 255 were not included in the report (1), but were shown in the mass spectrum of lipid-free CLB's at a recent meeting in Chicago (4). The mass spectrum showed a parent molecular ion at m/e 386 with fragment ions at m/e 368,

353, 301, and 275. These ions are not characteristic of vitamin A compounds but, when included with the fragment ions in the previous report (1), are identical to those of cholesterol (5). The nuclear magnetic resonance (NMR) data for the lipid-free CLB's are not inconsistent with the published NMR spectrum of cholesterol (6). The observed protons at 3.62 and 5.15–5.32 parts per million downfield from tetramethylsilane do not correspond to signals in published NMR spectra of the vitamins A (7). It should be noted that we have identified cholesterol as a contaminant in supposedly purified metabolites of retinoic acid many times. For example, cholesterol has cochromatographed with ^{14}C -labeled metabolites of retinoic acid on a silicic acid column, followed by sequential separation by thin-layer chromatography in four different solvent systems, and final-

ly, combination gas-liquid chromatography-mass spectrometry, where its identification was made. We have considered cholesterol complexed with retinoic acid. Such a complex would explain the findings of Wolfe *et al.* (1) as well as our own. However, no such complex has been demonstrated to our satisfaction.

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Nelson and Halley suggest that our data are more compatible with a retinoyl-cholesterol complex as the autofluorescent component in the neuronal storage material of Batten disease. We have found that although most of the phospholipids and cholesterol of CLB's are removed by multiple extractions with chloroform and methanol (2:1 by volume), the fluorescent residue, when subjected to basic or acidic methanolysis, still yielded small amounts of cholesterol and fatty acids together with large amounts of a fluorescent material that contained not only a compound which we reported as methyl retinoate but also more polar products which are in the course of investigation. All of these fluorescent components were clearly separated from cholesterol by thin-layer chromatography in benzene. It would thus appear that cholesterol in small amounts is indeed bound tightly to the retinoyl-peptide complex in CLB's, which explains the appearance of cholesterol in direct-inlet mass spectra of lipid-free CLB's. The cholesterol, however, was a minor component which eluted at 40°C. At higher temperatures (50° to

100°C) the major components eluted gave mass spectra with apparent molecular ions of m/e 482 and 576, together with prominent peaks at m/e 255 and below as reported in (1). Ions of m/e above 255 characteristic of cholesterol were not found in these mass spectra. Since cholesterol was eluted under electron impact, it is highly unlikely that it is covalently bound.

We disagree with the contention that the proton magnetic resonance spectra of the lipid-free CLB's dissolved in d_6 -dimethyl sulfoxide or treated with a strong base are "not inconsistent" with the published spectra of cholesterol. The bulk of the absorptions in cholesterol are in the region 0.67 to 1.2 parts per million (2), unlike our reported spectra. That our spectra do not correspond exactly to re-

ported spectra of the free A vitamins is not surprising since we were dealing with both the intact retinoyl-peptide complex and a base-treated material. More detailed chemical evidence for our initial report will be published elsewhere (3).

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Variations in the Earth's Orbit: Pacemaker of the Ice Ages?

Hays *et al.* (1) have "concluded that changes in the earth's orbital geometry are the fundamental cause of the succession of Quaternary ice ages." They reached this conclusion by statistical analysis of three time series (obtained by

combining data from two deep-sea sediment cores) without attempting to identify or evaluate "the mechanisms through which climate is modified by changes in the global pattern of incoming radiation. . . ." Such a procedure places stringent

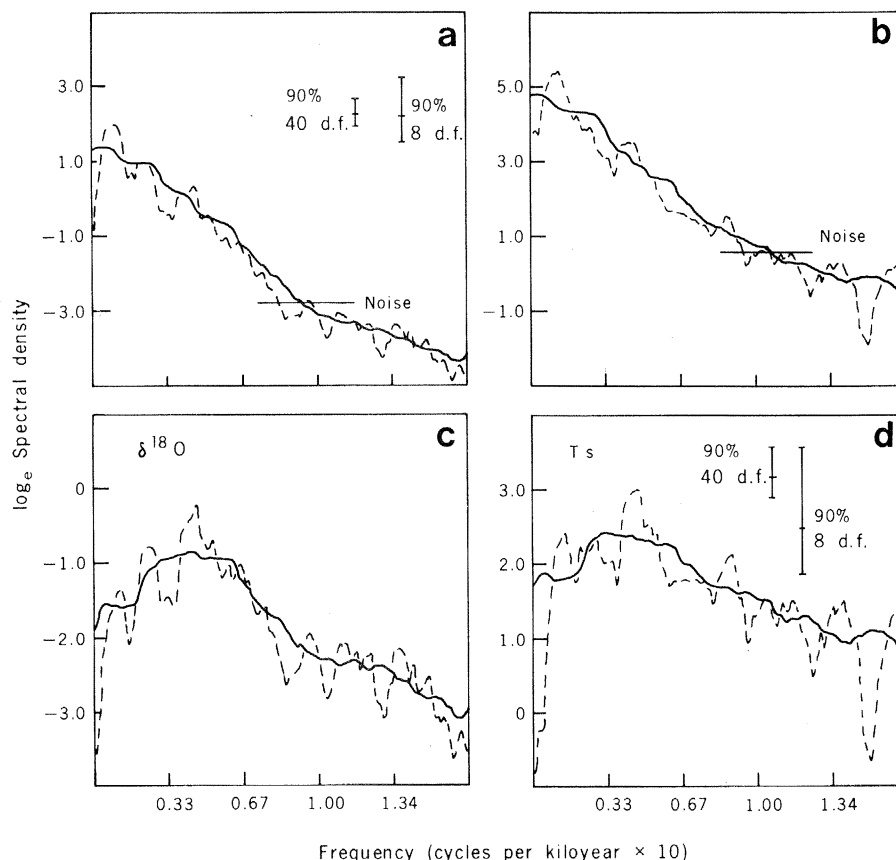


Fig. 1. Spectra of climatic variations in the combined (PATCH) record from two subantarctic deep-sea cores based on the TUNE-UP age model (1). (a and b) High-resolution spectra (dashed lines) and low-resolution spectra (solid lines) expressed as the natural logarithm of the variance per unit frequency as a function of frequency. (c and d) The same spectra after prewhitening with a first difference filter. Confidence intervals are the same for (a) and (b) and for (c) and (d).