Our experimental results seem to give strong support to our presumption that in injuries of the skin caused by burning or freezing, especially in the vesicles and in the cutis, large quantities of periodic acid–Schiff-positive material arise which in all probability correspond to neutral mucopolysaccharides. Shortly following the injury, increase of acid mucopolysaccharides may be observed, but beginning with the second or third day following the injury, the local appearance and the increase of neutral mucopolysaccharides are striking. The hexosamine content of the blood was found also to double shortly after the injury and slowly decrease from the third or fourth day following the injury.

We think that our results add support to our statement that the histological appearance *in situ* of neutral mucopolysaccharides is the consequence of a metabolic process following a general biological rule—a process which seems to occur whenever a local hypoxia or anoxia arises in the tissues without the immediate destruction of the whole tissue.

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HISTOLOGY

Collagen and a Cellulose-like Substance in Fossil Dentine and Bone

The first direct evidence that certain organic components are retained in the fossil remains of vertebrates comes from the analysis by paper chromatography of specimens of *Dinichthys* of Middle Devonian age (380 million years old)[1]. This work has shown that degradation products of collagen can still be recognized. More recently[2], it has been demonstrated that fossil dentine and bone-like tissues in Devonian ostracoderms are capable of being decalcified and sectioned on a microtome. Further work at the Royal Dental Hospital, London, using normal histological staining techniques, has now indicated the presence of polysaccharides as well as collagen in the dentine and bone-like tissue of the ostracoderms. Using fossil bone belonging to a bison from the most recent Ice Age, and to *Dremotherium* from the Miocene (25 million years old), electron microscope photographs have been obtained at the Nuffield Orthopaedic Centre, Oxford, showing collagen fibrils and the intact walls of canaliculi[3]. Furthermore, X-ray diffraction of the same material has established that it is the tubular form of collagen that is present.

In the work now in progress, an attempt has been made to isolate the organic content in the bone of a prosauropod dinosaur from the Upper Trias (200 million years old), and in the dermal armour of further Devonian ostracoderms. One of the main difficulties encountered, however, has been that since only dilute acids or alkalis at room temperature can be used to isolate the collagen, although most of the mineral content can be removed, certain minerals have so far resisted solution. In the dinosaur, a manganese phosphate has been the major obstacle, while in the ostracoderms there is a residual aluminium silicate. These minerals have been identified by their X-ray diffraction patterns.

Nevertheless, electron microscope investigations of patches of almost completely demineralized bone in the dinosaur, and dentine and bone-like tissue in the ostracoderms, reveal a fibrillar structure; an electron-diffraction examination of the same material shows a mixture of mineral and collagen patterns. In addition, in the dentine of the dermal armour of the ostracoderms, electron microscopy shows that the dentine tubules are intact, while the electron-diffraction pattern indicates that their walls are composed of an organic compound. The material is similar in appearance and staining characteristics to other mammalian tissue components, which have been isolated for X-ray diffraction and have given a cellulose-like pattern.

Our sincere thanks are due to Prof. J. Trueta of the Nuffield Orthopaedic Centre, Oxford, and to Prof. R. B. Lucas of the Royal Dental Hospital, London, for the provision of facilities. Financial assistance from the Nuffield Foundation is gratefully acknowledged by one of us (L. B. H. T.).

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PATHOLOGY

Paired Helical Filaments in Electron Microscopy of Alzheimer's Disease

In the light microscope, the characteristic change in the neurones of the cerebral cortex in Alzheimer's disease is the presence of dense bundles of argyrophilic fibrils. They are coiled into skeins or 'squash racket' shapes, and appear to fill most of the perikaryal cytoplasm, sometimes giving the cell a swollen appearance. It has been suggested by Divry[1] that the fibrils are extra-cellular except in the later stages of the change. The fibrils stain with congo red, and this results in a type of birefringence suggesting the presence of longitudinally arranged micelles in the fibrillar bundles. These well-known findings would lead one to expect the presence of fine filaments associated with these cells in the electron microscope, and if intra-cellular, these might be neurofilaments, which are suggested by Gray and Guillery[2] to be the basis of neurofibrillary argyrophilia.

This is a preliminary report of observations in the electron microscope on cortical biopsies from three cases of Alzheimer's disease, confirmed by light microscopy. In each case the biopsy was taken from the parietal lobe through a burr hole prior to ventriculography. The specimen was cooled rapidly below 20° C after removal and cut into small pieces in the fixative within 5 min of removal. The fixatives were 1 per cent OsO_4 or 0·6 per cent $KMnO_4$ buffered to *p*H 7·2, and fixation was continued for 4 h. The tissue was then dehydrated in alcohol and embedded in 'Araldite'. Most of the observations were made on material which had been stained in 1 per cent alcoholic phosphotungstic acid before embedding.

Most of the neurones seen were normal, being similar to those seen in biopsies from normal animals and from human cortex exposed for removal of tumours. A number of neurones, however, were very different from normal.