Fixatives and fixation: a review

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Introduction

Fixation in some form lies at the beginning of many morphological techniques from embalming to electron microscopy. The processes involved have grown up out of empirical systems or have been borrowed from other disciplines and the understanding of the mechanisms involved is not great.

The present review deals with the literature between 1960 and August 1968. A few papers which appeared before 1960 are included. For the literature before 1960 the reader is referred to the various excellent reviews on fixation which appeared at about that time: Wolman, 1955; Baker, 1960; Gersh, 1959; and Pearse, 1960. Since then have appeared reviews by Lojda (1965), Pease (1964) and Trump & Ericsson (1965), the latter two dealing mostly with electron microscopy. For the practical aspects of the subject the reader is referred to textbooks of histochemistry and electron microscopy (Pearse, 1960, 1968; Pease, 1964).

Fixation may be described phenomenologically, that is in terms of change using living tissue as a standard. The major processes which tissue fixation must ideally prevent have been listed by Baker (1960): autolysis, attack by bacteria, and change in volume and shape especially during subsequent preparative treatment. To these one may add loss of tissue constituents and change in spatial relationship of organelles and macromolecules. Ideally then, the fixed tissue should just "mark time".

Fixation may also be described in terms of molecular processes such as the formation of a macromolecular network between the various cellular constituents or in more specific terms in reactions between the fixative and some chemical group. A complete definition of fixation is difficult or even impossible as the changes brought about are necessarily compared with living tissues which themselves are not by any means completely characterized. At the present time, however, a number of fixatives are available each with its own potential usefulness, but none of which is universally applicable.

The chemistry of fixation

The chemical events which occur during fixation are beginning to be understood in greater detail. The fundamental reactions have been reviewed earlier by Baker (1960) and French & Edsall (1945). Some of the information is not due to work directed to the understanding of fixation but is a by-product of biochemical investigation into the structure and denaturation of proteins and nucleic acids by various methods. Denaturation has been defined by Scheraga (1960) as an intramolecular change from an ordered to a disordered state without rupture of covalent bonds, due to an altered environment. Under certain conditions denaturation may be reversible. Other data are derived from