A HISTORY OF PHOTODYNAMIC THERAPY

M. D. DANIELL AND J. S. HILL

Higginbotham Neuroscience Research Institute, Department of Surgery, Royal Melbourne Hospital, Parkville, Victoria

The origins of light as a therapy in medicine and surgery are traced from antiquity to the modern day. Phototherapy began in ancient Greece, Egypt and India but disappeared for many centuries, only being rediscovered by Western civilization at the beginning of the twentieth century through the Dane, Niels Finsen, and the Germans Oscar Raab and Herman von Tappeiner. The discovery of the tumour-localizing ability of haematoporphyrin, together with its phototoxic effect on tumour cells led to the development of photodynamic therapy, a promising tool in modern cancer treatment.

Key words: cancer, haematoporphyrin, history, laser, photodynamic therapy, phototherapy, tuberculosis, tumour.

Introduction

The use of light as a therapeutic tool in surgery is becoming increasingly important, with the routine use of lasers for photocoagulation and in the photodynamic therapy of cancer. The use of light as a therapy in human diseases has a very long history, stretching back into antiquity. There was a long period in which its uses were not appreciated, however, and only this century, through photodynamic therapy and psoralen molecules and ultraviolet A radiation (PUVA) therapy of some dermatological conditions, has light undergone a renaissance as a useful therapeutic tool in medicine and surgery. The rediscovery and development of phototherapy is also remarkable in that it was not until the second half of the 20th century that the English-speaking world began to appreciate its full potential. It is only by translating the old German, French and Danish texts that the discoveries of these early pioneers can be appreciated. The origins of photodynamic therapy have been investigated by reviewing this early literature that, until now, has been largely neglected. This paper traces the development of light as a treatment and the use of photodynamic therapy in surgery.

The interaction of light with some living cells is vital for their survival and yet under certain circumstances can lead to their destruction. Light is necessary for the production of carbon dioxide and oxygen in plants via its interaction with magnesium dihydroporphyrin, better known as chlorophyll, in the photosynthetic process which forms the basis for life on this planet. Yet there are simultaneous phototoxic reactions, the result of singlet oxygen formation, that would prove rapidly lethal if they were not quenched by the orange and yellow carotene pigments of plants. In humans, naturally occurring porphyrins, usually in iron complexes such as haemoglobin, myoglobin and cytochrome, are also essential for life and are operative in all aerobic cells. However, disturbance of synthesis of porphyrins responsible for the haem group leads to a class of diseases called porphyrias, each with a unique pattern of over-production, accumulation and excretion of intermediaries of haem biosynthesis. The main clinical manifestations are intermittent episodes of nervous system dysfunction and sensitivity of the skin to sunlight. This skin photosensitization is due to porphyrin accumulation and the consequent photodynamic action, after light activation, of singlet oxygen induced tissue damage.[1,2]

Similar phototoxic reactions have been used for the treatment of a variety of diseases including psoriasis, vitiligo and, more recently, cancer, via photodynamic therapy. This technique exploits naturally occurring but usually suppressed reactions. A photosensitizing dye is administered which localizes specifically in the tumour and is subsequently activated by light (usually a laser). When the sensitizer absorbs light of the appropriate wavelength it is converted from a stable electronic structure (ground state) to an excited state (singlet state). The short-lived singlet state may undergo conversion to a long-lived excited state (triplet state), which is the photo-active species responsible for the photochemical generation of cytotoxic products. Interaction of the triplet state with oxygen

Correspondence: Dr M. D. Daniell, Department of Surgery, Royal Melbourne Hospital, Parkville, Vic. 3052, Australia.

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