



The fundamental contribution of James Maxwell Ross Cormack (1909–1975) in suggesting the term “apoptosis”

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Abstract

This study highlights the historical contribution of Professor James Cormack by providing a Greek term that describes the process of programmed cell death. In 1972 the ancient Greek word “apoptosis” first appeared in the scientific literature. This short manuscript will examine the actual meaning of the term and its historical and philological background. The word “apoptosis” contains a variety of semantic nuances that are perfectly suited to describe such a complex set of biological events as programmed cell death.

Keywords Apoptosis · History · James Cormack · Ancient Greek sources

Dear Editor,

The ancient Greek word ἀπόπτωσης was introduced into the scientific literature by James Cormack (Fig. 1), M.A., B.A., epigraphist, archaeologist and Regius Professor of Classical Greek at the University of Aberdeen, Scotland, to denote what is now universally regarded as the process of “programmed cell death”. We know indeed that John Kerr and co-workers openly acknowledged the contribution of Professor Cormack in a footnote to their 1972 seminal paper [1], which has since had a strong impact in the biomedical literature being cited 11,700 times. They recognised that the “shrinkage necrosis” they had previously described in ischemic hepatocytes and other tissues should properly be renamed “apoptosis” according to the suggestion of the classicist they had consulted. Cormack apparently equated this cellular process with the “dropping off or falling off of petals from flowers, or leaves from trees”.

Much thought has been given to how “apoptosis” should be pronounced but little to the actual meaning of the word and its historical and philological background. The term derives from the prefix ἀπο- that means “off, from, away” plus πῶσις, whose meaning is “fall”. The prefix

ἀπο- conveys the sense of separation, the noun πῶσις the idea of downward movement or ruin. On what literary sources did Professor Cormack draw? According to Liddell-Scott-Jones’s Greek-English lexicon, ἀπόπτωσης has four main meanings. The first is “falling off or away”. In this respect, the term is cited in the *Hippocratic corpus*, namely *Mochlikon* or *Instruments of reduction* 35 (V-IV century BC), where it denotes the falling off of small pieces of bone and fragments of tissue from necrotic areas of the legs. Next, in *In Hippocratis librum de alimento commentarius III* (XV 343 K) Galen himself (II century AD) made use of this noun to denote the falling away of scabs from a wound. The botanist and pharmacologist Pedanius Dioscorides (I century AD) mentions the dropping off of flowers in the *Praefatio* of *De materia medica*. All these examples involve the concept of some kind of structure detaching from its context and falling off. Undoubtedly apoptotic cells shed condensed remnants from superficial cytoplasmic buds that detach and “fall off” or “fall away”, being rapidly phagocytosed by macrophages or internalised by cells of the same type. In the medical and biological literature, ἀπόπτωσης is often equated with the “falling off of leaves” from tree branches. This interpretation is reminiscent of a passage in *Iliad* VI 146–149, where the lives of mortal men are compared to the continuous process of leaves falling off in autumn and new buds bursting forth in spring. This simile fits the modern concept of apoptosis, in that one generation of men comes to life while the other dies away. Notably, however, Homer does not use the term ἀπόπτωσης to define this dying event but the verb ἀπολήγειν

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Fig. 1 Professor J.M.R. Cormack studying a funerary monument at Ure Museum of Greek Archaeology at the University of Reading (Courtesy of the Center for Epigraphical and Palaeographical Studies, The Ohio State University. With permission)

(to cease, end, stop, halt). The second meaning of the word ἀπόπτωσις is “vanishing, disappearance, negation”. Actually, apoptotic cells are rapidly degraded into picnotic microbodies that lead to the dissolution and disintegration of the original cell. In essence, apoptosis is a clean and elegant process of cell fading and disappearance that leaves no trace. The third meaning is “declension from”, which again implies a dimensional reduction or downward movement of apoptotic cells. Thus, the term ἀπόπτωσις is a felicitous word that includes a spectrum of semantic nuances ranging from decay to spoiling, from shrinkage to detachment, from loss of bonds to disappearance, from compression and condensation to migration and vanishing away.

As early as 1972, Kerr and Searle discovered ultrastructural features typical of “shrinkage necrosis” in basal cell carcinomas [2, 3]. Apoptosis can indeed be found in cutaneous diseases, particularly lichen ruber planus, lichenoid keratosis, discoid lupus erythematosus, graft-versus-host disease, adverse drug reactions, and cutaneous ultraviolet damage. When examined by light microscopy, these dermatoses show eosinophilic ovoid bodies with homogeneous appearance. They are variably referred to as Civatte bodies, or colloid bodies, or hyaline or cytooid bodies, or sunburn cells. These are apoptotic-diskeratotic keratinocytes found in the deeper layers

of epidermis and/or in the superficial dermis. These apoptotic keratinocytes migrate from the epidermis to the subepidermal papillary derma. In this case, the apoptotic process consists of the detachment of apoptotic cells and their descent to a deeper, underlying level. Here we can imagine encountering the fourth meaning of the term ἀπόπτωσις, namely the “direction in which a force is exerted”. The III century BC physicist and writer of mechanics, Phylo of Byzantium, the pupil of Ctesibius, adopted the word ἀπόπτωσις in his work *Belopoiika, On artillery*. He used this term to define the direction of a force acting on a missile. In the case of epidermal apoptosis, then, the word seems to imply a form of downward motion determined and directed by unknown forces.

We can only admire the extraordinary lexicographical insight and exquisite etymological skill of Professor James Cormack in finding a Greek word perfectly suited to describe such a complex biological process as programmed cell death. Professor Cormack died suddenly at the age of 65 and was buried in Aberdeen cemetery.

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