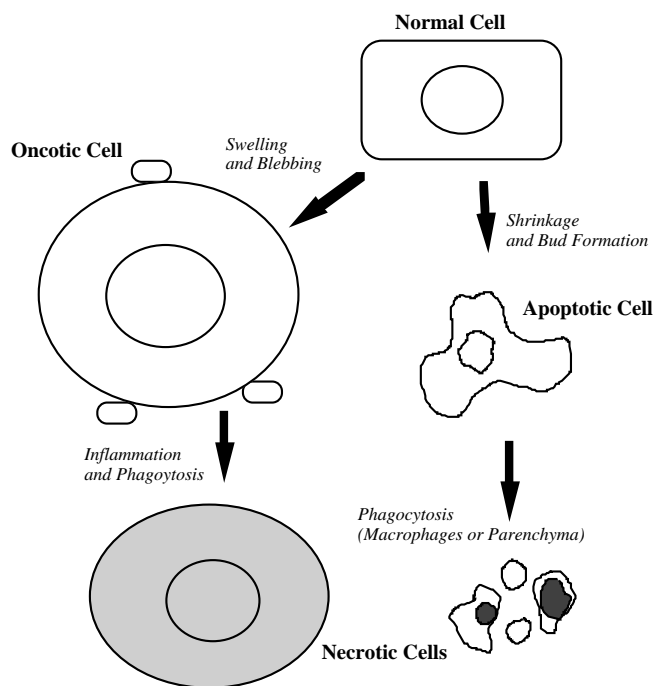


## EDITORIAL

# What's in a Name? Necrosis - Apoptosis and Oncosis

As emphasized in the commentary on surrogate markers in this volume (Ito, 2000), so-called 'programmed single cell death' or apoptosis is an important indicator of processes involved in neoplasia, with obvious impact on risk assessment. Cell death and division are the opposing events determining growth and it has long been realised that necrosis, from the Greek word for death, is of profound significance as a factor leading to regeneration. It has further been argued that apoptosis has wide ranging implications for tissue kinetics (Kerr et al., 1972). However, there remains a great deal of confusion in the nomenclature of cell death, as evidenced by the deliberations of an ad hoc committee of the Society of Toxicological Pathologists, whose recommendations, along with a number of related editorials, appeared in the journal *Toxicological Pathology* in 1999 (Levin, 1999; Levin et al., 1999; Lockshin, 1999; Majno and Joris, 1999; Mohr, 1999; Shirai, 1999). As stated by Majno and Joris (1999), since words represent concepts, their misuse points to a lack of conceptual understanding. In this case the problem arises because of the mistaken idea that apoptosis and necrosis are separate processes, rather than one being a subset of the other.

When apoptosis resurfaced, first as shrinkage type necrosis in 1971 (Kerr, 1971), and then as apoptosis (Kerr et al., 1972), an earlier description of the process leading having sunk without a trace (Gräper, 1914), it was heralded as a major new finding, with the possibility stressed of induction, for example in neoplasms, for clinical control of disease. The ensuing explosion of the literature has cast a great deal of light on underlying mechanisms although the situation *in vivo* as opposed to *in vitro* has proved complex indeed. Notwithstanding this fact we need to clearly differentiate forms of cell death actually encountered in toxicological pathology. The suggestion of Majno and Joris (1995) that the term 'oncosis', originally coined by von Recklinghausen in 1910 for osteocytes which died after swelling ('onco' in Greek), is most appropriate to contrast with the shrinkage characteristic of apoptosis has led to its recommendation for general use, naturally with the proviso that it does not encompass all non-apoptotic death, with autophagocytosis as one possible exception (Zakeri et al., 1995). Whatever, swelling related cell death is in fact well known from experimental investigations of ischemia in a variety of organs, including the liver, heart and nervous system, also being induced by a range of toxins.



**Figure. Schematic Representation of Oncosis and Apoptosis leading to Necrosis**

The emphasis should perhaps now be on further evaluation of processes to allow clearer distinction between forms of cell death and methodology for their demonstration. It appears clear from the ad hoc Committee's conclusions that the terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) technique is imperfect for this purpose, giving both false positive and false negative results. Obviously, interest will continue to be concentrated on mechanistic aspects and the degree to which apoptosis can be considered as 'programmed'. As stressed by Lockshin (1999) there may be a role for K<sup>+</sup> loss and consequent acidification of the cytoplasm, dependent on the amount of adenosine triphosphate available. While, his comment that 'in a pathological situation, there is no absolute dichotomy between physiological or apoptotic and a necrotic or oncotoc death' may be pertinent, the obvious differences evident at the morphological level demand a precise nomenclature.

As noted by Levin (1999), there are obvious concerns that introduction of a new system of nomenclature at this stage, when so many people around the world have accepted the dogma of the apoptosis-necrosis dichotomy, will encounter a great deal of resistance. Furthermore the likelihood that

scientists might find the similarity between oncosis and oncology a major disadvantage must be taken into account. However, these are not insurmountable problems and education efforts are clearly necessary on the basis of scientific validity (Levin 1999). The APJCP should add its voice to dispelling confusion among the toxicological pathology community involved in various aspects of cancer prevention, so that a real appreciation of physiological processes underlies our research efforts. Therefore is it not to be recommended that every effort be made to make use of the new paradigm ourselves in all our work, especially in the training of younger personnel, and alert biologists in other disciplines to its usage?. Comments on this and related questions are warmly welcomed in the APJCP.

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## Malcolm A Moore

APJCP Managing Editor/APOCP Secretary  
Editorial Office, Asian Pacific Training Center for Cancer Prevention, Bangkok Thailand  
T +81-52-853-8177 F 842-3830 malcolm812@yahoo.com



**Memorable Moments:** In place of a second photograph of authors of papers in the APJCP, they will be given the opportunity to provide pictures of occasions which they feel are deserving of human interest in the context of cancer prevention. This example from my own past illustrates particularly well the international flavour of the group of scientists that have had the pleasure of working as guests in Dr Nobuyuki Ito's lab in Nagoya over the years. The countries represented are Brazil, Portugal, Korea, Thailand, the United Kingdom, the USA, and of course, last but not least, Japan