Tissue Culture of Mammalian Cells

Richard G. Lynch, MD
Originally published in ASIP Pathways, Volume 3, No. 2 - May 2008

MILESTONES

Eagle H: **Nutrition Needs of Mammalian Cells in Tissue Culture.** *Science* 1955, 122:501-504

Harry Eagle

Virtually anyone who has ever grown mammalian cells in culture has encountered the term Eagle's medium. But only some of them will know much about the medium's formulator Harry Eagle. In his 1955 *Science* paper[1] Eagle summarized his extensive investigations that identified a chemically-defined medium that supported the *in vitro* growth of two cell lines, one a mouse fibroblast, the other a human carcinoma. Eagle's studies proved to be a tremendous breakthrough in the field of *in vitro* culture of mammalian cells.

Prior to Eagle's pioneering studies, the growth of mammalian cells *in vitro* involved explants of tissue pieces, a biological matrix such as a plasma or fibrinogen clot where the growing cells attached, and a liquid medium composed of human placental serum or adult serum, chicken embryonic extract and a balanced salt solution. Usually the cells grew for variable lengths of time and then the culture died. Established cell lines that grew by attaching to the surface of the bottle or flask were uncommon. Efforts by many investigators had established that growing mammalian cells in culture was not the simple matter that characterized the laboratory growth of bacteria.

In a meticulous body of work, Eagle identified 27 components – 13 amino acids, 7 vitamins, glucose, and 6 salts – that in the presence of a small amount of human or bovine serum supported the *in vitro* growth of the murine fibroblast and human carcinoma cells. Omission of any one of the 27 components resulted in cytopathic effects that initially could be reversed by replenishing the missing component. If the missing component was not replaced, the culture died in two to three days. Eagle observed that the amino acid requirements were met only by the L-enantiomorphs but that the presence of the D-enantiomorphs were not inhibitory of the L-forms.

Eagle worked out the optimal concentrations of each of the 27 components and was struck by the similarity in the results for the murine and human cell lines. He inferred that all mammalian cells might have similar requirements for *in vitro* growth. This proved generally correct and led to Eagle's success in establishing many new lines of human and murine cells. Eagle's discovery of a chemically defined medium launched decades of extraordinarily productive investigations of mammalian cell metabolism, physiology and pathology, many carried out in his laboratory or by many of the scientists he trained. Eagle was the first to show that mammalian cells contain a pool of free amino acids and that the cells could maintain the pool against a concentration gradient. He also showed that a minimal intracellular concentration of each of the amino acids was required for protein synthesis and optimum cell growth. Eagle's lab carried out studies on the undefined components present in serum that were necessary for continued cell growth. Those studies launched the field of cellular growth factors. His laboratory made major contributions to understanding amino acid metabolism in mammalian cells and the effects of population density and contact inhibition on macromolecular synthesis.

Reference

1. Eagle H: Nutrition Needs of Mammalian Cells in Tissue Culture, *Science* 1955, 122:501-504