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DISCUSSION.—DR. ORVAR SWENSON, Boston, Massachusetts: I wish to commend Dr. Dunphy for opening up a new field of investigation. Some years ago we investigated the composition of fracture hematoma, and it is through Dr. Dunphy's work that our interest in this field has been renewed. We have been able to demonstrate that in the first four days of wound healing there is a spectacular rise in mucoprotein. The problem is sampling. Dr. Dunphy's idea of using a sponge is indeed an ingenious one.

DR. JOHN A. SCHILLING, Rochester, New York: I, too, would like to commend Dr. Dunphy for this work, which, along with the work of Dr. Howes, is very fundamental and emphasizes that the so-called lag phase is a period of intense biologic activity. Perhaps it is in this period that all of us as surgeons can learn factors that will help us to push this curve to the left as we look at it from a clinical point of view.

We have used a somewhat different method for a number of years to secure wound fluid, namely, the implantation of a wire mesh cylinder, which is obliterated by granulation tissue, enabling a cellular study as well as analysis of fluid. The most recent study * really raises more questions than it answers, but it was related to the ultracentrifugal analysis of this fluid and to the Tiselius patterns.

There is a marked difference in the low density lipoprotein levels in wound fluid secured this way. First, in wound fluid the low density lipoproteins are low, yet they are high in the serum of a wounded animal. At the same time, if you look at the Tiselius pattern, the alpha and beta globulins are significantly elevated, and may be included in this category. In other words, some chemical changes occur. Thirdly, the gamma globulin is elevated in wound fluid; fibrinogen is absent.

The significance of this is a matter of conjecture, but the study of wound fluid and the fluid phase, as emphasized by Dr. Dunphy, seems certainly a fundamental contribution. Again, I would like to congratulate him on his study.

* Proc. Soc. Exp. Biol. & Med. 89: 189–192, 1955.

DR. AMOS R. KOONTZ, Baltimore, Maryland: Every surgeon certainly ought to be interested in wound healing. Whether he is or not, this paper by Dr. Dunphy is most stimulating. I would like to ask him one question about the role of fibrin in wound healing.

In about 1903, I believe, Hertzler showed that in intestinal anastomosis, when fibrin collects in the trough between the loops of the anastomosed bowel, it intensely facilitated wound healing. Baitsel, at Yale, in around 1916 demonstrated in tissue culture the advantage of fibrin in wound healing. He believed that fibrin was actually converted into connective tissue fibers.

I would like to know exactly how fibrin plays a part. I never have exactly understood it. Does it increase the growth of fibroblasts by furnishing more protein, or just how does it work? Thank you very much.

DR. DAVID ROBINSON, Kansas City, Kansas: This very interesting and fascinating study which Dr. Dunphy has just reported is of importance because it gets to the fundamentals of wound healing, or at least it tends to add basic knowledge.

One of the difficulties we have had when studying wound healing has been a lack of adequate tools other than just observation. Could one grow cells in tissue culture and measure them quantitatively, one might be able to get a quantitative assay of some meaning. Unfortunately there are too many imponderables and difficulties in tissue culture to make a good quantitative cell count unless one might employ the hela cell as a tool for the study of stimulator or inhibitor substances.

We have been especially interested, first, in stimulator substances, and have come to no very basic conclusions in tissue cultures studies. Of late we have been interested in inhibitor substances, particularly the role of the mast cell in wound healing, hoping that we might identify the mucopolysaccharide that is present in the wound as the inhibitor substance. There is some evidence to believe that the mucopolysaccharide released from mast cells may be an inhibitor; it may be heparin; it may be histamine; it may be some other substances which to date cannot be identified. One of

the difficulties of histochemical assays is that we cannot be quite sure what the chemical substance is that combines with the dye which is being studied.

I appreciate and have enjoyed this presentation by Dr. Dunphy and his associates. It is a real contribution to our knowledge today.

DR. J. ENGLEBERT DUNPHY, Boston, Massachusetts: I don't think I can answer Dr. Koontz's question. Fibrin may contribute to the first stage in the formation of collagen as part of certain soluble protein precursors. What is in it, I really don't know, but I suspect that when it is added to tissue culture or to a wound it is providing some of these precusors of collagen. Beyond that, I cannot go. It is one of the things we are interested in.

I would like to thank the discussants very much for their remarks.