The paper showed how permeability of blood capillaries could be determined quantitatively after a single passage of test solutes lasting a few seconds. The method was applied to different organs, with special emphasis on exchange between blood and brain. [The SCI® indicates that this paper has been cited in over 355 publications since 1963.]

Christian Crone
Department of Medical Physiology
Panum Institute
University of Copenhagen
2200 Copenhagen
Denmark

October 22, 1983

"Pappenheimer and associates introduced quantitative studies of capillary permeability. Their method, however, required isolation and artificial perfusion of organs. Chinard and his collaborators devised a principle which allowed organs to be studied in situ but their method was not quantitative. I solved this problem by making certain simplifying assumptions which made it possible to arrive at a simple mathematical expression from which capillary permeability could be calculated. The 'inaccessible' capillary membrane thus became accessible for quantification under in vivo conditions. The paper obviously filled a gap because very little was known about capillary permeability at that time. Interestingly, another solution to the same problem appeared almost in the same year from the other part of the globe, from Martin de Julián and Yudilevich in Chile.

"I was doing my thesis work in the late 1950s. The peculiar fact that the blood-brain barrier has an extremely low permeability aroused my interest. How could this be reconciled with knowledge that D-glucose virtually pours into the brain from the blood? The blood-brain barrier had, so far, largely been characterized with semiquantitative methods having a very poor time resolution. The 'indicator diffusion' method now made it possible to approach this structure. However, it was necessary to cut through a lot of mystifications about the blood-brain barrier to postulate that it was just another capillary with properties of its own. This immediately made it possible to apply the strict analysis used in capillary physiology in general—a reductionist view which paved the way for an impressive development in this area.

"With the method established, I went on to assess brain capillary permeability—a true gold mine—and I was lucky enough to find a real piece of gold: the nonlinear, facilitated, glucose transport across the blood-brain barrier—perhaps the best spin-off of the method.

"For quite a few years, there was considerable resistance against using the indicator diffusion technique, but things changed, and in the 1970s a surge of papers appeared based on this approach. The first to give the work full credit were my American colleagues, who chose me as the first recipient of the International Zweifach Award in 1979—given for work in microcirculation."

---