The need for a method allowing the pro-
tracted direct study of the liver uncompli-
cated by the contributions of other organs led to development of the isolated rat liver perfusion technique. The perfused rat liver closely simulated the physiological behavior of the liver in vivo with respect to metabolism of glucose and amino acids, synthesis of plasma proteins, and bile secretion. [The SCI® indicates that this paper has been cited over 600 times since 1961.]

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"Our first perfusion apparatus was a 'do it yourself' project. The 'heart-lung' was made from the multi-bulbed tube of an Allihn condenser, hand-ground glass valves, and fingers of surgical gloves. Our first rat liver perfusions were encouraging, but short-lived because of blood clotting; a pre-liver filter made of a piece of nylon stocking removed small clots and extended perfusion time to six or seven hours. Within a short time, with 14C-lysine, we demonstrated that the liver was producing 14C-labeled albumin, fibrinogen, and plasma globulins. Collaborating in this early work were graduate students Chauncey G. Bly and Michael L. Watson. Bly's PhD thesis was based on these early studies."

"There are two reasons for the frequent citation of this paper, (a) It afforded the first unequivocal demonstration of the dominant role of the liver in the biosynthesis of serum albumin, fibrinogen, and approximately 80% of the remaining plasma globulins. Several years later, by utilizing preparative zone electrophoresis to fractionate perfusates from liver perfusions and from rat hindquarters, we were able to document the view that the normal liver is the site of synthesis of virtually all of the plasma proteins with the notable exception of the gamma globulins. (b) It afforded a relatively inexpensive reproducible system for studying the direct interaction of various agents, on and with the liver, under conditions closely approximating the physiological, and with the aid of isotopically labeled metabolites. Over the intervening years the originally described operative technique and the apparatus have been substantially improved so that perfusions 24 hours in duration are routine."

"The technique of isolated rat liver perfusion has been widely and fruitfully applied to problems in biochemistry, physiology, and pharmacology, it will continue to be used by those seeking to explore further the unknowns of liver metabolism and function."