The purpose of this discussion is to review briefly the mechanisms of water flow in the biliary system as a prelude to the rest of this symposium which is primarily concerned with the flow of solutes - especially the lipid constituents which contribute to the pathogenesis of gallstones. It is convenient on anatomic as well as functional grounds to divide the discussion of water flow into a consideration of three regions: the bile canaliculi which produce a net fluid secretion, the gallbladder which performs net fluid absorption, and an intervening segment comprising the bile ducts and ductules in which water flow may be in either direction depending on the circumstances. In each of these regions the fundamental mechanism is osmosis, i.e. transepithelial water flow occurs in response to the active transport of solutes. With the possible exception of ductular secretion, however, the transported fluid is nearly isotonic with plasma. This means that the driving forces for bile production are completely dissipated before the final product becomes available for analysis, and this in turn adds greatly to the difficulty of learning the details of its original formation. Progress is being made, nevertheless, so that it is possible to outline at least the general features of this process and to explain the bases for currently promising speculations.

Absorption by the Gallbladder

As illustrated in Figure 1, the fluid absorbed by the gallbladder is for all practical purposes an isotonic mixture of NaCl and NaHCO₃. Over a period of hours this process leads to an increase in the concentration of bile acids and the other organic
constituents by a factor of six to eight. The luminal pH drops by approximately one unit and the concentrations of K⁺ and Ca²⁺ increase. The pH change is attributable to the removal of HCO₃⁻ while the pCO₂ remains in equilibrium with plasma. The concentrations of K⁺ and Ca²⁺ also remain in equilibrium, but owing to a diffusion potential which renders the lumen electrically negative and to the increase in bile acid concentration which decreases the activity coefficients of K⁺ and Ca²⁺, the concentrations of these counter-ions increase. Despite the substantial increase in total solute concentration, the osmolality of the luminal fluid is unchanged. This discrepancy is attributable to the aggregation of bile acid anions as micelles with an attendant decrease in their osmotic coefficient.

The mechanism of this remarkable process has been studied extensively (1-4) and it is now possible to suggest a reasonable working model to explain the following observations. 1) In contrast to the lumen negative diffusion potential which develops across the gallbladder in vivo, isolated preparations bathed on both sides by buffered saline show a negligible transepithelial P.D. 2) The transepithelial electrical resistance is much lower than the resistance of the mucosal cell membrane. 3) The transepithelial hydraulic conductivity is large by comparison with the values obtained for a variety of so-called "tight" epithelia such as the frog skin and the toad bladder which unlike the gallbladder separate solutions of very different osmolality. The importance of these characteristics extends well beyond the immediate problem of water transport in the gallbladder, because they also apply to a number of other so-called "leaky" epithelia including the small intestine, proximal renal tubule and the choroid plexus.