Salt and Water Transport
by Rabbit and Guinea Pig Gallbladder:
Effect of Amphotericin B on NaCl Influx

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Summary. Previous studies have led to the suggestion that salt and water absorption
by rabbit and guinea pig gallbladders exposed to Amphotericin B proceeds by a rheogenic
Na pump at the basolateral cell membrane. The present study in vitro was designed to
further characterize transport properties of rabbit and guinea pig gallbladders under control
conditions and to identify the properties of gallbladder mucosa which are altered by Am-
photericin B to allow for the induced serosa-positive electrical potential differences (PD).
Potassium is required in the bathing solution at a low concentration to maintain normal
tissue O_2 consumption, fluid absorption and the ability of the tissue to develop the maximum
Amphotericin B-induced PD; the relative effectiveness of alkali metal cations in substituting
for K is K > Rb > Cs > Li > Na. The carrier mechanism for coupled influx of Na and Cl
across the mucosal border of gallbladder appears to be functional in the presence of
Amphotericin B; in addition, the diffusional influx of chloride is not significantly altered
by the antibiotic. The primary action of Amphotericin B which appears to modify rabbit
and guinea pig gallbladders from having transmural PD's of less than ±1 mV to having
serosa-positive PD's of 5–30 mV is an increase in the mucosal cell membrane permeability
to Na. This permeability change has the effect of partially uncoupling NaCl influx. A
rheogenic Na pump mechanism at the basolateral membrane, presumably in operation
under control conditions also, may account for the PD.

The gallbladders of rabbit and guinea pig in vitro develop no signifi-
cant spontaneous transepithelial PD under control conditions, perhaps
because the active transport mechanism is an electrically neutral NaCl
pump (Diamond, 1962a) or because Na and Cl enter the cell across
the mucosal border by a neutral, coupled process (Frizzell, Dugas &
and Rose and Nahrwold (1976) have indicated that exposure of the
mucosal surface of gallbladders from rabbit, guinea pig, tortoise, toad
and frog to Amphotericin B results in the development of serosa-positive
transepithelial PD's as great as 20 mV. The PD was characterized in
the latter report as possibly being the result of an active rheogenic Na
pump at the serosal border, which was presumed also to function in net electrolyte absorption by the tissue. There are several apparent similarities between the electrical properties of rabbit and guinea pig gallbladders exposed to Amphotericin B and the properties under control conditions of intestine, gallbladders of goose, monkey and man, and certain other epithelial tissues. Thus, it was considered important to further characterize in gallbladder epithelium the dependence of the Amphotericin B-induced PD and the rate of fluid absorption on the ionic composition of the bathing solution; this may be helpful in identifying similarities between the ion transport mechanism of rabbit and guinea pig gallbladders and the corresponding properties of other epithelial tissues. The results of some studies on human gallbladder, which develops a spontaneous PD of 8 mV under control conditions, are included for comparison. Because the rates of most active transport processes are highly temperature sensitive, certain experiments performed on rabbit gallbladder by Cremaschi et al. (1971) at 27 °C were repeated in the present study at 37 °C.

Rose and Nahrwold (1976) mentioned several possible effects of Amphotericin B on rabbit and guinea pig gallbladders which could account for the induced serosa-positive transmural PD; three possibilities which currently deserve consideration are that Amphotericin B might A) increase the diffusional movement of Cl across the mucosal membrane, B) uncouple the mucosal membrane carrier-mediated NaCl transport mechanism, or C) increase the diffusional movement of Na across the mucosal membrane. In the present work the unidirectional influxes of Na and Cl across the mucosal membrane have been determined; possibility C appears to account for the Amphotericin B-induced PD.

Materials and Methods

Gallbladders from rabbit and guinea pig were removed shortly after sacrifice of the animal by Pentobarbital injection and placed immediately in control bathing solution at 0 °C. Human gallbladders were obtained at the time of cholecystectomy performed for cholelithiasis by members of the Department of Surgery. All patients were symptomatic. The fundus of human gallbladders was used for research and the remainder of the organ was sent to the Department of Pathology for histologic examination. Only results on human tissue having histologically normal mucosa are reported in this paper. Gallbladders were washed with cold Ringer’s solution to remove bile. The serosa of human gallbladder was removed by blunt dissection, which causes only minor changes in electrical parameters (Rose, Gelarden & Nahrwold, 1973).