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THE GALLBLADDER EPITHELIUM

IN EXPERIMENTAL CHOLELITHIASIS

A thesis
submitted in partial fulfilment
of the requirements for the degree of
DOCTOR OF PHILOSOPHY
in the
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by
SUM PING LEE
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This work is dedicated to my wife, Mary.

ABSTRACT

1. The behaviour of the gallbladder epithelium in three models of experimental cholelithiasis has been studied. The models are : (a) rabbits when fed a lithogenic diet containing 0.75% dihydrocholesterol for 7 days (b) mice when fed a lithogenic diet containing 1% cholesterol and 0.5% cholic acid for 42 days, and (c) guinea pigs when given subcutaneous injections of Lincomycin (60 mg/kg) for 7 days.
2. The morphological changes in the gallbladder epithelium during gallstone formation have been studied with light microscopy and autoradiography. In all three models, there was a marked increase in cell proliferation early in the lithogenic process before stones were formed. Epithelial dysplasia was common. In the mouse and guinea pig, these cellular proliferative and dysplastic changes progressed to metaplasia with new gland formation.
3. The quantitative and qualitative presence of mucus (glycoproteins) in the gallbladder epithelium has been studied by glycoprotein histochemistry of

microscopic sections, by scanning and transmission electron microscopy, and by chemical extraction and analysis of the monosaccharide radicles of the soluble glycoproteins. In all three models, a progressive increase in histochemical staining reaction in the epithelial cells was observed and commenced at a time before stones were formed. Results of the electron microscopic studies supported the histochemical study and in addition, demonstrated the presence of increased amounts of mucus droplets in the subapical zones of gallbladder epithelial cells. Extraction and chemical analysis of the soluble glycoproteins showed a quantitative increase in the glycoprotein content of the gallbladder, starting before stones were formed and persisted to when stones had formed. Both the histochemical and the chemical studies failed to demonstrate a qualitative difference in the mucus produced at different stages.

4. Fluid transport across the gallbladder mucosa has been quantitated by an in vitro preparation (Diamond 1964) in the rabbit and the guinea pig models. In both models, there was an

increase in the rate of fluid transport detectable before stones were formed, and returned to normal values when stones were formed and after the lithogenic treatment was stopped.