SUMMARY AND CONCLUSION

1) A peptic ulcer is a 'mucosal hole' in any portion of gastrointestinal tract exposed to acid and pepsin secretion. At least 98% peptic ulcers are located either in first portion of duodenum or in stomach. About 5% individuals with gastric ulcers develop duodenal ulcers, but 20% of those with duodenal ulcers develop gastric lesions. Duodenal ulcer is a chronic and recurrent disease. It may be superficial involving erosions of outer layer or deep penetrating through submucosa or often perforating through the wall of the duodenum.

The prevalence of duodenal ulcers in a population ranges from 6 to 15%. It is striking fact that duodenal ulcers are more common in males than in females. It is also known that this immunity is increased during pregnancy, so much so that the ulcer may heal up during this period but reappears at the end of the pregnancy. This suggests hormonal role in healing of ulcers. Not only is duodenal ulcer much less common in women but it also appears to run a less severe course, at any rate judged by liability to perforation. It was shown that chance of a man developing a duodenal ulcer remains remarkably constant between ages of 20 and 65 but chance of a woman developing duodenal ulcer remains relatively low throughout whole of her active
reproductive life but increases sharply at the time of menopause. Sex difference in the formation of induced duodenal ulcers is shown by some workers.

The peptic ulcer is believed to be developed when there is unfavourable balance between gastric secretion and gastric or duodenal mucosal resistance. Various physiological abnormalities alone or in combination may lead to stimulation of hyperacidity. It may be a temporary phenomenon associated with stressful life events. The hyperacidity may also have genetic basis. The hypersecretion is related to an abnormally large total mass of parietal cells or either increased responsiveness of parietal cells to secretory stimuli or lack of normal regular controls. Increased level of gastrin or unusual sensitivity of parietal cells to gastrin stimulation may also be involved.

A number of chemicals have been used as duodenoulcerogens, one of them is cysteamine. During cysteamine-induced duodenal ulceration, the Brunner’s gland function was observed to be impaired. Bicarbonates and mucus glycoproteins are secreted by the Brunner’s gland and some other cells like pyloric gland cells, goblet cells, etc., which contribute to form an unstirred layer over the gastric and duodenal mucosa and serves as a mixing barrier to acid. Thus,
the important biological functions of glycoproteins are protection, lubrication and transport. In duodenum these glycoproteins are mainly secreted by the Brunner's glands, duodenal goblet cells and mucus-secreting cells of crypts of Lieberkuhn.

The glycoprotein can be classified as neutral and acidic glycoproteins. Goblet cells of duodenal mucosa and mucus-secreting cells of crypts of Lieberkuhn secrete neutral and acidic type of glycoproteins whereas Brunner's gland secrete mainly neutral glycoprotein.

2) Critical evaluation of the above review indicates that:

i) in peptic ulcers, main ulcers are duodenal ulcers;

ii) duodenal mucosa is mainly protected by glycoproteins and bicarbonate secretions from anterior part of the duodenum;

iii) there may be influence of sex hormones in the protection of duodenal mucosa from damaging effect of acid secretion from stomach;

iv) the chief source of glycoprotein is the Brunner's gland cells and some mucus-secreting cells of the duodenum.
The present work is undertaken to discover whether there is effect of sex hormones in the protection of duodenal mucosa or not. The plan of work consisted the following studies:

i) critical evaluation of cysteamine-induced duodenal ulcers in normal, gonadectomised and gonadectomised + hormone-injected male and female mice;

ii) morphology and histology of pyloroduodenal junctions of cysteamine-treated and control male and female mice;

iii) histochemistry of pyloroduodenal junctions of cysteamine-treated and control male and female mice,

iv) colorimetric estimations of protein and constituent sugars like hexose, fucose, sialic acid from Brunner's gland glycoprotein of cysteamine-treated and control male and female mice.

For the present investigation male and female mice weighing 25 to 30 gm and about 2 months of age were used. Different methods of duodenal ulcer induction were tried and cysteamine-induced gastrointestinal ulceration (Selye and Szabo, 1973) was selected. Initially, the mice were divided into six groups. They
were starved for 24 hours, during which only water was supplied *ad libitum*, and injected with cysteamine-HCl in water (40 mg/100 gm BW) subcutaneously twice at the interval of 4 hours. The controls received water only. Twentyfour hours after the second dose, the mice were sacrificed by cervical dislocation. The pyloroduodenal junctions were dissected out as a single unit, opened along the greater curvature of stomach and mesentery of duodenum and processed for different studies.

Cysteamine Treated Mice

<table>
<thead>
<tr>
<th>Cysteamine Treated Mice</th>
<th>Control Mice</th>
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<tbody>
<tr>
<td>1. Normal $\sigma^+$ Cysteamine (CM$_1$)</td>
<td>Normal $\sigma^+$ (M$_1$)</td>
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<td>2. Castrated $\sigma^+$ Cysteamine (CM$_2$)</td>
<td>Castrated $\sigma^+$ (M$_2$)</td>
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<tr>
<td>3. Castrated $\sigma^+$ Testosterone + Cysteamine (CM$_3$)</td>
<td>Castrated $\sigma^+$ Testosterone (M$_3$)</td>
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<td>4. Normal $\varphi^+$ Cysteamine (CF$_1$)</td>
<td>Normal $\varphi^+$ (F$_1$)</td>
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<tr>
<td>5. Ovariectomised $\varphi^+$ Cysteamine (CF$_2$)</td>
<td>Ovariectomised $\varphi^+$ (F$_2$)</td>
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<tr>
<td>6. Ovariectomised $\varphi^+$ Estrogen + Cysteamine (CF$_3$)</td>
<td>Ovariectomised $\varphi^+$ Estrogen (F$_3$)</td>
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5) Following studies were carried out:

1. Gross Morphology

i) The mucosa of pyloroduodenal junction was stained for alkaline phosphatase to highlight the mucosal nature and changes in mucosa. Coloured photographs were taken wherever necessary.

ii) The ulcers were critically evaluated under steriomicroscope and ulcer index were calculated.
using Szabo's (1978) method. The ulcer index of male and female were compared statistically to find out whether the differences were significant.

2. Histology

The pyloroduodenal junctions were fixed and routinely processed for histological technique. Histology of pyloric glands, duodenal villi, crypts of Lieberkühn and Brunner's glands was studied.

3. Histochemistry

To study the nature of glycoproteins from pyloroduodenal junction, histochemical techniques were used. Not all histochemical methods were adopted for this study because we wanted to know broadly the nature of glycoproteins secreted in the duodenum.

i) Study of glycoproteins in general by PAS technique.

ii) Study of acidic glycoproteins by AB pH 2.5 technique.

iii) Study of sulphated glycoproteins by AB pH 1.0 technique.

iv) The difference between acid mucins and neutral mucins was evaluated by AB + PAS technique and between sulphated and carboxy mucins by acid hydrolysis technique.
4. Biochemistry

With the help of present techniques available it was not possible to separate pyloric glands, crypts of Lieberkuhn and goblet cells but Brunner's glands were isolated by using method described by Satakopan and Kurup (1977). Estimation of different constituents sugars and protein from the glycoprotein was carried out.

6) Cysteamine given in double dose produced duodenal ulcers in both male and female mice. There was no significant difference in ulcer index of male and female mice but the damage was more in male. In ovariectomised and castrated mice the severity of ulcers increased; and also the ulcer index. In gonadectomised + hormone-injected mice the severity of ulcers was reduced. Histologically, changes were observed in the intensity of eosin staining, changes in size and shape of secretory cells and nuclear changes. Pyloric glands were strongly alcinophilic in nature while pyloric pit cells were strongly PAS-positive. Some goblet cells and cells from crypts were PAS-positive and some were alcinophilic at both AB pH 2.5 and AB pH 1.0. The cells were stained blue purple in AB + PAS technique. The Brunner's glands were strongly PAS-
positive. With AB(pH 2.5) duct cells and some acini stained blue, indicating presence of acidic mucosubstances. With acid hydrolysis the alcianophilia was partially or at some places totally lost, indicating presence of carboxy mucins in their cells. In cysteamine-treated mice in general, the staining for both neutral glycoprotein and acidic glycoprotein was reduced. In operated and cysteamine-treated mice the reduction was more and in operated + hormone injected + cysteamine-treated mice the reduction was like that in normal cysteamine-treated mice. In colorimetric estimations the values of protein and sugars were decreased considerably in cysteamine-treated mice. The reduction was pronounced in cysteamine-treated operated mice which were recovered in hormone-treated mice. No sex difference was observed at histochemical or biochemical level.

The results of present investigation showed there was duodenal mucosal damage in the cysteamine-treated and gonadectomised cysteamine-treated mice. The damage was recovered after due treatment of hormones. Introduction of cysteamine caused the formation of ulcers in both sexes. However, they did not show any significant sex difference in the production of ulcers. In gonadectomised mice there was an increase in average incidence of ulcers upon the administration of

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estrogen and testosterone ulcer index was reduced significantly.

The studies on histochemistry and biochemistry of glycoproteins showed that there was a loss of glycoproteins in ulcerated mice which was very prominent in ovariolectomised and castrated mice; upon respective hormone therapy the loss was recovered.

Though the mechanism of anti-ulcer action of hormone is not fully understood but from the present investigation it is clear that

i) there is no sex difference as far as duodenal protection from acid chyme is concerned,

ii) both the sex hormones influence the secretion of glycoproteins from various parts of duodenum, the substance involved in the production of the duodenal mucosa, and

iii) this is well proved in Brunner's gland, which were studied histochemically as well as biochemically. In Brunner's gland there is neutral glycoprotein in majority of the animals, described in detail in the introductory chapter. In the present investigation acidic nature of glycoprotein is also been described in the anterior part of the duodenum. This nature may be very important in the protection of the duodenal mucosa.