Abstract. Background: Pyloric cells with “glassy” cytoplasm were detected 20 years ago in the human gastric mucosa, and subsequently in the gastric mucosa of two baboons and of transgenic mice. These pyloric cells, called glassy cells (GCs) show a homogeneous, eosinophilic material that pushes the nucleus towards the free border of the cell.

Materials and Methods: The frequency of baboons having pyloric glands with GCs was assessed in the stomachs of 92 consecutive animals, dying of non-gastrointestinal disorders. Results: High power examination of the apparently normal gastric mucosa revealed that 10.9% (n=10) of the 92 baboons had GCs. Periodic acid Schiff (PAS) and PAS-diastase stains suggested that the glassy material might be a glycoprotein. Conclusion: The relatively high frequency of GCs in the gastric mucosa of baboons suggests that this animal might be a useful model for investigating the effect of the environment in the development of GCs, as well as ascertaining the true nature of the retained “glassy” material.

In 1836 Boyd (1) described the normal structure of the human gastric mucosa. Since then, with the introduction of suitable tissue fixatives, embedding and staining procedures and the improvement of ancillary techniques, such as electron microscopy and immunohistochemistry, many workers have studied the normal histology of that mucosa in more detail (2-8). It is now known that the gastric mucosa operates through two main systems – the exocrine and the endocrine. The specialized exocrine cell system includes three glandular phenotypes, the cardia glands, not recognized by all authors (9), the fundic glands and the pyloric glands. Authors concur that the exocrine glands of the gastric antrum are lined by only one phenotype of pyloric epithelial cell (2-8). These cells have ill-defined borders with a mucus secreting, micro-vacuolated cytoplasm (7, 8).

Recently, however, several reports have indicated the presence of other phenotypes of gastric cells in the gastric antrum, namely pyloric cells with cilia (10-11), with large (mucin negative) vacuoles (12), with small (mucin negative) vacuoles (12), with a dense luminal border (12), with eosinophilic granules (13) and with pancreatic features (14). We have also detected another phenotype of gastric cells in humans (13). These cells, which are characterized by a homogeneously eosinophilic cytoplasm with “ground-glass” appearance, are usually found in one gland or in a group of pyloric glands. The “glassy” material pushes the nuclei of the pyloric cells towards the free border of the cells. Because of their appearance, they were called “glassy cells” (GCs).

In subsequent studies the frequency of GCs in populations dwelling in disparate geographical regions was investigated (15-19). In a more recent comparative survey of gastrectomies (20) it was found that GCs occurred in 2.1% of the 1,261 gastrectomies reviewed in the Pacific basin, but only in 0.6% of the 1,942 gastrectomies reviewed in the Atlantic basin (p<0.05). Interestingly, the proportion of gastrectomies with GCs was higher in Vancouver Canadians than in New Yorkers and in Chileans than in patients living in Buenos Aires, despite those populations residing at approximately the same geographic latitude, respectively, but in different basins (20). This results suggested that GCs occurred independently of the race of the individuals and that its presence might had been evoked by the dissimilar environmental exposures in the two basins. This suggestion seemed to be validated by the fact that other histological parameters influenced by environmental factors, such as extensive intestinal metaplasia (21) and ciliated metaplasia (22), were also higher in the same
inhabitants of the Pacific than in those of the Atlantic basin. It was concluded that environmental factors might be able to modify the histological make-up of the gastric mucosa.

We also found GCs in the gastric mucosa of two baboons (23) and more recently in the gastric mucosa of transgenic mice (24). The latter finding suggested that the development of GCs might be also be provoked by genetic manipulation.

In the present survey the frequency of baboons having GCs in the gastric mucosa was assessed.

Materials and Methods

The stomachs (sampled at autopsy), of 92 olive or olive/yellow hybrid baboons (Papio hamadryas anubis, P.h. cynocephalus, respectively) were investigated. The non-human primates (NHPs) were members of colonies at the Southwest National Primate Research Center, Southwest Foundation for Biomedical Research. The conditions of animal housing have been reported elsewhere (25). Briefly, the NHPs were housed in metal and concrete indoor-outdoor cages and were fed commercial monkey diets occasionally supplemented with a variety of fruit and vegetables. Water was available ad libitum.

The NHPs were euthanized with a commercial barbiturate euthanasia agent or died naturally. All the procedures were conducted in accordance with the Institutional Animal Care and Use Committee guidelines.

At necropsy, longitudinal tissue samples from the stomach, including the distal esophagus and the proximal duodenum, were fixed in 10% neutral buffered formalin, processed conventionally, embedded in paraffin, cut at 5 μm, stained with hematoxylin and eosin (H&E), and evaluated by light microscopy.

Three cases having “glassy cells” were stained with Periodic Acid Schiff (PAS) and with PAS-diastase (PAS-D). The gastric sections were scrutinized at 200x to disclose the presence of GCs.

Results

GCs (Figure 1) were detected in H&E stains, in 10.9% or in 10 of the gastric specimens in the 92 baboons. In 9 out of the 10 cases, GCs were found in the antrum and in the remaining one, both in the antrum and the cardia region (i.e. in areas having mucous secreting pyloric cells). At their luminal border, GCs usually showed remnants of the normal, micro-vacuolated, mucin-secreting cytoplasm (Figure 1).

One animal had one gland showing GCs, two animals had two glands with GCs, 5 had 3 glands with GCs and of the remaining 2 animals, one had 6 glands with GCs and the other the entire length of the pyloric antrum showed GCs (Figure 2).

In all 3 cases stained with PAS and PAS-D, the “glassy cells” were faintly PAS positive but PAS-D negative.

Discussion

A variable number of GCs were found in the pyloric glands in about 10.9% of the baboons investigated, a proportion that was higher than that reported in specimens from human subjects (20), namely 1.2% (38/3203) (20). Since environmental factors are assumed to influence the presence of GCs (20), the possibility that environmental factors acting in the baboons at the Southwest Foundation for Biomedical Research, San Antonio might have contributed to the presence of GCs, cannot be totally rejected.

Despite the fact that GCs can easily be recognized in H&E stained sections, we have been unable to determine the true nature of the “glassy” material. The faint positive
staining with PAS and the negative reaction following PAS-diatase suggest that the “glassy” material might be a glycoprotein (20). The faint PAS reaction in GCs differed from the strong PAS positive reaction found in “ground-glass” hepatocyte from patients with B hepatitis, with Lafora’s disease or with liver-transplantation (26).

We have previously tested several histochemical and immunohistochemical stains to highlight the nature of the accumulated material in the cytoplasm of GCs including alcian blue pH 2.5, high iron diamine, Small Intestinal Mucinous Antigen (SIMA), oil red staining on wet sections, alkaline Congo red, Chromogranin A, Prussian blue, lysozyme, hepatitis B core antigen, Cystatin C, orcein and hepatitis B surface antigen (20). All were negative. These negative reactions suggest that the material is not lipid, amyloid, sialomucin, sulphomucin, iron, lysozyme, or neuroendocrine. The negative reaction with Cystatin C indicated that the “glassy” material was not the same as the Cystatin C-positive eosinophilic, “glassy” material found in the cytoplasm of human duodenal cells (27).

The proteinaceous, “glassy” material secreted by GCs-organelles is, for unknown reasons, being retained in the cytoplasm of the pyloric cells. In this respect Kopito and Sitia (28) have claimed that all cells are equipped with a proteolytic apparatus that eliminates misfolded and damaged proteins. The 26S proteasome, the principal engine of cytoplasmic proteolysis, requires unfolded substrates but is ineffective at degrading aggregated proteins. When the production of aggregated proteins exceeds the cell capacity to eliminate them, a phenomenon of cellular indigestion of the endoplasmic reticulum (ER) occurs. This is the case for plasma cells with accumulated immunoglobulins in their cytoplasm, known as Russell bodies (29, 30). The condensation of Russell immunoglobulins suggests that the mechanism of protein transport in the ER is ineffectual in those plasma cells and that the accumulated immunoglobulins are neither degraded nor excreted, thus remaining stored in dilated cisternae (28). Although our studies at the Transmission Electron Microscopy (TEM) level of GCs in transgenic mice were not conclusive (24), a similar mechanism to that described by Kopito and Sitia (28) might be valid for GCs.

In conclusion, the findings in the baboon confirm the identification of GCs, a phenotype also detected in the gastric mucosa of human subjects (20) and of genetically manipulated mice (24) and the possibility that GCs might be found in other species should be entertained.

The relative high frequency of GCs in baboons suggests that this animal might be a useful model to carry out investigations aimed to disclose the true nature of GCs, as well as to study the effect of the environment in the development of these cells.

References