

## **Ghrelin physiology in a species (sheep) that has continuous gastric function**

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Sheep are ruminants and maintain gastric function for many days, even on a fast, since the rumen is adapted to the digestion of cellulose. We have measured plasma ghrelin levels around feeding time and also have examined effects of ghrelin on voluntary food intake (VFI) and the secretion of growth hormone (GH) in this species. Plasma ghrelin levels are increased preprandially when sheep are on a programmed feeding regimen; this is followed by a rise in plasma GH levels. Such a response (in anticipation of feeding) is seen in Lean, Normal and Fat animals. Unlike data from other species we observed that plasma ghrelin levels are higher in Lean sheep. A large dose of ovine ghrelin given i.v. had no effect on the VFI. Central administration of ovine and human ghrelin in various paradigms caused the secretion of GH, but did not affect VFI. Human ghrelin was more potent than ovine ghrelin in causing the secretion of GH. These data suggest that ghrelin has a more significant role in the regulation of the GH axis than in the regulation of feeding in this species. Whilst ghrelin is known to be secreted from the stomach in monogastrics, it is found in the abomasum of the sheep. Using polymerase chain reaction, we have also found mRNA for ghrelin in the hypothalamus. Immunoreactive ghrelin was found in the median eminence. With this evidence of production by the brain, we measured plasma levels of ghrelin in the hypophyseal portal blood and peripheral jugular blood. Higher levels in the portal blood indicated secretion from the brain. It is possible, therefore, that brain secretion of ghrelin is relevant to the control of GH secretion from the pituitary gland. These novel studies in sheep provide new information about the physiology of ghrelin that indicates a predominant role in the regulation of the GH axis.