did not result in any significant change in the plasma concentration of GIP, pancreatic glucagon, enteroglucagon or insulin.

Discussion. We have shown that a substantial release of various gastrointestinal hormones occurs after ingestion of water by normal subjects. The mechanisms involved in the release of these hormones, however, appear to differ. The release of PP was blocked in the atropinised subjects suggesting an important influence of the cholinergic innervation. This observation is in accord with that of Schwartz et al.[10] where the PP rise after gastric distension was also blocked by atropine. Adrian et al.[11] have shown that the PP release following insulin hypoglycaemia, caerulein and Boot's secretin can also be abolished by atropinisation. Thus both the present study and previous work emphasise the importance of cholinergic tone in control of PP release.

Plasma motilin appears to have a different release mechanism. Levels rose following ingestion of the water load and this rise was not significantly affected by atropine. It is interesting to note that the peak rise of motilin occurred at least 20 min after ingestion of water when presumably a significant amount of water had left the stomach. It is thus possible that direct stimulation of the duodenum was responsible for the motilin release. Motilin in man is indeed found mainly in the duodenum and jejunum with only minute amounts being present in the stomach.

Vasoactive intestinal polypeptide (VIP) is found in fine nerves in the plexuses of the bowel wall and it is thought to function as a peptidergic neuromodulator or neurotransmitter[12]. There are only a few stimulants causing systemic release of VIP but small rises are seen after intraduodenal instillation of hyperosmolar solutions[13] and acid[14]. Ingestion of water can now be added to this list. It is known that considerable VIP destruction may occur in the liver[15], thus when the systemic plasma dilution factor is taken into account, it is possible that the VIP levels in the local venous drainage are much higher than those found in the systemic plasma. Like motilin, the rise of VIP occurred late (30') and was not blocked by atropine.

Gastric distension in the dog is a powerful stimulant of gastrin release[16] but its influence in man is less well established. Richardson et al.[17] recently reported that 500 ml or 750 ml isotonic saline meals stimulated gastric acid secretion but had no effect on gastrin release. This appears to be in contrast to the gastrin release found in the present study. The discrepancy, however, may be due to the different methodologies used. Richardson et al. infused the saline intragastrically in their subjects and maintained the antral pH constant at 5.0 throughout their experiment. In the present study the gastric pH was not monitored. A rise in gastric pH may thus have been an important factor. This study has provided additional evidence that the PP release is under vagal tone. In addition, it has been shown that water ingestion releases PP, VIP, motilin and gastrin, although except for the first mentioned, the mechanisms involved are presently quite unknown.

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Seasonal variations in vasopressin secretion in rats

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Summary. Plasma vasopressin concentrations and vasopressin content in neurohypophysis in rats show seasonal variations; namely, high in summer and low in winter.

MacFarlane and Robinson[1] first documented seasonal changes in plasma vasopressin (VP) concentration in humans and sheep, higher in summer and fall and lower in winter and spring. When the heat stimulus was apllied in warm seasons, plasma VP concentration increased, but it did not change in cold seasons. Therefore, season-related sensitivity to stimuli was suggested. Later, Morimoto et al.[2] also described the same seasonal variations in man. We are presenting data accumulated during 1976–1978 providing evidence of seasonal variations in VP secretion in rats.

Materials and methods. Adult male Sprague-Dawley rats were kept at constant room temperature (22.5 ± 1.0 °C) with a 12:12 dark-light cycle at least 2 weeks before the experiment. Rat Purina Chow diet and tap water were given ad libitum. A minimum of 6 rats was used in each experiment for each season (table). The rats were decapitated, trunk blood collected into heparinized dishes, and plasma kept frozen for VP extraction. Neurohypophysis (NH) including the intermediate lobe, and the hypothalamus (HT) tissue block bound by chiasma opticum anteriorly, corpora mamillaria posteriorly and approximately 2 mm lateral to the midline on each side at the base of the brain were quickly removed and dried in acetone before VP extraction. Plasma VP was extracted with cold acetone and

cold petroleum ether[3]. Dried NH and HT were homogenized in 0.25% acetic acid, boiled for 2 min, quickly chilled on ice and centrifuged. The extract was kept at 4 °C for the assay and a drop of concentrated acetic acid added to keep its pH below 3. VP was measured by a double antibody radioimmunoassay[4] with modification. The Student t-test was used for statistical analysis.

Results. Plasma VP concentrations showed a significant difference ($p < 0.01$) between the values measured in winter (1.0 ± 0.2 μU/ml in Jan. 1976, or 1.5 ± 0.5 μU/ml in Feb. 1977 and 1.2 ± 0.3 μU/ml in Feb. 1978) and those measured in summer seasons (14.5 ± 2.0 μU/ml in July 1976 and 11.5 ± 1.5 μU/ml in Aug. 1977) (figure). The values measured in spring (3.5 ± 1.0 μU/ml in March 1977 and 2.9 ± 0.7 μU/ml in April 1978) were not significant from those measured in summer. In fall, the mean values (6.5 ± 3.0 μU/ml in Oct. 1976 and 5.5 ± 2.5 μU/ml in Nov. 1977) are between those measured in winter and in summer, but the difference is not significant because of a large scatter (0.8–16.9 μU/ml).

VP content in neurohypophysis had a trend similar to plasma VP concentration; namely, high in summer (270 ± 50 mU/gland in July 1976 and 350 ± 30 mU/gland in Aug. 1977) and low in winter (162 ± 12 mU/gland in Feb. 1977 or 166 ± 10 mU/gland in March 1977 and 160 ± 13 mU/gland in Feb. 1978). However, the winter values are significantly different only when compared to the value for Aug. 1977 (350 ± 30 mU/gland, $p < 0.01$). VP content in hypothalamus did not vary significantly. Even the highest value (17.6 ± 2.5 mU/gland in Aug. 1977), is not significantly higher ($p > 0.05$) than the lowest value (11.5 ± 1.5 mU/gland in Nov. 1977).

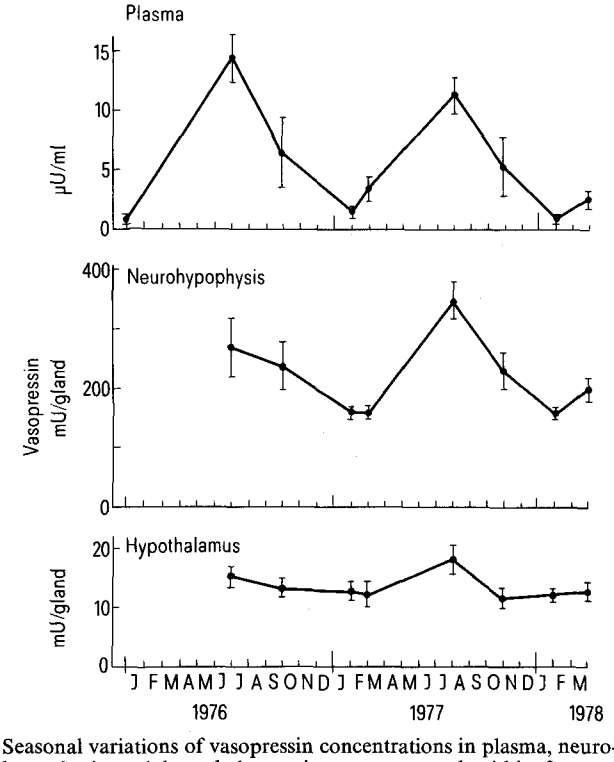
Discussion. Despite the fact that the animals were kept at a constant temperature with a 12:12 dark-light cycle, higher VP values in plasma and NH, with unchanged VP content in HT, were found in summer. It may suggest that VP synthesis, its transport to NH and release into the circulation, are increased in summer and decreased in winter. Recently, similar seasonal changes were also found in the uptake capacity of the suprachiasmatic nucleus (SCN) for 3H-serotonin in rats kept in an identical laboratory regimen[5]. Also, VP is produced in SCN, but its release from the parvocellular SCN neurons into the bloodstream has not been proven[6]. Nevertheless, a possible relation of summer-high SCN activity and summer-high VP secretion might be speculated.

VP is a potent vasoconstrictor which decreases cardiac output, heart rate and increases peripheral vascular resistance[7]. Interestingly, seasonal variations of cardiac output in rats; i.e., summer-low and winter-high, have been documented[8]. The low cardiac output was accompanied by decreased heart rate and increased peripheral resistance, which surprisingly correlates with the effect of VP. However, the authors did not measure plasma VP concentrations and we did not measure cardiac output; therefore, these 2 complimentary observations need further verification.

Our results on plasma VP are in agreement with those from humans and sheep[1,2] and are further supported by the fact that diminished nuclear volume of the neurones in supraoptic nuclei found in May and Nov. is coupled with a very high content of neurosecretory materials in the NH[9]. These authors suggested that the release of VP from NH is diminished in these months, but plasma VP concentration and VP content in NH were not measured. In our fall experiments (Oct. 76 and Nov. 77) 2 distinct subgroups with low and high plasma VP concentrations were detected. The animals appear to react to seasonal changes in an individual way. Some of them had already begun the winter-low and some still had summer-high VP concentrations. Why such a 'biological clock' also exists in laboratory animals kept under constant conditions is not yet established.

The protocol of the experiments

Season and date of experiments	Number of rats	Body weight g ± SE
Winter		
Jan. 20, 1976	6	263 ± 7
Feb. 10, 1977	10	270 ± 8
Feb. 9, 1978	8	264 ± 9
Spring		
March 15, 1977	6	238 ± 12
April 12, 1978	9	257 ± 5
Summer		
July 23, 1976	10	224 ± 8
Aug. 21, 1977	9	268 ± 11
Fall		
Oct. 20, 1976	6	309 ± 9
Nov. 3, 1977	6	252 ± 9



Seasonal variations of vasopressin concentrations in plasma, neurohypophysis and hypothalamus in rats measured within 2 years. Values are expressed in means ± SE.

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