which promotes biliary lipid excretion by formation of micellar complexes[4].

The present data indicate the complete reversal of EE-induced cholestasis and related biliary lipid abnormalities 7 days after the last dose of the estrogen, and confirm the ability of this hormone to affect only transiently the mechanisms of bile formation. To the substances, i.e. phenobarbital[10], S-adenosyl-L-methionine[11], Triton WR-1339[12], which by different mechanisms inhibit the effects of EE on bile secretion, we can add the possibility that a lag period of only some days reverses EE-induced bile flow impairment. This finding is consistent with clinical reports in humans which demonstrate that recurrent cholestasis of pregnancy resolves spontaneously approximately 2 weeks after delivery when endogenous gonadal and placental derived estrogens decrease[13]. Our data support the hypothesis[14] that EE-induced cholestasis depends by a transient failure of the canalicular pumps responsible for bile salt and sodium active transports with no irreversible damage to the hepatocytic structures involved in bile formation.

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Naltrexone influence on hibernation

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Summary. In the garden dormouse, opiate receptor blockade by naltrexone decreased the score for sleeping behaviour during hibernation at 24.00 h, indicative of a possible involvement of endorphins in the control of hibernation.

In a preliminary open study, the influence of opiate receptor blockade on hibernation was investigated in the garden dormouse (Gartenschläfer; *Eliomys quercinus*). This investigation was prompted by the observation that various changes in body functions (such as sensitivity to pain, respiratory function and circulation) which occur during hibernation, may also be caused by endogenous ligands of opiate receptors, endorphins (for review[2,3]).

During November 1978, 2 groups of animals (body weight 80–110 g; 4 animals in each group, housed individually at a normal dark-light-rhythm at 21 °C) were injected i.p. 4 times a day at 06.00 h, 12.00 h, 18.00 h and 24.00 h with the opiate antagonist naltrexone (25 mg/kg) or saline, volume 0.1 ml. The relatively high dosage of naltrexone was chosen to get a reliable occupancy of opiate receptors throughout each 6-h interval. 2 days after having started the injection schedule the animals were housed in darkness at 4 °C and deprived of food. The first 3 days of hibernation conditions (adaptation period) and the following 5 experimental days were evaluated separately. Altogether, the injection schedule was run for 10 days. Each animal was scored 5 min prior to and 10 min after each injection. Hibernation was rated as follows: Animals which were wide awake (eyes open, fast escape movements) received score 0, those which were sleepy (eyes open, but no escape movements or eyes closed, slow rigid movements) received score 1, and those which were sleeping (typical hibernation posture, as shown in figure 1) received score 2.

Injections were stopped after 10 days; all animals were again housed at a normal dark-light-rhythm at 21 °C, and

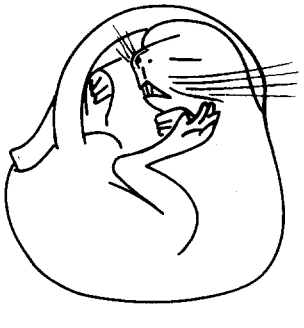

Fig. 1. Typical hibernation posture of the garden dormouse.

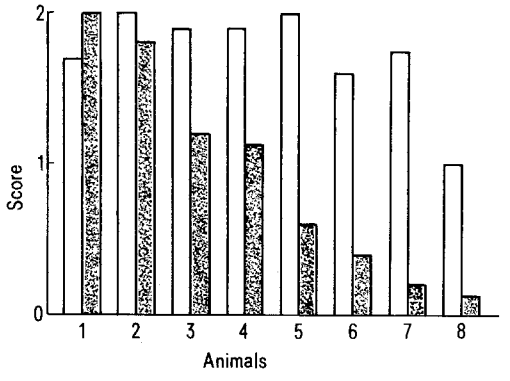

Fig. 2. Score for sleeping behaviour at 24.00 h. Mean values from 5 experimental days, starting at the end of the period of adaptation to hibernation conditions. Animals are ordered according to the increasing magnitude of effect. ☐ Saline treatment, ▨ naltrexone treatment.

received food and water ad libitum. 2 weeks later the experiment was repeated once in a crossed-over-design.

All score values refering to a certain injection time and a certain treatment condition were averaged for each animal separately and the mean values obtained under either saline or naltrexone treatment were compared to one another, using the Wilcoxon test for paired samples.

Naltrexone had no influence on the sleeping behaviour during the adaptation period (days 1-3 of hibernation conditions). Thereafter, naltrexone decreased the score for sleeping behaviour at the observation period prior to and after the midnight injection by an average of 46% ($p < 0.05$; figure 2), as compared to saline treatment. At the other 3 observation periods, no statistically significant changes were observed.

These preliminary results seem to indicate an involvement of endogenous opioids in the control of hibernation, possibly dependent upon regular endogenous fluctuations over time. Endorphins are known to modulate neurotransmitter systems. For example, they inhibit the release of noradrenaline[4], whose turnover is changed during hibernation in the same direction, i.e. depressed[5]. Thus, opiate receptor blockade may cause disturbances of neurotransmitter systems participating in the control of hibernation. However, the endorphins seem to have only a partial influence upon neuronal mechanisms involved in the control of hibernation, which may explain why no effect of naltrexone could be seen in a few animals.

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Action of histamine on phasic and tonic components of vascular smooth muscle contraction[1]

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Summary. The isometric contractile response of rabbit aortic strips in response to histamine was studied. Biphasic dose-dependent contractions reflecting release of internal Ca^{2+} (phasic component) and simultaneous mobilization of external Ca^{2+} stores (tonic component) were produced.

Vascular smooth muscle constitutes an important effector system permitting appropriate adjustment of vascular tone to the existing physiological state. Hence, functional properties and effects of drugs acting on this tissue have been widely studied. Recently, it has been appreciated that activation of vascular smooth muscle may involve mobilization of internal and/or external Ca^{2+} stores depending upon the agonist used. Biphasic contractions of vascular smooth muscle in response to catecholamines have been described as consisting of an initial rapid rise in tension (fast component) reflecting release of intracellular Ca^{2+} followed by a slower (slow component) phase dependent on extracellular calcium[3-15]. The endogenous vasoconstrictor, angiotensin, activates arterial smooth muscle by a process independent of extracellular calcium while histamine produces a biphasic response similar to that elicited by norepinephrine[3,4,13]. The above findings have led to the concept of phasic and tonic components of contraction as being functional properties of vascular smooth muscle. However, those descriptions relate only to maximal effective agonist concentrations and do not provide quantitative information about these functional properties of vascular smooth muscle. Recently, we have developed a new approach for studying the effects of drugs on the phasic and tonic components of vascular smooth muscle contraction which affords detailed information about the functional properties of vascular smooth muscle[16,17]. The purpose of the present study was to examine the actions of histamine on phasic and tonic components of vascular smooth muscle contraction.

Materials and methods. Aortic strips were prepared from 2-3 kg New Zealand White rabbits according to the method of Furchgott[18]. Strips were mounted isometrically in isolated organ baths containing 28 ml of Krebs-Henseleit bicarbonate solution[19] (KHB, 37±1 °C) equilibrated with a 95% O_2 5% CO_2 gas mixture (pH=7.4). Isometric contractions were recorded with Grass FTO3 linear force displacement transducers and were displayed on a Grass Model 7 polygraph. For experiments using Ca^{2+}-free KHB, Ca^{2+} was

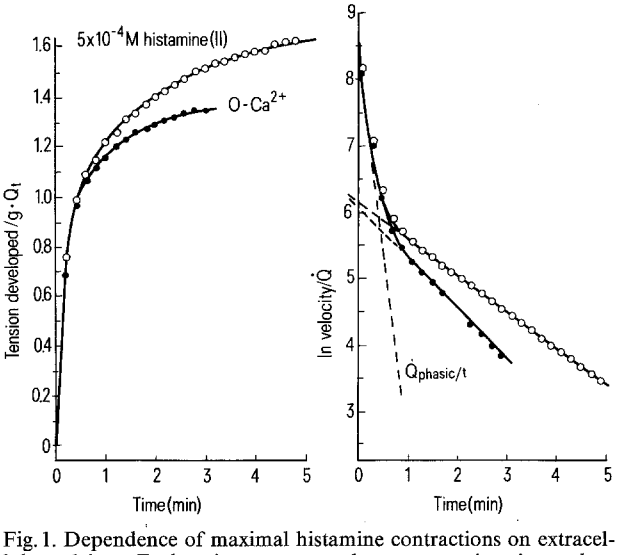

Fig. 1. Dependence of maximal histamine contractions on extracellular calcium. Each point represents the mean tension-time values for control ○ and calcium-free ● contractions. ( )=number of rabbit aortas. Dashed lines indicate resolved components of contraction.