24 Sprague-Dawley male rats of uniform age and weighing 266 ± 15 g were used. 12 of the animals were given 2 g of AMCA in water solution per kg bodyweight a day in their drinking water for 8 weeks. The animals, which did not receive any other fluid, willingly drank the solution. 12 rats served as controls. At the end of this period, the rats were killed and the hearts immediately removed together with the large heart vessels. The specimens were immediately frozen in liquid nitrogen. Cryostat sections were placed in a plane through the large vessels (aorta, arteria and vena pulmonalis) immediately after their origin in the heart; others in a plane passing through the sulcus coronarius. The sections were cut 8 µm thick and collected on cleaned glass slides. 4 slides with 6 sections on each were prepared for every sample. The fibrinolytic activity was determined histochemically with the method of TODD[5], as modified and graded in arbitrary units by PANDOLFI[6].

The results are given in the Table. No significant differences were found between the rats treated with AMCA and the controls of the fibrinolytic activity in the walls of the large heart vessels or of the coronary vessels. These findings are compatible with observations in organ culture of veins in medium with an addition of AMCA. The activator content of these vessel explants did not differ from that of explants cultured without AMCA (ÅSTEDT, to be published).

Occurrence of microthrombi in the glomeruli[7–10] has been reported in some patients and a thrombotic state in one[11] during treatment with EACA. But in extensive clinical investigations, no increase in thrombotic complications has occurred during such traetment[12–15].

In the previous study, the potent fibrinolytic inhibitor AMCA was given in a large dose with no effect on the fibrinolytic activator content in the vessel wall. In agreement with the clinical experience, the results thus argue against AMCA, favouring the development of thrombosis.

Zusammenfassung. Ratten wurden mit hohen Dosen des Fibrinolyseinhibitors Tranexamsäure gefüttert. Die fibrinolytische Aktivität der grossen Herzgefässe und der Coronargefässe wurde histochemisch untersucht und mit einer Kontrollgruppe verglichen, wobei sich ergab, dass der Gehalt der Gefässwände an Fibrinolyseaktivatoren durch die Tranexamsäure nicht beeinflusst wurde.

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Fibrinolytic activity in the wall of the large heart vessels (aorta, art. and v. pulmonalis) and the coronary vessels of rats after treatment with AMCA 2 g/kg body weight a day for 2 weeks

Groups	Large heart vessels	Coronary vessels
AMCA	7.5 (6–8.5)	4.5 (2.0–6.0)
Controls	6.0 (3.0–9.5)	4.25 (3.0–7.0)

Arbitrary units. Median value and range.

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Ciliary Action and Normal Movement of Odorant Wavefronts in Garfish Nasal Capsule of *Lepisosteus osseus*

The olfactory receptors of most fish are distributed on lamellae within the nasal capsule. Odorants ordinarily reach the olfactory receptors of fish when streams of water enter the anterior nares and exit through the posterior nares. In fish, this flow is normally produced by various combinations of active and passive mechanisms[1].

Since movement of an odorant wave-front across the mucosa may be a relevant parameter of olfactory input[2], information concerning the normal movement of odorant wave fronts would be useful to those studying the physiology of olfactory stimulation. In fish, flow patterns in the nasal capsule have been studied only in the eel[3].

The present report shows the relationship in the capsule between flow patterns and distribution of receptors on the lamellae of the garfish, *Lepisosteus osseus*. We suggest that ciliary currents are responsible for the efficient delivery of odorant molecules to the olfactory receptors, and prevent the existence of an unstirred layer along the epithelium.

Figure 1 illustrates the left nasal capsule after the dorsolateral wall has been removed. The lamellae are attached to the capsule along their medial and ventral borders. The nasal capsule of the garfish has no ancillary pumping structures such as are present in most teleosts[1], and flow is produced by action of cilia. In a 0.75 m fish, the capsular volume (determined by a paraffin-casting procedure) was 0.04 cm³, while that of a 1 m fish was 0.065 cm³. These volumes may be over-estimates because of tissue shrinkage caused by fixation and treatment with hot paraffin.

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The flow patterns indicated in Figure 1 were constructed a) by applying the dye streams to the various quadrants of the anterior naris, while measuring the time and location of their first appearance at the posterior naris in fish having intacts capsules and b) from observations of dye movement in fish with a portion of the capsular wall removed. Water flow was observed by allowing a microdrop of methylene blue solution, formed in front of an anterior naris, to be drawn into the nasal capsule by the ciliary currents within the capsule. A dye stream entering the anterior naris through its antero-medial quadrant traversed a much longer path past the anterior lamellae to the posterior naris than dye entering any other quadrant (Figure 1). Dye entering other quadrants of the anterior naris passed between more posterior lamellae. The dye taking the longest path required approximately twice as long to appear at the posterior naris as that taking the shortest path. In different fish the times were 3 to 9 sec for the long path versus 2 to 5 sec for the short path. Physiological condition of the fish was also a variable.

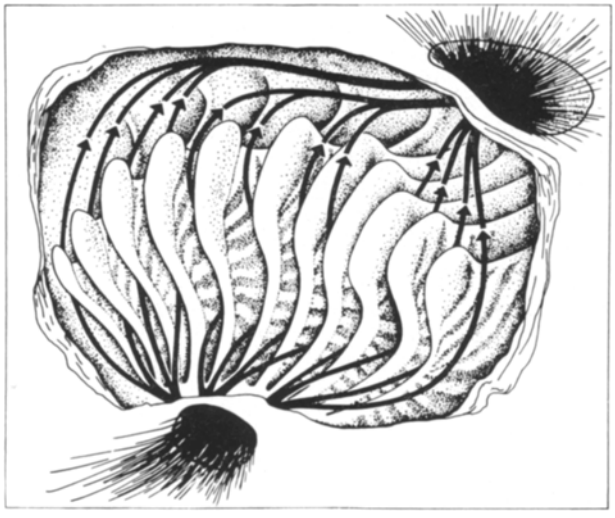

Fig. 1. Drawing of left nasal capsule of garfish, illustrating directions of water flow through the nasal capsule. Anterior is to the left, dorsal is upward. Linear dimensions of the capsule varied with size of fish.

Observation of dye streams in partially opened capsules showed that, when a water stream approached the surface of a lamella, it was drawn against the surface and propelled along the depressions that contain the receptors. Therefore, the velocity of flow is greatest along the surface of the lamellae. To measure velocity of dye fronts across the receptor surface and to observe flow patterns, individual lamellae were carefully removed from the capsule under the dissection microscope and transferred to a dish of garfish Ringer solution[4]. The dye droplet apparatus was then used to produce fronts which were observed moving across the lamella. In excised lamellae, the velocity of a dye front across the lamellar face varied between 1.5 and 2.9 mm/sec (average, 2.2 mm/sec). A lamellar face would then be traversed in 400–600 msec.

Scanning electron microscopy and light microscopy show that the cell types which cover the surface of the lamellae and capsule walls are separately grouped, presumably according to functional type. Cells having motile cilia, together with mucus-secreting cells, are found lining the walls of the capsule. These cell types are also found along the lateral and dorsal edges of the lamellae, as well as on the ridges of the lamellar surface. A pattern of ridges and depressions, as shown in the scanning electron micrograph[5] in Figure 2A, is present on both sides of all the lamellae in the nasal capsule. Such ridges also

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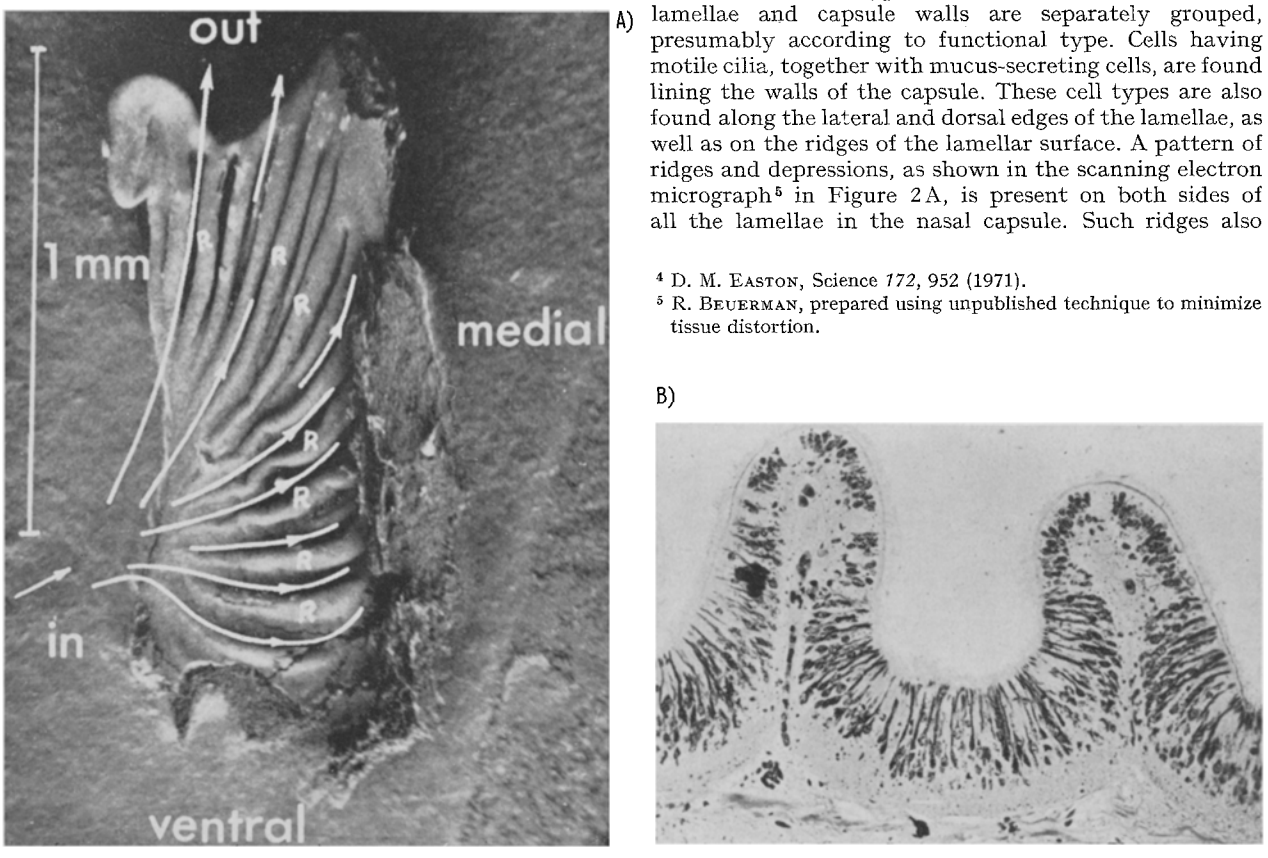

Fig. 2. A) SEM of single excised lamella, showing pattern of alternating ridges and depressions on the surface. Directions of flow are indicated by arrows. B) Bodian silver stained cross section of 2 ridges and intervening depression of single lamella. Olfactory receptors are seen in the depression, while nuclei of non-sensory cells are seen on the ridges. Some mucous containing cells are also present. White bar represents 20 μm.

exist in the sea trout[6]. Directions of flow across the lamellar surfaces are indicated by arrows. A silver-stained section of ridges and a depression (Figure 2B) shows numerous large cells containing mucous droplets. Some of these cells appear to have spilled their contents onto the ridge surface. WILSON and WESTERMAN[7] reported the presence of many mucous cells of similar appearance in goldfish olfactory lamellae. In the lamellar depressions, the receptor cells appeared quite numerous and densely packed; receptor cells were not observed on the ridges. A similar localization of receptors on the nasal epithelium recently has been reported in the smolt and sea trout[8]. Figure 2B shows that there are cells with cilia on the ridges. The mucus-secreting cells are not found in the depressions on the lamellae, but the olfactory receptors are concentrated there.

TEICHMAN[3] demonstrated that a volume of water flowing through the nasal capsule of the eel circulates past many lamellae consecutively. However, our observations show that in the garfish a volume of water passes over a lamella, and thus over the receptor surface, only once.

Water forced by outside pressure through the nasal capsule would move most rapidly in the bulk solution and more slowly close to the surfaces[9]. The rhythmic action of the cilia ensures that the hydrodynamic situation in fish nasal capsule is quite the reverse. We infer that the ciliary action, making for highest velocity of flow close to the surfaces, provides for efficient delivery of odorant to the receptors.

Résumé. Le cours d'un courant d'eau produit par les cils dans la capsule nasale de *Lepisosteus osseus* est décrit. Un certain volume d'eau ne passe sur l'épithelium nasal qu'une seule fois avant de sortir de la capsule, une situation différente de celle qui s'observe chez l'anguille. L'eau effectue son parcours en 2–9 sec, selon la route suivie à travers la cavité et la condition physiologique du poisson. Des cils sur des lamelles réséquées produisent à la surface un écoulement d'une vitesse moyenne de 2.2 mm par sec.

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Physostigmine Attenuation of Δ^9-Tetrahydrocannabinol Induced Hyperthermia in Rats

Administration of low doses of Δ^9-tetrahydrocannabinol (Δ^9-THC) may produce hyperthermia in rats[1,2]. Hypothermia appears after higher doses[1–3]. A similar dissociation of temperature effects is also reported for morphine[4–6].

A cholinergic link in central body temperature regulation is implied from experiments showing that when central cholinergic transmission is blocked, a rise in temperature appears; the opposite effect appears after acethylcholine (ACh) application[7–9]. That the morphine-induced hyperthermia may result from diminished ACh release has gained experimental support[6]. Physostigmine (0.1 mg/kg) attenuated morphine-induced hyperthermia whereas neostigmine (0.08 mg/kg) did not. Thus, only the centrally active esterase inhibitor exerted the attenuating effect[6].

This finding prompted us to investigate whether physostigmine would also attenuate THC-induced hyperthermia. Administrations of equimolar doses of neostigmine would indicate whether the THC hyperthermia was of central or peripheral origin.

Materials and methods. To answer these questions, male Sprague-Dawley rats, weighting 310–320 g, individually housed with free access to food and water, were treated with 1.0 mg/kg of Δ^9-THC alone or in combination with physostigmine (0.1 and 0.2 mg/kg) or neostigmine (0.08 and 0.16 mg/kg). The effects of the choline esterase inhibitors and the THC vehicle when given alone were also assessed. The drugs were administered in a balanced order according to a Latin square design[10], and the treatments were spaced 5 days apart. The effects of a moderate dose of morphine (2.5 mg/kg) given alone or in combination with physostigmine (0.1 or 0.2 mg/kg) were also studied.

We used 3 latin squares ($2\times5\times5$, Figure A; $2\times5\times5$, Figure B; $2\times3\times3$, Figure C) in order to minimize the number of injections. Physostigmine sulphate, neostigmine bromide, and morphine hydrocloride were dissolved in isotonic saline, whereas Δ^9-THC was given as a suspension of propylene glycol and saline plus Tween-80. Control rats received the THC vehicle. The i.p. route was used throughout and the volume injected was 0.1 ml per 100 g body weight. In the week preceeding the first experimental session, the animals were sham-injected and accustomed to the recording technique.

All recordings were performed in a room varying between 22–24 °C in temperature. The rectal temperature was measured by a thermistor rectal probe, inserted 4 cm into the rectum. Before each session 1 control measure-

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