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HISTAMINE-STORING CELLS IN ORAL TISSUES

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INTRODUCTION

The chemical assay of histamine in biological samples utilizes o-phthalaldehyde (OPT)-induced fluorescence (*Shore, Burkhalter & Cohn*, 1959). The histochemical application of OPT stain for cellular histamine stores was developed independently by *Juhlin & Shelley* (1966) and *Ehinger & Thunberg* (1967). Subsequent experimental work with this method has mainly been concentrated on histamine in the gastrointestinal system and in the skin.

The main histamine stores in the body are believed to be the mast cells, which, depending on the tissue concerned, also contain heparin, 5-hydroxytryptamine and various enzymes (*Selye*, 1965). In the rat, gastric histamine is stored in cells of three types; in the mast cells, in a specific nonmast-cell system and in cells also capable of producing and storing monoamines (*Håkanson & Owman*, 1967; *Thunberg*, 1967). Additional variation in histamine cells has been found in the dog stomach (*Aures, Håkanson, Owman & Sporrong*, 1968). In the skin, histamine has been detected in the mast cells and in the vascular walls (*Juhlin*, 1967a).

Studies with the histamine-releasing compound 48/80 also indicate differences in the histamine-storing cells. The content of mast cell histamine

Received for publication, April 16, 1969.

in the rat is high, but about one-half of the total histamine in tissues other than the skin resists the action of compound 48/80 (*Mota, Beraldo, Ferri & Junqueira*, 1956). A similar duality is seen in other animals too (*Burkhalter, Cohn & Shore*, 1959). *Johnson, Beaven, Erjavec & Brodie* (1966) concluded that histamine is stored in two forms. Histamine in mast cells has a slow turnover rate and can be released by compound 48/80. Histamine in nonmast-cell sites has a high turnover rate and is not affected by compound 48/80.

Histamine probably plays a basic role in the initial phase of the inflammatory process, although it cannot be responsible for the entire inflammatory response (*Stern*, 1966). In the oral cavity, numerous mast cells are present in the tongue and gingiva; see reviews by *Selye* (1965) and *Hall* (1966). It has been convincingly demonstrated that mast cell counts decrease in chronically inflamed gingiva (*Carranza & Cabrini*, 1955; *Calonius*, 1959; *Shelton & Hall*, 1968; *Zachrisson*, 1968). The sharp contrast between the tongue and gingiva in disposition to inflammation is puzzling, in view of the high mast cell counts of both tissues. That mast cells play any role in the inflammatory process of the dental pulp is doubtful. No mast cells are found in pulps (*Todaro*, 1939; *Dockrill*, 1961; *Anneroth & Brännström*, 1964) and in addition to histamine other biologically potent substances have attracted attention as mediators of the inflammatory reaction (*Schultz-Haudt & Sölna*, 1966).

The differences found in tissue stores of histamine and the desire to achieve selective identification of histamine among other mast cell components led us to try the histochemical OPT stain. The present paper describes histamine stores in various mammalian oral tissues, as revealed by a method based on this staining principle.

MATERIAL AND METHODS

Small tissue specimens were dissected from gingiva and lining mucosa of rats, guinea pigs, rabbits, cats and man. Tongue specimens were obtained similarly, but not from man. Incisors of rats, guinea pigs and rabbits, cuspids of cats, and various human teeth were split open and the pulps removed. Samples from the submandibular glands of rats and rabbits were included in the study. Additionally, the mesenteries of rats and guinea pigs were used as material for comparison.

The specimens were pulverized with talcum (*Moline & Glenner*, 1964), quenched and stored in liquid nitrogen until transferred to a freeze-drying unit described earlier by *Pohto & Antila* (1968). The transfer was accomplished in a copper cup half filled with paraffin wax (Gurr Ltd., London, m.p. 45°C). The vessel was filled up with liquid nitrogen and the coded specimens were dropped on frozen paraffin.

After the freeze-drying below —35°C, the specimens were allowed to attain room temperature. Warming was continued with a waterbath at 50°C around the freeze-dryer compartment, in which there was still a vacuum. One hour was enough for melting the paraffin and for infiltration of the specimens. It was important to keep the »cold finger» of the apparatus chilled in order to prevent the access of volatile paraffin components into the diffusion pump.

Sections cut at 8—16 μ from re-embedded blocks were flattened by melting. The fluorophore from histamine was induced in a moist chamber with a relative humidity of 100 % at room temperature by covering the slide with 1 % OPT (o-phthal(di)aldehyde, Fluka AG, Buchs) in anhydrous ethylbenzene (Fluka AG, Buchs) for 2—4 min (*Shelley, Öhman & Parnes*, 1968). The sections were washed with ethylbenzene, and mounted in an ethylbenzene-Entellan® mixture. The classical mast cell staining with a metachromatic dye, toluidine blue 0 (E. Merck, Darmstadt), was applied as a histological method of comparison. Microscopic analysis was carried out with a Carl Zeiss Nf microscope equipped with a high pressure mercury lamp (Osram, HBO 200), heat absorption filters, excitation filter (Schott UG 1, 2 mm), red absorption filter (Schott BG 38, 2.5 mm), barrier filter (Wild GG 13 Combi) and bright-field condenser. For photographing Agepe-FF (Agfa-Gevaert) or CT 18 Agfacolor films were used.

The method used for the demonstration of monoamine fluorescence (noradrenaline, 5-hydroxytryptamine) has been described by *Pohto* and *Antila* (1968).

The following drugs were given:

Reserpine (Lääke Oy, Turku) 0.5 mg/kg 12 hours and 1.0 mg/kg 3 hours before decapitation subcutaneously to rats.

Compound 48/80 (Wellcome Research Laboratories, Beckenham) intraperitoneally 1.0 mg/kg to rats and 2.0 mg/kg to guinea pigs 30 min before decapitation.

Histamine phosphate (The British Drug House Ltd., Poole) as an approximate LD_{50} dose to rats (500 mg/kg i.v. and i.p.) to rabbits (1.0 mg/kg i.v.) and to guinea pigs (5 mg/kg i.p.) 1 or 2 hours before decapitation. The histamine values given refer to the base.

RESULTS

Gingiva and lining mucosa

In man histamine-containing mast cells were numerous in the specimens of clinically healthy gingiva and alveolar mucosa (Fig. 1). In two samples of chronically inflamed attached and free gingiva histamine staining revealed only a few faintly fluorescent mast cells. The picture was clearly different from the degranulation of marginal mast cells caused by an excision injury.

Concomitant demonstration of histamine, 5-hydroxytryptamine and noradrenaline in the rat gingiva was accomplished (Figs. 2 and 3). The fluorophore of noradrenaline in the vascular sympathetic nerves and that of 5-hydroxytryptamine in the mast cells were induced with formaldehyde gas. In the same section histamine fluorescence was located identically with 5-hydroxytryptamine fluorescence.

Acute reserpine treatment released 5-hydroxytryptamine from the gingival mast cells of the rat, but had no detectable effect on histamine. When all histamine fluorescence had disappeared from the gingival mast cells after treatment with compound 48/80, some residual fluorescence was found in the tongue mast cells of the rat. Perivascular mast cells were seen, but the fluorescence of the blood vessel walls was not conspicuous in the gingival tissue (Fig. 4).

More histamine-fluorescent mast cells were observed in the rat cheek mucosa than in the lining mucosa of any other animal species studies. Mast

Fig. 1. Human alveolar mucous membrane. The bright white spots represent histamine in mast cells. The yellow o-phthalaldehyde-induced histamine fluorescence is seen on a faint blue background. ×100.

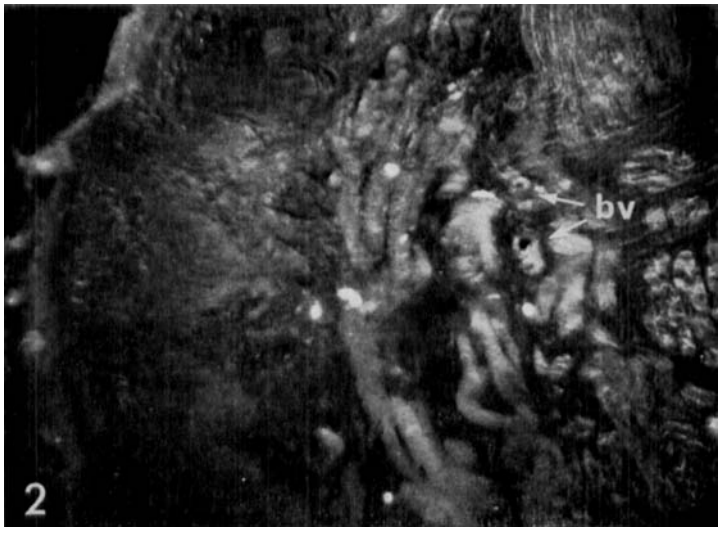

Fig. 2. Rat gingiva. Histamine-fluorescent mast cells are observed. Note the lack of specific fluorescence around the blood vessels (bv). ×240.

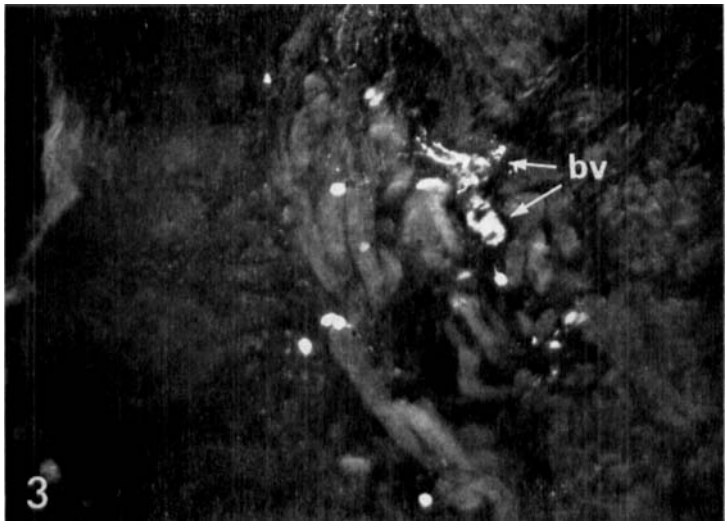

Fig. 3. The same section as in Fig. 2. The formaldehyde-induced yellow 5-hydroxytryptamine fluorescence in mast cells and the green noradrenaline fluorescence in sympathetic terminals around the blood vessels. ×240.

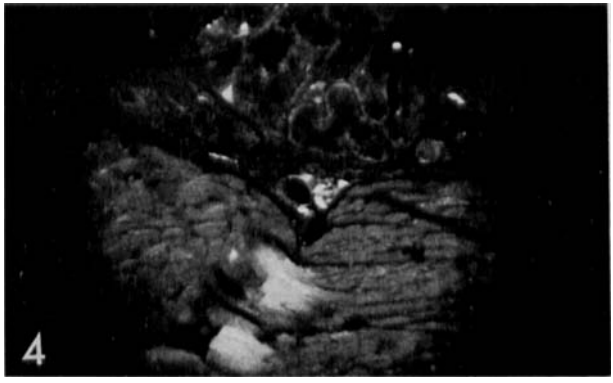

Fig. 4. Perivascular mast cells of an arteriole and a venule in cat gingiva. The endothelial fluorescence is not prominent. ×100.

cells located in the submucosal layer of the cheek were not so intensely stained as those in the rat tongue. Only occasional mast cells were found in the *lamina propria*, a layer which is rich in mast cells in the rat gingiva and tongue. A strong blue fluorescent band coinciding with the *stratum corneum* of the epithelium was observed in the keratinized mucosa. Pretreatment with compound 48/80 abolished the yellow fluorescence of the mast cells, but the blue band or the yellowish spots corresponding to the nuclei of the *lamina propria* were not affected (Figs. 5 and 6).

Tongue

The mast cells in the tongue of the cat, rat, rabbit and guinea pig were found to contain histamine (Fig. 7). In the rat and cat tongue the fluorescence from these histamine stores was clearly more frequent and intense than in the guinea pig and rabbit. The methylene blue staining coincided with the histamine fluorescence. Around the walls of the blood vessels histamine was concentrated in the perivascular mast cells, although sometimes a faint yellow OPT-induced fluorescence could be seen within the blood vessel walls.

Treatment with compound 48/80 led to liberation of histamine from the tongue mast cells of the rat, but not from those of the guinea pig. An intraperitoneal injection of an LD_{50} dose of histamine caused no detectable increase in the intensity of fluorescence of the tongue mast cells of these animals.

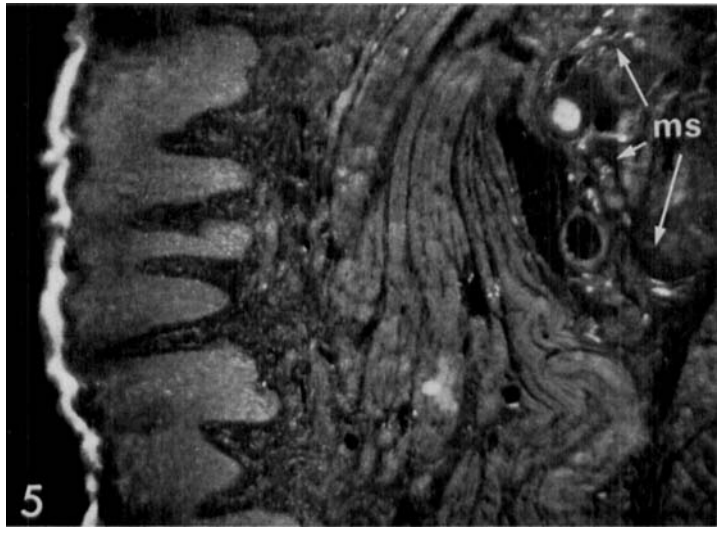

Fig. 5. Rat cheek. A faint histamine fluorescence in mast cells lying deep in the submucous layer (ms). A blue fluorescent band of the *stratum corneum* is probably caused by glutathione. ×240.

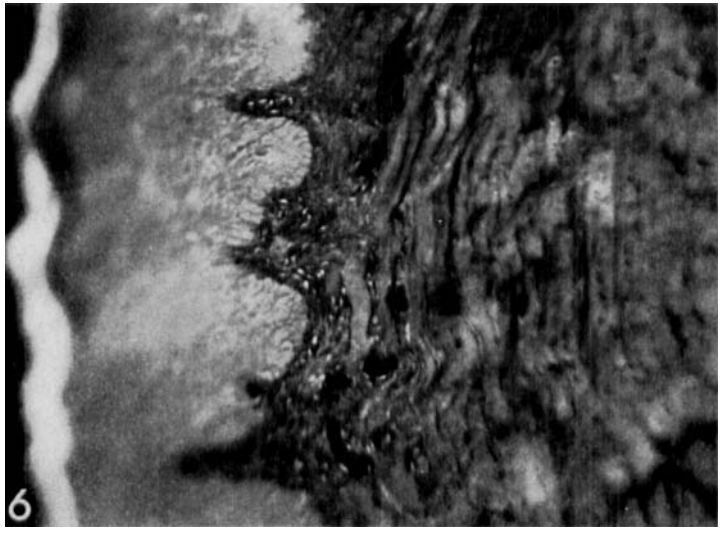

Fig. 6. Rat cheek after an intraperitoneal injection of the histamine-releasing compound 48/80. No mast cells can be detected. The blue band of the *stratum corneum* or white spots corresponding to endothelial nuclei in the lamina propria are not affected. ×240.

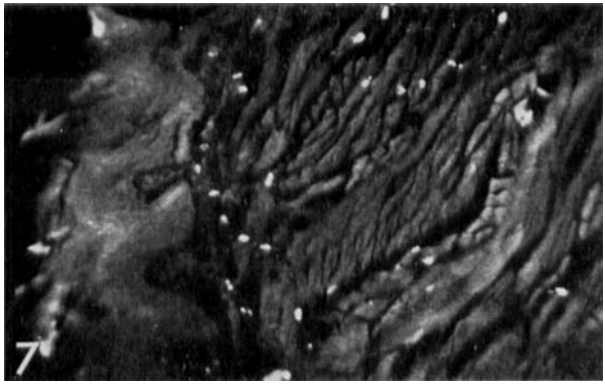

Fig. 7. Histamine fluorescence reveals numerous mast cells in the submucous layer and between interlacking muscle bundles in the antero-lateral part of the rat tongue. ×100.

Dental pulp

No histamine fluorescence demonstrating the presence of mast cells could be found in the pulps examined. Yellow OPT-induced fluorescence was observed in the walls of the blood vessels of the rabbit, cat and human pulps, but not in those of the rat or guinea pig (Figs. 8, 9 and 10). The fluorescence was most intense in the vascular endothelial cells, especially in their ovoid nuclei. A similar fluorescence was seen in the blood vessels of guinea pig and rat mesentery and was not abolished by compound 48/80. On the contrary, this fluorescence was intensified in the mesenteric blood vessels, but did not appear in the pulpal vessels, after intraperitoneal injection of compound 48/80, which depleted histamine from the mast cells of the mesentery (Figs. 11, 12 and 13). Intravenous administration of an LD_{50} dose of histamine to rabbits caused no detectable increase in the fluorescence in the pulpal vessels. Neither did there appear a vascular fluorescence in the pulps of rats after corresponding treatment.

The fibroblasts of rat incisor pulps showed an OPT-induced fluorescence (Fig. 10). The fluorescent fibroblasts were most numerous in the periphery of the proximal part of the pulps. The incisor pulps of the guinea pig and the rabbit contained fibroblasts of the same kind, although not so numerous or intense (Fig. 9). No fluorescent fibroblasts were found in the pulps of the cat or man (Fig. 8).

When the pulps were detached from the dentine with deep excavations, the odontoblastic bodies attached to the pulps displayed no histamine-like fluorescence.

Fig. 8. Pulp of the intact human bicuspid. Yellow histamine-like fluorescence in the walls of blood vessels (bv). Especially endothelial nuclei are stained. No mast cells or fluorescent fibroblasts are seen. ×150.

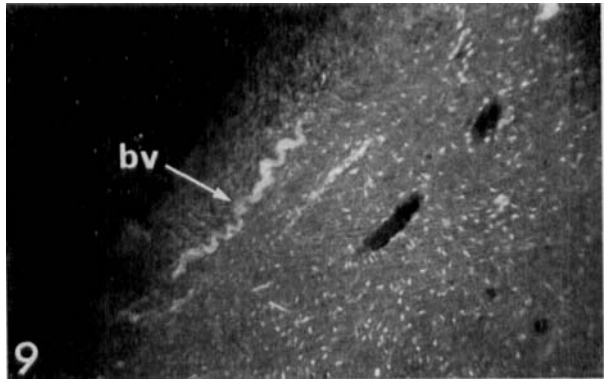

Fig. 9. Rabbit incisor pulp. OPT-induced fluorescence outlines a blood vessel (bv). Scattered fibroblasts show the same kind of fluorescence. ×80.

Submandibular gland

The submandibular glands of the rat and the rabbit were studied. Normally, OPT-treated sections had a non-specific pale blue background fluorescence and a specific yellow histamine fluorescence of the mast cells in the *stroma*. One hour after intravenous injection of an LD_{50} dose of histamine a new yellowish brightness appeared in the acini and striated ducts of the submandibular glands in the rat (Fig. 14). After 2 hours the intensity of fluorescence was diminished, although the bright emission often clearly de-

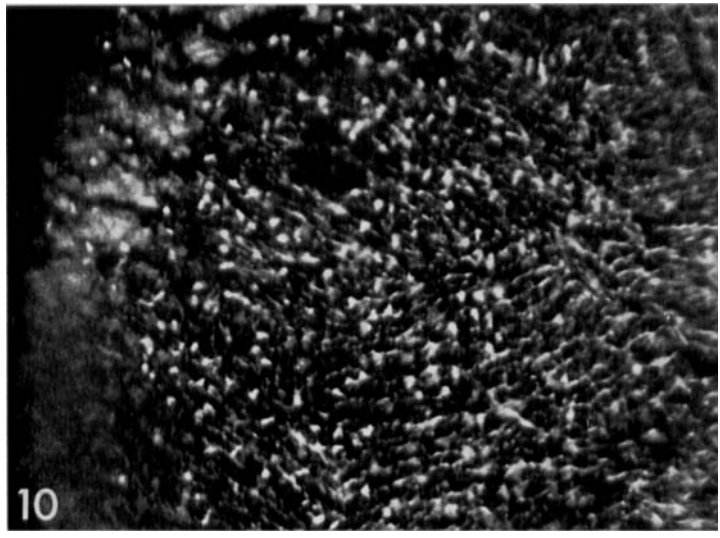

Fig. 10. Rat incisor pulp. Fibroblasts emit an intense histamine-like fluorescence. Autofluorescence of collagenous elements is disturbing. No fluorescence of vascular origin can be distinguished. ×280.

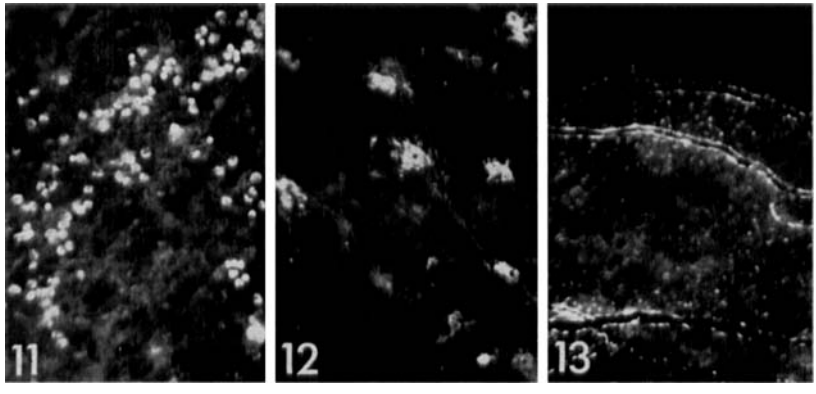

Fig. 11. Numerous mast cells are observed in a normal rat mesentery. ×100.

Fig. 12. Disruption of mesenteric mast cells of rat 30 min after an intraperitoneal injection of compound 48/80. ×200.

Fig. 13. Histamine depleted from mast cells enhances the fluorescence of mesenteric blood vessels in the rat. A clear reduction of intact mast cells is found. ×80.

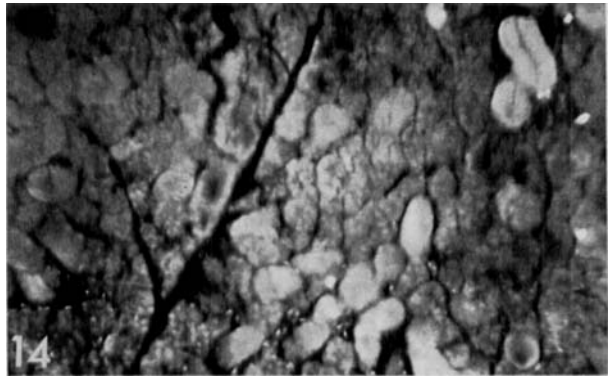

Fig. 14. Rat submandibular gland. One hour after an intravenous injection of an LD_{50} dose of histamine, a yellowish fluorescence can be detected in the acini and striated ducts. A few histamine-fluorescent mast cells are located in the *stroma*. × 100.

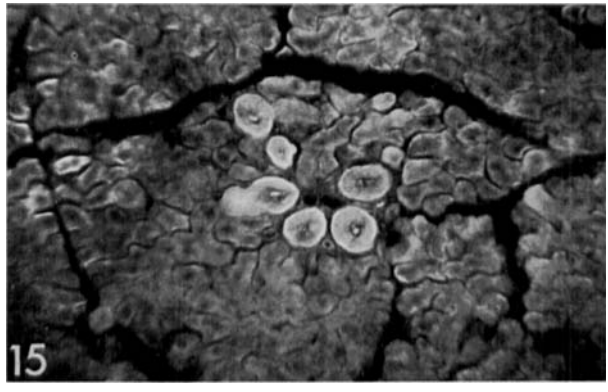

Fig. 15. Two hours after a histamine injection the parenchymal fluorescence is diminished in the rat submandibular gland. However, some striated ducts with their secretory contents exhibit the histamine-like fluorescence. × 100.

marcated the striated ducts with their yellow secretory contents, suggested to contain histamine or its metabolites (Fig. 15). This suggestion is further substantiated by the fact that the fluorescence of the secretion turned from yellow to the less intense blue in the excretory ducts (Fig. 16). The same »dilution change» in the fluorophores of histamine is often seen within the partially depleted mast cells.

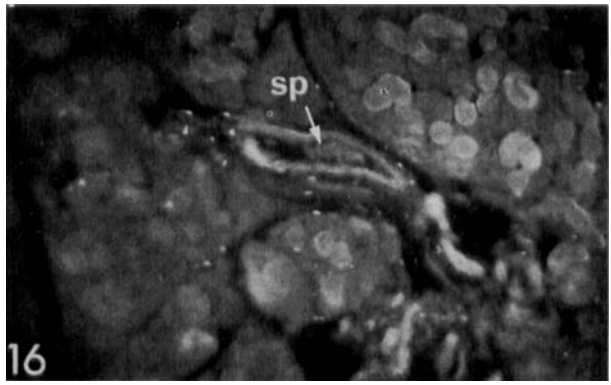

Fig. 16. Two hours after histamine administration secretory products display a faint blue fluorescence in the excretory ducts. For details see text. × 100.

DISCUSSION

Method and specificity

The blue and yellow OPT-induced fluorophores of histamine described by *Ehinger* and *Thunberg* (1967) were found to be reproducible in our preliminary investigations with histamine crystals, rabbit platelets and mast cells of rat tongue and mesentery. However, in the frozen sections and freeze-dried frozen sections consistent staining of mast cells was not achieved owing to the diffusion of histamine. Introduction of freeze-dried paraffin-embedded tissues standardized this stage of the procedure and made the method more convenient.

In the preliminary studies, we used gaseous OPT for the induction of fluorescence according to *Ehinger* and *Thunberg* (1967), but the proper micro-moistening in the humidity chamber was difficult to control and the blue fluorophore, which is less visible on the blue background, was often formed owing to diffusion of the histamine or to overdry conditions. More consistent results were obtained with 1 % OPT in xylene. Induction became most reliable when we changed over from xylene to ethylbenzene, which was recommended for this purpose during the course of the present work (*Shelley, Öhman & Parnes*, 1968). Thus it was possible to standardize the second stage of the procedure as well. A prerequisite for the proper visualization of histamine was a definite thickness of the ethylbenzene layer on the slides to provide constant water absorption.

Recent studies have confirmed that OPT-induced staining is indicative of the presence of histamine. The fluorescent reactions of OPT are numerous

(*Turner & Wightman*, 1968), but among substances occurring in normal tissues in substantial amounts histamine is the only one giving measurable fluorescence. The reaction with the metabolite, methylhistamine, is weaker and the fluorophore from the precursor histidine bleaches rapidly (*Ehinger & Thunberg*, 1967). It is probable that the blue fluorescence of cornified epithelium is due to the OPT-glutathione reaction (*Juhlin*, 1967a).

Mast cells

The OPT-induced fluorochrome from histamine proved to be a reliable means for the demonstration of mast cells. Fluorescence microscopy has been utilized before in oral mast cell studies (*Zachrisson*, 1968), but the present method has the advantage that one of the biologically active components of a mast cell is specifically shown. Although the method is not a quantitative one, a clear idea can be achieved of the dynamics of histamine when the changes are marked and the method strictly controlled.

No mast cell counts were made but the large population in the rat and the low one in the rabbit were conspicuous in the oral tissues. The situation is analogous in the other tissues, with the exception of the rabbit skin, which is rich in mast cells (*Selye*, 1965).

If the morphological aspects are ignored, only two types of mast cells are found in the tissues studied. 5-hydroxytryptamine of mast cells is restricted to the mast cells of the mouse and rat (*Parrat & West*, 1957a). In agreement with this, no formaldehyde-induced monoamine fluorescence could be seen in any but the rat mast cells. On the otherhand, when histamine fluorescence revealed the mast cells, they were also stainable with toluidine blue.

A histamine-releasing compound 48/80 depleted histamine from rat, but not from guinea pig mast cells. Simultaneous disruption of rat mast cells was seen. When reserpine was given to rats, 5-hydroxytryptamine fluorescence was abolished but not that due to histamine. No mast cell damage or degranulation was observed. The results are consistent with those obtained using other methods in rat and guinea pig tissues (*Parrat & West*, 1957b; *Mota & Vugman*, 1956). Mast cells can release histamine without degranulation (Smith, 1963).

It is difficult to see how dormant histamine in mast cells can be important in regulating rapid physiological processes. Loosely bound histamine in dynamic endogenous pools would be more suitable (*Johnson, Beaven, Erjavec & Brodie*, 1966; *Johnson*, 1968). Against this background the lack

of mast cells in dental pulps and the suggested nonmast-cell histamine stores render the pulp an interesting object for further studies.

Blood vessels

OPT-induced fluorescence was observed in the walls of the blood vessels of the pulps of all the species examined except the rat and the guinea pig. In human skin, arterioles and capillaries probably act as an accessory histamine store besides the mast cells (*Juhlin*, 1967a). In monkey kidney most of the yellow fluorescence indicating histamine is seen in the capillaries of the glomeruli (*Juhlin*, 1967b). *Juhlin* and *Shelley* (1966) regarded this kind of vascular fluorescence in various tissues as derived from histamine-containing smooth muscle and endothelial cells. Especially the endothelial cell nuclei of the *vasa recta* of the kidney show the histamine-like fluorescence (*Öhman & Shelley*, 1969).

We did not detect an extinction of this kind of fluorescence in the pulpal vessels after pretreatment with compound 48/80. *Johnson* (1968) has emphasized that mast cell degranulation by compound 48/80 may increase loosely bound histamine stores, although the augmentation may also be due to the separate stimulating effect of compound 48/80 on synthesis in nonmast-cell sites.

There is evidence of histamine synthesis at sites with properties different from those characteristic of mast cells (*Kahlson, Rosengren & Thunberg*, 1963). Histamine is believed to be synthesized continually within microvascular smooth muscle cells and possibly also in endothelium (*Shayer*, 1962). According to this view, histamine is loosely bound in the cell wall and liberated molecules can act on intrinsic receptors. Reactive hyperemia, spontaneous vasomotion, hyperemia of warmth, and slowly developing dilator responses in the slow phase of inflammation are explained on this basis (Shayer, 1965). Histamine is also the potential mediator of active reflex dilation after the action of vasoconstrictor substances (*Beck*, 1965). Thus it can be hypothesized that vascular histamine maintains a circulatory homeostasis and forms a counterbalance to nervous vasoconstriction. We found no evidence of the presence of vasodilator parasympathetic fibers in the dental pulps (*Pohto & Antila*, 1969). *Lahiri* and *Sanyal* (1967) have pointed out that a vascular inflammatory response may be affected by a dynamic balance between phlogistic histamine and monoamines having an opposite action. The absence of mast cell histamine in the pulps studied agrees well with earlier findings suggesting that no pulpal mast cells exist. This does not imply that nonmast-cell histamine should be excluded, e.g. as a possible mediator in the inflammatory processes.

Fibroblasts

A physiological function is proposed for histamine in rapidly growing tissues. Nascent histamine is said to be important for growth in some fetal tissues and in wound and granulation tissues during healing (*Kahlson & Rosengren*, 1965). A continuously growing tooth can be regarded as a rapidly growing tissue. Against this background it was interesting to find an OPT-induced histamine-like fluorescence in the pulpal fibroblasts of rat, guinea pig and rabbit incisors. Teeth with closing apexes did not display such fluorescence. These possible nonmast-cell histamine stores were not depleted by compound 48/80, although a simultaneous disappearance of mast cells was observed elsewhere in the rat.

Experimentally enhanced intracellular histidine decarboxylase and histamine levels accelerate collagen formation (*Sandberg*, 1962). *Schultz-Haudt* and *From* (1961) have proposed that the gingiva exists in a state comparable to continuous wound healing. To confirm the role of histamine in growth more detailed information on the dynamics of histamine synthesis is required (*Burkhalter*, 1965). Histamine formation in normal and reparative growth has been extensively discussed by *Kahlson* and *Rosengren* (1968).

Salivary gland parenchyma

Stimulation of salivary secretion is a characteristic effect of histamine (*Emmelin*, 1966). *Beaven, Erjavec* and *Brodie* (1965) have shown that exogenous histamine is incorporated by nonmast-cell stores in the cat submandibular gland. A subsequent secretory stimulus released both labeled and unlabeled histamine into the saliva, mainly as metabolites. When *Johnsson, Beaven, Erjavec* and *Brodie* (1966) studied several tissues of rats treated with compound 48/80, the highest concentration of exogenous histamine was retained for few hours in the submandibular gland.

The present finding that exogenous histamine or its metabolites can be detected histochemically in the acinar and tubular cells of the rat submandibular gland is consistent with the earlier results above. The fluorescence of secretory products seen in the duct system may also originate from metabolites, e.g. from 1,4 methylhistamine, which is the first step in the main pathway of histamine inactivation. The failure to obtain the same findings with the rabbit is obviously due to the unavoidable use of a small dose of histamine.

Acknowledgements. The expenses of the work were met by grants from the Chancellor of University of Helsinki and the Finnish Dental Society.

SUMMARY

o-Phthalaldehyde-induced fluorescence was employed for the demonstration of histamine-storing cells in oral tissues. The tissues studied were gingiva, lining mucosa, tongue, dental pulp and submandibular gland. Specimens from the rat, guinea pig, rabbit, cat and man were used.

Mast cells on a blue background were revealed by the yellow histamine fluorescence in all tissues studied except pulps, which were devoid of mast cells. In the rat gingiva concomitant demonstration of 5-hydroxytryptamine, noradrenaline and histamine was accomplished.

In human, cat and rabbit pulps the walls of the blood vessels displayed a distinct histamine-like fluorescence. A similar fluorescence was observed in the pulpal fibroblasts of continuously growing incisors. In the *parenchyma* of the rat submandibular gland, an OPT-induced fluorescence appeared after a large intravenous dose of histamine.

The effects of reserpine, histamine and compound 48/80 on the mast cells and nonmast-cell histamine stores suggested above were studied.

RÉSUMÉ

CELLULES DE MISE EN RÉSERVE DE L'HISTAMINE DANS LES TISSUS BUCCAUX

La fluorescence provoquée par l'o-phtalaldéhyde a été utilisée pour mettre en évidence les cellules des tissus buccaux dans lesquelles l'histamine est mise en réserve. Les tissus suivants ont été étudiés: gencive, muqueuse de revêtement, langue, pulpe dentaire et glande sous-maxillaire. Les prélèvements ont été faits sur le rat, le cobaye, le chat et l'homme.

Des mastocytes sur fond bleu ont été mis en évidence par la fluorescence jaune de l'histamine dans tous les tissus, à l'exception de la pulpe, qui ne contenait pas de mastocytes. Dans la gencive du rat, on a pu mettre en évidence en même temps l'hydroxy-5 tryptamine, la noradrénaline et l'histamine.

Chez l'homme, le chat et le lapin, les parois des vaisseaux sanguins de la pulpe présentaient une nette fluorescence du type de l'histamine. Une fluorescence semblable a été observée dans les fibroblastes des incisives à croissance continue. Dans le *parenchyme* de la glande sous-maxillaire du rat, une fluorescence provoquée par o-phtalaldéhyde est apparue après administration intraveineuse d'une forte dose d'histamine.

Les auteurs ont étudié les effets de la réserpine, de l'histamine et du composé 48/80 sur les mastocytes et sur les réserves d'histamine suggérées ci-dessus en dehors des mastocytes.

ZUSAMMENFASSUNG

HISTAMINSPEICHERNDEN ZELLEN IM MUNDGEWEBE

Die durch o-Phthalaldehyd hervorgebrachte Fluoreszenz wurde zur Sichtbarmachung von histaminspeichernden Zellen im Mundgewebe verwendet. Die untersuchten Gewebe waren Gingiva, Deckepithelgewebe, Zunge, Zahnpulpa und die Submandibulardrüse. Die Präparate stammten von Ratten, Meerschweinchen, Kaninchen, Katzen und Menschen.

Die gelbe Histaminfluoreszenz machte die Mastzellen auf blauem Grund in allen untersuchten Geweben sichtbar, ausser der Zahnpulpa, in der sich keine Mastzellen befanden. In der Gingiva der Ratten wurde gleichzeitig 5-Hydroksitryptamin, Noradrenalin und Histamin nachgewiesen.

Die Blutgefässwände der Pulpa von Menschen, Katzen und Kaninchen enthielten eine eindeutige histaminähnliche Fluoreszenz. Die gleiche Fluoreszenz wurde in den Fibroblasten der Pulpa von wachsenden Vorderzähnen nachgewiesen. Nach grosser intravenöser Histamindosis erschien in dem Parenchym der Submandibulardrüse der Ratten eine histaminähnliche Fluoreszenz.

Es wurde die Wirkung von Reserpin, Histamin und Compound 48/80 auf die histaminspeichernden Mastzellen und die oben vorgeschlagenen Nicht-Mastzellen untersucht.

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