Acta odont scand 1971 *29:* 663—681

Keywords:
Mouth mucosa
Biological transport
Water
Sodium
Potassium
Permeability

From:
The Department of Prosthetic Dentistry, Royal Dental College, Aarhus and the Department of Clinical Chemistry, University Hospital, Aarhus, Denmark

STUDIES ON THE PERMEABILITY OF HUMAN ORAL MUCOSA

II. THE PERMEABILITY OF DRY PALATAL MUCOSA TO WATER, SODIUM AND POTASSIUM

SVEND KAABER

The permeability of normal human palatal mucosa after suspended oral secretion was studied in 14 young adults by analysing the increase of weight and the sodium and potassium content in standardized filter paper discs applied to regions with and without visible glands. Samples taken from mucosa without visible glands exhibited a relatively uniform and individually constant increase in weight, the variation in which proved to be a linear function of the relative humidity of the surrounding air during sampling. Samples taken with direct contact between the mucosa and the filter paper regularly contained small amounts of sodium and potassium, and small amounts of desquamated epithelium. Corresponding samples taken with a cytological filter contained no demonstrable traces of the two electrolytes and showed a strong reduction in the number of epithelial cells. The simultaneous samples from the glandular mucosa region showed greater variability in weight increase and content of the two electrolytes, especially of sodium. The results showed a continuous outward diffusion of water and an apparent impermeability to sodium and potassium of the dry palatal epithelium.

The oral epithelium, like the epidermis, provides a route for the transport of solutes to and from the organism. Whereas the permeability of human epidermis has been studied systematically for more than fifty years (*Tregear*, 1966b), the corresponding properties of the oral mucosa have received only minor attention. Interest has mainly been focused on the inward transport, owing to the importance of the oral mucosa in the absorption of drugs (*Walton*, 1944; *Gibaldi & Kanig*, 1965; *Beckett & Triggs*, 1967). The outward transport under physiological conditions has been studied in only a few investigations. The observations indicate that there is no regular permeability to urea in human palatal mucosa (*Jensen et al.*, 1964) or to amino acids in nonkeratinized periodontal mucosa (*Löe & Holm-Pedersen*, 1965; *Egelberg*, 1966). The permeability of the oral mucosa to water and

Received for publication, July 1, 1971.

electrolytes has not previously been studied. Animal experiments have demonstrated an inward transport of sodium and potassium through vital excised sublingual mucosa from dogs (*Kawamura & Takata*, 1960). Similarly, Na^{24} is readily absorbed from the surface of various mucosal areas in rabbits, including the hard palate (*Aoyama*, 1968).

The latter observations indicate that an outward passage of electrolytes through oral mucosa without secretory potential is possible. The purpose of the present investigation has been to study the permeability of intact human oral epithelium to water, sodium and potassium in two similar types of mucosae, one with and one apparently without glandular tissue.

MATERIALS AND METHODS

The material comprised 14 healthy adult persons, 8 men and 6 women aged 22—25 years. All subjects had a natural dentition and healthy oral mucosae. None of them were regular smokers. The experiments were carried out on the hard palate, in two regions with an even mucosal surface, one without visible gland openings and lying about 10 mm from the gingival border of the second premolar and the other containing a varying number of gland openings and lying about 10 mm from the second or third molar. In all cases, both the right and left halves of the palate were used for sampling.

For sampling, standardized 6.3 mm wide discs of 0.15 mm thick ash-free filter paper (Frisenette type 644—25)* were employed, partly alone and partly with similar discs of a 0.13 mm thick porous cellulose ester membrane (Millipore MF filter, type 11301)** with a pore diameter of 5 μ. The discs were stored separately in closed polyethylene bottles, which served as transport and weighing containers (*Kaaber*, 1971). The containers were cleaned by (a) immersion in deionized water containing an anionic detergent for 24 hours at 50° C, (b) washing in three portions of deionized water and three portions of freshly made glassdistilled deionized water and (c) drying between layers of ash-free filter paper in clean plastic containers for 24 hours at 70° C. Electrolytes in the discs were removed by (a) elution in 15 mmol LiCl solution for 48 hours, (b) immersion in double-distilled water for 24 hours and (c) drying between layers of clean, ash-free filter paper. For manipulation of discs and containers, separate sets of clean, chromium-plated steel tweezers were employed. The closed polyethylene bottles were stored in closed glass containers, the surface of which had been treated against static electricity

*A. G. Frisenette & Sons, Farum, Denmark.
**Millipore Corp., Bedford, Mass. U.S.A.

by washing with a 0.1 % solution of quaternary ammonium bases (Rodalon ®)*.

Sampling technique

Before sampling, salivary secretion was suspended by submucosal injection of 0.5 ml 0.05 % scopolamine nitrate solution in the oral vestibule. After 30 minutes, the palate was dried with cotton rolls and a saliva ejector. The mucous membrane was then cleansed with a water spray and dried gently with clean gauze and ash-free filter paper. The four sampling areas were covered with pieces of semitransparent surgical tape (Blenderm ®)**, to the contact surface of which was attached a disc of 0.01 mm thick transparent plastic (Styroflex)*** with a diameter of 7.5 mm. The area under the plastic disc was used for sampling, and the transparency of the covering permitted repeated sampling from the same area. The sampling area was protected from saliva contamination by a ring of filter paper 2 mm wide stuck to the tape (Fig. 1A and 1B). Sampling from the right half of the palate was made by direct contact between the filter paper disc and the mucous membrane, whilst in the left half a disc of membrane material was interposed between the mucosa and the filter paper. A contact period of 30 minutes for each sample was used, five samples on filter paper being taken from each of the four sites. Where membrane filters were used the same filter served throughout the period. During the entire sampling period the mouth was kept open. All sampling was effected at room temperature (21 $\pm$ 3° C), the relative humidity being registered with a hygrometer. The transfer of the discs from the mucosa to the weighing bottle lasted 10—15 seconds. For each subject, 8—10 discs of filter paper and 2—3 of membrane filter were used as controls.

Gravimetric technique

Before and after mucosal contact, the disc was weighed in the closed polyethylene container, using a microbalance (Mettler M5) with a reading accuracy of 2 micrograms. Preweighing was carried out for 60 minutes before actual weighing was performed, and only containers antistatic after surface treatment with 0.5 % Rodalon solution were used. The two weighings were carried out 30—45 minutes before and after the contact of the disc with the mucous membrane. After the difference in weight had been found,

* Ferrosan A/S, Copenhagen, Denmark.
** Minnesote Mining & Mfg. Co., St. Paul 6, Minn. U.S.A.
*** Norddeutsche Seekabelwerke AG, Oldenburg, W. Germany.

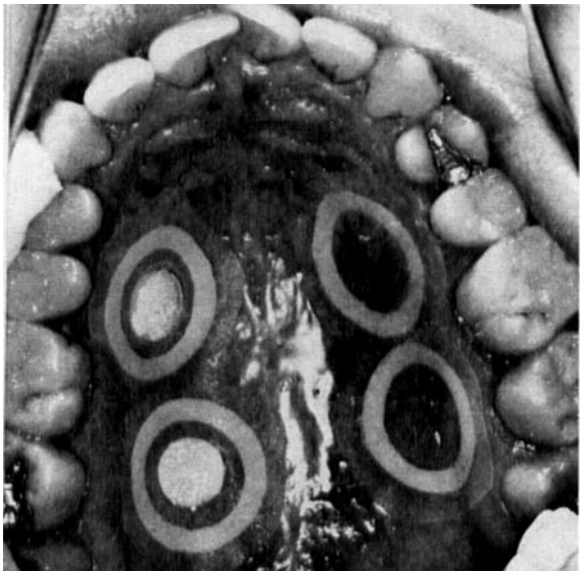

Fig. 1A. Location of the sampling sites on the hard palate.

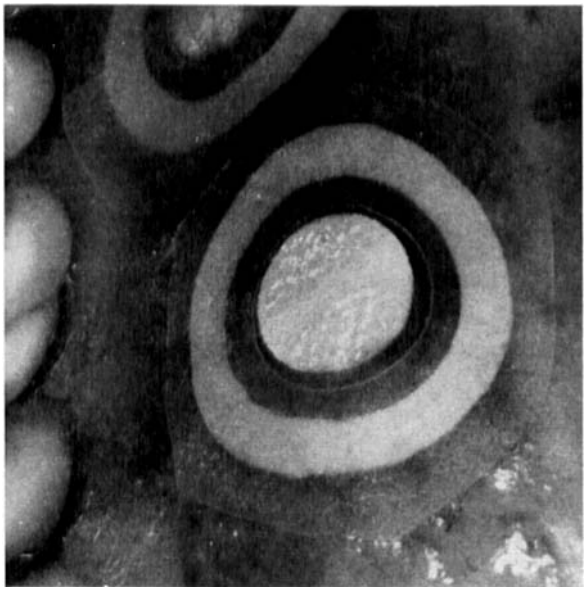

Fig. 1B. Sampling chamber with a disc of filter paper located on a glandular area of palatal mucosa.

this value was corrected for loss of water from the disc during transfer from the mucosa to the bottle. Correction was obtained from theoretical evaporation values, on the basis of temperature, relative humidity and the length of the transfer period (*Kaaber*, 1971).

Flame photometric technique

After the second weight determination, 600 microlitres 15 mmol LiCl solution were added to the weighing bottle. After at least 20 hours' elution of the disc, the content of sodium and potassium was determined with a flame photometer (IL model 143), using lithium chloride as internal standard (*Boling*, 1964). The photometer was adjusted to a standard containing 10 mmol Na and K/l, diluted 1:200, and the reading range increased from 10 to 40.

The sensitivity of the instrument was tested on samples of 300 and 600 nanolitres of double distilled water, containing 1, 2, 5 and 10 mmol Na and K/l. The quantities were transferred to filter paper discs with a microsyringe (Hamilton type 7001), whose reading accuracy and variation in yield had been previously ascertained (*Kaaber*, 1971). The tests were carried out three times with at least 14 days' interval using 8 samples of each solution and a similar number of controls of double distilled water. Solutions containing 30 nanograms sodium and more exhibited only a moderate discrepancy (<5 %). Readings of the potassium content were significant and without error at 25 nanograms and above. The reading variation proved to be of the same magnitude for both electrolytes, the standard error being ½ unit (= 1/8 of an ordinary scale unit of the instrument) (Fig. 2).

Cytological method

The transfer of cytological material to the sampling media during their mucosal contact was investigated in three separate series each consisting of four samples with and four samples without use of membrane filter. One side of each disc was marked with ink. After the first weighing and subsequent mucosal contact, the disc was placed in the weighing bottle with the contact side up. After the second weighing, the container was opened, the disc carefully removed, and its cytological material fixed to the surface with a thin layer af albumin-glycerine. After air drying, the disc was stained with haematoxylin-eosin. Filter paper discs were mounted in cedarwood oil or Eukitt*, while discs of membrane material were cleared after mounting in immersion oil under cover-slips. The surface of the filter paper was examined

* O. Kindler AG, Freiburg, W. Germany.

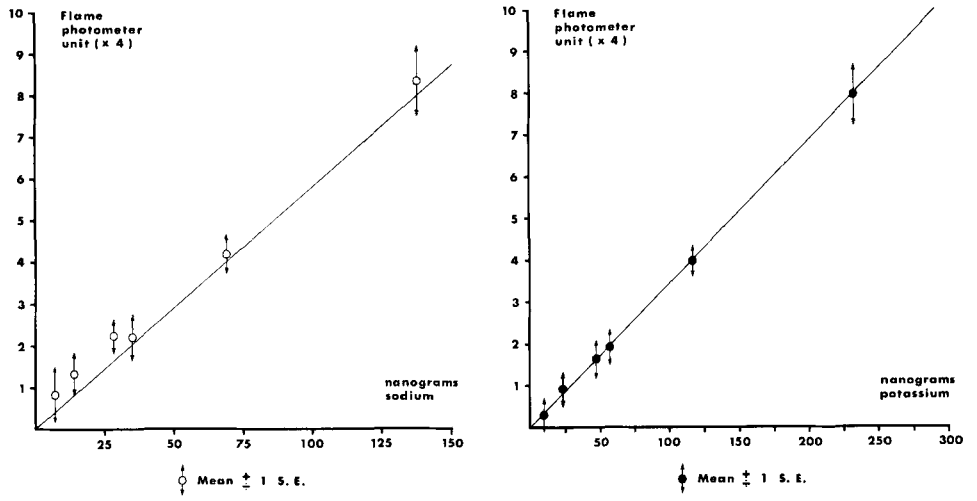

Fig. 2. The reading sensitivity of an IL—143 flame photometer to microquantities of sodium and potassium. The drawn line represents the theoretical reading level of the instrument.

at 250 times magnification with reflected light and dark field illumination in a Reichert-Zetopan microscope equipped with an opaque illuminator. The membrane filters were examined at the same magnification with transmitted light. For each disc, all nucleated cells were registered, using double counts. A discrepancy of more than 5 % elicited a recount.

Statistical methods

The statistical analysis employed parameters calculated by conventional methods (SOKAL & ROHLF, 1969). Parameter values with a significant deviation at a 5 %, a 1 % or a 0.1 % level are indicated in the following tables with 1, 2 and 3 asterisks respectively. Differences in variances were tested with Snedecor's F-test, and differences between mean values with Student's t-test, or with the Wilcoxon test for unpaired data. An electronic computer was used for all calculations.

RESULTS

The weight increase after sampling is recorded in Table I. Compared with the corresponding controls, the filter paper discs showed a strong increase in weight, the mean values of which were significantly higher in samples

Table 1.

Mean weight increase of sampling materials after contact with palatal mucosa with suspended secretion (values in micrograms)

Mucosal type		Filter paper discs: Samples without filter	Filter paper discs: Samples with filter	t	Filter paper discs: Controls		Membrane filter discs: Samples	Membrane filter discs: Controls
Without visible glands	N	70	70		111	N	14	37
	range	234—417	260—396		0—40	range	9—88	0—55
	$\bar{x}$	320.19	332.48	2.06*	12.70	$\bar{x}$	45.44	15.40
	S.E.	38.27	31.82		10.33	S.E.	21.84	12.46
With visible glands	N	50	50		111	N	10	37
	range	260—651	262—710		0—40	range	22—111	0—55
	$\bar{x}$	412.10	384.50	1.60	12.70	$\bar{x}$	54.71	15.40
	S.E.	93.92	77.67		10.33	S.E.	25.68	12.46
	t	7.39***	5.05***			t	1.03	

Table II.

Mean weight increase in filter paper discs after contact with palatal mucosa with suspended secretion (values in micrograms)

Variation according to sex and sampling procedure

Mucosal type	Sex		Samples without filter	Samples with filter	Analysis of variance: Source	Sum of squares	Mean of squares	Degrees of freedom	F
Without visible glands	Males (N:8)	N	40	40	Filter	7254	7254	1	6.17*
		$\bar{x}$	330.55	334.47	Sex	5172	5172	1	4.40*
		S.E.	37.69	29.52	Interaction	3162	3162	1	2.69
	Females N:6)	N	30	30	Error	159886	1175	136	—
		$\bar{x}$	306.40	329.53	Total	175476	—	139	—
		S.E.	34.80	34.90					
With visible glands	Males (N:6)	N	30	30	Filter	19803	19803	1	3.08
		$\bar{x}$	384.37	372.93	Sex	12996	12996	1	2.02
		S.E.	102.23	75.57	Interaction	4845	4845	1	0.75
	Females (N:4)	N	20	20	Error	616727	6424	96	—
		$\bar{x}$	427.30	387.45	Total	654372	—	99	—
		S.E.	74.35	88.43					

Table III.

Relation between weight change level and relative humidity of air during sampling from palatal mucosa without visible glands

Relative humidity in % (mean values)	Number of series ♂	♀	Weight changes in micrograms		Value of t
30—35	4	2	N	29	
			$\bar{x}$	364.82	
			S.E.	33.33	3.1784**(*)
40	4	—	N	20	
			$\bar{x}$	336.50	
			S.E.	26.18	3.1544**(*)
45—50	8	6	N	70	
			$\bar{x}$	317.51	
			S.E.	23.06	4.7106***
55—60	—	4	N	20	
			$\bar{x}$	287.55	
			S.E.	31.41	

from the glandular mucosa, $P<0.001$. The membrane discs exhibited a more moderate but still significant weight increase without local variation. The weight increase in filter paper discs according to sex and sampling technique is shown in Table II. Samples from females and samples taken without a membrane filter from the non-glandular mucosa showed a smaller weight increase than the corresponding male samples and those taken with filter. This difference was almost significant, $P<0.05$. The individual variation for the non-glandular mucosa is shown in Fig. 3. The mean values for the male and female series were between 270 and 410 micrograms with standard deviation values of 10—30 micrograms. Table III shows the relation between the weight change levels in this mucosal area and the relative humidity of the air during the sampling period. The mean values demonstrated a significant decrease with an increase in humidity. The two parameters exhibited a distinct linear connection (Fig. 4).

The relation between the weight increase in the samples and their electrolyte content is shown in Table IV. Samples from the glandular areas exhibited an increasing weight level compared to the non-glandular areas, the difference being most pronounced for electrolyte-containing samples from the glandular mucosa.

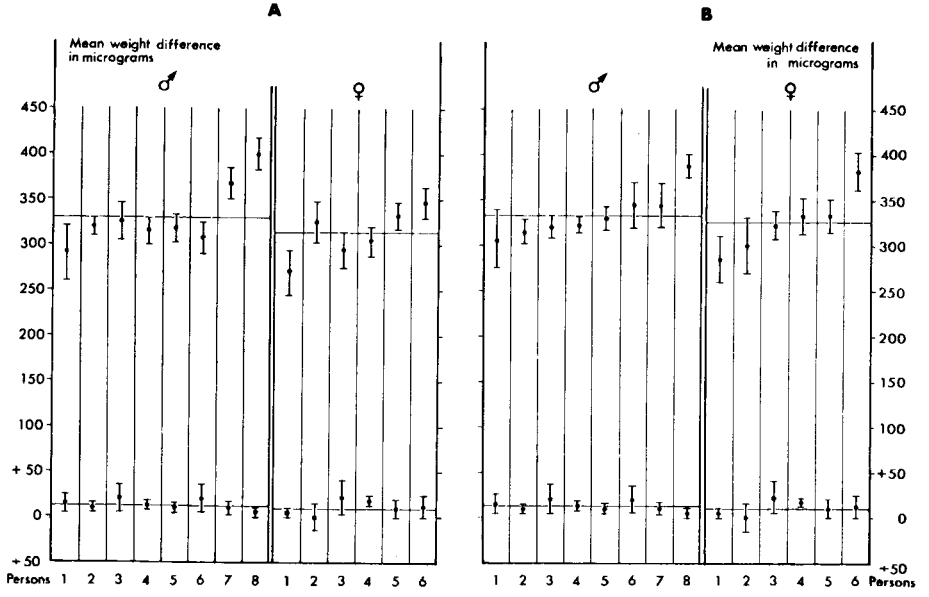

Fig. 3. Mean weight changes (+/÷ 1 S.E.) in filter paper discs after contact with non-glandular palatal mucosa (upper row), and in corresponding controls (lower row).
A: Samples taken without use of membrane filter.
B: Samples taken with use of membrane filter.

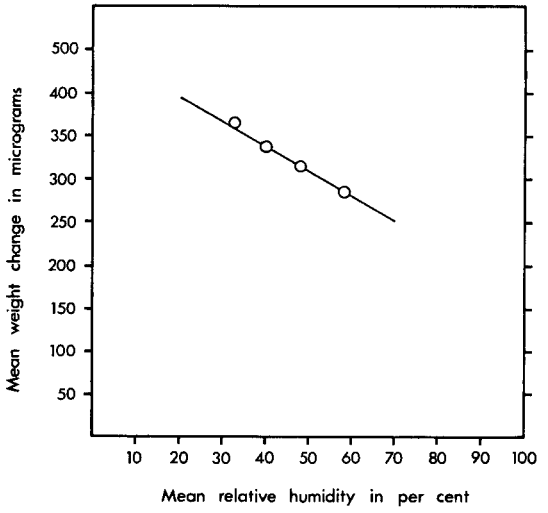

Fig. 4. Mean weight changes of samples from non-glandular palatal mucosa related to the relative humidity of the air during sampling.

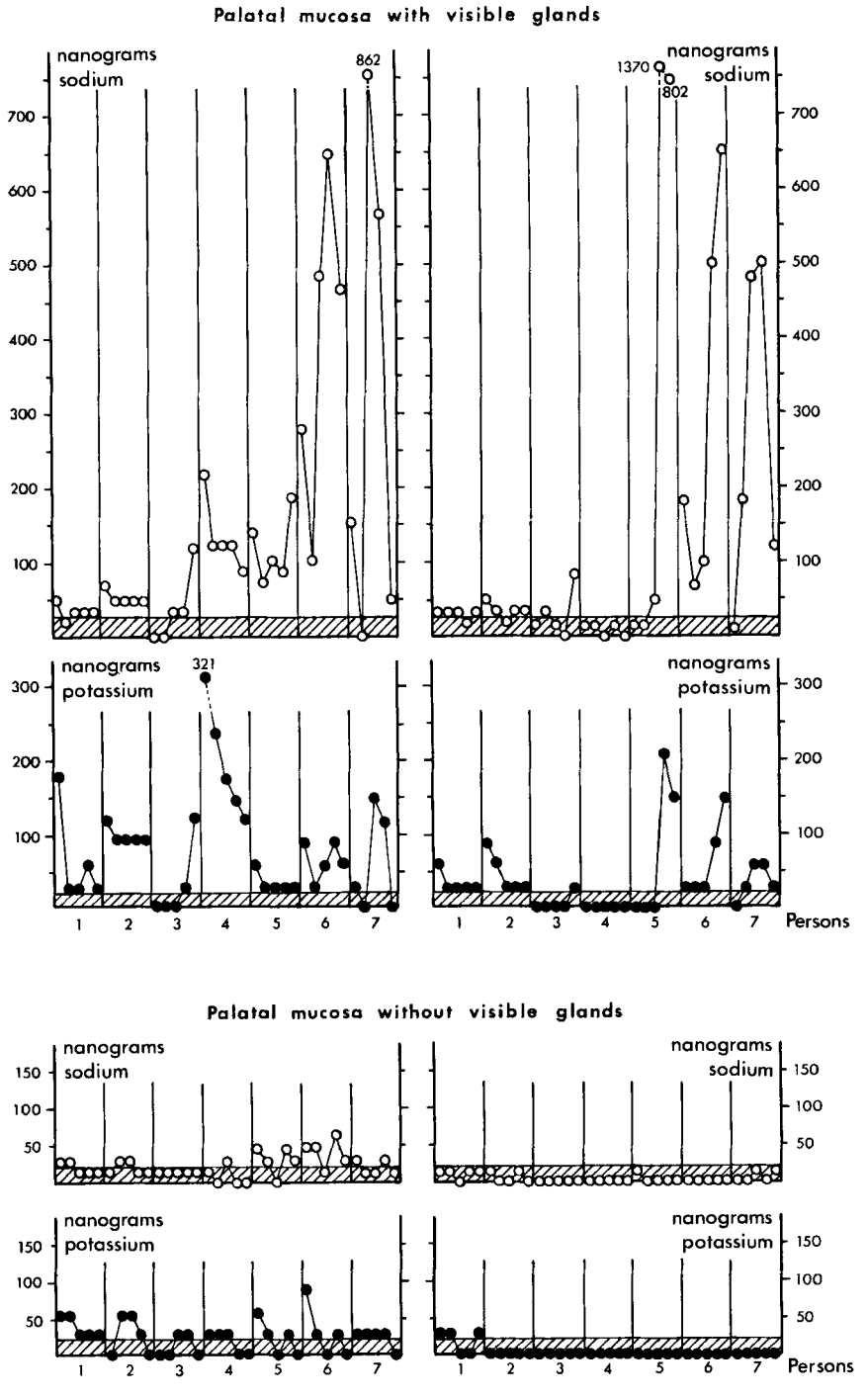

Fig. 5. Variations in electrolyte content during consecutive sampling from the same area of palatal mucosa.
Left row: Samples taken without use of membrane filter.
Right row: Samples taken with use of membrane filter.

Table IV.

Relation between weight increase and electrolyte content of samples from palatal mucosa with suspended secretion

Mucosal type	Samples without content of electrolyte (values in micrograms)			Samples with content of electrolyte (values in micrograms)			Value of t
	N	$\bar{x}$	S.E.	N	$\bar{x}$	S.E.	
Mucosa without visible glands	88	320.76	46.68	52	321.11	24.96	0.99
Mucosa with visible glands	29	343.16	31.21	71	406.06	87.06	4.03***
Value of t		2.09*			6.29***		

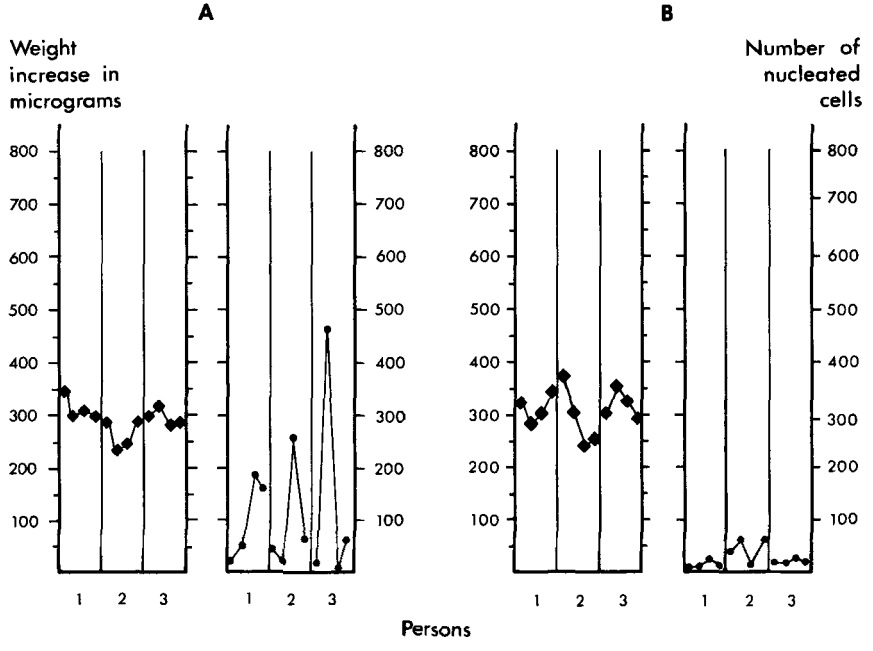

Fig. 6. Weight changes in filter paper discs and their content of nucleated epithelial cells after consecutive sampling from non-glandular palatal mucosa.
A: Sampling taken without use of membrane filter.
B: Sampling taken with use of membrane filter.

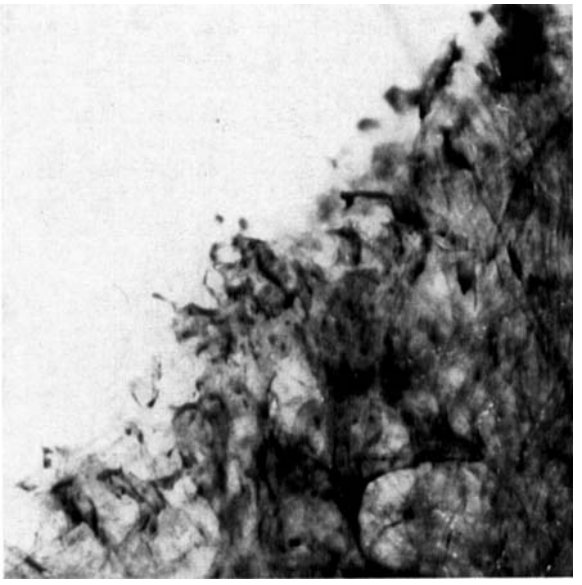

Fig. 7. Nucleated epithelial cells on the surface of a filter paper disc after sampling from non-glandular palatal mucosa without use of a membrane filter. Haematoxylin-Eosin, × 250.

The variation in the content of sodium and potassium in the material is apparent from Table V and Fig. 5. In samples from the non-glandular area small amounts of sodium and potassium were regularly found, whereas demonstrable traces of the two electrolytes were only rarely found in the filter paper when a membrane filter was used. The filters themselves contained demonstrable traces of sodium and potassium in only relatively few cases (Table V A). A corresponding reduction in the number of samples with appreciable amounts of electrolytes was observed in the material from the glandular mucosa (Table V B). The electrolyte content of these samples showed a strong quantitative variation, especially in the case of sodium (Fig. 5). The membrane filters regularly showed a varying content of electrolytes with a similar strong variation in sodium content (Table V B). The relation between the weight level and the number of nucleated epithelial cells in samples from the mucosa without visible glands is shown in Fig. 6. In samples obtained without use of a membrane filter, varying numbers of cells, mainly at the periphery, were observed (Fig. 7). The use of membrane filters caused a strong reduction in the number of cells present in the filter paper, without corresponding changes in the weight level. The membrane

Table V A.

Electrolyte content of sampling materials after contact with palatal mucosa with suspended secretion

Mucosa without visible glandular structures

Electrolyte	Sampling material	Number of samples	Samples without electrolyte content N	%	Samples with electrolyte content N	%	Electrolyte content in nanograms ≤75 N	%	≤150 N	%	≤150 N	%
Sodium	FP—MF	70	39	55.7	31	44.3	29	93.6	2	6.4	—	—
	FP+MF	70	69	98.6	1	1.4	1	100.0	—	—	—	—
	MF	14	10	71.4	4	28.6	4	100.0	—	—	—	—
Potassium	FP—MF	70	25	35.7	45	64.3	43	95.6	2	4.4	—	—
	FP+MF	70	66	94.3	4	5.7	4	100.0	—	—	—	—
	MF	14	11	78.5	3	21.5	3	100.0	—	—	—	—

(FP: filter paper MF: membrane filter)

Table V B.

Electrolyte content of sampling materials after contact with palatal mucosa with suspended secretion

Mucosa with visible glandular structures

Electrolyte	Sampling material	Number of samples	Samples without electrolyte content N	%	Samples with electrolyte content N	%	Electrolyte content in nanograms ≤75 N	%	≤150 N	%	≤150 N	%
Sodium	FP—MF	50	8	16.0	42	84.0	17	40.5	12	28.6	13	30.9
	FP+MF	50	22	44.0	28	56.0	17	60.7	3	10.7	8	28.6
	MF	10	4	40.0	6	60.0	2	33.3	3	33.3	3	33.3
Potassium	FP—MF	50	7	14.0	43	86.0	25	58.2	13	30.2	5	11.6
	FP+MF	50	26	52.0	24	48.0	18	75.0	4	16.7	2	8.3
	MF	10	7	70.0	3	30.0	3	100.0	—	—	—	—

(FP: filter paper MF: membrane filter)

filters contained only sporadic epithelial cells of both ortho- and parakeratotic type.

DISCUSSION

Methylated scopolamine nitrate, which was used in the present investigation to inhibit salivary secretion, is an atropine derivative with an effect 3.6 times as strong as that of atropine sulphate (*Nyman*, 1943). An intraoral injection of 0.25 mg of the former causes after 15—30 minutes a strong blocking of all salivary glands lasting 90—110 minutes (*Nyman*, 1943; *Hultin*, 1956; *Östlund & Åkesson*, 1959). The central reactions to this dose are moderate and limited to a weak or moderate tachycardia, frequently accompanied by a slight rise in blood pressure (*Nyman*, 1943; *Östlund & Åkesson*, 1959; *Pohto & Ahtee*, 1966). Peripheral reactions such as strong vascular dilatation, which has been observed after intravenous injection of 5 mg atropine sulphate (*Webb, Garlington & Schwarz*, 1956) have not been described. The administration of 0.25 mg scopolamine in the present material caused a pronounced inhibition of secretion in the larger salivary glands (parotid, submaxillary and sublingual glands). This effect was also pronounced in the palatine gland in 10 subjects, but inadequate in 2 men and 2 women. Samples taken from the glandular mucosa were in these cases excluded from the analyses.

The permeability of palatal epithelium to water. The distinct sample weight increase indicated an accumulation of water in the filter paper during the contact with the mucosa, as the influence from epithelial cells on this increase was only negligible (Fig. 6). Besides acting as a cytological filter, the membrane disc protected the mucosal surface against the direct effect of the capillary forces in the dry filter paper. A comparison between the two sampling methods indicated, however, that this factor was of no importance (Table II). The uniform increase in weight in the individual sample series from non-glandular mucosa (Fig. 3) indicated a continuous diffusion of water through the epithelium at an individually constant rate. The transmucosal water loss proved to be a straight line function of the relative humidity of the air during the experiments (Fig. 4). This observation corresponded to the similar connection between epidermal water loss and the ambient humidity of the air (*Buettner*, 1953, *Thauer & Zöllner*, 1953; *Zöllner & Thauer*, 1954; *Kaufmann, Thauer & Zöllner*, 1955; *Brebner, McKerslake & Waddell*, 1956; *Heerd & Ohara*, 1961; *Bettley & Grice*, 1967) and the water diffusion through intact epidermal horny layers (*Kligman*, 1964). The trends towards

sexual variation in the water loss (Table II) could be readily explained by the generally higher humidity level during sampling from the females, cf. Table III. The corresponding difference between the two sampling methods in the non-glandular area indicated the presence of local rate-limiting factors in the mucosa. An important factor determining the rate of transport of water through epidermis is the thickness of the stratum corneum (*Burch & Winsor*, 1946; *Blank*, 1953; *Mali*, 1956; *Scheuplein*, 1965, 1967). The significance of this factor seemed, however, to be limited in the palatal mucosa. The non-glandular area was in close topographical relation to the central glandular parts of the palate. Histologically, this area is characterized by a submucosal layer with varying amounts of connective and adipose tissue and strands of glandular tissue but a rather uniform keratinizing epithelium (*Sicher*, 1966). The variation in the material in Table II and III might thus be ascribed to other factors, such as differences in the regional density of the capillary network and in the local hydrostatic pressure, although a similar connection between the rates of transepidermal water loss and local vascular changes has not been established (*Ohara, Kondo & Ogino* 1962, *Bettley & Grice* 1967, *Baker & Kligman* 1967). The hydrostatic pressure in oral tissue does not yet seem to have been investigated. The values in Fig. 4 indicating an outward water transport through the dry mucosa even at an ambient humidity of 100 % thus reflected a positive pressure in the palatal region.

The mean weight increase values in Table I and II corresponded to a water content of 11—13 micrograms per sq. mm filter paper. These values were undoubtedly too low to reflect the actual rate of water loss, as the small volume of the sampling chamber and the length of the sampling period implied a gradual increase of the vapour pressure in the chamber and a corresponding decrease in the diffusional rate. Further investigations are therefore necessary to establish the true penetrational rate in the palatal area.

The permeability of palatal epithelium to sodium and potassium. Significant amounts of sodium and potassium were recognized in samples from the glandular area only (Table V A and B). In two cases — persons 5 and 6 in Fig. 5 — a parallellity was observed in the sodium content of the corresponding samples from the two areas, probably due to a weak secretory activity. Otherwise, samples from the non-glandular area contained only traces of the two electrolytes, nearly always after sampling with direct contact between the mucosa and the filter paper.

The demonstration of a considerable amount of parakeratotic epithelial cells with this procedure accorded with earlier observations on the pre-

dominance of this cell type in the keratinized palatal mucosa in young persons (*Shklar*, 1966). The concurrent presence of cells and electrolytes in these samples suggested that the occurrence of the two electrolytes was due to cellular contamination. This supposition was confirmed by the use of membrane filters which could simultaneously reduce the extent of the contamination and eliminate the electrolyte content in the filter paper. The membrane filters showed a similar correspondence between a small number of cells and a paucity or absence of sodium and potassium and no sign of ionbinding properties in the material.

The samples from the glandular mucosa exhibited a distinct relation between an increased and variable weight level and a corresponding electrolyte content (Table III) which further confirmed the importance of secretory activity for the electrolyte content of the samples. Such activity could be demonstrated, in spite of the scopolamine, during the entire sampling period (Fig. 5). It was propably provoked by the unavoidable stimulation of the mucosa during sampling, as the secretory activity of the palatine glands is strongly affected by mechanical stimuli (*Östlund*, 1953; *Butcher & Mitchell*, 1967). The clear reduction in the number of samples with electrolyte content when a membrane filter was used for the glandular mucosa (Table V B) was probably due to the protection afforded by the filter.

The present investigation showed that the human palatal epithelium, in spite of its permeability to water, is apparently impermeable to sodium and potassium. These results confirm earlier investigations of the human epidermis, which exhibits absorption of sodium and potassium to only a very limited extent (*Bettley*, 1965, *Tregear*, 1966a). They conflict, however, with the earlier mentioned observations in rabbits, where a distinct penetration of the palatal mucosa by Na^{24} has been demonstrated (*Ayoma*, 1968). The reason for this aberrant reaction is difficult to establish both on account of the differences in sensitivity of the methods employed and on account of inductive permeability changes in the rabbit mucosa due to the systematic cleansing with 70 % ethanol. A quantitative difference in the permeability reaction of the oral mucosa can not be excluded, as the rate of penetration of Na^{24} through the epidermis of the rabbit is 50 times that in man (*Tregear*, 1966a). This difference may, however, be due to the larger number of hair follicles in rabbit skin, on account of the differing diffusion constants for follicle tissue and the stratum corneum (*Scheuplein*, 1967). The qualitatively different permeability of the palatal mucosa to sodium which is indicated by the present animal and human experiments, is, however, in accordance with the reactions of the isolated surviving frog skin in which the outward-facing membrane of the transporting cells is passively permeable to sodium,

while the inwardfacing membrane is impermeable to this electrolyte (*Koefoed-Johnsen & Ussing*, 1958). The heterogenous structure of human epidermis has hitherto complicated an analysis of the barrier functions of the stratified keratinized epithelium. The present study has demonstrated that the hard palatal mucosa on account of its areas with a uniform epithelial structure, is suited to more detailed studies of this barrier function.

Acknowledgements. The valuable criticism and advice from Mr. C. J. Andersen, cand. polyt., Department of Clinical Chemistry, The University Hospital, during the flame photometric analyses, and from lecturer S. Terp, cand. oecon., Institute of Economics, University of Aarhus, during part of the statistical calculations is gratefully acknowledged.

REFERENSES

Aoyama, W., 1968: The experimental study on the permeability of the oral mucosa with sodium-24 solution. (Japanese with English summary) Odontology (Tokyo) *56:* 555—578.

Baker, H. & A. P. Kligman, 1967: Measurement of transepidermal water loss by electrical hygrometry. Arch. Derm. *96:* 441—452.

Beckett, A. H. & E. J. Triggs, 1967: Buccal absorption of basic drugs and its application as an in vivo model of passive drug transfer through lipid membranes. J. Pharm. & Pharmacol. 19 (suppl.): 315—415.

Bettley, F. R., 1965: The influence of detergents on epidermal permeability. Brit. J. Derm. *77:* 98—106.

Bettley, F. R. & K. A. Grice, 1967: The influence of ambient humidity on transepidermal water loss. Brit. J. Derm. *78:* 575—581.

Blank, I. H., 1953: Further observations on factors which influence the water content of stratum corneum. J. invest. Derm. *21:* 259—271.

Boling, E. A., 1964: A flame photometer with simultaneous digital readout for sodium and potassium. J. Lab. & Clin. Med. *63:* 501—510.

Brebner, D. F., D. McKerslake, & J. L. Waddell, 1956: The diffusion of water vapor through human skin. J. Physiol. *132:* 225—231.

Buettner, K., 1953: Diffusion of water and water vapor through human skin. J. appl. Physiol. *6:* 229—242.

Burch, G. E. & T. Winsor, 1946: Diffusion of water through dead plantar, palmar and dorsal human skin and through toe nails. Arch. Dermat. *53:* 39—41.

Butcher, E. O. & O. G. Mitchell, 1967: Structure and secretory mechanism of rodent and primate palatine glands. J. dent. Res. *46:* 672—674.

Egelberg, J., 1966: Permeability of the dento-gingival blood vessels II. Clinically healthy gingivae. J. periodont. Res. *1:* 276—286.

Gibaldi, M. & J. L. Kanig, 1965: Absorption of drugs through the oral mucosa. J. oral. Ther. Pharmacol. *1:* 440—450.

Grice, K. & F. Bettley, 1967: The effect of skin temperature and vascular change on the rate of transepidermal water loss. Brit. J. Derm. *79:* 582—588.

Heerd, E. & K. Ohara, 1961: Untersuchungen über die Wasserdampfabgabe kleiner Hautflächen beim Menschen. I. Die Abhängigkeit vom Wasserdampfdruck in der umgebenden Luft bei normaler Hauttemperatur. Pflügers Arch. ges. Physiol. *276:* 32—41.

Heerd, E. & C. Oppermann, 1966: Untersuchungen über die Wasserdampfabgabe kleiner Hautflächen beim Menschen. II. Der Einfluss der Hauttemperatur auf die Perspiratio insensibilis. Pflügers Arch. ges. Physiol. *291:* 163—173.

Hultin, M., 1956: Methylskopolominnitrat (skopyl) i standarddos för salivhämning inom odontologien. Sverig. Tandläkarförb. Tidn. *48:* 145—153.

Jensen, K. E., V. Lund, G. Tryde, & G. C. Bruun, 1964: The effect of inflammation on the permeability of human palatal epithelium to urea. Acta odont. scand. *22:* 322—331.

Kaaber, S., 1971: Studies on the permeability of human oral mucosa. I. Gravimetric determination of biological fluids at microgram levels. Acta odont. scand. *29:* 653—662.

Kaufmann, W., R. Thauer, & G. Zöllner, 1955: Der insensible Gewichtsverlust als Funktion der Umweltbedingungen. Der Wasserdampfdruck der Hautoberfläche und die Wasserdurchgangszahl der Haut in Abhängigkeit von Temperatur und Wasserdampfdruck der umgebenden Luft im thermoindifferenten Bereich. Pflügers Arch. ges. Physiol. *261:* 189—198.

Kawamura, Y. & M. Takata, 1960: Studies on the permeability of the oral mucosa. I. Permeability of inorganic ions. J. dent. Res. *39:* 517—524.

Kligman, A. M., 1964: The biology of stratum corneum — in »The Epidermis» p. 387—433. Montagna, W. & Lobitz, W. C. (ed.). New York & London.

Koefoed-Johnsen, V. & H. H. Ussing, 1958: The nature of the frog skin potential. Acta physiol. scand. *42:* 298—308.

Löe, H. & P. Holm-Pedersen, 1965: Absence and presence of fluid from normal and inflamed gingivae. Periodontics *3:* 171—177.

Mali, J. W. H., 1956: The transport of water through the human epidermis. J. invest. Derm. *27:* 451—469.

Nyman, E., 1943: N-methylierte Skopolaminderivate. Acta physiol. Scand. *6:* 256—265.

Ohara, K., M. Kondo & I. Ogino, 1963: Fluctuations in insensible perspiration. Jap. J. Physiol. *13:* 441—453.

Pohto, P. & L. Ahtee, 1966: Effect of atropine, methylatropine, methylscopolamine and pilocarpine on salivary secretion and heart rate in man. Ann. Med. exp. Fenn. *44:* 411—414.

Scheuplein, R. J., 1965: Mechanisms of percutaneous absorption. I. Routes of penetration and the influence of solubility. J. invest. Derm. *45:* 334—346.

Scheuplein, R. J., 1967: Mechanism of percutaneous absorption. II. Transient diffusion and the relative importance of various routes of skin penetration. J. invest. Derm. *48:* 79—88.

Shklar, G., 1966: The effects of aging upon oral mucosa. J. invest. Derm. *47:* 115—120.

Sicher, H. (ed.), 1966: Orban's oral histology and embryology. 6th ed. St. Louis.

Sokal, R. R. & F. J. Rohlf, 1969: Biometry. The principles and practice of statistics in biological research. San Francisco.

Thauer, R. & G. Zöllner, 1953: Der insensible Gewichtsverlust als Funktion der Umweltbedingungen. Seine Abhängigkeit von dem Wasserdampfdruck der Luft im indifferenten Temperaturbereich. Pflügers Arch. ges. Physiol. *258:* 58—71.

Tregear, R. T., 1966a: The permeability of mammalian skin to ions. J. invest. Derm. *46:* 16—23.

Tregear, R. T., 1966b: Physical functions of skin. London & New York.

Walton, R. P., 1944: Sublingual administration of drugs. J. Amer. med. Ass. *124:* 138—143.

Webb, P., L. N. Garlington, & M. J. Schwarz, 1956: Insensible weight loss at high skin temperatures. J. appl. Physiol. *11:* 41—44.

Zöllner, G. & R. Thauer, 1954: Der insensible Gewichtsverlust als Funktion der Umweltbedingungen. Seine Abhängigkeit vom Wasserdampfdruck der Luft in Lufttemperaturen oberhalb des Indifferenz-Bereiches. Pflügers Arch. ges. Physiol. *259:* 281—293.

Östlund, S. G., 1953: Palatine glands and mucin. Thesis. Malmø.

Östlund, S. G. & N. Å. Åkesson, 1959: Hämning och stegring av salivkörtlarnas verksamhet. Odont. Rev. *10:* 147—166.

Address:
The Department of Prosthetic Dentistry,
Royal Dental College,
8000 Aarhus C, Denmark