

Nevertheless, alternation of the phases of PA in the fasting state was accompanied by changes in the functional morphology of GPC in the antral part of the gastric mucosa of the dogs: in PR the hormone evidently diffuses from SG 1 and SG 2 (increased realization of secretion) whereas the secretion potential is unchanged and the reserve increased (an increase in the number of SG 4). PW is characterized by activation of granule formation accompanied by weakening of the release of the hormone from SG.

#### LITERATURE CITED

1. V. N. Boldyrev, "Periodic work of the digestive tract with an empty stomach," Dissertation for the Degree of Doctor of Medical Sciences, St. Petersburg (1909).
2. N. N. Lebedev, Biorhythms of the Digestive System [in Russian], Moscow (1987).
3. V. D. Sukhodolo and I. V. Sukhodolo, Periodic Activity of the Principal Digestive Glands [in Russian], Tomsk (1987).
4. A. Bennet, Mechanisms of Gastrointestinal Motility and Secretory Processes, New York (1983), p. 87.
5. M. Grusha et al., Pflügers Arch., 403, 40 (1985).
6. R. Hakanson et al., Cell Tissue Res., 222, 479 (1982).
7. P. Layer and H. Goebell, Z. Gastroent., 25, 769 (1987).
8. M. Nagata et al., Jpn. J. Pharmacol., 5, 932 (1982).
9. J. Rahier et al., Gastroenterology, 92, 1146 (1987).
10. R. Salmon et al., Chronobiology, 3, 267 (1982).

## FUNCTIONAL ANATOMY OF THE HUMAN ESOPHAGEAL MUCOSA DURING POSTNATAL DEVELOPMENT

M. M. Parshin

UDC 612.315:612.642]:66

**Key words:** esophagus; ontogeny; mucous membrane

The study of the human esophageal mucosa has been the subject of numerous publications [1, 2, 4, 6, 10], on account of the special position of the esophagus in the digestive tube [8, 9]. Some investigators have attached great importance to the combined study of the structure of the boundary segments of the esophageal wall, separating functionally different regions of the digestive tube [3, 7, 11, 12]. However, despite the large number of investigations, we could find no information on the dynamics of morphological changes in the mucosa (in successive layers) during postnatal development, confirmed morphometrically.

The aim of this investigation was a morphometric study of the layers of the human esophageal mucosa in the pharyngo-esophageal, aortic-bifurcational, and esophago-gastric segments of the organ in postnatal ontogeny.

#### EXPERIMENTAL METHOD

The layers of the human esophageal mucosa were measured in 2400 serial microscopic preparations varying from 15 to 25  $\mu$  in thickness, from 122 cadavers of persons aged from birth to 90 years. The causes of death were unrelated to diseases of the esophagus. Transverse and longitudinal sections were cut at the level of the pharyngo-esophageal, aortic-bifurcational, and

---

Department of Pathological Anatomy, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 109, No. 4, pp. 412-414, April, 1990. Original article submitted July 19, 1989.

TABLE 1. Thickness of Epithelial Layer of Human Esophageal Mucosa in Postnatal Ontogeny\* ( $\bar{X} \pm S_x$ )

| Age           | Pharyngo-esophageal segment, $\mu$ | Aortic bifurcational segment, $\mu$ | Esophago-gastric segment, $\mu$ |
|---------------|------------------------------------|-------------------------------------|---------------------------------|
| Under 10 days | 179,7 $\pm$ 5,9                    | 159,6 $\pm$ 4,6                     | 192,8 $\pm$ 4,9                 |
| Under 1 month | 175,3 $\pm$ 6,1                    | 157,2 $\pm$ 6,4                     | 181,4 $\pm$ 6,3                 |
| Under 1 year  | 175,4 $\pm$ 6,6                    | 158,0 $\pm$ 6,6                     | 180,8 $\pm$ 7,1                 |
| 1—2 years     | 181,7 $\pm$ 6,6                    | 157,7 $\pm$ 5,8                     | 194,3 $\pm$ 7,2                 |
| 2—3 "         | 204,9 $\pm$ 5,5                    | 172,9 $\pm$ 9,6                     | 234,5 $\pm$ 10,8                |
| 3—5 "         | 214,7 $\pm$ 9,5                    | 185,2 $\pm$ 6,4                     | 248,0 $\pm$ 9,7                 |
| 5—12 "        | 216,9 $\pm$ 5,5                    | 192,7 $\pm$ 8,8                     | 246,1 $\pm$ 6,6                 |
| 12—20 "       | 322,1 $\pm$ 5,7                    | 263,3 $\pm$ 6,3                     | 340,9 $\pm$ 5,8                 |
| 20—30 "       | 348,0 $\pm$ 28,0                   | 269,8 $\pm$ 3,0                     | 340,4 $\pm$ 5,0                 |
| 30—40 "       | 321,1 $\pm$ 3,3                    | 288,6 $\pm$ 4,7                     | 336,6 $\pm$ 7,9                 |
| 40—50 "       | 321,7 $\pm$ 8,0                    | 285,6 $\pm$ 12,3                    | 327,3 $\pm$ 7,4                 |
| 50—60 "       | 321,6 $\pm$ 6,0                    | 284,9 $\pm$ 4,2                     | 320,6 $\pm$ 8,1                 |
| 60—70 "       | 300,0 $\pm$ 4,4                    | 269,3 $\pm$ 3,0                     | 317,3 $\pm$ 7,9                 |
| Over 70 years | 297,6 $\pm$ 8,2                    | 245,5 $\pm$ 3,2                     | 298,0 $\pm$ 6,6                 |

Legend. \*All measurements in microns; coefficient of variation varies from 21.3 to 30.3%.

TABLE 2. Thickness of Tunica Propria of Human Esophageal Mucosa during Postnatal Development\* ( $\bar{X} \pm S_x$ )

| Age           | Pharyngo-esophageal segment, $\mu$ | Aortic bifurcational segment, $\mu$ | Esophago-gastric segment, $\mu$ |
|---------------|------------------------------------|-------------------------------------|---------------------------------|
| Under 10 days | 140,2 $\pm$ 2,9                    | 124,7 $\pm$ 3,2                     | 154,3 $\pm$ 3,7                 |
| Under 1 month | 145,6 $\pm$ 4,5                    | 127,3 $\pm$ 2,7                     | 157,6 $\pm$ 5,1                 |
| Under 1 year  | 169,9 $\pm$ 5,7                    | 141,6 $\pm$ 4,8                     | 179,2 $\pm$ 6,9                 |
| 1—2 years     | 178,8 $\pm$ 6,2                    | 149,8 $\pm$ 6,8                     | 193,7 $\pm$ 6,1                 |
| 2—3 "         | 189,7 $\pm$ 7,4                    | 159,6 $\pm$ 6,5                     | 206,8 $\pm$ 8,9                 |
| 3—5 "         | 207,4 $\pm$ 8,9                    | 167,4 $\pm$ 7,4                     | 247,6 $\pm$ 7,4                 |
| 5—12 "        | 226,8 $\pm$ 11,7                   | 179,3 $\pm$ 10,9                    | 265,5 $\pm$ 12,4                |
| 12—20 "       | 367,5 $\pm$ 14,8                   | 227,4 $\pm$ 28,8                    | 405,3 $\pm$ 13,9                |
| 20—30 "       | 388,7 $\pm$ 13,7                   | 269,5 $\pm$ 16,4                    | 425,2 $\pm$ 19,1                |
| 30—40 "       | 395,8 $\pm$ 18,2                   | 305,4 $\pm$ 17,9                    | 448,3 $\pm$ 18,8                |
| 40—50 "       | 399,6 $\pm$ 17,4                   | 321,6 $\pm$ 16,5                    | 458,1 $\pm$ 20,5                |
| 50—60 "       | 409,4 $\pm$ 16,5                   | 329,9 $\pm$ 17,2                    | 449,7 $\pm$ 21,9                |
| 60—70 "       | 412,7 $\pm$ 19,8                   | 326,3 $\pm$ 28,4                    | 443,4 $\pm$ 20,6                |
| Over 70 years | 402,4 $\pm$ 20,5                   | 317,4 $\pm$ 17,7                    | 435,8 $\pm$ 22,5                |

Legend. \*All measurements in microns; coefficient of variation varies from 7.4 to 17.9%.

esophago-gastric segments of the esophagus. Histological sections were stained with hematoxylin and eosin and by Van Gieson's, Bielschowsky—Gros, Foot's, and Mallory's methods. The layers of the mucosa in each segment of the esophagus studied were measured separately by means of an MOV-15 ocular micrometer on the MBM-1 and "Reichert" microscopes. The morphometric data were subjected to statistical analysis separately by the "Esophagus-1" program by "Fortran" computer [5].

The morphometric results were grouped in 14 age groups (Table 1). Microscopic sections of the mucosa were photographed on a "Reichert" microscope.

## EXPERIMENTAL RESULTS

Analysis of the morphometric data showed correlation between the growth of the layers of mucosa and the dynamics of the morphological changes in it within the limits of individual age groups. In particular, growth of the esophageal mucosa and its layers in thickness took place slowly from birth until the age of 1 year, and was cumulative in character, its rate increasing toward the end of each stage. Thus the thickness of the epithelial layer varied from  $159.6 \pm 4.6$  to  $194.3 \pm 7.2 \mu$ , of the tunica propria of the mucosa from  $124.7 \pm 3.2$  to  $179.2 \pm 6.9 \mu$ , and of the muscular coat from  $10.4 \pm 0.7$  to  $28.8 \pm 1.3 \mu$ . It has to be

TABLE 3. Thickness of Muscular Coat of Human Esophageal Mucosa in Postnatal Development\* ( $\bar{X} \pm S_x$ )

| Age           | Pharyngo-esophageal segment, $\mu$ | Aortic bifurcational segment, $\mu$ | Esophago-gastric segment, $\mu$ |
|---------------|------------------------------------|-------------------------------------|---------------------------------|
| Under 10 days | 10,4 $\pm$ 0,7                     | 10,9 $\pm$ 0,8                      | 12,3 $\pm$ 1,2                  |
| Under 1 month | 12,6 $\pm$ 0,6                     | 11,6 $\pm$ 1,1                      | 15,7 $\pm$ 0,9                  |
| Under 1 year  | 25,1 $\pm$ 1,9                     | 23,1 $\pm$ 2,1                      | 28,8 $\pm$ 1,3                  |
| 1—22 years    | 48,5 $\pm$ 3,5                     | 43,8 $\pm$ 3,7                      | 51,8 $\pm$ 2,9                  |
| 2—3 "         | 82,5 $\pm$ 7,2                     | 79,5 $\pm$ 5,2                      | 87,6 $\pm$ 4,8                  |
| 3—5 "         | 114,6 $\pm$ 8,7                    | 103,8 $\pm$ 8,9                     | 119,9 $\pm$ 10,2                |
| 5—12 "        | 148,3 $\pm$ 11,2                   | 137,4 $\pm$ 12,2                    | 157,4 $\pm$ 12,8                |
| 12—20 "       | 197,4 $\pm$ 16,7                   | 179,3 $\pm$ 16,5                    | 211,8 $\pm$ 16,7                |
| 20—30 "       | 245,8 $\pm$ 23,1                   | 228,8 $\pm$ 13,8                    | 263,7 $\pm$ 17,8                |
| 30—40 "       | 264,7 $\pm$ 20,9                   | 237,6 $\pm$ 21,6                    | 275,7 $\pm$ 22,9                |
| 40—50 "       | 271,8 $\pm$ 22,5                   | 245,7 $\pm$ 20,4                    | 282,3 $\pm$ 21,3                |
| 50—60 "       | 277,1 $\pm$ 21,8                   | 251,4 $\pm$ 18,3                    | 285,6 $\pm$ 23,4                |
| 60—70 "       | 280,2 $\pm$ 25,2                   | 258,9 $\pm$ 22,8                    | 289,1 $\pm$ 22,8                |
| Over 70 years | 283,9 $\pm$ 23,7                   | 262,1 $\pm$ 21,2                    | 293,7 $\pm$ 24,8                |

Legend. \*All measurements in microns; coefficient of variation varies from 21.6 to 30%.

pointed out that the parameters of the layers of the mucosa increased in the direction from the aortic-bifurcational segment to the pharyngo-esophageal, and still more, to the esophago-gastric segments. The muscular coat of the mucosa had no integral structure but consisted of collections of muscle cells measuring from 500 to 1200  $\mu$ . In the muscular coat, throughout this stage of development the connective-tissue framework was poorly developed and consisted mainly of large concentrations of reticulin fibers. As a result of secondary differentiation of the connective-tissue cells of the mucosa there was a gradual increase in thickness of the layers of the mucosa, and an increase in volumes of the connective-tissue papillae and the epithelial layer of the mucosa surrounding them. The coefficient of correlation between growth of the layers of the mucosa at this stage of development varied from moderately strong to very strong ( $R = 0.46-0.90$ ).

Between the ages of 1 and 3 years further growth of the layers of the mucosa took place, with an increase in the number of reticulin and elastic fibers in the tunica propria, and groups of cells of the lymphoid series appeared. The thickness of the epithelial layer increased to 170-230  $\mu$  (Table 1) of the tunica propria to 150-210  $\mu$  (Table 2), and of the muscular coat of the mucosa to 50-90  $\mu$  (Table 3). The latter still had no integral structure, but the distance between the separate fragments of the muscular coat lay between 400 and 600  $\mu$ . Further formation of its connective-tissue framework continued. The lumen of the esophagus became star-shaped because of the well developed folds, the number of which varied from 3-5 in the aortic-bifurcational segment to 4-6 in the pharyngo-esophageal and 6-8 in the esophago-gastric segments. This type of picture was the result of mixed growth of the layers of the mucosa, intensified differentiation of the connective-tissue elements of the mucosa, and an increase in the volumes of the epithelial layer and muscular coat of the mucosa on account of the reticuloelastic framework of the muscular coat. The coefficient of correlation for growth of the layers was very strong ( $R = 0.50-0.41$ ).

Between the ages of 3 and 12 years, growth of the layers took place more rapidly. The thickness of the epithelial layer increased to 185-260  $\mu$ , of the tunica propria to 170-270  $\mu$ , and of the muscular coat to 110-160  $\mu$ . The number of folds of the mucosa showed a very small increase, by only one or two. The coefficient of correlation of growth of the layers was strong ( $R = 0.63-0.90$ ).

Layers of the mucosa were completely formed by the age of 12-14 years. The epithelial layer was clearly divided into three strata: basal, intermediate, and squamous cells. The number of rows of the basal layer varied from five to 12, intermediate from 19 to 22, and squamous cells from 12 to 15. It must be emphasized that development of the basal layer took place more quickly in the pharyngo-esophageal and esophago-gastric segments than in the aortic-bifurcational segment, as shown by the considerable stratification of the intermediate layer and the small number of rows of squamous epithelial cells. The muscular coat of the mucosa at this age consisted of a well defined sheet of muscle cells with a tangential course. The thickness of the epithelial layer of the mucosa reached 195-350  $\mu$ , the tunica propria 230-430  $\mu$ , and the muscular coat 200-270  $\mu$ . The coefficient of correlation was 0.74-0.91.

Between the ages of 30 and 50 years, and still more, from 50 years to advanced old age, changes of an involutional character took place in the mucosa. Fat cells began to appear in the muscular coat, and collagen fibers along the course of the neurovascular bundles. The thickness of the epithelial layer increased up to the age of 50 years, but starting with 60 years, it decreased and varied from 340 to 240  $\mu$ . The tunica propria of the mucosa on the whole increased in thickness in the period from 30 years to advanced old age, but on account not of progressive morphological transformations, but rather of involutionary formations, and its parameters varied from 300 to 430  $\mu$ . The dynamics of growth of the muscular coat of the mucosa was similar in character, and it varied from 220 to 300  $\mu$  in thickness. Smoothing of the outlines and a reduction in the number of folds of the mucosa were observed, on account of a marked decrease in the volumes both of the connective-tissue papillae and of the epithelial layer surrounding them. The coefficient of correlation for growth of the layers of mucosa was appreciably reduced ( $R = 0.90-0.39$ ).

Thus the histological structure of layers of the esophageal mucosa during the postnatal period passes through alternate stages of progressive and regressive development. Six stages must be distinguished: 1) from birth to the age of 1 year — the stage of secondary differentiation; 2) from 1 to 3 years — the stage of mixed growth; 3) from 3 to 12 years — the stage of rapid growth; 4) from 12 to 30 years — the stage of extensive growth; 5) from 30 to 50 years — the stage of preinvolutionary growth; 6) from 50 years to advanced old age — the stage of involutionary growth. Each of the above-mentioned stages of individual development is characterized by a set of correlative features, of coordinated morphological changes in connective-tissue cells of the mucosa and growth of its layers.

#### LITERATURE CITED

1. A. N. Bazhanov, Properties and Distinguishing Features of the Esophageal Epithelium [in Russian], Alma-Ata (1978).
2. A. N. Liven, Proceedings of the 7th All-Union Congress of Anatomists, Histologists, and Embryologists [in Russian], Tbilisi (1969), pp. 408-410.
3. A. N. Maksimenkov, Vestn. Khir., 74, No. 3, 27 (1954).
4. F. F. Saks, M. A. Medvedev, V. F. Baitinger, and A. I. Ryzhov, The Neonatal Esophagus [in Russian], Tomsk (1988).
5. V. P. Yatsenko, "Morphology and reactive changes in afferent neurons of a sensory ganglion in ontogeny," Supplement to Dissertation for the Degree of Doctor of Medical Sciences, Kiev (1986).
6. N. R. Barret, Surgery, 39, No. 8, 290 (1963).
7. F. E. Fyke, C. F. Code, and J. F. Schleger, Gastroenterology, 86, No. 1, 19 (1956).
8. I. Jit, Ind. J. Med. Res., 62, No. 6, 838 (1974).
9. D. Rudnic, Ann. New York Acad. Sci., 55, No. 6, 109 (1952).
10. K. Roed-Petersen, Dan. Med. Bull., 26, No. 6, 275 (1979).
11. C. Zaino, H. G. Jacobson, H. E. Lepow, et al., The Pharyngo-Esophageal Sphincter, Springfield (1970).
12. C. H. Waddington, Principles of Development and Differentiation, New York (1966), pp. 163-172.