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Morphology and relationships of ultimobranchial body with pharyngeal pouches

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SUMMARY

The ultimobranchial body in humans is still controversial and different theories have been put forward. The aim of this study was to clarify the topographical anatomy of the ultimobranchial body and surrounding tissue during early development. Human embryos at 5-7 weeks of development were used for morphological observation. During the early stages, the sections displayed a ladder-like arrangement of the second to fourth endodermal pouches. The fourth pouch was located in front of the nodosa ganglion. The bilateral fifth pharyngeal pouches protruded anterolaterally to form a U-shaped lumen surrounding the arytenoid swelling. During the middle stages, the third pharyngeal pouch was identified near the fourth pharyngeal artery and the fourth pharyngeal pouch was located anterior to the parathyroid gland IV. We identified a cyst-like structure that is composed of a cell cluster facing to a small lumen as the ultimobranchial body. During the late stages, the lateral thyroid arising from the fourth pharyngeal pouch was located medial to the common carotid artery and joined to dorsal surface of the thyroid gland anlage. The thymus anlage arising from the third pharyngeal pouch was an independent structure that was located lateral to the common carotid artery. However, the ultimobranchial body had disappeared and did not integrate in the thyroid gland. We concluded that (1) the thymus originates from the third pharyngeal pouch; (2) the lateral thyroid originates from the fourth pharyngeal pouch; (3) the ultimobranchial body originates from the fifth pharyngeal pouch.

Key words: Ultimobranchial body – Pharyngeal pouch – Parathyroid – Lateral thyroid – Thymus – Human embryos

INTRODUCTION

It is well known that the third, fourth, and fifth pharyngeal pouches in the primitive pharynx differentiate into their derivatives to form in the lower anterior neck region. Hamilton and Mossman (1978) have pointed out that the fourth pharyngeal pouch gives rise to the superior parathyroid gland, lateral thyroid, the ultimobranchial body and part of the thymus. The fifth pharyngeal pouch is believed to be entirely taken up into the fourth pharyngeal pouch to provide the so-called caudal pharyngeal complex (Hamilton and Mossman, 1978). According to Moore and Persaud (1999), the third pharyngeal pouch contributes to the thymus and the fourth pharyngeal pouch forms the thyroid gland. The fifth pharyngeal pouch appears as a diverticulum of the fourth pharyngeal pouch and the endoderm of the fifth pharyngeal pouch forms the ulti-

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mobranchial body (Geoffrey et al. 2010). Mérida-Velasco et al. (1989) consider a cell cluster at the end of the fifth pharyngeal pouch to be the ultimobranchial body. Moreover, Rodríguez-Vázquez et al. (1984) and Garcia et al. (1984) have claimed that the so called lateral thyroid is derived from the fourth pharyngeal pouch and the third pharyngeal pouch forms the thymus. According to Sañudo and Domenech-Mateu (1990), the cranial growth of the laryngotracheal sulcus above the fourth pharyngeal pouch is identified during early development. However, normal derivatives of these pharyngeal pouches are still controversial.

There have been marked differences in the reported morphology of the ultimobranchial body (Rogers, 1927; Fontaine, 1979; Mérida-Velasco et al., 1989; Manley and Capecchi, 1995). According to Rogers (1927), the ultimobranchial body initially appears at the inferior end of the “third” pharyngeal pouch, but is then quickly incorporated into the cord-like thyroid anlage. Both a duct-like ultimobranchial body (Fontaine, 1979) and one appearing as a cell cluster between the lower groove and pouch (Mérida-Velasco et al., 1989) appear difficult to discriminate from usual pharyngeal arch structures.

The aim of the present study was to clarify the topographical anatomy of the ultimobranchial body. Additionally, we attempted to clarify the relationship between the ultimobranchial body and its surrounding tissue.

MATERIALS AND METHODS

The study was performed in accordance with the provisions of the Declaration of Helsinki 1995 (as revised in Edinburgh, 2000). We used tilted horizontal serial sections (5 micrometers in thickness) of 10 embryos (crown-rump length (CRL) 5-18 mm; 5-7 weeks; Carnegie Stages 13-19). The parameters used to determine the postconceptional age were greatest length and external and internal criteria (Patten, 1973; O’Rahilly and Müller, 1981). The sections had been stained with hematoxylin and eosin (HE) or azan. All specimens were part of the large collection kept at the Embryology Insti-

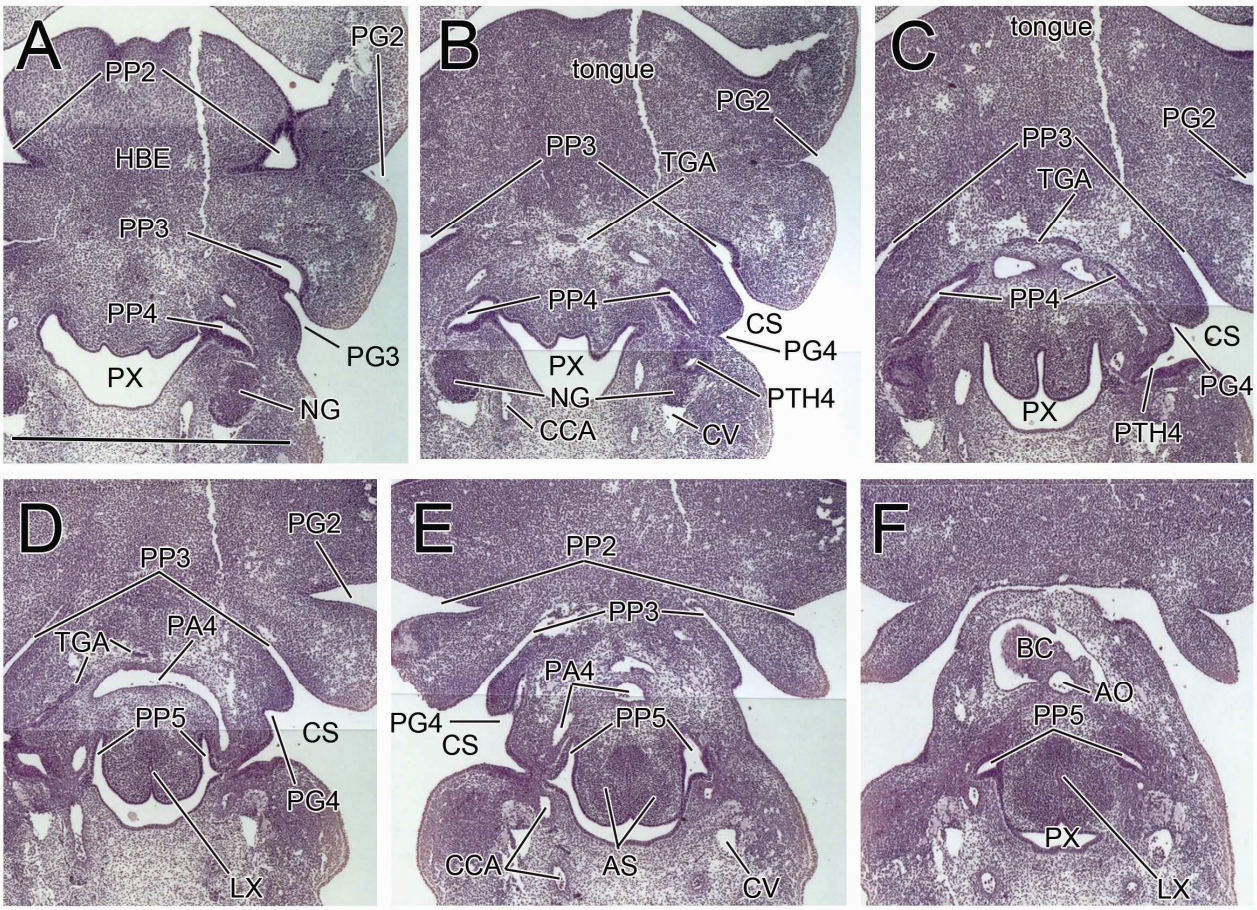

Fig 1. Ladder-like arrangement of the pharyngeal pouches in an 8-mm-CRL embryo. Tilted horizontal sections tangential to the pharyngeal arches. Panel A (Panel F) is the most anterosuperior (postero-inferior) side of the figure. Note the inferolateral end of the third-fifth pouches (PP3 in panels AB; PP4 in panels A-C and PP 5 in panels D-F). The thyroid gland anlage (TGA) is located anterosuperior to the fourth pharyngeal arch artery (PP4) (Panels B-D). The fifth pharyngeal pouch (PP5) provided a bilateral small mass of cells at the inferior end (Panel F) All panels are prepared at the same magnification (Scale bar in panel A, 1 mm).

tute, Universidad Complutense, Madrid, and were products of miscarriages and ectopic pregnancies managed at the Department of Obstetrics at the university. The study protocol was approved by our university ethics committee (No. B08/374). None of these specimens showed any morphological abnormality in the brain, the ganglia of the cranial nerves, the lungs, the liver and the intestinal loop including the pancreas.

RESULTS

Early stages of the development (CRL 5-8 mm; Carnegie Stages 13-15)

The second to fourth pharyngeal pouches were arranged in a ladder-like manner in a single section or near sections (Figs. 1 and 2). The fourth pouch was located in front of the nodosa ganglion (Figs. 1A-C and 2B-D). The bilateral arytenoid swellings sandwiched the slit-like primitive laryngeal cavity (the pharyngoglottic duct) and, in turn, the swellings were sandwiched by the U-shaped bilateral protrusions of the fifth pharyngeal pouches (Figs. 1D-E and 2F-H). The fifth pouch was identified near the fourth pharyngeal artery (Figs. 1D-E and 2F) and provided a bilateral small mass of cells at the inferior end (Figs. 1F and 2I). This inferior end was located anterior to the larynx (Figs. 1Fand 2I). In front of these lower pouches and developing larynx, the heart or the bulbus cordis was developing (Figs. 1F and 2H-I). The parathyroid gland III and IV was observed as a thickening ectoderm posterior to the third and fourth pharyngeal groove respectively, (Figs. 1B-C, 2B-E-F).

Middle stages of the development (CRL 11 and 13 mm; Carnegie Stages 16-17)

Multiple pharyngeal pouch-like structures (with a slit-like lumen lined by tall epithelium) were still evident lateral to the arytenoid swelling: these were regarded as the fourth and fifth pharyngeal pouches (Figs. 3B-E and 4B-D). The third pharyngeal pouch was identified near the fourth pharyngeal artery (Figs. 4C-D). The fourth pharyngeal pouch was located anterior to the parathyroid gland IV (Figs. 3B-C and 4A). We identified a cyst-like structure that is composed of a cell cluster facing to a small lumen as the most likely candidate of the ultimobranchial body. This candidate ultimobranchial body was located medial to the common carotid artery or fourth pharyngeal arch artery (Figs. 3C-E and 4C-D).

Late stages of the development (CRL 18 mm; Carnegie Stages 18-19)

With the development of embryos, the lateral thyroid arising from the fourth pharyngeal pouch was located medial to the common carotid artery and joined to dorsal surface of the thyroid gland anlage (Fig. 5A-D). The thymus anlage arising from the third pharyngeal pouch was an independent structure that was located lateral to the common carotid artery (Fig. 5A-D). However, the ultimobranchial body was not found, and did not have a relation with the thyroid gland (Fig. 5).

DISCUSSION

We found the ultimobranchial body as a bilateral small mass of cells at the inferior end of the fifth pharyngeal pouch during the early stages. During the middle stages, the fifth pharyngeal pouch was

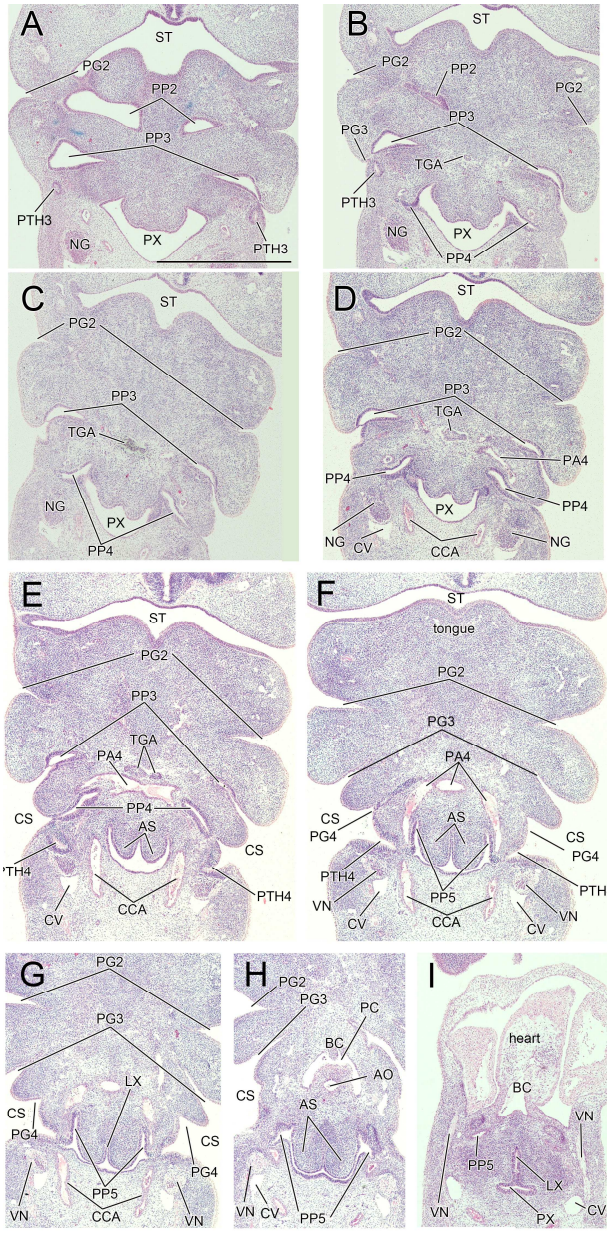

Fig 2. Ladder-like arrangement of the pharyngeal pouches in a 6-mm-CRL embryo. Tilted horizontal sections tangential to the pharyngeal arches. Panel A (Panel I) is the most anterosuperior (postero-inferior) side of the figure. A ladder-like arrangement of the stomodeum (ST) and the second and third pharyngeal pouches (PP2, PP3) are evident (Figs. 2 A-F). The fifth pouch (PP5) provides bilateral cell clusters near the bulbus cordis (BC) of the heart (Fig. 2I). All panels are prepared at the same magnification (Scale bar in panel A, 1 mm).

located medial to the fourth and third pharyngeal pouches, and near the fourth pharyngeal arch artery. During the late stages, the forth pharyngeal pouch contributed to the lateral thyroid, while the third pharyngeal pouch formed the thymus anlage. However, we could not identify the cyst-like structure as the ultimobranchial body in this stages . If so, at late stages, the ultimobranchial body might not appear as a definite structure that is discriminated from others with routine staining.

The ultimobranchial body has been defined as the origin of not only thyroid C cells or parafollicular cells (Pearse and Carvalheira, 1967; Sugiyama et al., 1969; Le et al., 1974; Fontaine, 1979) but also of specific cervical tumors containing nest-like structures (Williams et al., 1989; Harach et al., 1993; Carney, 2000; Michal et al., 2006; Bellevicine et al., 2012). Actually, an endodermal origin of the thyroid C cell (Johansson et al., 2015) is consistent with an endodermal ultimobranchial body by Fontaine (1979). The theory proposed by Rogers (1927) is most likely to provide a basis for the ultimobranchial origin of nest-like tumors in the adult neck, especially in the thyroid. The mitotic cell mass in the cord-like thyroid anlage is somewhat similar to the adult pathology. However, the thyroid anlage shows a significant change in morphology from a cord to a cluster of follicles. We found no intermediate morphology in which the endodermal tall epithelial cell lining of the fifth pharyngeal pouch (a hypothetical origin of the ultimobranchial body) differentiated into a thyroid anlage.

During embryonic development, the fourth pharyngeal pouch gives rise to the superior parathyroid gland, lateral thyroid, the ultimobranchial body and part of the thymus (Hamilton and Mossman, 1978). The fifth pharyngeal pouch is believed to be entirely taken up into the fourth pouch to provide the so-called caudal pharyngeal complex (Hamilton and Mossman, 1978). Hast (1972) stated that parts of the epithelial laminae obliterating the primitive laryngeal cavity originated from the fourth pouch. However, the ultimobranchial body is clearly described in several textbooks (Carmine, 1985; Geof-

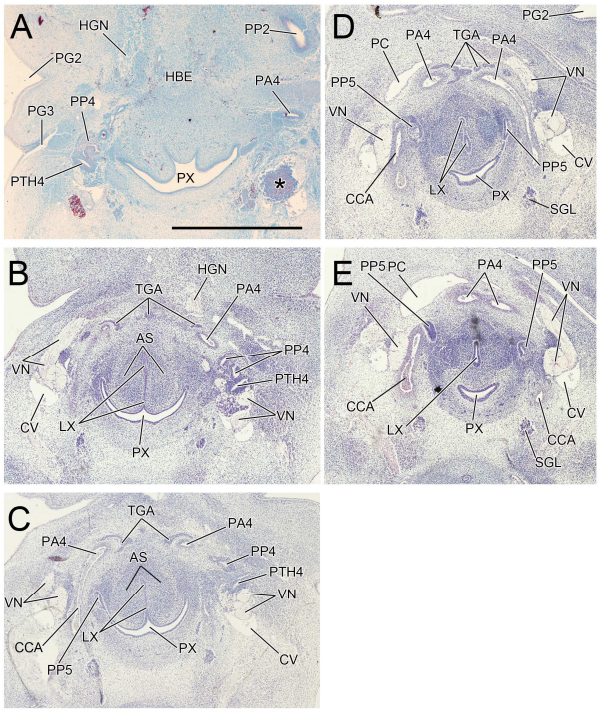

Fig 3. Remnants of the lower pharyngeal pouches in an 11-mm-CRL embryo. Tilted horizontal sections tangential to the pharyngeal arches. Panel A (Panel E) is the most anterosuperior (postero-inferior) side of the figure. A ladder-like arrangement is limited to the second and third ectodermal grooves (PG2, PG3) in panel A. A cyst-like structure as the most likely candidate of the ultimobranchial body (PP5) is identified (Panels C-E). Asterisk in panel A indicates blood retention due to unknown reason. Panels A-E are prepared at the same magnification (scale bar in panel A, 1 mm).

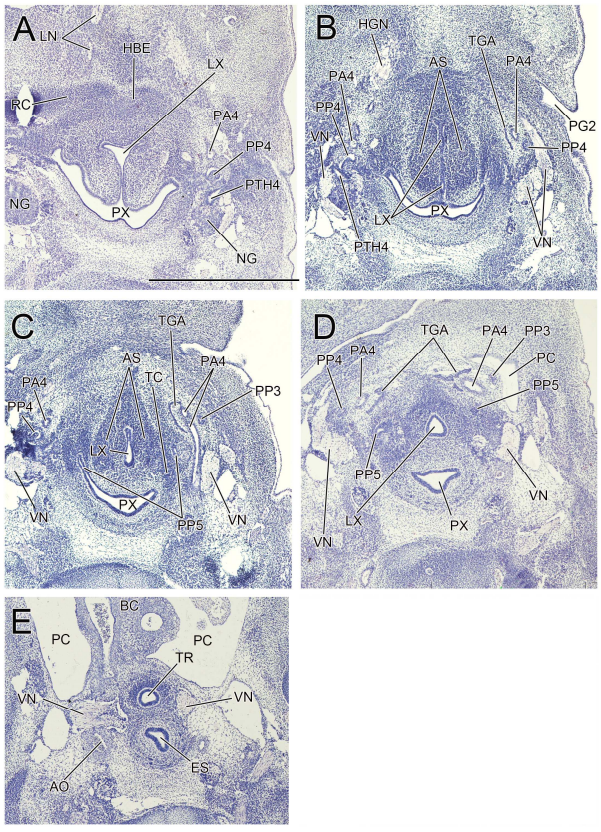

Fig 4. Remnants of the lower pharyngeal pouches in a 13-mm-CRL embryo. Tilted horizontal sections tangential to the pharyngeal arches. Panel A (Panel E) is the most anterosuperior (postero-inferior) side of the figure. A ladder-like arrangement of the pharyngeal arch is absent. A cyst-like structure as the most likely candidate of the ultimobranchial body (PP5) is identified (Panels C-E). The third pharyngeal pouch (PP3) was identified near the fourth pharyngeal artery (PA4) (Panels CD). The fourth pharyngeal pouch (PP4) was located anterior to the parathyroid gland IV (PTH4) (Panels AB). All panels are prepared at the same magnification (Scale bar in panel A, 1 mm).

frey et al. 2010). In our present study, the fifth pharyngeal pouch didn't appear as diverticulum of the fourth pouch. The lateral thyroid arising from the fourth pharyngeal pouch joined to dorsal surface of the thyroid gland anlage, and the thymus anlage arising from the third pharyngeal pouch was an independent structure, that was located lateral to the common carotid artery. Therefore, we concluded that (1) the thymus originates from the third pharyngeal pouch; (2) the lateral thyroid originates from the fourth pharyngeal pouch; (3) the ultimobranchial body originates from the fifth pharyngeal pouch (Fig. 6).

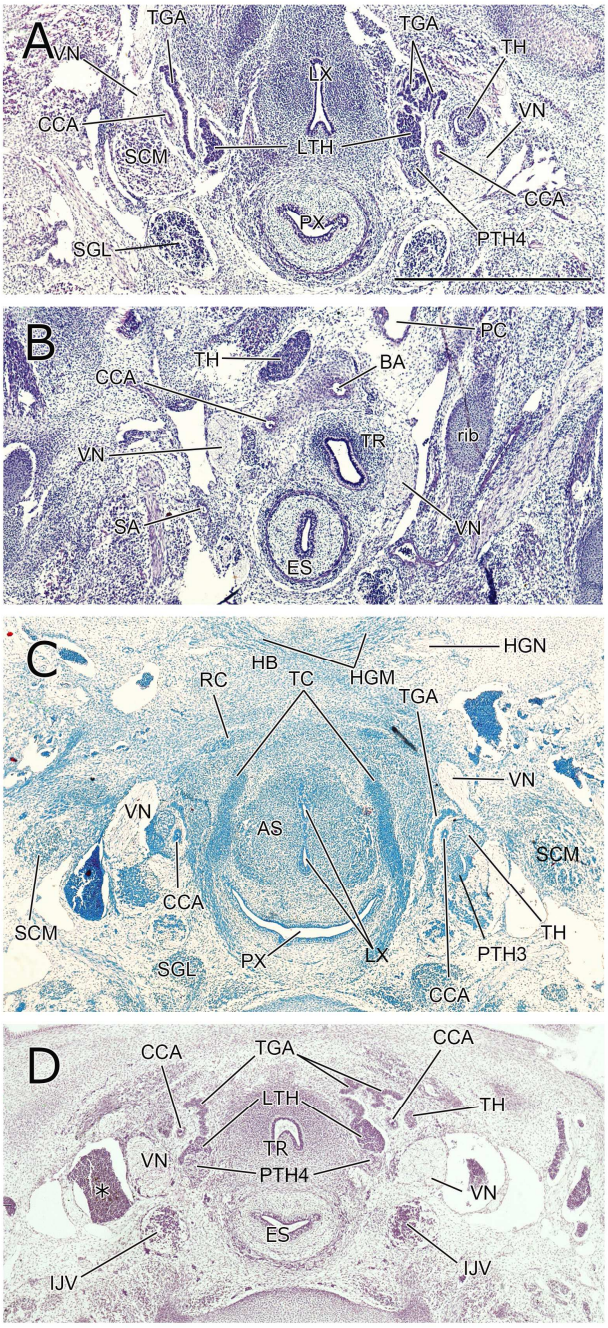

Fig 5. Thick mesenchymal tissue around the thymus, thyroid gland and larynx. Panels A and B (Panels C and D) display a 12-mm-CRL embryo (an 18-mm-CRL embryo). The lateral thyroid (LTH) was located medial to the common carotid artery (CCA) (Panels AD). A cell cluster is regarded as a part of the thymus anlage (TH) because it is lateral to the common carotid artery (CCA) (Panels AD). A cyst-like structure as the most likely candidate of the ultimobranchial body is not identified. Asterisk in panels C and D indicates blood retention in the cranial part of the cardinal vein due to unknown reason. Panels A-D are prepared at the same magnification (Scale bars, 1 mm in panel A).

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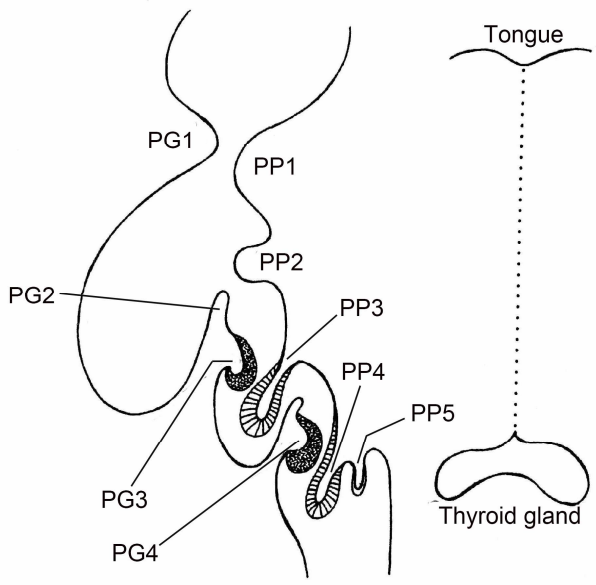

Fig 6. Schematic representation of the lower pharyngeal pouches and grooves. According to Hamilton and Mossman (1978), it is modified.

The fifth pharyngeal pouch (PP5) become distant from the surface ectoderm and is separated from the fourth pharyngeal pouch (PP4).

・The thymus originates from the third pharyngeal pouch (PP3).

・The lateral thyroid originates from the fourth pharyngeal pouch (PP4).

・The ultimobranchial body originates from the fifth pharyngeal pouch (PP5)

・The parathyroid III originates from the third pharyngeal groove (PG3).

・The parathyroid IV originates from the fourth pharyngeal pouch (PG4).

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Common abbreviations for figures:

- AO, aorta;
- AS, arytenoid swelling;
- BA, brachiocephalic artery;
- BC, bulbus cordis (outflow tract of the heart);
- CCA, common carotid artery;
- CS, cervical sinus;
- CV, cranial part of the cardinal vein;
- ES, esophagus;
- HB, hyoid body;
- HBE, hypobranchial eminence;
- HGM, hyoglossus muscle;
- HGN, hypoglossal nerve;
- IJV, internal jugular vein;
- LTH, lateral thyroid;
- LX, primitive larynx;
- NG, nodosa ganglion of the vagus nerve;
- PA4, fourth pharyngeal arch artery;
- PC, pericardial cavity;
- PG1, PG2, PG3, PG4, first, second, third, fourth pharyngeal ectodermal groove;
- PP1, PP2, PP3, PP4 or PP5, first, second, third, fourth or fifth pharyngeal pouch;
- PTH3, parathyroid III;
- PTH4, parathyroid IV;
- PX, primitive pharynx;
- RC, inferior segment of Reichert's cartilage;
- SCM, Sternocleidomastoid muscle;
- SGL, sympathetic ganglion;
- ST, stomodeum;
- TC, thyroid cartilage;
- TGA, thyroid gland anlage;
- TH, thymus anlage;
- TR, trachea;
- VN, vagus nerve;

In all figures, the left-hand side of the figure corresponds to the left side of the body according to morphologies of the heart and liver.