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A Human Embryo of Streeter Age Group XVII†

Je G. Chi* and Hee Jin Yang

Department of Pathology, College of Medicine, Seoul National University

= Abstract =A human embryo considered to belong to stage XVII of Streeter's developmental horizon was described. The embryo was surgically removed from a tubal pregnancy.

Although a certain portion of the back side of the embryo was lost during preparation, a total of 456 serial sections were made through the frontal plane. The ovulation age was thought to be 42±1 days, and the size of the embryo was 11mm in crown-rump length.

Characteristic features of the embryo included digital rays in the hand plate, foot plate of the lower limb bud, inward migration of retinal nuclei, definite pigment granules in the outer layer of the retina, actively elongating cochlear duct, initiation of semilunar valves, branches of the second order from stem bronchi, vermiform appendix, follicular lumen of the duodenum, fused dorsal and ventral pancreas, indifferent gonad and developing suprarenal gland.

Although the embryo derived from a surgical specimen of a tubal pregnancy, there was no change that could be considered abnormal in nature. Thus the embryo was designated as a normal one.

Key Words: ***Embryo, Normal development***

INTRODUCTION

It has been of the most envious and interesting subjects to study the temporal development of various organ systems in early human embryos. However, the most serious obstacle to this approach was the absence of universal and scientific criteria for the accurate determination of embryo age, especially in early stages of its development. To overcome the inaccuracy in the determination of embryo age on the basis of last menstrual period which had been generally applied, Streeter(1948) introduced the concept of "Developmental Horizon." He recognized the existence of close relationship between the gestational age and size of the embryo and the developmental status of internal organs, and classified developmental stages of embryo into I to XXIII with intervals of 2 to 3 days.

In this study, microscopic observation on a serially sectioned human embryo was made in order to reconstruct the organs in development, and to classify the developmental stages of the embryo according to Streeter's criteria.

* Author for correspondence

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CASE REPORT

The embryo (ERS# 68) was a surgical specimen harvested from a tubal pregnancy. Its size was 11mm in crown-rump length. After removing the ovisac the whole embryo was fixed in 10% formalin, embedded in paraffin and serially sectioned in 4 micrometer thickness through the frontal plane. A total of 456 consecutive sections were obtained, and stained with hematoxylin and eosin. During the embedding procedure the position of embryo was unintentionally tilted slightly to the right side.

1. External Appearance

Left lateral view of the embryo is presented in Fig. 1. The head part of the embryo was proportionally large. The embryo exhibited a suggestion of lumbar flexure and nasomaxillary groove. The nostrils were invisible laterally. The embryo showed distinct auricular hillocks that were located between the first and second pharyngeal arch, along with six distinctly developed mesenchymal proliferations-

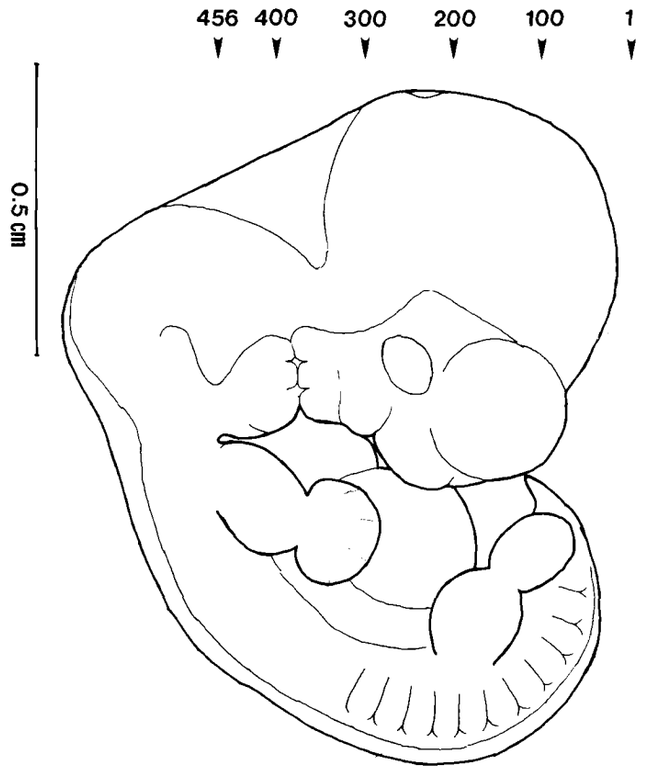

Fig. 1. External apperance of the embryo, right lateral view.

(Plate 1).

The arm bud contained a hand plate with digital rays which were recognized in section slides as the indentations at margins. The leg bud also had a foot plate but no digital ray was recognizable. The somites were prominent only in lumbosacral region where the development of subcutaneous tissue was rather incomplete.

2. Central Nervous System and Sense Organs

The brain exhibited well developed cerebral vesicles and cervical, pontine and cephalic flexures. The olfactory evagination was invisible. A thickened portion of the lamina terminalis indicative of future optic chiasm was recognizable in sections, No. 268-273. In sections No. 280 and 285 the Rathke's pouch enveloped the evaginating neurohypophysis in both sides (Plate 2 and Plate 3). The Rathke's pouch became widened in sections No. 274-290 to be connected with the pharyngeal cavity. The dorsally evaginating epiphysis appeared in section No. 119, as a small outpocketing of the primitive ependyma (Plate 4).

Ganglia of three cranial nerves, i.e., trigeminal, facial, and vestibulocochlear could be seen, and nerve fibers running from the brain to these ganglia and to the periphery were also identified (Plate 5). There was no indication of choroid plexus formation in the hindbrain.

Eyes were visible in sections No. 219-273 and 234-277 in the left and the right side, respectively (Plate 6). The pigmentation of the outer layer of the retina was distinct (Plate 7). The lumen of lens vesicle was semilunar shaped due to the thickening of the posterior wall. The inward migration of retinal nuclei was evident in section No. 250(Plate 8).

The otic vesicles (Fig. 2). were visible in sections No. 362-426 and 372-446 in the left and the right side, respectively. The nerve fibers connecting the brain and ganglion to the inner ear vesicle were also observed. An actively elongating cochlear duct, and thinning-out and approximation of walls of the vetibular part of the labyrinth were observed. There was no indication of absorption of the contacting walls and formation of semicircular canals (Plate 9).

The rhombencephalic wall was thick but no distinct alar or basal nuclear area was visible. The spinal cord had a well-developed ventral mantle layer, causing a narrow ventral portion of the neural tube lumen. Relatively large and distinct dorsal root ganglia and nerve fibers were seen at some levels

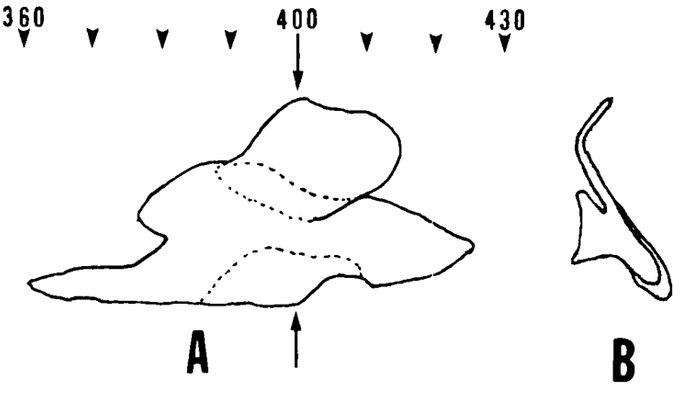

Fig. 2. A: Schematic reconstruction of the left otic vesicle, medial view. Number represents the section number.
B: The contour of the cut surface made through the arrow in Fig. A.

of spinal axis(Plate 10).

3. Respiratory System

The bronchial tree had lobar bronchi and segmental bronchial buds (second order branches). The lung parenchyme did not show the fully-developed external appearance, but exhibited a tendency of lobe formation along with the lobar bronchi (Plate 11). Fig. 3 shows the schematic reconstruction of the bronchial tree. The separation

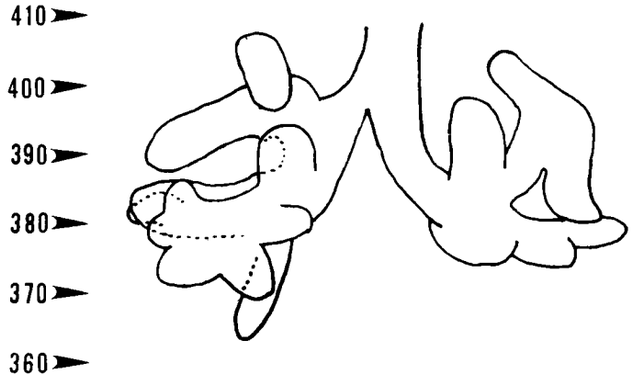

Fig. 3. Schematic reconstruction of bronchial tree, frontal view. Number represents the section number.

of airway from the esophagus began in section No. 436 and progressed considerably until the airway made its own connection with the pharyngeal cavity. The nasal apparatus could be seen in sections No. 204-267 in the left and 219-274 in the right side. There appeared nostrils in sections No. 219 and 221, and nasal fins in sections No. 245-267 and 259-274 in the left and the right side, respectively (Plate 12).

The espohagus and trachea became separated by the mesenchymal tissue. There was no condensation of the visceral mesenchyme surrounding the trachea that would become the tracheal cartilage.

4. Cardiovascular System

The pericardial cavity was observable from section No. 188, and ventricles were visible from section No. 219. The heart had 4 distinct chambers and clearly separated greater arteries. The ventricular wall was thick and showed trabecular carneae (Plate 13). Cross striations of the cardiac muscle could be seen only in some areas. The interventricular septum did have a muscular part but not a membranous part. The right and left atrioventicular canals were incompletely separated (section No. 326). The sections indicated that the endocardial cushions had not met yet (Plate 14). Atrioventicular valves were not recognized.

The heart had the septum primum and ostium secundum, both of which were visible from section No. 362. The septum spurium could be seen at the left side of the septum primum, which was composed of leaflets of valve of the sinus venosus (Plate 15). The septum secundum just began its growth which was visible from section No. 366. The initiating of semilunar valves was observed (Plate 16).

The aortic trunk was bifurcated in section No. 373. The pulmonary artery had two small pulmonary arteries and one large pulmonary trunk (future ductus arteriosus). In section No. 421, two dorsal aortae fused to form a single one. It gave a celiac branch in section No. 352 and a mesenteric branch in section No. 322. This dorsal aorta also gave several segmental mesonephric branches. It gave left and right common iliac arteries in sections No. 188 and 179, and became median sacral artery. It could be seen that the ductus venosus was connected with the vitelline vein which was connected to the sinus venosus and to the right atrium. The right posterior and anterior cardinal veins were identified in section No. 396.

5. The Gastrointestinal System

The cloaca began to emerge from section No. 135. The separation fo the urogenital sinus and the hindgut began from section No. 145. The duodenum exhibited a follicular lumen owing to the active proliferation of epithelium (Plate 17). The vermiform appendix was seen in sections No. 193 to 203 (Plate 18). The intestinal loop had a hint of rotation but it was minimal. In Fig. 4, the schematic reconstruction of the gastronitestinal system is presented. The lumen of the intestine was well communicated and no luminal obstruction was observed except in the duodenum. The dorsal and ventral pancreas were separated in section No. 283 but fused in section No. 289 (Plate 19). In section No. 298 the common bile duct branched from the ventral pancreatic duct. The gallbladder began to appear from section No. 160 and became connected to the biliary passage. The intrahepatic biliary passage could be seen in slide No. 43 (Plate 20).

The esophagus had a characteristic reticular coat enclosing the epithelium which was different from those of the airway. In section No. 357 the transition from the stomach to the esophagus became apparent. The liver was located in sections No. 135-376, which was the biggest organ of the embryo and well developed. The liver cell cords were visible as multiple cell plates, among which hemopoietic foci including nucleated red blood cells were manifest in the sinusoidal space.

The splenic bud was identified in sections No. 308-357 in the dorsal mesogastrium as a localized condensation of mesodermal cells with a wide base (Plate 21).

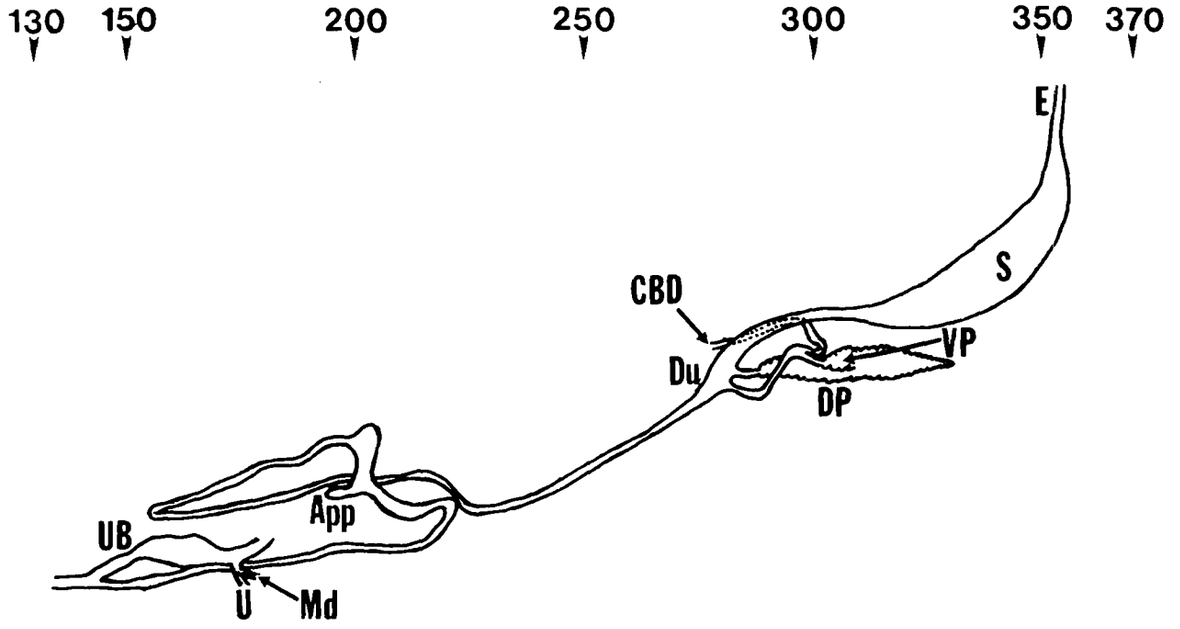

Fig. 4. Schematic reconstruction of the gastrointestinal tract. Number represents the section number. UB: urogenital sinus U: ureter Md: mesonephric duct App: appendix Du: duodenum CBD: common bile duct VP: ventral pancreas DP: dorsal pancreas S: stomach E: esophagus

6. Urogenital System

Mesonephric ducts and ureteric buds branched outward from the urogenital sinus in the same position (section No. 174 in the left side). The metanephroi could be traced through sections No. 145-198 and 150-208 in the left and the right side, respectively. The schematic reconstruction of the right kidney (Fig. 5) showed upper and lower

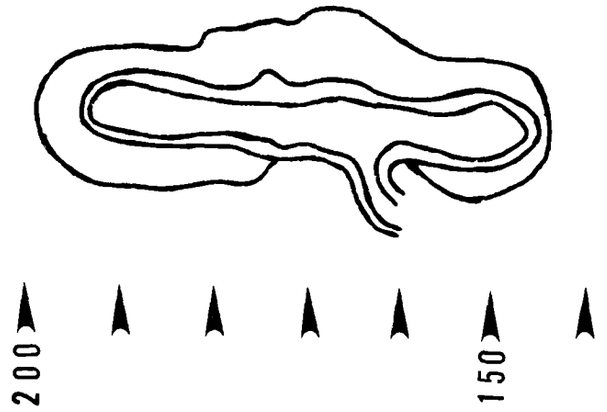

Fig. 5. Schematic reconstruction of the right kidney, lateral view. Number represents the section number.

poles but no calyces (Plate 22). The metanephric blastema consisted with elongated hyperchromatic cells were also observed.

The mesonephroi were identified through sections No. 209-402 and 214-408 in the right and the left side, respectively. The lumen of the mesonephric duct was wide, and there were many mesonephric tubules and glomeruli along its medial side (Plate 23). A number of segmental mesonephric arteries branched out from the dorsal aorta and drained to right and left posterior cardinal veins. The pramesonephric duct was not oberved.

The gonads were visible from sections No. 165-183 in both right and left sides as triangular ridges at each side of the dorsal mesentery. Cords of epithelial cells were found growing into the mesenchyme. But the gonads remained in indifferent forms, and no specific differentiation of sex could be made. Primordial germ cells were observed, and they had large vesicular nuclei and pale cytoplasm.

Adrenal cortices were visible from section No. 185 in the right and left sides at the medial aspect of mesonephroi as a thickening of the coelomic epithelium.

7. Other Systems

A mesenchymal codensation that would become the humerus was observed in the upper limb bud. But there exhibited no distinct mesenchymal condensation in the lower limb bud. Both the nerve trunk and nerve fibers were recognizable in the

lower limb bud.

The thyroid gland which developed near the thyroglossal duct was seen in sections No. 387-402. It was solid and separated into right and left masses.

Thymic primordia, frontal evaginations of the 3rd pharyngeal pouch, were visible from section No. 396 and 400 in the left and the right side, respectively, as solid cell nests with the lumen of varying size and shape. The lumen was generally narrow and the lining epithelium was stratified. Their posterior continuation represented a solid nodule with little or no lumen.

Parathyroid glands were seen as round nests of clear vesicular cells in section No. 407 and 423 in the right and the left side, respectively.

DISCUSSION

Summarizing the observations made in this study on the differentiating process of an embryo it could be pointed out that the embryo was fairly young probably belonging to Streeter's develomental stages between XVI to XVIII.

There exists a distinct difference between Streeter's stages XVI and XVII. The eyeball, gastrointestinal tract, otic vesicle, and heart are main organs that would provide clues to distinguish between these two stages. The embryo did show some features that could not be observed in stage XVII, i.e., digital rays in the upper limb bud, inward migration of retinal nuclei, follicular lumen of the duodenum, second order branches from stem bronchi, initiation of semilunar valves of the heart, appearance of the vermiform appendix and intrahepatic biliary passage, thinning-out and approximation of the walls of the vestibular part of the labyrinth, and fusion of the dorsal and ventral pancreas. But the incomplete separation of right and left atrioventricular canals in the heart and the absence of the calyceal development in metanephroi indicated that the embryo was possibly in the developmental status of Streeter's stage XVI as long as these features were concerned.

In comparison with stage XVII, stage XVIII has developmental features such as bifuracation of secondary branches of bronchi, branching calyces of plevis in kidney, vomeronasal organ of Jacobson, formation of semicircular canals of the membranous labyrinth, appearance and rapid growth of the Muellerian duct, sharply defined semilunar valves of the heart, primordium of the nasolacrimal duct, and established respiratory bypass. In this study there observed no such findings pertaining to stage XVIII of the embryonal development. Therefore, it appeared that the embryo under study belonged to the early stage of Streeter's developmental horizon XVII.

The embryo ages given by Streeter(1948) were based on the comparative study made with embryos of macaque monkey, and are now know to be modified a little particularly for stages XIV to XXIII. For example, the embryo at stage XXII are generally believed to be at least 56 days of gestation instead of 47 ± 1 days (Moore 1982).

The embryo used in this study derived from a tubal pregnancy, and this fact should be taken into consideration for the determination of the embryo age. In general, the embryo in the ectopic pregnancy tends to have smaller ovisac and size than the embryo of normal pregnancy (Chi and Lee 1980). As indicated in the test, the crown-rump length of the embryo was 11mm. The size of 25 embryos falling in stage XVII ranged in the greatest length from 10.0 to 14.5 mm (Streeter 1948). Excluding 5 of the largest and 3 of the smallest specimens, there remained 17 embryos (68%) ranging from11.0 to 13.6 mm in length.

The embryo size appeared to be inappropriate for the age determination of this embryo. since the size of the embryo in the range of stage XVII was not significant in the age determination, the developmental status of internal organs should be applied in such cases including ours.

No abnormal features were observed through serial sections of this embryo, and therefore it was to be appropriately designated as normal.

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LEGENDS FOR PLATES

Plate 1. Gross appearance of the embryo, right lateral view. Note the digital rays of the upper limb buds and distinct somites in lumbosacral region.

Plate 2. Rathke's pouch enveloping the evaginating neurohypophysis. RP, arro: Rathke's pouch N: neurohypophysis ×40(#280)

Plate 3. Dorsoventrally flattened Rathke's pouch(RP) and neurohypophysis(n). ×40(#285)

Plate 4. Dorsally evaginating epiphysis(arrow). It is small outpocketing of the primitive epenoyma. ×40(#119)

Plate 5. Trigeminal nerve ganglion(TG). Note the nerve fibers(arrow) connecting the thickened portion of the hindbrain and ganglion. ×40(#306)

Plate 6. The left eye. Note the thickenining of the posterior wall of the lens vesicle. ×40(#243)

Plate 7. Outer layer of the retina. Note the definite pigment granules. ×200(#243)

Plate 8. The left eye. Note the inward migration of retinal nuclei(arrow). ×100(#250)

Plate 9. The otic vesicle (left side). Thinning-out and aproximation of the walls of the vestibular part of the labyrinth are visible(arrow). Note the thin 4th ventricular roof(R). ×40(#403)

Plate 10. The spinal cord exhibits dorsal root ganglion(1) and thickened ventral mantle layer(2). Note the notochord(arrow) and dorsal aorta(A). ×40(#198)

Plate 11. Representative section of the lung. Note the reticular coat enclosing the esophagus(E). S are stem bronchi. ×40(#391)

Plate 12. Nasal apparatus. Note the nostril (N) and nasal fin (F). The repiratory bypass is not completed yet. ×40(#252)

Plate 13. Representative section of the heart. The atrioventricular canals (right side) and the bulbus cordis(B), right atrium(RA) and left atrium(LA) are shown. Note the thick ventricular wall(V). ×40(#288)

Plate 14. Incomplete separation of the right and the left atrioventricular canals. Not that the endocardial cushions(E) do not met yet. ×40(#326)

Plate 15. The septa of the heart. Note the septum spurium(S), septum primum(P), and septum secundum(SS). ×40(#371)

Plate 16. Initiation of the semilunar valves(arrow). LA left atrium RA: right atrium ×40(#342)

Plate 17. Duodenum(1). It has follicular lumen due to active epithelial proliferation. Note the dorsal pancreatic duct(2). ×40(#283)

Plate 18. Vermiform appendix(1) and cecum(2) are visible. ×40(#194)

Plate 19. Fused dorsal and ventral pancreas(1). Note the ventral pancreatic duct(2) and common bile duct(3). ×40(#302)

Plate 20. Liver. Liver cell cords are visible. Note the intrahepatic biliary passage(arrow). ×40(#194)

Plate 21. Splenic bud(SP) at dorsal mesogastrium. S is stomach ×40*(#337)

Plate 22. Metanephros(1) and Urogenital sinus(2). Note the mesonephric duct and the ureter branch out from the urogenital sinus at the same position(arrow). ×40(#174)

Plate 23. The gonad (1) and mesonephros(2). Note the mesonephric glomeruli and mesonephric tubles. The hind gut(3) and mesenteric vessel are also visible. ×40(#250)

= 국문초록 =

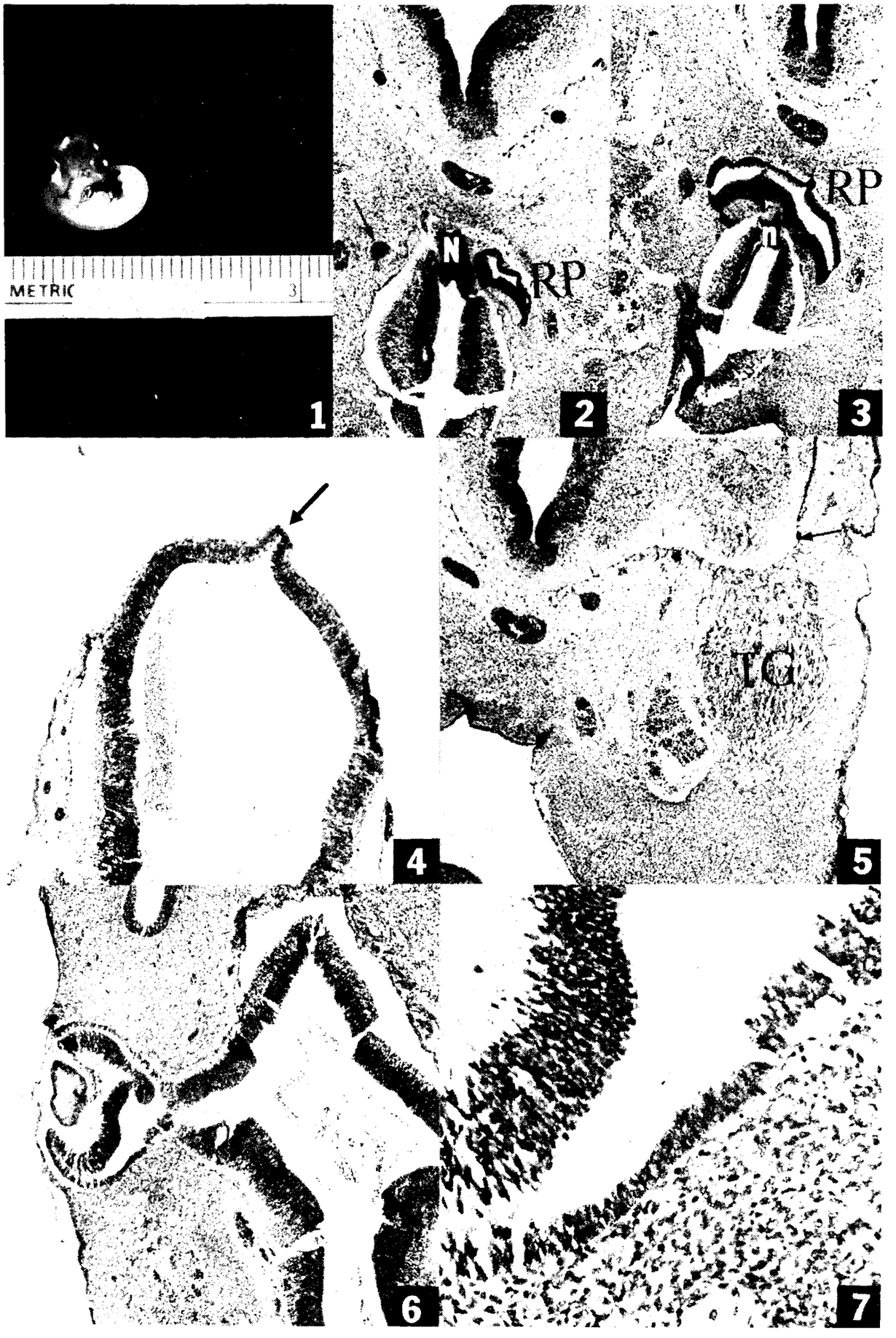
사람배아(Streeter 연령군 XVII)의 1예

서울대학교 의과대학 병리학교실

지제근 · 양희진

난관임신으로 적출된 난관내에서 잘 보존된 배아를 관찰하고 이를 고정하고 연속절편하여 태생학적 관찰을 하였다. 456연속절편을 판독하고 재구축한 결과 본 배아는 정상발육중의 배아였고 Streeter의 연령군에는 XVII단계에 해당한다고 생각되었다.

본 배아는 정둔장이 11 mm였으며 형태학적인 특징은 손에서의 digital ray, foot plate, 망막핵의 내방이동, 망막외층에서의 색소과립의 출현, 세장되는 와우관, 심장반월판의 시작, 폐의 간기관지의 2차 분지, 충수의 출현, 십이지장의 여포성 내강, 배 및 복췌의 유합, 미분화 정소 및 부신의 발달 등이었다.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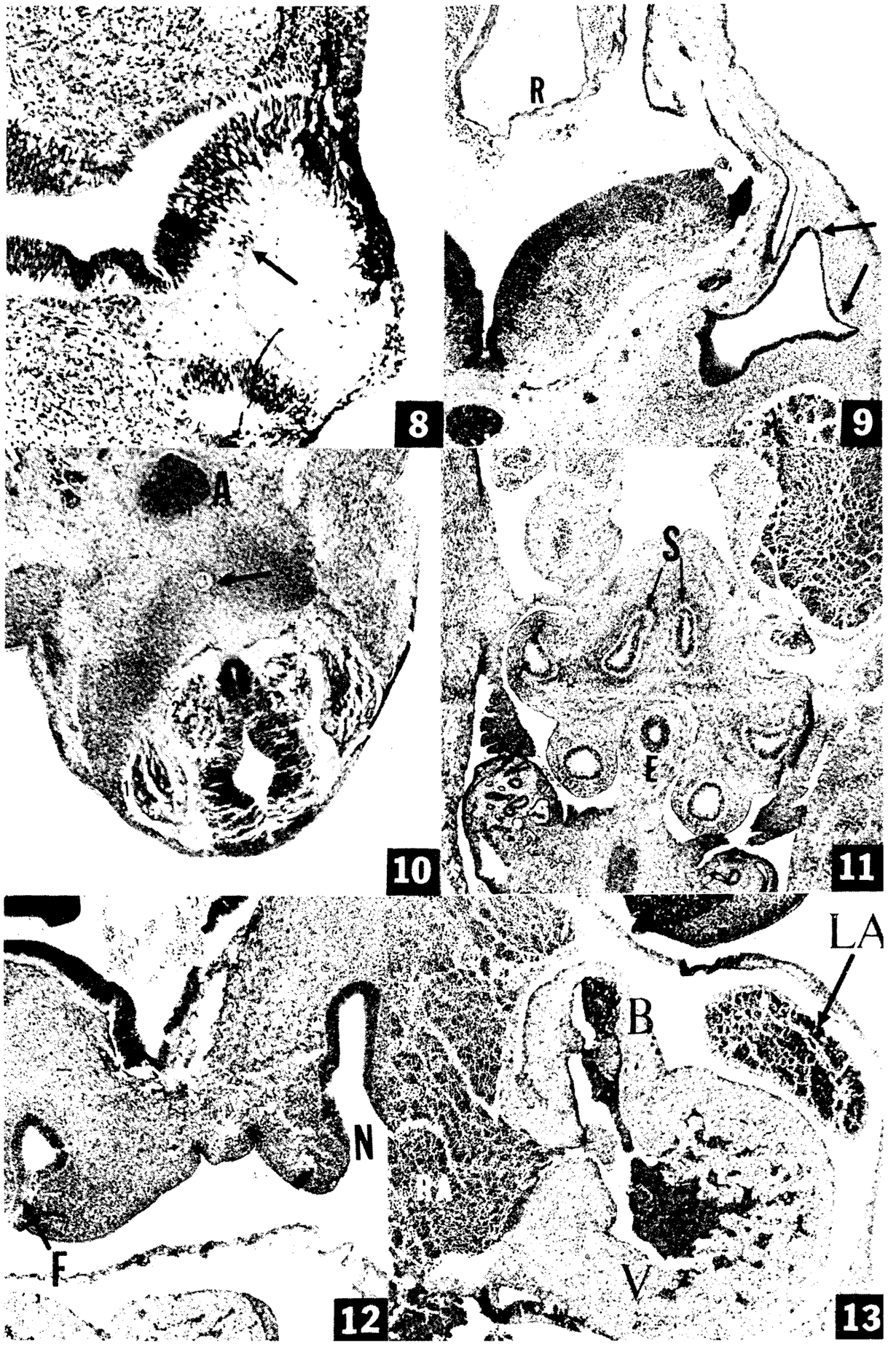
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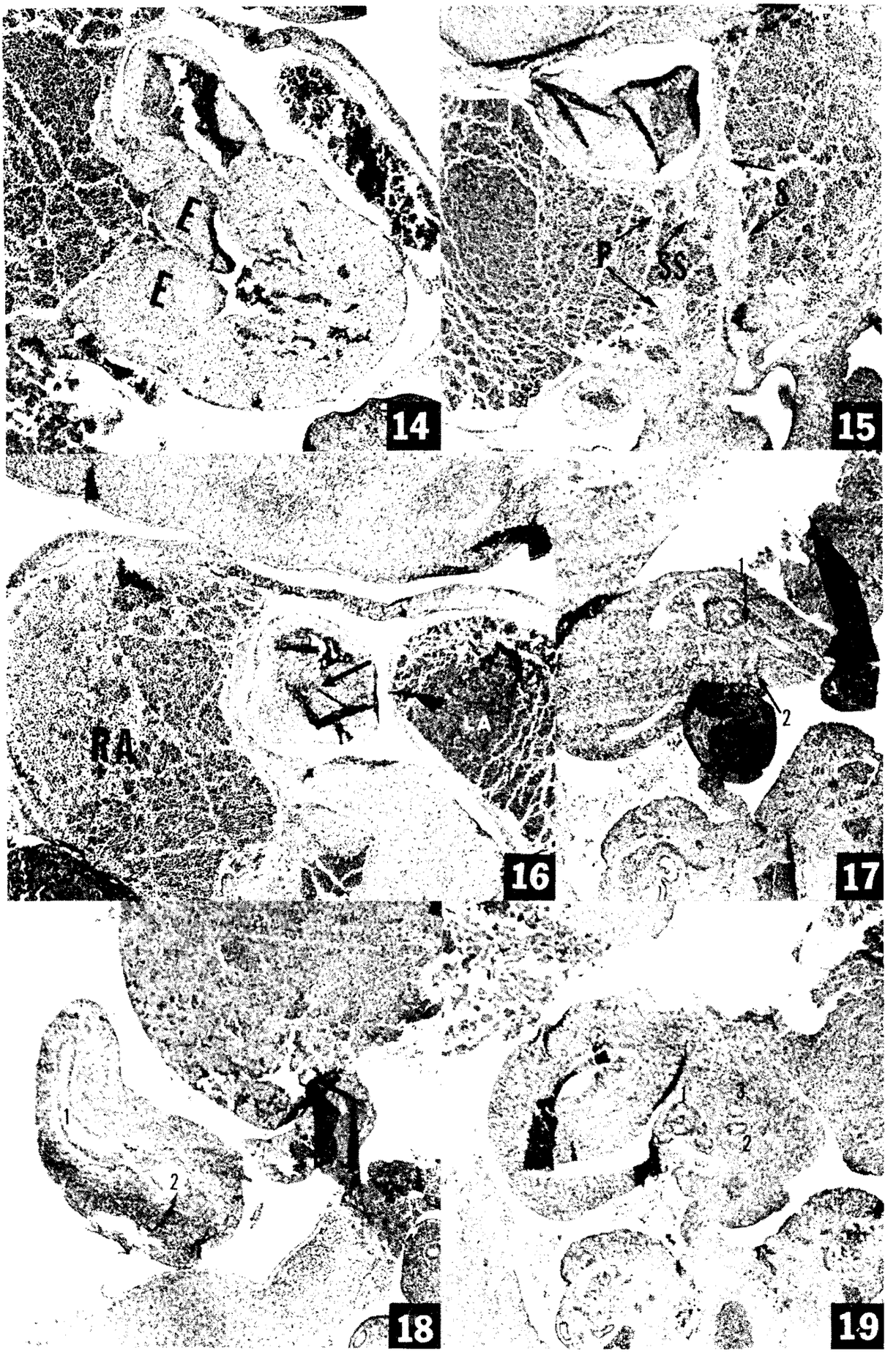
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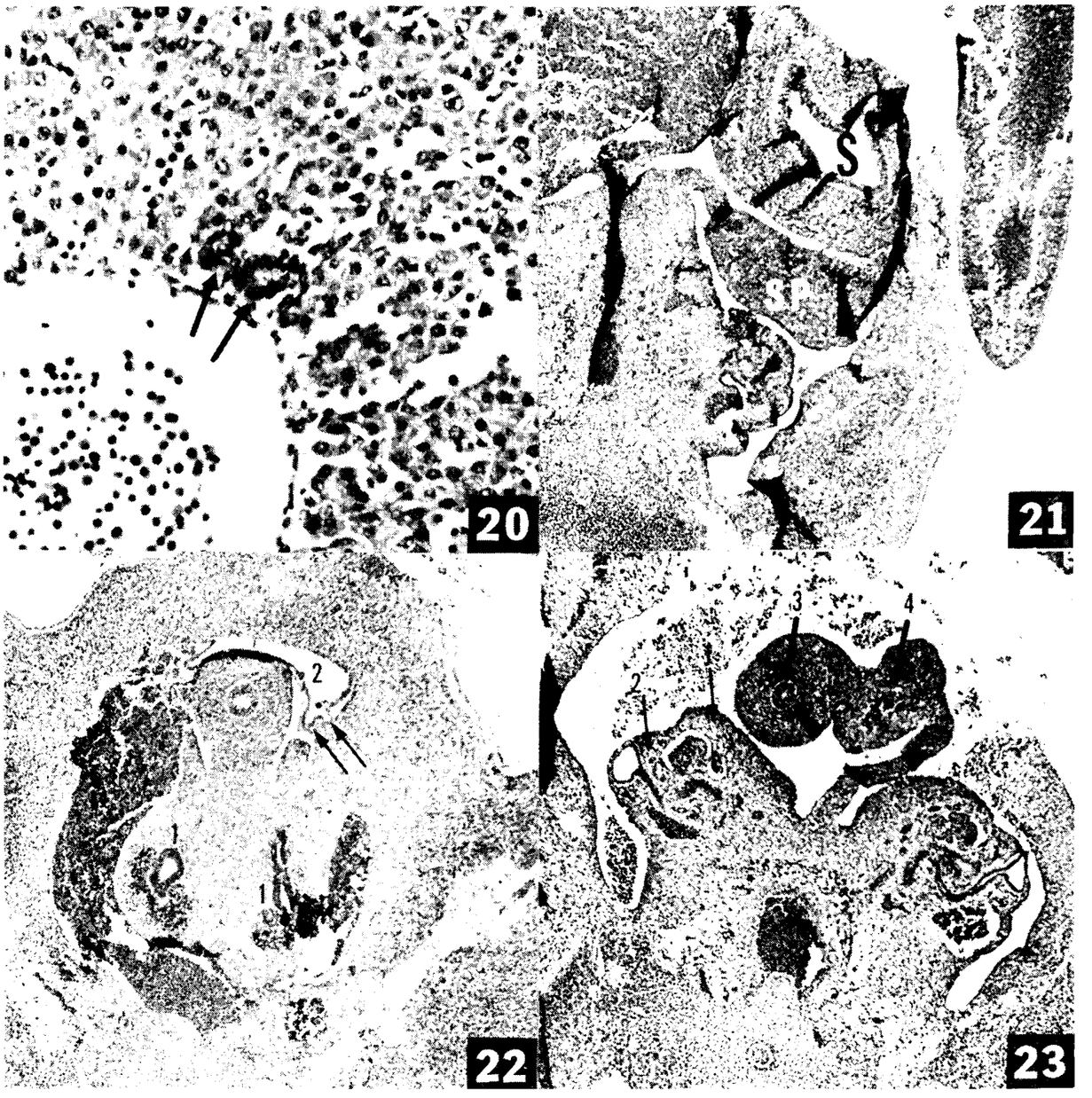
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