# Development of the Heart in 4-12 mm Golden Hamster Embryo

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## ABSTRACT

The developing heart in this study is focused on serial sections of 4-12 mm golden hamster embryos, which were stained with hematoxylin and observed under a light microscope, compared to 10 mm pig embryos. The developing hearts of Golden hamster and pig embryos are very similar. Although the partition of the hamster's heart is still incomplete, it is clearly divided into four chambers. Two atria are separated by septum primum which grows ventrally but does not reach the endocardial cushion; the foramen primum still remains in the 4 mm stage. This is just a very minor difference compared to that of the 10 mm pig embryo. This foramen is later closed at the older stage. Two ventricles are incompletely separated by the interventricular septum, remaining the interventricular foramen. The ventricle is connected to the bulbus cordis and truncus arteriosus, draining blood to the aortic sac. This study indicates that the developing heart of a golden hamster embryo can be used as a laboratory model instead of that of a pig embryo in order to study the development of a human heart. This will solve the problem of insufficient pig embryos and maintain the efficacy in the study embryology.

**Keywords:** Development; Embryo; Golden hamster; Heart

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The heart is a part of the cardiovascular system, which appears in the middle of the third week as a paired endocardial heart tube, formed by splanchnic mesoderm. These tubes fuse with each other to form a slightly bent single tubular heart, which is composed of three layers, the endocardium, the cardiac jelly and the epimyocardium. During the fourth to the seventh week the heart is divided into 4 chambers.

The endocardial cushions are formed at the central part of the anterior and posterior walls of the heart chamber. They fuse with each other to divide the atrium superiorly and the ventricle inferiorly, which remains connected through the right and left atrioventricular canals. The fused endocardial cushion contributes to the formation of the tricuspid valve on the right, the bicuspid or the mitral valve on the left and a part of the septum membranaceum.

The septum primum develops dorsocranially from the roof of the atrium as a crescentic membrane grows towards the endocardial cushion to divide the atrium into the right and left sides. The degeneration occurs at the central part of the septum primum, called the foramen secundum, the important connection between the right and left atrium of the embryo. The septum secundum is formed ventrocranially on the right side of the septum primum as a thickening crescentic membrane. It does not reach the fused endocardial cushion so there is a remaining foramen, called the foramen ovale, which will eventually be closed by the septum primum when the pressure of the left atrium increases after birth.

The interventricular septum consists of a thick muscular part and thin membranous part. The thick muscular part is formed at the floor of the ventricle with a concave free edge towards the endocardial cushion. The remaining interventricular foramen is closed by the septum membranaceum.

Understanding the normal development of the heart brings a better understanding of congenital abnormalities. Chick and pig embryos of different sizes are normally used as models for laboratory study. At present, obtaining pig embryos for slide preparation is not possible. Therefore, it is important to study the development of other mammal embryos, which are easily available and may be used as models instead of pig embryos in the future. Hamsters are selected for this study because they are laboratory animals and commonly used in a wide range of researches. In addition, a hamster has a short gestation period with a large litter.[1-6]

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## MATERIALS AND METHODS

Maternal Syrian hamsters or golden hamsters *(Mesocricetus auratus)* were obtained from the Department of Animal Laboratory, AFRIMS. They were maintained and fed at the Department of Anatomy, Faculty of Medicine, Siriraj Hospital until they were ready for breeding. Pregnant golden hamsters at 9-11 days old (4-12 mm) were used for this study. They were sacrificed at each period of gestation by ether. The uteri were dissected from the abdominal cavities and each embryonic mass was cut as a segment. The uterine wall and amnion were dissected to complete the infiltration of the fixation. Then they were fixed in Bouin's solution for at least 24 hours for preservation of their morphologies and preventing the process of autolysis. They were placed in 70% ethyl alcohol for removal of the fixative. Then after, they were dehydrated, cleared, embedded and serially sectioned. These serial sections were stained with hematoxylin. The cardiac region was observed under a light microscope and compared to that of a 10 mm pig embryo.

## RESULTS

### A 4-5 mm Hamster Embryo (Fig 1.)

The heart is composed of two atria and two ventricles, occupying the pericardial cavity. The atrium and the ventricle are separated externally by the deep sulcus, the coronary sulcus, and internally by a mass of subendocardial tissue, the endocardial cushion. The atrium begins to divide into the right and left atria by the septum primum which extends as a crescent-shape from the dorsocranial wall towards the endocardial cushion. The partition of the atrium is not completed at this stage because the septum primum does not reach the endocardial cushion but leaves a foramen between them known as the foramen primum. The left horn of the sinus venosus drains the blood into the right horn caudal to the sinuatrial orifice forming the transverse portion to shunt the blood from the left to the right. Then the right sinus horn drains the blood into the right atrium through the sinuatrial orifice, guarded by the right and left sinuatrial valves. The ventricle has a thick and spongy wall with a meshwork of muscular trabeculae. The partition of the ventricle begins to form by a thick median muscular ridge, the interventricular septum, on the floor of the ventricle near the apex and grows upward towards the endocardial cushion as a crescentic fold but the formation is not complete at this stage. The right and left ventricles connect to each other through the foramen between the endocardial cushion and the interventricular septum, the interventricular foramen. The ventricle continues to the bulbus cordis, which forms the longitudinal subendocardial thickening, the right and left bulbar ridges that continue to the truncus arteriosus, the truncal ridge. These ridges will eventually fuse and separate the lumen into the ascending aorta and the pulmonary trunk. The truncus arteriosus drains the blood to the aortic sac that connects to the aortic arches.

### A 6-7 mm Hamster Embryo (Fig 2.)

The heart is slightly bigger than that in the previous stage. The septum primum extends towards and fuses with the endocardial cushion. As a result, the foramen primum is closed but there is another foramen which forms at the center of the septum primum, the foramen secundum, and connects both atria. This foramen is very important for the blood circulation of the embryo. The left sinus venosus drains the blood to the transverse portion of the sinus venosus and continues to the right sinus venosus before opening into the right atrium. The ventricle is divided into right and left chambers by the interventricular septum internally and the interventricular sulcus externally. The interventricular septum extends from the floor of the ventricle to the fused endocardial cushion. The connection between right and left ventricles still remains as the interventricular foramen which is later closed by the septum membranaceum. The ventricle continues to the bulbus cordis and truncus arteriosus with their right and left thickening walls, the bulbar and truncal ridges, respectively.

### A 10-12 mm Hamster Embryo (Fig 3.)

The heart is larger than that of the 6-7 mm. hamster embryo with incomplete partition of the chambers, two atria and two ventricles. The right and left atrioventricular canals are narrowed by the subendocardial tissue which forms the tricuspid valve on the right and the bicuspid valve on the left. The atrium is separated by the septum primum with

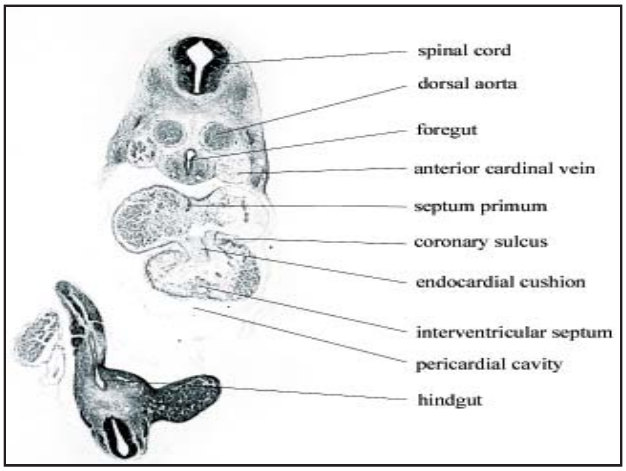



**Fig 1.** Transverse section of 4-5 mm hamster embryo at the level of septum primum.

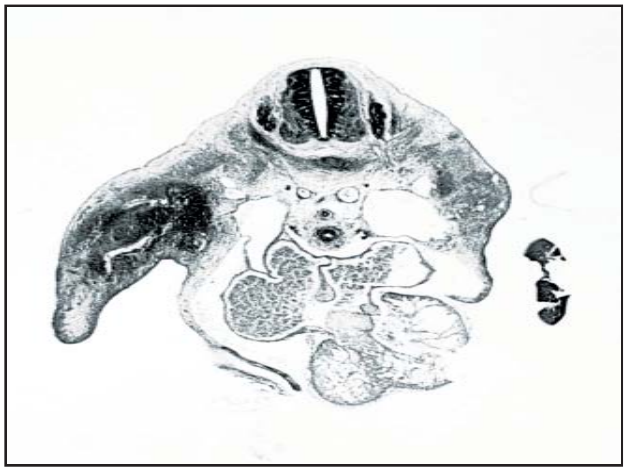


**Fig 2.** Transverse section of 6-7 mm hamster embryo at the level of sinuatrial valve.

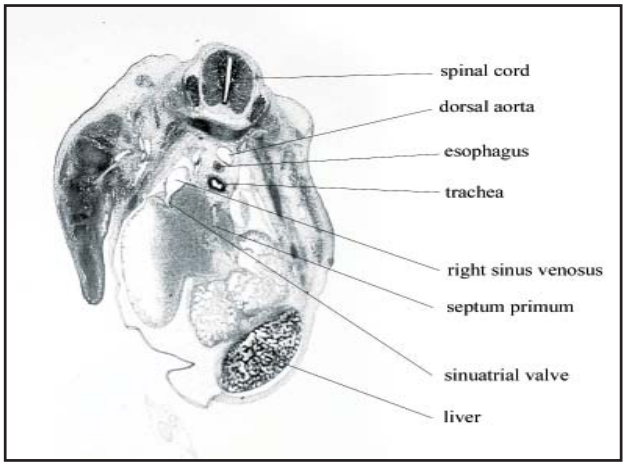



**Fig 3.** Transverse section of 10-12 mm hamster embryo at the level of sinuatrial valve.

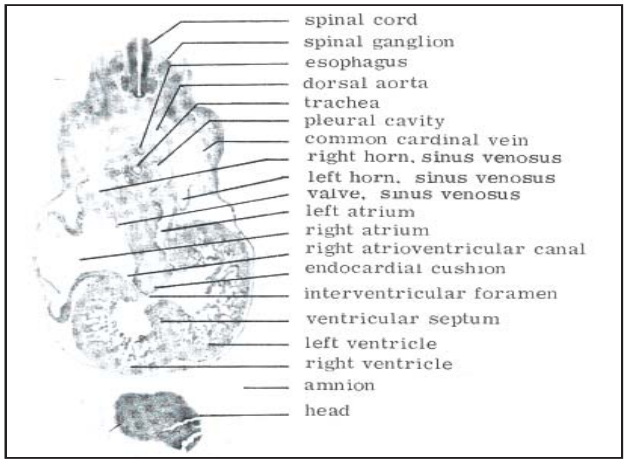



**Fig 4.** Transverse section of 10 mm pig embryo at the level of interventricular foramemn.

the foramen secundum at its center. The septum secundum does not develop at this stage. The ventricle is separated by the folding of the myocardium which arises from the floor of the ventricle and grows towards the endocardial cushion as the muscular portion. The lower part of the right and left bulbar ridges fuse with the endocardial cushion to form the membranous portion of the interventricular septum but the fusion is still not complete at this stage. The ventricle appears as a thick spongy wall and forms the tendinous cords and papillary muscles to control the tricuspid and bicuspid valves. The right, left bulbar and truncal ridges fuse to form the septum, separating the aorta and pulmonary trunk, the aorticopulmonary septum. This septum will later have a spiral orientation by the pressure of the blood flow. The semilunar valves are formed around the orifices of the aorta and pulmonary trunk. The pulmonary arteries continue to the right and left sixth aortic arches while the left pulmonary artery forms the ductus arteriosus to drain into the left dorsal aorta.

### A 10 mm Pig Embryo (Fig 4.)

The heart of a 10 mm pig embryo closely resembles the heart of a hamster embryo. It is composed of two atria and two ventricles. The atrium and the ventricle are separated by the fused endocardial cushion which still leaves two communications between them, the right and the left atrioventricular canals. The ventricle is separated into the right and left sides by the muscular interventricular septum which does not reach the endocardial cushion but leaves an opening known as the interventricular foramen. The right and left atria are separated by the septum primum which is already fused to the endocardial cushion. The foramen secundum occurs with the rupture of the septum primum. The right sunus venosus opens into the right atrium through the sinuatrial orifice which is guarded by the right and left valves of the sinus venosus. The right common cardinal vein drains the cephalic blood into the right sinus venosus while the left horn drains the blood through the transverse portion to the right horn.

## DISCUSSION

There is no significant difference between the heart of 4-12 mm golden hamster embryos and 10 mm pig embryos. But the developing heart of a 4-5 mm golden hamster embryo is younger than that of a 10 mm pig embryo because the septum primum does not reach the endocardial cushion so the foramen primum still persists. The septum primum of two bigger stages fused with the endocardial cushion results in the closing of the foramen primum, but another foramen appears on the septum primum, the foramen secundum, which is an important connection for blood circulation in the embryo. The right atrium receives blood from right horn of sinus venosus through the sinuatrial orifice, which is guarded by the right and left sinuatrial valves. The septum secundum does not develop in all three stages. The interventricular septum develops from the floor of the ventricle as a muscular ridge and slightly extends towards the endocardial cushion but does not reach it and leaves an opening, the interventricular foramen. This foramen is partially closed by the membranous part of the interventricular septum, which is formed by the right and left bulbar ridges and endocardial cushion. Moreover, the closure is still not complete. The atria and ventricles are communicated by the right and left atrioventricular canals, which are later guarded by the tricuspid and bicuspid valves, respectively. The bulbus cordis is separated distally into an ascending aorta and the pulmonary trunk.[7-10]

## CONCLUSION

The developing heart of 4-12 mm golden hamster embryos is almost similar to those of 10 mm pig embryos. There are two atria, which are separated by the septum primum with the foramen secundum on it, and two ventricles, separated by the muscular interventricular septum. The atrium is divided from the ventricle by the endocardial cushion, which also separates the atrioventricular canal into the right and left sides. The bulbus cordis continues to the truncus arteriosus, which is later divided into the ascending aorta and pulmonary trunk. This evidence indicates that the developing heart of a golden hamster embryo can be used as a laboratory model instead of a pig embryo to study the development of the heart of humans.

## REFERENCES

1. Arey LB. Developmental Anatomy. A Textbook and Laboratory Manual of Embryology, 7th ed. WB Saunders, 1966:375-95.

2. Beynon PH, Cooper JE. Manual of Exotic Pets. British Smali Animal Veterinary Association. West Sussex, 1991:39-50.
3. Carlson BM. Human Embryology and Developmental Biology. Mosby. USA, 1994: 372-406.
4. Langman J. Langman's Medical Embryology, 7th ed. Williams & Wilkins. USA, 1995:183-231.
5. Larsen WJ. Human Embryology. Churchill Livingstone, Inc., Singapore, 1993:131-65.
6. Moore KL. The Developing Human. Clinically Oriented Embryology, 6th ed. WB Saunders, 1998:349-403.
7. Rojananin J, Sangvichien S. The development of the mice embryo's heart. Siriraj Hosp Gaz 1992;44:969-74.
8. Rojananin J. The observation of serial sections of rat embryo related with pig and chick embryos. Siriraj Hosp Gaz 1987;39:617-23.
9. Pilakasiri K. The heart of rat embryo. Siriraj Hosp Gaz 1988;40:725-30.
10. Chakorn T, Roongruangchai J, Pilakasiri K, Pilakasir C. The development of rabbit embryo's heart: serial sections of 4-14 mm rabbit embryos compared to a 10 mm pig embryo. Siriraj Hosp Gaz 2003;55:226-33.

## บทคัดย่อ

# การเจริญพัฒนาของหัวใจในตัวอ่อนของหนูแฮมสเตอร์ขนาด 4-12 มิลลิเมตร

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ในการศึกษาการเจริญพัฒนาของหัวใจนี้ ได้ศึกษาจากซีเรียลเซ็คชั่นของตัวอ่อนของหนูแฮมสเตอร์ขนาด 4-12 มิลลิเมตร ซึ่งนำมาย้อมด้วยสีสีมาทอกซิลิน แล้วศึกษาด้วยกล้องจุลทรรศน์ชนิดใช้แสง และนำมาเปรียบเทียบกับตัวอ่อนของหมูขนาด 10 มิลลิเมตร ผลปรากฏว่า การเจริญพัฒนาของหัวใจในสัตว์ทั้ง 2 ชนิด ไม่แตกต่างกันมากนัก แม้การแบ่งช่องของหัวใจจะยังไม่สมบูรณ์ แต่ก็สามารถเห็นเป็น 4 ห้องได้ชัดเจน คือเอเตรียม 2 ห้องทางด้านบน และเวนตริเคิล 2 ห้อง ทางด้านล่าง เอเตรียมแบ่งเป็น 2 ห้องซ้ายขวาโดยเสปตัมปริมัม ซึ่งในตัวอ่อนขนาด 4 มิลลิเมตร เสปตัมปริมัมยังไม่ติดรวมกับเอ็นโดคาร์เดียลคูชั่น จึงมีฟอราเมนปริมัมเหลืออยู่ ซึ่งนี่เป็นข้อแตกต่างเพียงเล็กน้อยเมื่อเทียบกับตัวอ่อนของหมูขนาด 10 มิลลิเมตร ที่รูนี้จะปิดลงในตัวอ่อนที่มีขนาดใหญ่ขึ้น เวนตริเคิลแบ่งเป็น 2 ห้องโดยอินเตอร์เวนตริคูลาเสปตัม เวนตริเคิลนี้ต่อเนื่องไปเป็นบัลบัสคอร์ดิส นำเลือดไปสู่เอออร์ติกแสคการศึกษานี้แสดงให้เห็นว่าตัวอ่อนของหนูแฮมสเตอร์สามารถนำมาเตรียมสไลด์แทนตัวอ่อนของหมูได้ เพราะปัจจุบันนี้ ตัวอ่อนของหมูหาไม่ได้อีกแล้ว ถ้าสามารถใช้ทดแทนได้ก็จะสามารถแก้ปัญหาขาดแคลนตัวอ่อนของหมู และยังดำรงศักยภาพทางด้านการเรียนการสอนวิชาวิทยาเอ็มบริย์โอให้คงอยู่ต่อไป