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Vascular ontogeny within selected thoracoabdominal organs and the limbs

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ABSTRACT

The cardiovascular system is fundamental to life. Its vessels are the conduits for delivery of nutrients and oxygen to organs and the removal of wastes. During embryonic development, the vascular system is instrumental in the formation of organs. It contributes to the form and pattern of organs as diverse as the limbs and the gonads. Recent advances in molecular biology and genomics have afforded great insight to the control of vascular development at subcellular levels of organization. Nevertheless, there is little assembled information concerning the vascular development of the organ systems of the body. This paper begins by reviewing the modes of formation of embryonic blood vessels. This is followed by summaries of the ontogeny of the vasculature that supplies selected major thoracic and abdominal organs (heart, gut, liver, gonads, and kidney). The paper concludes with a description of the arterial development of the upper and lower extremities.

1. Introduction

A functioning, competent and structurally well-defined cardiovascular system is essential for life both in utero and post-partum. The cardiovascular system begins development during early embryonic life and its patterns of distribution evolve as the embryo matures and acquires adult characteristics. This paper will assemble the extant information relative to the morphogenesis of the vascular tree in several major organs in the body, including the upper and lower extremities, kidneys, gastrointestinal tract, liver, gonads and heart. Most of the vascular trees are formed by a combination of vasculogenesis (assembly by differentiation of mesenchymal cells that are indigenous to the territory under study or that migrated into the area) and angiogenesis (formation of new vessels by sprouting of endothelial cells from pre-existing vessels). Only when the development of a new blood vessel under consideration is known to occur predominantly by one or the other of the processes, will it be mentioned.

Embryology has been the subject of numerous textbooks [1–9]. The following descriptions are summarized from these sources and the scientific literature. Most of the dates for gestational events are provided in terms of human development. Because mammals undergo similar sequences of developmental events, albeit under different schedules due to their diverse gestational periods, interspecies adjustments for timing of embryological events can be gleaned by consulting tables of gestational milestones (e.g. [10–15]). Table 1 presents the comparative timing for a selection of gestational milestones in the human, rat, mouse, rabbit, and monkey.

2. Development of mesoderm

Shortly after implantation of the zygote, the embryo exists as a bilaminar plate of cells interposed between the amniotic and yolk sac cavities. The cellular layer that faces the amniotic cavity is the epiblast; the hypoblast faces the yolk sac cavity. Beginning on approximately gestational day 13–14 [14], a groove (the primitive streak) appears at a single location perpendicular to the circumferential edge of the epiblast (Fig. 1). In that region, cells of the epiblast migrate medially towards the primitive streak, change their shape, and pass through the streak to take a position beneath the epiblast. The migrating cells push the hypoblast towards the periphery to form the endoderm and then fill in the territory between the epi-

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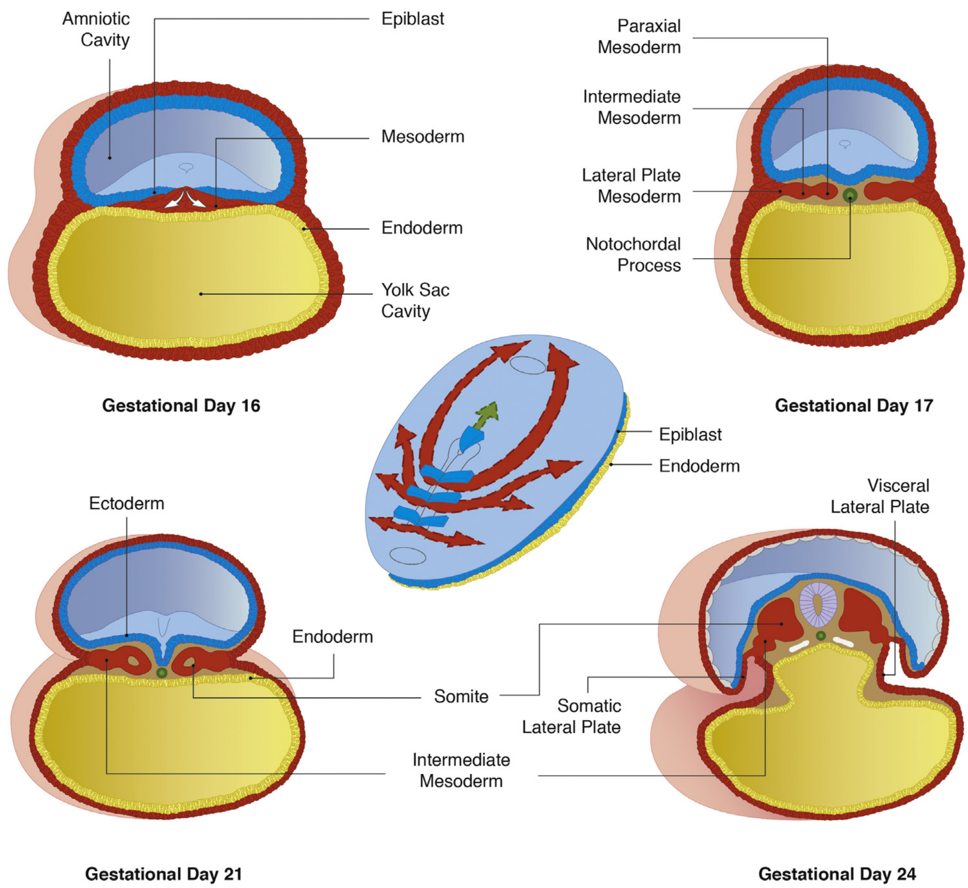

Fig. 1. Formation of Mesoderm.
Formation and segregation of the mesodermal germ layer is illustrated. The central image depicts a dorsal view of the embryonic disc during the process of ingression. The arrows denote the movement of epiblast cells towards and through the primitive streak and the migration of newly formed mesoderm (red arrows) throughout the embryo. The green arrow denotes the notochord. The four surrounding cross-sections illustrate the organization of the mesoderm during succeeding days of gestation. At gestational day 16, the epiblast is shown actively migrating through the primitive streak to form mesoderm. At gestational day 17, the mesoderm has become organized into 3 areas: paraxial mesoderm, adjacent to the notochord; lateral plate mesoderm at the periphery; and intermediate between the two. By gestational day 21, the paraxial mesoderm has increased in size and has organized itself into a somite. By gestational day 24 the somite has enlarged and the lateral plate has split into a somatic layer (associated with the ectoderm) and a visceral layer associated with the endoderm. Note that the visceral lateral plate layer of intraembryonic mesoderm is continuous with the mesoderm that is on the surface of the yolk sac (extraembryonic mesoderm).

Table 1
Selected Comparative Gestational Milestones.[a]

(Gestational Days)					
Gestational Milestone	Human	Rat	Mouse	Rabbit	Monkey
Gestation length	266	22	20	32	166
Implantation	6–7	5.5–6	4.5	7–7.5	9
Primitive Streak	13.5	8.5	7	7.25	15
First Somite	~20	10	8	8	21–22
Fusion of Heart Tubes	21	9.5	7	9	22
Foregut & Oropharyngeal Mem	21	9.5	7.8	8.5	20.5
Hindgut & Cloacal Plate	21.5	11	8.5	9	21
First Aortic Arch	22	10	8.5	9.25	22
Anterior Neuropore closes	25	10.5	9.1	9.5	25
Liver Primordium appears	23	11	8.8	9.5	~25
Anterior Cardinal Vein	24	10.5	8.5	–	–
10 Somites	25	10.5	8.5	8.5	23
Mesonephros appears	24–25	11.5	9.5	9.5	–
Fore Limb Buds appear	26	11	9.5	10.5	26
Posterior Neuropore closes	28	11.5	10	10.5	29
Hind Limb Buds appear	28	12	10.3	12	29
Ureteric Bud appears	28–29	12.3	11.5	13	29–30
Forelimb Digital Rays	36	14	12.3	14.5	34–35

[a] Data from DeSesso [14].

blast and endoderm by a process known as ingression. This process establishes the germ layers of the embryo: the layer of cells facing the yolk sac is the endoderm; the cellular layer facing the amniotic cavity is the ectoderm; and the layer between them is the mesoderm. The mesoderm gives rise to the vascular system of the limbs and the trunk of the body.

3. Early development of the vascular system

Prior to describing the detailed embryology of the vasculature, the terminology to be used must be defined [8,9]. Formation of embryonic vessels occurs by one of 2 processes: vasculogenesis or angiogenesis (Fig. 2). Vasculogenesis refers to the process whereby endothelial cell precursors (including neighboring mesenchymal cells) form condensations which develop into capillary tubes with lumens. Eventually, these tubes join together into webs of small vessels that merge, expand and invade tissues to create primitive vascular trees. In contrast, angiogenesis always begins with pre-existing vessels. The existing vascular tree can be enlarged through sprouting of new vessels from pre-existing vessels or by the longitudinal splitting of a single vessel into 2 vessels (intussusceptive angiogenesis). Remodeling the vascular tree by resorbing (pruning) unnecessary vessels is also a form of angiogenesis.