THE SCIENCE WORLD
A Monthly e Magazine
ISSN:2583-2212
November, 2022; 2(11), 1751-1756

An Overview: Embryonic and Fetal Mammalian Haematopoiesis

P.I.Sindhi[1]*., P.B.Rathod[2]., S.P.Modh[3]., S.H.Raval[1].,R.D. Singh[1].,R.S.Parmar[1].,K.D.Thakor[1]
[1]College of Veterinary Science and Animal Husbandry, Kamdhenu University,Sardarkrushinagar -385505.
[2]Polytechnic in Animal Husbandry (PAH), Kamdhenu University (KU), Rajpur (Nava), Himmatnagar-383010.
[3]V-Cross, Veterinary pathology laboratory, Palanpur-385001
https://doi.org/10.5281/zenodo.7295178

Introduction

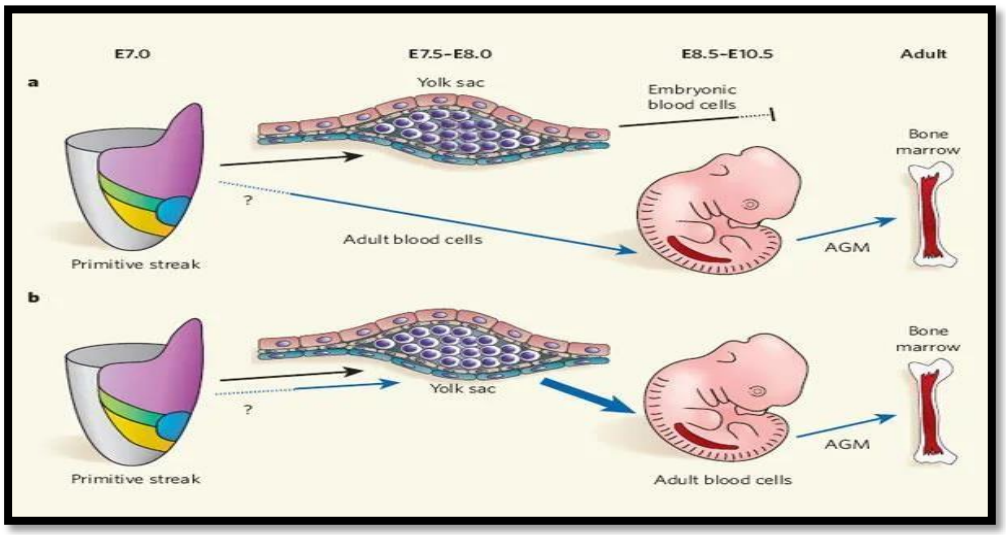
The blood is specialized body fluid made up of plasma and cells. Cellular constituents of blood are RBCs/erythrocytes, WBCs/Leukocytes and platelet/thrombocytes. Each these cellular components have very specific role. Leukocytes involved in immunity, erythrocytes provide O2 and CO2 transport, whereas platelets involve in blood clotting and wound healing. Each these cells have limited life span and died after performing their duties. For example, after 150 days of circulation, cattle RBCs are removed by macrophages when passing through the splenic and hepatic sinusoids. Like that millions of blood cells are destroyed every day and same blood cells should be produced by the body to maintain homeostasis.

Hematopoiesis, or Hemopoiesis, continuous process by which the cellular constituents of blood are reproduced and restocked as needed. In adult, all cellular component of blood, arise from hematopoietic stem cells (HSCs) that reside mainly in the bone marrow. In comparison to adult, embryonic and fetal hematopoiesis is quite different. Multiple sites are responsible for hematopoiesis occur.

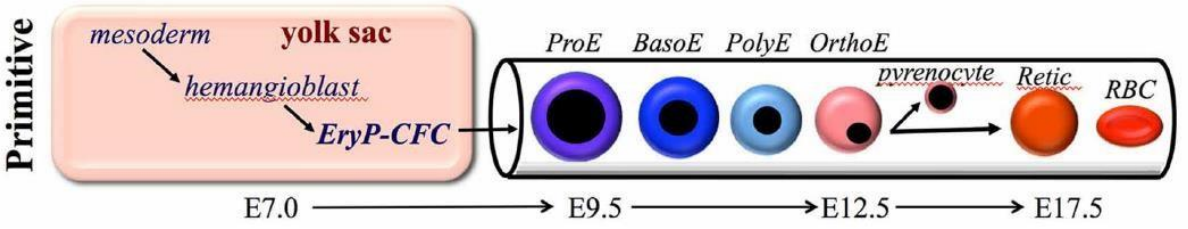
Embryonic and Fetal Hematopoiesis

Blood development in vertebrates involves two waves of hematopoiesis: the primitive wave and the definitive wave. During early life, heart and blood vessels are not formed. The fast-growing embryo cells require oxygen and nutrition which are provided by surrounding environment through diffusion. But after certain stage of development, diffusion methods unable to provide enough oxygen. From 8th day of embryo, vasculature formation starts and to fulfil the oxygen requirement in early life, embryo first start primitive wave of hematopoiesis which last for very few days. The main purpose of primitive wave hematopoiesis is production of red blood cells. These red blood cells provide oxygen to the developing embryo cells. It takes place in the visceral yolk sac beginning at approximately embryonic day (E) 7.0 (Palis et al., 2010; Palis, 2014). The primitive wave is transitory, however, and these erythroid progenitors are not pluripotent and do not have renewal capability (Jagannathan-Bogdan and Zon, 2013). The term definitive hematopoiesis is used because hematopoietic stem cells (HSC) acquire the ability to provide long-term hematopoiesis when they are transplanted into wild-type irradiated adult recipients (Medvinsky et al., 2011). Initiation of definitive

hematopoiesis ranges between E8.5 and E9.25, with definitive HSCs evident in the AGM by no later than E10 (Boyd and Bolon, 2010).



In mouse, two theories exist for in utro haematopoiesis. Model 1 suggests that the mouse embryo generates primitive and definitive hematopoietic systems independently. The primitive system emerges first, serves the short-term needs of the developing embryo and exists transiently. The definitive hematopoietic system emerges independently through the specification of dHSCs, which ensure life-long hematopoiesis. Model 2 suggests a common origin for the embryonic and adult hematopoietic hierarchies. This model implies the existence of a common hematopoietic ancestor cell, which first generates a 'wave' of embryonic hematopoiesis and later produces dHSCs (Ueno and Weissman, 2007; Medvinsky et al., 2011).



In primitive hematopoiesis, primitive erythroid progenitor's colony forming cells (EryP-CFC). These cells multiple and form proerythroblasts (ProE), than basophilic erythroblasts (Baso), than polychromatophilic erythroblasts (PolyE), and orthochromatic erythroblasts (OrthoE). Now inwards multiplication stops and OrthoE remove their nucleus to to form a pyrenocyte, that contains the condensed nucleus, and a reticulocyte (Retic), that goes on to mature in to a RBC (Palis, 2014).

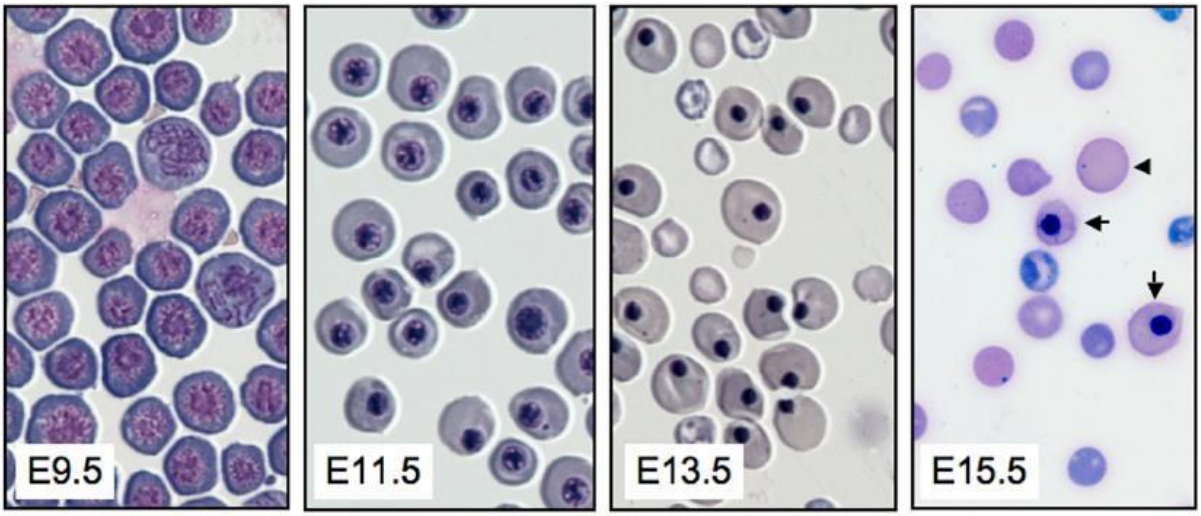
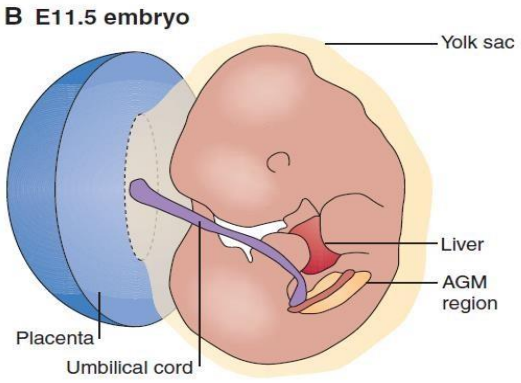


Fig. 2. Peripheral blood cells from E9.5, E11.5, E13.5 and E15.5 of mouse development. *The synchronous, progressive maturation of primitive erythroid cells from immature erythroblasts to enucleated erythrocytes (arrowhead) is evident.*

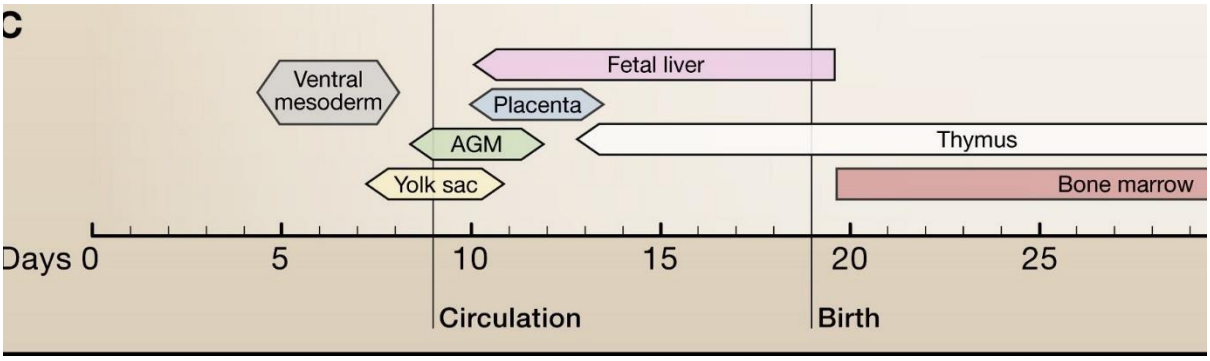
Primitive erythroid precursors mature with progressive characteristics like 1) symmetric cell divisions (up to orthochromatic E stage) 2) accumulation of hemoglobin's which increased pink staining 3) decrease in cell size 4) nuclear pyknosis and 5) decrease in RNA content which decreased blue staining. Initially, a nucleated form of primitive erythroid cells circulates in the embryonic blood stream. Eventually, these primitive erythroid cells enucleate between E12.5 and E16.5 (Yamane, 2018). Primitive erythroid cells remain in circulation up to 5 to 7 postnatal lives. How these cells are cleared from circulation is still not completely elucidated.

Recent studies suggest that other hematopoietic cell lineages also are generated in the yolk sac during this primitive stage of hematopoietic development. However, their role is not clearly characterized.

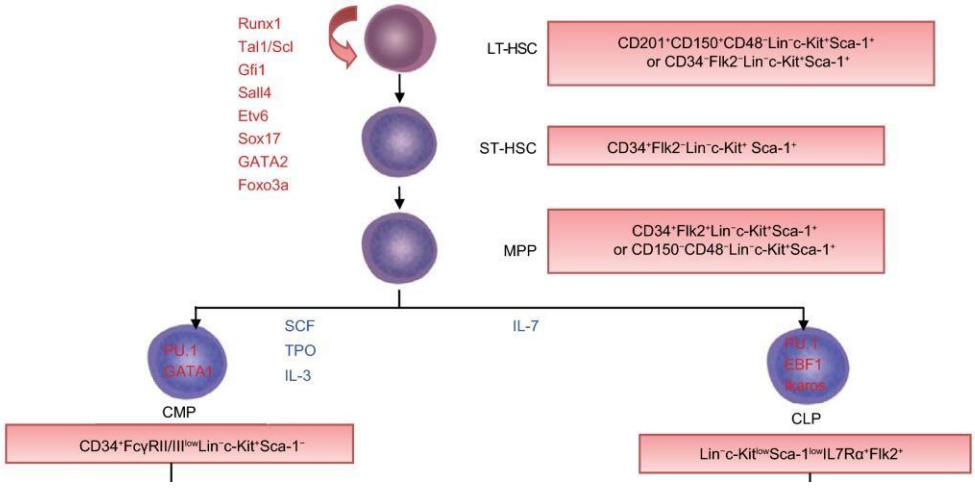
The term definitive hematopoiesis is used because hematopoietic stem cells (HSC) acquire the ability to provide long-term hematopoiesis when they are transplanted into wildtype irradiated adult recipients. They are responsible for hematopoiesis in embryo, fetus as well as entire post-natal life. Definitive HSCs that possess a full set of adult HSC properties emerge only at a certain stage of development. The direct transplantation of even large numbers of embryonic cells prior to E10.0 into adult wild-type irradiated recipients does not produce long-term hematopoietic repopulation (Muller et al., 1994). Definitive hematopoiesis thought to arise primarily from the AGM no later than E10.



As discussed earlier, there is some debate that these cells come from other place and reside in AGM or develop inside the AGM. Regardless of the origin of the cells, HSCs multiple in AGM and occupy 10% cell population of AGM by E11.5. Some AGM - independent HSCs may also arise from the placenta, umbilical arteries, yolk sac and other anatomical site. Even though these sites are responsible for de novo synthesis HSCs they do not provided facility for their expansion, hence they migrate in other anatomical sites. The vitelline artery and umbilical vein are two important routes by which HSC travel to embryonic liver and other anatomical sites. HSCs may directly migrate/seed the liver without circulatory route, but this theory is not completely supported by research experiments.

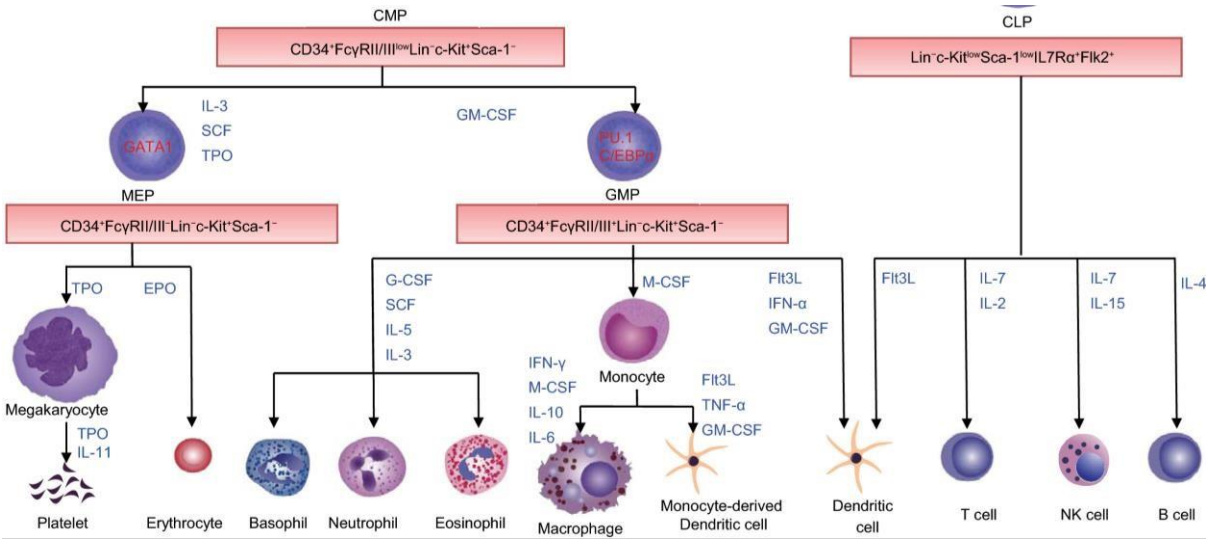


The embryonic liver is first organ which is seeded/colonized by HSCs, because it shares many molecular and functional similarities with the yolk sac (McGrath et al., 2011). After embryonic liver, embryonic thymus, fetal spleen, and bone marrow are colonized by HSCs (Boyd and Bolon, 2010). Embryonic thymus and fetal spleen are seeded either from the liver or AGM, or both, beginning about E13 for thymus and E15 for spleen. The thymus typically accepts only those HSCs that are responsible for production of T cells. The bone marrow first receives HSCs from liver at days before birth.

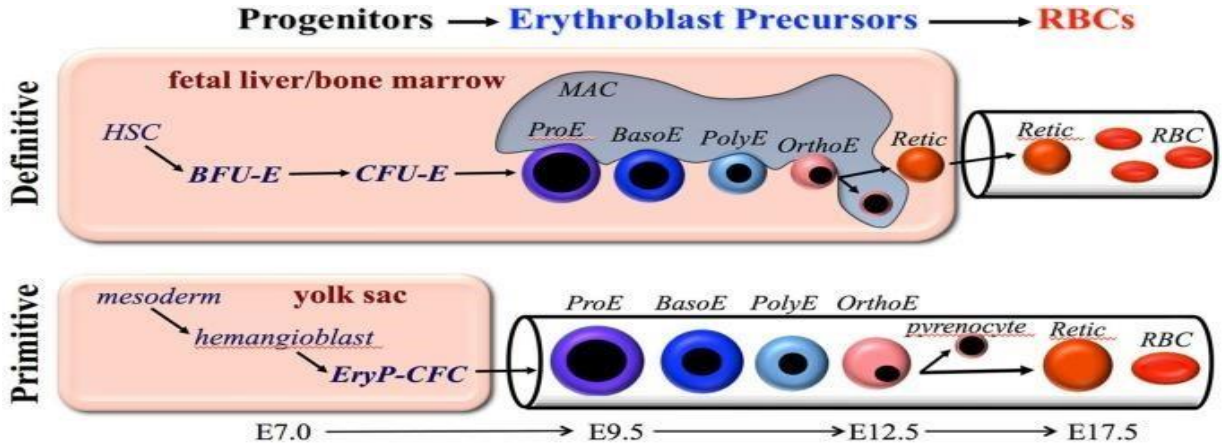


Stems cells responsible for formation blood cells are first converted to long-term (LT)-HSCs in fetal liver and bone marrow. LT-HSCs name given because, when they are transplanted into wild-type irradiated adult recipients, they do hematopoiesis for more than 3 to 4 months. LT-HSCs differentiate into ST-HSCs. ST-HSCs name given because, when they are transplanted into wild-type irradiated adult recipients, they do hematopoiesis for less than 1 month. ST-HSCs differentiate into multipotent progenitors (MPPs), which have no detectable self-

renewal ability (Orkin et al., 2010).



MPPs are differentiating into common myeloid progenitors (CMPs, with myeloid, erythroid and megakaryocytic potential) and common lymphoid progenitors (CLPs, with only lymphoid potential). CLPs further form T, B, NK and dendritic cells. The CMPs segregates bipotent granulocyte-macrophage (GMPs) and megakaryocyte-erythrocyte progenitors (MEPs). GMPs differentiate into granulocytes/monocytes and MEPs generate megakaryocytes/erythrocytes (Cheng et al., 2020).



We already discuss that primitive erythroid precursors mature within circulation, however in definitive hematosepsis, proerythroblasts (ProE), than basophilic erythroblasts (Baso), then polychromatophilic erythroblasts (PolyE), and orthochromatic erythroblasts (OrthoE) mature in fatal liver or bone marrow and only mature non nucleated RBCs enter in the circulation.

References

Boyd, K.L. and Bolon, B. (2010). Embryonic and fetal hematopoiesis. In: Weiss, D.J. and Wardrop, K.J. (eds) Schalm's Veterinary Hematology. Blackwell Publishing, pp. 3–7. Cell. 132(4): 631–644.

Cheng, H.; Zheng, Z. and Cheng, T. (2020). New paradigms on hematopoietic stem cell differentiation. Protein & Cell. 11(1): 34–44.

Jagannathan-Bogdan, M. and Zon, L. I. (2013). Hematopoiesis. Development, 140(12), 24632467.

McGrath, K. E., Frame, J. M., Fromm, G. J., Koniski, A. D., Kingsley, P. D., Little, J., and Palis, J. (2011). A transient definitive erythroid lineage with unique regulation of the β-globin locus in the mammalian embryo. Blood. 117(17), 4600-4608.

Medvinsky, A., Rybtsov, S. and Taoudi, S. (2011). Embryonic origin of the adult hematopoietic system: advances and questions. Development, 138(6), 1017-1031.

Müller, A. M., Medvinsky, A., Strouboulis, J., Grosveld, F., & Dzierzakt, E. (1994). Development of hematopoietic stem cell activity in the mouse embryo. Immunity, 1(4), 291-301.

Orkin, S.H. and Zon, L.I. (2008). Hematopoiesis: an evolving paradigm for stem cell biology. Palis, J. (2014). Primitive and definitive erythropoiesis in mammals. Frontiers in Physiology. 5(1): 1–9.

Palis, J., Malik, J., Mcgrath, K. E., & Kingsley, P. D. (2010). Primitive erythropoiesis in the mammalian embryo. International Journal of Developmental Biology, 54(6-7), 10111018.

Ueno, H. and Weissman, I. L. (2007). Blood lines from embryo to adult. Nature, 446(7139), 996-997.

Yamane, T. (2018). Mouse Yolk Sac Hematopoiesis. Frontiers in Cell and Developmental Biology. 6(80):1-8.