

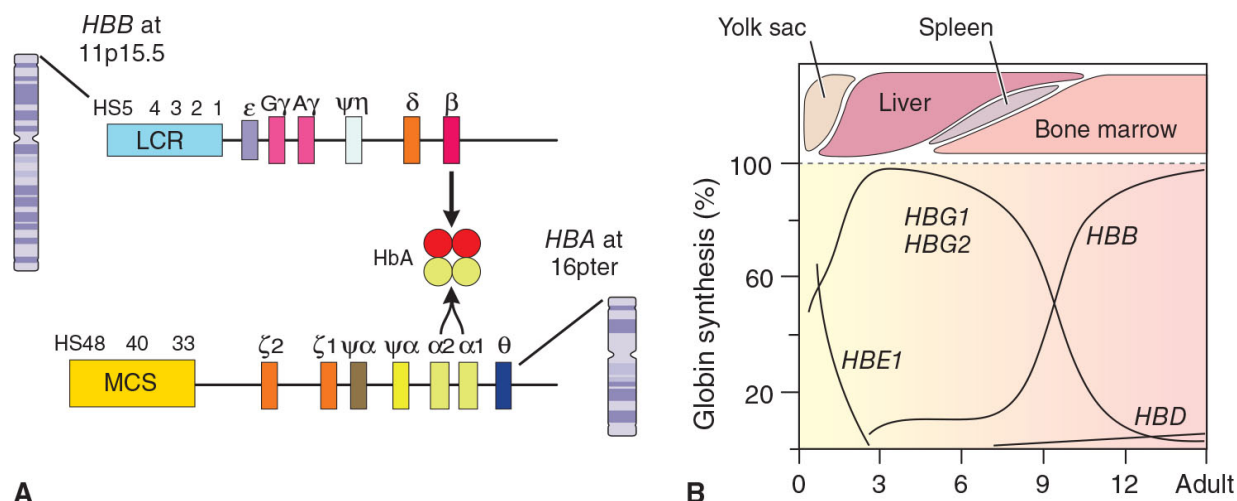


FIGURE 98-1 Globin gene clusters and their hemoglobin products during gestation. **A.** The order of globin genes in the β - and α -globin gene clusters along with their upstream enhancers, the locus control region (LCR) and multispecies conserved sequences (MCS). Normal hemoglobin tetramers contain two α -globin chains and two non- α -globin chains. In the example shown, this is adult HbA. **B.** Sites of erythropoiesis and globin synthesized from the yolk sac and the early embryo (months 1–3), the fetus (months 3–9), after delivery (months 9–12), and afterward (adult).

■ GLOBIN GENE CLUSTERS

Globin is encoded in two nonallelic gene clusters. The β -globin gene cluster is on the short arm of chromosome 11 (11p15.4); the α -globin gene cluster is on chromosome 16 (16p13.3) (Fig. 98-1). The β -globin gene cluster contains an embryonic ϵ -globin gene (*HBE*), two nearly identical fetal γ -globin genes (*HBG2*, *HBG1*) a major adult β -globin gene (*HBB*), and a minor adult δ -globin gene (*HBD*). The α -globin gene cluster contains an embryonic ζ -globin gene (*HBZ*) and duplicated α -globin genes (*HBA2*, *HBA1*) with identical proteins. Embryonic hemoglobins include Gower I ($\zeta_2\epsilon_2$), Gower II ($\alpha_2\epsilon_2$), Portland I ($\zeta_2\gamma_2$), and Portland II ($\zeta_2\beta_2$). Fetal hemoglobin (HbF, $\alpha_2\gamma_2$) production begins at 6–8 weeks' gestation, peaks during mid-gestation, then falls to <1% of total hemoglobin during the first 6 months of extrauterine life. Adult hemoglobin A (HbA; $\alpha_2\beta_2$) production follows a pattern reciprocal to that of HbF. The hemoglobin composition of normal adults is >95% HbA, ~1% HbF, and 2–3% HbA₂ ($\alpha_2\delta_2$). In adults, HbF and HbA₂ have little functional