# Thrombosis in the Neonatal Intensive Care Unit



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#### **KEYWORDS**

- Neonatal thrombosis
   Anticoagulation
   Prothrombotic disorder
   Thrombolysis
- Perinatal arterial ischemic stroke
   Cerebral sinovenous thrombosis

#### **KEY POINTS**

- Thrombosis is a significant problem affecting both term and preterm neonates.
- Most neonates that develop thrombosis have acquired risk factors or prothrombotic disorders.
- Proper imaging is essential for accurately identifying thromboses.
- The use of central venous/arterial catheters significantly increases a neonate's risk for thrombosis.
- Recommendations for neonatal treatment are based on expert opinion and data from case studies/series.

#### INTRODUCTION

Neonates have the highest risk for thrombosis among Pediatric patients (Box 1).<sup>1,2</sup> The placement of central venous and arterial catheters significantly increases this risk. Many prothrombotic disorders have been implicated in the pathogenesis of neonatal thrombosis, yet their exact role remains unclear. Despite treatment recommendations, there is a significant lack of randomized controlled trials demonstrating the efficacy of these treatments. Management of neonatal thromboses should occur at an experienced tertiary center that has proper support in place. This review focuses on a brief discussion of the neonatal hemostatic system highlighting why neonates are at risk for thrombosis, discusses the most common locations of neonatal thromboses and how to accurately image for them, reviews prothrombotic disorders' role in neonatal thrombosis, and discusses possible treatment modalities.

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### Box 1 Incidence of neonatal thrombosis

- Incidence of symptomatic neonatal thrombosis is 5.1 per 100,000 live births<sup>1</sup> and 2.4–6.8 per 1000 neonatal intensive care admissions<sup>2,7</sup>
- Term and preterm and male and female neonates are affected equally. 1, 2, 25

#### **NEONATAL HEMOSTASIS**

The neonatal coagulation system (anticoagulation and fibrinolytic systems) differs from those of children and adults (**Table 1**).<sup>7,8</sup> These differences shift the neonate into a somewhat prothrombotic state, which is balanced by other factors preventing spontaneous thromboses in well neonates.<sup>9</sup> However, numerous acquired and prothrombotic disorders may disrupt this balance, placing a neonate at risk for developing a clinically significant thrombosis (**Table 2**).<sup>3–6,9</sup> Age-appropriate reference ranges of coagulation and anticoagulation proteins are published.<sup>3,5,6</sup>

#### TYPES AND LOCATIONS OF NEONATAL THROMBOSES

Common locations, presenting signs and symptoms, and imaging modalities recommended for different types of thromboses are presented in **Table 3**.

#### Arterial Thromboses

#### Perinatal arterial ischemic stroke

Perinatal arterial ischemic stroke (PAIS), which affects both preterm and term infants, mainly occurs in the left hemisphere within the distribution of the middle cerebral artery, with multifocal cerebral infarctions usually being of embolic origin.<sup>12</sup>

The exact pathophysiologic mechanisms responsible for PAIS are unknown. A patent foramen ovale allowing thrombi from the placental circulation to pass into the cerebral arterial vasculature resulting in vessel occlusion has been one suggested theory.<sup>32</sup> Pathologic examination of the placenta from any high-risk delivery may

Table 1 Anticoagulant and procoagulant protein levels in neonates compared with adults		
	Protein	Neonatal Level Compared with Adult Level
Neonatal Procoagulant proteins	Factor VIII von Willebrand factor activity	Increased
Neonatal anticoagulant proteins	Factor II Factor VII Factor IX Factor X Factor XI Factor XII Protein C Protein S Antithrombin Heparin cofactor II	Decreased

Adapted from Manco-Johnson M. Controversies in neonatal thrombotic disorders. In: Ohls RY, editor. Hematology, immunology and infections disease: neonatology questions and controversies. Philadelphia: Saunders Elsevier; 2008. p. 59; with permission.

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