

# A History of Pulmonary Embolism and Deep Venous Thrombosis

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## KEYWORDS

- Pulmonary embolism • Deep venous thrombosis
- Thrombolytic therapy • Heparin • History

Pulmonary embolism (PE) remains a common and lethal entity that continues to diagnostically and therapeutically challenge contemporary physicians. As with many aspects of medicine, insights into the historical perspective of the disease are useful in configuring contemporary advances. The purpose of this article is to review the sentinel developments related to PE and enable readers to appreciate the current status of the diagnosis and therapy of PE while providing background to facilitate the development of future strategies. A comprehensive review of the history of PE is beyond the scope of this article and interested readers are referred to works of James Dalen and his extensive historical review of PE for greater detail.<sup>1,2</sup>

The first written reference to thrombotic disease is probably found in the ancient Indian medical texts of the great Ayurveda physician and surgeon, Susruta (circa 600–1000 BCE), in which he describes a patient who had a “swollen and painful leg which was difficult to treat.” Giovanni Battista Morgagni recognized the presence of large blood clots in the pulmonary vessels of patients suffering sudden death in his 1761 text, “De Sedibus et Causis Morborum per Anatomen Indagatis,” but was unable to provide an explanation for their presence. In the mid-1800s, Jean Cruveilhier, a prominent French pathologist of the time, proposed a central role for venous inflammation and thrombosis in all disease conditions (“phlebitis dominates all of pathology”) in his texts, “Anatomie Pathologique du Corps Humain” and “Traite d’Anatomie Pathologique Generale.”

The brilliant nineteenth-century German pathologist, Rudolph Virchow (**Fig. 1**), began his research studies into thrombosis specifically to investigate Cruveilhier’s proposal (at the suggestion of his anatomy professor, Robert Froriep). He since has been credited with “discovering” PE in 1846.<sup>3,4</sup> Virchow recognized the relationship between venous thrombosis and obstruction of the pulmonary arteries by the embolic phenomenon as depicted in his classic description: “the detachment of

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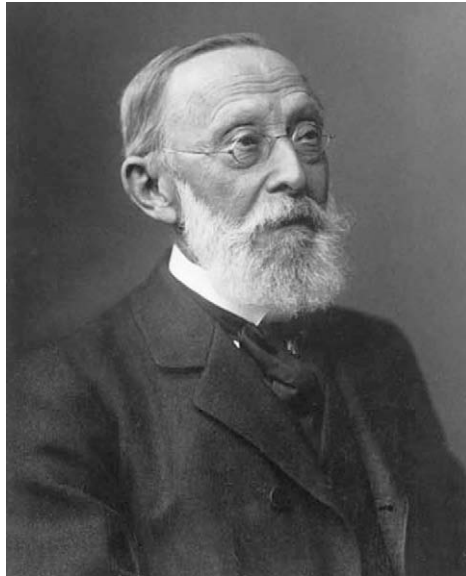


Fig. 1. Rudolf Virchow (1821–1902), who first described PE.

larger or smaller fragments from the end of the softening thrombus which are carried along the current of blood and driven into remote vessels. This gives rise to the very frequent process on which I have bestowed the name Embolia.” Virchow recognized that “these stoppers originated in part of the cardiovascular system upstream of the lungs, namely the veins and right heart. They are then carried to the pulmonary artery by the blood stream.” Virchow has a more dubious distinction of being among the foremost opponents of the germ theory of disease. His prominent and passionate opposition to the theory proposed by Lister and Pasteur led to prolonged delays in acceptance of this disease paradigm.<sup>5,6</sup> The contemporary approach regarding the genesis of venous thromboembolism (VTE) disease continues to reflect the triad, described by Virchow, consisting of intimal vessel injury, stasis, and hypercoagulability.

Clinical confirmation of Virchow’s discovery occurred in 1880 when Luzzatto reported a series of 160 cases that defined the clinical aspects of PE and began to recognize the role of underlying cardiopulmonary disease.<sup>6</sup> In 1884, Picot recognized that “venous thrombosis is always a severe disease and often fatal, because fragments of the thrombi may detach and occlude branches of the pulmonary artery....the occlusion of the main branches of pulmonary artery causes a striking rise of the blood pressure in these vessels. This rise—which the right heart must fight to insure circulation may sometimes lead to cardiac arrest.”<sup>7</sup> The remainder of this article reviews the sentinel events related to the diagnosis and treatment of PE.

#### DIAGNOSIS OF PULMONARY EMBOLISM

Before the development of the objective diagnostic standards in the 1960s, the diagnosis of PE ostensibly was made on clinical grounds. The lack of sensitivity and specificity in the accuracy of the physical examination is evident in reports that reveal the majority of PEs that were defined at autopsy were not diagnosed ante mortem. Dalen

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