CC/NUMBER 52
DECEMBER 24-31, 1979

This Week's Citation Classic

Negus D, Pinto D J, Le Quesne L P, Brown N & Chapman M. ^{125}I-labelled fibrinogen in the diagnosis of deep-vein **thrombosis and its correlation with** phlebography. *Brit. J. Surg.* **55**:835-9, 1968. [Depts. Surgical Studies, Nuclear Med., and Radiology, Middlesex Hosp., London, England]

Ninety-three post-operative patients were investigated by intravenous ^{125}I-labelled fibrinogen and leg scanning. A 93% correlation with phlebography was observed in 26 legs with deepvein thrombosis, and 100% correlation in normal veins. Most thrombi were detected within 48 hours of operation, and physical signs were present in only a few. [The *SCI*® indicates that this paper has been cited over 285 times since 1968.]

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September 18, 1979

"It is flattering for a surgeon to find himself among scientists, and it gives me much pleasure to be able to include some of the many people who were involved directly or indirectly in this paper. After a year's work on the post-thrombotic syndrome at St. Thomas' Hospital, I was given three opportunities: First, to remain there as a surgical registrar (resident). Second, to spend a year at the Mayo Clinic in vascular physiology, which was very tempting, but I was more interested in clinically-orientated research. I was therefore delighted with the third opportunity—to work in Professor Le Quesne's department at the Middlesex Hospital on problems related to thrombosis. My predecessor, John Ham, now in Queensland, had been interested in the relationship between platelet adhesiveness and lipoprotein lipase activity. I was encouraged to continue this and also to investigate ^{125}I-fibrinogen uptake in the diagnosis of deep vein thrombosis. This had been started by Hobbs and Davies in 1960,[1] and later developed by Atkins and Hawkins.[2] We also decided to combine these projects and to investigate platelet adhesiveness in relation to deep vein thrombosis. I was kindly allowed to investigate the patients of several surgeons and, apart from one lady who maintained that all surgical researchers were little better than murderers, these were most co-operative. Much help was also provided by Dr. (now Professor) Williams of the Nuclear Medicine Department; Nicholas Brown, medical physicist, who organised the radiation counting and suggested the useful modification of comparing 'leg counts' with 'heart counts' to compensate for biological decay; and Malcolm Chapman, consultant radiologist, whose phlebograms demonstrated that an increased isotope labelled fibrinogen uptake did accurately indicate radiologically-demonstrable thrombus.

"Atkins' and Hawkins' work at King's College Hospital, continued by Flanc and Kakkar,[3] confirmed the validity of the method. Unfortunately we were unable to demonstrate any relationship between early deep vein thrombosis and platelet adhesiveness, and the search for a simple and reliable 'early warning system' goes on. Dominic Pin to completed the work and undertook other studies with ^{125}I-fibrinogen.

"^{125}I-fibrinogen uptake has subsequently been widely used in investigating the natural history of deep vein thrombosis, and in assessing methods of prevention. Paradoxically, its extreme accuracy is its main defect in clinical research, and argument still continues as to whether these small early thrombi are 'clinically significant' or not.

"My year at Middlesex was stimulating and enjoyable, and I only regret that, by going there, I was unable to visit the Mayo Clinic. I hope to correct this deficiency in my medical and scientific education before too long."

1. **Hobbs J T & Davies J W L.** Detection of venous thrombosis with ^{125}I-labeled fibrinogen in the rabbit. *Lancet* **2**:134-5, 1960.
2. **Atkins P & Hawkins L A.** Detection of venous thrombosis in the legs. *Lancet* **2**:1217-9, 1965.
3. **Flanc C, Kakkar V V & Clarke M B.** The detection of venous thrombosis of the legs using ^{125}I-labelled fibrinogen. *Brit. J. Surg.* **55**:742-7, 1968.