

V. V. KAKKAR *ET AL.*: LATE RESULTS OF TREATMENT OF DEEP VEIN THROMBOSIS



FIG. 1

FIG. 1.—Phlebogram one year after extensive thrombi in the popliteal and tibial veins. The initial treatment was by streptokinase, and this resulted in complete dissolution of the thrombus. (a) The valves in tibial veins are competent. (b) Arrow indicates the popliteal valve, which is open. (c) The same valve, which is closed.

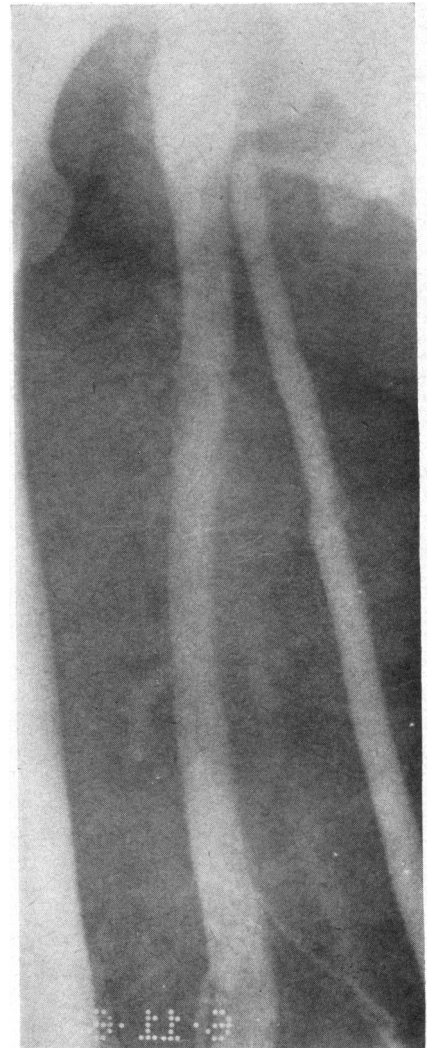


FIG. 2

FIG. 2.—Phlebogram showing completely recanalized vein. This patient was treated initially with Arvin, with a failure to clear the thrombus. Nine months later, after long-term oral anticoagulants, there was complete recanalization but no valves could be seen.

R. D. SPICER *ET AL.*: RENAL MEDULLARY CYSTIC DISEASE

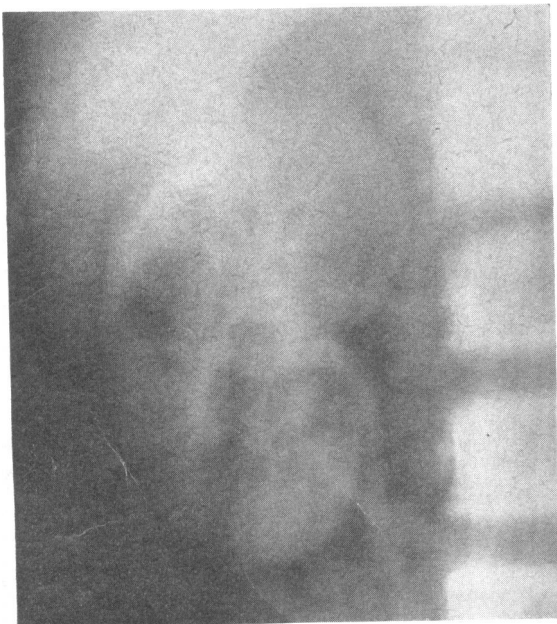


FIG. 1.—Nephroto-gram of right kidney.

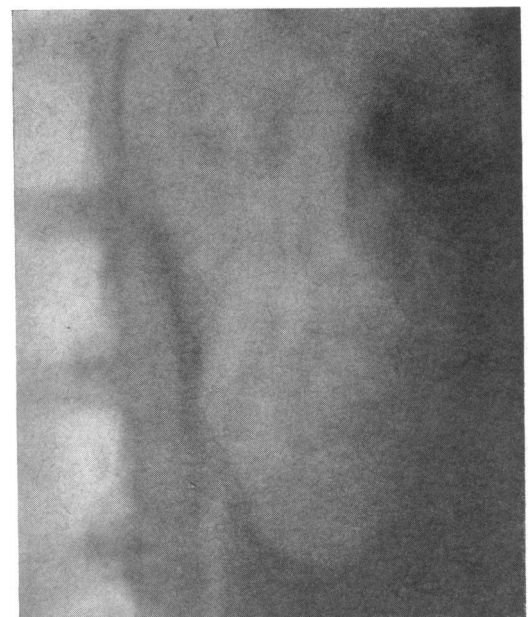


FIG. 2.—Nephroto-gram of left kidney.

Kakkar, V. V., and Flanc, C. (1968). *Brit. J. Surg.*, 55, 384.  
 Kakkar, V. V., Flanc, C., O'Shea, M., Flute, P., Howe, C. T., and Clarke, M. B. (1968). *Brit. J. Surg.*, 55, 858.  
 Kakkar, V. V., Flanc, C., O'Shea, M., Flute, P. T., Howe, C. T., and Clarke, M. B. (1969a). *Brit. J. Surg.*, 56, 178.  
 Kakkar, V. V., Howe, C. T., Laws, J. W., and Flanc, C. (1969b). *Brit. med. J.*, 1, 810.

Merskey, C., Kleiner, G. J., and Johnson, A. J. (1966). *Blood*, 28, 1.  
 Negus, D., Pinto, D. J., Le Quesne, L. P., Brown, N., and Chapman, M. (1968). *Brit. J. Surg.*, 55, 835.  
 Robertson, B. R., Nilsson, I. M., and Nylander, G. (1968). *Acta chir. scand.*, 134, 203.  
 Verstraete, M., Vermylen, J., Amery, A., and Vermylen, C. (1966). *Brit. med. J.*, 1, 454.

## Late Results of Treatment of Deep Vein Thrombosis

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[WITH SPECIAL PLATE FACING PAGE 809]

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**Summary:** Twenty-two patients who had an acute episode of thrombosis in the deep veins of the legs were studied by a new technique of ascending functional cinephlebography 6 to 12 months after the episode of thrombosis.

If the condition was diagnosed within 36 hours and the thrombus was dissolved rapidly valve function was preserved. When diagnosis was delayed there was a very great risk of permanent damage to the valves.

### Introduction

The preceding article (Kakkar *et al.*, 1969) described the immediate results of the treatment of deep vein thrombosis of the legs, in which the dominant complication was the risk to life from pulmonary embolism. By contrast, this paper is concerned with the long-term sequelae. When thrombosed veins recanalize, the valves are either destroyed (Edwards and Edwards, 1937) or they become incompetent, resulting in a sustained high pressure in the veins of the legs (Beecher, 1937; Linton and Hardy, 1948). Subsequently there may follow pain in the legs, swelling, varicose veins, eczema, ulceration, and other trophic changes.

In the present study 22 patients with deep vein thrombosis who had been treated during the acute phase with heparin, streptokinase, or Arvin were followed up in an attempt to answer the following questions: What form of initial treatment was most successful in the eventual return of the veins to normal? What are the critical factors involved in the preservation of function of venous valves?

### Materials and Methods

Twenty-two patients (described in the preceding paper) have so far been restudied after an interval of up to 12 months after the initial treatment with heparin, streptokinase, or Arvin (see Table). In eight patients who had complete clearance (see Table) long-term oral anticoagulant therapy was not used. Of 14 patients in whom there was partial clearance after the initial treatment eight had oral anticoagulants for six to nine months

and six had none. The dose of oral anticoagulant was regulated to maintain the prothrombin time between one and a half and twice the control value, rabbit brain thromboplastin being used.

The legs were re-examined several months after the original treatment by ascending functional cinephlebography—a technique which was developed to show valvular function and completeness of recanalization.

### Ascending Functional Cinephlebography

The patient lies on a fluoroscopic x-ray table which is tilted to an angle of 60 degrees to the horizontal. A pneumatic cuff is placed just above the ankle, and is distended to a pressure of 100 mm. Hg in order to prevent filling of the superficial veins of the leg and to direct the contrast medium into the deep venous system. A scalp-vein 21G thin-wall (20G bore) infusion cannula is introduced into a vein on the dorsum of the great toe; this vein is selected because it is easy to cannulate and directly joins the plantar plexus through the first interosseous space. Therefore any contrast medium which is injected through this vein flows directly into the deep veins. The cannula is attached to a 50-ml. syringe filled with 45% sodium diatrizoate which has been warmed to body temperature, and the contrast medium is injected slowly. The patient is instructed to plantar flex and dorsiflex the foot in order to propel the contrast medium. As the contrast medium progresses in the tibial veins, continuous observations are made on the television monitor. The function of the valves, seen on the television monitor, is recorded on both cine and static films. The contrast medium is now followed into the popliteal and femoral veins and the function of their valves is assessed. The effect of the Valsalva manoeuvre on these valves is also recorded. Lastly, the contrast medium is followed into the iliac veins to confirm their patency. At the end of the examination the contrast medium is washed out of the deep veins by 150 ml. of normal saline containing 2,500 units of heparin. Clearance is confirmed by screening the leg.

The valvular function was considered to be normal when both the valve cusps were seen to open and close with onward flow of blood and no retrograde flow occurred. It was considered that function was poor when the valve cusps were present but did not open and close and retrograde flow occurred. A completely recanalized vein was evenly filled with contrast medium and had a smooth lumen. Recanalization was considered to be incomplete when filling of the vein was constantly uneven with an irregular lumen.

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## Results

The Table gives an outline of the results. Of the 22 patients studied only eight had complete clearance of veins after the initial treatment. Five of these showed normal function of valves when re-examined 6 to 12 months later by cinephlebography (Special Plate, Fig. 1). In all instances where valvular function returned to normal the diagnosis had been made early, within 36 hours of onset of thrombosis. In all the thrombi had been cleared rapidly, within 72 hours of the beginning of treatment, as judged by phlebography. Patency of veins in all eight patients remained complete 6 to 12 months after the initial thrombotic episode.

*Valvular Function and Recanalization After Deep Vein Thrombosis*

Initial Treatment	No. of Patients	Valvular Function 6-12 months after Complete Clearance		Degree of Recanalization 6-12 months after Incomplete Clearance	
		Normal	Poor	Complete	Incomplete
Heparin ..	8	1	1	3	3
Streptokinase ..	7	4	1	1	1
Arvin ..	7	0	1	4	2

The remaining 14 patients had only partial clearance of thrombi after completion of the initial treatment. In none of these could valves be demonstrated subsequently (Special Plate, Fig. 2). In the eight who had received long-term oral anticoagulants seven showed complete recanalization within 6 to 12 months. In the remaining six who did not receive long-term oral anticoagulants only one had complete recanalization.

## Discussion

The sequelae of deep vein thrombosis—varicose veins, bursting pain, swelling of the legs, eczema, ulceration, and other trophic changes—are among the commonest and most intractable problems in medicine. What can be done about this problem?

The ideal to aim at is the prevention of deep vein thrombosis. The new techniques of radioactive labelled fibrinogen and phlebography, which lead to much greater precision in the diagnosis of venous thrombosis than was previously possible, give us every hope that prophylaxis can be made more effective in the future. At the present moment, despite the physiotherapy regimen used in most hospitals to prevent deep vein thrombosis, it still occurs in more than 30% of patients after operation (Flanc *et al.*, 1969).

When deep vein thrombosis has occurred it seems likely that prevention of late sequelae can best be brought about by the rapid and complete dissolution of thrombus with preservation of valvular function. In the past valvular function has been assessed by ascending phlebography (Scott and Roach, 1951) or by retrograde phlebography (Luke, 1941; Bauer, 1948;

Shumacker *et al.*, 1954). These methods demonstrated only the presence or absence of valves, but not their function. The technique in this study showed the function of valves, with the patient in an almost upright position.

What are the main factors in preserving valvular function? It seems likely from this study that early diagnosis is of paramount importance. This is possible by the use of the <sup>125</sup>I-labelled fibrinogen test. At this stage the clot is small and no organization has taken place, so that complete clearance may be obtained more readily. To be as certain as possible of preserving valvular function the diagnosis must be made within 36 hours of onset and the clot must be dissolved rapidly. Streptokinase, which actively lyses the thrombus, is the most effective agent at present for doing this. When heparin or Arvin were used the initial clearance of the veins was slower and consequently valvular function was less satisfactory.

The completeness and rapidity of recanalization have been recorded in this study. The majority of workers have claimed that recanalization seldom occurs under two years (Stulz and Froehlich, 1952; Rispoli and Moschen, 1965; Bergvall and Hjelmstedt, 1968). Without oral anticoagulants recanalization was slow and incomplete in all but one patient studied up to 12 months. The process was more rapid and complete if oral anticoagulants were given for six to nine months after the initial treatment.

We conclude that if deep vein thrombosis can be diagnosed within 36 hours of onset thrombi can be dissolved completely and valvular function preserved. When dissolution of the thrombus is delayed or incomplete then valvular function in the affected segment of vein is defective.

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## REFERENCES

- Bauer, G. (1948). *J. int. chir.*, **8**, 937.  
 Beecher, H. K. (1937). *J. clin. Invest.*, **16**, 733.  
 Bergvall, U., and Hjelmstedt, A. (1968). *Acta chir. scand.*, **134**, 219.  
 Edwards, E. A., and Edwards, J. E. (1937). *Surg. Gynec. Obstet.*, **65**, 310.  
 Flanc, C., Kakkar, V. V., and Clarke, M. B. (1968). *Brit. J. Surg.*, **55**, 742.  
 Flanc, C., Kakkar, V. V., and Clarke, M. B. (1969). *Lancet*. In press.  
 Kakkar, V. V., and Flanc, C. (1968). *Brit. J. Surg.*, **55**, 384.  
 Kakkar, V. V., Flanc, C., Howe, C. T., O'Shea, M., Flute, P. T. (1969). *Brit. med. J.* In press.  
 Linton, R. R., and Hardy, I. B., jun. (1948). *Surgery*, **24**, 452.  
 Luke, J. C. (1941). *Surg. Gynec. Obstet.*, **73**, 472.  
 Rispoli, F., and Moschen, M. (1965). *Chir. Organi Mov.*, **53**, 343.  
 Scott, H. W., jun., and Roach, J. F. (1951). *Ann. Surg.*, **134**, 104.  
 Shumacker, H. B., jun., Moore, T. C., and Campbell, J. A. (1954). *Surg. Gynec. Obstet.*, **98**, 257.  
 Stulz, E., and Froehlich, C. (1952). *Presse méd.*, **60**, 1432.