South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL : VAN DIE REDAKSIE

ANTICOAGULANT THERAPY

The treatment of thrombotic and potentially thrombotic states with anticoagulant drugs has now become commonplace. Numerous patients receive this form of therapy for acute conditions, and the number of patients who are being maintained on continuous long-term therapy for chronic cardiovascular disease is growing daily.

The technical problems of anticoagulant therapy are relatively simple. For rapid treatment of an acute condition intravenous heparin is unsurpassed, as is deep subcutaneous or intramuscular concentrated heparin during the following 48 hours. There is, as yet, no oral form of heparin which has therapeutic value. The administration of oral anticoagulant drugs is started simultaneously with the first dose of heparin and forms the basis of maintenance therapy. There appears to be little to choose between the various oral preparations in common use. The original dicoumarol is still widely used, but in South Africa and Britain phenindione (dindevan, indema, hedulin) is perhaps the most widely used drug of this group. Warfarin sodium (coumadyn, marevan) has gained in popularity in recent years, and there are other satisfactory drugs as well. The main point would appear to be to learn to know one of these drugs well, much as one gets to know one or two drugs of the digitalis or antihistamine groups. Many of the drugs in common use are satisfactory if used intelligently.[1]

The dose should not be varied excessively since too frequent tests may be as dangerous as too few. There is a tendency to attach too much importance to the actual figures of the prothrombin estimation. It matters little if the estimation is expressed as a percentage or an index; what is important is to know the therapeutic range, and this is sometimes quite wide. If anything, one should perhaps err on the side of keeping the prothrombin too high rather than too low, though there is evidence that too lax a control can also be dangerous.[2] The accepted practice is to keep the figure as low as can be done with safety, but a much higher level might possibly be equally satisfactory. A fixed dose is the ideal, and many patients have received the same dose for years. Once the readings are reasonably stable the dose need not be varied by more than perhaps half to one tablet per week. It is often better to check a divergent reading than to vary the dose. If the prothrombin reading is near the therapeutic levels the dose should not be altered at all. It is only when repeated readings are well outside optimum levels that the dosage schedule need be revised. Once the patient is well stabilized, tests need be done only once every two to three months.

An important cause of a divergent reading is that the patient has omitted to take the prescribed dose. It is not easy to remember to take a pill every day and, sooner or later, even the most conscientious pill-swallower begins to doubt whether he did in fact take his medicine. A useful trick is to advise the patient to put a week's supply of pills in one bottle and to take these pills during the week. The dose on the seventh day is whatever remains in the bottle!

There are surprisingly few contraindications to anticoagulant treatment. Severe bleeding diathesis, liver disease, ulceration in the gastro-intestinal tract, and possibly pregnancy are perhaps the most important contraindications. It is useful to remember that unexpected haemorrhage, when the prothrombin is not too low, is an indication for search for a local cause of bleeding.

It is probably wise to interrupt treatment if surgery is required. Major surgical operations without excessive blood loss, performed while the patients are being treated with such drugs as dicoumarol,[3] have been reported, but in general this is not advised. There is a difference, too, between patients who have been on these drugs for only a week or two and those who have received treatment for an extended period. Other coagulation factors, like Christmas factor, may become depressed and this will not necessarily be reflected in the prothrombin reading. Minor surgery, e.g. dental extraction, can usually be performed with safety two or three days after stopping phenindione, and the administration of the drug can be restarted within twenty-four hours after the operation when most of the pills which had been omitted will probably still be required. For emergency use vitamin K_1 is available, but it should only rarely be needed.

Are all the efforts and cost which are currently being expended in the therapeutic application of these drugs worth while? It would appear that this type of treatment has some value, though the proof is far from being satisfactory despite the many years which have elapsed since its introduction into medicine. It would also appear that a patient, who is admitted to hospital for an acute coronary thrombosis, has a better chance of leaving the hospital alive if he is given anticoagulant therapy than if this is not done. This might be due to the prevention of pulmonary embolism rather than the prevention of further coronary thrombosis. If this is the case the treatment would appear to be equally justifiable for any patient with chronic congestive cardiac failure or even for an (elderly) person who has to remain in bed. In chronic coronary artery disease there is room for even more scepticism despite some enthusiastic reports.[4-6] A recent MRC trial[7] has found this treatment beneficial, but some authors remain unconvinced.[8]

Anticoagulant treatment does appear to be of value in the prevention of cerebral embolism in chronic rheumatic heart disease,[9] but its use in the immediate treatment of cerebral embolism or in patients with cerebral thrombosis is not clearly established, although some reports tend to suggest that it might be of help.[10-12] It is not clear how long this treatment of patients with established vascular disease should continue—for the rest of their lives, or for a year or perhaps less?

These questions require an urgent answer and a clear case would appear to exist for a properly controlled study along these lines. The number of patients for whom this treatment is being prescribed is growing at an alarming

rate. Let us hope that clear-cut answers will be obtained before we are overwhelmed by the avalanche which is now rapidly gaining speed.

REFERENCES

1. Rodman, T., Ryan, C. S., Pastor, B. H. and Hollendonner, W. J. (1959): Amer. J. Med., **27**, 415.
2. Toohey, M. (1959): Brit. Med. J., **1**, 920.
3. Storm, O., Müllertz, S. and Tybjaerg Hansen, A. (1955): *Thrombosis and Embolism*, p. 959. Basel: Benno Schwabe.
4. Wright, I. S., Bourgain, R. H., Foley, W. T., McDevitt, E., Gross, C., Burke, G., Simon, E., Lieberman, J., Symons, C. and Huebner, R. (1954): Circulation, **9**, 748.
5. Suzman, M. M., Ruskin, H. D. and Goldberg, B. (1955): *Ibid.*, **12**, 338.
6. Bierkelund, C. J. (1957): Acta. med. scand., **158**, suppl. 330.
7. Medical Research Council Report (1959): Brit. Med. J., **1**, 803.
8. McMichael, J. (1959): *Ibid.*, **1**, 970.
9. Wright, I. S. and McDevitt, E. (1954): Ann. Intern. Med., **41**, 682.
10. Carter, A. B. (1957): Quart. J. Med., **26**, 335.
11. Wells, C. E. (1959): Arch. Neurol. Psychiat., **81**, 667.
12. McDevitt, E., Groch, S. N. and Wright, I. S. (1959): Circulation, **20**, 215.