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THE PROPHYLACTIC USE OF ANTICOAGULANT THERAPY IN THE PREVENTION OF PULMONARY EMBOLI IN ONE HUNDRED CONSECUTIVE SPINAL INJURY PATIENTS

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PULMONARY embolism is the major cause of death in the first few weeks after an acute spinal injury. Walsh and Tribe (1965) found that of 500 cases of traumatic spinal injuries admitted within 14 days at the National Spinal Injuries Centre, 15 died of pulmonary emboli. Cheshire (1968), in a comparable group of 325 admissions, had two deaths from pulmonary emboli. Watson (1968) found that among 413 acute admissions over a ten-year period there were seven deaths from pulmonary emboli and a further 15 patients were diagnosed clinically as having this condition although they recovered. This high incidence of pulmonary emboli is not restricted to spinal injury patients.

Sevitt and Gallagher (1959, 1961) found that 65 per cent of patients following major injury developed deep-vein thrombosis and 20 per cent of them had pulmonary emboli of which four-fifths were major. In order to reduce the morbidity and mortality from this condition, they instituted a regime of prophylactic anticoagulant therapy.

They showed that the veins of the lower limbs became thrombosed within a few days of injury, 50 per cent of patients developed a thrombosis by one week. They believed that pulmonary emboli arose as the result of the detachment of thrombi from the lower limbs. The use of anticoagulants after an overt deep-vein thrombosis or a pulmonary embolus did not prevent subsequent pulmonary emboli. The only effective way to stop pulmonary embolism was to prevent the leg veins thrombosing. They achieved this by anticoagulating on admission those patients that they considered to be at risk—initially patients with a fracture of the femoral neck. But they subsequently enlarged their experience and anticoagulated other patients with major injuries. However, they considered that the presence of a spinal injury was a contra-indication to therapy in view of the risk of bleeding into the spinal cord.

At this Centre, when a patient developed a swollen leg, anticoagulants had been given therapeutically on accepted principles for a period of two to three weeks, but as this failed to prevent pulmonary emboli a regime of prophylactic anticoagulant therapy was instituted in the late 'sixties. This was followed at the Liverpool Regional Paraplegic Centre (Silver & Moulton, 1970; Silver, 1971 *a*, *b*). As greater experience has been gained with this technique it seemed worth while to report the detailed management of this regime on a hundred consecutive spinal injury patients at the National Spinal Injuries Centre.

CLINICAL MATERIAL

The series consists of a hundred consecutive spinal injuries admitted to a male ward of the National Spinal Injuries Centre Stoke Mandeville Hospital

between 15.4.71. and 17.3.73. Details of their levels, severity, causes, delay in admission and ages are given in Table I. There were 51 cervical patients, 38 thoracic and 11 lumbar. The main causes were road traffic accidents in 41 patients and falls in 36 patients. Forty-two of the patients were admitted within two days of injury and 59 within seven days. There were two deaths. Seventy-five patients had major associated injuries, 12 had tracheostomies performed. The high incidence of cervical injuries and road traffic accidents is in keeping with the experience throughout the rest of the country.

TABLE I

Level and degree of completeness

Year	Number	Levels					
		Cervical (51)		Thoracic (38)		Lumbar (11)	
		Complete	Incomplete	Complete	Incomplete	Complete	Incomplete
1971–73	100	31	20	24	14	1	10

Cause of injury

Road traffic accidents	Falls	Blows	Dive	Gunshot wound	Miscellaneous
41	36	9	5	3	6

REGIME OF TREATMENT

Admission and General Care. No patients were admitted directly to the Centre following their spinal injury. They were always admitted to a receiving hospital and transferred subsequently to the Centre. On admission the spine and chest were X-rayed, haemoglobin, white blood count, blood group, blood urea and liver function tests were carried out. The urine was cultured; careful enquiry was made for any past history of peptic ulceration or other bleeding tendency and particularly jaundice or alcoholism and the administration of any drugs that might interfere with anticoagulant therapy such as aspirin, barbiturates or a broad-spectrum antibiotic.

The neurological and general condition was assessed to determine whether any further operative or medical treatment was required. Then following the routine treatment at the Centre, they were turned two-hourly either manually or on a turning-bed. Their bladders were drained by intermittent catheterisation or when contra-indicated by continuous drainage. The size of the lower limbs and the presence of swelling was determined. The patency of the veins was studied by means of a sonic aid. This was repeated subsequently if there was any question of a deep vein thrombosis occurring. When doubt still existed, venography was carried out. This was done on 14 occasions. If a patient had an established

deep-vein thrombosis on admission or developed one subsequently, no passive movements were given to the lower limbs until the patient had been adequately anticoagulated for one week. If deep venous thrombosis was not present and there was no contra-indication such as existing fracture, physiotherapy began immediately and consisted of passive movements to the lower limbs. In tetraplegic and thoracic patients postural drainage and percussion were administered to the chest. When the fracture of the spine was stable the patient was mobilised usually at about 12 weeks.

Anticoagulant Therapy (Table II). A period of 24 hours was allowed to lapse before anticoagulant therapy was commenced, and bowel sounds were present and they were taking solid food. Initially, especially in cervical lesions and in

TABLE II

Anticoagulant treatment

Total number on anticoagulants	68
Number who stopped early course of anticoagulants	6
Number who restarted early course of anticoagulants after brief delay	2*
Number who started anticoagulants later	6
Pulmonary infarcts	2
Deep-vein thrombosis	4
Number who needed later courses because of deep-vein thromboses and swollen legs	4*†

* During the interval one patient had a deep vein thrombosis and a pulmonary infarct and he later required a further course.
† One deep-vein thrombosis occurred late—after the patient had got up. Anticoagulants were stopped after a haemarthrosis but started again for oedema.

patients with lower lesions who have an extensive retro-peritoneal haemorrhage paralytic ileus is common. This is treated by a regime of 'suck and drip' and if necessary prostigmine injections. Anticoagulants are not given. Under these conditions stretching of the stomach can give rise to bleeding and at any event absorption of drugs is unpredictable. It is recognised that Warfarin has less side-effects and complications than Phenindione (Dindivan). But Phenindione (Dindivan) was used in all cases since this was the drug which had been in general use. The dosage varied from 25 to 100 mg. daily and was controlled by one-stage prothrombin test using the British Comparative Thromboplastin, the aim being to keep the prothrombin efficiency between 15 and 30 per cent; (prothrombin ratio 3 : 1 ratio to 1.8 : 1) Initially these were estimated at 48 hours then daily and eventually twice a week. The duration of the Phenindione treatment was varied. It was usually about 12 weeks before the patient was sitting up in bed. Discontinuation of the treatment was arbitrarily set at 12 weeks. Previously, shorter periods of six weeks had been used but this had resulted in late deep-vein thrombosis. Routine nursing and overall management of the patient was not modified by the use of this regime. If the patient had a deep venous thrombosis on admission as diagnosed by the sonic aid or the lower limb being overtly swollen, then

intravenous heparin therapy was commenced immediately, in addition to Phenindione since it takes some 72 hours before Phenindione becomes effective. This was given by means of a saline drip with 50,000 units of heparin being given over a 24-hour period.

Criteria for Diagnosis of Pulmonary Embolism

1. Post mortem.
2. Pleuritic pain of sudden onset lasting for more than 12 hours, with the exclusion of chest infection or minor cardiac infarction.
3. Supporting evidence from haemoptysis and enzyme studies.
4. The use of sonic aid and venography to determine if there was a concurrent deep-vein thrombosis which could be the source of the emboli.

Contra-indications. Thirty-two patients did not receive anticoagulants on admission. Seven arrived so late after injury that the risk of pulmonary embolism was considered to have passed. The largest group of 11 patients had associated injuries of such severity that the risk of further bleeding into vital organs was thought to outweigh the advantages of therapy. Six of these had severe skull fractures, three severe chest injuries with a haemothorax or pneumothorax. Two had severe bleeding into the renal tract, one around the kidney from trauma, the other a severe haemorrhagic cystitis from an irritant bladder wash-out given prior to admission. The high incidence of severe associated injuries is hardly surprising since a fractured spine seldom occurs in isolation. Seventy-five of the patients had associated injuries of whom 39 had head injuries and 32 chest injuries. Nevertheless they were only thought to be severe enough to contra-indicate treatment in 11 patients. In the case of head injuries it was the presence of a severe fracture of the base of the skull, bleeding from the ear, nose or throat or a prolonged loss of consciousness that stopped the institution of anticoagulation therapy.

If a patient had a haemothorax on admission this was aspirated. An intercostal drain was inserted only if it re-accumulated on several occasions. When there was no further blood in the chest anticoagulant therapy was commenced.

Three patients had a history of peptic ulceration and in view of the known risks of acute bleeding from the gastro-intestinal tract were not anticoagulated.

Two patients had so little neurological involvement that the risk of bleeding into the cord although slight was thought to outweigh the advantages. Finally there was a miscellaneous group of nine patients where general treatment on medical grounds precluded the use of anticoagulants. They included several alcoholics, and patients who had a previous episode of renal failure and one whose tetraplegia was caused by ankylosing spondylitis.

Complications. The only complications that necessitated discontinuation of treatment was bleeding. Treatment was stopped for this cause in six patients, in four it was from gastro-intestinal tract; two into the chest. Immediately after spinal injury acute bleeding from gastro-intestinal tract is a recognised risk. Seven patients developed an acute haemorrhage. Five patients presented with a melaena and two patients with a haematemesis. This occurred between three days and eight weeks after injury. Four of the patients had been anticoagulated on admission and this was stopped. Three patients were not anticoagulated. Four

patients had duodenal ulcers, only one had a definite stress ulcer diagnosed at laparotomy. No patients were treated with steroids (Table III).

TABLE III

Intestinal haemorrhage

Name	Anticoagulation	Days after injury	Diagnosis
M	+ ——→ –	20	Duodenal ulcer
C	+ —→ –	56	Duodenal ulcer
L	– ···→ –	16	Stress ulcer
H	+ ——→ –	15	No ulcer
G	– ——→ –	3	No diagnosis
W	– ——→ –	27	Perforated duodenal ulcer
G	+ ——→ –	6	Duodenal ulcer

Delay in commencing Therapy. Six of the 32 patients initially rejected for anticoagulant therapy for reasons mentioned earlier had to be anticoagulated despite risks involved. In two patients this was because of pulmonary embolism and in four, deep-vein thrombosis. There was no deterioration in their general condition.

RESULTS

Deep-Vein Thrombosis (Table IV). Three patients had deep-vein thrombosis on admission, and of the group of 32 who were not anticoagulated, eight (25 per

TABLE IV

Deep vein thrombosis

On admission	3
No anticoagulants	8
On anticoagulants	4
Off anticoagulants	3
Total	18

cent) developed deep-vein thrombosis, whereas of the 68 on anticoagulants only four (5 per cent) developed deep venous thrombosis, a further three patients developed deep-vein thrombosis when the therapy had been discontinued.

Pulmonary Embolism (Table V). One patient had a pulmonary embolism prior to admission, four patients (12½ per cent) out of 32 who were not anticoagulated had pulmonary embolism—one patient who had stopped therapy had an embolism; only one patient who was poorly controlled out of the group of 68 on anticoagulants

had a pulmonary embolism (less than 2 per cent). Therewere no fatalities from this condition.

TABLE V

Pulmonary infarcts

Before admission	1
No anticoagulants	4
Anticoagulants stopped	1
On anticoagulants—possible defect in control	1
Total	7

CASE HISTORIES

On 22.11.72, T. V., a 63-year-old man, sustained a severe head injury, multiple fractured ribs and a fracture dislocation of 6/7 cervical vertebra resulting in a complete cord transection below the 5 cervical segment. Initially he had several episodes of cardiac arrest secondary to pulmonary obstruction, a tracheostomy was performed and he also had several melaenas necessitating repeated transfusions. In view of the severity of his head injury and poor general condition he was not anticoagulated. On 25.1.73 he developed septicaemia and collapsed and died. At post-mortem he had a ruptured urethra, a coronary thrombosis and pulmonary emboli originating from the popliteal and post-tibial veins which were thrombosed. He also had multiple peptic ulcers including a perforated duodenal ulcer. In his case his general condition precluded anticoagulant therapy—he developed deep-vein thrombosis with pulmonary emboli which contributed to, but did not cause, his death.

On 13.4.72, T. L., a 14-year-old boy, whilst playing with his father's pistol, shot himself and sustained an injury to his liver, chest and spinal cord which was complete below T7. His abdomen and chest were explored by a thoracic abdominal operation. In view of the operation he was not anticoagulated. This view was confirmed by the fact that he had repeated melaenas which failed to respond to repeated transfusions. A laparotomy was performed on 9.5.72 which showed acute stress ulcers of the stomach. On 17.5.72 he collapsed from a massive pulmonary embolus originating in the left calf. The diagnosis of pulmonary embolism was supported by E.C.G. and enzyme studies. In view of the melaena he was still not anticoagulated. Despite the multiple injuries and the pulmonary embolism he survived and is now back at school.

On 13.10.72, K. S., aged 23 years, suffered a complete lesion at T12 as the result of a fall. He had a laparotomy at the receiving hospital for intra-abdominal haematoma and was therefore not given anticoagulants. He complained of pain in his left chest on 2.11.72. An X-ray showed a collapse. The next day a venogram showed a thrombosis in the left femoral vein the right being clear and the sonic aid negative. Anticoagulants were started on 4.11.72 but on the 6.11.72 although the prothrombin time was 26 per cent he had severe pain on the right-hand side of the chest accompanied by a haemoptysis and he subsequently developed a pleural rub. In his case the institution of anticoagulant therapy after an established deep-vein thrombosis did not prevent a subsequent pulmonary embolism. Two days' anticoagulant therapy will not prevent pulmonary emboli when the leg veins are already thrombosed.

DISCUSSION

This consecutive series of a hundred patients is comparable to those described by Guttmann (1963), Silver (1968) and Harris (1968) in composition

aetiology and incidence of associated injury. A similar incidence of deep venous thrombosis and of pulmonary embolism can thus be anticipated by other Units which follow a similar pattern of initial management to the National Spinal Injuries Centre. The rationale behind the treatment is that pulmonary emboli arise as a result of detachment of thrombi from the veins of the pelvis and lower limbs. To be effective, treatment must commence before they become thrombosed and continue after the risk period. The methods routinely performed—clinical inspection, the sonic aid and measurement by tape—will not diagnose pelvic vein thrombosis, they only detect thrombosis at the thigh and calf; only venography will do this and this was only carried out on 14 occasions. Nevertheless, it is striking that three patients who were not anticoagulated prior to admission had deep-vein thrombosis, and of the group of 32 who were not anticoagulated, eight developed overt deep-vein thrombosis, an incidence of 25 per cent, whereas of the 68 on anticoagulants only four developed deep-vein thrombosis, an incidence of five per cent, moreover, a further three patients developed deep-vein thrombosis after therapy was discontinued. Just as there is difficulty in establishing a diagnosis of deep-vein thrombosis, so too the diagnosis of pulmonary embolism can be difficult as it has so many different presentations even in normal subjects. It is especially difficult in paraplegic patients who cannot cough—so that the sign of haemoptysis will not be apparent and they are anaesthetic over the chest wall. So reliance has to be placed on ancillary methods of investigations such as E.C.G. enzymes and chest X-rays. Notwithstanding, there was a striking difference in incidence of pulmonary embolism in the treated and the untreated groups.

Only one patient out of seven had a pulmonary embolism while on anticoagulants and he (K. S.) had only been anticoagulated for two days before therapy could become effective.

Six patients had pulmonary embolism who were in the non-anticoagulant group. It might be argued that the groups are not comparable and that the 32 patients who were not anticoagulated were much more ill and more likely to develop deep-vein thrombosis. However, that is not borne out by inspection of the two groups. This is far less than in the untreated paraplegic patients. Comparison with the other series of Walsh and Tribe (1965), Cheshire (1968) and Watson (1968) would have led one to anticipate at least one death in this series of 100 patients—it is apparent that anticoagulant therapy does reduce the incidence of deep-vein thrombosis and that this has been accompanied by a reduction in the incidence of pulmonary embolism.

The length of treatment is controversial. Treatment was arbitrarily discontinued at 12 weeks since this was the time that bladder surgery was considered if the patient was not passing urine. This may be too short a time since three patients developed deep-vein thrombosis after treatment was discontinued. The therapy did not interfere with other forms of treatment. There were occasional small bleeds from the bladder; at such times therapy was discontinued, a catheter put into the bladder and a warm saline wash-out given. If the patient developed a haemothorax, therapy was stopped for 24 hours and vitamin K_1 was administered, the chest aspirated and therapy recommenced. There was nothing to suggest that it caused bleeding from the gastro-intestinal tract although four patients developed a bleed while on anticoagulants and a further three patients who were not on anticoagulants also bled. There were no cases of ascent of the lesion nor of hepatitis. Recently some of the patients who could not be anticoagulated have

been given low-dosage subcutaneous heparin. But as yet the numbers are too small to form an opinion as to its effectiveness. Apart from this series many other patients at this Centre and at the Liverpool Regional Paraplegic Centre have been anticoagulated and no patient who has been adequately anticoagulated has had a major pulmonary embolus. That means that they have been anticoagulated soon after injury before the leg veins have thrombosed. Once the leg veins have thrombosed anticoagulant therapy will not prevent a clot being detached.

The reason why patients with spinal injuries develop deep-vein thrombosis is of great theoretical and practical importance. Virchow showed that there are three major factors in any patient: one, an alteration in the properties of the flowing blood; two, a defect in the vein wall; and three, a stagnation of the venous return; all these factors are operative in paraplegic patients. In a paraplegic patient the paralysis of the muscles in the lower limb will reduce the venous return. This will be aggravated by immobilisation in bed. The reduction in speed of the blood changes the axial flow of the blood so that the platelets tend to be dispersed to the periphery and will be more likely to cause a thrombosis. The pelvic veins and vena cava are in close proximity to the pelvis, the vertebra and the bladder. When there are fractures of the vertebra there may be direct trauma to the veins at the time of injury and the development of a severe bladder infection may be transmitted through to pelvic veins, predisposing to thrombosis. In addition, in any major injury there are a complex of metabolic factors that predispose to deep-vein thrombosis.

It is apparent that there is a high incidence of deep-vein thrombosis and pulmonary embolism in acute paraplegic patients. This is certainly no less than in other patients with similar severe injuries not accompanied by severe paralysis. Perhaps all patients have small subclinical pulmonary emboli and this is in accordance with the views of Morrell and Dunhill (1968), who regard pulmonary emboli as a universal phenonema in a hospital population. The use of prophylactic therapy does seem to reduce the incidence of massive pulmonary emboli, and although it is a difficult regime to manage it can be carried out successfully.

Summary

One hundred unselected consecutive patients with acute spinal injuries were admitted between 15.4.71 and 17.3.73. Sixty-eight patients received prophylactic anticoagulant therapy by means of Phenindione. The dose was between 25 and 100 mg. daily and the duration of treatment was 12 weeks. Thirty-two patients were rejected for treatment due to severe associated injuries or on medical grounds. In the treated group there were only four deep-vein thrombosis and one pulmonary embolus. In the untreated group, there were eight deep-vein thrombosis and four pulmonary emboli. There were few complications and treatment was only discontinued in six patients. The regime appears to convey considerable benefits in preventing deep venous thrombosis and pulmonary embolus. The regime, results and complications are discussed.

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