Discussion

According to Herndon (1927), one of the most characteristic features of Charcot's spine is the disproportion between the severity of the process disclosed by the x-ray film and the slight discomfort and disability complained of by the patient. Usually, clinical evidence of tabes is present. One of the earliest and most constant signs is deformity which is due to bone destruction and subsequent compression of the vertebral body with posterior or lateral displacement. This process is usually limited to one or two vertebrae, and is most often found in the lower dorsal and lumbar spine. The resulting deformity is usually a kyphus with more or less lateral curvature and rotation. There is usually no tenderness and no muscle spasm.

Considerable discomfort is often caused by pressure of the collapsing spine or that of hypertrophic bone formation upon the spinal nerves. These root pains are usually gradual and insidious in onset and of moderate severity. Occasionally, however, they attain considerable intensity, somewhat simulating gastric crises or peptic ulcer pain. The mobility of the spine is little involved unless in cases of excessive destruction.

The existence of hereditary Charcot's spine has long been doubted, but it is now an acknowledged fact. Various observers consider many cases of apparent Pott's disease associated with other joint involvement in young children as luetic.

It is claimed that radiologically the alternation between sclerosis and rarefaction, bone absorption and bone apposition, is the most striking feature in Charcot's spine. In some cases the destructive, in others the proliferative, changes prevail. Often both are seen concomitantly.

The treatment of Charcot's spine consists in general anti-luetic therapy and local measures for support and immobilization of the spine.

Summary

Tabetic Charcot's spine probably occurs much more commonly than most textbooks lead us to believe. Severe persistent shooting pains, especially of a girdle distribution, should indicate an x-ray examination of the spine in order to rule out Charcot's disease. Brief case histories of eight tabetics with Charcot's spine are presented.

In Case 7 trauma would appear to have been a pre-disposing factor in the aetiology of the Charcot's spine.

We are indebted to Drs. M. M. Beveridge and A. I. Morrison, of the Department of Venereology, for assistance in the preparation of this paper.

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Because reports were being received that some nurses and doctors working both in hospital and in public health services were suffering from dermatitis after giving injections of streptomycin and penicillin, an inquiry was instituted into the best way of preventing it. As a result, recommendations for an improved injection technique for giving antibiotics were approved by the Standing Medical Advisory Committee of the Central Health Services Council and announced to hospitals and local health authorities (see *British Medical Journal*, 1953, 2, 40). The Ministry of Health has now made a ten-minute 16-mm. film to illustrate the technique. The film is for use in teaching student and postgraduate nurses, and is also suitable for showing to doctors, pharmacists, and medical students. Copies of the film may be hired (5s. for the first day, 1s. for subsequent days) from the Central Film Library, Government Building, Bromyard Avenue, Acton, London, W.3. The film was written and directed by Margaret Thomson and made by Basic Films.

VITAMIN K₁ IN ANTICOAGULANT THERAPY

BY

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Vitamin K₁ has proved to be a most potent antidote to anticoagulant drugs with a prothrombopenic action, and is clearly the antidote of choice in controlling the dangers of anticoagulant therapy. The use of large doses of vitamin K₁ in patients on anticoagulant therapy, with the consequential restoration of the blood prothrombin to normal or near normal levels, only, however, replaces the danger, or possible danger, of haemorrhage by that of a possible further thrombotic or embolic episode. In addition, large doses of vitamin K₁ are very likely to make the patient refractory to further anticoagulant therapy. Valuable time may therefore be lost in assessing the correct dose of the anticoagulant drug required to restore and maintain an adequate reduction in the blood prothrombin level. Therefore, whenever it is intended to continue anticoagulant therapy it is essential to use vitamin K₁ with the utmost discretion and to prescribe, so far as is possible, the *minimum* effective dose.

Assessment of Minimum Effective Dosage

To assess the minimum effective dose of vitamin K₁ required to antagonize the action of anticoagulant drugs is not easy. In addition to the actual level of the blood prothrombin (which is, of course, in itself very important) and the presence or otherwise of haemorrhage, several other factors must be considered, including the type of anticoagulant used and the general condition of the patient. Long-acting cumulative anticoagulants such as dicoumarol, phenylpropyl-hydroxycoumarin ("marcoumar"), and cyclocumarol ("cumopyran") require larger doses of vitamin K₁ than the short-acting anticoagulants, such as phenylindandione ("dindevan") or ethyl biscoumacetate ("tromexan").

The stage of anticoagulant therapy reached must also be taken into account; sometimes in the first few days of anticoagulant therapy, owing to the unavoidable difficulty of assessing the correct dose of the anticoagulant, the blood prothrombin may be reduced to too low a level. In most cases merely withholding further doses of the anticoagulant will then be sufficient to restore the prothrombin content to within a therapeutic and safe range. Where, however, the blood prothrombin is so severely reduced that haemorrhage is likely it is wise to give vitamin K₁, but small doses will in most cases be effective. This is because, unless the dose of the anticoagulant has been grossly miscalculated, there is no large accumulation of the anticoagulant in the body which would require large doses of vitamin K₁ to counteract its effect.

The general condition of the patient is also of prime importance in assessing the minimum effective dose of vitamin K₁ required to antagonize the action of anticoagulant drugs. For example, the presence of heart failure, shock, or deficient renal or liver function will mean that large doses of vitamin K₁ are needed if it is to be effective. The only failure met with in vitamin K₁ therapy has been in desperately ill patients who subsequently died within a short period.

It has been shown previously (Toohey, 1952) that 500 mg. of vitamin K₁, given orally, is entirely effective in antagonizing and controlling haemorrhage due to massive doses of such anticoagulants as dicoumarol, phenylindandione, and ethyl biscoumacetate. Such massive doses of anticoagulants as were used in these experiments would not, however, normally be given in clinical practice; nor, therefore, are

such large doses of vitamin K₁ needed. In the series of experiments under review in this paper doses of vitamin K₁ varying from 5 to 50 mg. were given orally on approximately 96 different occasions to 70 patients on anticoagulant therapy, and as a result it was found that these smaller doses of vitamin K₁ were always effective in counteracting the action of the anticoagulant drugs except in two instances (see later).

Classification of Cases

Most of the uses of vitamin K₁ in anticoagulant therapy may be considered in connexion with the following three groups of cases. Group 1: Cases of frank haemorrhage or of a severe lowering of the blood prothrombin to a dangerous level in which it is not intended to continue with anticoagulant therapy. Group 2: Cases of frank haemorrhage in which it is intended to continue with anticoagulant therapy. Group 3: Cases of severe lowering of the blood prothrombin to a dangerous level, with or without minimal haemorrhagic manifestations, in which it is intended to continue with anticoagulant therapy.

Group 1.—In this group little difficulty should arise. As anticoagulant therapy is not being continued, fairly large doses of vitamin K₁ can be given. If the anticoagulant in use is one of the short-acting variety (phenylindanedione, ethyl biscoumacetate), then 20–25 mg. of vitamin K₁ will be sufficient. If, however, long-acting anticoagulants (dicoumarol, phenylpropyl-hydroxycoumarin, cyclocoumarol) are in use, the initial dose of vitamin K₁ should be 25 to 50 mg., according to the degree of haemorrhage. This dose may in a few cases have to be repeated. Doses of vitamin K₁ in the region of 25 to 50 mg. will in nearly all cases result in the blood prothrombin level returning to normal or near normal. In addition, the patient may become refractory to further anticoagulant therapy for some days. As, however, it is not intended to continue with anticoagulant therapy this factor can be ignored.

Group 2.—It is in this group of patients that most anxiety will arise. Here it is essential to give a dose of vitamin K₁ sufficient to restore the blood prothrombin quickly to a safe level. At the same time the prothrombin must be kept within a safe therapeutic range, otherwise a further thrombo-embolic episode may occur. Also, as mentioned above, too large a dose of vitamin K₁ may render the patient refractory to further anticoagulant therapy for a few days. If the patient is receiving the short-acting anticoagulants, 15 mg. of vitamin K₁ should in most cases be enough. Larger doses than 15 mg. should be given only in exceptional cases. If, however, the patient is receiving the long-acting anticoagulants, 15 to 25 mg. of vitamin K₁ should be given, depending on the urgency of the case. The lower the blood prothrombin level, the more severe the haemorrhage, and, most important, the more seriously ill the patient, the larger the dose of vitamin K₁ required. It is in this group of patients with a severe reduction in the blood prothrombin accompanied by frank haemorrhage that most difficulty will arise in estimating the correct dose of vitamin K₁. Frequent blood prothrombin estimations are essential to assess the response to treatment and to decide whether further doses of vitamin K₁ are necessary.

Group 3.—In this group, in which there is a severe reduction in the blood prothrombin, but no or only minimal haemorrhagic manifestations, the urgency and anxiety are not as great as with patients in Group 2. For nearly all patients receiving the short-acting anticoagulants 5 to 10 mg. of vitamin K₁ will be sufficient. Patients receiving the long-acting anticoagulants will need slightly larger doses of vitamin K₁, but it is rarely necessary to give more than 15 mg., at least as an initial dose.

For all patients it is best to assess the response to vitamin K₁ therapy by means of prothrombin estimations taken about eight hours after the initial dose. In patients in Group 3, however, in whom there is no evidence of bleeding, it is usually sufficient to do the first prothrombin estimation after vitamin K₁ therapy the following day if this is

more convenient. In Group 2 patients, however, especially those receiving the long-acting anticoagulants, prothrombin estimations should be *routinely* made eight (or even six) hours after the initial dose of vitamin K₁. If an appreciable rise in the blood prothrombin level has not occurred a larger dose of vitamin K₁ should then be given.

Results of Vitamin K₁ Therapy

Given in the doses quoted above, in only 2 out of 70 patients did vitamin K₁ fail to have an effect. Both patients were seriously ill, suffering from myocardial infarction accompanied by shock and heart failure, and both died several days after admission to hospital. It was realized that each was desperately ill, and smaller doses than usual of the anticoagulant drugs were given. Nevertheless, the blood prothrombin fell to a dangerously low level, with microscopical haematuria in one case. Repeated doses of 20 to 25 mg. of vitamin K₁ had only a slight effect in raising the blood prothrombin. At necropsy there was no sign of haemorrhage in either case.

Desperately ill patients with signs of shock and heart failure therefore need initial doses of 25 mg. of vitamin K₁, even when there is little or no haemorrhage, in order to counteract the effect of anticoagulants, especially the long-acting ones. If there is no response to this initial dose—that is, if there is no rise in the blood prothrombin after six to eight hours—then 50 mg. of vitamin K₁ should be given. If a patient fails to respond to vitamin K₁ therapy it is an ominous prognostic sign, and it will be found that most such patients die.

In conclusion it should be stressed that vitamin K₁ is a most powerful drug, and unless the dose is carefully controlled its use will give rise to added difficulties in anticoagulant therapy. Vitamin K₁ should therefore be used only if haemorrhage has occurred as a result of anticoagulant therapy or if the reduction in the blood prothrombin is so great that haemorrhage is very likely to develop. In most patients, except those who are extremely ill, merely withholding further anticoagulant therapy will be enough to raise the blood prothrombin to a safe level without the need to use vitamin K₁. This is especially true when the short-acting anticoagulants are used. With the long-acting cumulative anticoagulants vitamin K₁ therapy will, however, be more often required.

Conclusions and Summary

In 68 patients out of 70 on anticoagulant therapy, vitamin K₁, in oral doses of 5 to 50 mg., was entirely effective in counteracting the action of the anticoagulant and restoring the blood prothrombin to a safe level. In two of these patients in whom slight haemorrhage (haematuria) had occurred the bleeding soon ceased. In only 2 of the 70 patients did vitamin K₁ fail to have effect. Both these patients were extremely ill and died from heart failure and shock following myocardial infarction.

Vitamin K₁ should be used only if haemorrhage has actually occurred or if the blood prothrombin is so low that haemorrhage is very likely to develop. Uncontrolled vitamin K₁ therapy may rescue the patient from the danger or possible danger of haemorrhage, only to render him liable to the risk of further thrombo-embolic phenomena.

In all cases in which it is intended to continue with anticoagulant therapy the *minimum* dose of vitamin K₁, which will be effective in restoring the blood prothrombin to a safe therapeutic range must be aimed at. In assessing this minimum effective dose of vitamin K₁, the general condition of the patient and the type of anticoagulant used are most important, in addition to the actual blood prothrombin level.

Patients receiving the short-acting anticoagulants require only small doses of vitamin K₁ to restore the blood prothrombin to a safe therapeutic level. In nearly all cases 5 to 15 mg. will be sufficient, and it is rarely necessary to exceed 15 mg.

Patients receiving the long-acting anticoagulants require larger doses of vitamin K₁ if the desired effect is to be achieved, but 10 to 25 mg. will usually be enough. The larger doses of vitamin K₁ should be given if haemorrhage has actually occurred or if the patient is desperately ill, especially if there are signs of shock and heart failure.

In cases of frank haemorrhage in which it is not intended to continue with anticoagulant therapy 25 to 50 mg. of vitamin K₁ should be given. The larger dose should be administered to patients who had been given the long-acting anticoagulants and also to the more seriously ill patients.

Response to vitamin K₁ therapy should be assessed by estimation of the blood prothrombin six to eight hours after the initial dose of vitamin K₁. If an appreciable rise in the prothrombin level has not occurred a larger dose of vitamin K₁ must be given.

I wish to thank Roche Products Ltd. for the generous supplies of the vitamin K₁ used in this work.

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Medical Memorandum

Orthograde and Retrograde Intussusception

Although it is stated that 80% of cases of intussusception occur in patients under 2 years of age, this was not my experience in North Szechwan, China. A number of cases were seen in adults of all ages and some in older children, but none in infants or young children. Although sometimes there was obvious cause such as a pedunculated tumour of the ileum or inflammatory swelling of a mobile caecum, often none was found. The following two cases were different from usual in that both also had retrograde intussusceptions. Although such a condition is not unknown, it seems uncommon enough to merit reporting.

CASE 1

A man aged 24 was seen in the out-patient department on October 31, 1949, complaining of abdominal pain for a little more than a month. He was admitted with a diagnosis of intussusception. Amoeboma was thought to be a possible cause, and therefore general treatment and a course of emetine injections were prescribed. This seemed justified by improvement in symptoms and resolution of the palpable mass, but one week later acute symptoms recurred with an enlarging mass in the right upper abdomen.

Laparotomy was performed under general anaesthesia. There was an intussusception of the terminal 3 in. (7.5 cm.) of ileum into the caecum and ascending colon, almost to the hepatic flexure. In addition there was a reverse intussusception of about 3 in. of the right half of the transverse colon, thus leaving a small length of normal colon at the hepatic flexure. Both intussuscepta were reduced with comparative ease; a lump about the size of a walnut could then be felt in the caecum. An end-to-side ileo-transverse colostomy was then performed. Three weeks later, under spinal anaesthesia, right hemicolectomy was performed, from which the patient made a good recovery.

On macroscopic examination of the specimen the wall of the caecum was found to be much thickened; there was no ulceration or definite tumour. Unfortunately, microscopical examination was not possible.

CASE 2

A boy aged 11 was admitted on November 3, 1951, with a diagnosis of intussusception and acute intestinal obstruction for about one day. During the previous six weeks he had been seen at intervals in the out-patient department complaining of abdominal pain and a lump. Apart from slight distension and poor nutrition, no definite physical signs had been noted. Ascariasis had been treated successfully, and the possibility of tuberculous peritonitis (which is common in the district) had been considered.

On admission he was seriously ill and dehydrated; the abdomen was distended and there was a large firm mass on the left side: this seemed to be a large mass in the left hypochondrium, with a smaller one rather lower and a small gap between. The apex of the intussusception could be felt about 1 in. (2.5 cm.) within the anal canal.

After saline infusion, laparotomy was performed under general anaesthesia (ether with an Oxford vaporizer). Considerable difficulty was experienced in determining the true condition—namely, an intussusception starting in the terminal ileum and traversing the whole colon to the anus; and also a secondary reverse intussusception of the primary intussusception (all three layers) starting about the middle of the descending colon and extending back to the middle of the transverse colon, thus making the big mass palpable before operation. The apex of the intussusception could be reached only with the help of an assistant pressing digitally per anum, but even then reduction could not be effected. With considerable difficulty the secondary intussusception was first reduced by combined movements—digital dilatation of the secondary intussusceptions, pressure on the secondary apex, and gentle traction. When this was eventually reduced the primary intussusception was reduced with great ease. The gut was carefully examined, but, apart from deep congestion, oedema, and plastic exudate, there was no obvious pathological condition to account for the intussusception, nor was there serious question of viability. The whole colon from caecum to rectum was exceedingly mobile with long mesenteries. The colon was replaced in the approximate anatomical position and the abdomen closed.

The patient made an uninterrupted recovery; two and a half months later he was well and obviously gaining weight.

COMMENT

Aetiology.—The cause in Case 1 was thought to be inflammatory thickening of the caecum, but in several such cases I have wondered whether the caecal thickening was primary or secondary to the intussusception. Histological examination has not been possible. In Case 2 it was obviously a chronic condition with partial resolution over a period of several weeks, possibly initiated by ascariasis; the exceptionally mobile colon can be regarded as a facilitating factor. Disordered peristaltic movements seem the only explanation of the retrograde intussusceptions, though not a complete one.

Treatment.—The remittent course of both these cases raises the question whether intussusception ever undergoes complete reduction spontaneously. At operation one often finds that reduction is comparatively easy except for the last inch or so. Is this the condition during symptomatic remissions? If so, then earlier exploration is called for. In Case 2 the diagnosis was missed and operation delayed till it was almost too late, because insufficient importance was attached to the boy's description and no lump was felt when he attended the out-patient department. It is not usual to do anything to prevent recurrence unless there is an obvious removable cause. Such has been my practice, except that resection, immediate or delayed, has been done in cases with a suspicious lesion in the caecum. This course was successfully followed in Case 1. In Case 2 nothing was done beyond replacing the colon anatomically, in the hope that the exudate would form some anchoring adhesions. The condition at operation precluded anything further, and the subsequent course seemed entirely satisfactory.

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