Discussion

When pethidine alone is used as an analgesic in labour it has been found that from 9 to 21% of the babies are depressed at birth (Gilbert and Dixon, 1943; Gallen and Prescott, 1944; Cripps *et al.*, 1944; O'Reilly, 1948; Davis and Tupper, 1949; Paterson and Prescott, 1954) even though the drug is withheld for a few hours before delivery. Series A confirmed this. By mixing an antagonist with pethidine this effect can largely be eliminated. However, if too much antagonist is used the analgesic action of pethidine may be interfered with, so that the least amount of antagonist required to prevent respiratory depression is thought to be the correct amount to use.

In series D depression at birth attributable to the pethidine mixture was virtually unrecognizable, so that it is likely that there is no lack of levallorphan in the mixture used. The results of using a mixture of pethidine 100 mg. with levallorphan 1.25 mg. in a larger series of 1,000 cases will be offered for publication.

Summary

A series of 130 patients consecutively admitted in early labour to one of two maternity wards were given intramuscular doses of pethidine 100 mg. premixed with levallorphan 2 mg., with the object of preventing neonatal respiratory depression. In all, 317 injections were given. The mean dosage of pethidine to each patient was 242 mg. Injections were started at two fingerbreadths' dilatation of the cervix, and were repeated as required through labour. Gas-air or "trilene"-air was given in the later stages.

Of the patients 42% had two injections, 26% had one, one patient had nine, and the remainder (33%) had three to eight injections. Analgesia from the injections was good in 76%, poor or nil in 3%, and fair in the remainder. Of 48 patients questioned on the point, 60% preferred the injections to gas-air as more effective. Amnesia was good in 33%, nil in 3.2%. 89% of the babies cried within 60 seconds and required no treatment; 8% were moderately and 2% severely depressed at birth, but none required stimulants, intubation, or intragastric oxygen. There was one stillbirth due to ante-partum haemorrhage. The incidence of operative deliveries, prolonged labours, and post-partum haemorrhage was not increased. The results of this series are compared with three previous series from the same unit, in which pethidine alone and mixtures of pethidine and nalorphine were used.

It is suggested that, by mixing an antagonist with pethidine, more of the latter drug can be given, providing better analgesia without causing an increased incidence of neonatal asphyxia.

Relevant statistics from the maternity unit at Dartford over the years before and after the introduction of pethidine-antagonist mixtures are given, showing no evidence of adverse effects on mothers and babies.

Roche Products Ltd. supplied ampoules of premixed pethidine and levallorphan. Burroughs Wellcome Ltd. supplied ampoules of premixed pethidine and nalorphine. The patients were under the care of Drs. G. Dalley, W. A. Chester, and W. Gross, obstetricians to the maternity unit, West Hill Hospital, Dartford. Anaesthetics were given by the consultant and junior staff of the Dartford Group of Hospitals. Labours were conducted by, analgesia was administered by, and statistical data were collected by the

staff midwives (superintendent Miss M. Gantry), to whom special thanks are due for their co-operation.

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SUBACUTE COMBINED DEGENERATION OF SPINAL CORD AFTER EXTENSIVE RESECTION OF ILEUM IN CROHN'S DISEASE

REPORT OF A CASE

BY

C. N. BEST, M.B., M.R.C.P.Ed.

Senior Medical Registrar, St. Peter's Hospital,
Chertsey, Surrey

Subacute combined degeneration of the spinal cord (S.C.D.) due to non-Addisonian megaloblastic anaemia is a rare but well-authenticated entity, and the subject has been comprehensively reviewed by Richmond and Davidson (1958).

This report records a case following extensive ileal resection performed for Crohn's disease.

Case Report

A man aged 46 was admitted to this hospital in August, 1958, complaining of paraesthesiae in the feet and hands, tightness and a burning sensation affecting the feet, with weakness of the ankles and knees for six weeks. For about three months he had noticed progressive visual fatigue during his clerical occupation and had become progressively irritable, depressed, and disinterested. He had been unable to feel the ground with his feet for a few days, and admitted that his tongue had recently been sore around the margins.

Past History

In 1940, after appendicectomy at another hospital, a faecal fistula developed, and in 1941 a short-circuit operation was performed for what was found to be Crohn's disease. In 1942 the diseased area of bowel was excised and an end-to-end anastomosis performed.

He was first seen at this hospital in 1949 with recurrent abscess formation in the right inguinal fossa and small-

intestine obstruction. The abscess was drained on two occasions, and later a short-circuit operation was performed.

In 1955, after further episodes of abscess formation and intestinal obstruction, the whole diseased area of bowel was excised and end-to-end anastomosis performed. The specimen showed several kinked loops of ileum adherent to a mass of mesenteric fat containing many enlarged lymph nodes. The microscopical appearances were those of long-standing Crohn's disease complicated by the presence of considerable talc granuloma changes.

Prior to operation his haemoglobin was 9.3 g./100 ml. (63%) and the red cells showed anisocytosis and polychromasia, but appeared well haemoglobinized. After operation his condition improved considerably and he gained 30 lb. (13.6 kg.) in weight in spite of a tendency to pass frequent soft stools, one of which contained 59% fat by dried weight and showed on microscopy a few undigested meat fibres and soap plaques.

In June, 1956, he was readmitted with a marked macrocytic anaemia, recent loss of weight, and frequent soft, pale stools. Though there was macroscopic steatorrhoea a single stool analysis showed only 27% fat by dried weight. His haemoglobin was 6.4 g./100 ml. (43%), M.C.V. 153 cubic microns, and M.C.H.C. 32%. There were 2,000 white cells per c.mm., with a normal differential count. He was treated with a low-fat, high-protein diet and oral folic acid 5 mg. twice daily. On this regime his haemoglobin rose to 10.7 g./100 ml. (72%), with a maximum reticulocyte response of 33% on the sixth day. His stool frequency decreased to twice daily and he gained weight. He continued taking folic acid, but was not seen again until the time of his latest admission.

Condition on Admission

He was a swarthy-complexioned, well-built man weighing 140 lb. (63.5 kg.). Apart from a much-scarred anterior abdominal wall the abnormal physical findings were confined to the nervous system. The tongue was well papillated.

His gait was ataxic, with absent joint sense in the feet and ankles. Vibration sense was absent in the ankles and feet, and there was bilateral loss of light touch, with some hyperaesthesia to pinprick, in a sock distribution. The calf muscles were not tender and there was mild weakness of dorsiflexion of the right ankle-joint. There was bilateral unsustained patellar clonus with brisk knee- and ankle-jerks. The biceps, supinator, and triceps jerks were all equal and brisk; both upper abdominal reflexes were present, and both plantar responses were extensor.

Investigation

Haemoglobin, 12.2 g./100 ml. (82%); M.C.H.C., 31%; reticulocyte count, 2%; white-cell count 7,000/c.mm., with a normal differential. The red cells appeared normochromic, with a moderate degree of anisocytosis. Serum vitamin-B₁₂ level, 25 µg./ml. (normal, 140-900). Sternal-marrow examination showed active megaloblastic erythropoiesis with normal leucopoiesis. A histamine test meal showed a normal level of free acid. Faecal fat studies showed a daily excretion averaging 19.5 g. over a three-day period on a normal ward diet.

Absorption of ⁵⁷Co-labelled Vitamin B₁₂.—After several days of intramuscular vitamin-B₁₂ therapy, urinalysis following an oral dose of ⁵⁷Co-labelled vitamin B₁₂ showed that there was no significant absorption of this from the gastro-intestinal tract, even when intrinsic factor was administered at the same time. Six months later, after a five-day course of oral chlortetracycline, 250 mg. q.d.s., there was no improvement in vitamin-B₁₂ absorption when accompanied by intrinsic factor.

X-ray Studies.—No abnormality was observed in a chest x-ray film, and small-bowel studies showed a normal mucosal pattern with no stasis.

Progress

On cessation of folic-acid therapy and the intramuscular administration of 250 µg. of vitamin B₁₂ twice daily, the patient made a remarkable recovery. After 48 hours he was able to feel the ground again, and in eight days the only abnormal finding was of diminished vibration sense in the metatarsus.

Six months later he was symptom-free on a low-fat diet and a weekly intramuscular injection of 1,000 µg. of vitamin B₁₂. He had gained weight, and the optic fundi showed no abnormality. His haemoglobin had risen to 14.1 g./100 ml. (95%), with an M.C.V. of 90 cubic microns and an M.C.H.C. of 30%. He said that his legs had taken six weeks and his visual and personality changes three months to return to their normal state.

Discussion

Though the diagnosis of S.C.D. in this case rests mainly on the transient extensor plantar responses, the visual and personality symptoms suggest that there was more than peripheral neuritis present. The serum vitamin B₁₂ was also at the very low level at which S.C.D. occurs.

The acute onset of symptoms may be attributable to the previous administration of folic acid, and the rapid recovery to the withdrawal of folic acid and the administration of large doses of vitamin B₁₂.

There is no doubt that during the various operations the major portion of this man's ileum had been removed, and microscopic submucosal extension of Crohn's disease may have further impaired absorption from the remaining ileum. There was no evidence of the presence of intestinal blind-loops.

Though in recent surveys of the effects of massive resection of the small intestine (Jackson, 1958; Pullan, 1959) it is stated that megaloblastic anaemia has not been shown to follow resection of the small bowel, it has been observed (Mollin *et al.*, 1957; Booth and Mollin, 1959) that not only is vitamin B₁₂ normally absorbed from the ileum, but that vitamin-B₁₂ absorption was grossly impaired in five cases of massive ileal resection. One of these cases showed a marked megaloblastic anaemia, with a serum vitamin-B₁₂ level of 25 µg./ml., and was presumably at risk of developing S.C.D. In these cases a course of oral chlortetracycline produced no increase in vitamin-B₁₂ absorption, in contrast to the frequent subsequent increase when intestinal blind-loops are present.

The above case illustrates the danger of a too facile administration of folic acid to patients with megaloblastic anaemia secondary to lesions of the small intestine.

As Booth and Mollin (1959) suggest, after operations involving resection of more than 6-8 ft. (1.8-2.4 metres) of ileum, patients should be kept under regular haematological observation. However, demonstration of a normal vitamin-B₁₂ uptake about one year after operation would presumably make this lifelong supervision unnecessary, assuming that iron intake is adequate.

Summary

The case of a patient with subacute combined degeneration of the spinal cord following extensive ileal resections for Crohn's disease is reported.

The very low serum vitamin-B₁₂ level was compatible with the diagnosis, and there was no significant

absorption of radioactive vitamin B₁₂ from the intestine either when administered with intrinsic factor or after a course of chlortetracycline.

The dangers of folic-acid therapy in this type of case are confirmed.

I thank Dr. O. R. L. Plunkett for permission to publish this case, and Dr. D. L. Mollin for the vitamin-B₁₂ studies carried out at the Postgraduate Medical School of London.

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TWO TYPES OF LUPUS ERYTHEMATOSUS CELL FACTOR, SHOWN BY INDUCED L.E. CELL PHENOMENON IN MAN

BY

G. BENCZE, M.D.

J. KOVÁCS, M.D.

AND

J. CSERHÁTI, M.D.

From the First Medical Clinic, University of Szeged,
Hungary

In a previous publication we have shown that typical lupus erythematosus (L.E.) cell formation can be induced by the transfusion of plasma from cases of systemic lupus erythematosus into patients with various other diseases (Bencze *et al.*, 1958a).

The present communication reports further experiments on similar lines and shows that the plasma factor from patients with systemic lupus erythematosus may or may not be transferable.

Method

Plasma was taken from six patients with typical clinical signs of systemic lupus erythematosus in whom the L.E. cell formation had been repeatedly demonstrated. The blood was taken into citrate (16 ml. of 3.8% sodium citrate per 100 ml. of blood) and kept for 23 hours at +4° C. It was then kept at 37° C. for one hour and transfused (at 24 hours from taking).

The examination for L.E. cells was made by Zinkham and Conley's (1956) rotation method, and was positive at that time in all donors.

The recipients chosen had neoplastic disease (detailed in column 2 of the Table, which also includes the three experiments previously reported). One recipient was transfused with plasma from three systemic lupus erythematosus donors and another with plasma from two such donors. Before transfusion, the L.E. cell phenomenon was absent in all recipients.

Results

Plasma from patient O.P. produced L.E. cells in all five of the subjects transfused, even when given in amounts as small as 70 ml. (see Table). These cells lasted for between 6 and 27 days. In two of these five subjects previous transfusions from other L.E. patients had been negative. (In one of them the negative transfusion had been given from two systemic lupus erythematosus cases 21 and 26 days before, and in the other a negative transfusion was given 18 days before.) Nucleophagocytosis and tart cells were present in patient P.F. at two, four, and six hours, but no L.E. cells. The L.E. cells produced were typical and showed a positive Feulgen reaction (Bencze *et al.*, 1958b). In one of the experiments (fifth line of Table) guinea-pig complement was added *in vitro* without producing L.E. cells since Formijne and van Soeren (1958) have claimed that complement is necessary for the phenomenon. Only one other out of the total of six donors gave positive results (line 10 of Table).

Discussion

We deduce from the above experiments that the failure to show L.E. cells after transfusion of plasma from a lupus erythematosus patient is not due to a peculiarity of the recipient but because there are two types of L.E. plasma factor, one transferable and one not transferable.

Summary

Further experiments on the transfusion of plasma from patients with systemic lupus erythematosus into patients with neoplastic disease have shown that only two out of six donors gave positive results. This did not seem to be related to the amount transfused.

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Table of Results

Recipient			S.L.E. Donor			Recipient (Days After Transfusion)										
Age and Sex	Diagnosis	Blood Group	Initials	Blood Group	Vol. Given ml.	2/24	6/24	1	2	4	6	8	10	15	27	Transfusion Reaction
M 24	Hodgkin's disease	B	O.P.	AB	200	++++	++++	++++	++++	+++	++++	++++	++	+	+	0
M 72	Cancer of prostate	O	O.P.	AB	200	++++	++++	++++	++++	++++	++++	++	++	+	+	0
F 52	" " ovary	A	O.P.	AB	140	++++	++++	++++	++++	+++	++	++	++	+	+	+
M 65	" " lung	A	A.J.	B	190	0	0	0	0	0	0	0	0	0	0	0
M 65	" " "	A	P.J.	O	170	0	0	0	0	0	0	0	0	0	0	+
M 65	" " "	A	O.P.	AB	180	+++	+++	+++	++	++	+	0	0	0	0	0
M 68	" " "	O	P.F.	A	200	0	0	0	0	0	0	0	0	0	0	++
F 45	" " breast	B	J.J.	A	200	0	0	0	0	0	0	0	0	0	0	0
F 45	" " "	B	O.P.	AB	70	+++	+++	+++	++	++	++	+	0	0	0	0
M 60	" " prostate	AB	T.I.	A	200	+++	++++	+	+	+	0	0	0	0	0	+