previous authors. In part, this is due to an increasing proportion of minimal lesions and fewer with moderately or far-advanced disease, but half of our patients were already moderately advanced. Comparison of the pattern of haemoptysis showed curiously larger amounts of blood recorded by those with minimal disease (six out of seven patients had noted 5 ml. or more of blood, compared with three out of seven with moderately advanced disease). But those with cavitary disease recorded a *repeated* haemoptysis in six out of seven, compared with only three out of seven with minimal disease. Apart from these differences, we could determine no other feature peculiar to haemoptysis in active pulmonary tuberculosis. Only one of these patients presented with a normal *x*-ray picture. She was a young woman aged 20 who was already attending the contact clinic. Her minimal lesion came to light 10 months after her haemoptysis and would, in any case, have been discovered.

Among those with quiescent pulmonary tuberculosis the haemoptysis was usually a single episode with only streaking of the sputum. In none of these patients was there any late reactivation of their tuberculous foci and, indeed, the haemoptysis was probably coincidental.

The character and degree of bleeding among our patients with bronchiectasis approximated to the pattern, for patients with active pulmonary tuberculosis. There was no difference between patients with cylindrical (8) or saccular (9) bronchiectasis.

In bronchial carcinoma the notable feature of the haemoptysis was its *duration*, which in the majority was at least two weeks. During this same year we saw 26 new patients with bronchial carcinoma, of whom 14 had haemoptysis. In 13 of these 14 patients a tumour was seen at bronchoscopy, and in 11 there was histological proof (seven squamous cell, one adenocarcinoma, and three anaplastic). These numbers were too small to recognize differences in the history of haemoptysis.

The problem of the patient with haemoptysis and a normal *x*-ray picture of the chest has been discussed by Mitchell (1955), who, among 30 such patients, found four with proved carcinoma and another two probable. Somner *et al.* (1958) report 93 patients, five of whom had bronchogenic carcinoma, and they note that these tumours all came from the 55 patients over the age of 40. Including 26 with calcified primary foci, 194 of our patients had a normal *x*-ray picture of the chest and only three of these were found to have a bronchial carcinoma (two proved, and one probable in an elderly patient who died at home). These three patients were men over the age of 40. The likelihood of carcinoma in a man over the age of 40 with an *x*-ray picture of the chest which shows nothing abnormal is therefore probably no higher than one in eight. We agree, however, with Somner *et al.* (1958) that bronchoscopy is advisable in men over 40 with a record of haemoptysis, even though their chest radiographs are normal.

At the start of this survey we felt that some follow-up of patients with haemoptysis was necessary, but it was a matter of conjecture how long this should be. We believed then that a year was necessary and two years desirable. The evidence we have accumulated from this series of patients shows that follow-up is not necessary.

Conclusions

Among 324 patients with haemoptysis we have been unable to find a cause in 145 (44%). Inflammatory conditions of the bronchi, chronic bronchitis, and bronchiectasis accounted for 30% of the total and were more than seven times as frequent as either bronchial carcinoma or active pulmonary tuberculosis. Calcified primary complexes may render patients more prone to haemoptysis, though the mechanism is in doubt and we have no proof of a causal relation. Systemic hypertension is an uncommon cause of haemoptysis.

In carcinoma, haemoptysis tends to be minimal but persistent; a frank haemoptysis is unusual and the certainty of the haemoptysis may be in doubt. It is still an important and frequent symptom in this disease.

In active pulmonary tuberculosis there is a brisker bleeding of short duration and the incidence of this symptom has declined.

We confirm that the amount of bleeding is no index of the underlying pathology.

Over a two-year period 89.8% of these patients were followed up. So little change was shown that we believe that follow-up is not necessary, provided the patients are carefully assessed at the first examination. In men over the age of 40, in whom the risk of carcinoma is higher, bronchoscopy is an essential part of the initial investigation.

We gratefully acknowledge the help and interest of Professor I. G. W. Hill in the preparation of this paper. We are indebted to Mr. Martin Fallon for details of patients investigated in the regional thoracic surgical unit, and to many practitioner colleagues for help in tracing patients.

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CLINICAL EVALUATION OF PROMAZINE AS AN ADJUNCT TO PREDELIVERY SEDATION

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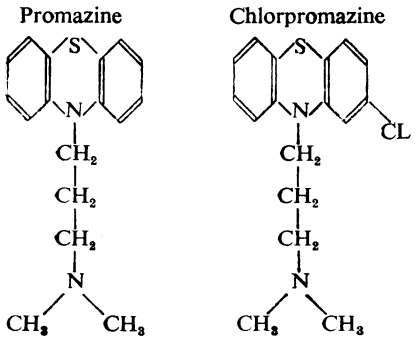
In recent years little progress has been made in obstetric practice with regard to analgesia and sedation in labour. The principal drugs used universally are still the barbiturates, pethidine hydrochloride, morphine and its derivatives, and scopolamine. None of these, however, satisfies the requirements of the ideal analgesic in obstetric practice. With the advent of the tranquillizing drugs, it was hoped that a new agent might be found which would provide satisfactory neuromuscular relaxation with relief of pain and tension in labour without untoward side-effects on either the mother or child.

Attention was directed to the phenothiazone series because of the potentiating effect of the various compounds in this group on hypnotics and analgesics. The effect of chlorpromazine as a sedative in labour has been reported by several authors (Karp *et al.*, 1955; Anz and Smith, 1956; Schaffer, 1956; Norton *et al.*,

1956). The results, however, have been disappointing and unreliable, and the risk of a precipitate fall in the blood-pressure when the drug is administered intravenously has proved an alarming side-effect.

A related compound, promazine ("sparine"), has a similar chemical structure to chlorpromazine, but lacks the chlorine atom. The difference in chemical structure is shown in the formulae.



Promazine has a depressive action on the subcortical centres of the central nervous system, reducing the intensity of abnormal stimuli without producing undue sedation or alteration in autonomic function. This blocking of afferent stimuli lessens emotional tension and decreases the awareness of pain, which should be of value during labour (Carlo, 1957; Himwich, 1958).

Toxic Effects

Few toxic effects of the drug have been published. Woodward and Solomon (1956) first reported a fatal case of agranulocytosis on the forty-eighth day of promazine therapy in a psychiatric patient. Several other cases have been published since (Cook *et al.*, 1957; Earle, 1957; Glaser and Adams, 1958). In a report to the A.M.A. Council on Drugs (1957) 18 cases of blood dyscrasia associated with promazine hydrochloride were listed, four of which ended fatally. In each of these reports the drug had been given for a prolonged period in the treatment of psychiatric conditions. Moore (1957) discussed the development of local reaction at injection sites, due probably to leakage into subcutaneous tissue. Opinsky *et al.* (1958) reported a case, which was later commented on by Root (1959) and Hamelberg (1959), in which arterial spasm and peripheral gangrene followed the presumed intra-arterial injection of promazine hydrochloride.

Buckmaster (1957) described a case of overdosage of promazine in a barbiturate addict who had taken 2,200 mg. of the drug. Though there was a considerable fall in blood-pressure, no respiratory depression or anoxia occurred.

Promazine hydrochloride would therefore seem to be a less dangerously toxic drug than chlorpromazine hydrochloride.

Previous Work Carried Out

Numerous publications have appeared describing the use of promazine in psychiatric disorders, but there have been only four reports on its use in labour. Sprague (1957) reported a series of 677 unselected cases in which promazine was administered during active labour. After an initial trial in 27 cases, 650 patients were given promazine hydrochloride, 50 mg., combined with pethidine hydrochloride, 50 mg., and scopolamine, 1/100 gr. (0.65 mg.), by intravenous injection when labour was established. He claimed excellent analgesia in 86% of cases and a good result in a further 13%. Labour was generally shorter and no foetal respiratory depression was observed. Side-effects were claimed to be minimal, two cases developing a mild hypotension and one a thrombophlebitis at the site of injection.

Kuntze and Sison (1957) studied the effect of promazine hydrochloride in 100 unselected cases, 50 mg. being administered intravenously to all patients in established labour. All but 16 required pethidine or atropine in addition. 70% had excellent relaxation and 25% a good result. No side-effects were noted.

Wegryn and Marks (1958) discussed the value of promazine and pethidine in association with spinal anaesthesia for labour and delivery in 100 unselected cases. All patients were given promazine hydrochloride, 50 mg. intravenously, when labour was established, followed by the intravenous injection of pethidine hydrochloride, 50 mg., as and when necessary. An excellent result was obtained in 57% of cases, a good result in 29%, and 31% had amnesia of some degree. No adverse side-effects were noted.

Sippel (1958) reported the use of promazine intramuscularly in 100 patients in labour and claimed results as satisfactory as with intravenous administration.

In none of these trials was a control series observed simultaneously, and it was evident that this would have to be done before a correct evaluation of the drug in labour could be made.

Clinical Procedure

Unselected cases admitted in labour were allocated to one of four groups consecutively, so far as their initial sedation was concerned.

Group 1. Promazine hydrochloride, 50 mg., and pethidine hydrochloride, 50 mg., combined and given intravenously.

Group 2. Promazine hydrochloride, 50 mg. intravenously alone.

Group 3. Pethidine hydrochloride, 50 mg. intravenously alone.

Group 4. Any other sedation, but consisting usually of an initial dose of pethidine hydrochloride, 100 mg. intramuscularly.

After the initial drug was injected, further sedation was given as required, in the majority of cases pethidine hydrochloride being injected intramuscularly. The patients were all nursed under the same conditions, and gas and air and "trilene" analgesia were available in the second stage of labour. Most of the patients were confined to bed during labour.

In all, 400 cases were investigated, 50 primigravid and 50 multigravid patients being studied in each group.

Sedative and Amnesic Effects

The response of the patients with regard to sedative and/or amnesic effects was graded as (1) good, (2) fair, and (3) little or no benefit. Subjective impressions were assessed by interview with the patients at various times after delivery. Of the patients receiving the combination of pethidine and promazine, 60% had a good result, as did 52% who had the promazine alone.

These patients became quiet and relaxed within four to five minutes of the injection and some slept soundly, even during contractions. Others were roused by the pains. In groups 1 and 2 20% had varying degrees of amnesia.

A fair sedative result was obtained in 26% and 28% respectively in groups 1 and 2. Few of these had any amnesia. Little or no benefit was found in 14% of group 1 as compared with 20% in group 2.

It was noted that those who had only a fair result, or who had no benefit, had received the initial sedation relatively later in labour, in each instance the cervical dilatation having been estimated at four fingerbreadths or over at the time of injection. If given at this stage the nursing staff occasionally found the patients less co-operative in the second stage of labour.

In groups 3 and 4, which were taken as controls, 42% had good effect, 26% fair, and 32% little or no benefit. No amnesia was found.

In Table I these findings are compared with those of Kuntze and Sison.

TABLE I.—*Comparison of Sedative Effect*

Effect of Sedation	Group I	Group 2	Groups 3 and 4	Kuntze and Sison's Figures
Good	60%	52%	42%	70%
Fair	26%	28%	26%	25%
Little or no benefit	14%	20%	32%	5%

Promazine hydrochloride would appear to be as effective as a sedative, especially if given early in labour, as other drugs in common use.

Effect on Length of Labour

The average length of labour in primiparae and multiparae in each group is shown in Table II. It should be stated that the term "multiparae" includes patients who may not previously have had a full-term pregnancy but had been gravid before. Cases in which labour was terminated by caesarean section are excluded. There is surprisingly little difference among the four groups. These patients who received intravenous pethidine alone seem to have had, on average, a slightly shorter labour. The interval between the initial injection and delivery was also calculated

TABLE II.—*Average Duration of Labour*

	Group 1	Group 2	Group 3	Group 4
Primiparae ..	20 h. 8 m.	19 h. 30 m.	18 h. 25 m.	22 h. 51 m.
Multiparae ..	14 h. 5 m.	14 h. 20 m.	12 h. 52 m.	13 h. 13 m.

TABLE III.—*Initial Injection to Delivery Interval*

	Group 1	Group 2	Group 3	Group 4
Primiparae ..	9 h. 29 m.	9 h. 14 m.	6 h. 6 m.	13 h. 13 m.
Multiparae ..	3 h. 30 m.	6 h. 18 m.	3 h. 24 m.	4 h. 14 m.

(Table III). As would be expected, a fairly consistent figure is present in each group. At least it can be said that promazine has not an adverse effect on the length of labour.

Effect on Amount of Analgesic Used in Labour

A surprisingly high number of patients, both primiparous and multiparous, had only the initial amount of sedation during the whole of labour (Table IV). The initial high dose of pethidine hydrochloride given in group 4 accounts for the high figure in the multiparous patients in this group. There is a corresponding lower figure for the primigravid patients in this group. It is interesting to note also that the figures for promazine and pethidine and for

TABLE IV.—*Number of Patients in Whom Initial Dosage was Sufficient (50 Primiparae and 50 Multiparae in Each Group)*

	Group 1	Group 2	Group 3	Group 4
Primiparae ..	29	24	29	20
Multiparae ..	41	31	31	42

TABLE V.—*Total Amount of Sedation as Averaged Per Patient, Expressed in mg. of Pethidine Hydrochloride*

	Group 1	Group 2	Group 3	Group 4
Primiparae ..	79	74	86	136
Multiparae ..	72	40	79	129

pethidine alone given intravenously are similar in primigravid patients. In the multiparous patient, however, the combined dose seemed to be sufficient for the whole of labour on more occasions.

The actual total amount of pethidine hydrochloride given per patient was also calculated (Table V). This calculation excluded patients delivered by caesarean section and two or three patients in each group who had been given morphine or other drug in labour. There would appear to be little difference among the first three groups, apart from the fact that the giving of promazine would seem to reduce the amount of pethidine required. It is very striking, however, how much more efficient intravenous therapy is than intramuscular therapy, using the same drug. The total amount of pethidine used is much reduced when given intravenously.

Effect on Mode of Delivery

The mode of delivery is shown in Table VI. The patients were not separated into primiparous and

TABLE VI.—*Mode of Delivery in Each Group*

	Group 1	Group 2	Group 3	Group 4
Spontaneous vaginal delivery	80	82	81	79
Forceps delivery	16	16	14	17
Caesarean section	4	2	5	4

multiparous. Promazine would appear to have no adverse effect on the outcome of labour and the spontaneous vaginal delivery rate is not lowered.

Effect on the Third Stage of Labour and the Perineum

To ensure that there was no harmful effect on the third stage of labour with regard to post-partum haemorrhage or retained placenta, the percentage rate of these conditions was compared in groups 1 and 2 (those receiving promazine) with groups 3 and 4 as controls (Table VII). Similarly, the percentage rate for episiotomy and perineal tears was

TABLE VII.—*Percentage of Post-partum Haemorrhage and Manual Removal of Placenta After Promazine and in Controls*

	Promazine Groups	Control Groups
Post-partum haemorrhage ..	3·5%	3%
Manual removal	3%	4%

calculated (all cases of caesarean section were naturally excluded) and corrected to the first decimal figure: promazine groups, 50.8% ; control groups, 50.8%.

Effect on Actual Uterine Action

External tocographic records were made before and after injection in six cases receiving promazine alone or combined with pethidine hydrochloride. In no case was there any indication of alteration of uterine muscle activity.

Effect on the Foetus

In the two groups who had received promazine there were five still-births out of 199 cases in which the foetus was still alive at the onset of labour. Two of these, however, had gross degrees of foetal abnormality. In the control groups there were three stillbirths out of 198 similar cases. One of these had a gross degree of foetal abnormality. None of the stillbirths could be attributed to the sedation given. In three cases of the whole series there was evidence of intrauterine death before the onset of labour.

In all other cases the condition of the foetus at delivery was classified as (1) active, where the child cried within two minutes of birth, and (2) lethargic, where active resuscitative measures were required.

In Table VIII the total number of lethargic babies in the series is reviewed.

TABLE VIII.—*Incidence of Lethargic Babies in Each Group*

Group	Total Lethargic	Lethargic after Spontaneous Vaginal Delivery	Lethargic after Forceps Delivery		Lethargic after Caesarean Section
			Local	General	
1	19	10	1	7	1
2	16	8	1	7	0
3	15	6	1	4	4
4	25	10	2	11	2

There was a relatively higher number of lethargic babies after forceps delivery under general anaesthesia, irrespective of the nature of the previous medication. Table IX shows the relationship in this respect between

TABLE IX.—*Condition of Baby After Forceps Delivery by Local and General Anaesthesia. All Groups. Excludes Two Cases of Intrauterine Death and One Stillbirth*

Baby	General	Local
Active	26%	76%
Lethargic	74%	24%

those delivered by forceps under pudendal-block local anaesthesia and those under general anaesthesia. Where operative delivery is concerned it would seem that the condition of the child is more often attributable to the anaesthetic than to the predelivery sedation.

It can be concluded that the use of promazine has no effect on the foetal respiratory centre, even when given shortly before delivery, since in the series some cases received the injection within two hours of delivery.

Side-effects

With regard to the mothers, no patient had an untoward reaction to the intravenous injection of promazine, such as fall in blood-pressure, sensitivity, reaction, or pain at the site of injection. As stated previously, these patients were mainly confined to bed.

One interesting feature observed in those cases in which promazine was administered was a rise in the foetal heart rate occurring within one to two hours after the injection and often, though not invariably, accompanied by an increase in the maternal pulse rate. The foetal heart rate in about 15% of cases rose to between 160 and 180 beats a minute, and was maintained for several hours at this rate. There was no other evidence of foetal distress. In no case did this phenomenon seem to influence the condition of the child at birth. No satisfactory explanation for this has been found.

Summary and Conclusions

A clinical evaluation of the obstetrical use of a tranquillizing drug, promazine hydrochloride, is described and its safety established. A brief review of the previous literature concerning tranquillizers in labour is given.

Promazine hydrochloride, when used in labour, would seem to have no adverse effect on the course of labour and, by its use either alone or in combination with pethidine hydrochloride, will cause a degree of amnesia in some cases and adequate sedation in most. Its use also will tend to lower the total amount of analgesic and sedative required, which may benefit both the mother and foetus. The phenomenon of rise in the foetal heart rate does not seem to affect the foetus, but requires further consideration. The findings in this clinical trial have been contrary to previous work, in that the high frequency of successful sedation, and shortening of labour, have not been confirmed. Promazine, however, would seem to have a definite place in the nervous primigravid early in labour.

It is readily appreciated also that pethidine hydrochloride given intravenously is as efficient in smaller dosage (such as 50 mg.) as when a larger dose (such as 100 mg.) is given by intramuscular injection.

We thank Professor Ian Donald for initially stimulating interest in promazine and Dr. D. McKay Hart for allowing his patients to be subjected to the trial. We also thank Dr. B. W. Cromie, of John Wyeth and Brothers Ltd., for his helpful advice and criticism.

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