AN EVALUATION OF HIGH-DOSAGE SYNTHETIC OXYTOCIN* INTRAVENOUS INFUSION IN THE TREATMENT OF MISSED ABORTION

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The meaning of the term missed abortion is controversial. According to Eastman[1] it is customary to define it as retention of a dead foetus under 500 G in weight for a period in excess of 2 months. British writers, however, refrain from establishing time limits for the diagnosis of missed abortion. Stallworthy[2] writes: '. . . in this variety of abortion the dead ovum or foetus is retained for an abnormally long time, even for several months, before it is expelled.' The qualification 'abnormally long' cannot be defined with precision.

In this paper, the term is used to describe the situation in which development of the embryo or foetus has been at a standstill for at least 4 weeks beginning before the 28th week of gestation. The meaning is in accordance with the definition of Appelberg,[5] Borglin,[4] and Cosgrove.[5]

According to Kinch[6] 6% of intra-uterine deaths will result in retention of the dead foetus for more than 5 weeks. Streeter,[7] however, found that on an average the foetus was retained for a period of about 6 weeks, with a tendency for a longer period of retention in advanced gestation and shorter in the earlier stages.

Considerable evidence has recently accumulated to explain why the uterus retains the dead foetus. The working hypothesis advanced by Csapo and co-workers[8-11] from experimental studies was that missed abortion results from an imbalance between uterine volume, progesterone block and oestrogen stimulation. Retention of the dead foetus is further enhanced by the reduction in uterine size which requires less progesterone for an effective block of the propagated activity of the myometrium. The studies of Cassmer[12] showed that foetal death results in a drastic reduction in urinary oestrogen but not pregnanediol. However, when the foetus and placenta die simultaneously, as in saline-induced abortion, Bengtsson and Stormby[13] showed that the placental production of oestrogen and progesterone falls rapidly and simultaneously. The experiments of Bengtsson[14] prove his hypothesis that missed abortion only occurs when the foetus dies, while placental function is maintained. Consequently he describes 2 stages of missed abortion. Stage I is characterized by a progesterone-dominated myometrium, resulting from partial functioning of the placenta. In stage II, the myometrium is 'castrated' (atrophic) because of severe reduction of both oestrogen and progesterone.

Once a diagnosis of missed abortion has been unequivocally established, most will favour some form of active treatment. Eastman and Hellman[15] have recently revised their recommendation for the handling of missed abortion from conservative watching to an attempt at induction with the use of high concentrations of oxytocin. Many of the disadvantages of an expectant policy have been concisely stated by Corbett[16] as 'inconveniency, varying degrees of mental distress, continued abeyance of reproductive function, restriction of full activity and, finally, the dread of the abortion completing itself awkwardly in time or place.' To this list can be added the possibility of intra-uterine infection as encountered in a case in this series and another reported by El-Sherbini.[17] Kemp and Stallworthy[18] reported a case of infection of the dead foetus in an intact amniotic sac. Furthermore, there are several reports in the literature[19-21] concerning severe haemorrhage and hypofibrinogenaemia occurring in cases of missed abortion. According to Kinch[6] defects of coagulation associated with fibrinogen depletion, will occur in less than 1% of unselected cases of intra-uterine death. As a general rule there need be no anxiety unless the pregnancy has progressed beyond 16 weeks. The longer the dead foetus is retained, the more likely is fibrinogen deficiency to occur. Many[15,22,23] point out that the uterus should be emptied as soon as possible if the concentration of fibrinogen falls below 150 mg./100 ml.

Until recently the management of missed abortion was problematic. Suffice it to say that the use of intra-uterine packing, catheters, laminaria tents or chemicals not infrequently leads to morbidity from infection or excessive bleeding. Abdominal or vaginal hysterotomy involves major surgery to deliver a macerated foetus, leaving a scarred uterus. Thus a satisfactory non-surgical method was sought, which proved difficult because of low oxytocin sensitivity and low spontaneous myometrial activity, which are the features characteristic of missed abortion. Since Loudon[24] described the successful treatment of 18 cases of missed abortion with high concentration 'pitocin' intravenous drip, several laudatory reports have followed.[25-29] More recently, Maxwell[30] has reported on the use of buccal 'pitocin' citrate in 3 cases of missed abortion.

Several reports have appeared which refer to the use of intra-amniotic injections of saline or glucose in the treatment of missed abortion. Jaffin *et al.*[31] are among those who have introduced 200 ml. of 20% saline via the trans-abdominal route into the amniotic cavity. Because a varying amount of saline passes into the circulation, producing osmotic changes characterized by headache, thirst, paraesthesia, changes in blood pressure, and haemolysis, it would appear that the use of 50% glucose solution, as employed by Wood *et al.*[32] and Van der Wat,[33] is preferable.

Although it is not proposed to debate the merits of the various methods, the hitherto described disadvantages of the high-dosage 'syntocinon' infusion must be mentioned. A further complication has been noted in the series presented.

Reinberger and Mackey[34] described a case of coronary ischaemia attributed to spasm induced by pitocin. However, synthetic oxytocin (syntocinon, Sandoz) which is free from vasopressin, was used in this series. Despite the last-mentioned fact, Kitchin *et al.*,[35] who investigated the cardiovascular effects of oxytocin, found no difference between pitocin and syntocinon. Their findings showed that the intravenous administration of oxytocin produces a vasodilator action affecting particularly the skin. This

*Syntocinon (Sandoz).

was associated with a fall in blood pressure, tachycardia and rise in cardiac output. On the other hand, marked hypertension occurred in 2 cases in the series described by Toaff and Ayalon.[29] However, one patient was pregnant with a hydatidiform mole and the other suffered from essential hypertension and an inactive rheumatic lesion. Kitchin *et al.*[35] suggest that a simultaneous visceral vasoconstriction occurs. The magnitude of effects decreases during continuous infusion. A feeling of warmth or flushing of the skin occurs in about 50% of patients. Vasoconstriction is frequently noted at the site of injection. Liggins[26] noted similar cardiovascular effects.

Quinn and Harper[19] and also Vitiliante and Behrninger[36] have raised the question as to whether uterine contractions enhanced by oxytocin stimulation might cause the fibrinogen levels to fall by extruding thromboplastin or fibrinolysin into the maternal circulation.

Abdul-Karin and Assali[37] showed that natural oxytocin and syntocinon causes antidiuresis. The antidiuretic action became evident before the oxytocic effect and lasted for the duration of the infusion. This effect is apparently a direct action on the kidneys. Liggins[26] also found that a marked fluid retention occurred in all patients during syntocinon administration. He encountered one case of water intoxication and suggests discretion in applying the method in patients suffering from chronic renal or cardiac disease. Of interest are the experimental studies of Cross *et al.*,[38] which show that antidiuresis only occurs in the recumbent position.

Rinne *et al.*[39] found that synthetic oxytocin administration in high doses caused marked adrenal-ascorbic acid depletion in male rats, indicating ACTH release.

The experiments of Chaudhury and Nayyar[40] showed that in rabbits synthetic oxytocin had a definite hyperglycaemic effect. The mechanism appeared to be the release of epinephrine—this may be important in diabetics.

Liggins[26] noted anorexia throughout the course of administration and vomiting was common when the concentration of the infusion exceeded 300 milliunits per minute. Other side-effects are malaise and a feeling of fullness in the head.

The series presented below relates to the clinical experience at the Pretoria General Hospital, with high-dosage oxytocin intravenous drip in the management of missed abortion.

MATERIAL AND METHODS

Eleven patients were studied. Despite the small size of the series, a hitherto unreported complication encountered provided the basis for this paper. In accordance with the definition previously outlined, no case was included where the dead foetus was considered to have been retained for less than 4 weeks or where the uterus approximated 28 weeks gestational size. Surgical evacuation by dilatation and curettage was regarded as the treatment of choice where the uterine size was less than that of a normal pregnancy of 10 weeks' duration and this series does not therefore include such cases.

The uterine size varied from 12 to 24 weeks and the period of retention from 4 to 14 weeks (Table I). In most cases the time of foetal death could only be estimated.

The diagnosis was established by the usual clinical signs and symptoms, together with biological (*Xenopus*) pregnancy tests which were negative in all cases. X-rays and foetal electroencephalography were carried out where indicated. Incidentally, the pulsed ultrasound as described by MacVicar and Donald[41] appears to enable a positive diagnosis in doubtful cases where re-examination after 2 weeks shows a similar scan.

The fibrinogen level was determined by the method of Stirland,[42] in 10 cases on admission, and during induction in 4 cases. The clot observation test, described by Wiener *et al.*,[43] was performed in all cases.

Artificial rupture of the membranes was not attempted in any case.

Dried human fibrinogen and cross-matched whole blood were always readily available.

Four cases received 100 mg. of stilboestrol before administration of syntocinon.

The method of syntocinon infusion was similar to that employed by Loudon.[24] 1 or 2 ml. (10 - 20 units) of syntocinon was thoroughly mixed with 1 litre of dextrose in water or saline solution. The drip was run in through a needle in a forearm vein at a rate of 25 - 30 drops p.m. In the absence of uterine contractions, the strength of the solution in the first bottle was not increased but the rate gradually increased to a maximum of 60 drops p.m. The second vaculitre contained 40 units, and the third 80 units. The infusion rate was varied according to uterine contractions. The arbitrary limit for the fourth and subsequent vaculitres (rarely required) was 160 units of syntocinon,

TABLE I. 11 CASES OF MISSED ABORTION TREATED WITH HIGH-DOSAGE SYNTOCINON INTRAVENOUS INFUSION

Case no.	*Age*	*Parity*	*Duration of amenorrhoea in wks.*	*Estimated duration of intrauterine retention (wks.)*	*Uterine size at induction in wks.*	** Highest milliunits (mU/min.)*	*Estimated total dose (units)*	*Induction to delivery interval (hr.)*	*Curettage performed*	*Fibrinogen on admission (mg./100 ml.)*	*Remarks*
1	28	4+0	28	6	20	180	60	15	No	71·4	No fibrinogen given
2	22	1+0	20	8	14	120	45	31½	Yes	?	—
3	19	0+0	26	12	12	240	85	68	Yes	100·0	Only one vaculitre infused per day. Hydatidiform mole
4	24	2+0	24	6	18	40	110	6½	No	217	Stilboestrol 100 mg
5	40	5+4	38	14—16	24	640	250	Laparotomy after 72 hrs.	—	446	See text
6	38	10+0	22	4	16	120	30	8	Yes	230	Evacuation for retained products. Stilboestrol 100 mg.
7	30	6+0	32	14	18	320	160	30	Yes	111·6	3 G fibrinogen administered
8	28	1+0	24	10	12	640	290	55	Yes	140	—
9	30	6+1	30	6	22	180	30	11	No	348	—
10	31	0+1	39	12	22	480	300	Laparotomy after 83 hrs.	—	86·2	See text. Progressive decrease of fibrinogen to 4 mg.
11	33	4+1	26	4	18	160	25	7	No	320	Stilboestrol 100 mg.

*1 ml. of syntocinon = 10 U = 10,000 mU. Thus 100 U/l infused at 40 drops p.m. = 400 mU/min. ('Baxter' administration set 10 drops = 1 ml.).

and the rate of infusion in such instances was not allowed to exceed 40 drops p.m.

The drip was discontinued in the late evening, unless it appeared that expulsion would soon follow. The infusion was resumed the following morning.

Pethidine was usually employed as the analgesic. There was no constant supervision of the patient who was only seen at regular intervals. As a precaution, syntocinon infusion was continued for 4 - 6 hours following abortion to prevent haemorrhage.

RESULTS

The results of treatment are summarized in Table I. The infusion failed to induce abortion in 2 of the 11 presented cases. The importance of these failures is magnified when compared with other series. Loudon[24] had no failures in 18 cases. Toaff and Ayalon[29] had no failures in 21 cases which included 3 cases of hydatidiform mole and 8 cases of foetal death before the twelfth week of gestation. Liggins[26] reported 3 failures out of 30 cases. In 2 instances the uterine size was at most that of a pregnancy of 8 weeks' duration. Misdiagnosis of a normal pregnancy accounted for the third failure.

There was one case of hydatidiform mole in this series, which was diagnosed after expulsion following syntocinon infusion. In the 9 successful cases the induction-delivery interval varied from 6½ to 68 hours. The total duration of infusion could not be calculated since in most cases the time of discontinuation in the evening was not recorded. The total dosage of syntocinon required to cause expulsion varied from 10 to 290 units, with an average of 85 units. As reported by Liggins,[26] a tendency was noted for a higher dose rate and total dose to be required where retention of a dead foetus was longest.

Curettage was performed following abortion in 5 of the 9 successful cases. The indications were: 1 for retained products, 1 because of haemorrhage and possible retained products, 1 in accordance with the general policy adopted in hydatidiform mole, and in the other 2 cases as a precaution because of uterine size. In only 1 instance was any significant amount of placental tissue removed.

Five out of 10 cases had a fibrinogen level below the commonly accepted critical level of 150 mg./100 ml. Despite this, fibrinogen was administered only on 1 occasion.

A representative case of missed abortion treated by high-dosage syntocinon infusion in this series, and the 2 failures, which are of considerable interest, are presented below.

CASE REPORTS

Case 7

A Bantu, para-6, with no previous abortions, aged 30 years had amenorrhoea for 32 weeks. Foetal movements were felt for only 2 weeks and had ceased 14 weeks before admission. All signs and symptoms of pregnancy had subsequently disappeared. There was no vaginal blood-stained discharge or haemorrhagic tendency. On examination the uterus was of firm consistency, enlarged to 18 weeks' gestational size. The cervix was of normal consistency, uneffaced and multiparous. No foetal parts were outlined. X-ray of the abdomen showed a small collapsed foetus with a Spalding sign. The *Xenopus* pregnancy test was negative. Venous blood clotted after 7 minutes without evidence of clot lysis. Plasma fibrinogen was 111·6 mg./100 ml. Serological tests for syphilis were negative and the Rhesus factor was positive.

The day following 'priming' with 100 mg. of stilboestrol and 1·2 G of quinine, an intravenous infusion containing 20 units of syntocinon/l. was begun at 25 drops p.m. and gradually increased to a maximum of 60 drops p.m. No objective or subjective contractions ensued. A second infusion containing 40 units syntocinon/l., was set up and allowed to run in at a rate of 30 drops p.m. Weak subjective uterine contractions occurred towards the end of the vaculitre. The infusion was discontinued in the late evening and re-started the following morning with a third vaculitre to which 80 units of syntocinon had been added. The infusion was commenced at a rate of 30 drops p.m. Subsequently it was necessary to vary the infusion rate of 30 drops p.m. Weak subjective uterine contractions occurred towards the end of the vaculitre. The infusion was discontinued in the late evening and re-started the following morning with a third vaculitre to which 80 units of syntocinon had been added. The infusion was commenced at a rate of 30 drops p.m. Subsequently it was necessary to vary the infusion rate between 20 and 40 drops p.m. to maintain regular painful contractions which were also palpable. The maximum milliunits p.m. was 320. Since uterine contractions were strong and regular the amount of syntocinon was not increased to 160 in the fourth vaculitre but maintained at 80 units. After 250 ml. of this solution had been infused, the patient aborted a macerated foetus weighing 625 G, and a friable pale thin placenta. A total of 160 units of syntocinon had been given. The infusion was continued for a further 6 hours. Uterovaginal bleeding followed abortion despite good uterine contraction. The fibrinogen level had decreased to 71·5 mg./100 ml. Reconstituted fibrinogen (3G) was given, and during curettage under general anaesthesia only a minimal quantity of retained placental tissue was removed. The fibrinogen level on the following day was 116 mg./100 ml. No further haemorrhage occurred and the patient made an uneventful recovery. No cause was established for the intra-uterine death.

Case 5

The patient was a Bantu woman aged 40 years. This was her 10th pregnancy, having had 5 full-term deliveries and 4 previous abortions. Her last menstrual period had occurred 38 weeks previously. Foetal movements were felt for only a few weeks. She was admitted to hospital 3½ - 4 months after she had last felt foetal movements. The patient was dehydrated, anaemic and pyrexial. The uterus was enlarged to the size of a 24-weeks pregnancy and felt softer than normal. Bimanual examination confirmed that the abdominal mass was indeed the uterus. The cervix presented a multiparous os with a tightly closed internal os; there was an offensive purulent discharge from the endocervix. Culture showed β-haemolytic streptococci and *Escherichia coli*. Blood cultures were negative and the fibrinogen was 446·6 mg./100 ml. Intensive appropriate antibiotic therapy and blood transfusion were given.

On the first day of syntocinon induction, an infusion containing 10 units/vaculitre was followed by one containing 40 units. No contractions were noted. On the second day a vaculitre containing 40 units (in error) was followed by one to which 160 units were added. The patient complained of slight pain, but no contractions were palpable. Laparotomy was performed, and the thinned out, pale anterior uterine wall was densely adherent to the peritoneum. Only with great difficulty could the attached friable thickened peritoneum be dissected from the uterus. Hysterotomy was performed and it was established that the infected, partly mummified products of conception were intra-uterine and not in a secondary abdominal gestational sac. Marsupialization was carried out. The postoperative course was stormy but the patient made a complete recovery.

Case 10

Mrs. R. S., a gravida-2, para-0, 31 years of age was admitted to the Pretoria General Hospital on 17 July 1961. Her last menstrual period was in the middle of October 1960 (39 weeks earlier). The attending practitioner had heard foetal heart sounds until approximately the 28th week of pregnancy. Subsequently foetal movements were arrested and the signs and symptoms of pregnancy had disappeared. Her only previous pregnancy 2 years earlier, had ended in the delivery of a macerated foetus at 24 weeks.

On examination the breasts were pendulous, but no colostrum could be expressed. Abdominal examination showed a uterus displaced slightly to the left of the midline, enlarged to 22 weeks' gestational size. No foetal parts were palpable and

no foetal heart sounds were heard. On vaginal examination a rudimentary midline septum was noted in the upper third of the vagina. The exocervix was shortened, multiparous, lacerated and displaced to the left. The external os admitted a finger tip, and a small amount of dark brown discharge was noted from the endocervical canal.

In the upper right vaginal fornix a rubbery hard nodule was noted. On examination with a speculum only one cervix was visualized. Bimanual examination confirmed the abdominal findings. However, lateral to the right isthmus region of the uterus a regular firm mass 4 cm. × 2·5 cm., was felt. It could not be unequivocally established whether it was attached to the uterus. The findings were consistent with a pregnancy in a fibroid uterus or a bicornuate uterus or a uterus didelphys.

The *Xenopus* biological pregnancy test was negative and X-rays of the abdomen showed a single foetus of about 22 weeks' size with complete collapse of the skeleton. The serological tests for syphilis were negative. The blood was group O, Rh-positive. The clotting time was 6 minutes, but after 10 minutes 75% clot dissolution occurred. Fibrinolysins were not tested for. Plasma fibrinogen was 86·2 mg./100 ml. Three days later the fibrinogen level was 59·8 mg./100 ml. 2 G of fibrinogen were given and syntocinon induction commenced in the manner previously outlined, after establishing that the fibrinogen level was now 116 mg./100 ml. Stilboestrol (100 mg.) had been given on the day preceding infusion. Fairly strong uterine contractions were experienced for the first time during administration of the 3rd vaculitre, which contained 80 units of syntocinon. The fibrinogen level decreased to 71·5 mg./100 ml. during this infusion. On the third day of induction an infusion containing 160 units of syntocinon caused fairly strong, regular and very painful contractions at an infusion rate of 25 - 30 drops p.m. (maximum milliunits p.m. 480). The rate of infusion was decreased to 20 drops per minute. However, tetanic contractions followed towards the end of the infusion. The patient was extremely nauseous, vomited frequently, and complained of dizziness and fullness of the head and continuous intense abdominal pain. Infusion was discontinued. Vaginal examination showed no change and laparotomy was decided upon.

At laparotomy there was clear evidence of a uterus didelphys and the ligament of Carus (recto-vesical ligament) as described by Hunter[44] was seen (Fig. 1). The antero-medial wall of the pregnant uterus showed a well-demarcated atonic, thinned out, necrotic area. Hemihysterectomy was performed. The uterus contained a partially decomposed foetus which

Fig. 1. Double uterus showing excessive thinning of the antero-medial wall of the 'uterus' containing the pregnancy and the well-demarcated area of infarcted muscle. There is no evidence of diverticulum. The ligament of Carus is clearly seen.

weighed 450 G, and the placental tissue was markedly degenerated. The necrotic area in the uterine wall was 2 - 3 mm. in thickness and there was no evidence of sacculation or of a diverticulum. The uterus was inadvertently 'fixed' in saline, and was unsuitable for histological examination.

Immediately before the laparotomy the fibrinogen level was 4·0 mg./100 ml. and during operation dropped to 0 mg./100 ml. In view of the absence of bleeding, fibrinogen administration was withheld. The following day the fibrinogen level was 60 mg./100 ml. without evidence of prolonged clotting or fibrinolysis. Two days later the fibrinogen level had increased to 317 mg./100 ml.

The patient made an uneventful recovery.

DISCUSSION

The fibrinogen determinations are of interest. In 5 out of 10 cases the fibrinogen level was below the accepted critical value of 150 mg./100 ml. However, according to Bach[45] the critical level is between 80 and 100 mg./100 ml. Despite the low fibrinogen levels, uterovaginal bleeding occurred only in one instance, necessitating the administration of 3 G of fibrinogen. In case 10, fibrinogen was given prophylactically when the level had decreased to 71·5 mg./100 ml. In the same case the well-known observation of spontaneous progressive decrease in fibrinogen was confirmed. The dramatic and sudden decrease in fibrinogen subsequent to uterine contractions and especially following uterine tetany, was probably the result of oxytocin stimulation which extruded thromboplastin or fibrinolysin from the uterus into the maternal circulation. This effect must be recognized and for that reason clotting derangements must be carefully excluded during induction for missed abortion. Although the fibrinogen level fell to 4 mg./100 ml. immediately before laparotomy and to 0 mg./100 ml. during operation, fibrinogen administration was withheld since there was no evidence of abnormal bleeding. Within 2 days the fibrinogen level had returned to normal. Thus this case again demonstrates that afibrinogenaemia cures itself spontaneously after the removal of the degenerated products of conception. Jeffcoate[46] reported cases in which there was a definite hypofibrinogenaemia in whole blood but in which this did not lead to uterovaginal bleeding. Jeffcoate[47] states: 'Afibrinogenaemia can exist without causing bleeding and by itself is not an indication for treatment. The administration of fibrinogen or concentrated plasma, can merely add fuel to the process of intravascular clotting. Because of this and because of the real risk of causing serum hepatitis, such treatments should be withheld until the occurrence of haemorrhage makes them essential and preferably until the cause of the pregnancy is removed.' I am in agreement with this view, although it is at variance with the generally accepted opinion that fibrinogen administration is indicated as prophylaxis when the level approaches 70 mg./100 ml.

In view of recent knowledge based especially on the hypothesis of Goldstein and Reid,[20] it would appear that the interests of a patient with clot dissolution would be better served by the administration of epsilon-aminocaproic acid rather than by fibrinogen, because the aforementioned can block the activity of some fibrinolysins.

The 2 patients with necrosis of the uterine wall merit further evaluation. It is submitted that the findings in case 5 were not the result of oxytocin, since hardly any contractions were noted, and dense adhesions could not develop within 3 days. Furthermore there was evidence of infection of the uterine wall, and El-Sherbini[17] has described similar findings in a case where an 8-months foetus was retained *in utero* for 2½ years. There was no mention of administration of an oxytocic.

The necrosis of the wall in the malfused uterus raised several questions. The total dose of oxytocin employed and the maximum milliunits p.m. were well below the highest value reported by other authors.[26,29] It is thought that because of known variations which exist in the uterine musculature of the 2 uteri in uterus didelphys, a smaller dose was sufficient to produce ischaemia. A didelphic uterus is not really 2 uteri developmentally, but each side represents one-half, a uterus, and cervix with resultant decreased distensibility of the deformed myometrium and poor vascularity. Holmes,[48] however, concluded that the foetal and maternal risks are greatest in the uterus bicornis unicollis and uterus subseptus and least in didelphys and uterus unicornis. Gergely and Mason[49] report an interesting case of a pregnancy in a non-communicating rudimentary horn, where attempts to induce labour with intravenous pitocin (dose not mentioned) were unsuccessful and 2 months later a laparotomy was performed. There was no reference to uterine necrosis.

Tetanic uterine contractions occurred suddenly in the patient in question. As the clinical observer by palpating the abdomen can tell frequency, but only give a vague idea of contraction amplitude and tonus between contractions, it appears that absolute safety with high-dosage syntocinon infusion can only be obtained if contractions are monitored.

Liggins[26] states that his present tendency is towards a commencing concentration of 50 units of syntocinon/pint at no more than 30 drops p.m., and to make a single increment to 100 units/pint at the end of 2 hours if contractions have not started. In view of the experience in the case encountered, it would appear that such a dosage may produce necrosis of the uterine wall or even gangrene in the presence of putrefaction if the method is employed in cases where there are uterine developmental anomalies. Since the inactive myometrium is often thin and fragile in missed abortion (Bengtsson[14]), it is logical to assume that an associated poor vascularity and distensibility will favour further complications when maximally stimulated by oxytocin. These conclusions must be drawn despite the fact that Bengtsson and Csapo[50] showed that the barely active human uterus of midpregnancy responded only with 20 mm.Hg active pressure on massive oxytocin infusion, whereas following the replacement of 200 ml. of amniotic fluid by 20% saline at least 50 mm.Hg spontaneous pressure developed 16 - 24 hours later.

In the series presented it was noted that oestrogen administration appeared to shorten the induction-delivery interval as well as the dosage of oxytocin required. These findings are in accordance with the view held by Eastman.[51] The author is of the opinion that 'priming' the uterus with stilboestrol is beneficial, despite the fact that Martin and Menzies[52] repudiated the earlier claims of Jeffcoate.[46] I have come across 2 consecutive cases of missed abortion which were scheduled for high-dosage syntocinon infusion, but which aborted during the night following administration of 150 mg. of stilboestrol and 1·2 G of quinine. The periods of intra-uterine retention were 4 and 14 weeks, and the uterine size 22 and 12 weeks respectively.

The work of Bengtsson[14] had added substantial support to the view regarding the value of oestrogen administration in missed abortion. In stage I missed abortion (referred to earlier) the treatment of choice appears to be destruction of the placenta alone (by intra-amniotic injection of saline or glucose) to remove the progesterone. Bengtsson[14] claims that oestrogen may be useful in such cases but not necessary. In stage II, however, oestrogen alone (in adequate doses and for long enough) will usually start abortion. Bengtsson[14] treated 11 patients with oestrogens in whom the pregnanediol levels were low. Only in 6 was oxytocin combined. All aborted spontaneously.

Since it is difficult to decide without vaginal smears and urinary levels of oestriol and pregnanediol, which stage of missed abortion is present in a particular patient, it is suggested that stilboestrol should be employed as a routine procedure in all cases of missed abortion before definitive induction.

SUMMARY

1. The treatment of 11 patients, diagnosed as having missed abortion, with high-dosage syntocinon intravenous infusion is described. Treatment was unsuccessful in 2 cases, which were of interest, and are presented in detail.

2. Necrosis of the uterine wall was noted in one of the failures associated with a uterus didelphys. Developmental anomalies are mentioned as a possible contraindication for this method of induction. The complications of oxytocin infusion are reviewed.

3. Fibrinogen levels were below the accepted critical value of 150 mg./100 ml. in 5 out of 10 cases studied. Haemorrhage requiring fibrinogen administration, occurred in only 1 patient, when the fibrinogen level had decreased to 71·5 mg./100 ml. These findings are in accordance with the experience of Bach,[45] who found the critical level to be 80 - 100 mg./100 ml. Oxytocin infusion caused a rapid decrease in the fibrinogen level to 4 mg./100 ml. in one instance. Fibrinogen administration was withheld and spontaneous correction ensued. It is stressed that afibrinogenaemia by itself, in the absence of haemorrhage, is not an indication for treatment. In one instance fibrinolysis was noted, illustrating the necessity for easy access to epsilon-aminocaproic acid, in addition to fibrinogen and compatible whole blood.

4. Routine employment of oestrogen to 'prime' the uterus before definitive induction is advocated. Recent experimental evidence to support this view is presented.

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