

Oxytocin: Pharmacology and Clinical Application

Jerry Kruse, MD
Quincy, Illinois

Oxytocin is a potent uterine stimulant that is used for the induction and augmentation of labor, antenatal fetal assessment, and control of postpartum hemorrhage. If used improperly, oxytocin can lead to such complications as uterine hypercontractility with fetal distress, uterine rupture, maternal hypotension, water intoxication, and iatrogenic prematurity. These complications can almost always be avoided if oxytocin is given in proper dosages and with careful fetal and maternal monitoring. Recent interest in active management of labor policies has resulted in a reexamination of the use of oxytocin in the augmentation of the labors of nulliparous women.

Since the production of synthetic oxytocin in the 1950s, there has been increasingly widespread use of oxytocin for a variety of obstetric situations. Oxytocin is a potent stimulant of uterine contractions that can cause severe adverse side effects for mother and fetus. In recent years the safety of oxytocin has been greatly enhanced by the use of continuous maternal and fetal monitoring and by the use of controlled intravenous infusion of the drug. A thorough knowledge of the pharmacology and proper clinical use of oxytocin is needed by all physicians who deliver babies.

THE PHARMACOLOGY OF OXYTOCIN

PRODUCTION

Oxytocin is one of two neurohormones released by the posterior lobe of the pituitary. It has potent primary effects on the myometrium during pregnancy, and also has secondary effects on the breasts, kidneys, and peripheral vessels. Both oxytocin and vasopressin (ADH), the other posterior pituitary neurohormone, are octapeptides. Their structures are similar and they have somewhat overlapping effects.

Submitted, revised, July 22, 1986.

From the Southern Illinois University Department of Family Practice, Quincy Family Practice Residency Program, Quincy, Illinois. Requests for reprints should be addressed to Dr. Jerry Kruse, Quincy Family Practice Residency Program, 1246 Broadway, Quincy, IL 62301.

FORMS

Oxytocin was first used for the management of labor in the form of a pituitary extract (Pituitrin), which consisted of oxytocin, vasopressin, and various impurities. Oxytocin was synthesized first in 1953¹ and then became available commercially in pure form (Pitocin, Syntocinon).

PHARMACOLOGIC ACTIONS

Oxytocin has three distinct effects on the myometrium: It increases the excitability of the myometrium, increases the strength of contraction, and increases the velocity and frequency of the contraction waves.² In addition to increasing the intrauterine pressure of the uterus, oxytocin facilitates the correction of ineffective and irregular uterine contractions.

The uterine response to oxytocin depends on the circulating levels of progesterone and estrogen and upon the gestational age. As estrogen levels rise and progesterone levels fall (which occurs late in pregnancy and to a lesser degree at midcycle of the menstrual cycle), the uterine response to oxytocin increases.² Indeed, at times other than midcycle of the period, the uterus in a nonpregnant state is almost refractory to large doses of intravenous oxytocin.

During pregnancy there is a progressive, though irregular, increase in sensitivity of the myometrium to oxytocin. The increase in sensitivity begins at 20 weeks, and there is a sharp rise after 30 weeks. The

sensitivity is maximal during spontaneous labor at term.³

Oxytocin has pharmacologic action on organs other than the uterus. It causes milk ejection from the gravid or puerperal breast.¹ Suckling, breast stimulation, and uterine manipulation cause oxytocin release and subsequent contraction of myoepithelial cells in the breast.³ Oxytocin also has mild properties of antidiuretic hormone, and water intoxication can occur if large amounts of oxytocin are given with large amounts of dilute electrolyte solution.⁴ Usually, a total of 40 to 50 units of oxytocin is required for antidiuretic effects to occur.

OXYTOCIN AND THE NATURAL OCCURRENCE OF LABOR

There is evidence that the concentration of circulating oxytocin rises gradually throughout pregnancy and peaks during the second stage of labor.⁵ This progressive rise in concentration is probably due to low-level spurts of oxytocin from the posterior pituitary, which increase in frequency until delivery. There is also evidence that there is significant excretion of fetal oxytocin during labor.⁶

There is probably a complex interaction between endogenous oxytocin and prostaglandins that initiates labor. Recent evidence suggests that prostaglandin production is a prerequisite for the maintenance of efficient uterine contractions, and that oxytocin stimulates production of prostaglandins in the uterus during pregnancy under conditions predisposing to the occurrence of labor.^{7,8} So it seems plausible that oxytocin from maternal and fetal sources triggers uterine contractions that become efficient when oxytocin induces an increase in uterine prostaglandin production.

The normal uterine contraction begins in the fundus at the cornual areas, the thickest parts of the uterine wall. The contraction wave is propagated in all directions and covers the entire uterus in 20 to 30 seconds. The origin, propagation, strength, and duration of an effective contraction all predominate in the fundus and progressively diminish as they reach the cervix. Intravenous infusions of oxytocin can often correct contraction patterns that do not follow this orderly sequence.²

QUANTIFICATION OF UTERINE ACTIVITY

Quantification of uterine activity is important in understanding the proper use of oxytocin. Uterine activity is conveniently measured in Montevideo units. Montevideo units measure the uterine work done in 10 minutes. The uterine work is defined as the summation of the intensity of uterine contractions, which is the amplitude of the contraction minus the baseline tonus of the uterus. Montevideo units can be calculated in the following two ways:

1. Montevideo units = The summation of the intensity of each contraction (mmHg) occurring in a 10-minute period

or

2. Montevideo units = Intensity of one contraction (mmHg)

$$\times \frac{10 \text{ min}}{\text{interval (min) from peak of contractions}}$$

The average number of Montevideo units generated at various times during normal pregnancies is shown in Table 1.⁸

PREDICTABILITY OF RESPONSE

During spontaneous labor, about 90 percent of women will have increased intensity of contraction and about 75 percent will have increased frequency of contractions when oxytocin is infused.² After maximal efficiency of contractions is reached, an increase in the infusion rate will result in a decrease in the intensity of contraction. This decrease in intensity occurs because the base-line uterine tonus increases and also because the frequency of contraction increases to such a degree that the relaxation phase of the contraction is interrupted by the next contraction.⁹

The uterus always responds to oxytocin infusion with an increase in tonus, even with small doses. The important increases in tonus are seen, however, when oxytocin is given with an already maximal uterine contractility or when starting an infusion at a high rate.⁹

CLINICAL APPLICATION OF OXYTOCIN

ADMINISTRATION

Oxytocin should be administered as a dilute intravenous solution. Usually 10 or 20 units of oxytocin is mixed with 1 L of balanced salt solution. The starting dose should be small, 0.5 to 1.0 mU/min. (In a solution of 20 units of oxytocin per liter, an infusion rate of 3 mL/h equals 1 mU/min).

The maximal effect of oxytocin occurs in 20 to 60 minutes, depending on the concentration of oxytocin.¹⁰ Lower concentrations will require more time than higher concentrations to reach maximal effect. If the rate of infusion is increased too rapidly, hyperstimulation may occur. The rate of infusion should be doubled every 20 to 30 minutes until the desired effect is obtained.

At term, 2 to 8 mU/min is usually sufficient to obtain labor-like contractility. Seldom is more than 20 mU/min required. When oxytocin is used to stimulate the preterm uterus, much higher concentrations may be required to obtain comparable uterine activity. At 32 weeks' gestation an average of 20 to 40 mU/min is required.²

TABLE 1. AVERAGE UTERINE ACTIVITY AT VARIOUS TIMES OF PREGNANCY

	Uterine Activity (Montevideo Units)
Prelabor (Braxton-Hicks contractions of late pregnancy)	50
Early first stage	125
Mid-first stage	180
Second stage	250

There is a continuous increase in spontaneous uterine activity throughout labor that will be superimposed on the effects of infused oxytocin. Needless to say, careful monitoring of the fetal heart rate and maternal contractions is mandatory when oxytocin is being administered. The dose of oxytocin may need to be decreased or discontinued altogether as labor progresses.

PRECAUTIONS AND RISKS WITH THE USE OF OXYTOCIN

When used carefully, intravenous oxytocin is a very safe pharmacologic agent. Complications caused by oxytocin are almost always due to improper dose or inadequate supervision.

Uterine Hyperstimulation and Fetal Distress. Uterine hypercontractility is by far the most common complication of the use of oxytocin. Uterine hypercontractility is usually defined as either uterine activity exceeding 250 Montevideo units, coupling of uterine contractions, or more than five contractions in a ten-minute period. Hypercontractility causes a decrease in the intravillous blood flow, and fetal distress is often the result. Hypercontractility is usually quickly reversible by discontinuation of the oxytocin. To maximize fetal oxygenation, oxygen should be administered and the patient should be placed in the left lateral position. Morbidity from hypercontractility can be minimized by careful fetal monitoring.

Hypercontractility may progress to tetanic contractions. Tetanic contractions may be quite prolonged, up to 10 to 20 minutes, after oxytocin is discontinued.² With proper monitoring, hypercontractility should be noted before tetanic contractions occur. There is no scientific basis for the notion of "pitting through hyperstimulation" by continuing to increase oxytocin infusion rates.

Uterine Rupture. Uterine rupture is an extremely rare occurrence, particularly in the primigravid uterus. When oxytocin is being used, uterine rupture appears to occur only when oxytocin is grossly misused, when the uterus is defective (eg, from a previous cesarean

section scar), or when the uterus is manipulated. Cibils² reports only one case of uterine rupture in 6,000 consecutive oxytocin inductions over a ten-year period at the Chicago Lying-In Hospital. No cases of uterine rupture occurred during the oxytocin inductions of 1,022 high-risk patients in South Africa in 1976.¹¹ In a review of 181 consecutive cases of uterine rupture, Trivedi et al¹² reported no cases of uterine rupture among nulliparous patients.

Hypotension. Oxytocin in bolus intravenous doses causes significant hypotension.¹³ As little as 2 units given by rapid intravenous bolus can cause a 30 percent drop in mean arterial pressure.^{2,14} Accordingly, oxytocin used for control or prevention of postpartum hemorrhage should be given by controlled intravenous infusion or intramuscular injection. Bolus intravenous doses should never be given.

Water Intoxication. Chemically, oxytocin is closely related to vasopressin and has weak intrinsic antidiuretic properties. Water intoxication can occur when large doses of oxytocin are given with electrolyte-free intravenous solutions.⁴ Water intoxication is completely preventable if intravenous fluids of the proper amount and composition are given.

Neonatal Hyperbilirubinemia. There is disagreement about the effects of oxytocin upon the development of neonatal jaundice. The most recent evidence suggests that infants at a higher risk of developing jaundice associated with oxytocin administration are those whose mothers received a total of 20 units of oxytocin or more during their labors.¹⁵ This dose is extremely large. For example, if oxytocin were infused at 12 mU/min, it would take about 20 hours to reach a total dose of 20 units.

Iatrogenic Prematurity. When oxytocin is used for the elective induction of labor, there is a chance that iatrogenically premature infants may be delivered. In a study of 1,000 newborn infants referred to a regional neonatal intensive care unit, Flaksman et al¹⁶ found that 32 were premature infants who had been born to mothers in whom labor had been electively induced. All 32 infants had serious respiratory complications. Twenty-five of these infants were born by "early" repeat cesarean section, and the other seven were products of oxytocin induction. All were presumed to be mature prior to delivery, but their gestational ages by Dubowitz scores were 33 to 37 weeks. Blacow et al¹⁷ studied 200 consecutive elective inductions and found that, when assessed by Dubowitz scores, 27 of the babies were more than 2 weeks younger than assumed. The true incidence of iatrogenic prematurity is unknown, but this complication should be preventable by accurate dating of pregnancies and the appropriate use of ultrasound examinations and amniocentesis.

TABLE 2. CONDITIONS IN WHICH THE INDUCTION OF LABOR MAY BE INDICATED

- Prolonged pregnancy
- Preeclampsia
- Chronic hypertension
- Diabetes mellitus
- Rh isoimmunization
- Previous stillbirth
- Advanced maternal age
- Intrauterine death
- Intrauterine growth retardation
- Major fetal anomalies
- Hydramnios

TABLE 3. THE BISHOP METHOD OF PELVIC SCORING*

	Score			
	0	1	2	3
Station	-3	-2	-1 or 0	+1 or +2
Cervix				
Dilation (cm)	0	1-2	3-4	5-6
Effacement (%)	0-30	40-50	60-70	80-100
Consistency	Firm	Medium	Soft	
Position	Posterior	Middle	Anterior	

*Reprinted with permission from the American College of Obstetricians and Gynecologists¹⁹

Abnormal Neurobehavioral Status of Infants. It has been suggested that infants born after oxytocin stimulation may have a higher risk of developing neurologic or behavioral abnormalities. The most recent studies suggest, however, that the neurologic and behavioral status at and before age 2 months of infants born after oxytocin stimulation is no different from that of those born spontaneously or after prostaglandin stimulation.¹⁸

Uterine Atony. In women of high parity, the use of oxytocin is thought to be associated with an increased incidence of uterine atony and postpartum hemorrhage.

THE INDUCTION OF LABOR WITH OXYTOCIN

Indications and Contraindications. Induction of labor may be indicated if continuation of pregnancy or spontaneous labor poses a threat to fetal or maternal well-being or if the fetus is dead. Conditions in which these criteria are often met are listed in Table 2. Obviously, the mere presence of these conditions is not an indication for the induction of labor. Careful consideration must be given to the optimal timing of the induction of labor, and before induction is begun, the following questions need to be addressed:

1. Do the risks of continuation of pregnancy outweigh the risks of the use of oxytocin?
2. Is delivery best accomplished by induction of labor or cesarean section?
3. Is the fetus mature? If not, do the risks of continuation of pregnancy outweigh the risks of prematurity?

As are the indications for the induction of labor, the contraindications for the use of oxytocin are quite controversial. In most textbooks of obstetrics, long lists of criteria for the use of oxytocin can be found. Petrie¹ suggests that the following criteria be met before using oxytocin: (1) data supporting fetal maturity or benefit of premature delivery outweighing prematurity, (2) absence of fetal distress, (3) absence of absolute cephalopelvic disproportion, (4) absence of uterine

overdistention from multiple gestation or hydramnios, (5) absence of major bleeding from placenta previa or abruptio placentae, (6) absence of uterine surgical scar, (7) absence of an unfavorable fetal position or presentation, (8) absence of grand multiparity, (9) absence of a history of uterine trauma or infection, (10) estimated fetal weight less than 4,300 g, and (11) Bishop score indicative of successful induction.

A more liberal use of oxytocin for induction is espoused by Cibils,² who writes "the only contraindication to the proper use of intravenous oxytocin are the contraindications to spontaneous labor." He finds no satisfactory reason to deny the potential benefit of a carefully controlled uterine stimulation with oxytocin to patients with twins, breech presentations, distended uteri, or grand multiparity.

Factors Affecting Success of Induction. By far the most important factor affecting the success of the induction of labor is the state of the cervix, or cervical ripeness. Various methods of assessing cervical ripeness have been developed, the most widely used being the Bishop method of pelvic scoring, which takes into account the cervical condition and station of the infant.¹⁹ This method was developed in 1964 and has been used to determine the optimal time for the induction of labor. The Bishop scoring method is shown in Table 3. Scores are assigned for station of the fetal head and for four characteristics of the cervix, which are then added to obtain the Bishop score. A score of 9 or more was uniformly associated with a successful induction.

Recently Lange et al²⁰ have proposed a modification of the Bishop method. This modification, which has better accuracy and reproductibility than the traditional Bishop method, eliminates the cervical consistency and position and weighs more heavily the cervical dilation. The modification by Lange et al is shown in Table 4.

Lange et al found that, in a series of over 1,000 patients, 100 percent of patients with a score of 8 or greater and 75 percent of patients with a score of 5 to 7

TABLE 4. THE MODIFIED BISHOP SCORING SYSTEM*

	Cm	Score
Station	-3	0
	-2	1
	-1 or 0	2
	+1 or 2	3
Dilation	0	0
	1-2	2
	3-4	4
	>4	6
Length of cervix	3	0
	2	1
	1	2
	0	3

*Reprinted with permission from the American College of Obstetricians and Gynecologists²⁰

TABLE 5. FREQUENCY OF CESAREAN DELIVERIES ACCORDING TO DIAGNOSTIC CATEGORIES*

	Percentage of Births	
	United States 1978	Dublin 1980
Dystocia (Cephalopelvic disproportion)	4.7	0.7
Repeat section	4.7	1.1
Breech	1.8	0.6
Fetal distress	0.8	0.5
Other	3.2	1.9
Total	15.2	4.8

*Reprinted with permission from the American College of Obstetricians and Gynecologists²⁶

undergo successful inductions. Induction of labor invariably fails in patients with scores of 4 or less.

ELECTIVE INDUCTION OF LABOR

The elective induction of labor at a predetermined time in pregnancy, the so-called planned delivery, has gained widespread acceptance in many parts of the world. It is estimated that 35 to 50 percent of all hospital deliveries in Britain are induced, and many of these inductions occur in the absence of clearcut medical indication.²¹ Advocates of the planned delivery argue that this type of delivery can be of great practical and social benefit to both obstetrician and mother.²²

Despite the widespread use of this method, the only controlled trials comparing the outcomes of electively induced labors and spontaneous labors have involved too few cases to draw definite conclusions.²³ Since there are definite, though infrequent, complications associated with the use of oxytocin, elective induction of labor purely for the sake of convenience or social benefit seems unwise in most instances.

AUGMENTATION OF LABOR WITH OXYTOCIN

When there is a failure of progression of labor due to inadequate uterine activity, oxytocin may be used to augment labor by the same technique as used for induction. The timing of the use of oxytocin in such circumstances is controversial. Recently much attention has been given to the "active management of labor" method espoused by O'Driscoll et al.²⁴⁻²⁷ The obstetricians at the National Maternity Hospital in Dublin, Ireland, have made a systematic attempt to curtail the duration of labor and to promote early delivery. Their goal is to assure every woman that the duration of labor will not exceed 12 hours. The active management policy includes the following: During the

first stage of labor, progress is measured in terms of cervical dilation, which is plotted on a graph. The slowest acceptable rate is 1 cm/h, which allows ten hours for complete dilation. In nulliparous women, lack of acceptable progress is treated promptly with oxytocin if there is a single fetus in vertex presentation and no fetal distress. Lack of progress in multiparous women is seldom treated with oxytocin. A prospective study of this policy was reported for the labors of 1,000 nulliparous women in 1973.²⁵ Only 45 of their infants were not delivered within 12 hours, and only nine cesarean sections were performed for cephalopelvic disproportion or prolonged labor. About 40 percent of the women received oxytocin.

For the past 15 years this active management policy has been used at the National Maternity Hospital. The cesarean section rate has remained at 4.8 percent, compared with a rise from 4 percent to over 15 percent in the United States. The perinatal mortality rate has fallen from 42.1 per 1,000 to 16.8 per 1,000 infants, a decrease similar to that seen in the United States. The rates of cesarean section for various indications for O'Driscoll's group and for the United States are listed in Table 5.²⁶⁻²⁸

The difference in cesarean section rates between the Dublin group and similar centers in the United States seems to be accounted for mainly by a different approach to the management of labor in nulliparous women and by a rejection of the precept once a cesarean section, always a cesarean section. The diagnosis of cephalopelvic disproportion was made in less than 1 percent of these women.

Though the views of O'Driscoll's group represent one extreme, the results of their work are impressive. Considering the potential complications of prolonged labors in nulliparous women (eg, maternal fatigue, complications of prolonged rupture of membranes, complications of prolonged anesthesia), the active

management of labor method, even in a modified form, may be of great benefit to mother, infant, and physician.

ALTERNATIVE METHODS FOR INDUCTION AND AUGMENTATION OF LABOR

Induction and augmentation of labor have been attempted using other methods and techniques, both alone and in combination with oxytocin. Some of these methods are summarized briefly below.

Prostaglandins. Prostaglandins have become widely used in many countries for the induction of labor but have not yet gained approval from the Food and Drug Administration for this indication. They are usually given either intravenously or as intravaginal suppositories. Prostaglandins also may be very effective when used to ripen the cervix.

Amniotomy. Rupture of the membranes results in the rapid release of prostaglandin metabolites into the bloodstream.²⁹ In nulliparous women at term, rupture of membranes will be followed by labor within 12 hours in about 80 percent of women.³⁰ The onset of labor following amniotomy in multiparous women is not nearly so predictable.

Vigorous Vaginal Examination. In animals any vigorous vaginal examination results in the release of prostaglandins from fetal membranes.³¹ There is no evidence, however, that vigorous vaginal examinations help to initiate labor in humans.

Stimulation of the Breasts. Stimulation of the breasts results in the release of endogenous oxytocin. If the uterus is sensitive to oxytocin (eg, late pregnancy), uterine contractions theoretically should result. This method of inducing labor has not been well studied.

Maternal Position. Several studies have shown that the vertical position is associated with an increased intensity and frequency of contraction and a decrease in the duration of labor.^{32,33} Ambulation, however, requires a nonmedicated, nonexhausted patient with no evidence of fetal distress and a fetal head firmly applied to the cervix. The use of ambulation for the augmentation of labor may become more feasible with the development of telemetry systems.

OTHER USES OF OXYTOCIN

Postpartum Hemorrhage. Oxytocin is used to control postpartum hemorrhage. It can be administered by intramuscular injection or intravenous infusion of dilute solution. It should never be given by rapid intravenous bolus. If hemorrhage is brisk, more active oxytocic agents such as ergots may be needed.

Contraction Stress Test. The contraction stress test (CST, or oxytocin challenge test) is used in the antepartum period to assess fetal well-being when there is a possibility of fetal compromise. The indications for and administration of the CST will not be discussed here. Only rare complications have been reported. One concern about the use of CSTs prior to 38 weeks' gestation has been the possibility of the initiation of premature labor. Recent studies have shown that there is no difference in the incidence of spontaneous labor in a five-day period for women who receive a CST prior to that period or for women who receive no test.³⁴

Placental Separation. Oxytocin is often given after the delivery of the anterior shoulder to hasten placental separation. This technique seldom offers any real advantages. It also does not appear to increase the chance of placental entrapment.

CONCLUSIONS

Oxytocin is a potent stimulant of uterine contractions that has widespread use among all physicians who deliver babies. In addition to increasing the intensity and frequency of contractions, oxytocin facilitates the correction of ineffective or irregular uterine contractions during labor. If properly used, oxytocin is a very safe pharmacologic agent. Complications resulting from the improper use of oxytocin can be severe, but can usually be avoided by proper administration of the drug and careful fetal and maternal monitoring. Recent evidence suggests that a more aggressive use of oxytocin in the augmentation of labor, particularly in nulliparous patients, may be of great benefit. Oxytocin should probably not be used to induce labor in the absence of medical indications.

References

1. Petrie RH: The pharmacology and use of oxytocin. *Clin Perinatol* 1981; 8(1):35-47
2. Cibils LA: *Electronic Fetal-Maternal Monitoring: Antepartum/Intrapartum*. Boston, PSG, 1981
3. Caldeyro-Barcia R, Serono JA: The response of the human uterus to oxytocin throughout pregnancy. In Caldeyro-Barcia R, Heller H (eds): *Oxytocin*. New York, Pergamon, 1961
4. Whalley PJ, Pritchard JA: Oxytocin and water intoxication. *JAMA* 1963; 186:601-603
5. Dawood MY, Rhagavan KS, Pociask C, et al: Oxytocin in human pregnancy and parturition. *Obstet Gynecol* 1978; 51:138-143
6. Dawood MY, Wang CF, Gupta R, et al: Fetal contribution to oxytocin in human labor. *Obstet Gynecol* 1978; 52:205-209
7. Husslein P, Fuchs AR, Fuchs F: Oxytocin and the initiation of human parturition: I. Prostaglandin release during induction of labor by oxytocin. *Am J Obstet Gynecol* 1981; 141:688-693
8. Fuchs AR, Husslein P, Fuchs F: Oxytocin and the initiation of human parturition: II. Stimulation of prostaglandin production in human decidua by oxytocin. *Am J Obstet Gynecol*

1981; 141:694-697

9. Poseiro JJ, Noriega-Guerra L: Dose response relationships in uterine effects of oxytocin infusions. In Caldeyro-Barcia R, Heller H (eds): *Oxytocin*. New York, Pergamon, 1981
10. Sica-Blanco Y, Sala NC: Uterine contractility at the beginning and end of an oxytocin infusion. In Caldeyro-Barcia R, Heller H (eds): *Oxytocin*. New York, Pergamon, 1981
11. Knutzen VK, Tannenberger U, Davey DA: Complications and outcome of induced labor. *S Afr Med J* 1978; 52:482-485
12. Trivedi RR, Patel KC, Swami NB: Rupture of the uterus: A clinical study of 181 cases. *J Obstet Gynaecol Br Comm* 1968; 75:51-54
13. Hendricks CH, Brenner WE: Cardiovascular effects of oxytocic drugs used postpartum. *Am J Obstet Gynecol* 1970; 108:751-760
14. Caldeyro-Barcia R, Poseiro JJ: Fetal and maternal dangers due to misuse of oxytocin. *II Int Cong Gynecol Obstet (Montreal)* 1958; 2:450-463
15. Beazley JM, Alderman B: Neonatal hyperbilirubinemia following the use of oxytocin in labor. *Br J Obstet Gynaecol* 1975; 82:265-271
16. Flaksman RJ, Vollman JH, Benfield DG: Iatrogenic prematurity due to elective termination of the uncomplicated pregnancy: A major perinatal health care problem. *Am J Obstet Gynecol* 1978; 132:885-888
17. Blacow M, Smith MN, Graham M, et al: Induction of labor, letter. *Lancet* 1975; 1:217
18. Ounsted MF, Boyd PA, Hendrick AM, et al: Induction of labour by different methods in primiparous women: II. Neurobehavioral status of the infants. *Early Hum Dev* 1978; 2/3:241-253
19. Bishop EH: Pelvic scoring for elective induction. *Obstet Gynecol* 1964; 24(2):266-268
20. Lange AP, Secher NJ, Westergaard JG, et al: Prelabor evaluation of inducibility. *Obstet Gynecol* 1982; 60:137-147
21. Tipton RH, Lewis BV: Induction of labour and perinatal mortality. *Br Med J* 1975; 1:391-392
22. Ounstead M, Simons C: Maternal attitudes to their obstetric care. *Early Hum Dev* 1979; 3/2:201-204
23. Martin DH, Thompson W, Pinkerton JH, et al: A randomized controlled trial of selective planned delivery. *Br J Obstet Gynaecol* 1978; 85:109-113
24. O'Driscoll K, Jackson RJ, Gallagher JT: Prevention of prolonged labour. *Br Med J* 1969; 2:477-483
25. O'Driscoll K, Stronge JM, Minogue M: Active management of labor. *Br Med J* 1973; 3:135-137
26. O'Driscoll K, Foley M: Correlation of decrease in perinatal mortality and increase in cesarean section rates. *Obstet Gynecol* 1983; 61:1-5
27. O'Driscoll K: Active management of labor as an alternative to cesarean section for dystocia. *Obstet Gynecol* 1984; 63:485-490
28. National Institutes of Health consensus development statement on cesarean childbirth. *Obstet Gynecol* 1981; 57:537-545
29. Sellers SM, Hodgson HT, Mitchell MD, et al: Release of prostaglandins after amniotomy is not mediated by oxytocin. *Br J Obstet Gynaecol* 1980; 114:788-795
30. Turnbull AC, Anderson AB: Induction of labour: Part I. Amniotomy. *J Obstet Gynaecol Br Comm* 1967; 75:849-854
31. Flint AP, Forsling ML, Mitchell MD: Blockade of the Ferguson reflex by lumbar epidural anaesthesia in the parturient sheep: Effects on oxytocin secretion and uterine venous prostaglandin F levels. *Horm Metab Res* 1978; 10:545-547
32. Read JA, Miller FC, Paul R: Randomized trial of ambulation versus oxytocin for labor enhancement: A preliminary report. *Am J Obstet Gynecol* 1981; 139:669-672
33. Caldeyro-Barcia R, Noriega-Guerra L, Cibils L, et al: Effect of position changes on the intensity and frequency of uterine contractions during labor. *Am J Obstet Gynecol* 1960; 80:284-290
34. Braly PS, Freeman RK, Carite TJ: Incidence of premature delivery following the oxytocin challenge test. *Am J Obstet Gynecol* 1981; 141:5-8

OXYTOCIN
 AND
 THE
 PARTURIENT