Appendix F

Ambulatory Tocodynamometry

Introduction

About 8 percent of all live births in the United States, on the order of **300,000** per year, occur before 37 weeks of gestation. A large percentage of these premature, or preterm, babies are of low birthweight, accounting for roughly half the low birthweight babies born each year. Many of these infants require intensive care, some will die in their first month or year of life, and some will have permanent disabilities as a result of their premature birth. Ambulatory tocodynamometry is designed as an aid to secondary prevention, an "early warning system" for detecting preterm labor, with the hoped-for effect of greater success of stopping early labor from progressing to an immediate birth.

The ambulatory tocodynamometer has an electronic sensor (a resistance strain gauge of sorts) that detects uterine contractions through the wall of the abdomen. The device is worn by a pregnant woman, strapped on with a belt. Signals from the device are stored in an attached recorder and later transmitted by telephone line to be plotted on a paper strip so the pattern of activity can be interpreted by a nurse or other trained professional. If preterm labor is diagnosed more than about 4 weeks before the due date (full term considered to be **36** weeks gestation), attempts to stop the labor can be made, assuming there are no medical reasons for the pregnancy to end early. How well tocodynamometry will play a part in averting preterm births still is unsettled, though information is accumulating as studies of the device are completed. There remain considerable uncertainties about the appropriate use of ambulatory tocodynamometry in clinical practice, though current information suggests that it may be effective under certain conditions. Whatever the clinical usefulness of ambulatory tocodynamometry, it is clear that research about the natural history of uterine activity in pregnancy, normal and abnormal, could benefit greatly from the information-gathering abilities of the device.

The underlying causes and events precipitating most cases of preterm labor are not well understood, and attempts at primary prevention of preterm labor—avoiding or averting its occurrence at all—have been, by and large, unsuccessful. It is possible, however, to identify some women who have a high likelihood of the premature onset of labor, based on their previous obstetric history and some characteristics of their current pregnancy. The preexisting conditions that set apart women at high risk for preterm labor include preterm labor or preterm birth in a previous pregnancy and certain abnormalities of the uterus. In the current pregnancy, an initial episode of preterm labor, twin (or higher multiple) pregnancy, cervical dilation, and "uterine irritability" (excessive uterine activity, not necessarily with full, high-amplitude contractions characteristic of labor) indicate a high risk of preterm labor. Many episodes of preterm labor and subsequent preterm births occur among a much larger pool of women without those specific risk factors. Clinically, ambulatory tocodynamometers have been used mainly by the former group of women—those with known risk factors. There has also been interest in developing a means to use the devices for identifying women from the larger group who are likely to experience preterm labor.

Another strategy that addresses the problem of preterm labor and might be placed in the category of tertiary prevention—trying to prevent or minimize untoward consequences of preterm labor—is the aggressive treatment of premature infants. Although large gains have been achieved through neonatal intensive care, the margin for further improvements is shrinking, and the already high costs are still rising. [1]

Strategies for Stopping Preterm Labor

The tocodynamometer itself is an information-generating technology that can be used to diagnose preterm labor in early stages, and its potential for improving the outcomes of preterm labor depends entirely on the availability of interventions to alter the natural course of events. Studies adequate to characterize the efficacy and safety of nearly all the available "tocolytic," or labor-stopping, interventions are lacking, though some approaches appear to be more effective than others.

One of the impediments to evaluating tocolytic interventions has been the fact that women do not readily recognize the very early stages of labor, when it is generally believed that the process is most amenable to intervention (Newman, Gill, Wittreich, et al., 1986). Once significant physical change in a woman's

[1] For information on the costs and effectiveness of neonatal intensive care units (NICUs) see ch. 2 and OTA's 1987, case study entitled *Neonatal Intensive Care for Low Birthweight Infants: Costs and Effectiveness* (U. S. Congress, OTA, 1987).

cervix occurs, a preterm birth may be unavoidable, given the currently available tocolytic strategies.

The idea for using ambulatory tocodynamometry developed out of the apparent success in certain highly motivated women of "self-palpation" of the uterus to detect contractions before the women would normally become aware of them. The aim was to shift the detection of labor to an earlier point when successful long-term tocolysis is thought to be more likely, The disappointing overall success rates of tocolysis, as reported in the literature, stem from a combination of the low probability of stopping labor in advanced stages and the effectiveness of the interventions. Using tocodynamometry in studies of tocolytic interventions could help clarify the effects of the interventions themselves when conditions appear more favorable for success. The discussion of tocolytic interventions presented here reflects the current literature and the experience with these techniques as they have been used generally.

The idea of intervening to stop the course of premature labor, or to prevent its occurrence entirely, is not new, and a number of pharmacologic and physical approaches have been tried over the years. Hydration is usually tried, with or without other measures. Some classes of pharmacologic agents—e.g., tranquilizers, spasmolytics, opiates, anesthetic agents—are no longer considered to be effective. There still is some minor interest in ethanol and hormonal agents (e. g., progesterone) for stopping preterm labor. Estrogen, in the form of diethylstilbestrol (DES), was at one time considered useful (on the theory that estrogen deficiency was the cause of preterm labor), but this substance is no longer used. The earliest approach to attempt prevention of preterm births, and one still current despite a lack of evidence of efficacy, is bedrest. Cervical cerclage, a surgical procedure which was introduced about **40** years ago in which the mouth of the cervix is physically cinched together with a suture, also is still used, though its popularity has waned.

Tocolytic Drugs

Beta-mimetic drugs and magnesium sulfate are the most recent, and probably the most effective, drug interventions for stopping labor. Ritodrine hydrochloride, a beta-mimetic, is the only drug approved by the U.S. Food and Drug Administration (FDA) for the inhibition of uterine contractions in threatened preterm labor. Developed specifically for this use and tested in clinical trials (including randomized trials) during the 1970s, ritodrine was approved in 1980, one of a small number of drugs approved in recent years for use during pregnancy (Barden, Peter, and Merkatz, 1980). Another beta-mimetic, terbutaline, a commonly prescribed bronchodilator used by asthmatics, is widely used for tocolysis, though it has not been approved for that indication.

Beta-mimetic drugs act by altering the cascade of events that leads to contraction. "Receptors" on the surface of smooth muscle cells play a role in mediating the ionic balance of the cells, including the influx and outflow of calcium ions, which are instrumental in the events leading to muscle contraction. Ritodrine and terbutaline selectively stimulate receptors that predominate in uterine muscles—''$beta_2$ receptors"-although they also affect the "$beta1_1$ receptors" of the heart muscle and other organs. Stimulation of the $beta_1$ receptors results in quickening of the heart beat, one of the major side effects of beta-mimetic drugs. All beta-mimetics may stimulate a wide range of organ receptors, which may cause severe adverse effects on the cardiovascular system.

A recent overview of randomized trials of beta-mimetic drugs concluded that they can be effective in halting preterm labor in the short term—e.g., for **24** to **72** hours—but there is insufficient evidence from those trials to conclude anything about their efficacy in the longer term (King, Keirse, Grant, et al., **1985).** Part of the problem in interpreting those trials to understand the potential of the tocolytic agents used is that in most women, preterm labor is far advanced before it is recognized, and tocolysis fails. The pertinent question with the use of tocodynamometry is whether tocolytics will, as is often assumed, be more effective overall when preterm labor is diagnosed in earlier stages. Randomized clinical trials of the tocodynamometry / tocolysis combination will be required to adequately characterize the safety and effectiveness of this approach. Potential negative effects include overdiagnosis of preterm labor, resulting in unnecessary tocolytic treatment, and treatment of women in whom preterm labor would resolve spontaneously.

Bedrest and Cervical Cerclage

In the realm of strategies to avoid the onset of preterm labor, at least one randomized trial has been conducted of hospital bedrest. That study compared hospital bedrest against hospitalization as needed from **32** weeks of gestation for women with twin pregnancies. Hospital bedrest conferred no benefit at all in preventing the occurrence of preterm labor. In fact, preterm deliveries were more common among women in the group randomized to compulsory hospitalization than among women in the ambulatory group (Saunders, Dick, Brown, et al., 1985). Despite this negative finding and no reliable positive studies, routine bedrest still is commonly prescribed.

The first randomized clinical trial of cervical cerclage was published in 1984 (Lazar, Gueguen, Dreyfus, et al., 1984). Because cervical cerclage has been so widely accepted by obstetricians for women with a high-risk profile for premature delivery due to cervical incompetence, the trial included only women at "moderate" risk. In the end, the rate of preterm births was no different in the cerclage and the control groups. The trial had two important results. First, it provided clear evidence that cervical cerclage was not effective in reducing the rate of preterm births among women at average risk. Second, it raised enough doubt about the usefulness of the procedure to plan a further trial of cervical cerclage in women at high risk.

Women at high risk of preterm delivery were recruited for the second randomized trial of cervical cerclage (Rush, Isaacs, McPherson, et al., 1984), The findings parallel those of the first trial. No evidence of benefit, either in lowering the preterm delivery rate or improving survival, was detected. In several ways, women with cerclage fared worse than those without, having longer hospital stays (excluding the time spent in hospital for the cerclage itself), receiving more tocolytic drugs, and having more fevers (though the latter two differences were not significant statistically).

It still is possible that cerclage may be beneficial to a specific group of women with cervical incompetence, but its use has not been so limited. Further studies may elucidate an appropriate role for this procedure.

Risk Factors for Preterm Labor and Preterm Birth Prevention Programs for High-Risk Women

Certain factors have been identified that set apart women at high risk for preterm labor, some of the factors present before the pregnancy and some related to what is experienced during the pregnancy. Preexisting risk factors, some being stronger predictors than others, include: preterm labor in a previous pregnancy, uterine anomalies, being a "DES daughter" (a woman exposed in utero to the drug DES during her mother's pregnancy), and previous spontaneous or therapeutic abortions. Risk factors associated with the pregnancy itself include: twin (or higher multiple) pregnancy (also called "multiple gestation"), arrested preterm labor in the current pregnancy, and recurring uterine "irritability, " or infection. (There also are sociodemographic factors that seem to be associated with a higher risk of preterm birth—e.g., teenage low-income women are more likely to experience preterm labor—but these factors are not such strong predictors on an individual basis.)

Using this type of information, investigators have developed risk scoring scales to identify women at high risk of preterm labor. The French obstetrician Dr. Emile Papiernik developed such a scale in the late 1960s, and he applied it in an area of France in a broad-based educational program aimed at bringing down the rate of preterm births during the early 1970s. Although the success of particular aspects of the French program could not be evaluated independently, the preterm birth rate did drop gradually over a 12-year period from 5.4 to 3.7 percent. That drop suggests the possibility of influencing the preterm birth rate (Papiernik, Bouyer, Dreyfus, et al., 1985); however, other factors might have been changing over time as well, and the change cannot be clearly attributed to any particular factor.

In the late 1970s, Dr. Robert Creasy, who built on Papiernik's scoring system, introduced the first preterm birth prevention program in the United States based on self-detection of uterine contractions (Herron, Katz, and Creasy, 1982). That program laid the groundwork for ambulatory tocodynamometry. Specifically, Creasy and his colleagues used a risk scoring method, which included both medical and sociodemographic factors, to divide their population of patients into low- and high-risk groups. Women in the high-risk group were educated about the early signs and symptoms of preterm labor and were taught the technique of self-detection of painless contractions by palpating the uterus, These women had weekly cervical monitoring at a special clinic. The clinic staff also had special training and education to optimize their responses to the women in the program and to recognize the subtle symptoms seen at the onset of preterm labor. The low-risk women got their usual obstetric care. No controlled studies were carried out in conjunction with this program,

During the first year of the program, **24 (2.5** percent) of the **974** low-risk and **30 (17** percent) of the 176 high-risk women entered labor prematurely (before **36 weeks gestation). Beta-mimetic** drugs were given to most of the women (those who had not progressed beyond specific stages of labor and for whom there were no contraindications for continuing the pregnancy) with final results of full-term deliveries for 23 of the high-risk women and for 15 of the low-risk women who had experienced preterm labor.

The overall preterm birth rate (including those women who had intentional preterm deliveries for medical reasons) during 1979, the year after the program was initiated, was **2.4** percent. The preprogram **1977 rate was 6.75** percent. The authors also reported that the annual rates from 1977 through 1979 at an

affiliated institution remained above 6.5 percent. While no causal inferences could be drawn because there was no control population, it is possible that the program accounted for some or all of the change. In any case, the generalizability of results from the program is limited because the population enrolled was a self-selected, highly motivated group of women,

The positive result of this program, however, was to spur the initiation of a randomized trial of the Creasy program at five institutions around the country, sponsored by the March of Dimes. The results of this study are not yet available.

Development and Current Use of Ambulatory Tocodynamometry

The ambulatory tocodynamometer is intended as an adjunct to a preterm birth prevention program such as Dr. Creasy's. This device should be more reliable than self-detection of early labor and would allow women to stay at home when they otherwise might be hospitalized or have emergency room or office visits. Three such devices have been developed in the United States. One, TermGuard®, made by the Tokos company, was developed by Dr. Michael Katz, who was a fellow of Dr. Creasy's, and the other devices were developed by the Litton and Healthdyne companies. All three ambulatory devices are considered "substantially equivalent" to hospital-based stationary tocodynamometers that have been marketed since the 1950s, and the manufacturers have obtained FDA clearance on that basis. Currently, these devices cannot be advertised as being effective for use in detecting preterm labor or in preventing preterm births, but only for detecting uterine activity, the function of the stationary devices. The Tokos company is seeking FDA approval to market TermGuard® with a claim that the device prevents preterm births, based on completed and ongoing clinical trials. On the basis of current approval, however, thousands of pregnant women have been monitored over the past few years, most with Tokos' equipment.

Although there are differences in the capabilities of the three brands of tocodynamometer, the most important difference among them is in the way they are marketed. While the Litton device is sold to be used by independent practitioners or institutions, Tokos' TermGuard® is marketed not simply as **a** device, but as a service, to be prescribed by doctors. (Healthdyne has followed Tokos' lead, though it is quite new to the market.) Once the service has been prescribed, nurses employed by Tokos at special centers interact with patients, teaching them how to monitor, talking to them each day, and receiving their monitoring transmissions. In general, patients on the Tokos system are asked to monitor twice daily for an hour at a time, during which time they may move around. With the "sensor" strapped on, uterine activity is detected, and the electronic signals are stored in the attached recorder. During telephone contact, the daily signals are sent to the nursing center over an ordinary phone line and printed out on a graphing tape, similar to the printout in a hospital setting. The pattern of low- and high-amplitude contractions is interpreted immediately after transmission by a trained perinatal nurse.

Tokos nurses confer with the prescribing physicians to define criteria for notifying them of unusual uterine activity and to inform them of when those criteria are met. The notification criterion is typically four or more contractions in an hour. Following notification, the doctor decides on the appropriate action. If preterm labor is confirmed by physical examination (a finding of cervical effacement), intervention with a tocolytic agent may be prescribed.

Tokos does not currently sell its devices and therefore retains considerable control over how they are used. Litton does not offer such a service and sells its devices (including the monitors, recorders, and readout units) outright. Most have been bought by hospitals, private physicians, and private companies.

Tokos currently operates **30** nursing centers around the United States and 1 in France. Since **1984,** more than 10,000 women have been monitored, an average of 53 days each and at a cost of about $75 per day. As of October 1987, 10 State Medicaid programs had approved tocodynamometry for coverage (not all had set reimbursement rates) and most of the major private insurance companies, including several Blue Cross/Blue Shield plans, provided some coverage, primarily for patients who have had preterm labor stopped and been sent home from the hospital with the device.

Studies of the Effectiveness of Tocodynamometry

The first studies of ambulatory tocodynamometry as part of a program for women at high risk of preterm delivery were carried out, as is often the case with new technologies, by the device's proponents, including one of its developers. These early studies, which did have control groups but which did not use random allocation, had very positive results: significant numbers of preterm births were avoided and no unintended adverse effects were found. They also answered affirmatively some basic questions about the practicality of ambulatory tocodynamometry—e.g., can

uterine activity patterns be accurately and reliably transmitted over existing phone lines?

So far, few studies of ambulatory tocodynamometry in clinical practice have been completed, so available evidence on which to judge the effectiveness of the technique is limited. In general, however, findings from the more recent studies have been more modest. All of the studies reviewed here involve the Tokos service or a similar set of services, so the results cannot be interpreted as strictly attributable to the device itself. In particular, there is a suggestion that the daily contact between the pregnant women and the Tokos nurses that is included in the service may account for at least part of the benefit found in earlier studies. Other differences in results among studies may be explained at least in part by other factors, including underlying differences in study populations, e.g., in the definitions of "high risk, " in the effective use of tocolytic interventions by physicians, and in the treatments given to the "control" groups.

The first report of ambulatory tocodynamometry was published in August 1985 (Katz and Gill, 1985). The authors aimed to answer basic questions about the device itself (TermGuard®, Tokos Medical Corp.) and the information it provides. First, do TermGuard® readings correlate with readings from stationary external uterine activity monitors with regard to the frequency of contractions? Second, do TermGuard® external readings correlate well with readings from internal uterine pressure catheters in measuring intrauterine pressure, a measure of intensity, during contractions? And last, can the device be used successfully by a pregnant woman at home? Those questions were all answered in the affirmative.

Questions about the overall effectiveness of tocodynamometry in preventing preterm birth have been addressed in later studies, with more mixed results, though generally positive findings. None of the studies to date, however, has been free of major design flaws or been large enough to give results that are unequivocal.

The first published evaluation of ambulatory tocodynamometry as part of a program to prevent preterm births, carried out by the device's developers and proponents, appeared in December 1986 (Katz, Gill, and Newman, 1986). The study reports the experience of **76** women at very high risk of having a pre-term birth as judged by their past obstetric history or the existence of uterine anomalies. The birth outcomes for these women were compared with those of a group of 76 women who were matched on risk factors, parity, and age. Most of the women (87 percent of monitored and 82 percent of unmonitored) were given instruction about the signs of preterm labor and were taught to palpate themselves for uterine activity. About half the women in both the monitored and unmonitored groups went into preterm labor. All women in preterm labor, except those with extreme cervical dilation, were treated with intravenous ritodrine; then, if tocolysis was successful, they were switched to oral ritodrine or terbutaline. Overall, 67 of the 76 monitored women (88 percent) had deliveries at or beyond 37 weeks; 45 of the 76 unmonitored women (59 percent) reached at least 37 weeks.

In March 1987, a controlled study of ambulatory tocodynamometry was reported (Morrison, 1987).[2] The study compared the Tokos system (34 women) with self-palpation (33 women) for monitoring uterine activity in **a** group of women at very high risk of having a preterm delivery. Only women with one of the following risk factors were eligible for entry into the study: 1) multifetal gestation (meaning twin or higher multiple pregnancy), 2) uterine abnormalities, or 3) history of two or more preterm births. (These criteria are more stringent than those used in the earlier studies, resulting in a higher overall rate of preterm labor in the study population.)

The tocodynamometry group wore monitors to record uterine activity twice daily for an hour at a time, and both groups were instructed about the signs and symptoms of preterm labor. Women in the tocody - namometry group had regular daily contact with Tokos' nurses, and those in the self-palpation group, twice weekly. All women were advised to call if they had symptoms of preterm labor.

Overall, the results favored ambulatory tocodynamometry over self-palpation: 18 of the 33 women in the self-palpation group, and 29 of the 34 women in the group with tocodynamometers, carried their pregnancies to term. About two-thirds of the women in each group (22 in the self-palpation group and **24** in the Tokos group) had a diagnosis of preterm labor, but more of the self-palpation women were farther along in the course of labor than were the Tokos women at the time of diagnosis. The investigators attribute the difference in overall outcome largely to the greater success of tocolytic intervention (most with magnesium sulfate, and a few with ritodrine hydrochloride) in the Tokos women because they were treated in earlier stages of labor. Although this is a relatively small study, the results are quite striking and appear to represent a positive effect of the Tokos system, though the true size of the effect cannot be estimated reliably.

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[2] Although the study is described as "randomized," in fact, it was not. Women were allocated to one group or the other according to whether the last digit of their hospital numbers were odd or even, Whether this affected the results is unknown.

A second study comparing the Tokos system with self-palpation appeared in September 1987 (Iams, Johnson, O'Shaughnessy, et al., 1987). The advantage of this study is that the self-palpation group had a level of contact with the Tokos nurses similar to that of the tocodynamometry group, so the difference in the interventions was narrowed as much as possible to the device itself. The following risk factors qualified women for entry into the study: 1) previous preterm delivery, 2) twin pregnancy, 3) previous second trimester loss, 4) cervical cerclage in this pregnancy, 5) uterine anomaly or DES daughter, and 6) bleeding after 14 weeks of pregnancy. The report states that 157 women were randomly allocated[3] in a ratio of 1:2 to either education and self-palpation (50 women, referred to as group E) or education and tocodynamometry (107 women, referred to as group EM).

The two groups had similar rates of preterm labor (about 37 percent of the women), and the progress of labor was not generally farther along in group E women than it was among group EM women when it was diagnosed. The rate of preterm birth was about the same in each group (20.4 percent before 35 weeks gestation in group E, and 23.5 percent in group EM), and there were no significant differences in the rate of successful tocolysis, gestational age, birthweight, or days gained from first preterm labor to delivery between the two groups.

The conclusion from this study in this group of patients is that tocodynamometry and self-palpation, both accompanied by intensive nursing support, produced about equal rates of preterm birth in a high-risk population. Because there was no group without intervention, the size of the effect relative to no intervention cannot be estimated directly. The investigators concluded that the role of "frequent and supportive patient contact in preterm birth prevention" should be given greater attention, and further that "the role of ambulatory contraction monitoring has yet to be defined." The finding of no major difference in outcome between the two groups is difficult to interpret because of the lack of a true control. The study does, however, point out the need to clarify what elements of monitoring—those centering on the device versus those centering on the interaction between the patient and provider—make a difference, as well as which women are most likely to benefit from monitoring.[4]

Results of a third study of ambulatory tocodynamometry in high-risk women who have not yet had an episode of preterm labor in the current pregnancy were presented at the 1987 meeting of the Society of Perinatal Obstetricians (Porto, Nageotte, Hill, et al., 1987).[5] In this study, high-risk women were randomly assigned to one of three groups. " Groups 1 and 2 were supplied with Tokos monitors and taught to use them, and the third group had no special intervention. The first two groups had daily contact with the Tokos nurses and transmitted their recorded data to the Tokos center, but the data were used to manage only group 1. For group 2, data were not used for patient management. A total of 136 patients were entered in the trial, 44 in group 1, 46 in group 2, and 46 in group 3. The investigators excluded "noncompliant" women from the analysis (3 women from group 1 and 4 women from group 2). The results indicated a similar rate of preterm labor in all three groups, but a lower rate of preterm deliveries in groups 1 and/or 2 compared with group 3 (reaching conventional levels of statistical significance). The analysis was based on small numbers of preterm births, however (4 in group 1, 6 in group 2, and 11 in group 3), and the exclusion of the noncompliant women may well have had an effect on the analyses. It is not possible to draw strong conclusions from this study.

Using Tocodynamometry To Screen for Women at Increased Risk of Preterm Labor

"Risk scoring" methods exist to identify women with a high probability of delivering a preterm baby. Some of the risk factors that go into these systems are discussed above, While a high percentage of the identified high-risk group will have preterm labor and go on to a preterm delivery, the group that can be so identified is small, and in fact, approximately half of all preterm births are to women not so identified, but who are part of a much larger pool with a lower overall risk of preterm birth. One potential use for the ambulatory tocodynamometer is as a method to "screen" for women likely to proceed to preterm labor but who have no specific risk factors. Three studies comparing high-amplitude uterine contraction patterns (the type of contractions that occur at short intervals during labor and delivery) of women who experienced first spontaneous labor preterm, at term, and postterm, were presented at the 1987 annual meeting of the Society of Perinatal Obstetricians.[7] Another recent study looked at patterns of low-amplitude contractions (which, when occurring frequently, are termed *"uter-*

[3]The method of randomization is not given

[4]A methodologic problem with the study is that six women dropped out of the study from group E and nine from group EM, and these women were excluded from the analysis; their exclusion could have biased the results, though it is impossible to say whether this is the case

[5]Abstract only available

[6]The randomization scheme was not specified

[7]All available as abstracts only

ine irritability"). One study in the first group (Main, Katz, Chiu, et al., 1987) took a practical screening approach in which uterine activity of a group of low-risk women was followed—measured with an ambulatory tocodynamometer for 1 hour once a week at a clinic between **27 and 34 weeks gestation.** The tracings were read by individuals with no knowledge of the women's status, and after the deliveries took place, the tracings were analyzed according to the two groups into which these women fell: 1) those who experienced preterm labor (less than 37 weeks gestation), and 2) those who had spontaneous labor for the first time at term **(37** or more weeks gestation). As early as 28 weeks gestation, the group of women who would go on to preterm labor had a higher average number of contractions per hour than did the rest of the women, but the ranges of uterine activity between the two groups overlapped considerably. According to the investigators, 12 of the 17 women who developed preterm labor would have been identified by a criterion of five or more contractions in an hour anytime between **28 and 32 weeks gestation,** It would also have incorrectly picked out **34** of the 108 women who labored at term.

One of the other studies focused on a population of women with known risk factors for preterm labor who used ambulatory tocodynamometry as prescribed, monitoring for an hour twice daily (Tomasi, Eden, Canlas, et al., 1987). Distinct differences in uterine contraction patterns, beginning at about **29 weeks gestation,** were found in the group of women who would experience preterm labor compared with the group who would go on to term or later.

Little detail was given about the population studied in the third report, but the data support a general trend toward increased uterine activity among women who will experience preterm labor several weeks before labor actually begins (Nageotte, Dorchester, Porto, et al., 1987).

A study of low-amplitude contractions (Newman, Gill, Campion, et al., 1987) was undertaken because these contractions occurring at high frequency, a condition called "uterine irritability, " are considered a risk factor for preterm labor. In this study, 92 women at high risk of preterm labor and 50 at low risk were monitored with the Tokos system. The authors found that, in fact, many women who experienced low-amplitude contractions for a relatively high proportion of the time (more than **30** percent of the time) did enter labor prematurely. For a number of women, preterm labor was not preceded by that pattern, however. Those who demonstrated this pattern less than 10 percent of the time were much more likely to have term labor. Although the findings are of clinical and biologic interest, the authors concluded that a pattern of high-frequency, low-amplitude contractions could not be used as a screening technique because, overall, such a finding was not highly predictive of preterm labor.

Net Health Care Costs of Tocodynamometry

It is relatively easy to develop a simple model to determine the net monetary costs of ambulatory tocodynamometry, but it rests on a major assumption about the level of effectiveness of the device and associated services in reducing the frequency of preterm delivery. Basically, the costs of monitoring a group of women must be balanced against the savings in neonatal care for the percentage of women whose pregnancies are prolonged. Costs of monitoring can be measured directly, and savings can be measured as the average costs of treating preterm babies in neonatal intensive care units (NICUs). The preterm birth rates in different groups of women and the success rate for arresting preterm labor must be estimated from data from the few comparative studies of tocodynamometry that have been carried out and from other women who have been monitored. Net costs would decrease the more "efficiently" tocodynamometry were used, i.e., the larger the percentage of women in the monitored group who experience preterm labor, the greater the benefit would be. With a low rate of preterm labor, many more women would be monitored than would benefit, making a greater contribution to the cost side than to the savings side.

The following example uses data from Tokos' clinical experience (Tokos, 1987) and from studies of women at high risk of preterm labor and preterm delivery. Among a group of women who either have had a previous preterm delivery, have a uterine anomaly, or have a multifetal gestation, about 40 percent would be expected to have a preterm delivery, given accepted obstetric practice in the United States. About **30** percent would be expected to experience preterm labor, of whom **80 to 90** percent would go on almost immediately to a preterm delivery. The remaining 10 to **20** percent would extend their pregnancies by an average of about 4 weeks. Of those with no preterm labor, about 20 percent would have an intentional delivery before term.

In this example, the Tokos service could potentially extend the pregnancies of women who experience preterm labor, but for whom tocolysis would be too late without tocodynamometry (the **80 to 90** percent of 30 percent), and also extend for more than 4 weeks the pregnancies of those 10 to 20 percent (of the original

30 percent) whose labor would have been successfully stopped initially without Tokos. The effectiveness data, which come largely from nonrandomized studies and the patient files of the Tokos Medical Corp., currently are inadequate to select a number with confidence, but the existing data are consistent with a reduction in the overall preterm delivery rate from about **40** percent to about **25** percent. This reduction is assumed in the following analysis.

Net health care costs for society would be equal to the difference between the total cost of monitoring high-risk women and the savings resulting from reduction in the care required for the extra 15 percent of deliveries that would be carried to term as a result of the program. Using average figures, the cost of monitoring 100 women (for an average of **53 days at $75** per day) would be **$397,500.** The cost avoided for caring for the 15 babies brought to term, had they been born instead at the time of preterm labor, can be considered a savings. Costs include not only the extra care needed around the time of birth, but also some excess hospital readmission during the first year of life particularly and the long-term costs of caring for the proportion of preterm babies with lifelong handicaps due to prematurity. In addition to direct costs to society, families may bear extra emotional and financial costs at the birth of a premature baby, particularly one with severe disabilities.

Using data from the State of Maryland, OTA estimates the extra cost of hospital care for each preterm baby (assuming that all would have weighed less than **2,500** grams at birth) at between **$3,763 and $5,236.** [a] Extra initial physician costs are estimated at between **$475 and $1,487** per baby. Rehospitalization costs in the first year of life are an estimated **$802 extra** per preterm baby. The estimated cost of long-term care per low birthweight baby (up to age 35) is between $9,000 and $23,000. Based on these figures, the monetary cost of each low birthweight birth, therefore, totals between $14,040 and $30,525.[9] The potential savings in delaying 15 births (from the original 100 above) would be between $210,600 and $457,875, so there may or may not be a cost-saving when compared to the **$397,000.**

[a] "The figures for initial and first-year costs used in this analysis are based on data from the State of Maryland See ch. 4 of this report for details. Details of the long-term care costs are given in app G. Hospital and physician costs are given in 1986 dollars

"The figures are not charges, but estimates of resource costs Many analyses of the costs of caring for preterm babies have been based on actual charges, which may be considerably higher than resource costs, thus altering the balance in a cost analysis OTA's analysis, from the societal point of view, is more appropriately based on costs The distribution of birthweights at 28 to 31 weeks gestation was taken from U S national vital statistics for 1985 (U S. DHHS PHS 1987) A weighted average hospital cost per preterm birth was derived by allocating birthweight-specific costs by the proportion of births at 28 to 31 weeks in each birthweight category

In a complete analysis, several other costs must be considered, some of which would fall on the net cost side and others on the saving side. Extra costs would be incurred for women treated for preterm labor detected initially through tocodynamometry, in whom the labor would not otherwise have been detected and which would not have progressed to an immediate birth. The potential rate of such "false positive" diagnosis is not known at present. Hospitalization for initial tocolysis, plus oral tocolysis after discharge would be included. Potential adverse effects of tocolytic agents on the mother and/or fetus, which currently are poorly known, might also eventually become costly in dollars and certainly have human costs.

An additional benefit of tocodynamometry, which might result in cost savings, is the possibility of discharging women from the hospital on oral tocolytic agents earlier than they might otherwise be. In this case, the tocodynamometer may be used to calibrate the tocolytic dose and give feedback on uterine activity otherwise available only while the woman is hospitalized. It is possible also that women who have had a successfully arrested episode of preterm labor may be able to return home on ambulatory tocodynamometry, rather than be hospitalized for the remainder of the pregnancy.

Summary

As a machine, the ambulatory tocodynamometer must be seen as a valuable information-generating technology. It provides reliable information about the activity of the uterus during pregnancy. It has already increased knowledge about that activity in its use as a research tool. The machine does not, however, allow interpretation of the information it produces in a way that would provide a definite diagnosis of preterm labor. As more experience with the device is gained, using the information for diagnosis should improve. The most uncertain part of all is deciding on a course of action once preterm labor is detected, presumably early in its course, with daily tocodynamometry. Certain drugs appear to be effective in stopping labor from proceeding to delivery, but the evaluations have been spotty. Part of the difficulty in testing interventions in the past has been that most women are not aware that labor has begun until it has progressed to a point that it cannot be stopped. Interventions have been attempted anyway, mostly unsuccessfully. Older studies, in which most women were treated far along in labor, may not be relevant to the use of tocolytic interventions with early detection. Until there is a direct demonstration of the effectiveness of early tocolysis in a program that uses tocodynamometry, however, the actual value of the system cannot be judged.

Unfortunately, public sector research has focused almost entirely on learning about the natural history of labor, while the few intervention trials have been supported largely by manufacturers.

Ambulatory tocodynamometry may have the potential for significantly reducing preterm birth rates and perhaps saving money, if used in appropriate populations and if interventions are applied appropriately. It might also foster the development and evaluation of more effective means of tocolysis. The "ifs" cannot be taken as inevitable, however, and the consequences of the "if nets" include much greater use of tocolytic agents, with their known and unknown adverse effects, as well as potentially great cost. As more and more physicians use the Tokos service, and as more companies enter the market, the widespread dissemination of the ambulatory tocodynamometer may precede answers to questions about appropriate populations and about the use of tocolytic agents.

Tocodynamometry is still considered investigational by professional groups (e.g., the American College of Obstetricians and Gynecologists), and there are a large number of skeptics in the medical community. There is a pressing need for well-designed randomized trials of tocodynamometry in conjunction with the best tocolytic treatments available, across the sociodemographic spectrum of pregnant women at risk of preterm labor. Without additional careful studies soon, it may be impossible to place this device in its appropriate and rational niche.

Appendix F References

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