A Supplement to Ob.Gyn. News®

CLINICAL UPDATE

The Latest Techniques for Preventing Adhesions in Cesarean Delivery

Hector Chapa, MD, FACOG
Medical Director and Outreach Coordinator
Women's Specialty Center
Clinical Faculty
Obstetrics and Gynecology Residency Program
Methodist Medical Center
Dallas, Texas

According to the Centers for Disease Control and Prevention (CDC), cesarean delivery (CD) remains one of the most common surgeries in women of reproductive age. The US national cesarean delivery rate was 4.5% in 1965, when first tracked and reported.[1] The cesarean rate has increased over the last few decades and currently has reached an all-time high of 31%, which represents a doubling of the rate since 1996.[2,3] By extrapolation of trends, it is projected that "cesarean deliveries will make up approximately 50% of the more than 4 million annual deliveries by 2020."[4] This trend is global. In Brazil, local area hospitals report cesarean rates of 100%, with health districts reporting rates of 85%.[5]

Two main factors help explain this change in obstetric practice. The first is the litigious climate in which physicians practice. According to The American College of Obstetricians and Gynecologists (ACOG) 2009 Medical Liability Survey of 5,644 obstetricians-gynecologists, 29% reported performing more CDs, and 25.9% stopped offering or performing vaginal births after cesareans (VBACs) specifically because of liability concerns.[6] Not surprisingly, this is not a new occurrence. Another survey in 1999 found that 82% of physician survey participants in Ireland had decided to perform a CD specifically to avoid a malpractice claim.[7] It is this decrease in VBAC allowance that has fueled the overall rate of cesarean births since 1996.

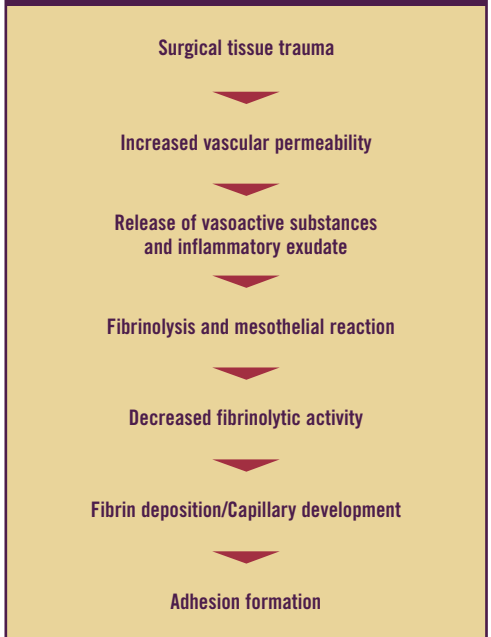
The second factor is the advent of CDs upon maternal request. Although traditionally not recognized, CD "on demand" has established a foothold in current practice. Though difficult to track, current estimates place the rate of CD "on demand" at 4% to 18% in the United States.[8]

Both nonmodifiable and modifiable morbidities are associated with increased CDs. Chief among the nonmodifiable morbidities is the rise in abnormal placentation that results from multiple CDs, which will not be the focus of this review. Chief among the modifiable morbidities is adhesion formation and its related morbidities. This review will address the pathophysiology, morbidity, and prevention tools relevant to abdominopelvic adhesive syndromes.

Adhesiogenesis

Central to adhesion formation is peritoneal trauma and injury. Devascularization and mesenchymal ischemia initiate the reparative process leading to reepithelialization (**Figure 1**).[9] Mesothelial cells migrate across areas of injury and lay a supportive matrix to allow for regeneration. The first 5 to 7 days are most influential for adhesion formation, and it is questionable whether any new adhesions form after that period. However, complete organization and remodeling may occur up to 3 to 4 weeks after formation.

FIGURE 1. Pathogenesis of Postoperative Peritoneal Adhesions



Source: The Practice Committee of the American Society for Reproductive Medicine.[9]
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Faculty Disclosure

Dr Chapa has received clinical grant funding from Johnson & Johnson Medical Affairs for clinical trials of Interceed® in cesarean section, is a medical consultant for ETHICON Women's Health & Urology, and serves as a speaker for Adhesion Prevention in Surgery.

This supplement was produced by International Medical News Group, a division of Elsevier Medical Information, LLC. Neither the editor of Ob.Gyn. News, the Editorial Advisory Board, nor the reporting staff contributed to its content.

INTERNATIONAL MEDICAL NEWS GROUP

The pregnant patient possesses additional factors favoring adhesion formation. The postpartum uterus resting against the abdominal wall/peritoneum has been postulated to be the reason for cohesive adhesions between the anterior abdominal wall and uterine serosa.[10] Additionally, the hypervascularity and tissue inflammation of pregnancy, as well as the substerile nature of the operative field, may further influence adhesion formation.

Although no formal grading system for adhesions currently exists, most adhesions are classified as grade 1 (filmy/peritoneal), grade 2 (moderate thickness), or up to grade 3/4 (severe/dense or cohesive).

Adhesion Frequency in Cesarean Deliveries

In one retrospective study, adhesions of all grades were found in 46% of second cesarean births, 76% of third cesarean births, and 83% of fourth cesarean births.[11] Similarly, Tulandi et al[12] documented adhesion frequencies in 24% of second cesarean births, 43% of third cesarean births, and 48% of fourth cesarean births. Percent differences between the two studies can be explained by the subjective grading scales employed in each cohort. The percentage of moderate-severe adhesions in each cohort varied less because of the more reproducible classification of cohesive disease (**Table 1**). Additionally, Nisenblat et al[13] compared 277 women undergoing a third or more CDs to 491 women undergoing a second CD. Excessive blood loss (7.9% vs 3.3%; $P<0.005$), difficult delivery of the neonate (5.1% vs 0.2%; $P<0.001$), and dense adhesions (46.1% vs 25.6%; $P<0.001$) were significantly more common in the group of women undergoing a third or more CDs, validating what practicing obstetricians have known for years.

General and Obstetric Sequelae of Adhesions

The morbidity associated with abdominopelvic adhesions is well documented. Published reports place small bowel obstruction (SBO) as one of the most dreaded complications of adhesion formation, with a rate of 50% to 75% of all SBOs being related to postoperative adhesions.[14-16] As related to CD, Al-Sunaidi et al[17] documented an SBO rate of 7/6,500 cases. Additionally, infertility,[9] chronic pelvic pain,[18] and subsequent surgical bowel/bladder injury have all been ascribed to adhesive disease.[19-20]

CD-related adhesions contribute to longer delivery times and total operating times during subsequent CDs. Tulandi et al[12] reported skin incision to fetal delivery times of 8.9 minutes for a first CD, 10.7 minutes for a second CD, and 12.8 minutes for a third CD. Similarly, Morales et al[11] reported an 18-minute delay of a fourth CD as a result of adhesions. This delay results in economic as well as infectious ramifications for the individual patient. Additionally, adhesions at CD increase the risk of bladder injuries, greater blood loss, and lower umbilical cord potential hydrogen (pH).[13, 21-24] In fact, lower umbilical blood pH is twice as likely during a repeat CD, when compared to a primary nonurgent CD; this is a direct consequence of adhesions.[25]

TABLE 1. Adhesions Following Cesarean Section Delivery

Procedure	N	% with adhesions
At time of 2nd C-section[11]	217	46%
At time of 3rd C-section[11]	64	76%
At time of 4th C-section[11]	6	83%
At time of 2nd C-section[12]	955	24%
At time of 3rd C-section[12]	255	43%
At time of 4th+ C-section[12]	73	48%
% Dense (moderate-severe) Adhesions		
Morales: 55% (2nd C/S), 54% (3rd C/S), 60% (4th C/S)		
Tulandi: 48% (2nd C/S), 56% (3rd C/S), 56% (≥4th C/S)		

Sources: Morales et al[11]; Tulandi et al.[12]
C/S=cesarian section.

Where Are Adhesions Most Likely to Develop?

Adhesions favor two anatomic areas in patients who have had a CD: (1) between the hysterotomy site/bladder flap and anterior peritoneum and (2) between the anterior uterine serosa and anterior abdominal wall. The medical literature points to the latter as the more frequent (**Figure 2**). It is proposed that the postpartum uterus resting on the traumatized peritoneal edges facilitates junction of the two by the regenerating peritoneal edges (**Figure 3**). The influence that peritoneal suturing may have on this phenomenon will be discussed later.

FIGURE 2. Cesarean Section Adhesion Locations

Author	Anterior Uterine/ Abdominal Wall (Fascia)	Bladder Flap/Anterior Uterine
Morales et al	77%	Not Applicable
Tulandi et al	48%-53%	26%-35%
Lyell et al	27%*	12%*

*Nonperitoneal closure group.
Sources: Lyell et al[10]; Morales et al[11]; Tulandi et al.[12]

FIGURE 3. Images Taken at Diagnostic Laparoscopy in Two Separate Patients Following Low Transverse Cesarean Sections

Grade 2 adhesion at time of C/S
Adhesion is between lower uterine segment and abdominal wall (peritoneum and rectus muscles)

Grade 3 adhesion at time of C/S
Exteriorized post-cesarean uterus. Band of adhesion between lower uterine segment and abdominal contents (peritoneum/bowel to uterine serosa).

Photos courtesy of H.O. Chapa, MD
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Adhesion propensity also is influenced by choice of abdominal entry. Brill et al[26] documented a 27% incidence of adhesions via Pfannenstiel entry, a 55% incidence with a midline supraumbilical incision, and a 67% incidence following a midline infraumbilical incision. The distribution (omentum alone or omentum and bowel) and severity of adhesions also varied with the type of incision made. With Pfannenstiels, 87% had adhesions to the omentum, with 13% adhesions involving the bowel. In the midline infraumbilical group, 83% had omental adhesions, with 17% of adhesions to the bowel; in the midline supraumbilical group, 60% had omental adhesions, with 40% adhesions involving the bowel.[26]

Should We Do Peritoneal Closure?

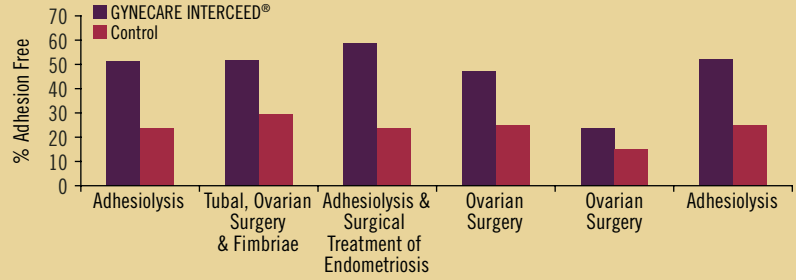
Controversy exists about whether or not to close the peritoneum. A recent Cochrane Review concluded that "there was improved short-term postoperative outcome if the peritoneum was not closed. This in itself can support those who opt not to close the peritoneum. [However], long-term studies following caesarean section are limited; there is, therefore, no overall evidence for non-closure until long-term data become available."[27-29] However, recent data support the theory that peritoneal suturing will reduce adhesion formation and its sequelae.[10,30] Lyell et al[10] concluded that "the practice of nonclosure of the parietal peritoneum at cesarean delivery should be questioned" in an effort to reduce adhesion formation.

Adhesion Prevention

Surgeons should incorporate several techniques to reduce the risk of adhesions. Avoiding excessive tissue handling and trauma and minimizing foreign body reactions—which includes exposure to medical glove powder—are two essential measures. To prevent tissue desiccation, clinicians should use intraabdominal electrocautery judiciously. Electrocautery produces eschar, which is carbon debris that causes periteonal injury. Similarly, one should avoid tissue ischemia by use of nontraumatic clamps, achieve hemostasis, irrigate the surgical field, use nonreactive suture material, and apply a barrier product approved by the US Food and Drug Administration (FDA). Good surgical technique should include all these measures.[31-32]

Currently, there are two absorbable barriers that are FDA approved for use in laparotomy for adhesion prevention: oxidized regenerated cellulose (ORC) (Interceed®) and sodium hyaluronic-carboxymethyl cellulose (SHCC) (Seprafilm®). Current labeling lists frank infection as a contraindication to ORC placement. The safety and efficacy of either barrier has not been fully evaluated in laparoscopy and is currently considered "off label." Neither is indicated as a hemostatic agent.

FIGURE 4. Gynecare Interceed Absorbable Barrier Effectiveness



- Adhesion-Free Outcomes: GYNECARE INTERCEED® was 1.6 to 2.5 times more effective than good surgical technique alone in achieving an adhesion-free outcome.
- Studies include adhesiolysis, endometriosis, ovarian, tubal, and fimbria procedures.

Source: Wiseman et al.[36]
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ORC forms a gelatinous protective coat over the surgical site, maintaining tissue integrity during peritoneal healing and organization/maturation. It is degraded by hydrolysis and completely removed from the body within 28 days. The mechanism of action for ORC is twofold. First, it acts as a hydrated gel to prevent the "sticking" of healing peritoneal edges between structures. Second, published data have shown a biochemical aspect influencing the proinflamatory cascade (tissue plasminogen activator and plasminogen activator inhibitor-1) to prevent adhesiogenesis. Reduction in fibroblast activation and macrophage activity has also been documented as ORC activity.[33-34]

ORC becomes a fully hydrated gel matrix 8 hours after application, in contrast to SHCC, which takes 24 to 48 hours for complete activation.[35] Per label description, ORC remains at the surgical site for 28 days, whereas SHCC remains for 3 to 5 days.

Data on Clinical Effectiveness

The efficacy of ORC for adhesion prevention in laparotomy is well established. A meta-analysis evaluating 560 laparotomies concluded that ORC was twice as effective as was good surgical technique alone in achieving an adhesion-free outcome (both in primary formation and in reformation after adhesiolysis).[36] Similarly, a recent Cochrane Review of 16 randomized clinical trials stated that "the absorbable adhesion barrier Interceed reduces the incidence of adhesion formation following [surgical intervention]. There was no evidence of effectiveness of Seprafilm and Fibrin sheet in preventing adhesion formation."[37] Theorized reasons for the differences in effectiveness of these two barriers stem from the residence time after application of each, with ORC maintaining tissue separation through adhesiogenesis and organization.[9] The difficult handling and placement of SHCC is also theorized to be responsible for the difference in clinical effectiveness (level C opinion).

Data presented at the American Society for Reproductive Medicine and illustrated in **Figure** 4 likewise support the value of ORC in several surgical scenarios, including ovarian surgery and adhesiolysis.[36] Among ORC-treated patients, more than 50% were free from subsequent adhesions after adhesiolysis, when compared to about 24% without ORC treatment. Reviewing the data for all patients in that study, Wiseman el al[36] concluded that ORC was 1.6 to 2.5 times more effective than good surgical technique alone in preventing adhesions.

Research on ORC in patients who had CD, although less extensive, also specifically documents its success in adhesion prevention. In a recent prospective case series involving eight patients receiving ORC and 37 patients as controls, none of the ORC group was found to develop adhesions at the bladder flap area when evaluated at a subsequent CD (single-site ORC application). All patients in the control arm were found to possess some grade of adhesions at the same site ($P<0.001$).[38]

Using ORC at Cesarean Delivery

Before applying ORC to the surgical site, a sheet should be cut in two by length. The organ surface must be dry before application. After ORC is applied, moisten with 1 to 2 mL of saline. ORC stays at the area of application by capillary action and surface tension. It is important to irrigate the pelvic cavity to remove clots/debris prior to placement. ORC should be

placed with the uterus in situ. There is no known risk if in contact with amniotic fluid, vernex, or meconium.

Although ORC should not be applied in a patient with active infection (chorioamnionitis), it does not promote bacterial growth. A patient who develops subsequent postoperative metritis will not be at higher risk of harboring an abscess if ORC was applied. The FDA-approved pivotal trials demonstrated that ORC does not promote bacterial growth. The concern that the barrier causes an allergic or local reaction in a sensitized patient is theoretical; no reported cases of anaphylactic or local allergic reaction exist in the peer reviewed literature.

When applying ORC, meticulous hemostasis should be employed per standard good surgical technique. No barrier is recommended with active bleeding as the presence of blood contributes to fibrin deposition and peritoneal trauma, thereby promoting adhesions.

Expert opinion (level C) for ORC placement at CD has been termed the "inverted T" method (**Figures 5A and 5B**). One strip is applied horizontally across the closed hysterotomy/bladder flap, another vertically and perpendicular over the anterior uterine serosa. This technique will provide maximal benefit for prevention of CD-associated adhesions as found in the literature.

As a specialty, obstetricians/gynecologists are responsible for the most common laparotomies in the United States, namely CD. The Cochrane Database clearly indicates that ORC is an effective tool in reducing the risk of CD-related adhesions. This, in addition to "good surgical technique," will help reduce morbidity in this patient population.

FIGURE 5B. Suggested Application – Inverted T

Photo courtesy of ETHICON Women's Health & Urology.
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FIGURE 5A. Suggested Application – Inverted T

Suggested Application of GYNECARE INTERCEED® Absorable Adhesion Barrier

Based on the location where adhesions are most likely to occur, the following application is recommended for C-section:

1. Irrigate abdominal cavity sufficiently during entire procedure

2. Ensure meticulous hemostasis and dry area thoroughly

3.

Cut GYNECARE INTERCEED® into two pieces

4.

Place one dry single layer on the uterine incision

5.

Place the other layer perpendicular on the uterine incision, over the anterior uterine serosa

6. Moisten layers with a few drops of irrigation solution

7.

Close the peritoneum

8.

Final skin closure

Photos courtesy of ETHICON Women's Health & Urology.
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