

Clinical implications of postsurgical adhesions

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Adhesion development can have a major impact on a patient's subsequent health. Adhesions are a significant source of impaired organ functioning, decreased fertility, bowel obstruction, difficult re-operation, and possibly pain. Consequently, their financial sequelae are also extraordinary, with more than one billion dollars spent in the USA in 1994 on the bowel obstruction component alone. Performing adhesiolysis for pain relief appears efficacious in certain subsets of women. Unfortunately even when lysed, adhesions have a great propensity to reform. Adhesions are prevalent in all surgical fields, and nearly any compartment of the body. For treatment of infertility and recurrent pregnancy loss, lysis of intrauterine adhesions results in improved fecundability and decreased pregnancy loss.

Key words: adhesions/bowel obstruction/economics/infertility/pain

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Introduction

Clinical ramifications of postsurgical adhesive disease have become increasingly familiar over the last 100 years. Adhesions have been defined as abnormal fibrous connections that may contain vascular channels, which join tissue surfaces in abnormal locations (Diamond, 2000). At the turn of the last century, most well conducted surgery was concerned with anaesthesia administration and infectious morbidity, with little fore-thought centred on the possible need for re-operation and later postoperative complications. As improved anaesthesia and the practice of antisepsis made repeated laparotomy a possibility, the true impact of postsurgical adhesions became evident. It is currently appreciated that abdominopelvic adhesive disease is a major cause of small bowel obstruction and infertility in the general surgery and gynaecology disciplines. However issues of chronic pain, impaired organ functioning, and difficult re-operations, permeate throughout many surgical specialties, representing a general pathological process that may affect almost all parts of the human anatomy.

Incidence of postoperative adhesions

The aetiology of adhesions is varied. Many different insults (e.g. infections, chemical irritation, surgery, endometriosis) that disrupt the peritoneum and produce inflammation may prompt adhesion development. Infection-induced adhesions arise most commonly from appendicitis, diverticulitis, pelvic inflammatory disease, and less often from regional enteritis, ulcerative colitis, and tuberculosis (Perry *et al.*, 1955; Raf, 1969). Chemicals precipitate adhesion development through a generalized peritonitis, and may occur with spillage of dermoid cyst contents into the pelvis (Rosen *et al.*, 1998; Nezhat *et al.*, 1999), or from the presence of, and dialysates from, continuous ambulatory peritoneal dialysis (CAPD) catheters (Rubin *et al.*, 1991; Brandt and Ricanati, 1996; Cochran *et al.*, 1997). Adhesions may even be congenital in some circumstances (Keddie and Mannam, 1988).

In a review of postmortem examinations conducted in 1973 by Weibel and co-workers, 298 subjects were identified as having prior laparotomies. In these 298 men and women, the incidence of adhesions after minor, major, and multiple operations was 51, 72 and 93% respectively (Weibel *et al.*, 1973). A prospective study performed by Menzies and Ellis in 1990 compared the incidence of adhesions in patients undergoing first time versus repeat laparotomy. They demonstrated that of the 210 patients undergoing a repeat laparotomy, 195 (93%) had adhesions believed to be secondary to prior surgery (Menzies and Ellis, 1990). In the comparison arm of 115 first-time laparotomy patients, 12 (10.4%) had adhesions, of these 12, 11 were felt to be inflammatory in nature, and one was congenital.

Adhesions occur frequently after initial surgery, and when lysed, have a tremendous propensity to reform. In his chapter,

'Incidence of Postsurgical Adhesions', Diamond remarks that adhesion reformation occurs postoperatively in 55–100% of patients, with a mean incidence of 85% (Diamond, 2000). This reformation will occur regardless of whether the adhesiolysis is performed via laparotomy or laparoscopy, and independently of the character of the initial adhesion (Diamond *et al.*, 1987).

In 1987, Diamond and associates evaluated 120 women by second-look laparoscopy (SLL) who 7–70 days prior had a laparotomy performed for reproductive surgery. At the time of the initial laparotomy all were noted to have some form of adhesions, which were scored and lysed. Adhesions that were more extensive at original laparotomy were noted at SLL to have had a greater decrease in their adhesion score after lysis. However, adhesion reformation still occurred in every adhesion type and all sites monitored (Diamond *et al.*, 1987). Also appreciated was the fact that 51% of the women had de-novo adhesion formation between the laparotomy and SLL at sites previously unencumbered by adhesions, with the majority of these new adhesions (82%) being fine and filmy.

Original expectations that laparoscopy might be less adhesiogenic than laparotomy have largely disappeared. In 1991, a prospective, multi-centre report was published showing considerable adhesion reformation after laparoscopic adhesiolysis. A total of 68 women had adhesions scored and lysed at an initial laparoscopy, and underwent a second look procedure within 90 days. Adhesions scores did decrease by 52% at second look; but, again, 66 of the 68 women (97%) had adhesion reformation occur. Most favourably, de-novo adhesion formation between the two laparoscopies occurred in only 12% of these women, compared with the 51% de-novo rate in the previously mentioned laparotomy study (Diamond, 1991). Therefore, we see that adhesion reformation is frequent after both laparotomy and laparoscopy; however, de-novo adhesion formation appears to be reduced with laparoscopy. Appropriately designed and conducted trials will be necessary to prove the latter point.

Adhesions and infertility

Infertility is a major morbidity suffered by many women with adhesive disease. Adhesions may originate from endometriosis, pelvic inflammatory disease (PID), peritoneal infections such as appendicitis or tuberculosis, or surgery. The impairment of reproductive performance occurs through a variety of mechanisms. A common endpoint for adhesion derangement is distortion of the normal tubo-ovarian relationships preventing ovum capture and transport by the fimbriated end of the Fallopian tube. Adhesions causing this can range from a thin, filmy avascular band that pulls the fimbriae outward to the pelvic sidewall; to dense, matted structures causing thick-walled hydrosalpinges and complete distal tubal obstruction (DTO).

Various adhesion classification systems have been introduced through the years in an attempt to quantitate the amount of disease, and predict reproductive potential (Rock *et al.*, 1978; Caspi *et al.*, 1979; Hulka, 1982; Society, 1988). These systems focus mainly on the gross appearance of the adhesions, external appearance of the tube, and extent of ovarian involvement for assessment. Recently, it has become increasingly clear that endotubal health is a key element for reproductive success. However, this component is largely overlooked in the existing

adhesion scoring systems. Only Rock's classification of the extent of tubal disease with distal fimbrial obstruction includes any tubal lumen evaluation by examining the rugal pattern of the Fallopian tubes in a preoperative hysterosalpingogram (Rock *et al.*, 1978).

Marana and co-workers routinely evaluate the endosalpinx via salpingoscopy, whether at laparotomy or laparoscopy (Marana and Muzii, 2000). Using Puttemans' tubal mucosa grading system, they have compared intraoperative endotubal luminal morphology against the American Fertility Society (AFS) 1988 classification of adnexal adhesions and DTO, in prognosticating reproductive surgical success (Puttemans *et al.*, 1987). Puttemans' system is as follows: Grade I, normal mucosal folds; Grade II, major folds are separated, flattened, but otherwise normal; Grade III, focal adhesions present between mucosal folds; Grade IV, extensive adhesions between the mucosal folds and/or disseminated flat areas visible; Grade V, complete loss of the mucosal fold pattern. In his 1995 prospective study, Marana used intraoperative rigid salpingoscopy to assess endoluminal health, and scored external adnexal adhesions according to the AFS system in 55 patients undergoing laparotomy for reconstructive tubal surgery due to PID. At surgery, 29 patients had salpingo-ovariolysis performed, and 26 had neosalpingostomy. Mean patient age was 30 years (range 22–38), mean length of follow-up was 54 months (range 29–71), and no one was lost to follow-up. In the salpingo-ovariolysis cohort, the overall term pregnancy was 66% (19/29), with this number increasing to 86% (19/22) when considering only those patients with salpingoscopic tubal mucosa grades of I and II. For the neosalpingostomy group, the term pregnancy rate was 31% (8/26) for the entire group, with this number increasing to 73% (8/11) in patients with grades I and II. AFS criteria however, yielded no ability to predict postoperative reproductive success in this study. Intrauterine pregnancies occurred in all AFS severity groups (Marana *et al.*, 1995; Marana and Muzii, 2000).

Marana validated these prior findings in a laparoscopic setting in 1999. Again, in this prospective study, 51 patients with tubal infertility due to PID undergoing laparoscopic salpingo-ovariolysis or neosalpingostomy had their tubal lumens graded by rigid salpingoscopy, and adnexal adhesions classified by the AFS system. A total of 24 patients with adnexal adhesions underwent adhesiolysis, and 27 women with hydrosalpinges underwent salpingoneostomy. The mean duration of follow-up was 33 months (range 14–67), with no one lost to follow-up. For the salpingo-ovariolysis group, total cumulative pregnancy rate was 50% (12/24), with this number rising to 71% (12/17) in patients with endoluminal grades I and II. For the neosalpingostomy cohort, the crude term cumulative pregnancy rate was 26% (7/27), with this number increasing to 64% (7/11) in grades I and II. No intrauterine pregnancy occurred in patients with tubal mucosa grades III, IV, and V. When postoperative reproductive success was evaluated using the AFS system, term pregnancies were evenly distributed throughout all classes (Marana *et al.*, 1999).

Other authors have produced results similar to Marana. DeBruyne and associates conducted a prospective study in 1997 of 226 women undergoing salpingo-ovariolysis ($n = 130$) or neosalpingostomy ($n = 96$) for post-PID tubal infertility by microsurgical laparotomy. Cumulative pregnancy rates were calculated after 42 months of follow-up. Puttemans' salpingoscopic grading was used, as was the AFS scoring system. Again,

statistically significant higher cumulative intrauterine pregnancy rates were noted for salpingoscopic grades I and II in both the salpingo-ovariolysis and neosalpingostomy groups. AFS scoring did not provide statistically significant correlation for post-operative reproductive outcome (DeBruyne *et al.*, 1997). Vasquez in 1995 provided evidence that operative microscopic examination of the tubal mucosa is superior to adnexal adhesion presence in predicting reproductive success after surgery. When adhesions within the tubal lumen were present, the subsequent intrauterine pregnancy rate was 22%, which increased to 58% when adhesions were absent (Vasquez *et al.*, 1995).

Some authorities believe adhesions also act to decrease fertility by hindering oocyte development and maturation. Adhesions, it has been argued, may kink or constrict the ovarian blood supply, preventing adequate delivery of gonadotrophins and growth factors to growing follicles (Nagata *et al.*, 1998). Supporting this contention is a retrospective study by Nagata and associates measuring human chorionic gonadotrophin (HCG) concentrations in the follicular fluid of retrieved oocytes from women with periadnexal adhesions undergoing IVF. Within the 12 months preceding their IVF treatment, or immediately after a treatment cycle, diagnostic laparoscopy was performed on 26 tubal infertility patients and their adhesions were graded according to AFS criteria. All women underwent a standard long IVF stimulation protocol, and utilized 10 000 IU of HCG i.m. to complete oocyte maturation. Follicular HCG concentrations of the transvaginally retrieved oocytes were compared to the patient's serum HCG concentration, and a ratio determined. They believed lower follicular to serum HCG concentrations indicated poorer diffusion and/or transport of the exogenously administered HCG into the developing oocytes. A negative correlation was noted between the extent of adhesions, and follicular HCG/serum HCG ratios. This negative correlation with adhesions was also observed with respect to total number of oocytes retrieved (Nagata *et al.*, 1998). In opposition to these observations, however, we observed no such relationships in our own prospective study of 1988, in which 49 women received long-protocol IVF stimulation, and had laparoscopic retrieval of their oocytes. Ovaries were assessed for extent of adhesion involvement at retrieval. Serum oestradiol concentrations, follicular size and number were recorded. No correlations were identified between the amount of ovarian adhesion involvement and the measured variables of oestradiol, follicle size and number (Diamond *et al.*, 1988).

Intrauterine adhesions

Another type of adhesion responsible for infertility and recurrent pregnancy loss (RPL) is the intrauterine adhesion (Asherman, 1957). Even though these are located within the uterus and not the peritoneum, they still form as a consequence of the general pathological process of pronounced wound healing. Intrauterine adhesions most often follow a vigorous pregnancy-related dilatation and curettage, infection, or uterine surgery. The adhesions may obstruct the tubal ostia of the uterine cavity, diminish the amount of receptive endometrium available for embryo implantation, and thwart development of an implanted embryo due to space-limiting factors or an impaired blood supply. Hysteroscopic adhesiolysis is the current standard for treatment. Good success rates for this minimally invasive technique have

been described. Goldenberg and colleagues published a 1995 study of 36 women treated for intrauterine adhesions and either infertility or RPL. Their adhesions were graded using the March classification system and then treated by hysteroscopic adhesiolysis (Goldenberg *et al.*, 1995). The March system is as follows: minimal, less than one-fourth of the uterine cavity is involved, and the adhesions are loose and filmy; moderate, adhesions affecting one-fourth to three-fourths of the uterine cavity, without agglutination of the walls or ostial areas, and with partial occlusion of the upper fundus; severe, adhesions involving greater than three-fourths of the uterine cavity, with agglutination of the walls or thick bands, and occlusion of the ostial areas and upper fundus (March *et al.*, 1978). Postoperatively, the 12 women with recurrent loss saw their pregnancy wastage decrease from 86.5 to 42.8%. The overall pregnancy rate in the 24 women with infertility was 48% after adhesiolysis. The mean time to conception for this group of women was positively correlated with age: ≤ 10 months post-procedure, 28.5 ± 2.9 years; > 10 months post-procedure, 34.0 ± 3.6 years; and failed to conceive, 35.4 ± 6.3 years.

In 1997, Pabuccu and associates described good results for hysteroscopic therapy of intrauterine adhesions in restoring normal menstruation and fertility (Pabuccu *et al.*, 1997). Their retrospective review included 40 women with complaints of infertility or RPL. Again, adhesions were graded by the criteria of March. Of the 40 women, 10 had mild adhesions, 20 had moderate, and 10 severe. All patients had re-evaluation of the uterine cavity by either hysterosalpingogram (HSG) or hysteroscopy postoperatively. Adhesion re-formation was absent or rare in the initially mild and moderate adhesion groups. However, there was adhesion re-formation in 60% of the severe patients. These re-formed adhesions were considered mild in 30%, moderate in 10%, and severe in 20%. All 24 women with RPL conceived after adhesiolysis, and 17 (71%) resulted in term or

Table 1. Intrauterine adhesion severity and treatment outcome by category

	Infertility		Recurrent pregnancy loss			
	Conceptions	%	Pregnancy rate	%	Birth rate	%
Goldenburg <i>et al.</i> (1995) ^a						
Mild	–	–	–	71	–	–
Moderate	–	–	–	68	–	–
Severe	–	–	–	14	–	–
Totals	11/23	48	–	–	8/14	57
Pabuccu <i>et al.</i> (1997) ^a						
Mild	7/8	88	–	–	–	–
Moderate	3/4	75	–	–	–	–
Severe	0/4	0	–	–	–	–
Totals	10/16	63	24/24	100	17/24	71
Valle and Sciarra (1988) ^b						
Mild	6/9	67	34/34	100	32/34	94
Moderate	29/42	69	47/55	85	24/47	89
Severe	13/30	43	14/17	82	11/14	79
Totals	48/81	59	95/106	90	85/95	89

– = not provided.

^aMarch criteria.

^bStudy-specific criteria.

Table II. Obstructive adhesion aetiology

Authors	Subjects	Small bowel adhesions <i>n</i> (%)	Small bowel—Other abdominopelvic structures <i>n</i> (%)	Unknown/others <i>n</i> (%)
Menzies and Ellis, 1990	80	19 (24)	50 (62)	11 (14)
Maetani <i>et al.</i> , 1984	88	26 (29)	42 (48)	20 (23)

viable preterm infants. Of the infertile patients, 7 of 8 with initially mild adhesions conceived, 3 of the 4 with moderate disease conceived, and the two women presenting with severe disease did not conceive postoperatively. Both Goldenberg's and Pabuccu's studies are corroborated by the earlier work of Valle and Sciarra (Valle and Sciarra, 1988), though Valle used his own grading system and not the March classification (see Table I). It can be seen that while hysteroscopic adhesiolysis does not restore normal fecundity to these women, it does provide real benefit with minimal invasiveness and risk.

Bowel obstruction

In the early 20th century, most cases of intestinal obstruction were due to strangulated external hernias. As abdominal and gynaecological surgeries began to be performed more routinely, the number of intestinal obstructions caused by postsurgical adhesive disease surpassed those produced secondary to hernias. This statistic, however, only holds true for the western world where laparotomy is commonplace. In those poorer regions where such surgery is not routine, the percentage of obstructions from hernias is still greater than that caused by adhesions. Currently, 40% of all cases of intestinal obstruction in advanced countries is attributable to adhesions, with this figure rising to 60–70% when only small bowel obstruction is considered (Menzies, 1993). However, in the Third World, hernias account for 25–75% of intestinal obstruction, while adhesions produce only 4–23% of cases (Ellis, 1997).

Certain types of adhesions appear to have an enhanced predilection for causing intestinal obstruction. In the previously mentioned study, Menzies and Ellis also evaluated 80 patients requiring surgery specifically for postoperative adhesive obstruction. The original operations that were the culprits of the obstructions were catalogued and tabulated. Procedures involving the left side of the colon or rectum constituted the highest percentage at 25%, appendectomies accounted for 15%, gynaecological procedures totalled 14%, and total colectomies were 9%. Altogether, 76% of those index surgeries resulting in later adhesive obstruction occurred in the peritoneal cavity below the transverse mesocolon (Menzies and Ellis, 1990).

Looking at what types of adhesions cause intestinal obstruction, a Japanese group investigated a total of 88 adhesive obstructions. They categorized adhesions into those involving the small bowel alone versus those adhering the small bowel to other peritoneal surfaces (e.g. viscera, retroperitoneum). 29% of the obstructive adhesions were small bowel to small bowel, while 48% consisted of small bowel to other abdominopelvic surfaces. These two groups together implicate the small bowel in 77% of postoperative obstructive adhesions. In the remaining cases, the adhesive complexes were such intimate combinations of both forms of adhesion that it was not possible to confidently identify the dominant adhesion type (Maetani *et al.*, 1984). Examining

Menzies and Ellis' 80 patients in the same manner as the Japanese study reveals small bowel to small bowel adhesions produced 24% of their obstructions, while small bowel to other abdominopelvic structures amounted to 62% of obstructions—taken together these totalled 86% (see Table II).

The adhesions that most often lead to intestinal obstruction are not the adhesions that most often occur after surgery, however. The single greatest type of postoperative adhesion in Menzies and Ellis' study of 210 patients with prior abdominal surgery was from the omentum to the previous scar. This was followed by adhesions at the site of prior surgery alone, and lastly from the omentum to the site of prior surgery. In total, the omentum was involved in 57% of all adhesions, while the small bowel was involved in only 27% (Menzies, 1993). In contrast to this, small bowel adhesions create the majority of obstructive adhesions, collectively producing 77% of obstructive adhesions in the Japanese study and 86% of Menzies and Ellis' cohort. The omentum's contribution to obstruction, despite its prevalence in postoperative adhesions, was only 2.5%.

When a postoperative adhesive bowel obstruction might strike is variable. Early postoperative small-bowel obstructions (within four weeks of surgery) are quite possible. Stewart and colleagues in 1987 observed an overall incidence of early obstruction of 0.69% while evaluating over 8000 patients who underwent a variety of abdominal procedures, and 92% of these obstructions were a result of adhesions (Stewart *et al.*, 1987). From 1976 to 1988, Menzies and Ellis followed a cohort of 2708 prospective patients who underwent laparotomy. Mean follow-up was for a period of 14.5 months, with a corresponding range of 0–91 months. Of their group, 0.52% developed an adhesive obstruction within one month after surgery. At one year, 0.96% of patients had endured an adhesive obstruction that necessitated an interventional procedure for resolution (Menzies and Ellis, 1990; Menzies, 1993).

Menzies and Ellis also catalogued a group of 80 consecutive patients presenting with postoperative adhesive bowel obstruction. A total of 17 patients, or 21.3%, developed an obstruction >10 years after their original surgery (Menzies and Ellis, 1990). Unfortunately recurrence of bowel obstruction will remain a lifelong issue for these patients. One study found a 12.5% recurrence rate after conservative management for their initial obstruction (Bizer *et al.*, 1986). In studies with patients undergoing simple adhesiolysis to relieve an obstruction, recurrence rates ranged from 11 to 21% (Ellis, 2000). In the special instance of early postoperative bowel obstruction, Pickleman contends that the majority of these (80–90%) will resolve with conservative measures of nasogastric suction, hydration, and parenteral nutrition (Pickleman and Lee, 1989).

Lower and associates recently performed a broader analysis of the adhesion-produced clinical burden. They tabulated adhesion-related re-admission rates over a 10 year period for 8489 female

patients who had a laparotomy performed for reproductive tract surgery in 1986. In this cohort of 8489 women, none had a laparotomy for any reason within the five years prior to their 1986 surgery. During this 10 year period, 2931 of the 8489 women (34.5%) had a total of 5433 re-admissions, rendering a mean of 1.9 re-admissions per re-admitted woman. These 5433 re-admissions break down as follows: 245 (4.5%) were directly due to adhesion complications; 2479 (45.6%) were possibly due to adhesions; and the remaining 2709 (49.9%) involved other abdominal or pelvic surgery that was potentially complicated by adhesions. The authors noted a noticeably higher re-admission rate following ovarian or Fallopian tube surgery, 48.1 and 41.2% respectively, compared with uterine or vaginal surgery, 32.1 and 34.6% respectively. 16% of all re-admissions were seen in the first postoperative year, but re-admissions persisted in all categories for the 10 year study period without decline (Lower *et al.*, 2000). This paper is among the first to examine the comprehensive long-term clinical burden of gynaecological postoperative adhesions.

Surgically, adhesions may create difficult re-operations even if the patient is symptom-free and does not develop an obstruction. The difficulties usually manifest themselves through increased operative time and bowel injury during adhesiolysis. A prospective study conducted by Moran evaluated 93 patients undergoing elective laparotomy. In 47 patients without prior surgery, incision time averaged 5 min, with a corresponding range of 3–9 min. In the group of 46 patients who had prior abdominal surgery, incision time averaged 10 min, with the time necessary for adhesiolysis in the range 0–120 min with a mean of 19 min. In the 'extensive' adhesions sub-group, the mean adhesion division time rose to 30 min (Moran, 1998). Coleman in 2000 presented data on 120 patients who underwent midline laparotomies, 89 elective and 31 emergency cases. Prior abdominal surgery had occurred in 51% of the elective cases, and 71% of the emergency cases. No significant differences were seen in abdominal entry times between the emergent and elective cases. Comparing those patients with previous surgery to those without, it was found that previous surgery prolonged the combined median incision and adhesion division times by 18 min (Coleman *et al.*, 2000).

Published reports have also demonstrated a significant risk for inadvertent enterotomies during adhesiolysis in patients undergoing repeat laparotomy. van Goor analysed 274 patients between June 1995 and September 1997 who underwent 291 repeat laparotomies. In 61 of the 291 repeat laparotomies (21%), one or more iatrogenic bowel perforations occurred. Those patients sustaining bowel perforation had higher rates of postoperative complications at 54% (such as wound infection, anastomotic leak, and haemorrhage), than those without bowel perforation, 36% ($P < 0.05$). Using multivariate analysis, the number of prior laparotomies and patient age were shown to be independent risk factors for perforation. Surgical skill, time interval from previous laparotomy, and urgency of the procedure were not identified as risk factors (van Goor, 1998). A.A. van der Krabben and colleagues found in a retrospective review of 270 consecutive patients requiring an abdominal reoperation that 52 patients, or 19%, had sustained an inadvertent enterotomy, with two or more enterotomies occurring in 40% of these 52 patients. They identified both the number of prior laparotomies and patient age as independent risk factors for inadvertent enterotomy. Having

three or more previous laparotomies resulted in a ten-fold increased risk (odds ratio 10.4; 95% CI 5.0–21.6) of enterotomy compared with patients with two or fewer laparotomies. For patients 60.3 years and older, the odds ratio was 1.9 (CI 1.3–2.7) for receiving an inadvertent enterotomy, compared with patients 54.1 years or younger. In this study, those patients with enterotomy had statistically significant higher rates of post-operative complications (e.g. bowel obstruction, sepsis, wound dehiscence) and intensive care unit admissions than those without enterotomy (van der Krabben *et al.*, 2000).

Financial consequences of adhesions

The financial impact of adhesions is enormous. Ray and associates published a report evaluating the direct in-patient costs of adhesiolysis in the USA during calendar year 1988. Data was acquired from three population information systems: the National Hospital Discharge Survey; the Medicare Provider Analysis and Review File; and the Part B Medicare Annual Data beneficiary file. From these sources, information including diagnostic related groups (DRGs), surgical procedures coded with *International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM)*, dates of admission/discharge, and Medicare reimbursements, was obtained. Two groups of patients were evaluated to determine the costs secondary to adhesions: the first group consisted of patients whose admissions were completely and entirely attributable to adhesions; the second group was composed of patients whose admissions were complicated by, but not entirely due to, adhesions. To be placed into the first group, patients needed both a surgical procedure of adhesiolysis and a corresponding adhesion DRG present in their hospitalization information. The authors felt that the complete costs of care for patients in the first group were directly attributable to the need for adhesiolysis. In the second group, the authors only wanted to consider the excess cost to a hospital admission caused by adhesiolysis. To figure excess cost, the nationwide mean cost for a hospitalization not complicated by adhesiolysis was subtracted from the mean cost of a hospitalization for an identical reason, but with adhesive disease present. Indirect costs, such as outpatient rehabilitative services and time missed from work, were not included.

Ray learned that in 1988, there were 281 982 hospitalizations during which adhesiolysis was performed, and of these 54 100 were directly due to adhesions (first group). This translates to 115.51 hospitalizations per 100 000 population. The 54 100 hospitalizations had an average length of stay of 11.24 days, resulting in a total of 608 084 inpatient days. For the second group, excess hospitalization due to adhesiolysis accounted for 340 643 inpatient days. Reimbursement for hospitalization was \$593 million in the direct group and \$332 million in the excess group. Surgeon fees amounted to \$49 million and \$206 million, for the direct and excess cost groups respectively. In total, adhesiolysis hospitalizations in 1988 accounted for \$1 180 million in health care expenditures, with \$925 million going towards hospital expenses, and \$255 million in surgeon fees (Ray *et al.*, 1993). Importantly, to calculate the total cost to society, factors such as time lost from work, reduced productivity, and lost pay would have to be added. Thus the direct medical costs represent only a portion of the actual cost to society.

Six years later in 1994, Ray and her colleagues re-examined this issue. The same study design from the 1988 report was utilized. In 1994, there were 303 836 hospitalizations during which adhesiolysis was performed, and of these 58 241 were caused directly by adhesions. This corresponds to a rate of 117.3 hospitalizations per 100 000 population, representing 1% of all hospitalizations in the USA that year. The 58 241 hospital admissions directly due to adhesions averaged 9.7 days per stay to total 564 938 inpatient days. The additional amount of inpatient days for patients who required adhesiolysis as a secondary, but not primary, procedure was 281 477. Hospitalization costs were \$764 million in the direct group and \$562 million in the excess group. The total adhesiolysis expenditure from the 1988 study converted to 1994 dollars amounts to \$1 437.1 million, compared to the 1994 study total of \$1 325.9 million (see Table III). This drop in expense is mainly attributable to the decreased average length of stay in the hospital, as the total number of admissions for adhesiolysis remained fairly constant (Ray *et al.*, 1998).

In a related analysis, Ivarsson and associates evaluated the cost of small bowel obstruction due to adhesions in Sweden during a five-month period from October 1992 to February 1993. 40 patients in total were treated for small bowel obstruction. 34 of these 40 obstructions, or 85%, were felt to be precipitated solely by adhesions, as determined by a history of prior surgery, clinical examination and radiological studies. 12 of the 34 patients were discharged early (within 24 h) after medical therapy. The remaining 22 required extended hospitalization, and 10 of the 22 needed surgical intervention to relieve their obstruction. Extrapolating these figures to the national level, Ivarsson believes adhesive bowel obstruction may cause 2330 annual hospital admissions, with a direct cost of \$13 million U.S. dollars (Ivarsson *et al.*, 1997). These outlays include the services of surgery and radiology, medicines, laboratory evaluation, room, rehabilitation costs, home-health care and sick leave. Again, the indirect costs of loss of income and loss of production were not included.

Harold Ellis and others took advantage of data available from the Information and Statistics Division of the Common Services Agency in the National Health Service of Scotland to compile a

detailed follow-up of patients who underwent first-time abdominal surgery (open, laparoscopic and endoscopic procedures) in 1986. Over the next 10 years, these patients were monitored for hospital re-admission. Any re-admissions complicated by adhesions, or triggered solely due to adhesive disease were identified. Of the original cohort of 52 192 patients that were followed, 20 418 (39.1%) required a total of 42 557 re-admissions for adhesion-related issues. Of these re-admissions, 2002 (4.7%) were precipitated directly by adhesions. The index operations causing hospitalizations for adhesions alone were tabulated. Re-admission rates particular to the type of surgery were: midgut/hindgut 7.1%, female reproductive tract 3.9%, and foregut 3.4% (Ellis, 2000).

Do adhesions cause pain?

The question of whether adhesions cause pain does not have an entirely satisfactory answer. Opinions range from Alexander-Williams' infamous declaration that it is 'a poorly substantiated myth that adhesions can cause abdominal or pelvic pain' (Alexander-Williams, 1987), to 'adhesions can cause pelvic pain and that adhesiolysis relieves it in 60–90% of cases' (Duffy *et al.*, 1996). Mechanistically, adhesions have been postulated to produce pain by restricting pelvic organs or placing them under tension (Kresch *et al.*, 1984). Visceral sensations are transmitted via the parasympathetic pathway, and parietal peritoneum receives innervation from the phrenic, thoracoabdominal, subcostal and lumbosacral nerves (diZerega and Rodgers, 1992). Kligman showed that adhesions themselves can contain nerve fibres. Adhesive tissue obtained from 17 patients, 10 with chronic pelvic pain (CPP) and 7 without, was subjected to immunohistochemical analysis. 10 of the 17 specimens had evidence of nerve fibres within them—however the nerve fibres were distributed among samples from both the CPP and pain-free groups (Kligman *et al.*, 1993). While obviously not providing the definitive answer to adhesion pain generation, this finding does suggest one possible avenue of pain production.

In terms of clinical studies, Kresch in 1984 compared 100 women with the complaint of pelvic pain in the same location for a minimum of six months against 50 women presenting only for laparoscopic tubal ligation and without pelvic pain (controls). In

Table III. Financial impact of intraperitoneal adhesions in the USA (Ray *et al.*, 1993, 1998)

	1988	1994
Admissions directly attributable to adhesions	54 100	58 241
Admissions indirectly complicated by adhesions	227 882	245 595
Total adhesion-related admissions	281 982	303 836
Hospital days directly attributable to adhesions	608 084	564 938
Hospital days indirectly complicated by adhesions	340 643	281 477
Total adhesion-related hospital days	948 727	846 415
Hospital cost of admissions directly attributable to adhesions	769.8	715.2
Excess cost from admissions indirectly complicated by adhesions	431.3	356.3
Total hospital cost of adhesion-related admissions	1201.1	1071.5
Surgeon fees for admissions directly attributable to adhesions	45.3	48.7
Excess fees from admissions indirectly complicated by adhesions	190.7	205.7
Total surgeon fees for adhesion-related admissions	236.0	254.4
Combined total, hospital cost + surgeon fees for all adhesion-related admissions	1437.1	1325.9

Hospital costs and surgeon fees in millions of 1994 US dollars.

the 100 females with chronic pelvic pain, laparoscopic inquiry revealed 83% with pathological findings, with 48% of women having adhesions involving their reproductive organs or bowel and 32% having endometriosis. In the asymptomatic tubal ligation group, only 29% of women demonstrated abnormalities—adhesions were present in 14 and 15% had endometriosis. This difference was significant at the $P < 0.001$ level. Kresch remarked that the adhesions identified in the control group were noticeably loose, allowing the involved organs to move freely. The adhesion quality in the chronic pain group, however, was more restrictive and limited mobility and expansibility of the adhered organs. Kresch felt that their highly significant findings were attributable to the selection criterion they employed of pain in a *consistent* location, regardless of its character. Careful patient screening should therefore increase one's yield of positive findings after diagnostic laparoscopy for pain (Kresch *et al.*, 1984). This study is one of the strongest to date implicating adhesions in a causative role for pain.

Stout, Steege, and others in 1991 corroborated Kresch's earlier report. 102 women scheduled for laparoscopy for a variety of reasons had pain assessment scoring by the McGill Pain Rating Index and West Haven-Yale Multidimensional Pain Inventory prior to surgery. Of the 102 laparoscopies, 64% were being done for reasons of pain alone, 35% to evaluate infertility, 19% as follow-up of abnormal findings identified in other testing (e.g. sonograms) and 15% for sterilization. According to the patient questionnaires, 90 women were self-assigned to the pelvic pain group, and 12 women reported no pain. During the laparoscopy, surgeons blinded to the patient's self-reported pain data completed AFS classifications for endometriosis and adhesions. There were no significant differences between the pain and no-pain groups with regard to demographics, marital satisfaction, prior surgeries, or fertility desires. Upon analysis, the pain cohort had a statistically significant higher mean AFS scoring than the no-pain patients (7.2 versus 1.6; $P \leq 0.01$). Within the pain group itself however, AFS scorings were not correlative with duration of pain, pain intensity, pain frequency, dyspareunia, dysmenorrhoea, the McGill Pain Index or the Yale Pain Inventory. The authors concluded on the basis of these findings that the majority of women reporting pelvic pain may be expected to have some type of physical abnormality, primarily adhesions or endometriosis, with the location of the abnormality almost always corresponding to the pain location. The fact that the amount of disease identified did not have a positive relationship with the self-report of pain severity demonstrated the differences in how patients experience or interpret noxious sensory input (Stout *et al.*, 1991).

Steege has gone on to advance the newer theories of pain perception, such as the gate control theory of pain and cognitive-behavioural theory, to explain the lack of quantitative relationships between organic disease burden and pain severity as noted above. In these theories, the influences of culture, psychological conditioning, sensory threshold, cognitions, affect, and stress, all participate in a patient's pain perception and response. When pain persists, and develops into affective, behavioural, and cognitive manifestations, a chronic pain syndrome (CPS), has begun (American College of Obstetricians and Gynecologists, 1989; Steege *et al.*, 1993). With this in mind, Steege and Stout published another study in 1991, evaluating 34 women in a tertiary care centre for chronic, constant pelvic pain of ≥ 6 months duration,

who underwent laparoscopic adhesiolysis. Prior to laparoscopy, patients rated their dysmenorrhoea, dyspareunia, and pain during daily activities. Also scored by a clinician was presence or absence of incomplete relief by prior therapy (medical and surgical), impaired physical functioning, vegetative signs of depression, and altered family roles. A patient was considered as having CPS if four or more of these characteristics were present. The laparoscopic procedure was videotaped and adhesiolysis performed. Interceed (Johnson & Johnson, Newark, NJ, USA) was placed upon areas of pelvic sidewall dissection, and moistened with heparin. Adhesions were scored with the surgeons blinded to the patients' pain score measures. A total of 20 patients had chronic pelvic pain alone, and 10 were diagnosed with CPS. Preoperative levels of dyspareunia, dysmenorrhea, daily pain, and adhesion scoring did not differ between the simple pelvic pain and CPS groups. Patient-reported pain location corresponded with the laparoscopically identified adhesion location in 90% of all patients. Patients without CPS were significantly more likely to have continued relief of dyspareunia ($P < 0.05$) and pain during daily activities ($P < 0.05$) following surgery than women with CPS. This study supports the role of adhesiolysis for pain relief, but it also emphasizes the need for continued follow-up to monitor for pain return and the importance of considering psychosocial factors in pain management (Steege and Stout, 1991).

Four other studies implicate a role for adhesions in pain production, as they demonstrate a diminution in pain after adhesiolysis. Daniell performed enterolysis in 42 patients suffering from chronic pelvic pain. The patients included 38 females and 4 males. All patients had prior surgery and developed pain and adhesions involving the bowel and abdominal wall. 40 of the 42 patients were able to have entero-adhesiolysis accomplished via the laparoscope, and two required laparotomy (one due to a trocar injury). After a minimum of four postoperative months, questionnaires were sent, and patients queried about the surgery's effectiveness. A total of 28/42 patients, 67%, had improvement of their pain symptoms, the remaining 14, or 33%, felt their symptoms were unchanged or worse (Daniell, 1989). Chan and Wood reported on symptom relief in patients after pelvic adhesiolysis, with 156 patients having laparoscopy and adhesiolysis for varied reasons (e.g. CPP, infertility, menstrual disorders) followed-up after a minimum of six months. Of the 156 women, 43 had complaints of pain. In these 43 women, 28 (65%) noted an improvement of symptoms, 5 (11%) considered their symptoms worse, 9 (21%) were unchanged, and 1 did not respond to the questionnaire. The degree of adhesive disease was not quantitated and the distribution of adhesions among the women presenting with other complaints was not recorded (Chan and Wood, 1985). Sutton and MacDonald performed laparoscopic laser adhesiolysis on 65 patients for lower abdominal pain. Pain duration and quality were not detailed. A total of 63 of the patients had follow-up over a period of 1–5 years, and 53 of the 65 patients, or 82%, reported relief of their pain, 3 (5%) had initial improvement but relapsed, and 7 (11%) felt no improvement (Sutton and MacDonald, 1990). Lastly, Saravelos and associates compared open microsurgical adhesiolysis versus laparoscopic adhesiolysis for pain relief in 123 women with CPP. Seventy-two patients had microsurgery and 51 laparoscopy for adhesiolysis. Follow-up data was obtained from hospital records and postal

questionnaires, and life-table analysis was utilized to compare cumulative rates of pain recurrence. The mean length of follow-up was 13.7 months (range 2–53). Sustained postoperative pain relief was noted in 71% of microsurgical cases, and 61% of laparoscopy cases (not statistically significant). Overall cumulative rates of pain persistence by life-table analysis were 40.0 and 51.0% at 12 and 24 months respectively. When broken down into different variables, only a history of prior laparotomy, for any reason, was identified as a risk factor for continued pain, with a 3× higher rate. Women having no prior laparotomy had a cumulative rate of pain persistence of 20.0 and 32.0% at 12 and 24 months respectively, while women with prior laparotomy had pain persistence rates of 54.0 and 64.0% at 12 and 24 months respectively. The authors feel the reason for this is an intrinsically increased rate of adhesion formation and reformation in patients with previous laparotomy, as the observed effect did not depend on whether the first laparotomy was for pain or another indication (Saravolos *et al.*, 1995). Though these studies are without controls, their results are quite similar and point to a beneficial role of adhesiolysis in reducing pelvic pain.

As early as 1973 there are reports arguing the other point, that a causal relationship of adhesions to pain is lacking. Lundberg and associates retrospectively reviewed the laparoscopy results of 95 patients with pelvic pain. Patient age ranged from 16–68 years, and pain was the only indication for the laparoscopy. The medical records were not detailed enough however, for the authors to determine the character of pain the patients were experiencing. Of the 95 laparoscopies, 37 (39%) had a normal anatomic pelvis, 17 (18%) patients had adhesions, chronic PID was seen in 12 (13%), endometriosis was isolated in 13 (14%), and the remaining cases consisted of other findings (Lundberg *et al.*, 1973). In this early report, patients demonstrating adhesions were less abundant than patients with a normal pelvis. In 1983, a report by Cunanan and colleagues concurred with Lundberg's findings. They reviewed 1194 charts of consecutive patients who had laparoscopy performed for pelvic pain. Patient ages ranged from 15–60 years, and 511 of the patients (42.8%) had a history of prior pelvic surgery. They found 355 (30%) to have a normal pelvis, 229 (19%) patients had adhesions, PID was found in 264 (22%), and endometriosis was surprisingly uncommon in only 43 or 4% of patients (Cunanan *et al.*, 1983). Again, the number of women without pathology exceeded all other pathology categories. No explanation was given for the relatively small endometriosis cohort.

Rapkin performed a retrospective review in 1986 comparing the incidence of adhesions in 100 consecutive women undergoing laparoscopy for CPP against 88 women having laparoscopy for reasons of infertility. Adhesions were scored from the surgeons' operative notes as to location and quality. In the 100 women with CPP, 26% demonstrated adhesions and 37% had endometriosis. Of the 88 women in the infertility (control) group, 34 (39%) had adhesions, and endometriosis was present in 29 (33%). While obviously all 26 women with adhesions in the CPP cohort had pain, only 4 of the 34 (12%) women in the infertility group had complaints of pain. When comparing the adhesions between the two groups in terms of location or density, no differences were found (Rapkin, 1986). While many of the previously cited adhesiolysis studies were prospective but uncontrolled, Rapkin's was retrospective, and as such has received criticism that the

infertility (control) arm was self-selected to contain an inordinately high percentage of patients with adhesions, as they were subfertile (Sutton and MacDonald, 1990).

A randomized clinical trial to assess the benefit of adhesiolysis in patients with CPP was performed by Peters and colleagues. A total of 48 women with CPP for more than 6 months underwent laparoscopy. Pain was calculated prior to laparoscopy by using the McGill pain score, subjective pain assessment, and disturbance of daily activities. At laparoscopy their adhesions were graded. Women with more than sparse, filmy non-vascularized adhesions were randomized into one of two treatment groups: lower midline laparotomy for adhesiolysis, or expectant 'wait-and-see' management. The time interval from laparoscopy to laparotomy was not given. The demographics, preoperative pain scores, and degree of adhesive disease did not differ between the two groups. Upon follow-up 9–12 months later, in which clinicians were blinded to the patient's intervention, there was no difference noted between the two groups overall with regard to pelvic pain. Only in the sub-group of women with severe, vascularized, and dense adhesions involving the bowel was there a statistically significant decrease in pelvic pain in the adhesiolysis cohort ($P < 0.01$) (Peters *et al.*, 1992). The authors believe these results lend support to the notion that adhesions do not contribute to pelvic pain. Given the fact that de-novo adhesiogenesis is greater after laparotomy than after laparoscopy, this may have contributed to the negative findings in this trial as compared to the positive findings in the laparoscopic studies. Peters' study also provides credence to the observation advanced by Kresch that adhesions restricting movement or distensibility of pelvic organs are more likely to cause pain than those that do not.

In his letter to the British Medical Journal, Alexander-Williams, in addition to declaring that it is 'a poorly substantiated myth that adhesions can cause abdominal or pelvic pain', focuses in on the important point of the placebo effect (Alexander-Williams, 1987). A significant proportion of women undergoing adhesiolysis for relief of pelvic pain will experience a placebo effect after surgery. Of the three studies evaluating adhesiolysis for pain relief, it is likely that only one (Sutton and MacDonald, 1990) followed patients long enough (1–5 years) to eliminate a placebo effect.

Obviously the 'gold-standard' study to determine the utility of adhesiolysis for pain relief would be a double-blinded, randomized, prospective trial with a control arm, and follow-up occurring past the point of the expected placebo effect. Not surprisingly such a study would be difficult to execute because of the need to recruit a large number of patients, to perform a second-look procedure to ascertain whether adhesion reformation occurred in those patients having pain relapse after adhesiolysis, and to debate the method to use to 'quantitate' patient pain. In the absence of such a perfect trial, we have to rely on the data we have available. Adhesions do not always cause pelvic pain, as demonstrated by many studies that have cohorts of women with adhesions but no reports of pelvic pain. Will some women with adhesions and pelvic pain benefit from adhesiolysis? Obviously. Can we identify which women those will be? Maybe. Patients with adhesions tethering and restricting pelvic or abdominal viscera, and those who have pain without a pain syndrome should be most likely to experience relief after adhesiolysis.

Adhesions in other surgical fields

The gynaecological and general fields of surgery are not the only ones plagued by adhesions. In cardiothoracic surgery, reoperative sternotomies can be particularly troublesome if the pericardium is not or could not be closed in the original operation. Adhesion development in this location causes increased bleeding and cardiac injury due to close contact of vital structures to the posterior surface of the sternum (Dobell and Jain, 1984). Resternotomies result in cardiac injury in 2–6% of patients, and if massive bleeding ensues, mortality ranges from 37–50% (Lahtinen *et al.*, 1998). These retrosternal adhesions can be seen on computed tomography (CT), and various adhesion prevention substances have been used in an attempt to reduce these adhesions, namely polytetrafluoroethylene (PTFE). Adhesions are noted widely in patients with reoperated chests undergoing thoracoscopic surgery, and currently represent a relative contraindication to thoracoscopy (Yim *et al.*, 1998).

In orthopaedics, joints often demonstrate reduced mobility after surgery. 'Captured shoulders' with tightness in the joint and moderate to severe pain with activity can be caused by subdeltoid adhesions after rotator cuff repair. This requires a second-look arthroscopy for adhesion takedown and relief (Mormino *et al.*, 1996). Adhesion development in the digital canal after repair of an injured digital flexor tendon is a well-known complication of the procedure. Tenolysis is the procedure of choice to correct this (Drape *et al.*, 1996). The problem of postoperative knee ankylosis has prompted the evaluation of the use of a porcine biomembrane to prevent adhesions after surgery (Wang *et al.*, 1997).

Neurosurgery has its share of adhesion-related misery. Retethering of the spinal cord by postoperative intradural fibrous adhesions at the repair site after initial tethered spinal cord surgery is not uncommon. Prevention of such adhesions was found effective through the use of Gore-Tex surgical membrane (expanded PTFE) (Aliredjo *et al.*, 1999). Even ophthalmology has seen the development of peripheral vitreo-retinal adhesions in the region of the vitreous base as a consequence of age-related remodelling, which can lead to retinal tears (Pierro *et al.*, 1997). Recently, recombinant tissue plasminogen activator (TPA) has been used for prophylaxis and treatment of fibrin reactions occurring within the anterior chamber of the eye following combined cataract and glaucoma surgery (Rehfeldt and Ho, 1999).

Conclusions

Currently adhesions remain a clinically relevant problem. In general surgery, and obstetrics and gynaecology we see bowel obstruction, infertility, difficult re-operations, and possibly pain, all attributable to adhesive disease. Other surgical specialties also encounter problems due to adhesions that are more germane to their specific fields. Consequently, this has sparked attempts in all surgical disciplines to reduce adhesions. This attention to adhesions along with increased biotechnology company interest, suggests the years ahead will bring more rapid developments that hopefully will lead one day to prevention, not reduction, of all undesired adhesions.

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