

I. RESEARCH OBJECTIVES:

The objective of the proposed study is to contrast in statistically sound form the utility of the figure-of-eight through-and-through closure over wound splints with closure by a more habitually employed method in terms of the following items:

- a. Appearance
- b. Comfort
- c. Wound infection
- d. Dehiscence
- e. Evisceration - disruption
- f. Late herniation

Since the wounds of operations in an infection-free patient without entry into hollow viscera are expected to heal uneventfully, they will not be included. Certain incisions such as the McBurney incision for appendectomy,¹ the Zierold incision for cholecystectomy,² the rectus-reflecting paramedian incision, and the midline incision through the linea alba are not suited to mass closure and regularly heal promptly without dehiscence or infection, they too will be omitted.

The study, therefore, will involve vertical, oblique, or transverse rectus incisions for operations

- a. with frank infection at the time,
- b. with overt contamination,
- c. with other high risk factors such as the "clean contaminated" group (cholecystectomy, bowel resection, pancreatic resection, gastrectomy, splenectomy), diabetes, uremia, widespread malignancy, evidence of malnutrition (e.g., plasma albumen below 2.8 mg/dl), chronic or acute obstructive pulmonary disease, morbid obesity, age over 70, and a record of current steroid therapy (over the equivalent of 40 mg. prednisone daily).

II. INTRODUCTION AND RATIONALE:

The incidence of complications in the healing of elective surgical abdominal wounds is not easy to establish, for few surgeons are inclined to rush into publication with accounts of personal failures and disasters. Infection, separation, and late herniation are the commonly mentioned complications. The major threat

to the patient lies in separation, which may be superficial or may involve all layers with exposure or actual extrusion of bowel. The term "dehiscence" is used to include all separations in which abdominal viscera are visible or palpable to the exploring finger.

Higgins et al.³ found 51 dehiscences in 2,377 laparotomies, exclusive of gridiron incisions and herniorrhaphies, an incidence of 2.1%. Customary layered closure in this retrospective study carried a 3.7% incidence of dehiscence and a mortality of 16% among those with dehiscence, or 0.6% of the entire group so closed. A mass closure of the Smead-Jones type^{4,5} resulted in a dehiscence rate of 0.7%, but among these 55% died of the dehiscence. This corresponds to a mortality from dehiscence of 0.6% after layered closures and 0.39% after the mass closure. The mass closure used steel wire sutures, which produced pain both early and late, at times requiring re-exploration for removal. This report included all laparotomies using the specified incisions, including those with excellent wound expectancy.

Other reports are somewhat at variance. Spencer et al.⁶ virtually eradicated evisceration by mass buried wire closures. Goligher et al.⁷ found a 14% incidence of either dehiscence or late hernia after layered catgut closure and of 0.9% with buried wire alone. Combination of layered catgut and wire tension sutures carried a 4.8% incidence of dehiscence or late herniation, but resulted in more wound sepsis than the other methods. Altemeier⁸ estimates the true incidence of dehiscence to be about 2.5% of all cases, and 10% in infected cases.

We have not found reports of studies on abdominal pain resulting from abdominal wound closures. One of us has been impressed in his personal experience with the minimization of postoperative pain after procedures in which strangulation of tissues and unnecessary trauma have been meticulously avoided. The proposed figure-of-eight closure over wound splints is believed to fulfill these requirements.

The investigators propose that there is need for a prospective, randomized, psychologically blind study in which two selected methods of closures can be compared as to (1) appearance, (2) pain, (3) infection rate, (4) dehiscence incidence, (5) disruption, and (6) occurrence of late herniation.

Abdominal wall closure after elective intra-abdominal surgical procedures is uncomplicated and secure in most cases. Multiple technical factors may impair healing and result in wound infection, dehiscence, frank evisceration, or late herniation. The major technical factors are:

- a. strangulation of tissues
- b. poor hemostasis
- c. undue trauma to the tissues
- d. failure to obliterate dead space
- e. placement of excessive foreign bodies during closures (such as gross or porous sutures)
- f. contamination from unsterile hollow viscera, the skin of the patient, or the environment, including the surgical team.

A method to provide secure closure without strangulation, without persistence of dead space in the interstices, and without placement of more than the least feasible amount of suture material in the wound was described by the Principal Investigator and associates in 1953.⁹ During 25 years of use in patients with poor wound expectancy, no case of evisceration occurred. It is now proposed for the first time to run a statistically valid, randomized, prospective study of this method compared with a habitual or customary method of abdominal closure.

Figure-of-8 Method of Closure:

The method of closure is illustrated in Figure 1.¹⁰

"When the time comes for closure, wound towels are removed and the skin about the wound is reprepared with antiseptic solution. Sutures are placed 2 cm. apart, first in the musculofascial structures 2 cm. back from the line of incision. In so doing, a bite of posterior fascia or rectus sheath and peritoneum is taken on each side (Figure 1). The large round Mayo needle used for this is removed, and hemostatic forceps are applied to the suture ends to permit progression of placement of sutures in this layer. Large trocar needles are now applied for passage of each end of each suture through the subcutaneous tissue and skin of the opposite side of the wound.

A length of wound splint is selected which is appropriate to approximate all layers without unduly pulling on the skin. Prior to drawing snug each of these sutures over the selected splint, the area between it and that just tied is explored with a finger, and, if necessary to avoid herniation between figure-of-8 sutures, a simple fine approximation suture of peritoneum and posterior fascia is placed and tied.

Snugging up the musculofascial layers and tying over the splints commonly completes the closure, although inaccuracies in placement occasionally must be corrected by three or four fine silk

sutures or adhesive strips to approximate the skin precisely. In case the monofilament suture is steel wire of the diameters indicated, it is more convenient simply to twist the wires than to tie knots. This has proved entirely adequate.

Routinely, the fine accessory skin stitches or adhesive strips are removed in one week, and the figure-of-8 sutures and splints are removed 18 to 21 days after closure, longer if the patient has been on heavy steroid therapy, has low serum protein levels, has carcinomatosis, or has other reason to suggest impairment of wound healing. Ordinarily this suture removal is done on an outpatient basis."

The processes of wound healing have been studied by many investigators. Howes, Sooy, and Harvey¹¹ first introduced determination of tensile strength as a measure of completeness of healing, and found that in many tissues there is an initial lag phase of three days following closure, after which fibroblastic activity rises and the tensile strength (disruptive strength) rises in linear fashion as the days pass for 11 or 12 days.

Fast, Nelson, and Dennis¹² reported the earliest studies on the tensile strength of the sutured leporine abdominal wall during the healing period. Their findings are presented in Figure 2 and show a total tensile strength, i.e., the tensile strength of sutures plus tissues, of 40% for the first three days and a rise to 80% of the unincised opposite side at 15 days. Because of the reports by Babcock of the minimal tissue reaction to stainless steel sutures,¹³ Nelson and Dennis¹⁴ repeated their studies in the rabbit and determined the tensile strength of the tissues both before and after removal of the wire sutures with an eye to leaving a wound with no foreign material in it (Figure 3).

The decision to use a minimally reactive monofilament suture toward this objective had been suggested by many observers earlier but was impressively supported later by the observation of Elek and Conen¹⁵ that the burial of braided silk sutures in man enhances the virulence of contaminating staphylococci by a factor of 10,000.

The technical factors involved in surgical wound healing have been studied since the time of Lord Lister. Postlethwaite has summarized our painfully gained understanding.¹⁶ The major factors are: asepsis, gentleness in handling the tissues, precise hemostasis, minimization of residual foreign bodies, and elimination of dead space. He expands regarding sutures, "Since their function is to appose tissues, the spacing of sutures, the depth of the bite taken, and the tension applied on tying should accomplish this without strangulation of the tissue or excessive foreign body implantation."

Technical factors were further documented by Condie and Ferguson.¹⁷ They deliberately contaminated abdominal wounds in dogs with a standard laboratory culture of virulent bacteria and found a meticulous space-obliterating pattern of closure to reduce the inci-

dence of infection from 11 out of 12 in conventionally closed wounds 3 out of 12 in experimental ones. They also reported that monofilament closures were strikingly effective in reducing the infection rate as compared with closures with braided silk or dacron.

The mechanical inadequacy of retention sutures without splints was expounded by Price,¹⁸ who devised a closure with a bar frame (Figure 4) as a means of achieving a more solid apposition of the fascial layers than can be gained by simple through-and-through retention sutures such as the monofilament silver wire sutures first proposed by Reid, Zininger, and Merrell¹⁹ (Figure 5). Price noted that this inadequacy of approximation is not significantly lessened by use of "booties" and is compounded by painful and unsightly cutting of the skin by the sutures.

It was in awareness of these principles but in advance of several of the above specific studies that Dennis, Nelson, and Ankner reported in 1953⁹ closure with figure-of-8 monofilament wire sutures over wound splints. An almost identical closure was reported by Taylor and Jontz in 1959;²⁰ it differed in not entering the peritoneal cavity and in being used only as reinforcement upon a standard closure, not as the sole closure.

Other factors of technical importance were reviewed in the report of Dennis and Aka in 1973.¹⁰ "As to fear of cutting bowel by bow-stringing intraperitoneal portions of the figure-of-8 sutures, Taylor and Jontz report an instance, and we have seen an instance, in totally buried wire closure in other hands elsewhere. We have not seen this complication in our own experience.....We had nonetheless respected the possibility and chose to catch the wound edges with the figure-of-8 suture in the mid-fifties after seeing the tragedy noted above with totally buried steel sutures. We concur in the opinion of Taylor and Jontz that precautions should be taken but prefer passage of the through-and-through suture at the holding extremes of the suture loop because of the greater certainty of engaging the posterior rectus sheath or posterior fascia and taking advantage of the strength of these structures.

"In 1963, 1964, and 1965 we studied variations in technique which might simplify the tedious closure as described. Polypropylene monofilament sutures were employed for a time; the elasticity appeared to us, as an elastic closure had appeared to Taylor and Jontz, to be accompanied by rapid loosening and the need for frequent re-tying to maintain the desired tension. Surgaloy suture was employed in some cases, but too often became so anchored as to make removal impossible. We have seen no untoward effects from division of such anchored sutures under tension at skin level when withdrawal is impossible, but prefer to remove the figure-of-8 sutures altogether, and therefore do not use braided wire.

"As previously reported by Howes and Harvey¹¹ in several tissues, and by Fast, Nelson and Dennis¹² in the abdominal wall of the rabbit, most (80%) of the ultimately achieved tensile strength across the wound is gained in the first 15 days. The occasional unexpected failure of a normal pace of strength gain has led us to delay suture removal until 18 to 21 days, particularly in instances in which poor healing had already been demonstrated."¹⁰

Control Closures:

The closures to be used as controls have been vigorously discussed among members of the Surgical Service. The figure-of-8 method was devised for wounds with poor healing expectancy and in general would be used in situations in which some type of retention suture is commonly employed. For this reason it was agreed that a reasonable comparison should be between:

- a. the figure-of-8 monofilament closure with wound splints, and
- b. closure employing Reid-type through-and-through sutures,

both closures to be applied to a specified class of cases. The control closure may include incidental sutures of polyglycolic acid or dacron suture material in one or more layers, but the figure-of-8 may supplement the test closure only with an occasional posterior rectus sheath-peritoneal stitch as needed to prevent herniation or an occasional skin stitch to maintain approximation.

It is appreciated that other factors have been demonstrated to play a part in the incidence of wound infection, and for the present study should be borne in mind. In 1964 the Cooperative Study Group reported that post-operative infections occurred with increasing frequency as the number of pre-operative days in the hospital increased. Those in the hospital less than two days had an infection rate of 6%, while those in the hospital over three weeks had an infection rate of 14.7%.²¹

Burke reported that the infection rate increased with increase in the length of operations up to three hours, levelling off after that time.²² He noted that obesity and advanced age also were factors.

III. SPECIFIC AIMS:

A. To identify patients at risk of less than optimal laparotomy wound healing due to existing infection, gross contamination, "clean contamination", albumin in the plasma below 2.8 gm/dl, diabetes, uremia, cirrhosis with ascites, carcinomatosis, leukemia, acute or chronic pulmonary disease with cough, advanced age (over 70), or steroid administration greater than the equivalent of 40mg/day of prednisone.

B. To randomize closure after rectus incisions, whether sagittal, transverse, or oblique, between

1. figure-of-8 monofilament closure over wound splints, and
2. control closure with Reid-type retention sutures.

C. To compare the two methods in terms of:

1. appearance of the wound
2. comfort
3. dehiscence
4. disruption
5. infection, and
6. late herniation.

D. To achieve a sufficient number of cases to permit statistically valid conclusions by the normal approximation test for comparison of two proportions, estimating in advance an incidence of 3% disruptions for the control group and 0% for the figure-of-8 closure, the latter based on the history of 1,500 cases without disruption reported in 1973.

IV. EXPERIMENTAL DESIGN:

A. Patient Selection:

1. Included Cases: Patients will be asked to participate and sign the consent form if they are: (a) scheduled to have laparotomies through sigittal, transverse, or oblique incisions, and (b) at higher than average risk of poor healing. These include:

- a. clean-contaminated cases such as bowel resections or anastomoses, gastrectomies, biliary tract operations, appendectomies, splenectomies, and pancreatectomies
- b. contaminated cases
- c. already infected cases
- d. cases with chronic obstructive pulmonary disease
- e. heavy smokers with cough
- f. cases with unrelieved distension
- g. diabetic cases
- h. uremic cases
- i. cirrhotic cases with any complications
- j. cases with disseminated neoplasia
- k. malnourished cases, specifically those with serum albumin levels below 2.8 gm/dl, low vitamin C levels
- l. patients receiving more than the equivalent of 40 mg/day of prednisone
- m. patients classed as obese
- n. patients over age 70

2. Excluded Cases: The excluded cases are:

- a. Patients having clean operations in a clean field, and
- b. patients having plastic surgical types of incisions which regularly heal without complicated courses, such as:
 - (1) McBurney incisions¹
 - (2) variations on the McBurney incision^{2,3,24}
 - (3) Zierold² incisions for cholecystectomy or exploration of the common duct
 - (4) paramedian muscle reflecting incisions
 - (5) midline incisions through the linea alba above the linea semilunaris.

B. Method of Study:

1. Each entrant into the study will be prepared by the best of current surgical methods as to nutrition, hydration, electrolyte balance, decompression, bowel preparation, and general care.

2. Each entrant will receive 1 gm of Cefoxitin sodium at 8 hours before operation, at the start of operation, and 8 hours after the start of operation.

3. Each entrant may have oral intestinal antibiotic preparation as the surgeon may wish.

4. At the time of start of closure on each entrant into the study, a numbered sealed envelope containing a randomized card will be opened in the presence of the operating team by a member of the operating room personnel not a participant in the study in any other sense.

5. Closure will be by the method stipulated on that randomized card.

6. Post-operative observations of the psychologist collaborators. In order to determine possible differences in pain experienced by patients due to the two surgical techniques, psychologists will assess pain levels on each of the first five days post-operative. Pain levels will be assessed in two ways.²⁵ First, in a heuristic fashion, patients will rate their subjective experience of pain on a scale of 0 to 100, where 0 is no pain at all and 100 represents intense, intolerable, unbearable pain.²⁶ Second, patients will fill out the McGill-Dartmouth Pain Questionnaire (Attachment 1),²⁷ a recently standardized, multidimensional psychometric device.²⁸

7. Post-operative surgical observations. The patient and his wound will be examined by two surgical collaborators 48 hours post-operatively. They will make the following notations:

- a. age
- b. weight and height
- c. number of preoperative days in hospital
- d. duration of operation
- e. type of closure, experimental or control
- f. delayed closure of extrafascial subcutaneous tissues
- g. reason for inclusion in the study
- h. surgeon.

Twice weekly thereafter until 30 days, if the patient remains in hospital that long, the two surgical collaborators will examine the wound and make the following notations:

(1) Appearance of the wound

- A - Excellent
- B - Cutting of skin by stay sutures
- C - Severe cutting and scarring

In order to permit consistent comparisons, they will photograph the wound weekly, using standard exposure, distance, and light with equipment to be purchased.

(2) Suppuration

- A - None
- B - Stitch drainage only
- C - More than 1 ml. of pus with positive culture
- D - Frankly septic wound

(3) Dehiscence

- A - Yes
- B - No

(4) Disruption

- A - Yes
- B - No

(5) 30-day outcome

- A - Alive
- B - Dead

There will be a further observation by the surgeons one year post-operatively:

(1) Survival

- A - Alive
- B - Dead

(2) Intestinal obstruction

- A - Yes
- B - No

(3) Appearance of wound

- A - Excellent
- B - Ugly scars of stay sutures
- C - Ugly scar of line of apposition

Photograph as above

(4) Hernia in wound

- A - Yes
- B - No

C. Analysis of Results:

1. Sample Size Considerations:

The sample size needed to detect a statistically significant difference in outcome between the figure-of-8 and the habitual closure study group will depend on the expected size of this difference. If a small difference in outcome is expected, the sample size required will be large. Therefore, the determination of sample size was based on the outcome which was expected to show the smallest difference between the two study groups. This was assumed to be the percentage of disruptions occurring in each group, since larger differences between the study groups were expected with regard to the other outcomes (e.g., wound appearance, suppuration, and dehiscence).

Based on previous studies, the expected incidence of disruption in the habitual closure group is 3%. However, no disruptions were observed among an estimated 1,500 figure-of-8 surgical cases, while 45 would have been expected to occur with a disruption rate of 3%. This finding cannot easily be explained by sampling variation, thus suggesting that the percentage of disruptions with the figure-of-8 method is nil. Rather than basing the sample size calculations on an expected difference of 3% vs. 0% disruptions between study groups, a more conservative approach was followed. Instead of zero, the figure used was 0.2%, which is the highest percentage of disruptions that would have been likely to occur in a sample of 1,500 with a disruption rate of 0%. This percentage was obtained by estimating the upper limit of the confidence interval for a Poisson variable expected to be zero.²⁹ Therefore, the sample size was calculated assuming 0.2% of disruptions for the figure-of-8 group and 3% of disruptions for the control group. The significance level was set at 5% ($\alpha = 0.05$, one-tailed test) and the power of the test was set at 90% ($\beta = 0.10$). By these specifications, the sample size required was 343 for each group, or approximately 690 patients.

The sample size calculations are based on the assumption that no disruptions occurred among 1,500 cases. It must be emphasized that this is a minimum sample size requirement. If a smaller difference than the one expected does occur, the sample size will be insufficient to detect a statistically significant difference at the 5% level, with 90% power, between the two groups. Because of the available data on the favorable outcome of the figure-of-8 cases, the sample size calculations assumed that one-tailed tests would be used to test the significance of the differences found.

2. Statistical Significance Testing:

Randomization of patients will be done to increase the likelihood that the two study groups will be comparable with regard to major variables such as age, diagnosis and length of pre-operative stay. After randomization, the composition of the two groups will be

compared with regard to variables of possible prognostic importance, in order to evaluate any differences. Duration of the operation in the two groups will also be compared. Statistical tests to be used are the Student's t-test (or where applicable, Welch's) for continuous variables and by continuity corrected chi-square for categorical variables.

After surgery, observations regarding outcome will be done in such a way as to decrease the possibility of observer bias. Observations most susceptible to this bias are degree of discomfort and appearance. Degree of discomfort will be evaluated on a scale of 0 (no discomfort) to 100 (unbearable discomfort) by an observer who will be unaware of the type of closure used. Because of the large inherent subjectivity in these evaluations, these "discomfort" categories will be strictly defined. Since only two observers will evaluate for all patients, interobserver variation will be minimized.

In order to decrease observer bias in grading appearance, the wound will be photographed under standardized conditions. An independent observer, who will be unaware of the type of closure used, will grade these photographs on a scale of 1 (excellent) to 3 (severe cutting and scarring). Appearance of the wound will again be noted after one year and photographs taken which will also be ranked by an independent observer.

The presence of suppuration, dehiscence, disruption, intestinal obstruction, hernia and survival will also be noted. Since all the outcome variables are of a qualitative nature, differences in outcome between the two study groups will be tested by statistical significance by the normal approximation test for comparison of two proportions. Differences in composition between groups with regard to variables of prognostic significance (such as age) will be taken into account in all comparisons.

3. Sequential Testing:

It is desirable to find an existing difference between the two groups as early in the study as possible. Rather than waiting until the end of the trial to conduct statistical significance tests, ongoing assessment of the accumulating data will be carried out by group sequential methods.³⁰ In the group sequential design, the decision to stop or continue the trial is based on repeated significance testing of the available data on groups of patients. The number of patients at each stage and the number of stages are chosen to maximize the chance of ending the study earlier than in a one-stage design. The level of significance at each stage is determined by the number of patients at each stage, the number of stages and the overall α or significance level. For this trial, differences in outcome between the two types of closure, such as in percentage of disruptions, will be tested for statistical significance following a three-stage group sequential design. Following

the method outlined by Pocock, it can be estimated that the number of patients per study group needed at each stage is 133 and the level of significance testing is $\alpha' = .0344$. Therefore, statistical testing will be done after data are available on the above number of patients.

4. Data Handling:

Information on each patient will be abstracted in a form, coded and entered in a computer. The computing facilities used will be those of the Computing Center at the State University of New York at Stony Brook. Analyses will be programmed and evaluated by staff in the Department of Community and Preventive Medicine. The Department has on-site computer terminals which can access remote computers via telephone couplers. In addition to the physician epidemiologist involved in this project (Dr. Leske), available staff includes two statisticians; a full-time programmer is being recruited.

V. RESEARCH REQUIREMENTS:

This study will be carried out on the Surgical Service at the VAMC Northport using the facilities provided for the routine care of surgical patients. No laboratory studies will be needed other than those routinely used. The Principal Investigator will obtain the wound splints from the machinist at Downstate Medical Center who manufactures them from methylmethacrylate.