Postoperative Function of "Free" Jejunal Transplants for Replacement of the Cervical Esophagus

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The postoperative function of "free" jejunal autotransplants for replacement of the pharyngoesophagus after palliative resection was evaluated in nine patients using clinical assessment, cinefluoroscopy, manometry, and electrical studies. After an initial period of adjustment, all patients swallowed solids and liquids with minimal difficulty, gained weight appropriately and were satisfied with their operations. Cinefluoroscopy and esophageal manometry demonstrated normal function of the intact distal esophagus, which correlated with the absence of reflux symptoms. The grafts were capable of contraction in response to local distension and maintained an intrinsic myoelectrical activity. These results indicate that jejunal autotransplantation may provide excellent palliation with restoration of a near normal swallowing mechanism for patients with large resectable lesions of the pharyngoesophagus. An additional observation was that the instillation of food directly into the gastric antrum caused a change in the motor activity in the transplanted jejunum, indicating physiological hormonal control of intestinal motility.

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THE VARYING SUCCESS of the large number of surgical methods for palliation in carcinoma of the pharyngoesophagus indicates that the ideal esophageal replacement has not been found. The high mortality and morbidity of patients treated with colon interposition[19] and isoperistaltic gastric tubes[18] stimulated us to pursue an alternative for treatment of cancers involving the cervical esophagus. Autotransplantation of the jejunum seemed to have three theoretical advantages: 1) a short vascular pedicle, thereby minimizing the danger of necrosis, 2) preservation of the distal esophagus which would reduce regurgitation and reflux, and 3) the possibility of functional peristalsis within the graft which could contribute to an effective swallowing mechanism.

Carrel in 1906 first described the autotransplantation of a loop of intestine into the neck "as a preliminary study of the substitution of such a tube for the oesophagus".[3] The intestinal vessels of a dog were anastomosed to the carotid artery and jugular vein and the intestine immediately achieved normal color and peristalsis. In 1957 Seidenberg reported the first successful intestinal autotransplant in man.[20] He used a segment of jejunum to replace a segment of esophagus resected for recurrent carcinoma. Unfortunately, the patient died on the seventh postoperative day of a cerebrovascular accident. Since then, gastric antrum,[9] colon[14] and ileum[15] have been transplanted successfully into the neck.

The principal objective of the present report was to evaluate the postoperative swallowing function of a series of patients with jejunal autotransplants in order to determine whether jejunal autografting offers a potential functional advantage over the other methods of esophageal reconstruction. We wanted to learn whether the patients were satisfied with their ability to swallow both liquids and solids. A secondary objective was to define the roentgenographic and motility characteristics of the jejunal autograft. In addition, we studied the effects of distension and of instillation of nutrients into the stomach on the myoelectric and motor activity of the jejunal autograft.

Materials and Methods

Patients

Over the past two years nine patients have undergone "free" jejunal transplantation after extensive resections of the larynx, pharynx, and cervical esophagus (Table 1). The patients' ages ranged from 48 to 87 years. Five patients were male and four patients were female. All had large squamous cell carcinomas involving the pharyngoesophagus and regional lymph nodes. Seven of the nine patients underwent surgery for recurrent tu-

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TABLE 1. *Patient Population*

Patient	Age	Diagnosis	Status	Months Postoperatively
1	57	Recurrent sq. cell CA esophagus	Alive	25
2	69	Rec. sq. cell CA larynx	Died	23
3	48	Rec. sq. cell CA piriform sinus	Died	4
4	65	Sq. cell CA esophagus	Alive	17
5	68	Rec. sq. cell CA pharyngoesophagus	Alive	12
6	55	Rec. sq. cell CA right neck	Died	10
7	87	Sq. cell CA larynx	Alive	9
8	61	Sq. cell CA piriform sinus with extension into esophagus	Alive	6
9	70	Rec. sq. cell CA pharynx	Alive	1½

mor. Before surgery they had severe dysphagia and a mean (±SEM) weight loss of 24.1 (±3.8) pounds. The patients have all had follow-up examinations as thought clinically appropriate and have been questioned in detail for symptoms. They have all been observed multiple times while swallowing solid and liquid food.

Surgical Procedure

The procedure is performed in one stage by two surgical teams. During the completion of the cervical dissection, a segment of jejunum with appropriate diameter and length, and a single nutrient artery and vein is selected and removed. Following removal the segment is perfused with Sack's solution until it is interposed between the remaining pharynx and esophagus. The jejunal artery and vein are anastomosed to an external carotid artery branch and the internal jugular vein using microsurgical technique. Throughout the period of ischemia the jejunum is cooled by slushed ice within a condom placed intraluminally.

Radiologic Studies

Each patient was studied with routine barium swallows two to six times. Cinefluoroscopy was performed on six patients, during swallows of both plain barium and barium-coated marshmallows. Manometry leads and electrodes were positioned during fluoroscopy.

Manometric Studies

Six patients underwent manometric studies of the jejunal graft and esophagus. The apparatus, calibration and procedure was as described by Duranceau.[5] A triple lumen catheter was used with openings 5 cm apart for simultaneous pressure recording. The pressures were transmitted from columns of water perfusing each lumen continuously at 1.91 ml/min. Pressures were recorded in millimeters of mercury with the zero reference point being atmospheric pressure. The patient sipped 2 ml of water with each swallow ("wet swallows") in the supine position. Normal laboratory values were determined by the range of pressures of 10 normal patients and are listed in Table 2. Manometric studies of the transplant patients were compared to a group of 10 patients with laryngeal carcinomas who were about to undergo laryngectomy with primary closure. A point midway between the upper and lower esophagus sphincter (LES) was selected as the division between the "proximal" and "distal" esophagus. Because the transplant patients no longer had an upper esophageal sphincter, that location was estimated. Peristalsis in the body of the esophagus was "coordinated" when the wave peaks were separated by more than 1.25 seconds, corresponding to a maximum wave speed of 4 cm/sec. The LES was "coordinated" when the phase of LES relaxation entirely encompassed the oncoming peristaltic wave.

TABLE 2. *Esophageal Manometry**

Body	35 ± 4 (Normal 15–90)
Lower esophageal sphincter	
peak contraction	21 ± 4 (Normal 10–35)
relaxation	−4 ± 4 (Normal −5–5)

* Distal esophageal pressures of transplant patients in mmHg with laboratory range of normal values in parentheses.

Intrinsic graft motor activity was measured by leaving manometric leads within the jejunal segment for periods varying between three and 13 hours. Four patients were studied on two different occasions and one a total of three times. They were fasted for a minimum of ten hours before the studies. One patient was studied overnight. In four patients a small feeding catheter was placed in the distal antrum prior to the studies and 150 ml of a liquid nutritional formula (Ensure® or a liquified meal) at room temperature was administered through the feeding tube after establishment of fasting activity. Following the studies there was no demonstrable reflux of contrast from the feeding tube into the esophagus during infusion of barium or gastrografin.

Simultaneous Electrical and Pressure Recordings

The methods used for simultaneous recording of electrical and intraluminal pressure was previously re-

ported.[1] Electrical activity of the jejunal graft was recorded using bipolar platinum suction electrodes positioned in an 18F vinyl tube. The electrodes were soldered at right angles to insulated copper wires, and the soldered junctions mounted within the vinyl tube with vinyl glue. The vinyl glue not only fixed the electrodes on the inner wall of the vinyl tube but also insulated the soldered junction. The shaft of the electrodes projected from its base towards an opening cut on the opposite side of the tube, so that the tips of the electrodes were flush with the outside wall of the vinyl tube. The shafts of the electrodes were insulated with vinyl paint and their tips electrolytically coated with silver chloride. The side holes through which the electrodes projected communicated freely with the lumen of the tube, so that when suction was applied at the open end of the tube, the intestine pulled onto the electrodes. The closed end of the tube was weighted with a mercury-filled "bullet." The insulated copper wires led from the electrodes down the center of the tube towards its open end near which they exited through the wall of the tube.

Plugs were attached to the ends of the wires. The plugs were connected via a "universal" amplifier to a channel of a Gould Brush 4600® alternating current, direct-writing pen recorder (time constant: one second).

The balloon was carefully mounted opposite the electrode pair. The balloon measuring about 2 × 4 cm was fitted with a polyethylene catheter which led from the balloon to a Gould Statham (Cleveland, Ohio) pressure transducer. The transducer signals were translated into pressure, in centimeters of water, by prior calibration of the Gould Brush pressure amplifier and recorder. With the transducer placed at a height level with the middle of the neck, the pressure inside the balloon was continuously recorded. Intraluminal pressure was recorded when the balloon and polyethylene catheter was filled with 5 ml water and again with 10 ml, taking precautions against air entering the system. Another balloon system with 5 ml water was positioned in an esophageal segment distal to the jejunal graft in order to measure simultaneously intraluminal esophageal pressure.

Results

Postoperative Complications and Patient Survival

Two patients had anastomotic leaks postoperatively which were clinically inconsequential. There were no postoperative problems with mediastinitis, empyema, other abscess, or delayed gastric emptying. Six of the nine patients remain alive. Our first patient, who had carcinoma of the esophagus, is alive and well at 25 months following transplantation. Our second patient died 23 months following surgery of pulmonary and cerebral metastases. Patients 3 and 4 died with extensive locally recurrent disease at four and nine months postoperatively.

Graft Viability

At the end of each operation, the grafts were seen to have normal color and normal appearing peristalsis. There has been no graft necrosis. A biopsy of the graft of our first patient 24 months postoperatively showed normal jejunum (Fig. 1).

Clinical Function (Table 3)

Initially following the procedure and resumption of oral intake, all patients had some nasal regurgitation of liquids. In all patients this was mild, and for seven patients this rarely occurred after the first two weeks. Following this initial period, however, graft function was excellent. All patients stated they could eat whatever they desired and each gained weight appropriately. Two patients (patients 3 and 6) developed large local recurrences which caused graft stenoses at 2 and 4 months postoperatively; after which deterioration of graft function was noted. Patient 2, who died 23 months postoperatively with systemic disease, had no dysphagia and gained weight until approximately one month before death. No other patient has had dysphagia with solid food. The patients have not had reflux symptoms, abdominal pain, early satiety, gastric emptying problems or marginal ulceration.

Radiologic Findings

Barium studies showed all grafts to be widely patent (Fig. 2) during the period of good graft function. The motility of the distal esophagus was normal and there was no demonstrable reflux from the stomach. Liquids passed freely through the grafts, and the grafts exhibited normally appearing small bowel contractions (Fig. 3), which seemed to be stimulated by the barium bolus. The patients experienced no dysphagia with swallowing barium coated marshmallows, 3 cm in diameter (Fig. 4). However, on cinefluoroscopy, there was delayed passage of the marshmallows through the graft. They passed easily down the esophagus after the patient swallowed a small amount of water.

Motility

The response of the graft to a bolus of water ("wet swallows") was variable. Twenty-nine per cent of swallows produced no appreciable pressure deflection within the graft. Thirty-two per cent of swallows produced deflections similar to normal esophageal contractions, with the wave peaks separated by more than 1.25 seconds from the esophageal peak 5 cm distal. Thirty-nine

FIG. 1. Biopsy of jejunal graft from patient 24 months after surgery showing normal jejunal architecture.

TABLE 3. *Symptoms After Initial Period of Adjustment*

Patient	Dysphagia with Liquids	Dysphagia with Solids	Regurgitation	Reflux	Pain	Early Satiety
1	–	–	–	–	–	–
2	–	–	–	–	–	–
3	–	–	–	–	–	–
4	+ (mild)	–	+ (mild)	–	–	–
5	–	–	–	–	–	–
6	–	–	–	–	–	–
7	–	–	–	–	–	–
8	+ (mild)	–	+ (mild)	–	–	–
9	–	–	–	–	–	–

per cent of swallows produced more sustained deflections in the graft than the associated esophageal contractions; the peak of the jejunal graft wave occurred before the peak of the esophageal wave, but relaxation did not occur until several seconds after esophageal relaxation (Fig. 5). All three patterns occurred in all the patients tested and there was no correlation of any pattern with dysphagia or nasal regurgitation.

Pressures and coordination of the intact remaining esophagus were within normal limits (Table 2). In comparison to the group of ten patients about to undergo laryngectomy with primary closure, there were no significant differences either in pressure or coordination

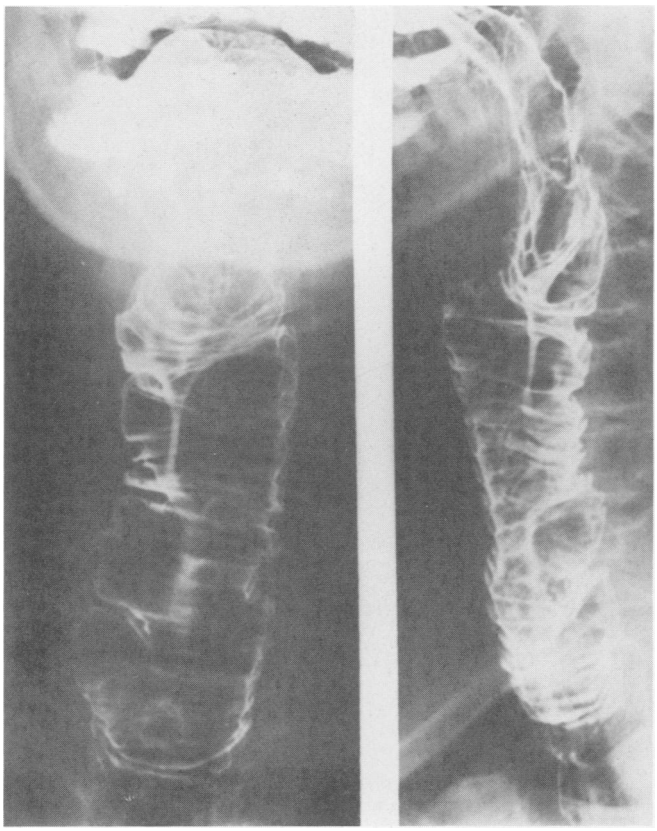

FIG. 2. Anterior and lateral films of jejunal interposition graft. Note patent proximal and distal anastomoses as well as normal appearing mucosal folds.

in the motility of the preserved esophagus between the transplant patients and the prelaryngectomy patients (Tables 4 and 5).

Intrinsic Motor and Electrical Activity During Fasting

During fasting the grafts exhibited periodic bursts of motor activity between which the grafts were relatively quiescent (Fig. 6a). Each burst of activity would last 5–20 minutes and the intervals between bursts varied from five to 35 minutes. The intervals between bursts decreased progressively over a 45 minute to two-hour period in a cyclical pattern until a longer burst occurred, lasting 15–20 minutes. The longer bursts were followed by a longer period of relative quiescence, sometimes lasting 25–30 minutes.

Slow waves and control potentials were consistently recorded from the jejunal graft (Fig. 7). The configuration, amplitude, and duration of the pacesetter potentials varied from cycle to cycle with the frequency of cycles being nine to ten per minute. Action potentials accompanied the pacesetter potentials and were consistently recorded when changes in intraluminal pressure were occurring in the jejunal graft. There was no consistent relationship between the small changes in jejunal graft pressure and distal esophageal pressure.

Distension of the balloon within the jejunal graft with 10 ml water changed its electrical and motor patterns markedly (Fig. 8). Action potentials occurred in bursts, sometimes spanning several pacesetter potentials. The action potential bursts were associated with phasic changes in pressure (amplitude: 50–55 cm H_2O, duration: 13–18 seconds). These phasic changes in pressure were frequently soon followed by changes in intraluminal pressure in the distal esophageal segment. The pattern resembled that induced by "wet swallows" (Fig. 5).

Motor Activity of Jejunal Graft During Instillation of Food Into the Stomach

Administration of a liquid nutritional formula directly into the gastric antrum, through a feeding tube, and without coming into contact with jejunal graft or esophageal mucosa, produced a dramatic change in motor activity within the jejunal graft (Fig. 6b). The jejunal graft immediately increased its motor activity. The periodic bursts of motor activity during the fasting state promptly ceased and the resultant pattern was a much more disordered, continually active one which continued for 2.5 hours before it began to convert back to the fasting pattern.

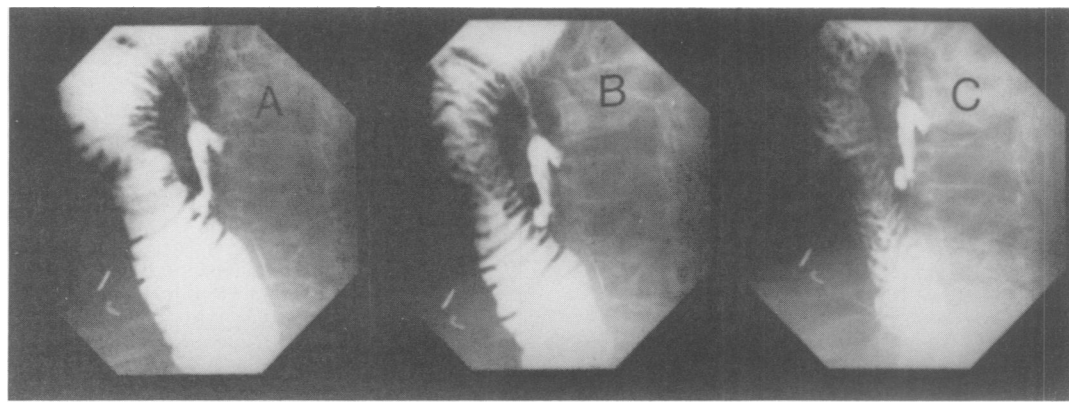

FIG. 3. Lateral films of jejunal graft during swallowing bolus of barium. (A) Jejunum filled with barium immediately after swallowing. (B) Mild contraction of jejunum forcing barium through graft. (C) Empty graft after barium has passed into esophagus.

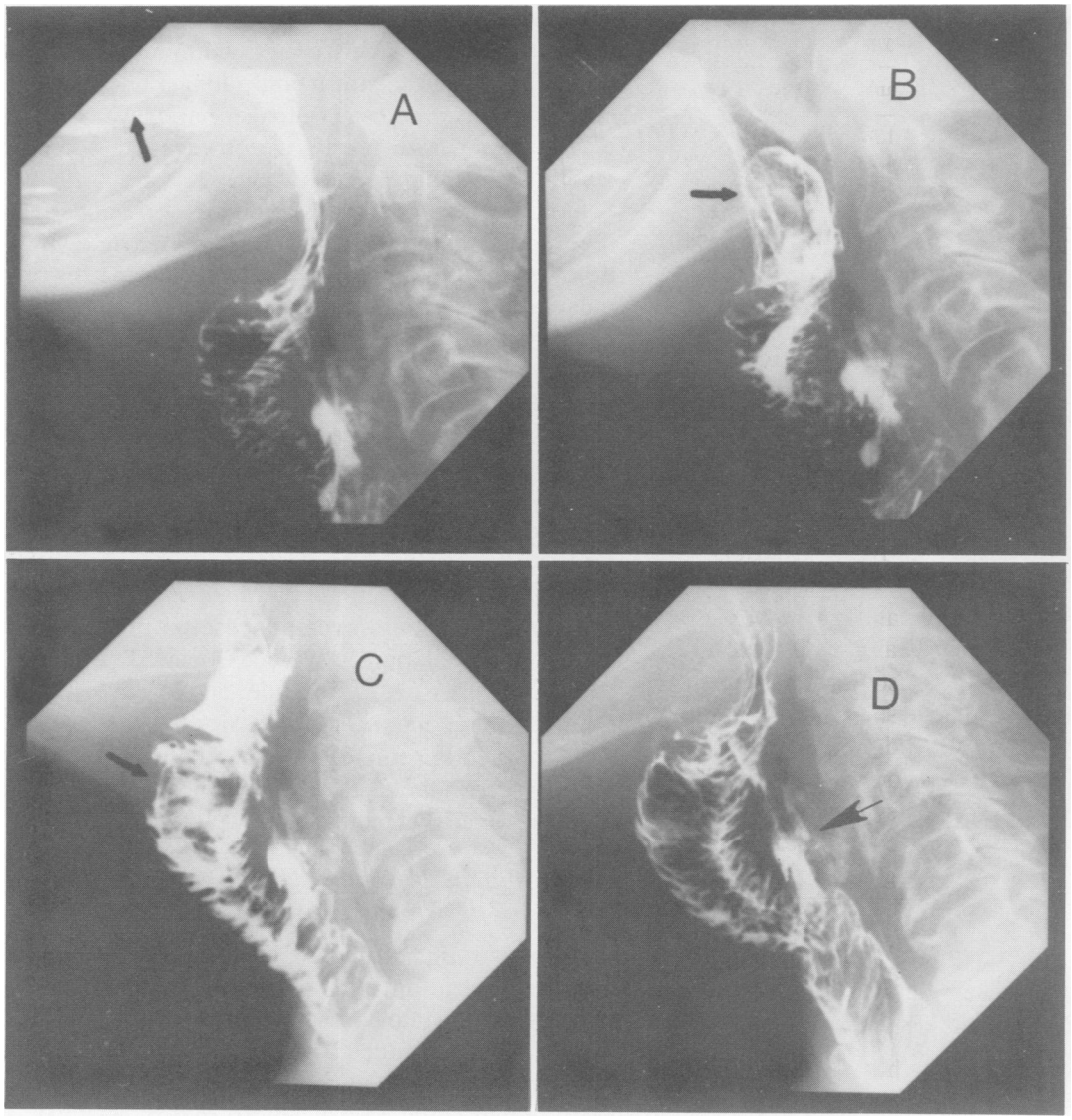

FIG. 4. Lateral views of jejunal graft during swallowing a barium-coated marshmallow. (a) Marshmallow (arrow) in oral cavity before swallowing. (b) Marshmallow (arrow) passing through proximal anastomosis. (c) Marshmallow (arrow) in upper portion of graft. (d) Empty graft after patient swallowed a small amount of water. Marshmallow passed easily through distal anastomosis down into the esophagus. Arrow marks small clinically insignificant sinus tract from proximal anastomosis.

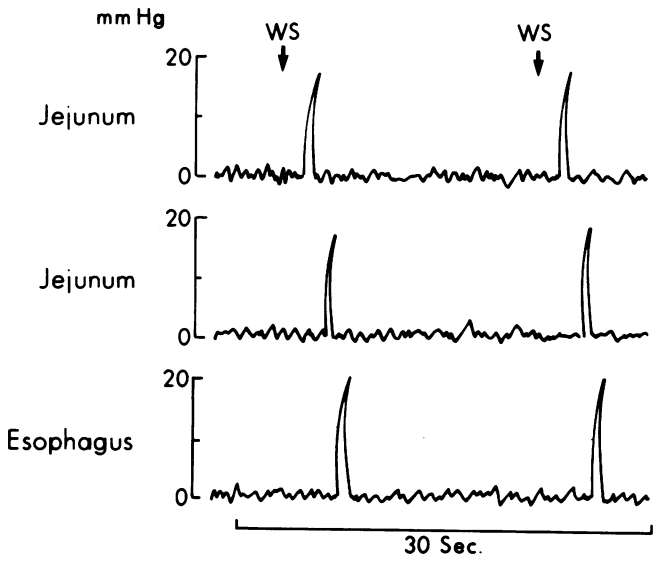

FIG. 5. Manometric tracing of a wet swallow (WS) passing through jejunal graft (top tracing), esophagus 5 cm distal (middle tracing), and esophagus 10 cm distal to jejunal graft pressure lead (bottom tracing). Note onset of jejunal contraction prior to esophageal and continuation of that contraction throughout the esophageal contractions.

Discussion

Survival for carcinoma of the esophagus, either by surgery or irradiation, is usually measured in months. Two year survival for those patients who have had resections is about 10% and for those without resection approaches 0%.[17] In our series, mean survival from carcinoma of the cervical esophagus with or without resection was 6.5 months compared to 8.4 months for the more distal lesions. Without surgery many patients die a slow death from inanition. The survival of patients with large pharyngeal or laryngeal car-

TABLE 4. *Esophageal Pressures of Five Transplant Patients Compared to a Group of Ten Prelaryngectomy Patients*

	Transplant	Prelaryngectomy
Proximal esophagus	21.1 ± 1.3	18.4 ± 1.3
Distal esophagus	30.3 ± 4.9	25.6 ± 2.7
Lower esophageal sphincter	24.2 ± 3.4	29.3 ± 3.9

Values are means ± SEM in mmHg.

TABLE 5. *Esophageal Coordination of Five Transplant Patients Compared to a Group of Ten Prelaryngectomy Patients*

	Transplant	Prelaryngectomy
Proximal esophagus	76.0 ± 10.9	82.6 ± 8.6
Distal esophagus	87.6 ± 9.7	89.9 ± 6.2
Lower esophageal sphincter	74.9 ± 10.1	80.5 ± 8.9

Values are mean ± SEM percentage.

cinomas involving the esophagus is probably longer although quality of the terminal course is similar.

Mustard found the Wookey operation satisfactory for pharyngoesophageal reconstruction, although he expressed dissatisfaction with the need for multiple stages.[13] Others[8,16] have considered this reconstruction with a tube of skin and platysma muscle satisfactory for palliation and have preferred reconstruction with pedicle grafts of colon or stomach. In our series' colon interposition[19] for malignant disease had a 25% postoperative mortality, and in hospital mortality after the isoperistaltic gastric tube[18] for esophageal bypass of malignant disease was 28%. One-fifth of the patients in the latter group, however, had tracheoesophageal fistulae. The major complications of colon interposition were gangrene of the interposed segment and anastomotic leakage. The incidence of cervical anastomotic leakage after the isoperistaltic gastric tube bypass was 43%. Using these methods there were also problems with mediastinitis, empyema, abdominal abscess, delayed gastric emptying, marginal ulceration, and reflux symptoms and complications.

At present for carcinomas involving the thoracic esophagus, pedicle grafts from the abdomen are still the most feasible procedures for resection or bypass. However, for large resectable carcinomas involving the pharyngoesophagus, the use of a "free" graft eliminates much of the abdominal and thoracic dissection. In the present series we did not encounter most of the problems seen with the other procedures including graft necrosis. In addition, there was preservation of the distal esophagus and its function. A retrospective study[5] suggested that there was distal esophageal motility abnormalities following laryngectomy with primary closure; however, the present study did not support this observation. Reflux was not a problem in the patients with jejunal grafts, and all the patients were satisfied with their swallowing function, particularly their ability to eat whatever they chose.

The postoperative functional results from this operation, assessed subjectively by the patients and their physicians, have indeed been good. Functionally a near normal swallowing mechanism was restored. However, the response to swallowing of the jejunal segment as measured by manometrics and barium studies clearly was different from the normal pharyngoesophagus. Motor activity, although functionally present, responded inconsistently to swallows. The barium studies suggested that the bolus of fluid stimulated the jejunal segment to contract like normal small bowel and the distal esophagus then continued its function of propelling the bolus into the stomach. The manometric studies indicated that the jejunal graft contraction began before esophageal contraction and was more prolonged. Since simple distension of the graft also caused repetitive forceful motor activity, it is likely that the process of distension by boluses of liquids and solids is responsible for the observed jejunal graft contractions during swallowing. However, distal esophageal response to simple distension of the graft was not well characterized in these studies.

It is too early, and the series too small to say whether the operation increased survival. The two patients with carcinoma of the esophagus are alive at 17 and 25 months

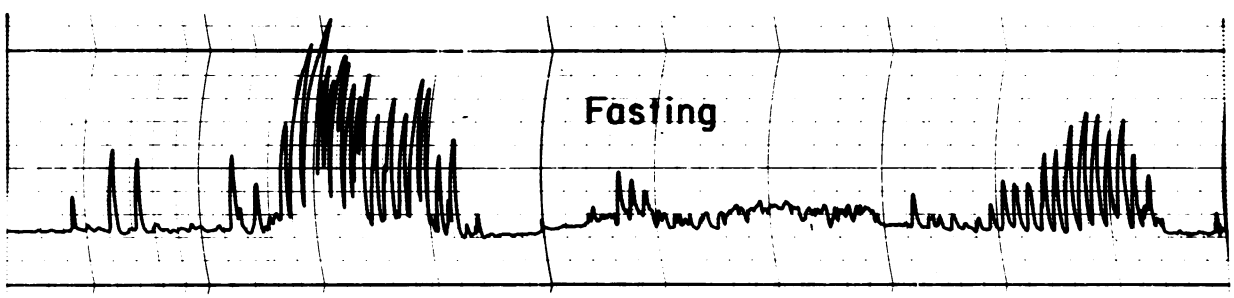

FIG. 6A. Manometric tracing of fasting motor activity over 30 minute period within jejunal graft.

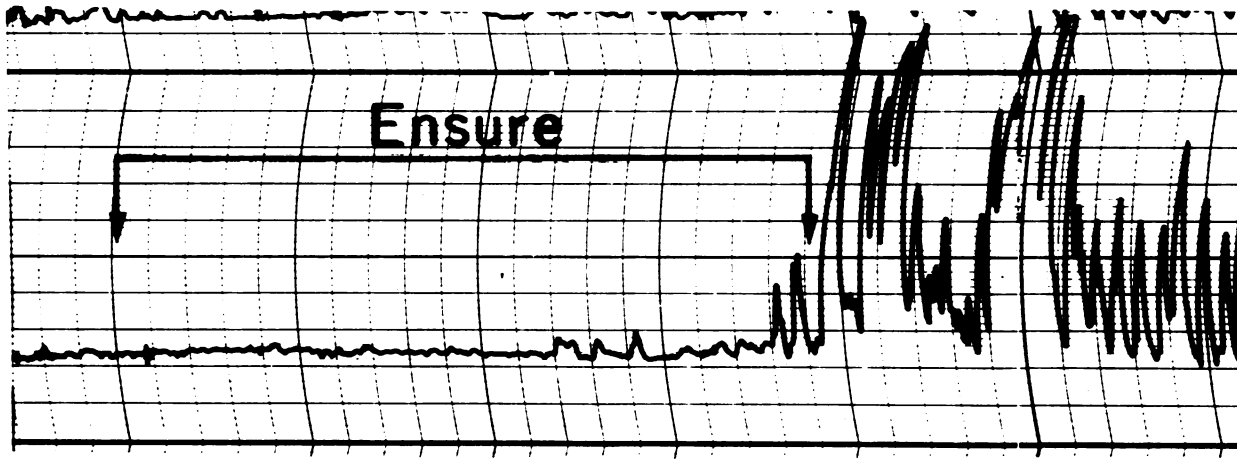

FIG. 6B. Transition from fasting to fed pattern of motor activity within jejunal graft. Note prompt change to continuous activity following administration of Ensure directly into distal antrum and bypassing the graft.

postoperatively. The early results indicate, however, that jejunal autotransplantation provided excellent palliation for this group of patients.

Several observations of the motor activity of these grafts are of scientific interest. The first is the observed fasting motor activity which was similar to that seen in intact human gut[4,7] and in dogs.[21] There were frequent intermittent bursts of motor activity which corresponded to action potential spikes during pacesetter potentials. In addition, every 45 minutes to two hours there was a longer burst of motor activity with action potentials. It will be important to determine whether the latter rhythmic bursts correspond to the "migrating electrical complex" described by Szurszewski.[7] A second observation was that the motor activity of the jejunal graft changed markedly by simple mechanical distension. There are two possible explanations for this phenomenon. Either distension stimulated the intrinsic contractile property of the intestine or there was release of a substance which controls this function. The present studies do not provide evidence for or against either of these explanations.

A third observation was that instillation of food directly into the stomach without coming into contact with the jejunal graft or esophageal mucosa completely abolished the fasting pattern of motor activity for over two hours. Previous dog experiments demonstrated that fasting motor activity is abolished by either dis-

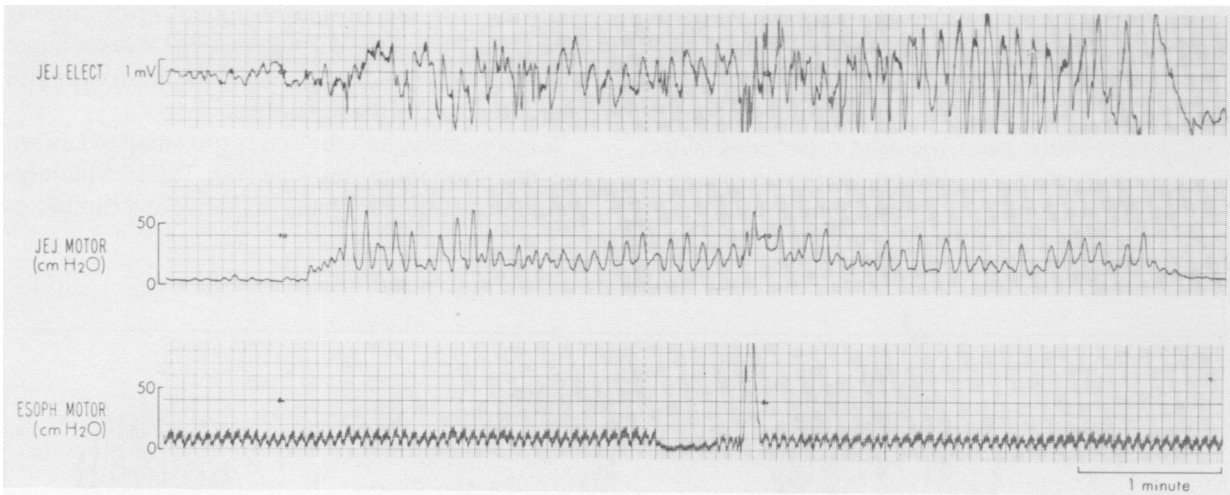

FIG. 7. Simultaneous recording of jejunal graft electrical (JEJ ELECT) and motor (JEJ MOTOR) activity, and esophageal motor activity (ESOPH MOTOR) during fasting burst. Note pacesetter potentials and action potential spikes in jejunal graft during motor activity.

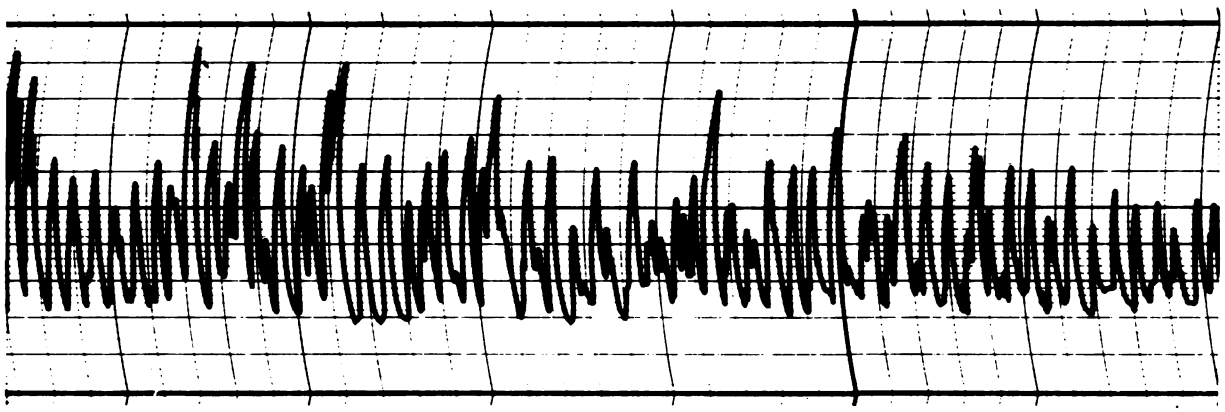

FIG. 6B. (*Continued*)

tension[4] or feeding.[2,10] Feeding produces a marked, continual increase in the activity. The evidence that this transition is regulated by hormones was based on a number of different experiments. Food administered into the intact gut of dogs caused a transition from the fasting to the fed myoelectric pattern in Heidenhain pouches[10] and Thiry loops.[2] Vagotomy did not abolish this phenomenon.[11] Several exogenously administered hormones, including pentagastrin and CCK stimulate the fed pattern of motor activity and others, such as secretin, inhibit it.[7,12] Administration of an extract of a gastrinoma caused stimulation of tone and motility of a canine Thiry loop followed by inhibition.[6]

The present study demonstrates that food instilled in a remote part of the gastrointestinal tract could produce this same transition from a fasting to a fed motor pattern in the jejunal autotransplant in the neck. In light of this observation, the hypothesis that these events are mediated by autonomic nerve fibers along the course of supplying blood vessels (10) is no longer a tenable alternative explanation because all the nerves in this transplanted loop of intestine were completely

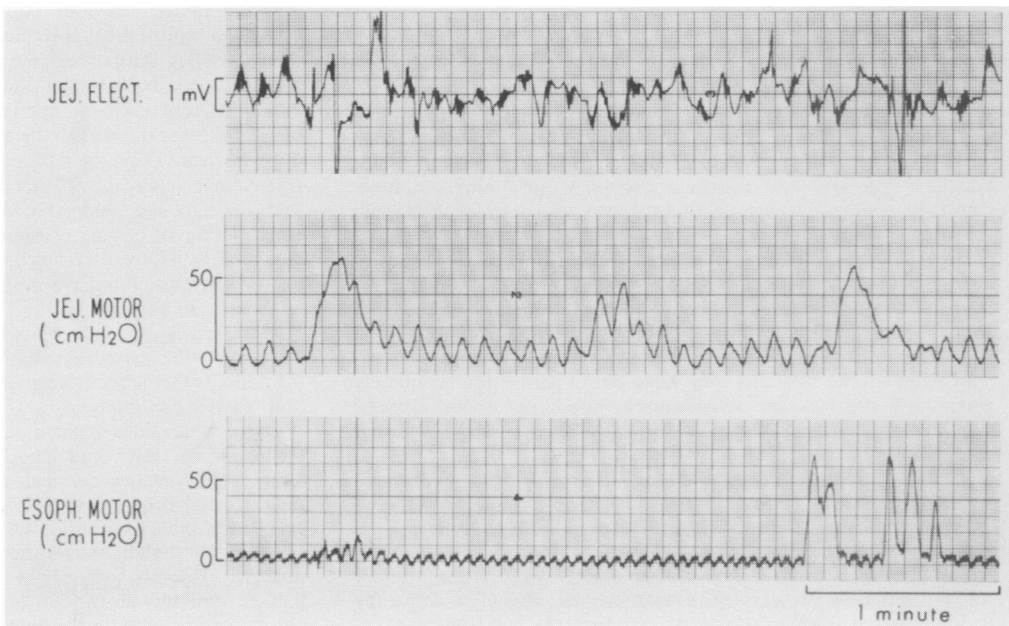

FIG. 8. Simultaneous recording of jejunal graft electrical (JEJ ELECT) and motor (JEJ MOTOR) activity, and esophageal motor activity (ESOPH MOTOR) during fasting and 10 ml balloon distension. Note series of strong jejunal contractions during graft distension.

severed. Therefore, the only plausible explanation for the mechanism of feeding motor activity in the jejunum in the human being is control by hormones.

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Discussion

Dr. William E. Neville (Newark, New Jersey): The technique of free bowel transplant with anastomosis of the accompanying artery and vein has intrigued me since a report by Seidenberg and the late Elliott Hurwitt at the *Surgical Forum* in 1959 of their successes in dogs. Subsequently, in my laboratory during the 1960's countless dogs met their demise as a result of our attempts to duplicate their results. The arterial anastomosis was not a problem, but the venous connections were insurmountable.

Obviously, in the 1960's we did not have fine monofilament sutures or sophisticated microsurgical techniques that were easily adaptable. With the advent of coronary artery operations, all of this has changed, and it is possible that the operation described by the group from Duke may well become the procedure of choice in the future.

In addition, we now not only have the expertise for adequately performing the vascular anastomoses, but have at our disposal stapling instruments, popularized by Mark Ravitch, and his former associate, Felix Steichen.

In regard to stapling techniques, it is interesting that Nakayama in 1964 reported 21 patients in whom autografts of the bowel were used to reconstruct the cervical esophagus, using a stapler for the vascular anastomosis.

Thus, at the present time we have several options for primary reconstruction of the cervical esophagus, thereby eliminating the multiple-staged Wookey procedure. We have the free transplant, as depicted in the previous paper; we have the gastric sleeve originally reported by Gavriliu, which can be done fairly quick with the GIA stapler and the use of an ileocolic segment whi retains its original vascular connection in the abdomen.

The ileocolic segment, can easily be transplanted from the abd men into the neck through the anterior mediastinum. My experien over the years using the right colon and leaving an attached segme of terminal ileum, as described by George Clowes and me nea 25 years ago, has made this technique preferable with me for constructing all or part of the esophagus. The only impediment that mother nature may not be kind enough to give one the blo vessel distribution to perform the procedure with a reasonable se of security in all patients.

My experience with pharyngolaryngoesophagectomy with without a neck dissection, has been limited to six patients. In the patients the ileocolic segment was used successfully to establi oral–gastric continuity.

These three slides depict a patient with a large cervical carcino on whom Dr. Rush and I both operated. The first slide shows large lesion in the cervical esophagus which has invaded t pharynx and the larynx. We removed en bloc the larynx and t cervical esophagus but did not do a concomitant neck dissectio

The second slide shows the terminal ileum anastomosed to t pharynx. There is some slight narrowing in that area, but this m had no difficulty in swallowing. The last slide shows the dila colon retrosternally in the anterior mediastinum.