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Curling's Ulcer:

A Clinical-Pathology Study of 323 Cases

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ACUTE ulceration of the stomach or duodenum, first described in a burn patient by Swan in 1823 [35] and which occurred in ten burn patients of Curling in 1842,[4] is the most frequent life-threatening gastrointestinal complication in burn patients. Numerous etiologies and pathogenetic mechanisms have been proposed to explain this entity,[15] and each has been found lacking as a completely satisfactory single explanation. Ulcerogenic factors active in other clinical situations [19] are known to be present in burn patients, and although overwhelming importance may not be attributed to any one factor, the added stress may tip the physiologic scales toward ulceration of the gastroduodenal mucosa. This clinical review records the experience of the U. S. Army Institute of Surgical Research in the treatment of 323 burn patients with a clinical or autopsy diagnosis of Curling's ulcer. This report relates the importance of burn size and pre-existent sepsis to the development of Curling's ulcer, and advances suggestions regarding indications for surgery and choice of operation based on results recorded in 42 patients with Curling's ulcer who have undergone operation.

Materials and Methods

The hospital records of 323 patients treated at the U. S. Army Institute of Surgical Research from 1954 through 1969 were reviewed. Where possible the clinical characteristics of each patient, the location and number of ulcerations and the morphology of the ulcer were recorded. In the case of the 42 operative patients, the indication for surgery, the quantity of preoperative blood replacement, the operative procedure employed, postoperative complications, and, in those who died, the cause of death were noted.

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TABLE 1. *Mortality and Causes of Death in 98 Burn Patients with Curling's Ulcer Treated in 1967–1969*

Total Patients		98
Deaths Total	68 (69.4%)	
Due to Sepsis	52 (77%)	
Related to Ulcer or Operation	13 (19%)	
Other Cause	3 (4%)	
Mean Postburn Day of Death	23.4	
Survivals		30

The criteria used to make the diagnosis of Curling's ulcer in these burn patients were (1) ulceration of the stomach or duodenum present at operation or autopsy; (2) gastric or duodenal ulcers in the burn patient noted by x-ray; (3) clinical evidence of upper gastrointestinal bleeding after the third postburn day requiring transfusion in excess of that anticipated in the normal course of the burn patient; and (4) massive upper gastrointestinal bleeding at any time postburn, resulting in a hematocrit fall of 10 points or shock, and requiring immediate transfusion. Iatrogenic "tube" erosions were excluded as was hemorrhagic gastritis in which no discrete ulcers were apparent.

Morphologically, a Curling's ulcer is characteristically round, shallow (though extending through the full thickness of the mucosa), sharply demarcated and small, although individual lesions may be extensive, irregular, and penetrate all layers of the gastric or duodenal wall. In general, there is little inflammatory reaction noted histologically, and no fibrosis is evident. Extension of these ulcers through the muscularis mucosa with erosion into a mural vessel is characteristic of those ulcers associated with major bleeding. As noted above, transmural extension may also occur with perforation into the free peritoneal cavity, perforation into the lesser sac or penetration into the head of the pancreas.

In order to determine what, if any, effect pre-existent sepsis had on the occurrence of Curling's ulcer, the records of 394 consecutive burn patients treated at this Institute in 1968 were reviewed. The frequency of occurrence of Curling's ulcer in patients with and without sepsis was determined, with subsequent analysis of occurrence rates of Curling's ulcer within the groups compared by means of standard statistical methods.

The hospital records of the 98 burn patients with Curling's ulcer treated in 1967–1969 were reviewed in particular detail to provide a current assessment of this disease in a group of patients treated entirely with topical chemotherapy and to illustrate the influence of burn size on the frequency of Curling's ulcer.

Results

Of 2,772 burn patients treated at the U. S. Army Institute of Surgical Research during the years 1954 through 1969, 323 patients (11.7%) had autopsy or clinical evidence of Curling's ulcer of the stomach and/or duodenum. This group of Curling's ulcer patients included 253 males and 70 females, and ranged in age from 35 days to 82 years. A mortality of 77 per cent was observed in this entire ulcer population. The mean burn index determined by summation of the entirety of third-degree burn plus one-half of the second-degree burn was 42.3, with a range of 2 to 95. The average burn index for all burn patients during the period considered was less than 30.

The records of the 98 burn patients with Curling's ulcer treated during the years 1967–1969 were examined in particular detail to provide a more current description of the clinical characteristics of the patient with Curling's ulcer. This "recent" group consisted of 93 males and five females who ranged in age from 35 days to 58 years. The average burn size within this group was 52 per cent of the total body surface with an average third-degree component of 23 per cent. The mean time of diagnosis of

TABLE 2. *Means of Diagnosis of Curling's Ulcer in 98 Burn Patients Treated in 1967–1969*

	No. of Patients	% of Patients
Clinical Diagnosis	74	75.5
Clinical only	19	194.
Clinical Confirmed by X-ray	7	7.1
Clinical Confirmed at Surgery or Autopsy	48	49.0
Autopsy Diagnosis Only	24	24.5

Curling's ulcer was the 15th postburn day. Sixty-eight (69.4%) of these 98 patients died.

The mean time of death of the 68 patients in the 1967–1969 group who died was the 24th postburn day. Fifty-two (77%) patients died with sepsis; 13 (19%) died of a cause directly related to their ulcer or operation thereupon, and three (4%) died of other causes. Thirty patients survived (Table 1). The diagnosis of Curling's ulcer was made at autopsy without a preceding clinical diagnosis in 24 (24.5%) of the 98 patients. A clinical diagnosis of Curling's ulcer was made in 74 (75.5%) of this group. The clinical diagnosis was confirmed at operation or autopsy in 48 patients (49%), by x-ray in seven patients (7.1%), and rested on clinical grounds alone in 19 patients (19.4%), as shown in Table 2.

In the 1967–1969 group, 74 of the 98 patients had premortem diagnoses of Curling's ulcer; 63.5 per cent (47) of these patients had pre-existing sepsis at the time of diagnosis of Curling's ulcer. In the 24 patients in whom the diagnosis of Curling's ulcer was first made at autopsy, 91.7 per cent (22) had septic complications diagnosed prior to discovery of Curling's ulcer, reflecting not only that septic complications may obscure a Curling's ulcer but that most burn patients with Curling's ulcer die of septic complication rather than of ulcer. Within this group of 69 patients with Curling's ulcer and pre-existing sepsis, the septic process which was diagnosed earliest in the postburn course was pneumonia in 37, septicemia in 17, suppurative thrombophlebitis in seven, burn wound sepsis in four, and other septic processes in nine. The mean interval between the diagnosis of sepsis and the diagnosis of Curling's ulcer was 5 days in both the autopsy and the clinical diagnosis groups.

The hospital records of 394 consecutive burn patients treated during the year 1968 were reviewed and the occurrence of sepsis, Curling's ulcer and the temporal relationship of the two were recorded. Within this entire group, 77 patients had septic complications, and 14 (18.2%) subsequently developed Curling's ulcer. Three hundred seventeen patients had no septic complication during their hospital course, and only nine (2.8%) developed a Curling's ulcer. The incidence of Curling's ulcer in these two groups was then compared by means of a Chi square analysis, and the higher incidence of Curling's ulcer in the group of patients with sepsis was found to be highly significant ($p < 0.0005$). These patients were then subdivided into those with burns of less than 50 per cent of the total body surface and those with burns of 50 per cent or more of the total body surface. In the patients with 50 per cent or more of the body surface involved in the burn injury, those with sepsis showed a 17.2 per cent incidence of Curling's ulceration, while those without sepsis showed an 8.8 per cent incidence, suggesting a slight additive effect which was, however, not significant statistically. In the group of

TABLE 3. *Influence of Pre-existing Sepsis on Incidence of Curling's Ulcer in 394 Consecutive Burn Patients Treated in 1968*

		n	% With Ulcer	
Burn <50%	Sepsis	48	18.8	$p < 0.0005$
	No Sepsis	283	2.1	
Burn >50%	Sepsis	29	17.2	N.S.
	No Sepsis	34	8.8	

TABLE 4. *Presenting Signs and Symptoms in 98 Cases of Curling's Ulcer Treated in 1967–1968*

		No. of Patients	% of Patients
Gastrointestinal Bleeding		68	69.4
Hematemesis	51		
Melena	17		
Massive Bleeding and/or Shock	30		
Pain		4	4.1
Distention		2	2
No Symptoms		24	24.5

patients with burns of less than 50 per cent, however, those with sepsis had an incidence of Curling's ulcer of 18.8 per cent, while those without sepsis had an incidence of Curling's ulceration of only 2.1 per cent, with this difference in incidence being highly significant statistically ($p < 0.0005$), as shown in Table 3.

The presenting sign or symptom could be determined in 291 of the total occurrences. Sixty-six patients (22.7%) had no symptoms or signs referable to their ulcer, and it was these patients in whom the diagnosis was first made at autopsy. Pain was the presenting symptom in 11 (3.8%), and this was frequently an accompaniment of perforation, or, as in the case of two patients, immediately preceded an exsanguinating hemorrhage. Distention was believed to be the initial sign in 28, or 9.6 per cent, of these patients. In 186, the first sign was upper gastrointestinal hemorrhage, hematemesis in 135, and melena in 51. In 85 of these latter patients (45.7%), the hemorrhage was classified as massive, i.e., an hematocrit drop of 10 points or more, and/or clinical shock. In the more recent (1967–1969) group of patients with Curling's ulcer, the distribution of presenting signs and symptoms was similar, with 69 per cent of the patients having upper gastrointestinal bleeding as the first sign, and 25 per cent having no symptoms, with the diagnosis first made at autopsy (Table 4).

Of the 227 ulcer patients in the 1954–1969 group in whom the lesion was anatomically localized, 47.1 per cent (107 patients) had gastric ulcers, of which 83 per cent were multiple and the remainder had single gastric ulcers. Eighty-five patients (37.1%) had ulcers situated in the duodenum, 72 per cent had a single duodenal ulcer and the remainder had multiple duodenal ulcers. In 35 patients (15.4%), both gastric and duodenal ulcers were identified, some with a single ulcer in each location, others with multiple ulcers in one or both sites.

Of the most recent 98 patients (1967–1969), 18 recovered without operation in whom the site of the ulcer remained unknown. Of the 80 patients in whom the ulcer could be localized, duodenal ulcers have been slightly more frequent, occurring in 42.5 per cent as opposed to 40 per cent for gastric ulcers and 17.5 per cent for coexistent gastric and duodenal ulcers (Table 5). In the burn patients with gastric ulcers, we were unable to confirm the preponderance of fundal lesions noted by others in patients with stress ulcers.[17] Of particular interest was the frequency of perforation noted in this group in which six gastric ulcers, five duodenal ulcers and one gastric ulcer in a patient in whom both gastric and duodenal ulcers had perforated, an occurrence rate of 12.2 per cent. Although Curling's ulcers occurring in burned children have been reported to be largely duodenal in location,[1, 3] the ulcers encountered in the 10 children of 12 or less years in 1967–1969 were in the duodenum in five, in the stomach in four, and in both stomach and duodenum in one, the same distribution as observed in the adult.

Review of the histology of the ulcer bed in the 65 patients treated in 1967–1969 on whom specimens were available showed microorganisms to be present in the ulcer base in 34 (52.3%). Bacteria were identified in the ulcer bed in seven, yeast in 12,

TABLE 5. *Site of Curling's Ulcer in 98 Burn Patients Treated in 1967–1969*

Location	Single	Multiple	Total	%	Perforation
Gastric	7	25	32	40.0	6
Duodenal	24	10	34	42.5	5
Gastric and Duodenal		14	14	17.5	1
Unknown			18	—	—

bacteria and yeast in 12, bacteria and virus in two, and yeast and virus in one.

During the years 1954 to 1969, 42 burn patients required operation for treatment of Curling's ulcer. The indications for operation in these 42 patients were massive hemorrhage in 32, perforation in six, and prolonged hemorrhage in four. The operations performed and the number of patients in whom each was performed were: subtotal gastrectomy 20, vagotomy and antrectomy 14, plication of ulcer and gastrostomy 3, vagotomy and pyloroplasty 4, vagotomy and gastrojejunostomy 1. A gastrostomy was performed in association with the above procedures as deemed necessary by the individual surgeon. Of the 42 operated patients, 27 died. Twenty (47.6%) of the operated patients died either in the early postoperative period or later from a cause which could be related to operation. Seven patients (16.7%) recovered from operation and resumed alimentation only to succumb to other complications of burn injury. Fifteen patients survived operation and other complications of burn and left the hospital, comprising 35.7 per cent of the total operative group.

Preoperative conditions and complications such as pneumonia, other foci of sepis, and burns of the abdominal wall contributed to a high occurrence of postoperative complications. The most frequent postoperative complications related to these pre-existing conditions were, in order of prevalence, pneumonia, abdominal wound infections, wound dehiscence, and suppurative thrombophlebitis.

The primary cause of death in the 27 patients who died in the early postoperative period was pneumonia in six, burn wound sepis in five, anastomotic or "stump" leak in four, peritonitis in three, suppurative thrombophlebitis in two, cardiac disease in two, massive bleeding in two, intraperitoneal hemorrhage in one, renal failure in one, and hepatic necrosis in one.

Discussion

Curling's ulcer has been estimated to occur in up to 25 per cent of all burn patients on the basis of observed autopsy and clinical incidence with addition of an estimated incidence of unrecognized asymptomatic disease in burn patients who survive.[21] The incidence of 11.7 per cent in the 2,772 burn cases reviewed in this study is more in accord with the experience of others and represents the minimum occurrence of the disease in our burn population.

Hemorrhagic gastritis, which frequently occurs in the early postburn period and is often manifested by coffee-ground emesis or nasogastric drainage,[16] though excluded by the criteria employed, deserves mention. This hemorrhagic gastritis, often associated with ileus, may be particularly prominent at post-mortem examination of patients with extensive burns who died early postburn. The suggestion that such morphological change represents postischemic congestion and edema following closure of arteriovenous shunts initially opened in response to neural stimuli during the early postburn period of hypovolemia and diminished blood flow is appealing. The presence of such shunts in the gastric wall and associated mucosal changes as observed in an autopsy specimen from a patient dying early postburn are docu-

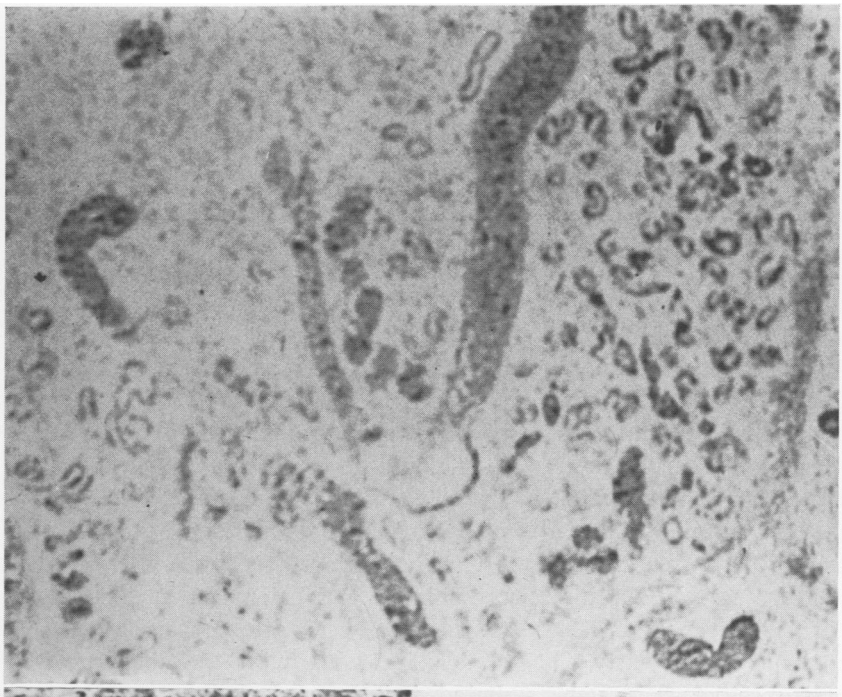

FIG. 1. Arteriovenous shunt in gastric wall of burn patient. The mercury-barium injection mixture fills both the thin arteriolar limb on the left and the wider venous limb on the right which connect through a bulbous dilation. Note the adjacent engorged vessels. Early vascular changes appear to cause focal mucosal injury.

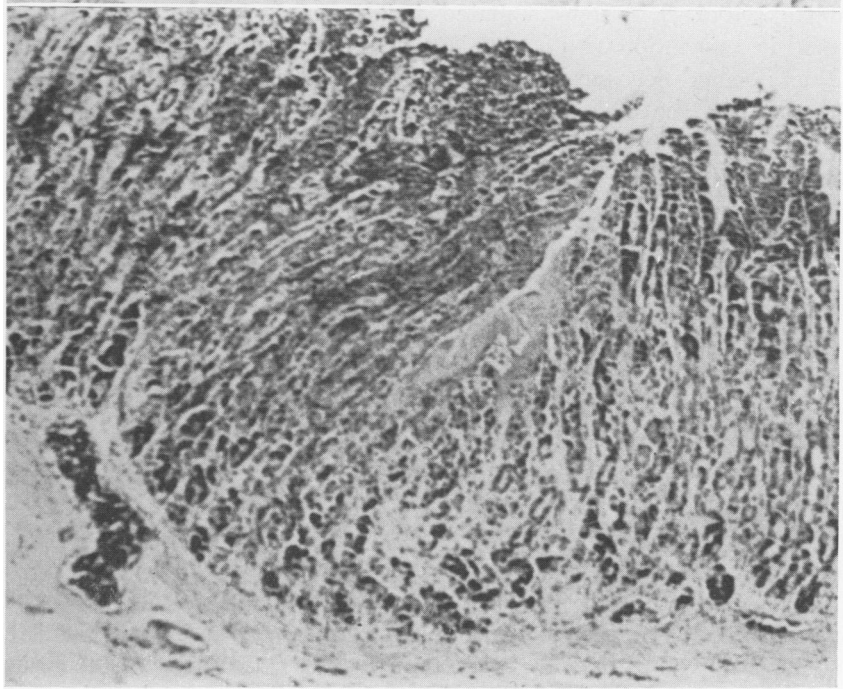

FIG. 2. Photomicrograph of margin of focal area of gastric mucosal injury. Note congested, engorged submucosal capillary on left, paucity of inflammatory reaction and sharp demarcation of necrotic mucosa showing cellular degeneration to left, and viable, apparently uninjured mucosa on the right.

mented in Figures 1 and 2. They lend support to our belief that this hemorrhagic gastritis, if not direct precursor lesion of Curling's ulcer, at least damages the mucosa and renders it more susceptible to ulceration as suggested by Goldman and Ros-

loff.[13] Bleeding from this entity is commonly trivial and ceases with resumption of gastrointestinal function. Any evidence of gastrointestinal bleeding later in the postburn period should suggest the dianosis of Curling's ulcer.

The predominance of males in the group of patients with Curling's ulcer in this study is in accord with the predominance of males in the burn population seen at this Institute and does not suggest any sex predeliction for the disease. Curling's ulcer is a complication most commonly encountered in patients with larger burns. Such is confirmed by the larger burn index of the patients with Curling's ulcer over the entire 16-year period and is particularly well illustrated in those with Curling's ulcer encountered over the past 3 years who had average burns of 52 per cent of the total body surface with a 23 per cent full-thickness injury. The relation of burn size to occurrence of Curling's ulcer is illustrated in Figure 3 in which the incidence of Curling's ulcer is shown to increase with increasing burn size. It is of particular interest to note that the incidence appears to follow a sigmoid curve which resembles a drug dose-response curve. The peak incidence of approximately 40 per cent in this group of patients suggests that there is a segment of the entire burn population which is susceptible to Curling's ulcer, while a larger group of the burn population is resistant. The absence of Curling's ulcer in patients with burns of more than 90 per cent of the body surface probably reflects the early demise of these patients, before Curling's ulcer develops.

The mortality of 77 per cent noted in this entire group of patients with Curling's ulcer is in accord with our previous communications and reflects not only the seriousness of Curling's ulcer but the prevalence of coexistent complications in these patients with extensive burns. Within the group of 98 patients treated in the years

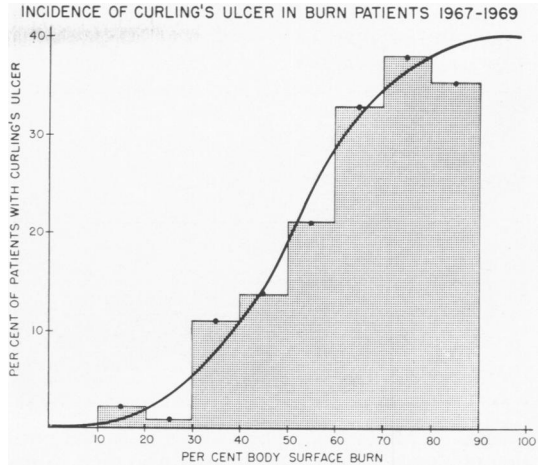

FIG. 3. Incidence of Curling's ulcer as related to burn size, 1967–1969. Note increasing incidence of Curling's ulcer with increasing burn size up to approximately 40% in patients with burns of 70% and more of body surface.

1967–1969, 77 per cent of the deaths were due to a septic complication while only 23 per cent were due to ulcer, operation for ulcer, or some other cause.

The influence of sepsis on the incidence of Curling's ulcer has been previously denied on the basis of the relation of Curling's ulcer to septicemia. Clinically, however, it is difficult to disregard the frequent occurrence of Curling's ulcer in those burn patients with other septic complications. In the 1967–1969 group, 64 per cent of those patients with premortem diagnosis of Curling's ulcer had some sort of infection preceding diagnosis of ulcer by a mean interval of 4.4 days. In the burn patients in this recent group in whom the diagnosis of Curling's ulcer was first made at autopsy, 91.7 per cent had clinical and morphologic evidence of pre-existing sepsis. The most common type of sepsis present in these patients was pneumonia, followed by septicemia, suppurative thrombophlebitis, burn wound sepsis, and other septic foci.

The additive effect of sepsis in predisposing burn patients to Curling's ulcer can be best appreciated by consideration of the review of 394 consecutive burn patients treated in 1968 at this Institute. In the pa-

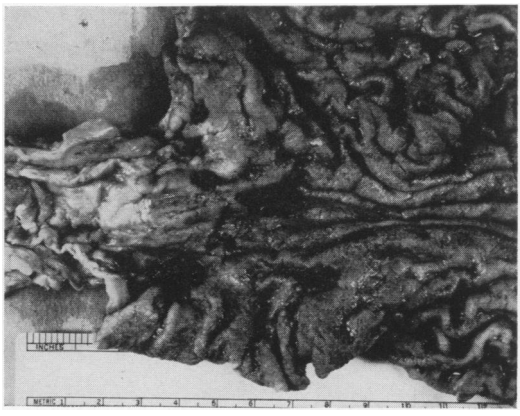

FIG. 4. Multiple Curling's ulcers in fundal portion of stomach from burn patient who died. Note the sharply defined margins, absence of edema at the periphery, and the variation in size and outline of these ulcers.

tients with 50 per cent or more of the body surface burned, the occurrence of Curling's ulcer in patients with sepsis was approximately twice that of the patients without sepsis, suggesting an additive effect which was on closer analysis not significant statistically. In those burns of less than 50 per cent of the total body surface, however, a striking effect of sepsis was observed with an incidence of ulcer of 18.8 per cent in the smaller burns with sepsis, as opposed to 2.1 per cent in the smaller burns without sepsis, a highly significant difference statistically. This difference in significance

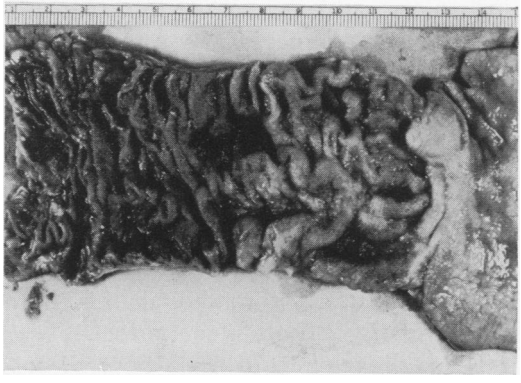

FIG. 5. Multiple Curling's ulcers in duodenum of same patient whose gastric ulcers are shown in Figure 4. Gastric and duodenal ulcers coexist in 15% of Curling's ulcer patients, an important consideration at time of operation.

of sepsis related to burn size is regarded as strong confirmation of the additive effect or stress of sepsis, tipping the physiologic scale in the direction of gastrointestinal ulceration in the small burns but having a much reduced and statistically insignificant effect in patients with larger burns who do not require additional stresses to develop gastrointestinal ulceration.

In an earlier report,[24] we recorded that 60 per cent of burn patients with Curling's ulcer were symptomatic within the first 8 postburn days. In the past 3 years, the mean postburn day of diagnosis of Curling's ulcer was the 15th, reflecting the control of the bacterial population in the burn wound by Sulfamylon topical therapy[29] and the resulting decrease of burn wound sepsis as well as the influence of relatively late occurring septic complications. The average time of onset of airborne or bronchopneumonia, the most frequent pre-existing septic complication in these ulcer patients, is the 10th postburn day or 5 days before the average postburn day of ulcer diagnosis.[26]

The anatomical site of Curling's ulcer in the entire group reveals a slight predominance of gastric ulcers which are most commonly multiple, as noted by others.[30] Duodenal ulcers, on the other hand, are most commonly single. It is important that one bear in mind that in one out of seven patients with Curling's ulcer, both gastric and duodenal lesions will be present (Figs. 4 and 5). In those patients treated in the past 3 years, there has been a slight predominance of duodenal ulcers, 71 per cent of which were single. An increase in the occurrence of perforation has been noted in the past three years, with perforation present at the time of diagnosis in 12 patients (12.2%).

The frequently occult nature of this disease can be appreciated by the fact that in 25 per cent of the 98 patients encountered in the years 1967–1969, the diagnosis was

made only at autopsy, with no antemortem symptoms or signs referable to the lesion. In 56 per cent of the patients within this group, a clinical diagnosis of Curling's ulcer was made and confirmed either at operation or autopsy or by x-ray. Nineteen per cent of the patients had only clinical diagnoses without confirmation; in these patients, the basis of diagnosis was gastrointestinal bleeding after the third postburn day requiring blood transfusion in amounts above that anticipated for a burn patient.

The most frequent initial symptom or sign in patients with Curling's ulcer was gastrointestinal hemorrhage, which occurred in 64 per cent of the study group. Within the patients with gastrointestinal hemorrhage as the first sign, hematemesis was almost three times more common than melena. In 46 per cent of these patients with initial gastrointestinal hemorrhage, the hemorrhage was so extensive as to result in shock or an hematocrit drop of 10 or more points and required prompt transfusion and often immediate operation. Pain was present in only 11 or 4 per cent of patients with signs or symptoms. In general, this was associated with perforation, although two patients complained of severe abdominal pain immediately prior to massive hematemesis and exsanguination.

Ten per cent of patients in whom a clinical diagnosis was made manifested distention as the first sign of Curling's ulcer. It should be noted that approximately half of all the patients with Curling's ulcer had ileus or distention at or shortly prior to the time of gastrointestinal bleeding. The frequent association of this entity with sepsis and other complications in the patient with large burns renders it difficult to relate it directly to Curling's ulcer. Nevertheless, otherwise unexplained ileus should suggest the possibility of an acute ulceration of the upper gastrointestinal tract in a burn patient, as should acute upper abdominal pain or other signs of a perforated viscus.

An infected burn of or near the abdomen, the frequent coexistence of pneumonia and other complications generate a reluctance to intervene surgically in burn patients with Curling's ulcer and a tendency to manage such patients in a nonoperative manner. Although we are in accord with an initial attempt at nonoperative management, it has been our experience with a variety of nonoperative regimens that one-third of the patients with massive hemorrhage treated in such manner will rebleed even if the initial hemorrhage relents.[24] The authors therefore advocate initial nonoperative therapy consisting of decompression and evacuation of the stomach, gastric lavage with iced saline, blood transfusion as necessary, and general supportive measures. As others have pointed out,[6, 7, 32] however, one must not permit the burn wounds or other complications of the burn patient to lead to inappropriate delay in surgical intervention.

O'Neill *et al.*[23] noted in 1968 that burn patients with Curling's ulcer who ultimately required operation had received an average of 5,500 cc. of blood prior to operation. In the 32 patients reported herein who underwent operation for massive hemorrhage, 4,839 cc. of blood had been administered prior to operation. It is the opinion of the authors that inordinate delay and prolonged transfusion therapy is often unrewarding and may adversely influence the outcome in these patients. In the 12 burn patients operated upon for massive hemorrhage from Curling's ulcer in the past 3 years, the average amount of blood given preoperatively has been 3,767 cc., indicating our greater willingness to operate upon these patients.

At the present time, our indications for surgery in patients with Curling's ulcer are uncontrollable hemorrhage and perforation. Uncontrollable hemorrhage is defined as (1) massive bleeding unresponsive to blood replacement, (2) failure of blood replacement to restore the hematocrit during several hours of therapy, (3) need for more

TABLE 6. *Indications for Operation in 42 Patients with Curling's Ulcer Requiring Surgery, 1954–1969*

Indication	No. of Patients
Massive Hemorrhage*	32
Perforation	6
Prolonged Hemorrhage	4
Total	42

* Average amount of blood given preoperatively: 4,839 CC.

than 2,500 cc. of blood over a 12-hour period, or (4) bleeding of lesser magnitude for over 48 hours. A surprisingly large blood volume deficit may exist at the time of initial observation of bleeding in these debilitated, sometimes obtunded, critically ill patients in whom occult hemorrhage may have been present for some time. Prompt resuscitation is mandatory in this setting of pre-existing hypovolemia, and continued significant hemorrhage requires early operative intervention. The indication for operation in all 42 operative patients is shown in Table 6.

A consideration of the ulcerogenic factors felt to be present in burn patients is helpful in guiding the selection of the best operation for the individual patient. These factors range from the hemoconcentration and diminished organ blood flow of the initial postburn period to the pulmonary complications associated with an elevated P_{CO_2} which occur later in the postburn period.

Although laboratory studies have implicated acid production as a prime factor in Curling's ulcer development,[11] a study of overnight gastric acid secretion in 34 burn patients carried out by O'Neill *et al.* in 1967 [24] and expanded in 1970 [22] revealed no absolute hyperacidity in burn patients who subsequently developed Curling's ulcerations. The presence of microorganisms (reported by Sevitt in 1966 [31]) in the ulcer bed of 52.3 per cent of 65 cases reported here in whom the ulcer was examined microscopically also militates against hyperacidity as a causative factor in these patients. Calculation of the mean overnight gastric acid secretion in the patients studied by O'Neill *et al.*[24] reveals that in the group who subsequently developed Curling's ulcer, the mean acid secretion was normal, as opposed to the subnormal mean acid secretion in those who did not develop Curling's ulcer. While this difference is not significant statistically, it does suggest that a relative hyperacidity may have existed with more acid being secreted and bathing a susceptible mucosa in those who subsequently developed Curling's ulcer.

The hypovolemia, increased peripheral resistance, and diminished cardiac output characteristic of the immediate postburn period [28] may result in diminished organ blood flow. These influences as modified by autonomic control of the aforementioned vascular shunts in the gastric wall appear to account for the initial mucosal ischemia and rebound hyperemia previously noted. Such local "injury" could well set the stage for ulceration of an impaired damaged mucosa as suggested by Friesen.[12] Another factor which may be operative in the immediate postburn period is hemoconcentration, the adverse rheological effects of which may further decrease gastric blood flow in the immediate postburn period.

Recently, Curreri *et al.*[5] have identified striking elevations of platelets, fibrinogen, Factor V and Factor VIII in the immediate postburn period, and a few cases of intravascular coagulation have been described by those authors. Local factors in areas of damaged tissue as noted in the hyperemic stomach may well promote focal intravascular coagulation, the importance of which in ulcerogenesis remains speculative at this time.

Elevated blood levels of the catecholamines noted by others [2] to be present in the immediate postburn period also serve to augment initial gastric ischemia by intensification of vasospasm. These secretions

of the adrenal medulla have no known direct effect on the gastric or duodenal mucosa. The steroid hormones, conversely, influence the stomach directly by altering mucus and perhaps by virtue of their antiphlogistic action. Elevated adrenal cortical hormone secretion has been shown to occur in the early postburn period.[2, 10] These adrenal secretions have been shown by Menguy and co-workers to alter gastric mucus both quantitatively and qualitatively.[18, 20] The adverse effects of "vago-adrenal" stimulation on gastric mucus have also been shown in an ulcerogenic laboratory preparation by Spicer and Sun.[33] A decrease in gastric mucus production in burned dogs has been documented by O'Neill *et al.*[25] and this decreased production of mucus could result in normal or even low gastric acid production, sufficient to produce mucosal damage.

The influence of sepsis on the development of Curling's ulcer has been noted, and while it cannot be regarded as the single etiologic agent, it does appear to be an additive stress, particularly important in those patients with smaller burns. Other authors have also attributed to sepsis a significant effect on the incidence of stress ulcers.[9] Of special interest is the observation by Douglass and LeVeen[8] that the incidence of "stress" ulcers increases with sepsis and that the peak incidence of ulceration occurred on the fourth post-stress day. The infection to Curling's ulcer interval in our burn patients averaged 4.5 days.

Another recently reported ulcerogenic factor deserving consideration in these patients is the regurgitation of intestinal chyme into the proximal duodenum and the stomach. Guilbert *et al.*[14] have shown in a hemorrhagic shock preparation that such chyme decreases gastric mucus and is associated with acute gastric ulcerations. The frequent occurrence of ileus in both the immediate postburn period and later in burn patients with septic complications suggests that such regurgitation may play a role in Curling's ulcer development.

The multiplicity of factors exerting some influence on integrity of the gastroduodenal mucosa indicates to us that no one mechanism is responsible for ulceration in all patients. Rather, the balance between protective and ulcerogenic influences may be disturbed in a variety of ways through a variety of mechanisms which differ greatly between patients. It does seem important in surgical treatment to diminish acid production as much as possible, to prevent gastric stasis, to remove the locally diseased tissue (the ulcer) and of course to treat and hopefully eliminate any pre- or coexisting sepsis.

The precarious status of these patients and the frequency of coexisting sepsis certainly militate toward as limited an operative procedure as is consistent with adequate treatment. In general, our results with non-resectional surgery have been discouraging. Eight patients have had non-resectional operative procedures (vagotomy and pyloroplasty, four; plication of an ulcer, three; and vagotomy and gastrojejunostomy, one). There were two cases of massive rebleeding, one suture line disruption, and two survivors. Vagotomy and pyloroplasty has not seemed to be effective in patients with significant hemorrhage. The one survivor in the vagotomy and pyloroplasty group had a perforated fundal ulcer without evidence of significant hemorrhage, and the patient who survived following vagotomy and gastrojejunostomy had a superior mesenteric artery syndrome with vascular obstruction of the third portion of the duodenum. Our unsatisfactory experience with lesser operative procedures has led us to reserve suture closure for patients with perforation who are in a particularly critical condition. Lesser sac abscess formation which may result from a posterior perforation will obviously require drainage, and resection in the presence of

TABLE 7. *Type of Operation Employed and Mortality in 42 Patients with Curling's Ulcer Undergoing Surgery, 1954–1969*

Operation	Total Number	Survivors	Deaths
Subtotal Gastrectomy	20	8	12
Vagotomy and Antrectomy	14	5	0
Vagotomy and Pyloroplasty	4	1	3
Plication of Ulcer	3	—	3
Vagotomy and Gastro-jejunostomy	1	1	—
Totals	42	15	27

such established infection is contraindicated.

Our initial resection of choice was a 60 to 80 per cent subtotal gastrectomy, and of 20 patients who underwent that procedure, there have been eight survivors. Once the Curling's ulcer patient recovers from burn, there is no greater incidence of chronic ulcer disease than in the general population, and we consequently prefer at the present time the more limited resection of antrectomy to preserve as much stomach as is consistent with adequate control of the acute problem. Vagotomy is important to decrease any acid secretion present, for its beneficial effect on any gastritic component of the disease, and to combat the effect of elevated serum carbon dioxide levels which may occur with postoperative pulmonary complications noted in approximately half of the operated patients. Despite this preference for vagotomy and antrectomy, we will not hesitate to perform a subtotal gastrectomy if necessary to remove the offending ulcer. The operations employed in all 42 of our surgically treated patients with Curling's ulcer are shown in Table 7.

In general, the duodenum can be closed primarily at the time of resection, reflecting the acute nature and absence of severe inflammation and fibrosis in these acute lesions. If any question exists about the adequacy of duodenal closure, however, a tube duodenostomy should be employed since rupture of the duodenal stump has been associated with universal mortality in our operative patients. The malnutrition and impaired alimentation in these patients require careful construction of all suture lines, since an anastomotic leak and resulting peritonitis would be poorly tolerated in these seriously ill patients. Rebleeding noted in only four of the 34 patients undergoing resection occurred either in those in whom a duodenal ulcer had not been excised or in those with suture line disruption and/or peritonitis.

The multiplicity of ulcers in these patients requires that a generous gastrotomy be made with a thorough inspection of the stomach and duodenum. If at all possible, the ulcer should be resected to remove the lesion which is a possible source of recurrent bleeding due to the continued influence of existing ulcerogenic factors. In the non-resected operative patients in whom control of hemorrhage was attempted by suture technic, the ulcers were noted to have enlarged at autopsy. Fundal lesions may be excised by wedge resection, and vagatomy and antrectomy carried out. In those patients with an ulcer in close proximity to the ampulla of Vater, the compromise of careful oversewing of the ulcer may have to be accepted. The simultaneous presence of both gastric and duodenal ulcers in 15 per cent of patients with Curling's ulcer necessitates that even if a source of bleeding is identified in one of

TABLE 8. *Operative Results in 42 Burn Patients with Curling's Ulcer Requiring Surgery, 1954–1969*

Operated Patients		42
Death Related to Operation	20 (47.6%)	
Late Deaths—Recovered from Surgery	7 (16.7%)	
Survivors	15 (35.7%)	

these locations, a careful search for associated ulcers in the other should be made.

The high incidence of postoperative abdominal wound infection in these hypermetabolic patients with impaired alimentation and hypoproteinemia and infected burns necessitates the use of retention sutures. Primary skin closure is avoided, and the wound can be initially covered with cutaneous homograft and closed secondarily.[34] Operative mortality in five patients could be directly related to a technical error, i.e., postoperative intraperitoneal hemorrhage in one, and an anastomotic or "stump" leak in four. There were, however, four other patients in whom an anastomotic leak was a significant contributing factor to their death. The causes of death in the remaining patients were frequently related to complications of burn injury which existed preoperatively. In similar fashion, postoperative complications were common and frequently related to preoperative complications.

Fifteen (35.7%) of the 42 operated patients survived and were discharged from the hospital (Table 8). Seven of the patients who died following operation had resumed alimentation, and their death was attributed to other complications of burn injury. These two groups when combined indicate that there was a potential salvage rate of slightly over 50 per cent in the operated patients compared to the overall survival of only 23 per cent in this entire group of 323 Curling's ulcer patients.

Summary

1. Over a 16-year period, 1954 through 1969, Curling's ulcer occurred in 323 (11.7%) of 2,772 burn patients treated at a burns unit.

2. The incidence of Curling's ulcer increases with increasing burn size to a maximum of approximately 40 per cent in burns of 70 per cent or more of the total body surface.

3. Pre-existing sepsis has been shown to be an additive stress predisposing the burn patient to development of Curling's ulcer. This effect is highly significant in patients with burns of less than 50 per cent of the total body surface.

4. Approximately one-fourth of patients with Curling's ulcer will have no symptoms or signs of Curling's ulcer during life, with diagnosis first made at autopsy.

5. Two-thirds of the patients with Curling's ulcer had gastrointestinal bleeding as the presenting clinical sign, and in 45 per cent such bleeding was massive.

6. Gastric ulcers were slightly more frequent in occurrence in the entire group of 323 patients but in the 98 patients treated in the past three years a slight predominance of duodenal ulcers was noted.

7. Of importance at the time of operation is the fact that gastric and duodenal ulcers coexist in 15 per cent of these patients.

8. Forty-two patients with Curling's ulcer required operation, 32 because of massive hemorrhage.

9. Vagotomy and antrectomy is the authors' operation of choice, but equally good results have been obtained with subtotal gastrectomy. The surgical procedure must be tailored to meet the individual patient's needs, and a variety of procedures has been employed.

10. The occurrence of operative mortality and postoperative complications are high and relate closely to the preoperative complications which existed in these seriously ill patients.

11. Fifteen (36%) of 42 operated patients survived both the ulcer operation and burn injury and were discharged from the hospital.

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