

# Exfoliative Cytology and Early Carcinoma of the Stomach\*

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## Introduction

GASTRIC CARCINOMA is still largely an incurable lesion in the far-advanced stage in which it is usually encountered. Since survival is increased by early extirpation,<sup>14</sup> hope of bettering the survival rate centers on the earlier recognition of gastric cancers. Mass x-ray studies, however, have detected only a disappointingly small number of asymptomatic gastric tumors.<sup>6</sup> Gastric cytologic examination, which is highly reliable,<sup>2, 7, 11, 12</sup> should be a useful method for detecting cancer before gross radiologic evidences of tumor are manifest. As it is used more widely in the investigation of relatively minor gastro-intestinal complaints, in the follow up of patients with achlorhydria, and in the evaluation of relatives of patients with gastric cancer, more early carcinomas of the stomach will be recognized.

The purpose of this paper is to report an unusual case of gastric malignancy in which gastric cytologic examination played an important diagnostic role; a case which may have some bearing on the pathogenesis of gastric carcinoma.

## Case Report

C. B., a 69-year-old man, entered the Grace-New Haven Community Hospital in October of 1957 because of a gastric ulcer. He had noted an

inability to eat large meals and experienced sensations of bloating and gaseous eructation. X-rays of his stomach performed five weeks prior to admission had revealed a prepyloric gastric ulcer; repeat study three weeks later failed to demonstrate any evidence of healing. A gastric analysis showed achlorhydria by Topfer's reagent. Gastric cytology demonstrated numerous cancer cells. Gastroscopy was technically unsuccessful and Wood's tube biopsy of the stomach failed to reveal any evidence of carcinoma. At operation on October 25, 1957, an adenocarcinoma of the greater curvature of the stomach was demonstrated. Seventy-five per cent subtotal gastrectomy and omentectomy were performed with a retrocolic gastro-enterostomy. Histologic examination of the specimen revealed its margins to be free of tumor. There was no evidence of lymph node involvement by carcinoma.

Following operation, the patient gained weight and did very well. Repeat gastric cytologic examination in October, 1959 was read originally as negative, but as the slides were reviewed in 1962, it was believed that there were, in fact, malignant cells present. In another gastric washing obtained in October, 1960, malignant cells were readily identified. Because of this, the patient was readmitted to the hospital, although still asymptomatic. Physical examination was within normal limits. Hemogram, urinalysis, and liver function tests were all within normal limits. The gastric aspirate following histamine showed no free acid. Gastroscopic examination was indeterminate. X-ray studies revealed a functioning gastro-enterostomy without gross evidence of recurrence. A roentgenographic series was negative for bony or pulmonary metastasis.

Because of the positive gastric cytology and the absence of evident widespread disease, re-exploration was carried out on November 16, 1960. At operation, inspection and palpation of the stomach remnant and other intra-abdominal organs revealed no abnormality. At gastrotomy, no mucosal lesions were evident. Resection of the major portion of the gastric remnant was nevertheless carried out, leaving approximately ten per-

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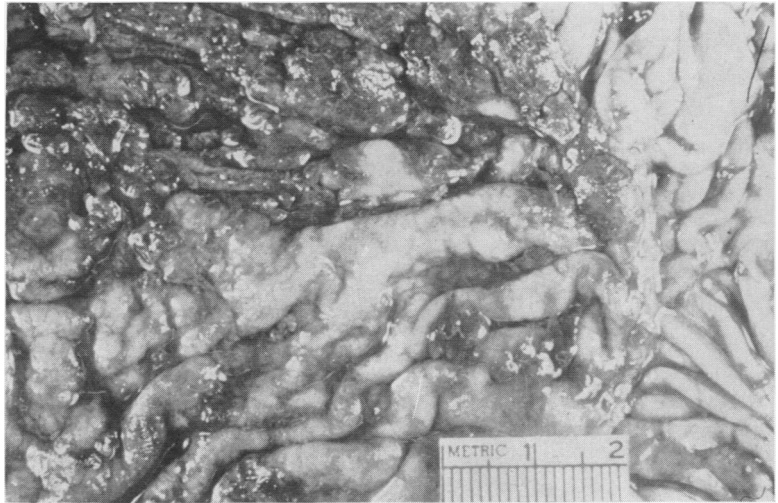
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FIG. 1. Gross surgical specimen from second gastric resection shows no evidence of malignant mucosal change.



cent of the original stomach. Splenectomy was performed in order to facilitate the high resection. Postoperatively, a left subdiaphragmatic abscess developed, and extraperitoneal drainage was required; the patient recovered without incident. Histologic examination of the resected stomach and gastro-enterostomy revealed changes limited to the mucosa adjacent to the gastro-enterostomy that were interpreted as carcinoma *in situ*. Dr. Arthur Purdy Stout reviewed the slides and concurred in the diagnosis.<sup>15</sup>

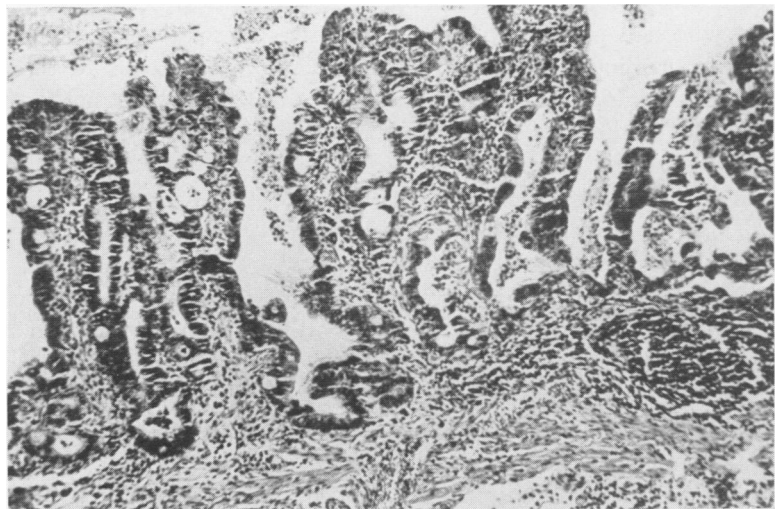
In April 1961, repeat gastric cytology showed no malignant cells. The patient continued to be asymptomatic and was again gaining weight when malignant cells were again found in a gastric washing done in December 1961. Although this constituted grounds for removal of the remaining stomach, the patient refused further surgery.

### Discussion

Perhaps the most difficult gastric carcinomas to recognize are the surface tumors. In carcinoma *in situ*, the earliest variety, the microscopic findings of cellular atypism and loss of polarity are restricted to the mucosa,<sup>10</sup> while in Golden and Stout's "superficial spreading carcinomas," there is actual invasion of the structures underlying the mucosa. These two types of early cancers must be carefully distinguished.

Since superficial carcinomas do not usually manifest radiologic findings until they are widespread, and since they are not palpable at laparotomy and may not even

FIG. 2. Low power photomicrograph from the same specimen demonstrates very little architectural abnormality.



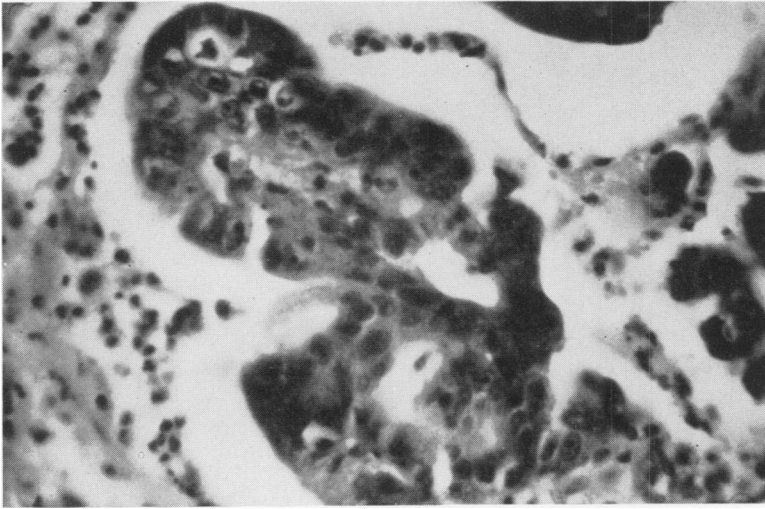


FIG. 3. High power view of the gastric mucosa demonstrates hyperchromatic large nuclei with prominent nucleoli. There is loss of cellular polarity.

be visible in the unfixed surgical specimen, as demonstrated in this case, cytologic examination remains the only available means of arriving at an early diagnosis.

In a recent study of 258 cancers of the stomach by Schade, 16 (6.2%) were found to be surface carcinomas and were discovered by gastric cytology after radiologic examination had failed to demonstrate the lesion.<sup>13</sup> Prior to this report, only nine such cases diagnosed by gastric cytology had been recorded, three by Klayman<sup>8</sup> and six by Graham.<sup>5</sup> Review of the literature has failed to disclose a single example of the cytologic detection of new malignant changes in the stomach remnant of a patient who had previously undergone resection for carcinoma of the stomach. This may be explained in part by failure to do cytologic studies following subtotal gastrectomy<sup>7</sup> since there are technical problems in obtaining an adequate specimen<sup>7</sup> and since it may be difficult to interpret correctly the cells that are seen.<sup>2</sup>

Most carcinomas found in gastric remnants undoubtedly represent recurrences of the original tumor. A certain number, however, may be new primary lesions, the result of *de novo* malignant change in an organ which has already demonstrated an ability to undergo such change. A number

of reports in the literature indicate that gastric cancer may be multicentric in origin.<sup>1, 4, 9</sup> Using over-sized tissue sections, Collins and Gall<sup>1</sup> have shown that a significant number of carcinomas probably result from the coalescence of independent neighboring foci of malignant epithelium. The present case may represent such multicentricity of origin. Since the margins of the specimen initially resected were free of tumor, the carcinoma *in situ* found in the second specimen may well represent a second focus of independent malignant mucosal change. Similarly, since the proximal edge of the second specimen was found to be free of malignant change on numerous sections, the recent reappearance of malignant cells in the gastric wash may represent still another focus of independent malignancy.

In a sense, it is fortunate that the 1959 cytology in this patient was erroneously read as negative. The resultant delay has given us further insight into the natural history of gastric carcinoma *in situ*. Our findings confirm Schade's conclusion that surface carcinoma may exist for prolonged periods of time before the *tumor stage* develops.<sup>3, 13</sup> Metastases, however, can take place even though these carcinomas appear to be limited to the mucosa<sup>9, 16</sup> so that ex-

tirpative surgery is justified despite the apparent localization.

A positive gastric cytology, even in the absence of other positive corroborating diagnostic studies, is evidence enough for exploratory celiotomy and gastrotomy.<sup>5,13</sup> When the tumor cannot be palpated through the stomach wall and is not visible on gastrotomy, the surgeon faces a difficult decision. The use of phase contrast microscopy to examine cellular material scraped from various portions of the gastric mucosa, and the employment of a rapid Giesma stain to examine material obtained in the same fashion have been suggested as methods of establishing the diagnosis.<sup>8</sup> Multiple gastric biopsies may be obtained for immediate frozen section examination. When these examinations are negative, the possibility still exists that the lesion has been missed. Total gastrectomy under these circumstances must certainly be considered. Whether our knowledge of carcinoma *in situ* of the stomach as a lethal disease justifies the morbidity and mortality cannot be answered until there has accumulated further information concerning the natural history of this disease.

### Summary

A case is presented of gastric carcinoma *in situ* developing in a man who had undergone resection of an invasive gastric cancer three years previously.

The carcinoma *in situ* was recognized by gastric cytologic examination when other available diagnostic studies were of no help.

The multicentric origin of certain gastric carcinomas is supported by the evidence in this case.

The dilemma of the surgeons confronted with a negative gross exploration in the face of a previously positive gastric cytology is considered.

### Acknowledgment

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