Biopsy Diagnosis of the Digestive Tract

Heidrun Rotterdam · Sheldon C. Sommers

Biopsy Interpretation Series

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Preface

The advent of fiberoptic endoscopy 20 years ago has resulted in an ever-increasing number of biopsies of all parts of the digestive tract. The contributions of endoscopy and endoscopic biopsy to the understanding of gastrointestinal disorders are comparable in many ways to the contributions of colposcopy and guided cervical biopsy to the understanding of cervical neoplasia. The ability to biopsy sequentially almost all parts of the digestive tract under visual control has led to a better understanding of the exact localization, extent, and natural history of conditions such as esophagitis, chronic gastritis, duodenitis, Crohn's disease, and ulcerative colitis. The early forms of neoplasia, especially in the stomach and colon, are now recognized with increasing frequency and have prompted the need for new classifications and terminology. The definition and clinical significance of some of the new terms, such as dysplasia in the various parts of the digestive tract, are still in the process of clarification.

For pathologists, these recent developments mean increasing exposure to biopsy specimens and the need to familiarize themselves with early pathologic changes and to recognize conditions in a small, often poorly oriented specimen.

We have tried in the present book to supply all the information that is pertinent to the biopsy diagnosis of diseases of the digestive tract. In contrast to already existing volumes of similar content we have included the chapters on the esophagus and anus. Furthermore, discussion has not been limited to inflammatory and degenerative conditions but also includes tumors and any other conditions that conceivably may appear in a biopsy.

The first chapter, by Dr. Jerome D. Waye, discusses the historical and technical aspects of endoscopy and endoscopic biopsy. Each subsequent chapter is devoted to one particular segment of the digestive tract and treats that segment's full complement of diseases. A certain degree of repetition was unavoidable but has the advantage of saving the reader the frustration of searching for the various bits of information on different pages.

The volume addresses itself primarily to the surgical pathologist, in training or in practice, but the endoscopist and gastroenterologist will find this volume helpful in correlating clinical, gross, and microscopic findings and in learning about indications, diagnostic accuracy, and handling of biopsy specimens.

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Sincere appreciation is expressed to the senior authors and publishers listed below for permission to reproduce the following figures: **Chapter 2:** Figs. 7 & 8. M Meurer and *Arch Dermatol*; Fig. 17. L Ozzello and *Pathol Annu*; Fig. 32. JV Johannessen. **Chapter 3:** Figs. 4, 5 & 42. J Lechago and *Pathol Annu*; Fig. 6. K Mukai and Masson Publ Co.; Fig. 8. HA Oberman and *N Engl J Med*; Fig. 36. H Belandria; Fig. 54. A Watanabe and *Gastroenterology*; Figs. 55 & 56. M Tatsuta and *Cancer*; Figs. 88 & 89. FR Smith and *Am J Gastroenterol*; Figs. 91 & 92. WC Black and *Cancer*. **Chapter 4:** Figs. 3 & 13. BM Schuman and *Henry Ford Hosp Med J*; Figs. 24 & 26. E Solcia and Masson Publ Co; Figs. 25 & 27. H Kaneko and *Cancer*. **Chapter 5:** Figs. 2, 19, 59 & 72. JV Johannessen and McGraw Hill Book Co.; Figs. 9 & 10. J Lechago and *Pathol Annu*; Fig. 14. WW Olmsted and *Am J Roentgenol Radium Ther Nucl Med*; Fig. 21. ME Ament and *Gastroenterology*; Fig. 25. JL Rollo; Figs. 29–31. WA Morningstar and *Human Pathol*; Fig. 37. RM Albrecht and *N Engl J Med*; Figs. 39–41. RL Owen and *Gastroenterology*; Figs. 50 & 51. RR Rickert and *J Clin Gastroenterol*; Fig. 56. TD Bohane and *Gastroenterology*; Fig. 56. M Ranchod and *Am J Surg Pathol;* Figs. 57 & 58. VJ Ferrans and *Am J Pathol*; Fig. 82. NS Mann and *Am J Gastroenterol*. **Chapter 6:** Fig. 10. MC Duffy and *Am J Clin Pathol*; Fig. 23. FV McClurg and *Am J Clin Pathol*; Fig. 24. N Lane; Fig. 78. RG Estrada and *Am J Surg Pathol*; Fig. 84. HJR Bussey and *Pathol Annu*; Fig. 107. T Nasemann and WB Saunders Co.

Contents

Chapter 1

Digestive Tract: Biopsy Instruments, Procedures, and Specimens

Jerome D. Waye

Several types of biopsy equipment are available for sampling tissue from the intact digestive tract. Specimens may be obtained through the rigid tube of the sigmoidoscope, by small bowel biopsy capsules, or via the flexible fiberoptic endoscope. Deep biopsies may perforate the wall of the intestinal tract, and the operator should try to provide sufficient tissue for histologic examination while avoiding harm to the patient.

The oldest method for obtaining tissue from the intestinal tract is the proctoscopic biopsy taken through a rigid sigmoidoscope with an alligator-type cutting forceps. An ample piece of tissue may be obtained from portions of the rectum and lower sigmoid with this technique.[5] Multiple biopsies are easily achieved, as the rigid forceps need only be reintroduced through the open proctosigmoidoscopic tube. The biopsy specimen is punched cleanly from the attachment to the surrounding mucosal surface and may be removed from the forcep jaws with a needle or toothpick. An attempt should be made to orient the flattened specimen on a carrier (plastic mesh, lens tissue paper, or Gelfoam®) for fixation purposes. Proper positioning of the tissue with the cut surface flat against the carrier permits orientation in the paraffin block for subsequent histologic sectioning perpendicular to the surface, along the long axis of the crypts.[12]

Small bowel biopsies are usually "suction biopsies" obtained by applying negative pressure to a portion of small bowel mucosa through a small port on a biopsy cylinder. The knuckle of tissue sucked through the small opening is severed by a guillotine-like action of a knife blade adjacent to the biopsy port activated by pulling a wire, or by the action of negative pressure tripping a spring-loaded blade. The amount of tissue obtained is directly related to the degree of negative pressure generated within the biopsy cylinder. In the small bowel it is important to obtain muscularis mucosae so that the individual glandular structure will be preserved, as the muscularis mucosae maintains the villous architecture. In the absence of muscularis mucosae, the villi may spread out laterally and shorten, rendering an inaccurate reading of crypt height. The self-contained biopsy capsule, activated by negative pressure alone, retrieves a single piece of small intestinal mucosa approximately 4 to 5 mm in diameter. A "multipurpose" biopsy tube with different-

sized biopsy capsules can obtain one, two, or four pieces of tissue at one time. For research purposes, there is a hydraulically activated biopsy tube in which a stream of water injected through one channel forces the biopsy specimen to be delivered through another channel, so sequential biopsy specimens may be obtained without removing the biopsy tube. Fluoroscopy or X-ray must be used to ensure proper localization of the biopsy site near or distal to the ligament of Treitz. Precise placement for obtaining biopsy specimens is not possible, as this is a "blind" biopsy technique. Utilizing the "multipurpose" suction biopsy tube, specimens may be taken in any accessible area of the intestinal tract, including esophagus, stomach, and rectosigmoid.

Flexible fiberoptic endoscopy became available approximately 20 years ago, and biopsy capabilities were soon expanded. Current endoscopes are sophisticated mechanical devices of variable length whose widths vary from 9 to 15 mm in diameter (Fig. 1). The entire large bowel can be completely intubated in a high percentage of cases with the flexible fiberoptic colonoscope, and frequently the terminal ileum may be intubated through the ileocecal valve. Biopsy specimens may be taken from any portion of the visualized mucosa of the colon, and any lesion in the colon is accessible for direct vision and tissue sampling. The upper intestinal tract is totally available for fiberoptic instrumentation, including the small bowel down to the midjejunum. A very long enteroscope is available for total small bowel intubation, but it is not possible to obtain biopsy specimens through this specialized instrument.

Through the use of flexible fiberoptic endoscopes, biopsies are obtained under direct vision, and precise placement of the biopsy forceps (target biopsy) can be accomplished. The technique of biopsy through the fiberoptic endoscope is the same whether biopsies are taken from the upper or lower intestinal tract. All biopsies are of the avulsion type, as the small forceps extended through the biopsy channels are neither sharp enough nor have enough pressure to cut a piece of tissue cleanly. Once tissue is grasped within the jaws of the forceps, it is held tightly and the

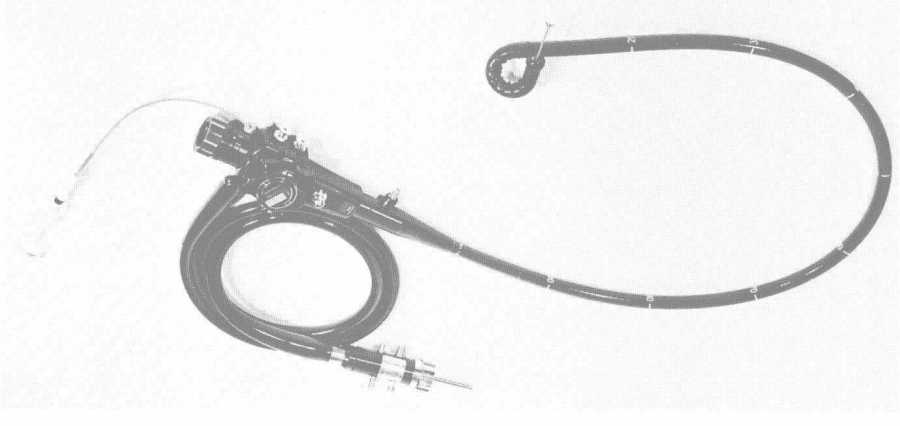

FIG. 1. Flexible fiberoptic upper gastrointestinal endoscope demonstrating tip angulation capability, with biopsy forceps extruded.

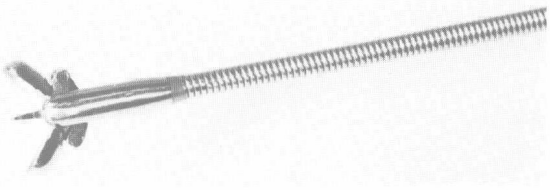

FIG. 2. Biopsy forceps with central spike, which allows better tissue orientation. The distance between the tips of the forcep cups is 7 mm.

biopsy is obtained by withdrawing the closed forceps toward the tip of the endoscope. As the forceps are retracted within the biopsy channel, the mucosa surrounding that portion captured in the jaws is pulled up to the distal tip of the endoscope. Continued forceps withdrawal tears the captured piece from surrounding mucosa, after which the elasticity of the stretched bowel rapidly returns the bowel's configuration toward normal. The tissue is retrieved by withdrawing the full length of forceps from the instrument. The forceps have bivalved cups which open symmetrically and are of variable length. Bleeding is not a problem with the endoscopic biopsy, which is usually obtained through a standard channel of 2.8 mm diameter. Pediatric instruments have smaller biopsy channels and can only accommodate a forceps of 2.0 mm diameter; the tissue specimens retrieved are correspondingly smaller. Newer instruments are designed with a larger biopsy channel and accept forceps of 3.7 mm diameter. These large-jaw forceps provide a larger piece of tissue, but their safety has not been tested in clinical situations.

Some standard biopsy forceps have a needle-like spike in the center of the forceps which protrudes as the forcep jaws open (Fig. 2). The needle tip impales mucosa and stops the forceps from sliding along the wall of a curved organ, e.g., the stomach or esophagus.[2]

Simultaneous biopsy and fulguration may be performed with a "hot biopsy" forceps that is insulated to protect the instrument and operator from harm during electrical activation (Fig. 3). A current passes down the entire length of the forceps and around the metal jaws to coagulate tissue at the site of biopsy, while the tissue within the cups is only slightly heated. The specimen within the forceps undergoes no thermal damage, but the surrounding tissues are burned to the point of protein denaturation. This technique is useful for tissue identification and simultaneous fulguration-obliteration of small polyps less than 8 mm diameter.[11]

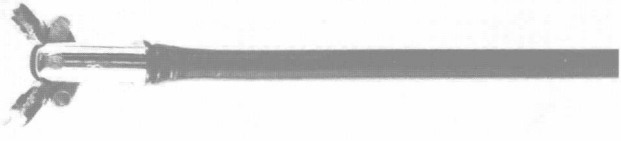

FIG. 3. Insulated biopsy forceps (hot biopsy).

Various techniques for obtaining biopsy specimens are available:

1. Biopsies may be done as previously described. Multiple biopsy specimens can be obtained by repeated passage of the forceps through the biopsy channel, with retrieval of each specimen individually. The greater the number of biopsies, the more accurate is the diagnosis, with one report[3] of overall endoscopic biopsy accuracy rate in the upper gastrointestinal tract of 99.8% when multiple specimens are taken. Not all endoscopists achieve this degree of success, but one should expect about 95% accuracy.[13]

2. When deeper biopsies are desired (e.g., when attempting to biopsy submucosa when a large fold is covered by normal mucosa), multiple specimens may be taken from the same site, with each biopsy biting successively deeper into the tissue.[1] Three samples are usually taken in this method, which is known as the "well technique."

3. A "large-particle" biopsy may be achieved using a wire snare of the type employed for polypectomy purposes. A segment of a large fold may be entrapped within a snare loop and, after tightening, electrocautery current applied; in this way a portion of tissue may be cleanly severed, with hemostasis achieved by the coagulation current. A "button" of mucosa and submucosa approximately 1.0 cm in diameter may be obtained using this technique. The specimen may be retrieved by grasping it within the snare loop again and removing the instrument and snare simultaneously, or suctioning the biopsy specimen onto the tip of the endoscope with the internal suction mechanism of the instrument and removing the instrument along with the biopsy specimen. The large-particle biopsy technique is applicable to thickened folds within the stomach; it should not be performed in the colon or small bowel because the wall is considerably thinner there. If desired, a snare biopsy may be performed on exophytic tumors presenting anywhere in the lumen of the intestinal tract. The technique is similar to that described above.

4. Large clumps of tumor tissue may be impacted into the jaws of the forceps and retrieved by repeatedly pushing the open forcep jaws into a tumor. A large tissue sample, approximately 5 to 8 mm in diameter, may be retrieved. This technique is successful only when a tumor is encountered that is fixed to the wall. Each pass of the biopsy forceps and its retraction removes a fragment of a fixed tumor without the tendency for the tumor (as occurs with normal tissue) to stretch up to the faceplate of the endoscope before being torn off. The fixation of the tumor permits the specimen to be torn off without complete retraction of the forceps into the biopsy channel of the instrument. Once a large mass of tissue has been collected into the forcep cups and bulges out from all sides, the forceps is partially withdrawn, so only the jaws and mass of tissue remain extruded from the instrument tip. The endoscope is then removed with the forceps in its partially retracted position just outside the distal tip. Once outside the patient, the forceps may be pushed out several inches from the instrument tip, opened, and the specimen retrieved. At any time during withdrawal, or even when outside the patient, if the forceps tip is pulled into the biopsy channel all the excess tissue outside of the forcep jaws will be cleanly severed at the instrument face and lost. This technique is not applicable to biopsy of normal tissue or in instances where crush artifact is likely to interfere with the histologic diagnosis, e.g., when mucosal detail is important.

It is difficult to orient biopsy specimens taken through a flexible fiberoptic endoscope because the entire compressed piece of tissue is approximately 1 to 2 mm in diameter (Fig. 4). Tissue should be obtained by teasing it from the open forcep jaws with a needle or toothpick onto a carrier material. The specimens are extremely small, and the assistant must be cautioned to place the tissue gently onto the carrier and resist the tendency to smear the small biopsy fragment from the cups to the carrier. The spike forceps frequently permits orientation of the specimen, as the open forceps with the biopsy specimen impaled will have the specimen stretched from one cup to the other, with the spike through its mid-portion. The jaws can be placed on a carrier and the specimen teased down flat. Tissue should be placed immediately in fixative and labeled as to the site of biopsy.

When a large operative specimen is presented to the pathologist, tissue sampling is performed in the laboratory; in cases of endoscopy, however, the pathologist must accept the sampling provided by the endoscopist. Sampling errors are common when obtaining such small segments of tissue, and care must be taken to direct the forceps precisely at the area where the yield will be highest. If multiple samples are taken from the same site, they may all be placed within one container of fixative. If various sites are sampled, each biopsy specimen should be placed in a different container and labeled as to the location of origin.

Nowhere is endoscopic sampling error greater than in the biopsy of polyps, which has prompted endoscopists to advocate total removal of all polyps, so that the entire specimen may be submitted for histologic examination, rather than a portion of its surface. Because of the small sample provided, it is important to supply adequate clinical data with each endoscopic biopsy submitted. The most informative results are obtained when there is close cooperation between the endoscopist and the histopathologist, so that the best interpretation can be rendered from the small fragments of tissue delivered.

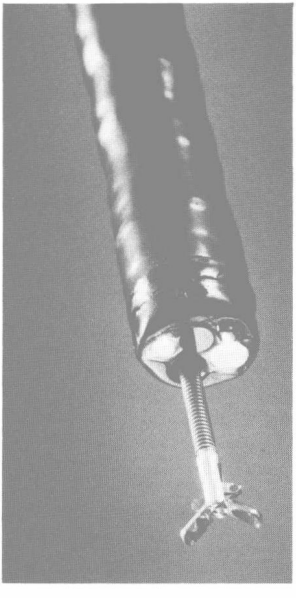

FIG. 4. Fenestrated biopsy forceps protruding from the tip of a pediatric instrument. Holes in the jaws permit a larger fragment of tissue to be contained within the closed cups. The width of the instrument (Olympus GIF P-3) is 9.0 mm.

Rectal biopsies with the sigmoidoscopic forceps should be done on a rectal valve which protrudes into the lumen of the rectum. Under direct vision, samples may be taken from any lesion seen through the sigmoidoscope. To prevent bleeding from the large biopsy site, pressure must be placed on the area using a long cotton-tipped applicator.

Small bowel biopsies are retrieved in a blind fashion, and the physician does not know if the portion of tissue obtained is adequate until the biopsy capsule has been completely withdrawn (unless a hydraulically operated biopsy device is available). The biopsy capsule must be disassembled to retrieve the tissue specimen. A dissecting microscope can be a great aid in orientation of the small bowel biopsy specimen. The spring-loaded biopsy capsule responds to the amount of negative pressure applied by the operator. The "pull-wire" biopsy tube is equipped with a pressure gauge, and various pressures are used for biopsies through different parts of the intestinal tract. Although complications of small bowel biopsies are rare, attention must be directed to the amount of negative pressure applied lest too large a portion of mucosa (and submucosa) be drawn into the biopsy capsule and guillotined. Free perforation is unusual, as is bleeding.

Flexible fiberoptic endoscopy is performed under direct vision, and visible submucosal blood vessels should be avoided during biopsy, if possible. There is very little problem with persistent bleeding following endoscopic biopsy, except in patients with an underlying bleeding diathesis. The major problem involved in the endoscopic biopsies performed through the flexible fiberoptic endoscope is sampling error due to the small amount of tissue obtained.

Several studies have shown that at least six[10] or seven[6] biopsy specimens must be taken from the edge of a gastric ulcer to avoid missing a carcinoma on one edge of the ulcer. It is not always possible to recognize an early malignancy within a gastric ulcer by gross inspection, although the magnification factor is 10 × to 12 ×. Biopsies should be aimed at the inner edge of a gastric ulcer, where the base meets the mucosal surface. One report states that accuracy of biopsy may be increased by biopsying the base as well as the edge of ulcers.[7]

Sampling errors are increased with the current generation of flexible fiberoptic endoscopes, which are end-viewing instruments. The original endoscopes were side-viewing, with the biopsy forceps exiting at 90° (perpendicular) to the long axis of the instrument. Utilizing these older instruments, a gastric ulcer could be viewed directly and samples taken from all aspects of the ulcer. The end-viewing instruments, although easier to use and affording a view of long tubular organs as well as hollow organs (esophagus and duodenum, as well as stomach), permit an ulcer to be seen only tangentially. In this instance, multiple samples should be taken from the visible distal hemicircumference and some from the proximal mound of mucosa. A U-turn maneuver may be performed with the endoscope, and it is especially helpful when ulcers are present on the angulus of the stomach (junction between body and antrum). When ulcers are located at the angulus, a total face-on view may be obtained with this maneuver and biopsies taken from all edges.

Thickened folds within the stomach may have the mucosal surface easily biopsied with the standard "avulsion" biopsy technique previously described. If deeper tissue

is desired (i.e., submucosal infiltration by tumor), multiple, increasingly deeper biopsies can be taken through the same surface biopsy site, while the endoscopist maintains precise positioning of the endoscope under direct vision. A much larger tissue specimen may be obtained from large gastric folds by placing a snare around a portion of a fold and removing it with an electrocautery technique. When multiple biopsies (described above) are taken, they may all be placed in the same bottle of formalin, each on a separate carrier. Thickened folds elsewhere in the intestinal tract should not be biopsied with a snare technique or with the well technique, as the wall of the stomach is considerably thicker than that of the intestinal tract at other locations.

Random biopsies are recommended when sampling a postgastrectomy stomach remnant because of the tendency for carcinoma to develop many years following surgery.[4]

When patients with inflammatory bowel disease are examined for dysplasia, multiple biopsies should be taken from at least eight locations throughout the large bowel, e.g., the cecum, ascending colon, hepatic flexure, mid transverse colon, splenic flexure, descending colon, upper and lower sigmoid colon, and rectum.[8,9] Areas of obvious inflammation should be avoided if possible. Each specimen should be placed in a separate container and labeled as to its site. Pseudopolyps need not be biopsied, but if they are this information should be noted on the pathology requisition form.

The clinician should not rely on tissue sampling from colonic polyps, which frequently does not reflect the histologic pattern of the entire polyp. Colonoscopy and polypectomy have progressed to the stage where it is possible to remove almost all colonic polyps encountered, either pedunculated or sessile. The entire polyp should be endoscopically resected and an attempt made to identify the base of the polyp by marking it with a thread, suture, or needle. Identification of the base is important, as retraction of the tissue around the small base may completely obscure its location and result in tangential histologic sectioning.

SUMMARY

Many types of biopsy instruments are available for providing tissue specimens during endoscopic examinations. Flexible fiberoptic endoscopy has revolutionized the approach to patients with gastrointestinal disease, and histologists are presented with an increasing number of tiny fragments of tissue obtained through the flexible endoscope. Proper interpretation of these tiny tissue fragments can best be provided by close communication between the histopathologist and the endoscopist concerning the reason for the examination, the type of lesion biopsied, and the site from which tissue was obtained.

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Chapter 2

Esophagus

The esophagus extends from the pharynx to the stomach and is 23 to 25 cm long. The lining epithelium is stratified, squamous, and glycogen-rich. Grossly, it appears white because of its thick epithelial layer. It is normally not keratinized and closely resembles mature vaginal epithelium. Underneath are the lamina propria connective tissue, muscularis mucosae, and the submucosa, which contains mucous glands with lymphocytes around the acini and small lymph nodules around the ducts.

Endoscopic biopsy specimens most often contain only the esophageal epithelium peeled off and sometimes rolled up, with little or no attached connective tissue. The diagnosis then is esophageal epithelium or negative esophageal mucosa. In such cases there is only a single layer of basal cells, the epithelium is very little interdigitated with the lamina propria, and the total mucous membrane is 0.5 to 0.8 mm thick (Fig. 1).

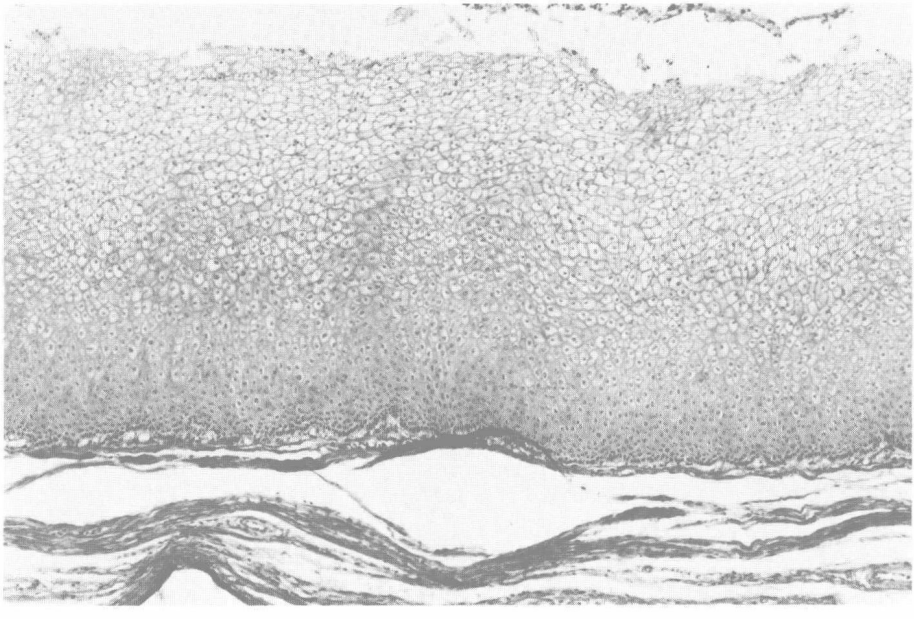

FIG. 1. The normal esophageal mucosa is a stratified squamous epithelium rich in glycogen, attached at the base along a rather smooth surface. Its epithelial thickness is slightly less than 1 mm. Hematoxylin-phloxin-safranin (HPS) stain. ×45.

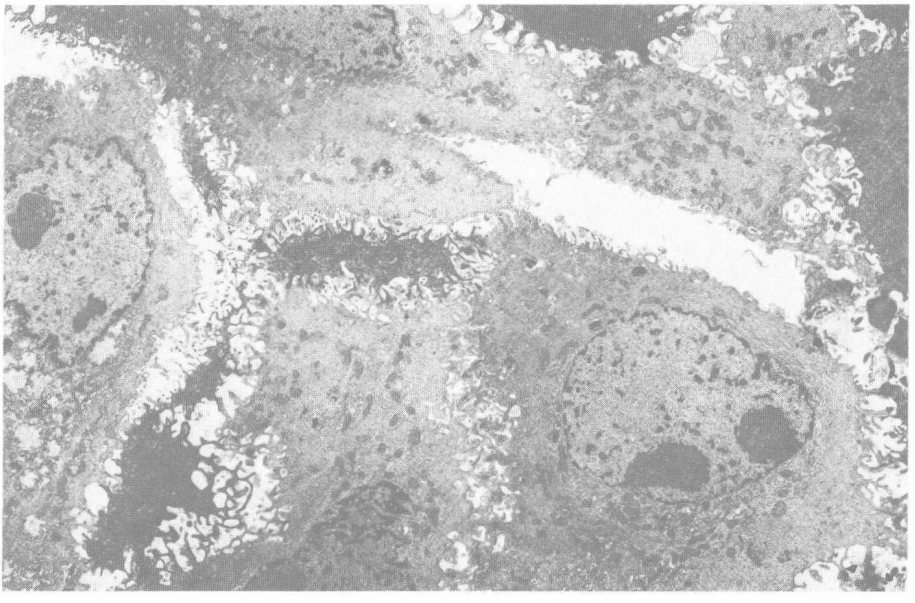

FIG. 2. Squamous epithelium of esophageal type shows the complex interdigitations of the individual cells, locally artifactually separated. The minute black cytoplasmic granules represent glycogen. × 3,095.

Ultrastructurally, the esophageal epithelium comprises basal, prickle, and functional cell layers. The basal and prickle cells have microvillous surface processes, desmosomes, and cytoplasmic tonofilaments. There are wide intercellular spaces containing debris. Prickle cells contain glycogen rosettes, and the functional cell layer contains abundant glycogen and tonofilaments. Intercellular spaces are narrow. Membrane coating granules in the upper prickle cells and functional cells persist slightly in the surface cells. Normally, no keratohyaline granules are present (Fig. 2). Some lamina propria capillaries have a fenestrated endothelium.[50]

About 28% of esophagi have unevenly distributed argyrophilic cells in the deeper epithelial strata, representing the neuroendocrine, or "APUD" (amine precursor uptake and decarboxylation), disseminated endocrine cells of Pearse.[125] The related amphicrine cells of Feyrter, which stain for mucus as well as argyrophilic or argentaffin granules, are also seen here.[107] About 4 to 8% of esophagi possess intraepithelial melanocytes.[82,125] Cancers may arise from these three specialized cell types. The results of 366 consecutive esophageal biopsies performed at Lenox Hill Hospital over a 3-year period are shown in Table 1.

CONGENITAL ANOMALIES

Many congenital abnormalities evident early in life would not likely yield endoscopic biopsy specimens and are mentioned only briefly. These include the relatively common esophageal atresia, usually with an associated tracheoesophageal fistula, the less common duplications and congenital cysts, and the rare columnar

TABLE 1. *Diagnoses of 366 consecutive esophageal biopsies, LHH, 1976–1979*

Diagnosis	No.	%
Normal	57	(16%)
Foreign bodies	30	(8%)
Esophagitis	100	(27%)
Ulcer	53	(14%)
Barrett's esophagus	8	(2%)
Benign neoplasm	4	(1%)
Dysplasia/carcinoma *in situ*	32	(9%)
Carcinoma	50	(14%)
Miscellaneous	32	(9%)

epithelium-lined esophagus.[105,131] Biopsy of an esophageal cyst reveals that its epithelium is columnar and ciliated. This is the normal embryologic esophageal epithelium from the 9th to the 11th week of life. Sometimes the cyst is lined by squamous, flat, cuboidal, ciliated, or pseudostratified columnar cells.[131]

Congenital esophageal webs or membranes are rare and are curable by dilatation without biopsy.[41] Lower esophageal ring (Schatzki's ring) is a radiologic, not an esophagoscopic, diagnostic entity.[64] The more common mucosal type of ring is located at the squamocolumnar junction and at the constrictor cardiae level.[43] It is a nearly circular wedge-shaped shelf or diaphragm covered by squamous epithelium on the upper surface and gastric mucosa on the lower side.[79] Combined manometry and measurements of transmural potential differences have shown that these mucosal rings mark the lower end of the esophagus and do not represent a dislocation of the gastroesophageal mucosal junction away from the lower esophageal sphincter.[33b] The less common muscular ring is situated more proximally, covered by squamous epithelium, and corresponds to the inferior esophageal sphincter.[43] These rings may or may not be symptomatic and are said to be always associated with a hiatus hernia.[63]

Mechanical Injuries, Strictures, and Diverticula

Foreign bodies impacted in the esophagus may be removed endoscopically. They produce superficial erosive injuries that usually heal promptly. In England coins and fish bones are common in children, and chicken or fish bones in adults.[95] In New York meat and potato pancakes are found. Occasionally the bone ulcerates and fistulizes into the trachea, a bronchus, or the aorta.[94,95] Iatrogenic instrumental injuries were recognized clinically in only 2% of a consecutive autopsy series, but some esophageal trauma was found in 60%. Metal instruments, soft flexible tubes, and suction catheters produce mucosal injury. Patients with thrombocytopenia are the most susceptible.[133]

Stricture of the esophagus most often follows liquid lye burns, e.g., from sodium hydroxide drain cleaner.[67] Biopsies show keratinized regenerated squamous epithelium and fibrosis of the underlying connective tissue (Fig. 3). Stricture may complicate Crohn's disease or scleroderma.[33a]