*Bulletin* of the

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and
Minnesota Medical Foundation

# Epithelial Tumors of the Large Intestine

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BULLETIN OF THE
UNIVERSITY OF MINNESOTA HOSPITALS
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UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

Visitors Welcome

November 22 - 27, 1948

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Monday, November 22

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Staff; Veterans' Hospital.

11:00 - 11:50 Physical Medicine Seminar; E-101, U. H.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:00 - 1:00 Physiology Seminar; Studies on Circulation in Mouse Tails; Arnold Lehman; 214 M. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; 104 I. A.

12:30 - 1:50 Surgery Grand Rounds; A. A. Zierold, Clarence Dennis and Staff; Minneapolis General Hospital.

1:00 - 2:00 Kellogg Lecture; The Normal and Pathologic Physiology of the Thyroid Gland; F. R. Keating, Jr., Mayo Clinic; Eustis Amphitheater, U. H.

2:00 - 3:00 Kellogg Lecture; The Use of Radio-Iodine in the Study and Treatment of Thyroid Disease; F. R. Keating, Jr., Mayo Clinic; Powell Hall Amphitheater.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

2:00 - 3:00 Surgery Problem Case Conference; C. Dennis and Staff; Small Class Room, General Hospital.

3:45 - Pediatric Seminar; Newer Methods of Treating Acute Poisonings; Wallace Lueck; 6th Floor, Child Psychiatry, U. H.

4:00 - 6:00 School of Public Health Seminar; 113 MeS.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

Monday, November 22, Cont.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy and H. M. Stauffer and Staffs; M-109, U. H.

Tuesday, November 23

8:30 - 10:20 Surgery Reading Conference; Lyle Hay; Small Conference Room, Bldg. I, Veterans' Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and Robert Hebbel; Veterans' Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans' Hospital.

2:00 - 4:00 Kellogg Lecture; The Physiology of the Testis and Male Hypogonadism; Warren Nelson; Eustis Amphitheater, U. H.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans' Hospital.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

5:00 - 5:50 Urology Pathological Conference; C. D. Creevy and Staff; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; Dr. Aurelius and Staff; Powell Hall Amphitheater.

Wednesday, November 24

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515, U. H.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans' Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker and Joe R. Brown; Veterans' Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; O. H. Wangensteen, C. J. Watson and Staff; Todd Amphitheater, U. H.

12:00 - 12:50 Radio Isotope Seminar; Emission and Absorption of Beta Rays; J. C. Wang; Rm. 216, Hospital Court, Temporary Bldg.

1:00 - 3:00 Kellogg Lecture; Dysplasias and Dystrophies of Bone; James Braillsford, England; Todd Amphitheater, U. H.

4:00 - 5:00 Infectious Disease Rounds; Medical Conference Room, Veterans' Hospital.

4:00 - 5:30 Surgery-Physiology Conference; O. H. Wangensteen and M. B. Visscher;

Thursday, November 25 - Holiday

Friday, November 26

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Staff; Veterans' Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, A. V. Stoesser and Staffs; Minneapolis General Hospital.

11:30 - 12:50 University of Minnesota Hospitals General Staff Meeting; Football Pictures; Administration; Powell Hall Amphitheater.

12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Minneapolis General Hospital; Small Classroom.

1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

2:00 - 3:00 Kellogg Lecture; The Role of Irradiation in Therapy of Carcinoma of the Breast; K. W. Stenstrom; Eustis Amphitheater, U. H.

Saturday, November 27

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 21, U. H.

8:00 - 9:00 Pediatric Psychiatric Rounds; Reynold Jensen; 6th Floor, West Wing, U. H.

8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Minneapolis General Hospital, Small Classroom.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-101, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 12:00 Surgery-Roentgenology Conference; O. H. Wangensteen, L. G. Rigler, H. M. Stauffer, and Staff; Todd Amphitheater, U. H.

9:00 - 12:00 Neurology Conference; Powell Hall Amphitheater.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - 11:50 Urology Seminar; Aortography; Michael Feeney; E-101, U. H.

11:00 - 12:00 Anatomy Seminar; Therapy of Transmitted Mouse Leukemia, Sister Teresita Judd; Localization of Lesions in Aphasia, Roger A. Smith; 226 I.A.

## II. EPITHELIAL TUMORS OF THE LARGE INTESTINE

Walter A. Fansler
Howard M. Frykman

The increase in the knowledge that malignant tumors of the colon frequently arise from lesions which were previously considered insignificant has added new importance to the search for epithelial tumors of the colon and rectum. We purposely do not intend to spend much time in the discussion of far advanced lesions. If they are viewed through the proctoscope the diagnosis is usually apparent and a biopsy will confirm the clinical findings. Since the diagnosis, prognosis and accepted forms of treatment are quite well standardized in these advanced lesions we would like to call attention to those cases in which the growth is small, the prognosis more hopeful and the methods of treatment less well agreed upon.

Considerable confusion in the literature dealing with the occurrence of benign tumors of the large intestine has resulted from the designation of the word "polyp". With most authors it refers only to form and not to the histological appearance of the tumor. The word polyp is properly used to designate any sessile or pedunculated tumor arising from the bowel wall and projecting into the lumen of the intestine. However, many people consider the term polyp to be synonymous with adenoma. Hypertrophied anal papillae and thrombosed fibrous internal hemorrhoids are frequently incorrectly called rectal polyps, as are leiomyomas, lipomas, and fibromas. This group of tumors are not considered to be precancerous lesions and require removal only for mechanical reasons. To the true epithelial tumors, however, which include the adenomas, papillomas and carcinoids, we have learned to attach a much greater significance.

### Adenomas

Adenomas constitute the great majority of polyps found in the large intestine. They may be single or multiple, sessile or pedunculated, and may be found in any portion of the large bowel. Initially they appear as slightly raised areas on the mucous membrane 1 to 2 millimeters in diameter and are usually no different in appearance from the normal mucosa. Whatever the original appearance of the adenomas, as they gradually increase in size they become reddened in color and eventually assume the dusky red lobulated raspberry appearance of the typical adenomatous polyp. These changes occur at different stages of development but most pedunculated polyps 5 millimeters in diameter are of this characteristic type. Benign sessile adenomas, however, usually do not show this change so early. Occasionally they may be seen to attain a diameter of 1 cm. and are found to be still maintaining their light color and appearing as nothing more than rounded slight elevations of the mucous membrane. Most adenomas are flat or sessile in their early stages of growth although the majority will eventually become pedunculated. Pedunculation is the natural consequence of the enlarging tumor mass, dragging on its mucosal attachment caused by the peristalsis attempting to propel the tumor mass onward with the intestinal contents.

The microscopic appearance of a mature adenoma varies considerably. The typical pedunculated variety may be described as a connective tissue stalk with terminal branching, the branches of which are covered by atypical epithelium. Well developed blood vessels usually course through the stalk or pedicle which is usually covered with normal bowel mucosa. In the large sessile type of adenoma several stalks may be fused together to form a broad base and in this type the normal mucosa of the bowel extends only to the base of the tumor. The covering epithelium of the adenoma per se varies from normal mucosa of the large intestine to irregular branching glands lined with tall columnar epithelium with large vesicular nuclei and prominent nucleoi and frequently contain mitotic figures. The histological structure of these tumors is indeed quite variable and different sections of the same tumor may show a very different cytological picture. In all benign adenomas, however, the mucosa is of fairly even thickness and

usually shows well defined boundaries from the connective tissue stroma. The amount of mucous secretion produced by adenomas varies greatly, but as a class they produce much less than do villous papillomas. This is due to the lesser number of goblet cells in the typical adenoma.

Most observers have accepted Erdmann & Morris' classification of polyps of the colon into two distinct groups, the acquired and congenital types. 1) The acquired types consist of single or multiple polyps developing as simple neoplasms of the mucosa, or secondary to or in association with acute or chronic inflammatory diseases, such as ulcerative colitis. 2) The congenital type consists of those cases of diffuse multiple polyposis of the colon. In this disease there is a marked hereditary and familial tendency for its occurrence and there exists a great tendency for the development of carcinoma of the colon at an early age. It has been shown repeatedly that of the hundreds of polyps diffusely distributed throughout the colon in multiple polyposis, all are true adenomas and differ in no way grossly or microscopically from the single adenomas found in the large intestine. Multiple polyposis is quite different, however, from those cases in which a single adenoma or a few adenomas are found and it will not be considered other than its relationship to the simpler condition. A complete report on multiple polyposis citing several recent cases is forthcoming.

Helwig states that one person in five who reaches the age of 60 has an adenoma of the large intestine with a slight predominance in males. His figures are obtained from 1460 consecutive autopsies which were exclusive of cases of familial multiple polyposis. He found that from the first through the third decades the average incidence of adenomas in both males and females was approximately 3 per cent and with the beginning of the fourth decade there was an appreciable progressive increase with a maximum being reached in the eighth decade in which 24 per cent of his patients were found to have one or more adenomas of the colon. The over all incidence of adenomas found by Helwig in his study was 9.5 per cent. He also found adenomas in the colon were much less common in Negroes than in white people, the ratio being 1:5. Swinton and Haug, in 1843 autopsies, found adenomas in the colon in 7 per cent of their cases with 42 per cent showing two or more benign polyps, while 58 per cent had single lesions. Adenomas were found with the greatest frequency in the sigmoid colon and rectum and it was estimated that approximately 70 per cent wer within the reach of the 25 cm. sigmoidoscope. Seventy per cent of the malignancies of the colon also occurred in this same segment of the bowel. In familial multiple polyposis, too, there is an increasing frequency of polyp formation as the rectum is approached. Rankin states that adenomas in multiple polyposis have a tendency to appear approximately eight times more frequent in the rectosigmoid and rectum than in other sections of the colon. The greatest percentage of malignancy also occurs in the distal segments of the colon in this disease. It has been postulated that the reason for the great frequency of malignancy in multiple polyposis is due to the fact that the presence of the innumerable adenomas offer a much greater opportunity for malignant degeneration to occur than if only a single or a few adenomas are present.

Estimates of the incidence of adenomas vary greatly with the type of material used for investigation. Very different statistics are quoted in the literature of the adenomas found as a result of clinical symptoms rather than those obtained from autopsy specimens. Brust has reported that only 20 per cent of his patients with benign polyps presented symptoms referable to the tumor and this has also been true in our experience. Rectal bleeding is the outstanding symptom of adenomas of the colon. In fact, in most instances it is the only symptom noted by the patient. In the case of very large polyps abdominal cramps or intussusception may occur but this is extremely rare. Profuse bleeding from adenomas is rare and can occur only with the traumatization of a large

vascular polyps or by tearing a polyp from its pedicle leaving the vessels in the stalk exposed. Usually the bleeding from a polyp is rather small in amount and is frequently mixed with mucous. It may consist of bright red blood or small dark clots but more characteristically small dark stringy masses of coagulated blood are passed. Proctoscopic examinations done on patients in which the preparatory enemas are omitted will show dark streaks of blood and mucous adhering to the bowel wall. If these flecks extend as high as the proctoscope can reach it is indicative of pathology higher in the colon and a very diligent search with x-ray should be made to find the lesions.

Approximately 80 per cent of benign adenomas of the rectum and sigmoid colon are discovered as an incidental finding on proctoscopic examination. In these cases no symptoms of any kind can be elicited from the patient referable to these benign tumors. The reason for this is the complete lack of symptoms produced by the tiny sessile or pedunculated tumors a few millimeters in diameter which constitute the great majority of adenomas found. They are too small to produce any appreciable amount of mucous and it is difficult to traumatize them with hard stool because of their minute size and consequently they remain completely silent. The adenomas producing symptoms at the time of their discovery are usually found to be pedunculated and to measure approximately 1 cm. in diameter. Adenomas 3 or 4 cms. in diameter are occasionally seen and rarely a much larger one is reported. We believe this characteristic 1 cm. size is due to the fact that unless the patient is unusually careless or unobservant, enough rectal bleeding has occurred to cause the patient to seek medical advice.

In the majority of instances a single polyp is present -- 58 per cent in Swinton's series. This is especially true in children in which the lesion is almost invariably single and malignant change is unusual. Occasionally a second polyp is found in children but this is unlikely. Proctoscopic examinations in children are usually not done unless symptoms are present so the adenomas are usually well developed when found. In the first decade of life painless bleeding unassociated with other symptoms is usually found to be due to a polyp in the large bowel which is usually found to be in the rectum or sigmoid. These tumors are almost invariably pedunculated and occasionally may become 2 or 3 cms. in diameter before they are discovered. In these young children it is usually possible to find and destroy them through a sigmoidoscope, but occasionally laparotomy is necessary.

A portion of the confusion concerning the incidence of adenomas of the large intestine has resulted from the inclusion of pseudopolypoid tumors which arise as a result of gross inflammation. These are usually classified as acquired polyps of the colon. Occasionally innumerable small pseudopolypoid tumors will be found throughout the large bowel but this has been generally accepted as an entity distinct from multiple polyposis. Recent studies, however, have shown that considerable importance should be attached to these cases because of the much greater frequency of cancer when they are present.

Brust and Bargen found 10 per cent of their cases of chronic ulcerative colitis developed polyps which represented isolated areas of granulation tissue and mucosal remnants in which the inflammatory hyperplasia was conspicuous. They thought that there was a transition of inflammatory polyps to adenomatous polyps and that subsequent malignant degeneration occurs. In their series of cases of chronic ulcerative colitis in which carcinoma developed, polyps were found in 60 per cent. In familial multiple polyposis 100 per cent of the polyps were adenomatous while in the pseudopolyps arising as a complication of chronic ulcerative colitis Bargen has demonstrated approximately 20 per cent to be adenomatous and of this percentage 21.9 per cent were carcinomatous. Helwig, however, states that he has found no evidence to support the conception of associated inflammation as

an inciting agent in the development of adenomas. In 1460 consecutive autopsies only one example of association of colitis and adenomas was observed.

In our patients with chronic ulcerative colitis in which healing of the chronic ulcerative process has occurred, we have occasionally seen polypoid tumors which were thought to be true adenomas to decrease in size or entirely disappear. In following these patients with proctoscopic examination or in specimens removed following colectomy, these mucosal irregularities have frequently been found to have completely disappeared or to have greatly diminished in number. The regression or disappearance of true adenomas is never seen except where pedunculated adenomas have been broken off at the base of the pedicle. When any adenomatous changes have occurred in these pseudopolypoid tumors any regression which may occur is incomplete and they become precancerous lesions with a marked tendency to early malignant degeneration as is shown by the high incidence of cancer in chronic ulcerative colitis. The development of carcinoma in patients with ulcerative colitis has been reported to be as high as 13 per cent in Dennis' series.

True adenomas of the colon have been definitely shown to be dangerous precancerous lesions. Swinton and Warren have demonstrated that 14 per cent of the carcinomas of the colon in their series arose from benign polyps and they believed the percentage to be much higher. In many instances the overgrowth of the tumors has made it impossible to determine whether a polyp had existed prior to the development of the malignancy. It cannot be predetermined which adenomas will undergo malignant degeneration or when this might occur. Some adenomas appear to stay stationary in size and benign for an indefinite period of time while others seemingly show cancerous change from their inception. It is also impossible to tell how long the average adenomas must remain in situ before cancerous changes occur. In some cases of multiple polyposis which have been followed over a period of years in which the patient has refused surgery it has been estimated that from 6 to 12 years is necessary for the development of malignancy. There is no way of determining whether the situation in multiple polyposis parallels that of patients with solitary adenomas. It is also possible for carcinomas to develop directly from the normal mucous membrane. In Helwig's extensive study he found two cases in which an adenocarcinoma had developed spontaneously from the mucous membrane without an adenoma having been present. These cases, however, are believed to constitute a minority with most of the malignancies developing secondary to a cancerous change in a benign mucosal polyp.

No indication can be had as to the presence of malignant degeneration in a polyp from its size but in Helwig's series the adenomas with malignant foci were larger as a group than the benign adenomas. In his study the average diameter of polyps with cancerous changes was 1.8 cms. Saint has also reported that the polyps in which malignant degeneration was found were larger than the average benign adenomas. This would tend to indicate that the majority of these benign epithelial tumors must attain a certain size before cancerous degeneration can occur. This may be true, but the frequency with which small adenomas show malignant changes warrants their removal and microscopic study whenever they are found. We have seen three cases in which small sessile adenomas approximately 5 millimeters in diameter showed malignant degeneration upon microscopic examination.

At one time it was thought that malignant foci in adenomas usually occurred at the apex of the tumor. It has been shown, however, that cancerous changes can occur anywhere within the adenoma. Areas of malignant degeneration may be found at the periphery, in the center, at the apex or at the base of a previously benign adenoma. This is of importance in the larger sessile or broad based pedunculated lesions because of the possibility of early metastasis. In pedunculated aenomas with long narrow pedicles the chances of early metastatic spread are much less, and frequently local excision

close to the base of the stalk constitutes adequate definitive therapy if microscopic examination of the pedicle shows no involvement.

Whenever adenomas are visualized an effort should be made to determine whether these tumors are benign or malignant since it greatly affects the type of therapy to be used and the prognosis. Biopsy specimens alone are frequently unreliable because of the possibility of malignant changes having occurred in a portion of the polyp which was not removed for examination. It is also difficult to distinguish transitional forms histologically. Adequate visualization and palpation of epithelial growths are very important in establishing a diagnosis of malignancy. Firmness, fixation or induration in a polypoid tumor are almost pathognomonic of malignant change. If any of these gross changes are present repeated biopsies should be done until a definite diagnosis of carcinoma is established or definitely ruled out.

The high frequency with which multiple adenomas have been found in published autopsy series and the frequent finding of benign adenomas along with carcinomas of the colon has made it very important to seek out and destroy additional polyps if any type of epithelial tumor of the large bowel is discovered. Helwig has shown that in over 50 per cent of the cases of carcinoma of the colon and rectum additional adenomas were found, while Swintin reports 25.1 per cent in his series. The frequent multiplicity of adenomas of the colon is probably the explanation for the frequent finding of multiple malignant tumors of the large bowel. In the Lahey Clinic series it was found that 4 per cent of 195 patients had multiple cancers of the colon at the time of autopsy. This means that there is a possibility that one in 25 of all patients operated upon for carcinoma of the large intestine may have an additional malignancy of the colon at the time of surgery.

If one or more adenomas are discovered on proctoscopic examination regardless of their tiny size or harmless appearance the patient should have careful x-ray examination of the colon as a routine measure to rule out pathology beyond the reach of the sigmoidoscope. We use air contrast barium enemas routinely since we feel that the ordinary barium enema is unsatisfactory in the detection of polyps. Even with the best radiologic techniques it is difficult to demonstrate polyps less than 1 cm. in diameter and it is impossible to find the small sessile adenomas which are encountered most frequently. This means of examination, however, is the best available method we have at the present time. After removal or destruction of any visible polyps the patient is urged to return for re-examination at six month intervals for an indefinite period of time, which should include air contrast barium enemas once each year. If any unexplained rectal bleeding occurs in these patients and the sigmoidoscope examination rules out lesions in the terminal colon, x-ray studies should be ordered. If no lesion can be demonstrated and symptoms persist, however slight, the air contrast barium studies are repeated at frequent intervals. In the event that small lesions exist, it may be possible with frequent, repeated studies to demonstrate these early growths after they have increased slightly in size. This is the only manner in which an early diagnosis of benign polyps or early malignancy can be made above 25 cm. from the anal margin.

With malignancies of the large bowel if adequate colon studies are impossible prior to surgery because of varying degrees of obstruction, the entire colon should be carefully palpated at the time of surgery and a diligent effort should be made to discover additional lesions of any type. With frank malignancies palpation of the colon will usually suffice but the detection of adenomas other than the large pedunculated type is practically impossible. Because of the frequent multiplicity of lesions it is very important to search for and destroy any additional epithelial tumors which might be present. We have found direct visualization of the interior of the large bowel with a sigmoidoscope to be

very valuable, especially with lesions of the left colon. We routinely use an open type of anastomosis in resecting pathology of the large intestine and it is a simple procedure to pass a sterile sigmoidoscope through the open ends of the bowel and determine by direct visual examination the presence or absence of additional pathology. The lighted instrument can be passed with ease proximally to the splenic flexure and distally to the rectosigmoid. In this way adenomas too small to be demonstrated with standard roentgenographic methods or discovered by palpation may be detected and destroyed by fulguration at the time of surgery. The known incidence of additional adenomas in at least one third of the cases of malignancy of the colon justified this procedure which we believe can be done safely in patients who have had adequate preoperative preparation with non-absorbable sulfonamides. We also do this routinely in cases in which a colostomy is necessary to remove polyps inaccessible through the rectal approach. Similarly, in our patients with permanent colostomies following resections for carcinoma of the rectum, we feel that no interval postoperative examination is c complete without visualization of the mucosa of the terminal colon by the passage of a sigmoidoscope through the colostomy stoma. Endoscopic examination of the colon through colostomy stomas has been badly neglected. The presence of a colostomy gives an opportunity, which is frequently temporary, for direct examination of a segment of colon to determine the presence or absence of pathology which might not be demonstrable by the routine roentgen studies. If this procedure is done routinely the number of lesions which can be detected is surprising and gratifying.

Papillomas

Villous papillomas are another type of epithelial tumor occasionally encountered in the colon. These growths are also termed villous polypi, papillary adenomas and papillary polypi. Bacon and other authorities believe that papillomas represent a type of epithelial tumor which should be classified separately, although this seems of academic importance since the pathologic tendencies of papillomas and adenomas are the same. The villous tumors are characterized by a soft almost gelatinous appearing growth consisting of a large number of arborescent villae arising from the mucous membrane. These villae are composed of a very loose fibrous stroma covered by tall columnar epithelial cells. The covering mucosa usually shows increased cell layers, increased nuclear staining and occasionally mitotic figures but everywhere the regular relation of the mucosa to the basement membrane is preserved. There is a tremendous increase in the number of goblet cells in this type of tumor which accounts for the large amount of mucus produced. Although these tumors are very vascular they usually appear pinkish or grayish red and are often slightly lighter in color than the normal mucus membrane. This is in contrast to the larger adenomas which are very similar to a raspberry in color and appearance. The lobulated soft spongy mass of light color is characteristic of the villous papillomas. They may be either sessile or pedunculated and of any size. Papillomas are frequently larger than the other types of epithelial tumors encountered in the colon. At times they may become tremendous in size, almost occluding the lumen of the bowel without producing any marked obstructive symptoms because of the very soft nature of the growth. They are a slow growing tumor and occur almost exclusively in adults.

These growths characteristically produce large amounts of mucus and because of their friable nature they bleed easily. Consequently it is not unusual for a patient with this type of tumor to give a history of passing numerous diarrheal stools consisting mostly of blood tinged mucus. Villous papillomas, like adenomas, are definitely precancerous lesions. Rankin states that approximately 20 per cent eventually undergo malignant degeneration to form papillary adenocarcinomas. Dixon considers this type of malignancy to offer as poor a prognosis as colloid adenocarcinomas of the colon. In 523 cases of carcinoma of

the terminal colon in which non-palliative resections were done, 5 were of the papillary type and none of these 5 patients lived for 3 years following surgery. Eighteen of twenty patients with colloid carcinoma were also dead within three years.

Treatment of choice in this type of tumor is radical excision if the tumor is of large size or if any areas of induration or ulceration are present regardless of size. Induration or ulceration in these growths is usually indicative of malignant degeneration. Repeated biopsies should be done but they are notoriously inadequate in large papillomas because of the large mass of tissue present. With tumors higher in the colon the histologic diagnosis can only be made by the pathologist after the usual type of resection has been done. With small papillomas within the reach of the proctoscope, however, in which no induration is present and the growth is freely movable with the mucosa, we feel that local removal is indicated. If the tumor is pedunculated this can be done readily with the electric snare and the mass completely removed for microscopic examination. With the sessile type of papillomas complete removal is more difficult. Local recurrences following removal are not uncommon and it may be necessary to destroy these small recurrences several times before they are completely eradicated. Villous papillomas have been likened to condylomata accuminata with small or tiny tumors studding the wall around the larger growth, and they are almost as difficult to eradicate permanently. We feel that if these patients can be carefully followed at frequent intervals local removal or destruction can be done with relative safety. In our experience the recurrences have been benign histologically and after repeated irritation of these tumors with fulguration we have never seen malignancy supervene. David reports the same type of experience following the local removal of villous papillomas. With the large sessile growths of this type even though no indications of malignant change are present the mechanical difficulties involved in attempting local removal do not make this method feasible and resection is indicated.

Carcinoids

Carcinoids or argentaffinomas are quite rare in the large intestine. The senior author has never seen a carcinoid tumor of the colon in one of his own patients in almost 30 years of active proctological practice. The reports appearing in recent literature, however, suggest that the lesion is more frequent than was previously realized.

Carcinoids arise from argentaffin cells which are found diffusely distributed through the mucosa of the gastrointestinal tract. They were originally thought to be a benign tumor, but they now have been found to infiltrate and metastasize in a manner similar to adenocarcinoma of the intestine. Grossly these tumors have been found to appear as single or multiple firm, yellowish masses varying in form from sessile plaques or nodules to pedunculated tumors covered with intact mucosa. The reported tumors have also varied from small lesions to large tumors. If the mucosa over the tumor has become ulcerated and infected it is frequently impossible to distinguish them from true adenocarcinomas. Usually, however, the mucosa is intact over the mass but the covering mucus membrane is quite firmly attached to the underlying tumor. The mass itself is usually freely movable in the bowel wall, however. Histologically, carcinoids are found to consist of anastomosing cords and nests of cells which are extremely uniform in size and either cylindrical or polygonal in shape. They usually show no evidence of gland formation but may form pseudorosettes. The uniformity of the individual cells and their nuclei plus the absence of mitotic activity differentiates this tumor from carcinoma. Altman states that a comparison of the histological features in cases exhibiting metastases and those remaining as local tumors revealed no essential difference; and he is of the opinion that all carcinoids have the potential power to metastasize. To date, according to Rietz, 400 malignant intestinal carcinoids have been reported.

The appendix is the most frequent site of carcinoids, however the tumors reported from this organ have shown the least tendency to metastasize. The small intestine is the next most common site, and Wyatt found 22 per cent of all the reported carcinoids of the small bowel to be malignant. Carcinoids of the large intestine are much less frequent than those found in the small bowel but they apparently have the same malignant tendencies. At the present time 32 carcinoid tumors of the rectum have been collected and reported by Pearson and Fitzgerald, 12.5 per cent of which showed metastases. It is interesting to note that a high percentage of the cases were completely symptom free at the time of the examination with the tumor being discovered as an incidental finding. In those cases with erosion of the mucosa, however, the typical symptoms of bleeding and change of bowel habit were present. With carcinoids above the reach of the sigmoidoscope the histologic diagnosis is made by the pathologist after resection. With the carcinoids that are visible in the distal sigmoid and rectum, however, Pearson and Fitzgerald feel that local excision is indicated because of the apparent low grade of malignancy shown by most of these tumors. Mallory reported one case in which a carcinoid with metastases was removed from the small intestine and 20 years later the same metastases were found at autopsy in a relatively unchanged state. In the majority of reported cases with extensive metastases, however, death has occurred in approximately 2 years from the time of surgery.

In the differential diagnosis of carcinoids and other epithelial tumors one must consider the extra-rectal masses arising in adjacent structures and either eroding and invading the rectum or colon or encroaching upon the lumen of the bowel. In cases in which the mucosa covering the mass is normal there is no question but when the mucus membrane is ulcerated or when the tumor has broken through the mucosa and is projected into the bowel lumen some confusion may arise. The malignancies which most commonly produce this complication are carcinomas of the prostate, ovary and cervix and metastatic tumor masses in the rectovesical pouch or culdesac of Douglas. Punch biopsies in those cases with intact rectal mucosa or the removal of tissue with a biopsy forceps in ulcerated cases will usually establish the diagnosis.

A relatively rare benign condition which may also produce a similar situation is found in endometriosis with the formation of an endometrioma, which clinically may be indistinguishable from a malignancy of the rectum or distal sigmoid. Usually, however, the bowel mucosa is intact, the endometrioma producing a constriction of the lumen without actually eroding the mucosa. Certain other tumors arising in the bowel wall such as fibromas, lipomas or leiomyomas may also give this picture as may benign masses originating entirely outside the bowel as in the case of presacral dermoid cysts. Enlarged lymph follicles and inflammatory fibrous reaction at the site of injection therapy must also be considered. Determination of the exact nature of these nodules is frequently impossible without excision and histologic study of the tissue removed. Likewise, inflammatory conditions with ulceration such as lymphopathia venereum, tuberculosis, syphilis with gumma formation, amebiasis and other inflammatory conditions may simulate to some degree epithelial tumors. If the existence of these conditions is kept in mind, differentiation is usually not particularly difficult either from the gross appearance of the mass or from other physical observations and laboratory data.

Benign epithelial tumors and early malignancies of the terminal colon are being discovered much more frequently in recent years as more and more patients are being subjected to proctoscopic examination. This is indeed a step in the right direction since only with the discovery and treatment of these early tumors can we hope to reduce the mortality rate from cancer of the large bowel. For some reason adequate rectal examinations are badly neglected in the course of most general physical examina-

tions. Frequently this is due to the lack of time on the part of the busy doctor as well as the annoyance of having to set up equipment which is infrequently used. In many cases, however, it seems that even the simple digital examination of the rectum has been omitted. Frequently we see patients on whom the practitioner has resorted to x-ray studies in the presence of symptoms rather than conducting an adequate examination. A false sense of security is obtained with a negative barium enema although it is well known that barium studies of the rectum are notoriously inadequate. A portion of the blame may be laid upon the medical schools for not offering more adequate treatment in undergraduate and postgraduate education in the manner of conducting a proper proctoscopic examination. Early diagnosis is primarily a medical responsibility and it requires better education of the doctor as well as the education of the patient to the point where he will cooperate with the doctor in the necessary examination.

Treatment

The discussion of treatment will be limited to those lesions which may be visualized through the proctoscope or sigmoidoscope. In eradication of polyps through the rectal approach fulguration, coagulation or surgical excision is utilized. The method to be used varies with the size and configuration of the tumor and also its relation to the peritoneal reflection.

The tiny sessile adenomas 2 or 3 millimeters in diameter which are seen most commonly we usually destroy directly with fulguration without biopsy. The amount of fulguration necessary to destroy them is very small and it can safely be done anywhere in the bowel within the reach of the sigmoidoscope. It is sometimes advantageous to destroy these tiny lesions at the time they are found since it is occasionally very difficult to locate them again. We often do this as a safe and simple office procedure with no more discomfort to the patient than a routine proctoscopic examination. Small pedunculated polyps may be destroyed with direct fulguration or an electric snare may be employed. The electric snare has the advantage of saving the entire specimen for laboratory examination. If fulguration is used to char the polyps, representative biopsies should be routinely taken before the lesions are destroyed.

The uncertainty of the location of the peritoneal reflection adds a hazard in the adequate treatment of the large rectal lesions. This is especially true in removing tumors from the anterior rectal wall in females because of the great variability in the depth of the culdesac. Pedunculated polyps with a long thin pedicle usually present no great difficulties regardless of the size of the adenoma itself, but with sessile growths or with pedunculated lesions with a short thick stalk considerable more difficulty is encountered. Flat or sessile tumors on the posterior or lateral rectal walls below the peritoneal reflection may be fulgurated or coagulated almost with impunity. The charring may extend through the entire thickness of the rectal wall if it is thought necessary for the destruction of the tumor. A charred crater remains which heals slowly but usually uneventfully. On the anterior wall, however, it is much safer to be more conservative with the destruction of the tumor and to repeat the fulguration later if any tumor tissue remains. This also holds true for any lesion above the peritoneal reflection. It is much better to err on the side of conservatism and destroy the tumor in stages than to run the risk of perforation and peritonitis. There is no evidence to indicate that stage destruction of a tumor by fulguration increases the tendency to malignant degeneration in epithelial tumors of the bowel. It is often possible with benign lesions in the rectal ampulla to dilate the sphincter sufficiently so that a surgical excision can be done. This is especially applicable in the larger broad based lesions which are freely movable on the mucosa. An incision can be made through the mucus membrane around the base of the tumor and the entire lesion along with a margin of normal tissue can be easily dissected free. Tumors of the

same type higher in the ampulla can frequently be removed using a modified Harrison-Cripps procedure if sufficient exposure cannot be obtained through the intact sphincter. The entire sphincter mechanism and the rectal wall are severed in the midline posterior and the coccyx excised. This opens the posterior wall of the rectum widely and will give adequate exposure for the removal of large benign mucosal tumors. The rectal wall and sphincter are then repaired in layers. The advantage of surgical excision is that the entire specimen can be removed intact and studied microscopically for signs of malignant degeneration. Freely movable submucosal rectal nodules should also be excised surgically.

Extreme caution must be used in the destruction of polyps definitely above the peritoneal reflection. The bowel wall is normally quite thin and a definite respect for this thinness must be maintained at all times. If care is not exercised it is very easy to expose a lesion in the end of a sigmoidoscope and with slight pressure to produce "tenting" of the bowel wall. This stretches the wall of the bowel over the open end of the scope like a drumhead which greatly reduces its thickness and also the margin of safety. In this case the slightest error in judgment as to the strength or amount of fulguration used will cause perforation. We never use coagulation current above the peritoneal reflection because of the difficulty of determining the depth of penetration of the coagulating process. With fulguration on the other hand the destructive process is more restricted to a superficial area and consequently is much easier to control. It is unfortunate that if one does err in the type or amount of current used and perforation does ensue it is often 48 to 72 hours before a diagnosis can be made. This delay is due to the time necessary for the excessively fulgurated area to slough out leaving a hole in the bowel wall. Immediate perforation of the bowel with over zealous destruction of adenomas has been known to occur at the time of the fulguration. If this should happen immediate recognition by the operator of this disaster is imperative and a laporotomy done to close the defect. It is for this reason that the fulguration of adenomas, except for the very tiny ones, should be done as a hospital procedure.

In the removal of adenomas above the peritoneal reflection other than the tiny sessile or pedunculated variety the patients should be routinely prepared with non-absorbable sulfonamides. Usually sulfathaladine is used in a manner identical with routine preparations for colon resections. This is strictly an expectant measure and is used as insurance against the possible development of peritonitis in the event that a small delayed perforation should occur. We also use sulfathaladine in those cases in which a large or extensive area is fulgurated below the peritoneum as well as in those cases in which surgical excision is used. We feel that the postoperative course is smoother and the healing more rapid if the secondary infections in these raw surfaces can be controlled. The preoperative preparation of these patients with non-absorbable sulfonamides is usually begun at home. The patient can then enter the hospital the day before the procedure and thus greatly reduce the length of the period of hospitalization. The sulfonamides are continued during the postoperative phase for as long as they seem indicated.

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## III. MEDICAL SCHOOL NEWS

### Visiting Lecturers

Dr. James Braillsford of the Department of Radiology, St. Chad's Hospital, Birmingham, England, will visit our campus November 23 and 24. He will give a special Kellogg lecture in Todd Amphitheater at 1:00 p.m. Wednesday, November 24. His subject at that time will be "Dysplasias and Dystrophies of Bone." He will also give a special lecture on Tuesday, November 23, at 8:00 p.m. in the Medical Sciences Amphitheater. The subject for the Tuesday evening lecture will be "Diagnosis of Bone Tumors." Everyone interested is welcome to attend both these lectures.

Distinguished physicians who will visit our campus next week to deliver Kellogg lectures include.Dr. F. R. Keating, Jr., of the Mayo Clinic, Rochester, and Dr. Warren Nelson of the University of Iowa, Iowa City. Dr. Keating will discuss "The Normal and Pathologic Physiology of the Thyroid Gland" and "The Use of Radio-Iodine in the Study and Treatment of Thyroid Disease." Dr. Nelson's subject will be "The Physiology of the Testis and Male Hypogonadism." Time and place of the presentations are listed elsewhere in Bulletin.

### To Members of the Medical Foundation and Alumni of University Medical School:

The "Bulletin of the University of Minnesota Hospitals and Minnesota Medical Foundation" welcomes news items regarding alumni of the University Medical School which may be of interest to its readers. Such material may be telephoned or may be mailed directly to the Editor at the University of Minnesota Hospitals.

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### Minnesota Foundation Members

The Bulletin will print from time to time the names of all those who have recently become members of the Minnesota Medical Foundation.

Morris H. Lax, 438 Hamm Bldg., St. Paul
S.E. Gilkey, 400 Shubert Bldg.,St. Paul
H.O. Hoff, 501 E. 4th St., Duluth
E.R. Hudec, Echo
T.J. Jensen, 2031 W. Superior St., Duluth
Eugene M. Kasper, 372 St. Peter St., St. Paul
John B. McAdams, 1015 Lowry Bldg., St. Paul
Harold H. Fesler, 1144 Lowry Bldg., St. Paul

### Kellogg Foundation Lectures

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| Dr. F. R. Keating, Jr. | The Normal and Pathologic Physiology of the Thyroid Gland - The Use of Radio-Iodine in the Study and Treatment of Thyroid Disease - | Monday, November 22, 1:00-2:00 Eustis Amph. 2:00-3:00 Powell Hall Amph. |
| Dr. Warren Nelson | The Physiology of the Testis and Male Hypogonadism - | Tuesday, Nov. 23, 2:00-4:00 p.m., Eustis Amph., U. H. |
| Dr. James Braillsford | Dysplasias and Dystrophies of Bone | Wed., November 24, 1:00-3:00 p.m., Todd Amphitheater, U. H. |
| Dr. K. W. Stenstrom | The Role of Irradiation in Therapy of Carcinoma of the Breast | Fri., November 26, 2:00-3:00 p.m., Eustis Amph., U. H. |