Relying on this feature alone, one would be justified in so classing them. It is when the tissue is stained by the Hasagawa method that the similarity ceases, for we were unable to obtain a reduction of the alkaline silver solution in cases of basal cell epithelion from other locations. The argentaffin character of the cells in the tumor of the ileum, as well as the two growths of the appendix, is clearly demonstrated.

115 West Franklin Street—1609 Linden Avenue.

CARCINOMATOUS DEGENERATION OF RECTAL ADENOMAS

REPORT OF SEVEN CASES

FRANK C. YEOMANS, M.D.

NEW YORK

Adenomas are the commonest variety of benign intestinal tumors and may occur in any segment of the intestinal tract; chiefly, however, they are found in the rectum and then, in the order of frequency, in the ileum, colon, ileocecal valve and duodenum.

Dewis reported 219 benign intestinal tumors, 101 of which were in the rectum. Of the latter, eighty-one were adenomas; ten, myomas; six, lipomas; two, fibromas, and two angiomas.

In form these tumors are either sessile or pedunculated. Adenomas develop as the solitary polyp, multiple polyposis or villous tumor. They have a common origin from the mucous membrane and are of the same histologic structure; namely, glandular, with connective tissue intermingled.

In the majority of instances, a single or a few adenomas occur most frequently in children from 3 to 10 years of age, although they are not unusual in adults.

In my series of thirty-five cases in children and young adults, no single growth has been larger than an English walnut.

On the other hand, in adults the tumors may reach an enormous size, completely filling the bowel lumen.

When the solitary type assumes the polypoid form, the attenuated pedicle frequently breaks and the tumor is cast off, spontaneous cure resulting. Adenomas may undergo hyaline, myxomatous or cystic degeneration.

In adults, single adenomas are usually sessile or have only short pedicles. Bleeding and a sense of weight in the pelvis are the characteristic symptoms. Unless thoroughly removed at the base, they are likely to recur and are prone to malignant degeneration.

Villous tumor is a rare neoplasm, usually single and occurring in adults. It arises from the mucosa and is attached by a broad base, planarlike rather than spherical. Grossly, its surface is covered with soft, wavy papillae which bleed freely on contact. When palpable in the rectum, it imparts a soft, velvety feel. Ordinarily the size of an egg, it may become fist size (Cripps), or fetal head size (Allingham), filling the rectum; it then tends to drag down the mucous membrane as a pedicle or to become the apex of an intussusception. The usual site is the rectum or pelvic colon.

Because of the pronounced tendency of villous tumor to recurrence and to malignant change, thorough extirpation of the base should always be practiced.

MULTIPLE POLYPOSIS

The pathologic changes, course and treatment of multiple polyposis differ in so many important respects from those of simple adenomas that the condition demands separate consideration as a distinct disease entity. It is a comparatively rare condition but is the most important and serious type of innocent neoplasm of the intestine.

The usual site of these neoplasms is the distal colon and rectum. Yet the tumors may literally rud the mucosa from the ileocecal valve to the anus, becoming less numerous in the higher levels. In a review of thirty-four cases, Thorebecke found the rectum involved in twenty-three; the colon and rectum in five, and the colon alone in six.

In Doering's 3 compilation of fifty cases, children were affected more frequently than adults.

The earliest instances that I have seen were in boys of 5 and 7 years. Approximately two thirds of the cases occurred in males.

In the early stages of multiple adenomas there is a diffuse, marked hyper trophy of the epithelial lining. This accords with the view of Verse that irritation (bacterial, chemical or mechanical) is a predisposing factor.

Clinical experience justifies the opinion that the greater number of these cases are inflammatory in cause. The theory of a congenital defect or a pre-natural sensibility of the tissues, furnishes a basis for the disseminated adolescent type of multiple polyposis, without demonstrable gross evidence of associated irritation. A familial tendency, observed in several instances, favors this view.

In 1839, Rotkansky interpreted the adenomas developing at the margin of healed ulcers as islets of mucosa caught by the cicatrical tissue in the process of repair.

The several polypi, noted by Mummery and others, in the immediate vicinity of old intestinal stricture and hyperplastic tuberculosis are most probably secondary to irritation of the lesion with which they are associated.

The tumors are small and mostly sessile at first, but in their later development many, in some cases the majority, become pedunculated. In diameter they vary from 0.5 cm. to 2 or 3 cm. The intervening mucosa usually shows chronic inflammatory changes.

As a result of traumatism by the feces and hyperperistalsis, ulceration of the tumors is frequent.

The two essential elements comprising the adenomas are the fibrous tissue stalk, derived from and continuous with the submucous connective tissue, and the epithelium covering this stroma, which is continuous over the pedicle with the normal epithelium lining the intestinal wall. Both the epithelium and the stroma participate in the diffuse neoplastic process.

The course of the disease is slow but progressive, usually over a period of from one to five or more years.

As a result of dysenteriform bowel movements, multiple adenomas per se may have a malignant constitutional effect, but the chief danger in their neglect or improper treatment is their proneness to malignant degeneration. In fifty cases reviewed by Doering, and eleven by Soper, adenocarcinoma was present in twenty-six (43 per cent). 5 reported eight cases, five of which showed malignant growth.

Another series of recorded cases showed a malignant change in approximately 50 per cent. Accumulating clinical experience tends to show that practically all cases of multiple polyposis eventually undergo malignant degeneration when allowed to take their natural course.

Both clinically and by histologic study of the specimens, the transition from simple inflammatory hyperplasia to tumors pathologically cancerous can be traced through the stages of inflammation, gland cell hypertrophy and hyperplasia, and adenoma to definite adenocarcinoma. It is a logical inference that continuation of the irritative factors that induce the adenosas stimulate epithelial hyperplasia until it breaks through normal bounds and becomes malignant. Malignant transition may occur in widely separated tumors. For this reason negative observations in one or more excised growths do not exclude the possibility of others in the same case being malignant.

Metastasis to the abdominal lymphatics, and the liver, kidney and spleen has been noted.

**DIAGNOSIS**

The diagnosis of intestinal polyposis is based on the history, frequently of a colitis and a discharge of blood, and on the physical conditions present.

Digital palpation will usually detect one or more tumors in the rectum, but proctoscopy is essential when they are situated at a higher level. In no case should inspection be omitted to determine the number, size, character and distribution of the growths. In cases of segmental or disseminated polyposis of the colon, the roentgen rays often show a striking and characteristic picture. Roentgenographic examination is also invaluable in demonstrating associated lesions, such as chronic ulcerative colitis, multiple diverticulitis and obstruction. In rare instances biopsy is essential for a positive diagnosis.

**TREATMENT**

Tumors in the rectum and sigmoid, accessible through the proctoscope, should be snared off. Snaring and cautery may result in a cure. Moreover, this procedure should precede more radical intra-abdominal operations, for even when colectomy is performed, unless the tumors in the rectum have been removed, the symptoms persist in a modified form.

In the disseminated type, the prognosis is best when the tumors are localized to a segment of the bowel that can be excised. This frequently means a partial or total colectomy, which the weakened condition of the patient may interdict. Less radical surgical procedures are appendicostomy or colostomy for irrigation; ileostomy by the Brown technic to divert the fecal current and for colonic flushing and colosigmoidostomy. These measures are largely palliative, but in some instances the neoplastic process is held in check, the tumors regress, and the general condition of the patient is so improved that colectomy can be undertaken with more favorable prospects of success.

Of four cases of polyposis that I observed, one developed carcinoma.

**REPORT OF CASES**

Case 1.—J. T., a man, aged 29, who had had intermittent bloody diarrhea of fourteen months' duration, showed typical multiple adenosas at sigmoidoscopy, varying in size from that of a pea to that of a hazelnut, and extending beyond the reach of the tube. I did a colostomy in the transverse colon, as tumors were not palpable through the bowel wall above the sigmoid. Unfortunately, when the bowel was opened on the fifth day it was found that adenoma extended to the hepatic flexure and presumably to the cecum. By irrigation through the colostomy, the greater number of growths distal to the stoma disappeared, and those remaining regressed. The growths proximal to the colostomy were influenced to a less degree, but the patient was restored to health and carried on his usual occupation for three years. Then intractable diarrhea recurred through the colostomy, and he died of exhaustion three weeks after ileostomy.

The excised colon showed many small adenosas on the mucosa distal to the colostomy, while large areas of adenocarcinomatous degeneration were present proximal to the colostomy.

Case 2.—F. L., a woman, aged 33, illustrates the development in the same person, in sequence, of infective ulceration, adenoma and cancer. Ulcerative colitis had existed for seventeen years with remissions and exacerbations. Several small sessile adenosas observed in the course of treatment were removed. Six years later, the patient noticed some blood in the stools for one month, and digital examination showed on the left side of the rectal ampulla an elevated tumor 4 cm. in diameter, with a soft, smooth surface and indurated base, the entire mass freely movable with the mucosa. Sections of the tumor, after removal one month later, demonstrated typical adenocarcinoma. This was, in my experience, the earliest case of carcinoma of the rectum to come to operation.

Case 3.—M. B., a woman, aged 37, after suffering from constipation and rectal bleeding of six months' duration, had been subjected to a hemorhoidectomy under the mistaken diagnosis of "bleeding piles." Blood clots continued to pass with, and independent of, the stools. The examining finger felt a freely movable growth, the size of a hen's egg, at the level of 3 inches, and examination of sections of a biopsy specimen resulted in a diagnosis of malignant adenomatous poly. Local excision relieved all symptoms and was followed by a restoration of health for three years. Then there was a recurrence. Local removal of the growth with wide excision of the base resulted in a clinical cure that is now of more than five years' duration.

Case 4.—D. C., a woman, aged 57, had complained of "bleeding piles" for many years, and for several months of a protrusion at stool which had to be replaced. A small pedunculated polyp just above the anal canal was removed by ligature. The pathologist reported malignant degeneration of an adenoma. The site of attachment was then excised broadly, the tissues showing only chronic inflammation. Nearly five years has now elapsed without signs of recurrence.

Case 5.—K., a man, aged 76, had had rectal bleeding for eight years, with progressive constipation and a protrusion which at first occurred at stool and could be replaced but which in time protruded permanently from the anus, forcing the patient to sit on one buttock. Examination showed a reniform tumor 3½ by 2 inches attached just within the anal verge of the left side and to both commissures for about two thirds of the circumference of the anal ring. Treatment consisted in local wide excision. Histologic examination of the growth confirmed the clinical diagnosis of adenocarcinoma. This is a striking example of a simple adenoma becoming malignant as a result chiefly of repeated and prolonged trauma.

Case 6.—E. P., a man, aged 60, had had bleeding from the colon for seven months with frequent stools and tenesmus, and a loss in weight of 10 pounds (4.5 Kg.). The examining finger could just reach a tumor about the size of a hickory nut, hard, and with a nodular surface. Its rather broad base of attachment was not indurated. Proctoscopy showed that the tumor was attached to the margin of the highest valve of Houston. In May, 1925, the base of the tumor was coagulated by surgical endotherapy applied through the operating proctoscope, and a biopsy specimen taken which showed adenocarcinoma. All symptoms were relieved and now a smooth scar marks the site of removal.

Case 7.—C. M., a man, aged 67, during the six months prior to consultation had been passing bright red blood with the stools and had had two large hemorrhages. He had lost 8 pounds (3.6 Kg.), and felt weak and dizzy.
Digital examination was negative, but proctoscopy showed a growth 3 cm. in diameter, at a level of 5 inches, attached to the upper surface of the highest Houston valve. The base, 2 cm. in width, did not convey the impression of being indurated when a probe was applied to it. In May, 1926, without anesthetic, the growth was snared off, very slowly through the proctoscope, a small portion of the adjacent mucosa being grasped in the loop. Hemorrhage was slight, and the wound was phenolized. The pathologist's report on the growth was adenocarcinoma. Five days later, six seeds, each containing 0.3 millicuries of radon, were implanted around the site. A soft, smooth scar is present now, and there have not been any signs of recurrence.

COMMENT

Although a solitary adenoma may exist for years without becoming malignant, the instances here reported justify the conclusion that every neoplasm of this type should be considered a precancerous lesion and promptly eradicated.

In general, the more sessile a growth the greater is its liability to malignant change.

It may be reasonably assumed that many cancers of the rectum and rectosigmoid develop from adenomas that could be detected and removed while still innocent, if proctosigmoidoscopy were employed more regularly in routine examination.

A polypoid adenoma that is accessible can usually be ligated and cut off safely. If sessile, wide excision of the base is indicated and cautery or coagulation of the site of removal.

Solitary growths beyond reach of the finger but accessible through the operating proctoscope often present a difficult problem. If pedunculated, they may be snared off. I have had a practical strong snare made for this purpose.

When sessile, but removable, the possibility that the growth is already malignant must be borne in mind. Under these circumstances electric coagulation (surgical endothermy), or radon implantation, when the tumor is snared off, are efficient safeguards against dissemination in case the growth has already undergone malignant change. Otherwise, approach to these high-lying growths must be made through the abdomen, which involves the risk of peritoneal infection when the colon is laid open.

171 West Seventy-First Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. MCLLANNA N AND MCLLEARY AND DR. YEOMANS

Dr. Joseph C. Bloedsoe, Baltimore: In 1913 when I reviewed every case of tumor of the stomach and the colon, including the rectum, all benign polypoid tumors of the stomach and colon were found at autopsy. Then came a period in which we operated for certain reasons, and found a polypoid tumor in the portion of the resected colon in which there also was a carcinoma. We have gone over all the tumors of the small intestine, and the paper published by a Chinese surgeon, now professor of surgery at Peking, is most enlightening. This is a submucous tumor. There is every reason to believe that the submucous tumor, whether we find it in the appendix, small intestine or stomach, can produce carcinoma. I myself have had for the first time seen and operated on a man with a tumor clinically cancerous and of three months' duration. There are tumors that may precede cancer. There is every reason to believe that cancer never begins as cancer, and now we are getting those things that ultimately develop into cancer. I believe that in cases of polypoid tumor in the stomach or intestine it is a good plan to resect just as if it were a cancer. I have quite a number of cases in which the abdomen has been opened and the tumor taken out by the pedicle, perhaps not with the cautery and perhaps not followed by radium treatment, but in which there was a recurrence and death. It is just as easy to resect. There is no danger in the resection of an intestinal tumor, but removal of a tumor in the rectum by the combined operation is one of the most difficult operations in surgery. When one sees a small polyloid tumor and can get at it with a wire or with diathermy, the temptation, of course, is to remove it that way. There is danger in the partial removal of these apparently innocent tumors. Perhaps in twenty years, with dangerous growths, will be entirely treated in a milder way, but whenever a radical operation can be done for a tumor in the wall of the stomach, the small intestine or the large intestine, or rectum, one should do it.

Dr. Curtice Rossor, Dallas, Texas: James Ewing has said that it is very fortunate that cancers are preceded by various forms of chronic irritation, many of which we can detect and eliminate and thus prevent cancer. Practically all anorectal cancers fall into one of two divisions: adenocarcinomas arising from the rectal glands, and squamous cell neoplasms from anal tissues. Dr. Yeomans has brought to our attention the fact that adenomas, single or multiple, are preceded by irritation, chiefly inflammatory, and has stressed the high incidence of those benign adenomas in which the stages of inflammation, gland cell hypertrophy and hyperplasia have been continued to hyperplastic degeneration. Dr. Yeomans (I am one) will go further and make the statement, difficult to prove but nevertheless impossible to refute, that all glandular rectal cancers were first benign adenomas, and that their detection and elimination is, therefore, the logical prophylaxis of this division of anorectal malignancy. The general dissemination of what is already known about the origin of the squamous cell division should make it as preventable as the other forms of malignant epithelial growths. When, in other words, we are all ready to admit that the antecedent hemorrhoid, the neglected fissure or fistula, the chronically infected anal canal are the exciting factors and the precursors of squamous cell malignancy, the complete prophylaxis of both divisions of anorectal cancer will be apparent.

Dr. Louis B. Graham, Indianapolis: A rectal adenoma is an excessive overgrowth of the normal glandular elements of the rectal mucosa. The only difference between it and a malignant adenoma is that it does not perforate the muscularis mucosae or basement membrane. Otherwise, it very closely resembles the malignant growth. Although they are referred to usually as innocent epithelial tumors, it is very important to remember the established fact that these seemingly simple tumors of the rectum when viewed by the naked eye are often of the adenomatous type, that is affected by a tendency to undergo malignant transformation. This transformation occurs more frequently in the multiple variety; yet we must look on the single adenoma with suspicion and consider the possibility of its being a precancerous condition. In fact, malignant changes have been found in some part or another of large adenomas. So marked is the tendency of these apparently simple tumors to become malignant that Mummery regards them as merely a stage in the development of malignant disease. Therefore, every rectal adenoma, being regarded as a definite precancerous condition, should be removed as soon as it is diagnosed, regardless of the symptoms presented. These adenomas are easily diagnosed. The diagnosis as to whether malignant transformation has occurred will be determined a microscope. A section of a single polypoid or multiple variety, the observation that several tumors do not show any malignant transformation means nothing so far as the other tumors are concerned. It has been clearly demonstrated that a benign adenoma may be almost contiguous with a malignant adenoma. It occurs to me that it is good teaching to state that all rectal adenomas, if let alone, will eventually develop malignant transformation at some point or another.

Dr. Alexis McGlannan, Baltimore: As far as our knowledge goes, the attack for which this colored man came to the hospital was his first gastro-intestinal upset. Carcinoid as a precancerous lesion, I think, depends on what we believe about the cells from which it is derived. Certainly, there is some difference from the ordinary epithelial cell. The argentaffin granules are characteristic of this type of cell, and these
granules are not found in the ordinary epithelium that makes up the usual adenoma of the gastro-intestinal tract. We have tested this reaction in studying this particular tumor. We took a carcinoid of known malignancy and put it through the silver solution; we were unable to get any argentaffin granules in the known cancer, while we got them in all of our sections from the carcinoid tumor. With a tumor of the intestinal wall it is better to resect than it is to attempt to take out the small tumor, and leave the wounded intestinal wall to heal in the best way that it can under the surgery. We resected the bowel in this man because of the intussusception.

**TRANSFUSION IN INFANCY AND CHILDHOOD**

**REVIEW OF FIVE HUNDRED AND FIFTY-SIX CASES**

J. BUREN SIDSBURY, M.D.
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Transfusion in infancy and childhood is a relatively recent therapeutic measure. The first transfusion of blood for hemorrhagic disease of the new-born was performed in New York City by Dr. Alexis Carrel in 1908. During the next ten years, transfusion in infancy was mainly confined to this condition. It has been only within the past decade that transfusion in infancy and childhood has been more generally used. In 1921, Robertson, Brown and Simpson made this significant statement: "From a perusal of the literature we have only been able to find two reports of blood transfusion in childhood [report of nine cases by Kerley and thirteen cases by Lowenburg]. This does not include hemorrage of the new-born."

It has been only in the last twenty-five years that the existence of isoagglutinins in the blood has been known. This discovery was made by an Englishman, Shattuck, and an Australian, Landsteiner, in 1900. Following this, Jansky, in 1900, demonstrated that blood could be divided into four groups according to agglutinins. In 1910, Moss independently made a similar classification of agglutinins in blood. Since these discoveries, blood transfusion has been put on a rational basis, and its use as a therapeutic measure is becoming more general.

**BLOOD GROUPING**

It is now universally agreed that some form of blood matching is absolutely essential before giving a transfusion. Exceptionally, there may arise a need for immediate transfusion when a delay of a few minutes would seem to cost the life of the patient, but the few minutes required for the matching is time well spent, even though the emergency seems great.

The chief value of blood grouping today is as an aid in eliminating donors. I do not consider it a safe method of selecting a donor—that is, if only the grouping is to be done before the transfusion is given. So frequently has it been found that donors of the same group do not match that only cross-matching is relied on. This is the only safe method of selecting suitable donors. In my experience the so-called universal donor has not always matched, nor have the donors in the same group matched any more frequently. In the last two years, I have found universal donors incompatible in twelve cases. This incompatibility was due to agglutination in eight cases, and to hemolysis in four cases.

Dr. Glover H. Copher states that:

Until 1920 the universal donor was used for transfusion of any group. The practice was discontinued because of reactions traceable to the use of such blood. In spite of the high dilution to which the incompatible plasma is brought after introduction into the veins of the recipient, fatal accidents were recorded from the agglutination of the red blood cells of the recipient by the donor's plasma when the recipient belonged to a group other than that of the universal donor.

Reports of the Inter-Allied Surgical Congress state that fatal accidents have occurred from hemolysis of the blood corpuscles of the recipient by the donor's plasma.

It was once taught that infants under 6 months could always be transfused with safety from the mother. We now know this to be untrue. Hallan found that the mother's blood had greater agglutinating power than blood from the umbilical vein of her infant. Unger states that 13 per cent of new-born infants show the presence of agglutinins in the serum as against 97 per cent of adults, and that 25 per cent of the cells in the new-born can be agglutinated as against 50 per cent in adults.

According to Jones, 197 specimens of blood from young infants were examined, and 78.8 per cent could be placed in one of the four groups. He showed that the different groups occurred with approximately the same frequency in the new-born as in adults. Iso-agglutinins have been demonstrated in the blood of a seven months fetus.

In 1920, 160 specimens of umbilical cord blood were examined by Minot and Weld, who found that 70 per cent could be definitely grouped. Happ established the group by both serum and cell reaction in 22.7 per cent of infants between 1 and 3 months of age; in 31.8 per cent of infants from 4 to 6 months, and in 69.7 per cent of infants from 6 to 12 months. He states that after 1 year the group can be established in practically every case.

One infant in this series, who was operated on for pyloric stenosis at 3 weeks of age by Dr. T. M. Green, developed a postoperative hemorrhage twenty-four hours after operation and came near being exsanguinated. Her blood was cross-matched with her mother's, maternal grandmother's and father's blood. The serum of both the mother and the maternal grandmother completely agglutinated the baby's cells. The father's blood matched perfectly both ways. A transfusion was given, in which the father's blood was used, and the child made a complete recovery.

Another baby, 4 weeks old, very anemic from congenital malaria, would not match either father or mother. The mother's serum agglutinated the baby's cells, and the baby's serum agglutinated the father's cells. Six or eight donors were tested before a suitable one was found.

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