# The Adenoma-Carcinoma Sequence of the Colon and Rectum

*Friedrich J. Gloor*
*Institut für Pathologie, Kantonsspital, CH-9007 St. Gallen*

The concept of a polyp-cancer sequence is gaining increasing evidence as an important factor in the development of colorectal cancers [6]. With the introduction of colonoscopy of the entire large bowel, endoscopic removal of most colonic polyps has become possible. If the adenoma-carcinoma concept of evolution is valid, endoscopic resection of colonic polyps is a means of reducing the incidence of colorectal cancers. Of the various types of polyps encountered in the colon, only true adenomas are neoplasic. The neoplasic adenomatous polyps include tubulous, tubulovillous and villous adenomas of the WHO classification [10].

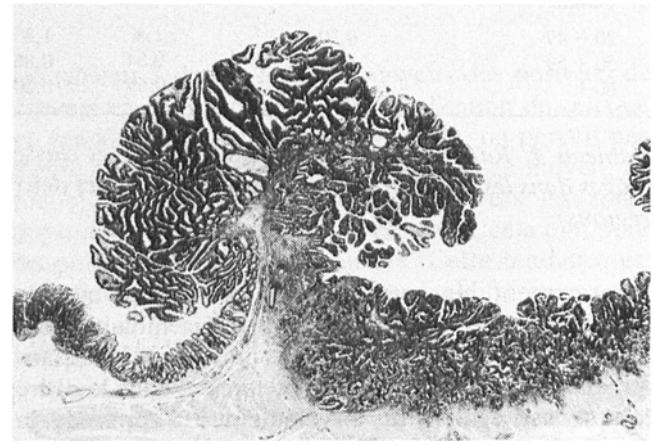

*Fig. 1. Colon sigmoides. Male, 66 years.*
*Invasive carcinoma developing within a tubulous adenoma. Contiguous changes from normal mucosa with goblet cells (at the left side) to adenomatous changes with mucus depletion into invasive carcinoma (at the right side).*

What are the arguments in favour of such an evolution?

1. A comparison of the *age distribution* of adenomas and carcinomas shows that the peak age of appearance of adenomas lies about 7–8 years earlier than that of carcinomas, if we look at asymptomatic patients with adenomas [6]. This corresponds well with the experience in familial polyposis coli [11].
2. The marked *geographical variations* in incidence of colorectal carcinomas are well established [3]. The incidence of adenomas is less well known. Several workers, however, have shown that adenomas are significantly more common in countries with a high incidence of colorectal cancers compared to low incidence areas [4, 5]. A comparative histological study of adenomas in Japan, a low incidence area of colorectal cancers, and England, a high incidence area, has shown that the malignant potential of colonic adenomas varies with size, histological pattern and grade of cellular atypia in the same way in Japan and England, but adenomas in England grow larger, show a villous pattern and severe cellular atypia more often than those in Japan, and therefore have a greater malignant potential [12].
3. The question if adenomas and carcinomas have the same *site of predilection in the large intestine* is hard to answer. Although the sites of carcinomas are well known from cancer incidence statistics, there are problems about the exact distribution of adenomas in different parts of the colorectum, even when we are looking at autopsy figures [6]. There seems to be some excess of adenomas in the right colon [11].
4. *Morphological arguments* also speak in favour of an adenoma- carcinoma concept. Careful microscopic examination of colorectal tumors reveal contiguous histological transformation from benign to malignant tissue changes in the same tumor *(Fig. 1)* [7, 11]. More recent immunhistochemical studies with identification of a number of tumor-associated antigens in tumor cells have detected a remarkable similarity between adenomas and carcinomas [14].

The question as to how often *remnants of adenomas* can be found *in invasive carcinomas* has been a matter of much discussion, but now it is evident that the percentage of remnants depends on the size of the carcinomas as well as on the number of histological sections taken from the margins of the tumor. Remnants are detected frequently in small carcinomas, but rarely in large carcinomas with extramural spread [11].

*Carcinomatous changes in adenomas* can be found rather often, as is well known by every surgical pathologist looking at endoscopically removed adenomas. The percentage of carcinomatous foci in adenoma depends on size, histological pattern and grade of cellular atypia [2, 11].

For the clinician it is important to know that cancerous changes must penetrate the muscularis mucosae for an adenoma to be regarded as clinically malignant. Superficial focal cancer of the mucosa is not known to metastasize (with some rare and debated exceptions) and is therefore not regarded as a true carcinoma [2, 7, 10].

5. If adenomas give rise to the development of carcinomas, *prophylactic removal of all adenomas* found in a given population should have the effect of

reducing the incidence of invasive carcinomas subsequently observed in that population. There are interesting, but somewhat debated, studies which seem to prove this concept [8, 9]. Controlled prospective studies in asymptomatic persons with flexible proctosigmoidoscops have to be awaited before giving a conclusive answer to this question.

6. If colorectal cancer does not arise from preexisting adenoma, what would the *alternative mechanism of histogenesis* be? The most convincing evidence of carcinoma independent of adenoma would be the demonstration of minute carcinomas in the normal flat mucosa. Such small carcinomas less than 5mm in diameter without ulceration, excluding an eroded preexisting adenoma, are extremely rare, except in the special circumstances of long- standing ulcerative colitis [6, 11, 13].

**Summary**

**The Adenoma-Carcinoma Sequence of the Colon and Rectum**

Morphological and epidemiological arguments in favour of an adenoma-carcinoma concept of evolution in the development of colorectal cancers are presented. It is highly probable that most colorectal cancers arise in adenomas. Therefore detection and endoscopic removal of adenomas is a means of reducing the incidence of colorectal carcinomas.

**References**

[1] *Arminski, T.C.* and *D.W. McLean,* Incidence and Distribution of Adenomatous Polyps of the Colon and Rectum based on 1000 Autopsy Examinations. Dis. Colon Rectum, *7,* 249–261, 1964.

[2] *Arnold, K.* and *H.F. Otto,* Frühformen des kolorektalen Karzinoms. Therapiewoche, *28,* 5001–5009, 1978.

[3] *Berg, J.W.* and *M.A. Howell,* The Geographic Pathology of Bowel Cancer. Cancer (Philad.), *34,* 807–814, 1974.

[4] *Bremer, C.G.* and *L.V. Ackermann,* Polyps and carcinoma of the large bowel in South African Bantu. Cancer (Philad.), *26,* 991–999, 1970.

[5] *Correa, P., Strong, J.P., Reif, A.* and *W.D. Johnson,* The epidemiology of colorectal polyps. Prevalence in New Orleans and International Comparisons. Cancer (Philad.), *39,* 2258–2264, 1977.

[6] *Enterline, H.T.,* Polyps and Cancer of the Large Bowel, In: Morson, B.C., Pathology of the Gastro-intestinal Tract. Current Topics in Pathology, *63,* 97–141, 1976.

[7] *Fenoglio, C.M.* and *N. Lange,* The anatomical precursor of colorectal carcinoma: Cancer (Philad.), *34,* 819–823, 1974.

[8] *Gilbertsen, C.A.,* Proctosigmoidoscopy and Polypectomie in reducing the Incidence of Rectal Cancer. Cancer (Philad.), *34,* 936–939, 1974.

[9] *Hertz, R.E., Deddish, M.R.* and *E. Day,* Value of periodic examination in detecting cancer of the rectum and colon. Postgrad. Med., *27,* 290–294, 1977.

[10] *Morson, B.C.* and *L.H. Sobin,* Histological Typing of Intestinal Tumours. Internat. Histol. Classification of Tumors Nr. 15 WHO, Geneva, 1976.

[11] *Muto, T., Bussey, H.J.R.* and *B.C. Morson,* The Evolution of Cancer of the Colon and Rectum. Cancer (Philad.), *36,* 2251–2270, 1975.

[12] *Muto, T., Ishikawa, K., Kino, I., Nakamura, K., Sugano, H., Bussey, H.J.R.* and *B.C. Morson,* Comparative Histological Study of Adenomas of the Large Intestine in Japan and England, with Special Reference to Malignant Potential. Dis Colon Rectum, *20,* 11–16, 1977.

[13] *Shamsuddin, A.K.M., Bell, H.G., Petrucci, J.V.* and *B.F. Trump,* Carcinoma in situ and "micro-invasive" Adenocarcinoma of Colon. Path. Res. Pract., *167,* 374–379, 1980.

[14] *Skinner, J.M.* and *R. Whitehead,* Tumor-associated Antigens in Polyps and Carcinoma of the Human Large Bowel. Cancer (Philad.), *47,* 1241–1245, 1981.