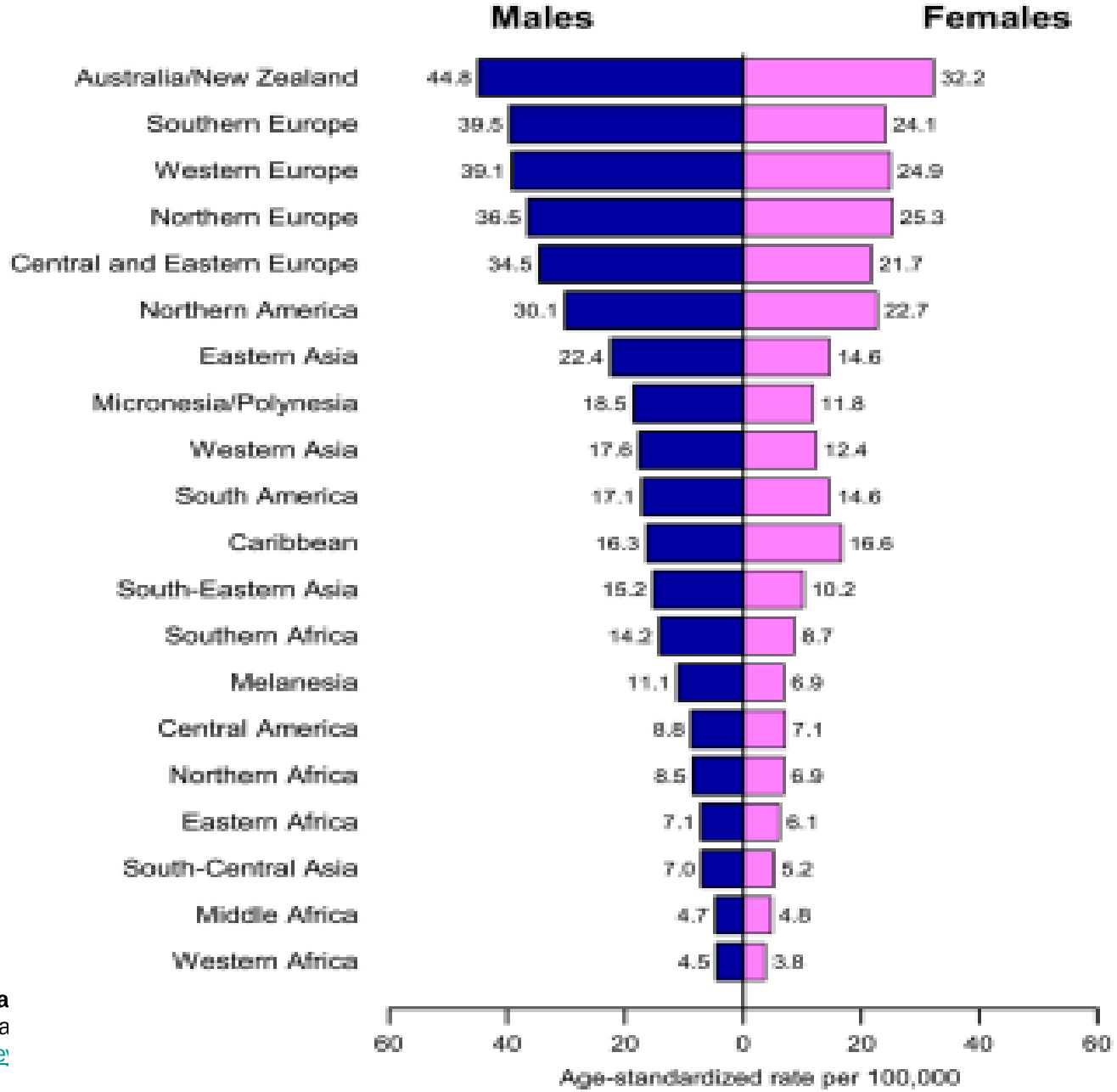
CARCINOMA OF LARGE INTESTINE

The malignant tumor
developing from elements
of a epithelium mucous a large intestine

C18 Malignant neoplasm of a colonic intestine (including caecum and appendix)
C19 Malignant neoplasm of rectosigmoid part
C20 Malignant neoplasm of a rectum

Colon Cancer Incidence Rates by Sex and World Area



CA: A Cancer Journa
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Incidence in USA 35,8 per100,000

In developing countries < 10 per 100,000

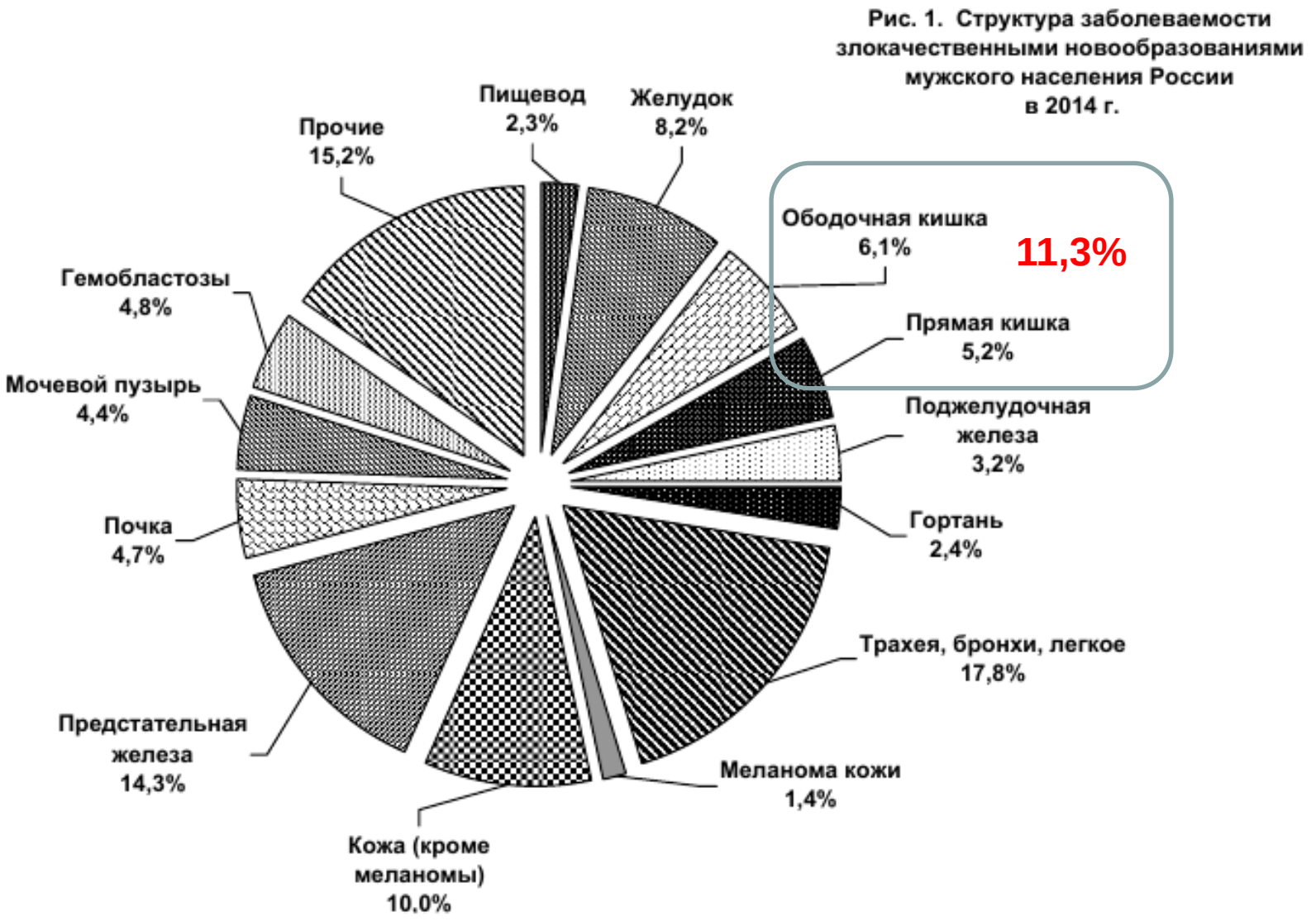
In India incidence - 7 per100,000

Mortality from a colon cancer on the second place after lung cancer

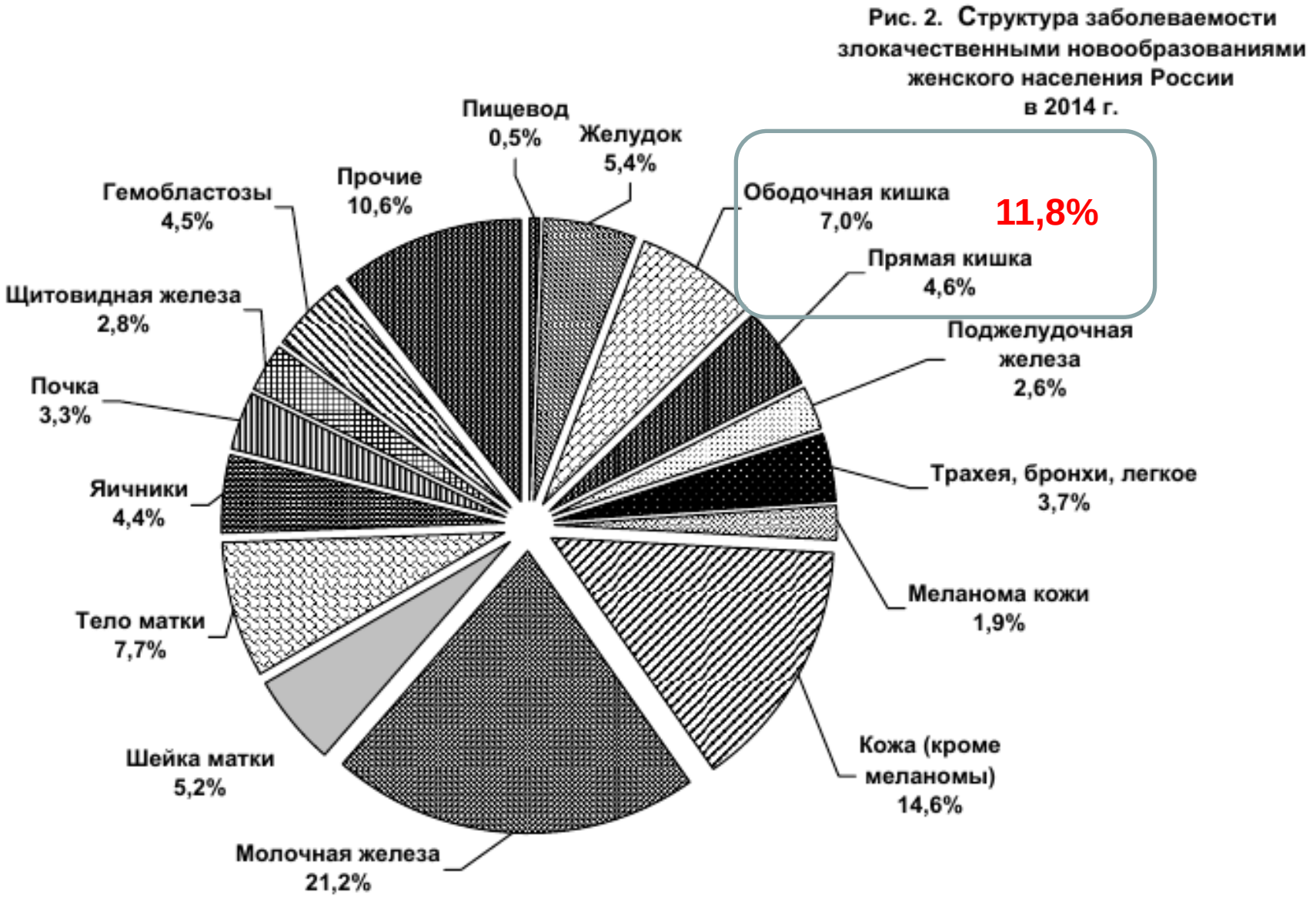
Динамика показателей заболеваемости населения России злокачественными новообразованиями в 2004-2014 гг.

Локализация, нозологическая форма	Годы											Среднегодовой темп прироста, %	Прирост, %
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014		
Оба пола («грубые» показатели на 100 000 населения)													
Все новообразования	**328,00**	**330,51**	**333,67**	**341,55**	**345,69**	**355,84**	**364,22**	**365,42**	**367,29**	**373,42**	**388,03**	**1,64**	**18,04**
Губа	2,96	2,83	2,70	2,51	2,49	2,42	2,36	2,07	1,97	1,89	1,82	-4,87	**-38,38**
Полость рта	4,53	4,49	4,55	4,78	4,89	5,08	5,18	5,37	5,36	5,55	5,77	2,58	**30,09**
Глотка	2,86	2,84	2,90	3,02	3,03	3,22	3,22	3,07	3,25	3,28	3,44	1,76	**19,46**
Пищевод	5,07	4,99	4,96	5,03	5,04	5,03	5,20	5,17	5,10	5,16	5,18	0,37	**3,82**
Желудок	30,99	30,56	29,43	29,51	28,61	28,41	28,03	26,8	26,10	25,99	25,88	-1,93	**-17,43**
Ободочная кишка	20,36	20,89	21,15	21,68	22,35	22,78	23,24	23,6	23,91	24,24	25,59	2,10	**23,80**
Прямая кишка, ректосигмоидное соединение, анус	15,97	16,61	16,58	16,83	16,9	17,64	18,02	18,00	18,38	18,36	19,03	1,62	**17,79**
Печень и внутрипеч. желчные протоки	4,60	4,57	4,34	4,43	4,56	4,67	4,55	4,56	4,39	4,73	4,96	0,56*	**5,82***
Желчный пузырь и внепеченочные желчные протоки	2,09	2,23	2,15	2,17	2,31	2,18	2,37	2,32	2,23	2,30	2,38	0,94	**9,94**
Поджелудочная железа	9,33	9,36	9,28	9,88	9,93	10,37	10,59	10,43	10,61	10,69	11,44	1,93	**21,62**
Полость носа, среднее ухо, придаточные пазухи	0,63	0,64	0,64	0,65	0,67	0,64	0,63	0,66	0,66	0,67	0,69	0,64*	**6,64***
Гортань	4,78	4,55	4,67	4,57	4,74	4,63	4,71	4,68	4,72	4,62	4,55	-0,10*	**-1,03***
Трахея, бронхи, легкое	41,39	40,6	40,16	40,23	39,99	40,2	40,15	39,19	38,74	39,06	39,48	-0,50	**-4,85**

Structure of cancer cases of men in Russia in 2014.



Structure of cancer cases of women in Russia in 2014.



Etiology

1. Heredity and family history (about 5% of patients)

- Familial adenomatous polyposis (FAP) is the second most common predisposing genetic syndrome, and is characterized by the development of hundreds to thousands of colorectal polyps in affected individuals.

Familial adenomatous polyposis Gross specimen of the colon from a patient with familial adenomatous polyposis shows innumberable small polyps. Courtesy of Robert Odze, MD.

Lynch syndrome families

Syndrome of a heriditary not polypostural colon cancer

- in the US found lifetime risks of 66% in men and 43% in women
- The mutation of genes of hMSH2 and hMLH1 is noted at 70% of patients. At the type «a» cancer arises only in a large intestine, in the type «b» at the same time there can be tumors in endometrium or a stomach, a brain, a mammary gland, or genitourinary, gepatobiliary system.

Li-Fromeni's syndrome, Gardner's syndrome, Peyttsa-Egers's syndrome, family juvenile polyposes.

2. Not heriditary-sporadic CRC

- Not heriditary-sporadic CRC makes about 95% of cases of a colon cancer
- APC gene mutations - loss of an allele in the 5th chromosome at - 30-50% of patients

Summary of Selected Risk Factors for Colorectal Cancer

that increase risk:	**Relative Risk***
Heredity and Medical History	**Factors**
Family history 1 first-degree	2.2
relative more than 1	4.0
relative with diagnosis before age 45	3.9
Inflammatory bowel disease Crohn disease (colon)	2.6
Ulcerative colitis colon	2.8
rectum	1.9
Diabetes	1.2

Summary of Selected Risk Factors for Colorectal Cancer

that increase risk:	**Relative Risk***
Behavioral factors	**Factors**
Alcohol consumption (heavy vs. nondrinkers)	1.6
Obesity	1.2
Red meat consumption	1.2
Processed meat consumption Smoking (current vs. never)	1.2
	1.2

Summary of Selected Risk Factors for Colorectal Cancer

Factors that decrease risk:	**Relative Risk* Factors**
Physical activity (colon)	0.7
Dairy consumption	0.8
Fruit consumption	0.9
Vegetable consumption	0.9
Total dietary fiber (10 g/day)	0.9

Precancerous diseases of a large intestine:

1. Single and multiple polyps

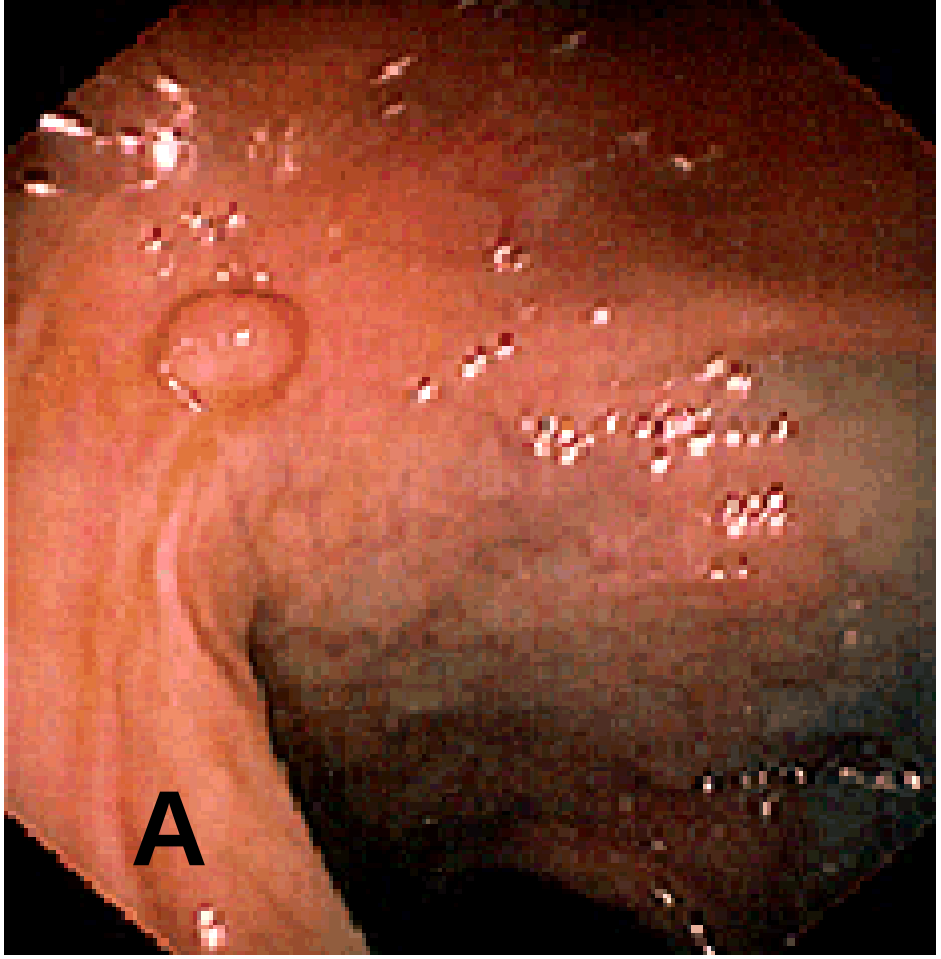
Risk of a malignancy of a polyp at the sizes to 1 cm-1,1 %, 1-2 cm-7,7 %, 2 cm – 42%.

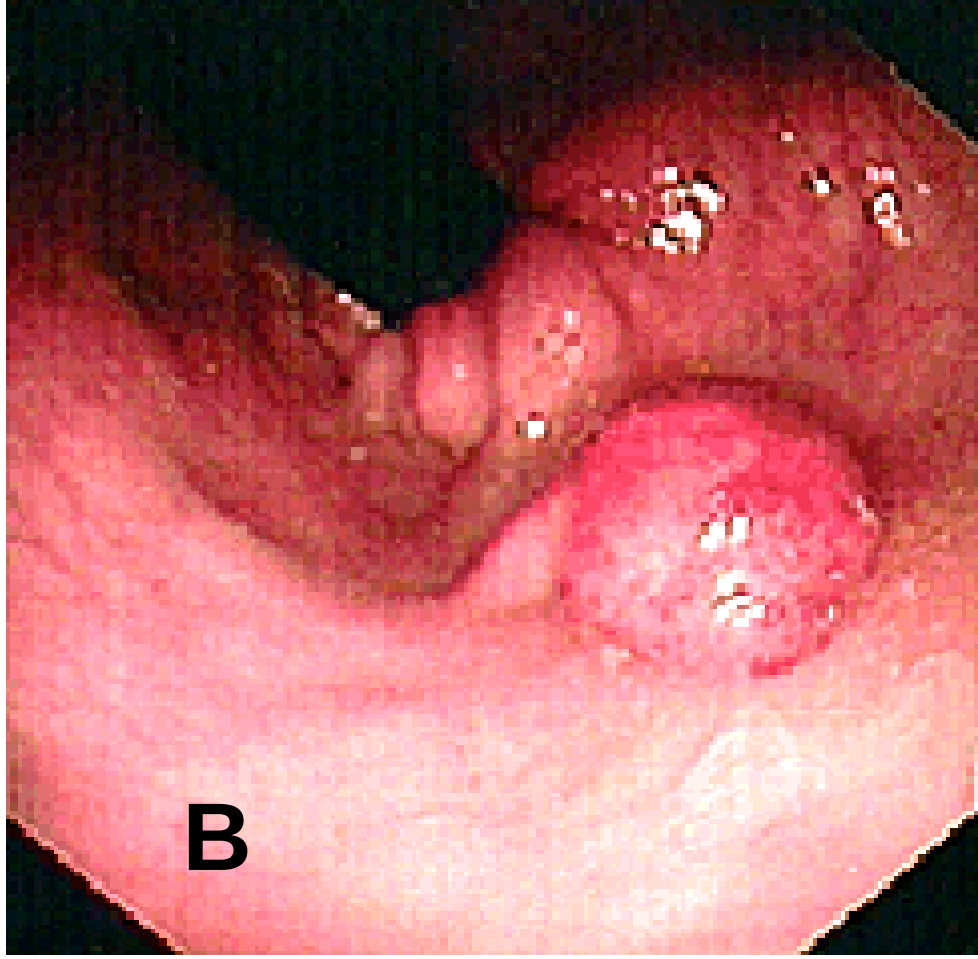
2. Nonspecific ulcerative colitis

The risk of development of cancer lasting disease more than 10 years increases up to 20%,

30 years – 60%.

3. Illness Krone of a large intestine.





Colonic polyps Over 95 percent of colonic polyps are hyperplastic or adenomatous. Although these two types have some distinctive features on gross appearance, they cannot be reliably distinguished endoscopically. Panel A: typical small sessile hyperplastic polyp that is less than 5 mm in size. Panel B: typical pedunculated adenomatous polyp. Courtesy of James B McGee, MD.

Classification

1. Patomorphological

A. Exophytic (Fungating)

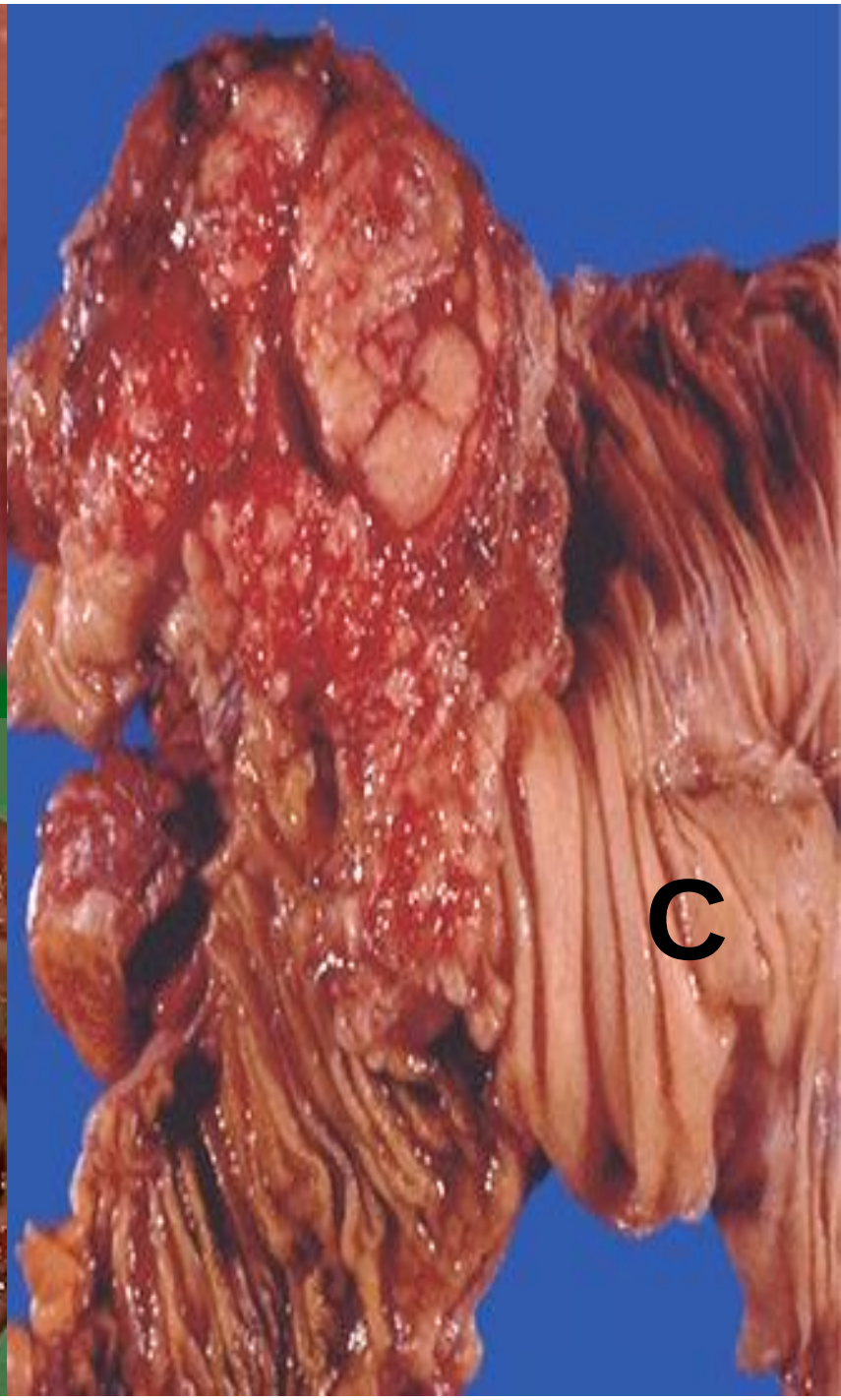
B. Endophytic (and Ulcerative)

C. Stenosing (annular, constricting, circumferrential)

D. Diffuse - infiltrative


A


B
SPECIMEN S3445-83
DATE 8-19-83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PATHOLOGY: WHO Classification

I. Epithelial
- •Adeno Ca >95%
- •Mucinous adeno Ca 17%
- •Signet ring cell Ca 2-4%
- •Squamous cell carcinoma
- •(SCC)
- •Adenosquamous
- •Undifferentiated
- •Unclassified

II. Neuroendocrinal – carcinoid

III. Nonepithelial (sarcoma)
- Leiomyosarcoma
- Liposarcoma
- Angiosarcoma etc.

IV. Hematopoietic/ lymphoid(DLBCL)

V. Unclassified

VI. Secondaries

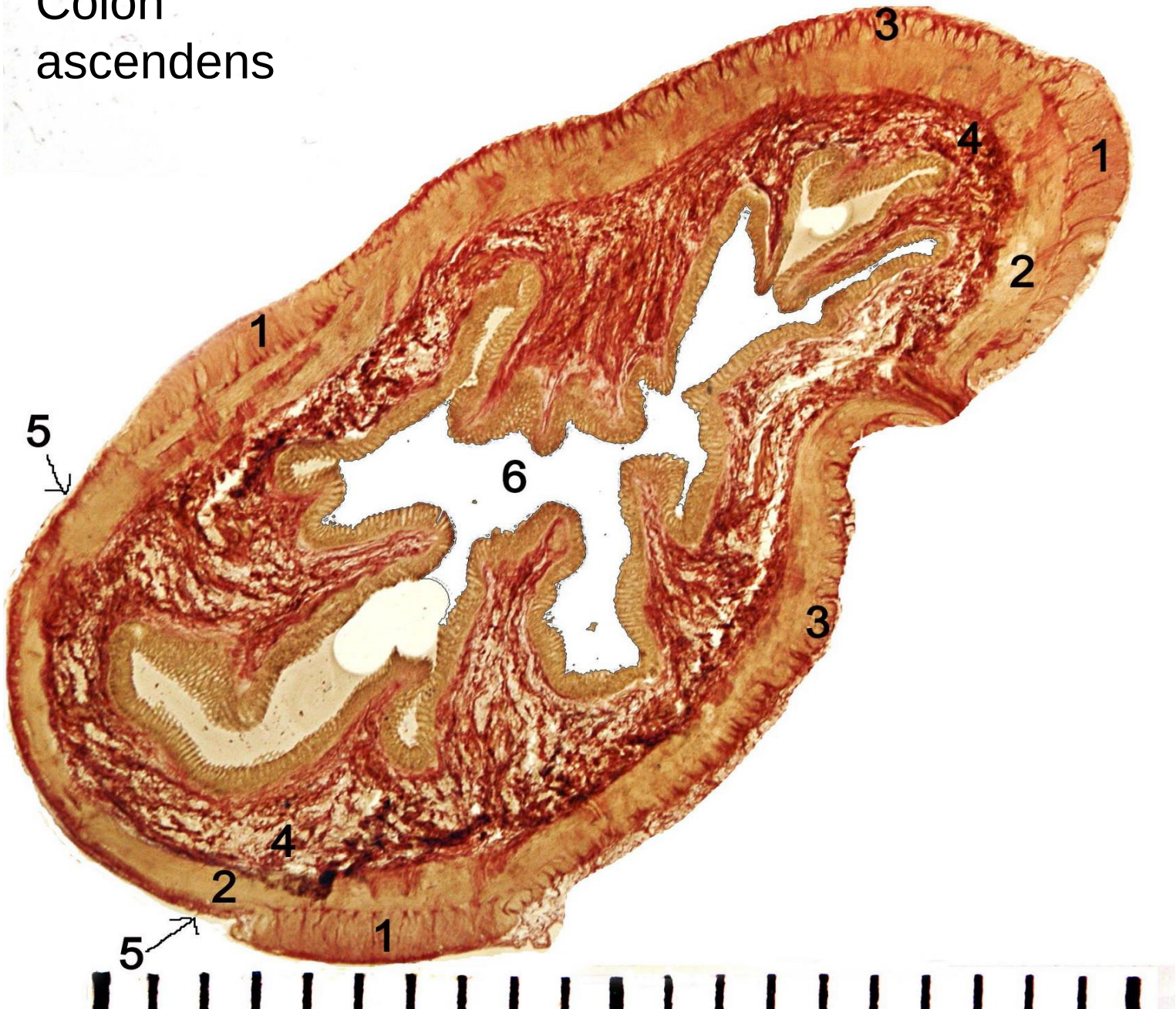
VII. Tumor - like lesions

VIII. Epithelial atypia in Ulcerative colitis

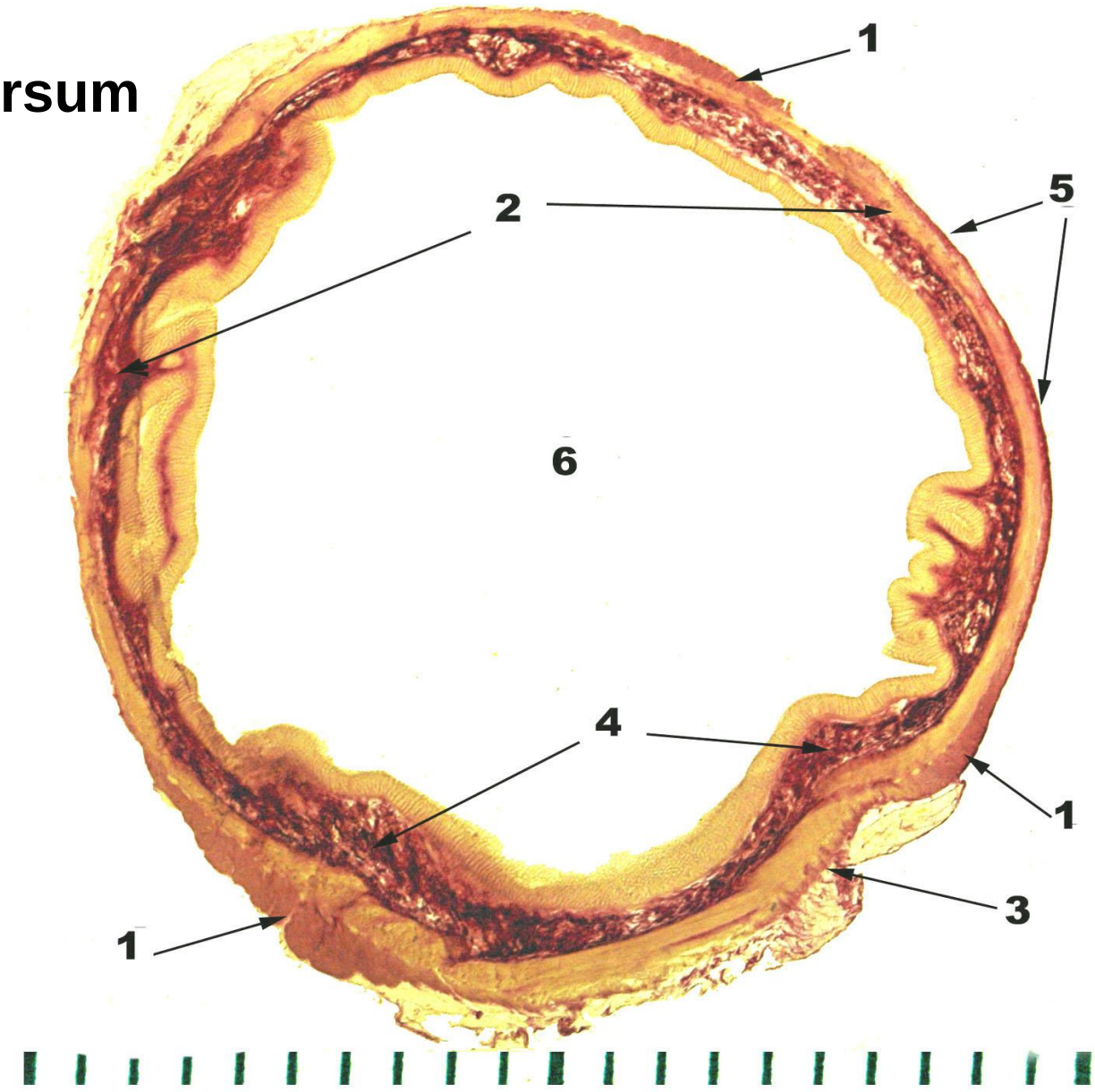
Features of microanatomy of a wall of a colonic intestine

- Thickness of a wall of a colonic intestine makes in the studied cases from 495 to 3501 microns in intertenial areas and from 1095 to 4007 microns in the field of tenia, on average respectively 1564,5±139,1 microns and 2588,2±242,5 microns
- The general width of tapes fluctuated from 14,2 mm to 25,6 mm and that averages about 30% lengths of a circle of an intestine. Width of a free muscular tape throughout a colonic intestine fluctuated from 4,3 mm to 10,3 mm, averaging 6,1±1,6 mm.
- Absolute thickness of a submucosa fluctuated on average from 308,7±110,7 microns to 401,4±114,8 microns and decreased in the distal direction, reaching a difference between the right and left departments of a colonic intestine by 1,5-1,7 times.

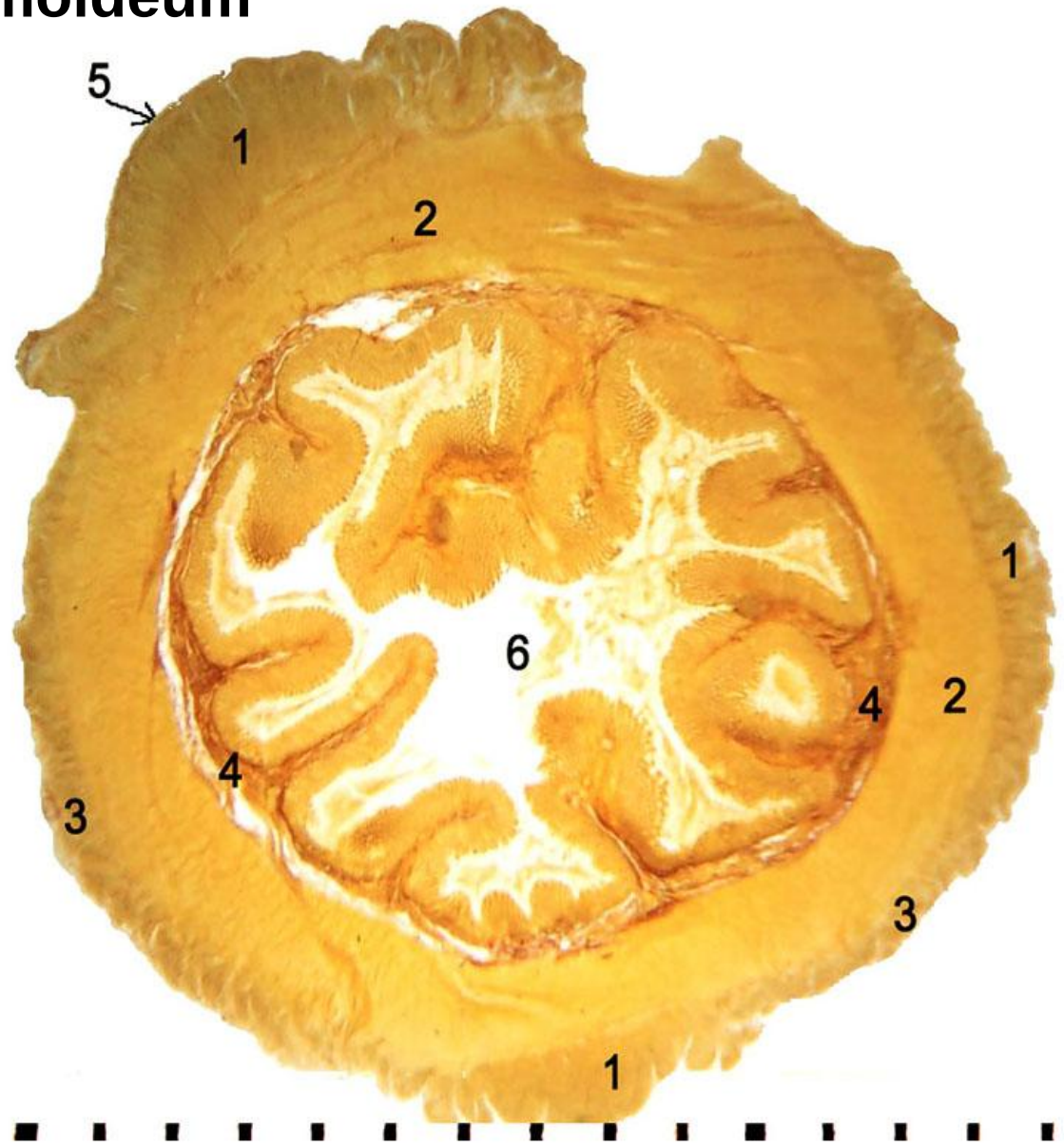
Colon
ascendens



Colon transversum



Colon sigmoideum



TNM Staging Classification of CRC

Primary tumor (T)

- TX - Primary tumor cannot be assessed
- T0 - No evidence of primary tumor
- Tis - Carcinoma in situ: intraepithelial or invasion of lamina propria
- T1 - Tumor invades submucosa
- T2 - Tumor invades muscularis propria
- T3 - Tumor invades through the muscularis propria into the subserosa or into nonperitonealized pericolic or perirectal tissues
- T4a - Tumor directly invades other organs or structures, and/or perforates visceral peritoneum
- T4b - Tumor directly invades other organs or structures, including other departments of a large intestine.

Regional lymph nodes (N)

- NX - Regional lymph nodes cannot be assessed
- N0 - No regional lymph-node metastasis
- N1 - Metastasis in 1 to 3 regional lymph nodes
- N2 - Metastasis in 4 or more regional lymph nodes

Distant metastasis (M)

- MX - Distant metastasis cannot be assessed
- M0 - No distant metastasis
- M1 - Distant metastasis:M1a-1 organ(hepar, lung etc.), M1b- 2 and more organs or peritoneum

Clinical forms CRC

- Toxico - anemia
- Coloenteritis-like
- Dyspepsia-like
- Obturative
- Pseudo-inflammatory
- Tumoral, or atypia

Clinical sings

- Related to tumor size, type, location
- Ascending colon- the tumor is large, exophytic, bulky and offer:
  - Abdomen Pain
  - Bleed PR
  - Unexplained anemia
  - fatigability or weight loss
- Descending colon- offer infiltrating, annular, obstructive tumor
  - Altered bowel habits
  - Decreased stool calibre
  - Frequent gas pains, bloating, fullness, cramps
  - Mass P/A

CLINICAL SIGNS

- Abdominal pain 44%
- Change in bowel habit 43%
- Hematochezia or melena 40%
- Weakness 20%
- Anemia without other gastrointestinal symptoms 11%
- Weight loss 6%
- Some patients have more than one abnormality
- 15 to 20% of patients have distant metastatic disease at the time of presentation

DIAGNOSIS

- Complete history
- Physical examination /DRE
- Routine investigations
- Confirmatory- Biopsy
- Staging workup
  - CXR
  - Barium enema
  - Colonoscopy
  - USG
  - CECT abdomen-pelvis
  - Virtual colonoscopy
  - MRI
  - PET
- Gold standard- Colonoscopy+ Biopsy

- Others
  - FOBT
  - Stool cytology
  - CEA
  - IHC markers- keratin
  - Molecular markers- oncogenes
  - DNA flow cytometry
  - Immunoscintigraphy
- Screening investigations

Diagnostic Tests

- Digital rectal exam (DRE) - obligatory research
- Barium enema (BE) with or without air contrast: used primarily to locate deformities of intestinal topography
- Sigmoidoscopy, rigid type or flexible fiber optic type: used to visualize local rectal tumors or for routine screening
- Colonoscopy (or colon endoscopy): Direct visual examination of the colon and rectum detects early polypoid tumors preoperatively and recurrences post-resection; Multiple biopsies may be performed at time of study to increase sensitivity
- Computed tomography (CT): Used to stage disease and identify metastases
- Transrectal ultrasound (TRUS): An excellent choice for preoperative staging of rectal carcinomas, included changes in mesorektum.
- Magnetic resonance imaging (MRI): very useful for diagnosing metastatic disease
- Laparoscopy, -tomy: Useful in detecting metastases to abdominal regions (especially omentum, peritoneum or liver) that often remain undetected by current imaging techniques

Performance & Benefits
Complexity, limitations of tests

Flexible Sigmoidoscopy • Fairly quick • Few complications • Minimal bowel preparation • Does not require sedation or a specialist	Performance: High for rectum & lower one-third of the colon Complexity: Intermediate	Views only one-third of colon • Cannot remove large polyps • Small risk of infection or bowel tear • Slightly more effective when combined with annual fecal occult blood testing • **Colonoscopy still needed if abnormalities are detected** • Limited availability
Colonoscopy • Examines entire colon • Can biopsy and remove polyps • Can diagnose other diseases • Required for abnormal results from all other tests	Performance: Highest Complexity: Highest	• Full bowel preparation needed • Can be expensive • Sedation of some kind usually needed, necessitating a chaperone to return home • Patient may miss a day of work. • Highest risk of bowel tears or infections compared with other tests

Performance & Benefits
Complexity, limitations of tests

Double-contrast Barium Enema • Can usually view entire colon • Few complications • No sedation needed	Performance: High (for large polyps) Complexity: High	• Full bowel preparation needed • Some false positive test results • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if abnormalities are detected • Very limited availability
Computed Tomographic Colonography • Examines entire colon • Fairly quick • Few complications • No sedation needed • Noninvasive	Performance: High (for large polyps) Complexity: Intermediate	• Full bowel preparation needed • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if abnormalities are detected • Not covered by all insurance plans

Complications of CRC

- Intestinal obstruction
- Perifocal inflammatory process
- Perforation of a tumor
- Intestinal bleeding
- Invasion on surrounding organs and tissues

SURGERY

- SURGRY is the GOLD STANDARD and principle therapy of primary and non metastatic Ca colon. Operation can be

  -Curative (radical)

  – Palliative
  – Accurate disease staging
  – Guides adjuvant treatment

- Likelihood of cure is greater when disease is detected at early stage

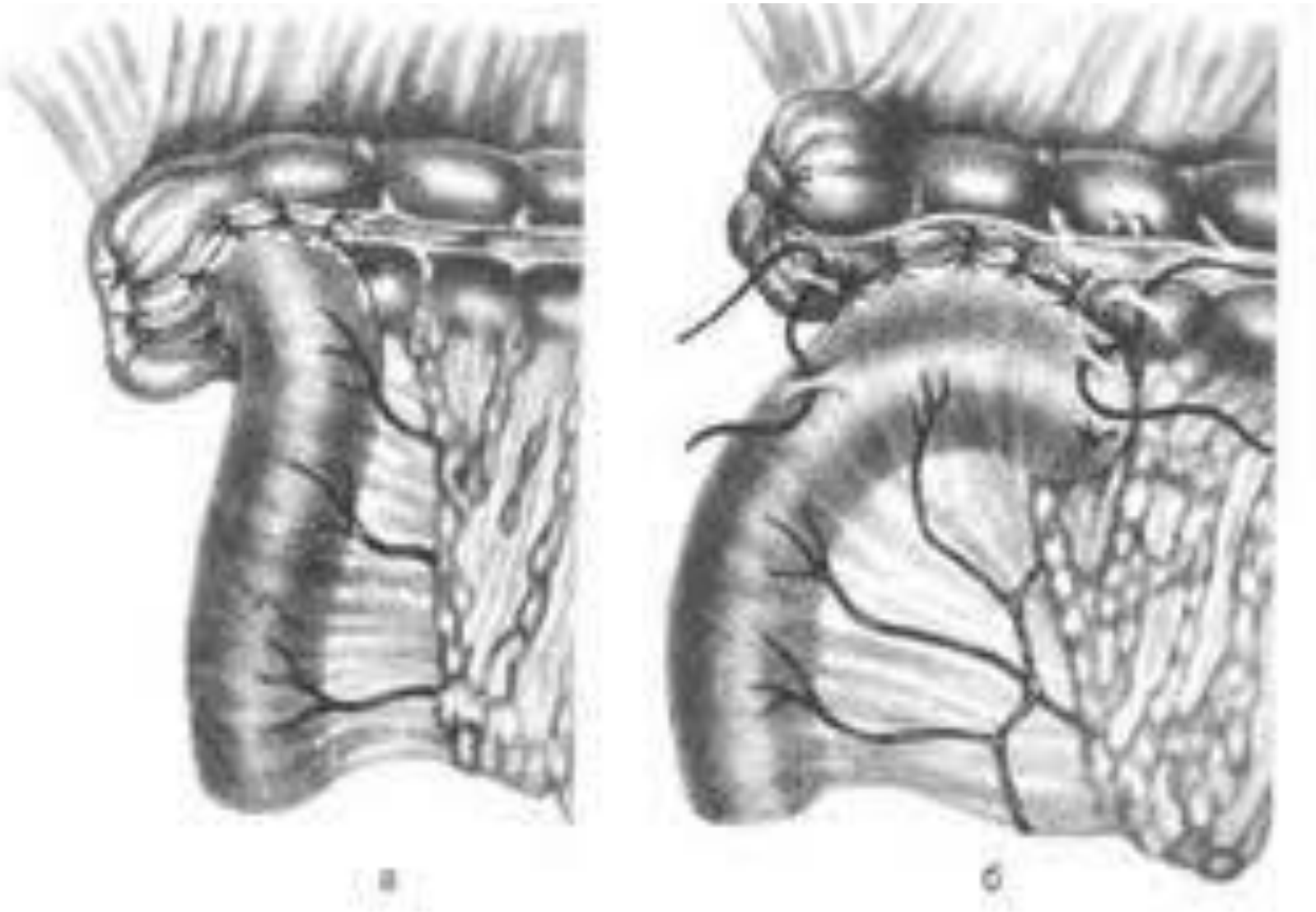
Treatment of CRC

Surgical excision:

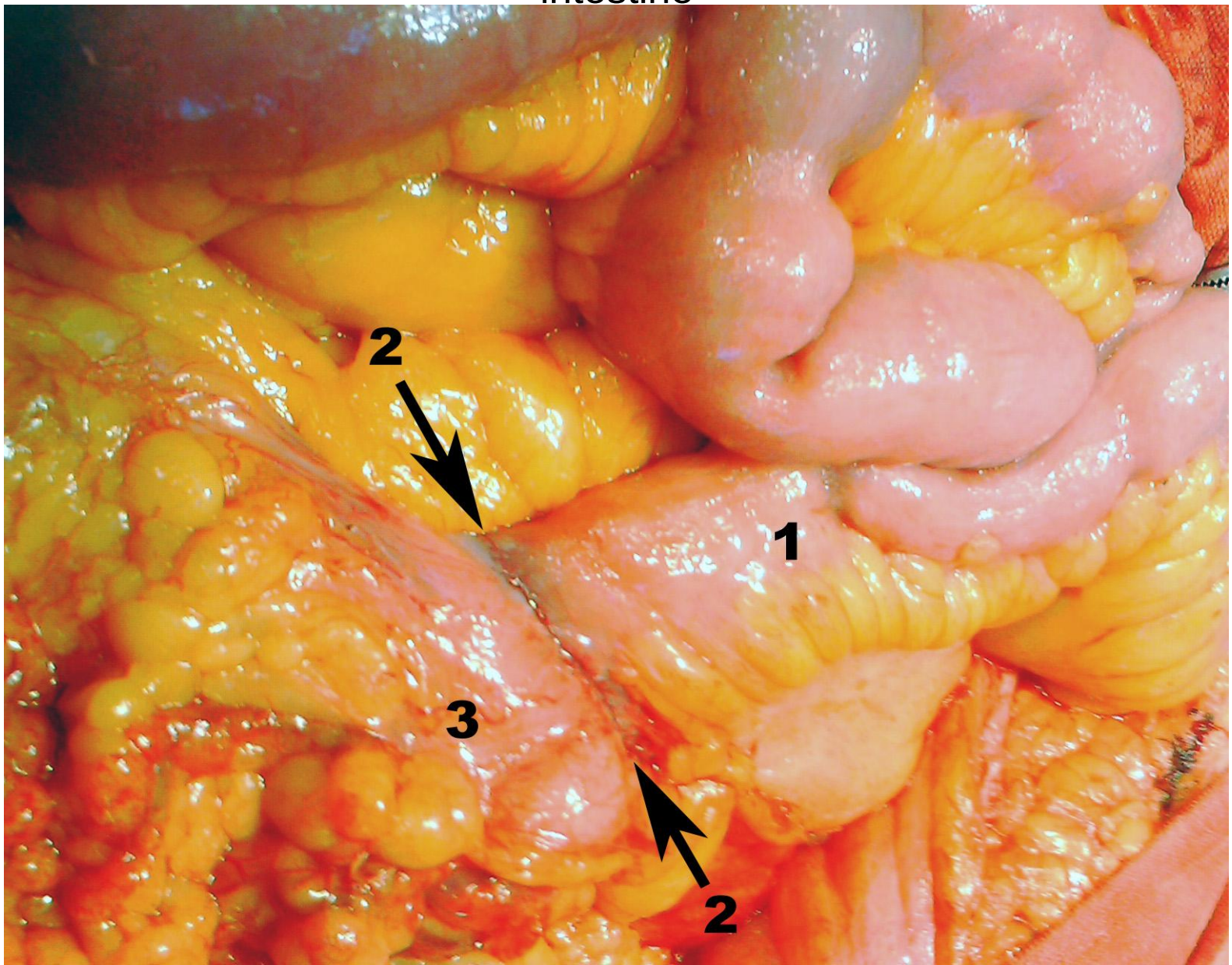
Specific procedure depends on the anatomic location of the cancer, but typically involves hemicolectomy. Performance of a resection of transversal and sigmoid intestines at localization of a tumor in an average third of departments and lack of metastasises in regionaly lymph nodes is possible

- Surgical resection of affected bowel with clear margins, along with the adjacent mesentery and at least 12 regional nodes
- For rectal tumors, total mesorectal excision with a distal surgical margin of at least 2 cm is recommended
- For tumors that are located within 6 cm of the anal verge, or involve the anal sphincter, wide surgical resection with abdomino-perineal resection and permanent colostomy is recommended
- Local excision, for palliative treatment or simple polyp removal

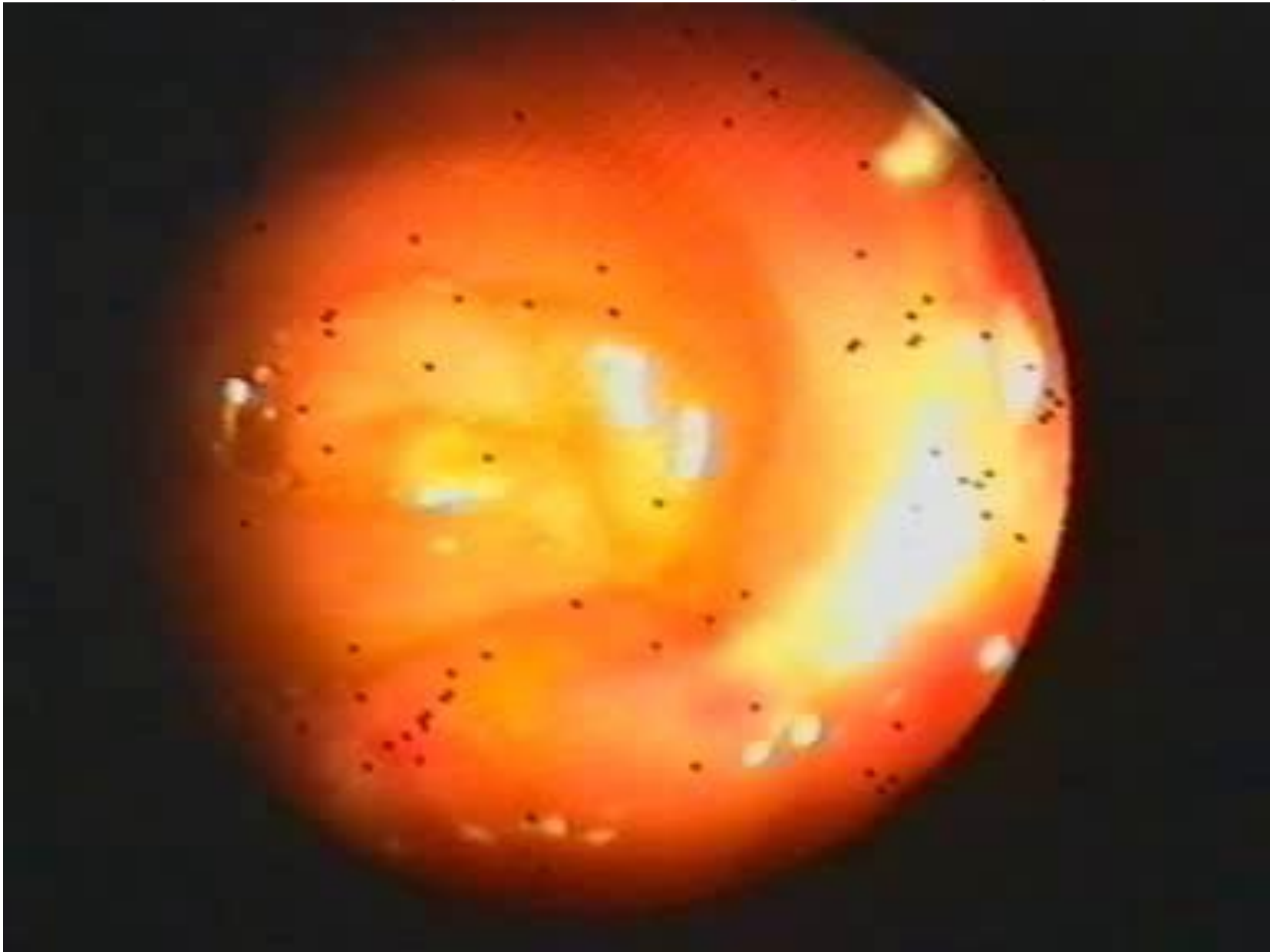
Ileotransversoanastomosis
а – «end-to-side», б – «side-to-side»



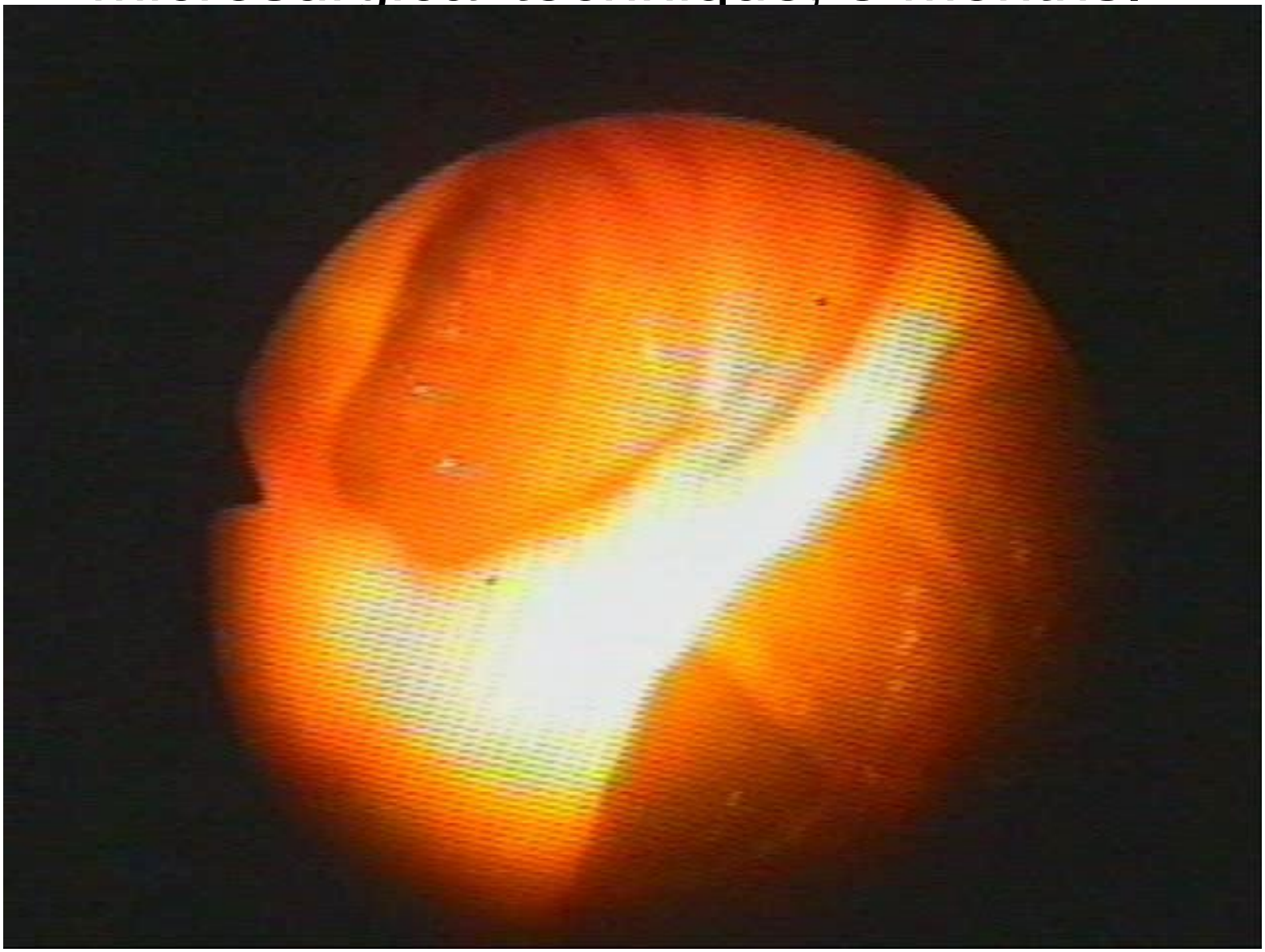
Ileotransversoanastomosis end-to-side by a microsurgical technique. 1 - an ileal intestine, 2 - an anastomosis suture line, 3 - a stump of transversal colonic intestine

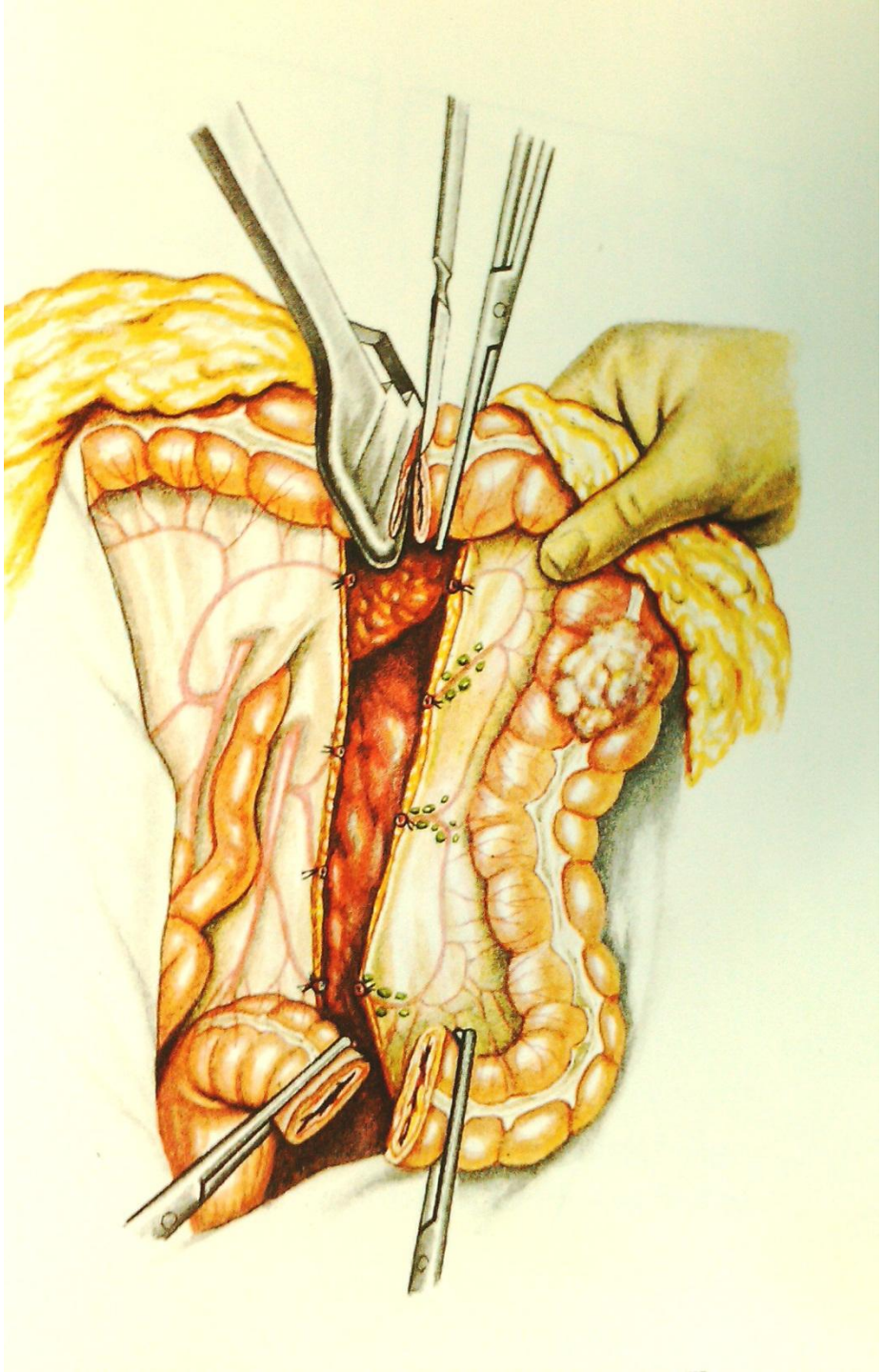


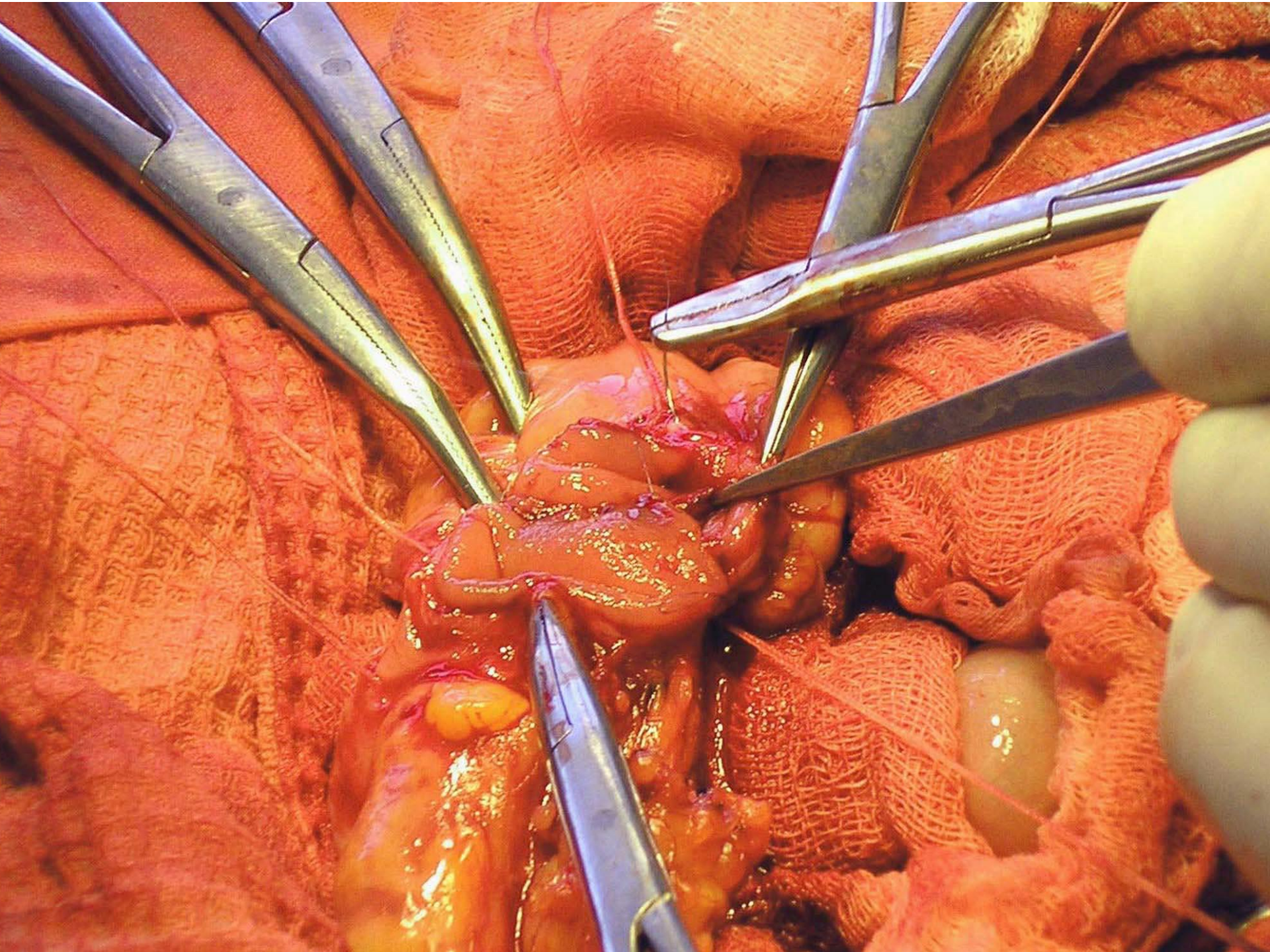
Ileotransversoanastomosis end-to-side by a microsurgical technique, 8 days.

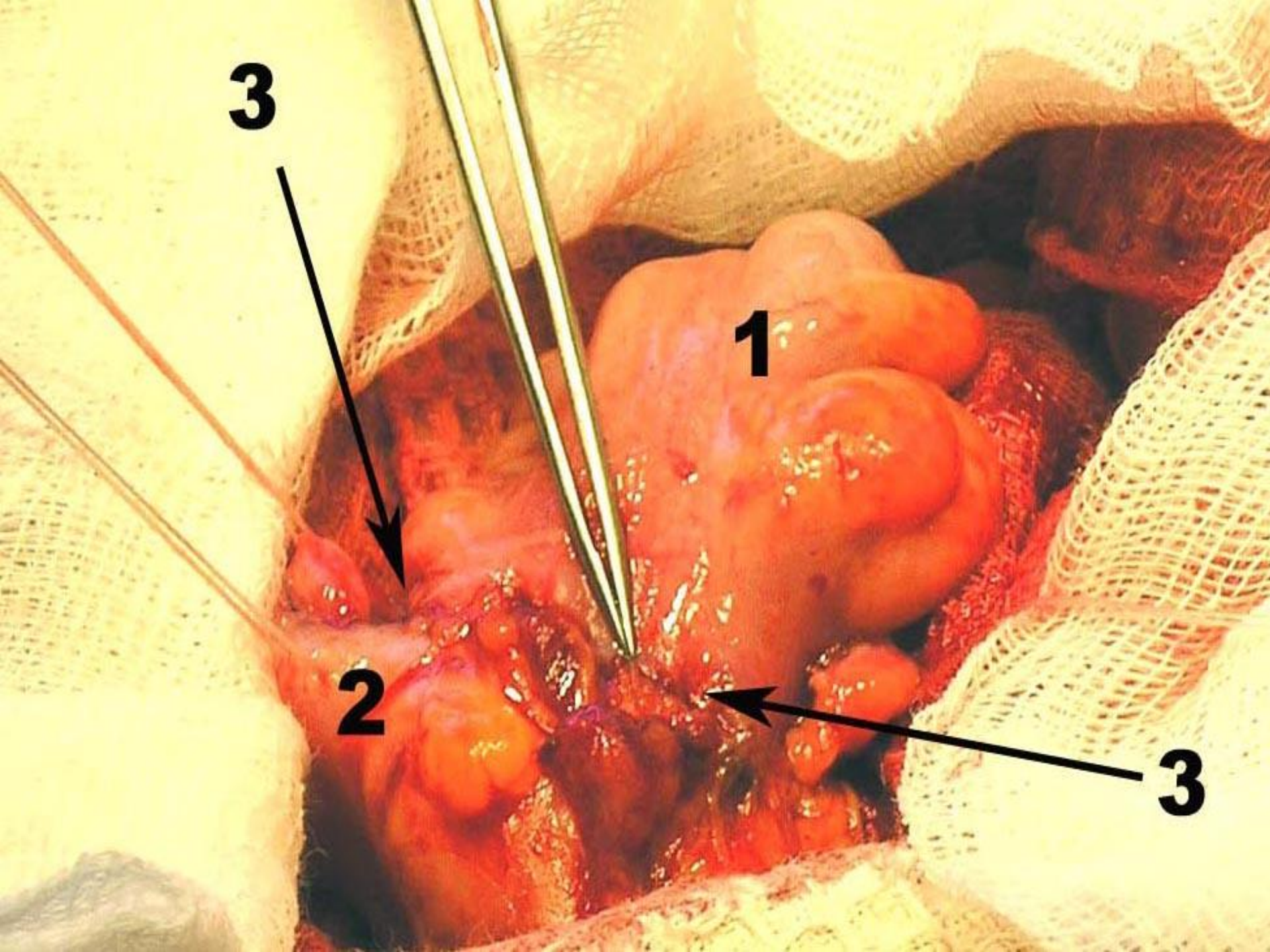


Ileotransversoanastomosis end-to-side by a microsurgical technique, 8 months.





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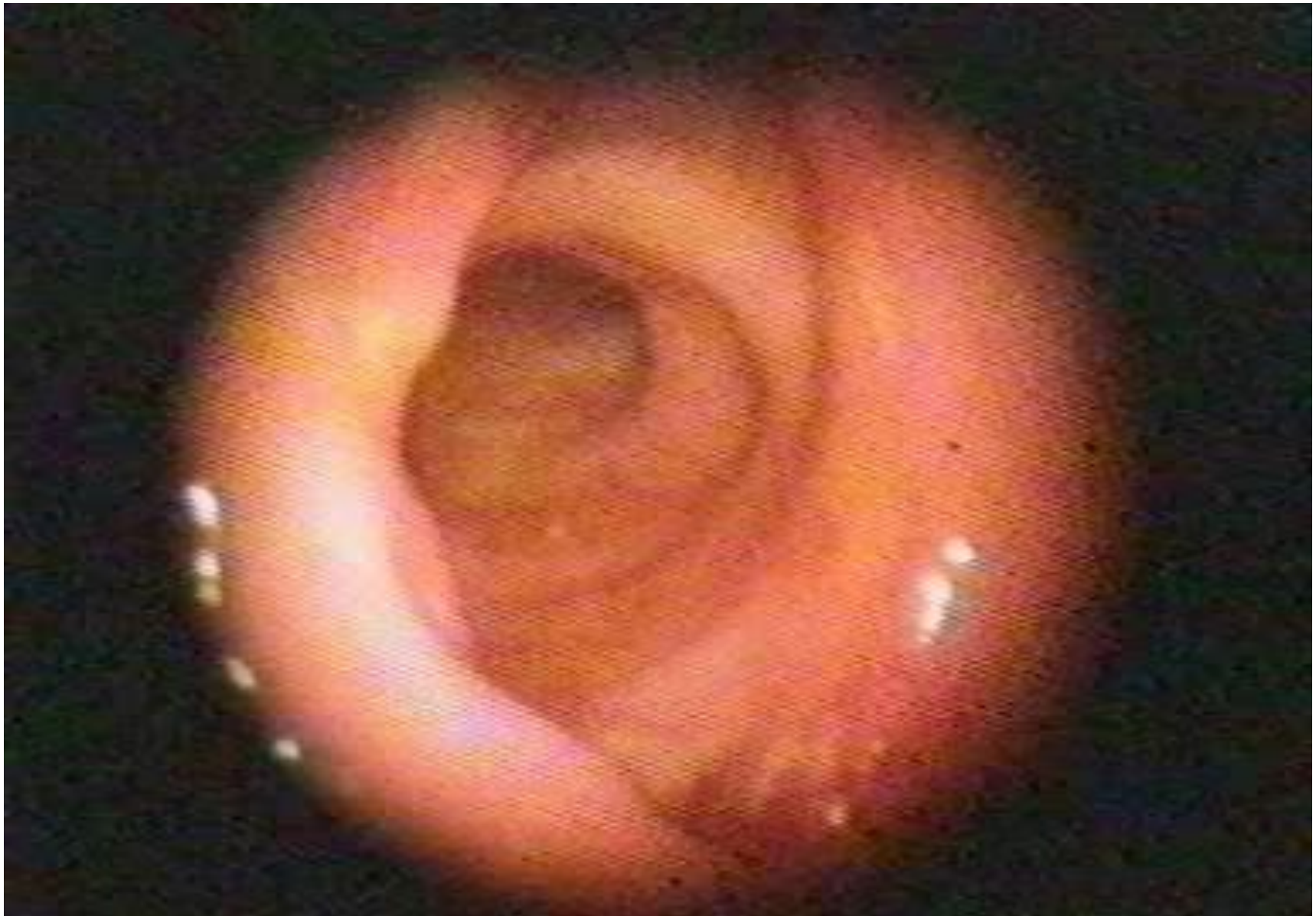
1
2
3

Sigmosigmoanastomosis end-to-end by a microsurgical technique, 6 days.



Radiation therapy:

Postoperative radiation, with or without chemotherapy, significantly reduces local recurrence rates

Common regimen incorporates infusional 5-fluorouracil (5-FU) as a radiosensitizer to boost the efficacy of pelvic radiation

Administered as 45 to 55 Gy over 5 weeks

Repeated as needed

Treatment

SYSTEMIC CHEMOTHERAPY

- 5-FU (5-fluorouracil) has been the mainstay of systemic chemotherapy for CRC
- Capecitabine was approved in 2001 as first-line therapy for metastatic CRC
- Irinotecan (Camptosar), Oxaliplatin (Eloxatin), Bevacizumab, Cetuximab

Electrocoagulation

- Mostly palliative treatment for rectal carcinomas
- Curative for small subset of patients

Screening for high-risk people

- A first-degree relative (sibling, parent, child) who has had colorectal cancer or an adenomatous polyp: Screening should begin at age 40 years

- Family history of familial adenomatous polyposis (FAP):

  Screening should begin at puberty

  Sigmoidoscopy - annually, beginning at age 10 to 12 years

  Colonoscopy - every five years

- Family history of hereditary nonpolyposis colorectal cancer (HNPCC):

  Screening should begin at age 21 years

  Sigmoidoscopy - annually, beginning at age 10 to 12 years

  Colonoscopy - every one to two years, beginning at age 20 to 25 years or 10 years younger than the earliest case in the family, whichever comes first

Screening for high-risk people

- Personal history of adenomatous polyps: Screening should be based on pathological findings
- Advanced or multiple adenomas (3 or greater): First follow-up colonoscopy should occur in 3 yrs; 1 or 2 small (< 1 cm) tubular adenomas: First follow-up colonoscopy should occur at 5 years
- Personal history of colorectal cancer:
- After colon resection
- Approximately six months after the surgery

If the colonoscopy performed at six months is normal, subsequent colonoscopy should be repeated at 3 years and then if normal, every 5 years

- Personal history of inflammatory bowel disease

Every one to two years after an eight year history of the disease with pancolitis or

Every one to two years after 15 years history of left-sided colitis or

For all patients beginning with eight to ten years of disease to document the extent of the disease