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GBETH Newsletter

Grupo Brasileiro de Estudos de Tumores Hereditários

Uma publicação semanal do Grupo Brasileiro de Estudos de Tumores Hereditários

Neste Número

Carcinogênese Ileal em Polipose Adenomatosa Familiar (FAP)

A FAP é uma síndrome hereditária rara, autossômica dominante, causada por alteração no gene supressor de tumor *APC*. A principal causa de morte na FAP é o câncer colorretal (CCR), por isso, a retirada cirúrgica do cólon é parte fundamental do tratamento. A cirurgia consiste na colectomia total com anastomose ilelorretal, ou proctocolectomia total com bolsa ileal e anastomose da bolsa no ânus. Nos casos submetidos à proctocolectomia total e bolsa existe a possibilidade de aparecimento de pólipos na mesma. Acredita-se que isso ocorra por dois motivos principais: a alteração germinativa do paciente no gene *APC*, e um processo de "colonização" da mucosa do íleo na bolsa. Existem várias hipóteses para esse processo de alteração da mucosa ileal, porém, nenhuma delas foi ainda comprovada. Os trabalhos aqui apresentados tentam estabelecer as bases para entender esse processo e propor novos estudos no sentido de entender melhor as causas da transformação ileal.

Artigo: Risco de pólipos na bolsa ileal

Incidence of neoplastic polyps in the ileal pouch of patients with familial adenomatous polyposis after restorative proctocolectomy.

Wu JS, McGannon EA, Church JM.

David G. Jagelman Center for Inherited Colorectal Cancer, Department of Colorectal Surgery, Cleveland Clinic Foundation, Ohio, USA.

Dis Colon Rectum. 1998 May;41(5):552-6; discussion 556-7.

PURPOSE: Although adenomatous polyps and even adenocarcinomas have been found in the terminal ileum of patients with familial adenomatous polyposis, the prevalence of neoplastic changes in the pouches of patients who have undergone restorative proctocolectomy is unknown. The objective of this study was to determine the frequency of pelvic pouch neoplasia in familial adenomatous polyposis patients after restorative proctocolectomy. METHODS: Patients in a polyposis registry who had undergone restorative proctocolectomy were recruited. Demographic, surgical, pathologic, and endoscopic data were obtained from patient records. Video pouchoscopy was done after two enemas and representative biopsies were taken.

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Artigo: Risco de pólipos na bolsa ileal

RESULTS: Of 102 eligible patients, 26 (17 males and 9 females) participated. Median age at ileal pouch-anal anastomosis was 31 (range, 12-58) years. Median follow-up period was 66 (11-156) months. Adenomas were found in the pouch of 11 (42 percent) patients, in the terminal ileum above the pouch in 1 patient, and in the anal canal of 4 patients. Among patients with pouch polyps, three patients had one lesion, three patients had two lesions, and five patients had more than ten lesions. The incidence of polyps increased steadily with time from restorative proctocolectomy. There was no relation between the incidence of pouch polyposis and the severity colonic or duodenal disease. CONCLUSIONS: Proctocolectomy and ileal pouch-anal anastomosis is associated with a significant risk of pouch neoplasia in familial adenomatous polyposis patients. The severity of pouch adenomas was not related either to the severity of colonic or duodenal disease. The pelvic pouches of all patients with familial adenomatous polyposis who have undergone restorative proctocolectomy should be examined periodically.

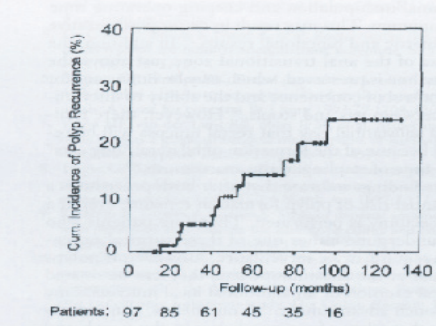

Figura 1. Incidência cumulativa de recorrência de pólipos na anastomose de pacientes com FAP submetidos a protocolectomia com anastomose ileoanal.

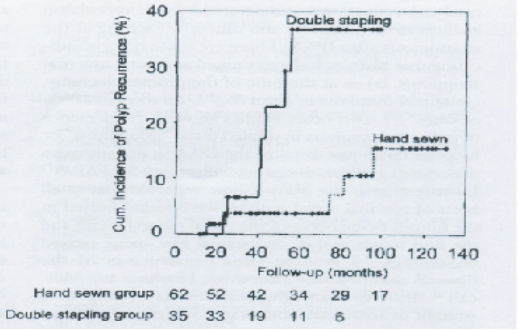

Figura 2. Incidência cumulativa de recorrência de pólipos na anastomose em pacientes com FAP. A linha superior presenta os pacientes submetidos a anastomose mecânica; a linha inferior representa pacientes submetidos a anastomose manual.

Artigo: Carcinogênese colorretal em múltiplos passos

Multistage carcinogenesis and the incidence of colorectal cancer.

Luebeck EG, Moolgavkar SH.

Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue North, P.O. Box 19024, Seattle, WA 98109-1024, USA. gluebeck@fhcrc.org
Proc Natl Acad Sci U S A. 2002 Nov 12;99(23):15095-100.

We use general multistage models to fit the age-specific incidence of colorectal cancers in the Surveillance, Epidemiology, and End Results registry, which covers approximately 10% of the U.S. population, while decrease the growth rate of adenomatous polyps, are very efficient at lowering colon cancer risk substantially, even when begun later in life.

Continuação: Carcinogênese colorretal em múltiplos passos

The incidence of colorectal cancers in the Surveillance, Epidemiology, and End Results registry is most consistent with a model positing two rare events followed by a high-frequency event in the conversion of a normal stem cell into an initiated cell that expands clonally to give rise to an adenomatous polyp. Only one more rare event appears to be necessary for malignant transformation. The two rare events involved in initiation are interpreted to represent the homozygous loss of adenomatous polyposis coli gene function. The subsequent transition of a preinitiated stem cell into an initiated cell capable of clonal expansion via symmetric division is predicted to occur with a frequency too high for a mutational event but may reflect a positional effect in colonic crypts. Our results suggest it is not necessary to invoke genomic instability to explain colorectal cancer incidence rates in human populations. Temporal trends in the incidence of colon cancer appear to be dominated by calendar year effects. The model also predicts that interventions, such as administration of nonsteroidal anti-inflammatory drugs. By contrast, interventions that decrease the rate of mutations at the adenomatous polyposis coli locus are much less effective in reducing the risk of colon cancer.

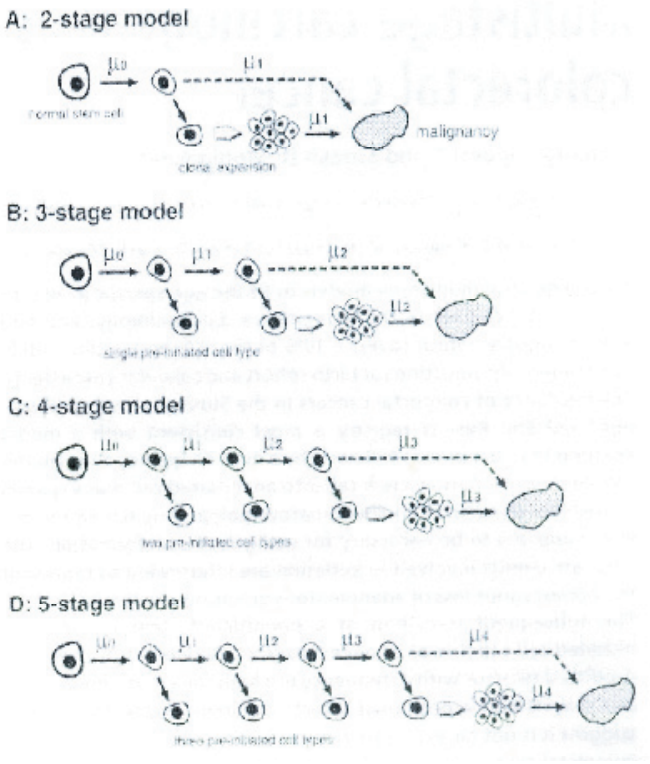

Figura 3. Representação esquemática do modelo TSCE (a) para câncer colorretal com três (b), quatro (c) ou cinco estágios (d). É demonstrada a progressão de uma célula normal a uma célula "iniciada".

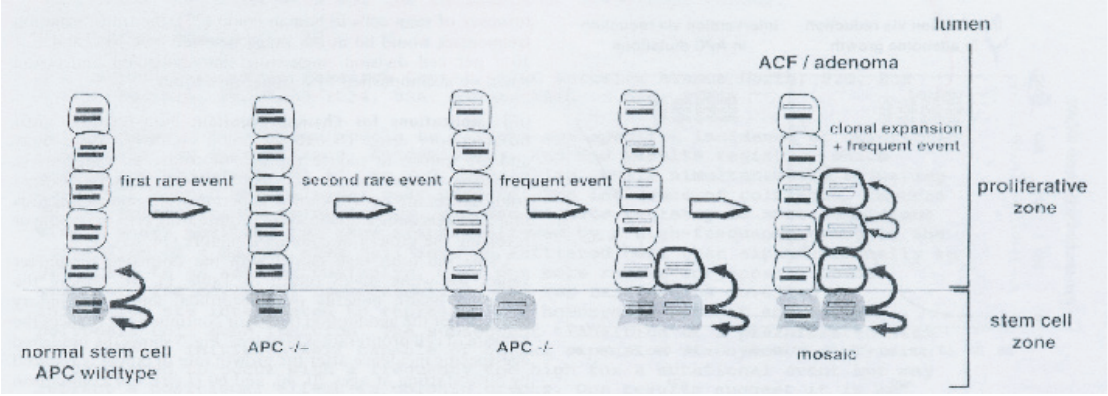

Figura 4. Formação de um adenoma no modelo em quatro estágios. Os passos básicos estão descritos na cripta colônia: a divisão da celúla tronco na cripta. Uma mutação rara na célula tronco inativa um alelo do gene APC. Um segundo evento raro leva a inativação dos dois alelos do gene APC. Divisões freqüentes das células APC -/-.

Programação das Próximas Reuniões

Dia/Horário: Terças-feiras das 9 às 10 horas
Local: Sala de Reuniões da Pediatria
Hospital do Câncer

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08/07/2003	Carcinogênese Ileal em FAP	Dr. Gilles/ Dr. Hugo