Prevalence of Colonic Polyps among Egyptians

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List of Abbreviations

- AFAP Attenuated Familial Adenomatous Polyposis
- APC Adenomatous Polyposis Coli
- CIN Chromosomal Instability
- CRC Colorectal cancer
- DCBE Double Contrast Barium Enema
- DRE Digital Rectal Examination
- FAP Familial Adenomatous Polyposis
- FCC Familial Colorectal Cancer
- FOBT Fecal Occult Blood Test
- FS Flexible Sigmoidoscopy
- gFOBT Guaiac-based Fecal Occult Blood Test
- HNPCC Hereditary Non-Polyposis Colorectal Cancer
- IBD Inflammatory Bowel Disease
- iFOBT Immunochemical Fecal Occult Blood Test
- MMR Mismatch Repair
- MSI Microsatellite Instability
- NIH National Institute of Health
- PJS Peutz-Jeghers Syndrome
- RER Replication Errors
- SEER Surveillance, Epidemiology and End Results
- TSG Tumor Suppressor Gene
- WHO World Health Organization

INTRODUCTION

Colorectal cancer (CRC) is one of the major causes of cancer mortality and morbidity worldwide. It accounts for 98% of malignant tumors of the bowel and affects men and women equally **(Tomlinson et al., 1997).** The lifetime risk for having CRC diagnosed is 6% **(Rieset al., 2001).** Generally, ninety percent of cases occur above the age of fifty but in Egypt colorectal cancer has no age predilection and more than one third of tumors affects a young population **(Abou-Zeid et al., 2002).**

Evidence from several studies suggests that screening for detecting and removing colorectal cancer and precancerous adenomatous polyps can reduce the incidence of colorectal cancer and colorectal cancer- related mortality **(Pignone et al., 2002).**

Screening asymptomatic persons for colorectal cancer can reduce mortality from the disease **(Lang and Ransohoff, 1998)** and has been advocated by many organizations and expert panels **(Winwar et al, 1997).**

CRC is considered a preventable disease as screening can potentially prevent most of cases by detection and removal of the precancerous lesions. CRC does not develop de novo and is almost always preceded by adenoma. Long term survival of patients with colon cancer is largely determined by the timing of the diagnosis **(Kolligs et al., 2002).**

The high mortality of advanced colorectal cancer lies in the fact that early cancers are asymptomatic while the symptomatic patient usually has advanced disease.

A full colonoscopy is the gold standard for diagnosis of colonic polyps and colorectal cancer. Colonoscopic screening can detect proximal colonic neoplasms in asymptomatic adults. Many of these lesions would not be detected with sigmoidoscopy **(Lieberman et al., 2000).**

The cancers arise over along period of time as a result of interactions between genetic predisposition and enviormental influences and therefore it is possible to identify and remove the preneoplastic lesions and improve survival rates.

In general screening is justified when :

1. A disease is common and associated with serious morbidity and mortality.
2. Screening tests are sufficiently efficient in detecting early stage disease, are acceptable to patients. and are feasible in general clinical practice.
3. When treatment after detection by screening has shown to improve prognosis relative to treatment after usual diagnosis.
4. Evidence exists that the potential benefit outweighs the potential harms and costs of screening.

   From the previous criteria we can conclude that screening can be applied in Egypt if the disease is prevalent.

AIM OF WORK

The aim of work is to study the prevalence of colonic polyps among a considerable number of Egyptian population, in order to obtain satisfactory data, and to suggest national surveillance programs for early detection of adenomas and early carcinomas to improve outcome and reduce disease mortality.

Chapter 1

Large bowel

The large bowel comprises the terminal 1 to 1.5 meters of the gastrointestinal tract. The rectum forms the distal 8 to 15 cm of the extraperitoneal large bowel that lies within the pelvis and ends at the anal canal. The large bowel is composed of four layers: mucosa, submucosa, muscularis externa (propria), and serosa (or, in the rectum, perimuscular tissues) ***(Rosai J, 2001)***

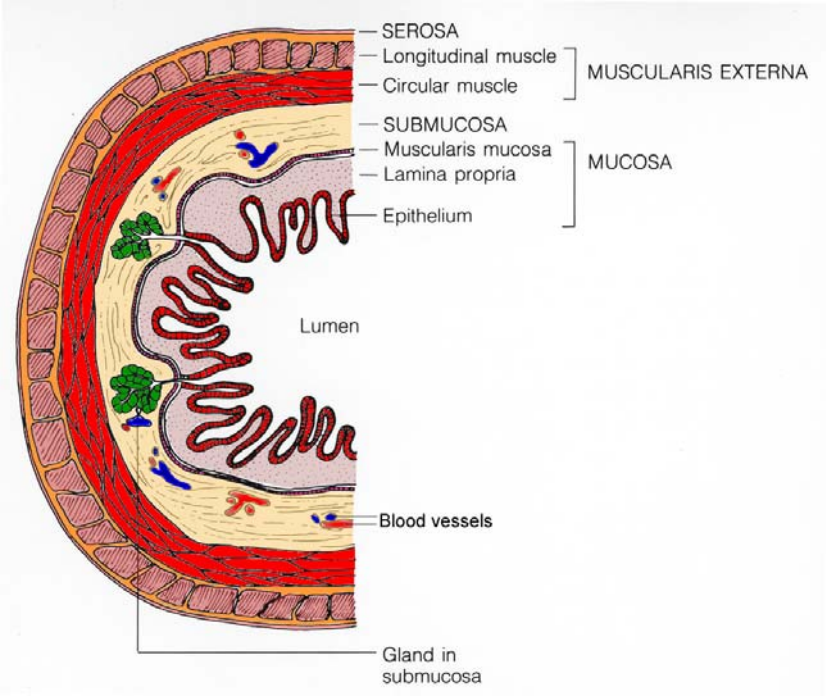

Figure 1: Layers of Large intestine from Colorado.edu

A- Large bowel mucosa

The large intestinal epithelium is composed of uniform test tube shaped crypts between which is the intervening lamina propria. The lamina propria, situated between the basement membrane of the epithelial crypts and the muscularis mucosae, consists of fibroblasts,

capillaries, macrophages, eosinophils, lymphocytes, plasma cells and nerve fibres. Occasionally, lymphocytes or eosinophils are seen between the epithelial cells. Crypt columnar cells contain a variable number of cytoplasmic mucous granules. Towards the upper portion of the crypts, the population of mucous containing cells decreases and cells with eosinophilic cytoplasm appear; however, mucous cells are still abundant and the granules appear larger, giving the cells a "wine glass" (goblet) appearance. The most important known function of goblet cells is secretion of mucin. There are qualitative and quantitative changes in the goblet cell population and mucin production during some colonic diseases such as ulcerative colitis and colon cancer. The surface epithelium, which lies between the crypts, is composed of eosinophilic columnar cells, which have been called absorptive cells and fewer mucous cells.

Compared to the rest of the large intestine, the rectum appears to have many more mucous cells, both in the crypts as well as in the surface in between the crypts ***(Whitehead, 1997)***.

The lymphoid cells in the large intestine are often aggregated into lymphoid follicles. These may be seen in the submucosa beneath the muscularis mucosae, or may be present as confluent masses on both sides of the muscularis mucosae or entirely in the lamina propria. Cells in the basal part of the crypts immediately adjacent to these lymphoid aggregates frequently show decreased amounts of mucous, cytoplasmic basophilia and an increased nucleo-cytoplasmic ratio. Rarely, these crypts may be seen within the lymphoid aggregates. When the lymphoid follicles extend from the mucosa to the submucosa, the crypts also extend into submucosa, forming so-called lympho-glandular complexes. These complexes have been suggested to be involved in carcinogenesis ***(Levine and Haggitt, 1997).***

The normal large intestinal epithelium contains three basic cell types: undifferentiated cells, mucous cells and endocrine cell. These same cell types are seen in all the segments, but their proportion, degree of differentiation and cytoplasmic content vary depending on their position

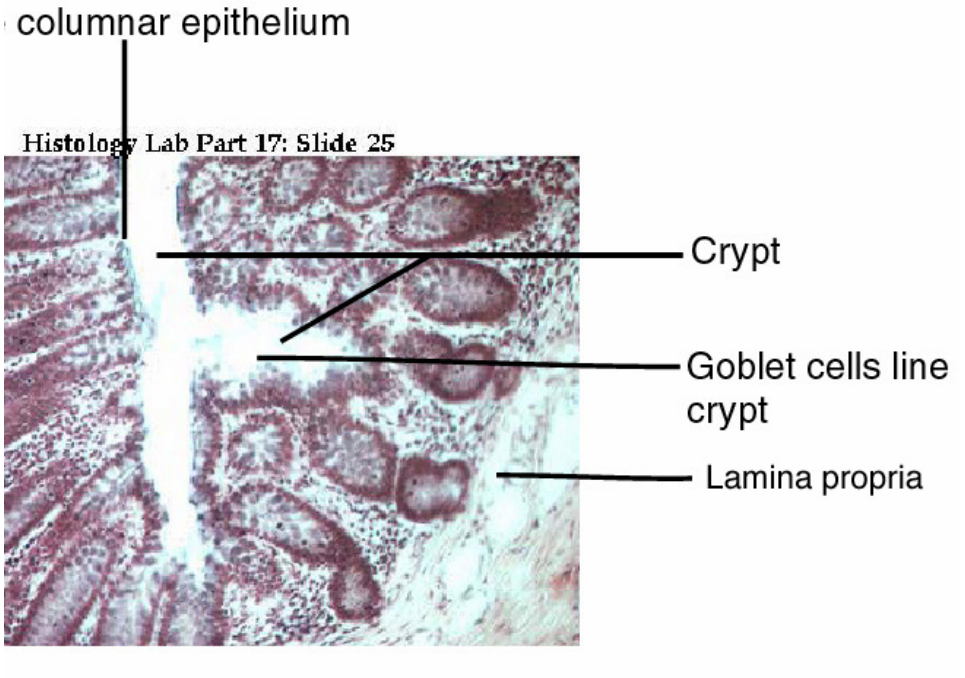

Figure 2:Histology of Large intestine from Colorado.edu

The surface epithelium, which lies between the crypts, contains between 5 to 10 cells, which are somewhat morphologically different from active mucous cells of the crypts ; these surface epithelial cells are designated as columnar cells ***(Levine and Haggitt, 1997).***.

I- Undifferentiated cells

The undifferentiated cells are located towards the basal aspect of the crypts and usually lie on the basement membrane, not reaching the crypt lumen. Undifferentiated cells have a rounded shape and the nucleus is markedly indented with a convoluted nuclear envelope. The first signs of differentiation to mucous cells or endocrine cell are the acquisition of Golgi and rough endoplasmic reticulum (RER) or dense core secretory granules, respectively ***(Levine and Haggitt, 1997).***

Colonic epithelial stem cells (undifferentiated cells) of the basal portion of the crypts comprise the proliferative compartment and a pluripotent capability for differentiation to epithelial cells, goblet cells (both called mucous cell) and neuroendocrine cells ***(Whitehead, 1997).*** A stem cell may be multipotent, or omnipotent, capable of giving rise to multiple lineages or a single lineage ***(Ming SC, Goldman H, 1998)*** **.**

II- Mucous cells

The mucous cell population shows marked variation in degree of differentiation. At the very early stage, they contain a few profiles of RER and Golgi. Mucous granules of various size and density are later seen in these cells, which appear to undergo cycles of mucous accumulation and discharge. Discharge seems to occur only when the cells become hyperdistended with mucin. During the process of discharge, individual mucous granules coalesce, their partitioning membranes disappear and the mucous assumes a fibrillar appearance ***(Levine and Haggitt, 1997).***

III- Columnar cells

The columnar cells have slender elongated cytoplasm with basal rounded nuclei and abundant supranuclear Golgi, mitochondria, some profiles of RER and free polysome. The apical part of the cytoplasm contains numerous clear secretory granules and microfilaments. They have the usual organelles for mucous production and indeed, mucus has been demonstrated in them. They are probably senescent mucous cells, which will soon be extruded from the surface ***(Levine and Haggitt, 1997).***

IV- Endocrine cells

A diverse population of endocrine cells is scattered among the epithelial cells lining the large intestinal crypts. The cytoplasm of gut endocrine cells contains fine eosinophilic secretory granules that are released at the basal surface of the cell. The cytoplasmic portion of the cell is at the base of the epithelium, and the nuclei reside on the luminal side of the cytoplasmic granules ***(Ming SC, Goldman H, 1998).***

B- Large bowel microvasculature

In the colonic mucosa, arteriolar branches from the submucous arterial plexus penetrate the muscularis mucosa, and then break up into a leash of capillaries between the bases of the colonic tubular glands.

The capillaries pass towards the colonic surface in the lamina propria with frequent cross-anastomoses. At the most luminal level of the mucosa, they join a polygonal array of capillaries and subepithelial postcapillary venule rings, which lie just beneath the colonic surface epithelial cells and surround the necks of the colonic glands ***(Ming SC, Goldman H, 1998).***

The venous drainage of the colon largely parallels its arterial supply. Straight veins drain the submucous, intermuscular and subserosal venous plexuses into an anastomosing marginal vein ***(Ming SC, Goldman H, 1998).***