

Gastrointestinal disease

Celiac disease

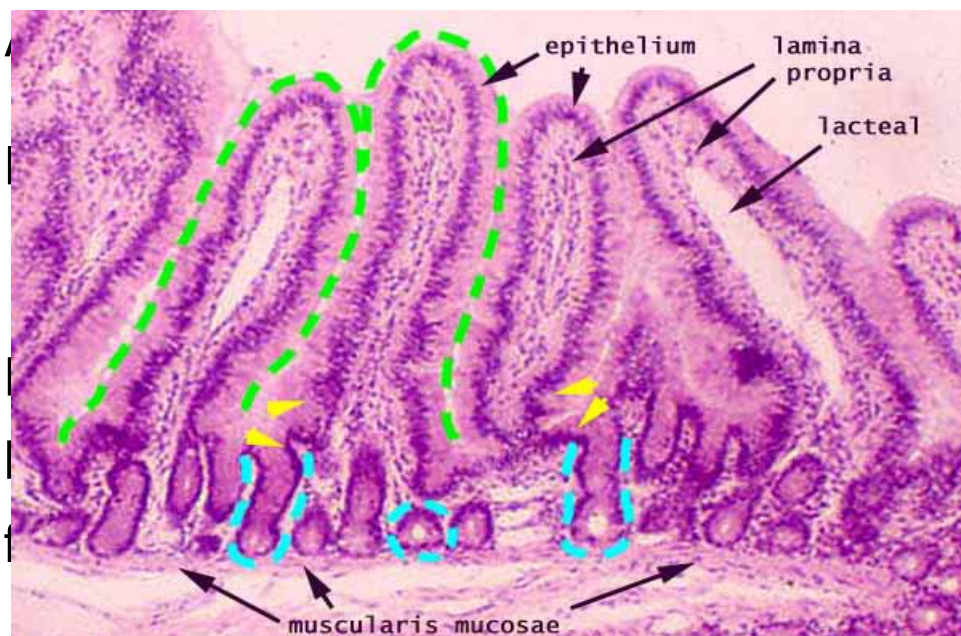
- More than Diarhea !?



Morphological damage of the proximal small intestine mucosa

- Atrophy of villi
- Hyperplasia of cryptae

T lymphocyte-mediated enteropathy with malabsorption



+ autoantigen)

position)

he

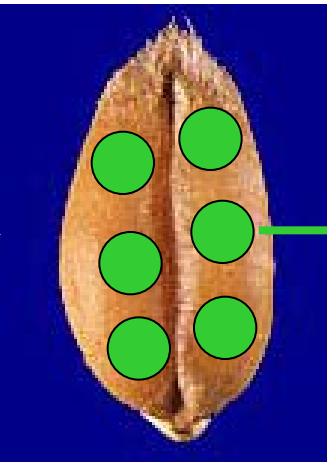
nder a strict lifelong gluten-

Gastrointestinal disease

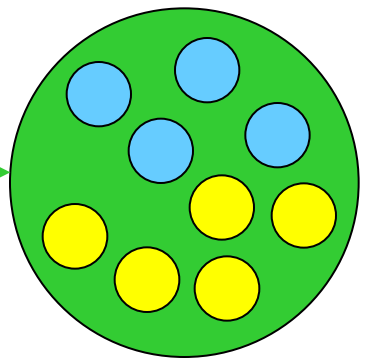
Celiac disease - Gluten



Wheat Rye Barley Oat
(7-15% protein, 90% of it Gluten)



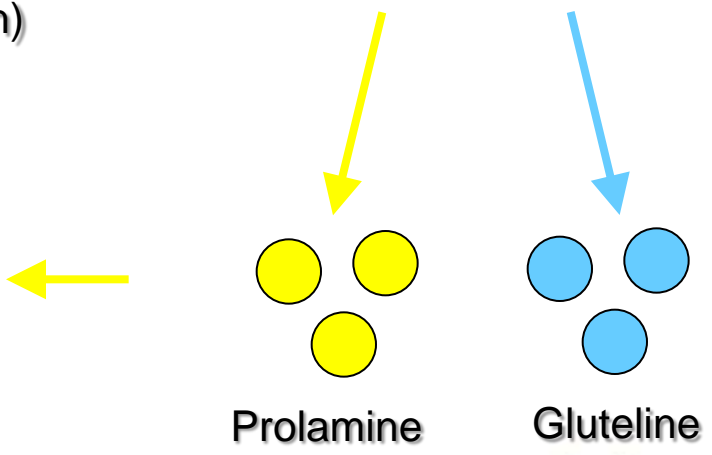
Cereal seed
(containing
Gluten)



Gluten
(Protein mixture)

Prolamines in Gluten:

- Wheat: **Gliadin**
- Rye: Secalin
- Barley: Hordein
- Oat: Avenin

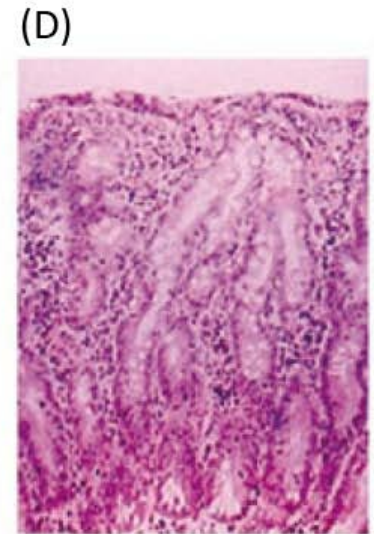
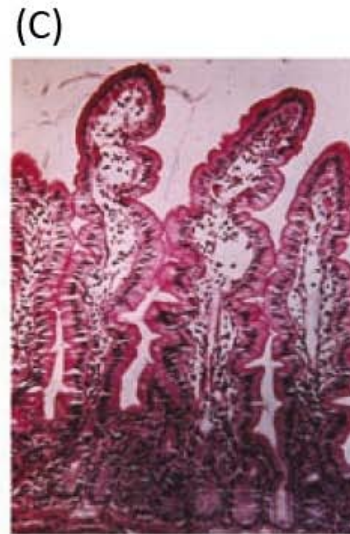


Gastrointestinal disease

Celiac disease - Pathology

=> Morphological damage of intestinal mucosa

-



Source: Kagnoff, M. F. (2007). Celiac disease: pathogenesis of a model immunogenetic disease. *J Clin Invest* 117, S. 41-49.

Prevalence

- much greater than previously estimated
- approaches **1%** in US and Europe
- the most common genetic disease in Europeans
- rare among African-Caribbean, Chinese, Japanese

Strong genetic susceptibility

- 75% concordance in monozygotic twins
- 4-12% prevalence among first-degree relatives

Age - 20% of cases diagnosed in people *over age 60*, most new cases between ages 10-40

Sex - slight female preponderance

Classical celiac disease - GI malabsorption symptoms and sequelae, positive serology, villous atrophy, improvement with gluten-free diet

Celiac disease with “atypical” symptoms
mostly extraintestinal symptoms, positive serology, villous atrophy, improvement with gluten-free diet.
May be the most common presentation!

Silent Celiac disease - asymptomatic. Positive serology, villous atrophy. Detected by screening high risk individuals or by biopsy for another reason.

Latent Celiac disease - asymptomatic. *Positive serology only.*
(normal biopsy)

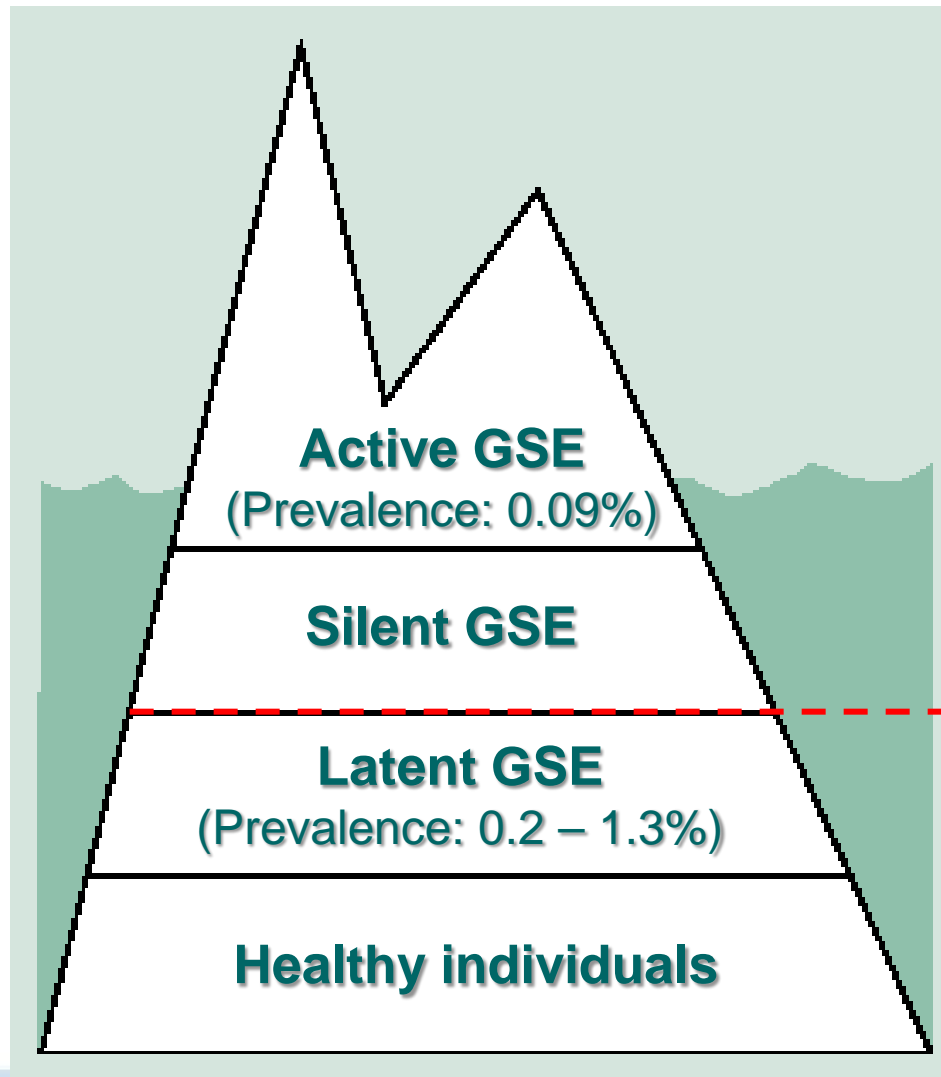
=> The clinical significance of these subtypes remains unclear

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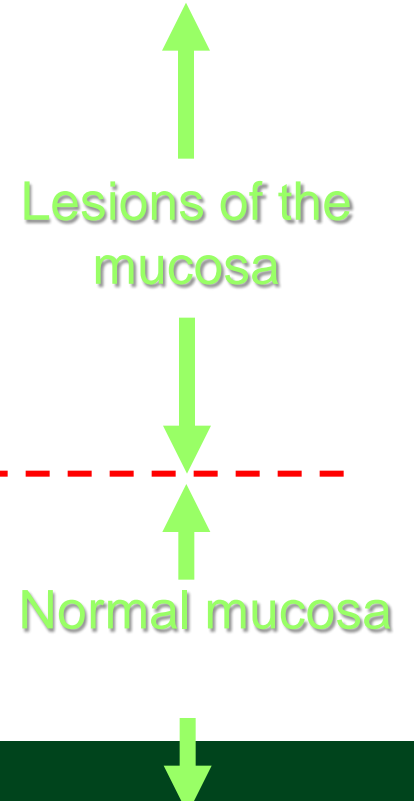
Celiac disease - Subphenotypes



Genetical predisposition



Morphology of mucosa



Gastrointestinal disease

Celiac disease - various clinical manifestations -



General:

- delayed adolescence
- anaemia
- malignancy

CNS:

- ataxia, seizures
- depression

Skin & Mucosa:

- dermatitis herpetiformis
 - stomatitis
 - loss of hair



Digestive

- diarrhea,
- abdominal distension
- malnutrition
- hepatitis, cirrhosis

Reproductive:

- infertility
- miscarriage

Bones

- osteoporosis, fractures
- arthritis
- dental anomalies

Autoimmune Diseases:

- Diabetes
- Thyreoiditis



Gluten, a substance in wheat and other grains, may be found in a variety of foods including breads, cakes, cereals, pasta, commercial dairy products and alcoholic beverages



CELIAC DISEASE



A
Lifetime Without
Beer

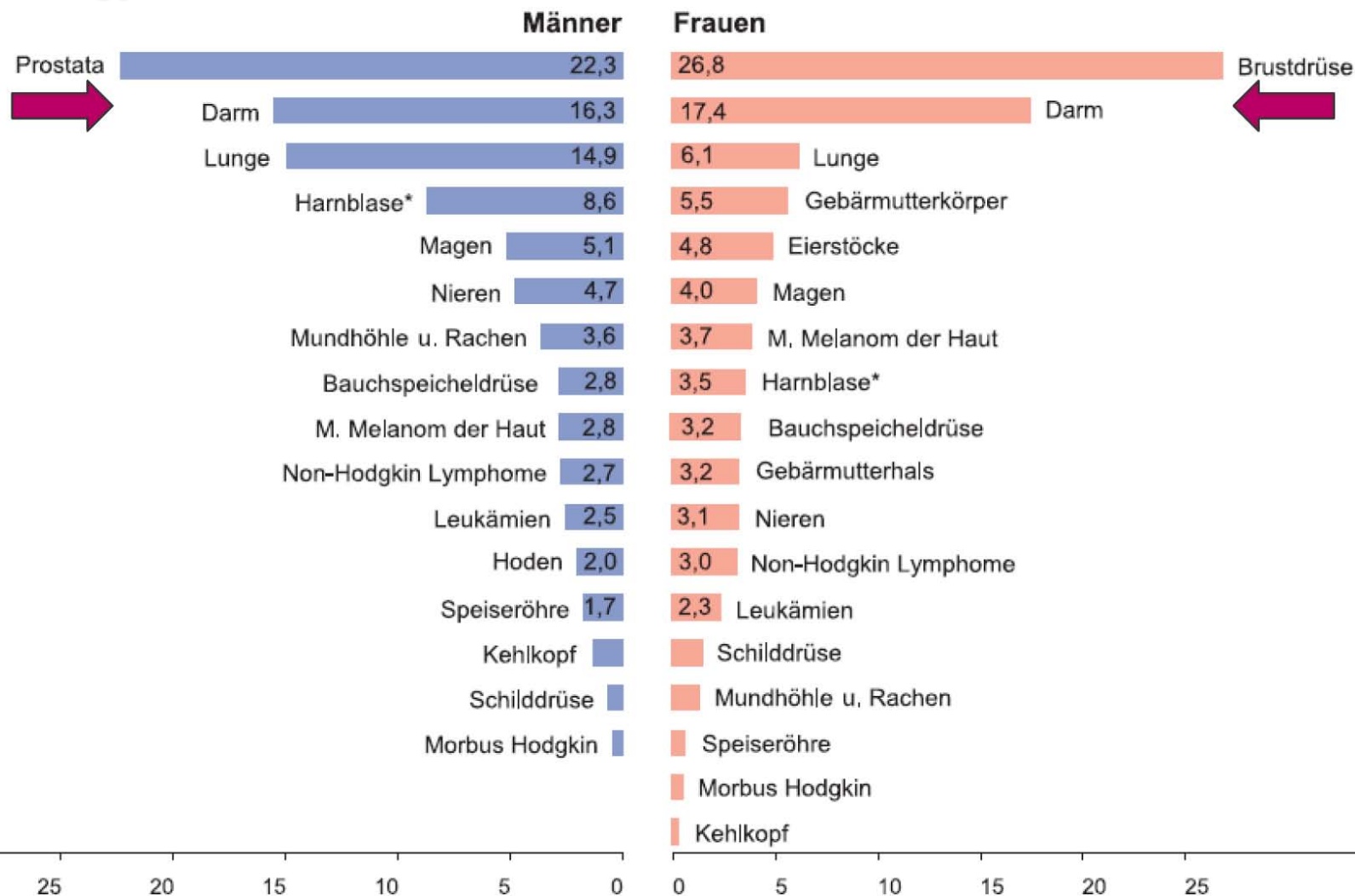


Colorectal Cancer

Gastrointestinal disease

Colorectal Cancer

Epidemiology



* einschließlich bösartiger Neubildungen in situ und Neubildungen unsicheren Verhaltens



Gastrointestinal disease

Colorectal Cancer (CRC)



Increased risk:

- western diets are low in dietary fibre which increase fecal mass and reduce colon transit time
- Fat and Meat consumption correlates with risk of CRC

Decreased risk:

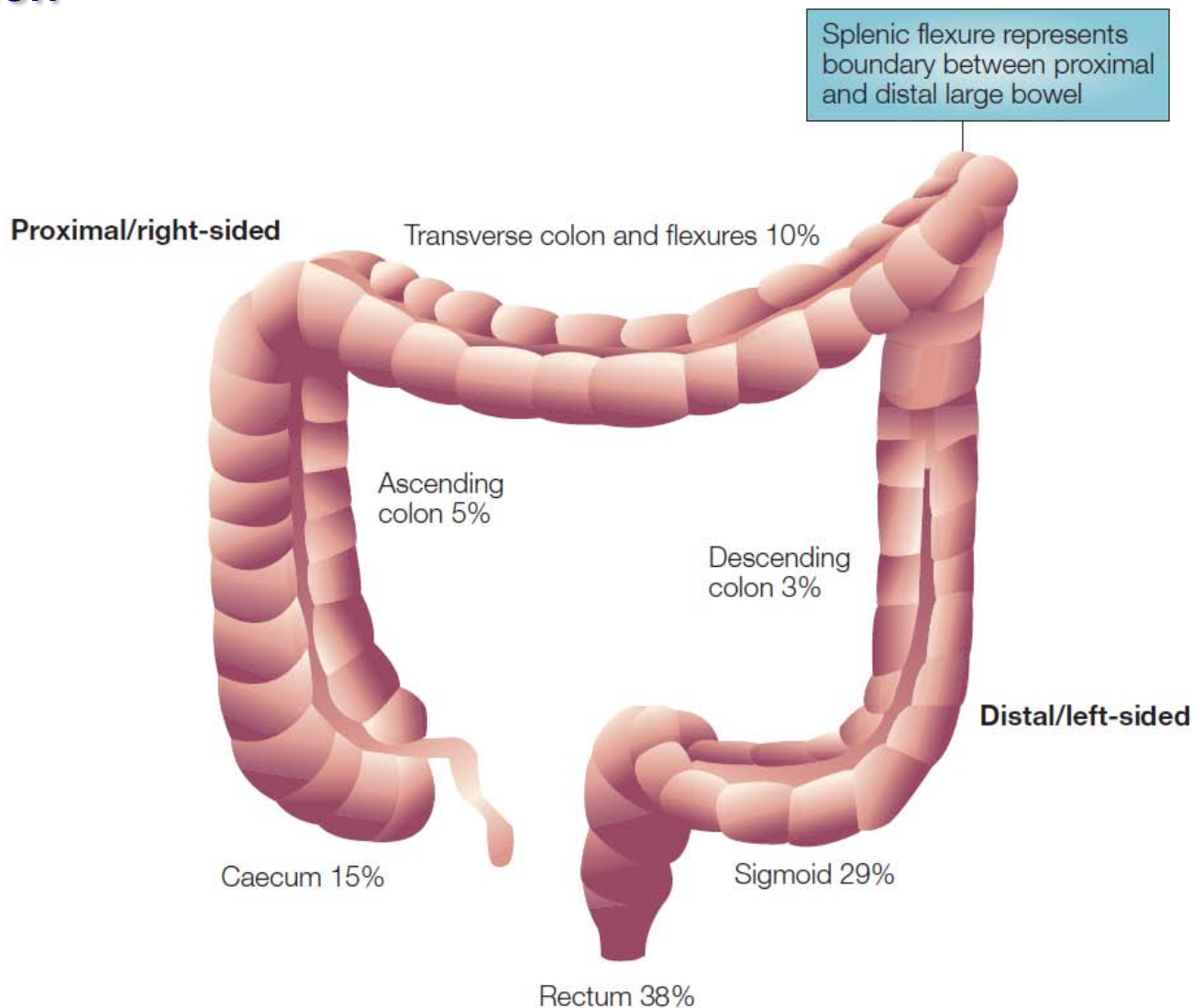
- Fruit and vegetables consumption has a protective effect
- increase fibre intake in the diet
- Exercise reduces the risk of CRC
- Aspirin and other NASIDs reduce the risk of developing both adenomas and cancers
- Hormone-replacement therapy (combined oestrogen and progesterone) may reduce the risk of CRC ?

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Colorectal Cancer



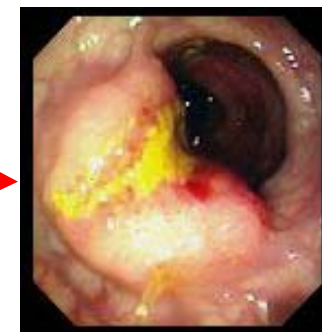
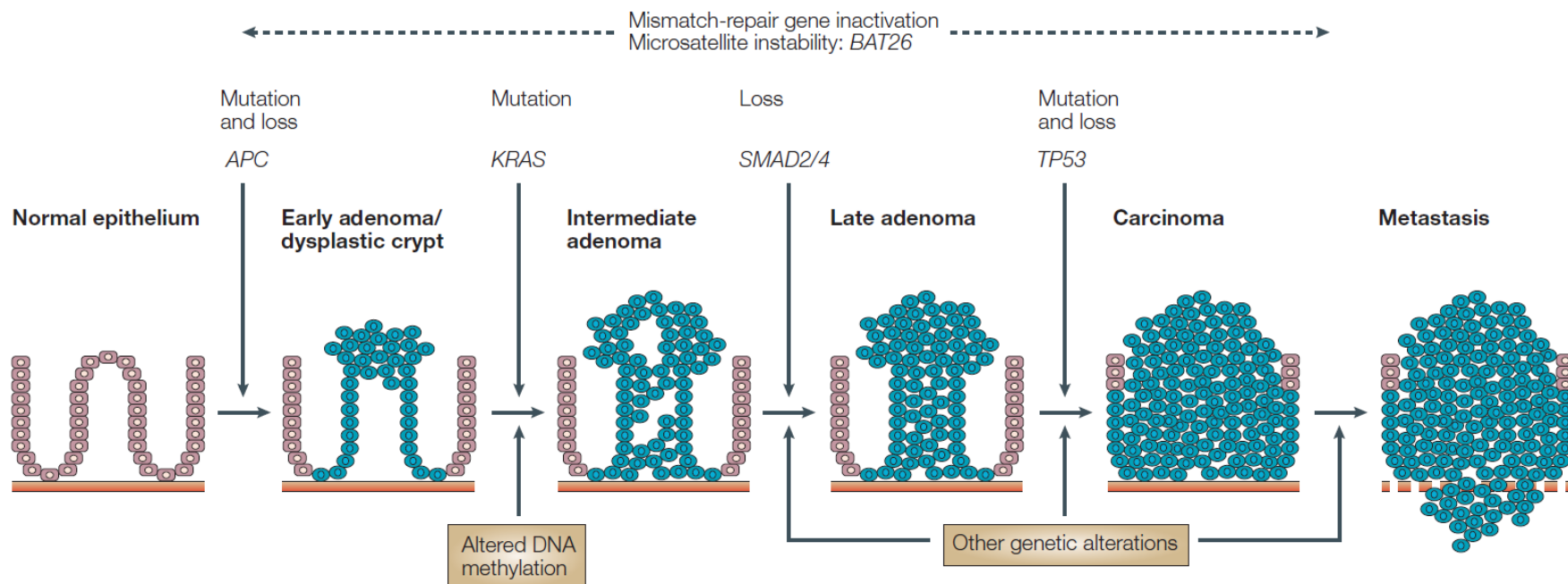
Localisation



Gastrointestinal disease

Colorectal Cancer

Pathogenesis: Progression from adenoma => carcinoma



10 – 12 years !



Screening

Box 2 | **Features of an ideal screening test for colorectal cancer**

- Cheap
- Simple to perform
- Non-invasive
- Represents the whole colon
- Unambiguous interpretation of results (that is, high sensitivity, specificity, positive predictive value and negative predictive value)
- Easy to teach
- Easy to maintain quality control

Test	Sensitivity	Specificity	Cost	Represents whole colon?	Non-invasive?	Other advantages	Other disadvantages
Faecal occult blood test*	Moderate to low	Moderate	Low	Yes	Yes	No bowel preparation needed; specimens transportable; can be combined with flexible sigmoidoscopy to improve detection of proximal lesions ⁹¹	Repeat samples needed; dietary and drug restrictions required
Digital rectal examination*	Low	Low	Low	No	No	Simple to perform	Patient discomfort
Flexible sigmoidoscopy*	Moderate to high	High	Moderate	No	No	Acceptable (to trial volunteers) ^{92,93} ; allows removal of precancerous polyps	Patient discomfort; bowel preparation or enema needed; risk of bowel perforation and bleeding; trained personnel needed; data from randomized control trials are pending
Barium enema*	Moderate	Moderate to high	Moderate	Yes	No	Lower risk of bowel perforation than endoscopic screening	Patient discomfort; bowel preparation needed; trained personnel needed
Colonoscopy*	High	High	High	Yes	No	Allows removal of precancerous polyps; evidence of reduced colorectal cancer incidence after polyp removal during colonoscopy screening ^{94,95} or colonoscopy following FOBT screening ³⁸	Patient discomfort; bowel preparation needed; risk of bowel perforation and bleeding; mortality rates of 1–3 per 10,000 reported ²² ; intravenous sedation required; highly trained personnel needed; no randomized control trials
Virtual colonoscopy [‡]	High	High	High	Yes	Yes	Speed; no sedation needed; extracolonic and pelvic organs can also be evaluated; high patient acceptability	Patient discomfort; bowel preparation required; high radiation dose; trained personnel needed; high inter-observer variability ⁹⁶ ; very small risk of bowel perforation ^{97,98} ; limited specificity; unknown sensitivity for flat adenomas ⁹⁹
Cellular markers [‡]	Moderate to high	Moderate to high	Unknown	Yes	Yes	Single stool sample adequate; no bowel preparation required; specimens transportable; high patient acceptability likely	Research stage of development; assay might be time consuming; technology for large-scale use lacking at present
DNA markers [‡]	Moderate to low	Moderate to high	Unknown	Yes	Yes	Single stool sample adequate; no bowel preparation required; specimens transportable; potential high patient acceptability	Research stage of development; often time consuming to perform assay; technology for large-scale use lacking at present
DNA markers: multitarget assays [‡]	High	High	High at present	Yes	Yes	Single stool sample adequate; no bowel preparation required; specimens transportable; potential high patient acceptability	Research stage of development; often time consuming to perform assay; technology for large-scale use lacking at present

*Tests that are currently available. †Newer tests that are at various stages of development. FOBT, faecal occult blood test.