Inflammatory Bowel Diseases (IBD)
Clinical aspects

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IBD- clinical features

Chronic inflammatory diseases of the GI tract characterized by periods of exacerbations and remissions.

- Diarrhea
- Abdominal pain
- Rectal bleeding
- Fever
IBD History - ulcerative colitis

- 1875 - Wilks and Moxon - were the first to identify the disease as being from a non-infectious cause.
IBD History- Crohn’s

- 1913- BMJ- T. Kennedy Dalziel: 13 patients-intestinal obstruction, inflamed gut, involving jejunal, ileal and colonic areas with transmural inflammation.

Crohn's disease-- 1913 T Kennedy Dalziel reported (BMJ) treating 13 patients who had suffered from intestinal obstruction. On autopsy he found that all had inflamed gut in the jejunal, ileal, and colonic areas with transmural inflammation. -- 1932-- Burril Crohn--J A M A--"terminal ileitis"." terminal ileitis".

Global map of Crohn's disease incidence.
ULCERATIVE COLITIS AND CROHN’S DISEASE

- Diffuse mucosal inflammation limited to colon
- Affects rectum
- May involve all or part of rest of colon

- Patchy transmural inflammation
- May affect any part of GI tract
IBD - Extraintestinal Manifestations Related to Disease Activity

- Aphthous stomatitis
- Episcleritis and uveitis
- Arthritis
- Vascular complications
- E. nodosum
- P. gangrenosum
EYE LESIONS
UC - Spectrum of Disease

Normal

Mild

Moderate

Severe
Anatomic Distribution

Freq. of involvement

most

least

Small bowel alone 33%

Ileocolic 45%

Colon alone 20%
CD - Clinical Patterns

Inflammation

- Pain
- Tenderness
- Diarrhea
- Low-grade fever
- Weight loss (anorexia)
CD - Clinical Patterns

Obstruction

- Post-prandial cramps
- Distention
- Borborygmi
- Vomiting
- Weight loss (food avoidance)
Fistulization

- **Enterocutaneous**
  - Drainage via scar

- **Enterovesical**
  - Recurrent UTIs, pneumaturia

- **Retroperitoneal**
  - Psoas abscess signs: back, hip, and thigh pain; limp

- **Perianal**
  - Pain, drainage

- **Rectovaginal**
  - Drainage: feces and/or air
The many faces of Crohn’s disease
UC - Complications

Risk of Colorectal Cancer

Cumulative probability %

Time from diagnosis (years)

UC  Control

Gut 2001, 48:526
More than 2 million patients around the world
In Israel

- Incidence 10/100,000/year for each of the diseases
- Over 20,000 patients.
Inflammatory bowel diseases: An increasing burden on patients and families, health systems, economy

Admissions, surgeries, symptoms-from mild to debilitating, the burden of IBD, increasing incidence, loss of school/workdays, psychosocial distress, treatment, side effects, cost, young age at diagnosis, chronic-lifelong diseases.
IBD Risk factors

- Genetic-
  - Common in twins and family members.
  - More common in Jewish people.
  - More than 160 susceptible genes loci.
GWAS in IBD

- Total of 163 IBD loci

- Most loci contribute to both phenotypes

Many variants are associated with the immune system, however most do not have an obvious function
IBD- Environmental factors

- Northern areas - “Hygiene theory” / “Old friends”
- Industrialization -
  Food (refined sugars, high fat, less vegetables)
- Vaccination
- Air pollution
- Protective - Multiple siblings, rural areas
IBD- Environmental factors

- Northern areas-
“Hygiene theory” / “Old friends”
IBD- Environmental factors

- Cigarette smoke
- Stress (?)
- NSAIDs
..inappropriate and ongoing activation of the mucosal immune system driven by the presence of normal luminal flora, in a genetically susceptible host.

Gut microbiota
- Increased pro-inflammatory
- Decreased beneficial

Genetic susceptibility
- Barrier function
- Bacterial killing
- Immunoregulation

Environmental triggers
- Infection
- NSAIDS
- Smoking
- Stress
- Diet

Effector immune response
- Increased Th1 and Th17
- Defective innate responses
IBD Diagnosis

- Clinical presentation, background
- Laboratory studies
- Colonoscopy, gastroscopy
- CT Enterography
- MR Enterography
- Capsule endoscopy
- Serologies?
- Genetics?
<table>
<thead>
<tr>
<th>Test</th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>pANCA</td>
<td>60-70%</td>
<td>15-20%</td>
</tr>
<tr>
<td>ASCA</td>
<td>&lt;5%</td>
<td>40-60%</td>
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Has not solved the problem of “indeterminate colitis”
<table>
<thead>
<tr>
<th></th>
<th>Acute Infections</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration symptoms</strong></td>
<td>&lt;2 weeks</td>
<td>&gt;4 weeks</td>
</tr>
<tr>
<td><strong>Onset of symptoms</strong></td>
<td>abrupt</td>
<td>insidious</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td>normal</td>
<td>&gt;450,000</td>
</tr>
<tr>
<td><strong>Hct</strong></td>
<td>normal</td>
<td>low</td>
</tr>
<tr>
<td><strong>Biopsy</strong></td>
<td>neutrophils predominate</td>
<td>mixed infiltrate, abnormal crypt architecture, lymphoid aggregates, basal plasmacytosis</td>
</tr>
</tbody>
</table>
Clinical features

- Anemia, ↑platelets, ↑sed. rate, ↓albumin
- Weight loss, fever
- Perianal disease
- Bloody stools, tenesmus
- Fecal WBC, occult blood

IBD - Differential Diagnosis

IBD

IBS
Conventional Drug Therapies

Supportive agents
- Antidiarrheal
- Bile sequestrants
- Bulk formers
- Antidepressants
- Pain management
- Anti-spasmodics

Aminosalicylates
- Sulfasalazine
- Mesalamine
- Olsalazine
- Balsalazide

Corticosteroids
- Prednisone
- Prednisolone
- Budesonide
- ACTH

Immunomodulators
- 6MP/Azathioprine
- Methotrexate
- Cyclosporine
- / tacrolimus
- Anti-TNF
- Anti-chemokine rec.

Antibiotics
- Metronidazole
- Quinolones
- Other
Euphoria
(though sometimes
depression or psychotic
symptoms, and emotional
lability)

(Benign intracranial
hypertension)

Buffalo hump

(Cataracts)

(Hypertension)

Moon face, with red
(plethoric) cheeks

Increased
abdominal fat

(Avascular necrosis
of femoral head)

Thinning
of skin

Easy bruising

Thin arms
and legs:
muscle wasting

Poor wound
healing

Also:
Osteoporosis
Tendency to hyperglycaemia
Negative nitrogen balance
Increased appetite
Increased susceptibility to infection
Obesity
Biologics side effects:

- **Hypersensitivity**
  - Immediate (22% vs. 9% placebo)
  - Delayed (serum sickness-like)

- **Infections (36% vs. 26% placebo)**
  - TB, fungal, bacterial and viral infections
  - Abscess in fistula patients

- **Auto antibodies (22-44%) /Lupus-like**

- **Malignancies: Lymphoproliferative; skin cancer?**

- **Neurologic events: demyelinating disease**

- **Cardiovascular deterioration**

- **Skin manifestations**
Crohn’s disease - surgery
Crohn’s Disease - Post-Operative Recurrence

Disease - free survival

Years

0 1 2 3 4 5 6 7 8

Reoperation

Clinical symptoms

Endoscopic lesions

Rutgeerts P et al. Gastroenterology 1990; 99:956
Experimental therapies

- Helminths - ova of Trichuris suis
- Fecal transplantation
תודה רבה