Natural History of IBD=
Inflammatory bowel disease

Ulcerative colitis (UC)
Crohn’s disease
Inflam bowel disease
unclassified (IBDU)
Are the definitions of MH reproducible? 
- On an individual or group level
Localisation of Crohn’s disease

Classification of CD at inclusion in the IBSEN study (1990 – 1994)

L1, terminal ileum: 64
L2, colon: 115
L3, ileocolon: 54
L4, upper GI: 4
Total: 237
Ulcerative colitis

Localisation of inflammation in UC in the IBSEN- study (1990-1994)

Proctitis: 17
Proctosigmoiditis: 101
Left sided: 81
Total colitis: 166
Total: 519
The frequency of IBD over time
Recording by the IBSEN study group

GP

G-1

G-1 1 year

G 2

PL

Communication

BjM, 93
Incidence according to age and gender

UC / IBDU

CD

Incidence 0-16 years

<table>
<thead>
<tr>
<th></th>
<th>IBSEN 1990-93</th>
<th>Ahus 1994-98</th>
<th>Ahus 1999-04</th>
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<tr>
<td>CD</td>
<td>2.7</td>
<td>1.9</td>
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<td>2.1</td>
<td>3.3</td>
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<td>0</td>
<td>0</td>
<td>0.7</td>
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<tr>
<td>total IBD</td>
<td>4.7</td>
<td>5.6</td>
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Incidence of CD

<table>
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<tr>
<th>Year</th>
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<td>1980-90</td>
<td>2.2</td>
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<td>1990-94</td>
<td>8.5</td>
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<td>1998-99</td>
<td>3.1</td>
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<td>1996-2003</td>
<td>3.6</td>
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<tr>
<td>1988-99</td>
<td>2.3</td>
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Ref. Table 3
Incidence of IBD in Europe - adults

Fig. 7
Incidence of IBD in the US

Fig. 6
Global incidence of IBD
Patogenesis of IBD

Balance between the bacterial-flora of the gut and a dysfunctional immune-system in a genetically disposed host
Etnicity and NOD2 mutations

The frequency of CARD15 (R702W) in Crohn's Disease in European countries
GENETICS and IBD

- Having a family member with IBD represents the strongest risk factor ("dose response effect")
  - First degree relative with IBD gives approx. 15% risk
- λs-"relative sibling risk"
  - (Crohn: 20-35, Ulcerative Colitis: 6-9)
- Twin studies:
  - Monozygotic twins risk vs dizygotic
    - Crohn 35% vs dizygotic 7%
    - Ulcerative Colitis 11% vs dizygotic 3%

The Hygiene hypothesis

The theory of reduced diversity of bakterial stimulation as an explanation for increased allergic and immunologic diseases

Faktors influencing our bakterial flora:
- Modern lifestyle
- Food consumption (milk- and meat products) and industrialisation of food products
- Antibiotics
- Birth release
Environmental factors

- **Smoking** gives increased risk for CD, but "protects" against UC
- **Breast feeding >3 mnd** gives reduced risk for IBD (bifidobact, anaerobe bact)
- **Antibiotics** early in life may give increased risk for IBD

Gearry et al, J Gastroent Hepatol, 2010; 25
Drinking water and IBD

- Analysis of drinking water and occurrence of IBD showed:
  By increase of iron concentration in drinking water by 0.1mg/L, the relative risk for development of IBD increased by 21%.
  - Iron catalysis oksidativt stress (inflammation and cell mutation)
  - Iron stimulates bacterial growth (influence on epithelial cell barrier and immune system)

Aamodt et al, Am J Epidemiol, 2008;168
Disease behaviour of IBD within a region
Cumulative probability of first surgery

Years after diagnosis of CD
Risk factors for surgery in CD

Disease location
- Small bowel (L1 or L4)
- Colonic (L2)
- Ileocolonic (L3)

Disease behaviour
- B1: Pure inflammatory
- B2: Stricturing
- B3: Penetrating

Non significant variables
- Gender
- Smoking status
- Familial IBD
- Systemic steroids

Cumulative risk of intestinal resection
- N = 237
- E = 85
- 13.6% = 27.0% = 37.9%

Cumulative hazard
- A1 (<40 yrs)
- A2 (>40 yrs)

Age
- P = 0.001
- P = 0.03

Time in years since diagnosis
IBSEN study: Disease course during the first 10-year period, patients’ perceptive

**Curve 1:** Remission or mild severity of intestinal symptoms after initial high activity

**CD 43%**

**Curve 2:** Increase in the severity of intestinal symptoms after initial low activity

**CD 3%**

**Curve 3:** Chronic continuous symptoms

**CD 19%**

**Curve 4:** Chronic intermittent symptoms

**CD 37%**
Remission rate (grey) during the first and second 5 years period of CD

I. First 5-years period

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<th>B1</th>
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<th>L2</th>
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<th>L4</th>
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p = 0.08

II. Second 5-years period

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p = 0.03

p = 0.2

p = 0.7
Figure V. Cumulative drug consumption (after initial treatment) in CD patients during the first 5 years period (patterned bars) vs. the second 5 years period (grey bars): = percentage of total number (N)
Conventional treatment in IBD:

- Combination of general guidelines and individual experience with a patient
- A close follow up from start of treatment should aim at detecting intolerance or lack of effect
- Drug therapy should aim at the lowest dose(s) giving relief of symptoms
- Biologics are the most effective drugs on disease activity and QoL short term, and anti-metabolites effective long term, in the complicated patient.
Chronic Inflammation: Imbalance Between Mediators

- Pro-inflammatory: TNFα, IL-1β, IL-8, IL-12, IFNγ, IL-4/IL-13
- Anti-inflammatory: TGFβ, IL-10
The introduction of biologics in the treatment of IBD

- Documented and experienced increased efficacy
  - an indication of top down strategy
- Still recommendation of step up strategy:
  - adverse reactions (hypersensitivity, infections)
  - long term complications (neoplasia)
  - cost benefit (price, resources)
5-ASA/ SASP/
Antibiotics/ Local

Budesonide

Steroids

Antimetabolites

Biologics
Epidemiology of IBD in SE Norway in 1990's

Diagnose

Gs1

QoL

IBD 2TK

Gs1

Rheu

Genetics

Gs1

Gs2

Pc

Diagnose

C-C

GP

Gs1

Gs2
National registration of IBD
Quartiles of incidences of ulcerative colitis in the study area

The municipalities in black represent the upper quartile etc.
USA: Rhode Island, Iowa
Switzerland: Zurich
Germany: Regensburg, Norway: Oslo, Czech: Prague, Hungary: Budapest
Croatia: Rijeka, Zagreb
Spain: Gijon
Argentina: Buenos Aires
Uruguay: Monevideo
Greece: Athens
Israel: Telaviv
Crete

Early IBD – International Consortium
Les deseamos los mejores augurios para cada uno de ustedes, deseando que la paz y felicidad, los colme de bendiciones y que el nuevo año que se inicia sea la recompensa de todo aquello que anhelan.

felices fiestas

ACCU Uruguay