Behçet’s Syndrome

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Disclosures

- Abbott
- BMS
- Celgene
- Genentech
- Janssen
- Merck
- Pfizer
- Samumed
- Takeda
- UCB
History

• Hulusi Behçet described (1937) 3 patients with
  – aphthous mouth ulcers
  – genital ulceration
  – hypopyon uveitis

• All 3 patients studied over 17 years

• First to describe “triple symptom complex”
• German medical journal (Dermatologische Wochenschrift)

• Prof. Mischner first proposed the name “Morbus Behcet” at a medical congress in Geneva (1947)
INTERNATIONAL STUDY GROUP CRITERIA FOR THE DIAGNOSIS (Classification) OF BEHÇET’S SYNDROME

Oral ulcers (100%)

+ 

2 of the following:

a. genital ulcers (80%)

b. eye lesions (50%)

c. skin lesions (80%)

d. pathergy (50%)
# Symptoms

**TABLE 1. Major and minor manifestations of Behçet’s syndrome (prevalence %)**

<table>
<thead>
<tr>
<th>Major</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral ulceration—recurrent</td>
<td>(97–98)</td>
</tr>
<tr>
<td>Genital ulceration</td>
<td>(80–90)</td>
</tr>
<tr>
<td><strong>Inflammatory eye disease</strong></td>
<td></td>
</tr>
<tr>
<td>iritis ± hypopyon</td>
<td>(50)</td>
</tr>
<tr>
<td>retinal vasculitis</td>
<td></td>
</tr>
<tr>
<td>Skin lesions</td>
<td>(80)</td>
</tr>
<tr>
<td>erythema nodosum</td>
<td>(45)</td>
</tr>
<tr>
<td>folliculitis/acne</td>
<td>(70)</td>
</tr>
<tr>
<td>pathergy test</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis and arthralgia</td>
<td>(45–50)</td>
</tr>
<tr>
<td>Neurological lesions</td>
<td>(5–25)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>(25)</td>
</tr>
<tr>
<td>aneurysm formation</td>
<td></td>
</tr>
<tr>
<td>arterial/venous thrombosis</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal lesions</td>
<td>(0–25)</td>
</tr>
<tr>
<td>Cardiovascular lesions</td>
<td></td>
</tr>
<tr>
<td>Pleuropulmonary lesions</td>
<td></td>
</tr>
<tr>
<td>Epididymitis</td>
<td>(8)</td>
</tr>
</tbody>
</table>
Demographics

• Mediterranean basin, Korea, Japan
  – Silk road?
    - Very few cases in India
• Before puberty or after 6\textsuperscript{th} decade, rare
• Usual onset 3\textsuperscript{rd} decade
• Male: female equal numbers,
• Worse disease in males

• 400/100,000 (16 yrs or older) in Turkey
• 1-3/100,000 in Olmstead County, MN
Distribution of Behçet’s disease
CLINICAL MANIFESTATIONS
Oral ulcers

• Virtually all patients
• Frequently first manifestation
• Minor aphthous ulcers are most common
  – Lips, gingiva, cheeks and tongue
  – Unlike herpes, skin covered part of lips not involved
  – Usually heal in 15 days without scarring
  – Some complain of premenstrual activation
• Major ulcers
  – Larger, may scar, lasts longer, less common
  – Recurrent aphthous stomatitis (RAS)
    • 20% in population
    • Very rare for RAS to have another clinical finding
    • No HLA B51 association
    • There are no differences among the two ulcers histologically
Genital ulcers

- Papules or pustules that ulcerate quickly
- Punched out appearance
- Aseptic ones heal in 3 weeks, very likely to get secondary infections
- In males usually scrotum is involved, scars, and absence of lesions on glans penis is typical

  - All females should have a gynecologic examination, scarring in the right clinical picture is good evidence
Skin manifestations of BS

- Papulopustular (acne) lesions (85%)
  - Indistinguishable from acne vulgaris
  - Later decades of life vs. teens
    - Atypical places, arms
  - Acne is androgen dependent, however, androgen levels are normal
    - Increased severity in males?
Acne and arthritis in BS

- 44 patients with BS and arthritis
- 42 patients with BS without arthritis
- 21 patients with RA
- 33 healthy controls

Acne scores were very significantly higher among BS patients with arthritis

E Diri et al Ann Rheum Dis 2001
Target organ associations in BS

An Analysis of 272 consecutive patients

- Factor I:
  - oral ulcers + genital ulcers + erythema nodosum

- Factor II:
  - superficial vein thrombosis + deep vein thrombosis

- Factor III:
  - Uveitis

- Factor IV:
  - acne + arthritis

Tunc R, et al J Rheumatol 2002
Enthesopathy

Figure 2. Mean (95% confidence interval [95% CI]) enthesopathy scores and power Doppler scores for each group. BSWA = Behçet’s syndrome without arthritis; BSAA = Behçet’s syndrome with acne and arthritis; AS = ankylosing spondylitis; RA = rheumatoid arthritis; HC = healthy control.

Hatemi G et al, Arthritis Rheum 2008
Nodular lesions of BS

- 60% of patients
  - 50% *e.nodosum like* lesions (more common in women)
  - 50% *superficial thrombophlebitis* (associated with major vessel involvement)
- Difficult to tell one from the other.
CNS involvement in BS

- CNS involvement has a frequency of ~ 4 % in prospective, cross-sectional studies.

- The frequency goes up to ~ 10 % in longer follow-up.

- Peripheral neuropathy is distinctly rare.

- CNS involvement has two distinct forms:
  A. Parenchymal disease (80%, bad prognosis)
  B. Dural sinus thrombi (20%, favourable prognosis)

- A and B rarely co-exist
CNS disease
differential diagnosis

- Brainstem, diencephalon and pontobulbar regions mainly affected
- Peripheral neuropathy very rare
- CNS lesions do not follow a specific vascular pattern
- Isolated cerebellar disease rare
- Meningeal symptoms and on occasion, convulsions can be seen
- Multiple sclerosis, and on occasion, sarcoidosis, can cause problems
# Behçet’s Syndrome vs Multiple Sclerosis

<table>
<thead>
<tr>
<th></th>
<th>MS</th>
<th>BS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>±</td>
<td>+++</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>+++</td>
<td>±</td>
</tr>
<tr>
<td>Sensory problems</td>
<td>+++</td>
<td>±</td>
</tr>
<tr>
<td>PV and SC lesions</td>
<td>+++</td>
<td>±</td>
</tr>
<tr>
<td>Brainstem lesions</td>
<td>Small, no upward extension</td>
<td>Large, with upward extension</td>
</tr>
<tr>
<td>Spinal cord lesions</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Inflammatory CSF</td>
<td>±</td>
<td>+++</td>
</tr>
<tr>
<td>OCB</td>
<td>&gt; 90%</td>
<td>~ 10%</td>
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</tbody>
</table>
Pulmonary Artery Aneurysms

- Unique complication of BS
- Diagnosed mainly at postmortem until 1980 – the most frequent arterial complication today
- Strongly associated with venous thrombosis
- Large proximal branches of pulmonary arteries
Mortality in PAA

- Survival rate: 62% at 5 years (new cohort)
- 70% of the deaths occurred within 1 year following emergence of PAA

*Figure 2.* Kaplan-Meier plot comparing survival of patients diagnosed as having pulmonary artery aneurysms since 1992 with that of the patients diagnosed and reported earlier (6).
Pathergy reaction

• Non-specific hyperreactivity to minor trauma

• Can also be seen in pyoderma gangrenosum

• Standard technique
  – 20 gauge needle
  – Papule or pustule in 48 hours
  – Induration required
  – More common in Middle East

• Interestingly PPD is not augmented in BS patients

  – Hatemi G et al. Rheumatology 2008
# BS vs. Crohn’s Disease

<table>
<thead>
<tr>
<th></th>
<th>Behçet’s syndrome</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perianal disease</strong></td>
<td>Very uncommon</td>
<td>Seen in 1/3</td>
</tr>
<tr>
<td><strong>Structures</strong></td>
<td>Uncommon*</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Deep mucosal ulcerations</strong></td>
<td>Uncommon*</td>
<td>Common</td>
</tr>
<tr>
<td></td>
<td>-multiple, superficial ulcers.</td>
<td></td>
</tr>
<tr>
<td><strong>Granuloma formation</strong></td>
<td>Uncommon</td>
<td>Common</td>
</tr>
</tbody>
</table>
Eye disease in BS

- Most serious when considering frequency and morbidity
- Leading cause of non-traumatic blindness after DM in Japan, Israel
- Non-granulomatous panuveitis and retinal vasculitis
- Over all 50%
  - 70% of males <25 yr
- Frequently present at onset or first 2-3 yrs
  - Rare after 5 years of disease
- Bilateral in 90%
- Hypopyon is classical finding in eye disease (20%)
  - Almost always accompanied by severe retinal vasculitis
DVT

- DVT in BS is an inflammatory reaction to the endothelium
- It is a sticky and very hard clot, no trailing tail formation
- Very rare for it to break off and embolise
- ? Anti-coagulation in DVT with BS
Thrombophilia in BS

- 1/3 of patients have thrombophlebitis

- Abundant evidence for functional impairment of the vessel wall;
  - an autoinflammatory endothelitis?

- Abnormalities in the coagulation cascade?
Long-term mortality and morbidity of BS:
Two decade outcome study

- 428 (286M / 142F) BS patients registered at Cerrahpaşa BS Multidisciplinary Outpatient Clinic between 1977-1992

- Found to have died: 42(9.8 %) - 39M / 3F

- Could not be reached: 41(9.6 %) - 24M / 17F
STANDARDIZED MORTALITY RATIOS OF 286 MALE PATIENTS WITH BS STRATIFIED AS TO THE AGE OF ONSET AND EVALUATED AT 7 YEAR INTERVALS
Main causes of death among 42 patients

- Vascular disease: 17 (venous 5)
- CNS disease: 5
- Amyloidosis: 3
- Malignancy: 4
- Suicide: 2
- Misc: 11

- PAA
  - Main reason for mortality
  - Frequently associated with thrombi in inferior vena cava and iliac-femoral system
  - Presents with hemoptysis, may look similar to PE
  - Anticoagulation contraindicated
Onset of eye disease in males

-1 0 1 2 3 4 5 6-10 11-20 21-30

Years

0 20 40 60 80 100 120

%
Other manifestations

<table>
<thead>
<tr>
<th></th>
<th>Beginning</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OU (%)</strong></td>
<td>345 (100.0)</td>
<td>220 (63.7)*</td>
</tr>
<tr>
<td><strong>GU (%)</strong></td>
<td>310 (89.9)</td>
<td>90 (26.1)*</td>
</tr>
<tr>
<td><strong>EN (%)</strong></td>
<td>223 (64.4)</td>
<td>88 (25.5)*</td>
</tr>
<tr>
<td><strong>Arthritis (%)</strong></td>
<td>140 (40.6)</td>
<td>34 (9.9)*</td>
</tr>
</tbody>
</table>

* P=0.001
Differential diagnosis

• Sacroiliitis and spinal joint involvement are not features of BS

• Skin lesions do not include psoriasis

• Urethral discharge is not a feature of BS

• GI involvement with ileocaecal ulceration and sometimes colonic perforation is distinct from typical IBD
Clinical evidence for autoimmunity in BS?

Uncommon/not seen in BS:
- Sjögren’s syndrome
- Association with other autoimmune diseases
- Raynaud’s phenomenon
- Polyserositis
- Hemolytic anemia
- Sun sensitivity
- No autoantibodies

Unique to BS:
- Pathergy
- Genital ulcers – scrotal
- Pulmonary artery aneurysms
- Clinical course
CAD in Patients with Severe Vascular Disease of BS

- 24 males
- Age: 37.5 ± 4.5 yrs.
- Disease duration: 13.2 ± 3.9 yrs.
- Smoking: 88%
- Steroid use: 63%
- 3/24 (12.5%) had angina pectoris

- Coronary calcification and stenosis: 3/24 (12.5%)

Seyahi-Kural E et al. Rheumatology, 2004
Prevalence of carotid artery plaques in male patients vs healthy controls

<table>
<thead>
<tr>
<th>Diseases</th>
<th>n (%)</th>
<th>Adjusted**</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS (n =162)</td>
<td>31 (19)</td>
<td>1.5 (0.7-3.4)</td>
<td>0.33</td>
</tr>
<tr>
<td>RA (n = 24)</td>
<td>11 (46)</td>
<td>3.5 (1.1-10.9)</td>
<td>0.033</td>
</tr>
<tr>
<td>AS (n =58)</td>
<td>9 (16)</td>
<td>1.3 (0.5-3.5)</td>
<td>0.64</td>
</tr>
<tr>
<td>HC (n = 83)</td>
<td>10 (12)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*: Mean age for BS: 40 ± 7, RA: 46 ± 7, AS: 39 ± 7, HC: 38 ± 8 years

**: Adjusted for age and presence or absence of diabetes mellitus and hypertension

Autoinflammatory?
(FMF as the prototype)

- Epidemiology
  - Mediterranean vs. Japan
    - Rare and almost all defined from the West
  - Children vs. adults

- Clinical findings

- Genetic aspects
  - HLA B51
  - Pyrin

- Response to treatment (colchicine story)
- Well defined mutations (TNF-receptor, pyrin or CARD/NOD) and transmission
- Usually a non-abating course
Genetics of Behcet

- HLA B51
  - ? HLA A26 in Japanese and Turkish
- GWAS
  - IL-10
    - IL-10 knockout mice intestinal inflammation
    - UC, Crohn’s
    - Increasing IL-10 may restore imbalance and control hyperinflammation
      - Interferon?-alpha?
  - IL-23R, shared between Japanese and Turks
    - Also found in spondyloarthritis group
      - AS, IBD, psoriasis
      - Genetic variants don’t overlap
  - IL-12RB2
Genetic ? Environmental ?

- Japanese living in Hawaii

- Turkish immigrants vs Germans in Berlin

- Arabs/Druzes vs Jews in Israel

- North African immigrants vs Europeans in Paris
Treatment
Systematic literature search: 2402 articles

Exclusions:
- Duplications
- Review articles
- Editorials
- Case reports
- Studies where the results for BD was not given separately

- 137 articles
- 20 randomized controlled trials
# Colchicine in BS

## Table 2. Mean number of mucocutaneous lesions and arthritic joints in each study arm

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Colchicine (n = 28)</td>
<td>Placebo (n = 27)</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td>15.6 ± 12.3 (0–40)</td>
<td>21.3 ± 13.6 (2–56)</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>0.1 ± 0.5 (0–2)</td>
<td>2.6 ± 4.6 (0–16)</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>1.4 ± 3.9 (0–17)</td>
<td>6.0 ± 14.9 (0–71)</td>
</tr>
<tr>
<td>Arthritic joints</td>
<td>0.3 ± 1.1 (0–6)</td>
<td>2.4 ± 6.0 (0–29)</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>4.1 ± 3.5 (0–12)</td>
<td>5.9 ± 5.2 (0–18)</td>
</tr>
</tbody>
</table>

* Values are the mean ± SD (range) unadjusted total number of mucocutaneous lesions or arthritic joints in patients during the whole trial irrespective of the length of time he/she remained in the trial. All outcome measures were based on the data obtained by the physicians at monthly clinic visits.
† Mann-Whitney U test (2-tailed).
Corticosteroids

A double-blind trial of depot corticosteroids in Behçet’s syndrome

C. Mat¹, S. Yurdakul¹†, S. Uysal, F. Gogus¹, Y. Ozyazgan², O. Uysal³, I. Fresko¹ and H. Yazici¹

Objectives. Corticosteroids are widely used in Behçet’s syndrome despite the absence of controlled studies. We assessed the effect of depot corticosteroids primarily for genital ulcers and secondarily for the other mucocutaneous manifestations of Behçet’s syndrome.

Methods. We randomized 86 patients who had active disease with genital ulcers to receive either intramuscular corticosteroid injections (40 mg methylprednisolone acetate) or placebo every 3 weeks for 27 weeks.

Results. Seventy-six patients (88%) completed the treatment. There were no significant differences in the mean number of genital and oral ulcers, or folliculitis between groups. The mean number of erythema nodosum lesions was less in the corticosteroid group as a whole ($P=0.0046$); subgroup analyses revealed that this was significant for females ($P=0.0148$) but not for males ($P=0.1$).

Conclusion. Low-dose depot corticosteroids did not have any beneficial effect on genital ulcers. However, it was useful in controlling erythema nodosum lesions, especially among the females.

Keywords: Behçet, Corticosteroids, Erythema nodosum, Genital ulcer, Therepy.
Corticosteroids in BS
(Skin-Mucosa Manifestations)

Table 2. Mean number of lesions during treatment and post-treatment periods among males and females

<table>
<thead>
<tr>
<th></th>
<th>Treatment period</th>
<th>Post-treatment period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Steroid (n = 41)</td>
<td>Placebo (n = 44)</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>0.3 ± 0.4</td>
<td>0.3 ± 0.4</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td>1.8 ± 1.0</td>
<td>1.8 ± 1.2</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>0.1 ± 0.3</td>
<td>0.3 ± 0.5</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>1.1 ± 0.7</td>
<td>1.0 ± 0.6</td>
</tr>
<tr>
<td>Joints with arthritis</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.3</td>
</tr>
</tbody>
</table>

Values are mean ± s.d. for the unadjusted total number of lesions in patients during the whole trial. All outcome measures were based on the data observed by the physician at three weekly clinic visits during the treatment period and monthly clinic visits during the post-treatment period.

<sup>a</sup>Mann–Whitney U-test (two-tailed).
Azathioprine in BS (I)

- Prevents emergence of eye disease in the unaffected ($p < 0.01$)
- Prevents eye disease becoming bilateral ($p < 0.001$)
- Prevents eye disease getting severe (thus leading to withdrawal from the study) among the affected ($p < 0.001$)
- Less frequent attacks of hypopyon ($p < 0.001$)
- Preserves vision
Azathioprine in BS (II)

- Less frequent oral ulcers ($p<0.005$)
- Less frequent genital ulcers ($p<0.001$)
- Less frequent arthritis ($p<0.02$)
- Less frequent thrombophlebitis ($p<0.10>0.05$)

Azathioprine in BS (III)

Reassessment after 8 years

- Total loss of vision more in those initially allocated to placebo ($p = 0.02$)

- Beneficial effects on visual acuity mainly among those who had been allocated to azathioprine within 2 years of onset of eye disease ($p = 0.05$ and $0.07$ for either eye)

- A trend for less frequent extraocular manifestations among the groups that received azathioprine

Azathioprine in BS (IV)

- Data available had been for the 2.5 mg/kg/day dose!
- Onset of action is slow (> 3 months)
- Leukopenia with azathioprine + interferon
Effect of etanercept on mucocutaneous manifestations of BS

• There was 40% chance of remaining oral ulcer (OU) free in the etanercept arm versus 5% in the placebo arm ($p_{log}=0.002$) at the end of 4 weeks.

• There were also significant decreases in the number OU, nodular lesions, acne lesions and arthritis with the expected exacerbations at 3 months after the trial ended.

• No effect on the pathergy reactions.

Infliximab for severe and treatment resistant uveitis of BS

4 studies (open):
- Fast (<24 hours) onset of action
- Complete (attack free) remission: 31 – 75%
- Infusions need to be continued for sustained remission

Ohno S et al J Rheumatol 2004
Tugal-Tutkun I et al. Arthritis Rheum 2005

Infliximab

Figure 1. Distribution of the types of uveitis attacks that occurred during the previous-treatment, infusion, and observation periods.
Apremilast

Hatemi G, et al. EULAR 2013
OU time to response

All patients in the PBO group switched to APR from week 12 visit
OU Pain over time

Placebo: 51.7 29.8 37.4 36.7 30.7 23.5 35.0 7.9 7.9 7.3 7.2 6.6 9.6 17.2 21.0
30 mg BID: 54.3 12.0 10.2 10.5 13.0 8.8 9.4 9.9 5.8 7.1 8.1 3.4 9.7 23.2 27.2
<table>
<thead>
<tr>
<th>Table 2. Disease Activity and Patient-Reported Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Behçet’s Disease Activity Index (n)</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Week 12 (LOCF)</td>
</tr>
<tr>
<td>Change from baseline</td>
</tr>
<tr>
<td>BDQoL (n)</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Week 12 (LOCF)</td>
</tr>
<tr>
<td>Change from baseline</td>
</tr>
<tr>
<td>MDHAQ (n)</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Week 12 (LOCF)</td>
</tr>
<tr>
<td>Change from baseline</td>
</tr>
<tr>
<td>Treatment-Emergent Adverse Events (TEAEs), n (%)</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Any TEAE</td>
</tr>
<tr>
<td>Any drug-related TEAE</td>
</tr>
<tr>
<td>Any severe TEAE</td>
</tr>
<tr>
<td>Any serious TEAE</td>
</tr>
<tr>
<td>Behçet’s flare</td>
</tr>
<tr>
<td>Diplegia</td>
</tr>
<tr>
<td>Anal fissure</td>
</tr>
<tr>
<td>Hemorrhoids</td>
</tr>
<tr>
<td>Pyrexia</td>
</tr>
<tr>
<td>Any serious drug-related TEAE</td>
</tr>
<tr>
<td>Any TEAE leading to drug interruption</td>
</tr>
<tr>
<td>Any TEAE leading to drug withdrawal</td>
</tr>
<tr>
<td>Behçet’s flare</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Anal fissure</td>
</tr>
<tr>
<td>Hemorrhoids</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Dysfunctional uterine bleeding</td>
</tr>
<tr>
<td>Any TEAE leading to death</td>
</tr>
</tbody>
</table>
Inflammatory eye disease with posterior segment involvement should be on azathioprine+corticosteroids

Severe eye disease, retinal disease
- Cyclosporine or infliximab added
- Interferon alpha

No firm guidelines for major vascular disease
- DVT= immunosupression
- PAA and peripheral aneurysm= CYC+corticosteroids

No data about use of anticoagulants, anti-platelet agents but not recommended

No evidence base for GI treatment
- Immunosupression, TNF

In most patients, arthritis can be managed with colchicine
EULAR guidelines (2)

• No data on CNS disease management
  – AZA, CYC preferred, IFN alpha, TNF inhibitors
• Cyclosporine should not be used in CNS, unless needed for eye inflammation
• Mucocutaneous lesions, systemic treatment if resistant to topical measures
Management in 2013

- Consider natural course, age, sex
- Steroids: not for long-term use
- Colchicine:
  - arthritis (M+F)
  - e. nodosum (M+F)
  - genital lesions among the females
- Thalidomide:
  - Good for all mucocutaneous lesions
  - toxicity precludes long-term use
- Azathioprine
  - slow-acting, usually under-dosed
- Cyclosporine
  - fastest acting agent for eye disease; CNS toxicity?
- Interferon:
  - masked studies in eye disease needed
- TNF inhibitors
  - Quick response, use in combination
- Plaquinil, MTX, Cellcept,...

- No anticoagulation for thrombophilia
NYU HJD Behçet’s Syndrome Evaluation, Treatment and Research Center

• Started in 2005

• ~1100 patient seen

• ABDA

• RCT
BSAS consists of 10 questions, each scored 0-10.

Patient reported measures

VAS for patient’s level of discomfort oral ulcers, genital ulcers, skin lesions or acne, and current disease activity.

The BSAS also categorizes the number of oral ulcers, genital ulcers, and acne lesions present, and records if there is GI involvement, vascular involvement, or eye involvement.
Current studies

• Anakinra
  – NIH

• Abatacept
  – OU, open label

• Tocilizumab
  – OU, double blind, placebo controlled

• Neurology NYU HJD and NIH
  – Functional imaging
Conclusions

- BS is not very rare.
- It has distinct features from “connective tissue” diseases.
- Disease clusters.
- In many patients it is a mild disease which can also go away by itself.
- We can successfully manage a substantial majority of the remaining patients.
  - CNS disease and thrombophilia are still problems.
- We are doing considerably better now than did 20 years ago.