Treatment with steroids and immunosuppressants

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Factors that will influence therapy

- **Clinical features**
  - Extent of disease
  - Areas of the body involved
    - Mucosa, palmar/plantar
  - Symptoms
    - Degree of itch or pain

- **Patient features**
  - Comorbidities
    - Dementia, renal failure, diabetes, malignancy
  - Medication list
Factors that will influence therapy

- **Disease features**
  - Bullous pemphigoid
    - Autoantibodies → inflammation, cellular infiltrate
  - Pemphigus
    - Autoantibodies → acantholysis with minimal inflammation
  - Others ...
    - Presence of IgA or IgE, type of cellular infiltrate, circulating autoantibodies (IIF or ELISA)
Factors that will influence therapy

- **Phase of disease**
  - Baseline – the day therapy is started by a physician
  - Control of disease activity – new lesions cease to form and old lesions begin to heal
  - End of consolidation – no new lesions have developed for 2 weeks and 80% of lesions have healed

Factors that will influence therapy

- Phase of disease - maintenance
  - Complete remission off therapy or on minimal therapy – no lesions for 2 months
  - Partial remission off therapy or on minimal therapy – lesions that heal spontaneously within 1 week
  - Mild disease activity – less than 3 new lesions per month that do not heal within 1 week
  - Flare/Relapse – greater than 3 new lesions per month that do not heal within 1 week

Factors that will influence therapy

Early and intermediate observation points

- Baseline: The day that BP therapy is started by a physician
- Time to disease control
- End of consolidation phase: no new lesions or pruritic symptoms for at least 2 weeks; 80% lesions have healed; when steroid tapering starts
- Complete remission during tapering: absence of non-transient lesions whilst the patient is receiving more than minimal therapy

Late observation endpoints

- Partial remission on minimal therapy: Presence of transient new lesions that heal within one week without treatment and while the patient is on minimal BP therapy for at least two months.
- Partial remission off therapy: Presence of transient new lesions that heal within one week without treatment and while the patient is off therapy including topical steroids for at least two months.
- Complete remission on minimal therapy: Absence of new or established lesions while the patient is on minimal BP therapy for at least two months.
- Complete remission off therapy: Absence of new or established lesions while the patient is off all BP therapy for at least two months.
- Relapse: Appearance of 2 or more new lesions or monitoring of cutaneous skin thickening on tapering or thinning treatment of remission or less than 1 month without treatment patients who have previous disease controls.

Approach to treatment

- Fast acting
- Slow acting

Dose vs. Time graph
Approach to treatment

<table>
<thead>
<tr>
<th>Time</th>
<th>Dose</th>
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<tbody>
<tr>
<td></td>
<td>Prednisone</td>
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<td></td>
<td>Steroid sparing agent</td>
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Bullous pemphigoid/MMP
Bullous pemphigoid/MMP

Localized or limited disease

- Clobetasol
- Dapsone
- Minocycline/doxycycline, nicotinamide

Bullous pemphigoid/MMP

Extensive disease

- Prednisone – 1-2mg/kg/day, 60-80mg daily with taper by 5-10mg weekly until 30mg daily, then alternating day taper
- Potent topicals such as clobetasol cream (20g/bid) are also very effective and may be safer – systemic absorption? $$$$

Bullous pemphigoid/MMP

Prednisone

- Works quickly, relatively inexpensive
- Short term side effects – insomnia, irritability, elevated blood glucose, increased blood pressure, increased appetite, water retention
- Long term side effects – diabetes, cataracts, glaucoma, weight gain, GI bleed, decreased bone density (compression fractures)

Bullous pemphigoid/MMP

Dapsone

- Old leprosy drug
- Very good at treating certain blistering skin disorders
- Usually well tolerated
- Dose related anemia
- Motor and sensory neuropathy

Methotrexate

- Weekly medication – oral or subcutaneous
- Effective at successfully tapering prednisone
- Can be used without prednisone (median time to remission 11 weeks)
- Relatively inexpensive
- Maybe slightly less immunosuppressive

Bullous pemphigoid/MMP

Methotrexate

- **Contraindications** – history of liver disease, heavy alcohol use, pregnancy
- **Side effects**
  - Nausea/vomiting, fatigue
  - Drop in blood counts, liver inflammation, lung irritation
  - Long term effects on the liver
Bullous pemphigoid/MMP

Azathioprine (Imuran)
- Dose based on TPMT enzyme activity level
- 100-200mg daily
- Contraindication – active infection
- Side effects – nausea/vomiting, decrease in blood counts, liver inflammation, infection
- Other considerations – drug interactions (gout)
Bullous pemphigoid/MMP

Mycophenolate mofetil (Cellcept)

- 500-1500mg twice daily
- Contraindication – active infection
- Side effects – nausea/vomiting, urinary symptoms, decrease in blood counts, liver inflammation, infection
- Other considerations – cost!
Bullous pemphigoid/MMP

Cyclophosphamide

- Good efficacy in severe ocular cicatricial pemphigoid
- Side effects - Bladder toxicity, drop in blood counts, liver inflammation, infection
Pemphigus
Localized disease

- Topicals – minimally effective
- Intralional steroids – useful in rare cases
Pemphigus

Extensive disease

- Prednisone 60-80mg daily with taper by 5-10mg weekly until 30mg daily, then alternating day taper
- Potent topicals – don’t work as well

Pemphigus

MTX
- Lower efficacy
- Cost effective

Azathioprine versus mycophenolate
- Equally effective in terms of steroid sparing ability
- Azathioprine has more GI related upset
- Mycophenolate costs more

Cyclophosphamide
- Efficacy in recalcitrant disease and/or vegetative plaques
B cells in pemphigus and pemphigoid

Bone Marrow

Pro-B  Pre-B

Immature  Mature

Spleen

Germinal Center

Ag

Memory

Plasma cell

Bone Marrow

Plasmablast

?
Approach to treatment

How can we tell if the treatment is working?

- Fewer to no new lesions
- Steroid sparing
- Titers of antibodies are lower/negative (pemphigus)
Approach to treatment

When to switch treatments?

- Intolerable side effects
- Serious side effect
- Ineffective – definitions for dose and length of treatment
- Not steroid sparing
- The list of options is not very long!
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