## Appendix 4: Prevention and treatment of less common adverse effects reported with insulin

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Description</th>
<th>Evidence level</th>
<th>Prevention and treatment</th>
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</thead>
</table>
| **Congestive heart failure (CHF)**

- CHF rates were highest in regimens that included insulin and lowest in regimens including metformin
- Addition of insulin to preexisting diabetes regimens significantly increased the rates of CHF relative to the addition of sulfonylureas (odds ratio [OR] 2.33, *p*<0.0001) and metformin (OR 2.66, *p*<0.0001) even after adjustment for relevant covariates

<table>
<thead>
<tr>
<th>27-mo observational study</th>
<th>Conventional medical management for CHF as needed</th>
</tr>
</thead>
</table>
| **Edema**

- Varies from mild peripheral edema to frank anasarca

<table>
<thead>
<tr>
<th>Case reports</th>
<th>Self-limiting, rarely requires treatment except for diuretic use with anasarca</th>
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</table>
| **Lipodystrophy**

- Most common cutaneous effect of insulin
- Consists of subcutaneous fat at injection sites
- Occurs in 3.6% of patients with type 2 diabetes and 28.7% of patients with type 1 diabetes
- Risk factors include: young age, low body mass index, abdominal injection site, and failure to rotate injection sites

| Case reports | Prevention:
- Regular rotation of injection sites.
Treatment:
- Rotation of injection sites and switching to rapid-acting insulin analogues so potential regression of affected sites may occur
- Insulin pump therapy
- Syringe assisted liposuction |
|--------------|---------------------------------------------------------------------|
| **Other cutaneous reactions**

- Lipotrophy:
  - Associated with older less purified insulin
  - Rare with modern insulins
  - Risk factors include: young age, individuals with previous dermal reactions to insulin
  - Skin abscesses, pigmentation, and keloid formation:
    - Rare

| Case reports | Lipotrophy:
- Prevention: regular rotation of injection sites
- Treatment: injection of a modern insulin into the edge of the area, co-administration of insulin with dexamethasone (4 mcg/unit) or switching to insulin pump therapy
Skin abscesses:
- Prevention: good hygiene and appropriate antiseptic measures, rotation of injection site |
|--------------|---------------------------------------------------------------------|
| **Allergic reactions and formation of antibodies to insulin**

- Associated with older less purified insulin
- Rare with modern insulins

| Case reports | Cutaneous allergic reactions:
- Tend to be short-lived and resolve spontaneously within a few weeks
- Antihistamines or corticosteroids if needed
- Switching insulin used (avoid use of insulins containing zinc or protamine)
- Dividing of dose and varying delivery sites
- Addition of 1 mcg dexamethasone to each unit of insulin per injection
- Use of insulin pump therapy
- Insulin withdrawal
- Densensitization in more serious cases |
|--------------|---------------------------------------------------------------------|
| **Other adverse effects**

- Insulin-induced transaminitis (> 10 times the upper limit of normal)
- Reversible nephrotic syndrome
- Beta-cell destruction (complete disappearance of C-peptide upon insulin initiation)

| Case reports | No specific prevention nor treatment strategy to avoid |
References


