A subgroup of severe COVID-19 patients experience cytokine release syndrome (CRS, also known as cytokine storm), where cytokines that coordinate the response to infection and trigger inflammation are released in excessive amounts. If uncontrolled, CRS can lead to tissue damage and patient death.

**Symptoms of severe disease:**
- Massive multi-organ tissue destruction
- Acute Respiratory Distress Syndrome (ARDS)
- Cytokine Release Syndrome (CRS)

**Viral infection**
- SARS-CoV-2
  - ACE2
  - TMPRSS2

**Acute inflammation**
- Type II alveolar cell
  - IL-18
  - IL-1
  - MCP-1
  - IP10
  - MIP1α
  - MIP1β
- +ve feedback
- Monocyte
  - +ve feedback
- Macrophage
- IFNγ

**Cytokine storm**
- Liver
  - ↑ CRP
  - ↑ Ferritin
  - ↑ Fibrinogen
  - ↑ TPO
  - ↑ Albumin
  - ↑ Complement C3
- Blood vessels
  - ↑ VEGF
  - ↑ IL-8
- Lymphocytes
  - ↑ Tα, 17
  - ↑ CD8+ T cell activity
  - ↑ IL-17A
  - ↑ IL-10
  - ↑ E-cadherin
  - ↓ Treg cells
  - ↓ IL-10
  - ↓ Plasma cells

**Three grades of illness**

- **Asymptomatic**
- **80%**
- **Non-severe**
- **Severe respiratory symptomatic**
- **20%**

**Symptoms of severe disease:**
- Massive multi-organ tissue destruction
- Acute Respiratory Distress Syndrome (ARDS)
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**Cytokine storm in COVID-19**

** IL-6** The most frequently reported cytokine to be increased in COVID-19 patients. Elevated levels of this cytokine are associated with higher mortalities.

** >65 yrs** Cytokine storm disproportionately affects the elderly. Immune system balance is regulated differently at different ages. Older people may make a more damaging response than the young.

**12+** Number of candidate coronavirus drugs targeting cytokine storm. Early results from the recovery trial show the steroid dexamethasone reduces mortality by one third for patients requiring respiratory support.

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