

Steroid and COVID19

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- **Steroids** (also known as cortisone or **corticosteroids**) are chemicals (hormones) that occur naturally in the body.
- **Steroids** decrease **inflammation**,
- suppress the body's immune system,
- block DNA from being made,
- blocking a chemical called histamine

- **Steroids** are hormones of **3 types**:
- 1. **Anabolic Androgenic Steroids** – like testosterone, that builds muscle and masculinize (hair, deep voice, sex).
- 2. **Glucocorticosteroids** – like cortisone or **prednisone**, that are anti-inflammatory or immunosuppressants used in swelling, rashes, asthma, or bronchitis.

- Steroids do not tend to cause significant side effects **if** they're taken for a short time or at a low dose.
- But sometimes they can cause **unpleasant side effects**, such as an increased appetite, mood changes and **difficulty sleeping**.
- This is most common with steroid tablets.

What are the benefits of steroids?

- Common uses for **steroids** include improving performance in sporting, increasing muscle mass in strength champions, and preserving muscle mass in those with muscle-wasting diseases.

- Corticosteroid drugs are used to treat **rheumatoid arthritis, lupus, asthma, allergies** and many other conditions.
- They also treat **Addison's disease**, a condition where the adrenal glands aren't able to produce even the **minimum amount** of corticosteroid that the body needs

- **Corticosteroids** are a class of drug that lowers inflammation
- They also reduce immune system activity.
Because **corticosteroids** ease swelling, itching, redness, and allergic reactions, asthma.

- Systemic **corticosteroids** must go through the body to treat the inflammation.
- Inhaled or intranasal **corticosteroids** go directly to where the inflammation is.
- In general, **corticosteroids** are **safe** and work well if the medicine is taken

- **Corticosteroids** are a class of [steroid hormones](#) that are produced in the [adrenal cortex](#) of [vertebrates](#), as well as the synthetic analogues of these hormones.
- Two main classes of corticosteroids, [glucocorticoids](#) and [mineralocorticoids](#), are involved in a wide range of [physiological](#) processes,
- including [stress response](#), [immune response](#), and regulation of [inflammation](#), [carbohydrate metabolism](#), [protein catabolism](#), blood [electrolyte](#) levels, and behavior.^[1]

- Some common naturally occurring steroid hormones are [cortisol](#) , [corticosterone](#) , [cortisone](#) and [aldosterone](#)
- (Note that aldosterone and cortisone share the same chemical formula but the structures are different.)
- The main corticosteroids produced by the adrenal cortex are cortisol and aldosterone

- **WHO** welcomes the initial clinical trial results from the United Kingdom (UK) that show **dexamethasone**, can be lifesaving for patients who are critically ill with COVID-19
- For patients **on ventilators**, the treatment was shown to reduce mortality by about **one third**,
- and for patients requiring only oxygen, mortality was cut by about **one fifth**, according to preliminary findings shared with WHO.
- The benefit was only seen in patients seriously ill with COVID-19, and was not observed in patients with milder disease.

- The **Recovery trial**, one of the biggest efforts to evaluate whether existing drugs can treat COVID-19, included **2104** patients given a relatively low dose of 6 milligrams of dexamethasone for 10 days.
- When their outcomes were compared with those of 4321 patients receiving standard care, the steroid reduced deaths by one-third in patients already on ventilators and by one-fifth in patients receiving supplemental oxygen in other ways,
- They did not find any benefit in patients not receiving respiratory support.

- Dexamethasone's effect is seemingly much stronger than that of **remdesivir**.
- That antiviral reduced the number of days critical patients were hospitalized, but it did not clearly reduce death
- **UK RECOVERY trial** assessed the mortality rate at day 28 in hospitalized patients with COVID-19 who received low-dose **dexamethasone 6 mg** PO or IV daily for 10 days added to usual care.
- Patients were assigned to receive dexamethasone (n = 2104) plus usual care or usual care alone (n = 4321).

- Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization ($P < 0.001$)
- In the dexamethasone group, the incidence of death was lower than the usual care group among patients receiving invasive mechanical ventilation (29.3% vs 41.4%)
- and among those receiving oxygen without invasive mechanical ventilation (23.3% vs 26.2%),
- but not among those who were receiving **no respiratory support at randomization (17.8% vs 14%).**

- Corticosteroids are not generally recommended for treatment of viral pneumonia.
- The benefit of corticosteroids in septic shock results from modulating the host immune response to bacterial toxin release

Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective

David M. G. Halpin, Dave Singh, Ruth M. Hadfield
European Respiratory Journal 2020

- Surprisingly, the prevalence of COPD among patients with SARS and COVID-19 appears to be lower than the general population
- Sadly, patients with underlying lung disease who develop COVID-19 and are hospitalised have worse outcomes with a case fatality rate of 6.3% compared to 2.3% overall in China
- At present, there is no evidence as to whether pre-morbid use or continued administration of ICS is a factor for adverse or beneficial outcomes in acute respiratory infections due to coronavirus

- in this COVID-19 pandemic, there is no evidence to support the withdrawal of ICS in patients treated with these drugs, and to do so is likely to be harmful.
- Patients with asthma and COPD who are stable while using ICS **should continue** on their treatment.
- If there is uncertainty about the diagnosis, physicians should be more careful about initiating ICS or ICS/LABA in patients without clear objective evidence of asthma.
- Similarly, there is no evidence to suggest a change in the advice for asthma patients to increase the dose of ICS at the onset of an exacerbation.

Efficacy and safety of corticosteroids in COVID-19 based on evidence for COVID-19, other coronavirus infections, influenza, community-acquired pneumonia and acute respiratory distress syndrome: a systematic review and meta-analysis
CMAJ July 06, 202

- In ARDS, according to 1 small cohort study in patients with COVID-19 and 7 RCTs in non-COVID-19 populations , corticosteroids may reduce mortality
- In patients with severe COVID-19 but without ARDS, direct evidence from 2 observational studies showed an **increase in mortality** with corticosteroids , as did observational data from influenza studies.
- Observational data from SARS and MERS studies showed a small or no reduction in mortality

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CMAJ July 06, 2022

- Randomized controlled trials in CAP suggest that corticosteroids may reduce mortality and may increase hyperglycemia

Inhaled steroid

- We identified three studies that investigated the antiviral potential of the inhaled corticosteroid **ciclesonide**
- One study investigated the antiviral potential of **ciclesonide** against the SARS-CoV-2 virus in vitro, one against the MERS-CoV, HCoV-229E and SARS-CoV viruses in vitro and one was a case series of three patients admitted to hospital with COVID-19 who were treated with inhaled ciclesonide.
- **Inhaled ciclesonide is expected to reduce viral replication and pulmonary inflammation**, whilst **having lower immunosuppressive effects when compared to systematic corticosteroids.**

- A single in vitro study that investigated the antiviral potential of **budesonide** observed **no reduction in viral replication in cells treated with budesonide and no reduction in inflammatory cytokine release**
- Additional data is required both in vitro and in vivo to help consider whether inhaled corticosteroids may be used for the treatment of COVID-19 pneumonia;
- one study underway investigating the safety and efficacy of inhaled ciclesonide for the treatment of COVID-19 in the **US** and three further studies due to start recruiting (one each in **Sweden, Canada** and **South Korea**).⁹

- **Dexamethasone** is generally safe.
- It presents a favourable benefit-risk profile, particularly in patients with **severe forms of pneumonia**, while the benefit is **less prominent in non-severe pneumonia**.
- As the treatment is short, even at high doses, corticosteroids are not associated with **serious side effects**.
- Potentially higher blood glucose levels (hyperglycaemia) are temporary
- **Prolonged use (more than two weeks)** may be associated with adverse events such as **glaucoma, cataract, fluid retention, hypertension, psychological effects (e.g., mood swings, memory issues, confusion or irritation), weight gain, or increased risk of infections and osteoporosis**.

- The **Recovery trial** used dexamethasone 6mg daily oral or intravenous for 10 days.
- Higher daily doses of dexamethasone have been used for other indications for a long time and are known to be safe
- **Can steroids be used in the elderly/children/pregnancy?**
- They can be used in children and the elderly.
- **In pregnancy**, the Recovery trial used **prednisolone orally** or **hydrocortisone by intravenous infusion** instead of dexamethasone.

- **In pregnancy or breastfeeding women**, patients were randomized to prednisolone (a milder corticosteroid) 40 mg administered by mouth. (or intravenous hydrocortisone 80 mg twice daily) should be used instead of dexamethasone
- It is permitted to switch between the two routes of administration according to clinical circumstances.

Interleukin Inhibitors

- Interleukin (IL) inhibitors may ameliorate severe damage to lung tissue caused by cytokine release in patients with serious COVID-19 infections.
- Several studies have indicated a “**cytokine storm**” with release of IL-6, IL-1, IL-12, and IL-18, along with tumor necrosis factor alpha (TNF α) and other inflammatory mediator(**in second week**)

Inhaled corticosteroids and COVID-19

- Many physicians are concerned about whether individuals positive for SARS-CoV-2 and taking ICS should **continue them**, **or stop them**, given that ICS are often regarded as immunosuppressive

Surprisingly, the **prevalence** of chronic respiratory disease among patients with SARS and COVID-19 appears to be lower than among the general population

Sadly, patients with underlying lung disease who develop COVID-19 and are hospitalised have worse outcomes, with a case fatality rate of 6.3% compared to 2.3% overall in China

- **budesonide**, in combination with **glycopyrronium** and **formoterol**, has inhibitory actions on coronavirus HCoV-229E replication and cytokine production
- Furthermore, **ciclesonide** blocks SARS-CoV-2 ribonucleic acid replication *in vitro* and inhibits SARS-CoV-2 cytopathic activity
- which may reduce the risk of developing of COVID-19 in response to SARS-CoV-2 infection or reducing the severity of the disease.