

**Effects of Inhaled Steroids on cell
mediated immunity (CMI) and possible
reactivation of tuberculosis in
asthmatic patients**

Thesis submitted for partial fulfillment of MSC degree in
Internal Medicine

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**تأثير الكورتيزون بالاستنشاق على المناعة الخلوية في مرضى
الربو الشعبي واحتمالية نشاط مرض الدرن الكامن**

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أمراض الباطنة العامة

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Recommendation

Because ICS have a dose-dependent systemic effect, although less than oral corticosteroid treatment, (**Lipworth et al., 1999**) careful follow up should be undertaken for patients with asthma who are treated with ICS. When acute pneumonia develops in these patients, atypical pulmonary tuberculosis should be taken into account as a differential diagnosis.

We thought that Careful observation of patients is considered to be important because pulmonary tuberculosis in association with ICS was found among inpatients, there was no relationship to the total dose or duration of administration of ICS, there were no clinical symptoms, and the patients exhibited atypical radiographic findings.

We recommend to apply this study in wider scale of patients and for a longer duration using the same dose of beclomethasone dipropionate inhaler and to assess other systemic side effects of inhaled corticosteroid to achieve safe form and dose for asthmatic patients.

Also using of the more recent accurate laboratory technique includes polymerase chain reaction assays for the detection of bacterial DNA to diagnose pulmonary tuberculosis especially atypical form.

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Introduction

An important advantage of inhaled corticosteroids (ICS) is that they have been shown to have a topical anti-inflammatory effect (**Lawrence et al., 1997**).

Up till now, there is no documented evidence that the incidence or the course of acute viral or bacterial respiratory infections is affected by the use of conventional doses of inhaled steroids in immune-competent hosts, and only occasional cases of reactivation of tuberculosis have been reported with the use of inhaled steroids (**Shaikh, et al., 1992**).

Although corticosteroids are known to be immunosuppressive, there have been no studies to show that use of corticosteroids increase the risk of developing new tuberculosis or reactivating old tuberculous lesion (**Dharam et al., 2002**).

Aim of the work

To assess the effects of ICS on cell mediated immunity (CMI) and whether this therapy reactivates latent tuberculous infection in asthmatic patients.

Inhaled glucocorticosteroids (ICS)

Introduction

In general, ICSs are favored over oral corticosteroids because their anti-inflammatory effect is directed at the airways, which reduces the risk of unwanted systemic effects (**Lawrence et al., 1997**).

Mechanism of action

The inflammatory process in asthma involves the increased expression of a wide variety of pro-inflammatory chemokines, cytokines, growth factors, lipid mediators, adhesion molecules, enzymes, and increased numbers of resident and invading inflammatory cells. That milieu leads to persistent or recurrent symptoms that require daily anti-inflammatory treatment to maintain appropriate symptom control and quality of life (**GINA 2009**).

Inhaled Corticosteroids reduce airway inflammation and hyperresponsiveness by altering the production of mediators of the asthmatic inflammatory process in the airways (involving dendritic cells, macrophages, eosinophils, lymphocytes and mast cells), ultimately

leading to improvement of symptoms and lung function **(Yudt et al., 2002 and Barnes et al., 2005).**

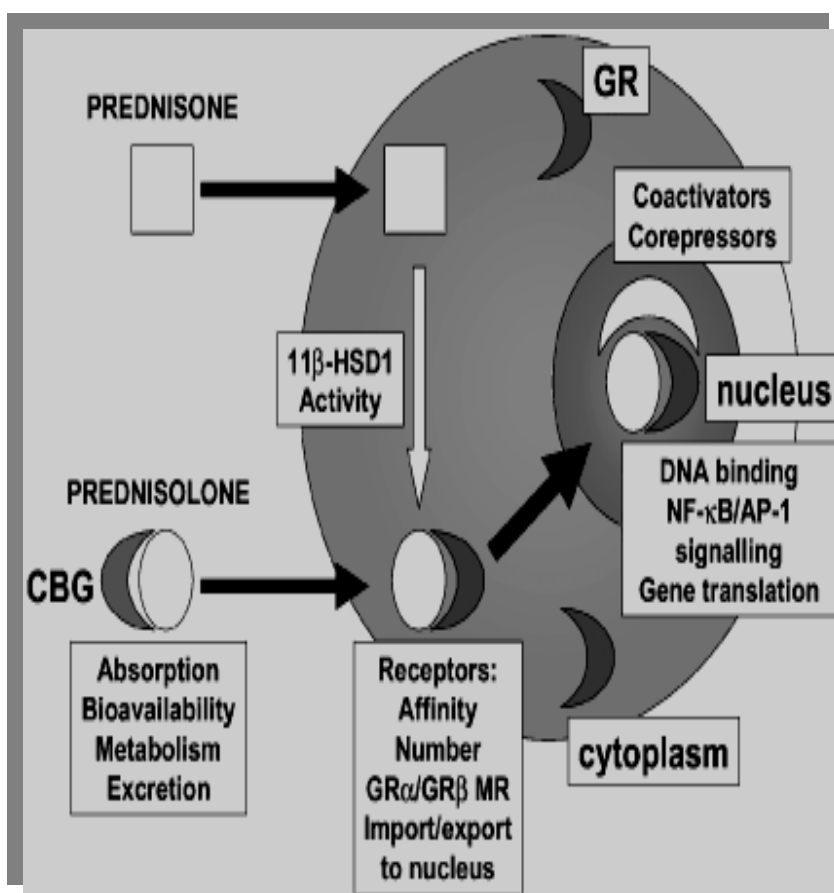
Glucocorticoids act by influencing gene transcription of molecules that are involved in the initiation and maintenance of the inflammatory response **(Umland et al., 2002 and Pelaia et al., 2003).**

Nowadays ICSs are believed to exert their effects after translocation into the nucleus of the respiratory epithelial cell and other cells in the airway, via the glucocorticoid receptor (GR) *(figure 1)* **(Leung et al., 2003).**

The GCS-GR complex, free from other proteins, enters the nucleus and binds to the DNA. There it affects gene transcription or modulates gene expression, thus altering protein synthesis. Release of the ligand (i.e. the GCS) from the GR causes the receptor to translocate back into the cytoplasm *(figure 2)* **(Barnes et al., 2005).**

Activated GR may bind to co-activators (e.g .cyclic adenosine monophosphate response element-binding protein) directly to inhibit their HAT activity thus reversing the unwinding of DNA around core histones and there by repressing inflammatory genes **(Cerasoli et al., 2006).**

Activated GR recruit histone deacetylase (HDACs) to the activated transcriptional complex, resulting in deacetylation of histones and thus a decrease in inflammatory gene transcription (**Ito et al., 2000**).



(**Figure 1**) effects ICSs via the glucocorticoid receptor adapted from (**Umland et al., 2002**).