

## Steroid Resistance in Allergic Disease and Asthma

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Steroid insensitivity in severe asthma is rare but has huge health care costs. About 5% of asthmatic patients account for ~50% of total health care costs in UK. Incorrect diagnosis, non-compliance with therapy and psychological problems are all confounding issues, and can account for a failure to respond to steroids in many of these patients.

At a molecular level, resistance to the anti-inflammatory effects of glucocorticoids can be induced by several mechanisms, and these might differ between patients. The reduction in corticosteroid responsiveness observed in cells from these subjects has been ascribed to a reduced number of GRs, altered affinity of the ligand for GRs, reduced ability of the GRs to bind to DNA, or increased expression of inflammatory transcription factors, such as AP-1, that compete for DNA binding.

Distinct treatments might have to be tailored to the individual patient; for example, drugs that enhance receptor nuclear translocation will only be effective in patients in whom this is a problem. Once issues of diagnosis, compliance and psychological disorders have been resolved, true steroid resistance or dependence is unlikely to be an issue for most clinicians, who will rarely, if ever, see these patients. However, management of those few patients with true steroid resistance will require novel therapies tailored to specific subgroups of patients.