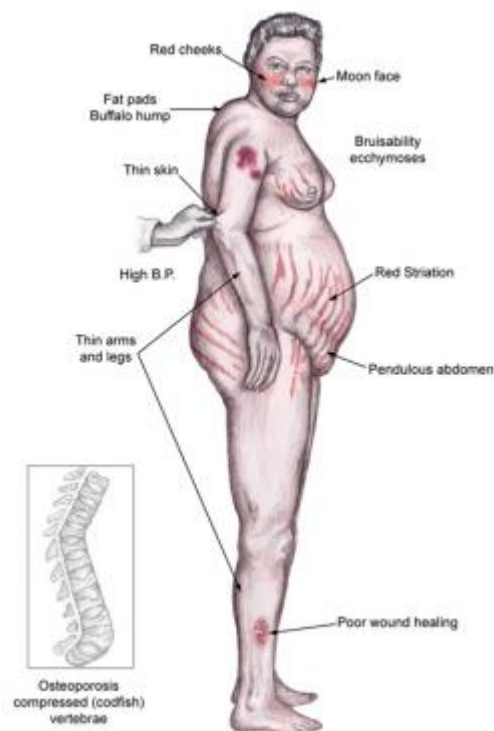


Cyclic Cushing's syndrome



Cyclic Cushing's syndrome is a rare variant of [Cushing's syndrome](#), which demonstrates periodic [cortisol](#) excess.

Cyclical Cushing's syndrome may render the diagnosis and management of Cushing's disease difficult.

It has been suspected that inhibition of a [glucocorticoid positive feedback](#) loop is associated with remission of [hypercortisolism](#) in [ACTH](#)-dependent cyclic Cushing's syndrome. However, the underlying mechanism to trigger the development of its hypercortisolism is still unknown.

Seki et al., from the [Tokyo Women's Medical University](#), experienced a case of ACTH-dependent cyclic Cushing's syndrome developed by exogenous glucocorticoids possibly through a glucocorticoid positive-feedback loop.

A 75-year-old woman had experienced cyclic ACTH and cortisol elevations 6 times in the previous 4 years. Her diagnosis was cyclic Cushing's syndrome. During the hypercortisolemic phase, neither low-dose nor high-dose dexamethasone suppressed her plasma ACTH and cortisol levels. Daily [metyrapone](#) therapy decreased her plasma cortisol and ACTH levels during every hypercortisolemic phase. After the sixth remission of a hypercortisolemic phase, she took 25 mg [hydrocortisone](#) for 4 weeks and developed ACTH-dependent hypercortisolemia. Treatment with 1 mg [dexamethasone](#) gradually increased both plasma [ACTH](#) and cortisol levels over 2 weeks resulting in the eighth hypercortisolemic phase. Treatment using a combination of dexamethasone with metyrapone did not increase plasma ACTH or cortisol levels and successfully prevented development of ACTH-dependent hypercortisolism.

It is an interesting case of cyclic Cushing's syndrome in which ACTH-dependent hypercortisolemic phases relapsed during exogenous glucocorticoid treatment. A glucocorticoid positive-feedback loop and endogenous glucocorticoid synthesis may play key roles in the periodicity of hypercortisolism in

cyclic Cushing's syndrome ¹⁾.

Alexandraki et al., analysed the case records of 201 patients with Cushing's disease in a retrospective case-note study. Cyclicity was considered as the presence of at least one cycle, defined as a clinical and/or biochemical hypercortisolaemic peak followed by clinical and biochemical remission, followed by a new clinical and/or biochemical hypercortisolaemic peak. The fluctuations of mean serum cortisol levels, as assessed by a 5-point cortisol day curve, defined the variability.

Thirty (14.9%; 26 females) patients had evidence of cyclicity/variability. 'Cycling' patients were older but no difference in sex or paediatric distribution was revealed between 'cycling' and 'non-cycling' patients. The median number of cycles was two for each patient, and 4 years was the median intercycle period. A trend to lower cure rate post-neurosurgery and lower adenoma identification was observed in 'cycling' compared with 'non-cycling' patients. In multivariate analysis, older patients, longer follow-up, female sex and no histological identification of the adenoma were associated with an increased risk of cyclic disease.

This large population study reveals that cyclicity/variability is not an infrequent phenomenon in patients with Cushing's disease, with a minimum prevalence of 15%. Physicians should be alert since it can lead to frequent problems in diagnosis and management, and no specific features can be used as markers ²⁾.

A 56-year-old male patient with cyclic Cushing's disease remained in a state of remission for more than one year with a relatively low dose of bromocriptine (2.5-3.75 mg/day). It has been reported that bromocriptine treatment for cyclic Cushing's disease induces only a transient remission; in the most effective cases, a relatively high dose (40 mg/day) was necessary. In the hypercortisolemic state, plasma adrenocorticotrophic hormone (ACTH) and serum cortisol were not suppressed by dexamethasone and did not respond to corticotropin-releasing factor (CRF). An antehypophysectomy was not effective, even though the resected tissue contained ACTH-positive microadenomas. The present observations thus indicate the effectiveness of bromocriptine for some patients with this rare disorder ³⁾.

A cyclic excess of cortisol secretion was detected in a patient with diabetes insipidus and diabetes mellitus. The cycles of hypercortisolism were of 7 days' duration, but during the nadir of these cycles urinary excretion of corticosteroids and 17-ketosteroids was within the normal range. The radiological appearance of the sella turcica was normal; however, computerized axial tomography of the head revealed a small tumor immediately superior to the sella turcica. At operation a small chromophobe adenoma superior to the diaphragma sellae and involving the hypophysial stalk was partially resected. Postoperatively, the patient continued to have 7-day cycles of increased corticosteroid excretion, but the amounts excreted were less than they had been preoperatively. Other patients have been described in whom Cushing's disease has been due to cyclic hypercortisolism. These cycles have been remarkably regular in individual patients, but of variable duration in different patients. Furthermore, cyclic hormonogenesis probably occurs in a variety of endocrinopathies ⁴⁾.

References

1)

Seki Y, Morimoto S, Saito F, Takano N, Kimura S, Yamashita K, Yoshida N, Bokuda K, Sasaki N, Yatabe M, Watanabe D, Yatabe J, Ando T, Amano K, Kawamata T, Ichihara A. ACTH-dependent Cyclic Cushing's Syndrome Triggered by Glucocorticoid Excess Through a Positive-Feedback Mechanism. *J Clin Endocrinol Metab*. 2018 Dec 17. doi: 10.1210/jc.2018-02268. [Epub ahead of print] PubMed PMID: 30561712.

2)

Alexandraki KI, Kaltsas GA, Isidori AM, Akker SA, Drake WM, Chew SL, Monson JP, Besser GM, Grossman AB. The prevalence and characteristic features of cyclicity and variability in Cushing's disease. *Eur J Endocrinol*. 2009 Jun;160(6):1011-8. doi: 10.1530/EJE-09-0046. Epub 2009 Mar 16. PubMed PMID: 19289537.

3)

Adachi M, Takayanagi R, Yanase T, Sakai Y, Ikuyama S, Nakagaki H, Osamura Y, Sanno N, Nawata H. Cyclic Cushing's disease in long-term remission with a daily low dose of bromocriptine. *Intern Med*. 1996 Mar;35(3):207-11. PubMed PMID: 8785455.

4)

Oates TW, McCourt JP, Friedman WA, Agee OF, Rhoton AL, Thomas WC Jr. Cushing's disease with cyclic hormonogenesis and diabetes insipidus. *Neurosurgery*. 1979 Nov;5(5):598-603. PubMed PMID: 534067.

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