# Acromegaly

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## Abstract

Acromegaly is a rare, chronic, debilitating condition. Untreated, it causes significant morbidity and reduces life expectancy by about 10 years. The disease process is insidious, and early presenting features can be non-specific (e.g. sweating, fatigue). Physicians, dentists and surgeons should consider this diagnosis if any of the more classically recognized features is present (e.g. dental malocclusion, symptoms of median nerve entrapment, sleep apnoea, type 2 diabetes mellitus without a family history). This is important because surgery remains the only hope of cure, and surgical outcome varies widely with the size of the adenoma (≥90% for microadenomata versus 40–45% for macroadenomata, even lower for tumours invading local structures), which is in turn is related to disease duration. The diagnosis of acromegaly is based on three key findings: clinical features, elevated age-adjusted serum insulin-like growth factor 1 concentration and serum growth hormone nadir >0.3 micrograms/litre following a 75 g oral glucose challenge. After biochemical confirmation of the disorder, magnetic resonance imaging of the pituitary is performed to assess the size and regional anatomy in anticipation of future surgery. Medical control of acromegaly has improved significantly in recent years, with the introduction of long-acting somatostatin analogues and the growth hormone receptor antagonist pegvisomant. Radiation therapy is a potential adjuvant therapy for patients with residual disease, but can take 5–10 years to have its full effect.

**Keywords** Acromegaly; GH; IGF-1; MRCP; pituitary

## Key points

- Acromegaly is rare and requires clinical suspicion in specific scenarios for diagnosis
- Prompt diagnosis improves outcomes
- Successful treatment reverses excess mortality

## Introduction

Acromegaly is an under-recognized and under-diagnosed chronic debilitating condition in adults that is associated with significantly increased morbidity and mortality. It is almost invariably caused by a growth hormone (GH)-secreting pituitary tumour. Life expectancy in untreated individuals with or without associated co-morbidities is reduced by several years, as shown in Figure 1.

## Epidemiology

Acromegaly typically starts to develop between the ages of 25 and 40 years, although the diagnosis is often delayed by many years. In Europe, the incidence is 3–4/million per year and the prevalence 40–60/million. Men and women are equally affected.

## Aetiology

In 99% of cases, acromegaly is caused by a GH-secreting pituitary adenoma. The tumour usually secretes GH alone, but in some cases there is co-secretion of prolactin and/or thyroid-stimulating hormone. Acromegaly caused by ectopic secretion of GH-releasing hormone is extremely rare. It occasionally occurs in the context of a rare genetic syndrome, such as multiple endocrine neoplasia (MEN) type 1, McCune–Albright syndrome or Carney complex.

## Clinical features

The clinical features of acromegaly are listed in Table 1. The condition develops insidiously, such that the average time from initial onset of symptoms to diagnosis is typically 5–10 years and often longer.[1] In view of the non-specific nature of many of the common symptoms (e.g. fatigue, joint pain), it is recommended that physicians, surgeons and dental practitioners consider the diagnosis in any patient with any of the symptoms or signs listed in Table 1 or co-morbidities shown in Figure 2.

Clinical assessment of patients with suspected acromegaly should focus particularly on the characteristic symptoms, and the syndromes mentioned under Aetiology. It should also include detailed neuro-ophthalmic evaluation and address the features that may suggest any of the common complications of acromegaly (hypertension, cardiac failure, large joint osteoarthritis, type 2 diabetes mellitus).

## Investigations and diagnosis

The major challenge in acromegaly is early diagnosis of a disease that develops insidiously. GH secretion is pulsatile, with 6–10 pulses of release separated by long periods during which GH concentrations are virtually undetectable. This means that measurement of a random serum GH concentration has little value in the diagnosis of acromegaly. Although insulin-like growth factor 1 (IGF-1) mediates almost all of the actions of GH, the assays for this peptide are less robust than those for GH, and circulating IGF-1 concentration is influenced by various factors (Table 2). For this reason, diagnostic tests for acromegaly include both serum IGF-1 concentration and the 75 g oral glucose tolerance test.

Variations in assay methodology dictate that no overall consensus exists for the nadir GH during an oral glucose

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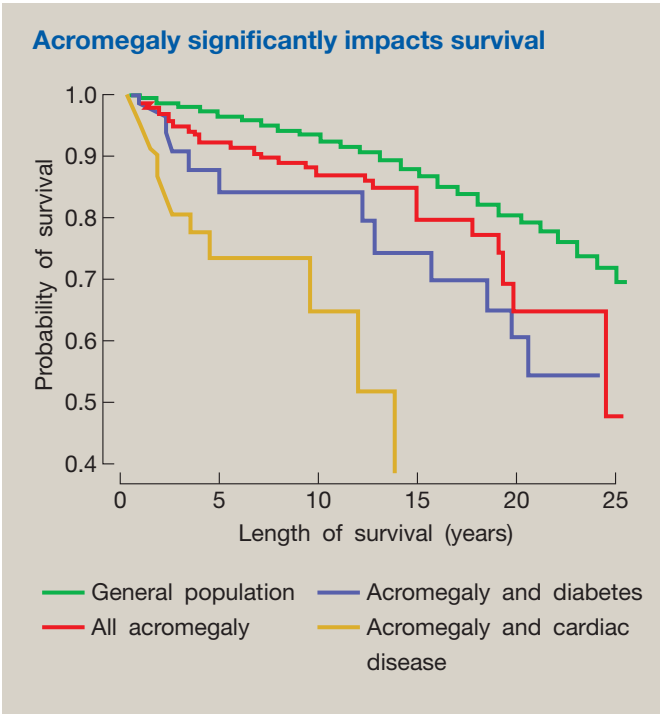


**Figure 1**

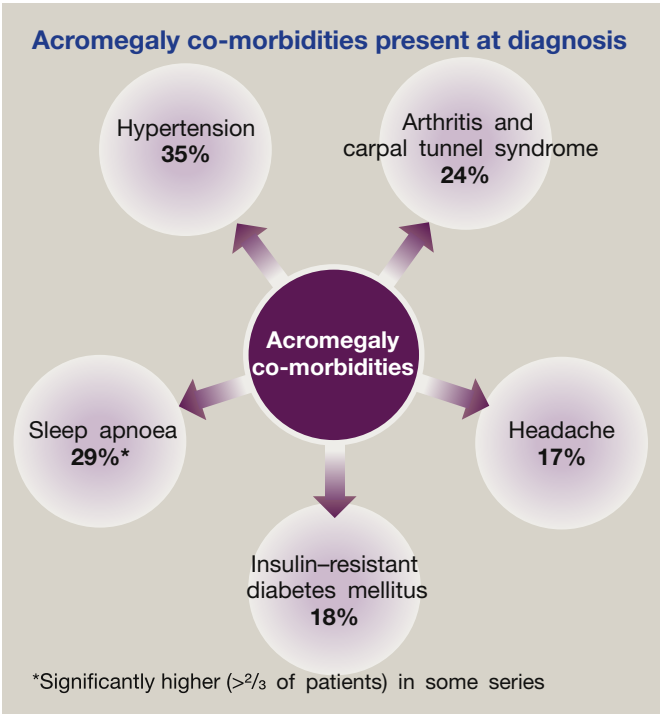


**Figure 2**

## Clinical features of acromegaly

- Increased sweating
- Headache
- Carpal tunnel syndrome
- Dental malocclusion
- Multiple skin tags
- Sleep apnoea
- Recurrent colonic polyps
- Oligomenorrhoea/amenorrhoea
- Type 2 diabetes mellitus (insulin-resistant) in the absence of a family history and/or appropriate phenotype
- Large joint arthritis

**Table 1**

tolerance test, but most endocrine physicians regard a value of 0.3 micrograms/litre (1 mU/litre) as an appropriate threshold for the diagnosis.

### Further assessment

Once the diagnosis has been established, further investigations are needed (Table 3). Most investigations are needed in every patient as a matter of routine, although some (as indicated) are only required if clinically indicated.

## Management

Acromegaly is best managed in a centre with an experienced endocrinologist, a pituitary surgeon and a radiotherapist. The aims of treatment are:

- control of the tumour and its mechanical effects
- relief of symptoms
- reducing serum GH/IGF-1 to 'safe' concentrations associated with improved prognosis
- preservation of normal pituitary function.

### Surgery

Surgical adenomectomy remains the treatment of choice in most patients. With an experienced surgeon, the 'disease control' rate (defined by normal age-adjusted and sex-adjusted IGF-1 and post-glucose GH nadir of <1 micrograms/litre) is about 90% in

## Factors affecting IGF-1 and GH

**Pitfalls when interpreting IGF-1 concentration**

*Low IGF-1*

- Poorly controlled diabetes mellitus
- Liver disease
- Exogenous oestrogen
- Malnourishment

*High IGF-1*

- Adolescence/puberty
- Pregnancy
- Hyperthyroidism

**Pitfalls in GH suppression**

*False-positive oral glucose challenge*

- Diabetes mellitus
- Liver disease
- Renal insufficiency
- Malnutrition
- Adolescence
- Women receiving oestrogen

**Table 2**



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