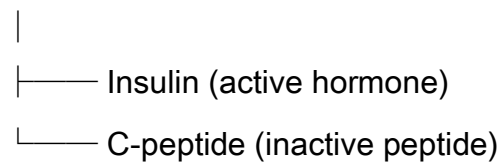


C-Peptide

C-peptide is a peptide that is cleaved from **proinsulin** when it is converted into **endogenous insulin** within pancreatic β -cells. Because insulin and C-peptide are released in **equimolar amounts**, C-peptide serves as a marker of a patient's **own insulin production**.

Physiology

Proinsulin



- Secreted 1:1 with endogenous insulin
- Not present in pharmaceutical insulin preparations
- Longer half-life (20–30 min vs insulin 3–5 min)
- Less hepatic extraction than insulin, making levels more stable

Clinical utility in Type 2 Diabetes

Clinical question	How C-peptide helps
Does the patient still produce insulin?	Direct measure of residual β -cell function
Is this really T2D?	Low levels suggest T1D, LADA, or advanced β -cell failure
Will insulin be required?	Very low C-peptide predicts need for insulin
Is insulin likely to work?	High C-peptide suggests insulin resistance rather than insulin deficiency
Can insulin potentially be de-escalated?	Preserved C-peptide suggests this may be possible if glycaemic control allows

Interpretation

C-Peptide	Suggests	Common Situations	Treatment Implicatons
High or Normal	• Preserved β-cell function • Insulin resistance • Typical early T2D • Hyperinsulinaemia	• Obesity • Metabolic syndrome • Early T2D	• Metformin • GLP-1 receptor agonists • SGLT2 inhibitors • Pioglitazone • Lifestyle interventions • Insulin often not immediately required
Low	• Marked β-cell failure • Long-standing T2D • Type 1 diabetes • LADA • Pancreatic disease		• Greater likelihood of requiring insulin • Sulfonylureas often become less effective • Limited endogenous insulin reserve

When should you measure it?

Useful when the diagnosis or management is uncertain.

Examples:

- Lean adult labelled as T2D
- Rapid deterioration despite oral therapy
- Recurrent ketosis
- Considering stopping insulin
- Suspected **LADA**
- Young patient with atypical diabetes
- Possible MODY
- Unexplained recurrent hypoglycaemia

Typical interpretation (values vary by assay)

C-peptide	Interpretation
<0.2 nmol/L	Severe insulin deficiency; consistent with absolute insulin deficiency
0.2–0.6 nmol/L	Reduced β -cell reserve
>0.6 nmol/L	Preserved endogenous insulin secretion
>1.0–1.5 nmol/L	Often indicates significant insulin resistance if hyperglycaemic

Always interpret alongside the plasma glucose at the time of sampling, as **hyperglycaemia stimulates insulin (and C-peptide) secretion**.

Role in choosing diabetes medications

Drug class	C-peptide implication
Metformin	Effective regardless of C-peptide if renal function permits
SGLT2 inhibitors	Effective with preserved or reduced C-peptide, provided some insulin is present; use caution in severe insulin deficiency due to increased ketoacidosis risk
GLP-1 receptor agonists	Better response when β -cell function is preserved
DPP-4 inhibitors	Require functioning β -cells; efficacy declines as insulin deficiency progresses
Sulfonylureas	Require functioning β -cells; poor response when C-peptide is very low
Insulin	Essential when C-peptide is markedly reduced or absent

Important limitations

- Renal impairment can **increase C-peptide concentrations** because it is cleared by the kidneys.
- Levels should be interpreted with a concurrent blood glucose; a low glucose at the time of sampling may suppress C-peptide secretion.
- Exogenous insulin does **not** affect C-peptide measurement, making it useful in insulin-treated patients.

Practical take-home points

- **C-peptide is the best readily available marker of endogenous insulin secretion.**
- In early T2D, C-peptide is usually **normal or elevated**, reflecting insulin resistance with compensatory hyperinsulinaemia.
- Over time, progressive β -cell dysfunction leads to declining C-peptide levels, indicating reduced insulin reserve.
- Measuring C-peptide can help distinguish insulin resistance from insulin deficiency, guide medication selection, identify patients likely to require insulin, and prompt evaluation for alternative diagnoses such as type 1 diabetes or LADA when clinical features are atypical.