2. Action on the *intracellular* (steroid or thyroid) receptors

a) At cytoplasmic receptors:
- Steroid hormones, Calcitriol
Feedback regulation of endocrine axes
Corticotropin releasing hormone (CRH) – corticoliberin, is a hypothalamic polypeptide for diagnostic use.
Corticotropin stimulates corticotropin cells to produce ACTH → synthesis of corticosteroids (of which the most important is hydrocortisone) and to a lesser extent of androgens, by the cells of the adrenal cortex.
1. Corticotropin releasing hormone (CRH) – corticoliberin

- Natural corticotropin (ACTH) is a 39-amino-acid polypeptide secreted by the anterior pituitary gland, obtained from animal pituitaries.

- The pituitary output of corticotropin responds rapidly to physiological requirements by the familiar negative-feedback homeostatic mechanism.

- Synthetic corticotropin tetracosactide has the advantage that contains shorter amino acid chain (devoid of amino acids 25–39) and so are less likely to cause serious allergy.

- In addition, they are not contaminated by animal proteins which are potent allergens.

- It consists of the biologically active first 24 amino acids of natural corticotropin (from man or animals) and so it has similar properties, e.g. t$_{1/2}$ 10 min.
Thyroid stimulating hormone (TSH), thyrotropin, a glycoprotein of the anterior pituitary, controls the synthesis and release of thyroid hormone from the gland, and also the uptake of iodide. There is a negative feedback of thyroid hormones on both the hypothalamic secretion of TRH and pituitary secretion of TSH.
Growth Hormone

**GH** is a 191-amino-acid peptide.

Two types of recombinant human growth hormone (rhGH) are approved for clinical use:

- **Somatropin** (identical with the native form of human GH)
- **Somatrem** (with an extra methionine residue at the amino terminal end).

*used in children with growth hormone deficiency*, while the bone epiphyses are still open,

- to prevent *dwarfism* (underdevelopment of the body) and provide normal growth.

- Treatment improves exercise performance and increases lean body mass.

- It may improve overall quality of life.
Urofollitropin \{Raavelle\}

- Purified FSH
- Derived from post-menopausal females
human Chorionic Gonadotropin (hCG)

- Diagnostic use
- Treatment of infertility
  - Induce ovulation
- Adverse reactions
  - Headache
  - Depression
Desmopressin (des-amino-D-arginine vasopressin) (DDAVP)

- For replacement therapy of pituitary diabetes Insipidus
- The longer acting analogue

has two major advantages:

- The vasoconstrictor effect has been reduced to near insignificance and the duration of action with nasal instillation, spray or s.c. injection, is 8–20 h ($t_{1/2}$ 75 min) so that, using it once to twice daily, patients are not inconvenienced by frequent recurrence of polyuria during their waking hours and can also expect to spend the night continuously in bed.
Desmopressin

- The adult dose for intranasal administration is 10–20 micrograms daily.
- The dose for children is about half that for adults.
- The bioavailability of intranasal DDAVP is 10%.
- It is also the only peptide for which an oral formulation is available, with a bioavailability of only 1%.