Q23 How do chemical messengers in the extracellular fluid bring about changes in cell function? Give an example of a chemical messenger for each mechanism noted (March 2013)

A receptor is a protein, often integral to a membrane, containing a region to which a ligand (chemical messenger) binds specifically to elicit a response. They may be grouped into three classes based on mechanism of action:

a. Altered ion permeability (ion channels / ionotropic)
   - Membrane spanning complexes with the potential to form a channel through the membrane
   - Three families:
     - Pentameric → contain 5 membrane spanning units (eg, nicotinic Ach receptor at the NMJ which allows an Na channel to form, GABA A receptor which allows a Cl channel to form, 5HT3 receptor)
     - Ionotropic glutamate → NMDA, AMPA and kainate iontropic ligand gated ion channels. They form Na, K and (NMDA only) Ca channels when glutamate binds
     - Purinergic receptors → PX1 and PX2 are activated by ATP, permeable to Na, K and Ca, and are associated with mechanosensation and pain.

b. Production of intermediate messengers
   - Membrane bound systems that transduce a ligand gated signal presented on one side of the cell membrane into an intracellular signal transmitted by intermediate messengers. These messengers may be:
     - G proteins (most common) → binding of a chemical messenger to a G-protein coupled receptor activates the G protein, which in turn amplifies and transmits the signal to the appropriate target molecules. This can be done in several ways:
       a. Activation of phosplipase C, with intracellular production of DAG, IP3 and other inositol phosphates (eg; angiotensin II, noradrenaline on alpha 1 receptors, vasopressin on V1 receptors)
       b. Activation or inhibition of adenylyl cyclase, causing increased or decreased levels of intracellular cAMP (eg, noradrenaline increases cAMP via beta1 receptors, noradrenaline decreases cAMP via alpha 2 receptors)
       c. Increase in cGMP (eg, atrial natriuretic peptide, nitric oxide)

     - Tyrosine kinase → eg, insulin activates tyrosine kinase resulting in the phosphorylation of various proteins
     - Guanylyl cyclase → eg, NO, atrial natriuretic peptide

c. Regulation of gene transcription
   - Steroids and thyroid hormones act through intracellular receptors to alter the expression of DNA and RNA, and indirectly alter the production of intracellular proteins.