• Antagonist – Has affinity but no efficacy so doesn’t activate receptor

Fast Synaptic Transmission – Receptor protein to pre-synaptic ligand is also an ion channel opened by ligand binding
• Excitatory – Opens channels causing depolarisation (ACh, glutamate)
• Inhibitory – Opens channels causing hyperpolarisation (glycine, GABA)

Slow Synaptic Transmission – Receptor is a GPCR or gates via an intracellular messenger

Receptor – Molecule that is silent at rest and recognises ligand to be activated
• Integral Ion Channels – Agonist binding causes change in shape & resultant opening of the gated ion channel
• Integral Enzyme Activity
  o Tyrosine Kinase – Binding causes autophosphorylation of tyrosine residues to produce a recognition site for enzymes to bind & produce an intracellular event
• Intracellular Receptors – Resting state stabilised by heat shock/chaperone proteins, when activated it enters the nucleus to cause changes in DNA expression
• G-protein Coupled Receptor – Bind causes GDP to become GTP which leads to G protein dissociation (to become G\textsubscript{p} & G\textsubscript{i}); dephosphorylation of GTP causes sub-units to re-bind and deactivate
  o $G_{\alpha_o}$ – $\uparrow$ adenylyl cyclase, $\uparrow$ ATP $\rightarrow$ cAMP, $\uparrow$PKA
  o $G_{\alpha_i}$ – $\downarrow$ adenylyl cyclase, $\downarrow$cAMP, $\downarrow$PKA
  o $G_{\alpha_q}$ – $\uparrow$phospholipase C, $\uparrow$IP\textsubscript{3} (Ca\textsuperscript{2+} release) & diacylglycerol ($\uparrow$ protein kinase C)

Desensitisation – May be desensitised by change in receptor properties, loss of receptors (receptor internalisation) or exhaustion of mediators
• Homologous Desensitisation – Only signal from the stimulated receptor is reduced
• Heterologous Desensitisation – Receptors for several agonists become less effective, even when only one is continuously stimulated

Supersensitivity – Treatment of hypersensitivity (agonist deprivation or excessive antagonist exposure) can mean the cell adapt a ‘rebound’ response to natural agonists when therapy ceases and becomes less sensitive; this occurs due to treatment causing an increased number of receptors, change in receptor number, receptor coupling to secondary messenger, availability of secondary messenger or cell responsiveness

ACh Uses:
• Pre-ganglionic SNS $\rightarrow$ nAChr on post-ganglionic receptor
• Pre-ganglionic PNS $\rightarrow$ nAChr on post-ganglionic receptor
• Post-ganglionic PNS nerve endings $\rightarrow$ mAChr on target organ
• Post-ganglionic SNS nerve endings $\rightarrow$ mAChr on sweat glands & piloerection muscles

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Adrenoceptor Subtype Involved</th>
<th>Physiological response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>$\alpha_1$, $\beta_2$</td>
<td>Glycogenolysis $\uparrow$</td>
</tr>
<tr>
<td>Vascular Smooth Muscle</td>
<td>$\alpha_1$, $\beta_2$</td>
<td>Vasoconstriction (Skin, GI, kidney &amp; brain)</td>
</tr>
<tr>
<td>Airway Smooth Muscle</td>
<td>$\alpha_1$, $\beta_2$</td>
<td>Minor bronchiole contraction</td>
</tr>
<tr>
<td>GI- tract Smooth Muscle</td>
<td>$\beta_2$ (Dominant)</td>
<td>Decreased motility</td>
</tr>
<tr>
<td>Bladder Smooth Muscle</td>
<td>$\alpha_1$</td>
<td>Contraction of detrusor urinae muscle</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$ (Dominant)</td>
<td>Relaxation of detrusor urinae muscle</td>
</tr>
</tbody>
</table>

mAChr: $M_1$ – q $M_2$ – i $M_3$ – q $M_4$ – i $M_5$ – q
Adrenoceptors: $\alpha_1$ – q $\alpha_2$ – i $\beta_1$ – s $\beta_2$ – s $\beta_3$ – s