Q18 Describe the processes of excitation and contraction within a smooth muscle cell (60% of marks). Briefly outline the mechanism by which nitric oxide affects smooth muscle cell activity (40% of marks) (March 2012)

Smooth muscle

- Either single unit (joined by gap junctions, act as a syncytium, found in blood vessels, the GIT and GUT) or multiunit (contain fibres that can contract independent of each other, such as in the ciliary, iris and piloerector muscles).
- Contain actin and myosin dispersed through the cell rather than in striations
- Some are autorhythmic and contraction is only modified by nerve activity, other smooth muscles resemble skeletal muscle and are primarily controlled by motor neurons from the CNS
- Contains calmodulin, a regulatory protein, but no troponin

Excitation/contraction coupling

- Unitary smooth muscle possesses an unstable membrane potential and continually contracts – ie, it has 'tone'.
- Multiunit smooth muscle contraction is more discrete and localized.
- Intracellular calcium concentration increases (either enters the cell via voltage or ligand-gated Ca channels or is released from the sarcoplasmic reticulum, although the SR is poorly developed and is only a minor source of Ca) in response to nerve stimulation, hormonal stimulation, stretch of the fibre or change in its chemical environment
- Calcium ions bind with calmodulin → Ca2+/calmodulin complex activates myosin light chain kinase → phosphorylates myosin → myosin head now able to bind with actin filament
- When calcium ion concentration falls below a critical level (because of active reuptake at the sarcoplasmic reticulum), myosin phosphatase splits the phosphate from the regulatory light chain and cross bridge cycling ceases.
- Cross bridge cycling much slower than in skeletal muscle

Nitric oxide

- Activates soluble guanylyl cyclase → catalyses the dephosphorylation of GTP to cGMP
- cGMP then causes smooth muscle relaxation, by →
    - Reduces intracellular Ca2+ concentration by inhibiting Ca2+ channels
    - Activates K channels which hyperpolarise the cell
    - Activates cGMP dependent protein kinase PKG, which activates myosin light chain phosphatase (dephosphorylates myosin light chains, thus ending muscle contraction)