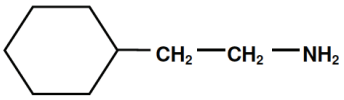
First 2008
VIVA 5

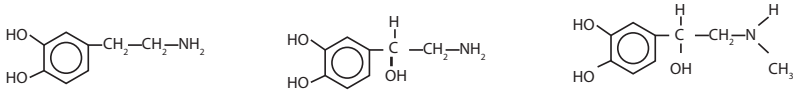
Viva 5 - Name this molecule?



How can we make this molecule biologically active?

"Could you please draw the steps in the generation of common catecholamines?"

tyrosine → (tyrosine hydroxylase, rate limiting step) → L- DOPA → (amino acid decarboxylase) → dopamine → (dopamine beta hydroxylase) → noradrenaline → (PNMT) → adrenaline



"Describe the structure activity relationships of catecholamines"

Increased length of the carbon chain confers greater affinity for the beta receptors
the synthetic catecholamines isoprenaline and dobutamine have long carbon chains
With the natural catecholamines at low doses the beta effect predominate, at higher doses alpha

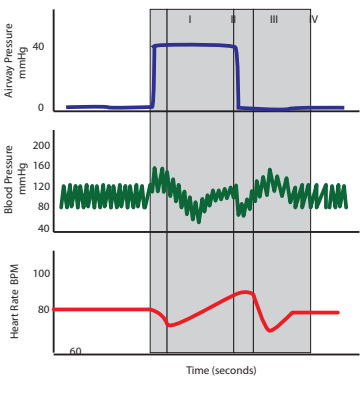
"Please describe the physiology and pharmacology of noradrenaline"

- is a naturally occuring catecholamine
  - produced peripherally in the adrenal medulla and at the postganlionic SNS
  - in the CNS in areas such as the locus ceruleus and other medullary and pontine nuclei
  - it is produced from dopamine as shown above and stored in granulated vesicles
  - acts on alpha 1 and 2 receptors and beta 1-3 receptors with a higher affinity for alpha
  - metabolised by MAO (oxidisation) and COMT (methylation)
- drug data
  - pharmacodynamics
    - action as above
    - effects - peripheral vasoconstriction, increased BP, possible reflex bradycardia (with associated decrease in CO, increase MVO2 and decreased hepatic and renal bood flow.
  - pharmacokinetics
    - doses 8-12 mcg/minute up titrated
    - doesn't cross the BBB
    - half life is around 2 minutes, metabolism as above
    - excretion in the urine as inactive metabolites

"What is the autonomic nervous system?"

is a division of the nervous system which maintains body homeostasis
it integrates signals from the somatic and visceral sensors in the medulla
this is modulated by the cortex, hypothalamus and mygdalla
the efferent components are the PNS and the SNS

"Please draw and describe the Valsalva manouvre"



Phase I Increased intrathoracic pressure causes a brief increase in preload as the pulmonary vasculature empties to the LA/LV. This causes an increase in CO and therefore blood pressure and a fast baroreceptor driven decrease in heart rate.

Phase II The increased intrathoracic pressure causes reduced venous return which leads to decreased preload and CO. As blood pressure now falls the baroreceptor response is an increase in HR and TPR. The increase in TPR means that the diastolic pressure will be increased more than the systolic and as a result the pulse pressure narrows.

Phase III The intrathoracic pressure now drops, transiently decreasing preload and CO as blood pools in the pulmonary vasculature. There is a transient decrease in blood pressure.

Phase IV As CO returns to normal, the residual increase in TPR (and probable venous constriction) means that there is an overshoot and blood pressure spikes (with associated fast baroreceptor decrease in HR) before stabilising.

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