Catecholamines, neurotransmitter, hormone

1) epinephrine (adrenaline)

\[
\begin{align*}
\text{Epinephrine} & \\
\text{HO} & \\
\text{HO} & \\
\text{C–CH₃–NH–} & \\
\text{H} & \\
\text{CH₃} & \\
\end{align*}
\]

2) norepinephrine (noradrenaline)

\[
\begin{align*}
\text{Norepinephrine} & \\
\text{HO} & \\
\text{HO} & \\
\text{C–CH₂–NH₂} & \\
\end{align*}
\]

3) dopamine

I. CNS

II. PNS

A) SNS

B) ANS

1) Parasympathetic (P)
basal metabolism

2) Sympathetic (S)
fight or flight

preganglionic neurons (spinal cord)

\[
\begin{align*}
\text{Ach} & \\
\text{Ach} & \\
\text{Ach} & \\
\text{Ach} & \\
\text{Ach} & \\
\end{align*}
\]

shorter

target effect organ

Figure 14.2: The autonomic nervous system. (From William T. Evans, Anatomy and Physiology, 2nd edn. p. 187, © 1930. Reproduced by permission of Prentice Hall, Inc., Englewood Cliffs, NJ.)
Postganglionic to Target Effector Organs

P  cholinergic transmission  S  adrenergic transmission

**neuroendocrine hormone**

peptide secreted from a nerve ending into a bloodstream reach target tissue hormonal effect
*neural crest → ? quadroblastic germ layer*
Pathways of Catecholamine Biosynthesis

1. Phenylalanine
   - Phenylalanine Hydroxylase
   - Tyrosine Hydroxylase

2. Tyrosine
   - Dopamine β-Hydroxylase
   - L-Aromatic Amino Acid Decarboxylase

3. Dopamine
   - Norepinephrine
   - Phenylethanolamine N-Methyltransferase (PNMT)

4. Norepinephrine
   - Epinephrine

5. Epinephrine

L-Tyrosine → DOPA → Dopamine → Noradrenaline → Adrenaline
Pathways of Catecholamine Metabolism

**Historical Perspectives**

1886 Bates: adrenal gland substance in New York Medical Journal
1895 Cybulski: isolated & identified epinephrine
1897 Abel: repeated discovery
1900 Takamine: discovered same hormone
1904 Elliot: sympathetic nerve impulses released epinephrine-like substance
  suggestion of neurohormor → neurotransmission
1904 Stolz: first artificially synthesized
1905 Langley: autonomic effector cells possess inhibitory & excitatory substances
1906 Dale: epinephrine elicit two opposing actions in same tissue
1921 Loewi: vagus nerve → excitatory epinephrine-like substance
1921 Cannon & Bacq: → referred this substance to sympathin
  blood pressure & heart rate
1931 Bacq: sympathin → norepinephrine
1933 Cannon & Rosenblueth: 2 sympathins E (excitatory) & sympathin I (inhibitory)
1935 Bacq: sympathin not identical to E; against sympathin E & I;
  same catecholamine opposite effect
1946 Von Euler: postganglionic substance → NE
1948 Ahlquist: dual adrenoreceptors → smooth muscle contraction & relaxation→
  a & β adrenoceptors → **adrenoceptor hypothesis**
1952 Carlsson & Hillarp: discovered dopamine
2000 Carlsson: Nobel Prize in Physiology or Medicine→ dopamine neurotransmitter
**ADRENAL MEDULLA (AM)**

I. chromaffin Gr. Chroma (color); L. affinis (affinity) pheochromocytes → color exposed to oxidizing agent chromate

II. medulla & cortex regions
   1) overlap in birds & mammals  \[\uparrow E : \downarrow NE\]
   2) variable in reptiles & amphibians  frogs: 55-70% NE
   3) highly separated in elasmobranchs & teleosts  dogfish shark → NE

III. human
   1) A-storing cells (adrenaline) → E
   2) N-storing cells (noradrenaline) → NE
   3) glycoproteins in A cells
   4) fetus: extra-adrenal chromaffin tissue → NE → ? Fetal circulation
      fetal: humoral control (NE); postnatal: sympathetic neural (NE)

IV. A/N ratio high in humans & guinea pigs: A & N cells found in
   1) birds
   2) reptiles
   3) amphibians
   4) elasmobranchs

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**B. secretes catecholamines**
   1) epinephrine (E)
   2) norepinephrine (NE)

**C. intimate association with sympathetic nervous system** → **sympathoadrenal system**

**D. AM located interiorly**
   1) blood flows from exterior (cortex) of adrenal gland to AM
   2) blood titers glucocorticoids influence hormone synthesis in AM
D. Anatomy
1) chromaffin cells - stained histologically with chromium
   a) pheochromoblasts = derived from neural crest
   b) functions as neuroendocrine cells
   c) similar structurally to postganglionic fibers of sympathetic nervous system
   d) preganglionic fibers to medulla directly innervate (no synaptic cleft) chromaffin cells
   e) stimulation → chromaffin cells secrete hormone E into blood
   f) E affects variety of effector organs throughout the body
   g) NE is secreted in small amounts
   h) NE is an intermediate in synthesis of E

E. Synthesis/Secretion of E
1) tyrosine
2) dihydroxyphenylalanine (DOPA)
   a. enzyme tyrosine hydroxylase (TH) converts tyrosine to DOPA
   b. rate limiting step in E synthesis
   c. nerve stimuli l enzymatic activity of TH
   d. subsequent steps proceed rapidly
3) NE
4) E
   a. enzyme phenylethanolamine-N-methy transferase (PNMT) converts NE to E
   b. PNMT stimulated by cortisol
   c. E packaged into vesicles = chromaffin granule
   d. stimulation of chromaffin cell → release of E from granules
F. Action of E and NE
   1) **fight-or-flight** response: capability of body to perform vigorous muscular activity for survival
   2) cardiovascular
      a) **cardiac output**:
         1. **heart rate**
         2. **strength of cardiac contractions**
      b) vasodilation in skeletal muscles: blood flow
      c) vasoconstriction in internal organ & skin: decrease blood flow
   3) other tissues
      a) relaxation of smooth muscles
         1. gastrointestinal tract
         2. urinary bladder
         3. lung airways: **$O_2$** transport
      b) contraction of spleen
         1. circulating blood volume & red blood cells: $O_2$ transport
      c) central nervous system: mental alertness
   4) metabolism: **blood glucose**
      a) **glycogenolysis** in liver: glucose release into blood
      b) **glycogenolysis** in muscles:
         1. glucose $\rightarrow$ lactate which released into blood
         2. lactate uptake by liver to conversion to glucose
      c) **lipolysis** in adipose tissue
         1. fat source for metabolism of heart/muscles
         2. glycerol released from lipolysis uptake by liver to convert into glucose
         3. "sparing effect" to offer fatty acids as fuel source to spare glucose utilization
      d) **insulin secretion**
      e) **glucagon secretion**
Glucogenesis

generation of glucose from carbon substrates:
- pyruvate
- lactate
- glycerol
- amino acids (primarily alanine & glutamine)

sympathetic: → feedback mechanisms for inhibition of sympathetic neuron secretion
Pathways of Catecholamine Metabolism

Norepinephrine
\[ \text{COMT} \]
3,4-Dihydroxyphenylalanine
\[ \text{COMT} \]
3-Methoxy-4-Hydroxyphenylglycol (Vanillylmandelic Acid or VMA)
\[ \text{COMT} \]
Epiinephrine
Metanephrine
Noradrenaline
\[ \text{COMT} \]
3,4-Dihydroxyphenylglycol
\[ \text{COMT} \]
Epiinephrine
Metanephrine
Noradrenaline
\[ \text{COMT} \]