Chapter 11

Catecholamines and the Sympathoadrenal System

Nam Deuk Kim, Ph.D.
Peripheral Nervous System

- Communication link by which CNS controls activities of muscles and glands
- Two divisions of PNS
  - Autonomic nervous system (ANS)
    - Involuntary branch of PNS
    - Innervates cardiac muscle, smooth muscle, most exocrine glands, some endocrine glands, and adipose tissue
  - Somatic nervous system
    - Subject to voluntary control
    - Innervates skeletal muscle
ANS

• Most visceral organs innervated by both sympathetic and parasympathetic fibers
• In general produce opposite effects in a particular organ
• Dual innervation of organs by both branches of ANS allows precise control over organ’s activity
AUTONOMIC NERVOUS SYSTEM (ANS)

An autonomic nerve pathway consists of a two-neuron chain.

Fig. 7-1. Autonomic nerve pathway.
ANS

• **Sympathetic system** dominates in emergency or stressful ("fight-or-flight") situations
  – Promotes responses that prepare body for strenuous physical activity

• **Parasympathetic system** dominates in quiet, relaxed ("rest-and-digest") situations
  – Promotes body-maintenance activities such as digestion
Autonomic Division: Homeostatic balancing

Homeostasis is a dynamic balance between autonomic branches.

Parasympathetic activity

Sympathetic activity
Fig. 7-2. Autonomic nervous system.
Parasympathetic postganglionic fibers release acetylcholine; sympathetic ones release norepinephrine.

**TABLE 7-2**

Sites of Release for Acetylcholine and Norepinephrine

<table>
<thead>
<tr>
<th><strong>ACETYLCHOLINE</strong></th>
<th><strong>NOREPINEPHRINE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>All preganglionic terminals of the autonomic nervous system</td>
<td>Most sympathetic postganglionic terminals</td>
</tr>
<tr>
<td>All parasympathetic postganglionic terminals</td>
<td>Adrenal medulla</td>
</tr>
<tr>
<td>Sympathetic postganglionic terminals at sweat glands and some blood vessels in skeletal muscle</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>Terminals of efferent neurons supplying skeletal muscle (motor neurons)</td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td></td>
</tr>
</tbody>
</table>
Structures Innervated by Sympathetic and Parasympathetic Nervous Systems:

Dual innervation
Dual innervation of sympathetic and parasympathetic nervous system.

### TABLE 7-3
Effects of Autonomic Nervous System on Various Organs

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>EFFECT OF SYMPATHETIC STIMULATION</th>
<th>EFFECT OF PARASYMPATHETIC STIMULATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Increased rate, increased force of contraction (of whole heart)</td>
<td>Decreased rate, decreased force of contraction (of atria only)</td>
</tr>
<tr>
<td>Blood Vessels</td>
<td>Constriction</td>
<td>Dilation of vessels supplying the penis and clitoris only</td>
</tr>
<tr>
<td>Lungs</td>
<td>Dilation of bronchioles (airways)</td>
<td>Constriction of bronchioles</td>
</tr>
<tr>
<td></td>
<td>Inhibition (?) of mucus secretion</td>
<td>Stimulation of mucus secretion</td>
</tr>
<tr>
<td>Digestive Tract</td>
<td>Decreased motility (movement)</td>
<td>Increased motility</td>
</tr>
<tr>
<td></td>
<td>Contraction of sphincters (to prevent forward movement of contents)</td>
<td>Relaxation of sphincters (to permit forward movement of contents)</td>
</tr>
<tr>
<td></td>
<td>Inhibition (?) of digestive secretions</td>
<td>Stimulation of digestive secretions</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>Relaxation</td>
<td>Contraction (emptying)</td>
</tr>
<tr>
<td>Eye</td>
<td>Dilation of pupil</td>
<td>Constriction of pupil</td>
</tr>
<tr>
<td></td>
<td>Adjustment of eye for far vision</td>
<td>Adjustment of eye for near vision</td>
</tr>
<tr>
<td>Liver (glycogen stores)</td>
<td>Glycogenolysis (glucose released)</td>
<td>None</td>
</tr>
<tr>
<td>Adipose Cells (fat stores)</td>
<td>Lipolysis (fatty acids released)</td>
<td>None</td>
</tr>
</tbody>
</table>

© 2007 Thomson Higher Education
<table>
<thead>
<tr>
<th><strong>Exocrine Glands</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exocrine pancreas</strong></td>
<td>Inhibition of pancreatic exocrine secretion</td>
</tr>
<tr>
<td><strong>Sweat glands</strong></td>
<td>Stimulation of secretion by most sweat glands</td>
</tr>
<tr>
<td><strong>Salivary glands</strong></td>
<td>Stimulation of small volume of thick saliva rich in mucus</td>
</tr>
<tr>
<td><strong>Endocrine Glands</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adrenal medulla</strong></td>
<td>Stimulation of epinephrine and norepinephrine secretion</td>
</tr>
<tr>
<td><strong>Endocrine pancreas</strong></td>
<td>Inhibition of insulin secretion; stimulation of glucagon secretion</td>
</tr>
<tr>
<td><strong>Genitals</strong></td>
<td>Ejaculation and orgasmic contractions (males); orgasmic contractions (females)</td>
</tr>
<tr>
<td><strong>Brain Activity</strong></td>
<td>Increased alertness</td>
</tr>
</tbody>
</table>

© 2007 Thomson Higher Education
ANS

- **Exceptions to general rule** of dual reciprocal innervation by the two branches of autonomic nervous system
  - Most arterioles and veins receive only sympathetic nerve fibers (arteries and capillaries are not innervated)
  - Most sweat glands are innervated only by sympathetic nerves
  - Salivary glands are innervated by both ANS divisions but activity is not antagonistic – both stimulate salivary secretion
Adrenal Gland

• 3 arterial supply sources
  – Perfuse gland
    • Peripheral → center
    • Sinusoids
    • Medulla receives blood w/ cortex prod’s
  – Medulla has own arterial supply
• Medulla, cortex different embryo origins
  – Cortex from posterior abdominal wall lining
  – Medullary pheochromocytes from sympathogonia
    • Neural crest cells
    • Also give rise to neuroblasts; → sympathetic ganglia
• SF-1 required for adrenal gland development
  – Also gonads, ventromedial nucleus of hypothalamus
  – Also DAX-1 required
• During development, pheochromoblasts migrate to other areas (aorta, organ of Zuckerkandl)
Adrenal Cortex

- Produces steroid hormones
- Cholesterol-processing enz’s in sER, inner mitoch. membrane
  - Tubulovesicular mitoch.
    - Much inner membrane surface area
    - Much P450scc
- Parenchymal cells can produce cholesterol de novo
  - Mainly endocytosis of LDL
  - Cholesterol-rich lipid droplets in cytoplasm
- Capsule + 3 cell layers
Adrenal Gland (40x)

- Capsule
- Zona Glomerulosa
- Zona Fasciculata
- Zona Reticularis
- Adrenal Medulla
Adrenal Medulla

- Modified sympathetic ganglion
  - BUT no axons at targets
  - Release catecholamines to ECF → bloodstream

- Cells = pheochromocytes
  - Axonless secretory cells
  - Two cell subpopulations
    - Same cell population under different physiologic states
      - Concent cortisol exposure
    - Norepinephrine (noradrenaline) producing cells
    - Epinephrine (adrenaline) producing cells
  - Secrete prod’s from granules → ECF by exocytosis
The adrenal medulla is a modified part of the sympathetic nervous system.

- **Adrenal medulla** is a modified part of sympathetic nervous system
  - Modified sympathetic ganglion that does not give rise to postganglionic fibers
  - Stimulation of preganglionic fiber prompts secretion of hormones into blood
    - About 20% of hormone release is norepinephrine
    - About 80% of hormone released is epinephrine (adrenaline)
Fig. 14-1. Structures of norepinephrine and epinephrine.
Fig. 7-4. Comparison of the release and binding to receptors of epinephrine and norepinephrine.
1. Adrenal Medulla

- Modified part of sympathetic nervous system
- Primary stimulus for increased adrenomedullary secretion activation of sympathetic nervous system by stress
- Releases epinephrine and norepinephrine
  - Secreted into blood by exocytosis of chromaffin granules
  - Vary in their affinities for the different adrenergic receptor types
- Epinephrine
  - Reinforces sympathetic system in mounting general systemic “fight-or-flight” responses
  - Maintenance of arterial blood pressure
  - Increases blood glucose and blood fatty acids
Catecholamines

- **Stimulators**: stress (psychological reactions), elevated sound levels, intense light, low blood sugar levels
- Synth’d from L-tyrosine \( \rightarrow \) L-Dopa
- Dopamine, norepinephrine, epinephrine
- L-tyr in plasma (1-1.5 mg/dL)
- Active transport into cells
- Conversion L-tyr by 4 enz’s
  - Compartmentalized (격벽화)
- Adrenal medulla catecholamine output approx. 80% epinephrine
  - BUT plasma ratio 8:2 norepinephrine: epinephrine
Adrenal Medullary Hormones

- Epinephrine (E): 80%
- Norepinephrine (NE): 20%

- Adrenergic receptor
- Different affinity of E and NE
- $\alpha_1\beta_1\beta_2$ 수용체 결합
- $\alpha_1\beta_1$: excitatory
- $\alpha_2\beta_2$: inhibitory
<table>
<thead>
<tr>
<th>ADRENERGIC RECEPTOR TYPE</th>
<th>LOCATION</th>
<th>AFFINITY OF CATECHOLAMINE FOR NE AND E</th>
<th>TYPICAL RESPONSE ELICITED</th>
<th>EXAMPLES OF RESPONSES ELICITED</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$</td>
<td>Most sympathetic target cells</td>
<td>NE $&gt;$ E</td>
<td>Excitatory</td>
<td>Generalized arteriolar vasoconstriction (↑ smooth muscle contraction)</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>Digestive system</td>
<td>NE $&gt;$ E</td>
<td>Inhibitory</td>
<td>Decreased motility in digestive tract (↓ smooth muscle contraction)</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>Heart</td>
<td>NE $=$ E</td>
<td>Excitatory</td>
<td>Increased rate and strength of cardiac muscle contraction</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>Skeletal muscle; smooth muscle of some blood vessels and organs</td>
<td>E only</td>
<td>Inhibitory</td>
<td>Breakdown of glycogen in skeletal muscle; bronchiolar dilation and arteriolar vasodilation in skeletal muscle and heart (↓ smooth muscle contraction)</td>
</tr>
</tbody>
</table>
2. Synthesis, Chemistry, and Metabolism of Catecholamines

Fig. 14-3. Pathway of catecholamine biosynthesis.
1) Tyrosine Hydroxylase

→ Ring hydroxylation to L-DOPA (L-Dihydroxy-PhenylAlanine)
  - Contains Fe$^{2+}$; tetrahydrobiopterin cofactor
  - Activity regulated by preganglionic nerves
    - Get phosph’n PKA, PKC and calmodulin-dependent kinases
  - Long-term stimulation → upregulation of transcription, translation
  - Increased L-DOPA → prod inhibition
2) DOPA Decarboxylase (L-aromatic amino acid decarboxylase)

- Pyridoxal phosphate cofactor
- End product in CNS
- Stored in secretory vesicles
  - Enter by active transport
  - MVATs (Vesicular MonoAmine Transporters)
3) Dopamine β-Hydroxylase (DBH)

→ side chain hydroxylation to noradrenaline
- Contains Cu; Vit C cofactor
- Rxn w/in secretory vesicle
- End prod in symp. nerves, most central catecholaminergic neural tracts
4) Phenylethanolamine N-MethylTransferase (PNMT)

→ N-methylation to epinephrine
  • Methyl donor = S-Adenosylmethionine
  • Cytoplasmic
    – Norepinephrine leaves vesicle
      • Passive transport
      • Concent gradient
    – Epinephrine must reenter secretory vesicle
      • Active transport

Copyright © 2007 Pearson Prentice Hall, Inc.
PNMT

• Expression depends on high local cortisol
  – From adrenal cortex
  – Through sinusoid system

• Transcriptional activation of PNMT gene through ligand-activated glucocorticoid receptor
  – Also other transcription factors

• Also activity stimulated by glucocorticoid

• Adrenaline $\rightarrow$ prod feedback inhibition

• Also found in kidney, lung, pancreas

• Also nonspecific NMT
  – Contributes to peripheral conversion norepi. to epi.
Secretory Vesicles

- Catecholamine storage
- Active transport via VMATs
  - ATP-driven proton pump
  - In vesicle membranes
  - pH, electrical gradient
  - Antiporter
- 12 transmembrane helical segments
  - Related to plasma membrane monoamine transporters
Catecholamine Release from Storage Vesicles

- ACh released from preganglionic fibers
  - Nicotinic receptors
  - Get depolarization of pheochromocytes
  - act’n voltage-gated Ca\(^{2+}\) channels
  - influx Ca\(^{2+}\)
  - exocytosis of secretory vesicles
    - Chromogranins, DBH, ATP, other peptides released
Actions of Catecholamines

- Circulating catecholamines reach most tissues
  - BUT cannot penetrate
    - BBB
    - Fetus
  - Fetal production (mostly norepi) through fetal zone
    - Impt in intrauterine life (cardiovascular responses)
    - Large
    - Placenta expresses catecholamine degrading enzymes

- Placental norepi. transporter
  - Delivers circulating fetal chatechol’s for degrad’n
Catecholamine Elimination

- Short-lived mol’s
  - 10 sec to 1.7 min
- 50-60% associated w/ albumin
- Elimination
  - At synapse, ISF near symp. neurons
    - Reuptake into nerve terminals
    - Reenter vesicles via VMAT OR
    - Become degraded by monoamine oxidase (MAO, MAOIs bind to MAO for inhibition)
  - In target cells
    - Degraded by Catechol-O-MethylTransferase (COMT)
  - 5% directly filtered into urine
Fig. 14-4. Pathways of catecholamine metabolism.
• MAO
  – In outer mitoch membr
  – Substr’s also serotonin, histamine
  – Oxidizes amino grp → aldehydes
  – Further ox’d by nonspecific aldehyde deHase
  – Ultimate prod dihydroxymandelic acid (DOMA)
  – MAO-A and MAO-B
• COMT – extraneuronal degradation
  – Uses SAM as methyl donor
  – Important to circulating catecholamines
• Get final conjugation
  – Sulfate, glucuronate in liver, gut
  – Excretion through urine
Fig. 14-5. Sympathetic negative feedback mechanisms for inhibition of sympathetic neuron secretion.
Inhibitors of Catecholamine Metabolism

- alpha-methyl-para-tyrosine (AMPT)
- tyrosine
- disulphiram
- reserpine
- tetrabenazine
- amphetamine
- NA
- MAO
- iproniazid (MAOI)
- deaminated products
- imipramine tricyclics
- COMT
- NM
- VMA
- MAO

40
3. Sympathoadrenal System Receptors

- Neurotransmitters: primary substances produced by neurons of ANS
  - **Acetylcholine** released by *cholinergic neurons*
  - **Norepinephrine** released by *adrenergic neurons*

- Certain cells have **receptors** that combine with neurotransmitters causing a response in the cell
  - **Cholinergic**: bind acetylcholine. Have two different forms: *nicotinic* and *muscarinic*
    - **Nicotinic**: all receptors on postganglionic neurons, all skeletal muscles, adrenal glands
    - **Muscarinic**: all receptors on parasympathetic effectors, receptors of some sweat glands
  - **Adrenergic receptors (adrenoceptors)** bind norepinephrine/epinephrine
    - **Alpha** and **beta** receptors:
      - Alpha (α) receptors: α1, α2
      - Beta (β) receptors: β1, β2
<table>
<thead>
<tr>
<th>Organ</th>
<th>Adrenergic Effects of Sympathoadrenal System</th>
<th>Adrenergic Receptors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td>Contraction of radial fibers of the iris dilates the pupils</td>
<td>$\alpha_1$</td>
</tr>
<tr>
<td>Heart</td>
<td>Increase in heart rate and contraction strength</td>
<td>$\beta_1$, primarily</td>
</tr>
<tr>
<td>Skin and visceral vessels</td>
<td>Arterioles constrict due to smooth muscle contraction</td>
<td>$\alpha_1$</td>
</tr>
<tr>
<td>Skeletal muscle vessels</td>
<td>Arterioles constrict due to sympathetic nerve activity</td>
<td>$\alpha_1$</td>
</tr>
<tr>
<td></td>
<td>Arterioles dilate due to hormone epinephrine</td>
<td>$\beta_2$</td>
</tr>
<tr>
<td>Lungs</td>
<td>Bronchioles (airways) dilate due to smooth muscle relaxation</td>
<td>$\beta_2$</td>
</tr>
<tr>
<td>Stomach and intestine</td>
<td>Contraction of sphincters slows passage of food</td>
<td>$\alpha_1$</td>
</tr>
<tr>
<td>Liver</td>
<td>Glycogenolysis and secretion of glucose</td>
<td>$\alpha_1, \beta_2$</td>
</tr>
</tbody>
</table>

Fig. 14-6. Experimental demonstration of epinephrine (catecholamine) reversal.
Fig. 14-7. Examples of $\alpha$-AR agonist and antagonist structures.

- $\alpha$-Adrenoceptors ($\alpha$-AR):
  - $\alpha_1$-Agonist: phenylephrine
  - $\alpha_2$-Agonist: clonidine
  - Mixed $\alpha$-Adrenoceptor antagonist: phentolamine
• **β-Adrenoceptors (β-AR):**

![Chemical structures of β-AR agonists and antagonists](image)

- **Practolol (β<sub>1</sub>-Antagonist)**
- **Butoxamine (β<sub>2</sub>-Antagonist)**
- **Prenalterol (β<sub>1</sub>-Agonist)**
- **Salbutamol (β<sub>2</sub>-Agonist)**
- **Isoproterenol**

*Fig. 14-8. Examples of **β-AR agonist and antagonist** structures.*
4. Adrenergic receptor

Fig. 14-9. Topological model of the ligand-binding pocket of the $\beta_2$-adrenergic receptor, which is inserted in the membrane. The ligand-binding region formed by the seven transmembrane domains is buried in the lipidic bilayer.
Adrenergic Receptors

- Heptahelical, G-protein-linked transmembrane receptors
- 2 categories: α and β, subcategories
  - α – affinity for epinephrine > norepinephrine
    - α1 (A, B, D) mostly use Gαq G prot’s
      - Usually activate PLC (→ PKC and DAG and intracellular Ca^{2+}
        through IP_{3})
      - And/or activate PLA2
    - α2 (A, B, C) varied
      - Gαi and G0 couple to decremented activity adenylyl cyclase
      - Can → act’n K^{+} channels, inhib’n Ca^{2+} channels, act’n PLC
        and/or PLA2
  - β – affinity for epinephrine > norepinephrine
    - All (1, 2, 3) use Gαs G prot → act’n ad cyclase
5. Adrenoceptor Signal Transduction

1) α-adrenoceptors: IP₃

![Diagram of multiple mechanisms of adrenoceptor signal transduction](https://example.com/diagram.png)

Fig. 14-10. Multiple mechanisms of adrenoceptor signal transduction.
2) β-adrenoceptors: cAMP

Fig. 14-11. Lipolytic action of catecholamines on adipocytes.
3) β-adrenoceptors desensitization:

- Molecular mechanisms underlying rapid β-AR desensitization do not appear to require internalization of the receptors.
- Uncoupling of β-AR by at least two kinases, PKA and the β-AR kinase (β-ARK).

Fig. 14-12. Mechanisms of β-AR desensitization.
6. Sympathoadrenal Functions

1) Catecholamines regulate intermediary metabolism.
   - Carbohydrate metabolism (β-AR): blood glucose levels increased
   - Fat metabolism (β-AR): activates a hormone-sensitive lipase, triglyceride lipase → metabolizes fats into fatty acids (FFAs) and glycerol (Fig. 14.11)
   - Protein metabolism (β-AR): decreases the release of amino acids from skeletal muscle

2) The sympathetic nervous system regulates thermogenesis.
   - Shivering thermogenesis:
   - Nonshivering (chemical) thermogenesis: brown adipose tissue in the rat

3) Adrenergic receptors mediate cardiovascular responses to stress (β-AR) →
4) Physiological implications of sympathoadrenal catecholamines

• General: activates fight/flight mech’s
  – Mobilizes energy, redist’s blood

• Opposes parasymp.
  – Promotes digestion, storage of energy
  – BUT distinct target cell pop’ns w/in organs

• Many targets; overall
  – Incr’s cardiac output, blood pressure
  – Bronchodilation ➔ matched perfusion w/ increased ventilation
  – Blood diverted from viscera and skin to muscle
    • Retain blood to brain
  – Mobilize fuel from energy stores
INTEGRATED STRESS RESPONSE

• Pattern of reactions to a situation that threatens homeostasis

• Stress
  – Generalized nonspecific response of body to any factor that overwhelms or threatens to overwhelm the body’s ability to maintain homeostasis

• Stressor
  – Any noxious stimulus that brings about the stress response
Stressors

- **Physical**: trauma, surgery, intense heat or cold
- **Chemical**: reduce O2 supply, acid-base imbalance
- **Physiologic**: heavy exercise, hemorrhagic shock, pain
- **Infectious**: bacterial invasion
- **Psychological or emotional**: anxiety, fear, sorrow
- **Social**: personal conflicts, change in lifestyle
Action of a stressor on the body

Stressor

Body

Specific response characteristic of type of stressor

Nonspecific generalized response regardless of type of stressor = Stress response

© 2007 Thomson Higher Education
Stress Response

- All the actions are coordinated by the hypothalamus

- Generalized stress response
  - Activation of sympathetic nervous system accompanied by epinephrine secretion
    - Prepares body for fight-or-flight response
  - Activation of CRH-ACTH-cortisol system
    - Helps body cope by mobilizing metabolic resources
  - Elevation of blood glucose and fatty acids
    - Decreased insulin and increased glucagon secretion
  - Maintenance of blood volume and blood pressure
    - Increased activity of renin-angiotensin-aldosterone system and increased vasopressin secretion
영국 해병이 전우를 구하기 위해 자기 체중의 13배에 달하는 트럭을 들어 올린 사실이 뒤늦게 알려지면서, 5일 영국 언론들의 집중 조명을 받았다. 2006년 11월 아프가니스탄에서 교전을 벌이던 중 부근에서 박격포탄이 터지면서 핀츠가우어 트럭이 뒤파지고 수로로 빠졌다. 트럭 밑에 갈린 마크 파(29)가 움짝달싹할 수 없었고 1미터 깊이의 물속에서 익사할 위기에 처했다. 칼 태튼 상사(38)는 마크 파의 고개를 올려 숨을 쉬게 하려 했지만, 여의치 않았다. 방법은 오직 하나 트럭을 드는 것 뿐 이었다. 천장 부근의 롤바를 잡고 힘을 쓰자 2톤에 달하는 트럭이 들어 올려졌고 마크 파는 빠져 나올 수 있었다. 탈레반의 박격포 공격 속에서 전우를 구하기 위해 용기와 ‘초인적’ 힘을 발휘한 칼 태튼은 ‘영웅’으로 떠올랐다. (사진: 해병대원들이 칼 태튼이 들어올렸던 군용 트럭 주변에서 조사를 벌이고 있다)
**Pinzgauer High Mobility All-Terrain Vehicle**

*Pinzgauer* is a high mobility all-terrain 4x4 and 6x6 military utility vehicle manufactured in Guildford, Surrey, United Kingdom, by Automotive Technik (ATL). ATL has been manufacturing the Pinzgauer since the year 2000. Before then the Pinzgauer was produced by *Steyr-Daimler-Puch* in Graz, Austria (hence the name, based on an Austrian breed of horse). ATL has since then been acquired by Stewart & Stevenson Services, Inc. in 2005, which in turn became a subsidiary of the aerospace and defence group Armor Holdings, Inc in May 2006. One year later Armor Holdings was itself acquired by BAE Systems.

*Pinzgauer 710M 4x4 model*
Control of cortisol secretion

Pro-opiomelanocortin (POMC)

- MSH
- β-Endorphin
- ACTH

Stress

Diurnal rhythm

Hypothalamus

Corticotropin-releasing hormone (CRH)

Anterior pituitary

Adrenocorticotropic hormone (ACTH)

Adrenal cortex

Cortisol

↑ Blood glucose
(by stimulating gluconeogenesis and inhibiting glucose uptake)

↑ Blood amino acids
(by stimulating protein degradation)

↑ Blood fatty acids
(by stimulating lipolysis)

Metabolic fuels and building blocks available to help resist stress

© 2007 Thomson Higher Education
## Activation of CRH-ACTH-cortisol system

### TABLE 19-3

<table>
<thead>
<tr>
<th>HORMONE</th>
<th>CHANGE</th>
<th>PURPOSE SERVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>↑</td>
<td>Reinforces the sympathetic nervous system to prepare the body for “fight or flight”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mobilizes carbohydrate and fat energy stores; increases blood glucose and blood fatty acids</td>
</tr>
<tr>
<td>CRH-ACTH-Cortisol</td>
<td>↑</td>
<td>Mobilizes energy stores and metabolic building blocks for use as needed; increases blood glucose, blood amino acids, and blood fatty acids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACTH facilitates learning and behavior</td>
</tr>
<tr>
<td></td>
<td></td>
<td>β-endorphin cosecreted with ACTH may mediate analgesia</td>
</tr>
<tr>
<td>Glucagon</td>
<td>↑</td>
<td>Act in concert to increase blood glucose and blood fatty acids</td>
</tr>
<tr>
<td>Insulin</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>Renin-Angiotensin-Aldosterone</td>
<td>↑</td>
<td>Conserve salt and H₂O to expand the plasma volume; help sustain blood pressure when acute loss of plasma volume occurs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Angiotensin II and vasopressin cause arteriolar vasoconstriction to increase blood pressure</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vasopressin facilitates learning</td>
</tr>
</tbody>
</table>

© 2007 Thomson Higher Education
Integration of the stress response by the hypothalamus.