ENDOCRINOLOGY:
Study of ductless glands/tissues & their hormonal products that regulate activity of other cells in body

COMPARATIVE ENDOCRINOLOGY:
Study of endocrine system of number of invertebrate/vertebrate systems

Endocrinology: Subdiscipline of Physiology: Includes study of:
1) physiological role of hormones
2) cellular source & synthesis of hormones
3) hormonal chemistry & storage
4) factors & mechanisms controlling hormonal secretion
5) cellular mechanisms of action of hormones
6) pathophysiology of endocrine system dysfunction

Classical definition of **Hormone**:
chemical messengers (hormones) or substances **secreted by cells of endocrine gland** (ductless glands) & tissues into **general circulation (blood)** that regulate activity of other **distant target cells**

Starling: Canadian physiologist, (1905) coined **Hormone** from the Greek "I arouse to activity or I excite"

Endocrine glands (**ductless**) contrast those of **exocrine** glands (**duct**) products of exocrine glands released into **ducts** that lead to digestive tract or to exterior of the body

Exocrine products include:
mucus, perspiration, oil, wax, & digestive enzymes

1) Salivary glands - mucus and digestive enzymes
2) Sweat glands - perspiration to cool the skin
Old definition stressed "source of the hormone"

New concepts of hormones through recent discoveries include "method of delivery"

Hormones produced in many sites and may be released into
1) blood
2) neuronal synapsis
3) immediate intercellular spaces to affect adjacent cellular activity

Historical perspectives: Endocrinology-infant science
1849 Berthold: First experiment
1818-78 Claude Bernard-father of comparative physiology
1878-79 constancy of the “milieu interieur”
organisms preserve a distinct internal environment despite changes in the external environment

William Bradford Cannon – mammalian physiologist
1932: The Wisdom of the Body → Homeostasis—physiological equilibrium
extended Bernard’s constancy of “milieu interieur”
1) to include internal environment of organism
2) surrounding cells/tissues—thus constancy within organisms

1) requires mechanisms acting to maintain this regulation of steady states:
glucose concentrations, body temperature & acid-base balance

2) steady-state conditions requiring any tendency toward change automatically meeting with factors that resist change:
e.g. increase in blood sugar → in thirst: body attempts to dilute sugar concentration in extracellular fluid

3) regulating system determining homeostatic state consists of a # of cooperating mechanisms acting simultaneously or successively:
blood sugar regulated by insulin, glucagons & other hormones controlling its release from liver or its uptake by tissues

4) homeostasis not occur by chance, but is result of organized self-government
1889-1902 (50 year lapse): Significant discoveries
1910 advances
By 1950 vertebrate/invertebrate endocrine systems complete
1950-1980 Endocrine chemistry
1980-present: Molecular biology:
   insights into evolutionary history of endocrine systems
   a) Structure of genes for hormones
   b) Receptors
Galenic theories
   physiological regulation to the movement of body fluids or humors.

19th century physiologists based on chemical & physical principles
regulation of bodily activities explained by reflex responses
mediated by neural pathways

19th century: microscopists
described detail the tissues and organs but functional significance was unknown

Early medical writings describe general symptoms of endocrine dysfunctions
Clinical correlations between tissue/organ abnormalities
(atrophy/enlargement) & physiological state were observed
First experiments: Effects of tissue/organ removal resulting in physiological alteration
Castration of cockerels:
1) no development of combs/wattles
2) failed to exhibit male behavior
3) replacement therapy:
   replacement of one or both testes back into
   abdominal cavity in either same/different bird
   1) normal development of combs/wattles
   2) male behavior
   3) one transplanted testis larger than normal intact testes

Compensatory hypertrophy:
increase in organ size to compensate functionally for activity of other lost organ

Significance:
1) transplanted testes functional & independent of nervous innervation
2) donor organ can be transplanted to another host & remain functional

Berthold conclusion: testes secreted something that "conditioned" blood;
blood then acted on body of cockerel to cause male characteristics
showed presence of testes maintained “maleness”
Organ transplants/extracts
replacement therapy for absent tissue or organ testes function:
1) activation/transformation of blood constituents into active agents (hormones)
2) removal of inhibitory substance from blood
3) release of hormone into circulation
Successful replacement therapy led to purification of physiologically active extracts
testes extracts could functionally replace testes of castrated animals
Identification of hormonal substances concerned
1935 testosterone purified in crystalline form

1889: Von Mering & Minkowski
Surgically removed pancreas from dogs
symptoms similar to human diabetes mellitus
  elevated blood glucose levels
Conclusions: diabetes defect of carbohydrate metabolism due to pancreatic malfunction

1922: Banting & Best
Islets of Langerhans, not pancreatic acini (bulk of pancreas) control carbohydrate metabolism through internal secretion rather modification of blood
preparation of pancreatic islets injected into diabetic dogs lowered blood glucose levels

1912: Schaefer named pancreatic protein hormone insulin
1953: Sanger characterized amino acid sequence of insulin (Nobel Prize)

A Chain

- His-Asn-Thr-
- Ala-Ser-Thr-
- Thr-Gly-Ile-
- Ala-Gly-Val-
- Ala-Ser-Val-
- Thr-Ser-Ile-
- Thr-Ser-Ile-
- Pig, Dog, Sperm Whale

Gly-Ile-Val-Glu-Gln-Cys-Cys-Thr-Ser-Ile-Cys-Ser-Leu-Tyr-Gln-Leu-Glu-Asn-Tyr-Cys-Asn

1 2 3 4 5 6 8 9 10 11 12 13 14 15 16 17 18 19 20 21

B Chain

Arg-Gly-Phe-Phe-Tyr-Thr-Pro-Lys-Thr

- Ala Pig, Dog, Sperm Whale
- Ser Rabbit
- Ala Cattle, Goat
- Ala Sheep
- Ala Horse
- Ala Sei Whale

1955: du Vigneaud → Nobel Prize

used Sanger methods synthesize peptide hormones: oxytocin & vasopressin
1962 Sutherland

adenosine 3', 5'-monophosphate (cyclic AMP or cAMP)

enzyme adenylate cyclase responsible for production of cAMP

Sutherland et al.

hormones could stimulate broken cell membrane preps to activate liver phosphorylase, enzyme responsible for breakdown of liver glycogen

hormones + Liver cell membrane particulate fractions --> factor (cAMP) --> activate phosphorylase enzyme in supernatant fraction of tissue homogenate

cAMP: second messenger involved in role of hormone action & cellular function

Implications in biochemistry, pharmacology, physiology, and medicine

Sutherland 1971 Nobel Prize in Physiology or Medicine