ENDOCRINOLOGY:

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

COMPARATIVE ENDOCRINOLOGY:

Study of endocrine system of number of invertebrate/vertebrate s ystems

Endocrinology: Subdiscipline of Physiology: Includes study of:

1) physiological role of hormones
2) cellular source and synthesis of hormones
3) hormonal chemistry and storage
4) factors and 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 the 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 are released into *ducts* that lead to the digestive tract or to the 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

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

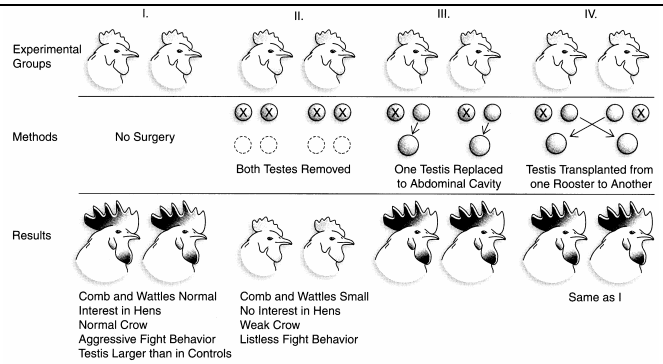


Figure 1.1 Berthold's experiment: the first endocrine experiment.

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 size of organ to compensate functionally for the activity of the other lost organ

Significance:

1) transplanted testes were functional and independent of nervous innervation

2) donor organ can be transplanted to another host and remain functional

Berthold conclusion: testes secreted something that "*conditioned*" the blood;

blood then acted on body of cockerel to cause male characteristics

showed that presence of testes maintained maleness

Organ transplants/extracts as replacement therapy for absent tissue or organ

testes function:

1) activation/transformation of blood constitutents 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 and 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

1912 Schaefer named the pancreatic protein hormone ***insulin***

1922 Banting & Best

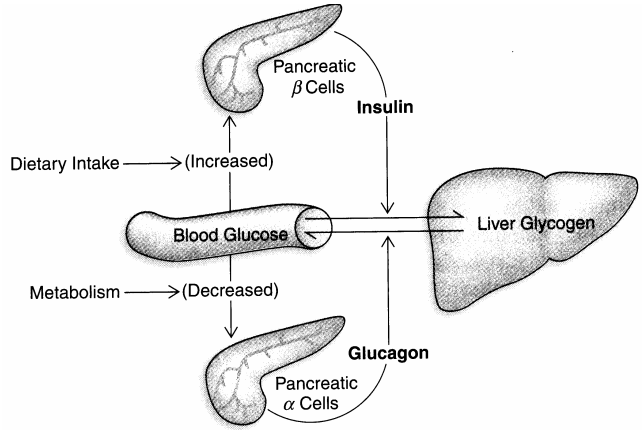
Islets of Langerhans, and not pancreatic acini (bulk of pancreas) control carbohydrate metabolism through internal secretion rather modification of the blood

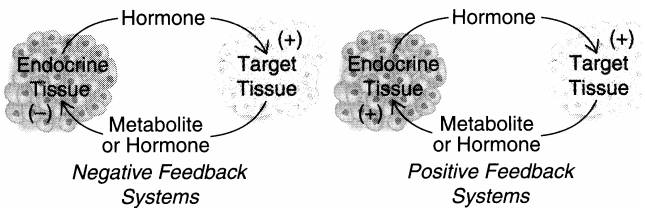
preparation of pancreatic islets injected into diabetic dogs lowered blood glucose levels

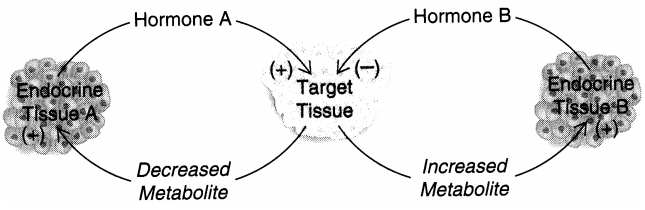
1953 Sanger characterized amino acid sequence of insulin (Nobel Prize)

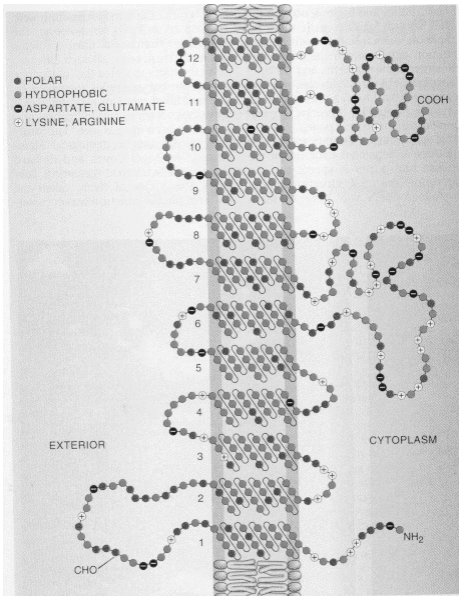
1955 du Vigneaud Nobel Prize

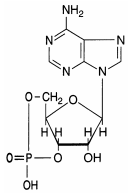
used Sanger methods synthesize peptide hormones: ***oxytocin*** & ***vasopressin***




Hormone
(+)
Endocrine Tissue
(–)
Target Tissue
Metabolite or Hormone
Negative Feedback Systems
Hormone
(+)
Endocrine Tissue
(+)
Target Tissue
Metabolite or Hormone
Positive Feedback Systems


Hormone A
Hormone B
(+)
(–)
Endocrine Tissue A
(+)
Target Tissue
Endocrine Tissue B
(+)
Decreased Metabolite
Increased Metabolite





1962 Sutherland

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

enzyme ***adenylate cyclase*** responsible for production of cAMP

Sutherland et al.

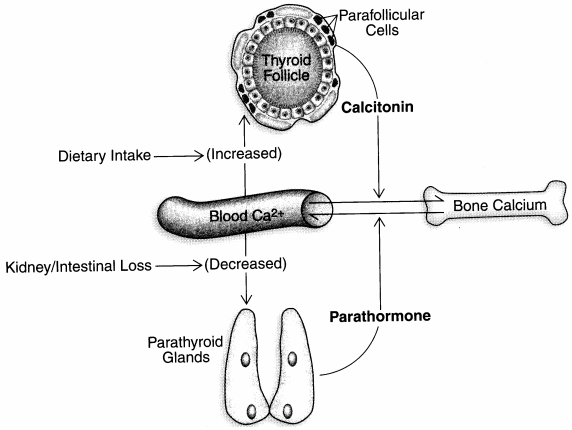
hormones could stimulate broken cell membrane preps to activate liver phosphorylase, enzyme responsible for breakdown of liver glycogen

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


Parafollicular Cells
Thyroid Follicle
Calcitonin
Dietary Intake
(Increased)
Blood Ca^{2+}
Bone Calcium
Kidney/Intestinal Loss
(Decreased)
Parathormone
Parathyroid Glands