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

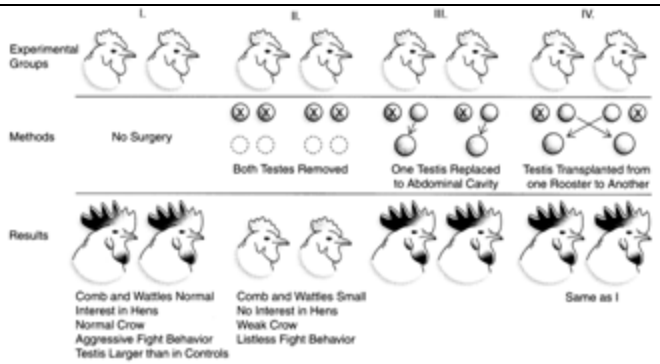


Figure 1.1 Berthold's experiment: the first endocrine experiment.

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 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 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 & 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

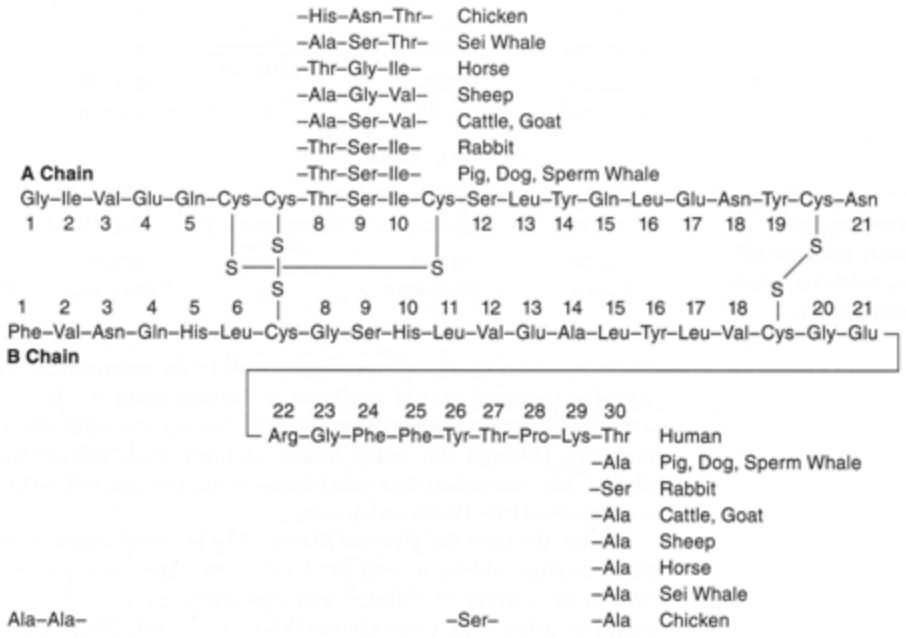
1922: Banting & Best

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

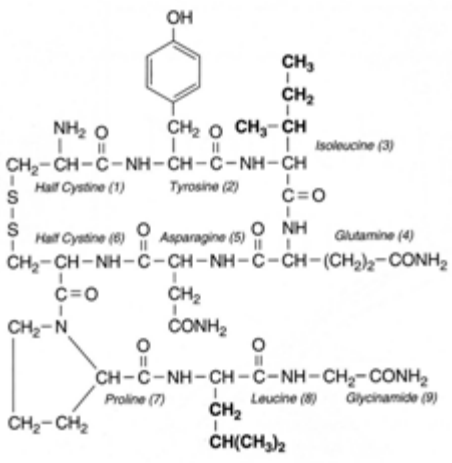
1912: Schaefer named pancreatic protein hormone ***insulin***

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

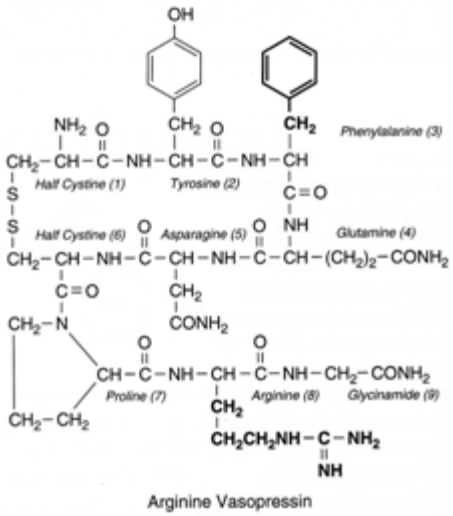


1955: du Vigneaud → Nobel Prize

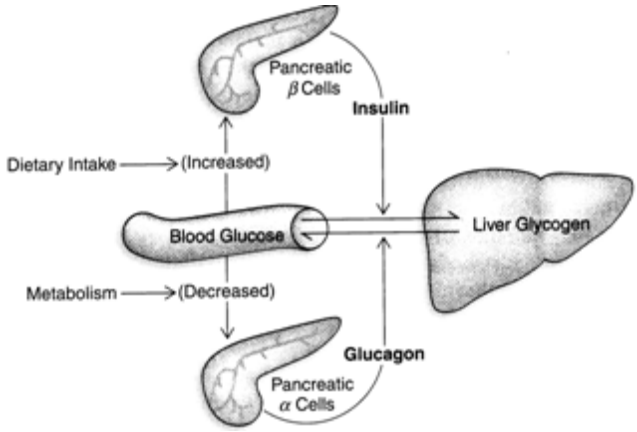
used Sanger methods synthesize peptide hormones: ***oxytocin*** & ***vasopressin***

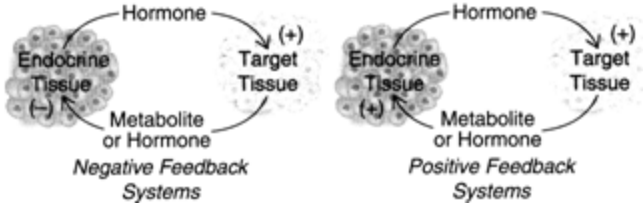


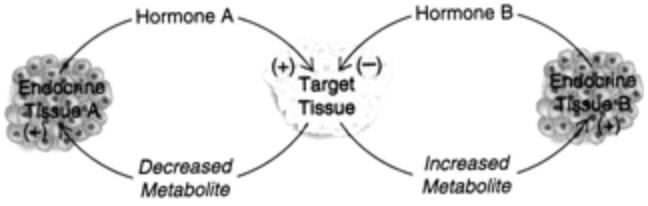
Oxytocin

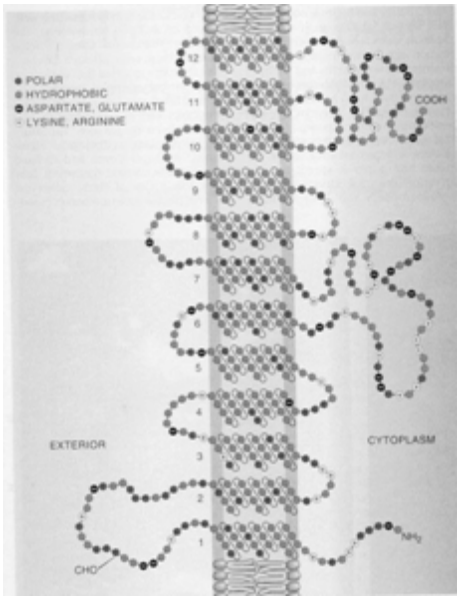


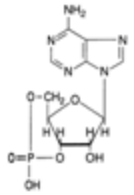
Arginine Vasopressin


Pancreatic
β Cells
Insulin
Dietary Intake
(Increased)
Blood Glucose
Liver Glycogen
Metabolism
(Decreased)
Glucagon
Pancreatic
α Cells


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


POLAR
HYDROPHOBIC
ASPARTATE, GLUTAMATE
LYSINE, ARGININE
COOH
EXTERIOR
CYTOPLASM
CHO
NH2
12
11
10
9
8
7
6
5
4
3
2
1



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