

INSULIN ISOLATION
FROM HEROPHILUS TO LANGERHANS AND BANTING
EARLY ANATOMY AND PHYSIOLOGY OF PANCREAS
AND THE UNIVERSITY OF ADELAIDE CONTRIBUTION

HISTORY: MAJOR CONTRIBUTORS: EGYPT, GREECE, ROME, BELGIUM, FRANCE, GERMANY, CANADA AND AUSTRALIA

- HEROPHILUS 335-280 BCE
- GALEN 125-200 ? 216 CE
- VESALIUS 1514-1564
- WIRSUNG, 1589-1643
- SANTORINI, 1691-1737
- VATER 1687-1751
- DE GRAAF 1641-1673
- CLAUDE BERNARD 1813-1878
- LANGERHANS 1847-1888
- BANTING 1891-1941
- THOBURN BRAILSFORD ROBERTSON
1884-1930

ALEXANDRIA AND HEROPHILUS 335-280 BCE

DYNASTY OF PTOLEMIES FOLLOWED ALEXANDER IN 323 AND CONTINUED TO SUPPORT SCIENCES AND CULTURE. ANATOMY THRIVED BECAUSE HUMAN DISSECTION WAS POSSIBLE. HEROPHILUS PERFORMED MANY DISSECTIONS, SOME IN PUBLIC AND WAS THE FIRST TO DESCRIBE THE PANCREAS

HEROPHILUS



LIBRARY IN ALEXANDRIA



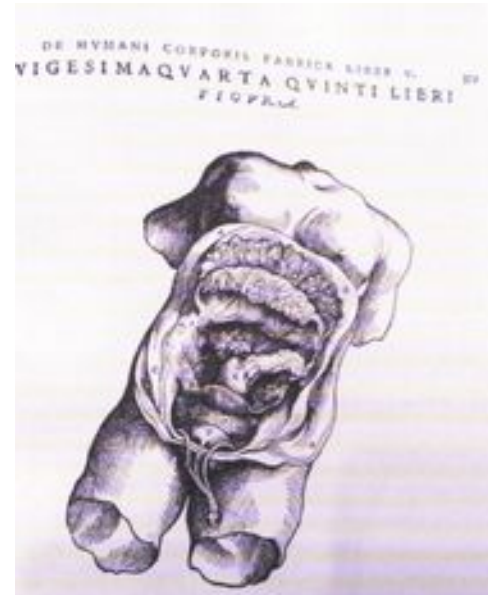
GALEN (CE 129-200)



- STUDIED MEDICINE AT THE AESCULAPIUM IN PERGAMON
- VISITED CENTRES OF LEARNING, THOUGHT PANCREAS PROTECTED BLOOD VESSELS
- SURGEON TO GLADIATORS
- 161 MOVED TO ROME
- MARCUS AURELIUS SUPPORT
- DISSECTIONS OF ANIMALS
- NUMEROUS PUBLICATIONS WHICH INFLUENCED ANATOMY FOR 1500 YEARS

CHRONOLOGY

- GRECO-ROMAN ERA: HEROPHILUS AND GALEN - 400 BCE TO 800 CE
- DARK AGES: ARABIC GOLDEN AGE, IBN SENA (AVICENNA)
- MEDICAL RENAISSANCE: VESALIUS 1514 TO 1546
- WIRSUNG AND SANTORINI
- VATER AND BRUNNER
- DE GRAAF AND BERNARD
- MICROSCOPE AND VITAL STAINS: LANGERHANS 1869
- DISCOVERY OF INSULIN: BANTING, BEST, MCLEOD AND COLLIP
NOBEL PRIZE 1923
- ROBERTSON MASS PRODUCES INSULIN IN ADELAIDE, c. 1924



PANCREAS?

ANDREAS VESALIUS 1514-1564

THESE WOODCUT FIGURES APPARENTLY DEPICT THE PANCREAS WHICH IS NOT NORMAL OR DESCRIBED CLEARLY IN THE "*DE HUMANI CORPORIS FABRICA*"

ANATOMY AND EXOCRINE FUNCTION

- **WIRSUNG AND SANTORINI DESCRIBED PANCREATIC DUCTS**
- **BRUNNER AND VATER DESCRIBED THE AMPULLA**
- **DE GRAAF COLLECTED PANCREATIC JUICE FROM DOG**
- **CLAUDE BERNARD NOTED THE EFFECT OF ENZYMES**
- **AWARDED A PRIZE FROM THE FRENCH ACADEMY OF SCIENCES**

DE
Succo Pancreatico: Or,
A Physical and Anatomical
TREATISE
Of the NATURE and OFFICE of the
Pancreatick Juice;

Shewing its generation in the Body, what Diseases arise by its Vitiation; from whence in particular, by plain and familiar examples, is accurately demonstrated, the Causes and Cures of Agues, or Intermitting Fevers, hitherto so Difficult and Uncertain; with sundry other things worthy of Note.

Written by *D. Reg. de Graaf*, Physician of *Delft*,
And Translated by *Christopher Pack*, *Med. Lond.*



London, Printed for *N. Brook* at the *Angel* in
Cornhil near the *Royal Exchange*, 1676.

TITLE PAGE FROM DE GRAAF'S TREATISE ON
PANCREATIC JUICE AND ITS COLLECTION
FROM A PANCREATIC FISTULA IN A DOG.

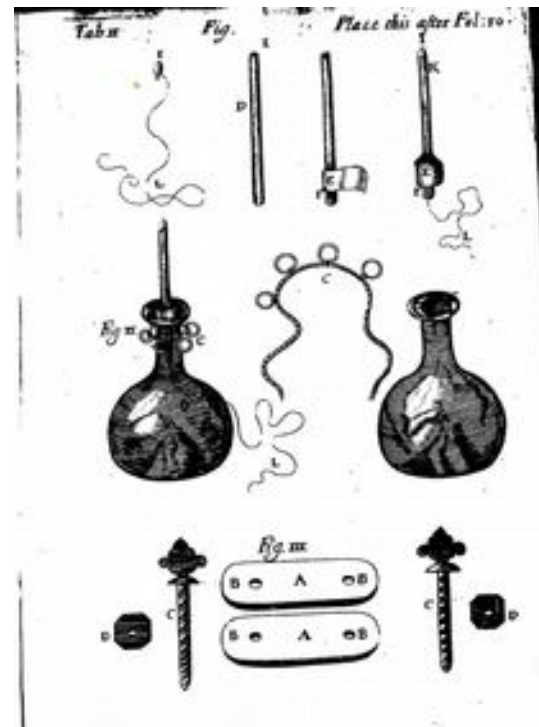
DE GRAAF

DE GRAAF HAD SEVERAL ATTEMPTS TO PRODUCE A FUNCTIONING FISTULA. THOUGHT THE JUICE TO BE ALKALINE AND POSSIBLY THAT THE FLOW INCREASED DURING FEEDING. BIOCHEMISTRY WAS PRIMITIVE

A DOG WITH A FISTULA

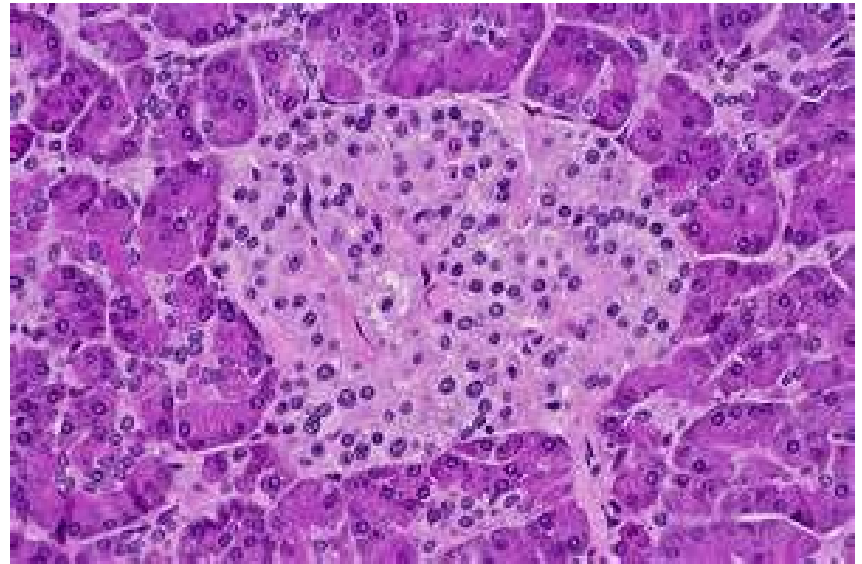


COLLECTING APPARATUS



PAUL LANGERHANS

THESIS AT THE BERLIN PATHOLOGICAL INSTITUTE 1869



HISTOLOGY OF A SINGLE
PANCREATIC ISLET, CENTER

ANATOMY AND ENDOCRINE FUNCTION

**LANGERHANS DESCRIBED THE ISLETS BUT THOUGHT THEY MAY BE LYMPHATIC
TISSUE**

**LANGUESSE SUGGESTED THE NAMING OF THE ISLANDS AFTER LANGERHANS
AND BELIEVED THEY PLAYED AN IMPORTANT ROLE**

MINKOWSKI AND VON MEHRING REMOVED CANINE PANCREAS AND PRODUCED DIABETES

**BARROW PRODUCED PANCREATIC FIBROSIS BY LIGATING THE PANCREATIC DUCT
IN DOGS**

BANTING, BEST, MACLEOD AND COLLIP ISOLATED INSULIN

THE TORONTO INSULIN TEAM



BANTING

**ORTHOPOEDIC SURGEON,
ISOLATED INSULIN**



BEST

**MEDICAL STUDENT
BANTING'S
COLLABORATOR**



**BANTING AND
GEST WITH THEIR
DIABETIC DOG**



MACLEOD

PROFESSOR OF PHYSIOLOGY



COLLIP

BIOCHEMIST

ISOLATION OF AN INSULIN CONTAINING PROTEIN

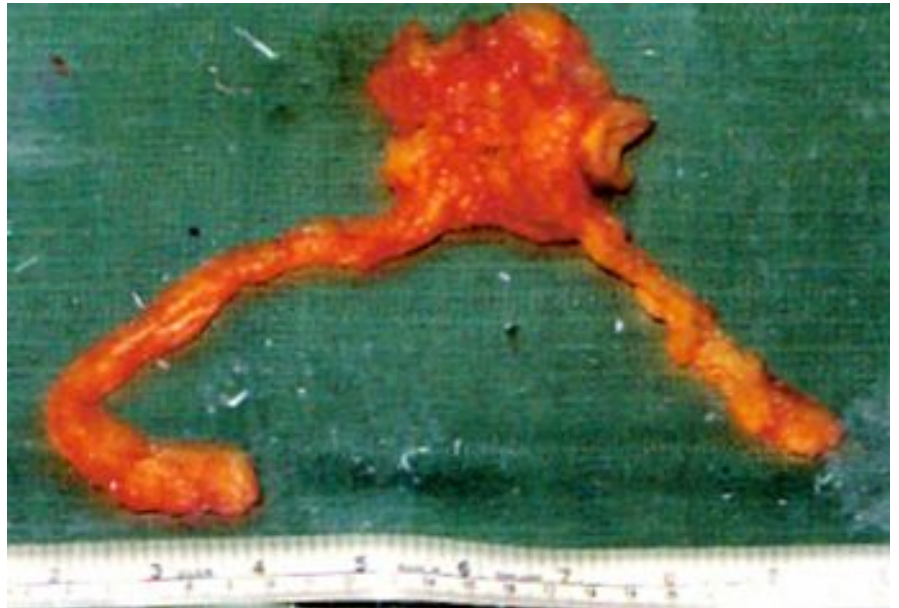
- **BANTING GRADUATED IN MEDICINE AND VOLUNTEERED IN WW1 (1918). HE RECEIVED A MILITARY MEDAL FOR BRAVERY UNDER FIRE AT CAMBRAI.**
- **BEST WAS IN A TANK REGIMENT. ON RETURN BANTING BECAME A PAEDIATRIC ORTHOPAEDIC SURGEON, BUT ALSO LECTURED IN PHARMACOLOGY. BEST BECAME A MEDICAL STUDENT.**
- **BANTING CONTINUED HIS INTEREST IN PANCREAS. AT THIS TIME MANY TRIED TO ISOLATE INSULIN BUT FAILED.**
- **BANTING FELT THAT THE PROTEOLYTIC ACTION OF PANCREATIC ENZYMES INTERFERED WITH THE PROCESS.**
- **HE WAS AWARE OF MINKOWSKI AND BEHRING'S WORK IN PRODUCING DIABETES IN DOGS AFTER TOTAL PANCREATECTOMY.**

ISOLATION OF AN INSULIN CONTAINING PROTEIN

- HE ALSO FELT THAT MOSES BARROW'S PUBLICATION (1920) ON PANCREATIC FIBROSIS AFTER DUCT LIGATION WAS IMPORTANT IN REDUCING THE ENZYME EFFECT.
- HE BELIEVED THAT REMOVING DOGS PANCREASES TO PRODUCE DIABETES AND USING A FIBROSED
- PANCREAS TO EXTRACT THE TISSUE WITHOUT THE ENZYMES COULD WORK.
- HE APPROACHED PROFESSOR MACLEOD AND AFTER SOME DEBATES HE WAS ALLOWED 10 DOGS AND AND BEST AS ASSISTANT.
- THE TISSUE FROM THE FIBROTIC PANCREASES WAS SLICED, MINCED AND DISSOLVED. IT WAS ALSO COOLED UNDER ICE SLUDGE AND THEN INJECTED INTO DIABETIC DOGS.
- THE RESULTS RESULTED IN A NOBEL PRIZE AWARD

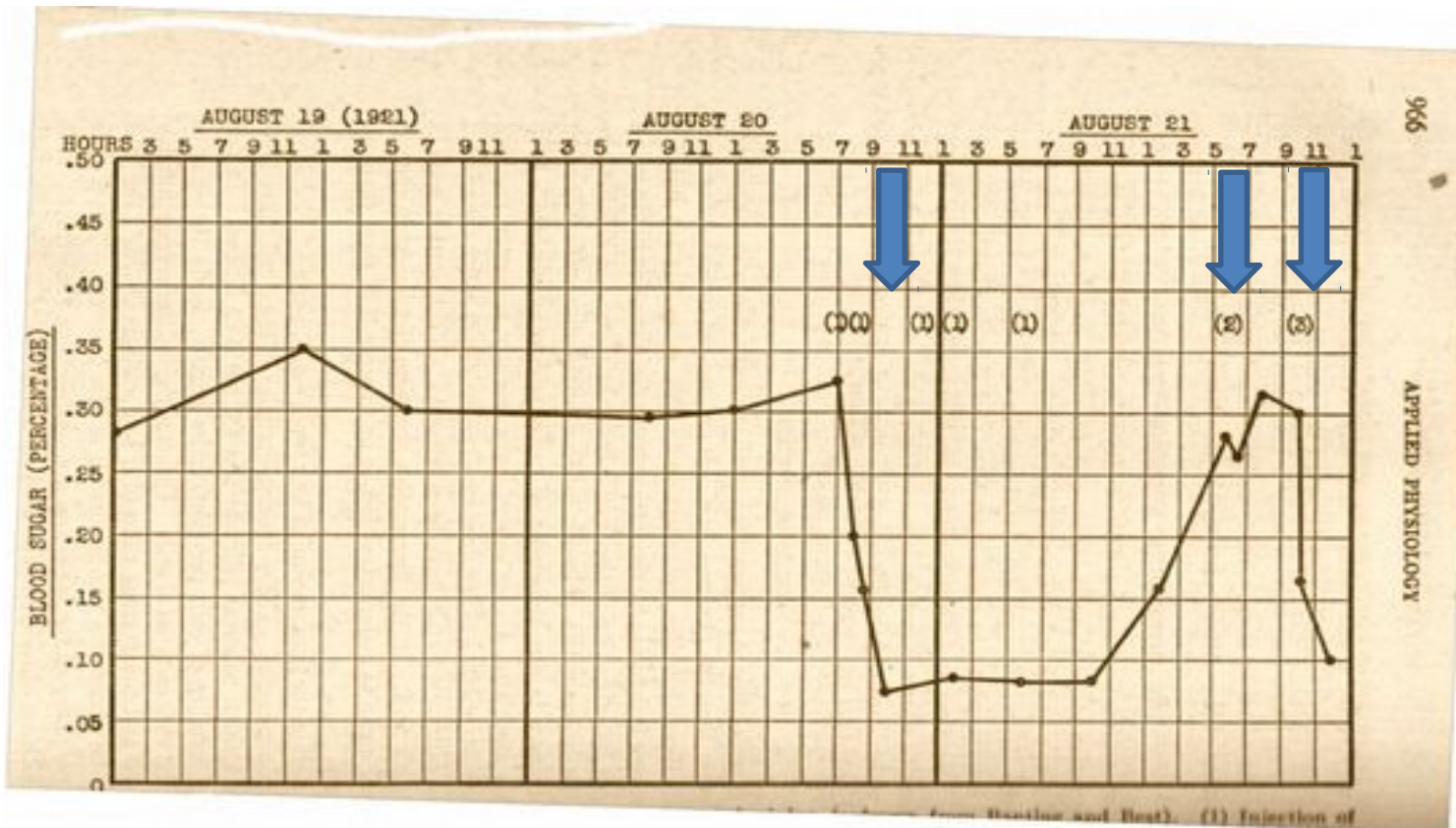
PATHOLOGY (1962) 14, pp 363-368.

DOG PANCREAS DRAWING BEFORE LIGATION OF THE CRANIAL HALF, LEFT. PHOTOGRAPH OF FIBROSED CRANIAL HALF, RIGHT.



IN THIS DOG ONLY THE CRANIAL DUCT WAS LIGATED. BANTING LIGATED BOTH DUCTS AND THUS MARKEDLY REDUCED THE ENZYME PRODUCTION.

PAGE 966 FROM BEST AND TAYLOR PHYSIOLOGY



The chart shows glucose levels on the vertical axis and the dates and years above. The glucose levels are from a diabetic dog after a total pancreatectomy. The first arrow (August 20 1920) indicates the injection of Bantings pancreatic extract and the glucose level fell to below 10. Twelve hours later as the glucose level rises, extract which was INCUBATED with pancreatic juice was injected with no effect, but re-injection with the pure extract lowered the glucose level again.

LIKELY REASONS FOR INCREASE IN KNOWLEDGE IN ANATOMY AND FUNCTION OF PANCREAS

RELAXATION OF REGULATIONS PROHIBITING DISSECTION

ESTABLISHMENT OF SCHOOLS OF LEARNING

TRANSLATIONS OF ORIGINAL GREEK AND OTHER TEXTS

DEVELOPMENT OF THE PRINTING PRESS

RENAISSANCE IN ANATOMY AND EXPLORATION

**ADVANCES IN ALLIED SCIENCES: MICROSCOPY , BIOCHEMISTRY AND
OTHER TECHNOLOGIES)**

CONCLUSION

- **2000 YEARS FROM PANCREAS DISCOVERY TO INSULIN**
- **ALEXANDER THE GREAT, THE PTOLEMIES AND GALEN**
- **RENAISSANCE : PRINTING, LATIN, NEW TECHNOLOGIES**
- **ATTEMPTS TO DRAW PANCREAS: VESALIUS, EUSTACHIUS**
- **EXOCRINE FUNCTION: DE-GRAAF AND CLAUDE BERNARD**
- **ENDOCRINE ROLE: LANGERHANS AND LAGUESSE,**
- **MNKOWSKI, MEHRING, BARROW**
- **THE INSULIN TEAM**

THE VITAL ROLE OF DOGS



PARKER AND SCRUFFY NETWORKING (LT), PARKER AND
PASSING BIGGER DOG AND CARER (RT)
MANY DOGS WERE KILLED/SACRIFICED TO ISOLATE
INSULIN THEY SHOULD BE REMEMBERED.