GAUCHER DISEASE.

DR. HYLTON SEVITZ.

DISCLOSURES.

- Travel grants – Genzyme, Shire & Pfizer.
- Investigator – International Gaucher Registry.

INCIDENCE.

- Ashkenazi Jewish 1:1 200.
- Non-Jewish 1:200 000.

- Wide spectrum of disease.

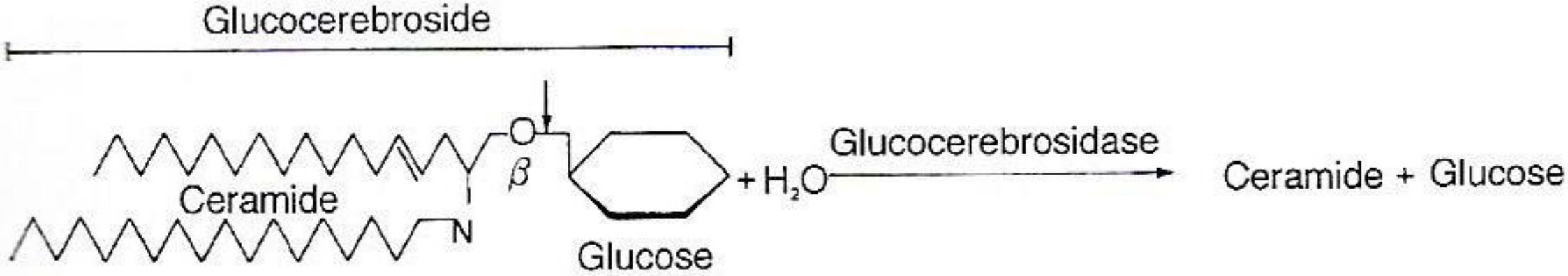

Figure 1. Structure of glucocerebroside that accumulates in Gaucher's disease. the vertical arrow indicates the site of hydrolytic cleavage of glucose catalysed by the enzyme glucocerebrosidase.

- ENDOPLASMIC RETICULUM TO GOLGI APPARATUS TO LYSOSOME.

- AUTOSOMAL RECESSIVE INHERITENCE.
- Chromosome 1.
- Over 200 genotype abnormalities.

ALLELE	JEWISH	NON-JEWISH
N370S	71.8%	43.6%
84GG	11.2%	0.2%
L444P	2.8%	25.6%

- TYPE 1 – Non-neuronopathic. 95% of patients.

- <u>NEURONOPATHIC.</u>
- Type 2
- Type 3 A
- Type 3B
- Type 3C

SYMPTOMS & SIGNS.
TYPE 1.

- Bleeding tendency
- Anaemia
- Hepato-splenomegaly
- Growth retardation
- Lethargy
- Recurrent infections
- BONE DISEASE
- Erlenmeyer flask deformity
- Osteoporosis
- Medullary cavity expansion
- Avascular necrosis-Bone crisis

- LUNG
- Interstitial fibrosis
- Pulmonary artery hypertension

- Parkinson’s disease

TYPE 2.

- Systemic symptoms
- Dysphagia
- Head hyperextension
- Strabismus
- Trismus
- Spasticity
- Myoclonus
- Seizures
- Psychomotor regression
- Laryngospasm & apnoea

TYPE 3A.

- Systemic symptoms
- Myoclonic epilepsy
- Horizontal supranuclear gaze palsy
- Ataxia
- Spasticity
- Dementia

TYPE 3B.

- Systemic symptoms
- Horizontal supranuclear gaze palsy
- Squint
- Retinal infiltrates
- Ataxia
- Spasticity
- Dementia
- Epilepsy

TYPE 3C.

- Calcification in heart & great vessels.

DIAGNOSIS.

- Glucocerebroside assay
- Bone marrow – Gaucher cells
- Genotyping

PSEUDO-GAUCHER CELLS.

- Chronic granulocytic leukaemia
- Myeloma
- Lymphomas
- Hodgkin’s disease
- Thalassaemia
- AIDS
- M. Avium infections

INVESTIGATIONS.

- FBC
- Renal & liver function
- Protein electrophoresis
- Thyroid & parathyroid function
- BIOMARKERS
- Chitotriosidase
- CCL18/PARC
- Lyso-GB1

RADIOLOGY.

- Skeletal survey
- DEXA
- MRI
- Liver & spleen volume
- Pulmonary artery pressure

TREATMENT.

- Not all patients will need treatment.

TREATMENT OPTIONS.

- Enzyme replacement therapy
- Substrate reduction therapy
- Chaperone therapy
- Gene therapy

ENZYME REPLACEMENT THERAPY.

- Aglucerase/Ceredase (Genzyme)
- Imiglucerase/Cerezyme (Genzyme)
- Velaglucerase/V-Priv (Shire)
- Taliglucerase alfa/ Elelyso (Protalix/Pfizer)
- Cerezyme generics

DOSAGE.

- 10-60 UNITS/Kg. EVERY 2 WEEKS BY INFUSION OVER 1 HOUR.
- Titrate against response
- Home infusions

SUBSTRATE REDUCTION THERAPY.

- Miglustat/Zavesca (Actelion)
- Eliglustat/Cerdalga (Genzyme)

- CYP2D6
- Not in children.

Splenectomy.

FOLLOW-UP.

- 3 monthly until stable/therapeutic goals reached, then 6 monthly.

- Clinical assessment
- Biomarkers
- FBC
- Renal & liver functions
- Protein electrophoresis
- Liver & spleen volumes
- Bone