- Bone marrow (useful, not mandatory): May show foam cells (filipin + if tested for this stain)
- If a liver biopsy is performed for cholestatic liver disease, fixation for EM study is essential
- Serum chitotriosidase: useful, not mandatory; generally (not always) elevated activity
- **Isolated (hepato)splenomegaly : enzymatic exclusion of Gaucher and Niemann-Pick B = prerequisite**
- **Provide the laboratory with sufficient clinical data** (essential for correct interpretation of the results)

SKIN BIOPSY

- If local situation permits: fixation and EM study
- **Fibroblast culture** (mandatory)

FILIPIN TEST

(cell biology) (done twice)

Highly positive « classical »
(85% of NP-C patients)

Nearly sure NP-C**

Moderately positive with pure LDL, « variant »
(15% of NP-C patients)

Probable "variant" NP-C***

Kinetics of LDL-induced cholesteryl ester formation

Difficult Interpretation*
(3-5% of NP-C patients)

Re-assess clinical features
Reference Centre Complementary investigations
If likely diagnosis, gene sequencing

NPC1 Gene
Mutation p.P1007A and codon 992****

Clearly negative

a priori, not NP-C

Sequencing of NPC1 and NPC2 genes

- Depending on countries, study first *NPC1* p. I1061T or other most prevalent common mutation
- Conclude quickly on *NPC2* if child < 8-10 months
- *NPC1*: numerous polymorphisms!!! – check allele segregation from parental study
- often need to study both gDNA and cDNA