Diagnostic Evaluation

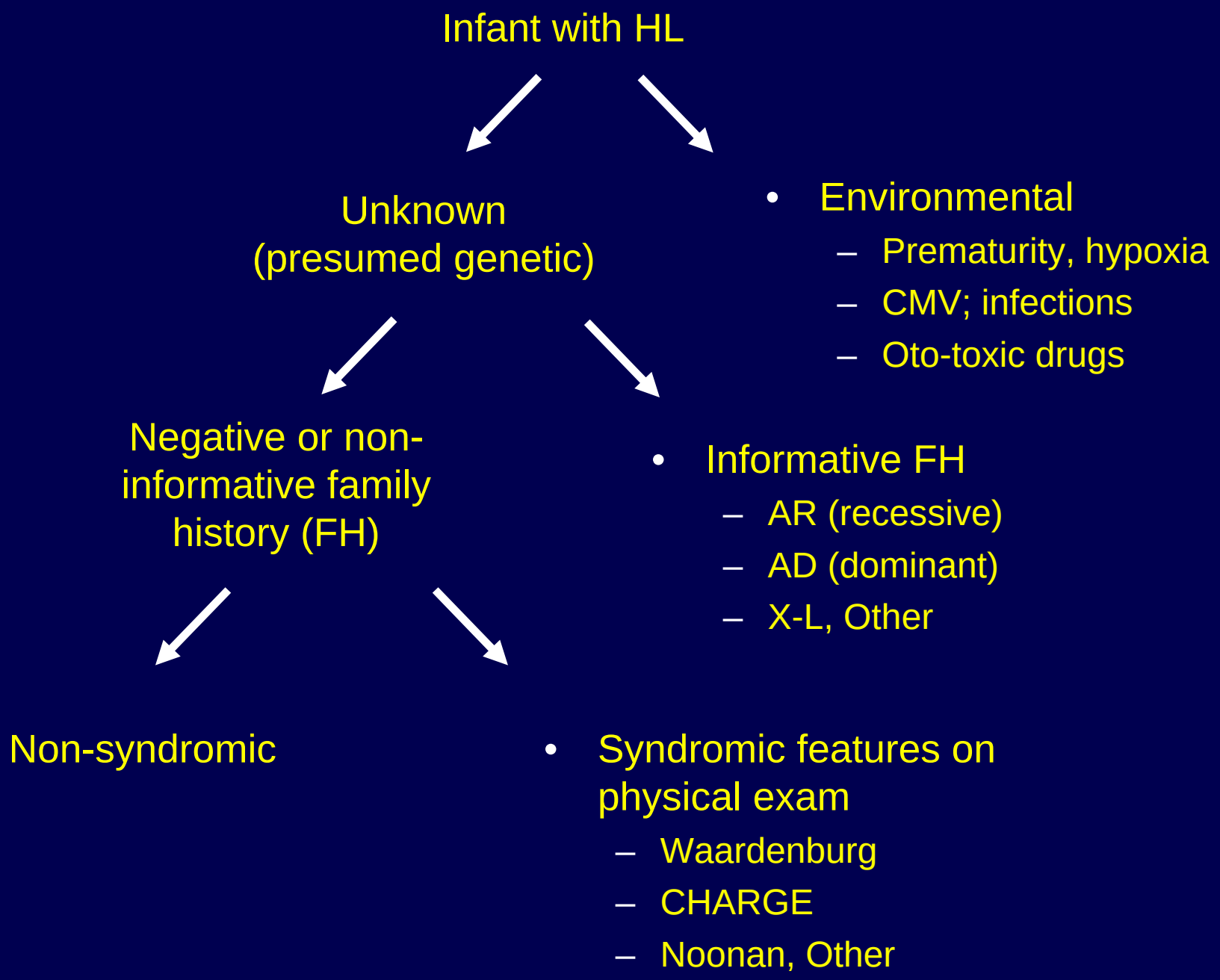
- Variable approach depending on
  - Time of onset
    - Infancy (prelingual), childhood, adult , older adult
  - Physical anomalies
    - External, middle and inner ear
  - Inheritance pattern
  - Audiogram profile
  - Type of HL: neural, conductive, cortical
  - Environmental factors
    - Infection, prematurity, hypoxia

Genetic Testing is Complicated

- Enormous number of genes cause HL
- A given gene can cause different types of HL
- Social and cultural factors important
- Access to testing may be limited

Prelingual Deafness Approach

- Assumptions
  - Diagnostic evaluation, <12 months age
  - Availability of physical examination and clinical testing (e.g., CT/MRI scans)
  - Genetic testing is offered to the family


Infant with HL
Unknown
(presumed genetic)
Negative or non-informative family history (FH)
Non-syndromic
• Environmental
– Prematurity, hypoxia
– CMV; infections
– Oto-toxic drugs
• Informative FH
– AR (recessive)
– AD (dominant)
– X-L, Other
• Syndromic features on physical exam
– Waardenburg
– CHARGE
– Noonan, Other

Non-syndromic HL

- Multiple screen
  - Cx26
  - SLC26A4
  - Cx30 deletion

Cx26 sequencing (50% detection rate In AR HL)

Get more information

- Type of HL
  - Conductive, sensory neural, auditory neuropathy, central (cortical/brainstem)
- CT/MRI temporal bone
- Gait disturbance/vestibular function
- Audiogram profile
- Ethnic background

- Candidate gene
  - Cx26, Cx30
  - SLC26A4
  - Others

- No candidate gene

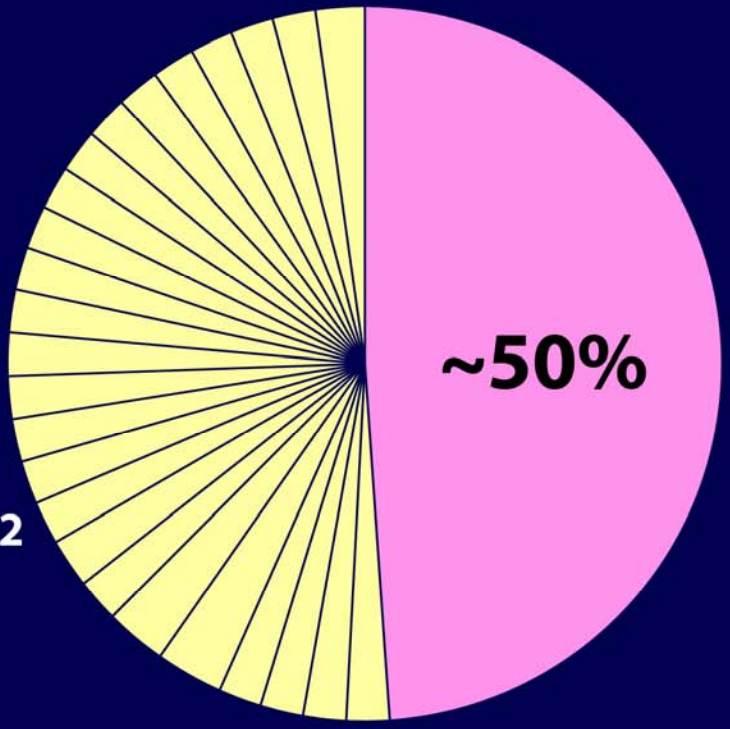
Cx26 (if no anomalies and AR suspected)

DNA screen for multiple genes

AR Genetic HL in infants

SLC26A5
GJB6
MYO7A
MYO15
SLC26A4
TMIE
TMC1
TMPRSS3
OTOF
CDH23
STRC
USH1C
TECTA

OTOA
PCDH15
RDX
TRIOBP
CLDN14
MYO3A
WHRN
ESPN
MYO6
MARVELD2
COL11A2
PJVK
LHFPL5



GJB2 (Cx26)

- Except for Cx26, no other major gene in pre-lingual onset AR deafness
- Multiplex DNA screening platforms needed