APHL New Disorders National Meeting: MPS I - Experience in Illinois

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OVERVIEW

- ILLINOIS NBS PROGRAM
- PREPARATION FOR MPS I
- EXPECTING THE UNEXPECTED
- OUTCOME: 2 YEARS LATER

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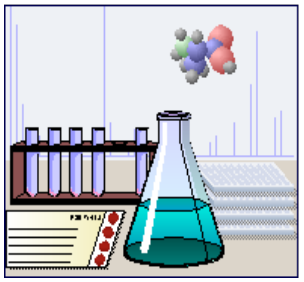
ILLINOIS NBS PROGRAM

Office of Health Protection

Laboratory (Chicago)



- Develop new tests
- Test for disorders ~150,000 births annually

Office of Health Promotion

Follow-up (Springfield)

- Report/Follow-up all abnormal results
- Compile case data
- Interact with specialists

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PREPARATION

- **FOLLOW-UP PROGRAM**
  (ADDED SCREENING FOR 5 LSDS JUNE 2015)
  - ADMINISTRATIVE CODE CHANGES/FEE INCREASE
  - DETERMINE STAFFING NEEDS
  - OBTAIN CLINICAL INPUT (LSD SUBCOMMITTEE)
  - DETERMINE REPORTING AND F/U PROTOCOLS
  - DEFINE DATA ELEMENTS
  - PROVIDE EDUCATION

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PREPARATION

- **ADMINISTRATIVE CODE CHANGES**
  - DEFINE CRITERIA FOR DESIGNATION OF SPECIALISTS
  - INCREASE NBS FEE
- **STAFFING**
  - HIRED TWO FOLLOW-UP STAFF MEMBERS TO SUPPORT ADDITION OF TESTING FOR MULTIPLE LSDS

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PREPARATION

- ## OBTAIN CLINICAL INPUT
  - ### DESIGNATE REFERRAL CENTERS
    - SEVEN HOSPITAL SYSTEMS
    - INCLUDES TWO IN THE ST. LOUIS AREA (MISSOURI)
  - ### MULTIDISCIPLINARY LYSOSOMAL STORAGE SUBCOMMITTEE
    - STAFF FROM ALL CENTERS INCLUDED
    - MET MONTHLY/CONTINUE TO MEET
    - PROVIDED INPUT ON WHAT DIAGNOSTIC AND LONG TERM FOLLOW-UP DATA TO COLLECT
    - ESTABLISHED STANDARDIZED CLINICAL DIAGNOSTIC PROTOCOLS

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PREPARATION

- ## REPORTING/FOLLOW-UP PROTOCOLS
  - ### UTILIZE SAME PROTOCOL USED FOR OTHER NBS DISORDERS
    - REPORT RESULTS TO PCP BY PHONE/FAX/MAIL
    - FOLLOW-UP WITH PCP IN 1-2 DAYS TO ASSURE REFERRAL
    - ONCE REFERRED, FOLLOW WITH SPECIALIST TO OBTAIN DX RESULTS (2 WEEK INTERVALS)

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PREPARATION

- DATA ELEMENTS
  - MAKE CHANGES TO PERKIN ELMER DATABASE
  - DEVELOP CONSENT FORM (ALLOW SPECIALISTS TO DISCUSS CASES/SHARE BLOOD SPOT)
  - DETERMINE DIAGNOSTIC INFORMATION TO COLLECT
    - ENZYME LEVELS
    - URINE GAGS
    - MOLECULAR RESULTS
  - DETERMINE ANNUAL LTFU DATA ELEMENTS TO COLLECT

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PREPARATION

- EDUCATION
  - DEVELOP PHYSICIAN FACT SHEET
  - NOTIFY BIRTH HOSPITALS
  - COLLABORATE WITH AAP (STATE CHAPTER) AND IAFP
  - ISSUE PRESS RELEASES

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EXPECTING THE UNEXPECTED

- **INSURANCE ISSUES**
  - TIME INVOLVED IN MOLECULAR TESTING APPROVAL
  - COVERAGE DENIED IN SOME CASES
- **CASE CATEGORIZATION CONUNDRUM!**
  - PSEUDODEFICIENCIES/VARIANTS OF UNKNOWN SIGNIFICANCE
  - DETERMINE RESPONSIBILITY OF STATE NBS PROGRAM RE: TRACKING VUS CASES-LONG TERM

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EXPECTING THE UNEXPECTED

MPS I CASE DETERMINATION

ASSESSMENT	Severe	Attenuated	Pseudo	Undeter-mined	Carriers
Enzyme	Deficient	Deficient	Deficient	Deficient	Deficient
Urine GAGS	Elevated	Elevated	Normal	Normal	Normal
	And 2 pathogenic variants predicting severe phenotype	And 1 or 2 pathogenic variants predictive of attenuated disease	And 1 or more Pseudodeficiency alleles (A79T, H82Q, D223N, and V322E)	And 1 pathogenic variant and one VUS (in trans)	And 1 pathogenic variant
Genetics	Or 1 or 2 VUS with clinical findings consistent with severe phenotype			Or 2 VUS (in trans)	
	Or 1 pathogenic variant with clinical findings consistent with severe disease				

OUTCOME: 2 YEARS LATER

- SCREENED ~320,000 BIRTHS
- ONE MPS I CASE DIAGNOSED
- NBS PROGRAM WILL TRACK VUS CASES ANNUALLY

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OUTCOME: 2 YEARS LATER

- MPS I
  - BORDERLINE SCREENING RESULTS (44%)
    - IDUA>14% AND ≤ 18%
    - 88% CLOSED AS NORMAL WITH SUBSEQUENT NBS
    - 10% CLASSIFIED AS CARRIER OR PSEUDODEFICIENCY
    - 2% VUS
  - POSITIVE SCREENING RESULTS (56%)
    - IDUA ≤ 14%
    - 56% CLOSED AS NORMAL (20% THROUGH DX ENZYME TESTING ALONE)
    - 38% CLASSIFIED AS CARRIER OR PSEUDODEFICIENCY
    - 6% VUS
    - <<1% MPS I

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OUTCOME: 2 YEARS LATER

- MANY PSEUDODEFICIENCIES
  - ABNORMAL SCREENING RESULTS WERE COMMONLY DUE TO PSEUDODEFICIENCIES
  - OF ALL IDUA VARIANTS, A79T – MOST COMMONLY IDENTIFIED (AA VARIANT)

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THANK YOU

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