CHALLENGES TO TREATMENT OF INHERITED METABOLIC DISORDES: THE SAUDI EXPEREINCE

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KING FAISAL SPECIALIST HOSPITAL & RESEARCH CENTRE
GENERAL ORGANIZATION

مستشفى الملك فيصل التخصصي و مركز الأبحاث
مؤسسة عامة

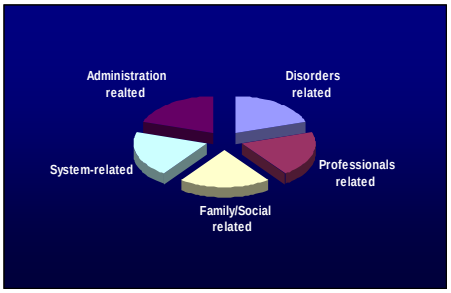
Saudi Population & Genetic Diseases

Saudi Population & Genetic Diseases

- High consanguinity rate
- Large family size
- Tribal structure
- Presence of isolates & semi-isolates

Treatment Challenges

Treatment Challenges



Professionals-Related Challenges

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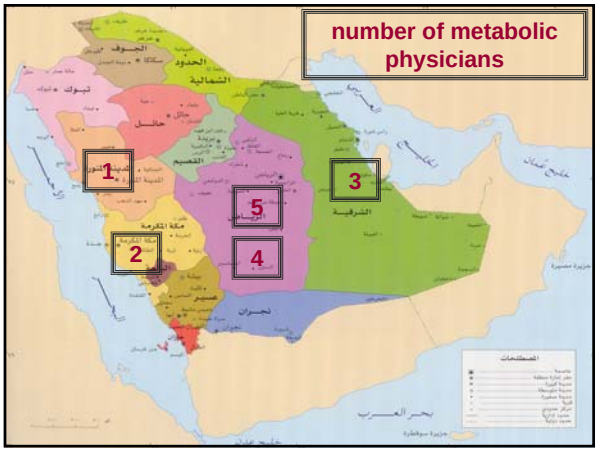
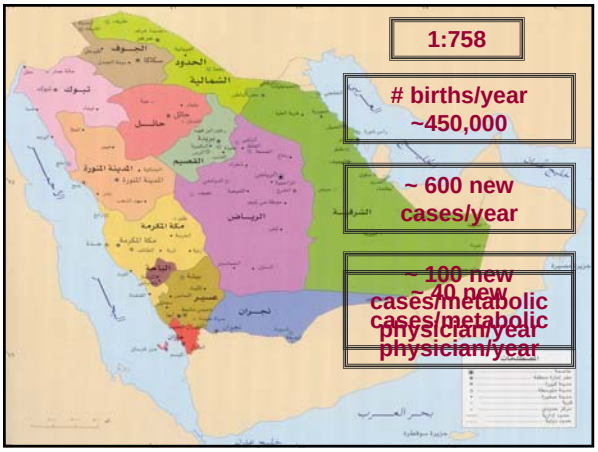
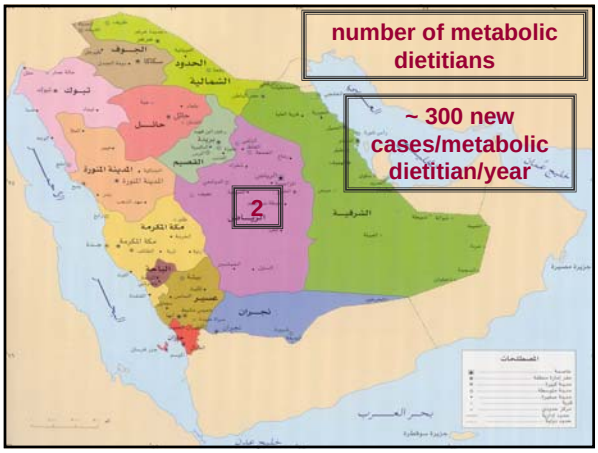
- Shortage of :
  - Metabolic physicians
  - Metabolic nutritionists
  - Counselors







Professionals-Related Challenges

- Inadequate assessment of neuropsychological outcome
- Inadequate professional education/awareness:
  - Delay in instituting treatment
- Generalization of the false impression of poor outcome in IMD:
  - Delay of prompt and properly aggressive ICU interventions

Laboratory-Related Challenges

Laboratory-Related Challenges

- Shortage/Unavailability of biochemical diagnostic facilities
- Confirmatory tests are not available
  - Enzyme assay
  - Metabolites (pterins)
  - Complementation studies (MMA)
  - Mutation detection

Laboratory-Related Challenges

- MS/MS related:
  - Fractionation of plasma isoleucine and leucine levels
- Delay of lab results:
  - Biochemical assessments for follow up cases

Disorders-Related Challenges

The National Neonatal Screening Program

- Organic Acidurias
  - Methylmalonic acidemia
  - Propionic acidemia
  - Isovaleric acidemia
  - Glutaric acidemia I
  - HMG CoA lyase def.
  - Beta-ketothiolase deficiency
  - 3MCC
  - Biotinidase deficiency
- Aminoaciopathies
  - PKU
  - MSUD
- FAOD
  - MCAD
- UCD
  - Citrullinemia
  - Argininosuccinic aciduria
- CHO disorders
  - Galactosemia
- Endocrine disorders
  - Congenital hypothyroidism
  - Congenital adrenal hyperplasia

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Organic Acidurias - Diagnostic Issues

- Confirmatory tests are not available
  - Enzyme assay
  - Complementation studies (MMA)
  - Mutation detection
- B_{12} responsiveness assays (MMA)
  - *in-vivo* and *in-vitro*

Organic Acidurias - Treatment Issues

- Nutrition:
  - Formula/synthetic food:
    - Cost
    - Availability
  - Evaluation of nutritional status:
    - Shortage of specialized/dedicated metabolic nutritionists
    - Inadequate frequency of follow ups
    - Inadequate family/nutritionist communication
    - Inadequate nutritional laboratory assessments

Organic Acidurias - Treatment Issues

- Carnitine / Biotin / Glycine:
  - Availability
  - Physicians knowledge (ER physicians, Pediatricians)
- Bicarbonate:
  - improper correction of severe metabolic acidosis :
    - cerebral edema
    - prolongation of imbalanced acid-base status

Organic Acidurias- Complications

- Acute complications:
  - Dialysis:
    - Lack of experts/experience on using hemodialysis
    - Delay of instituting dialysis in cases of severe unresponsive metablic acidosis:

      Call for guidelines

Organic Acidurias - Complications

- Chronic:
  - Neuropsychological outcome:
    - Shortage of pediatric psychiatrists and psychologists to assess neuropsychological outcome
    - Inadequate neurological evaluations for CNS deficits
    - Lack of psychosocial support and interventions
  - Renal complications:
    - Lack of interest/experience of adult nephrologists to follow organic acidurais cases.
    - The burden of kidney transplantation:
      - The Priority

Organic Acidurias - Complications

- Chronic:
  - Recurrent Pancreatitis
    - Prolonged hospital stay – recurrent
    - Hospital-acquired infections
    - The need for TPN – availability / cost
    - Social impact

The National Neonatal Screening Program

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MSUD

MSUD - Diagnostic Issues

- Mutation detection assays are not available:
  - Prevention
- MS/MS related:
  - Unknown plasma isoleucine level:
    - Over treatment
    - Improper a.a. supplementation
    - Skin changes
    - Poor growth
    - Unnecessary interventions:
      - High dextrose/Insulin infusion
      - ICU care
      - Dialysis
      - Delay of hospital discharge

MSUD - Treatment Issues

Nutrition

- Formula/synthetic food:
  - Cost
  - Availability
- Shortage/lack of amino acids (Val, Ile) supplements
- Evaluation of nutritional status:
  - Improper use of MS/MS for follow ups instead of plasma amino acids analysis
  - Shortage of specialized/dedicated metabolic nutritionists
  - Inadequate frequency of follow ups
  - Inadequate nutritional laboratory assessments
  - Inadequate family/nutritionist communication

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MSUD - Complications

- Acute complications:
  - Dialysis:
    - Lack of experts/experience on using hemodialysis
    - Delay of instituting dialysis in cases of severe leucine encephalopathy
    - Delay of the results of plasma amino acids:
      - On presentation
      - For monitoring
    - Clinical judgment – based intervention : not always accurate
    - Call for guidelines

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  - Dialysis:
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    - Delay of the results of plasma amino acids:
      - On presentation
      - For monitoring
    - Clinical judgment – based intervention : not always accurate
    - Call for guidelines

PKU

PKU - Diagnostic Issues

- Enzyme / Pterine measurements / Mutation detection assays are not available:
  - Confirmation of the hyperphenylalaninemia variant
  - Prevention

PKU - Diagnostic Issues

- No uniformity of protocols to detect biopterin metabolism defects
- Shortage / unavailability of biopterin to assess:
  - Biopterin metabolism defects
  - Biopterin-responsive PKU

PKU - Treatment Issues

Nutrition

- Formula/synthetic food:
  - Cost
  - Availability
- Underutilization of plasma amino acids analysis
- Evaluation of nutritional status

PKU - Treatment Issues

- Sinemet / BH4 / 5HT:
  - Availability
  - Cost

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UCD - Diagnostic Issues

- Enzyme and mutation detection assays are not available:
  - Confirmation
  - Prevention
- Spurious serum ammonia result – Unnecessary/Delay of interventions:
  - ICU care
  - Dialysis
  - Delay of hospital discharge

UCD - Treatment Issues

Nutrition

- Formula/synthetic food:
  - Cost
  - Availability
- Evaluation of nutritional status:
  - Underutilization of plasma amino acids analysis for follow ups
  - Shortage of specialized/dedicated metabolic nutritionists
  - Inadequate frequency of follow ups
  - Inadequate nutritional laboratory assessments
  - Inadequate family/nutritionist communication

UCD - Treatment Issues

Nutrition

- Formula/synthetic food:
  - Cost
  - Availability
- Evaluation of nutritional status:
  - Underutilization of plasma amino acids analysis for follow ups
  - Shortage of specialized/dedicated metabolic nutritionists
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UCD - Treatment Issues

- Arginine:
  - Availability
- Unavailable sodium phenylbutyrate (I.V.)

UCD - Treatment Issues

- Acute decompensation:
  - Dialysis:
    - Lack of experts/experience on using hemodialysis
    - Delay of instituting dialysis in cases of severe hyperammonemia

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MCAD - Treatment

- Management of acute decompensation:
  - Physicians awareness of:
    - S/S of acute presentation
    - The importance of prompt intervention

Galactosemia

Galactosemia - Diagnostic Issues

- Detection of partial GALT deficiency
- Unavailable assays:
  - Mutation detection
  - Epimerase

Family/Social - Related Challenges

Family/Social - Related Challenges

- Inadequate parents/family education
  - Compliance issues
- Implication of a “Genetic” disease on the family/tribe
- Inadequacy of counseling services
- No support groups

Family/Social - Related Challenges

- Inadequate services for other preventive measures:
  - Prenatal diagnosis
  - Preimplantation genetic diagnosis

System-Related Challenges

System-Related Challenges

- Maintaining the chain is a major undertaking:
  - Time of sampling/early discharge
  - Tracking of positive cases
  - Follow up of detected cases
- Efficiency of communication faces hurdles
- The wide geographic area poses a great challenge to every single element of the Program

System-Related Challenges

- Inadequate evaluation of nutritional status:
  - Shortage of specialized/dedicated metabolic nutritionists
  - Unavailability of dietary products (semisynthetic diet, mixtures of a.a., modified protein hydrolysates)
  - Inadequate frequency of follow ups
  - Inadequate family/nutritionist communication
  - Inadequate nutritional laboratory assessments

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System-Related Challenges

- Inadequate assessment of neuropsychological outcome:
  - Shortage of pediatric psychiatrists and psychologists to assess neuropsychological outcome
  - Inadequate neurological evaluations for CNS deficits
  - Lack of psychosocial support and interventions
- No plan for multidisciplinary approach

System-Related Challenges

- Lack of:
  - Treatment guidelines
  - Consistency of management interventions
  - Consensus on outcome measures

System-Related Challenges

- The infrastructure of the health care system and integrating the Screening Program

System-Related Challenges

- Facility for diagnosis and treatment:
  - A single comprehensive center (KFSH&RC) serving the whole country
  - The goal of a comprehensive and efficient system may not be achievable
  - The need for more specialized centers

Administration-Related Challenges

Administration-Related Challenges

<u>Vision of the Program administration</u>

- The comprehensiveness of the Program
  - Integration of follow-ups into the Program
- Pace of the Program expansion:
  - New disorders
  - New centers
  - New labs
- ? who evaluates/plans

Administration-Related Challenges

- Funding issues:
  - Screening (new technologies
  - Diagnosis
  - Management (formulas / medications)
  - Follow up and evaluation
  - Education
- Poor involvement of the public/media
- Bureaucracy – *not unexpected!*

Despite these challenges !

Despite these challenges:

A great opportunity still remains to overcome these issues

- The Program is still in its first stages.
- The high ambition, perseverance, and determination.
- Having the political support and decision has always been attainable.

THANK YOU