Endocrinology Emergencies in the Newborn

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Ambulatory Endocrine Care Manager

Objectives

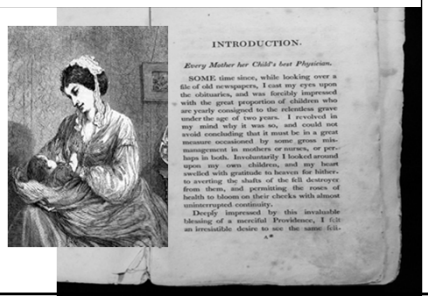
1. List the pathophysiology of an inheritance pattern of inborn errors of metabolism
2. Describe clinical presentation and symptoms of inborn errors of metabolism
3. Explain studies used to diagnose inborn errors of metabolism and the role of the nurse
4. Identify neonatal emergencies of the thyroid gland disorder, hypothyroidism, Grave's disease and understand the diagnostic tests and role of the nurse
5. Discuss the neonatal adrenal disorders and treatment
6. Discuss panhypopituitarism and hypoglycemia in the newborn

Conflict of Interest Disclosure

No conflict of interest related to the content of the presentation

Care of the Newborn

In 1811, care of the newborn was managed by nurses and midwives in the home



INTRODUCTION.

Every Mother her Child's best Physician.

SOME time since, while looking over a file of old newspapers, I cast my eyes upon the obituaries, and was forcibly impressed with the great proportion of children who are yearly consigned to the relentless grave under the age of two years. I revolved in my mind why it was so, and could not avoid concluding that it must be in a great measure occasioned by some gross mismanagement in mothers or nurses, or perhaps in both. Involuntarily I looked around upon my own children, and my heart swelled with gratitude to heaven for hitherto averting the shafts of the fell destroyer from them, and permitting the roses of health to bloom on their cheeks with almost uninterrupted continuity.

Deeply impressed by this invaluable blessing of a merciful Providence, I felt an irresistible desire to see the same feli-

A*

Care of the Newborn

1930's and 1940's

1960's

Care of the Newborn

2015

Nurse assessment skills remain critical

The nurse assessment and "concern" about a patient often influence the timeliness of diagnosis and interventions

Neonatal Metabolic and Endocrine Emergencies

- Uncommon and a challenge with diagnosis
- Significant overlap with other neonatal emergencies
- Challenge to implement screening programs & improve current tests

Neonatal Metabolic and Endocrine Emergencies

- Metabolic
  - Inborn Errors of Metabolism
- Endocrine
  - Neonatal Thyroid Disorders
  - Adrenal Disorder
  - Hypopituitarism

Neonatal Metabolic Emergencies Inborn Errors of Metabolism (IEM)

- Pathophysiology
  Gene mutation, deficiencies in enzymes and cofactors lead to a blocked metabolic pathway

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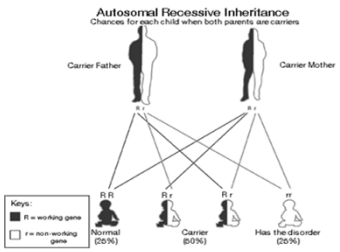
Inborn Errors of Metabolism (IEM)

- Pathophysiology
  Gene mutation, deficiencies in enzymes and cofactors lead to a blocked metabolic pathway
- Fetal effect
  Usually absent at birth due to placental protection
- Inheritance Pattern
  Generally autosomal recessive
  Some are X linked

Autosomal Recessive
X-Linked



MSUD Support

Clinical Presentation

- Usually appear normal at birth
- Within hours, days, sometimes weeks or months develop non-specific symptoms

Clinical Presentation of IEM

Signs and symptoms may mimic sepsis

Neuro-lethargy, irritability, seizures, coma	Respiratory-increased or decreased effort	Ketonuria
Jaundice	Cardiomyopathy, arrhythmias	Unusual color or odors

Ketonuria with IEM

- Ketonuria is uncommon in newborn infants.
- Anyone caring for newborn with severe illness and ketonuria must consider inborn error of metabolism

Photo: Wikipedia

May Point to Possible IEM

- Acute onset and rapid progression of symptoms after an interval of normal health
- Unusual severity of symptoms
- Symptoms may correspond with feeding
- In general, the accumulation of toxic intermediates takes place between day 2 and 5 of life
- History of unexplained neonatal or infant death in family

Diagnosis

- Prenatal
- Newborn Screening
- Neonatal Diagnosis
- Post Mortem

General Management of IEM

- Supportive care: respiratory support, IV fluids, antibiotics
- Nutrition: dietary restrictions
- Removal of toxic substances: dialysis
- Administration of cofactors (vitamin)
- Liver transplant

Role of the Nurse

- Acute assessment and comprehensive history
- Metabolic work-up: ABG, CBC, lytes, glucose, urinalysis, ammonia*
- Baby's advocate
- Parent / caregiver advocate
- Consult and coordinate care

Role of the Nurse

- Assisting the family with a crisis situation
- Assess the coping resources of parents and family
- Understand that grieving can occur as response to a hoped for "perfect" infant
- Anticipatory guidance

Nursing Care-Ambulatory

Keep a close eye on labs and follow-up care after discharge!

Specific Disorders of IEM

1. Amino Acid Disorders
2. Organic Acid Metabolism / Methylmalonic Acidemia
3. CHO Metabolism Disorder: Galactosemia
4. Urea Cycle / Hyperammonemia Disorder
5. Fatty Acid Oxydation Disorder: MCADD

Amino Acid Disorder Phenylketonuria (PKU)

Pathophysiology	Presentation	Inheritance Pattern
• Deficiency of enzyme, phenylalanine hydroxylase, needed for conversion of phenylalanine to tyrosine • Phenylalanine is part of all complete proteins	• Abnormal newborn screen • Vomiting • Difficulty feeding • Infantile spasms • Mousy smell • Hypopigmentation • Eczema	• Inherited autosomal recessive trait • Incidence 1:12,000 newborns

PKU Treatment

- Restriction of phenylalanine
  - Special low protein infant formula
- Diet is lifelong and awful
- DNA sequencing mutational analysis may be used to determine carriers in families
- Developmental delay if untreated
- Most people with PKU can live as long and healthy as anyone else if the diet is started as infants and continued throughout their life

Recipe for low Phe Pancakes

- 1/3 c wheat starch
- 1/4 c corn starch
- 1/3 c welplan baking mix
- 1/2 t methylcellulose
- 1/2 t cinnamon
- 1 t Ener-G egg replacer
- 1 t metamucil or other fiber product
- 1/2 t baking powder
- 1/2 c mocha mix
- 1/4 c apple sauce
- 1/2 c water

Photo Retrieved from You Tube

Case study

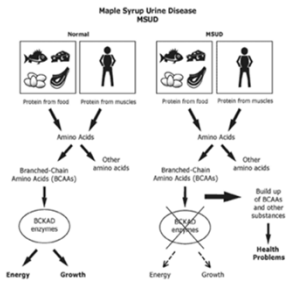
- Birth History: 8lb, 1 oz product of full-term, uncomplicated gestation. Apgar scores 8 and 8. No problems during newborn period
- History: Hospitalized with bronchiolitis at 5 months of age. No neurological abnormalities noted on physical exam. Parents note he walked at 1 ½ years of age
  At 4 years, he was referred for neurological eval because of lack of speech. He was not toilet trained, was unable to feed or dress himself, related poorly to others and occasionally engaged in rocking and head banging. He had eczema on the palms of his hands. An EEG showed seizure activity and he was started on phenytoin. At 6 years, he had progressive encephalopathy, severe mental retardation and seizure disorder.
- Lab: Plasma phenylalanine level was 23 mg / dL (0.40-1.6)
  Urinary ferric chloride test was positive for phenylketonuric derivatives, despite the lack of musty urine odor

The original newborn filter paper screen for PKU had been omitted

Amino Acid Disorder
Maple Syrup Disease (MSUD)

Pathophysiology	Presentation	Inheritance Pattern
• Missing enzyme-Branched Chain Ketoacid Dehydrogenase (BCKAD)- needed to change 3 branch amino acid: leucine, isoleucine and valine. Without enzyme-changed to toxic ketoacids	• Abnormal newborn screen • Vomiting-poor appetite • Metabolic acidosis-rapid respirations • Hypertonia • The urine smells like maple syrup	• Inherited rare autosomal recessive trait • Incidence: Less than 1:200,000 births • Mennonites have a higher incidence 1:380

MSUD



MSUD Treatment

- Peritoneal dialysis to reduce the amino acid level acutely
- Low protein infant formula
- Avoid cow's milk, regular formula, meat, fish, cheese and eggs Regular flour, dried beans, nuts and peanut butter may have branch chained amino acids and must be avoided or strictly limited
- Lifelong treatment with MSUD diet is necessary
- Children are at risk for metabolic crisis when they don't follow the diet
- Regular lab tests to measure amino acid levels
- Liver transplant
- Genetic testing

Role of the Nurse MSUD

Coordinate care Dietary Genetics Developmental Intervention	Call the doctor Poor appetite Behavioral changes Vomiting Infection or illness
Educate	Emotional support MSUD family support http://www.msud-support.org/

Nursing Care MSUD - Ambulatory

Keep a close eye on labs and follow up care after discharge

Example:
Branch chain amino acids (BCAA) due on Friday, June 8

Organic Acid Disorder Methylmalonic Acidemia (MMA)

Pathophysiology	Presentation	Inheritance Pattern
• Missing enzyme needed to break down certain fats and amino acids	• Newborn screen • Ketonuria • Vomiting • Poor appetite • Extreme sleepiness • Hypotonia • Hypoglycemia • Seizure	• Inherited rare autosomal recessive trait • Incidence 1:67,000

Methylmalonic Acidemia Treatment

- Special formula as infant
- Avoid meat, eggs and dairy products
  -Smaller amounts of the amino acids are found in flour, cereal, some vegetables and fruits
- Urine and blood testing
- Without treatment, brain and nerve damage can occur. Acutely, this can cause coma and death
- Even with treatment, some children continue to have problems with health and development

Nursing Care MMA

Coordinate Care	Call the doctor
Dietary Genetics Developmental intervention	Poor appetite Behavioral changes Vomiting Infection or illness
Educate	Emotional support Children Living with Inherited Metabolic Disorders (CLIMB) http://www.climb.org.uk

Nursing Care MMA-Ambulatory

Carbohydrate (CHO) Disorders Galactosemia

Pathophysiology	Presentation	Inheritance Pattern
• Missing enzymes that cause the rapid hepatic conversion of galactose to glucose following the ingestion of lactose • Enzymes GALK, GALT, Galactose 4, UDP • Usually it is a GALT deficiency	• Abnormal newborn screen • Feeding intolerance • Lethargy • Jaundice, large liver • Profound hypoglycemia after lactose ingestion • Cataracts • E Coli sepsis	• Galactosemia is inherited in an autosomal recessive pattern. • Incidence is 1:30,000 to 60,000 babies in US • It is more common in people from Ireland 1:24,000 are born with this disease

Galactosemia Treatment

Lactose free diet: soy formula as infant and no lactose for life

MSG, soy sauce	Butter	milk, cream, cheese, milk chocolate
Pizza		Ice cream
Dough conditioners, hydrolyzed protein	Lactose (many medications are cut with lactose)	Dry milk protein, whey, casein, yogurt

Nursing Care Galactosemia

Coordinate Care

Dietary
Genetics
Developmental intervention

Call the doctor with

Poor Appetite
Behavioral change
Vomiting
Infection or illness

Educate

Emotional Support

Galactosemia Foundation
http:glactosemia.org

Nursing Care Galactosemia Ambulatory

Follow up labs
Make sure pt has follow-up appointment

Urea Cycle Defects Hyperammonemia

Pathophysiology	Presentation	Inheritance Pattern
• Missing enzymes to convert ammonia and other organic acids to urea	• Abnormal newborn screen • Refusal to eat • Vomiting • Drowsiness • Seizure • Rapid breathing	• Inherited autosomal recessive trait • OTC (Ornithine transcarbamolylase deficiency) is inherited as X linked disease • Incidence: 1: 70,000 births

Urea Cycle Disorder Treatment

- Dietary restriction of protein
- Pharm treatment with sodium benzoate and phenylacetate
  - Reduce ammonia level
  - Arginine or Citrulline
- Dialysis for high ammonia levels
- Liver transplant

Nursing Care Urea Cycle Disorder

Coordinate Care
Dietary
Genetics
Developmental intervention

Call the doctor with
Poor appetite
Behavioral change
Vomiting
Infection or illness

Educate

Emotional support
National Urea Cycle Disorders Foundation
www.nucdf.org

Nursing Care Urea Cycle Disorder

Case Study

Birth History:	33 year old mother, G3, P2; insulin dependent due to gestational DM good BS control, GBS negative. Birth weight 8 lbs.
Family History:	Positive for maternal uncle died on the 3rd day of life from unknown cause
	Siblings; 2 healthy sisters, ages 2 and 4 years
Assessment:	2 day old newborn; rooming with mom
	Unable to nurse, sleepy and unresponsive with blood draw
	Mild jaundice
	Resp reg / rapid 80. Temp 97 Ax. HR 122, Non-reactive to stimuli; Decreased tone; no suck
Labs:	Normal Total Bilirubin, CBC, differential and blood culture
Treatment:	Transfer to NICU-IV D10W; amp and gent given

Within 24 hours he began having seizures

Case Study

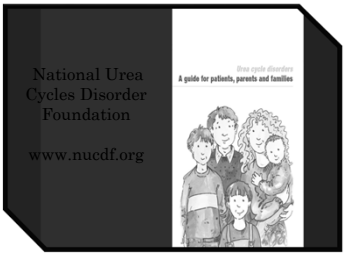
Differential:	Sepsis or IEM
Diagnostic Studies:	Ammonia level 1901 mcmol / L (less than 50)
	Glutamine 1632 mcmol / L (376-709)
	Citrulline Trace (10-45)
	Urine orotic acid 852 mmol / mol creatinine (0.12-3.07)
Diagnosis:	Orthine Transcarbinase Deficiency (OTC deficiency)
Treatment:	Remove Protein; Administer Sodium Benzoate, Phenylacetate and Arginine; Hemodialysis
Outcome:	Ammonia 70 mcmol / L after 36 hours
	Neurological status improved
First Year of Life:	2 metabolic crisis required hospitalization before Liver transplant

Nursing Care of Urea Cycle Disorder Advocate

I wanted to write just to thank you so much for everything, every word, every effort, every email…you made this period of my life easier…I don't have enough words to thank you.

C.C., Mexico

We were so scared and lost before we contacted NUCDF. They personally spent hours on the phone with us answering our questions. My husband and I learned more from about UCD in our first conversation than we learned from our doctors in eight months. Thank you for always being there for us and giving us the knowledge we need to help our daughter live every day with UCD.

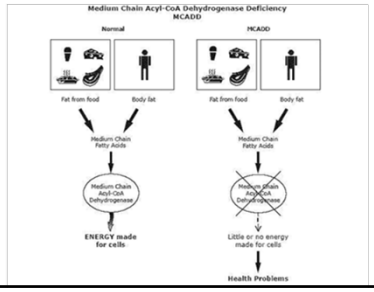


GuS

Fatty Acid Metabolism Medium Chain Acyl-CoA Dehydrongenase Deficiency (MCADD)

Pathophysiology	Presentation	Inheritance
• MCADD enzyme missing • Cannot use certain fat for energy-uses glucose	• Abnormal newborn screen • Extreme sleepiness • Irritability • Vomiting • Diarrhea • Hypoglycemia	• Inherited autosomal recessive trait • Incidence is 1:15,000 babies born in US • 1 in every 70 Caucasians is a carrier

Fatty Acid Metabolism: MCAAD



Treatment of Fatty Acid Metabolism: MCADD

- Treat and prevent hypoglycemia; avoid fasting; frequent small feeds; IV glucose during treatment
- Restricted LOW fat, high protein, high CHO
- L-Carnitine
- High mortality with the initial episode. In retrospect, some SIDS cases are probably a result of non-ketotic hypoglycemic seizure
- Genetic counseling
- Emotional support

Nursing Care MCAAD

Coordinate Care

Dietary
Genetics
Developmental Intervention

Call the doctor with

Poor Appetite
Behavioral Change
Vomiting
Infection or illness

Educate

Avoid going long periods without food

Emotional Support

Fatty Oxidation Disorders (FOD) Family Support
http://www.fodsupport.org

Nursing Care MCAAD

Genevieve Carbery, Irish Times

Neonatal Screening

Newborn Screening History

Mid 1950's
- PKU was the first metabolic disorder known to benefit from early dietary therapy
- Detecting PKU in all affected infants before irreversible brain damage occurred became the challenge

1962
- Guthrie developed a simple bacterial assay for phenylalanine that required only a small amount of blood soaked into filter paper
- Infants in newborn nurseries were routinely checked for PKU

2003
- As late as 2003-all but 4 states tested for only six disorders
- By April 2011, all states were testing for at least 26 disorders

Federal Newborn Screening Today

2014
- On December 18, 2014, President Obama signed the Newborn Screening Saves Lives Reauthorization Act of 2014
- The Act includes new timeliness and tracking measures to ensure newborn babies with deadly, yet treatable disorders, are diagnosed quickly
- The Act mandates a consent by parents for blood spots used in federally funded research
- Most states test for 31 disorders

Federal Newborn Screening Today

2015

- Expand newborn screening into Next Generation Sequencing (NGS)
- The National Institute of Child Health and Development is currently funding four 5-year research projects to examine the application of NGS to newborn screening.
  - Examine technical feasibility
  - Test the medical effectiveness of sequencing in neonatal setting
  - Address the ethical, legal and social implications

State Neonatal Screening Programs

- Federally mandated but state run
  While there are recommendations, each state may choose what tests will be included
- Know your state law
  Who is responsible for follow up of abnormal results
  Timing of testing, how it is to be drawn
- False positives and false negatives

Neonatal Endocrine Emergencies

Thyroid disease
Hypothyroidism
Thyrotoxicosis

Hypopituitarism

Adrenal disorders
Congenital Adrenal Hyperplasia
Adrenal insufficiency

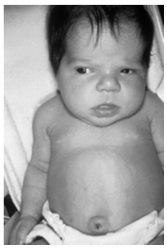
Hypoglycemia

Neonatal Thyroid Disease

Hypothyroidism	Thyrotoxicosis
Permanent or Transient Primary or Central Congenital or Acquired	Neonatal Grave's Disease

Question 1

- A 12-week old female was born at home and has received no medical care. She has a coarse face, with puffy eyelids, thickened protruding tongue, and thick hair. Her cranial sutures are easily palpable, and posterior and anterior fontanels are open. Her abdomen is protuberant and an umbilical hernia is present. Her skin is cool to touch and mottled. No masses are palpable in the neck.



Nicholson,Y MD (Date unknown)

Question 1

Of the following, the MOST likely long-term sequelae of this infant's condition is

A. Cerebral palsy
B. Corneal Opacities
C. Deafness
D. Hydrocephalous
E. Developmental Delay

Neonatal Hypothyroidism

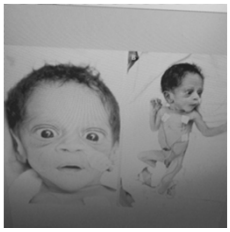
Pathophysiology	Presentation	Incidence
• Thyroid dysgenesis-85% • Sometimes radionuclide scanning studies using I-123 determine ectopic, lingual or sublingual or missing gland • Transient hypothyroidism	• Abnormal Newborn Screen • Birthweight > 4 kg. Gestation > 42 wk. • Umbilical hernia • Hypothermia • Jaundice • Bradycardia • Poor muscle tone • Poor feeding • Constipation	• 1: 3000 to 4000 • Most common congenital endocrine disorder

Treatment of Neonatal Hypothyroidism

- Confirm positive diagnosis by newborn screen with serum thyroid levels
- Thyroxine replacement-Initial evaluation and treatment should be done within 2-5 days
- Regular thyroid level blood tests essential-monthly with newborn
- Newborns diagnosed and treated in the first month of life usually have normal intelligence

Question 2

A term infant was born GA and develops irritability, jitteriness, and tremors at 7 days of life. Physical exam reveals flushed cheeks, sweating, prominent eyes and hepatosplenomegaly. Axillary temperature is 100.4 F, HR 210 bpm, RR is 48 and BP 88/56. Muscle tone is normal.



Biscschoo,P. ,Trotsenberg (2014)

Question 2

- Question 2
- Of the following the most likely diagnosis is
- A. congenital heart disease
- B. familiar dysautonomia
- C. Intrauterine infection
- D. Neonatal Thyrotoxicosis
- E. Neonatal withdrawal

Neonatal Grave's Disease

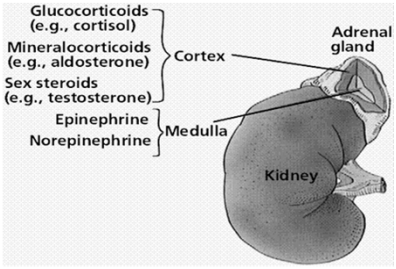
Pathophysiology	Presentation	Inheritance Pattern
• Transplacental passage of TSH receptor stimulating antibody (TSA) from a mother with active or inactive Graves disease	• Fetal tachycardia above 160 bpm should be suspicious for fetal Graves disease • In the newborn Grave's disease is manifested by irritability, flushing, tachycardia, hypertension, poor weight gain, thyroid enlargement and exophthalmos	• Uncommon due to the low incidence of thyroid toxicosis in pregnancy

Treatment of Fetal / Neonatal disease

- PTU (Propylthioracil) and Lugal's Solution (Potassium Iodide) decrease the thyroid hormone secretion
- Methimazole and Carbimazole
- Corticosteroids
- Beta blockers for cardiac protection–such as Propanalol to counter the effects of the excessive free T4
- A therapeutic response should be observed within 24-36 hours
- Neonatal Grave's disease resolves spontaneously as the maternal thyroid receptor antibody in the newborn is degraded
- Clinical course is 3-12 weeks

Nursing Care Neonatal Thyroid Disease

Neonatal Adrenal Gland Disorders



Neonatal Adrenal Disorders

Classic Congenital Adrenal Hyperplasia

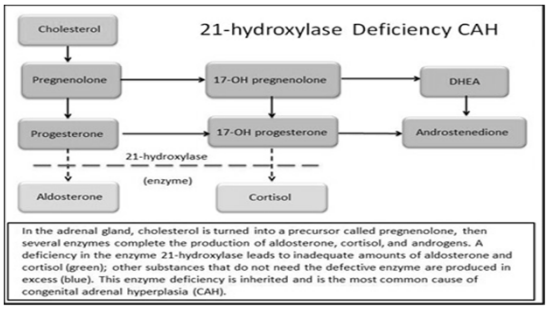
- Salt Losing*
- Simple Virilizing*

Severe hypoglycemia can result in death in the first 48 hours of life

Adrenal Hypoplasia

- In the absence of pituitary gland function, the adrenal glands fail to develop normally

Severe hypoglycemia can result in death in the first 48 hours of life



American Association for Clinical Chemistry (2015)

Congenital Adrenal Hyperplasia

Autosomal recessive; Defect in the synthesis of cortisol and sometimes aldosterone that results in increase ACTH and adrenal hyperplasia. Enzyme 21-Hydroxylase (21-OH) is missing or not working.

Female-Classic

- Ambiguous genitalia-virilization, large clitoris, labia may be fused and look like scrotum
- High levels of androgens does not usually affect the uterus and ovaries.

Male-Classic

Rarely diagnosed at birth unless they have ambiguous genitalia, are salt losers and manifest adrenal crisis; are identified in newborn screen, or have affected sibling

Adrenal Hypoplasia or Insufficiency

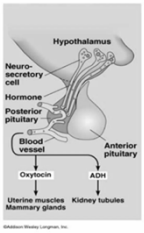
Pathophysiology	• Adrenal hemorrhage • Congenital
Clinical manifestations	• Hyponatremia, hyperkalemia, polyuria, dehydration • Failure to Thrive
Diagnostic Studies	• Lytes, Glucose, Cortisol (serum and urinary) • Adrenal ultrasound

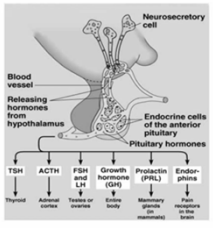
Treatment of Adrenal Hypoplasia and Adrenal Insufficiency

- Hydrocortisone (glucocorticoid)
- 9 alphafludrocortisone (mineral corticoid)
- Dietary sodium
- Management of ambiguous genitalia
- Genetic counseling
- Life long management
- In time of crisis-increased steroids
- Psychosocial support

Nursing Care Neonatal Adrenal disorder

Neonatal Hypopituitarism





Neonatal Congenital Pituitary Disorder

Gene mutation Pituitary agenesis
Holoprosencephaly Septo-optic dysplasia Other midline defects
Infection Hypovolemic shock

Neonatal Congenital Hypopituitarism

Anterior Pituitary
Cortisol, Growth Hormone, Gonadotropin, Thyroid deficiencies

Clinical manifestation

- Hypoglycemia
- Micropenis
- Jaundice

Diagnosis

- Hormone levels
- MRI

Neonatal Congenital Pituitary Disorder

Posterior Pituitary
Diabetes Insipidus

Clinical manifestation

- High urine output; excess of 5ml/kg/hr
- Low specific gravity
- Dehydration

Diagnosis

- Electrolytes
- Osmolality
- Plasma SDH level
- MRI

Treatment of Pituitary Disorder

- The immediate goals of management are to stabilize the neonate's blood sugar and ensure that the neonate is not at risk of life-threatening cortisol deficiency
- Hypoglycemia may not resolve without growth hormone treatment
- Correct the specific hormone deficiencies

Nursing Care Neonatal Pituitary Disease

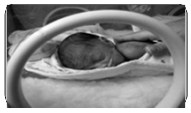
Take-away

- Competencies for non-genetics health care provider
  - Published by the National Coalition for Health Professionals Education in Genetics (NCHPEG, 2007)
- At minimum every health care professional should be able to:
  - Examine their own competence and identify areas of strength and opportunity for growth
  - Understand that health related genetic information can have social and psychological implications for individuals and families
  - Know when to make a referral to a genetics professional

Take-away

- Knowledge
  - Basic terminology
  - Patterns of inheritance
  - Difference between diagnosis and predisposition to disease
  - The potential limitations, and risks of genetic information
- Skills
  - Family history taking, explain the benefits of genetic services, use of credible resources
  - Seek coordination and collaboration with an interdisciplinary team of health professionals
  - Provide education, care and support

Achieve the best outcome



The nurse should make continued, repeated assessments of the neonate in the acute care setting

The nurse should track the labs in the acute and outpatient setting

Coordinate care

"To watch the infant form with anxious care
The lurking symptoms of disease detect,
And with the aid of sweet nutritious food,
Or potent herb, or kindly drug, to aid
Oppressed nature in her arduous task
Be thine! And thine the grateful rich reward
Of conscious duty done -- a mead more fair
Than all the laurels which bedeck the brow
Of modern Caesar".

Isaac Riley MD, 1811

Questions

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