PORPHYRIA

A Few Facts

- Used to be known as a blood/liver disease
- Came from the Greek word Porphyrus
  - Meant the color purple
  - Came from the color of the urine
  - King George III also had this disease

A Brief History

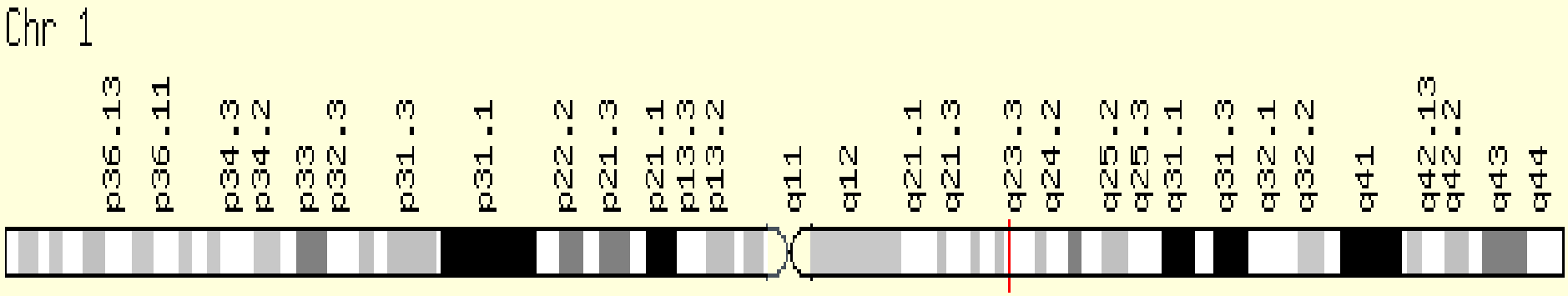
- Has been around for a long time
- Abdominal pain brought on the idea of it being a liver disease
- First identified/named by a Dr. Schultz in 1874
- First clinical description made by B. J. Stokvis
- The name Pyrrolia was also considered

People with Porphyria

Who does it affect?

- 1-2 people per 100,000 are effected world wide
- 2720 in affected in USA
- Male and Female alike
- About 0.3 deaths per million people
- Most amount of cases in Brazil
  - 20 deaths resulting from Porphyria
  - 12 in the US
- 40-60 year life expectancy (if well treated)

Location



- Also Located on Chromosome 11 at q23.1

So, What is it?

- A group of disorders affecting the nervous system and skin
- Eight types
  - Acute and cutaneous
  - Acute most severe
  - Cutaneous most common
- Characterized by a deficiency in the enzyme needed to make heme
  - Heme is located in the hemoglobin located in the bone marrow

Symptoms

ACUTE PORPHYRIAS

- Severe Abdominal Pain
- Constipation
- Vomiting
- Diarrhea
- Pain in arms/legs/or back
- Muscle Pain
- Seizures
- Fever
- Confusion
- Hallucinations
- Disorientation
- Paranoia
- Red urine
- High blood pressure

CUTANEOUS PORPHYRIAS

- Itching
- Painful skin redness (erythema)
- Skin swelling (edema)
- Blisters
- Red Urine

Common Signs

ACUTE PORPHYRIAS

- Begins with abdominal pain
- Accompanied by vomiting and/or constipation
- Can also be accompanied by:
  - Muscle pain
  - Confusion
  - Disorientation

CUTANEOUS PORPHYRIAS

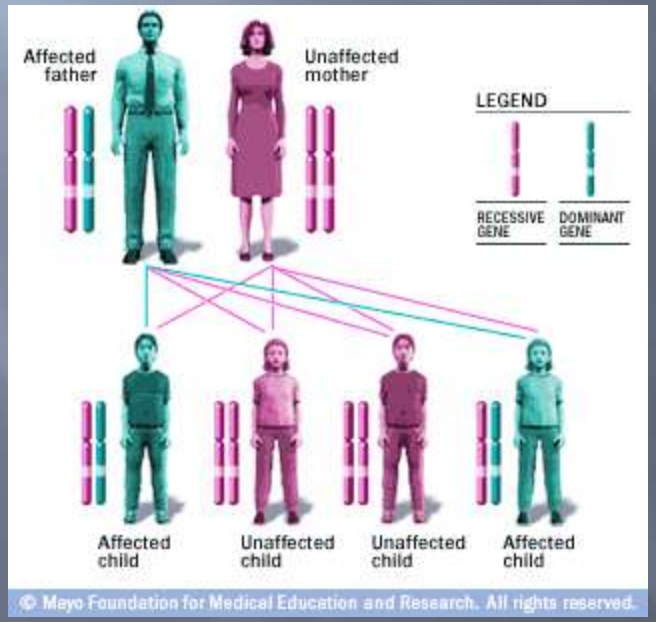
- Itching
- Painful skin redness
- Skin swelling
- Blisters that appear within several minutes of sun exposure

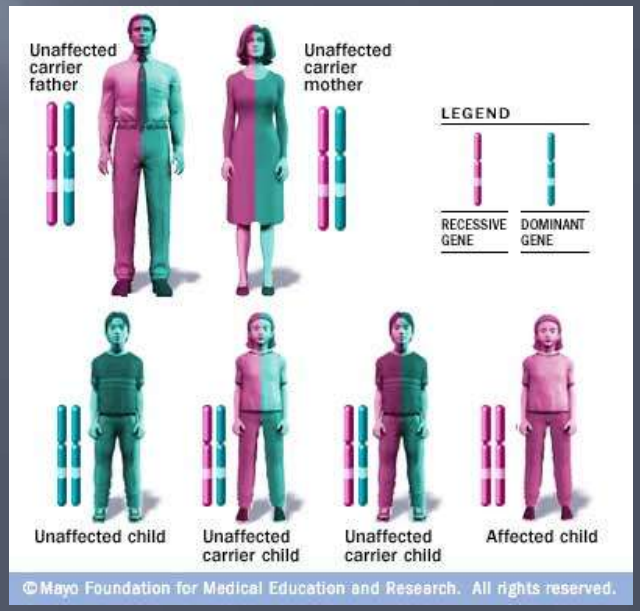
How does it effect your life?

- Sunlight avoidance
- Avoid Triggers:
  - Alcohol
  - Medicine
    - Contraceptive Pills
- Suffer Attacks
  - Major: Attacks from the body trying to produce heme
  - Minor: heart palpatations

Inheritance

- Most forms inherited
  - Autosomal dominant (one parent has it0
  - Autosomal recessive (both parents have it)
    - Majority is recessive inheritance of mutated alleles



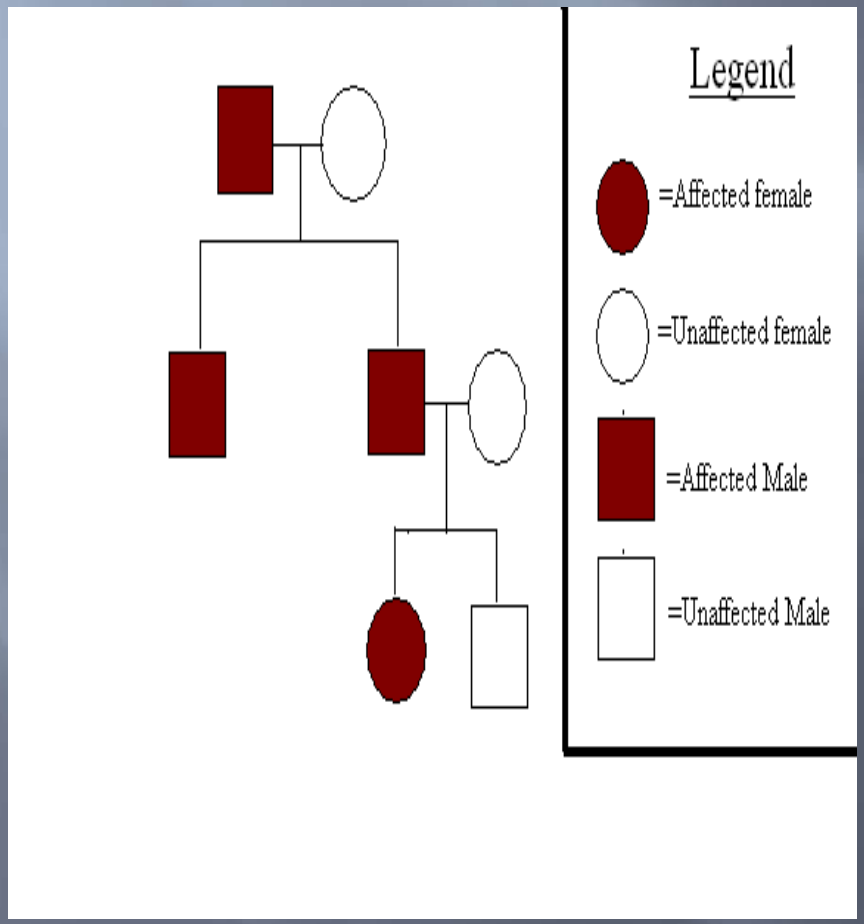


Appearance of Symptoms

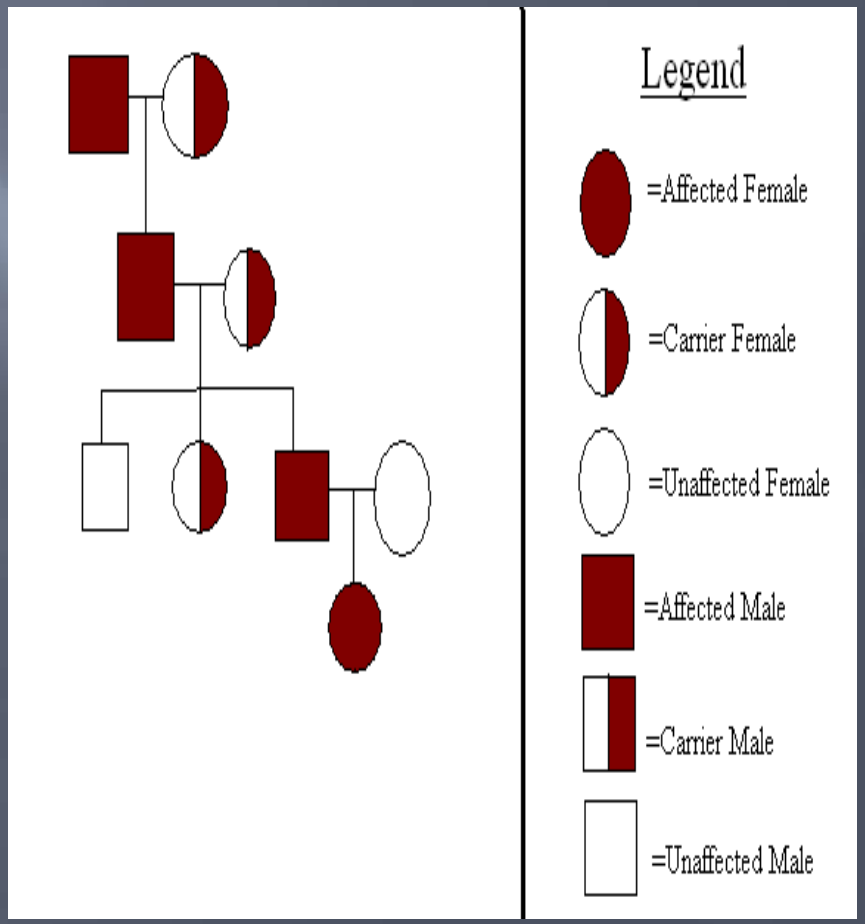
- Deficient enzyme does not always cause symptoms to appear
- Sometimes appears to the exposure of a trigger:
  - Drugs
  - Dieting/fasting
  - Smoking
  - Surgery
  - Infections
  - Stress
  - Alcohol use
  - Menstrual hormones
  - Sun exposure
  - Excess iron in body

Pedigree

AUTOSOMAL DOMINANT



AUTOSOMAL RECESSIVE

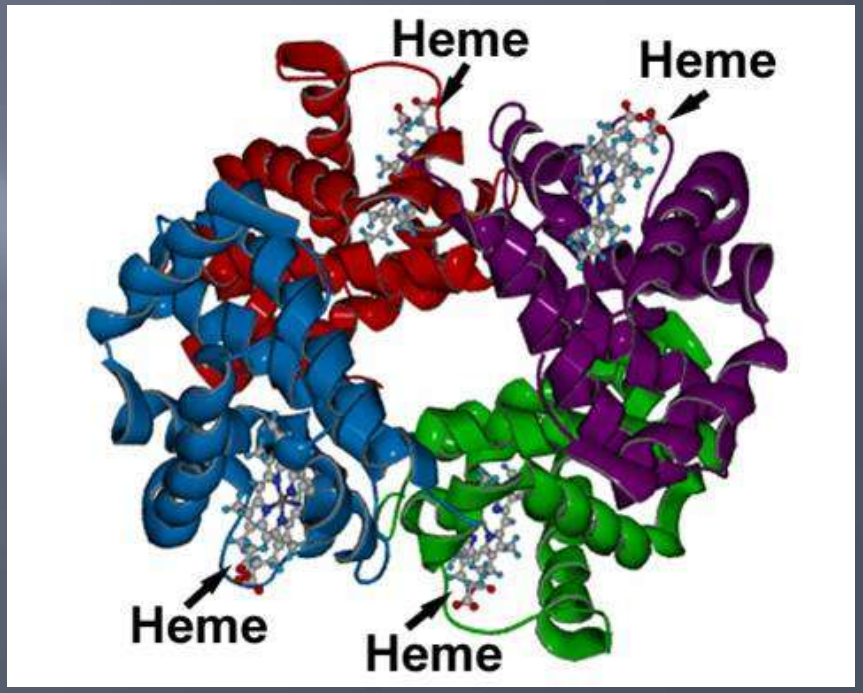


What would a genetic counselor say?

- Think about the consequences
  - What type do you have?
  - Recessive? Dominant?
  - What symptoms will the child display?
- Do you have the means to take care of the child?

How Heme Works

- Primarily found in red blood cells
  - Found in Myoglobin as well
    - Myoglobin is a protein found in muscle cells
- Major component of hemoglobin
  - Enables blood cells to carry oxygen from lungs to other parts of the body
- Eight components turn porphyrin into heme



How the Mutation Works

- Specific type of mutation unknown
- Porphyrin is a chemical that forms heme
- Caused by an inherited mutation in any of the eight genes that form heme
- Mutation causes heme deficiency
  - Causes porphyrins to build up
    - Causes high blood pressure, kidney failure, and liver damage

Where is the mutation?

- Located in the enzymes
- Each type has a different mutation
  - Acute:
    - ALAD Porphyria: Delta-aminolevunic acid dehydratase
    - Acute Intermittent Porphyria: Porphobilinogen deaminase
  - Cutaneous:
    - Congenital Erythropoietic Porphyria: Uroporphyrinogen III cosynthase
    - Porphyria Cutanea Tarda: Uroporphyrinogen decarboxylase
    - Hepatoerythropoietic Porphyria: Uroporphyrinogen decarboxylase
    - Erythropoietic Protoporphyria: Ferrochelatase
  - Two other types that can be both:
    - Hereditary Corproporhyria: Corproporphyrin oxidase
    - Variegate Porphyria: Protoporphyrinogen oxidase

Diagnosis

- Some symptoms are similar to other diseases
- Tests are required to determine form
  - Urine: reveals porpyrins such as porphobilinogen and delta-aminolevulinic acids
  - Blood: shows an elevation in porphyrins in blood plasma
  - Stool: shows elevated levels of porphyrins not evident in urine

Treatment

ACUTE PORPHYRIAS

- Stop medications that cause triggers
- Medication to control pain
- Prompt treatment of infections/illnesses that cause symptoms
- Injections into vein
  - Glucose
  - Fluids
- Hemin/Hematin injections

CUTANEOUS PORPHYRIAS

- Phlebotomy
  - Reduces iron in body and thus porphyrins
- Activated Charcoal
  - Absorbs excess porphyrins
- Beta Carotene
  - Increases skin tolerance to sunlight
  - Converts to Vitamin A

Current Research

- Attempting to find a cure
- More research being done into acute porphyria
- Organizations all over the world
  - America Porphyria foundation

The America Porphyria Foundtation
4900 Woodway, Suite 780
Houston TX, 77056-1837
(713)-266-9617
Toll free: (866)-APF-3635

  - European Porphyria Innitiative
  - British Porphyria Association

Implications

- Insurance is available for anyone
- Rare disease
  - Many surprised to find they have it
- Does not affect rights
- Does not cause stigmatization
- Testing should be allowed for all ages
- Genetic information should be restricted -- should not impact life

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