



Alpha₁-Antitrypsin Deficiency

Coram, Inc., an Apria Healthcare Company, is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Provider approved by the California Board of Registered Nursing, Provider #11609.

Copyright © 2009 by Coram, Inc.

Important Information Regarding Continuing Education

- o Sign in on the Attendance Record, **clearly**. This is used to print your certificate
- o Provide your RN License number and credentials
- o Provide a current address
- o If you do not have this information with you, please contact Coram's CE Dept. at 847-553-2555 or by email at cedept@coramhc.com with this information.
- o If this information is not received, a certificate will not be issued. This information is required by ANCC and CABRN.
- o The recent Apria program you attended has a Coram Infusion logo. This is because our current CE provider number is allocated to Coram. Your CE credits are not affected by this logo change.

Who is this guy???

- Aaron L Patterson
 - RPh; PharmD
 - Pharmacy Supervisor; Coram Minneapolis
 - Licensed: Iowa, Wisconsin, Minnesota

3

Continuing Nursing Education and Conflict of Interest Statement

- o Conflicts of interest or lack thereof
- o Commercial support received
- o Non-endorsement of products
- o Off-label product use

*Coram, Inc., an Apria Healthcare Company, is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.
Provider approved by the California Board of Registered Nursing , Provider #11609.*

4

Objectives

- Identify the incidence and pathophysiology of AAT
- Describe three (3) symptoms of AAT
- Identify diagnostic tests and treatment modalities
- Discuss the use of replacement therapy for AAT: Aralast, Glassia, Prolastin, Zemaira
- Identify how nutrition management helps in treatment of AAT
- Describe the psychosocial aspects of AAT

5

Overview

- **Disease referred to as:**
 - A1AD for Alpha₁- Antitrypsin Deficiency
 - AAT Deficiency
 - Genetic or Inherited Emphysema
 - Alpha-1
- **Discovered in 1963 in Sweden**
 - A trypsin inhibitory protein isolated from serum by Drs. Eriksson & Laurel

6

WHAT IS IT???

- Alpha 1 Antitrypsin is a glycoprotein produced by the liver and released into the bloodstream. It then travels to the lungs, where it bathes the alveolar lining and acts to inhibit the activity of neutrophil elastase, as well as other degradative enzymes. In this way, AAT puts the brakes on the inflammatory process before it can damage healthy lung tissue.

7

Summary of the issue

- Neutrophil elastase = good
 - Unchecked enzymes = bad (inflammation)
 - bad = degraded elastin
 - Bad = lung tissue damage
 - Bad = liver tissue damage
 - Bad = skin/blood vessel damage
- Alpha 1 Antitrypsin is good
 - Too little/ No AAT = unchecked enzymes

8

Characteristics of Alpha₁-Antitrypsin Deficiency

- Autosomal, co-dominant pattern of inheritance
- Recessive hereditary disorder
- The alpha₁- antitrypsin gene is found on the long arm of chromosome 14

9

Alleles

M (healthy)

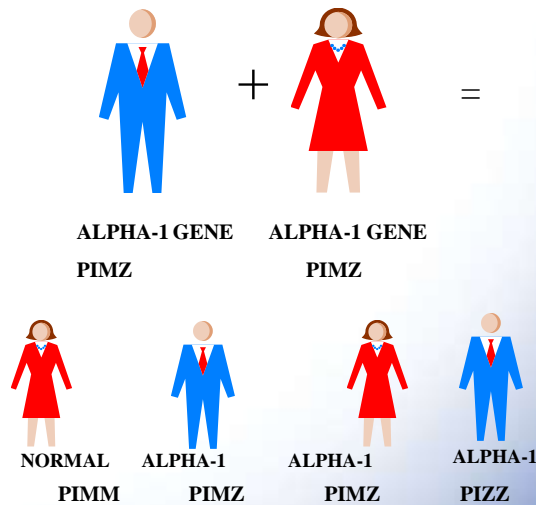
- Directs body to synthesize enzyme

S and Z (defective)

- Direct body to synthesize a non-functional enzyme.
- PiZZ
 - More than 95% with severe AAT deficiency have this
- PiMZ
 - Usually decreased levels of AAT

10

Alpha₁-Antitrypsin Deficiency The Heredity Pattern



11

Alpha₁-Antitrypsin Deficiency Genetics of Inheritance

- 75 Genetic Variants (protease inhibitor-PI types) are called Phenotypes.
 - PiZZ--Accounts for 95% of symptomatic patients with low levels of alpha-1 antitrypsin
 - 20 Rare Variants--i.e. PiSZ, Nulls, may be symptomatic
 - S, Z & Null genes are most common for symptomatic patients

12

Genetics of Inheritance continued...

- People that are PiMM have normal levels of alpha₁-antitrypsin
- People that have inherited one abnormal gene (Z) are called carriers
- Carriers have lower than normal levels of the protein
- PiZZ is the most severe form of the deficiency. Several other variants have been identified (i.e. S, Null)
- Alpha₁-Antitrypsin Deficiency, PiZZ, occurs when both parents pass on the abnormal gene, Z, to their child

13

Alpha₁-Antitrypsin Deficiency Disease Mechanisms

- Alpha₁-Antitrypsin (protein):
 - Is produced by the liver
 - Circulates in the blood
 - Inhibits neutrophil elastase (a protease) in the lungs--thus it is called a protease inhibitor
- Neutrophil elastase (enzyme):
 - Digests injured lung tissue (reaction to colds, flu, smoke, airborne irritants etc.)
 - If not inhibited by Alpha₁-Antitrypsin, it goes on to destroy alveolar lung tissue

14

So???

- How many AAT are there in US?
 - 10,000 ???
 - 100,000 ???
 - 1,000,000 ???

15

Similar disease populations

- Incidence range from 1:1500 to 1:3500
 - Comparator is 1:3000
- Frequently cared for by RT, transplant
 - Comparator is the same
- Frequently cared for in specialized centers
 - Comparator difference...
- [Alpha 1 Foundation](#)

16

Incidence

- Same frequency as Cystic Fibrosis:
 - 1 in 3000 live births
- Alpha-1 has been identified in virtually all populations
- Thought to be most common in individuals of Northern European (Scandinavian & British) and Iberian (Spanish & Portuguese) descent

17

Incidence

- Estimated that at least 100,000 Americans and a similar number in Europe have the most severe form of the disease (PiZZ)
- 21 Million are estimated to be carriers of Alpha₁-Antitrypsin Deficiency
 - Heterozygotes
 - 1 in 37 individuals carry a defective gene for Alpha-1

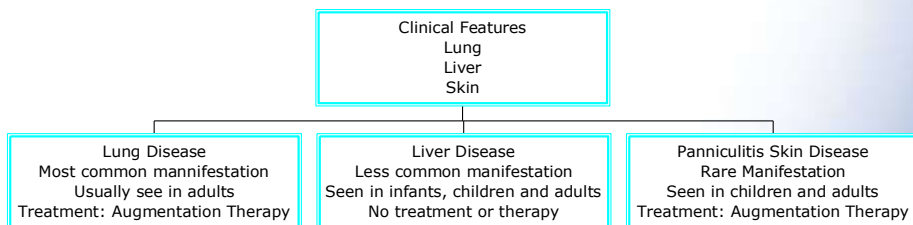
18

Incidence

- Widely under-diagnosed
 - Often misdiagnosed as asthma, allergies, COPD or chronic bronchitis
 - Up to 4% of patients with emphysema or COPD actually have A1AD
 - Variable symptoms make diagnosis complicated
 - Lack of awareness of disease in general population and parts of medical community also make diagnosis difficult

19

Alpha 1-Antitrypsin Deficiency Clinical Features



20

Common Signs and Symptoms

- Family history of lung disease or liver disease
- Recurring respiratory infections that do not respond to antibiotics
- Shortness of breath
- In the 3rd/4th decade of life in adults but sometimes as early as childhood
 - Before age 50 for smokers and nonsmokers alike
- Can have rapid deterioration of lung function without a history of significant smoking

21

Common Signs and Symptoms

- Decreased exercise tolerance
- Non-responsive asthma or year-round allergies
- Elevated liver enzymes
- Chronic liver problems

22

Clinical Features Lungs

- Insidious onset of progressive SOB between ages of 25 and 40
- Increasing dyspnea/evidence of airflow obstruction
- Chest X-ray abnormalities
 - *lung bases*-hyperinflation
- Concurrent chronic bronchitis in 20-30% of pts.
- Concurrent asthma in 4-34% of pts.
- Pursed-lip/diaphragmatic breathing, wheezing
- Chronic cough

23

Clinical Features Liver

- Liver symptoms vary in severity:
 - 12-15% have liver involvement.
 - 10% of newborns, with ZZ genotype, have liver disease leading to fatal childhood cirrhosis.
 - It is most common form of liver disease in children
 - Alpha-1 is the most common genetic reason for transplant in infants and children

24

Clinical Features Liver

- Of children with PiZZ Phenotype:
 - Up to 25% develop cirrhosis and portal hypertension, die of complications before age 12
 - 25% will die of the same process by age 20
 - 25% will have liver fibrosis but minimal hepatic dysfunction. They can live into adulthood.
 - 25% show no evidence of progressive disease

25

Clinical Features Liver

- Risk higher for adults:
 - 12-15% of all ZZ phenotypes develop liver disease
 - Risk is slightly higher in male ZZ's
- Excessive alcohol consumption, smoking and exposure to occupational toxins increases risk

26

Skin Clinical Features Panniculitis

- Inflammation of fat beneath the skin
 - Causes skin to harden
 - form lumps, lesions and patches
- Damage initiated by destructive action of unrestrained neutrophils
- May occur after an incident of trauma to the affected area
- Occurs in children as well as adults
- Treated with augmentation replacement therapy
- Panniculitis

27

Screening & Detection

- 5000 Alpha 1 patients have been identified in US
 - Many still unidentified or misdiagnosed
- The World Health Organization (WHO) recommends (1995) that all individuals with COPD, as well as adults and adolescents with asthma (an estimated 30 million Americans in total) be tested for Alpha-1.

28

Screening and Detection

- Targeted screenings are done to identify adults at risk who have:
 - Chronic bronchitis.
 - Symptoms of emphysema.
 - Asthma.
 - Family history of A1PI or history of a family member who died young of unknown lung or liver disease.

29

Alpha₁-Antitrypsin Deficiency Diagnosis

- Measure serum AAT concentrations
 - PiZZ - Have <35% of normal serum level
- If level is low or borderline, phenotyping is done
- Chest X-ray
 - (abnormalities in bases of lungs)
- Pulmonary Function Testing (based on decreased FEV1)
- Graded Exercise Test
- Arterial blood gases
- Liver function tests

30

ATS Standards for Screening and Detection of AAT Deficiency

...who to test? (American Thoracic Soc 2003)

- All patients with COPD merit testing
- Early onset emphysema
- Asthma patients that do not respond to inhalers
- Patients with reoccurring bronchitis and pneumonia that do not respond to antibiotics
- Patients with bronchiectasis
- Patients with Anti-Proteinase 3 positive vasculitis
- Family histories of lung or liver disease
- Unexplained liver disease
- Panniculitis

31

Differential Diagnosis

Acquired Emphysema

- Inhibitor normal
- Usually associated w/smoking
- Usually affects upper lobes of lungs
- Usually diagnosed in pts. 55-75 years

Alpha-1 or Genetic Emphysema

- Serum levels of A₁ Proteinase <35% of normal
- Usually affects lower lobes of lungs
- Usually diagnosed in pts. 30-40 years old but can be seen as early as 20's

32

Co-morbid Conditions and Complications

- Asthma
- Pneumonia
- Acute or Chronic Bronchitis
- Cor Pulmonale
- Pulmonary Hypertension
- Hypoxemia

33

Testing Family Members of Identified Alpha-1 Patients

- If a family member is already displaying symptoms, they should be told the test is available and discuss their options with their healthcare providers or a genetic counselor.
- Alpha-1 Coded Testing (ACT) Trial kits are available for those that want confidential results by calling 1-877-886-2383.
 - <mailto:alphaone@musc.edu>

34

Ongoing Interventions & Treatments

- Smoking cessation
- Supportive therapy:
 - Pulmonary rehab/exercise
 - Bronchodilators/anti-inflammatory
 - Immunizations
 - Influenza and Pneumococcal
- Augmentation therapy
- Early and aggressive Rx of respiratory infections
- Lay off the sauce...

35

Ongoing Interventions/Therapies

continued...

Oxygen Therapy for Lung Patients

Symptomatic Alpha-1 patients should all be evaluated at:

- Pulse oximetry at rest for O₂ saturations
- Pulse oximetry with mild exertion
- Pulse oximetry with strenuous exertion consistent with lifestyle; climbing stairs, treadmill etc.
- Overnight oximetry for all patients with decreased lung function

36

Supportive Treatment for A1PI

- Bronchodilators
- Anti-Infectives
- Pulmonary Rehabilitation
 - Accessory muscle strengthening
 - Breathing techniques
 - Maximize lung capability
- Augmentation Replacement Therapy
 - Aralast, Glassia, Prolastin, Zemaira

37

Interventions & Treatments

- Lung Transplant
 - When patient has declined to the point where therapies are no longer viable
- Liver interventions
 - No cure or treatment for liver damage caused by AAT Deficiency except liver transplant

38

Interventions & Treatments

Augmentation Replacement Therapy

- FDA approved; once weekly by intravenous infusion
- For patients 18 years of age For PiZZ and other variants with symptoms
- Not given if normal lung fxn
- Purified alpha₁-antitrypsin
- Derived and isolated from pooled human blood plasma
- Use of augmentation therapy should reduce further damage to the lungs caused by neutrophil elastase

39

Augmentation Therapy

continued...

- Purified Alpha₁-Antitrypsin
- Derived and isolated from pooled human blood plasma
- IV infusion recommended weekly
- Use of augmentation therapy should reduce further damage to the lungs caused by neutrophil elastase

40

Available Therapies

- Zemaira ®
- Prolastin ®
- Glassia ®
- Aralast NP®
- Recommended Dosing:
– 60 milligram/kg/week

41

Plasma Fractionation to Make Derivatives

Frozen Plasma

thaw 0-2°C

Cryoprecipitate

FVIII
II
vWF
Fibrinogen

Cryo-Free Plasma

FIX Complex
Coag. FIX
AICC
AT III

25% ETOH, pH5.2

IV-1
FIX/FVII
AICC, A1AT

20% ETOH, pH 6.7-7.1

Fraction

IGIV
IMIG

40% ETOH,
pH 4.8

V
Albumin

40% ETOH,
pH 6.8

IV-4

PPF

42

Interventions and Treatments

Side Effects from Augmentation Therapy

- Side effects are rare
 - Dizziness, lightheadedness, headache
 - Somnolence, transient HTN, peripheral edema
 - Pharyngitis, cough, bronchitis symptoms, sinusitis
 - Back pain and rash

43

Nutrition Management

- Treat weight loss
- Eat balanced diet in several small meals
- Multi-vitamin
- Rest before eating
- Exercise to increase appetite – 2 hours after meal
- Low fat, high calorie meals
- Eat sitting up
- Decrease sodium
- If patient has lots of congestion stay away from dairy products
- Nutritional consult

44

Psychosocial Impact

- Need for enhanced awareness of the disease by healthcare professionals and general public
 - Recent study by the Cleveland Clinic revealed:
“7.2 year delay between onset of symptoms and correct diagnosis. 7 years may be ample time for an untreated patient to needlessly progress from mildly symptomatic to severely disabled”
 - This delay of diagnosis can be very demoralizing for patients.

45

Psychosocial Impact

- Need for screening and detection programs to identify more patients, particularly those with COPD symptoms age 50 and under
- Patient Support is a vital part of treatment
 - Education
 - Counseling
 - Patient and family resource meetings

46

Customer Service and Patient Education

- Education, information, resources
- Access to insurance and financial assistance programs
- Personal advocacy, peer to peer mentoring and psycho-social support
- As members of the community (in most cases), advocates can be more effective

47

quiz

- [A1 quiz](#)
- pp33

48