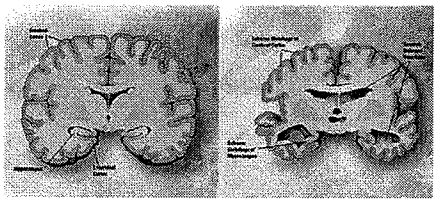
Alzheimer's

By: Patrick Stevens

Introduction

- Alzheimer's disease (AD), is most common form of dementia that gradually gets worse over time. It affects memory, thinking, and behavior.



Major Milestones

- 1906 Dr. Alois Alzheimer describes what would be later known as Alzheimer's.
- 1931 Electron Microscope allows further study of the brain.
- 1968 Devlopement of Cognitive Measurement Scale
- 1984 Beta-Amyloid identified-the chief component of Alzheimer's brain plaques and a prime suspect in triggering nerve cell damage.

Major Milestones Cont.

- 1986 Tau Protein Identified-tau protein is a key component of tangles—the second pathological hallmark of Alzheimer's disease and another prime suspect in nerve cell degeneration.
- 1987 First Alzheimer's Drug Trial
- 1987 First Alzheimer's gene Identified-Researchers identify the first gene associated with inherited forms of Alzheimer's disease. This gene on chromosome 21 codes amyloid precursor protein (APP), the parent molecule from which beta-amyloid is formed. Chromosome 21 is also the chromosome of which those with Down syndrome have three copies rather than two. Many individuals with Down syndrome develop Alzheimer's disease, often as young as their 30s and 40s.

Milestones Cont.

- 1993 Alzheimer's risk factor gene identified-Researchers identify APOE-e4, on chromosome 19, as the first gene that raises risk for Alzheimer's but does not determine that a person who has it will develop the disease.
- 1993 First Alzheimer's drug approved
- 1999 Alzheimer's Vaccine Sucessful in Mice-injecting transgenic "Alzheimer" mice with beta-amyloid prevents the animals from developing plaques and other Alzheimer-like brain changes.

Clinical Features

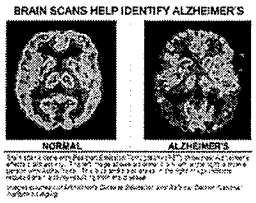
- The usual first symptom is short term memory loss which progresses from seemingly simple and often fluctuating forgetfulness
- a more pervasive loss of short-term memory, then of familiar and well-known skills or objects or persons.
- Aphasia, disorientation and disinhibition often accompany the loss of memory.
- Alzheimer's disease may also include behavioural changes, such as outbursts of violence or excessive passivity in people who have no previous history of such behaviour.

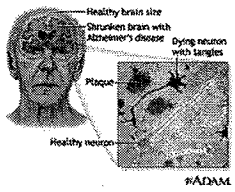
In the later stages, deterioration of musculature and mobility, leading to bedfastness, inability to feed oneself, and incontinence, will be seen if death from some external cause (e.g. heart attack or pneumonia) does not intervene.

What does Alzheimer's do

- build-up of amyloid plaques and tau-containing neurofibrillary tangles, which result in the death of brain cells and the breakdown of the connections between them.
- Plaques are dense deposits of protein and cellular material outside and around the brain's nerve cells.
- Tangles are twisted fibers that build up inside the nerve cells.

Your Brain on Alzheimers





Stages of Alzheimers

- **Stage 1 (mild):** common early symptoms of Alzheimer's disease include short term memory loss which progresses from seemingly simple and often fluctuating forgetfulness
- confusion, disturbances in short-term memory, problems with attention and spatial orientation, changes in personality, language difficulties and unexplained mood swings. Normally, these symptoms are very mild, and presence of the disease may not be apparent to the person experiencing the symptoms, loved ones or even health professionals. Lasts 2 to 4 years

Stages of Alzheimers

- **Stage 2 (Moderate):** This is generally the longest stage and can last 2 to 10 years. In this stage, the person is clearly becoming disabled. Individuals can still perform simple tasks independently, but may need assistance with more complicated activities. They forget recent events and their personal history, and become more disoriented and disconnected from reality. Memories of the distant past may be confused with the present, and affect the person's ability to comprehend the current situation, date and time. They may have trouble recognizing familiar people. Speech problems arise and understanding, reading and writing are more difficult, and the individual may invent words. They may no longer be safe alone and can wander

Stages of Alzheimers

- **Stage 3 (Severe):** This stage may last 1 to 3 years. During this final stage, people may lose the ability to feed themselves, speak, recognize people and control bodily functions, such as swallowing or bowel and bladder control. Their memory worsens and may become almost non-existent. They will sleep often and grunting or moaning can be common. Constant care is typically necessary. In a weakened physical state, patients may become vulnerable to other illnesses, skin infections, and respiratory problems, particularly when they are unable to move around.

Is Grandma just old?

What does Alzheimer's do to the Brain?

- Alzheimer's disease has been identified as a protein misfolding disease, or proteopathy, due to the accumulation of abnormally folded amyloid beta protein and tau protein in the brains of AD patients.
- Plaques are dense deposits of protein and cellular material outside and around the brain's nerve cells.
- Tangles are twisted fibers that build up inside the nerve cells.
- At an anatomical level, AD is characterized by gross diffuse atrophy of the brain and loss of neurons, neuronal processes and synapses in the cerebral cortex and certain subcortical regions.
- result in the death of brain cells and the breakdown of the connections between them.
- Levels of the neurotransmitter acetylcholine are reduced. Levels of the neurotransmitters serotonin, norepinephrine, and somatostatin are also often reduced. Glutamate levels are usually elevated.

Mode of Transmission

- Alzheimer's disease is believed to be etiologically heterogeneous: it may be genetic or sporadic.
- In the familial type it is believed that the disease is inherited as an autosomal dominant, with a wide range of age of onset within a family.
- gene is not usually expressed until over age 70.
- No clinical differences were found between the familial and the sporadic groups.
- Slightly higher chance of getting alzheimer's if someone in immediate family has disease.

Risk of getting Alzheimer's

- AD is primarily a disease of the aged.
- It is currently estimated that close to 50% of adults over the age of 85 have some form of dementia including AD.
- There is also a greater risk for AD associated with a family history of the disorder.
- common variations in some known genes, such as the APOE gene located on chromosome 19, influence risk for AD.

Detection

- There is no single diagnostic test to detect whether a person has Alzheimer's disease. The factors used to complete a diagnosis include:
- Medical History
- Mental Status Evaluation
- Physical Examination
- Neurological Examination
- Neuropsychological Evaluation
- Brain Scans (CT, MRI, PET)
- Laboratory Tests-blood, to eliminate other possiblities

Treatment

- No cure, aimed at slowing progression
- Treatment includes medication that helps increase certain brain chemicals affecting memory and reducing secondary damage to the brain from inflammation
- Medicine increase a neurotransmitter called acetylcholine in the brain.
- Treatment for patients family includes: family counseling and support groups

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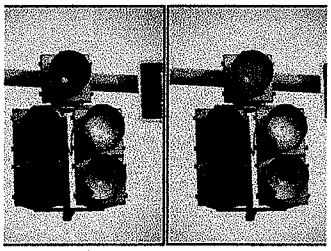
Jonathan Rogers



Color Blindness

X-linked Recessive Disorder
By: Jonathan Rogers

Introduction

Key Milestones

- Earliest known paper on Color Blindness was from John Dalton, who himself had deutanopia color blindness. Where daltonism is derived from.
- The X-Linked recessive characteristic was observed by Swiss ophthalmologist Horner in the 1870s
- Colorblindness genes were the first to be mapped to a specific chromosome in any mammal.
- Opsin 1 genes on Xq28 isolated and sequenced and made into cDNA clones in 1986

Introduction

Unique Features of the Disease

- Disorder causes an individual to have trouble distinguishing different colors and shades of light.
- Disorder is caused by mutations in the opsin 1 genes which causes a loss of function in the green and red cone pigments.

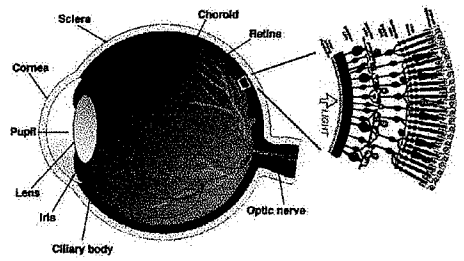
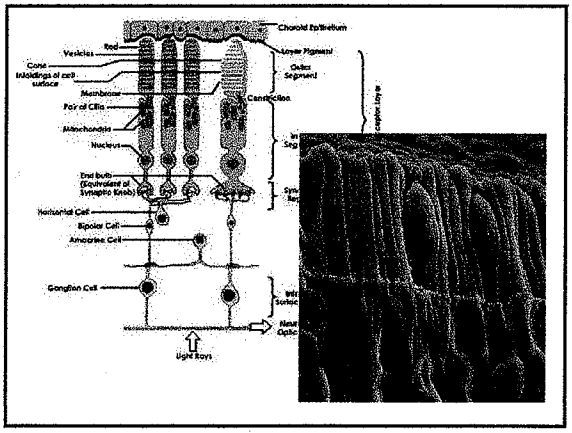
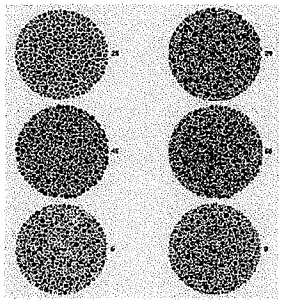


Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.



Clinical Diagnosis

- Trouble distinguishing between colors or shades
- Parental observation
- Ishihara colorblindness test
- Colored chip test



Four Sex-linked Traits

1) Normal Color Vision

A:29, B:45, C:–, D:26

2) Red-Green Color Blind

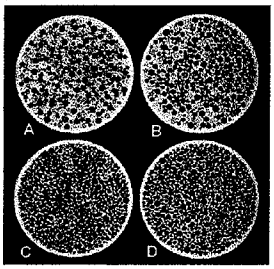
A:70, B:–, C:5 , D:–

3) Red Color Blind

A:70, B:–, C:5 , D:6

4) Green Color Blindness

A:70, B:–, C:5 , D:2



Clinical Phenotypes

•Normal color vision; trichromatic

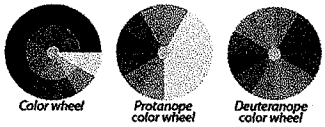
- 3 classes of photoreceptors that are maximally sensitive to light (SW blue, MW green, LW red)

•Abnormal color vision; dichromatic

- 2 normally functioning photoreceptors
- Blue + Green (protanopia)
- Blue + Red (deuteranopia)

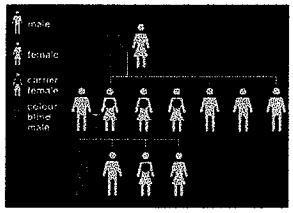
•Anomalous trichromacy

•Monochromatic



Mode of Inheritance

- Color blindness is an X-linked recessive disorder
- Males have higher risk
- If mother is carrier, then sons have 50% chance of having the disorder.
- If father has the disorder then all daughters will receive one copy of mutant allele and become carriers.



Population Genetics

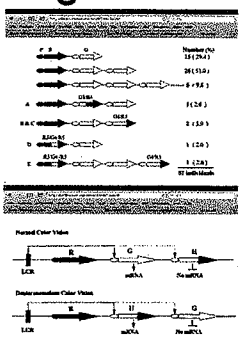
- Red-green color vision defects in northern European origin is around 8% of males and 0.5% females
- Abnormalities of color vision pigment genes in 15.7% of Caucasian men.

Molecular Diagnosis

- The red and green opsin gene repeats are in a head to tail tandem array, located on Xq28
- MW green and LW red opsin genes are 96% identical to each other and only 43% identity with blue pigment gene.
- The high homology between the red and green pigment genes have predisposed the locus to common unequal recombination events which gives rise to red/green hybrid genes and deletions of the green pigment genes. These constitute the most common cause of red-green color vision defects.

Molecular Diagnosis

- The locus control point (LCR), located between 3.1 kb and 3.7 kb 5-prime of the gene array, regulates the first red and green opsin gene in the tandem array.
- If hybrid gene is present in proximal locations then deuteranopia occurs.

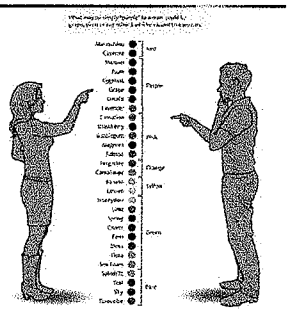


Treatments

- No current treatments available
- New aids available to help correct some color vision: specialized contacts and glasses
- Research being carried out on gene therapy through viral vector injections with opsin gene. Some success with monkeys.

Summary

- X-linked recessive disorder that affects a large number of men
- Not usually harmful or life threatening
- Can range from mild to severe in phenotype
- May affect individuals career options
- Often easily adjusted to by individuals



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Multiple choice questions

Name: Jonathan Rogers
Presentation on: Color Blindness X-linked recessive

1. X-linked recessive color blindness is a loss of function mutation that affects the vision of the patient. The X-linked gene family that has lost some function is referred to as the:

a. rod 3 genes
b. choroid 2 genes
c. opsin 1 genes
d. trichromatic 5 genes

2. A father has just verified that he has an X-linked recessive color blindness. His wife has no knowledge of the disorder occurring on her side of the family. They have two boys and a girl that show no phenotype. Assuming their daughter marries a man without colorblindness and has children, what would be the probability that she will have sons that express the colorblind phenotype? What would be the probability of her daughters expressing the phenotype?

a. Sons 50% / Daughters 50%
b. Sons 25% / Daughters 75%
c. Sons 0% / Daughters 100%
~~d. Sons 100% / Daughters 0%~~

Sons 50% daughters 0%