GRAND ROUNDS November 2, 1961

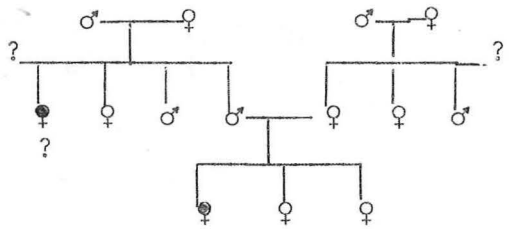
Parkland Memorial Hospital

THE RETINITIS PIGMENTOSA SYNDROMES

CASE #1 Retinitis Pigmentosa [redacted]

This woman was first seen in the [redacted] in 1949 at age 56. At that time she gave a history of night blindness beginning in childhood with slowly decreasing visual acuity for the remainder of her life. In addition when she coughed she noted sparks and balls of fire in both eyes. Ophthalmological examination revealed irregular, wavy, superficial areas of pigmentation in both fundi with yellow, waxy optic discs. The diagnosis was Retinitis Pigmentosa with optic atrophy.

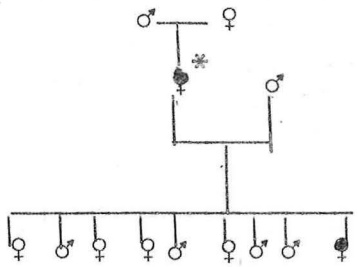
The family history was as follows:



She was subsequently admitted to PMH in 1957 for jaundice of unknown etiology. By that time her visual acuity had decreased so that she could only distinguish light and dark.

CASE #2 Retinitis Pigmentosa [redacted]

This 56 year old woman has been followed at [redacted] and [redacted] since 1953 for advanced pulmonary tuberculosis. At the time she was first seen she complained of a progressively decreasing visual acuity since 1930 culminating in almost complete blindness. Examination revealed pale optic discs with scattered streaks of black pigmentation, thought by the ophthalmology service to represent advanced retinitis pigmentosa with optic atrophy. This patient also has mild epilepsy, adequately controlled with phenobarbital. The family history is as follows:



Key

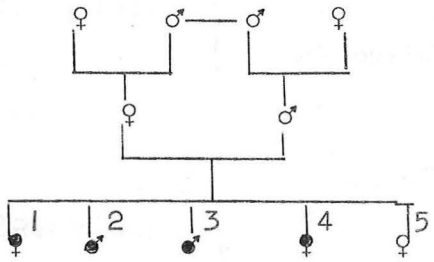
Epilepsy and Retinitis Pigmentosa

Epilepsy only

CASE # 3 Laurence-Moon-Biedl Syndrome [redacted]

This 14 year old girl appeared to be perfectly normal at birth; she walked at 15 months of age and talked at age 3. Excessive weight gain was noted beginning at about 3 years of age, and gradually it became apparent that she was retarded mentally. Poor visual acuity was first noted at age 5. At 6 years of age she was seen in Freeman Clinic where she was diagnosed as having the Laurence-Moon-Biedl syndrome. Since that time she has had a progressive decrease in visual acuity, now retaining only peripheral vision. In addition she has grown progressively more obese. Since infancy she has had repeated respiratory infections and pyelonephritis. Because of progressive lethargy, obesity, and dyspnea on exertion she was admitted to [redacted] in [redacted] of 1961 for a general workup.

The family history is as follows:



Key: 1. Polydactyly; died at 15 days when cyst on spinal column burst.

2. Laurence-Moon-Biedl Syndrome, polydactyly; died at 16 years of age.

3. Died at 2 hours of age after home delivery; probable Laurence-Moon-Biedl Syndrome.

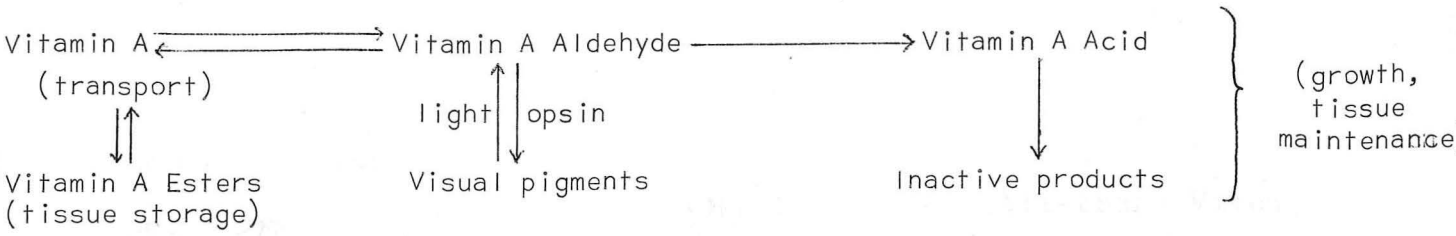
4. Patient.

5. Normal child except for congenital pyloric sterosis.

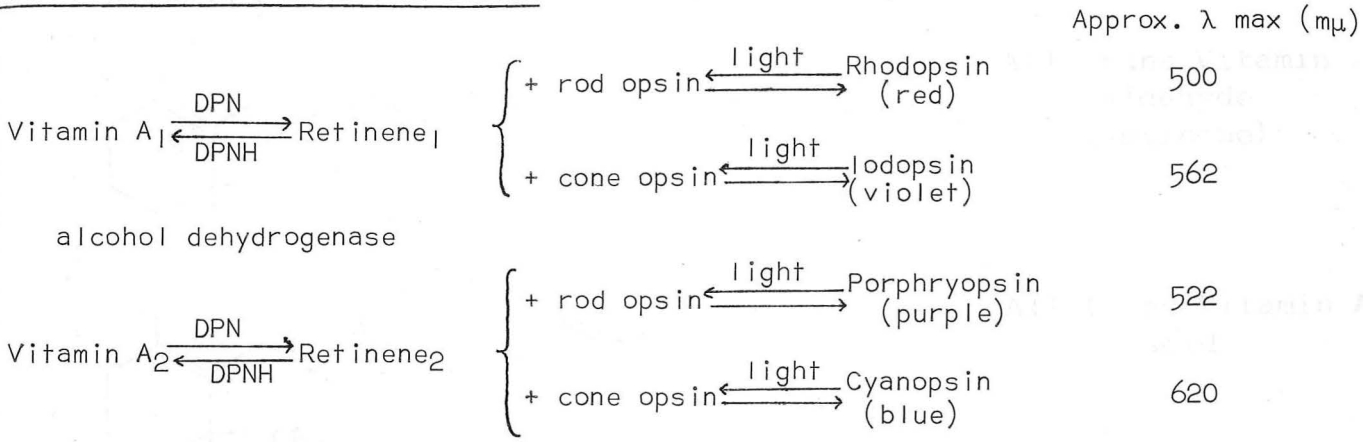
[redacted] on admission revealed a very obese young woman (weight 233 lbs.) with a B.P. of 150/110. Examination of the eyes revealed a lateral nystagmus and a marked corpuscular type pigmentation of the fundi, most marked in the mid-retineal area. Visual field studies could not be done, and the physical examination was otherwise unremarkable. There was no polydactyly. CBC and urinalysis were normal. BUN was slightly elevated (19), and she had a thymol turbidity of 19.9 and 13. PSP excretion was only 50% at the end of two hours. Several different parameters of thyroid, cardiopulmonary, and immune mechanism were all within normal limits. Urinary 17 keto steroids were 3.0 mg/24 hours. Chest x-ray and serum electrophoretic pattern were normal. Urine culture revealed a heavy growth of E. intermedius; this was treated with a subsequent reversion to a sterile urine.

On a weight reduction regimen she has subsequently lost about 35 pounds with a subsequent marked improvement in affect.

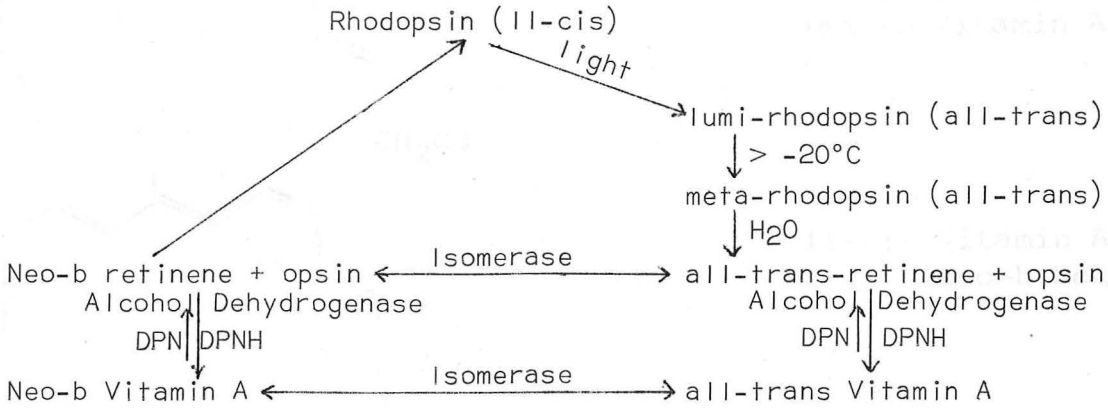
GENERAL METABOLISM OF VITAMIN A



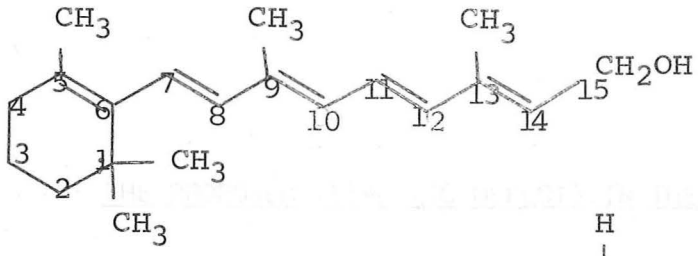
MAJOR PIGMENTS OF VERTEBRATE VISION



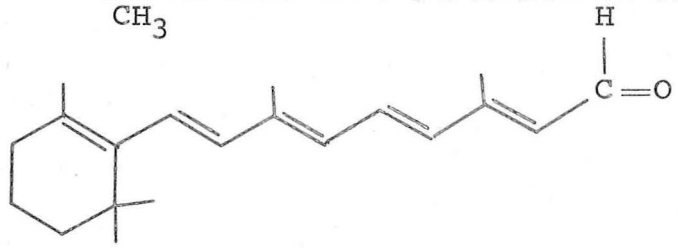
RHODOPSIN-RETINENE-VITAMIN A CYCLE



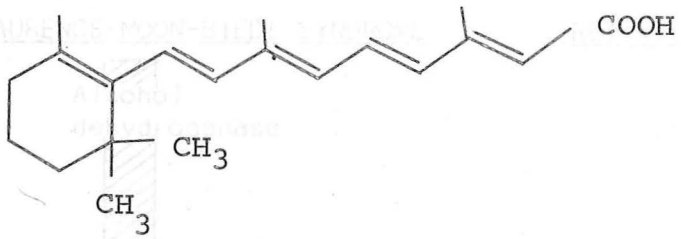
Physiological Isomers of Vitamin A and Retinene



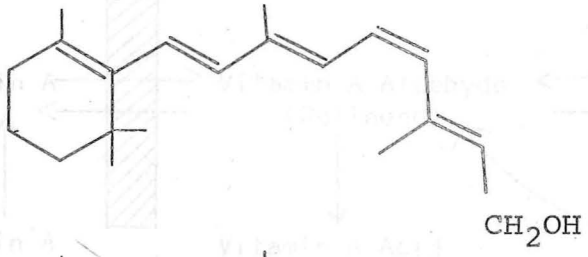
All-trans Vitamin A_1



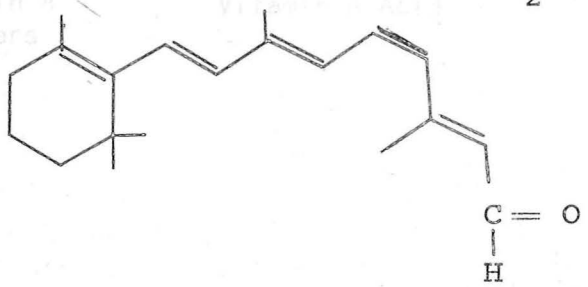
All-trans Vitamin A_1 aldehyde (Retinene)



All-trans Vitamin A_1 Acid



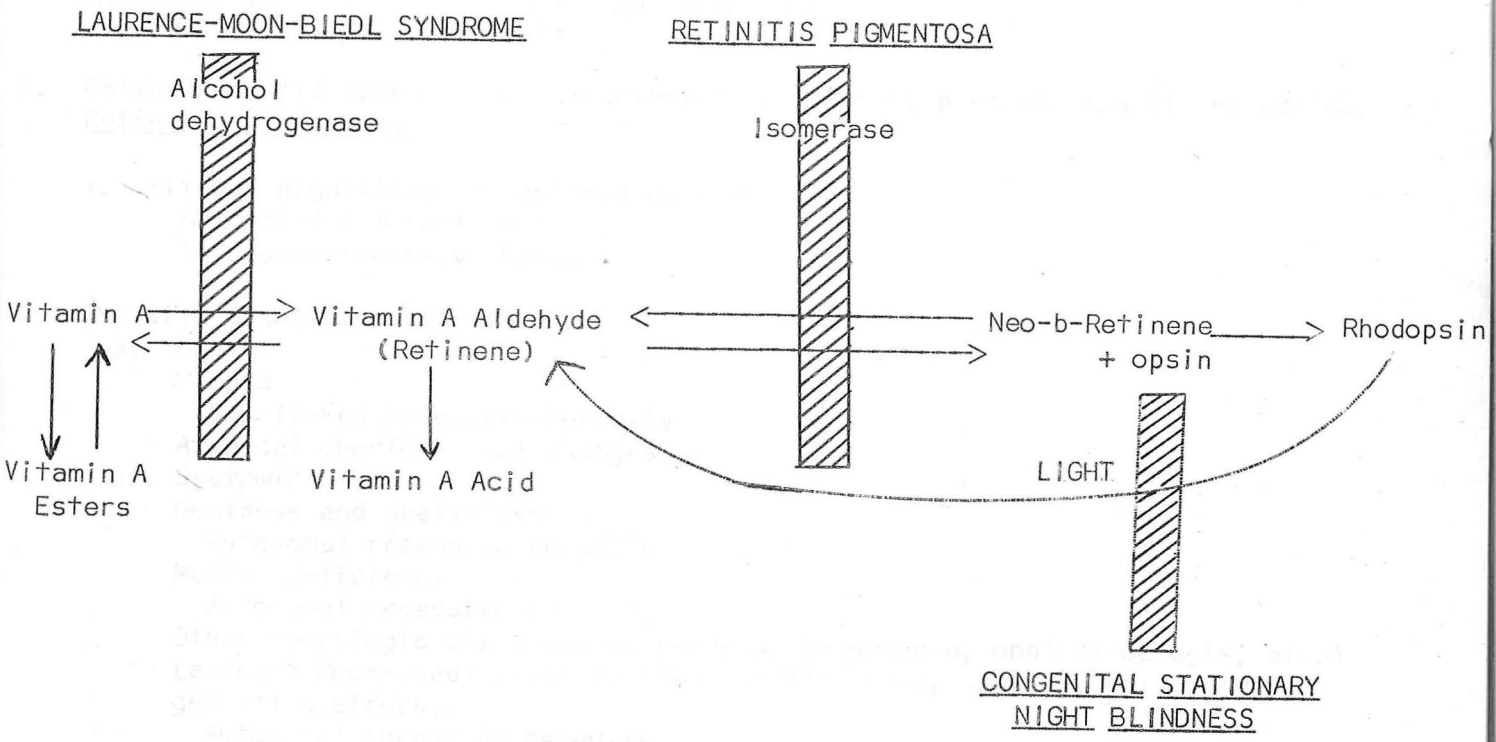
11-cis Vitamin A_1 (Neo-b Vitamin A_1)



11-cis Vitamin A_1 aldehyd (Neo-b Retinene)

Note: The Vitamin A_2 - Retinene$_2$ series differs only in that it contains a double bond in the 3-4 position. All visual pigments that have been analyzed contain as chromaphore the sterically hindered 11-cis isomen of retinene, or retinene$_2$ (neo-b).

THE PROPOSED METABOLIC DEFECTS IN THE CHORIORETINITIS SYNDROMES



PRIMARY CHORIORETINAL ABERRATIONS WITH NIGHT BLINDNESS
(after Leinfelder)

I. Congenital Stationary Night Blindness
A. Without ophthalmoscopic abnormality
Autosomal dominant heredity
Autosomal recessive heredity

B. Without ophthalmoscopic, but with other, abnormalities (myopia, amblyopia, nystagmus)
Sex-linked recessive heredity

C. Ophthalmoscopic appearances characterized by changes in color of the fundus.
Oguchi's disease.
Autosomal recessive heredity

D. Ophthalmoscopic appearances characterized by white dots in the fundus.
Retinitis punctata albescens (stationary type)
Autosomal recessive heredity

II. Delayed and Progressive Night Blindness
A. Ophthalmoscopic appearances characterized by white dots in the fundus.
Retinitis punctata albescens (progressive type)
Autosomal recessive heredity

B. Ophthalmoscopic appearances characterized chiefly by pigmentation of the retina.
Retinitis pigmentosa.

1. Without significant associated defects
Autosomal dominant heredity
Autosomal recessive heredity

2. With associated defects
a. Ocular
Myopia
Sex-linked recessive heredity
Atypical chorioretinal changes
b. Systemic
Deafness and deafmutism
Autosomal recessive heredity
Mental deficiency
Autosomal recessive heredity
Other neurologic disturbances (ataxia, paraplegia, ophthalmoplegis, etc.)
Laurence-Moon-Biedl syndrome (mental deficiency, obesity, polydactyly, genital dystrophy)
Autosomal recessive heredity

C. Ophthalmoscopic appearances characterized by depigmentation of the fundus.
Progressive atrophy of the choroid

1. Gyrate atrophy type
Autosomal recessive heredity

2. "Choroideremia" type
Sex-linked intermediate heredity
a. Male form
b. Female carrier form

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   This book includes a critical review of the difficulties in interpreting the large number of human studies on vitamin A deficiency.

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5. Dowling, F. E. and G. Wald. Nutritional night blindness. Proc. N. Y. Aca. Science 74:256, 1958.

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RETINITIS PIGMENTOSA

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Despite many suggestions of multiple alleles, at least 95% of the cases are due to a recessive defect, and it is possible that all cases are recessive in nature. Incidence of consanguinity is at least 20-30% of cases. Frequency of heterozygotes is 1 in 71 and of homozygotes 1 in 20,000. Most older reports in the literature of dominant varieties now thought to be examples of pseudodominance, although a few examples of true dominance may exist as well as a few cases of sex-linked recessive inheritance.

LAURENCE-MOON-BIEDL SYNDROME

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CONGENITAL NIGHT BLINDNESS

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COMPARISON OF COMMON NIGHT-BLINDNESS SYNDROMES

Disease	First Symptom	Course	Ophthalmological Examination	Mode of Transmission	Pathological Picture
Vitamin A Deficiency	Night Blindness	Progressive	Normal in Reversible Stages	Dietary Deficiency	Loss of Pigment Cell Layer with secondary degenerative changes
Retinitis Pigmentosa	Night Blindness	Progressive	Pigmentation of Retina	Recessive Defect (> 95%)	Resembles Vitamin A Deficiency
Congenital Stationary Night Blindness	Night Blindness	Stationary	Normal	Dominant (usually)	Normal
Laurence-Moon-Biedl Syndrome	Night Blindness	Progressive	Pigmentation of Retina	Recessive Defect	Resembles Vitamin A Deficiency