Pigment in animal tissue results from the union of 2 substances: a colorless chromogen and a ferment or enzyme which activates the chromogen. Where either of these is absent there is no pigment, or, if present but in insufficient amount, the tissue is lacking in pigment in a proportionate degree. Lack of pigment in tissue is known as albinism. It is a hereditary genetic defect. The entire body may be affected, or only certain parts may be albinotic, such as the hair, skin, or eyes. A portion of one organ may be albinotic without involving the whole.

Albinism is found among all vertebrates and in plants. I was unable to find any reference to albinism in invertebrates, but I know of no reason why it should not occur in the members of this division of zoology.

Albinism was known in antiquity. It was described by Hippocrates and was regarded by him as an inherited condition. The most complete investigation of the subject was conducted by Pearson, Nettleship and Usher, who published a 5-volume work in 1911. Their research was not limited to the eye, but considered albinism of all parts of the body. In their discussion of partial albinism they refer to a white forelock in several generations of a family.

In my own experience this was witnessed in 3 generations in direct lineage. A patient, aged 20 years, had a white forelock approximately 2 cm. in width which extended back from the hairline in the middle of the forehead for about 3 cm. The same condition was present in the mother and grandmother. Other tissues had normal pigment. The eyes presented no
anomaly. The patient’s mother stated that this white forelock had been present in several preceding generations of her family, was manifest only in females, and was transmitted by affected females. A full sister of the patient was not deficient in pigment.

In the discussion of ocular albinism, Pearson, Nettleship and Usher state: “The criterion of ocular albinism is lack or deficiency of the retinal epithelial pigment.” Then, they continued, “There is reason for believing that injurious deficiency of pigment may be restricted to the pigmented epithelium of the retina and possibly even to a part of the retina.”

In their publication they gave no record of any albinotic eye with a brown iris. The color was always blue or gray or there was even an entire absence of color. When there is an absence of pigment in the body of the iris the appearance is that of a pink membrane due to the fundus reflex being transmitted through the iris. According to their work, all of the physical manifestations of ocular albinism, besides the lack of color in the tissue—such as photophobia, nystagmus, and low visual acuity—are due to a deficiency of pigment in the epithelium of the retina. They were unable to find recorded or to obtain for microscopic examination human material that showed complete absence of pigment in the retina. They made the statement that total absence of pigment is found in the retinas of albino rabbits.

These authors give case records where senile cataract developed in human beings who successfully underwent surgery. They also state that many albinos are mentally deficient. Their researches showed that the life expectancy of the albino is not less than that for a normal person.

Waardenburg, according to Ida Mann, recognized 7 types of albinism as follows:

1. Universal albinism. The individual is totally deficient in pigment. There is underdevelopment of the macula and nystagmus.
2. Incomplete universal albinism. The patient is poor in pigment although it is not totally absent. The macula is underdeveloped. Nystagmus is not present in all cases. There may be head nodding.

3. Isolated eye or fundus albinism. The general pigmentation is normal, the eyes alone being deficient. The iris may be involved, sometimes only the fundus. The macula is underdeveloped. There may or may not be nystagmus and head nodding.

4. Aplasia or hypoplasia of the macula with or without deficient fundus pigmentation.

5. Aplasia or hypoplasia of the macula and the periphery of the retina with night blindness and contraction of the visual field.

6. Nystagmus with high myopia and poor visual acuity (probably defective macula) but with normal pigmentation.

7. Primary hereditary nystagmus without defective macula or albinism.

Waardenburg endeavors to classify each of the 7 groups according to inheritance and to state which is sex-linked, dominant, or recessive.

Ida Mann states that the existence of deficiency of pigment and underdevelopment of the macula in albinism are connected. A defect of the macula can occur with normal pigmentation, but the opposite condition, an albino with a normal macula, has not been reported. Her explanation is that normal pigmentation is necessary during the early stages of retinal differentiation and if such normal pigmentation has not taken place the higher differentiation of the retina can not occur.

Pipkin and Pipkin reported 11 albinos in 5 Negro families. They do not state interrelationship of the families. All had very fair skin with freckles in areas exposed to the sun. The iris color varied from light blue to cinnamon brown. Photophobia, nystagmus, low visual acuity, and strabismus were present in all members of the group. Evidently these persons
did not have complete ocular albinism; there was color in
the irides.

In another Negro family reported by the same authors, ear
pits and albinism were found to be dominant inherited char-
acteristics. Nothing was stated about the intelligence level or
of the fundus examination.

Riwchun reported a white male, aged 59, who had no pig-
ment in the skin, hair, or irides and who developed senile
cataract. Operation was successful with corrected vision
right eye 20/100, left eye 20/200 and near vision Jaeger No. 4
print. No statement was made concerning the intelligence
level but the impression was given that he had average men-
tal ability.

Wakefield and Dellinger reported albinism in identical
Negro twins whose parents had normal pigmentation. Exam-
ination of the ocular fundi revealed an absence of pigment.
There were photophobia, nystagmus, pink irides, and low
visual acuity. There was normal intelligence.

Windle and also McCracken reported albinism in twins.
The latter reported twins, not identical; one had normal pig-
ment and the other was an albino. No statement was made
about low mentality.

Swab reported albinism in one child, the progeny of Negro
and white parents. The intelligence level was low. There was
complete albinism of the skin, hair, and eyes. The suggestion
is made by him that photophobia may be overcome by use of
a dark contact glass with a small clear central opening. The
danger of this, as cited by him, is abrasion of the cornea from
nystagmus. I did not find record of anyone who had tried
this suggestion.

George M. Gould reported 9 cases of albinism in 2 fami-
lies. He described the affected individuals and their cardinal
ocular findings; namely, photophobia, nystagmus, amblyopia,
ametropia, the pink or colorless iris, and the absence of pig-
ment in the fundus.

I have 7 cases of ocular albinism to present for considera-
tion. Developmental anomalies of the eye other than albinism are present in 2 cases; associated anomalies of the central nervous system are present in 4 cases; horizontal movements of the head is present in 1 case; and anomalies of the ocular motor system other than nystagmus are present in 3 cases.

CASE REPORTS

CASE 1.—Waardenburg I. R. L. B., female, aged 13 years, is an example of complete albinism. Both parents are brunette and they are unrelated. There are 3 children older than the patient, 1 blonde and 2 brunette. The father stated that in his family a great-great aunt was an albino; that is, 3 generations removed from the patient. This is the only family history of albinism. The hair, eyebrows, and eyelashes are white and the skin has the characteristic pinkish-white color seen in albinos. When exposed to the sun, the skin becomes blistered but does not darken in color, and during the summer there is considerable trouble with inflammatory lesions of exposed skin.

Uncorrected visual acuity for each eye is 2/40. There are photophobia and nystagmus and each iris is pink in color. By oblique illumination each iris has a translucent gray color. The pupils are equal in size, round, and react in a normal manner to light and convergence stimuli. Color perception was tested on the Ishihara color plates and found to be normal. The visual fields are essentially normal. Retinoscopy under scopolamine disclosed 10 diopters of myopia. This correction did not improve the vision. There is no strabismus. Examination showed an almost complete absence of pigment in the eyegrounds. The blood vessels of the retina and choroid are visible over a light-colored background. There is no foveal reflex and no pathology of the discs. She has completed the sixth year of grade school. Difficulty is experienced in reading, and she was brought to me in the hope that something could be done to improve the vision. This child is not mentally deficient. The difficulty encountered in school is due to the low visual acuity. She should be in a sight-saving school.

CASE 2.—Waardenburg II. N. C., female, aged 23 years. This patient was employed in the office of a large manufacturing corporation. She complained that she suffered severe headaches, particularly when in bright light, and was subject to considerable ocular fatigue. She stated that her visual acuity had never been good. She
began wearing glasses at the age of 5. She had been able to complete her high school course, and since then had been employed in an office, typing and filing. There was no known family history of albinism.

The eyelashes, eyebrows, and hair were devoid of pigment. The skin was white but not so pale as in the first patient. She admitted that exposure to sunlight produced a marked erythema and she blistered very easily upon a short exposure. She stated that late in the summer her hands and exposed parts of her body would become darker in color than protected portions of her body, but that she always would blister if exposed for an hour or longer.

Each iris was a light blue color with a few brown flecks of pigment visible in the stroma. There was rapid horizontal nystagmus. The pupils responded promptly to light and convergence stimuli. Uncorrected vision was 5/40 for each eye. Corrected vision was 6/16. The lens determined for the right eye was minus 0.75 sphere plus 3.00 cylinder axis 90. For the left eye it was minus 0.75 sphere plus 3.50 cylinder axis 80. Examination of the fundi disclosed pale, washed-out, relatively colorless backgrounds over which the vessels of the retina and choroid were visible. There was slight pigmentation in the area of the macula. I was uncertain about the presence of a fovea.

When an effort was made to direct the gaze to the left, nystagmus became markedly increased in rapidity, and the excursions likewise were augmented. Nystagmus became slower as the gaze was directed to the right. Examination of the ocular motility in the cardinal directions of gaze showed partial paralysis of the left superior rectus muscle. Fixation was done with the right eye. It was necessary for her to turn the head somewhat toward the left and direct the eyes down and to the right in order to do her office work. There was no other disturbance of the central nervous or motor systems.

CASE 3.—Waardenburg II. H. F. R., male, aged 27 years, a graduate pharmacist, consulted me with the complaint of headache. Insofar as he knew there was no family history of albinism. His father was blond and his mother brunette. He was the only child of the family.

The eyelashes, eyebrows, and hair of the head and body were devoid of pigment. During the summer he was troubled greatly by various eruptive skin diseases affecting the exposed parts of the body. A brief exposure to sunlight produced blisters of the skin without darkening.
Uncorrected vision for each eye was 20/100. Corrected vision of the right eye 20/50, of the left 20/70. The correction was right eye plus 5 sphere plus 3 cylinder axis 75; the left eye plus 4 sphere plus 2 cylinder axis 120.

There was rapid horizontal nystagmus, and he had been troubled all of his life by bright light. The irides were of the translucent pale blue color. The pupils responded promptly to light and convergence stimuli. He stated that when he read it was necessary for him to turn his head to his left shoulder.

The patient was able to read 6-point print at approximately 30 cm. distance. It was observed that it was necessary for him to turn his head to his left shoulder and to direct the eyes down and to the right. Examination of the ocular motility in the different angles of gaze did not disclose any convincing evidence of a motor disturbance, and did not explain the peculiar position of the head and eyes when he read. It was found that nystagmus became more pronounced when the eyes were turned past the midline to the left. When the eyes were directed to the right, particularly right and down, the nystagmus was reduced to a barely perceptible movement.

The fundi showed an insufficient amount of pigment in the background, but not an absence as described in the first case. There was no pathology of the disc and there was a comparative increase in pigment in the region of the macula. I was unable to identify a fovea.

The patient returned to me 7 years after the first examination and complained of pain in the eyes and forehead. The right eye had become esotropic 15 to 20° when tested at 6 meters distance. He continued to read with the eyes turned down and to his right. I could not demonstrate the presence of a paretic muscle.

Case 4.—Waardenburg II. L. R. M., male, aged 7 months. There was no family history of albinism. The father was blond and the mother brunette. There was absence of pigment in the eyelashes, eyebrows, and hair. The skin was very fair. There was horizontal nystagmus.

The irides consisted of narrow bands of pale blue tissue of 1.5 to 2 mm. width. There was no evidence of an iris sphincter and consequently no movement of the pupil when the eye was exposed to light. Many fine spider-web strands of a congenital pupillary membrane passed across each pupil. The right fundus was devoid of pigment and the disc was white. The left fundus showed a very
Fig. 1.—Test charts.
Fig. 2.—Test charts.
pale background, but there was evidence of pigment about the macula, and the disc was no so pale as that in the right eye.

Light thrown upon the right retina did not elicit any response such as directing the eye toward the light. A light cast upon the left eye induced the infant to follow the light and also to forcibly squeeze the eyelids to defend itself from the light.

**Case 5.**—Waardenburg II. G. P., female, aged 3 years. The parents had observed that the eyes had peculiar rhythmical motion, and that the child was very sensitive to light. They had noted that she was awkward and did not appear to have vision comparable to other children. There was no family history of albinism or of ocular defects. The skin and hair were white. Horizontal nystagmus was marked. Bilateral anterior capsular cataracts were present. There was a coloboma of the mesodermal tissue of the pale blue iris of the right eye, and it was directed toward 7:30 o'clock. The right pupil was enlarged to approximately 6 mm. in diameter. It did not respond to light. The iris was not adherent to adjacent structures. The left pupil was approximately 5 mm. in diameter and responded promptly to direct and consensual light and convergence stimuli. The iris of the left eye presented no defect in structure, and was of the same color as the right one. Examination of the fundi showed an almost complete absence of pigment. I was unable to determine the presence of a fovea. Tactile tension was normal.

**Case 6.**—Waardenburg II. R. R., white male, aged 28 years. He reported to me in March, 1944 for removal of a foreign body from the cornea. He stated that his father was blond and his mother brunette. There is no previous history of albinism. A younger brother, the only other child of the family, also is an albino.

The skin, hair, eyebrows, and eyelashes of the patient are devoid of pigment. Exposure to sunlight does not tan the skin but produces blisters. During the summer he is troubled by eruptive skin diseases.

The irides are pale blue and the pupils respond promptly to light. A beam of light can pass through the body of the iris and illuminate the interior of the eye so that the fundus can be viewed with an unlighted ophthalmoscope. Conversely, if light is passed through the pupil it filters through the body of the iris and is visible to the observer. He suffers greatly from photophobia.

Uncorrected visual acuity is 6/60 for each eye. Corrected visual acuity, right eye 6/30; left eye 6/25. The best lens correction is
plus 2.00 sphere plus 1.00 cylinder axis 90 for each eye. Color perception and visual fields are normal.

The right eye is divergent. There is paralysis of the left inferior oblique muscle. Fixation is performed with the left eye. Horizontal nystagmus is present, the arc and frequency of which is lessened when the gaze is directed to the right but increased when the gaze is directed to the left. With his glasses he is able to read 5-point print when the eyes are turned down and to the right.

The fundi are of the exaggerated blonde type with a pinkish-white background over which pass the vessels of the retina and choroid. Each disc appears to be normal. There is no foveal reflex.

Case 7.—Waardenburg II. C. McC., white female, aged 8 years. There is no family history of albinism. At the age of 5 months it was observed by the parents that the patient turned her eyes to the right in order to view an object. Nystagmus and photophobia were observed. The skin, hair, eyebrows, and eyelashes are white and devoid of pigment. She is troubled during the summer with eruptive skin diseases.

Uncorrected visual acuity for each eye was 6/40. Corrected visual acuity for each eye was 6/20. The lens correction was found to be for the right eye minus 0.25 sphere plus 2.25 cylinder axis 90; for the left eye plus 2.25 cylinder axis 90. Color perception was tested on the Ishihara color plates and found to be normal.

The irides are pale blue. The pupils react normally to light and convergence stimuli.

The fundi are the extreme blonde type with a light pink background. The discs and blood vessels appear normal. There is no foveal reflex.

Horizontal nystagmus is present with an associated side-to-side movement of the head on the vertical axis. As the eyes are directed to the right the nystagmus and head movements slow down until the movements are imperceptible. When the eyes are rotated toward the midline the arc and frequency of the nystagmus, together with the head movements, increase. The right and left components of the nystagmus are equal. The patient is unable to rotate the eyes more than a few degrees past the midline to the left. The head cannot be turned to the left shoulder. The patient walks with the head erect with horizontal rhythmical movements of the head and eyes. There is no other defect found of the central nervous system.
DISCUSSION

According to the classification of Waardenburg, Case 1 is to be placed in group 1 since there was complete albinism of the skin, hair, iris, and fundus. The remaining 6 cases are to be placed in group 2 since there is some pigment in the iris. The patient listed as Case 7 presented side-to-side movement of the head which can be considered analogous to head nodding.

The 2 patients listed as Cases 4 and 5, respectively, have congenital anomalies of the eye other than albinism. The 4 eyes of these 2 patients present absence of the sphincter muscle and partial aniridia in 2 eyes, congenital pupillary membranes in 2, atrophy of the disc in 1, bilateral capsular cataract in 2, and coloboma of the mesodermal tissue of the iris in 1 eye.

Motor anomalies other than nystagmus are found in patients listed as Cases 2, 3, and 6, respectively. Case 3 developed esotropia, probably of accommodative origin. Cases 2 and 6 each presented paralysis of an extra-ocular muscle which evidently was present at birth; there was no history of injury or illness to account for the muscle paralysis.

The explanation of the congenital anomalies of the eyes found in Cases 4 and 5 will be left to those who have made a more thorough study of embryology of the eye than I have been able to accomplish. The interesting fact is that structural anomalies of the eye are present in addition to albinism.

Cases 2, 3, 6, and 7 give unmistakable evidence of anomalies of the central nervous system. This is shown by the change in the character of the nystagmus when the gaze is shifted from the right to the left. The nystagmus lessens to almost total abolition when the eyes are rotated to one side and then becomes accentuated in extent of arc and frequency as the eyes are rotated to the opposite side. This suggests an incomplete conjugate paralysis of the coordinated movements of the eyes. The lesion is on the side to which the nystagmus is increased. This cannot be explained upon the
basis of a paralyzed muscle because there was no clinical evidence of paralysis of a horizontal acting muscle and Case 6 had right exotropia.

Case 7 has in addition to nystagmus an associated side-to-side movement of the head, and the two are varied in time and intensity as the gaze is shifted from the right to the midline. This patient was unable to turn the head or eyes to the left. The head movement and nystagmus lessened when the gaze was directed to the right until there was a very slight movement.

This patient has complete paralysis of the associated movements of the eyes and head to the left.

The simplest and most common site of a lesion that produces paralysis of the conjugate movements of the eyes to one side is that part of the abducens nucleus which governs conjugate movements of the eyes.

An incomplete destruction of this part of one abducens nucleus would incompletely paralyze the conjugate movements of the eyes to that side. The clinical picture presented by the nystagmus would be altered by addition of the incomplete conjugate paralysis. This would explain the findings for Cases 2, 3, and 6, but does not explain the findings of Case 7.

The site of a lesion that would cause a marked variation in nystagmus when the eyes are directed from one side to the other, and also, as in Case 7, an associated side-to-side head movement, must be placed in the association track or centers of the central nervous system above the level of the nuclei of the individual muscles. The dorsal longitudinal bundle is such an association pathway. Aplasia of this tissue and of the adjacent nucleus of Deiters can explain the clinical phenomenon described.

**Summary**

Seven cases of generalized albinism have been described. Two had anomalies of the eye other than albinism and 4 presented evidence of anomalies of the central nervous system.
Two patients are infants and a fair consideration of their intelligence level cannot be made. The remaining 5 show no evidence of mental deficiency.

CONCLUSION

Albinism is aplasia of tissue of ectodermal origin in which there may occur anomalies of the central nervous system as well as deficiency of pigment of the skin, hair, ocular fundus, and iris.

BIBLIOGRAPHY


——, and ———: Ibid., 34:240, 1943.


DISCUSSION

Dr. HARRY S. GRADLE, Chicago, Ill.: This excellent paper by Dr. Clark presents so many opportunities for discussion of various phases that I wish to limit myself to one particular aspect; namely, the histologic picture.

The first description was made by Fritsch in 1907, but it was not until 1913 that Elschnig presented serial sections of the albinotic eye. I wish to quote from his article: "Serial sections showed the absence of a fovea centralis. In this central area of an albinotic eye the ganglion cell layer is somewhat thickened as in the normal eye, the nerve fibre layer is reduced to a layer of very delicate nerve fibres that can be differentiated sharply from the membrana limitans interna, in an area of about 6 mm. diameter. In the center of this area, the rods and cones are somewhat elongated, the external nuclear layer somewhat thinned and merges indistinctly with the sponged over inner nuclear layer. The other layers are about normal."
These findings were later corroborated by Gilbert, Velhagen and Usher.

Such lack of foveal differentiation easily can be detected ophthalmoscopically, in such cases where the nystagmus can be controlled. There is to be seen only a slight depression of the fovea and a marked diminution of foveal reflex.

Anatomically, this is very much the same picture as is shown in the embryonic eye at between the sixth and seventh, according to Bach and Seefelder. The correlation of the ophthalmoscopic and the histologic picture explains the poor vision of these cases.

May I add one point found in practical experience? When fitted between the ages of 8 and 12, such albinotic children are able to use telescopic spectacles so satisfactorily that their collegiate education can be completed without great difficulty.

AMYLOID DISEASE OF THE CONJUNCTIVA

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Amyloid is a term used to designate a product that appears as a formed element in certain intercellular regions during the course of seemingly diverse pathologic states. It is characterized morphologically by its deposition in elective sites, its more or less dependable affinities for several unrelated stains, and its homogeneity. Recent work indicates that amyloidosis is not a degenerative disease, but the result of a long-continued metabolic disorder, probably protein in nature.

The disease is referred to briefly by Fuchs,¹ Collins and Mayou,² De Schweinitz,³ Berens,⁴ Wolff,⁵ and more in detail by Duke-Elder,⁶ who states that: "The disease attacks as a general rule young adults, especially between 25 and 30 years of age, affecting either one or both eyes; about two-thirds of the cases are bilateral. The degeneration is local and its cause is quite unknown, for the sufferers are almost invariably healthy and are not subjects of general amyloid disease; but it has a parallel in localized degenerations elsewhere—in the larynx (Courvoisier, 1902), the lung (Hersheimer, 1903), and