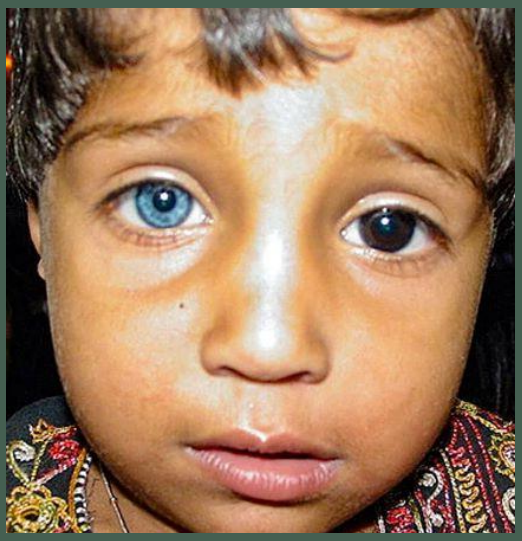


Waardenburg Syndrome and Homoeopathy

Dr. Rajneesh Kumar Sharma MD
(Homoeopathy)

Waardenburg Syndrome and Homoeopathy

© Dr. Rajneesh Kumar Sharma M.D. (Homoeopathy)
Homoeo Cure & Research Institute
NH 74, Moradabad Road, Kashipur (Uttarakhand) INDIA
Pin- 244713 Ph. 05947- 260327, 9897618594
E. mail- drrajneeshhom@hotmail.com
www.treatmenthomeopathy.com
www.cureme.org.in

Contents

Auditory-pigmentary syndromes are caused by physical absence of melanocytes from the skin, hair, eyes, or the stria vascularis of the cochlea. Dominantly inherited examples with patchy depigmentation are usually labelled Waardenburg syndrome (WS). (Psora/ Syphilis)

Definition

Waardenburg syndrome is a rare autosomal dominant disorder characterized by patchy depigmentation, sensorineural hearing loss, and other developmental defects (Psora/ Syphilis).

Incidence

Autosomal dominant inheritance	Autosomal recessive inheritance
Patient's siblings: not increased unless one of the parents is also affected	Patient's siblings: 25%
Patient's offspring: 50%	Patient's offspring: not increased unless the spouse is a carrier or affected

Types

The four types of Waardenburg syndrome				
Type	**MIM**	**Inheritance**	**Distinguishing feature**	**Comments**
I	193500	AD	Dystopia canthorum W> 1.95	Nearly all have PAX3 mutations
II	193510	AD	No dystopia	Heterogeneous; 15% have MITF mutations
III (Klein-Waardenburg)	148820	AD (most cases sporadic)	Hypoplasia of limb muscles; contractures of elbows, fingers	Variant presentation of WS 1; mostly PAX.3 heterozygotes; some may be homozygotes
IV (Shah-Waardenburg)	277580	Mostly AR	Hirschsprung's disease	Heterogeneous; includes homozygotes for EDN3 or EDNRB mutations

Inheritance: genetic heterogeneity

- Autosomal dominant
    - Type I (Waardenburg syndrome; presence of dystopia canthorum) (Psora/ Syphilis)

  - Type II (Waardenburg syndrome with ocular albinism; absence of dystopia canthorum) (Psora)
  - Type III (Klein-Waardenburg syndrome; presence of musculoskeletal abnormalities) (Psora/ Sycosis/ Syphilis)
- Autosomal recessive
  - Type IV (Shah-Waardenburg syndrome or Waardenburg-Hirschsprung disease) (Psora/ Sycosis)

Causes

- Type I and Type III
  - Mutations in PAX3 (paired box) gene on chromosome 2q35
- Type II
  - Mutations in MITF (microphthalmia associated transcription factor) gene on chromosome 3p12-p14.1
- Type IV
  - Mutations in the genes for endothelin-3 (EDN3) on chromosome 13q22 or endothelin B receptor (EDNRB) on chromosome 20q13.2–q13.3
  - Mutations in SOX10 gene on chromosome 22q13

Symptoms

1. Waardenburg syndrome has a wide clinical spectrum.

2. Facial appearance

a. Dystopia canthorum (lateral displacement of the medial canthi) (Psora/ Syphilis)

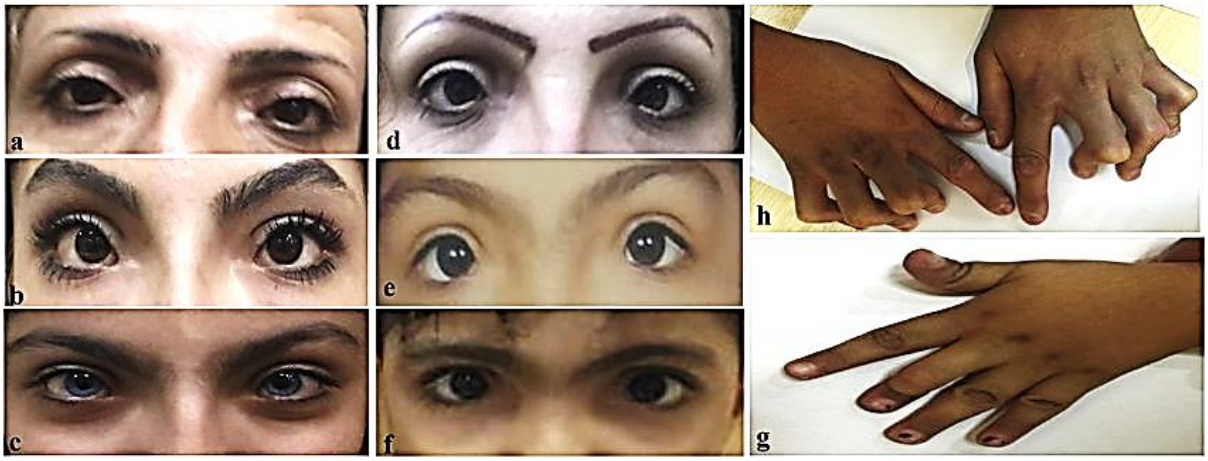
b. Bushy eyebrows with synophrys (Sycosis)

c. A narrow nose with prominent nasal root (Psora/ Sycosis)

d. Marked hypoplasia of the nasal bone (Psora)

e. Short philtrum (Psora)

f. Short/retro positioned maxilla (Psora/ Syphilis)



Facial characteristics and joints contractures - Dystopia canthorum in II8 (a), III-7 (b), III-8 (c), II-2 (d), III-1 (e), and III-2 (f); Blue irides in III-8 (c); Prominent/broad nasal root in II-8 (a), III-7 (b), III-8 (c), II-2 (d), III-1 (e), and III-2 (f); Limb joints contracture in II-2 (g) and III-2 (h)

3. Congenital sensorineural deafness (deaf-mutism) (Psora/ Syphilis)

4. Pigmentary abnormalities (Psora/ Syphilis)

a. Cutaneous pigmentary abnormalities

i. Achromatic spots, with sharply defined irregular borders and containing scattered islands of hyperpigmention, resemble those of piebaldism (Psora)

ii. Hyperpigmented macules on normally pigmented skin showing as “patchy skin” and giving a “dappled appearance” (Psora)

b. Hair pigmentary abnormalities

i. White forelock (may be evident at birth, soon afterwards, or develop later) (Psora)

ii. Premature graying of the scalp hair and of the eyebrows, cilia, or body hair (Psora/ Syphilis)

c. Fundus pigmentary abnormalities

i. Albinotic fundi (generalized retinal hypopigmentation) (Psora)

ii. Pigmentary mottling in the periphery (Psora)

d. Partial albinism (Psora)

e. Heterochromia (different color) of the iris (Psora)

f. Bilateral isohypochromia iridis (pale blue eyes) (Psora)

g. Ocular albinism (type II) (Psora)

5. Musculoskeletal abnormalities (type III, Klein-Waardenburg syndrome)

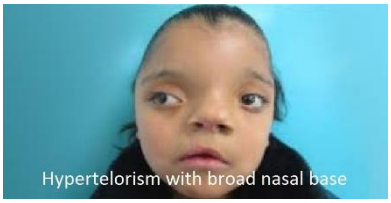
a. Ortho-osteomyo-dysplasia of the upper limbs (Psora/ Syphilis)

b. Bilateral upper limb defects (Psora/ Syphilis)

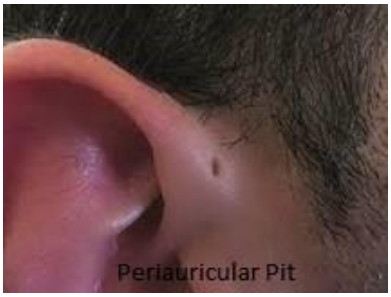
c. Flexion contractures (Psora/ Sycosis/ Syphilis)

d. Fusion of the carpal bones (Psora/ Syphilis)

e. Syndactyly (Psora)



6. Congenital aganglionic megacolon association (type IV, Shah-Waardenburg syndrome, Waardenburg-Hirschsprung syndrome) (Psora/ Sycosis)

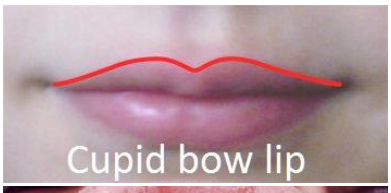


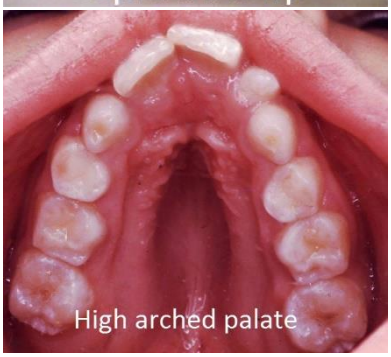
7. Occasional associated anomalies

- Cleft lip/palate (Psora/ Syphilis)
- Neural tube defects (Psora)
- Facial asymmetry (Psora)
- Facial palsy (Psora)
- Hypokalemic periodic paralysis (Psora)
- Preauricular pit (Syphilis)
- Hypoplasia of the middle ear ossicles (Psora)
- Blepharoptosis (Psora)
- Microphthalmia (Psora)

Blepharoptosis

- Iris coloboma (a hole in one of the structures of the eye, such as the iris, retina, choroid, or optic disc) (Psora/ Syphilis)
- Esophageal atresia with tracheo-esophageal fistula (Syphilis)
- Hypertelorism (Psora/ Sycosis)
- High arched palate (Psora/ Sycosis/ Syphilis)
- Fixed dilated pupil, anterior lenticonus (Psora/ Sycosis)
- "Cupid bow" configuration of the upper lip (Psora)
- Microcephaly (Psora/ Syphilis)
- Mental retardation (Psora/ Syphilis)
- Polythelia (the presence of an additional nipple) (Psora/ Sycosis)
- Prognathism (jaws protrude beyond a predetermined imaginary line in the coronal plane of the skull) (Psora/ Sycosis)
- Hyperkeratosis of palms and soles (Psora/ Sycosis/ Syphilis)
- Imperforate anus (Psora/ Syphilis)
- Bifid spine (Psora/ Syphilis)
- Vertebral agenesis (Psora)
- Absence of vagina and right adnexal uteri (Psora)
- Syndactyly (Psora)
- Cardiovascular anomalies (Psora/ Syphilis)
- Urinary anomalies (Psora/ Syphilis)
- Black forelock (Psora)
- Hyperpigmented skin lesions (Psora/ Sycosis)





Diagnosis

Diagnostic criteria for Waardenburg type 1 and type 2 as proposed by the Waardenburg Consortium. To be affected with Waardenburg type 1, an individual must have two major or one major plus two minor criteria. To be affected with Waardenburg type 2, an individual should show two major features.

a. Major criteria

i. Congenital sensorineural hearing loss

ii. Pigmentary disturbances of iris

a) Complete heterochromia iridum (two eye of different color)

b) Partial or segmental heterochromia (segments of blue or brown pigmentation in one or both eyes)

c) Hypoplastic blue eyes (characteristically brilliant blue in both eyes)

iii. Hair hypopigmentation (white forelock)

iv. Dystopia canthorum

v. Affected first degree relatives

b. Minor criteria

i. Congenital leukoderma (several areas of hypopigmented skin)

ii. Synophrys or medial eyebrow flare

iii. Broad and high nasal root

iv. Hypoplasia of alae nasi

v. Premature graying of hair (scalp hair predominantly white before age 30)

Common tests

1. Audiologic evaluation for hearing loss

2. Histochemical studies of achromic skin

a. Absent melanocytes

b. Presence of only a few dihydroxyphenylalanine (dopa)-positive cells

3. Ultrastructural findings of depigmented skin

a. Absence or dramatically reduced melanocytes

b. Dendritic cells containing poorly melanized melanosomes

c. Absence of melanosomes in the keratinocytes

4. Chromosome abnormalities observed in Type I Waardenburg syndrome

a. Inversion 2q35-q36.1

b. Deletion 2q35-q36.2

c. Del(2)(q34;q36.2)

5. Molecular studies of mutations for different types of Waardenburg syndrome

a. Waardenburg syndrome type I: PAX3 gene mutation

b. Waardenburg syndrome type II: 15–20% of cases have heterozygous mutation in the MITF gene

c. Waardenburg syndrome type III: interstitial deletion of chromosome 2(2q35-q36.2) including the PAX3 gene

d. Waardenburg syndrome type IV:

i. Mutations in the gene encoding endothelin-3 (Edn 3) or one of its receptors, the endothelin-B receptor (Ednrb)

ii. Mutations in SOX10

Differential diagnosis

Conditions Causing Albinism or Partial Albinism

Albinism is lack of pigment in skin, hair, or eyes. Major conditions simulating WS are-

Nevus anemicus

Nevus anemicus is a congenital deficiency of terminal blood vessels.

Hypomelanosis of Ito (Ito Syndrome)

This genetic condition occurs sporadically and presents with symmetric depigmented streaks, patches, swirls, or sprays on the skin. These problems are present at birth and are sometimes accompanied by wide-set eyes and anomalous auricles. Skeletal anomalies have been reported in some cases.

Piebaldism

It is an autosomal-dominant condition presenting with areas of depigmented skin frequently on the head and trunk, as well as in the eyebrows, eyelids, eyelashes, and forelock. Heterochromia iridis may be present. Deafness is not a characteristic of this syndrome, nor is broad nasal root or dystopia anthorum.

Oculocutaneous Albinism/Ocular Albinism

Oculocutaneous albinism produces total absence of pigment in all of the individual's skin, hair, and eyes. If pigment is lacking only in the eyes the condition is called ocular albinism. The patient often experiences photophobia, strabismus, nystagmus and low vision.

Vitiligo

Vitiligo is an autoimmune disorder that has been associated with mutations on chromosomes 1, 7, 8, and 4. Depigmented patches of skin are common on the face, hands, feet, elbows, knees, and chest. Hair may lose pigment, and the depigmented areas of skin may increase in size.

Conditions Producing Heterochromia Iridis

Heterochromia iridis occurs as an occasional anomaly in a number of syndromes, including Horner's syndrome and piebaldism. The condition may also be associated with disease and trauma.

Horner Syndrome

Horner syndrome or oculosympathetic paresis results from an interruption of the sympathetic nerve supply to the eye and is characterized by the classic triad of miosis (constricted pupil), partial ptosis, and hemifacial anhidrosis.

Eye Trauma

Eye trauma may destroy the pigment layer of the iris and lead to formation of scar tissue.

Treatment

Since this is a genetic condition, whole organism is badly affected and treatment becomes very difficult. The treatment of WS is directed toward the specific symptoms that are apparent in each individual. Such treatment may require the synchronized efforts of a team of medical professionals of dermatologists, ophthalmologists, orthopedists, gastroenterologists, speech-language pathologists, physical therapists, and many others. Thus, a holistic system of treatment is needed.

Homoeopathic treatment of Waardenburg syndrome

Homoeopathy is the science of individualization. It treats the person, not the disease. The whole constitution, including mental and physical components is entirely restored to health if Homoeopathic treatment is given to the sick individual. The common remedies for Waardenburg syndrome are-

Belladonna

Adapted to bilious, lymphatic, plethoric constitutions; persons who are lively and entertaining when well, but violent and often delirious when sick.

Women and children with light hair and blue eyes, fine complexion, delicate skin; sensitive, nervous, threatened with convulsions; tuberculous patients.

Great liability to take cold; sensitive to drafts of air, especially when uncovering the head; from having the hair cut; tonsils become inflamed after riding in a cold wind (Acon.; Hep.; Rhus takes cold from exposure of feet, Con., Cup., Sil.).

Bromium

It acts best, but not exclusively, on persons with light-blue eyes, flaxen hair, light eyebrows, fair, delicate skin; blonde, red-cheeked, scrofulous girls.

Sensation of cobweb on the face (Bar., Bor., Graph.). Fan-like motion of alae nasi (Ant. t., Lyc.).

Brom. and Iod. is, the former cures the blue-eyed and the latter the black-eyed patients."-HERING.

Calcarea carbonica

Leucophlegmatic, blond hair, light complexion, blue eyes, fair skin; tendency to obesity in youth. Psoric constitutions; pale, weak, timid, easily tired when walking. Disposed to grow fat, corpulent, unwieldy.

Children with red face, flabby muscles, who sweat easily and take cold readily in consequence. Large heads and abdomens; fontanelles and sutures open; bones soft, develop very slowly. Curvature of bones, especially spine and long bones; extremities crooked, deformed; bones irregularly developed.

Capsicum annuum

Persons with light hair, blue eyes, nervous but stout and plethoric habit.

Lobelia inflata

Best adapted to persons of light hair, blue eyes, fair complexion; inclined to be fleshy. For the bad effects of drunkenness in people with light hair, blue or grey eyes, florid complexion, corpulent, Lobelia bears the same relation that Nux vomica does to persons of the opposite temperament.

Pulsatilla pratensis

Adapted to persons of indecisive, slow, phlegmatic temperament; sandy hair, blue eyes, pale face, easily moved to laughter or tears; affectionate, mild, gentle, timid, yielding disposition- the woman's remedy.

Sulphur

Sulphur people may have any complexion, but the most common are fair or red haired, with blue, green or grey eyes, and black-haired with blue or grey eyes. The eyes frequently appear to have a sparkling quality, and also often have a dreamy, far-away look. The eyebrows are frequently very

bushy, and either curl up at both outer edges, or one end curls up and the other curls down, producing a somewhat comical appearance.

Tuberculinum bovinum Kent

Adapted to persons of light complexion; blue eyes, blonde in preference to brunette; tall, slim, flat, narrow chest; active. The potencies of Fincke and Swan were prepared from a drop of pus obtained from a pulmonary tubercular abscess or sputa.

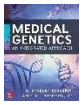
Bibliography

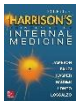

Atlas of genetic diagnosis and counseling.. HAROLD CHEN, MD, FAAP, FACMG.. Humana Press Inc. 999 Riverview Drive, Suite 208 Totowa, New Jersey 07512.. Waardenburg Syndrome 1035


Chapter 54. Hereditary Hearing Impairment > Waardenburg Syndrome CURRENT Diagnosis & Treatment in Otolaryngology—Head & Neck Surgery, 3e... Of the six genes identified in Waardenburg syndrome, four belong to the family of transcription factors that bind DNA and regulate its transcription. The other two genes are members of the group of endothelins and are involved in the development of neural crest-derived cells, which evolve...inheritance...

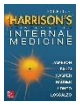

Chapter 73. Albinism and Other Genetic Disorders of Pigmentation > Waardenburg Syndrome Fitzpatrick's Dermatology in General Medicine, 8e... Table 73-2 Waardenburg and Tietz Syndrome Characteristics Disorder Clinical Signs Mutated Gene(s) Waardenburg syndrome (WS) type I Hypopigmented patches, heterochromia irides, dystopia canthorum, sensorineural deafness (~75%) PAX3 WS type II Same as type I...


Encyclopedia Homoeopathica


Key Genetic Diseases, Disorders, and Syndromes > Dysmorphology Syndromes/Malformations Medical Genetics: An Integrated Approach... stenosis Saethre-Chotzen syndrome Sotos syndrome VATER association van der Woude syndrome Waardenburg syndrome Williams syndrome ...


Principles of Human Genetics > Regulation by Transcription Factors Harrison's Principles of Internal Medicine, 20e... missense mutations) Spinobulbar muscular atrophy (CAG repeat expansion) Zinc finger proteins WT1 WAGR syndrome: Wilms' tumor, aniridia, genitourinary malformations, mental retardation Basic helix-loop-helix MITF Waardenburg's syndrome type 2A Homeobox IPF1...


Radar 10



Skin Manifestations of Internal Disease > HYPOPIGMENTATION Harrison's Principles of Internal Medicine, 20e... Incontinentia pigmenti (stage IV) Tuberous sclerosis Waardenburg syndrome and Shah-Waardenburg syndrome a Absence of melanocytes in areas of leukoderma. b Normal number of melanocytes. c Platelet storage defect and restrictive lung disease secondary to deposits of ceroid-like...

Waardenburg Syndrome Clinical Genomics: Practical Applications in Adult Patient Care


Radar Opus 2.1.11