

Cerebral Autosomal Recessive Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CARASIL) and Homoeopathy

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DEFINITION

CARASIL or Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy is an inherited condition, characterized by early-onset changes in the deep white matter of the brain observed on MRI and associated neurological findings including early-onset gait disturbances, premature scalp alopecia, ischemic stroke, acute dorsal to lower back pain with degeneration of the discs and progressive cognitive disturbances leading to severe dementia and ultimately fatal outcomes.

ETYMOLOGY

- CARASIL (Cerebral Autosomal Recessive Arteriopathy with Subcortical Infarcts and Leukoencephalopathy)- by Nemoto in 1960
- Familial young-adult-onset arteriosclerotic leukoencephalopathy with alopecia and lumbago without arterial hypertension
- Maeda syndrome- by Maeda in 1965
- Nemoto disease- by Nemoto in 1960
- In 2009, Hara et al identified homozygous mutations in the HTRA1 gene on chromosome 10q25

PREVALENCE

- Rare
- Primarily seen in Japan and China
- A male predominant disorder

ETIOLOGY

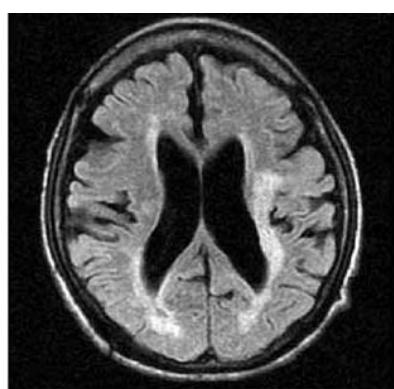
- CARASIL is a single-gene disorder
- Directly affects the cerebral small blood vessels
- Caused by mutations in the HTRA1 gene encoding HtrA serinepeptidase/protease 1 (HTRA1)

As its name suggests, this condition is inherited in an autosomal recessive pattern (Syphilis). The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

PATOPHYSIOLOGY

CARASIL presents with intense arteriosclerosis (Syphilis/ Sycosis), mainly in the small penetrating arteries, without granular osmiophilic materials (reacting to or staining with osmium tetroxide usually by the formation of a black deposit) or amyloid deposition (Sycosis). Histopathology slide shows-

- Fibrous intimal proliferation (Psora)
- hyaline degeneration of the media (Syphilis)
- thickening and splitting of the internal elastic lamina (Sycosis)
- concentric narrowing of the lumen (Psora/ Sycosis)

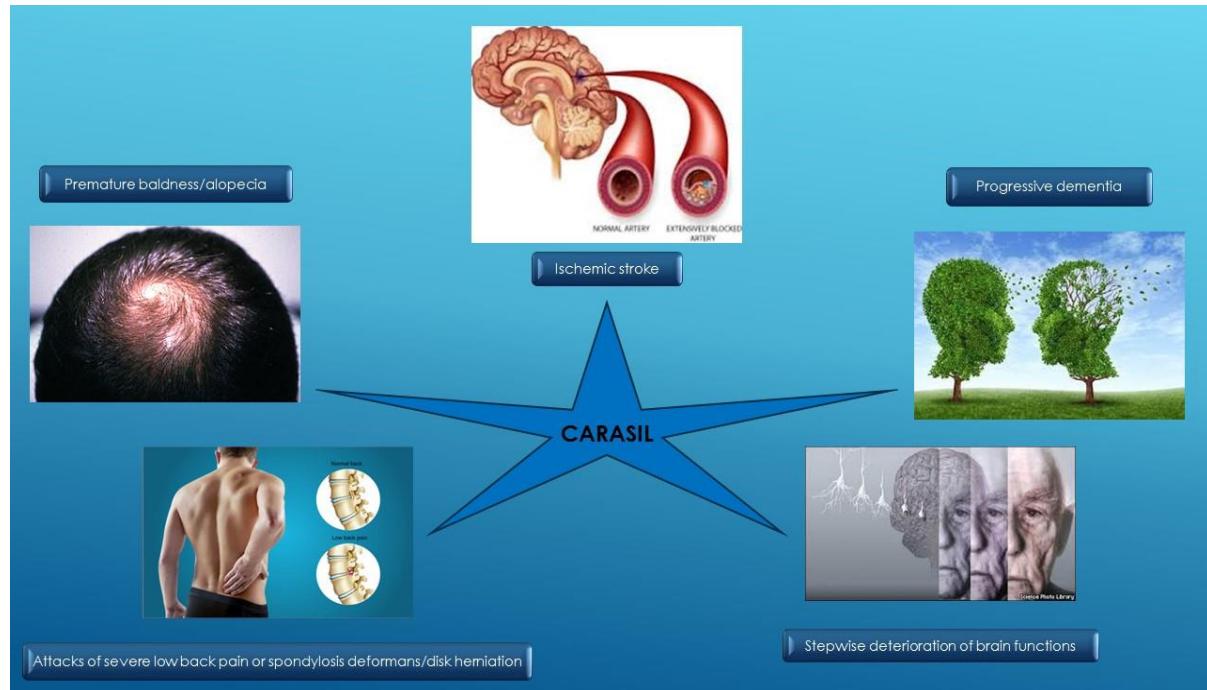


Flair Axial MRI Brain showing white matter hyperintensities with sparing of U fibres

Each of the small arterial changes is intense in the cerebral medullary and leptomeningeal arteries, leading to multifocal, confluent, or diffuse ischemic changes in the cerebrum.

SIGNS AND SYMPTOMS

CARASIL is a systemic disease, mostly driven by Syphilitic miasm. As soon as Psora intervenes it, the worst form of suffering is developed in long run. Sycosis often complicates it in terminal stage of the disease.



CARDINAL SYMPTOMS OF CARASIL

- Ischemic stroke (Psora)
- Stepwise deterioration of brain functions (Syphilis)
- Progressive dementia (Syphilis)
- Premature baldness/alopecia (Psora/ Syphilis)
- Attacks of severe low back pain or spondylosis deformans/disk herniation (Psora/ Syphilis)

At twenties or thirties of age, the abnormalities affecting the brain and other parts of the nervous system start to appear. The first signs of the disorder are-

- Muscle stiffness (spasticity) in the legs (Psora/ Sycosis)
- Problems with walking (Psora/ Syphilis)

Before age of 40, about half of affected individuals have a stroke or similar episode. As the disease progresses, most people with CARASIL develop-

- Mood and personality changes (Psora)
- Decline in thinking ability (Syphilis)
- Memory loss (dementia) (Psora/ Syphilis)
- Worsening problems with movement (Syphilis)

Other characteristic features of CARASIL are-

- Alopecia beginning during adolescence and limited to the scalp (Psora)
- Attacks of low back pain developing in early to mid-adulthood, caused by degeneration of the intervertebral discs (Psora/ Syphilis)

The signs and symptoms of CARASIL worsen slowly with time. After several years, affected individuals gradually become-

- Less able to control their emotions and communicate with others (Psora/ Syphilis)
- Helpless with personal care and other activities of daily living (Psora/ Syphilis)

PROGNOSIS

Most affected individuals die within a decade after signs and symptoms first appear, although few people with the disease may survive for 20 to 30 years.

DIAGNOSIS

Diagnosis is based on findings in MRI of brain and clinical evaluation.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of CARASIL includes-

- Adrenoleukodystrophy/adrenomyeloneuropathy
- BD (Binswanger's disease)
- CADASIL (Cerebral Autosomal-Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy)
- Chronic progressive multiple sclerosis
- Hereditary SVDs (subcortical vascular dementia)
- Hutchinson-Gilford syndrome
- Membraneous lipodystrophy (Nasu-Hakola disease)
- Primary angiitis of the nervous system
- Sporadic SVDs
- Werner syndrome

CARASIL is similar to CADASIL, but with differences, including the earlier onset of encephalopathy in CARASIL (32 years vs 45 years), different inheritance modes, the absence of migraine and severe depression in CARASIL, the absence of the peculiar extraneural symptoms in CADASIL, and different progression patterns of MRI white matter changes.

TREATMENT

Basic treatment includes genetic counseling, supportive care, and medications for treating dementia and secondary prevention of ischemic stroke.

HOMOEOPATHIC TREATMENT

Common remedies for CARASIL *abies-n.* *abrot.* *acet-ac.* *Acon.* *act-sp.* *adren.* **AESC.** *aeth.* **Agar.** *ago.* *ail.* *alco.* *all-c.* *all-s.* *allox.* *aloe* *alum-p.* **Alum-sil.** **ALUM.** **Alumn.** *am-c.* *Am-i.* *Am-m.* *am-p.* *am-van.* **Ambr.** *aml-ns.* **Anac.** *anag.* *anan.* **Ang.** *ant-ar.* *ant-c.* **Ant-t.** *anth.* **Apis** *apisin.* *apoc.* *aran.* *arb.* **ARG-MET.** **ARG-N.** *arist-m.* **Arn.** **Ars-h.** **Ars-i.** *ars-met.* *ars-s-f.* **ARS.** *arund.* *asaf.*

Asar. asc-t. aster. astra-m. **ATRO.** aur-ar. Aur-i. aur-m-n. aur-m. aur-s. **AUR.** bac. **Bapt.** bar-act. **BAR-C.** bar-i. bar-m. bar-s. barbit. bell-p. **BELL.** benz-ac. **BERB.** beryl. **Bol-la.** borx. bov. brach. brom. **BRY.** **Bufo** but-ac. cact. cadm-met. cain. calad. **Calc-ar.** calc-f. calc-i. **Calc-p.** calc-s. calc-sil. **CALC.** camph. cann-i. cann-s. **CANTH.** **Caps.** **CARB-AC.** Carb-an. Carb-v. carb-n-o. Carbn-s. carc. **Card-m.** carl. cass. castm. castn-v. **Caul.** **CAUST.** cench. **CHAM.** cheir. chel. **CHIN.** Chinin-ar. chinin-hcy. chinin-s. chlol. chr-ac. chr-o. **Cic.** **Cimic.** Cimx. **Cina** cinnb. cinnm. cist. clem. cob. **Coc-c.** coca **COCC.** **Coff.** Colch. **Coloc.** CON. conv. cop. cor-r. **Corn.** cortico. crat. croc. **Crot-c.** crot-h. **Crot-t.** cund. cupr-ar. **Cupr.** Cur. cycl. dig. dios. diosm. dros. dub. **DULC.** Echi. elaps ergot. ery-a. **EUP-PER.** Euphr. euphr. eupi. ferr-ar. **Ferr-i.** **Ferr-p.** Ferr. Fl-ac. form. fuc. gamb. **GELS.** gins. **GLON.** gnaph. **GRAPH.** grat. Guaj. Ham. hed. Hell. helo. Helon. Hep. hip-ac. hipp. hura hydr-ac. **Hydr.** hydrang. hydrc. **Hymos.** Hyos. hyper. ign. ind. **Iod.** Ip. ipom-p. iris jatr-c. jug-c. **Kali-ar.** Kali-bi. kali-br. **Kali-c.** Kali-i. kali-m. **Kali-n.** kali-o. kali-ox. **Kali-p.** Kali-s. kali-sal. kali-sil. **Kalm.** Kreos. kres. Lac-ac. Lac-c. Lac-d. Lach. lact. lapa. **Lath.** Laur. lec. **LED.** lepi. **Lil-t.** lith-be. lith-c. lob-c. lob-s. lob. lol. loxo-recl. luf-op. **LYC.** lycps-v. **Lyss.** m-ambo. m-arct. **M-aust.** macro. mag-c. mag-f. **Mag-m.** **Mag-p.** mag-s. mand. mang-act. **Mang.** Med. meli. **Meny.** Merc-c. **Merc.** merl. **Mez.** morg-p. morph. **Mosch.** **MUR-AC.** murx. **Mygal.** naja Nat-ar. **NAT-C.** Nat-i. Nat-m. nat-n. Nat-p. Nat-s. Nat-sal. nicc. **Nit-ac.** **NUX-M.** **NUX-V.** ol-an. ol-j. **OInd.** onos. **Op.** orch. osm. ost. ox-ac. oxyt. paeon. pall. par. Petr. Ph-ac. **PHOS.** phys. **Phyt.** **PIC-AC.** pimp. pix plan. Plat. Plb-i. **PLB.** Podo. Polyg-a. prun. psil. Psor. ptel. **PULS.** rad-br. ran-a. Ran-b. Ran-s. rat. rauw. rham-cal. rheum **Rhud.** RHUS-T. rhus-v. rob. rosm. **Ruta** sabad. sabal sabin. samb-c. samb. sang. sanic. sarcol-ac. sarr. sars. **Sec.** sel. senec. seneg. **SEP.** **SIL.** sin-n. slag spartin-s. spig. spira. **Spong.** Stann. Staph. stram. **Stront-c.** **Stront-i.** stroph-h. stroph-s. **Stry.** Sul-ac. sul-i. sulfon. sulfonam. **SULPH.** sumb. syc. syph. **Tab.** tanac. tarax. tarent-c. tarent. ter. teucr. thal. Thuj. thyroiod. til. trion. tub. tus-p. Valer. Vanad. **VARIO.** **VERAT-V.** **VERAT.** verb. vib. vinc. viol-o. viol-t. vip. **Visc.** wies. xan. xero. zinc-p. Zinc.

SHORT REPERTORY OF CARASIL

GENERALS - BLOOD VESSELS - degeneration of bar-c. bar-m. vanad.

GENERALS – ARTERIOSCLEROSIS adren. Am-i. am-van. ant-ar. arg-n. **Arn.** **Ars-i.** ars. asar. Aur-i. aur-m-n. aur-m. **Aur.** **Bar-c.** bar-i. bar-m. bell-p. cact. calc-ar. calc-f. **Calc.** chinin-s. chlol. con. crat. **Cupr.** ergot. fl-ac. form. fuc. **Glom.** hed. hyper. iod. kali-bi. **Kali-i.** kali-sal. kres. lach. lith-c. mag-f. naja **Nat-i.** phos. **Plb-i.** **Plb.** Polyg-a. rad-br. rauw. **Sec.** sil. spartin-s. **Stront-c.** **Stront-i.** stroph-h. sulph. sumb. **Tab.** thyroid. **Vanad.** **Visc.**

GENERALS - OSSIFICATION - Arteries; of aur. **Bar-c.** lith-c. vario.

MIND – DEMENTIA aeth. **Agar.** alco. alum. **Anac.** ant-c. anth. apisin. arg-n. ars. bell. bufo calc-p. calc. cann-i. carbn-s. carc. cic. coca con. croc. crot-c. crot-h. glon. graph. hell. **Hyos.** ign. kali-i. **Lil-t.** lyc. merc. **Nat-sal.** Nux-v. op. orch. Ph-ac. **Phos.** **Pic-ac.** plb. puls. sil. stram. sulph. sumb. tarent. **Verat.** vip. zinc.

MIND - DEMENTIA - senilis – premature **Ambr.** bufo **Lyc.**

HEAD - HAIR – baldness abrot. all-s. alumn. ambr. **Anac.** **Apis** arn. aur. **BAR-C.** Fl-ac. Graph. hell. hep. kali-c. lyc. med. morg-p. nat-m. **Phos.** pix rosm. **Sep.** **Sil.** sulph. syc. syph. thal. Thuj. vinc. Zinc.

HEAD - HAIR - baldness - young people arund. bac. **Bar-c.** **Sil.** tub.

HEAD - HAIR - falling - Vertex; from **BAR-C.** calc. carb-an. **GRAPH.** hep. **LYC.** Nit-ac. plb. sel. **Sep.** sil. thuj. zinc.

EXTREMITIES - WALKING – difficult **Ang.** aur. cact. chin. iod. kali-i. olnd. phys. sec. sil. ter.

EXTREMITIES - WALKING - shuffling gait **arn.** chin. colch. gels. led. nux-v. ol-an. op. **Psor.** **RHUS-T.** sec. sil. staph. tab. vip. **Zinc.**

EXTREMITIES - TOTTERING GAIT acet-ac. acon. aesc. **Agar.** agro. ail. **ALUM.** am-c. Am-m. am-p. Ambr. aml-ns. **Anac.** anan. ang. ant-c. **Apis ARG-MET.** arg-n. arn. ars-s-f. **Ars.** Asar. aster. astram. atro. aur-s. **AUR.** **BAR-C.** barbit. **BELL.** bov. **BRY.** bufo calc-p. **Calc.** camph. cann-s. canth. **Caps.** **Carb-ac.** carb-an. **Carb-v.** **Carbn-s.** **CAUST.** cham. chel. **Chin.** chinin-hcy. cic. **COCC.** **Coff.** colch. **Coloc.** **CON.** croc. crot-h. cupr. cycl. dros. dub. dulc. euph. ferr. **Fl-ac.** **Gels.** **Glom.** graph. **Hell.** helo. hydr-ac. hyos. ign. **Iod.** ip. kali-br. kali-c. kali-n. lac-ac. lach. lact. **Lath.** Laur. led. **lil-t.** lol. lyc. m-ambo. m-arct. m-aust. mag-c. **Mag-m.** **Mag-p.** mang-act. mang. **Merc.** Mez. morph. mosch. **Mur-ac.** **Mygal.** naja Nat-c. Nat-m. nit-ac. Nux-m. **NUX-V.** ol-an. **Olnd.** onos. Op. ox-ac. oxyt. paeon. par. petr. **Ph-ac.** **PHOS.** phys. phyt. **PIC-AC.** plat. **PLB.** prun. puls. rheum rhod. **RHUS-T.** ruta sabad. samb. **Sars.** sec. seneg. sep. **Sil.** spig. spong. stann. stram. stront-c. **Stry.** sulfon. **Sulph.** tab. tanac. tarax. tarent-c. **Tarent.** teucr. **Thuj.** trion. valer. **Verat-v.** **VERAT.** verb. viol-o. viol-t. vip. visc. zinc.

EXTREMITIES - WEAKNESS - Lower limbs acet-ac. acon. **AESC.** aeth. **Agar.** ail. all-s. aloe alum-p. **Alum-sil.** **ALUM.** alumn. am-c. Am-m. ambr. **Anac.** Ang. ant-c. ant-t. **Apis ARG-MET.** **ARG-N.** arn. ars-s-f. **ARS.** asar. aur-ar. aur-i. aur-s. **AUR.** **Bapt.** bar-c. bar-s. bell. benz-ac. berb. beryl. borx. bov. brach. **Bry.** **Bufo** but-ac. cadm-met. calad. calc-ar. calc-f. calc-i. calc-s. **CALC.** camph. cann-i. cann-s. canth. **CARB-AC.** carb-an. **Carb-v.** **Carbn-s.** carc. castm. **CAUST.** cham. chel. **Chin.** chinin-ar. **Cic.** **Cina** cist. clem. coc-c. **COCC.** colch. **CON.** **Corn.** cortico. croc. **Crot-c.** **Crot-t.** **Cupr.** cycl. dig. diosm. dros. dulc. ery-a. eup-per. **Euph.** euphr. **Ferr-i.** ferr. **GELS.** **GLON.** Graph. grat. guaj. ham. **Hell.** hep. hipp. **Hydr.** **Hyos.** ign. ind. iod. ip. **Kali-ar.** kali-bi. Kali-br. Kali-c. Kali-n. kali-ox. **Kali-p.** Kreos. lapa. **Lath.** laur. led. **lil-t.** lob-c. **Lyc.** m-arct. m-aust. mag-c. **Mag-m.** mand. mang. **Med.** **Merc-c.** merc. **Mez.** mosch. **MUR-AC.** murx. **Nat-ar.** **NAT-C.** **Nat-m.** nat-n. nat-p. nat-s. nicc. **Nit-ac.** Nux-m. **NUX-V.** olnd. onos. Op. ox-ac. par. Petr. Ph-ac. **PHOS.** **PIC-AC.** **Plat.** **PLB.** podo. psil. ptel. puls. **Ran-b.** **Rat.** rhod. **RHUS-T.** **Ruta** sabin. samb. sang. sarcol-ac. **Sars.** **Sec.** sel. seneg. **Sep.** **Sil.** spig. spong. **Stann.** stram. Stront-c. stroph-s. stry. **Sul-ac.** sulfonam. **Sulph.** tab. tarent. thal. **Thuj.** til. verat. verb. vip. wies. xan. zinc-p. **ZINC.**

EXTREMITIES - WEAKNESS - Lower limbs – paralytic agar. ambr. anac. arg-n. **COCC.** dig. rhus-t. ruta sars. thuj.

BACK - PAIN - Lumbar region abies-n. abrot. acon. act-sp. **AESC.** aeth. **Agar.** all-c. all-s. allox. aloe alum-p. alum-sil. **Alum.** am-c. Am-m. ambr. anag. anan. ang. ant-c. **Ant-t.** **Apis apoc.** aran. arb. **ARG-MET.** Arg-n. **Arn.** ars-met. ars-s-f. ars. arund. asaf. asar. asc-t. aur-ar. aur-m. aur-s. aur. **Bapt.** bar-act. **BAR-C.** bell. **BERB.** **Bol-la.** borx. bov. brom. **BRY.** bufo but-ac. cadm-met. cain. **Calc-ar.** calc-f. **Calc-p.** calc-s. calc-sil. **CALC.** camph. cann-i. cann-s. **CANTH.** caps. **Carb-ac.** carb-an. **Carb-v.** **Carbn-s.** **Card-m.** carl. cass. castn-v. **Caul.** **Caust.** cench. **Cham.** cheir. chel. **CHIN.** chinin-ar. chinin-s. chr-ac. chr-o. cic. **Cimic.** **Cimx.** cina cinnb. cinnm. clem. cob. coc-c. **Cocc.** coff. **Colch.** **Coloc.** **Con.** conv. cop. cor-r. corn. croc. crot-h. crot-t. cund. cupr-ar. cupr. **Cur.** cycl. dig. dios. dros. **DULC.** **Echi.** elaps **EUP-PER.** eupi. ferr-ar. ferr-i. **Ferr-p.** Ferr. fl-ac. gamb. **Gels.** gins. gnaph. **GRAPH.** grat. **Guaj.** Ham. hell. **Helon.** Hep. hip-ac. hura Hydr. hydrang. hydrc. **Hymos.** hyos. hyper. ign. ind. iod. ip. ipom-p. iris jug-c. kali-ar. Kali-bi. kali-br. Kali-c. Kali-i. kali-m. Kali-n. kali-o. kali-ox. **Kali-p.** Kali-s. kali-sil. **Kalm.** kreos. **Lac-c.** **Lac-d.** Lach.

lact. lath. lec. **LED.** lepi. **Lil-t.** lith-be. lob-s. lob. loxo-recl. lyc. lycps-v. **Lyss.** m-ambo. **M-aust.** macro. mag-c. **Mag-m.** **Mag-p.** mag-s. mand. mang. med. meli. **Meny.** merc. merl. **Mez.** Mur-ac. murx. naja nat-ar. **Nat-c.** **Nat-m.** **Nat-p.** **Nat-s.** nicc. **Nit-ac.** **NUX-M.** **NUX-V.** ol-an. ol-j. onos. Op. osm. ost. ox-ac. pall. petr. Ph-ac. **PHOS.** Phyt. Pic-ac. pimp. plan. Plat. plb. **Podo.** prun. psil. Psor. ptel. **PULS.** rad-br. ran-a. ran-b. **Ran-s.** rat. rham-cal. rheum **Rhod.** **RHUS-T.** rhus-v. rob. Ruta sabad. sabal sabin. samb-c. samb. sang. sanic. sarr. sars. **Sec.** sel. senec. **SEP.** **Sil.** sin-n. slag spira. spong. stann. **Staph.** stram. **Stront-c.** **Stry.** Sul-ac. sul-i. **SULPH.** syph. tarax. tarent, ter. thuj. tus-p. **Valer.** **VARIO.** verat. vib. visc. zinc-p. **Zinc.**

BACK - INFLAMMATION – Vertebrae aesc. ph-ac.

BACK - INFLAMMATION - Lumbar region ars. **Lath.** merc. **Rhus-t.**

EXTREMITIES - STIFFNESS – Legs alum. ang. arg-n. arist-m. ars. bapt. bar-m. bell. bry. calc. carb-v. **Cic.** colch. con. dios. **Eup-per.** ferr. gamb. guaj. **Ip.** **Lath.** luf-op. mang. merc. nat-m. nux-v. petr. phys. plat. ran-b. rhus-t. sarcol-ac. sars. sep. stry. verat. visc. xero. zinc.

EXTREMITIES - STIFFNESS - Legs – Calves **Arg-n.** cic. con. mag-m. sarcol-ac. verat. zinc.

EXTREMITIES - STIFFNESS - Lower limbs **Acon.** agar. alum-p. alum-sil. alum. am-m. ambr. aml-ns. anac. ang. ant-t. apis apoc. **Arg-met.** arg-n. arist-m. ars-h. ars. **ATRO.** aur-ar. **Aur-m.** aur. bar-c. **Bell.** **BERB.** brom. **Bry.** bufo calc-s. calc-sil. **Calc.** caps. carb-an. **Carb-v.** carb-n-o. **Carbn-s.** **Caust.** **CHAM.** chel. chin. chinin-ar. **Cic.** **Cina** **Coc-c.** **Cocc.** con. cupr. cycl. dig. dros. **EUP-PER.** ferr-ar. ferr-p. **Ferr.** **Guaj.** Ham. Hydr-ac. ign. jatr-c. kali-c. kali-i. **Lac-c.** lact. **Lath.** **Led.** **Lyc.** m-arct. **Mag-p.** **Mang.** merc-c. **Merc.** mosch. **Nat-m.** **Nat-s.** nit-ac. **NUX-V.** ol-an. **Olnd.** op. ox-ac. **Petr.** phos. phys. **PLAT.** plb. podo. puls. ran-b. rhod. **RHUS-T.** sars. sec. **SEP.** **SIL.** **Spong.** stram. **Stry.** sulph. tab. ter. thuj. tub. **Verat.** zinc-p. **Zinc.**

EXTREMITIES - STIFFNESS - Lower limbs - sensation of alum. arg-met. arg-n. asaf. caust. cham. chin. cocc. mang. merc-c. mosch. nit-ac. nux-v. plat. rhod.

BIBLIOGRAPHY



Cerebrovascular Diseases > LESS COMMON CAUSES OF STROKE Harrison's Principles of Internal Medicine... and leukoencephalopathy (CARASIL) and hereditary endotheliopathy, retinopathy, nephropathy, and stroke (HERNS). Fabry's disease also produces both a large-vessel arteriopathy and small-vessel infarctions. ...



Chapter 34. Cerebrovascular Diseases > Familial Subcortical Infarction (CADASIL and CARASIL) Adams & Victor's Principles of Neurology, 10e ... changes typical of CADASIL has been identified as a recessively inherited disease (cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy [CARASIL]) and is discussed separately below. The MRI and CT appearance is of multiple confluent white matter lesions of various...



Chapter 34. Cerebrovascular Diseases > Strokes in Children and Young Adults Adams & Victor's Principles of Neurology, 10e ... Phosphodiesterase 4D Phosphodiesterase 4D Complex

a CADASIL Notch 3 AD a CARASIL HTAR1 AR a Hyperhomocysteinemia Methylene tetrahydrofolate reductase AR a Rare 20 in young Homocysteinemia Cystathione beta-synthase AR...



Encyclopedia Homoeopathica



Radar 10



Stroke > INTRODUCTION Clinical Neurology, 9e ... CST3 Cystatin 3 AD ICH Arterial tortuosity syndrome SLC2A10 Solute carrier family 2, member 10 AR Ischemic Brain small-vessel disease with hemorrhage COL4A1 Collagen type IV, α-1 chain AD ICH CADASIL NOTCH3 Notch-3 AD Ischemic CARASIL...