U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Burnett JR, Hooper AJ, McCormick SPA, et al. Tangier Disease. 2019 Nov 21. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Tangier Disease

Synonyms: Analphalipoproteinemia, Familial High-Density Lipoprotein Deficiency 1, Primary Hypoalphalipoproteinemia 1

John R Burnett, MB ChB, MD, PhD, FRCPA,[1] Amanda J Hooper, PhD,[1] Sally PA McCormick, PhD,[2] and Robert A Hegele, MD, FRCPC, FACP[3]

Created: November 21, 2019.

Summary

Clinical characteristics

Tangier disease is characterized by severe deficiency or absence of high-density lipoprotein (HDL) in the circulation resulting in tissue accumulation of cholesteryl esters throughout the body, particularly in the reticuloendothelial system. The major clinical signs of Tangier disease include hyperplastic yellow-orange tonsils, hepatosplenomegaly, and peripheral neuropathy, which may be either relapsing-remitting or chronic progressive in nature. Rarer complications may include corneal opacities that typically do not affect vision, premature atherosclerotic coronary artery disease occurring in the sixth and seventh decades of life (not usually before age 40 years), and mild hematologic manifestations, such as mild thrombocytopenia, reticulocytosis, stomatocytosis, or hemolytic anemia. The clinical expression of Tangier disease is variable, with some affected individuals only showing biochemical perturbations.

Diagnosis/testing

The diagnosis of Tangier disease is established in a proband with absent or extremely low HDL-cholesterol and apo A-I levels and biallelic pathogenic variants in *ABCA1* identified by molecular genetic testing.

Management

Treatment of manifestations: Tonsillectomy in those with airway obstruction or mass symptoms; transient bracing (such as ankle-foot orthosis) and exercise for those with peripheral neuropathy; corneal transplantation for corneal opacities that interfere with daily living; standard treatment for hepatosplenomegaly, coronary artery disease, severe thrombocytopenia, and severe hemolytic anemia.

Author Affiliations: 1 Department of Clinical Biochemistry Royal Perth Hospital & Fiona Stanley Hospital Network PathWest Laboratory Medicine WA; School of Medicine Faculty of Health & Medical Sciences University of Western Australia Perth, Australia; Email: john.burnett@health.wa.gov.au; Email: amanda.hooper@health.wa.gov.au. 2 Department of Biochemistry University of Otago Dunedin, New Zealand; Email: sally.mccormick@otago.ac.nz. 3 Departments of Medicine and Biochemistry Schulich School of Medicine and Robarts Research Institute Western University London, Ontario, Canada; Email: hegele@robarts.ca.

Prevention of primary manifestations: Mitigation of cardiovascular risk factors, including improvement of plasma lipid profiles using statin therapy and a low-fat diet.

Surveillance: Assessment for hepatosplenomegaly by physical examination and imaging at each visit; neurology and ophthalmology evaluations annually; cardiovascular risk assessment of atherosclerotic plaque burden annually beginning in adulthood; complete blood count with differential as clinically indicated.

Agents/circumstances to avoid: Obesity (which makes walking more difficult); medications that are toxic or potentially toxic to those who are predisposed to the development of peripheral neuropathy; contact sports in those with hepatosplenomegaly.

Evaluation of relatives at risk: It is appropriate to measure a lipid profile (total cholesterol, HDL-cholesterol, triglyceride, and calculated LDL-cholesterol) and apo A-I concentration in at-risk sibs to identify as early as possible those who would benefit from appropriate treatment or measures to prevent disease complications.

Genetic counseling

Tangier disease is inherited in an autosomal recessive manner. Most parents are heterozygous for a pathogenic variant. At conception each sib has a 25% chance of being unaffected, a 50% chance of being a carrier (with no overt clinical manifestations, but with plasma HDL-cholesterol concentrations that are ~50% of normal), and a 25% chance of being unaffected and not a carrier. Carrier testing for at-risk relatives and prenatal testing for pregnancies at increased risk are possible if the pathogenic variants in the family are known.

Diagnosis

Formal clinical diagnostic criteria for Tangier disease have not been published.

Suggestive Findings

Tangier disease **should be suspected** in individuals with the following clinical and supportive laboratory findings.

Clinical findings

- Enlarged tonsils that are yellow and/or orange in children and young adults
- Peripheral neuropathy
- Hepatomegaly and/or splenomegaly
- Corneal opacities
- Coronary artery disease
- Lymphadenopathy
- Blood disorders (especially thrombocytopenia)

Supportive laboratory findings

- Major findings:
  - Very low plasma HDL-cholesterol concentration, typically <5 mg/dL (0.125 mmol/L), rarely 5-10 mg/dL
  - Very low or absent apo A-I concentration, usually <30 mg/dL (typically <5 mg/dL)
  - Small or absent alpha band on lipoprotein electrophoresis
- Other laboratory findings:
  - Low plasma total cholesterol concentration, typically <150 mg/dL (4 mmol/L)
  - Mild-to-moderate hypertriglyceridemia, up to 400 mg/dL (4.5 mmol/L)
  - Decreased LDL-cholesterol concentration

- Small beta or broad pre-beta band on lipoprotein electrophoresis

Establishing the Diagnosis

The diagnosis of Tangier disease **is established** in a proband with absent or extremely low HDL-cholesterol and apo A-I levels and biallelic pathogenic variants in *ABCA1* identified on molecular genetic testing (see Table 1).

Note: If clinical molecular genetic testing cannot be performed, the presence of accumulation of cholesterol esters in tissue biopsies in an individual with typical clinical features of Tangier disease can be considered.

When the phenotypic and laboratory findings suggest the diagnosis of Tangier disease, molecular genetic testing approaches can include **single-gene testing** or use of a **multigene panel**:

- **Single-gene testing.** Sequence analysis of *ABCA1* detects small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. Perform sequence analysis first. If only one or no pathogenic variant is found, perform gene-targeted deletion/duplication analysis to detect intragenic deletions or duplications.
- **A multigene panel** that includes *ABCA1* and other genes of interest (see Differential Diagnosis) is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests. For this disorder a multigene panel that also includes deletion/duplication analysis is recommended (see Table 1).

  For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Table 1. Molecular Genetic Testing Used in Tangier Disease

Gene [1]	Method	Proportion of Pathogenic Variants [2] Detectable by Method
ABCA1	Sequence analysis [3]	>90%
	Gene-targeted deletion/duplication analysis [4]	<10% [5]

1. See Table A. Genes and Databases for chromosome locus and protein.
2. See Molecular Genetics for information on allelic variants detected in this gene.
3. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
4. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.
5. Dron et al [2018]

Clinical Characteristics

Clinical Description

Tangier disease is characterized by severe deficiency or absence of high-density lipoprotein (HDL) in the circulation resulting in tissue accumulation of cholesteryl esters throughout the body, particularly in the reticuloendothelial system [Assmann et al 2001]. The major clinical signs of Tangier disease include hyperplastic yellow-orange tonsils, peripheral neuropathy, and hepatosplenomegaly. The clinical course of neuropathy may be either relapsing-remitting or chronic progressive [Mercan et al 2018]. However, the clinical expression of Tangier disease is variable, with some affected individuals only showing biochemical perturbation.

Histiocytic manifestations

- Hyperplastic yellow-orange palatine and pharyngeal tonsils are typically first noted in late childhood or adolescence. This finding does not usually cause any symptoms; however, it may occasionally cause difficulty breathing or swallowing, recurrent ear or sinus infections, or obstructive sleep apnea.
- Hepatomegaly and/or splenomegaly presents more commonly in adulthood.
- Orange-brown focal deposits of the intestinal and rectal mucosa may be seen on colonoscopy, but typically do not cause any symptoms.
- Lymphadenopathy may be found in the thoracic, axillary, and cervical regions of the body.

Neurologic manifestations. Peripheral neuropathy, the clinical course of which is commonly benign, can be relapsing-remitting with sensory abnormalities but in some individuals can be progressive. Findings may include the following:

- Multifocal mono- or polyneuropathy (monophasic or relapsing-remitting pattern)
- Syringomyelia-like neuropathy (slowly progressive weakness, muscle wasting, and loss of pain and temperature sensation mainly affecting the upper extremities)
- Subclinical or distal symmetric polyneuropathy (rare)

Ophthalmologic manifestations. Corneal opacities, which are diffuse or dot-like, occur later in life and generally do not affect vision.

Cardiac manifestations. Premature atherosclerotic coronary artery disease may develop in some affected individuals, usually in the 50s and 60s [Schaefer et al 2010], and usually not before age 40 years [Burnett et al 1994]. Some affected individuals may have heart valve involvement.

Hematologic manifestations

- Mild thrombocytopenia
- Reticulocytosis
- Stomatocytosis
- Hemolytic anemia

Dermatologic manifestations. The skin lesions of Tangier disease have not been extensively reported. However, prurigo nodularis, skin ulcer, and painless scald or burn scars have been reported in some affected individuals.

Prognosis. The prognosis in Tangier disease is usually good and depends mainly on the progression of peripheral neuropathy and/or atherosclerosis. Individuals with Tangier disease have a moderately increased risk of coronary artery disease (see **Cardiac manifestations**), which can be managed with conventional preventive therapies [Schaefer et al 2010, Schaefer et al 2016].

Genotype-Phenotype Correlations

Given the small number of individuals with Tangier disease reported in the literature, reliable data on genotype-phenotype correlations are lacking.

Prevalence

With the exception of small founder populations (e.g., Tangier Island, Virginia, after which the disorder is named), Tangier disease is rare; fewer than 100 cases have been published.

Genetically Related (Allelic) Disorders

No phenotypes other than those discussed in this *GeneReview* are known to be associated with pathogenic variants in *ABCA1*.

Differential Diagnosis

Artifactual and secondary causes of severe HDL deficiency. In the setting of an extremely low HDL-cholesterol in the absence of hypertriglyceridemia, artifactual causes (e.g., paraproteinemia) and secondary causes (e.g., androgenic anabolic steroids, paradoxic response to PPAR agonists, malaria, HIV infection, malignancy, liver disease) should be excluded [Rader & deGoma 2012].

Hereditary disorders with severe HDL deficiency. See Table 2.

Table 2. Disorders with Severe HDL Deficiency to Consider in the Differential Diagnosis of Tangier Disease

Disorder	Gene	MOI	Distinguishing Features
Apo A-I deficiency [1]	*APOA1*	AR	Plasma apo A-I is undetectable (compared w/very low plasma apo A-I in Tangier disease) [2]
LCAT deficiency [1] (OMIM 245900)	*LCAT*	AR	Marked corneal opacification (plus renal disease in individuals w/complete LCAT deficiency) [2]
Fish eye disease [1] (OMIM 136120)			

Apo A-I = apolipoprotein A-I; AR = autosomal recessive; LCAT = lecithin cholesterol acyltransferase; MOI = mode of inheritance
1. Oldoni et al [2014]
2. Only the biochemical perturbation is expressed in individuals who are heterozygous for an *APOA1* or *LCAT* pathogenic variant; the biochemical perturbation can be indistinguishable from that observed in individuals heterozygous for an *ABCA1* pathogenic variant [Geller et al 2018].

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with Tangier disease, the evaluations summarized in Table 3 (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Table 3. Recommended Evaluations Following Initial Diagnosis in Individuals with Tangier Disease

System/Concern	Evaluation	Comment
Histiocytic	Physical exam to assess tonsillar hypertrophy	Consider referral to otolaryngologist.
	Abdominal ultrasonography to assess for hepatosplenomegaly	

Table 3. continued from previous page.

System/Concern	Evaluation	Comment
Neurologic	Nerve conduction studies & electromyography to determine presence &/or extent of peripheral neuropathy	Consider referral to neurologist.
Ophthalmologic	Ophthalmologic eval to assess for corneal opacities	Consider referral to ophthalmologist.
Cardiovascular	Plasma lipid profile (total cholesterol, triglycerides, LDL-, HDL-cholesterol) & apo A-I concentration	Consider referral to cardiologist.
	Noninvasive imaging of carotid plaque burden by duplex ultrasonography	
	Coronary calcium score [1] &/or CT coronary angiography to assess for coronary atherosclerosis	
Hematologic	Complete blood count w/differential & peripheral blood film (also known as a blood smear)	Consider referral to hematologist.
Dermatologic	Dermatologic consultation if indicated	
Miscellaneous/ Other	Consultation w/clinical geneticist &/or genetic counselor	Incl genetic counseling

1. A cardiac calcium score involves a noninvasive CT scan of the heart that is able to measure the amount of calcified plaque in the coronary arteries. This score is used to estimate the risk an affected individual has of developing coronary artery disease.

Treatment of Manifestations

Table 4. Treatment of Manifestations in Individuals with Tangier Disease

Manifestation/Concern	Treatment	Considerations/Other
Enlarged hyperplastic palatine tonsils	Tonsillectomy	Consider if tonsils cause airway obstruction or mass symptoms.
Hepatosplenomegaly	Standard treatment	Incl standard precautions such as avoidance of high-impact sports or activities that could → splenic rupture. Abdominal masses may complicate splenectomy.
Peripheral neuropathy	Clinically proven effective treatments are not yet available.	
	Transient bracing (e.g., w/wrist splint or ankle-foot orthosis) may be useful.	Those w/residual foot drop may need to use an ankle-foot orthosis permanently.
	Exercise as appropriate to person's capacity	To maintain balance & strength
Corneal opacification	Corneal transplantation	Consider if this interferes w/daily living.
Coronary artery disease	Standard treatment, incl use of dietary & pharmacologic therapies	See Prevention of Primary Manifestations.
Thrombocytopenia / Hemolytic anemia	Standard treatment, if severe	

Prevention of Primary Manifestations

Mitigation of cardiovascular risk factors (including LDL-cholesterol concentrations using statin therapy and a low-fat diet) is indicated.

Surveillance

Table 5. Recommended Surveillance for Individuals with Tangier Disease

System/Concern	Evaluation	Frequency
Histiocytic	Assessment for hepatosplenomegaly by physical exam & abdominal imaging modalities	At each visit
Neurologic	Neurologic eval	Annually
Ophthalmologic	Ophthalmologic eval	
Cardiovascular	Cardiovascular risk assessment, incl noninvasive assessment of atherosclerotic plaque burden [1]	Annually beginning in early adulthood
Hematologic	Complete blood count w/differential	As clinically indicated

1. Duplex coronary ultrasonography (See Table 3.)

Agents/Circumstances to Avoid

The following should be avoided:

- Obesity, because it makes walking more difficult
- Medications that are toxic or potentially toxic to persons who are predisposed to the development of peripheral neuropathy, such as vincristine or taxols (paclitaxel)
- Contact sports, in those with hepatosplenomegaly

Evaluation of Relatives at Risk

It is appropriate to clarify the genetic status of apparently asymptomatic older and younger at-risk relatives of an affected individual in order to identify as early as possible those who would benefit from prompt initiation of treatment and preventive measures. Evaluations can include:

- A lipid profile (including total cholesterol, HDL-cholesterol, triglyceride, and calculated LDL-cholesterol) and apo A-I concentration;
- Molecular genetic testing if the pathogenic variants in the family are known.

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Pregnancy Management

See MotherToBaby for information on medication use during pregnancy.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Tangier disease is inherited in an autosomal recessive manner. Heterozygous carriers of an *ABCA1* pathogenic variant are asymptomatic but tend to have hypoalphalipoproteinemia (HDL-cholesterol concentrations that are ~50% of normal).

Risk to Family Members

Parents of a proband

- The parents of an affected child are obligate heterozygotes (i.e., carriers of one *ABCA1* pathogenic variant).
- Heterozygotes (carriers) are asymptomatic and have no clinical manifestations, but they may have plasma HDL-cholesterol concentrations that are approximately one half of normal.

Sibs of a proband

- At conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.
- Heterozygotes (carriers) are asymptomatic and have no clinical manifestations, but often have plasma HDL-cholesterol concentrations that are approximately 50% of normal.

Offspring of a proband. The offspring of an individual with Tangier disease are obligate heterozygotes (carriers) for a pathogenic variant in *ABCA1*.

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of a pathogenic variant in *ABCA1*.

Carrier (Heterozygote) Detection

Carrier testing for at-risk relatives requires prior identification of the *ABCA1* pathogenic variants in the family.

Related Genetic Counseling Issues

See Management, Evaluation of Relatives at Risk for information on evaluating at-risk relatives for the purpose of early diagnosis and treatment.

Family planning

- The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected, are carriers, or are at risk of being carriers.

Prenatal Testing and Preimplantation Genetic Testing

Once the *ABCA1* pathogenic variants have been identified in an affected family member, prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **National Library of Medicine Genetics Home Reference**
  Tangier disease

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Tangier Disease: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
ABCA1	9q31.1	Phospholipid-transporting ATPase ABCA1	ABCA1 @ LOVD	ABCA1	ABCA1

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Tangier Disease (View All in OMIM)

205400	TANGIER DISEASE; TGD
600046	ATP-BINDING CASSETTE, SUBFAMILY A, MEMBER 1; ABCA1

Molecular Pathogenesis

Introduction. The 49-exon gene *ABCA1* encodes ABCA1, a 2,261-amino acid member of the ATP-binding cassette transporter family, which is a large group of transporters involved in the transfer of different hydrophobic compounds across cell membranes. ABCA1 is a flippase, which promotes movement of lipid (chiefly unesterified cholesterol, but also phosphatidylcholine) across the cell membrane from inside to outside [Quazi & Molday 2011]. ABCA1 facilitates the formation of HDL particles by transferring cholesterol and phospholipids onto apo A-I within nascent HDL, and promotes the efflux of cholesterol from vascular endothelial cells and macrophages [Qian et al 2017]. Small apoA-I-containing particles are prone to degradation in the kidney. Defects in ABCA1 therefore reduce circulating HDL-cholesterol concentrations and result in the accumulation of cholesteryl esters in reticuloendothelial cells throughout the body (e.g., as in tonsils, lymph nodes, spleen, liver, and intestinal mucosa) as well as in an increased risk of coronary heart disease. Mild-to-moderate hypertriglyceridemia occurs because there is an increase in large triglyceride-rich VLDL production as a result of dysregulation related to the absence of ABCA1 [Liu et al 2012].

Mechanism of disease causation. Tangier disease is caused by loss-of-function variants in *ABCA1*, resulting in reduced ABCA1 synthesis or activity. Loss-of-function missense variants may disrupt binding with apo A-I or ATP or trafficking of the ABCA1 protein to the cell membrane. Large-scale deletions are rare but may affect a single exon, multiple exons, or the entire gene [Dron et al 2018].

Table 6. Notable *ABCA1* Pathogenic Variants

Reference Sequences	DNA Nucleotide Change	Predicted Protein Change	Comment
NM_005502.3 NP_005493.2	c.1824delG	p.(Thr609ArgfsTer27)	Founder variants on Tangier Island [Bodzioch et al 1999, Rust et al 1999]
	c.1881C>G	p.Tyr627Ter	

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.

References

Literature Cited

Assmann G, von Eckardstein A, Brewer HB Jr. Familial analphalipoproteinemia: Tangier disease. In: Scriver CR, Beaudet AL, Sly WS, Valle D, Vogelstein B, eds. *The Metabolic and Molecular Bases of Inherited Disease*. 8 ed. Vol 2. New York, NY: McGraw-Hill; 2001:2937-80

Bodzioch M, Orsó E, Klucken J, Langmann T, Böttcher A, Diederich W, Drobnik W, Barlage S, Büchler C, Porsch-Ozcürümez M, Kaminski WE, Hahmann HW, Oette K, Rothe G, Aslanidis C, Lackner KJ, Schmitz G. The gene encoding ATP-binding cassette transporter 1 is mutated in Tangier disease. Nat Genet. 1999;22:347–51. PubMed PMID: 10431237.

Burnett JR, Law AJJ, Yeong ML, Crooke MJ, Sharma AK. Severe aortic stenosis and atherosclerosis in a young man with Tangier disease. Am J Cardiol. 1994;73:923–5. PubMed PMID: 8184829.

Dron JS, Wang J, Berberich AJ, Iacocca MA, Cao H, Yang P, Knoll J, Tremblay K, Brisson D, Netzer C, Gouni-Berthold I, Gaudet D, Hegele RA. Large-scale deletions of the ABCA1 gene in patients with hypoalphalipoproteinemia. J Lipid Res. 2018;59:1529–35. PubMed PMID: 29866657.

Geller AS, Polisecki EY, Diffenderfer MR, Asztalos BF, Karathanasis SK, Hegele RA, Schaefer EJ. Genetic and secondary causes of severe HDL deficiency and cardiovascular disease. J Lipid Res. 2018;59:2421–35. PubMed PMID: 30333156.

Liu M, Chung S, Shelness GS, Parks JS. Hepatic ABCA1 and VLDL triglyceride production. Biochim Biophys Acta. 2012;1821:770–7. PubMed PMID: 22001232.

Mercan M, Yayla V, Altinay S, Seyhan S. Peripheral neuropathy in Tangier disease: a literature review and assessment. J Peripher Nerv Syst. 2018;23:88–98. PubMed PMID: 29582519.

Oldoni F, Sinke RJ, Kuivenhoven JA. Mendelian disorders of high-density lipoprotein metabolism. Circ Res. 2014;114:124–42. PubMed PMID: 24385507.

Qian H, Zhao X, Cao P, Lei J, Yan N, Gong X. Structure of the human lipid exporter ABCA1. Cell. 2017;169:1228–1239.e10. PubMed PMID: 28602350.

Quazi F, Molday RS. Lipid transport by mammalian ABC proteins. Essays Biochem. 2011;50:265–90. PubMed PMID: 21967062.

Rader DJ, deGoma EM. Approach to the patient with extremely low HDL-cholesterol. J Clin Endocrinol Metab. 2012;97:3399–407. PubMed PMID: 23043194.

Rust S, Rosier M, Funke H, Real J, Amoura Z, Piette JC, Deleuze JF, Brewer HB, Duverger N, Denèfle P, Assmann G. Tangier disease is caused by mutations in the gene encoding ATP-binding cassette transporter 1. Nat Genet. 1999;22:352–5. PubMed PMID: 10431238.

Schaefer EJ, Anthanont P, Diffenderfer MR, Polisecki E, Asztalos BF. Diagnosis and treatment of high density lipoprotein deficiency. Prog Cardiovasc Dis. 2016;59:97–106. PubMed PMID: 27565770.

Schaefer EJ, Santos RD, Asztalos BF. Marked HDL deficiency and premature coronary heart disease. Curr Opin Lipidol. 2010;21:289–97. PubMed PMID: 20616715.

Chapter Notes

Author Notes

Lipid Genetics Clinic

Robert A Hegele directs a tertiary referral lipid speciality clinic and a genomics core facility (London Regional Genomics Centre) in London, Ontario, Canada, and has a research program in genetics of dyslipidemias and related metabolic disorders.

Acknowledgments

Robert A Hegele is supported by the Jacob J Wolfe Distinguished Medical Research Chair, the Edith Schulich Vinet Canada Research Chair in Human Genetics, the Martha G Blackburn Chair in Cardiovascular Research, and operating grants from the Canadian Institutes of Health Research (Foundation Grant) and the Heart and Stroke Foundation of Ontario (G-18-0022147).

Revision History

- 21 November 2019 (ma) Review posted live
- 18 April 2019 (jb) Original submission

License