



# ISSVA classification for vascular anomalies<sup>©</sup>

(Approved at the 20th ISSVA Workshop, Melbourne, April 2014)

## Overview table

Vascular anomalies				
Vascular tumors	Vascular malformations			
	Simple	Combined <sup>◦</sup>	of major named vessels	associated with other anomalies
<a href="#">Benign</a> <a href="#">Locally aggressive or borderline</a> <a href="#">Malignant</a>	<a href="#">Capillary malformations</a> <a href="#">Lymphatic malformations</a> <a href="#">Venous malformations</a> <a href="#">Arteriovenous malformations*</a> <a href="#">Arteriovenous fistula*</a>	<a href="#">CVM, CLM</a> <a href="#">LVM, CLVM</a> <a href="#">CAVM*</a> <a href="#">CLAVM*</a> <a href="#">others</a>	<a href="#">See details</a>	<a href="#">See list</a>

◦ defined as two or more vascular malformations found in one lesion

\* high-flow lesions

**N.B.** The classification tables do not list exhaustively all known vascular anomalies. Some rare "dermatologic" vascular anomalies will be found in dermatology textbooks.

The tumor or malformation nature or precise classification of some lesions is still unclear. These lesions appear in a [separate provisional list](#).

[Abbreviations used](#)

For more details, click on the underlined links



[Back to overview](#)

<b>Benign vascular tumors</b>	
Infantile hemangioma / Hemangioma of infancy	<a href="#">see details</a>
<b>Congenital hemangioma</b>	
Rapidly involuting (RICH) *	
Non-involuting (NICH)	
Partially involuting (PICH)	
Tufted angioma * °	
Spindle-cell hemangioma	
Epithelioid hemangioma	
Pyogenic granuloma (aka lobular capillary hemangioma)	
Others	
<b>Locally aggressive or borderline vascular tumors</b>	
Kaposiform hemangioendothelioma * °	
Retiform hemangioendothelioma	
Papillary intralymphatic angioendothelioma (PILA), Dabska tumor	
Composite hemangioendothelioma	
Kaposi sarcoma	
Others	
<b>Malignant vascular tumors</b>	
Angiosarcoma	
Epithelioid hemangioendothelioma	
Others	

\* some lesions may be associated with thrombocytopenia and/or consumptive coagulopathy [see details](#)

° many experts believe that these are part of a spectrum rather than distinct entities

**N.B.** reactive proliferative vascular lesions are listed with benign tumors

<b>Simple vascular malformations I</b>	
<b>Capillary malformations (CM)</b>	
Cutaneous and/or mucosal CM (aka “port-wine” stain )	<a href="#">G</a>
CM with bone and/or soft tissue overgrowth	
CM with CNS and/or ocular anomalies (Sturge-Weber syndrome)	
CM of CM-AVM	<a href="#">G</a>
CM of MICCAP (microcephaly-capillary malformation)	
CM of MCAP (megalencephaly-capillary malformation-polymicrogyria)	
Telangiectasia	
Hereditary hemorrhagic telangiectasia (HHT) ( <a href="#">different types</a> )	<a href="#">G</a>
Others	
Cutis marmorata telangiectatica congenita (CMTC)	
Nevus simplex / Salmon patch / “angel kiss”, “stork bite”	
Others	

<b>Simple vascular malformations II</b>	
<b>Lymphatic malformations (LM)</b>	
Common (cystic) LM	
Macrocystic LM	
Microcystic LM	
Mixed cystic LM	
Generalized lymphatic anomaly (GLA)	
LM in Gorham-Stout disease	
Channel type LM	
Primary lymphedema <a href="#">(different types)</a>	<a href="#">G</a>
Others	

some lesions may be associated with thrombocytopenia and/or consumptive coagulopathy [see details](#)

click on [G](#) to see genetics

## Simple vascular malformations IIb

### Primary lymphedema

Nonne-Milroy syndrome

[G](#)

Primary hereditary lymphedema

[G](#)

Lymphedema-distichiasis

[G](#)

Hypotrichosis-lymphedema-telangiectasia

[G](#)

Primary lymphedema with myelodysplasia

[G](#)

Primary generalized lymphatic anomaly  
(Hennekam lymphangiectasia-lymphedema syndrome)

[G](#)

Microcephaly with or without chorioretinopathy,  
lymphedema, or mental retardation syndrome

[G](#)

Lymphedema-choanal atresia

[G](#)

Simple vascular malformations III	
<b>Venous malformations (VM)</b>	
Common VM	<a href="#">G</a>
Familial VM cutaneo-mucosal (VMCM)	<a href="#">G</a>
Blue rubber bleb nevus (Bean) syndrome VM	
Glomuvenous malformation (GVM)	<a href="#">G</a>
Cerebral cavernous malformation (CCM) ( <a href="#">different types</a> )	<a href="#">G</a>
Others	

some lesions may be associated with thrombocytopenia and/or consumptive coagulopathy [see details](#)

click on [G](#) to see genetics

Simple vascular malformations IV	
<b>Arteriovenous malformations (AVM)</b>	
Sporadic	
In HHT	<a href="#">G</a>
In CM-AVM	<a href="#">G</a>
Others	
<b>Arteriovenous fistula (AVF) (congenital)</b>	
Sporadic	
In HHT	<a href="#">G</a>
In CM-AVM	<a href="#">G</a>
Others	

<b>Combined vascular malformations*</b>		
CM + VM	capillary-venous malformation	CVM
CM + LM	capillary-lymphatic malformation	CLM
CM + AVM	capillary-arteriovenous malformation	CAVM
LM + VM	lymphatic-venous malformation	LVM
CM + LM + VM	capillary-lymphatic-venous malformation	CLVM
CM + LM + AVM	capillary-lymphatic-arteriovenous malformation	CLAVM
CM + VM + AVM	capillary-venous-arteriovenous malformation	CVAVM
CM + LM + VM + AVM	capillary-lymphatic-venous-arteriovenous m.	CLVAVM

\* defined as two or more vascular malformations found in one lesion



## **Anomalies of major named vessels**

(aka "channel type" or "truncal" vascular malformations)

### Affect

lymphatics

veins

arteries

### Anomalies of

origin

course

number

length

diameter (aplasia, hypoplasia, stenosis, ectasia / aneurysm)

valves

communication (AVF)

persistence (of embryonal vessel)

Vascular malformations associated with other anomalies		
Klippel-Trenaunay syndrome:	CM + VM +/- LM + limb overgrowth	
Parkes Weber syndrome:	CM + AVF + limb overgrowth	<a href="#">G</a>
Servelle-Martorell syndrome:	limb VM + bone undergrowth	
Sturge-Weber syndrome:	facial + leptomeningeal CM + eye anomalies +/- bone and/or soft tissue overgrowth	<a href="#">G</a>
Limb CM + congenital non-progressive limb hypertrophy		
Maffucci syndrome:	VM +/- spindle-cell hemangioma + enchondroma	
Macrocephaly - CM (M-CM / MCAP)		<a href="#">G</a>
Microcephaly - CM (MICCAP)		<a href="#">G</a>
CLOVES syndrome:	LM + VM + CM +/- AVM + lipomatous overgrowth	<a href="#">G</a>
Proteus syndrome:	CM, VM and/or LM + asymmetrical somatic overgrowth	<a href="#">G</a>
Bannayan-Riley-Ruvalcaba sd:	AVM + VM +macrocephaly, lipomatous overgrowth	<a href="#">G</a>

## Provisionally unclassified vascular anomalies

Verrucous hemangioma

Angiokeratoma

Multifocal lymphangioendotheliomatosis with thrombocytopenia / cutaneovisceral angiomatosis with thrombocytopenia (MLT/CAT)

Kaposiform lymphangiomatosis (KLA)

PTEN (type) hamartoma of soft tissue / "angiomatosis" of soft tissue

[G](#)

some lesions may be associated with thrombocytopenia and/or consumptive coagulopathy [see details](#)

click on [G](#) to see genetics

# Appendix 1

## **abbreviations used**

(excluding gene names)

AVF	arteriovenous fistula
AVM	arteriovenous malformation
CAT	cutaneovisceral angiomas with thrombocytopenia
CAVM	capillary arteriovenous malformation
CCM	cerebral cavernous malformation
CLAVM	capillary lymphatic arteriovenous malformation
CLOVES	congenital lipomatous overgrowth, vascular malformations, epidermal nevi, skeletal/scoliosis and spinal abnormalities
CLM	capillary lymphatic malformation
CLVAVM	capillary lymphatic venous arteriovenous malformation
CLVM	capillary lymphatic venous malformation
CM	capillary malformation
CM-AVM	capillary malformation-arteriovenous malformation
CMTC	cutis marmorata telangiectatica congenita
CNS	central nervous system
CVAVM	capillary venous arteriovenous malformation
CVM	capillary venous malformation
DIC	disseminated intravascular coagulopathy
GLA	generalized lymphatic anomaly
GSD	Gorham-Stout disease
GVM	glomovenous malformation
HHT	hereditary hemorrhagic telangiectasia

HI	hemangioma of infancy / infantile hemangioma
IH	infantile hemangioma / hemangioma of infancy
INR	international normalized ratio
JPHT	juvenile polyposis hemorrhagic telangiectasia
KHE	kaposiform hemangioendothelioma
KLA	kaposiform lymphangiomatosis
KMP	Kasabach-Merritt phenomenon,
LM	lymphatic malformation
LVM	lymphatic venous malformation
MCAP	megalencephaly-capillary malformation-polymicrogyria
M-CM	macrocephaly-capillary malformation
MICCAP	microcephaly-capillary malformation
MLT	Multifocal lymphangioendotheliomatosis with thrombocytopenia
NICH	non-involuting congenital hemangioma
PHACE	posterior fossa malformations, hemangioma, arterial anomalies, cardiovascular anomalies, eye anomalies
PILA	papillary intralymphatic angioendothelioma
PICH	partially involuting congenital hemangioma
RICH	rapidly involuting congenital hemangioma
TA	tufted angioma
VM	venous malformation
VMCM	venous malformation cutaneo mucosal

## Appendix 2-a

### *causal genes of vascular anomalies*

<b>Capillary malformations (CM)</b>	
Cutaneous and/or mucosal CM (aka “port-wine” stain )	<b>GNAQ</b>
CM with bone and/or soft tissue hyperplasia	
CM with CNS and/or ocular anomalies (Sturge-Weber syndrome)	<b>GNAQ</b>
CM of CM-AVM	<b>RASA1</b>
Telangiectasia	
Hereditary hemorrhagic telangiectasia (HHT)	
<i>HHT1</i>	<b>ENG</b>
<i>HHT2</i>	<b>ACVRL1</b>
<i>HHT3</i>	
<i>JPHT</i> (juvenile polyposis hemorrhagic telangiectasia)	<b>SMAD4</b>
Others	
Cutis marmorata telangiectatica congenita (CMTC)	
Nevus simplex / Salmon patch	
Others	

## Appendix 2-b

### *causal genes of vascular anomalies*

<b>Lymphatic malformations (LM)</b>	
<b>Primary lymphedema</b>	
Nonne-Milroy syndrome	<b>FLT4 / VEGFR3</b>
Primary hereditary lymphedema	<b>VEGFC</b>
Primary hereditary lymphedema	<b>GJC2 /</b>
<b>Connexin 47</b>	
Lymphedema-distichiasis	<b>FOXC2</b>
Hypotrichosis-lymphedema-telangiectasia	<b>SOX18</b>
Primary lymphedema with myelodysplasia	<b>GATA2</b>
Primary generalized lymphatic anomaly (Hennekam lymphangiectasia-lymphedema syndrome)	<b>CCBE1</b>
Microcephaly with or without chorioretinopathy, lymphedema, or mental retardation syndrome	<b>KIF11</b>
Lymphedema-choanal atresia	<b>PTPN14</b>

## Appendix 2-c

### *causal genes of vascular anomalies*

<b>Venous malformations (VM)</b>	
Common VM	TIE2 somatic
Familial VM cutaneo-mucosal (VMCM)	TIE2
Blue rubber bleb nevus (Bean) syndrome VM	
Glomuvenous malformation (VM with glomus cells)	Glomulin
Cerebral cavernous malformation (CCM)	
CCM1	KRIT1
CCM2	Malcavernin
CCM3	PDCD10

## Appendix 2-d

### *causal genes of vascular anomalies*

<b>Arteriovenous malformations (AVM)</b>	
Sporadic	
In HHT	
<i>HHT1</i>	ENG
<i>HHT2</i>	ACVRL1
<i>JPHT (juvenile polyposis hem. telangiect.)</i>	SMAD4
In CM-AVM	RASA1
<b>Arteriovenous fistulas (AVF)</b>	
Sporadic	
In HHT	
<i>HHT1</i>	ENG
<i>HHT2</i>	ACVRL1
<i>JPHT (juvenile polyposis hemorrhagic telangiectasia)</i>	SMAD4
In CM-AVM	RASA1



## Appendix 2-e

### *causal genes of vascular anomalies*

<b>Vascular malformations associated with other anomalies</b>	
Klippel-Trenaunay syndrome	
Parkes Weber syndrome	<b>RASA1</b>
Servelle-Martorell syndrome	
Sturge-Weber syndrome	<b>GNAQ</b>
Limb CM + congenital non-progressive limb overgrowth	
Maffucci syndrome	
Macrocephaly - CM (M-CM or MCAP)	<b>PIK3CA</b>
Microcephaly - CM (MICCAP)	<b>STAMBP</b>
CLOVES syndrome	<b>PIK3CA</b>
Proteus syndrome	<b>AKT1</b>
Bannayan-Riley-Ruvalcaba syndrome	<b>PTEN</b>

## Appendix 2 -f

### *causal genes of vascular anomalies*

<b>Provisionally unclassified vascular anomalies</b>	
Verrucous hemangioma	
Multifocal lymphangioendotheliomatosis with thrombocytopenia / cutaneovisceral angiomatosis with thrombocytopenia (MLT/CAT)	
Kaposiform lymphangiomatosis (KLA)	
PTEN (type) hamartoma of soft tissue / "angiomatosis" of soft tissue	<b>PTEN</b>

some lesions may be associated with thrombocytopenia and/or consumptive coagulopathy [see details](#)

## Appendix 3

### *infantile hemangioma*

<b>Pattern</b>	<b>Different types</b>
<ul style="list-style-type: none"><li>- focal</li><li>- multifocal</li><li>- segmental</li><li>- indeterminate</li></ul>	<ul style="list-style-type: none"><li>- superficial</li><li>- deep</li><li>- mixed (superficial + deep)</li><li>- reticular / abortive / minimal growth</li><li>- others</li></ul>

<b>Association with other lesions</b>	
PHACE association / syndrome	Posterior fossa malformations, Hemangioma, Arterial anomalies, Cardiovascular anomalies, Eye anomalies, sternal clefting and/or supraumbilical raphe
LUMBAR (SACRAL, PELVIS) association / syndrome	Lower body hemangioma, Urogenital anomalies, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Arterial anomalies, and Renal anomalies

### *possibly associated with platelet count / coagulation disorders*

<b>Anomalies</b>	<b>Hematological disorders</b>
Tufted angioma Kaposiform hemangioendothelioma	Profound and sustained thrombocytopenia with profound hypofibrinogenemia, consumptive coagulopathy and elevated D-dimer (Kasabach-Merritt phenomenon)
Rapidly involuting congenital hemangioma	Transient mild/moderate thrombocytopenia, +/- consumptive coagulopathy and elevated D-dimer
Venous malformations / Lymphatic-venous malformations	Chronic localized intravascular coagulopathy with elevated D-dimer, +/- hypofibrinogenemia, and +/- moderate thrombocytopenia (may progress to DIC after trauma or operation)
Lymphatic malformations	Chronic localized intravascular coagulopathy with elevated D-dimer and +/- mild to moderate thrombocytopenia <i>(consider Kaposiform lymphangiomatosis)</i> (may progress to DIC after trauma or operation)
Multifocal lymphangioendotheliomatosis with thrombocytopenia / Cutaneovisceral angiomatosis with thrombocytopenia	Sustained, fluctuating, moderate to profound thrombocytopenia with gastrointestinal tract bleeding or pulmonary hemorrhage
Kaposiform lymphangiomatosis	Mild to Moderate thrombocytopenia, +/- hypofibrinogenemia, and D-dimer elevation