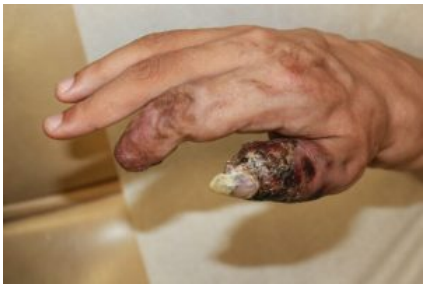
COURSE 05: INTERVENTIONAL RADIOLOGIC MANAGEMENT OF VASCULAR ANOMALIES OF THE EXTREMITIES

Dr. Robert Rosen

Introduction: Interventional radiologic management of vascular anomalies of the extremities



Vascular anomalies include vascular tumors and vascular malformations. Treatment of these anomalies is often multidisciplinary, combining surgery, pharmacologic agents, laser therapy, and interventional radiologic procedures which include embolic therapy and sclerotherapy. These latter techniques are playing an increasingly critical role in the management of these often complex anomalies. This module discusses the diagnosis and treatment of common vascular anomalies, with emphasis on the techniques, efficacy, and potential complications associated with interventional radiologic procedures.

Interventionalists have assumed a primary role in the management of children and adults with vascular anomalies. Most practitioners feel that a dedicatedmultispecialty group of physicians is necessary to provide proper care for these complex problems. The key to proper treatment is making the correct diagnosis and knowing the natural history of that condition.

The choice of interventional approach should be based on a careful risk/benefit analysis for each patient. The details of guidance techniques, delivery systems, and embolic agents will depend on the location and nature of the malformation as well as the expertise of the interventionalist. The ability and willingness to provide long-term follow-up and constant availability for clinical problems is essential in this patient population.

This module will focus on management of vascular anomalies of the trunk and extremities using interventional techniques. Making the correct diagnosis, using the appropriate nomenclature, and knowing the natural history of these conditions is key. The best diagnostic modalities will be briefly reviewed. A discussion of interventional techniques-including transcatheter embolization and direct puncture techniques as well as the appropriate embolic agents for each type of condition-will be presented.

Objectives

Upon successful completion of this activity, participants should be able to:

- Identify the role of the interventionalist in treating vascular anomalies
- Differentiate the various types of vascular anomalies in order to choose the appropriate interventional treatment option
- Distinguish treatment options that include and exclude the role of the interventionalist
- Describe interventional treatment options for treating vascular anomalies
- Identify treatment and post-treatment obstacles
- Outline treatment modalities used by the interventionalist
- Distinguish complex cases treated with interventional strategies
- Compare and contrast treatment options
- Explain the critical value of accurate diagnosis for the best outcome for the interventionalist
- Describe issues interventionalists should discuss with patients

Making the correct diagnosis

There are now extremely detailed and sophisticated classification systems for the various types of vascular malformations. The most current and comprehensive is the 2014 Updated ISSVA Classification, which is covered in detail in Module 1 of this course.

For the purposes of intervention, it is important to at least consider the four major categories of vascular lesion:

- Hemangioma (a benign tumor of infancy, not a malformation)
- True arteriovenous malformation (AVM, high-flow)
- Venous malformation (VM, low-flow)
- Lymphatic malformation (LM, low-flow)

Hemangioma

This is a benign endothelial cell tumor of infancy, characterized by various stages, including:

- Appearance – at birth or shortly thereafter
- Proliferative stage – lesion may grow rapidly and be associated with several clinical problems, including pain, bleeding, ulceration, and interference with normal structure/function
- Involution – spontaneous shrinkage of the lesion due to complex cellular factors. The final result may need no treatment or leave significant residual tissue damage

The drug Propranolol has now assumed a major role in accelerating the process of involution. The drug should be prescribed and monitored by pediatric specialists knowledgeable in its use and potential side effects.

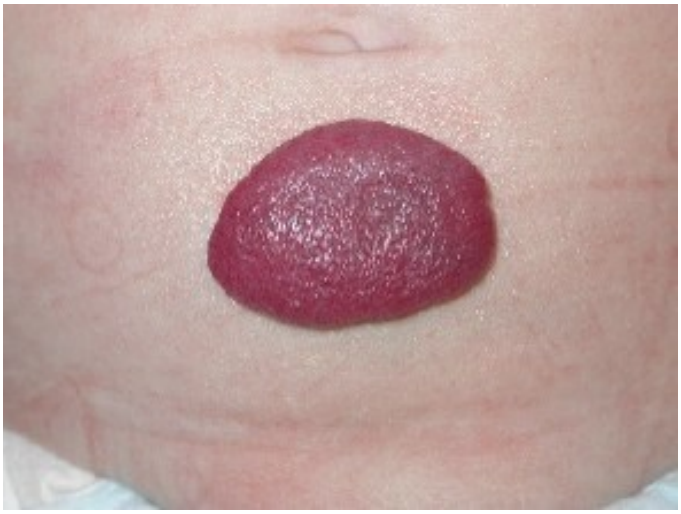
The term “hemangioma” has been misused for many years, leading to confusion in the literature and especially for patients and their families who, consequently, develop inaccurate expectations regarding the prognosis and appropriate treatment of the condition. Briefly put, the term “hemangioma” does not apply to any condition other than the benign tumor of infancy.

Hemangioma and other proliferative lesions vs. vascular malformations

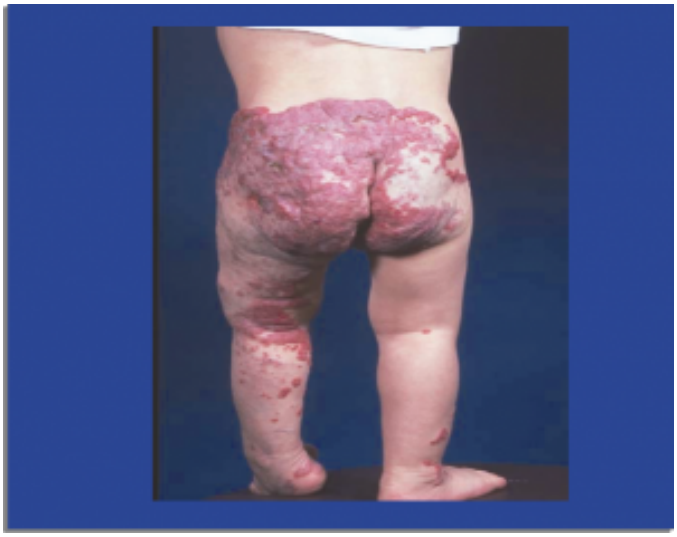
Vascular tumors	Vascular malformations
• Infantile hemangioma • Congenital hemangioma (RICH and NICH) • Tufted angioma (with or without Kasabach-Merritt syndrome) • Kaposiform hemangioendothelioma (with or without Kasabach-Merritt syndrome) • Spindle cell hemangioendothelioma • Other, rare hemangioendotheliomas (epithelioid, composite, retiform, polymorphous, Dabska tumor, etc.) • Dermatologic acquired vascular tumors (pyogenic granuloma, targetoid heman-gioma, glomeruloid hemangi oma, etc.)	Slow-flow vascular malformations • CM Port-wine stain Angiokeratoma • VM Common sporadic VM GVM (glomangioma) • LM Fast-flow vascular malformations • AM • AVF • AVM Complex-combined vascular malformations • CVM, CLM, LVM, CLVM, AVM-LM, CM-AVM

Taken from Updated 2014 ISSVA Classification

Infantile hemangioma: benign endothelial tumor



Focal infantile hemangioma



Diffuse segmental infantile hemangioma

These lesions are the only lesions that should be termed *hemangioma.*

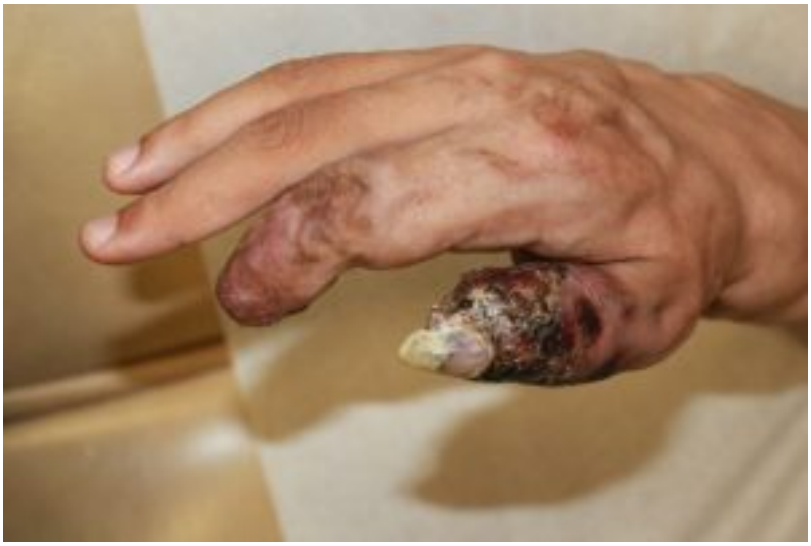
Arteriovenous malformations (AVM)

- A true arteriovenous malformation (AVM) is an abnormal connection between the arterial and venous systems at something larger than capillary level, leading to shunting.
- Most of these lesions are congenital (present at birth; actually they are present prior to birth). Most do not run in families, however there are some types of arteriovenous malformations that are hereditary (eg. HHT, RASA-1).
- The site of the actual AV communication is called the Nidus, which may range from a complex small vessel connection to a direct AV connection equivalent to an AV fistula.

AVM natural history

- While present at or before birth, by definition, clinical manifestations will depend on the size and location of the lesion; some will be obvious from birth while others may not become manifest until later in life.
- Growth is usually at the same rate as other normal body tissues, although increased growth may occur at times of increased hormonal activity, such as puberty, pregnancy, the use of birth control pills and, in some cases, after intervention.

Natural history of AVMs



Gangrenous thumb secondary to steal from a high flow AVM

Depending on the size and location, malformations may remain asymptomatic, in which case no treatment is required. Some malformations, however, may cause:

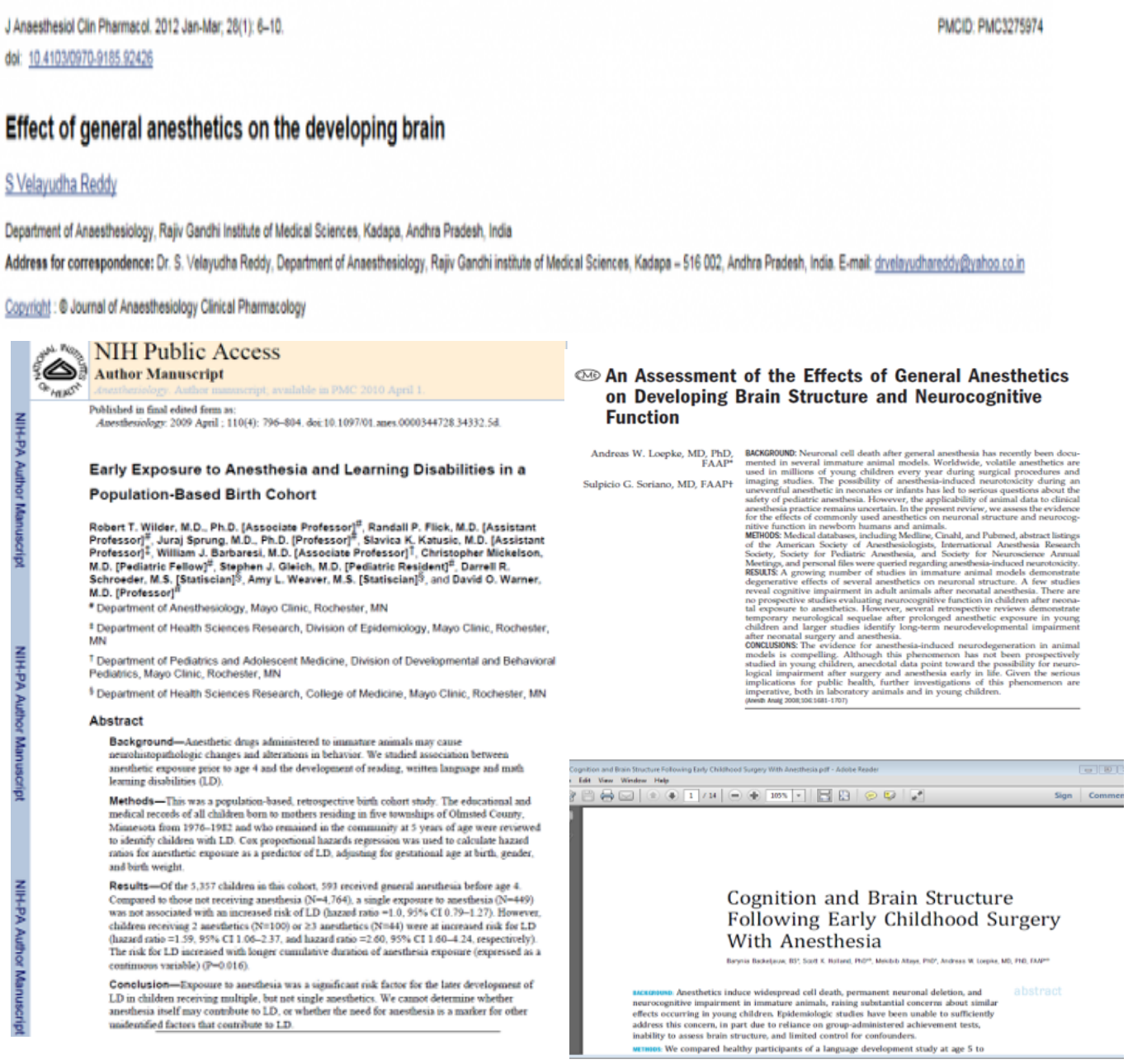
- Mass
- Pain
- Bleeding
- Ischemia
- Growth disturbance
- High output states

Early vs. delayed treatment

The decision as to when to treat is controversial, particularly in the pediatric age group. The pros of early treatment are:

- Better long-term result (generally)
- Anesthesia risks based on age are reduced (controversial)
- Psychological factors: infants and young children (<5 yrs.) may actually tolerate intervention better than when older
- Advantage to intervening before potential accelerated growth of malformation at puberty
- Cardiovascular considerations: generalized CV effects are unusual
- Function preservation, especially when the knee joint is involved (will be discussed in more detail)

Risks of anesthesia to developing brain?



J Anaesthesiol Clin Pharmacol. 2012 Jan-Mar; 28(1): 6–10. PMCID: PMC3275974
doi: 10.4103/0970-9185.92426

Effect of general anesthetics on the developing brain

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NIH Public Access
Author Manuscript
Anesthesiology. Author manuscript; available in PMC 2010 April 1.

Published in final edited form as:
Anesthesiology. 2009 April ; 110(4): 796–804. doi:10.1097/01.anes.0000344728.34332.5d.

Early Exposure to Anesthesia and Learning Disabilities in a Population-Based Birth Cohort

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Abstract

Background—Anesthetic drugs administered to immature animals may cause neurohistopathologic changes and alterations in behavior. We studied association between anesthetic exposure prior to age 4 and the development of reading, written language and math learning disabilities (LD).

Methods—This was a population-based, retrospective birth cohort study. The educational and medical records of all children born to mothers residing in five townships of Olmsted County, Minnesota from 1976–1982 and who remained in the community at 5 years of age were reviewed to identify children with LD. Cox proportional hazards regression was used to calculate hazard ratios for anesthetic exposure as a predictor of LD, adjusting for gestational age at birth, gender, and birth weight.

Results—Of the 5,357 children in this cohort, 593 received general anesthesia before age 4. Compared to those not receiving anesthesia (N=4,764), a single exposure to anesthesia (N=449) was not associated with an increased risk of LD (hazard ratio =1.0, 95% CI 0.79–1.27). However, children receiving 2 anesthetics (N=100) or ≥3 anesthetics (N=44) were at increased risk for LD (hazard ratio =1.59, 95% CI 1.06–2.37, and hazard ratio =2.60, 95% CI 1.60–4.24, respectively). The risk for LD increased with longer cumulative duration of anesthesia exposure (expressed as a continuous variable) (P=0.016).

Conclusion—Exposure to anesthesia was a significant risk factor for the later development of LD in children receiving multiple, but not single anesthetics. We cannot determine whether anesthesia itself may contribute to LD, or whether the need for anesthesia is a marker for other unidentified factors that contribute to LD.

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An Assessment of the Effects of General Anesthetics on Developing Brain Structure and Neurocognitive Function

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BACKGROUND: Neuronal cell death after general anesthesia has recently been documented in several immature animal models. Worldwide, volatile anesthetics are used in millions of young children every year during surgical procedures and imaging studies. The possibility of anesthesia-induced neurotoxicity during an uneventful anesthetic in neonates or infants has led to serious questions about the safety of pediatric anesthesia. However, the applicability of animal data to clinical anesthesia practice remains uncertain. In the present review, we assess the evidence for the effects of commonly used anesthetics on neuronal structure and neurocognitive function in newborn humans and animals.
METHODS: Medical databases, including Medline, Cinahl, and Pubmed, abstract listings of the American Society of Anesthesiologists, International Anesthesia Research Society, Society for Pediatric Anesthesia, and Society for Neuroscience Annual Meetings, and personal files were queried regarding anesthesia-induced neurotoxicity.
RESULTS: A growing number of studies in immature animal models demonstrate degenerative effects of several anesthetics on neuronal structure. A few studies reveal cognitive impairment in adult animals after neonatal anesthesia. There are no prospective studies evaluating neurocognitive function in children after neonatal exposure to anesthetics. However, several retrospective reviews demonstrate temporary neurological sequelae after prolonged anesthetic exposure in young children and larger studies identify long-term neurodevelopmental impairment after neonatal surgery and anesthesia.
CONCLUSIONS: The evidence for anesthesia-induced neurodegeneration in animal models is compelling. Although this phenomenon has not been prospectively studied in young children, anecdotal data point toward the possibility for neurological impairment after surgery and anesthesia early in life. Given the serious implications for public health, further investigations of this phenomenon are imperative, both in laboratory animals and in young children.
(Anesth Analg 2008;106:1681–1707)

Cognition and Brain Structure Following Early Childhood Surgery With Anesthesia.pdf - Adobe Reader

Cognition and Brain Structure Following Early Childhood Surgery With Anesthesia

abstract

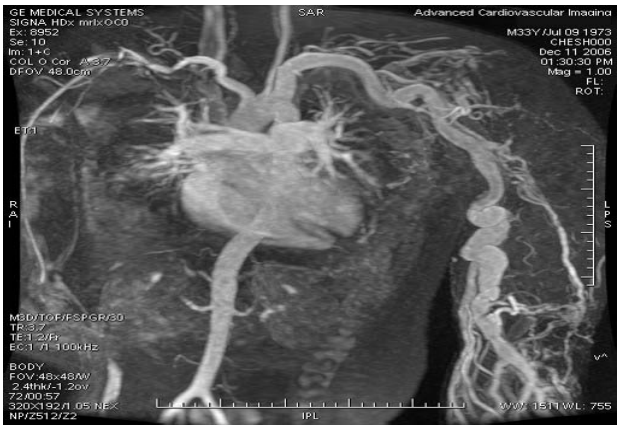
BACKGROUND: Anesthetics induce widespread cell death, permanent neuronal deletion, and neurocognitive impairment in immature animals, raising substantial concerns about similar effects occurring in young children. Epidemiologic studies have been unable to sufficiently address this concern, in part due to reliance on group-administered achievement tests, inability to assess brain structure, and limited control for confounders.

METHODS: We compared healthy participants of a language development study at age 5 to

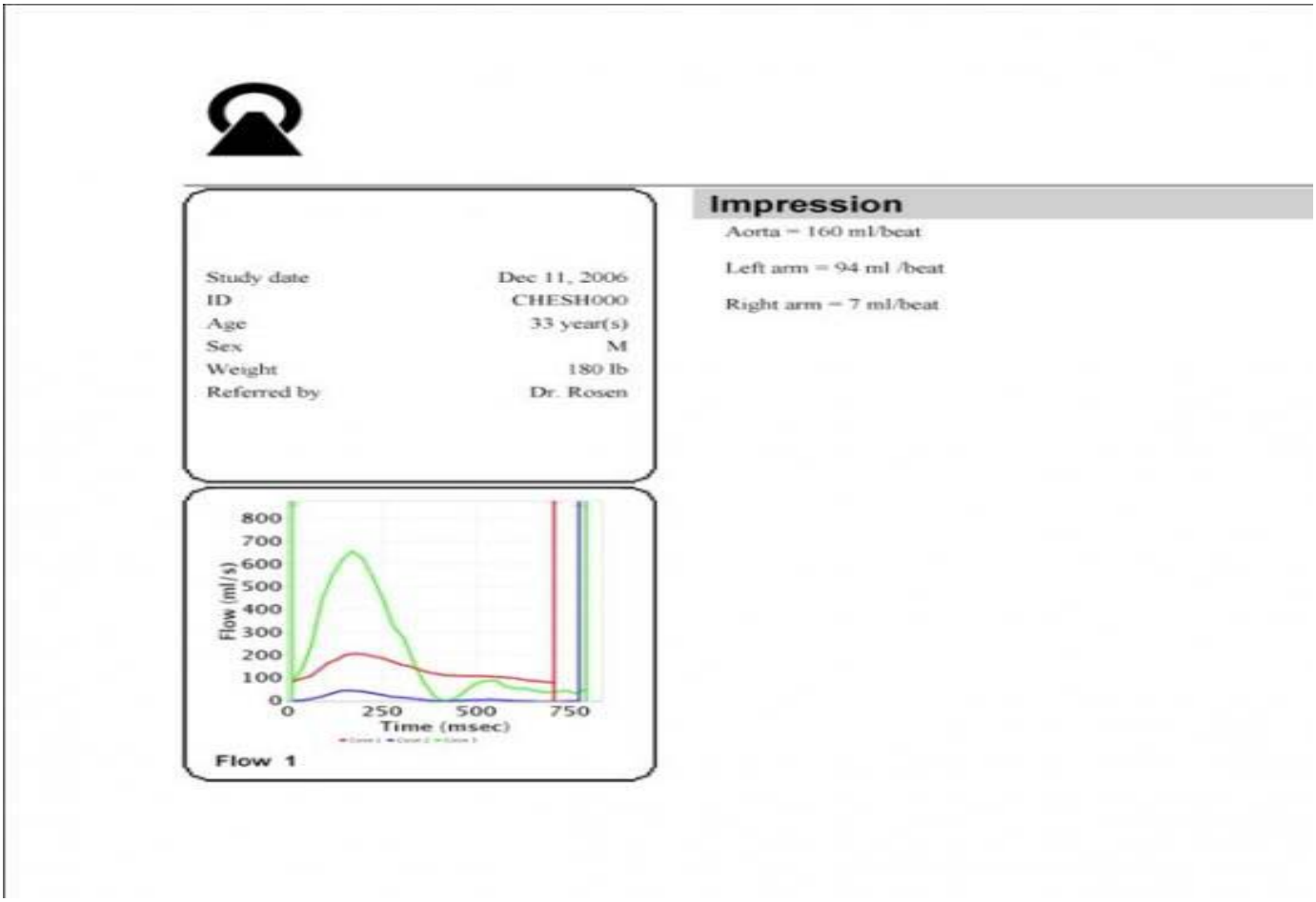
In recent years, animal studies have suggested risks of anesthesia to the developing brain. This suggestion has not yet been borne out in human studies, but the use of anesthesia should be restricted to truly necessary procedures (including MR imaging in young children who may require anesthesia).

High-flow AVMs

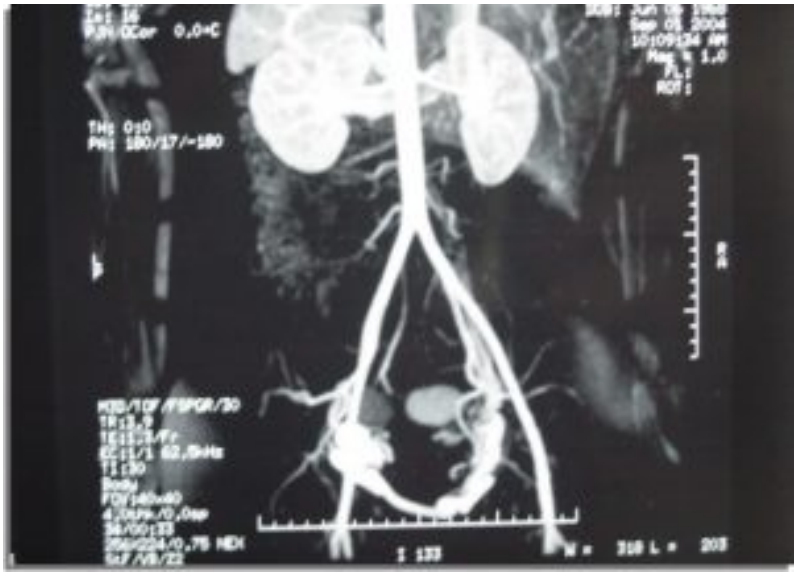
High flow AVMs can cause an increase in cardiac workload, but the actual incidence of high output cardiac states or failure is low.



The degree of shunting can be quantified by both echocardiography as well as quantitative MR and CT studies as seen above; this may also be useful for follow-up studies to evaluate disease progression or treatment response.



MRI/MRA and CT/CTA

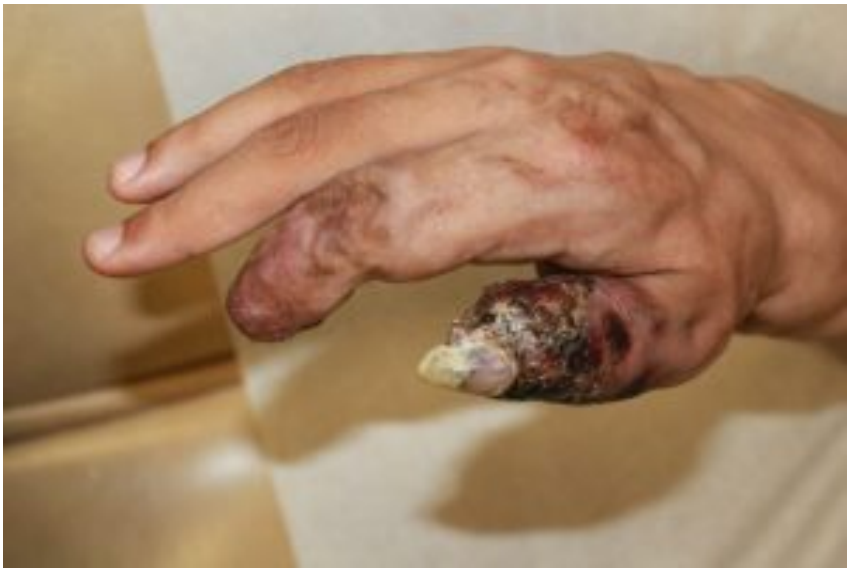


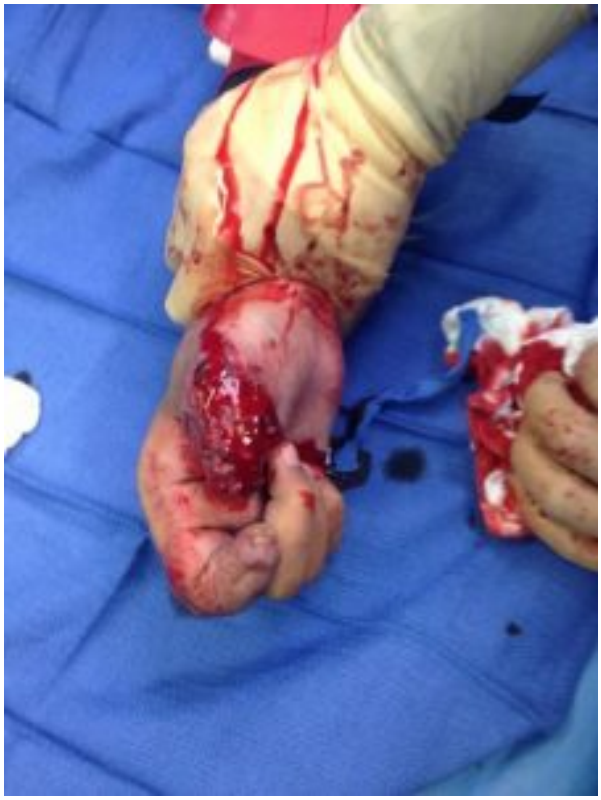
MRI/MRA and CT/CTA now show precise arterial supply and venous drainage in addition to multiplanar anatomy.
Thus, until treatment is planned, there is no reason to perform invasive diagnostic procedures, especially in pediatric patients.

Treatment option for high flow AVMs – Surgery

- Mainly suitable for localized, completely resectable lesions; ligating feeders ineffective or worse
- “Debulking” procedures may be helpful in extremely large lesions, but patient selection is critical
- Need detailed pre-op imaging studies to evaluate the true extent of lesion
- Must be prepared for blood loss – tourniquets, cell saver, possible pre- or intra-op embolization
- Significant likelihood of recurrence (many patients have surgical scars)

Even something as simple as a digital amputation can result in life-threatening bleeding

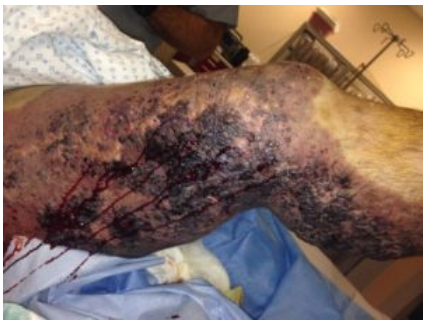




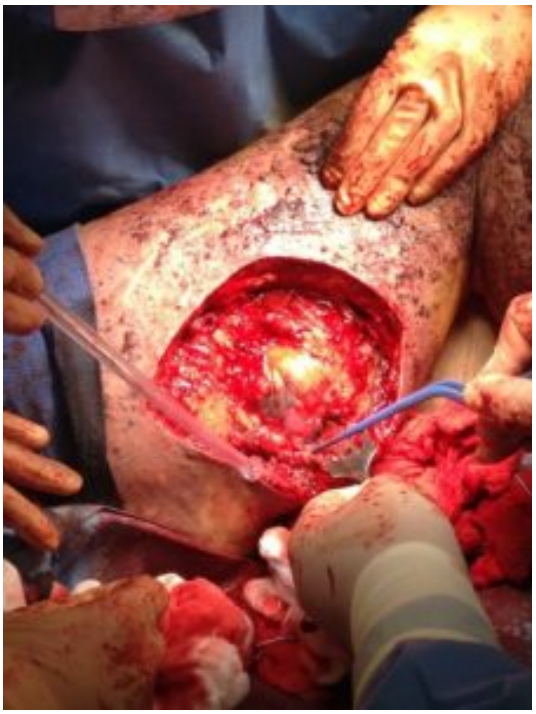
Amputation was planned for this gangrenous thumb secondary to steal from a high flow AVM. Even with an automatic tourniquet set at 300mmHg, bleeding due to the intra-osseous component of the AVM could not be controlled at surgery. Intra-operative embolization was necessary.

Role for surgery

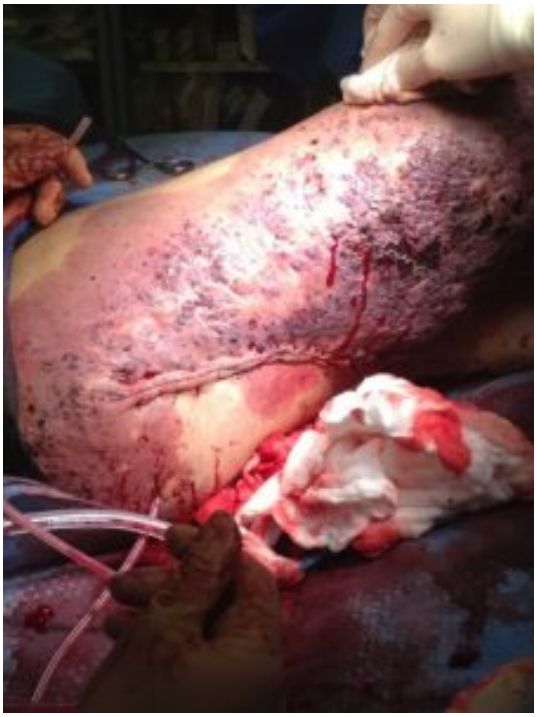
There is definitely a role for surgery when there are localized lesions, when there are extremely bulky lesions, or when there is extensive skin involvement.



Severe Klippel-Trenaunay Syndrome (KTS) with extensive skin involvement by angiokeratomas which bled constantly



Resection of involved skin

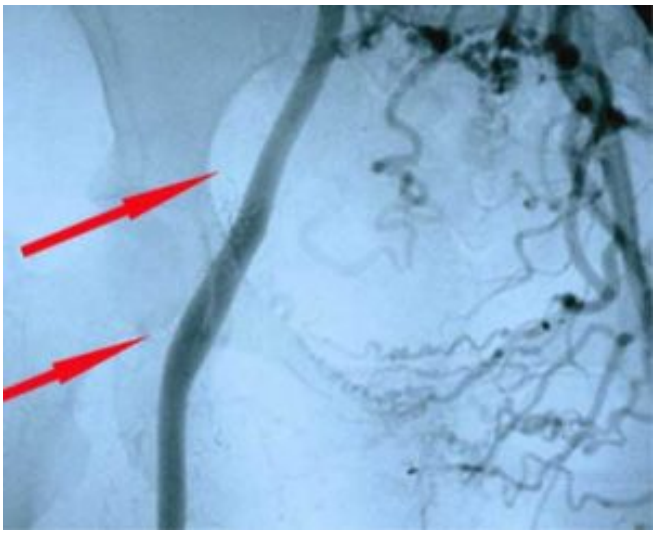


Primary closure was performed by plastic surgeon

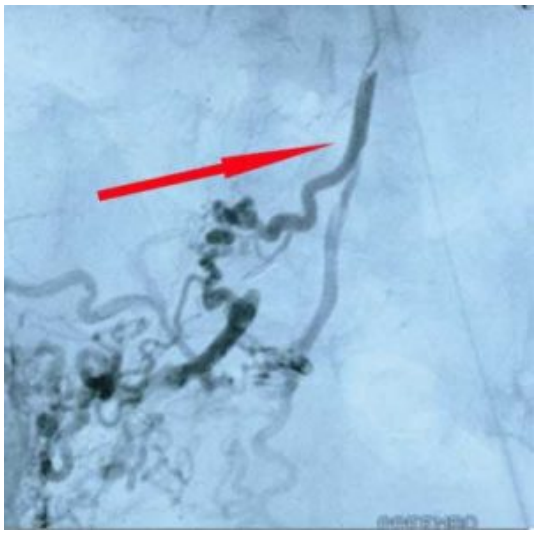
Ligating arterial branches

Ligating arterial branches feeding a high flow AVM is not only ineffective, but sacrifices catheter access to the nidus for a more definitive embolization procedure; coil embolization is equally ineffective.

28-year old female with pelvic pain
Right sided pelvic AVM with multiple feeders



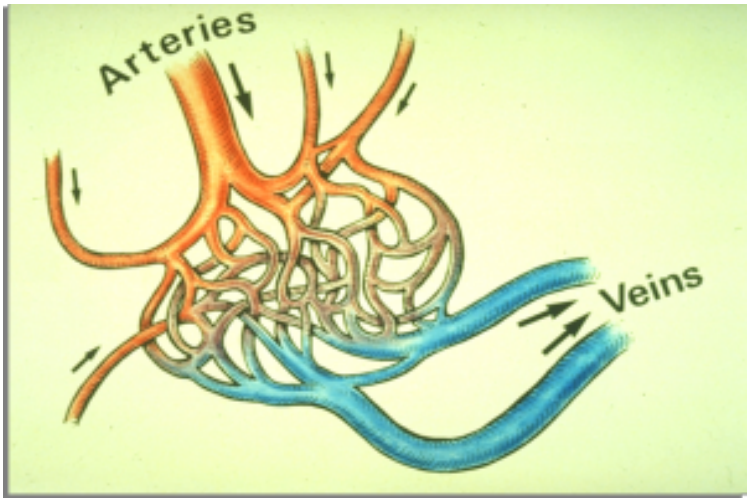
14 hour procedure with ligation of all hypogastric and femoral branches



Recurrent symptoms four months post-op Nidus resupplied by middle sacral branches

Nidus principle

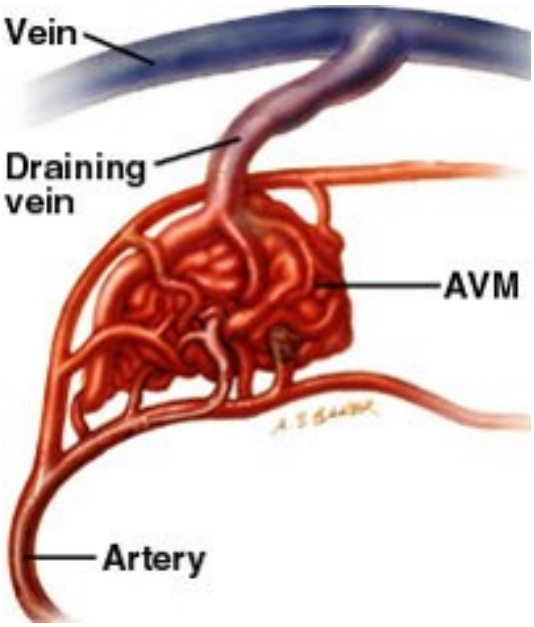
The principle is that only eradication of the nidus will provide a long-term result.



Pictured here is the “nidus,” the actual site of arteriovenous communication. The nidus varies in terms of vessel caliber and complexity.

Two primary mechanisms

There are two primary mechanisms at work in the tendency of AVMs to recur after treatment.



Physical factors (“Plumbing”)

- Pressure/flow realationships; blood flow will always find path of least resistance **More complex phenomena**
- Angiogenesis
- Local ischemia
- Events at cellular level

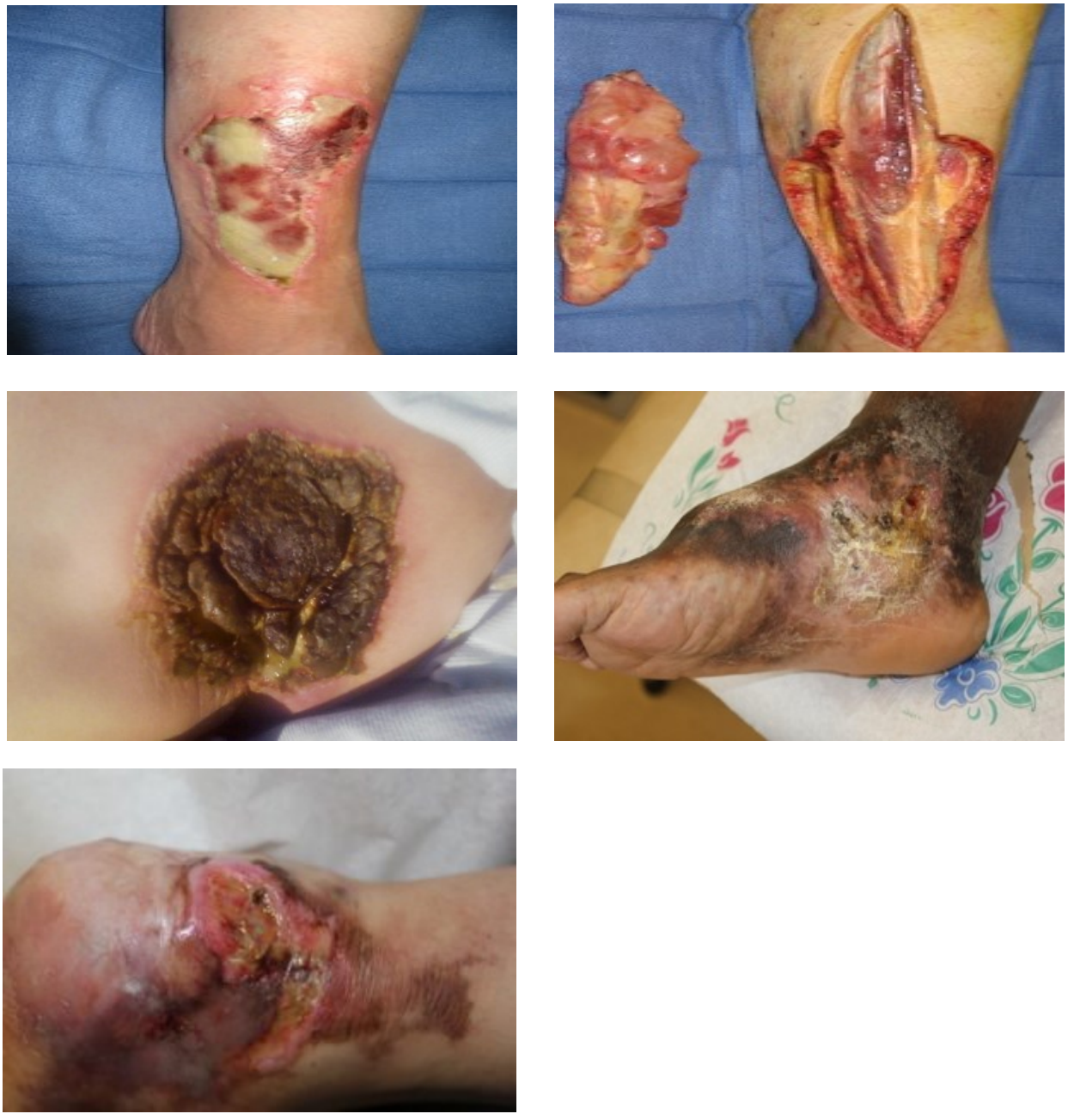
Ethanol

This agent can be used intra-arterially for high-flow malformations.

- Works by clotting blood and damaging endothelium.
- Must be used with caution due to tissue toxicity and radiolucency, risk of neurotoxicity, mucosal ulceration, skin sloughing.
- Can achieve cure in high-flow lesions, unlike most agents, but be aware of risks.

Intra-arterial ethanol

Be cautious with intra-arterial ethanol! There is a relatively small therapeutic margin; normal branches must be avoided.

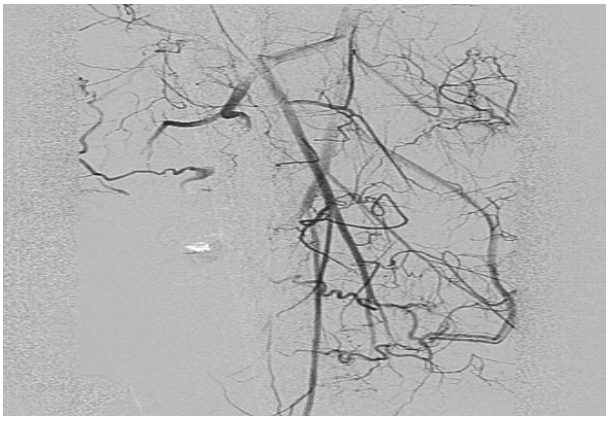


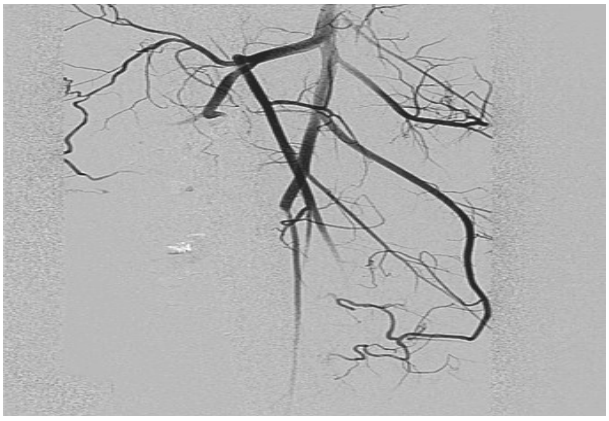
Examples of injury to normal tissues from intra-arterial ethanol.

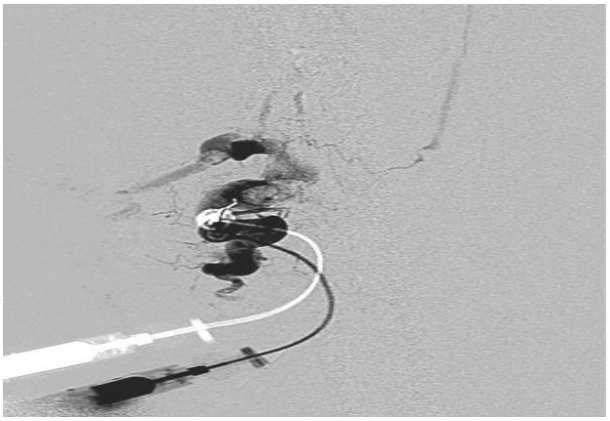
Considerable experience and detailed contrast studies are required to use this potent sclerosant intra-arterially. Ethanol which escapes into the venous circulation also carries a risk of generalized cardiovascular effects, including cardiac arrest.

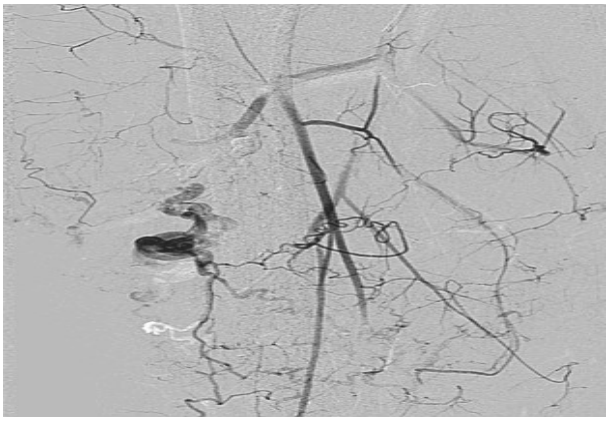
Injected ethanol

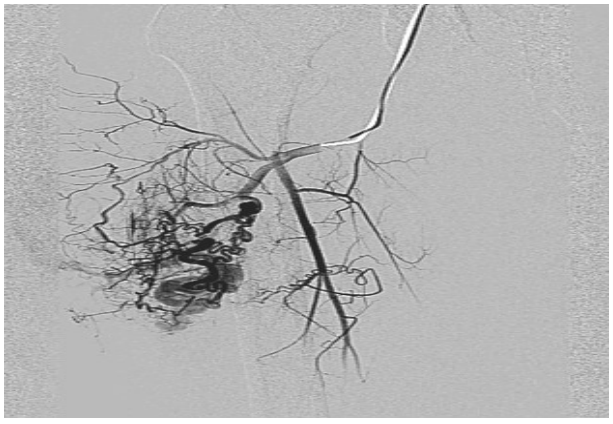
Ethanol injected directly into the nidus or into venous structures has much lower risk of toxicity.











Ethanol directly injected into nidus of thigh AVM with eradication of lesion.

Acrylic Adhesives – nBCA (“Glue”)

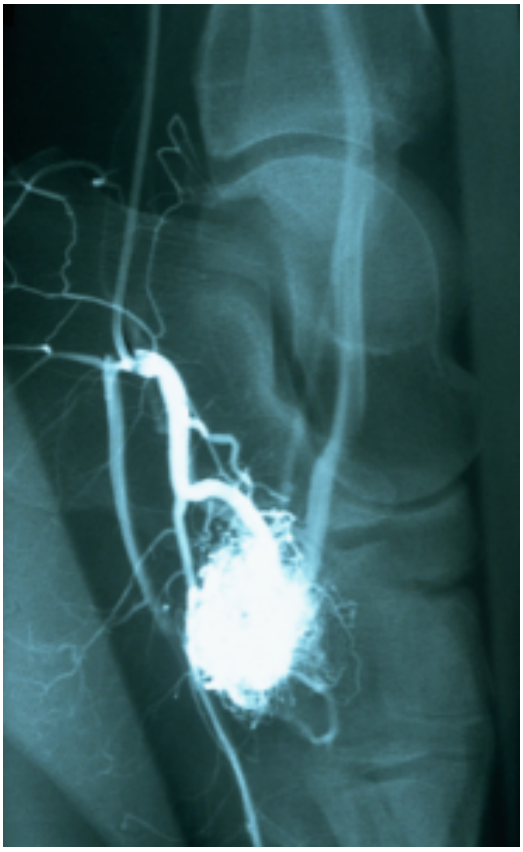
Advantages:

- Permanent (theoretically)
- Minimal tissue toxicity
- In use since 1965 (>1500 cases in literature) with no reported adverse long-term effects
- Low viscosity
- Rapid vessel occlusion; useful in high-flow lesions
- Can be made radiopaque without impairing occlusive properties

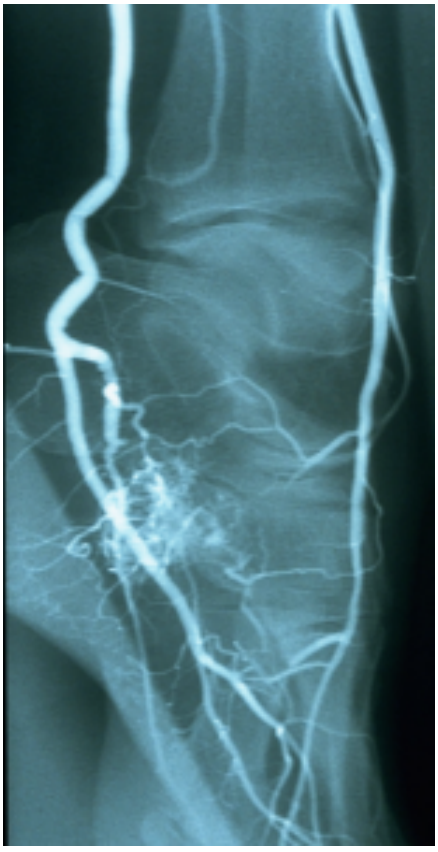
Disadvantages:

- Significant learning curve
- Requires strict maintenance of non-ionic environment
- Occludes catheter after each deposition
- Flow pattern not completely predictable; dynamic process
- Expensive

Shunts



Proximal shunt to distal ischemia



Reduce shunt to improve distal perfusion

33-year old male with ischemic ulceration of toes due to proximal AVM in forefoot; pre (top) & post (bottom) embolization using microspheres showing reduction in shunt, improved distal perfusion

Embolization for AVM

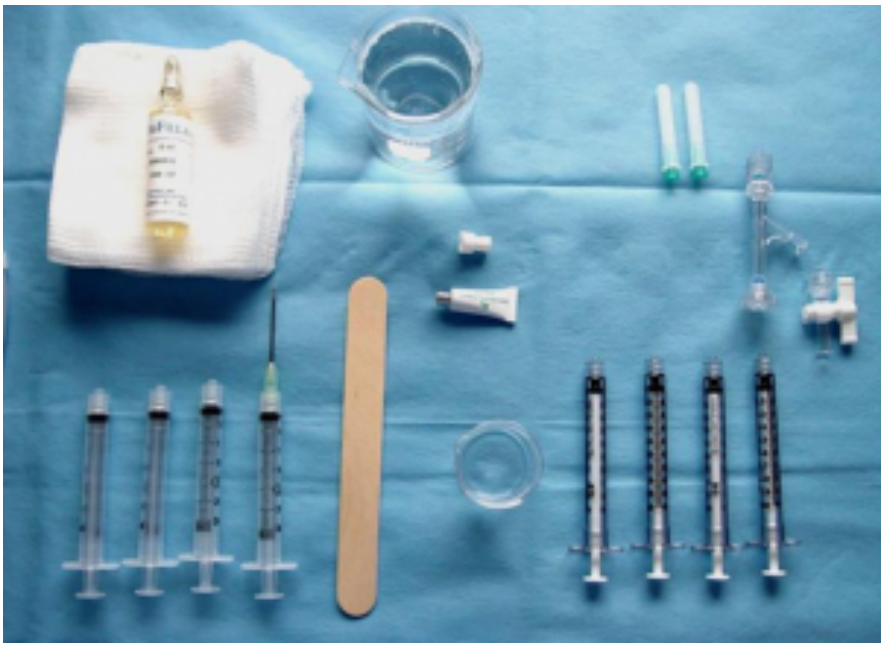
The ideal embolic agent would:

- Obliterate the nidus
- Be permanent
- Be controllable
- Be non-toxic including long-term

Unfortunately, this agent does not exist, at least not yet. Choice of embolic agents for AVM:

- Particles/microspheres
- Ethanol and other sclerosants
- Liquid adhesives (NBCA)
- Other liquid agents (EVAL, Ethibloc, etc.)

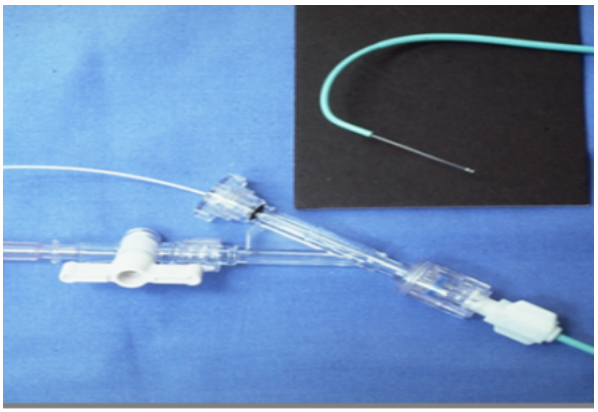
Glue preparation requires strict attention to detail



- Typical mixture – equal volumes (1:1) nBCA and Ethiodol oily contrast, but mixture can be varied for faster or slower polymerization
- Ethiodol provides radiopacity and slows polymerization
- Small volumes are used in each deposition (typically 0.2 – 0.5cc)
- Scrupulous attention to maintaining non-ionic environment, since glue polymerizes almost instantly on contact with any ionic environment (use D5W flush, separate table, new gloves)

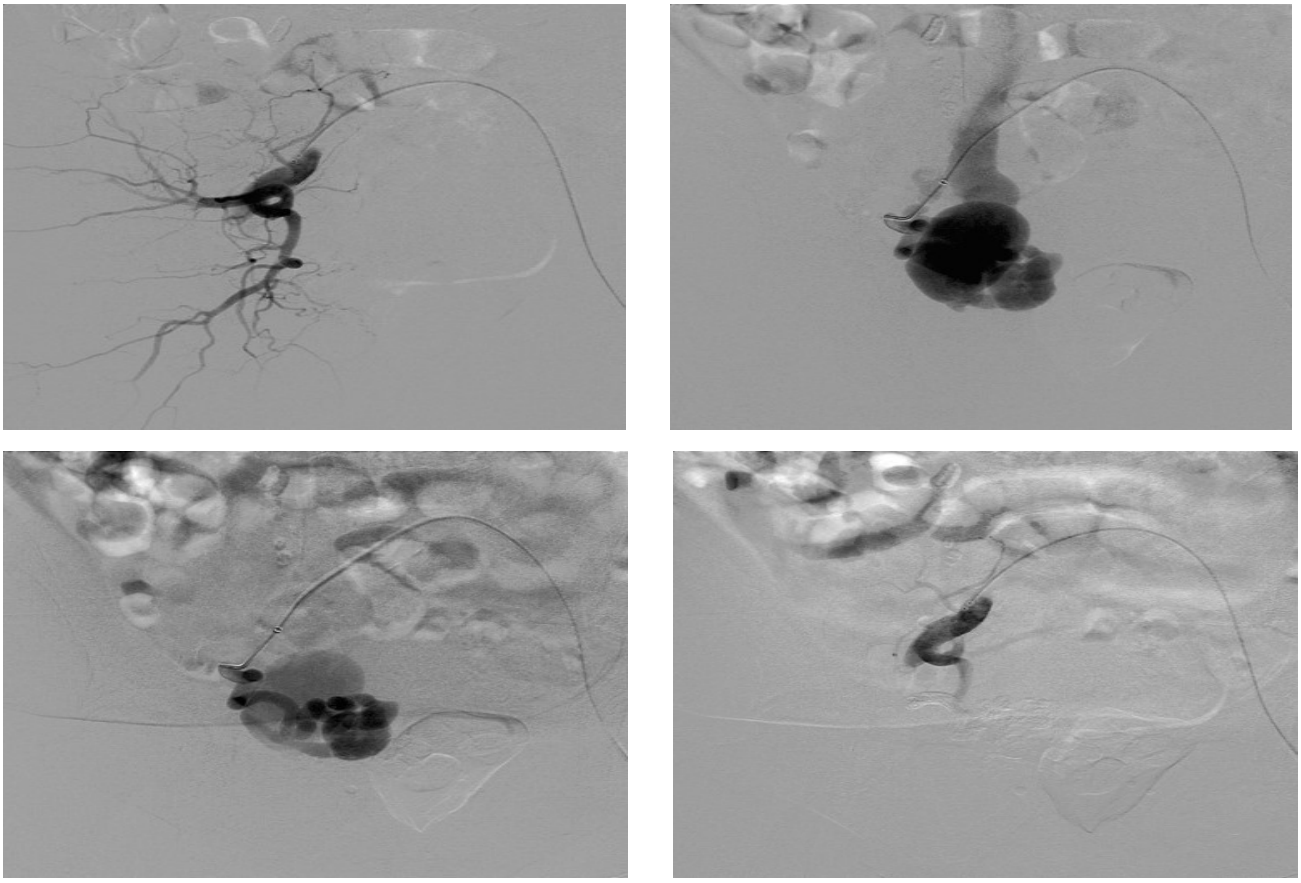
Advantage of glue

A major advantage of glue is that its low viscosity allows it to be delivered through microcatheters and even through fine (22g) needles by direct injection.



Another advantage is that a small volume of glue can create a much larger intravascular cast, due to the incorporation of blood elements. Even a large, complex AVM may require only 1 or 2 cc's of glue total, using multiple depositions of 0.2-0.4cc each.

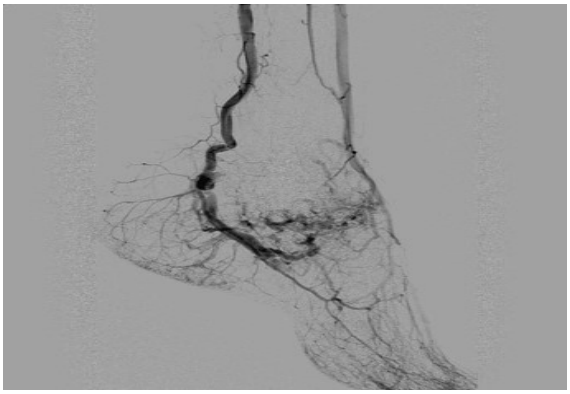
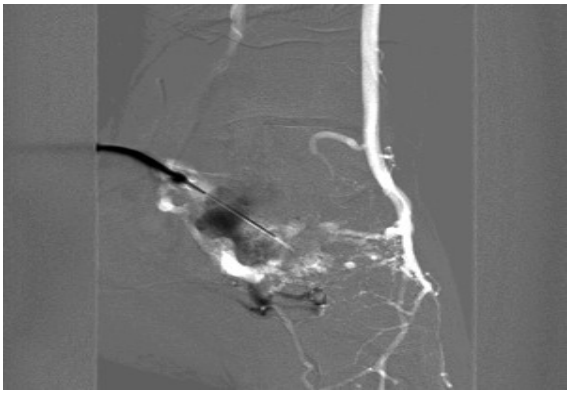
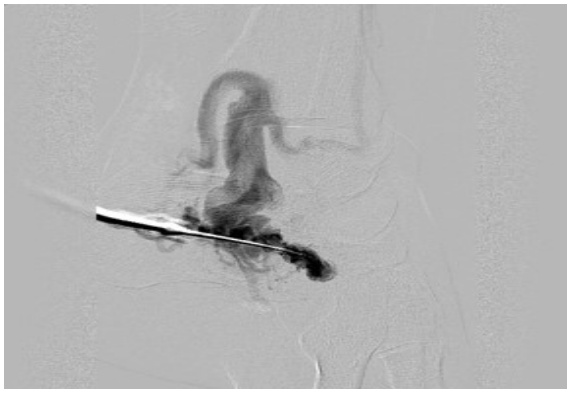
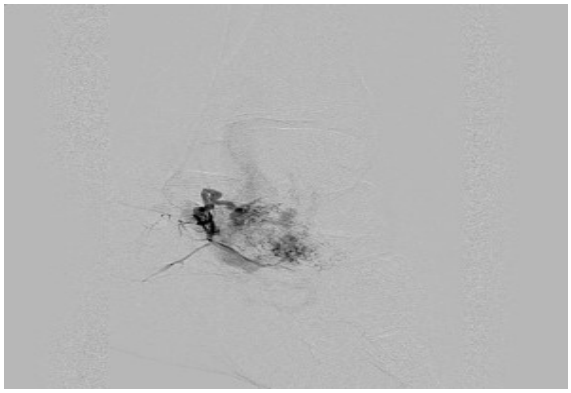
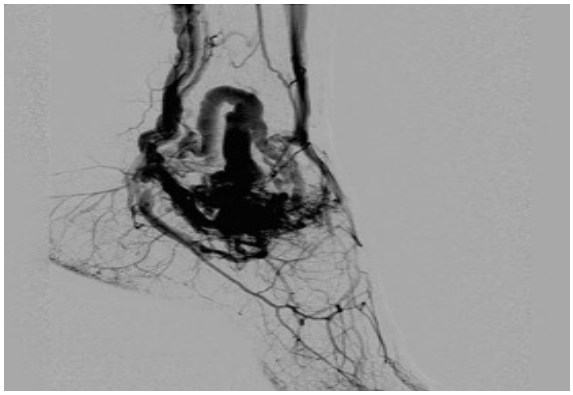
35-year old female with pelvic pain due to high flow AVM



Pictured: Stages 1 – 4 of embolization resolution of an AVM. One deposition of 0.3cc nBCA results in complete resolution of the AVM.

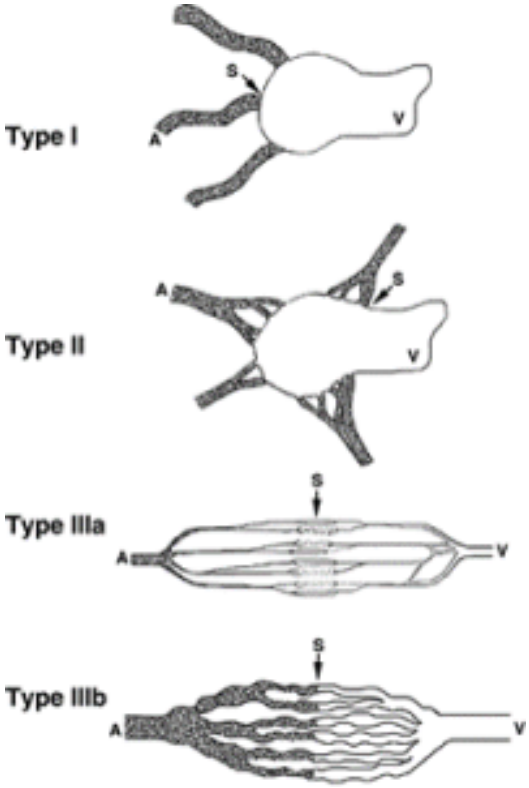
Nidus with glue using a fine needle

An approach used with increasing frequency is direct injection of glue into the nidus using a fine needle.

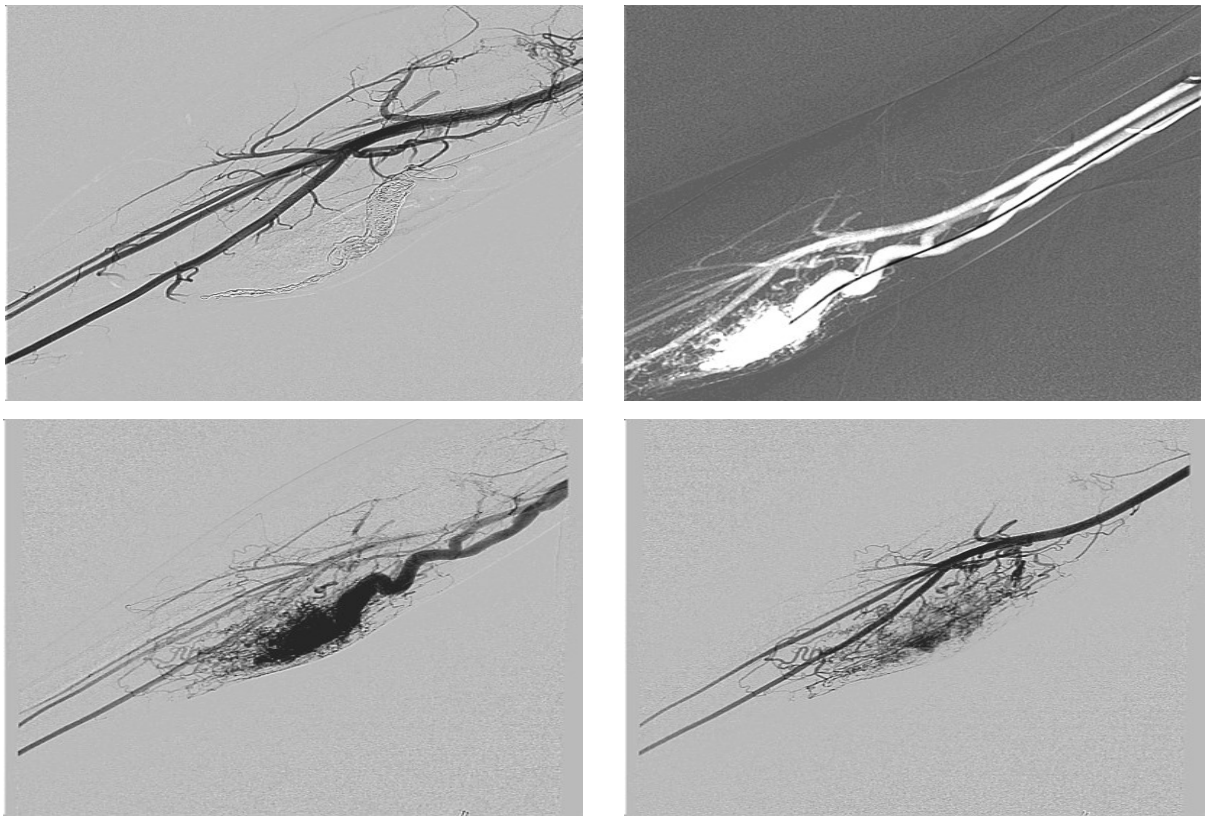
This approach permits direct accessto the nidus without risk to normal vessels in the area. The nidus is entered using ultrasound or by fluoroscopic puncture with angiographic roadmapping.

Modified classification of Houdart and Yakes



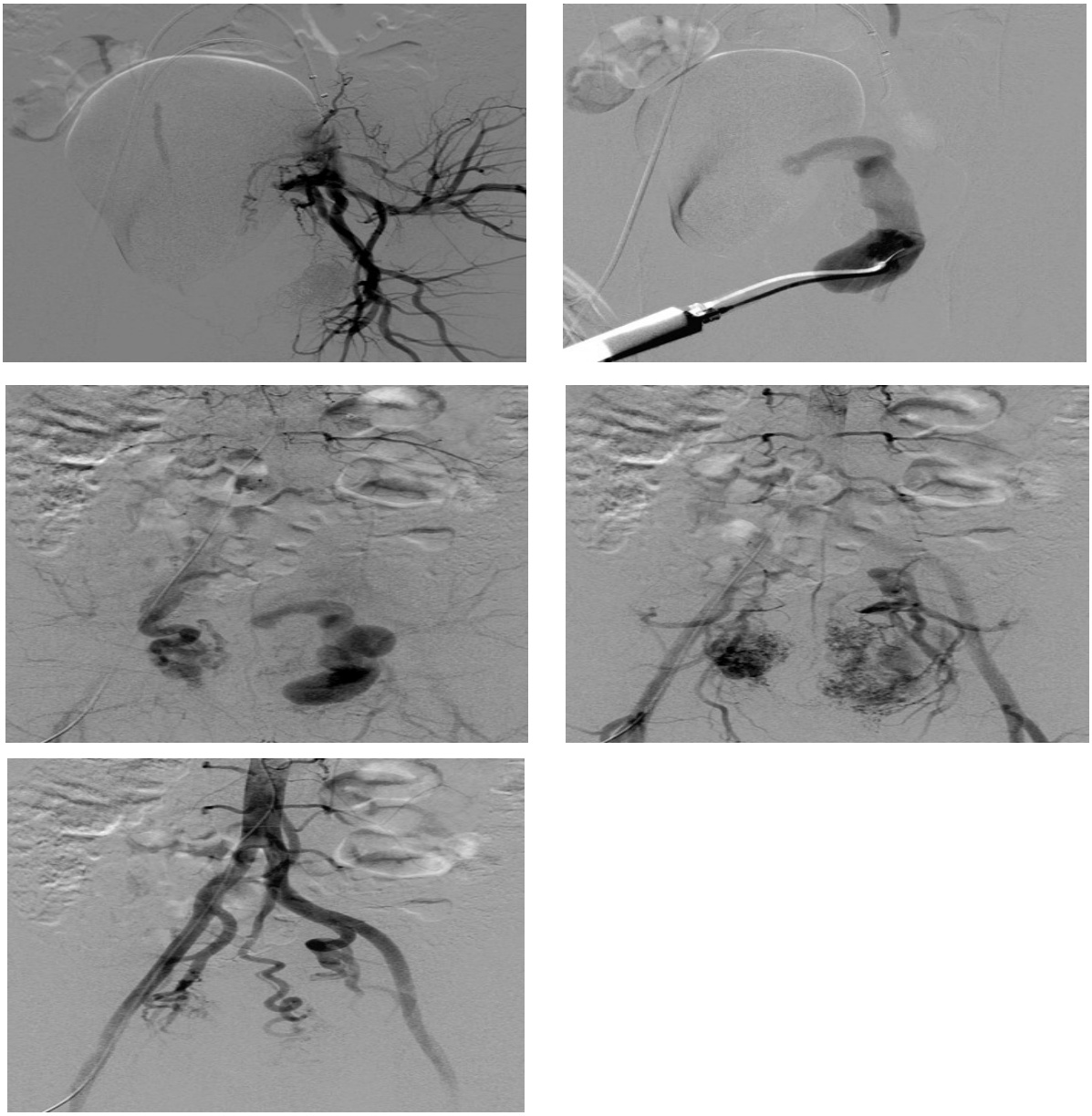
Depending on the architecture of the AVM, some lesions are most effectively treated by occluding the venous drainage rather than embolizing through the feeding arteries.
Pictured is a modified classification of Houdart and Yakes based on anatomic pattern of AVM.

Forearm AVM with dominant draining vein – venous approach



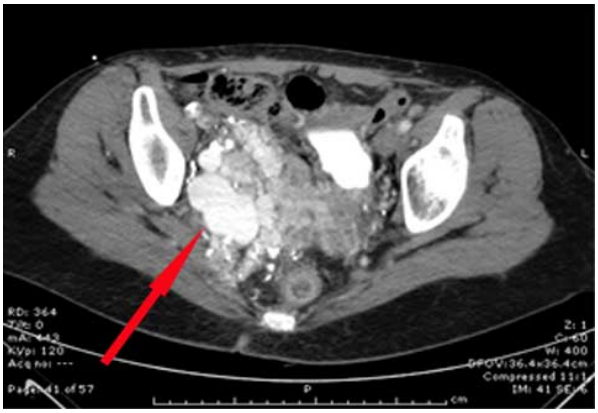
Forearm AVM with dominant draining vein- venous approach where innumerable small branches supply AVM – embolization of draining vein is the best approach.

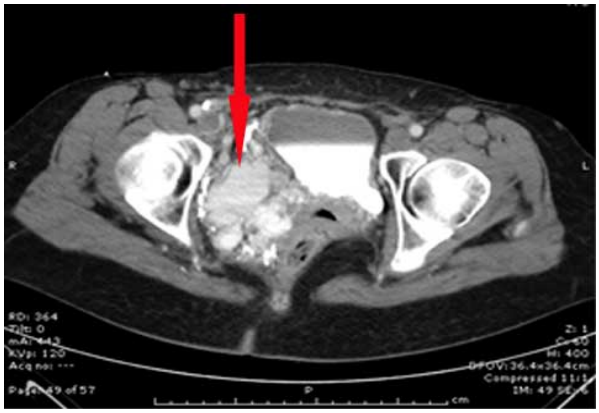
28-year old male with pain and lower GI bleeding



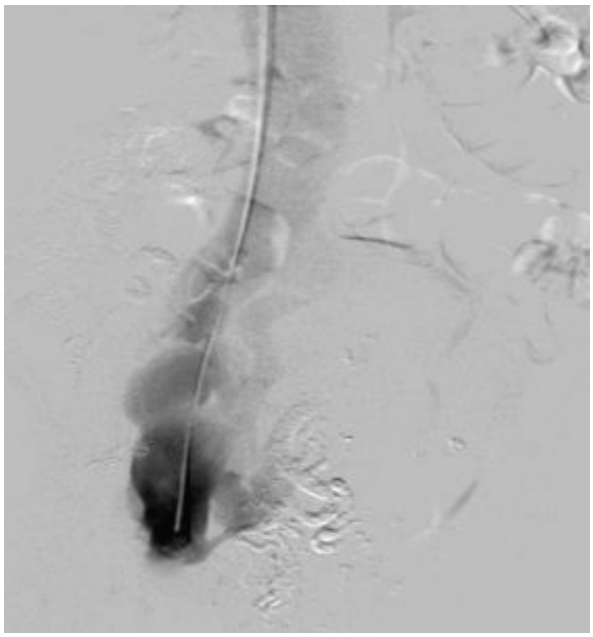
Pelvic AVM with multiple feeding arteries treated by direct percutaneous puncture embolization of aneurysmal draining veins.

Aneurysmal draining vein





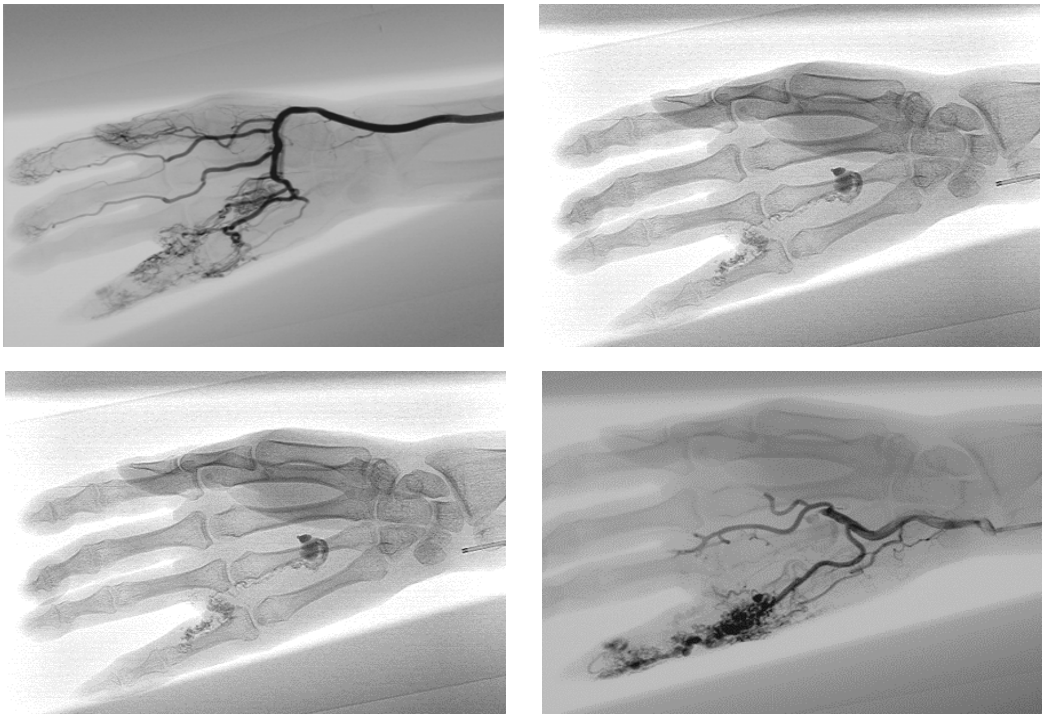
Percutaneous using US, Fluoro, CT (anterior or posterior approach



Transvenous via IJ or femoral approach

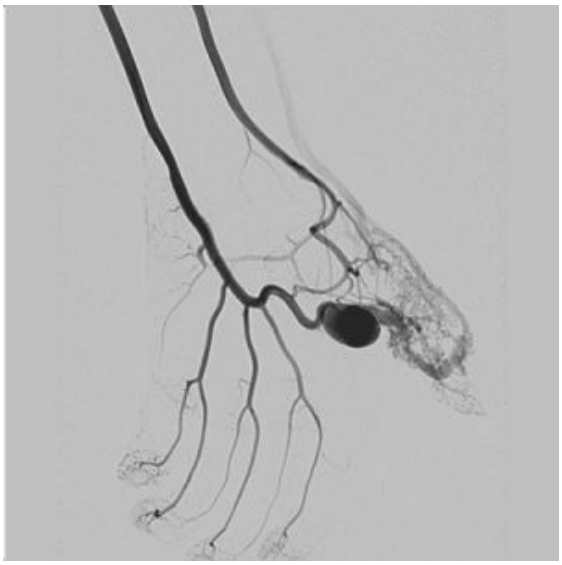
Distal arterial circulation

Lesions involving the distal arterial circulation are actually among the most difficult to treat.

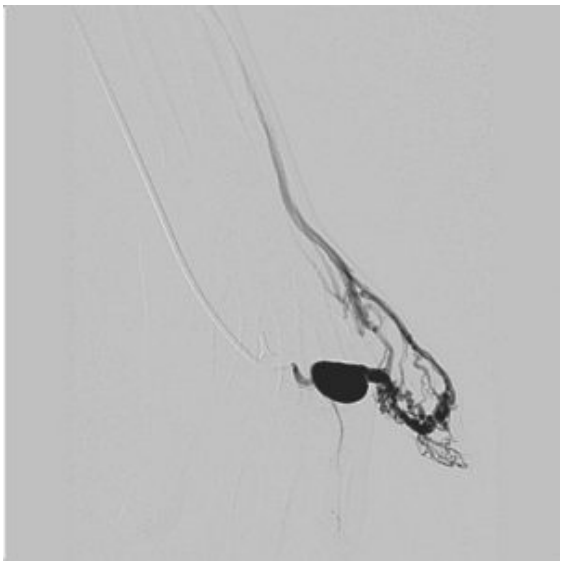


There is little margin for error in judging which branches can be embolized safely versus those supplying normal tissues.

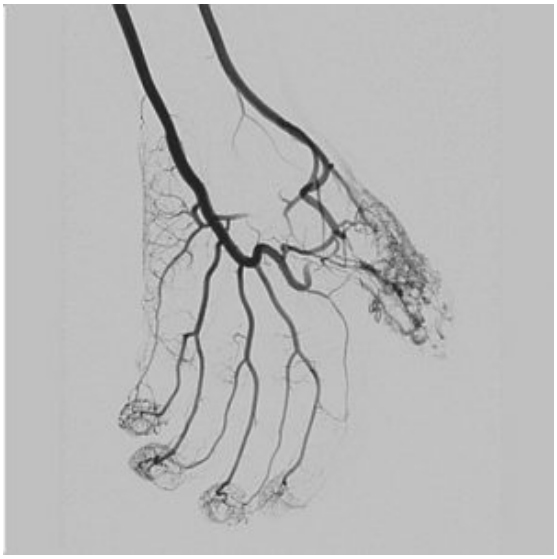
6-year old girl with aneurysm and AVM of left hand



Pre-treatment: aneurysm causing painful pulsatile mass

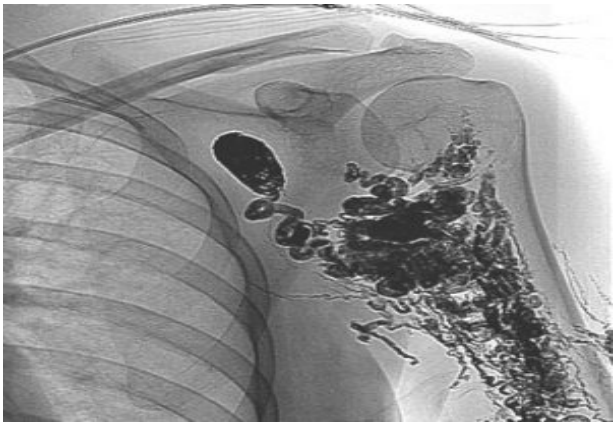


Outflow vessel compressed with clamp while aneurysm embolized using microcatheter



Post-treatment

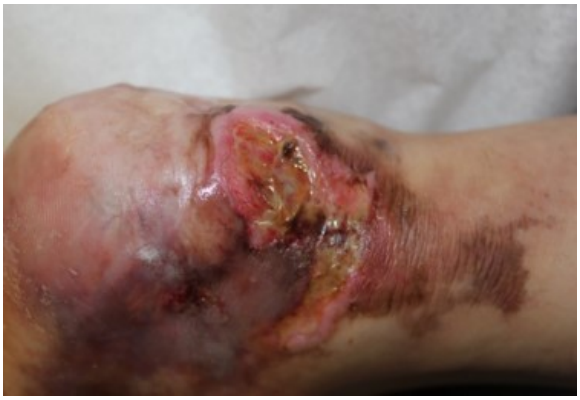
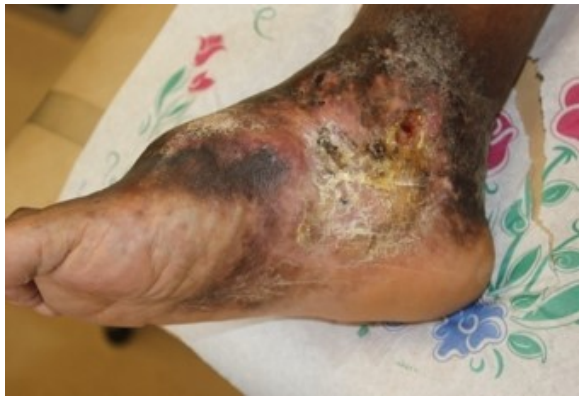
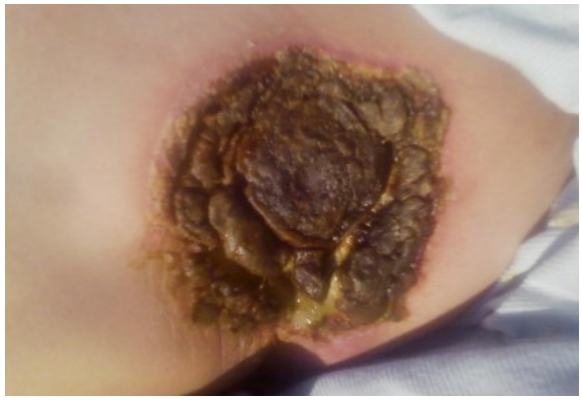
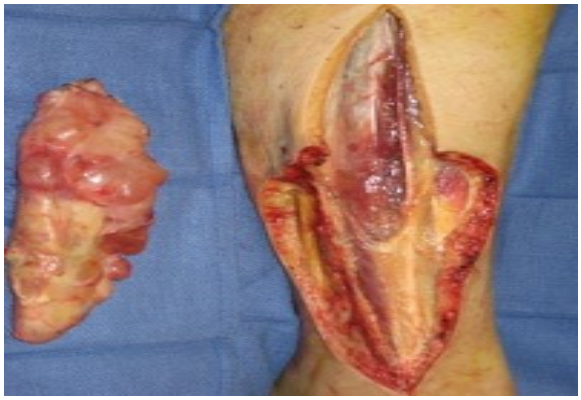
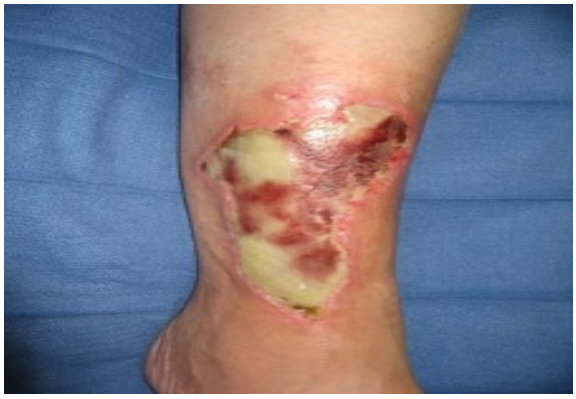
Onyx (ethylene vinyl alcohol co-polymer)



- Non-adhesive polymer
- Uses dimethyl sulfoxide (DMSO) as solvent
- Tantalum powder used for radiopacity
- Agent is injected slowly through microcatheter to form a cast of the nidus – result is very technique-dependent
- Very complete cast can be obtained, but if future embolization is required the density will make fluoroscopic visualization difficult
- Other drawbacks include some patients experiencing chronic pain post embolization

Intra-arterial ethanol

Be cautious with intra-arterial ethanol! There is a relatively small therapeutic margin; normal branches must be avoided.

Examples of injury to normal tissues from intra-arterial ethanol; considerable experience and detailed contrast studies are required to use this potent sclerosant intra-arterially. Ethanol which escapes into the venous circulation also carries a risk of generalized cardiovascular effects, including cardiac arrest.

Venous malformations

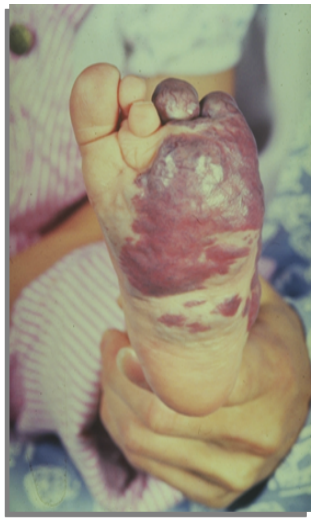
- Low flow
- Much more common than high flow AVMs, probably by a factor of anywhere from 3:1 to 10:1
- May be isolated malformations or occur as part of a venous syndrome
- Treatment is often not curative but symptoms can be significantly improved in the majority of patients

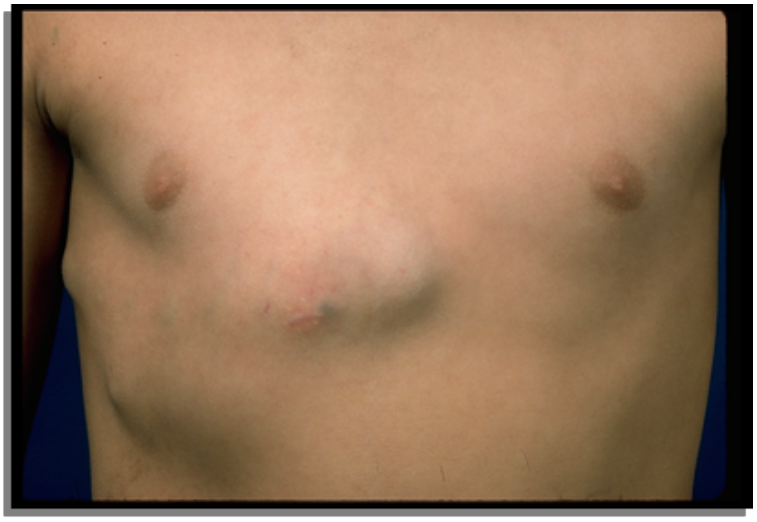
Venous Malformation types

- Cavernous
- Intramuscular
- Superficial (including port wine stain)
- Klippel-Trenaunay and other venous syndromes
- Mixed – seen in combination with lymphatic or other malformations

Venous Malformations

Clinical Presentation

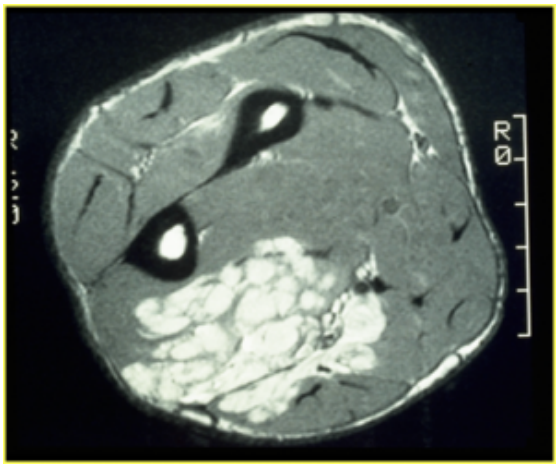




- Soft tissue mass – lesion can be emptied with compression or elevation
- Discoloration – bluish color, depending on depth of lesion; cutaneous port wine stain common
- Pain – especially when limb is dependent or after exertion
- Bleeding – deep or from superficial involvement, such as angiokeratoma
- Acute thrombosis – painful episodes, usually self-limited
- Thromboembolic complications are surprisingly uncommon

Venous Malformations

Radiologic evaluation of venous malformations



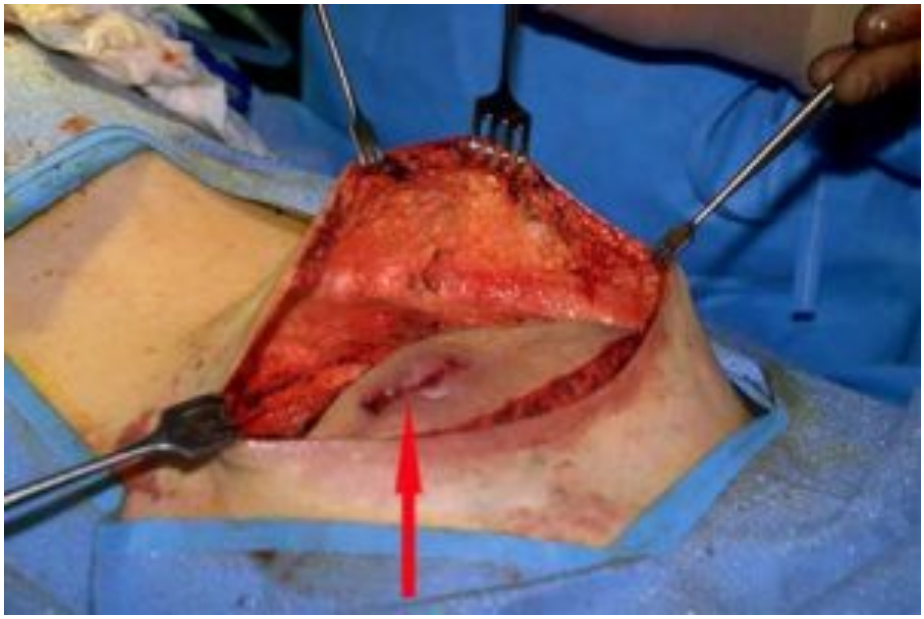
MRI of intramuscular venous malformation in forearm

- Ultrasound – easy office study, confirms low flow fluid filled spaces or channels
- Plain films – may show phleboliths, not otherwise helpful
- CT – usually not impressive
- MRI – the best imaging study
- Venography – shows anatomy of venous system and whether it is connected to malformation
- Arteriography – usually not necessary or helpful

Venous malformation treatment options

- Surgical resection
- Sclerotherapy – Ethanol, Sotradecol, Bleomycin, Doxycycline, etc.
- Laser for skin lesions, such as port wine stain, angiokeratoma, lymphatic vesicles

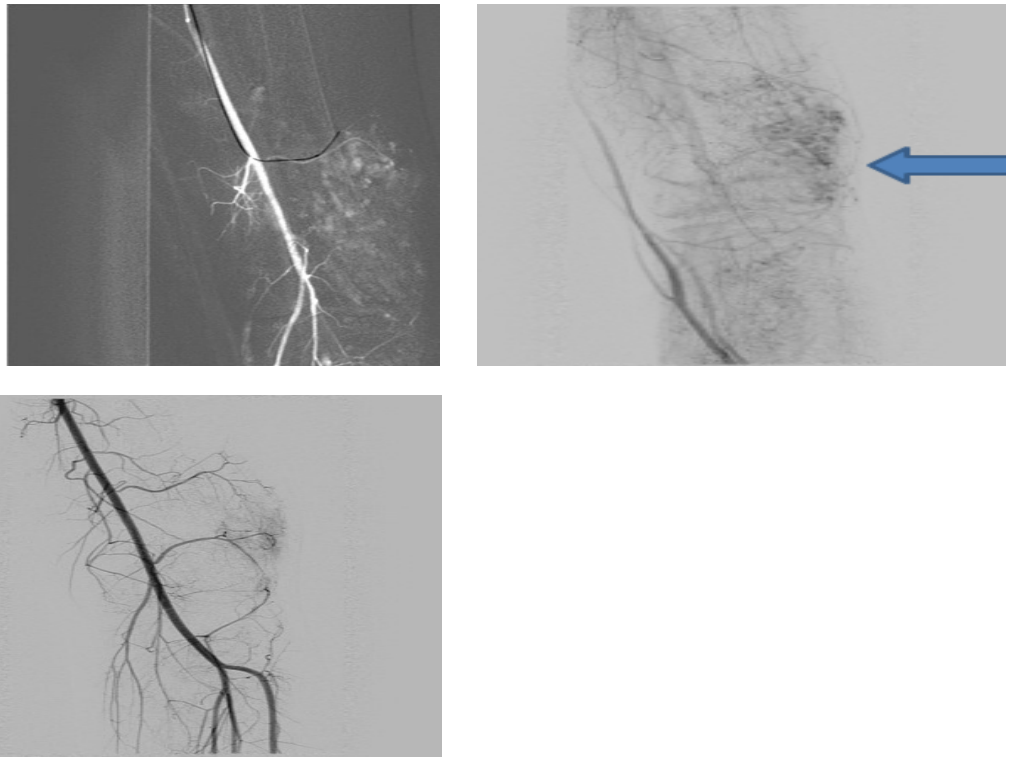
Surgery is feasible for selected cases, but there is significant likelihood of recurrence.



Arrow points to scar from previous “complete” resection.
Best application – completely resectable lesions, large bulky lesions, or those with severely affected overlying skin. Some evidence shows that early surgery in resectable lesions may produce a better long term outcome.

Is angiography necessary?

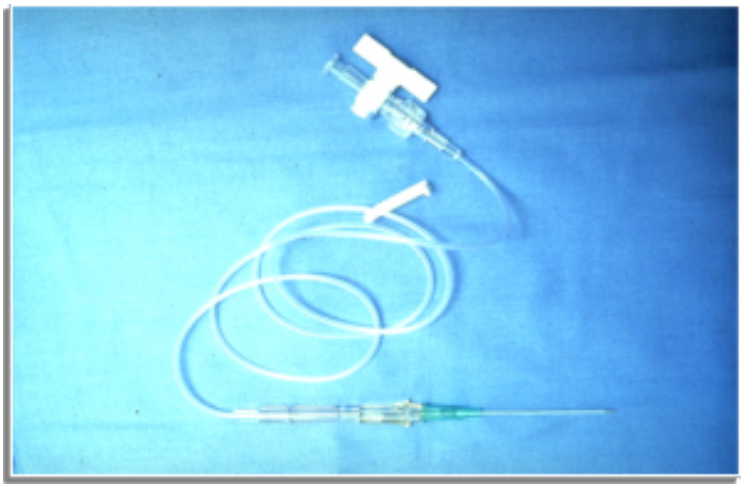
Is it worth embolizing “microshunts” prior to sclero?



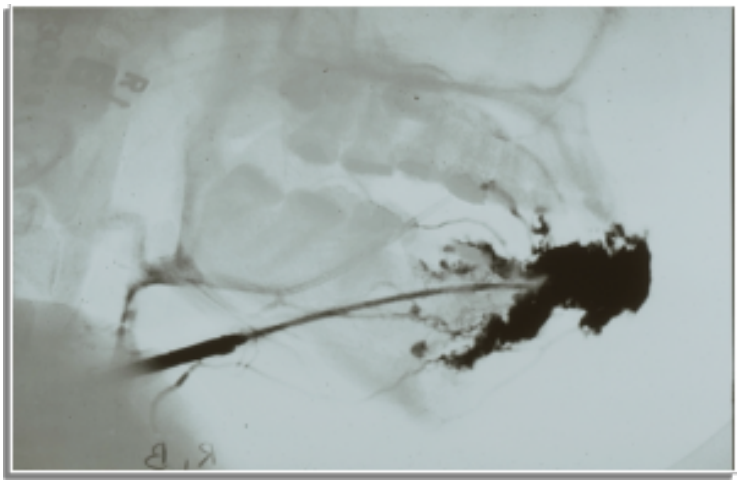
Angiogram of venous malformation shows late staining (arrow), no macroscopic shunting. Embolizing feeding arteries is not helpful.

Angiography isn’t needed in most cases, as non-invasive imaging will have clarified the nature of the lesion. Embolizing regional arteries has been tried in the past and is not effective.

Direct Puncture Study



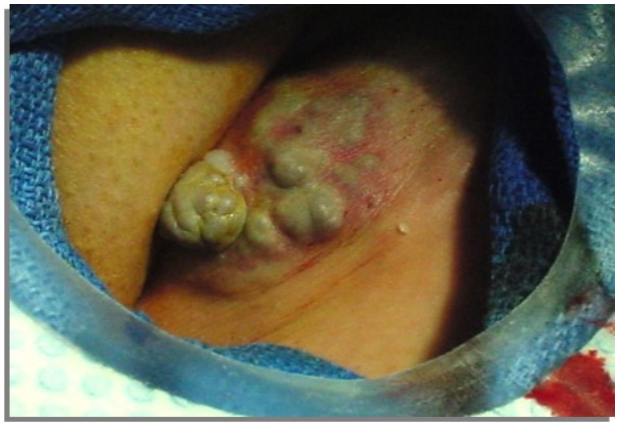
Direct puncture set-up: needle or angiocatheter and connecting tube

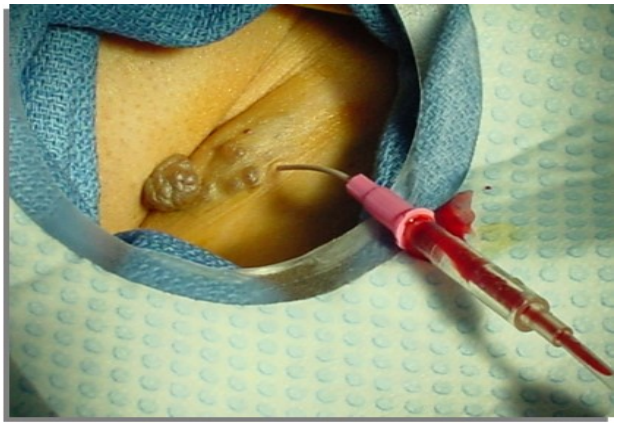


Injection of contrast

The lesion is entered using a needle or angiocath using palpation and/or US for guidance. Contrast is then injected with fluoroscopic monitoring. The malformation will have a “fluffy” appearance, with filling of draining veins once the capacity of the lesion has been reached.

Direct embolization or sclerotherapy





Once the lesion has been defined with contrast, the sclerosant is injected to fill the malformation, often using digital roadmapping to visualize the sclerosant. Depending on the architecture of the malformation, one or multiple entry sites may be needed to completely treat the lesion.

A collagen suspension is injected to fill the entry tract as the needle or catheter is withdrawn, stopping bleeding at the skin entry and preventing tracking of sclerosant to the surface where it can cause blistering or ulceration.

Sotradecol (Sodium tetradecyl sulfate)

- Our sclerosant of choice is STS, prepared as a foam with air and a small amount of ethiodol for radiopacity. This detergent agent is not as potent as ethanol but has a larger margin of safety in terms of tissue toxicity and potential cardiovascular effects.
- The liquid is available in concentrations from 1 to 3%. For deep lesions, we generally use 3%, while more superficial or mucosal lesions are treated with more dilute preparations, ranging from 0.5-2%.
- A maximum volume of 0.5cc/kg body weight generally provides an adequate safety margin. Giving significantly higher doses increases the risk of hemoglobinuria and renal dysfunction.

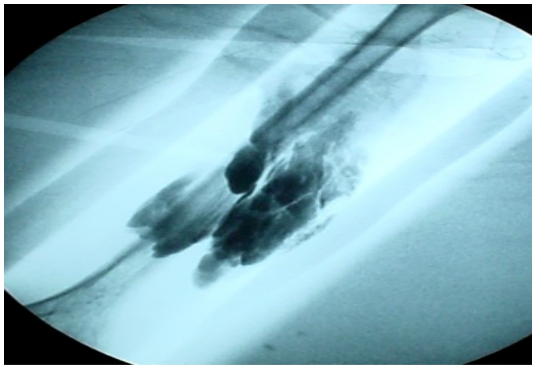
Prevention of thromboembolic complications

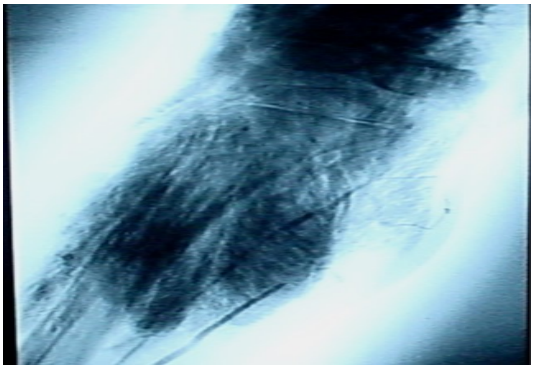
An automatic tourniquet placed proximal to the lesion is used to distend the malformation, presenting an easier target for ultrasound-guided puncture, as well as controlling outflow of the sclerosant into the venous circulation. The cuff is inflated to between systolic and diastolic pressure to allow arterial inflow while stopping venous outflow.

The deep venous system of the extremity is continuously flushed with a heparinized saline solution through a pressurized peripheral IV in the hand or foot to reduce the risk of DVT.

Pictured: automatic touniquet (left), pressurized IV heparin infusion (right)

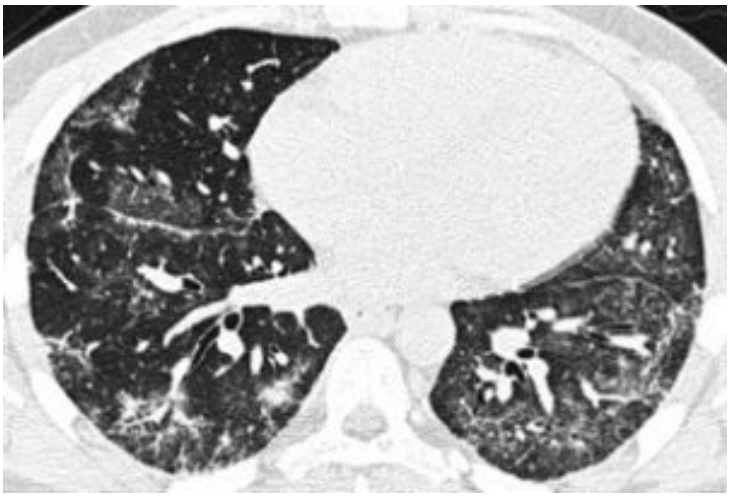
Calf and forearm intramuscular lesions: risk of compartment syndrome





When treating intramuscular lesions in the calf or forearm, treatment should be staged and conservative to reduce the risk of compartment syndrome. Steroids before and after the procedure should be used to reduce swelling.

Bleomycin

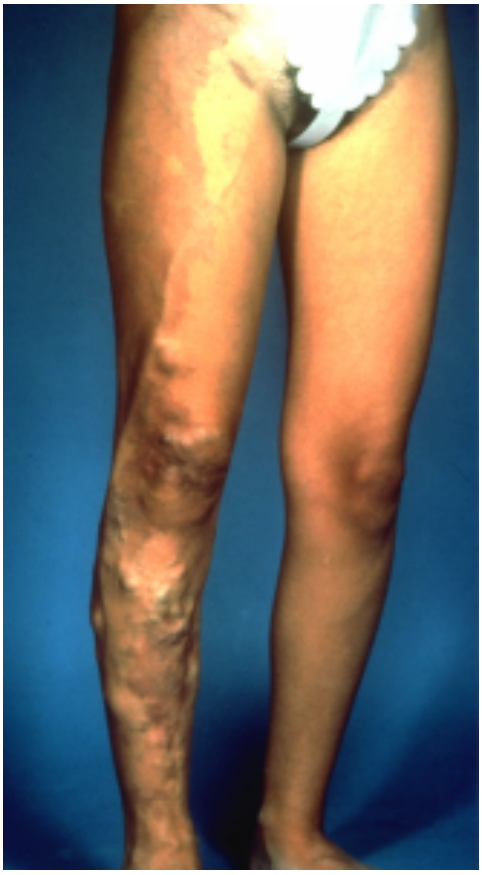


- Has been used as sclerosant in VMs for nearly 10 years.
- Dose range much lower than that used in chemotherapy; lifetime cumulative dose is the limiting factor.
- Causes less swelling than most other sclerosants, making it useful in areas such as the orbit and in proximity to the facial nerve.
- Primary concern has been pulmonary toxicity (fibrosis), a risk factor when used in higher doses as chemotherapeutic agent.
- There are scattered reports of both acute and longer term pulmonary toxicity when used as sclerosant but risk is generally considered low.
- Precautions necessary to prevent hyperpigmentation when skin adhesives are used (leave adhesive dressings and EKG pads on for 48h).
- Should it be used as first line agent or reserved for cases when other agents with longer track record have failed?

Direct embolization/sclerotherapy: post-op course

- Expect increased swelling, typically lasting 2-3 weeks
- Post-op pain is usually very mild, even in children
- If the lesion extends to the skin surface, blistering or ulceration may occur. This is usually self-limited and treated with topical agents (Silvadene cream)
- The lesion will shrink gradually over a period of up to six weeks post-procedure
- Many lesions will require multiple treatments, with limitations based on sclerosant volume and anatomic considerations
- Potential complications include DVT, skin ulceration, and nerve damage/contracture, particularly in deep hand and foot lesions

Klippel-Trenaunay syndrome

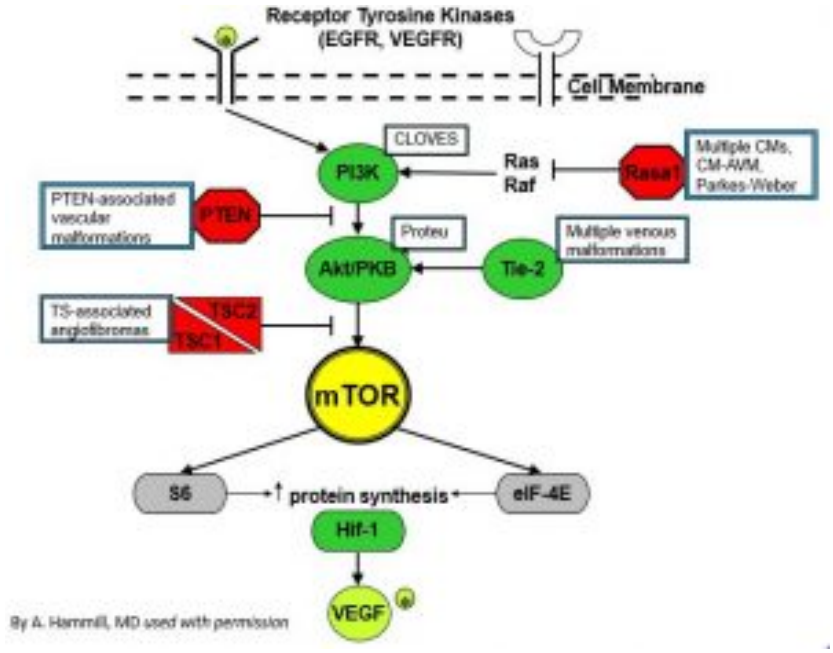


- One of the most common vascular malformations
- Usually a single extremity involved (typically leg)
- Venous anomalies & varicosities
- Some have hypoplastic deep veins (most do not)
- Cutaneous lesion (port wine stain – actually capillary venous malformation)
- Hypertrophy of bone/soft tissues
- No AV shunting on angiogram

KT Syndrome: why does it occur?

- Abnormality in mesodermal fetal development vs. segmental genetic mutation (mosaicism)
- Stereotypic clinical manifestations favor the latter
- Congenital but not genetically transmitted in vast majority

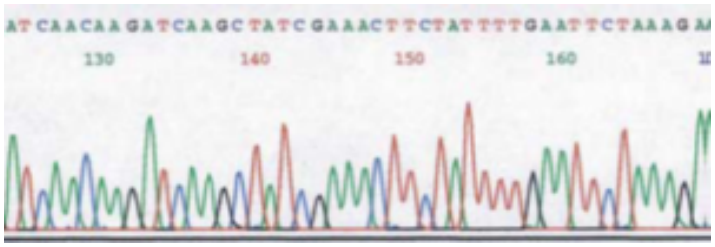
Receptor Tyrosine Kinases



Green: activating mutations (so all somatic, as germline mutation would presumably be fatal; also known/potential oncogenes) Red: (stop signs): tumor suppressor gene mutations (usually germline inheritance)

Mosaicism

An angiogenic factor has been identified that, when mutated, causes susceptibility to Klippel–Trenaunay Syndrome. This has been isolated from affected tissues (Mosaicism).



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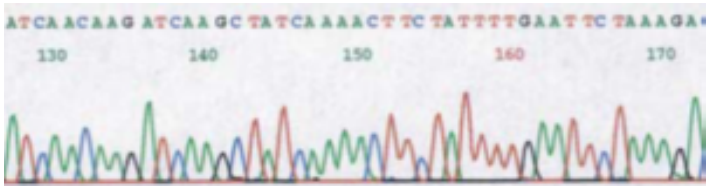

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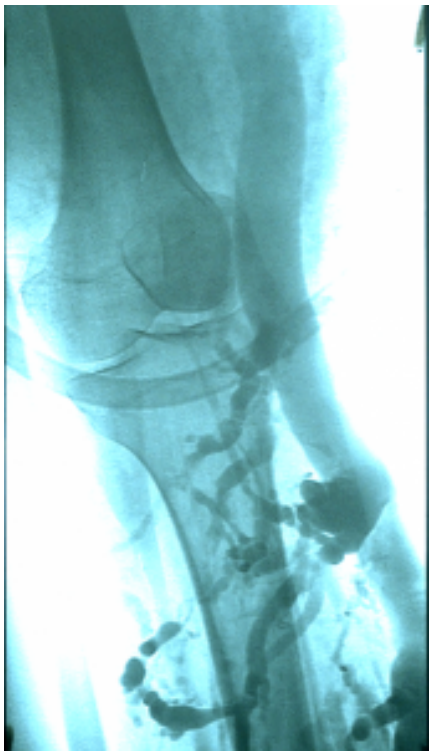
KT SYNDROME MANAGEMENT

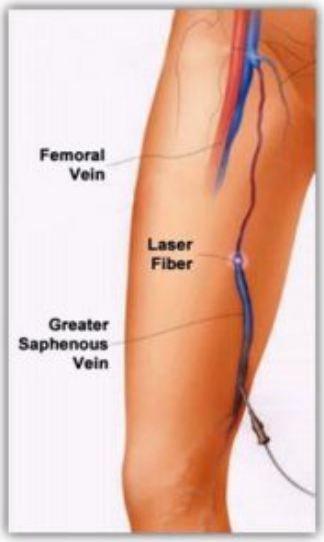


- Conservative: support stockings, elevation
- Baseline ultrasound and venogram to evaluate the entire venous system of the extremity
- Angiography only if there is suspicion of arterial involvement (as in Parkes Weber Syndrome)
- Avoid vein stripping/ablation if deep veins are hypoplastic or absent
- Associated intramuscular venous malformations are treated in the usual manner
- Increasing use of venous embolization and ablation when deep veins patent

Deep veins in KT syndrome

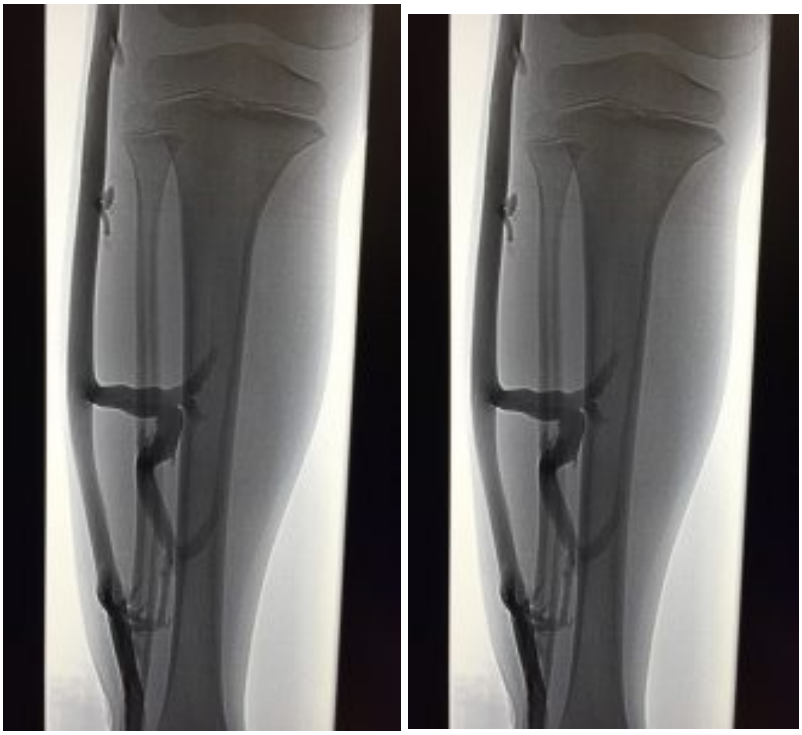
- Contrast venography is NOT the gold standard in evaluating the deep veins of KT patients; the majority (>80%) DO have patent and intact deep veins even when venography with tourniquets seems to indicate they are absent. Ultrasound is the best study to confirm this.
- This may mean that many KT patients have more treatment options than we thought in the past (Endovascular laser/RF, sclero, embolization, etc).

Venous ablation for anomalous KT veins?

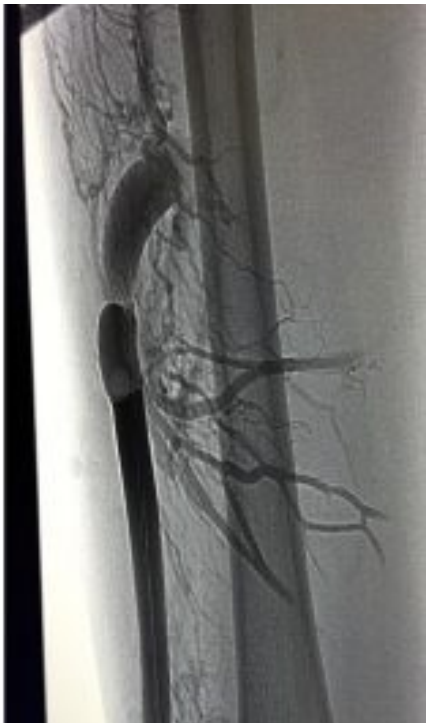


The marginal vein and other anomalous veins in KT Syndrome are often very superficial, creating a risk of skin injury when thermal ablation (RF, Laser) is used.

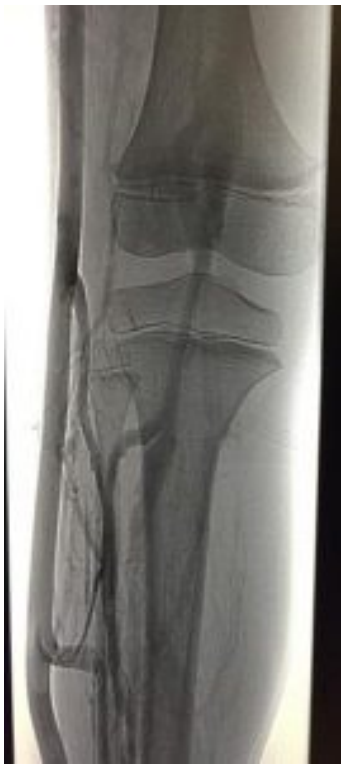
Embolization/sclerotherapy of anomalous veins in KTS



Initial venogram shows only filling of anomalous marginal vein which enters deep system via profunda vein (right).

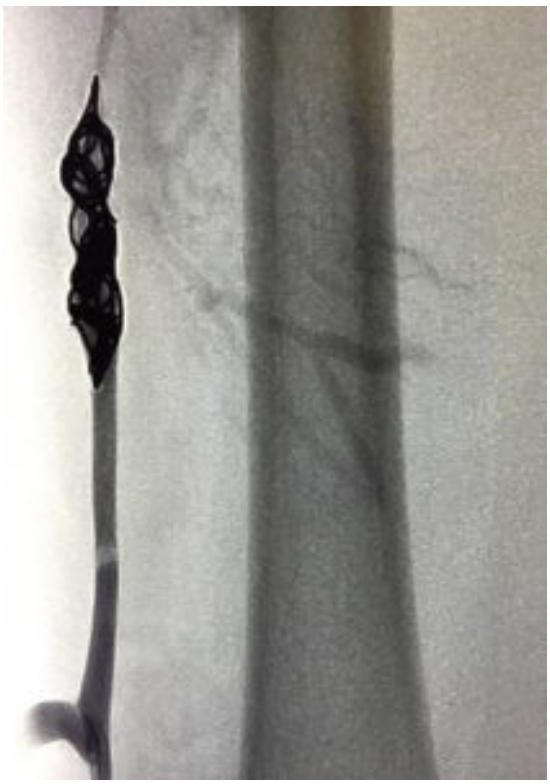


Patient was known to have a patent deep system by ultrasound. Repeat venogram with occlusion balloon in marginal vein.

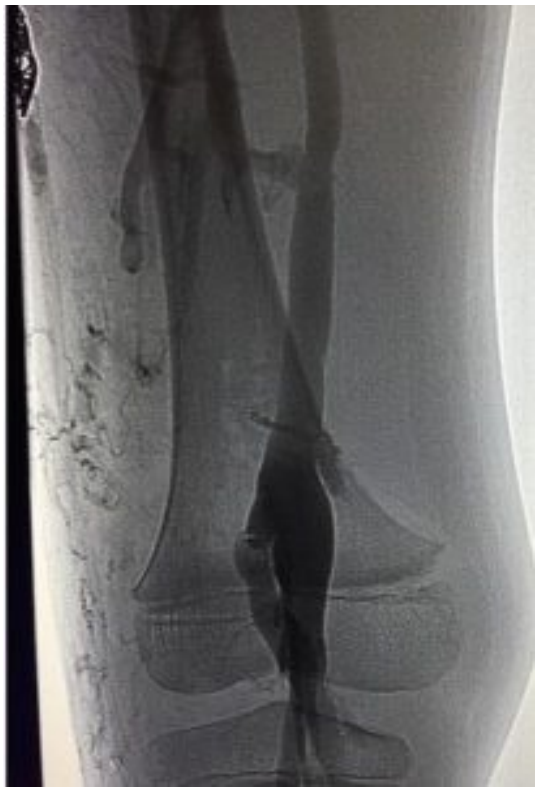


US shows filling of normal popliteal vein.

Embolization/sclerotherapy of anomalous veins in KTS (2)

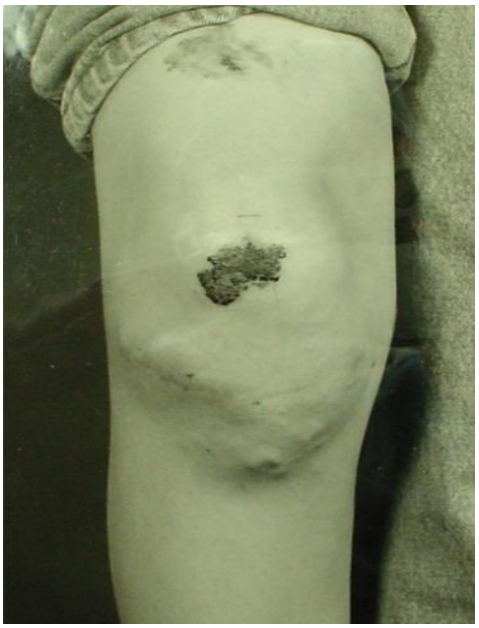


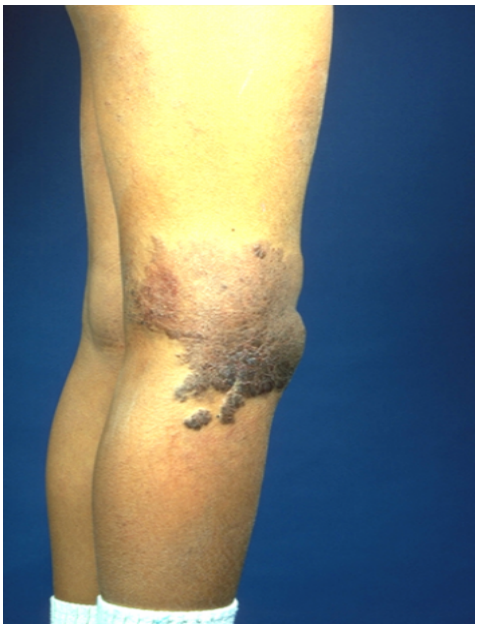
Once the status of the deep system has been confirmed, the marginal vein is embolized using coils and sclerosant.



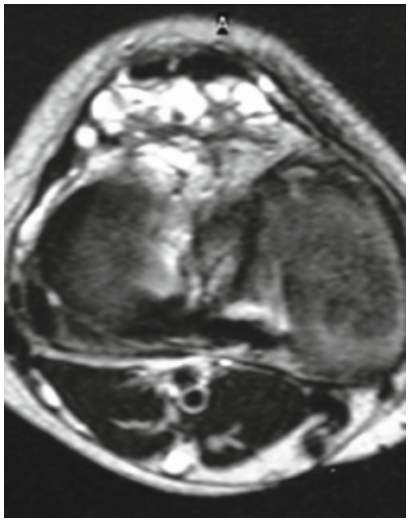
Post-embolization venogram shows filling of normal size popliteal vein.

The knee in KT syndrome





The knee is a fairly common location for venous malformations, most often as part of KTS, but in some cases as an isolated lesion. Involvement of the joint may be associated with recurrent hemarthrosis which causes pain and swelling, and eventually leads to cartilage destruction and arthritis.



Typical MR appearance and location of venous malformation involving the knee joint, bright on T2.

Joint involvement is often misdiagnosed

Scand J Rheumatol 1998;27:313–5

CASE REPORT

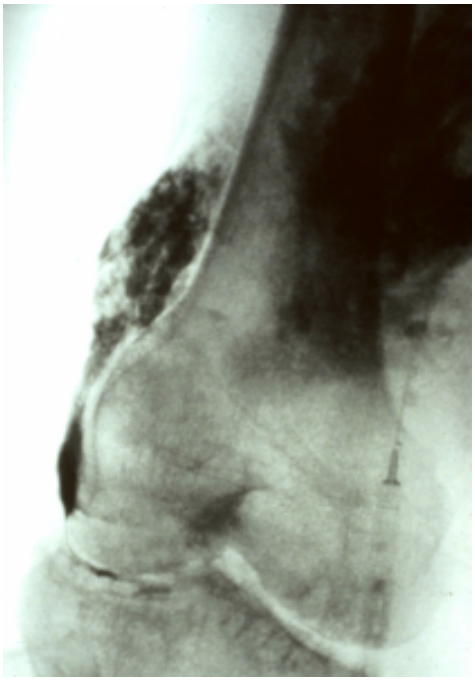
Arteriovenous Malformation of Knee Masquerading as Juvenile Arthritis

J. S. Goraya, Gurpreet Singh[1], Surjit Singh, S. S. Gill[2], Amit Goyal[3], S. K. Mitra[1], and Lata Kumar

[1]Departments of Paediatrics, Paediatric Surgery, [2]Orthopedics , [3]Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Lack of physical findings, especially when not in KT setting, may lead to misdiagnosis of JRA, PVNS, “growing pains”, etc. Only MRI confirms the diagnosis.
Joint changes are similar to that seen in hemophilia.

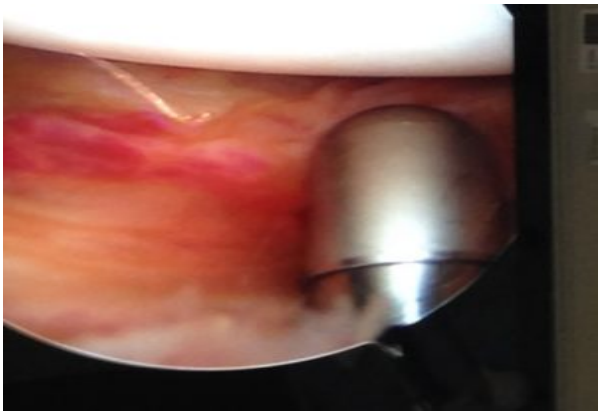
Knee involvement should be treated more aggressively

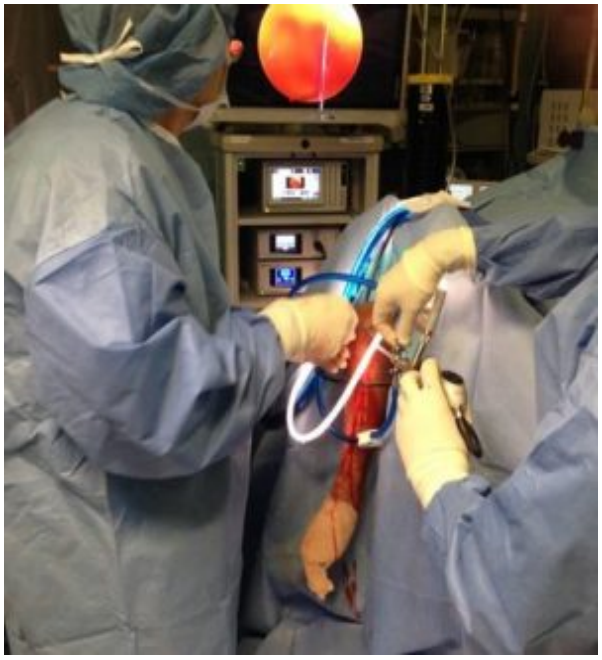


Treat early and aggressively, using sclerotherapy and arthroscopic surgery when necessary to remove hypertrophic synovium.

Pictured: contrast injection into malformation shows leakage into joint space, consistent with hemarthrosis. Note severe degenerative arthritis in this 22-year old patient.

Arthroscopic synovectomy



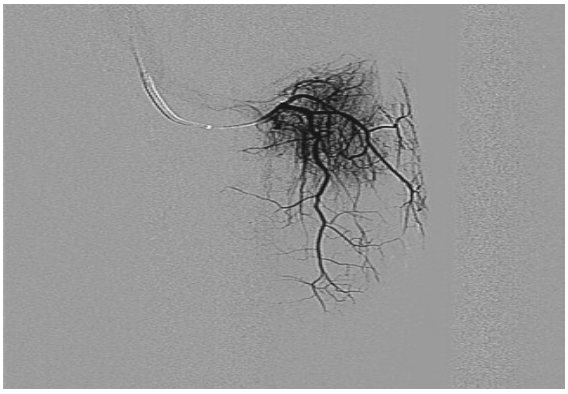


Arthroscopic synovectomy for venous malformation involving knee
Goals are:

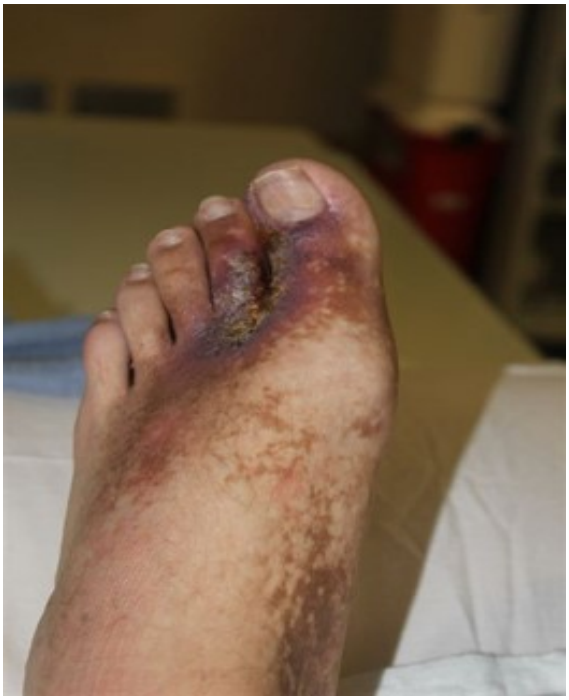
- Joint preservation
- Stop recurrent hemarthrosis and tissue hypertrophy
- Delay need for joint replacement
- Good working relationship with orthopedic surgeon essential

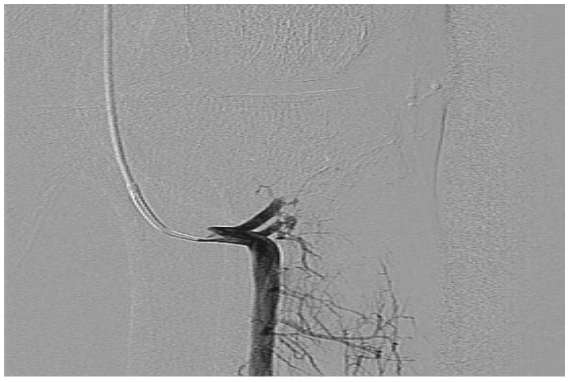
Parkes Weber syndrome

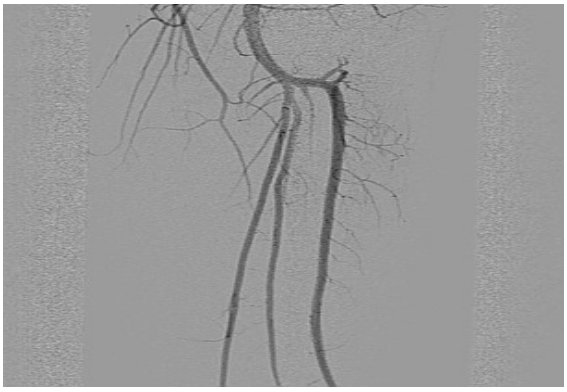
Parkes Weber syndrome is similar to KTS but with high flow component which may be diffuse



Small vessel shunting anterior tibial branch







Post-embolization (left) and one year later (right)
Symptoms, including those of venous hypertension, may be improved by embolizing the shunting vessels with microspheres.

Lymphatic malformations (LM)

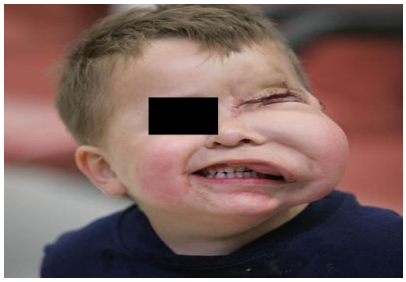
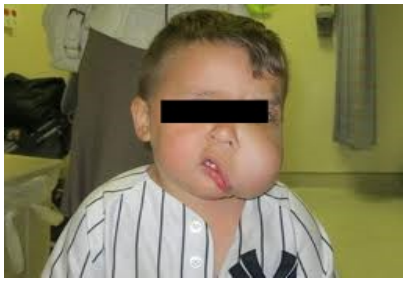
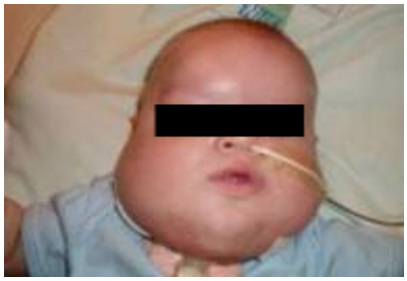
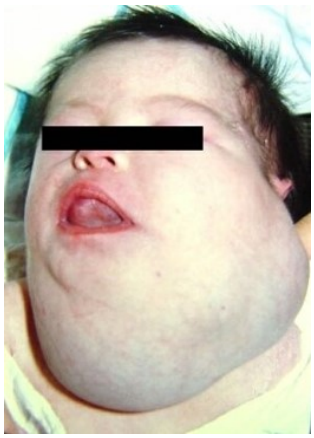
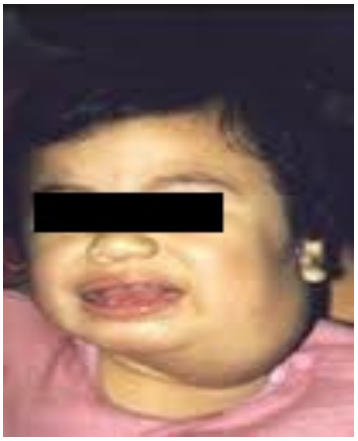
- Tendency to have spontaneous inflammation and infection (almost never occurs in other VMs). These patients can become septic very quickly and IV antibiotics should be started early.
- Macrocystic lesions respond well to treatment: drainage and sclerotherapy.
- Agents include Doxycycline, STS, Bleomycin, OK432 (not available in the U.S.).
- Microcystic and cutaneous malformations are more difficult to treat; laser or surgical resection may be best option.

Lymphatic malformations: types

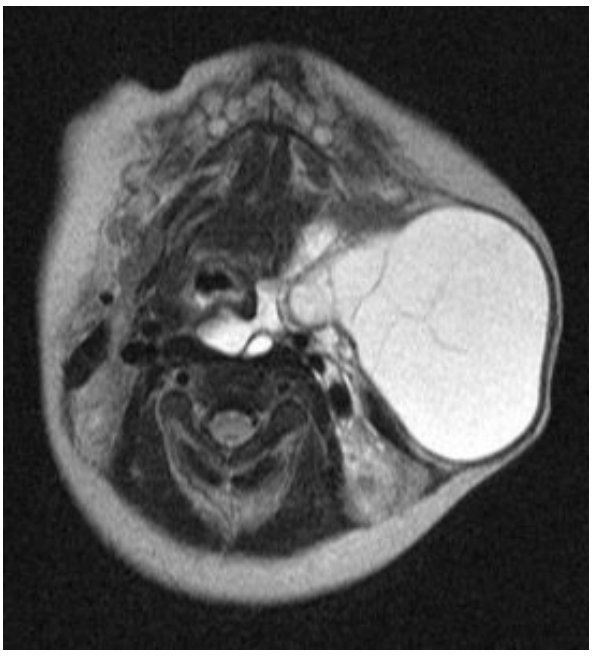
- Lymphedema Syndromes (congenital, acquired)
- Macrocystic lesions, including “cystic hygroma”
- Microcystic lesions
- Infiltrative lesions
- Cutaneous lesions
- Mixed with venous malformations, e.g. “venolymphatic malformations,” as sometimes seen in KTS

Common location for LM

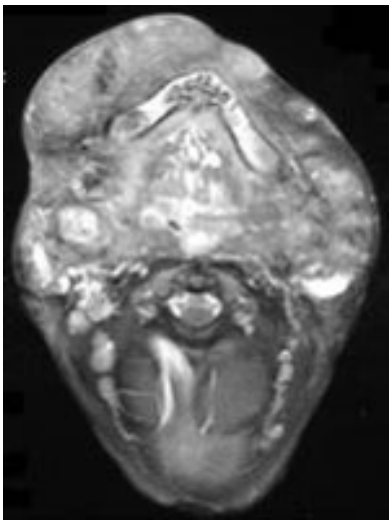
Head and neck are the most common location for lymphatic malformations, and are often disfiguring.


Macrocystic vs. microcystic LM



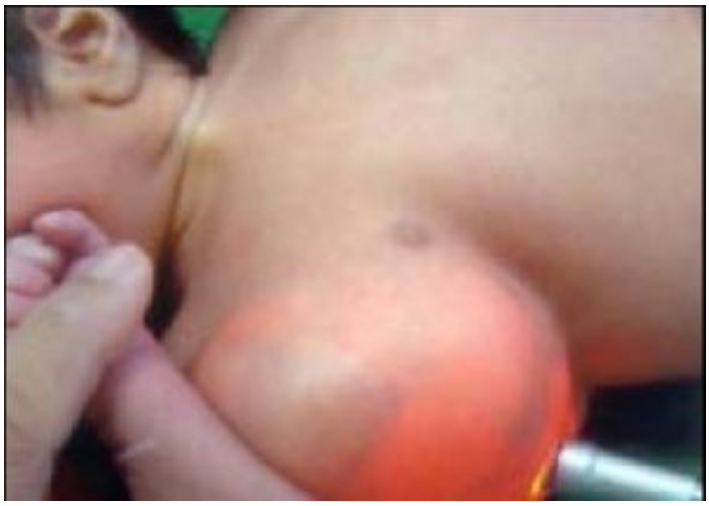
Macrocystic: easier to drain and treat



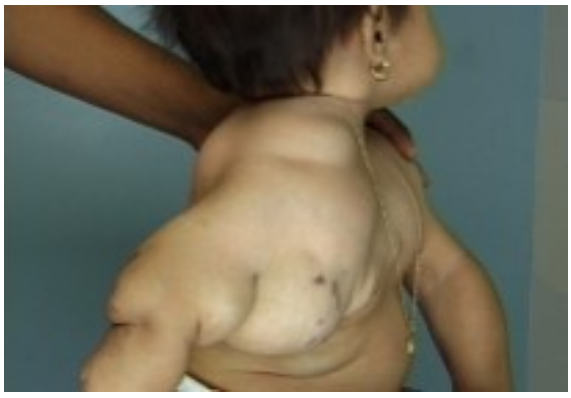
Microcystic: much more difficult to treat

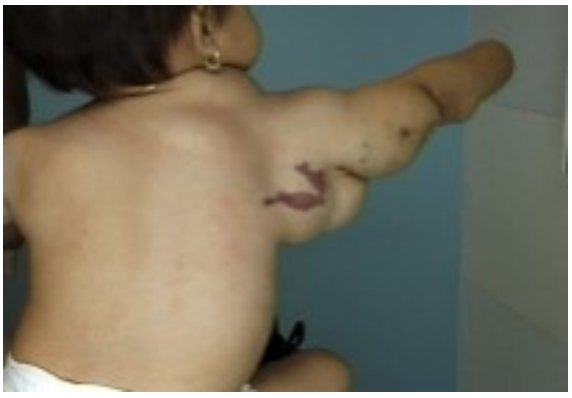
Common location for LM (2)

While head and neck are the most common areas, LM can occur anywhere

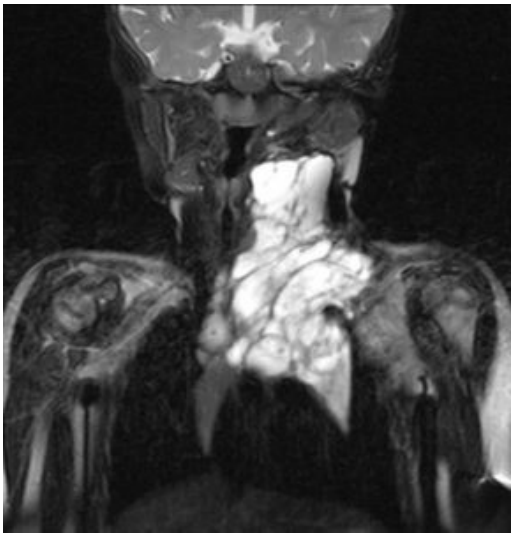


Transillumination



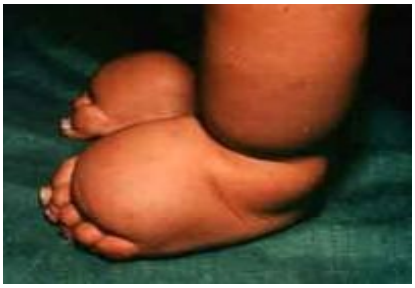
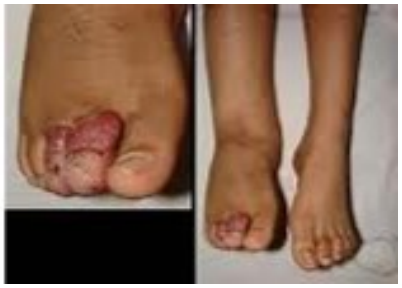
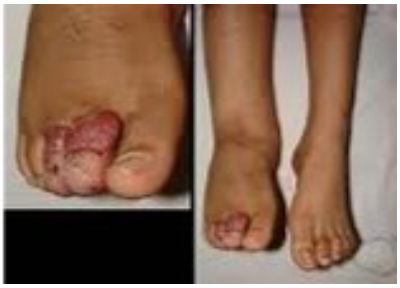


Often associated with venous component



Often multiloculated and infiltrative

May cause generalized limb enlargement or focal gigantism, especially toes

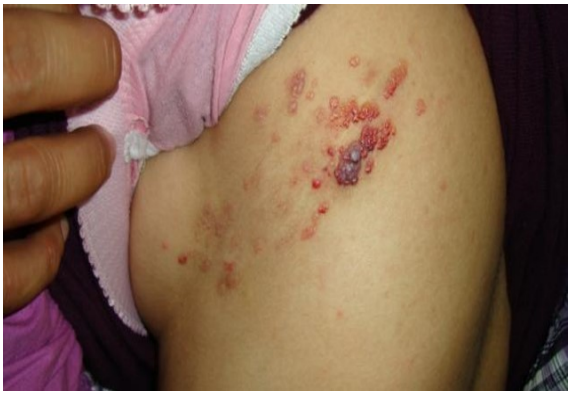
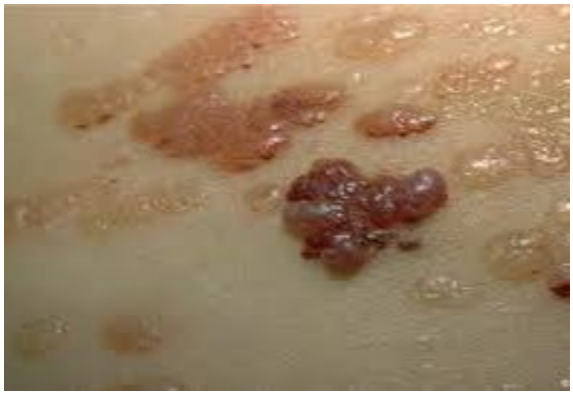
No good treatment other than conservative: compression stockings, lymphatic pumps, or decompressive massage. Occasionally, debulking surgery is indicated where massive enlargement exists or removal of severely affected digits is required.

Lymphatic malformations: treatment

- Among the most difficult/frustrating malformations to treat, results often unsatisfactory
- Surgery
- Drainage
- Sclerotherapy: Doxycycline, STS, Bleomycin, OK432 (Picinibil)
- Laser
- Systemic treatment (Sirolimus)
- Topical and supportive treatment: antibiotics, lymphatic massage (“decompressive therapy”)

Cutaneous involvement

Angiokeratomas, lymphatic vesicles often are mixed and may bleed or leak fluid.

Best treatment is laser or excision of involved skin if possible.

Summary

- AVMs are difficult management problems.
- Proper dignosis is essential and terminology is important.
- Surgery is best reserved for completely resectable lesions.
- High-flow lesions can be treated by transarterial embolization but the choice of agent is critical.
- Transvenous treatment of high-flow lesions is effective.
- Low-flow lesions are treated by direct injection of sclerosant.
- Results must always be judged over the long-term.
- These patients should be treated in specialized centers by a multidisciplinary team.

Course 05: Lesson Quiz

1. Which risk factor should be discussed prior to treatment of a vascular malformation or vascular tumor?

   A. The risk of seizure activity.
   B. The risk of kidney damage from contrast medium.
   C. The risk of anesthesia to the developing brain.
   D. The risk of hyperactivity following surgery.

2. Which of the following should be identified as an infantile hemangioma?

   A. Lesions that appear after birth and continue to grow.
   B. Lesions that appear at or shortly after birth, proliferate, and then regress.
   C. Lesions that are fully present at birth and have a rapid regression.
   D. Lesions that are diagnosed in utero and are fully present at birth.

3. Slow-flow vascular malformations include which of the following:

   A. CM, VM, and LM only
   B. CM, VM, LM, and AVM
   C. AV, AVM and CM
   D. AVM, CM, GVM

4. The characterized stages of the infantile hemangioma are as follows:

   A. Appearance, stabilization, regession
   B. Appearance, proliferation, and involution
   C. Appearance, intermittent growth cycles, stabilization
   D. Non-appearance, appearance, regression

5. Which of the following are some benefits of early vs. delayed intervention?

   A. Cardiovascular and neurological systems stimulate rapid healing.
   B. Immature vasculature and lymphatic system considerations.
   C. Heightened pain tolerance and joint preservation.
   D. Psychological factors can be circumvented and treatment may prevent growth that typically occurs during puberty.

6. Which of the following risk factor is increased in AVMs?

   A. Thromboembolism
   B. Cardiac workload
   C. Neurological sensitivity
   D. Lymphatic drainage

7. Surgery requires which of the following for definitive diagnosis?

    A. Ultrasound
    B. Patient's desire for surgery
    C. Detailed pre-op imaging studies
    D. Detailed history of lesion only

8. The treatment of venous malformations can best be summarized as:

    A. A frustrating process with frequent major setbacks
    B. Not curative but can greatly improve symptoms
    C. A cautionary tale of trial and error

9. Surgery is discussed in which of the following situations?

    A. When lesion is in early growth phase with no bulk to lesion.
    B. When lesion is localized, bulky, or has extensive tissue involvement.
    C. When lesion is localized and has history of profuse bleeding.
    D. When lesion is ulcerated.

10. Which of the following pertains to arteriovenous malformations?

    A. Complex malformation only
    B. Combination of vascular tumor and vascular malformation
    C. Fast-flow vascular malformation only
    D. Fast-flow vascular tumor only

Robert J. Rosen, MD, AVM Center Director

Interventional Radiology & Endovascular Surgery

Dr. Rosen is internationally recognized as a leader in the field of interventional radiology and endovascular surgery, having pioneered several techniques and medical devices now in common use. He attended college and medical school in Philadelphia, receiving his medical degree from Hahnemann University and post graduate training in interventional radiology at the Hospital of the University of Pennsylvania. After completing a fellowship in 1980, he was recruited to establish the Division of Interventional Radiology at New York University Medical Center, where he remained for 25 years, performing over 70,000 interventional and endovascular procedures and training 45 fellows, several of whom have become leaders in the field in their own right. In April 2005, Dr. Rosen joined the newly formed multidisciplinary cardiovascular group at Lenox Hill Heart and Vascular Institute in New York, where he continues to treat patients, train fellows, and conduct clinical research.

Dr. Rosen is best known for his original work in the management of children and adults with congenital vascular malformations, and is referred patients from around the world with these disorders. He has also developed techniques and instrumentation for the treatment of patients with aortic aneurysms, atherosclerosis, hepatic tumors, and uterine fibroids. He holds several patents for medical devices and has published nearly 100 original scientific papers and two textbooks, as well as book chapters in several standard medical texts. He also lectures extensively and has been a visiting professor in institutions throughout the United States and abroad. He was the youngest individual ever elected to fellowship in the Society for Interventional Radiology, and is a member of the Alpha Omega Alpha Honor Medical Society, the Radiological Society of North America, and the Cardiovascular Council of the American Heart Association.

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Course 05: Lesson Quiz Answer Key

1. C
2. B
3. A
4. B
5. D
6. B
7. C
8. B
9. B
10. C