Multidisciplinary Evaluation and Management of Complex Vascular Malformations

Cynthia K. Shortell, MD
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• **Vascular malformations?**
  
  – “Embryologically developed, inborn errors of vascular morphogenesis leading to true structural anomalies”\(^1\)

• **Etiology:**
  – Unknown, but genetic predilection
  – Molecular studies:
    • VMs are caused by dysfunctions in the signaling process regulating proliferation, differentiation, apoptosis, maturation and adhesion of vascular cells²

• Spectrum of disorders ranging from minimal to significantly disabling conditions impacting patient’s anatomic, functional and emotional integrity

• **Incidence VMs = 1.2-1.5%**
• **Obstacles to treatment and misconceptions about VMs**

  • Expectation that lesions will regress
  • Lack of knowledge around diagnosis and therapies
  • Fear/patients considered too high risk to treat
• **Importance of multidisciplinary approach**
  - Diversity of lesions and treatment options
  - The management of VMs *exceeds* the level of expertise of any *single medical specialty*
  - Consequently, many patients have been discouraged by the *lack of correct diagnosis* and *proper treatment* despite numerous visits to different clinics
• **Multidisciplinary approach advantages**
  
  – **Lessens** the need for **multiple office visits**
  – **Streamlines** and **expedites** patient care
  – **Gets all caregivers and staff on the same page**
  – **Best results** if patient evaluation and indication for treatment are based on the assessment of team members
  – **Important to establish treatment strategy and TREATMENT GOAL(S) for each patient**
• **Duke Multidisciplinary Vascular Malformation Team:**
  - Vascular Surgery
  - Plastic Surgery
  - Pediatric Surgery
  - Diagnostic Radiology
  - Interventional Radiology
  - Dermatology
  - Ophthalmology
  - Orthopedics
Management Challenges

Nomenclature & Classification
Diagnosis
Treatment Planning
Inconsistent, archaic terminology

• hemangioma simplex
• cavernous hemangioma
  • birthmarks (naevi)
  • port-wine stains
• angiomas / angiomatas
Nomenclature & Classification:

The greatest confusion exists around the difference between “hemangiomas” and vascular malformations.
Numerous classification attempts in the past:

- Mulliken and Glowacki
- Jackson et al.
- Belov (Malan, Degni): truncular and extratruncular
- International workshop on Vascular Malformations Hamburg, Germany

<table>
<thead>
<tr>
<th>Anatomopathologic classification of vascular defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Hamburg classification)</td>
</tr>
<tr>
<td><strong>Type</strong></td>
</tr>
<tr>
<td>Predominantly arterial defects</td>
</tr>
<tr>
<td>Predominantly venous defects</td>
</tr>
<tr>
<td>Predominantly lymphatic defects</td>
</tr>
<tr>
<td>Predominantly arteriovenous shunting defects</td>
</tr>
<tr>
<td>Combined/mixed vascular defects</td>
</tr>
<tr>
<td><strong>Forms</strong></td>
</tr>
<tr>
<td>Truncular</td>
</tr>
<tr>
<td>Extratruncular</td>
</tr>
<tr>
<td>Aplasia or obstructive</td>
</tr>
<tr>
<td>Dilation</td>
</tr>
<tr>
<td>Aplasia or obstructive</td>
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<tr>
<td>Dilation</td>
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<tr>
<td>Aplasia or obstructive</td>
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<tr>
<td>Dilation</td>
</tr>
<tr>
<td>Deep</td>
</tr>
<tr>
<td>Superficial</td>
</tr>
<tr>
<td>Arterial and venous</td>
</tr>
<tr>
<td>Hemolympathic</td>
</tr>
<tr>
<td>Limited</td>
</tr>
<tr>
<td>Infiltrating</td>
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<td>Limited</td>
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<tr>
<td>Based on seventh Meeting of the International Workshop on Vascular Malformations, Hamburg, Germany, 1988.</td>
</tr>
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</table>
Vascular Anomalies

Tumors
- Hemangioma
- Other

Malformations
- High Flow (AVM)
- Low Flow
  - Venous
  - Lymphatic
  - Combined
Hemangiomas vs. Vascular Malformations
• Vascular tumors:
  - Infantile hemangioma the most common type
  - Proliferative phase during the first year of life
  - Spontaneous involution
  - Treatment often not needed
  - Therapy: usually medical (corticosteroids, interferon α)

Retroauricular infantile hemangioma:
• Vascular malformations
  – Arterial, capillary, lymphatic, venous, combined
  – Do **NOT** regress
  – Treatment indicated if symptomatic
  – Therapy: surgery, or interventional
• Hemangiomas are **true neoplastic** disorders and pathohistologically they demonstrate **increased endothelial cell turn over rate**

• Vascular malformations arise by dysmorphogenesis **without increased endothelial proliferation**
Histopathology:

Malformations

• Normal endothelial cell turnover rate (Hypertrophy)

Tumors

• Increased endothelial cell turnover rate (Hyperplasia)
Histopathology:

Malformations vs. Tumors

- Vascular malformations DO NOT regress
- Infantile hemangiomas are characterized by proliferative phase during the first year of life followed by involutional phase of slow, spontaneous regression in most cases
<table>
<thead>
<tr>
<th></th>
<th>Infantile hemangioma</th>
<th>Vascular malformation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Infancy or childhood</td>
<td>Anytime during lifetime</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Proliferating, involuting, involuted</td>
<td>Commensurate growth or slow progression</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Increased cellular turnover</td>
<td>Normal cellular turnover</td>
</tr>
<tr>
<td><strong>Triggering factors</strong></td>
<td>Unknown</td>
<td>Hormones, trauma, spontaneous</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Spontaneous involution, corticosteroids, interferon α, surgery</td>
<td>Sclerotherapy, surgery, laser, embolization</td>
</tr>
</tbody>
</table>
Vascular Malformations
Management Challenges

Nomenclature & Classification

Diagnosis

Inadequate treatment
• **Diagnosis:**
  - H&P
  - Duplex scan
  - MRI
  - Arteriogram
• **Physical Exam:**
  - Assess presence and characterization of mass
  - Color / temperature of skin
  - Thrill / bruit
  - Dilated veins and variation of mass with Valsalva
  - Presence of limb asymmetry and presence of lymphedema
**Clinical Features**

- Present at birth
- May not be clinically apparent until *later in life*
- Growth and appearance may be stimulated by trauma, the effects of hormones (during puberty and/or pregnancy)
- May occur in the absence of any identified triggering factors
In some cases, it may be challenging to distinguish between low flow and high flow lesions....
• Every effort should be made to **differentiate** low flow from high flow malformations

• This process is the most **critical** step in the evaluation and management of VM
• **Duplex scan**
  - Useful to confirm the diagnosis, as it is rapid, easy and shows the low flow velocity and vascularization
  - Frequently *inadequate* to demonstrate the extent of the lesion
• **MRI** is the imaging modality of choice in the evaluation of VM:
  - Shows the lesion’s **flow characteristics**
  - Provides good soft **tissue definition**
  - Delineates the **extent** of the malformation throughout the involved tissues
  - Determines **relationship to normal circulation** and surrounding anatomic structures
  - Requires **exact and expert timing and protocol**
**ARTERIOGRAM**

- When MRI suggests the presence of a high flow/arterial component, the diagnostic workup should include an arteriogram.
- If the arteriogram confirms a high flow component, treatment can be done at the same time.
- If the arteriogram excludes a high flow component, treatment can safely be designed for a low flow lesion.
High Flow Vascular Malformations
• **High Flow** Vascular Malformations (Arterio-Venous Malformations)
  
  - Direct connection between arterial and venous system caused by congenital malformations resulting in fistulous A-V tracts
• **PE:**
  - Skin discoloration
  - Elevated cutaneous temperature
  - Dilated veins
  - Thrill / bruit
• Can be aggressive; cutaneous ischemia with ulceration, infection or hemorrhage
• Can be painful
• High output cardiac failure when extensive
• Duplex:
  - Multidirectional flow and high-amplitude arterial waveform with spectral broadening
• **MRI**
  
  - Best to evaluate extent of AVM and relationship to adjacent structures
• **Arteriogram**
  - Used to evaluate the extent of lesion and to plan treatment
  - Allows precise evaluation of feeding arteries and draining veins-feasibility of embolization

This arteriogram demonstrates AVM supplied by infraorbital and ophthalmic artery
• **Therapeutic mainstays**
  - **Multimodal treatment** including preoperative **embolization** and complete **surgical resection**, is usually necessary for the management of high flow vascular malformations.

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**Duke Medicine**
http://vascular.surgery.duke.edu
• **Treatment of high flow vascular malformations**
  - Coil embolization
• **Treatment of high flow vascular malformations**
  - Glue embolization
• **Treatment of high flow vascular malformations**
  - Glue embolization
• **Surgical treatment of high flow VMs**

  - **Surgical resection**
    • Pulsatile mass at the base of long and ring fingers
    • Severe ischemia of the long finger
• Angiogram demonstrates a lesion originating at the palmar arch and extending into the long finger
• Resection and revascularization with an autogenous vein graft
• One year after surgery
  – All motion and sensation had returned to all the digits
  – The color and turgor of the long finger pulp are dramatically improved
Low Flow Vascular Malformations
• **Clinical Presentation**
  - Affects both superficial and deep underlying anatomic structures (skin, muscles, abdominal viscera, CNS)
  - Sx severity variable based on size and extent
  - Can be isolated or part of a syndrome
• **Presenting symptoms:**
  - Skin discoloration
  - Varicosities
  - Pain
  - Decreased mobility
  - Swelling
  - Bleeding
  - Osteomuscular hypertrophy
• **Venous malformations**
  - Typically **bluish**
  - Soft and easily compressible lesions
  - Usually enlarge when affected extremity is dependent or after Valsalva maneuver
• **Venous malformations**
  - No increase in local skin temperature
  - No thrill or bruit

Venous malformation affecting fronto-temporal part of the face
• **Venous malformations**
  - Extensive extratruncular malformation causing swelling of the upper extremity
• Venous malformations
  - Malformation causing swelling of digit
• **Duplex** of venous malformation reveals mixed venous waveform

• **Duplex** is inadequate to demonstrate the extent of the lesion
• **MRI** gives a **bright hypersignal** on T2-weighted spin-echo sequences that delineates the extent of the malformation throughout the involved tissues
• **Lymphatic malformations**
  - Usually noted at birth or before the patient reaches the age of 2 years
  - Sponge-like lesions
  - Skin overlying lymphatic malformations is usually normal in color
• Lymphatic malformations
  – Microcystic
  – Macrocystic
  – Combined
• **Duplex** scan of lymphatic malformation shows complete absence of Doppler signal
• **Lymphatic malformations**
  – Most common complications:
    • Infection
    • Swelling/compression of vital structures
• **Capillary malformations**
  - Present at birth and grow in proportion to the growth of a child
  - Appear as localized pink or red lesions
• **Capillary malformations**
  - Commonly associated with enlargement and anomalies of underlying structures
  - Midline occipital capillary malformations can herald the presence of an encephalocele or ectopic meninges
• Capillary malformation associated with venous malformations and osteomuscular hypertrophy in patient with KTS
Vascular malformations can be isolated or as a part of a syndrome (ie Klippel Trenaunay Syndrome, Proteus, Maffucci, Parkes-Weber)
• Klippel-Trenaunay Syndrome:
  - Rare congenital anomaly
  - No arterial component (w/ arterial comp = Parkes Weber syndrome)
• **Klippel-Trenaunay Syndrome Triad:**
  - Capillary malformations ("port wine stain")
  - Venous/lymphatic malformation
  - Pathognomonic osteomuscular hypertrophy
• **Special diagnostic considerations:**
  - Aplasia or hypoplasia of deep venous trunks
  - Localized Intravascular Coagulopathy
Special diagnostic consideration: Aplasia or hypoplasia of deep venous trunk.

- Present in 8% of VM patients (with venous predominance)


Table II. Prevalence of deep venous anomalies in congenital vascular malformations of venous predominance

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (n)</th>
<th>Phlebectasia*</th>
<th>Aplasia/hypoplasia of deep * veins</th>
<th>Aneurysms*</th>
<th>Avalvula*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belov</td>
<td>347†</td>
<td>180/347; 52% (47%-57%)</td>
<td>29/347; 8% (5%-11%)</td>
<td>71/347; 20% (16%-25%)</td>
<td>N/R</td>
</tr>
<tr>
<td>Browse et al16a,16b</td>
<td>49‡</td>
<td>N/R</td>
<td>9/49; 18% (8%-29%)</td>
<td>N/R</td>
<td>3/49; 6% (0%-12%)</td>
</tr>
<tr>
<td>Gloviczki et al12</td>
<td>144</td>
<td>N/R</td>
<td>13/144; 9% (4%-14%)</td>
<td>N/R</td>
<td>N/R</td>
</tr>
<tr>
<td>Malan11</td>
<td>234†</td>
<td>96/234; 41% (35%-47%)</td>
<td>N/R</td>
<td>21/234; 8% (5%-13%)</td>
<td></td>
</tr>
<tr>
<td>Paes &amp; Vollmar39</td>
<td>114†</td>
<td>N/R</td>
<td>53/117; 46% (37%-56%)</td>
<td>17/117; 15% (8%-21%)</td>
<td>73/117; 64% (55%-73%)</td>
</tr>
<tr>
<td>Servelle38</td>
<td>768†</td>
<td>276/768; 36% (33%-39%)</td>
<td>48/768; 6% (5%-8%)</td>
<td>64/768; 8% (6%-10%)</td>
<td>N/R</td>
</tr>
<tr>
<td>Taute et al22</td>
<td>50†</td>
<td>71/50; 14% (4%-24%)</td>
<td>1/50; 2% (0%-6%)</td>
<td>N/R</td>
<td>N/R</td>
</tr>
<tr>
<td>Villavicencio et al40</td>
<td>257†</td>
<td>21/257; 8% (5%-12%)</td>
<td>5/257; 2% (0%-4%)</td>
<td>21/257; 8% (5%-12%)</td>
<td>10/257; 4% (2%-6%)</td>
</tr>
<tr>
<td>Median prevalence (%)</td>
<td></td>
<td>36</td>
<td>8</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

N/R, Not reported.

*Prevalence of deep venous anomalies in patients with congenital vascular anomalies of venous predominance were estimated. The data in parenthesis represent the lower and upper limits of prevalence of the 95% confidence interval for each prevalence. The homogeneity test showed that prevalence varied significantly (P < .001).

†Patients with congenital vascular malformations of venous predominance.

‡Patients with Klippel Trenaunay syndrome.
• Prevalence of deep venous anomalies is even higher (18%) in patients with KTS

• Ascending phlebography of patient with KTS: absence of the left iliofemoral vein segment
• MRI reconstruction of patient with KTS:
  - Absent left common iliac vein
• Evaluation of patency and anatomic variations of the **ENTIRE** venous system (deep and superficial)
• **Special diagnostic consideration II**
  – **Localized Intravascular Coagulopathy**
    • Thrombosis of intralesional blood
    • Usually latent and asymptomatic
    • If symptomatic: associated with painful inralesional thrombotic episodes
    • Patients can become **severely** coagulopathic even during diagnostic procedures
• **Localized Intravascular Coagulopathy**
  
  - Often erroneously labeled as Kasabach-Merritt Syndrome (a distinct clinical entity characterized by profound thrombocytopenia associated with *vascular tumors*)
• **Localized Intravascular Coagulopathy**
  
  - The platelet count in LIC is moderately diminished *(100-150 x 10^3/ml)*
  
  - The increased risk of bleeding in some of VM patients can be attributed to the increased consumption of coagulation factors⁴

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• Procoagulant states are also associated with low flow VMs, including chronic intermittent PE

• A **hypercoagulability** profile should be routinely performed in all VM patients prior to undergoing diagnostic evaluation, surgical intervention or sclerotherapy

• Most PC states will not be detected however
• **Treatment of low flow vascular malformations**
  - Small lesions may be cured
  - Extensive lesions therapy palliative/goal oriented
• **Treatment options**
  - Surgical resection
  - Sclerotherapy
• **Treatment options**
  
  – *Surgical resection:*
    
    • Most effective for **encapsulated** and **microvascular lesions**
    
    • Diffuse, deep, and macrovascular lesions are not amenable to surgical excision d/t risk of hemorrhage and damage to vital structures
• Treatment options
  – Sclerotherapy:
    A) Liquid
      – Ethanol
    B) Foam
      – Polidocanol (Aethoxysklerol®)
      – Sodium Tetradecyl Sulfate (Sotradecol®)
• **Ethanol sclerotherapy:**
  – Limitations:
    • Use in pediatric patients
    • General anesthesia required for all patients
• Ethanol sclerotherapy adverse effects:
  • EtOH toxicity
  • Severe pain
  • Ulceration and necrosis at injection site
  • Ischemic bullae
  • DVT and PE
  • Peripheral nerve injury
  • Pulmonary hypertension
Complications of absolute ethanol sclerotherapy

<table>
<thead>
<tr>
<th></th>
<th>Acute (n = 51)</th>
<th>Chronic (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor (n = 41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin only (n = 30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Bullae</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Skin or subcutaneous tissue damages (n = 5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrosis/ulcer</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous damage combined with deeper tissue/structure (n = 6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Tendon</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Major (n = 10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis (n = 5)</td>
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</tr>
<tr>
<td>Localized</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Combined with pulmonary embolism</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Combined with superficial thrombophlebitis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nerve damage (n = 5): facial or peroneal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Minor (n = 6)

- Gait difficulty due to calf muscle fibrosis: 3
  - Spontaneous relief with minimum supportive measurement
  - Ankle contraction due to calf muscle fibrosis to require physical therapy for the relief: 3

Major (n = 1)

- Ankle contraction due to calf muscle fibrosis to require Achilles tendon lengthening surgery: 1

However, another six cases with skin complications involved deeper tissue injury (e.g., muscle or tendon injury), necessitating a combination of two to three in one patient (e.g., skin damage together with DVT and superficial thrombophlebitis),
• **Foam sclerotherapy**
  
  – Sodium Tetradecyl Sulfate (USA)
    • Used widely in US and Europe in the treatment of varicose veins and superficial reflux
    • Not previously applied to the treatment of VMs
  
  – Polidocanol (Europe)
    • has shown benefit in the treatment of VM but is not FDA approved in US
“Sodium Tetradecyl Sulfate foam sclerotherapy may be an effective alternative to polidocanol in the treatment of LFVM$^5$”

• Foam sclerotherapy
  – Offers best visualization under US
  – Prevents sclerosant dilution by intralesional blood
  – Maximizes endothelial exposure
• **Foam sclerotherapy**
  
  – **Mechanism of vascular obliteration**
    
    • Disruption of endothelial cell membrane
    • Vasospasm due to exposure of subendothelial collagen to sclerosant
    • Platelet aggregation, inflammation and subsequent endofibrosis
    • *Ideally a sclerotic, not thrombotic* occlusion
• Foam sclerotherapy
  - Effectively used for varicose veins, telangiectasias and recently VMs
  - Expce primarily European using polidocanol
  - Duke experience the first reported use of STS for VMs
• **Foam sclerotherapy**
  – Treatment in the **office setting** under **local anesthesia**
  – *General anesthesia for pediatric patients*
Foam sclerotherapy

- When accessing deeper/non-visualized vessels
- To control foam delivery preventing entry into major venous structures through communicating vessels

http://vascular.surgery.duke.edu
• Foam sclerotherapy:
  – for visible subdermal malformations w/o deep communications

http://vascular.surgery.duke.edu
• **Clinical case 1**
  - 53 year old male with long history of left face and left ear vascular malformation
  - **Diagnosis:** Low flow (venous) vascular malformation
• **Clinical case 1**
  - **Initial treatments:** surgical resections over 20 years
• **Clinical case 1**
  - **Subsequent treatment:** STS Foam Sclerotherapy
  - Outpatient; visual guidance
  - Goals set primarily for:
    - cosmesis
    - pain relief
• Clinical case 1
  – **Outcome:** symptoms improved after the treatment
  – No complications

Before STS FS

After 3 STS FS
• **Clinical case 2**
  - 13 year old female c/o right leg swelling, discoloration, varicosities and severe discomfort with exertion.
  - Lesion present from birth but progressive
  - Referred by dermatologist
• **Clinical case 2**

  - **Diagnosis:** Klippel-Trenaunay Syndrome
  - Venous malformation on the right anteromedial thigh
  - **Initial treatment:** Ethanol Sclerotherapy
  - Complicated by popliteal DVT
• **Clinical case 2**
  
  – Subsequent therapy: STS foam sclerotherapy
  
  – Goals preset as:
    • Decreased pain
    • Decreased swelling
    • Improved cosmesis
    • Increased mobility
  
  – General anesthesia due to age
Clinical case 2

- **US Guidance**
- **Tessari method of mixing**
- **Percutaneous injection under US surveillance**
- **Displaces intralesional blood better**
- **Leg elevation**
- **Compression wrappings**

Clinical case 2 – Outcome

Before STS FS

After 4 STS FS
• Clinical case 2 – Outcome

  - 100% goal achieved after 7 treatments
  - No complications
  - No side effects
• **Clinical case 3**
  
  - 7 yo male with right leg pain, varicosities, discoloration, decreased mobility, bleeding since birth
  
  - **Diagnosis: Klippel-Trenaunay Syndrome**
• **Clinical case 3**
  
  - **Initial treatment:** Ethanol sclerotherapy (outside facility)
  - **Subsequent treatment:** STS foam sclerotherapy
  - **Goals set at:**
    - increased mobility
    - decreased bleeding risk @ hockey
• **Clinical case 3**
  Combination of therapies as with prior case
Clinical case 3
outcome:

• Symptoms resolved
• Able to play hockey
• Socially comfortable
• No complications
SUMMARY
VASCULAR MALFORMATIONS ARE NOT HEMANGIOMAS

DIFFERENTIATING BETWEEN HIGH FLOW AND LOW FLOW LESIONS IS VITAL TO DIAGNOSIS AND THERAPY OF VMs

MOST VMs ARE PALLIATED, NOT CURED AND REQUIRE MULTIPLE TREATMENTS

THE MULTI-DISCIPLINARY APPROACH IMPROVES CARE AND PATIENT EXPERIENCE
Thanks to Jovan Markovic MD, who helped prepare these slides
Questions?

Duke Multidisciplinary Vascular Malformation Team 2009