Haematological Aspects of VAD Therapy

London Regional Transfusion Committee
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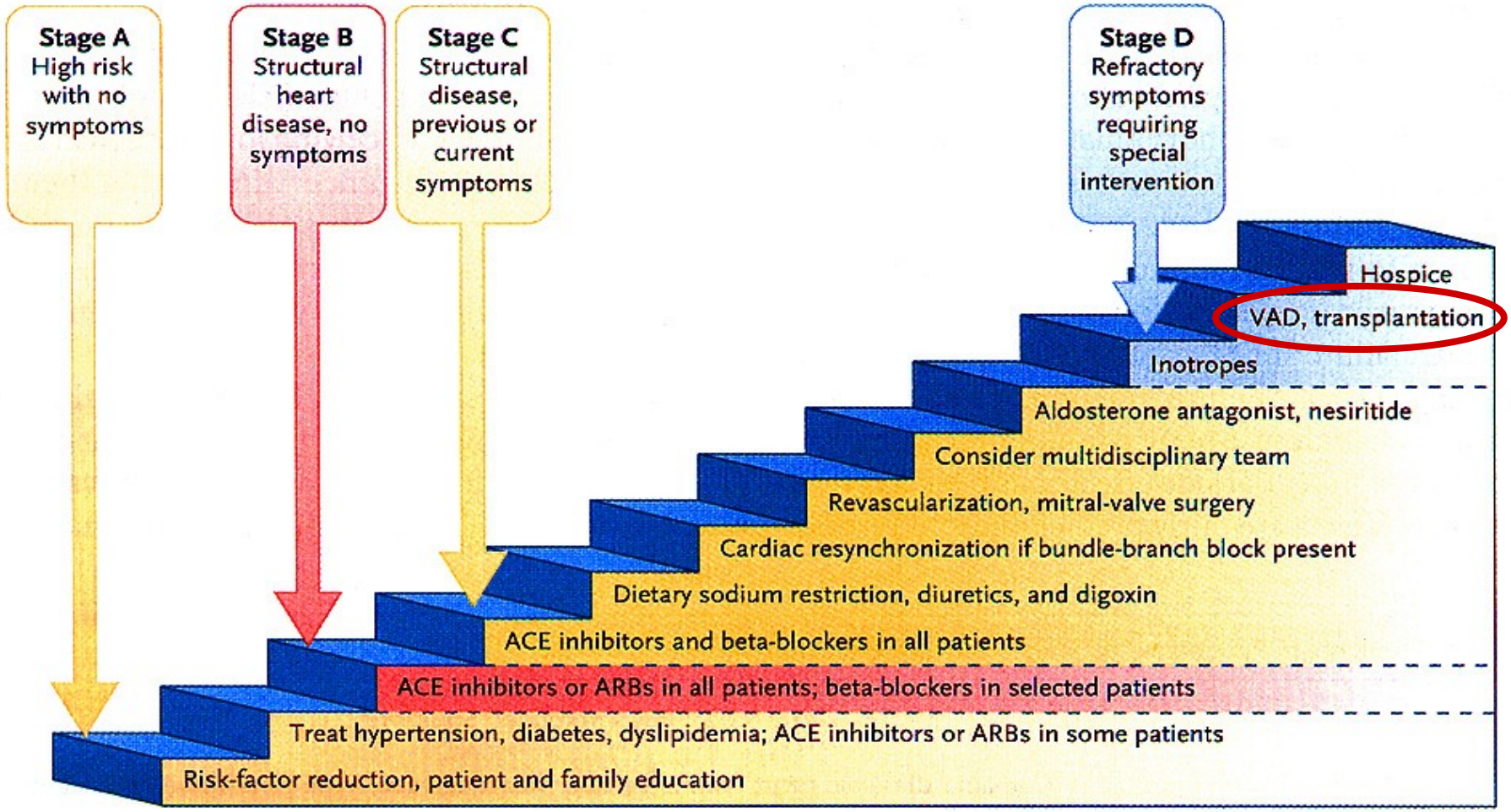
VAD therapy is a treatment for advanced heart failure



Jessup NEJM 2003;348:2007-18

C2 CB245, 08/02/2010

Mechanical Circulatory Support

Applications

- Post cardiotomy -salvage
- Bridge to transplantation
- Bridge to recovery “combination therapy”
- Chronic support “destination therapy”
- Adjunctive therapy

  (cell transplantation, gene therapy, etc.)

Blood flow quantity ?

Blood flow quality ?

What is the best method to pump blood ?

Peristaltic roller pump

Advantages

- Inexpensive
- Suitable for short term and intermittent use

Disadvantages

- Risk of tubing rupture
- Spallation
- Turbulence
- Haemolysis
- Inappropriate response to changes in pre- and afterload

Constrained forced vortex

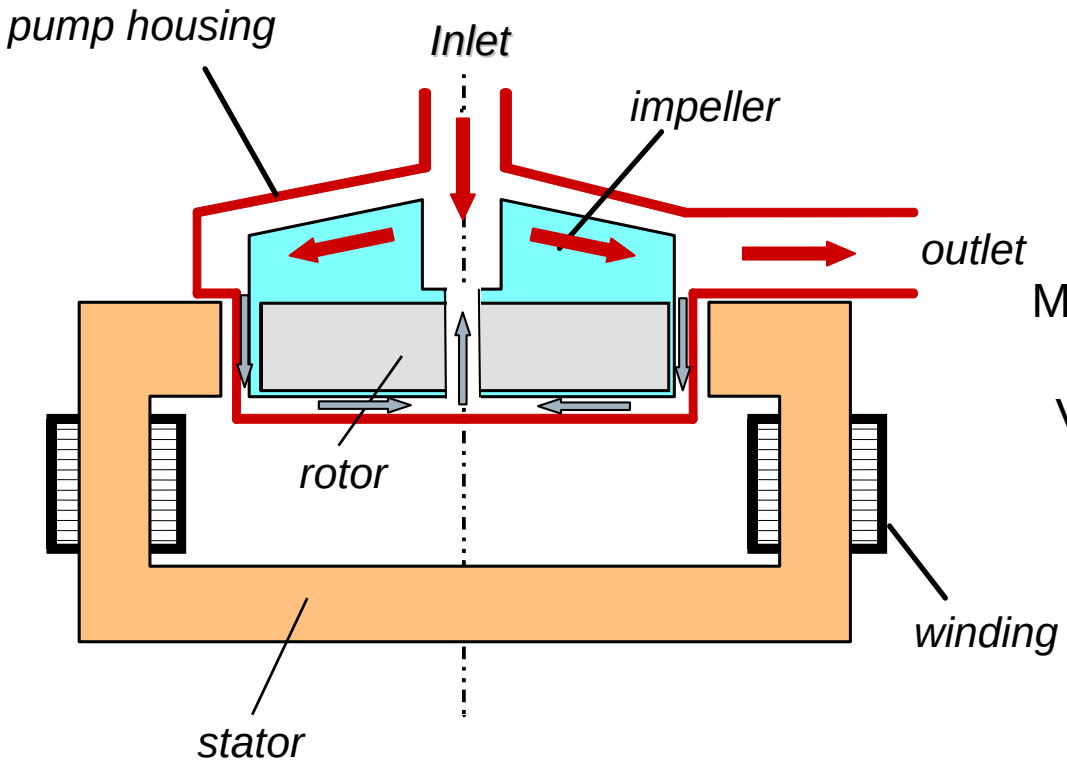
Advantages

- Inexpensive
- Suitable for short term
- No spallation
- No risk of tubing rupture

Disadvantages

- Lip seal
  - friction
  - heat
  - thrombus
- Risk of bearing failure
- Non-occlusive

Thoratec CentriMag



Advantages

Magnetic levitation –no bearings
Relatively inexpensive
Versatile, LVAD RVAD BiVAD
Ultrasonic flow probe
Patient transfer to ward

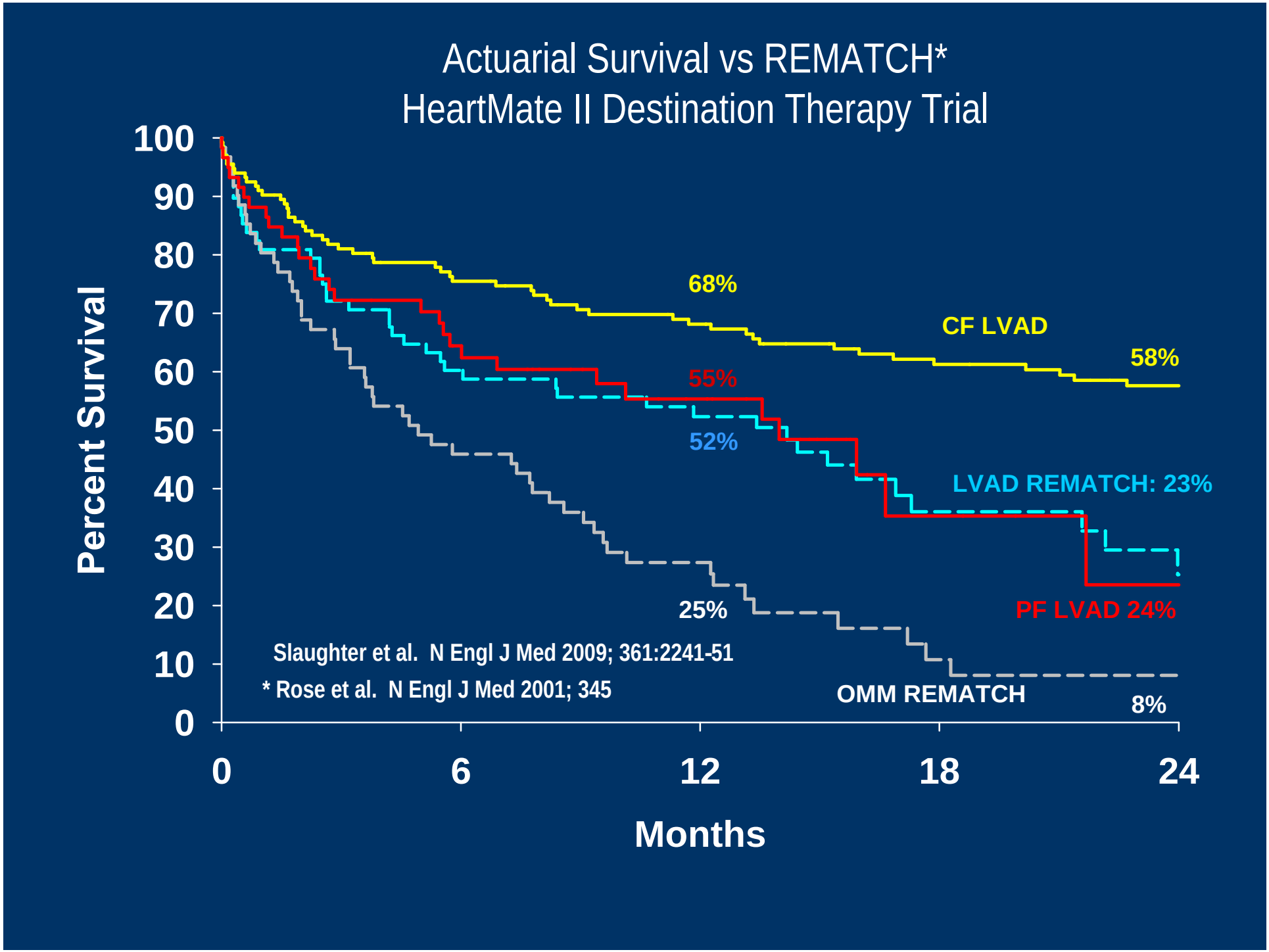
Disadvantages

Prone to thrombus accumulation
Atrium/cannula and lines
Unsuitable for long term support

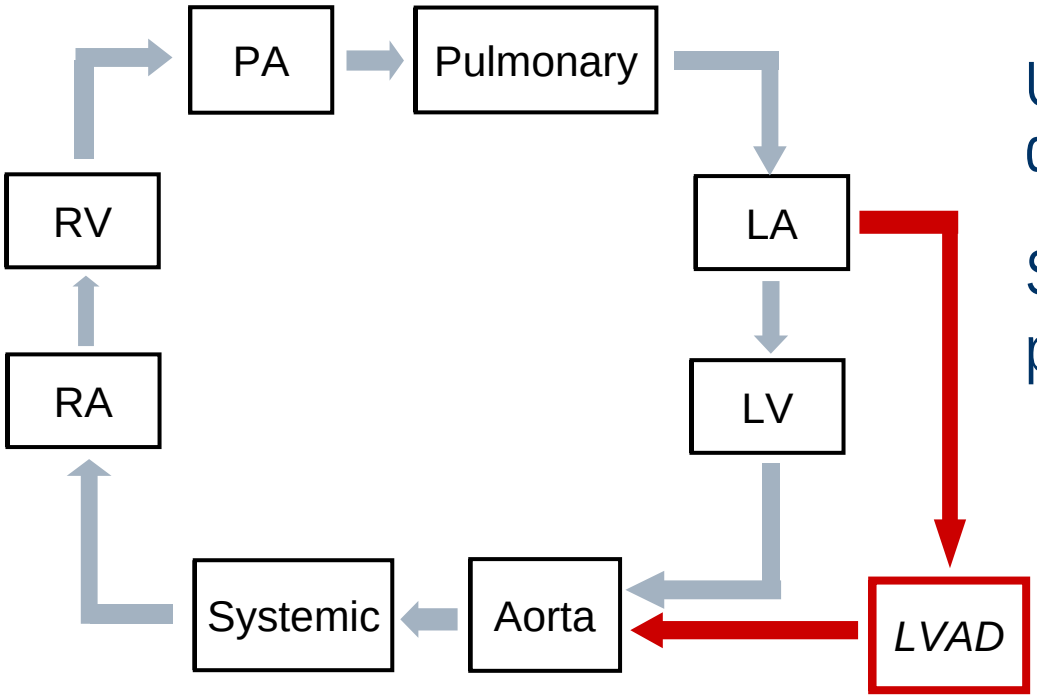
Long term support strategies

	Total artificial heart	Pulsatile VAD	Rotary VAD	
Natural heart	Removed	In situ	In situ	In situ
Blood flow replacement	Total	Total	Total	Partial
Support mode	Left and right	Left or right or BIVAD	Left or right or BIVAD	Left

	Pulsatile (first generation)	Rotary
Characteristics	Intra- or extracorporeal blood chamber with moving boundary (diaphragm or sac) Inlet and outlet valves for unidirectional flow (mechanical or tissue)	Intra- or extracorporeal Blood pumping achieved by high speed rotation of impeller located by: - Blood lubricated bearings (second generation) - Magnetic/hydrodynamic levitation (third generation)
Actuation	Pneumatic or electrical	Electrical
Implant size	Large	Small
VAD blood path	Occlusive	Non-occlusive (risk of retrograde flow)


Actuarial Survival vs REMATCH*
HeartMate II Destination Therapy Trial
Percent Survival
100
90
80
70
60
50
40
30
20
10
0
0
6
12
18
24
Months
68%
CF LVAD
58%
55%
52%
LVAD REMATCH: 23%
PF LVAD 24%
25%
OMM REMATCH
8%
Slaughter et al. N Engl J Med 2009; 361:2241-51
* Rose et al. N Engl J Med 2001; 345

Left ventricular assist device (LVAD)
Short term configuration

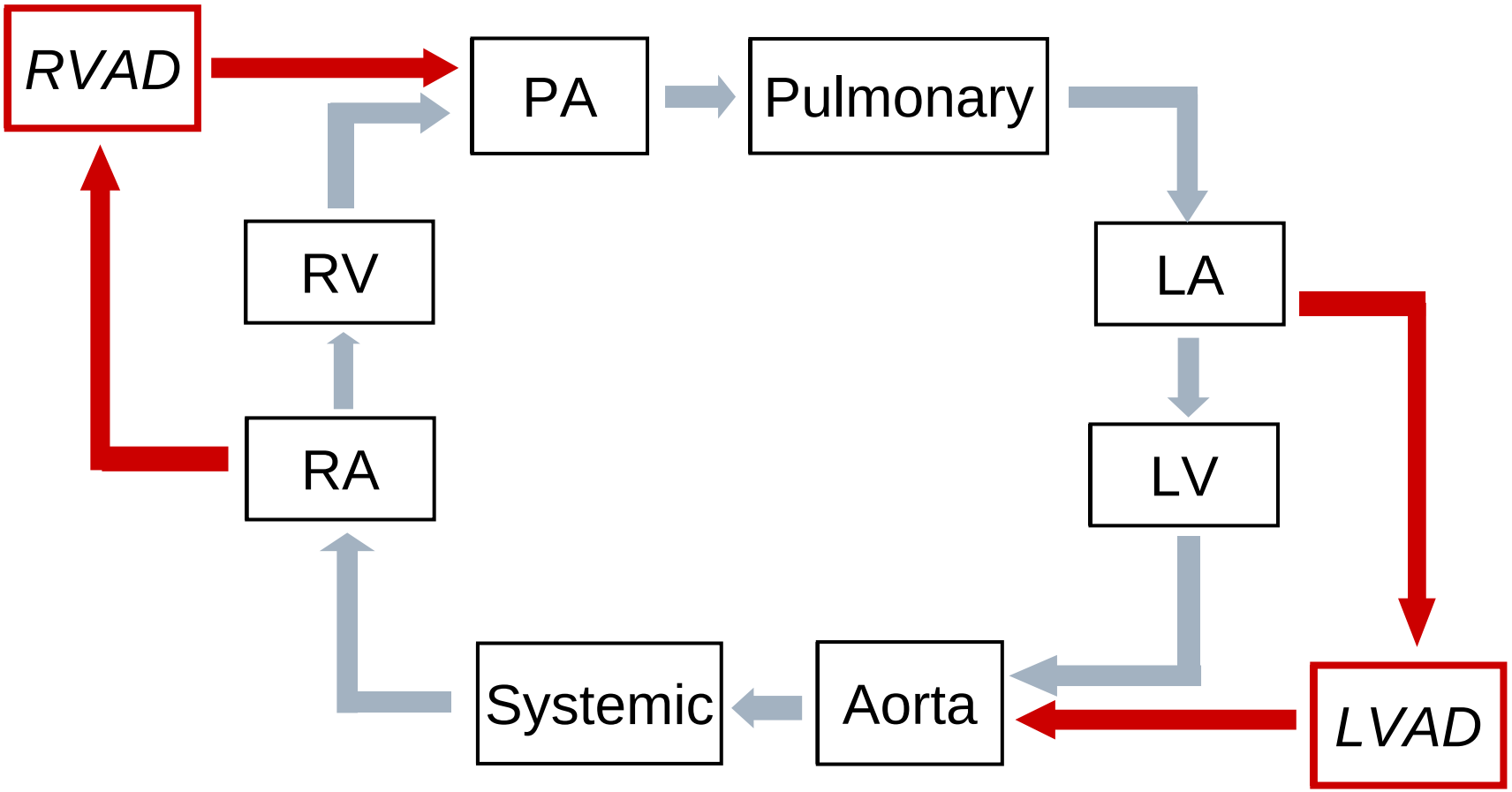


Relatively rapid implementation

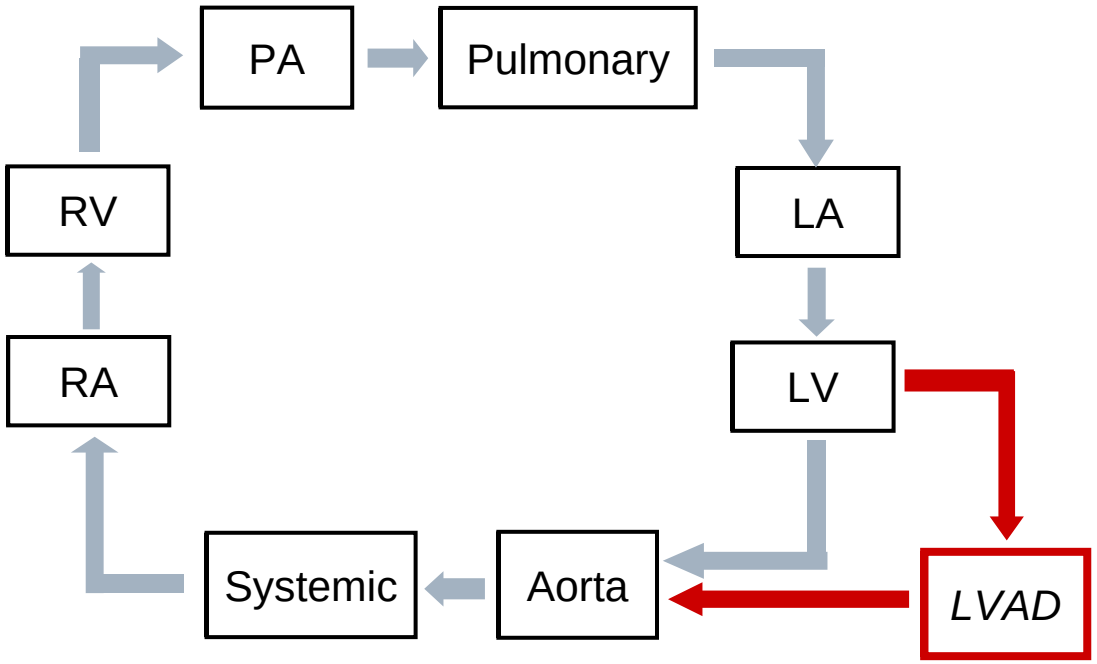
Unpredictable LV decompression

Suitable for long term partial support

BiVAD configuration



Long term LVAD Configuration



Complex implantation procedure

Profound LV offloading

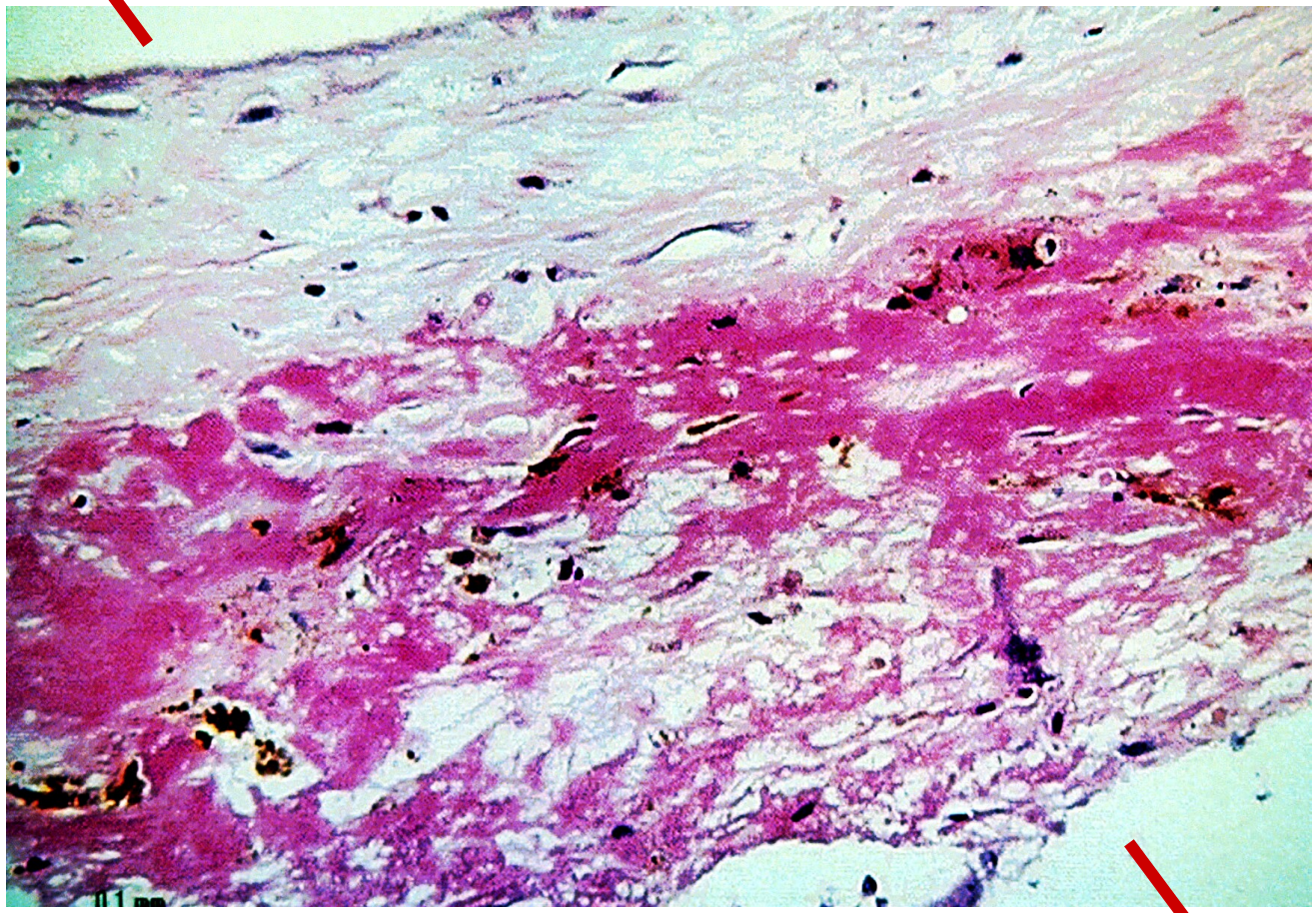
Blood flow quantity

- Adult cardiac index 2.8 – 4.2 L / min / m^2
- Mean adult body surface area: female: 1.6 m^2 male: 1.9 m^2
- Total replacement flow rate: 3 - 10 L / min
- Heart failure
  - cardiac index variable (typically 1.8 L / min / m^2)

Blood flow issues

- Vulnerability to thrombogenesis
  - Anticoagulation (heparin then warfarin + aspirin)
  - Avoid localised heat generation
    - (potential problem with bearings)
  - Moderate wall shear stresses (self cleaning)
  - Avoid flow separation /stagnation
  - Appropriate material selection (surface topography)
    - Smooth versus rough surface

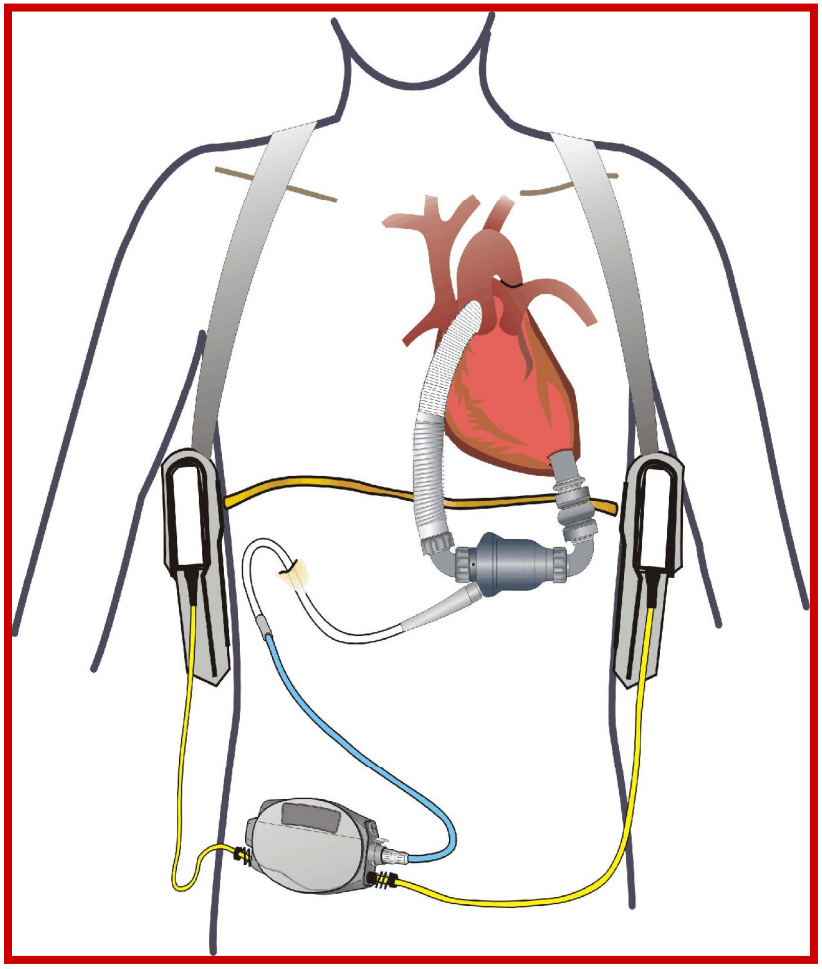
Blood



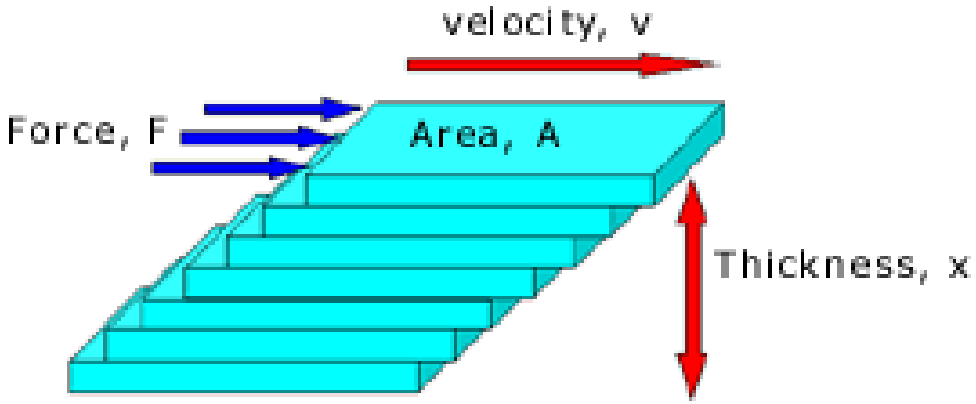
VAD surface

Blood flow issues

- Vulnerability of formed elements to trauma
  - Avoid excessive turbulence/shear stress
  - Minimise residence time in hostile microenvironment



Relationship between shear stress, shear rate and dynamic viscosity (Pouseille flow)



Laminar shear field due to applied shear stress

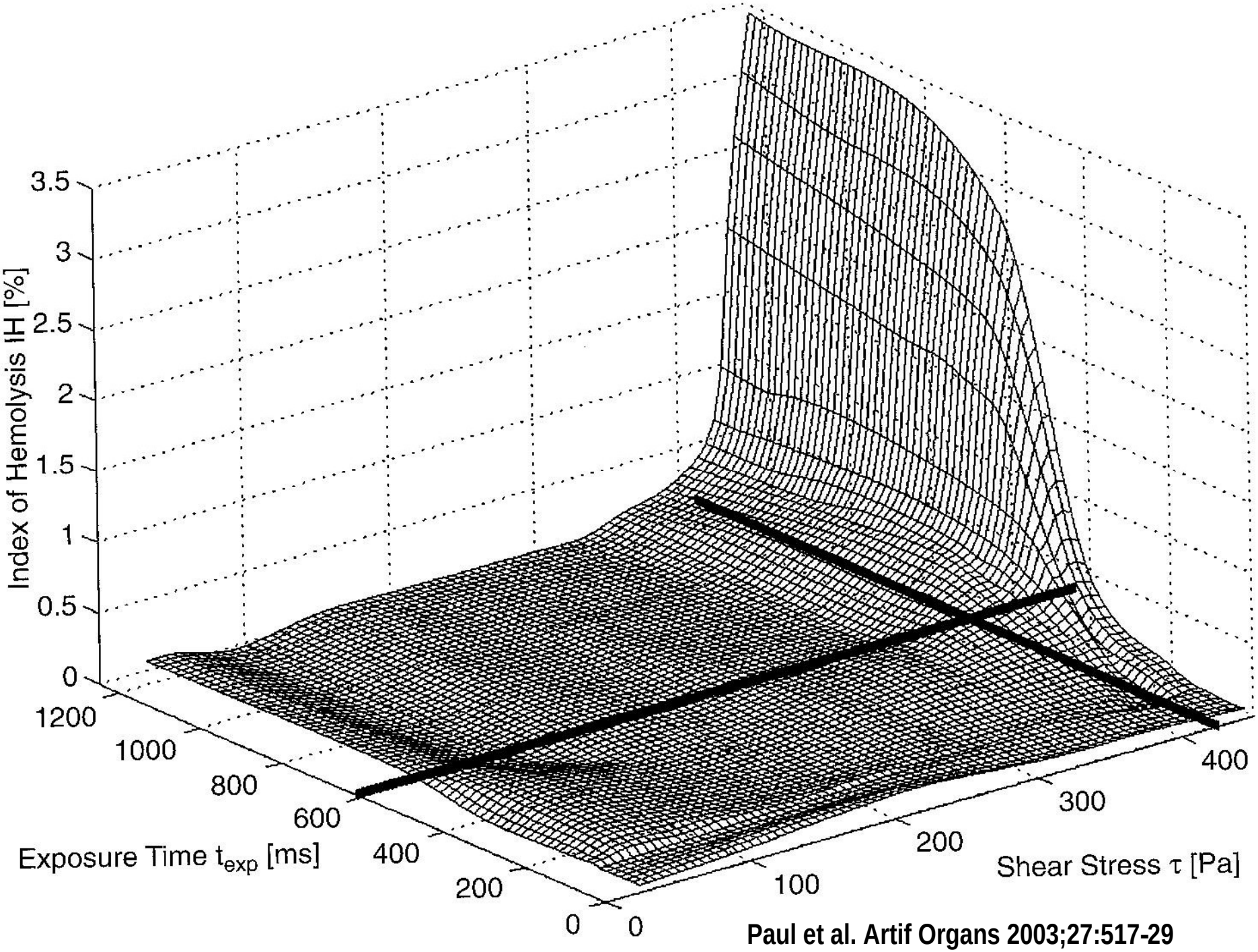
$$\text{shear stress, } \tau = \frac{F}{A} \quad (Pa)$$

$$\text{shear rate, } D = \frac{v}{x} \quad (s^{-1})$$

$$\text{viscosity, } \eta = \frac{\tau}{D} \quad (Pa.s)$$

shear work = τ t (Pa.s)

Impeller blade tip speed = shear rate
gap width



Paul et al. Artif Organs 2003;27:517-29

VAD therapy – a multifactorial pro-haemorrhagic state

- **Symptoms can range from**
  - **chronic mild anaemia to severe acute haemorrhage**

VAD therapy – a multifactorial pro-haemorrhagic state

The main contributory factors are:

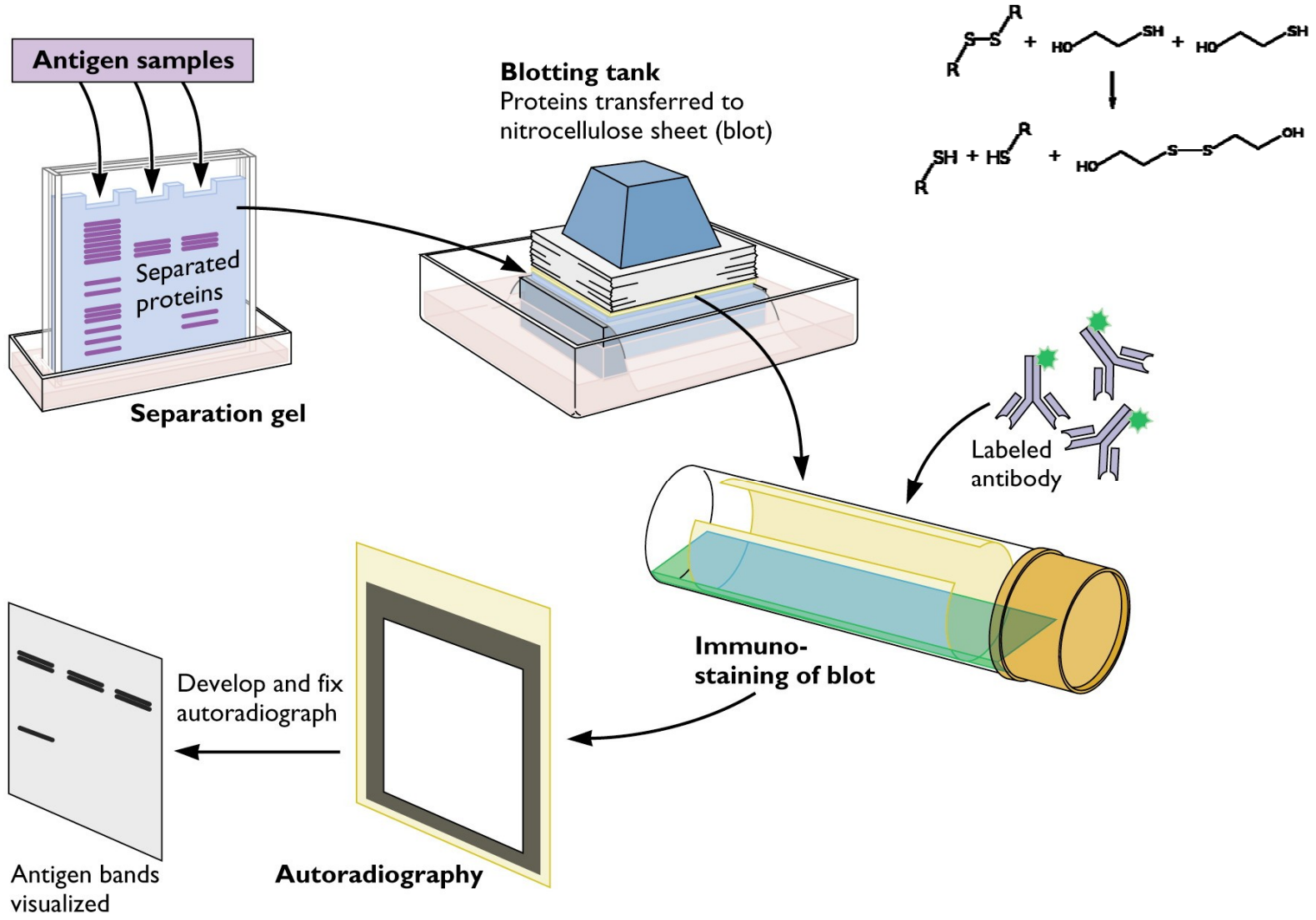
- **Pre-existing pathology**
  - **AVMs (brain and GI tract)**
  - **Stress ulceration of GI tract**
  - **Hepatic venous congestion secondary to HF => autoanticoagulation**
  - **Propensity to epistaxis**
  - **Anaemia of chronic disease**
- **Requirement for anticoagulation**
  - **Exacerbated by excessive dosage, poor control and drug interactions**
- **Secondary effects of infection**
  - **Bone marrow suppression (inflammatory cytokines)**
  - **Increased capillary permeability**
- **Device or flow related haemostatic abnormalities**
- **Blood path irregularities (e.g. kinked vascular conduit)**

Association between aortic stenosis and GI bleeding

- First reported by Heyde. *NEJM 1958:259:196* - Heyde's syndrome
- Association questioned – study limitations *Gastroenterology 1988;95:1670*
- Consensus remains that there is an association
- Many mechanisms have been proposed:
  - Altered intralumenal pressure
  - Neurovascular aetiology
  - Hypoperfusion
  - Diminished pulsatility
  - Acquired von Willebrand disease

    Vincentelli NEJM 2003;349:343-9.

vW-factor analysis of multimers by agarose gel electrophoresis & western blotting



Association between VADs and acquired von Willebrand disease

- Ulrich Geisen, Freiberg *Eur J Cardiothorac Surg 2008;33:679-84.*
- Comprehensive comparison of vWf parameters (incl. collagen and plt R binding) in:
  - OCTx (n=8)
  - HMII (n=7)
  - BiVAD PVAD (n=5)
- All vWf parameters attenuated in VAD patients (except no. monomers) with respect to controls
- No significant differences detected between pulsatile and rotary VADs

Diagnosis and treatment of GI bleeding in VAD patients

- **Initial diagnosis: Hb↓ and haem +ve stool**
  - **Gastroscopy, colonoscopy and if necessary capsule endoscopy**
  - **Mesenteric angiography (vascular tuft and early venous phase)**

- **Treatment :**
  - **Argon plasma coagulation**
  - **Cauterisation**
  - **Endoscopic embolisation**

Case Report 1

- 17yr, Male,
- Hx “flu-like illness” for 2 weeks
- Dx: DCM
- HMI (VE) May 2000
- Slow, steady post op progress
- POD 21 Lower GI bleeding
- OGD – normal, colonoscopy - no bleeding point
- POD 23 Angiography/embolization

Case Report 1

- Bleeding problem resolved
- Bridged to recovery after 234 d
- Alcohol consumption ++ -> HF
- OHTx 2.5 yr post explant
- Remains A&W 6.5 yr post Tx

Rotary LVAD thrombosis

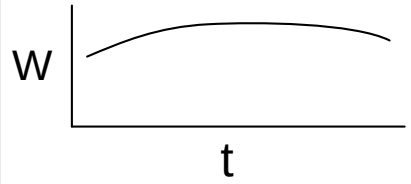
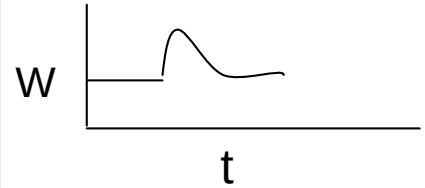
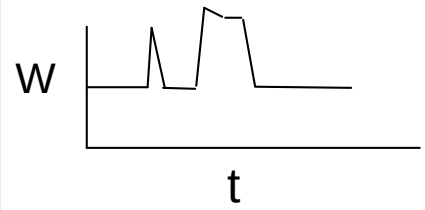
- Relatively infrequent but serious complication
- Characterised by:
  - substantial, refractory changes in estimated pump flow and power
  - ↑ LDH and plasma free Hb, haemoglobinuria
  - abnormal pump sound on auscultation
- Treatment options:
  - Elevated anticoagulation / thrombolytic therapy
  - LVAD replacement
  - Emergency transplantation

Rotary LVAD thrombosis

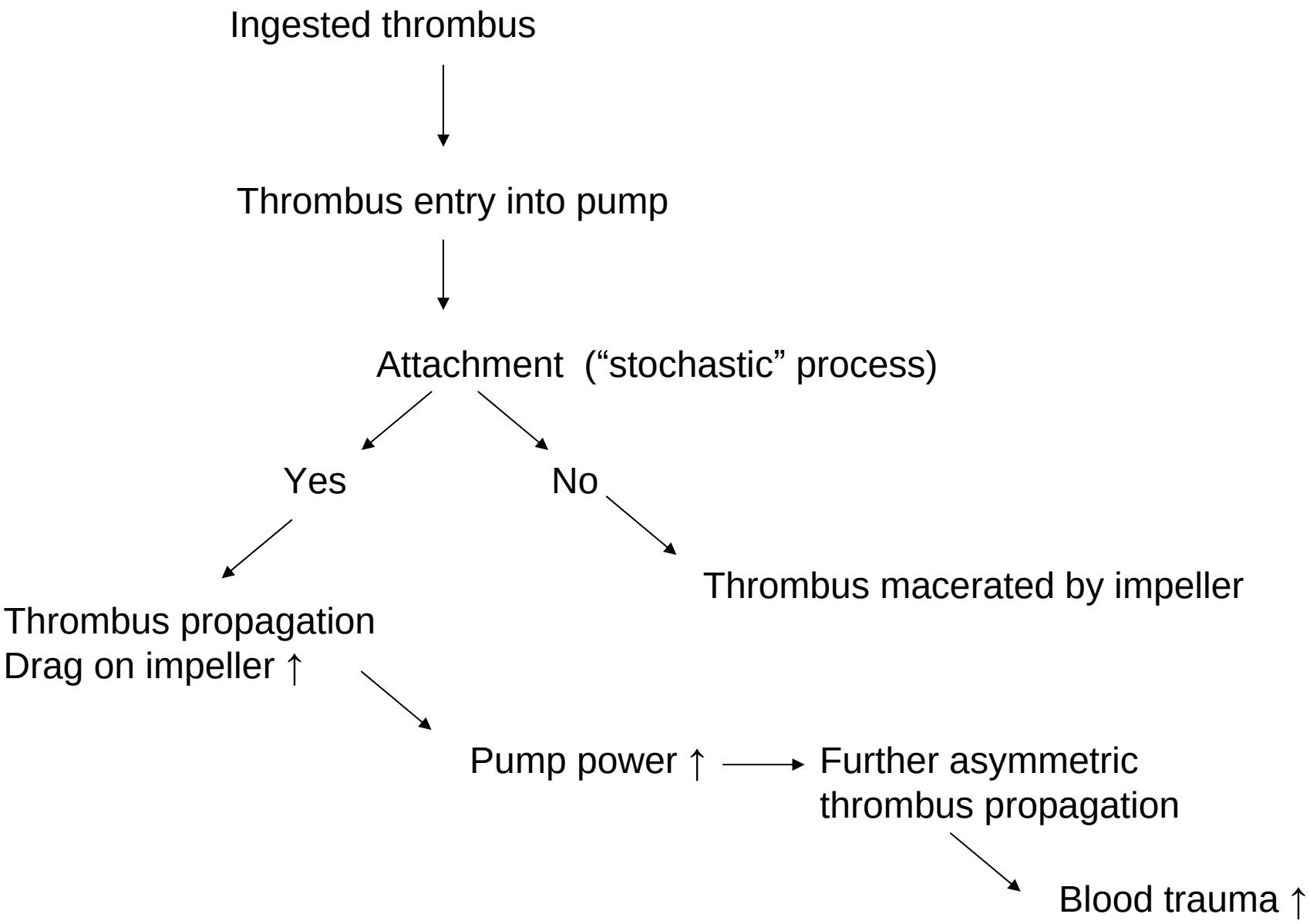
Two possibilities:

1. Elevated LVAD power and estimated pump flows
    - Increased drag on impeller
    - Accumulation of thrombus / fibrin
2. Decreased LVAD power and estimated pump flows
    - Restricted flow through blood path of LVAD

High power causes - HMII

Cause	Characteristics	Instantaneous power profile	dW/dt -dW/dt
Sepsis			Low
Exercise/ anxiety			Moderate-high
Impeller thrombus	Erratic changes Peak levels can be very high Very difficult to capture power spikes on controller data logger		Can be v high

Working hypothesis



Location of impeller thrombus

- Likely to be inlet bearing/impeller interface

  1. First point of entry of mobile thrombus

  2. Relatively constant and low Reynold's numbers upstream of impeller ?

  3. Thrombus likely to be dispersed during transit through pump

  4. High and variable Reynolds numbers in stator zone would tend to disperse thrombi attached to stator

Evidence of impeller thrombus

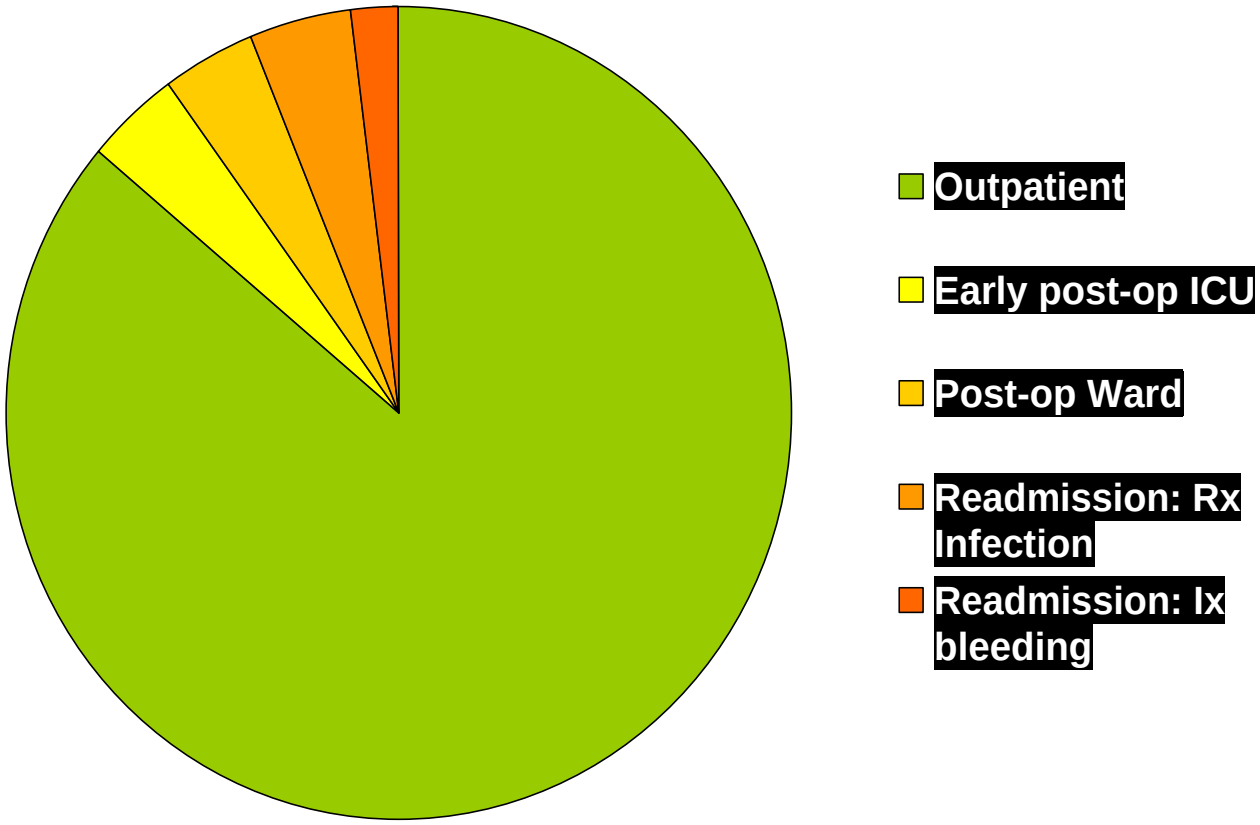
- Indirect
  - Elevated power levels particularly if power profile is erratic
  - Elevated plasma free hemoglobin (unexplained anaemia)
  - Elevated lactate dehydrogenase
  - Macroscopic haemoglobinurea (red urine)

  - Acoustic monitoring

- Direct
  - Examination of explanted pumps

Current status of NHS LVAD implants

27 February 2012 (N=49)



Remote monitoring of Harefield patient

Summary

- **Technology advancing rapidly**
- **Thromogenesis, bleeding and infection limit efficacy**
- **Totally implantable VADs within 5 years**
- **Improvements in pump design and anticoagulation regime should reduce hamatological complications**