

## Valve Related Hemolysis *Case Based presentation*

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## Hemolytic Anemia

- Shortened survival of red blood cells due to premature destruction
- Typical RBC lifespan is 120 days
- Normal aging of RBCs results in age-dependent destruction
  - Referred to as “random hemolysis”
  - About 1% of RBCs daily

## Hemolytic Anemia Classification

- Intracorporeal vs extracorporeal
- Immune vs non-immune
- Intravascular vs extravascular

## Hemolytic Anemia Classification

### Intracorporeal Defects

- Hemoglobinopathies
- RBC membrane/cytoskeletal defects
- RBC metabolic abnormalities

## Hemolytic Anemia Classification

### Extracorporeal Factors

- Antibodies directed against RBC membrane
- Enlarged spleen (hypersplenism)
  - stasis, trapping and destruction of RBCs
- Mechanical trauma to RBCs due to high velocity jets
- Exposure to compounds with oxidant potential
- Destruction of RBCs by bacterial pathogen
- Toxins, snake bites, thermal burns, Wilson's Dz

## Hemolytic Anemia Classification

### Immune Mechanisms

- Autoimmune hemolytic anemia
- Drug-induced hemolysis
- Hemolytic transfusion reactions
- Paroxysmal cold hemoglobinuria
- Cold agglutinin disease

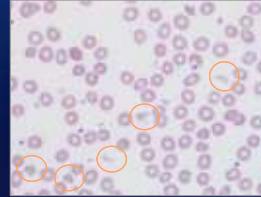
## Intravascular Hemolytic Anemia

- Shear stress (valve prostheses/rings)
- Heat damage (thermal burns)
- Complement-induced
  - paroxysmal cold hemoglobinuria
- Lysis from bacterial toxins
- Thrombotic microangiopathies
  - TTP, HUS and drug-induced
- Acute hemolytic transfusion reaction
- Direct trauma
  - Bongo drummers
  - runners (foot-strike)



## Hemolysis Due to Prosthetic Heart Valves And Prosthetic Rings

- Intravascular hemolysis
- Fragmentation hemolysis: Schistocytes



## 74 Year Old Woman With Mechanical Mitral Valve Prosthesis

- Rheumatic heart disease
- Mitral valve replaced with 30 M Braunwald-Cutter prosthesis at age 38 yr
- The B-C valve thrombosed and was replaced with 27 mm St. Jude Medical mechanical prosthesis at age 59 yr
- She also had surgical MAZE for PAF
- One year later, she required surgical repair for severe perivalvular MR



## 74 Year Old Woman With Mechanical Mitral Valve Prosthesis

- Two years ago she developed hematuria (on warfarin)
- Clot was removed from right renal pelvis during retrograde pyeloureterography
- She developed a large perinephric hematoma and underwent urgent right radical nephrectomy



## 74 Year Old Woman With Mechanical Mitral Valve Prosthesis

- One year later she began to experience dyspnea with one flight of stairs
- Her MVR appeared normal by echo, with MG 4 mmHg and with trivial MR
- Her LVEF was 55% and she had abnormal septal motion due to LBBB
- Her RVSP was 51 mmHg



## 74 Year Old Woman With Mechanical Mitral Valve Prosthesis

- During the next year her dyspnea worsened; she noted shortness of breath when walking 100 feet
- Her creatinine was 1.9
- NT-ProBNP 372
- She had multifactorial anemia, which had worsened, with hemoglobin 8.3
- She was transfused with 2 units of RBCs and her Hb rose to 11.3



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Hematology Testing*

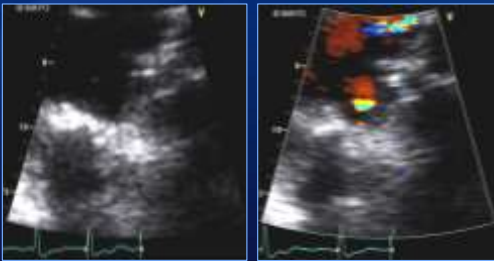
- Hemoglobin 8.3; normal MCV (92.8)
- Reticulocytes increased at 3.14% (0.6-1.3)
- Normal serum iron and % saturation
- No schistocytes on special smear
- Increased LDH at 1229 (122-222)
- Sedimentation rate 37
- Small, stable M-spike on SPEP
- Moderate hemoglobin on urinalysis



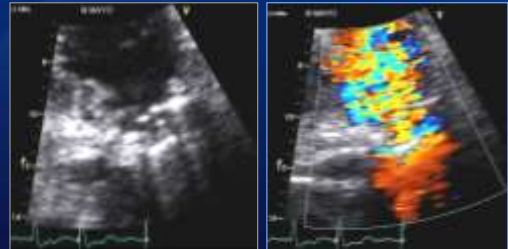
**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**



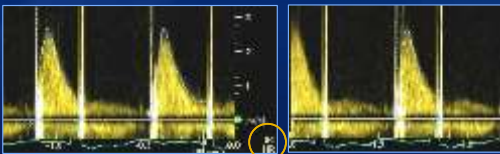
**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**



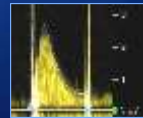
**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**



Mitral Prosthesis  
 E-velocity 2.6 m/sec  
 MG 9 mmHg  
 TVI 37 cm



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**



MVR TVI  
 37 cm



LVOT TVI  
 23 cm

$MVR TVI \div LVOT TVI$   
 1.8



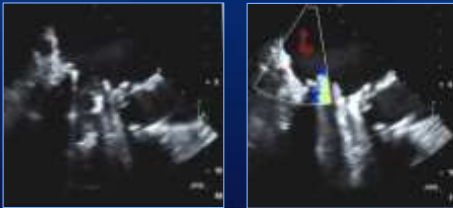
74 Year Old Woman With  
Mechanical Mitral Valve Prosthesis  
*Transesophageal Echo*



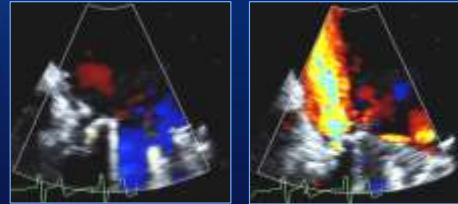
74 Year Old Woman With  
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74 Year Old Woman With  
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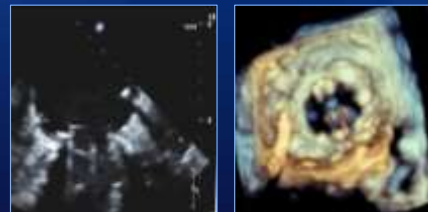
74 Year Old Woman With  
Mechanical Mitral Valve Prosthesis  
*Transesophageal Echo*



74 Year Old Woman With  
Mechanical Mitral Valve Prosthesis  
*Intra-procedural Transesophageal Echo*



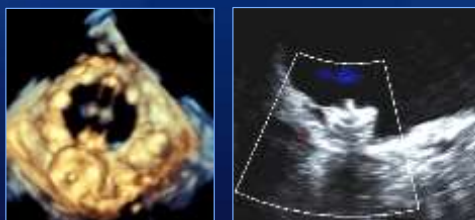
74 Year Old Woman With  
Mechanical Mitral Valve Prosthesis  
*Intra-procedural Transesophageal Echo*



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Intra-procedural Transesophageal Echo*



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Intra-procedural Transesophageal Echo*



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Three Month Follow-up*

- Dyspnea at the top of one flight of stairs (significant improvement from before procedure)
- Hemoglobin was 9.4; normal serum iron
- LDH 679 (previously 1229)
- No fragmented RBCs on special smear
- ESR had risen to 82 (previously 37)
- Two sets of blood cultures were negative



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Transthoracic Echo*

- Mild to moderate LV enlargement; EF 42%
- Akinetic basal inferoseptal segment
- Hypokinetic anterior septum, inferior wall and mid inferoseptal segment
- Abnormal septal motion (LBBB)
- Normal RV size and function
- Severe LA and moderate RA enlargement



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Transthoracic Echo*

- Mildly thickened AV with mild to moderate aortic regurgitation
- Moderately calcified mitral annulus
- MV prosthesis appeared normal with trivial transvalvular regurgitation
- No perivalvular leak evident
- Mild tricuspid regurgitation



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Hemodynamics (transthoracic Echo)*

- Mitral prosthesis E velocity 2.1 m/sec
- Mean gradient 7 mmHg (58 /min)
- Pressure halftime 53 msec
- Prosthesis TVI 27 cm; LVOT TVI 23 cm
- Prosthesis/LVOT TVI ratio 1.2
- RVSP 35 mmHg (BP 123/75 mmHg)



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis

- By 8 months after plugging of perivalvular leak, her Hb fell to 6.8
- She received 2 units of RBC and Hb rose to 7.2
- One month later her Hb fell to 6.7 and she received 2 more units of RBCs



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis *Ten Months After Plugging Perivalvular leak*

- Her Hb was 7.9 and she received 2 more units of RBCs
- Her urine suddenly turned red
- Her INR was 2.9
- She had no symptoms of UTI

The last time her urine turned red, she suffered iatrogenic perinephric hematoma, after a diagnostic procedure, and had to undergo right radical nephrectomy



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis *Ten Months After Plugging Perivalvular leak*

- Hemoglobin, after transfusion, was 8.4
- RBC MCV was normal at 93.9
- Reticulocytes increased at 2.38%
- Normal serum iron and % saturation
- Haptoglobin < 14
- Initial special smear did not show schistocytes, but a few were seen on repeat smear



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis *Ten Months After Plugging Perivalvular leak*

Smear Showed Schistocytes



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis *Ten Months After Plugging Perivalvular leak*

- Sed rate 62
- Normal RF and ANA levels
- Small, chronic spike in gamma region on SPEP; unchanged
- Creatinine 2.3
- NT-ProBNP 10,357



## 75 Year Old Woman With Mechanical Mitral Valve Prosthesis *Ten Months After Plugging Perivalvular leak*

### Urine testing

- Large amount of hemoglobin
- Hemosiderin present
- < 3 RBCs per HPF



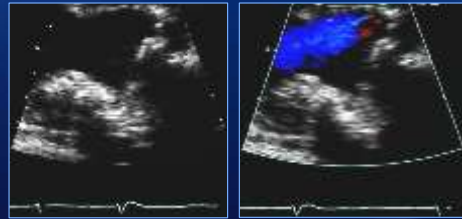


**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



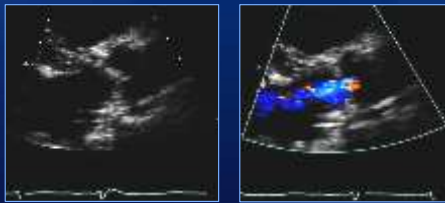
MAVO CLINIC

**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



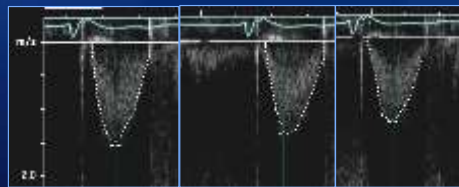
MAVO CLINIC

**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



MAVO CLINIC

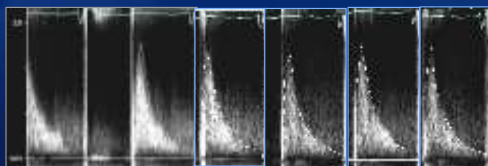
**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



LVOT TVI  
31 cm

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**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*

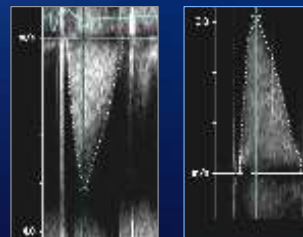


Mitral Prosthesis  
 E-velocity 2.3 m/sec  
 MG 5 mmHg  
 TVI 48 cm

HR 58/min

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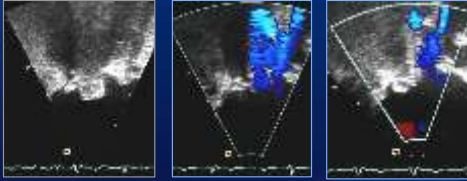
**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



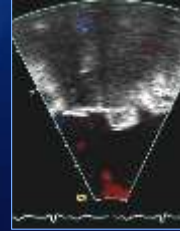
Aortic Valve  
 MG 17mmHg

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**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Ten Months After Plugging Perivalvular leak*



**75 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Coronary Angio*

- Right dominant
- Normal left main coronary artery
- 30% mid LAD stenosis
- 50% intermediate branch stenosis
- 30% stenoses in mid right coronary and in posterior descending branch



**74 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*Cardiac Surgery*

- Retrieved Amplatzer vascular plug
- Three interrupted mattress sutures were used to repair the mitral perivalvular leak
- No other areas of perivalvular leak identified



**74 Year Old Woman**  
*Surgical Repair Of Mitral Perivavular Leak*

- I visited her in ICU the evening after her surgery
- After establishing that she had no evidence of neuro deficits and was hemodynamically stable, my first question was

What color is her urine?



**78 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
*20 Month Follow-up*

- Physically active
- No cardiovascular symptoms





**78 Year Old Woman With Mechanical Mitral Valve Prosthesis**  
20 Month Follow-up

- Hemoglobin 11.8
- Serum iron normal
- Reticulocytes slightly decreased
- Serum LDH 258
- Sedimentation rate 50
- Urinalysis negative for hemoglobin



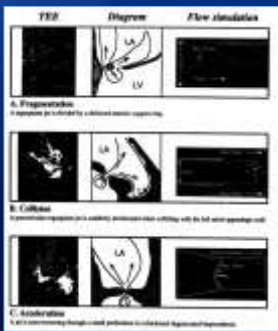
**Mechanisms of Hemolysis With Mitral Prosthetic Regurgitation**  
Study Using Transesophageal Echocardiography and Fluid Dynamic Simulation

MARCO J. GARCIA, MD, PIETER VAN DERVORST, MD, WILLIAM J. STEWART, MD, FACC,  
BRUCE W. LYTLE, MD, FACC, DELOS M. COGGROVE III, MD, FACC,  
JAMES D. THOMAS, MD, FACC, BRIAN F. GRIFFIN, MD, FACC  
Cleveland, Ohio

Journal of the American College of Cardiology 27(2)  
February 1996; 399-406



**Mechanisms Of Hemolysis With Mitral Prostheses**



Garcia M; JACC 27(2); February 1996



**Mechanisms of Hemolysis After Mitral Valve Repair: Assessment by Serial Echocardiography**

TJONG-CHENG YEO, MRCP, WILLIAM K. FREEMAN, MD, FACC,  
HARTZELL V. SCHAFF, MD, FACC,\* THOMAS A. ORSZULAK, MD, FACC\*  
Baltimore, Missouri

Journal of the American College of Cardiology 32(3)  
September 1998; 717-23



**Hemolysis After Mitral Valve Repair**

**Mechanism #1**  
Collision

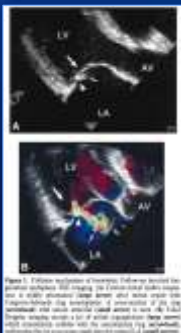


Figure 1. Collision mechanism of hemolysis. Following mitral valve repair, the anterior leaflet may impinge on the posterior leaflet, creating a high-velocity jet of blood that can cause hemolysis. The anterior leaflet may also collide with the posterior leaflet, creating a high-velocity jet of blood that can cause hemolysis.

Yeo TC; JACC 32(3); September 1998



**Hemolysis After Mitral Valve Repair**

**Mechanism #2**  
Acceleration



Figure 2. Acceleration mechanism of hemolysis. Following mitral valve repair, the anterior leaflet may impinge on the posterior leaflet, creating a high-velocity jet of blood that can cause hemolysis. The anterior leaflet may also collide with the posterior leaflet, creating a high-velocity jet of blood that can cause hemolysis.

Yeo TC; JACC 32(3); September 1998



## Hemolysis After Mitral Valve Repair

### Mechanism #3 Fragmentation

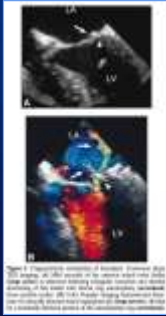
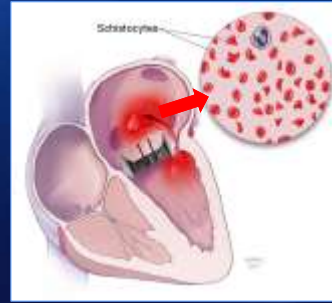


Figure 1. Fragmentation of red blood cells (RBCs) during mitral valve repair. The echocardiogram shows the mitral valve area with turbulent flow (color Doppler) and the presence of schistocytes (fragmented RBCs) in the blood. The echocardiogram shows the mitral valve area with turbulent flow (color Doppler) and the presence of schistocytes (fragmented RBCs) in the blood.

Yeo TC, JACC 32(3); September 1998

## Intravascular Fragmentation Hemolysis



## Intravascular Fragmentation Hemolysis



Red blood cells are sheared within the vascular space creating schistocytes

RBC breakdown products are released into bloodstream

- LDH
- Bilirubin (mainly indirect)
- Hemoglobin

## Intravascular Fragmentation Hemolysis

Red blood cells are sheared within the vascular space creating schistocytes



RBC breakdown products

- LDH
- Bilirubin (mainly indirect)
- Hemoglobin

## Intravascular Fragmentation Hemolysis



## Intravascular Fragmentation Hemolysis

- Free hemoglobin binds to haptoglobin
- Hemoglobin-haptoglobin complex rapidly removed by liver
- Serum haptoglobin level becomes low to undetectable
- Smaller dimers of alpha-beta globin, not bound to haptoglobin, are filtered by glomerulus, resulting in hemoglobinuria



## Intravascular Fragmentation Hemolysis

- Renal tubular cells take up hemoglobin and degrade it and store it as hemosiderin
- Hemosiderin is eventually shed into the urine



## Lab Testing For Intravascular Hemolysis

- Schistocytes on special smear (fragmentation)
- Increased reticulocytes
- Increased serum LDH
- Increased serum bilirubin (indirect)
- Decreased or undetectable serum haptoglobin
- Hemoglobin in urine
- Hemosiderin in urine



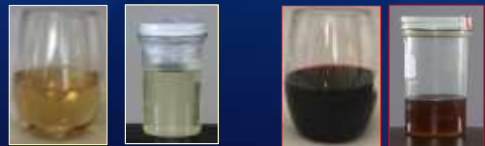
## Intravascular Hemolysis

- Patient loses iron in urine (serum iron decreased)
- Bone marrow responds by putting out young red blood cells (reticulocyte count is increased)
- If bone marrow cannot keep up, patient develops iron deficiency anemia
- Intervene if they become transfusion dependent
- Plugging perivalvular leak is about 50% successful in correcting hemolysis
- Often requires surgical repair of leak or replacement of valve prosthesis



## Pertinent to Patients with Valve Rings/Prostheses:

You want your patient's urine to look like chardonnay..... not cabernet



## Questions & Discussion

