

# Carcinoid Valve Disease

And other valvulopathies

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No Disclosures

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## Hedinger Syndrome

“Metastasizing carcinoid of the small intestine,  
tricuspid valve disease and pulmonary stenosis,  
a new syndrome.”

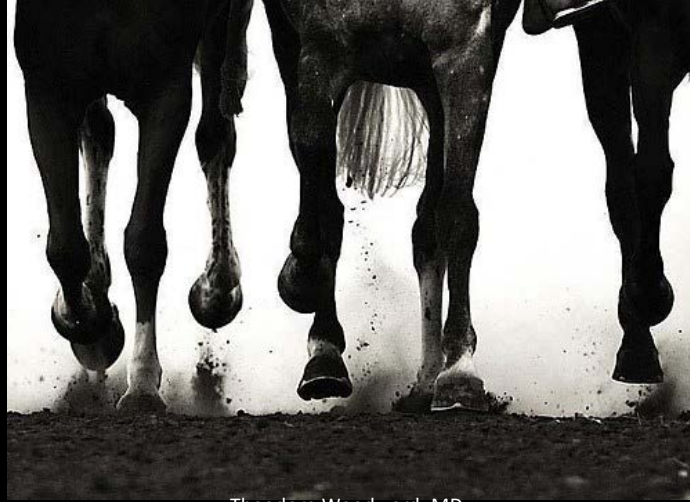
Hedinger C, Gloor R

Schweizerische Medizinische Wochenschrift, 31 Jul 1954, 84(33):942-946



2

## “When you hear hoof beats . . .”



Theodore Woodward, MD  
University of Maryland School of Medicine



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## The “Zebra” Community

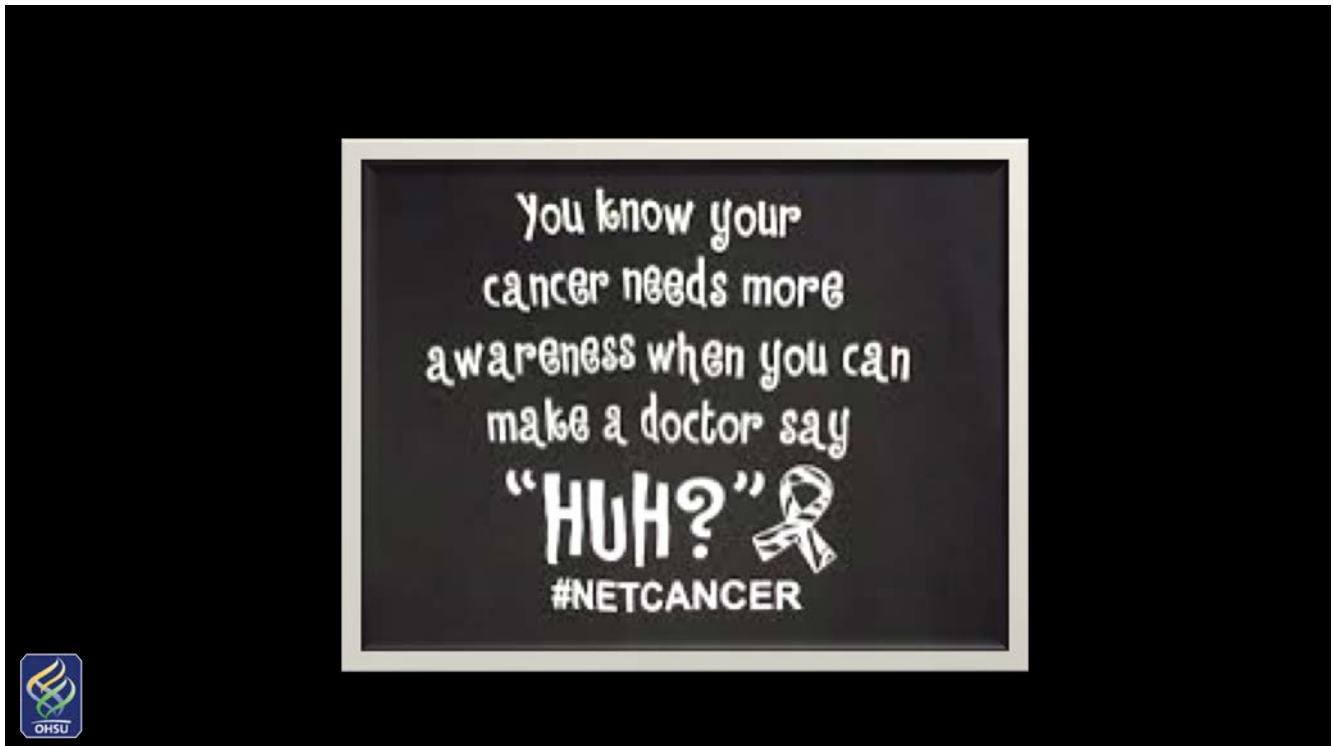
THE  
**CARCINOID  
CANCER**  
FOUNDATION

HOME ABOUT FOR PATIENTS FOR DOCTORS RE

**More Things Zebra for the Carcinoid and  
Neuroendocrine Tumor (NET) Community:  
From the Everyday to the Extraordinary**



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## Just how rare?

of 10,000,000 people

~400 Neuroendocrine tumors	}	Most will be referred for an echocardiogram
~150 Carcinoid tumors		
~50 Carcinoid heart disease		
~25 Undergo valve surgery		

~90 cases of AL amyloid diagnosed/year



Adapted from Davar, J, JACC Mar 2017; 69:1288–304

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## Why this topic matters to us?

Echo may provide first clue to an elusive diagnosis

Don't miss your chance to be the patient's hero.

Patients with neuroendocrine tumors will be referred for echocardiograms.

Because tumors are slow growing and fairly differentiated,  
Longevity means multiple serial studies over time.



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## Who Gets Valve Involvement?

Portland Carcinoid Experience

Valves affected in ~20% of carcinoid patients



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	<u>Carcinoid on Echo</u> (n=197)		<u>No Carcinoid on Echo</u> (n=41, 20%)		P value
Characteristic	mean/N	IQR/%	mean/N	IQR/%	
Age at diagnosis	59.7	(58, 61)	62.1	(59, 66)	0.22
Gender (Female)	83	42%	18	42%	ns
Small Bowel	103	53%	17	42%	0.16
Lung	25	13%	3	7%	ns



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Lung	25	13%	3	7%	ns
Peak Plasma CgA	164	(77, 616)	666	(222, 2917)	<0.0001
Peak Urine 5-HIAA	9.2	(4.2, 37)	76	(17, 220)	<0.0001
Liver mets	129	66%	36	84%	0.01



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## A matter of exposure

Valves are effected by circulating neuroendocrine “evil humours”

More exposure = more changes to the leaflets

Valve dysfunction develops after a certain amount of leaflet change



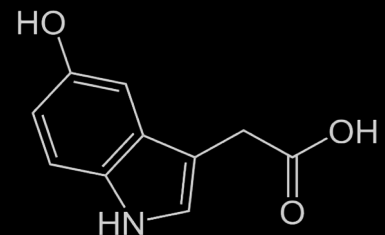
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## Mechanisms

Affected by 5-Hydroxyindoleacetic acid (HIAA)

Metabolite of 5-hydroxytryptamine

Receptors on heart valves



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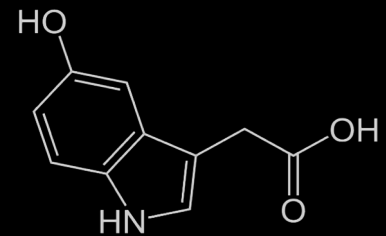
Receptors on heart valves

Induces mitogens, inflammatory cytokines,

TGFbeta, bradykinin, activin A

myofibroblasts, collagen, fibrous tissue

Endocardial plaques build up



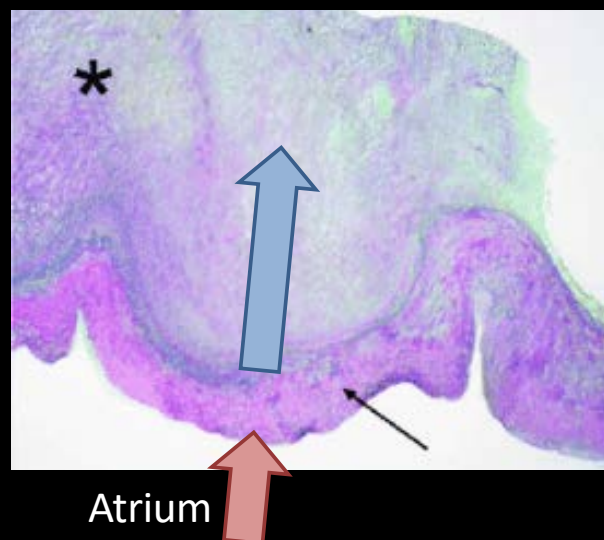
Bhattacharyya S, Circ Cardiovasc Imaging. 2010;3:103-111



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## Mechanisms

Changes mostly on  
"downstream"  
valve surface



Gujral, D. Future Cardiology 9(4):479-88



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## Valve Changes



Wicked Witch of the East



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## Valve Changes

Thickening, leading to retraction, stiffening, and immobility  
Shriveled, shortened, stiff, "board like"



Mild



Moderate



Severe



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## Reading the Echo: Context is everything



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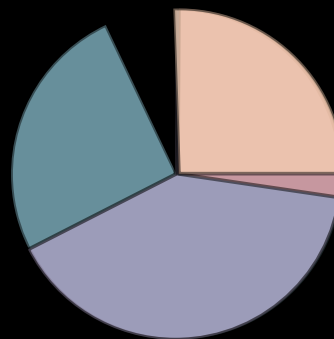
## Valves Affected

Tricuspid (90%)

Pulmonic (67%)

Mitral (29%)

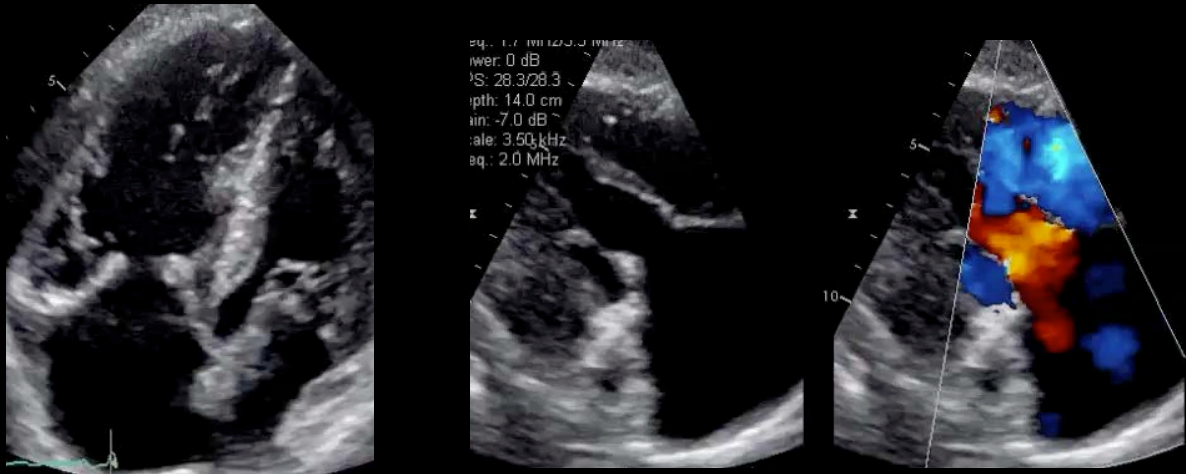
Aortic (27%)



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## Tricuspid Valve (99% of surgeries)

Leaflet thickening and restriction, mostly leads to regurgitation



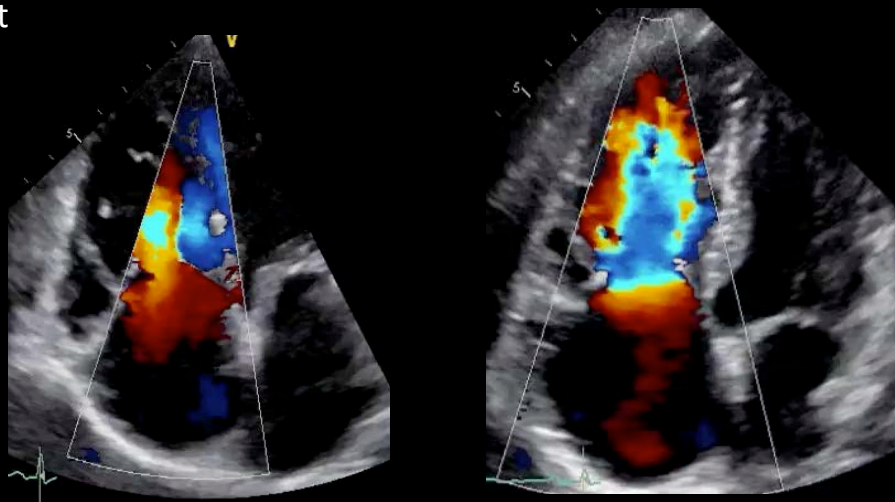
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## Tricuspid Valve (99% of surgeries)

Wide coaptation gap, large jets

RA enlargement

Elevated BNP



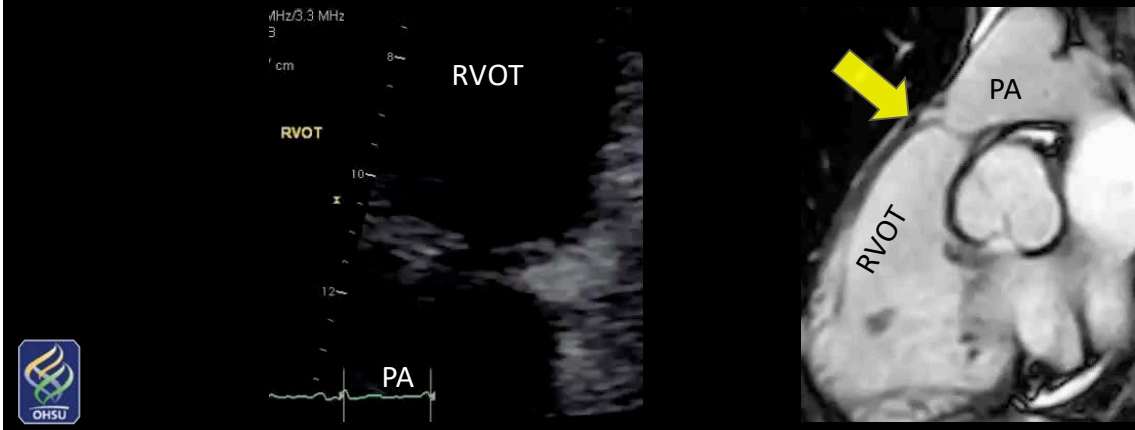
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## Pulmonary Valve (69%, 84% of surgeries)

Similar process. More difficult to visualize.

Leaflet restriction often leads to stenosis more than regurgitation

Sometimes annular retraction contributes to stenosis



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## Left-sided valve involvement (30%)

Usually seen with ASD/PFO (“ASD” may be “stretched PFO” from TR)

Coexisting tricuspid regurgitation raises RA pressure and promotes R-L shunt

Shunt allows for 5HIAA exposure to the left sided valves

Severity is dependent on the degree of shunting



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 Shunt allows for 5HIAA exposure to the left sided valves  
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If no atrial shunt, could be due to:

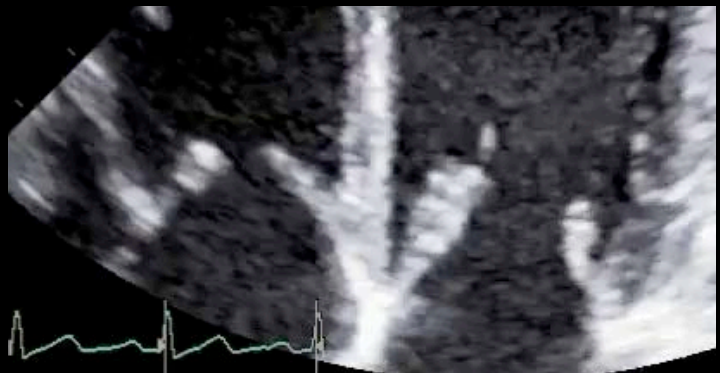
- intrapulmonary shunt
- intrapulmonary tumor
- intracardiac tumor
- very high levels of circulating neuroendocrine substances



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## Mitral Valve (11% of surgeries)

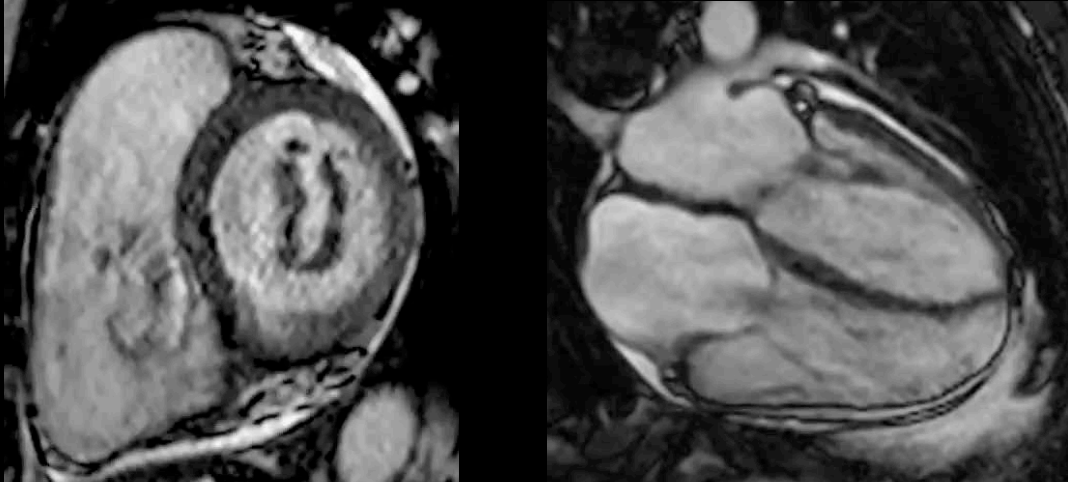
Diffuse thickening of valve leaflets  
 Thickened papillary muscles  
 and shortened chordae  
 Restricted leaflet mobility  
 Affects coaptation



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## Mitral Valve (29%, 11% of surgeries)

Similar changes; thickening and immobility



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## Aortic Valve (10% of surgeries)

Least involved

Ranges from mild thickening to severe retraction and immobility

Severity worse with larger atrial shunt (increased exposure)



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## Treatment

Medical therapy for valve regurgitation (diuretics)

Somatostatin analogues don't reverse (or even attenuate) valve progression

Tumor debulking is best way to avoid valve dysfunction



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## Surgical Indications

Progressive RV enlargement

Reduced RV EF

Symptoms of RV failure

Need for hepatic surgery (and control congestion)

At least one year life expectancy from tumor



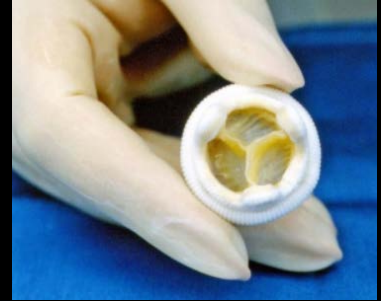
Dobson R, International Journal of Cardiology 173 (2014) 29–32

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## Surgical Treatment

Usually bioprosthetic valves (esp tricuspid)  
(avoid bleeding and thrombosis risks)



Repair usually isn't an option due to leaflet stiffness

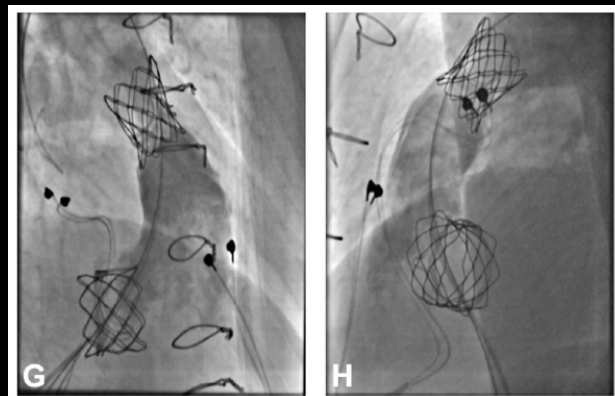
Transcatheter Clips aren't an option



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## Transcatheter Valves

Emerging experience; suggests reasonable durability thus far  
Often used if/when initial bioprosthetic valves fail



DeRosa R, Ann Thorac Surg 2017;104:e61–3)


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# Surgical Treatment

## Mayo Experience/European Experience

Single Valve Surgery	32	13%
Double Valve	175	73%
Triple Valve	24	10%
Quadruple Valve	9	4%
ASD/PFO closure	57	24%




Nguyen A, J Thor CV Surg, 2018 (in press)  
Bhattacharyya S, Eur J Cardio-thoracic Surg 40(2011):168—172

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Reoperation	27	11%
Reoperation due to bleeding	18	8%
Pacemaker implantation	14	6%
30 day mortality	22	9%



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# Surgical Treatment

## Risk Factors for Surgical Mortality:

Age  
NYHA Class  
Creatinine  
Diuretic use



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# Surgical Treatment

## Risk Factors for Surgical Mortality:

- Age
- NYHA Class
- Creatinine
- Diuretic use

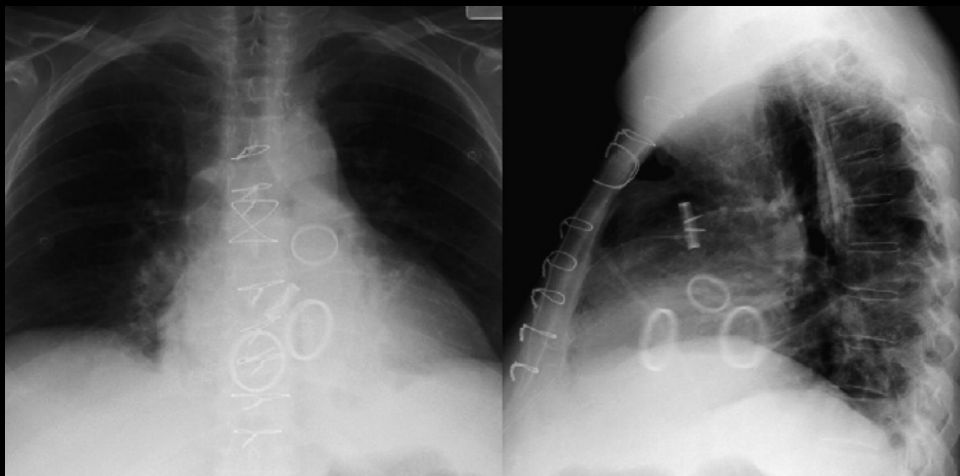
## Intraoperative carcinoid crisis

- Trigger for vasoactive substance release
- Produces hypotension, bronchospasm, arrhythmia
- Best to treat with octreotide infusions beforehand



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# Quadruple Valve Replacement



Arghami A, J Thorac Cardiovasc Surg 2010;140:1432-4

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# Quadruple Valve Replacement

Small case series in literature  
Operations usually successful  
Long-term survival varies

Serial valve gradients can be detrimental  
Can create physiologic restriction  
Fluid retention, orthostasis,  
renal insufficiency



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## Is this Carcinoid?



**NO**

Normal leaflet thickness and  
mobility

Poor coaptation from RV  
enlargement



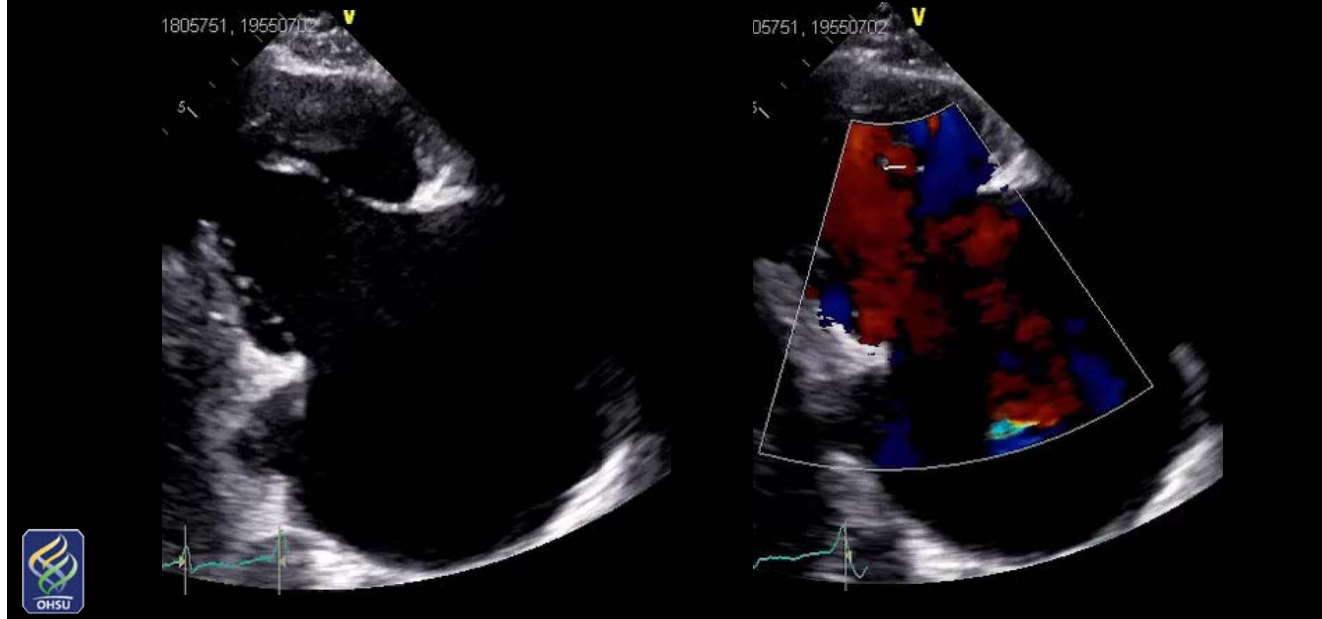
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## Dysplastic Tricuspid Valve



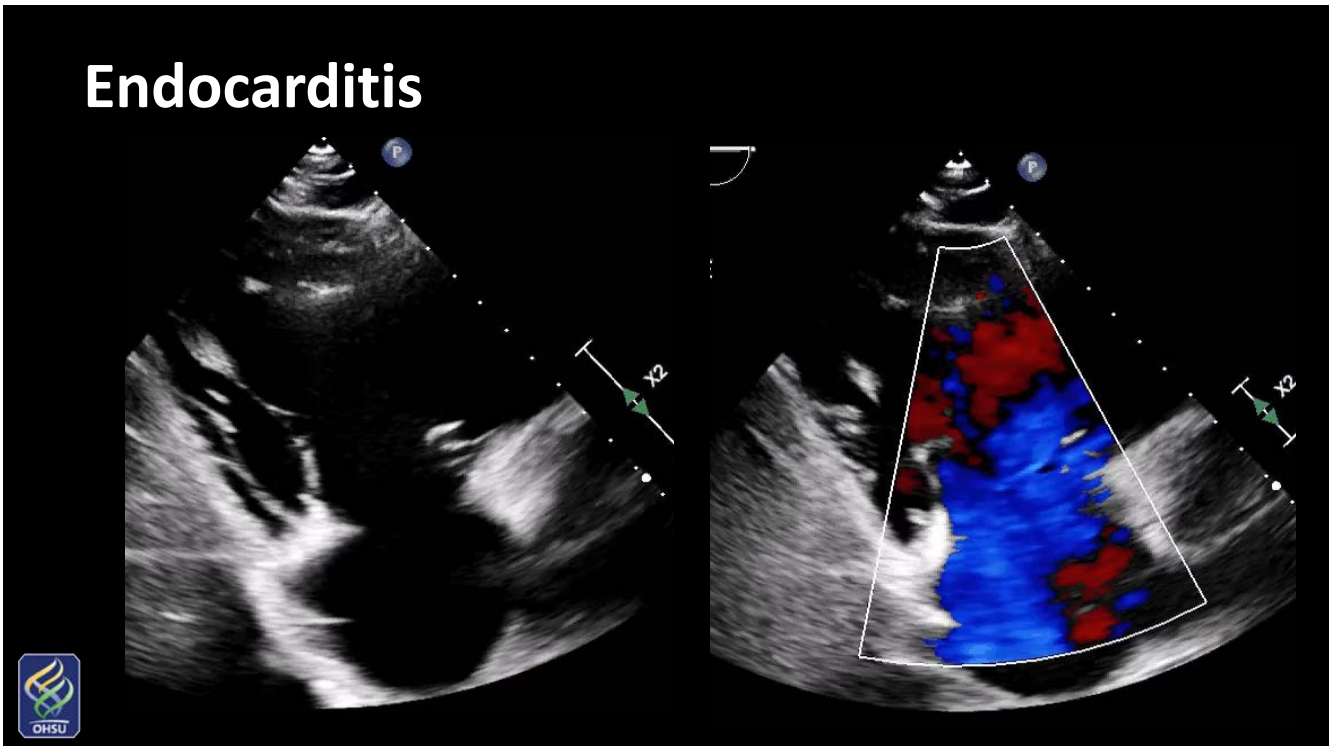
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## Severe pulmonary regurgitation



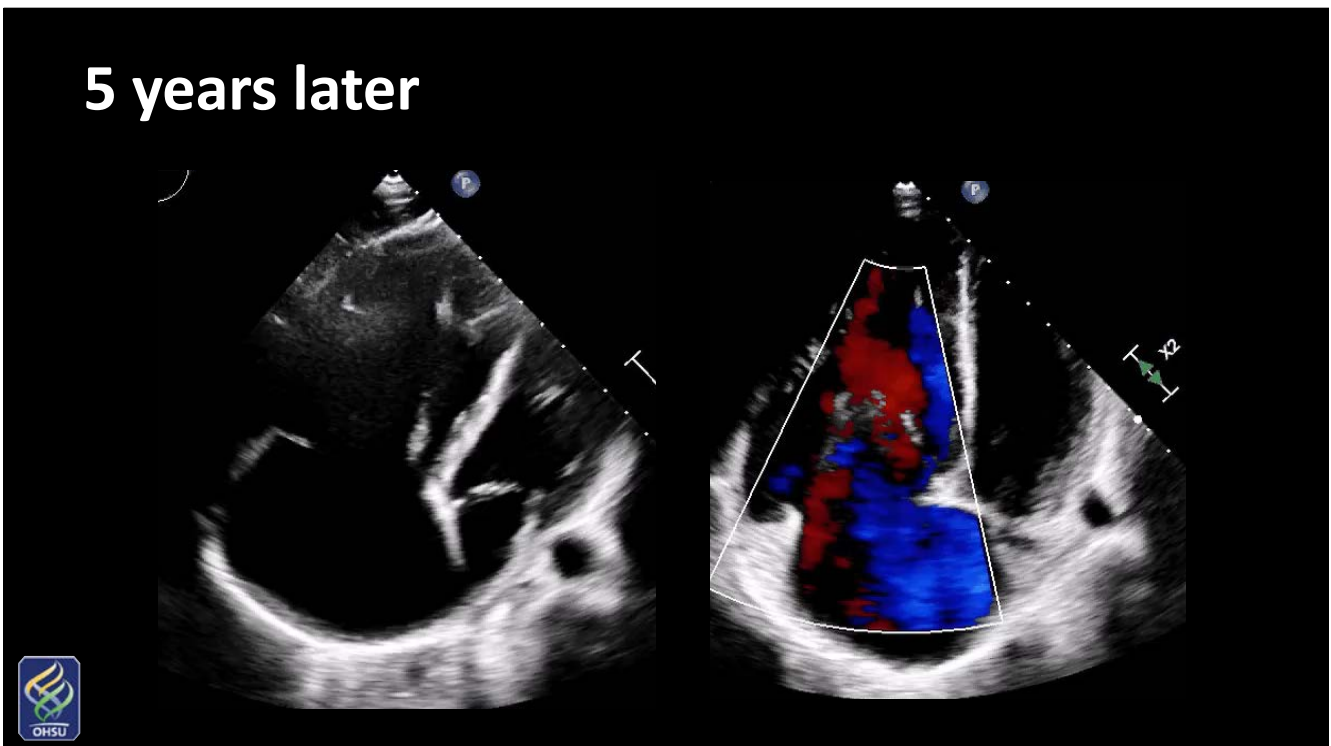
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## Endocarditis



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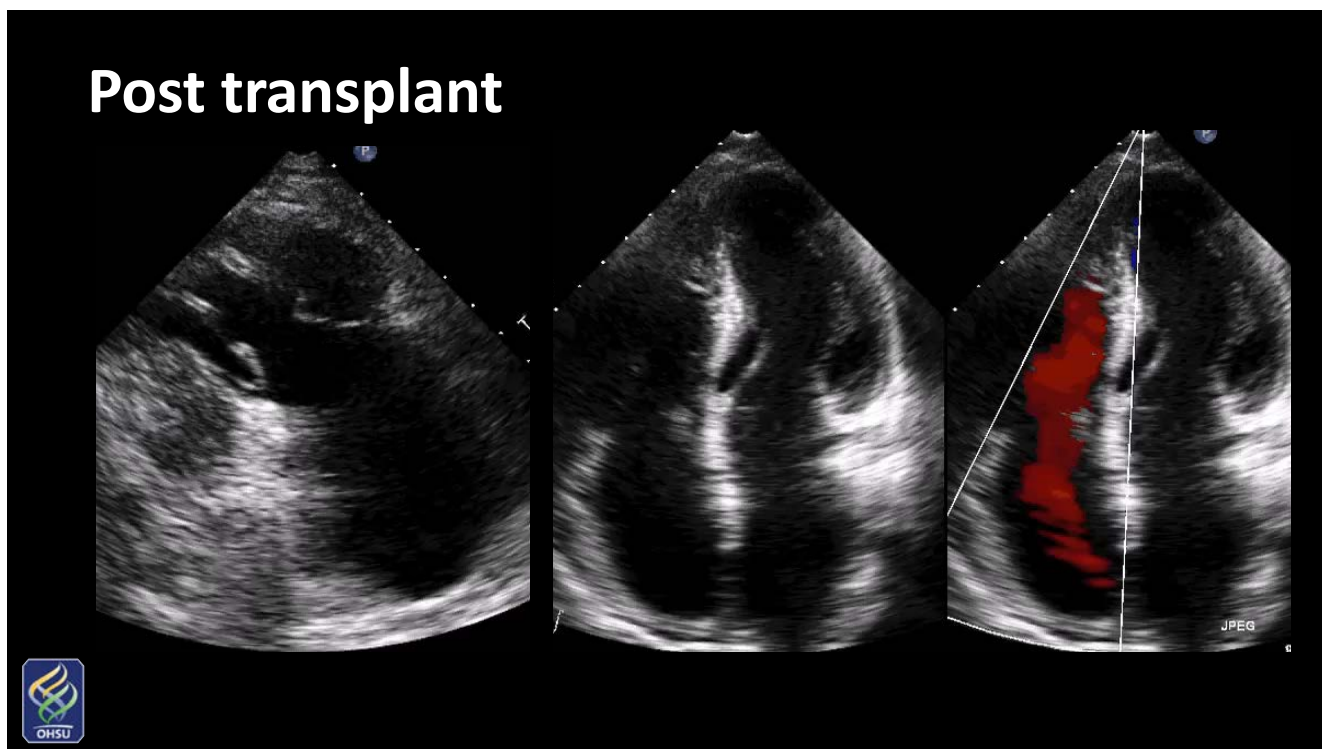
## 5 years later



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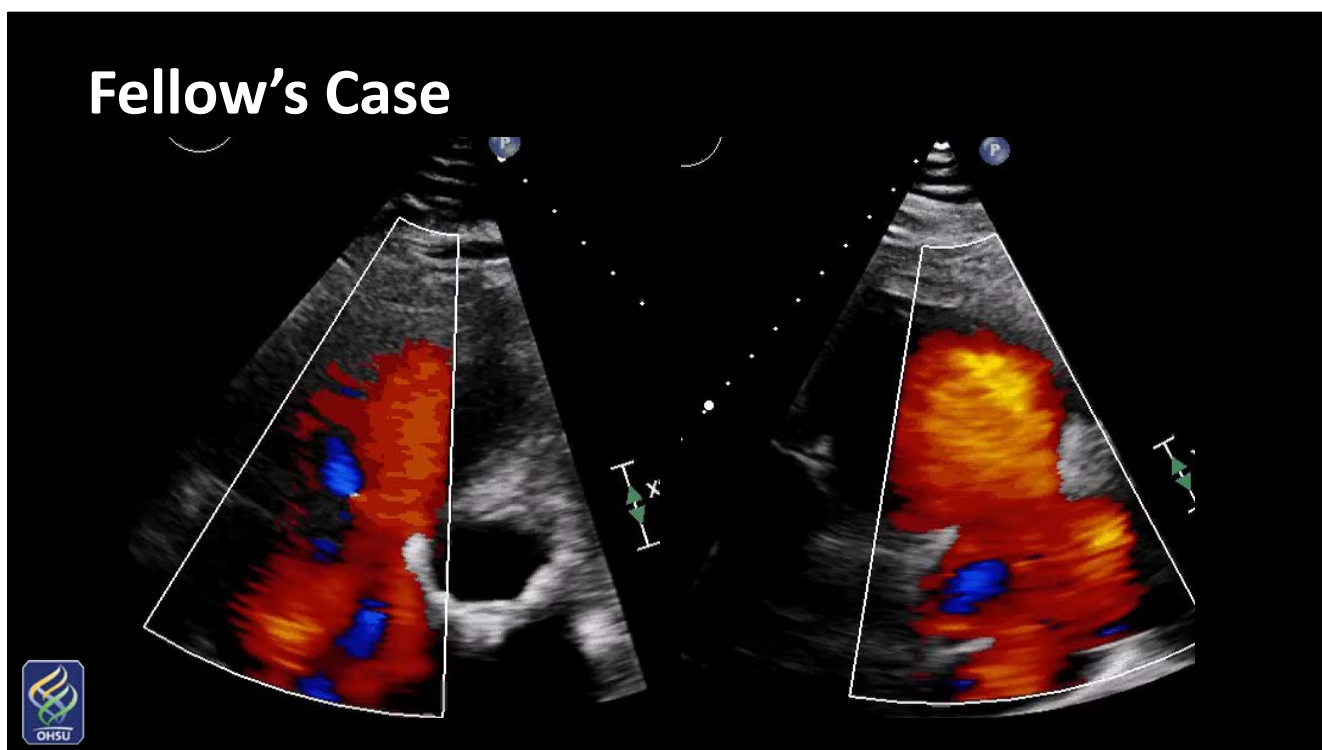


## Post transplant



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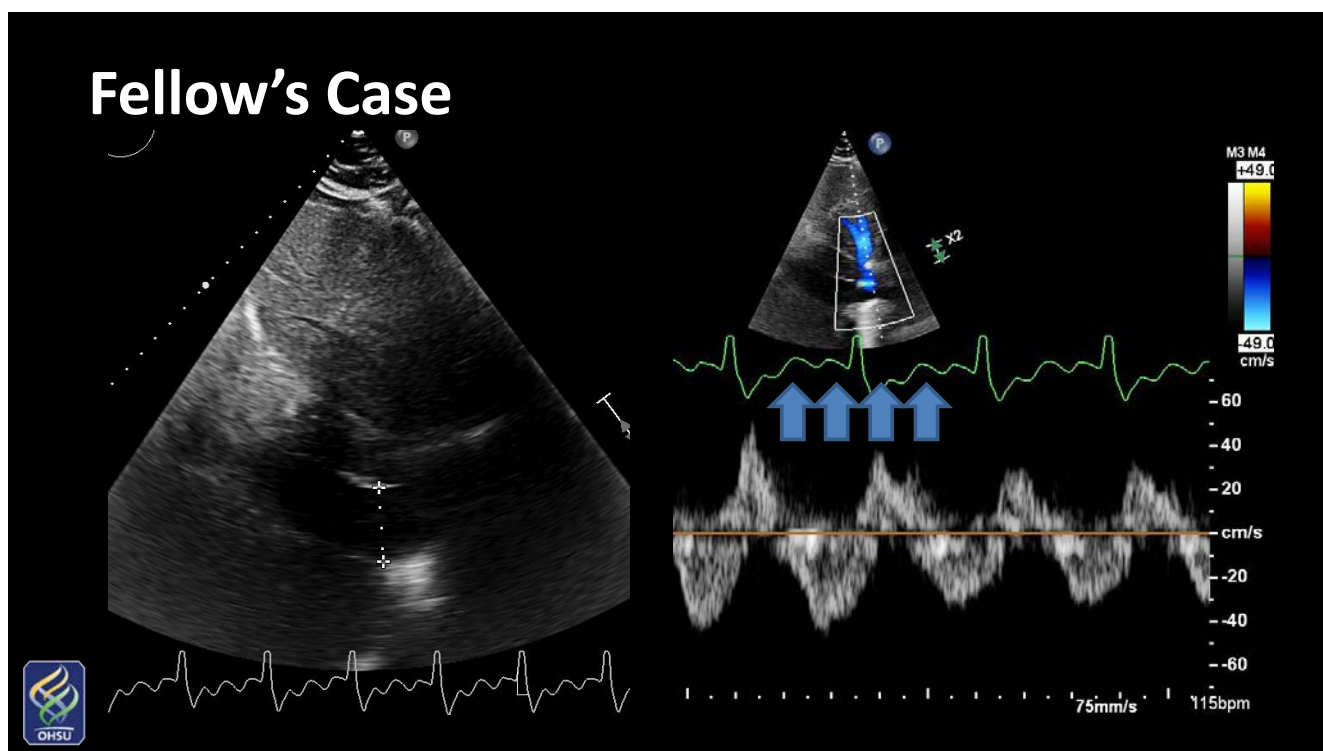
## Fellow's Case



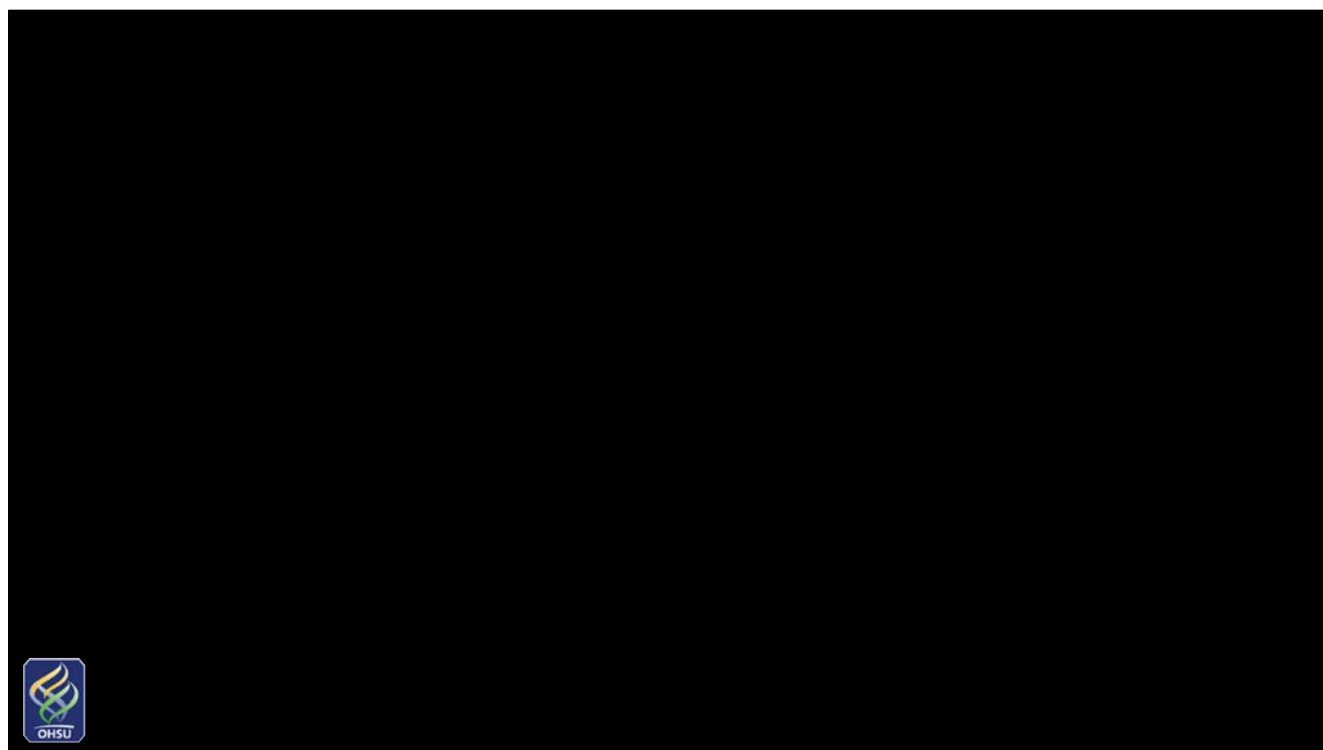
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## Fellow's Case



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# Carcinoid Summary

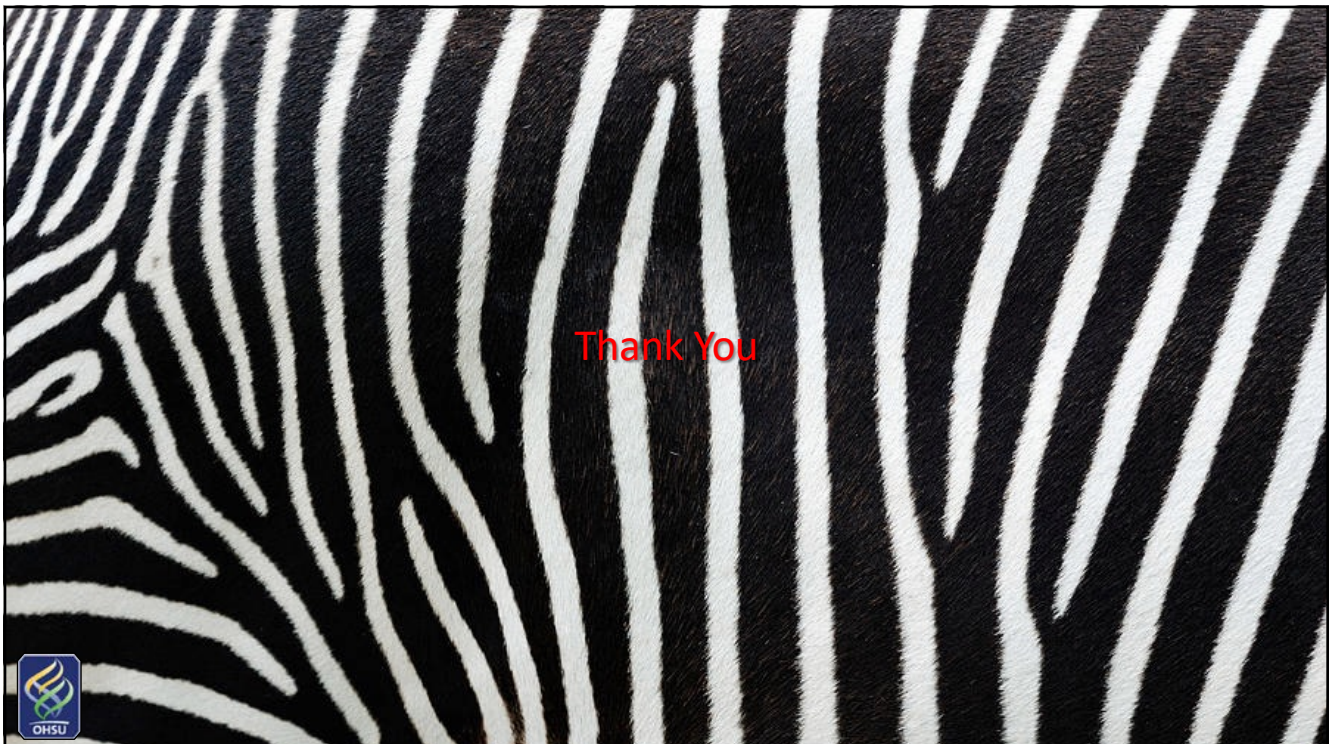
Recognize it when you see it!

Thick, stiff, short leaflets

TV > PV > MV > Ao



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