Keeping Up with a Failing Heart--2020

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So, what's the NUMBER 1 risk factor for heart failure? Your AGE! This cannot be modified…you can lie about it 😂, but that doesn't change the physiology…

- Simply aging from 35 to 85 increases the risk of dying from cardiovascular causes 1,000-fold
- Mean age of heart failure from 1950-1969 was age 63;
- Today? Age 80

And a few more numbers to ponder…

- 6.5 million Americans with heart failure in 2019 (cost of $31 billion - mostly hospitalization costs);
- ~8 million by 2030; ($70 billion projected)
- Why? We're living longer, with older hearts + coronary artery disease (CAD) and diabetes will continue to be of epidemic proportions AND

  diabetes and CAD are the top causes of heart failure today
- (In 1970 it was hypertension and valvular heart disease)

The aging cardiovascular system

- 1% rule of Geriatrics…reach our peak function of all organ systems by age 24…
- **1% rule**--maximal O2 consumption and cardiac output ***decrease*** by 1% per year **after the age of 30**
- Diminished responsiveness to beta-adrenergic stimulation **(fancy way of saying a decreased responsiveness to epinephrine)**—decreased heart rate reserve and maximum attainable heart rate

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The aging cardiovascular system

- **Endothelial** dysfunction—increased risk for atherosclerosis in the coronary arteries **—increased risk of coronary artery disease (CAD)** with angina and ischemia and subsequent heart failure due to ischemic heart disease (IHD)
- Increased atherosclerosis other major arteries including the aorta and it's tributaries—carotids to brain/stroke; renal arteries/hypertension/renal insufficiency and renal failure; peripheral arteries with peripheral arterial disease
- Is there any artery that doesn't fill with fat?

The internal mammary artery…Whaaaaaaattttt?????

- Fewer fenestrations in its endothelial layer and lower intercellular junction permeability
- greater anti-thrombotic molecules such as heparin sulfate and tissue plasminogen activator (tPA)
- higher endothelial nitric oxide production (maintaining vasodilation)
- All of the above make the IMA impervious to the transfer of lipoproteins, which are responsible for the development of atherosclerosis.(Otsuka F. et al. *Ann Cardiothorac Surg* 2013 Jul; 2(4): 519–526)

And that's why we use the the IMA for bypass…results?

- IMA grafts are associated with long-term patency and improved survival vs. saphenous vein grafts.
- IMA graft use has also been shown to be superior at 1-year and at five years compared to percutaneous procedures, including the use of drug-eluting stents for the treatment of coronary artery disease.
- Any problems with the IMA? Tends to be a short artery and can use both IMA's for triple vessel disease… or it can only be used for a single LAD bypass…unless… they're old breasts… 😁

The aging cardiovascular system

- Apoptosis (preprogrammed drop-out) of the cells of the SA node results in the loss of 50-75% of the atrial pacemaker cells, slowing the intrinsic heart rate. (sinus bradycardia)
- May result in **sick sinus syndrome** and the need for a pacemaker (50% of all pacemakers are due to sick sinus syndrome)

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Back to the aging cardiovascular system

- **Increased risk for atrial fibrillation (AF)** – aging is the number one risk factor for AF (10% in patients over 80; less than 0.1% in patients under age 55),
- Atrial fibrillation most often occurs with underlying cardiopulmonary disease most often observed in the elderly (hypertension, CAD, cardiomyopathy, heart failure, COPD)

The aging cardiovascular system

- Decreased contractile reserve (no "back-up" so to speak) leading to a progressive decline in peak cardiac performance **—increased risk of CHF**
- NO cardiac reserve? It's harder to recover when additional clinical conditions arise – either cardiac (MI, atrial fibrillation, or valvular disease such as aortic stenosis) or noncardiac conditions (pneumonia, flu, major surgery, renal failure)

In addition to aging, there are 4 general causes of heart failure*—easy to remember

1. **The broken heart**
2. **The betrayed heart**
3. **The befuddled heart**
4. **The defeated heart**

- ***some are overlapping**

Causes of heart failure— (1) The broken heart

- myocarditis and cardiomyopathy as primary causes of cardiac muscle failure
- myocarditis {usually viral}, Coxsackie B viruses, Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Hepatitis C, Herpes, HIV, Parvovirus, Chlamydia, Mycoplasma,
- Myocarditis (bacterial) – Strep, Staph, Borrelia burgdorferi (Lyme disease), Treponema (syphilis)
- Autoimmune disease—lupus myocarditis, rheumatoid arthritis

Causes of heart failure—
(1) the broken heart -- cardiomyopathy

- Chronic alcohol intake and thiamine {B1} deficiency) – ***why don't we just add thiamine to booze?***
- Cocaine and heroin
- cobalt cardiomyopathy
- Cancer therapies (anthracycline antibiotics (Adriamycin, daunorubicin), traztuzumab/Herceptin)
- Radiation to heart (mantle radiation, left breast radiation for DCIS, or invasive breast cancer)
- Vitamin E is linked to a 13% higher risk of heart failure and a 21% increased risk of hospitalization for heart failure. Small risk, but since the vitamin has no benefits at all it's not worth the risk

Causes of heart failure
(1) the broken heart -- cardiomyopathy

- **Anabolic steroids—the healthy left ventricle has a** 55% to 70% ejection fraction
- Eighty-three percent of anabolic steroid users in a small 12-person study had ejection fractions of less than 55%
- only one of the non-steroid users in the control group had a low ejection fraction. (Baggish AI et al.)

One more cardiomyopathy to be aware of: Tokotsubo ("fishing pot for trapping octopus")

- Takotsubo ("octopus pot") appearance of the left ventricular apex on echocardiogram
- stress **cardiomyopathy**, apical ballooning, or broken heart syndrome.
- surge of stress hormones cause short-term **heart** muscle failure

Stress, acute chest pain, and the heart in post-menopausal females-- Takotsubo cardiomyopathy

- 1 to 2% of patients who present with signs and symptoms similar to those of an acute myocardial infarction. Interestingly it is most frequently seen in females (89-90%), most of whom are postmenopausal (ages 58-77)(mean age 66.8 years).

Takotsubo cardiomyopathy--? pathogenesis

- Multivessel epicardial spasm
- Catecholamine-mediated myocardial damage
- Microvascular coronary spasm or dysfunction
- neurogenic stunning (defined as **myocardial** injury and dysfunction occurring after diverse types of acute brain injury as a result of imbalance of the autonomic nervous system)(stroke, SAH, AHI, ECT, seizure)
- In other words, the stress response has caused a major temporary malfunction. A high index of suspicion should be maintained even though the ECG shows an ST elevation; troponin and CK-MB can also be elevated but not to the extent observed in an ACS
- RX: beta-blockers (to immediately STOP the stress responses)
- Gentry K, Childers WA. Is takotsubo cardiomyopathy in your differential diagnosis? *The Clinical Advisor* March 2013; 43-48)(Templin C, et al. NEJM 2015 Sept 3; 373;10.

Causes of heart failure— (2) the betrayed heart

- The heart that is let down by its friends—lungs, arteries, thyroid, brain
- decreased O_2 (smoking* (next slide), COPD, pneumonia, the flu, and CAD)
- Atherosclerosiss (coronary artery disease)
- Diabetes – as many as 50% of people with T2DM develop heart failure (Diabetes Forecast. January/February 2020) "*Patients with diabetes are essentially treated as if they already have heart disease.*" Michelle Kittleson, M.D.
- Thyroid dysfunction (overlaps with the befuddled heart)
- Obesity
- Depression—2-3x greater than the general population

(2) The betrayed heart: Smoking

- Cigarette smoking/cigar smoking/cigarillo smoking and second-hand smoke contribute to ~30% of all deaths from heart disease.
- Smokers have a two- to fourfold increase in coronary artery disease and ~70 percent higher death rate from coronary artery disease than do nonsmokers.

(2) The betrayed heart—the lungs: pneumococcal pneumonia

- Increased workload on an already "taxed" old heart can throw the heart into HF
- VACCINATE: Pneumococcal vaccine!!

(2) The betrayed heart— The flu can precipitate heart failure

- A meta-analysis of more than 78,000 patients with heart failure, getting a seasonal flu vaccine was associated with a 50% drop in the risk of death (from any cause) during the flu season and a 20% drop in the risk of death during the rest of the year (Modin D. et al. *Circulation.* January 29, 2019;139 (5):575-586).
- Getting vaccinated was also linked to a **22 percent reduction** in the risk of being hospitalized with cardiac problems
- It's well-known that heart failure patients have an elevated risk of flu-related death, so it makes sense that vaccination can help—☺ right?

Obesity and heart failure

- Obesity and overweight are also linked to hypertension and an left ventricular hypertrophy, increasing risk for heart failure.

Obesity—even Mona has plumped up and is at risk for heart failure

- 11% of heart failure cases in men and 14% in women are attributed to obesity alone

Depression and anxiety are often observed in patients with chronic heart failure

- Both comorbidities complicate the treatment approach and increase hospitalizations
- Depression affects at least one-fifth of patients with CHF, worsening the NYHA class and increases hospitalizations
- Depression negatively affects the quality of life and functional status of the patient, decreasing the level of physical activity and worsening the survival rate.
- **SSRIs (except paroxetine—anticholinergic effects=tachycardia)**
- (Bordoni B, et al. Depression and anxiety in patients with chronic heart failure. Published online: 22 Jan 2018: https://doi.org/10:2217/fca-2017-0073)

Anxiety exacerbates the symptoms of CHF--

- …negatively affecting the quality of the breath, creating panic and chest pain.
- Sertraline is also prescribed as an anti-anxiety drug as well as an anti-depressant…
- Consider pet therapy…

Causes of heart failure— (3) the befuddled heart

The heart that beats funny (valvular problems)

- Atrial fibrillation
- Thyroid disease with bradycardia (hypo-) or tachycardia (hyper-) and excess levothyroxine can trigger atrial fibrillation)

Special relationship: Thyroid hormone and the heart

- The SA node and myocardial cells are covered with B1 receptors that respond to epinephrine
- Epinephrine increases the heart rate and boosts the strength of contraction
- **HOWEVER, the NUMBER of B1 receptors is not static; the number is influenced by thyroid hormone**
- **Always check the TSH in patients with heart issues**

Special relationship: Thyroid hormone and the heart—the number of B1 receptors is not static

- Too little thyroid hormone? Too few B1 receptors resulting in bradycardia
- Too much thyroid hormone? Tachycardia—resulting in atrial fibrillation and subsequent heart failure
- HEART FAILURE can result from either hypo- or hyperthyroidism (thyrotoxicosis can precipitate heart failure)

Heart failure from too much levothyroxine

- Caution when using levothyroxine in elderly—an initial starting dose of levothyroxine of 25-50µg per day in older patients who might have clinically silent cardiac disease
- in patients with a hx of cardiac disease, LT4 replacement may begin at even lower doses of 12.5-25 µg per day
- **Levothyroxine overtreatment is a cause of atrial fibrillation and can precipitate heart failure**
- P.S.—hyperthyroidism can also trigger A-fib and can trigger angina …
- Did I tell you this? ALWAYS check the TSH with heart issues

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Heart failure can also occur w/ severe hypothyroidism…myxedema coma

- Heart failure with bradycardia (45)
- Bradypnea (8)
- Hypothermia (94 F; 34 C)
- Metabolic acidosis

Causes of heart failure—(4) the defeated heart

- The heart that works too hard against a resistance
- Increased SVR—hypertension
- Aortic stenosis, mitral stenosis, aortic regurgitation, mitral regurgitation

Yeah, but they're old…why bother treating their predisposing conditions?

- Is it worth treating the conditions that cause heart failure?
- Better question…why don't we treat conditions that lead to heart failure BEFORE they cause heart failure?

Is it worth treating patients who are over 80 for hypertension?

- Yes, indeedy. In the HYVET (Hypertension in the Very Elderly Trial--2008), a trial involving 3845 patients 80 years and older found that active treatment with indapamide (Lozol) to start and adding perindopril (Coversyl, Coversum, Aceon) as needed was associated with a 21% reduction in the relative risk of death from any cause, a 64% reduction in the relative risk of heart failure, and a 30% reduction in the relative risk of stroke
- Start with the lowest dose possible and titrate up as needed or until side effects are not tolerable

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Is it worth treating hyperlipidemia?

- **YES! READ MY LIPIDS!!**
- LDLs are directly deposited into the walls of the arteries via the process of oxidation
- Triglycerides are elevated in patients with diabetes, causing the LDLs to be small and dense (small and dense LDLs easily deposit into the walls of arteries)
- This is an *accelerated process* in patients with diabetes
- All diabetics between ages 40 and 75**, regardless of their LDL level**, should be started on a moderate dose of a statin drug (AHA, CHA Guidelines 2018)
- Individualized recommendations for under 40 and over 75 and are based on assessing cardiovascular risks

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Lowering LDL cholesterol

High-intensity statins—daily dose lowers LDL by greater than or equal to 50%--want to reduce the LDL-C to 70 mg/dL (1.8 mmol/L)

- atorvastatin (Lipitor)—40-80 mg
- rosuvastatin (Crestor)—20-40 mg

Statin drugs for cardiovascular disease

Moderate-intensity statins—lower LDL by 30- 50%; <u>best choice for the elderly</u>

- Atorvastatin – 10-20 mg
- Rosuvastatin – 5-10 mg
- pravastatin (Pravachol)—40-80 mg
- simvastatin (Zocor)—20-40 mg
- (*Circulation* 2004;110:227-239)(Prescriber's Letter July 2014) The American College of Cardiology/American Heart Association guideline on the Treatment of Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Is it worth treating for Type 2 Diabetes Mellitus?

- YES, absoutely.
- Diabetes is **prothrombotic**, **proatherosclerotic**, and **proinflammatory** (triggers lipid plaque rupture), fills up arteries with fat, and increases the clotting risk…
- METFORMIN is the number one drug for Type 2 Diabetes, but renal function must be assessed before and during treatment
- Metformin has cardiovascular benefits: lowers BP, increases HDL, lowers LDL; weight loss (varies among patients)

Autonomic neuropathies can also be a big problem for the heart in diabetics—especially…

- The loss of the vagus nerve (CNX) (autonomic neuropathy) resulting in two major problems that lead to heart failure:
- The vagus nerve normally slows down the heart rate; NO VAGUS?

(1) **Tachycardia resulting in an increased workload that is already overworked due to the atherosclerosis of diabetes, and**

(2) The inability to feel chest pain. So, the individual may *not* be aware of the pain of angina or an acute MI – known as **silent ischemia**

- Silent ischemia increases the risk of myocardial damage; and, repeated silent episodes increase the risk of heart failure (HF) in the diabetic patient explaining the 10 x greater risk of HF in women with diabetes; 6 x greater risk of HF in men with diabetes

Diabetes and drugs that reduce the risk of heart disease

- The SGLT-2 inhibitors—the "flozins"—canagliflozin (Invokana), dapagliflozin (Farxiga),empagliflozin (Jardiance) *Patients with T2DM + high cardiovascular risk who received empagliflozin have **lower mortality rates due to CV causes, nonfatal MI's and nonfatal strokes (EMPA-REG study) cardiovascular benefits**—reduced the chances of death from CV disease by 38%, risk of hospitalization by 35%, and the risk of all-cause death by 32%.
- Empagliflozin canNOT be used in patients with moderate to severe renal insufficiency (eGFR less than 45 mL/min). (Prescriber's Letter, November 2015)
- The "glutides" – liraglutide (Victoza)—lowers the risk of CV events that lead to HF (the newest one semiglutide—OZEMPIC)

Diabetes drugs and other drugs that increase the risk of heart disease

- TZD (pioglitazone) causes fluid retention and weight gain in people with heart failure and increase the risk in patients who don't have heart failure.
- Patients on the oral dipeptidyl peptidase-4 inhibitors (alogliptin, linagliptin, saxagliptin, sitagliptin) increase the risk of heart failure (unknown as to why)www.WebMD.com) Accessed 10/19)
- (not diabetes drugs) (controversial)TNF-alpha inhibitors and receptor blockers—infliximab (Remicade), adalimumab (Humira), etanercept (Enbrel) (Cush)

Chronic Heart Failure—CHF

- Nomenclature has changed over the years—the "C" was tweaked from **congestive** to **chronic**; so we the acronym remains the same—CHF
- ***"Not all heart failure is congestive…"***
- Old-old classification? Left-sided vs. right-sided—made sense – there are only two sides, so these were apt descriptions
- Progressed to systolic and diastolic heart failure (still used today)

Chronic Heart Failure—CHF

- Newest classification is defined by ejection fractions (Silver):
- A systolic ejection fraction ≤ 40% **(reduced)** is called HF**r**EF (hef-ref) (systolic dysfunction)(66%);
- An ejection fraction of ≥ 50% indicates heart failure with **preserved** ejection fraction is called HF**p**EF (diastolic dysfunction)(34%)and;
- HF with an EF between 40-50% is HF**mr**EF (mid-range)—SERIOUSLY???
- Better prognosis with HFpEF vs. HFrEF (mortality 30% lower in HFpEF than HFrEF)

Left-sided symptoms of heart failure

- Early left-sided symptoms may be quite subtle and are often related to pulmonary congestion and edema. Cough and dyspnea (breathlessness), initially with exertion and later at rest, are two of the earliest complaints
- ***"Funny things happen in the middle of the night."*** As failure progresses, worsening pulmonary edema (with fluid in the alveoli and impaired diffusion) may lead to orthopnea (dyspnea when lying down that is relieved by changing to an upright position), requiring the patient to sleep sitting up in the Lazy Boy.

Early left-sided symptoms (continued)

- PND—paroxysmal **nocturnal** dyspnea (occurs at night—duh, see name—that is so severe it induces a feeling of suffocation)
- Nocturia—fluid returning to vascular space when lying down increases renal blood flow and urine output at night
- ***New onset*** nocturia in a diabetic may signal new onset heart failure

Signs and symptoms of heart failure--assessment

- Pulmonary rales (crackles)—Crackles scattered throughout both lung fields anteriorly and posteriorly—"frothing at the mouth" with all lung fields involved
- O2 saturation decreased with pulmonary edema; GOAL? Greater than 92% at a minimum
- Very old (over 85) patients will normally have a few crackles due to the loss of lung elasticity not due to pulmonary edema

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Symptoms of right-sided Heart Failure

- Liver and portal system—congestion of the hepatic and portal systems result in congestive hepatomegaly and congestive splenomegaly (portal hypertension can increase the size of the spleen 2-3 times—from 150 gm non-palpable organ to a 300 – 500 gram palpable organ)
- "Nutmeg" chronic passive venous congestion of the liver secondary to right-sided HF

If you're going to check the jugular vein in the elderly…

- Check the RIGHT jugular vein in the older patient—don't use the left jugular vein
- WHY?
- The left inominate vein dumps into the left jugular; this vein may be compressed between an elongated and unfolded aortic arch (as a function of aging) and the back of the sternum; increased mechanical pressure of the inominate vein may lead to increased left jugular vein distention continuously—i.e. falsely distended
- Abdominojugular reflex (hepatojugular)—compress abdomen and watch the right jugular vein—if the pressure causes a sustained rise of blood in the vein it's positive

Pleural effusion

- Systemic venous congestion can cause pleural, pericardial, and peritoneal effusions
- Transudation of fluid into the peritoneal cavity may cause ascites (free fluid in the abdomen)

Ascites—free fluid in abdomen with displaced suspenders ☺

Pitting edema—consider CHF

- Edema of the peripheral and dependent portions of the body, especially ankle (pedal) and pretibial edema, is a hallmark of right-sided heart failure
- Presacral edema may predominate in chronically bedridden patients
- If there is pitting at the ankles you can assume that the patient has at least 4.5 kg of excess fluid (10 pounds)—more fluid as the pitting ascends
- Subjectively measured—1+ to 4+

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Pretibial pitting edema

- Firmly depress 2-3 fingers over the anterior shin starting at the ankle and marching up to see how far the edema is present (instruct RNs in hospitalized patients to repeat each shift to assess the effectiveness of diuresis and current state of volume overload)
- 1/4th inch per + (or 2mm)
- 1+ = 1/4th inch, 2+ = ½ inch (2-4 mm), 3+ = 4-6 mm, 4+ = 6-8 mm

Pitting edema—fluid overload in CHF

- **Other conditions** and drugs can cause swollen ankles with NON-pitting edema (venous stasis, NSAIDS, the calcium channel blockers (CCBs) with the last name "dipine")
- Grapefruit juice with the NSAIDS or the peripherally-acting CCBs can exacerbate the problem
- DVTs, and various causes of hypoproteinemia (liver failure, nephrotic syndrome, kidney failure)

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Chronic Heart Failure— 4 compensatory mechanisms

- Regardless of the cause of heart failure, if the heart is unable to pump adequately four compensatory mechanisms occur

1) The increased release of BNP or NT-proBNP from the ventricular myocardium
2) The kidney--triggering the renin-angiotensin-aldosterone system which in turn increases preload and afterload (SVR) and remodels the heart
3) The adrenal gland and release of catecholamines—epinephrine and norepinephrine (remodels the heart)
4) The kidney again--production and release of neprilysin in the kidney

Chronic Heart Failure—compensatory mechanisms—the myocardium

#1) The increased release of BNP or NT-proBNP; the ventricular myocardium normally releases B-type ***natriuretic*** peptide (BNP) in small amounts. Endogenous BNP acts like our own "internal ACE inhibitor" and stimulates diuresis and vasodilation to decrease fluid overload and decrease systemic vascular resistance

BNP (B-type Natriuretic Peptide)

- The BNP **directly correlates** with cardiac ventricular wall stress and volume overload—as the left ventricle is stretched or stressed as in volume overload, BNP increases
- **The higher the BNP the greater the severity of ventricular wall stress and volume overload**
- BUT signs and symptoms may NOT correlate directly with the BNP level—
- The higher the BNP the worse the prognosis

BNP (B-type Natriuretic Peptide)—more notes and numbers

- BNP less than 40 pg/mL has a high negative predictive value for CHF vs. BNP of greater than 400-500 pg/mL with a high positive predictive value for CHF; a BNP of less than 100—CHF is unlikely
- Hospital discharge w/ BNP less than 400 pg/mL is associated with a decreased likelihood of readmission for CHF within 30 days—**MAKES MEDICARE HAPPY**
- Following the CHF patient's BNP is more accurate than checking for the classic signs of HF: jugular vein distention, pedal edema, S3, and hepatomegaly

Summary: Use the BNP for the following:

- Diagnosis of CHF (levels greater than 400 pg/mL)
- Monitoring the patient with CHF
- Determining the effectiveness of treatment regimens and treatment titrations in patients with CHF
- Early detection of CHF in patients with diabetes

Rapid BNP testing for the following situations:

- Evaluating a patient with dyspnea in the ER or office to confirm the S & S of new-onset heart failure
- Evaluating for occult CHF or cor pulmonale in patients with COPD who are not responding to treatment

What is NT-proBNP?

- N-terminal (NT)-pro-hormone BNP (NT-proBNP) is a non-active prohormone that is released from the same molecule that produces BNP.
- Both BNP and NT-proBNP can screen the general population for heart failure (Example: patient in ER with SOB, palpitations, pallor)
- Both BNP and NT-proBNP are released in response to changes in left ventricular pressure. It can be monitored for CHF patients just as BNP is monitored, but both tests are not necessary

Advantages of NT-proBNP

- NT-proBNP has greater sensitivity for detecting CHF in patients with a preserved LVEF (left ventricular ejection fraction)
- Has a longer circulating half-life (~120 minutes vs. 20 minutes for BNP), available for measurement for longer periods of time-reduces the possibility of a false negative report

One more note about the NT-proBNP

- NT-proBNP – the pre-discharge NT-proBNP is more strongly associated with outcomes than NT-proBNP level at admission.
- A higher NT-proBNP measured at discharge may serve as a prompt for an earlier clinic appointment or follow-up phone call to assess the patient's condition and **help prevent readmission**

Back to the compensatory mechanisms in chronic heart failure—the kidney

#2) The renin-angiotensin-aldosterone system is activated when the kidney senses low pressure and low volume from a failing pump (systolic heart failure) or diastolic heart failure (not enough "oomph" to get blood to the kidney…resulting in an increased preload (fluid retention)—

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What does "angie 2" do on any given day without heart failure? She's good…

- Low volume? this low volume state is "sensed" by the kidney and renin is released resulting in the production of angiotensin 2
- Angiotensin 2 ("ANGIE") triggers the release of "AL"—aldosterone (from the adrenal cortex to save sodium & H_2O in the kidney—increasing BP by increasing volume; excretes K+ in exchange for Na+)
- Angiotensin 2 is the most potent direct vasoconstrictor in the body—in other words, she "tenses" your "angios"—and increases blood pressure as needed
- She's beautiful…and good…

But, she's not such a good girl in heart failure patients…

- WHY? By doing what she does best in the setting of a failing heart…she tries too hard.
- HF is a 'hyper-reninemic' state--Excess renin triggers excess angiotensin
- IN EXCESS..she increases the workload of a failing heart by increasing systemic vascular resistance (afterload) and conserving fluid (increasing preload)—making the heart work even harder...

And, to add insult to injury…

- Excess angiotensin 2 acts as a growth hormone and contributes to "re-modeling" of the heart
- What does that mean? Isn't "re-modeling" a good word?
- Absolutely! In your 1920's-style kitchen…

But NOT in your heart!

- Remodeling enlarges the heart and interrupts the conduction system resulting in ventricular dysrhythmias—ventricular fibrillation and sudden cardiac death

Treatment?

- Drugs that block any or all of the RAA system
- ACE inhibitors – "PRILS"
- ARB receptor blockers or ARBS– the "SARTANS"
- Spironolactone—Aldactone a mild aldosterone inhibitor
- Eplerenone -- Inspra
- Sacubitril/valsartan (ARNI)--ENTRESTO

The 3rd compensatory mechanisms in chronic heart failure

3) The sympathetic nervous system (SNS) response--the adrenal gland pumps out the catecholamines, epinephrine and norepinephrine, to increase the heart rate and the contractile state (chronotropic and inotropic functions) via B1 receptors (epi) and vasoconstrict via alpha 1 receptors (norepi)

… this compensatory mechanism helps initially (may trigger palpitations)…BUT just like angiotensin,

epinephrine also "remodels" the heart…it enlarges the myocardium and increases the risk for ventricular fibrillation

Beta blockers to the rescue!

- Beta-blockers ("olols, alols, ilols")—block the effect of epinephrine on the heart and therefore reduce remodeling of the heart—may exacerbate heart failure initially so start with very low doses keep a close eye on the patient in the first 2 weeks; long-term effects are beneficial
- Metoprolol succinate (Toprol XL)—start low (12.5mg BID) and titrate up at no less than 2-week intervals or Carvedilol (Coreg)*—start low (3.125 BID) and titrate up; bisoprolol (Zebeta, Monocor) is the 3rd beta blocker approved for CHF (Carvedilol is a beta blocker + alpha one blocker—also causes vasodilation)
- **Don't give a beta blocker if the resting heart rate is less than 45 or SBP is less than 90-100 mm Hg**

The 4th compensatory mechanism in heart failure is the activation of neprilysin

Neprilysin is an enzyme (primarily produced by the kidney) that normally **inactivates (degrades)** vasoactive peptides that contribute to vasoconstriction and increased systemic vascular resistance, sodium retention and maladaptive remodeling of the heart (same old story, just a new "player"…

- Inhibition of neprilysin results in vasodilation, natriuresis, and inhibition of myocardial remodeling
- Is there a drug for that? YEP.
- Sacubitril/valsartan combination (brand name ENTRESTO) reduces the rate of cardiovascular death (by 20%) and hospitalizations related to heart failure compared to a PRIL alone, enalapril (Vasotec)
- (PARADIGM-HF Trial (Hegde, Voors)

What's not to love about the ACE Inhibitors? Side effects, of course…

- Hypotension—start low and go slow
- Hyperkalemia (high potassium) (excreting sodium and water and ***retaining*** potassium)
- Avoid ***excessive*** potassium intake when on the ACE inhibitors (includes KCl supplements)
- Advise patients to decrease potassium intake (certain foods) until they can get their potassium checked

What foods? Foods containing high K+ ≥200 mg/serving

- Avocado
- Artichoke
- Broccoli
- Carrots
- Cantaloupe
- Potatoes
- Dried beans, canned mushrooms
- Apricots
- Bananas
- Pumpkin
- Spinach
- Oranges
- **Prunes (6) (YIKES)—a problem in the elderly!!!**
- *Health.harvard.edu/heartextra* for K+ content of 1,200 foods

Bummer.

- Unfortunately chocolate also fits into the category of high-potassium foods…
- (Greene JH. Restricting dietary sodium and potassium intake: a dietitian's perspective. In Daugirdas JT. Handbook of Chronic Kidney Disease Management. Philadelphia, PA: Lippincott Williams & Wilkins;2011:81-96)

Additional aldosterone inhibition is sometimes needed

- Spironolactone (Aldactone), eplerenone (Inspra)—inhibit aldosterone –referred to as potassium-sparing drugs
- in HFrEF patients with a eGFR greater than 30 mL/min
- May contribute to hyperkalemia if also on a "PRIL"
- This increases the risk for cardiac arrhythmias but **usually only in patients with renal insufficiency (elderly and diabetics)**
- Reduce dietary intake of K+ containing foods

Does adding Aldactone (spironolactone) help with heart failure? absolutely…

- The RALES study (Random Aldactone Evaluation Study--1999)
- The good news: Adding spironolactone to the treatment of patients with HF postponed or prevented 200 deaths/1000 patients w/HF…
- The bad news...for every 1000 spironolactone prescriptions in HF patients, there were 50 more hospitalizations for hyperkalemia and cardiac dysrhythmias
- YIKES...CAREFUL...

Males on spironolactone…

- May complain of breast tenderness – reduce the dose
- 10% develop overt gynecomastia

Speaking of hyperkalemia—a few more notes on drugs and OTC products that increase potassium—

- NSAIDS increase K+ due to vasoconstriction of the afferent arteriole (ibuprofen, piroxicam, and naproxen are the biggest offenders)
- KCl supplements (potassium chloride as a salt substitute)
- Don't use Bactrim/Septra for UTIs when patients are on ACE inhibitors—it also increases K+ and can lead to life-threatening arrhythmias within 5 days of initiating treatment (and **especially** if on ACE inhibitors and spironolactone)
- "flozins"—SGLT2 inhibitors (canagliflozin/Invokana; empagliflozin/Jardiance; dapagliflozin/Farxiga) for Type 2 DM retain K+

Ivabradine (Corlanor) – 2nd line drug for heart failure

- Used in patients with stable, symptomatic chronic heart failure with LVEF of greater than 35 percent, who are in sinus rhythm, with resting heart rate greater than 70 and either are on maximally tolerated doses of beta blockers or have a contraindication to using beta blockers.
- Monitor for bradycardia, hypertension, or atrial fibrillation (15%). Temporary vision disturbance (flashes of light) may also occur. Dizziness, weakness or fatigue due to bradycardia and/or AF.
- The recommended starting dose of Corlanor is a 5 mg tablet twice daily with meals.

Digoxin may be used as an "add-on"

- Not first line therapy tho'
- When should dig be used? Persistent symptoms, despite optimum therapy with ACE inhibitors, diuretics, and beta blockers to reduce hospitalization in patients with a Class IIa indication…(Stage C with a reduced left ventricular ejection fraction)
- Mild inotropic effects; reduces hospitalizations; decreases symptoms; no effect on longevity
- Side effects are common in the elderly due to their decreased volume of distribution and decreased renal clearance—start with the low dose of 0.125 mg QD
- Use ventricular rate as the best indicator of the therapeutic dig effect

Dig levels

- Dig toxicity? Visual disturbances, anorexia, nausea, vomiting, bradycardia, dysrhythmias
- *Therapeutic dig levels are between 0.8-2.0 ng/mL; patients with AF may require higher dig levels; patients with HF may do better at lower levels
- Dig toxicity occurs more commonly with electrolyte imbalances— low potassium and low magnesium (high risk of toxicity if on Loop diuretics that tend to deplete all both electrolytes)

Loop diuretics—the big guns

- Go with furosemide—cheap and just as effective as torsemide and bumetanide
- Start with 20-40 mg in a.m. and titrate every few days—can titrate up to 80 mg in a.m. and give another 80 mg in p.m.
- Patients with renal insufficiency may need higher doses; maximum daily dose of 240 mg or up to 600 mg with renal insufficiency
- Can switch loop diuretics if the above doses don't work
- Watch the electrolytes! K+, Na+, and magnesium loss
- Add a thiazide if necessary; metolazone if eGFR is less than 30 mL/min (markedly less sodium excretion than loop diuretics)
- No need to give the thiazide 30-60 minutes before the Loop diuretic
- Prescriber' Letter February 2020

Lasix (furosemide)

- Oral Lasix – half life is 1.5 hours; takes 4 hours to clear (4 x 1.5 = 6 hours)—hence, it lasts 6 hours
- Lasix IV—onset 5 minutes, peaks in 30 minutes and duration of 1-2 hours
- Potent Loop diuretic—if response is poor (less than 200-300 mL after 2 hours) and if still in respiratory distress from pulmonary edema, a larger dose of furosemide will be necessary

Enter the Loop diuretics

- Bumetanide (Bumex)1: 40 (Lasix:bumetanide)—ie, 40 mg of Lasix = 1 mg of bumetanide—DON'T transpose those numbers… "Here's your 40 mg of bumetanide"…WHAAAAAAAAAAAAAAAAAAAAT?
- Torsemide (Demedex) 10-20 mg = 40 mg of furosemide = 1 mg bumetanide
- Ethacrynic acid (Edecrin)—an old, old, old Loop diuretic

Electrolytes to consider

- Potassium (3.5 – 5.0 mEq/L)* (the most rapidly depleted electrolyte with furosemide administration)(Monitor carefully, especially if K+ was low before starting furosemide)
- Sodium (135-145 mEq/L)—one of first signs of hyponatremia is confusion in the elderly
- Magnesium (1.6-2.0 mEq/L)(essential to normal conduction, as is K+. If too high or to low, can predispose the patient to rhythm abnormalities that can be life-threatening)

Co-morbidities in HF patients

- **Anemia** may be independently associated with HF disease severity and is associated with decreased exercise capacity
- Keep an eye on their hemoglobin, MCV and serum ferritin
- Patients with NYHA class II or III HF who also have **iron deficiency** (ferritin less than 100 ng/mL or 100-300 ng/mL if transferrin saturation is less than 20%) should receive IV iron
- **BP**—initiate therapies that maintain a systolic BP of 130 mm Hg with stage C reduced and preserved ejection fraction HF, noting that BP control is associated with fewer adverse CV events

Renal function

- Creatinine (0.6-1.2 mg dL)(watch the trending values)
- What was it upon admission, what is it today?
- Consider the onset of acute renal failure or acute renal failure on top of chronic renal failure

3 REMAINING RED FLAGS: Heart failure and NSAIDs

1. NSAIDs can exacerbate HF symptoms due to sodium, potassium and water retention (+peripheral edema, +↑ BP); HOW?
2. Administer appropriate vaccines
3. Reduce sodium in the diet—have your patients AVOID all boxes, cans, and bags of processed foods

Factors that may influence readmission rates

- Increase readmissions—Heart rate ≤ 80/min
- Abnormal troponin
- Serum creatinine 1.0-2.5 mg/dL
- SBP ＞130 mm Hg
- African American ancestry
- History of renal disease
- History of diabetes
- HF admission within 1 year
- Atrial fibrillation

(Ryan CJ, Bierle R, Vuckovic KM. The Three R's for Preventing Heart Failure Readmission: Review, Reassess, and Reeducate. Critical Care Nurse 2019 (April); 39(2):85)

Factors that may decrease readmission rates

- Normalization of hemoglobin 10-14 g/dL
- Normalization of sodium at discharge to 135-140 mEq/dL
- Pre-discharge BNP ≤ 430 pg/mL (less likely to be readmitted to hospital within 30 days)
- History of cardiovascular disease

(Ryan CJ, Bierle R, Vuckovic KM. The Three R's for Preventing Heart Failure Readmission: Review, Reassess, and Reeducate. Critical Care Nurse 2019 (April); 39(2):85)

Thanks!

- *"Learn from the mistakes of others. You can't live long enough to make them all yourself."*

---Eleanor Roosevelt

NYHA classification of HF

- Class I - No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
- Class II - Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
- Class III - Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20—100 m).Comfortable only at rest.
- Class IV - Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

CRT (cardiac resynchronization therapy) + ICD (implantable cardioverter defibrillator)

- CRT (aka biventricular pacing) + ICD and optimal medical therapy reduces the rates of death and hospitalization for heart failure among patients with mild-to-moderate heart failure (Class 2, 3 NYHA), a reduced left ventricular ejection fraction, and a wide QRS complex.
- CRT triggers left ventricular **reverse remodeling** in patients with advanced heart failure and those with milder heart failure, resulting in an improved ejection fraction, and a reduced left ventricular size.
- Significant reduction in the rate of death from any cause associated with the use of CRT in addition to ICD and optimal medical therapy.
- Relative risk of death was reduced by 25%,

VAD (ventricular assist device)

- LVAD, RVAD, BiVAD
- Assists ventricular pumping
- Waiting for heart transplant
- Not eligible for heart transplant but need a boost--VADs are increasingly being used as a long-term treatment for people who have heart failure but aren't good candidates for a heart transplant. Generally if you're older than age 65, you may not be eligible for heart transplantation.

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A normal level of NT-proBNP

- Based on Cleveland Clinic's Reference Range is:
- Less than 125 pg/mL for patients aged 0-74 years
- Less than 450 pg/mL for patients aged 75-99 years
- **If you have heart failure**, the following NT-proBNP levels could mean your heart function is unstable:
- Higher than 450 pg/mL for patients under age 50
- Higher than 900 pg/mL for patients age 50 and older