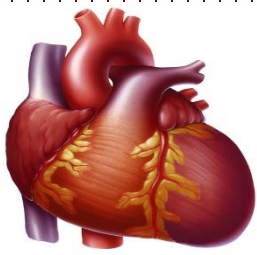
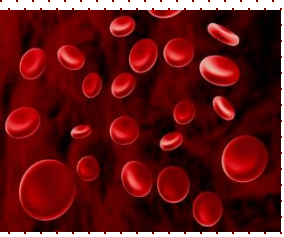


A large, multi-story, light-colored brick building with a central tower and many windows. The building is surrounded by green trees and a paved area with some people walking. The sky is blue with some clouds.

**V.N. KARAZIN KHARKIV NATIONAL
UNIVERSITY
INTERNAL MEDICINE DEPARTMENT**

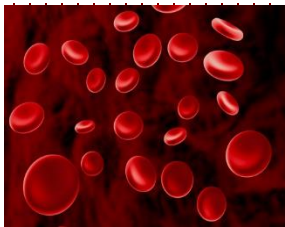
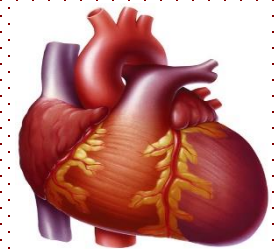


ANEMIA AND CHRONIC HEART FAILURE

SPEAKER: Nsikak-Abasi M. David (4th course)

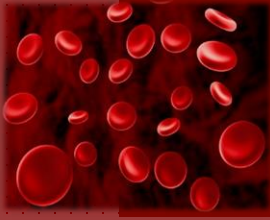
ADVISER: Ass. Kateryna I. Kornieieva, Ass. Daria I. Stehnyi

HEAD OF DEPARTMENT: Prof. Mykola I. Yabluchanskyi



INTRODUCTION

- Anemia has been frequently observed in patients with Chronic Heart Failure (CHF) and has been associated with increased mortality.
- Increased mortality as well as increased rates of hospital admissions and decreased quality of life or exercise tolerance increased attention from the medical societies around the world.
- Estimates of the prevalence of anemia in patients with CHF and low ejection fraction range widely from 4% to 61%
- Causes of anemia in patients with CHF, possibility of anemia contributing to more severe CHF, form(s) of anemia prevalent in CHF populations, recommended treatment to improve anemia and the general condition of patients with CHF, as well as a Clinical Case demonstrating the role of anemia in the developing heart failure will be further discussed.



INTRODUCTION

DEFINITION OF ANEMIA

- Anemia is the most common disorder of the blood, affecting about a quarter of the people globally.
- It is a reduction in the total amount of red blood cells (RBCs) in the blood.
- Reduction in the number of RBCs transporting O₂ and CO₂ impairs the body's ability for gas exchange leading to even more detrimental effects starting from the nervous system on to the other systems of the body.



INTRODUCTION

**WHO's Hemoglobin thresholds used to define anemia
(1 g/dL = 0.6206 mmol/L)**

Age or gender group	Hb threshold (g/dl)	Hb threshold (mmol/l)
Children (0.5–5.0 yrs)	11.0	6.8
Children (5–12 yrs)	11.5	7.1
Teens (12–15 yrs)	12.0	7.4
Women, non-pregnant (>15yrs)	12.0	7.4
Women, pregnant	11.0	6.8
Men (>15yrs)	13.0	8.1

WHO defines anemia as [hemoglobin (Hb) concentration <13.0 g/dL in men and <12.0 g/dL in women] whereas the National Kidney Foundation defines anemia as Hb ≤12 g/dL in men and postmenopausal women..

INTRODUCTION

CAUSE OF ANEMIA

1. As a result of impaired production

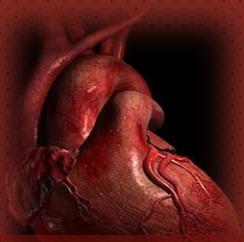
- **Disturbance of proliferation and differentiation of stem cells:** Pure red cell aplasia, insufficient erythropoietin production etc.
- **Disturbance of proliferation and maturation of erythroblasts:** Congenital dys-erythropoietic anemia, Iron deficiency, Vitamin B-12 deficiency, Folate deficiency, thalassemias, Starvation and generalized malnutrition etc
- **Others:** Myelophthisic anemia, Myelodysplastic syndrome

2. As a result of increased destruction:

- **Intrinsic (intracorpuseular) abnormalities** [Enzyme deficiencies (Pyruvate kinase etc.), hemoglobinopathies (Sickle cell anemia), hereditary spherocytosis, hereditary elliptocytosis, abetalipoproteinemia, Paroxysmal nocturnal hemoglobinuria]
- **Extrinsic (extracorpuseular) abnormalities** [Antibody-mediated (autoimmune hemolytic diseases such as Rh disease, transfusion reaction etc.)]
- **Mechanical Trauma to RBCs** [Microangiopathic hemolytic anemias, including thrombotic thrombocytopenic purpura (TTP) and disseminated intravascular coagulation (DIC)]

3. Blood Loss (from surgery, trauma, burns, menstruation, GIT lesions, infections from intestinal nematodes)

4. Fluid overload (hypervolemia)



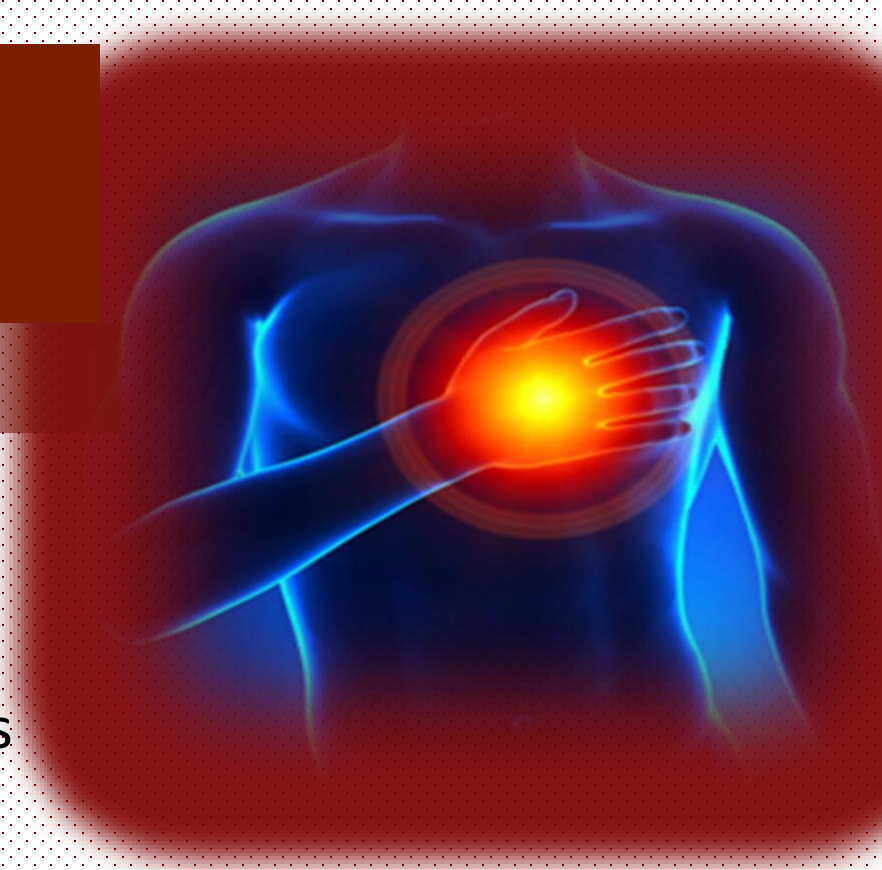
INTRODUCTION

DEFINITION OF CHF

- Heart Failure (HF), also known as Congestive Heart Failure (CHF) occurs when the heart fails to pump blood at the rate needed by the body.
- HF - is a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function.

The European Society of Cardiology (ESC) 2016 guidelines

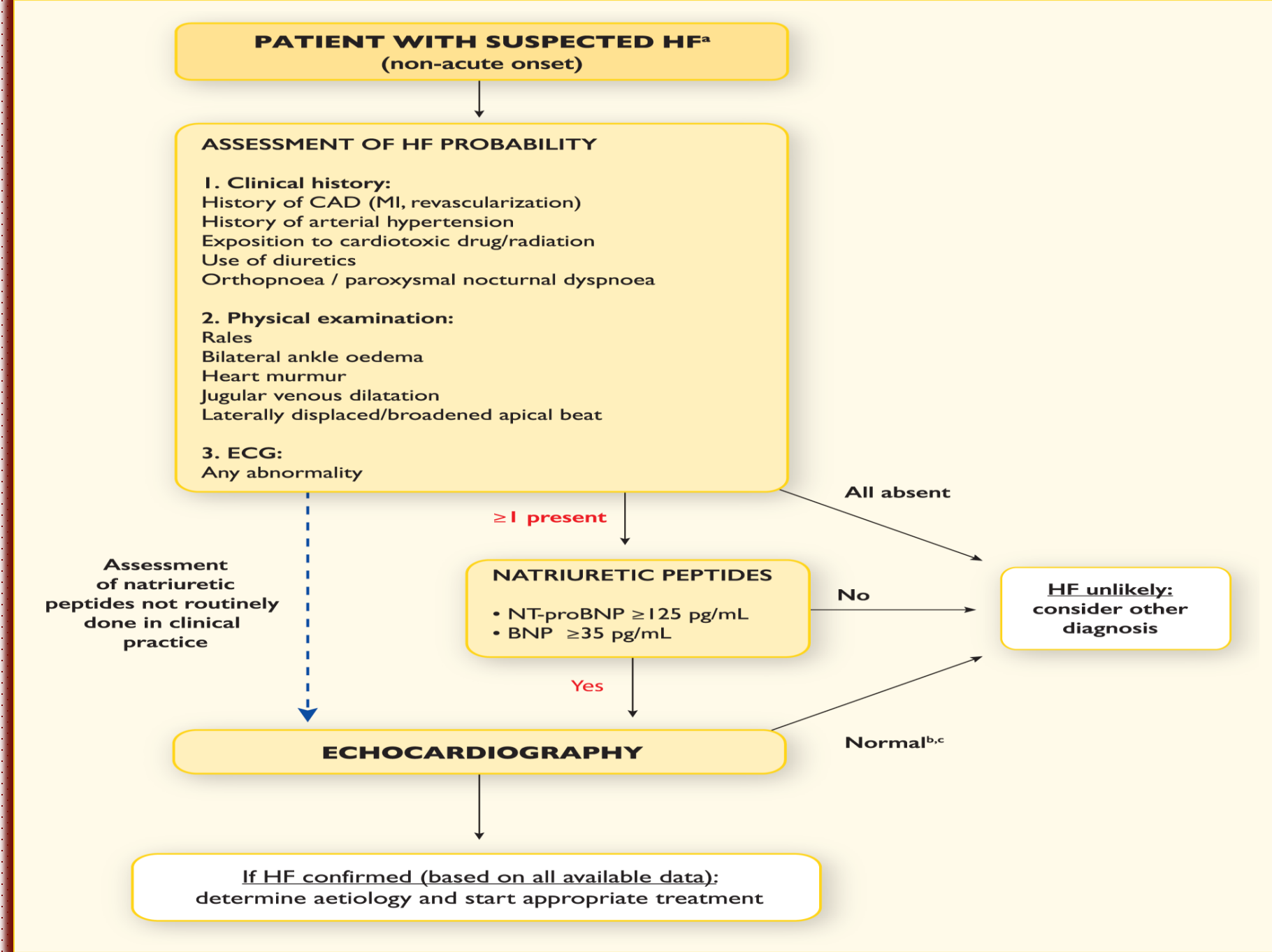
- More than 20 million people have HF worldwide with men having a higher incidence than women.
- In the year after diagnosis the risk of death is about 35% after which it decreases to below 10% each year



INTRODUCTION

DEFINITION OF CHF

- CHF results from injury to the myocardium from a variety of causes including ischemic heart disease, Coronary artery disease, amyloidosis, sarcoidosis hypertension, diabetes mellitus, cardiomyopathies, valvular disease, myocarditis, infections, systemic toxins, and cardiotoxic drugs.
- CHF is further exacerbated by sedentary lifestyles, anemia, hyperthyroidism, pregnancy, obesity, strenuous exercises, nutritional deficiencies (e.g., thiamine deficiency, beriberi) etc.

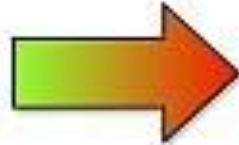


INTRODUCTION

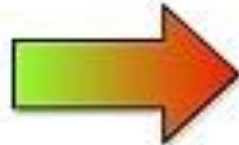
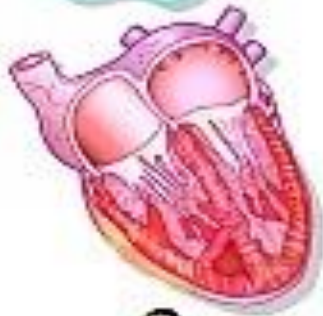
COMORBIDITY OF CHF

- Angina and coronary artery disease (CAD)
- Valvular heart disease
- Hypokalemia and hyperkalemia
- Hyperlipidemia
- Hypertension (HTN)
- **Iron deficiency and anemia**
- Cancer
- Obesity
- Diabetes
- Gout and arthritis
- Erectile Dysfunction (ED)
- Kidney dysfunction (including chronic kidney disease, acute kidney injury, cardio-renal syndrome and prostatic obstruction)
- Lung disease [including asthma and chronic obstructive pulmonary disease (COPD)]
- Cachexia and sarcopenia
- Central nervous system (including depression, stroke and autonomic dysfunction).
- Sleep disturbance and sleep-disordered breathing

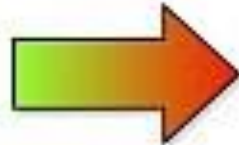
**Iron is Critical for Optimal
Functioning and Survival
of Alive Structures:**



**Mitochondrial Dysfunction
Deranged Activity of Enzymes
Abnormal Transport and Structural Proteins
Apoptosis**



**Tissue Remodeling
Impaired Organ Efficacy**

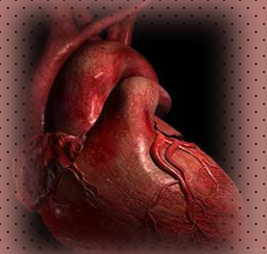


**Impaired Exercise Capacity
Reduced Work Efficacy
Impaired Cognitive Performance and Behaviour
Increased Morbidity and Mortality**



INTRODUCTION

ANEMIA ↔ CHF



- Anemia now occupies an important place in our present understanding of the pathogenesis of heart failure.
- In Europe, one in two patients with CHF has ID.
- ID is associated with a worse prognosis in the HF patient population and is an independent risk-factor for mortality, poor exercise capacity and low quality of life
- **Anemia has been found to be more prevalent in heart failure patients with a higher NYHA functional classification, greater degree of renal dysfunction, advanced age, female sex, and African-American race.**
- The relationship between anemia and CHF is mutual, the former produces or worsens the latter and vice versa.

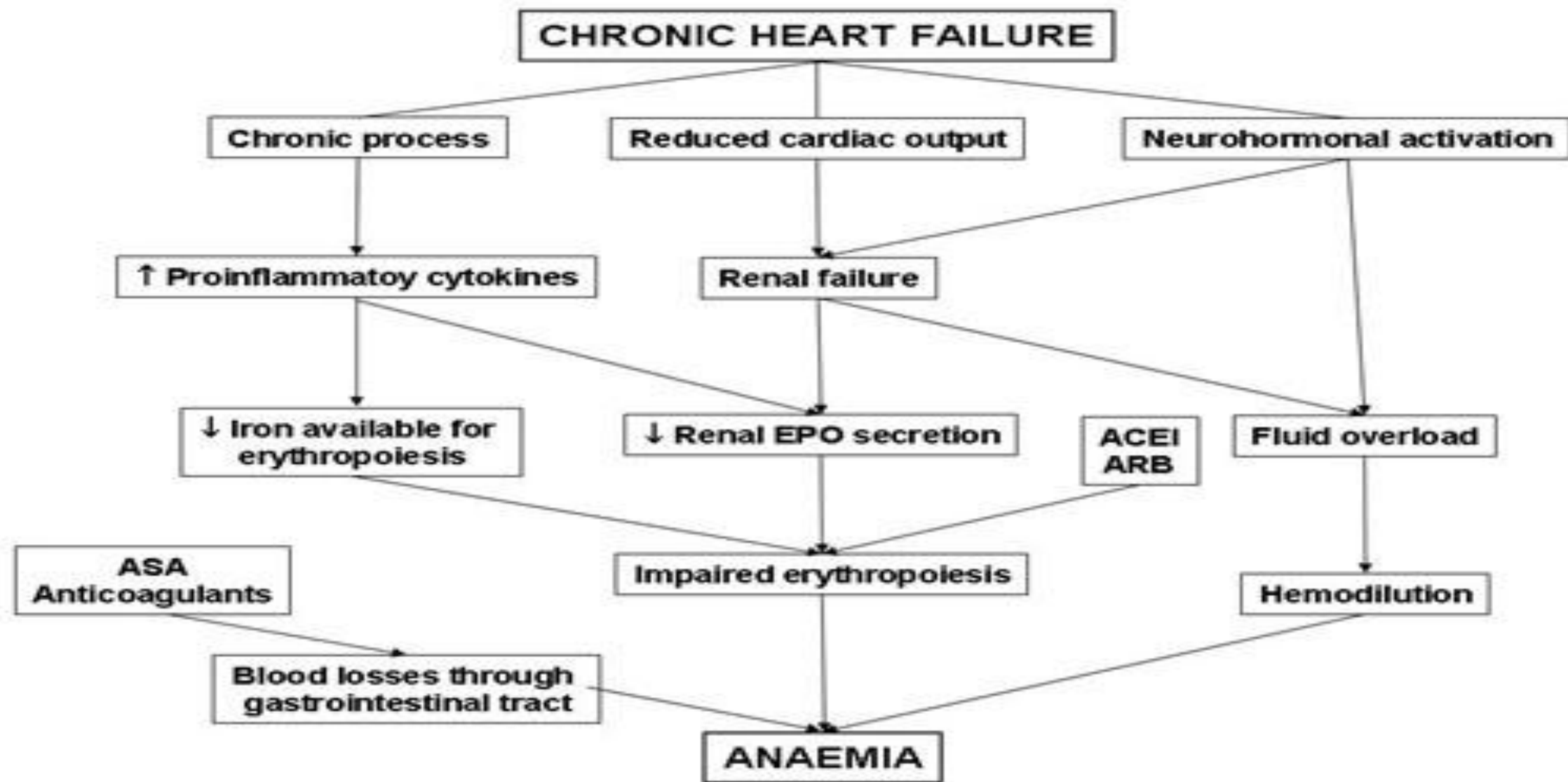
INTRODUCTION

ANEMIA → CHF

- Anemia depends nearly exclusively on hemorrhage, which sets in motion an integrated response with actions in different regions, which include vasoconstriction and thrombosis, fluid retention, stimulation of erythropoiesis, and vascular repair. All these as a result of the human adaptive mechanisms induced to maintain perfusion, O₂ supply to tissues, but also to preserve volume. As a consequence, left ventricular dilation and hypertrophy can occur, with the net result being the production or worsening of CHF.

CHF ← ANEMIA

- Potential causes for anemia in heart failure patients is likely to be a multifactorial [seen in the next slide]



INTRODUCTION

INTERACTION BETWEEN CKD, CHF ANEMIA AND SUBSEQUENT MORTALITY

PATIENT GROUP	NO. OF PATIENTS	2 YEAR DEATH RATE (%)	RR (95% CI)
CHF(-)CKD(-)Anemia(-)	848182	7.7	1.00
CHF(-)CKD(-)Anemia(+)	108926	16.6	1.90 (1.87 to 1.94)
CHF(-)CKD(+)Anemia(-)	12031	16.4	2.05 (1.96 to 2.15)
CHF(+)CKD(-)Anemia(-)	90886	26.1	2.86 (2.82 to 2.91)
CHF(-)CKD(+)Anemia(+)	7381	27.3	3.37 (3.23 to 3.53)
CHF(+)CKD(-)Anemia(+)	40364	34.6	3.78 (3.71 to 3.85)
CHF(+)CKD(+)Anemia(-)	7131	38.4	4.86 (4.67 to 5.05)
CHF(-)CKD(-)Anemia(-)	9404	45.6	6.07 (5.89 to 6.27)

CI	Confidence interval
RR	Relative risk

INTRODUCTION

DIAGNOSIS OF ID AND CHF

Routine diagnostic evaluation includes:

- Complete blood count with reticulocyte count and index
- Serum iron and total iron binding capacity
- Transferrin saturation
- Ferritin
- Serum B12 and folate
- Thyroid stimulating hormone
- Fecal occult blood test

Red blood cell distribution width (RDW) is a numerical measure of the variability in the size of circulating erythrocytes, taken during a standard blood count test. Ineffective erythropoiesis causes heterogeneity in erythrocytes size and a higher RDW. RDW has recently emerged as a new prognostic marker of HF, regardless of Hb levels

(Dickstein K, Cohen-Solal A, Filippatos G, et al. Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008)

SUMMARY OF PUBLISHED TRIALS ASSESING EFFECTS OF ESA IN PATIENTS WITH HF AND ANEMIA							
Ref.	Study design	Patients (n)	NYHA class	Follow-up (months)	Baseline Hb (g/dl)	Study drug	Outcome
Silverberg et al.	Single-center, uncontrolled, open-label	26	III-IV	8	10.2	Epoetin + iron	↓ serum creatinine; ↑Hb, NYHA class, LVEF, VO _{2max} & exercise capacity
Silverberg et al.	Single-center, randomized, open-label	32	III-IV	8	10.3	Epoetin	↓ serum creatinine; ↑Hb, NYHA class, LVEF
Mancini et al.	Single-center, single-blind, randomized, placebo-controlled	26	NA	3	11.0	Epoetin alfa vs. placebo	↑Hb, QoL, VO _{2max} & exercise capacity
Ghali et al.	Multi-center, double-blind, randomized, placebo-controlled	319	I-IV	6.5	11.4	Darbepoetin vs. placebo	No change in NYHA class, QoL, exercise capacity; ↑Hb

Left ventricular ejection fraction (LVEF), Quality of Life (QoL)

GOAL

The goal is to bring awareness to the prevalence of anemia and CHF, and influence of iron deficiency anemia in the progression of CHF while also focusing on diagnostic testing and treatment strategies.

CLINICAL CASE HISTORY

“You treat a disease, you win, you lose.

**You treat a person, I guarantee you, you’ll win, no matter
what the outcome”**

Patch Adams

CLINICAL CASE HISTORY

PATIENT MEDICAL PROFILE

- NAME: Patient N.
- GENDER: Female
- AGE: 58 years old
- OCCUPATION: retired

Patient N. was admitted to the hospital on 14th of November 2016

CLINICAL CASE HISTORY

CHIEF COMPLAINTS

- General weakness
- Palpitations
- Stabbing chest pain, without any radiation, that is relieved without medications
- Dyspnea during physical activity, absent at rest
- Numbness of fingertips
- Attention deficit disorder

CLINICAL CASE HISTORY

HISTORY OF PRESENT ILLNESS

- These complains were felt by Patient N. 1 year ago.
- Last exacerbation was 3 days ago, she didn't take any drugs
- After consulting with the physician, she was thus admitted to the hospital (14.11.2016) for further observation and tests.

CLINICAL CASE HISTORY

PAST MEDICAL HISTORY

- For over 5 years, Patient N. suffered from essential hypertension. Her therapist prescribed medications such as diuretics and B-blockers (name not specified), but she did not comply to the proper dosing and as such, her BP level was unstable (she recalled it rising up to 150-170/100 mm Hg)
- Patient N. also suffered from chronic gastritis since year 2000
- Patient N has had no history of viral hepatitis, Diabetes Mellitus.
- Patient N also denied any history of easy bruisability, menorrhagia.
- No surgical history

CLINICAL CASE HISTORY

FAMILY/SOCIAL HISTORY

- Patient's mother and sister suffers from essential hypertension
- No family history of anemia or any other hematologic disorder
- No family history of kidney and liver diseases
- Patient N denied any illicit drug history, alcohol use, smoking and allergic reactions both to environmental factors and to drugs
- Retired
- Patient N is married, has 2 children

CLINICAL CASE HISTORY

GENERAL EXAMINATION

- VITAL SIGNS
- Temp. – 36.7 C
- BP–150/80 mm Hg
- RP – 82 BPM
- RR – 19 breaths per minute

- Height – 160 cm
- Body Weight (BW) – 57 kg
- BMI – 22,2 kg/m²

CLINICAL CASE HISTORY

GENERAL EXAMINATION

- Elderly female, has correct orientation in space and surroundings, mild depressed
- Skin was pale with the absence of rashes and hemorrhages.
- Mucous membranes are pale and wet
- Tongue- clear and wet
- Turgor and elasticity of the skin is decreased , Koilonychia
- Subcutaneous fat tissue – normal
- Absence of any chest variations, surgical incision sites
- Edema of the lower limbs is observed (2+)
- Joints are normal, active and passive movements are painless
- The rest general inspection was unremarkable.

CLINICAL CASE HISTORY

GENERAL EXAMINATION

- PERCUSSION
- Percussion of the lungs showed was normal
- Heart borders extended to the left on 1,5 cm of mid-clavicular line

- AUSCULTATION
- Heart:
- Heart sound are decreased in all points of auscultation
- Also observed is an accentuation of S2 on aorta point
- Systolic murmur on the 1st point of the heart auscultation (apex of the heart)

- Lungs:
- Auscultation of the lungs were normal
- Abdomen:
- No abdominal bruits or rubs were observed

CLINICAL CASE HISTORY

PRELIMINARY DIAGNOSIS (Dx)

- Anemia
- Heart failure
- Arterial hypertension
- Gastritis

More specific laboratory and instrumental investigation should be further conducted.

CLINICAL CASE HISTORY

DIAGNOSTIC PLANS

Laboratory Investigation

- Complete blood count (CBC) any illicit
- Urinalysis
- Biochemical blood profile: [Glucose, Bilirubin, ALT, AST, Creatinine, urea and Blood lipid profile, Ferrum, ferritin, Tsat, TIBC, B-12 Vit]

Instrumental Investigation

- Abdominal (with barium contrast) and chest x-ray
- Upper Endoscopy
- Ultrasound of abdomen and heart
- 12 – lead ECG
- Stress test (6MWT)
- **ANP,**
- **H.pylori tests**

CLINICAL CASE HISTORY

COMPLETE BLOOD COUNT (CBC)

PARAMETERS	NORMAL	16.11.2016	22.11.2016	29.11.2016
Hb	120-140 g/l	40 g/l	55 g/l	70 g/l
RBCs	3.9-4.7	1.6	2.2	2.4
WBCs	4.0-9.0 g/l	3.9 g/l	4.2 g/l	4.1g/l
Platelets	160-320 g/l	190 g/l	195 g/l	190 g/l
Stab Cells	1-6%	1%	2%	3%
CPU	0.85-1.15	0.8	0.75	0.8
Segmented Neutrophils	47-72%	79%	74%	73%
Eosinophils	0.5-5.0%	1%	1%	1%
Basophils	0-1.0%	0.9%	0.5%	0.5%
Lymphocytes	19-37%	16%	18%	19%
Monocytes	3-11%	3%	4.5%	3.5%
ESR	2-15 mm/h	18 mm/h	18 mm/h	17 mm/h

CONCLUSION:

- Remarkable decrease in Hb, RBC; indicates a severe form of anemia.
- An increase in segmented neutrophils which could be as a result of an infection or inflammation process.
- A slight decrease in lymphocytes

The rest results are unremarkable.

RECOMMENDATION:

- More specific test to identify the type of anemia: Hb electrophoresis, reticulocyte count, tests for the level of iron and vitamin deficiencies.

CLINICAL CASE HISTORY

BIOCHEMICAL BLOOD TEST

Parameters	Normal	Date (16.11.2016)
AST	0.1-0.445	0.59
ALT	0.1-0.68	0.7
Creatinine	53-97	58
Urea	2.5-8.3	4.0
Total Bilirubin	0.5-5 mIU/L	8 μ mol/L
Fasting Glucose Test	4.2-6.1 mmol/l	5.3

CONCLUSION

- All parameters except AST, ALT are normal
- An increase in AST and ALT is an indicators of liver damage or muscle damage (cardiac muscle) or both.
- The interpretation of elevated AST and ALT results depends upon the entire clinical evaluation of an individual.
- Cardiac function has to be further assessed.

CLINICAL CASE HISTORY

BLOOD LIPID PROFILE

Parameters	Normal	Date (16.11.2016)
LDL	85-125 mg/dL	127 mg/dL
HDL	40-80 mg/dL	55 mg/dL
Total Cholesterol	3-5.5 mmol/L	5.5 mmol/L
Triglycerides	50-150 mg/dL	58 mg/dL
BNP	Less than 125 pg/mL for patients aged 0-74 years Less than 450 pg/mL for patients aged 75-99 years	-

CONCLUSION

All parameters except LDL are normal

- There is a slight increase in low density lipoprotein (LDL)

CLINICAL CASE HISTORY

URINE ANALYSIS

Parameters	Normal	16.11.2016			
Color	Yellow	yellow	Urobilirubin	(0.5-1 mg/dL)	normal
turbidity	Clear or cloudy	clear	Blood	≤3 RBCs	normal
pH	4.5-8	4.8	Proteins	≤150 mg/d	normal
Specific gravity	1.005-1.025	1.010	RBCs	≤2 RBCs/hpf	normal
Glucose	≤130 mg/d	normal	WBCs	≤2-5 WBCs/hpf	normal
Ketones	None	None	epithelial cells	≤15-20 squamous epithelial cells/hpf	normal
Nitrites	Negative	Negative	Casts	0-5 hyaline casts/lpf	normal
Leukocyte esterase	Negative	Negative	Crystals	Occasionally	None
Bilirubin	Negative	Negative	Bacteria	None	None
			Yeast	None	None

CONCLUSION:

- Urine analysis is normal

CLINICAL CASE HISTORY

UPPER ENDOSCOPY (16.11.2016)



The mucosa of the esophagus is normal. Gastric mucosa is reddened and swollen. The structure of the folds is not changed.

CONCLUSION:

- The signs of the gastritis

CLINICAL CASE HISTORY

Biochemical blood tests

Vitamin Levels

Parameters	Normal	Date (17.11.2016)
Vitamin B12	130-700 ng/L	685 ng/L

CONCLUSION:

- No vitamin deficiency anemia

CONCLUSION:

- Remarkable decrease in iron levels in the blood indication Iron Deficiency (ID) anemia

RECOMMENDATION:

- Refer patient to a hematologist for consultation to get started on treatment

Parameters	Normal	Previous Stats (17.11.2016)	Date (29.11.2016)
Serum iron	Male - 11.6-31.3mkmol/l Female - 9.0-30.4 mkmol/l	2.3 mkmol/l	8.4 mkmol/l
total iron-binding capacity (TIBC)	44.8-76.1 mkmol/l	35.7 mkmol/l	43.8 mkmol/l
Transferrin saturation	Male - 20-50 % Female - 15-50 %	6.4%	15%
serum ferritin	45-340 ng/mL	28 ng/mL	44 ng/ml

CLINICAL CASE HISTORY

ABDOMINAL ULTRASOUND 19-11-2016



Liver: normal. Gallbladder: normal. The spleen is enlarged. Size: 133*60 mm (N – 110*60)

CONCLUSION:

- Splenomegaly

CLINICAL CASE HISTORY

CHEST X-RAY (CXR) 21-11-2016

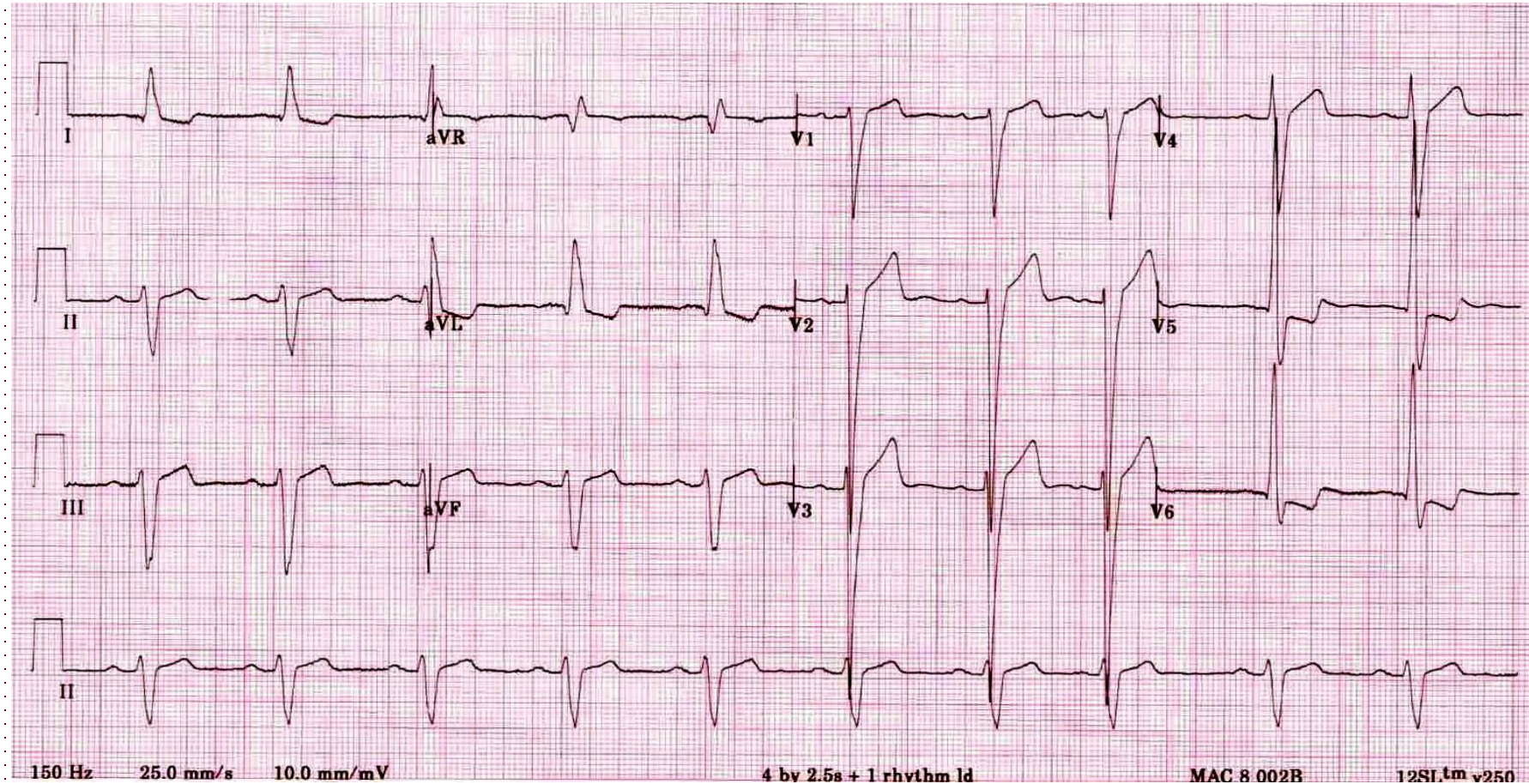


CONCLUSION:

- There are no infiltrative or local changes in the lung
- The sinus are without liquid
- Left heart border displaced sinisterly, inferiorly and posteriorly
- Rounding of the cardiac apex

CLINICAL CASE HISTORY

ECG 21.11.2016



CONCLUSION:

- Left-Ventricular Hypertrophy

CLINICAL CASE HISTORY

HEART ECHOCARDIOGRAPHY 22-11-2016



Name	Result	Normal
Acoustic window	normal	normal
Aorta d	28 mm	20-37 mm
Aortic Valve	20 mm	17-26 mm
Left Atrium	34 mm	To 38 mm
End-DV LV	120 ml	142±21 ml
End-SV LV	34 ml	47±10 ml
Mitral Valve	Regurgitation I degree	-
Posterior wall of the LV	13 mm	6-11 mm
Interventricular septum	12 mm	6-11 mm
Right Ventricle	14 mm	D.: (9-26 mm)
Right Atrium	26 mm	To 38 mm
Ejection Fraction	40 %	55-78%

CONCLUSION:

- Concentric left ventricle hypertrophy, decreased ejection fraction

CLINICAL CASE HISTORY

GI X-RAY 23.11.2016



Upper GI x-ray barium

CONCLUSION: Gastritis

CLINICAL CASE HISTORY

6MWT 25.11.2016

- Patient N. walked 450 feet in 6 minutes

CONCLUSION:

- The European Society of Cardiology (ESC) guidelines indicates the 6-minute walk test is a good indicator of functional status and prognosis in patients with heart failure. It evaluates distance walked, dyspnea index on a Borg scale from 0 to 10, oxygen saturation, and heart rate response to exercise.
- Normal value is walking more than 1500 feet. Patients who walk less than 600 feet have severe cardiac dysfunction and a worse short- and long-term prognosis.

CLINICAL SYNDROMES

CLINICAL SYNDROMES CLASSIFICATION

- 1. Anemia**
- 2. Iron deficiency**
- 3. Heart failure**
- 4. Arterial hypertension**
- 5. Gastritis**
- 6. Neutrophilic Leukocytosis**

CLINICAL SYNDROMES

ANEMIA CLASSIFICATION

CLASSIFICATION OF ANEMIA ACCORDING TO THE DEGREE OF SEVERITY

- Mild - hemoglobin - 120-90 g / l 2.
- Moderate - hemoglobin - 90-70 g / l
- **Severe - hemoglobin - less than 70 g / l**

CLINICAL SYNDROMES

STAGES OF IRON DEFICIENCY ANEMIA

STAGE 1	Characterized by decreased bone marrow iron stores; Hb and serum iron remain normal, but serum ferritin level falls to < 20 ng/mL. [The compensatory increase in iron absorption causes an increase in iron-binding capacity (transferrin level)]
STAGE 2	Erythropoiesis is impaired. Although the transferrin level is increased, the serum iron level decreases; transferrin saturation decreases. [Erythropoiesis is impaired when serum iron falls to < 50 $\mu\text{g/dL}$ (< 9 $\mu\text{mol/L}$) and transferrin saturation to $< 16\%$. The serum transferrin receptor level rises (> 8.5 mg/L)]
STAGE 3	Anemia with normal-appearing RBCs and indices develops
STAGE 4	Development of microcytosis and then hypochromia
STAGE 5	Iron deficiency affects tissues, resulting in symptoms and signs

CLINICAL SYNDROMES

CLASSIFICATION OF ID

ABSOLUTE ID

- Currently, the generally accepted serum ferritin cut-off level to diagnose absolute ID is $<30 \mu\text{g/L}$ and low Tsat ($<16\%$)
- In chronic diseases, absolute ID is typically diagnosed with higher cut-off ferritin values (i.e. $<100 \mu\text{g/L}$)

FUNCTIONAL ID

- functional ID, diagnosed with normal serum ferritin ($100\text{--}300 \mu\text{g/L}$) and low Tsat ($<20\%$).

Tsat - Transferrin saturation

CLINICAL SYNDROMES

CHANGE IN LAB VALUES IN IRON DEFICIENCY ANEMIA

CHANGE	PARAMETER		
↓ - Decreased	ferritin	Hemoglobin (Hb)	Mean corpuscular volume (MCV)
↑ - Increased	Total iron-binding capacity (TIBC)	Transferrin	Red blood cell distribution width (RDW)

CLINICAL SYNDROMES

CLASSIFICATION OF CHF

- **The New York Heart Association (NYHA) functional classification** has been used to describe the severity of symptoms and exercise intolerance
- **The American College of Cardiology Foundation/American Heart Association (ACC/AHA) staging system** complements the NYHA classification to reflect the progression of disease and comprises of four stages

CLINICAL SYNDROMES

American College of Cardiology and American Heart Association (ACC/AHA) Stages

At Risk for Heart Failure		Heart Failure	
Stage A	Stage B	Stage C	Stage D
Patients at high risk for developing HF in the future but no functional or structural heart disorder	a structural heart disorder but no symptoms at any stage	previous or current symptoms of heart failure in the context of an underlying structural heart problem, but managed with medical treatment.	advanced disease requiring hospital-based support, a heart transplant or palliative care

Hunt SA, Abraham WT, Chin MH, et al. (2005). "ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult"

CLINICAL SYNDROMES

CHF NYHA CLASSIFICATION

Class	Patient Symptoms
Class I (Mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

CLINICAL SYNDROMES

Classification of heart failure according to ejection fraction

Type of HF	HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2	LVEF <40%	LVEF 40–49%
	3	–	1. Elevated levels of natriuretic peptides ^b ; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

- ESC Clinical Practice Guidelines 2016 on ACUTE AND CHRONIC HEART FAILURE

CLINICAL SYNDROMES

AH stages (WHO-ISH, 1993)

- **Stage Signs I**

No objective signs of organic changes

- **Stage Signs II**

At least one of the following signs of organ damage:

- Left ventricular hypertrophy (x-ray film, electrocardiogram, echocardiogram) - Generalized or focal narrowing of retinal masses
- Proteinuria or slightly raised plasma levels of creatinine concentrations (106- 107 $\mu\text{mol/l}$), or both
- Ultrasound or radiological evidence of atherosclerotic plaque (carotid arteries, aorta, iliac, and femoral arteries)

- **Stage Signs III**

Both symptoms and signs have appeared as a result of end organ damage including:

- Heart: angina pectoris, myocardial infarction, heart failure
- Brain: transient ischaemic attack, stroke, hypertensive encephalopathy
- Optic fundi: retinal haemorrhages and exudates with or without papilloedema
- Kidney: plasma creatinine concentration $>177 \mu\text{mol/l}$, renal failure
- Vessels: dissecting aneurysm, symptomatic arterial occlusive disease

Summary of 1993 World Health Organization – International Society of Hypertension guidelines for the management of mild hypertension. – BMJ 1993; 307: 1541-1546

CLINICAL SYNDROMES

ESSENTIAL HYPERTENSION CLASSIFICATION

Normal	SBP <120 mm Hg	DBP <80 mm Hg
Optimal	<120	<80
High normal	130–139	85–89
Grade 1 hypertension	140–159	90–99
Grade 2 hypertension	160–179	100–109
Grade 3 hypertension	≥180	≥110
Isolated systolic hypertension	≥140	<90

CLINICAL SYNDROMES

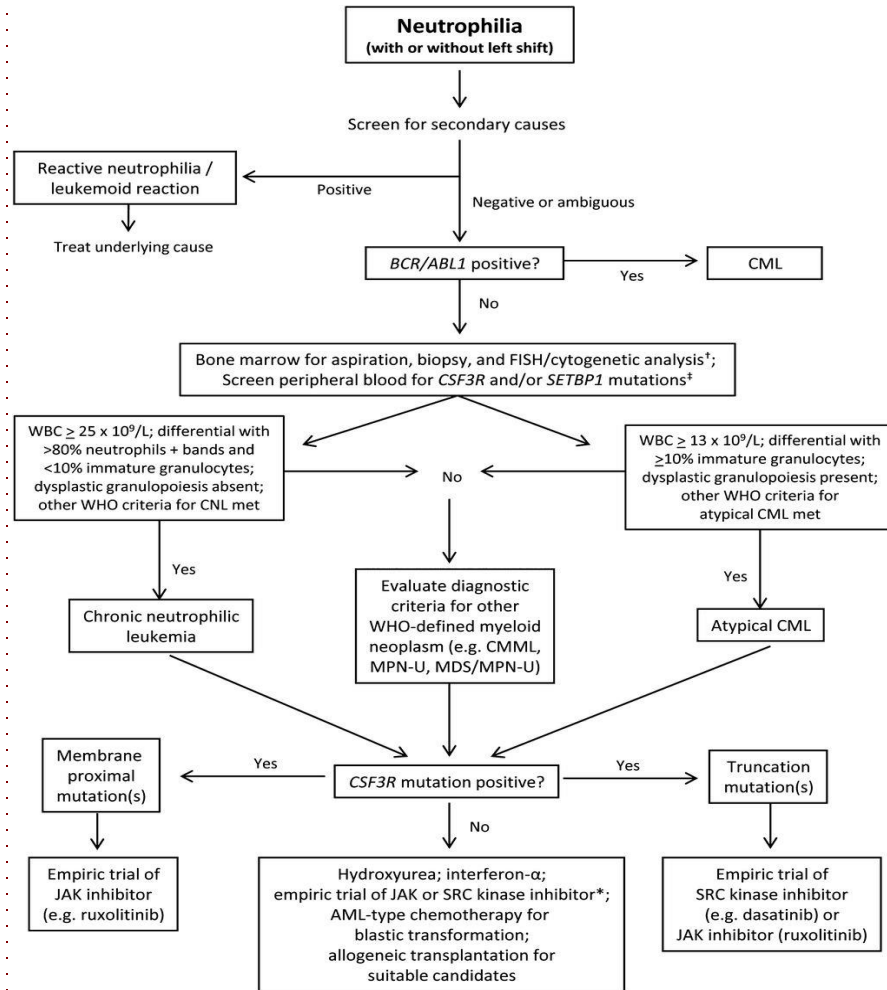
GASTRITIS CLASSIFICATION

There are follows forms of chronic gastritis:

- Type A gastritis (autoimmune atrophic gastritis) may be triggered by a physical or psycho-emotional stressor that causes the individual's immune system to produce antibodies against certain cells in the stomach (parietal cells); destruction of these cells results in atrophy of the stomach tissue
- Type B gastritis (simple atrophic gastritis) is more common and is strongly associated with the presence of a certain bacterium (*Helicobacter pylori*) in the stomach mucosa
- Type AB gastritis (environmental)
- Chemical gastritis (reflux gastritis)
- Uncommon forms

CLINICAL SYNDROMES

Neutrophilic Leukocytosis



Any process resulting in anaemia, including haemolysis and blood loss, can cause increased haematopoiesis to compensate for a low haemoglobin, leading to secondary elevation of the total leukocyte, neutrophil, and platelet counts.

<http://bestpractice.bmj.com/best-practice/monograph/1023/overview/aetiology.html>

<http://www.bloodjournal.org/content/122/10/1707?sso-checked=true>

CLINICAL CASE HISTORY

FINAL DIAGNOSIS

Main Disease:

- Iron Deficiency Anemia , stage 2, severe degree, mixed genesis

Concomitant Diseases:

- Essential Hypertension IInd stage 2nd grade
- Chronic Heart Failure (CHF) 2nd Class according to the NYHA classification, rEF
- Chronic gastritis

CLINICAL CASE HISTORY

HOSPITAL TREATMENT

RBCs transfusion BIII Rh+ 368,0 ml (16.11.16)

Tardyferon (Ferrous sulfate) 80 mg -1 tablet twice a day

Sufer 20 mg /ml IV

Bisoprolol 2.5 mg 1 tablet once a day

Perindopril 5 mg 1 tablet once a day

CLINICAL CASE HISTORY

EMERGENCY CASE

- Patients with severe (lower than 80), severely symptomatic (e.g., with symptoms of myocardial ischemia), or life-threatening anemia should be treated with RBCs transfusion because correction of iron deficiency anemia using iron replacement requires time for iron administration and incorporation into RBCs.
- RBC transfusion can be life saving for the patient who is hemodynamically unstable due to active bleeding, and/or when evidence of end-organ ischemia secondary to severe anemia is present.
- The following may be expected for each unit of packed RBCs transfused to an adult, as long as there is not ongoing bleeding:
 - Total volume – 300 mL
 - Volume of RBCs – approximately 200 mL
 - Iron – 200 mg (in the form of hemoglobin)
 - Increase in Hb – approximately 1 g/dL
 - Increase in hematocrit – approximately 3 percentage points
- Once the patient is stabilized with transfusion, the need for additional iron supplementation can be determined and evaluation for the cause can be pursued.

CLINICAL CASE HISTORY

MANAGEMENT OF PATIENT

- Diet modification
- Oral iron therapy
- Treatment of CHF, hypertension
- Patient should be seen every 3 months to have her CBC checked.

CLINICAL CASE HISTORY

NON-EMERGENCY CASE

Diet

- According to the American Society of Hematology:
“Meat: beef, pork, or lamb, especially organ meats such as liver; Poultry: chicken, turkey, and duck, especially liver and dark meat; Fish, especially shellfish, sardines, and anchovies; Leafy green members of the cabbage family including broccoli, kale, turnip greens, and collard greens; Legumes, including lima beans, peas, pinto beans, and black-eyed peas; Iron-enriched pastas, grains, rice, and cereals”
- Patients should be strictly warned against a “tea and toast diet” as tea strongly blocks iron absorption.

Activity Restriction

- Patients with moderately severe iron deficiency anemia and significant cardiopulmonary disease should limit their activities until the anemia is corrected with iron therapy.

CLINICAL CASE HISTORY

IRON THERAPY

Oral iron:

- Examples of available preparations (with the amount of elemental iron per dose) include:
- Ferrous fumarate - 324 or 325 mg tablet (contains 106 mg elemental iron per tablet)
- Ferrous gluconate - 325 mg tablet (contains 36 mg elemental iron per tablet)
- Ferrous sulfate - 325 mg tablet (contains 65 mg elemental iron per tablet) orally three times a day, lower doses (eg, 15-20 mg of elemental iron daily) may be as effective and cause fewer side effects.
Tardyferon 80 mg -1 tablet twice a day

Of the various iron salts available, ferrous sulfate is the one most commonly used.

CLINICAL CASE HISTORY

IRON THERAPY

Benefits of oral iron administration

- Oral iron provides an inexpensive and effective means of restoring iron balance in a patient with iron deficiency without complicating comorbid conditions
- Oral supplements are the only form of iron available to many patients, especially those in resource-poor settings.
- Use of oral iron avoids the need for IV access and monitored infusion.
- Use of oral iron eliminates the potential for infusion reactions and/or anaphylaxis

Side effects

- Possible side effects of iron tablets include abdominal discomfort, nausea, vomiting, diarrhea, constipation, and dark stools.

CLINICAL CASE HISTORY

Intravenous (IV) Iron

DRUGS	NUMBER OF DOSES	ELEMENTAL IRON CONCENTRATION (mg)	DOSES (ml)	CONCENTRATION PER ML (mg/ml)
Iron isomaltoside (Monofer) [available only in Europe]	single infusion	The elemental iron concentration is 100 mg/ml	20 mg/kg, over 15 minutes.	100 mg/ml
LMW iron dextran (INFeD, CosmoFer)	a single, large dose	equivalent to 100 mg elemental iron	multiple doses of 2 mL	50 mg/ml
Ferric gluconate (FG; Ferrlecit), ferric gluconate complex	multiple infusions	equivalent to 125 to 187.5 mg elemental iron	10 to 15ml	12.5 mg/ml
Iron sucrose (IS; Venofer), iron saccharate	multiple infusions	equivalent to 200 to 300 mg elemental iron	10 to 15ml	20 mg/ml
Ferumoxytol (Feraheme)	2 doses (three to eight days apart)	equivalent to 510 mg of elemental iron	17ml	30mg/ml
Ferric carboxymaltose (FCM; Ferinject, Injectafer)	Single dose	equivalent to 1000mg of elemental iron	20ml Or Max. dose of 20mg/kg	50 mg/ml

CLINICAL CASE HISTORY

IRON THERAPY

- In July 2013, the FDA approved ferric carboxymaltose injection (Injectafer) for the IV treatment of ID anemia in adults who either cannot tolerate or have not responded well to oral iron.

Benefits of IV iron administration:

- Patients who cannot (or prefer not to) tolerate the gastrointestinal side effects of oral iron.
- Patients who prefer to replete iron stores in one or two visits rather than over the course of several months.
- Ongoing blood loss that exceeds the capacity of oral iron to meet needs (eg, heavy uterine bleeding, mucosal telangiectasias).
- Coexisting inflammatory state that interferes with iron homeostasis.

Side effects:

- Allergic and infusion reactions
- Risk of infection

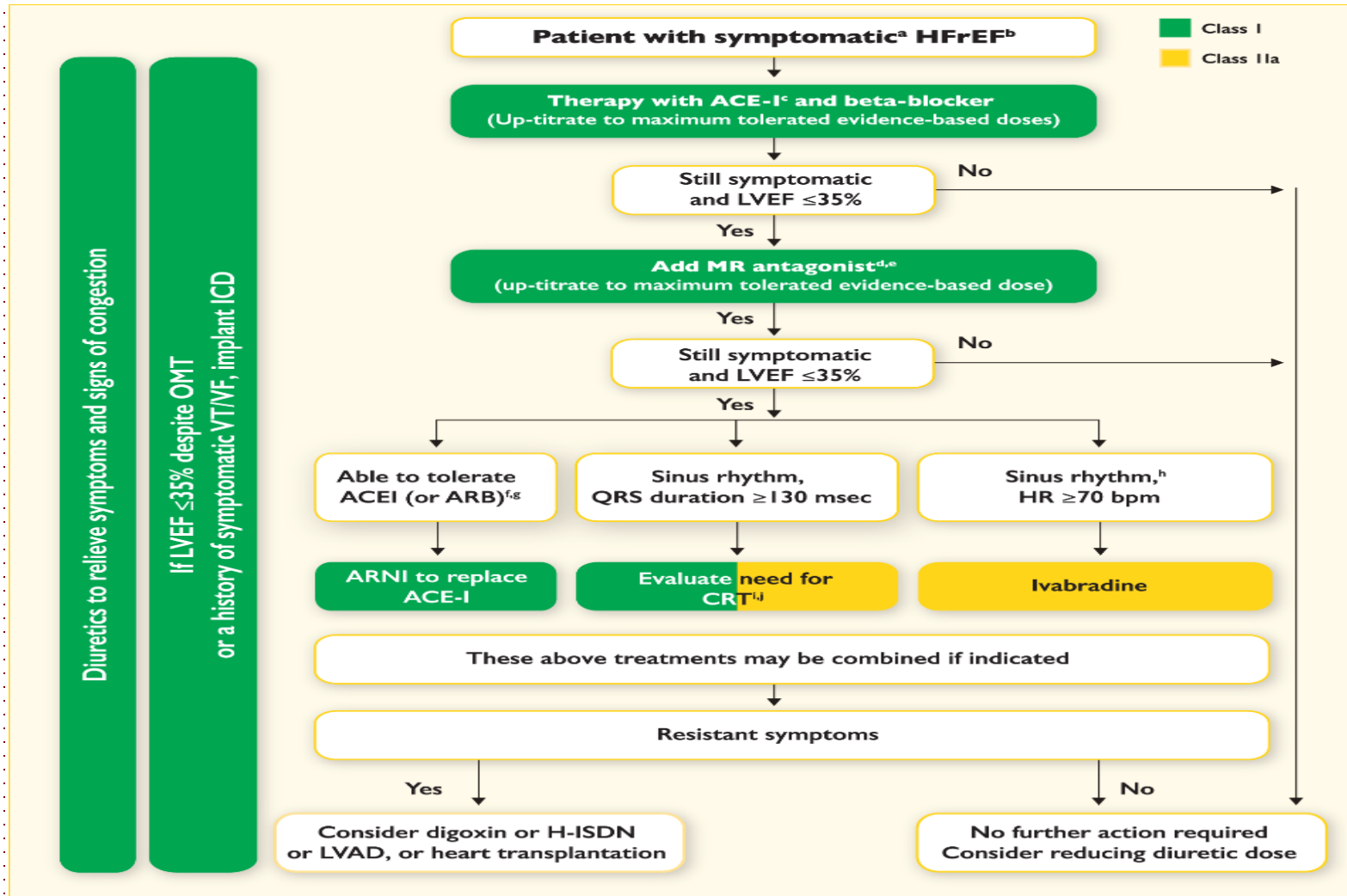
CLINICAL CASE HISTORY

IRON THERAPY and CHF

Recommendations	Class ^a	Level ^b	Ref ^c
Iron deficiency			
Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.	IIa	A	469, 470
Diabetes			
Metformin should be considered as a first-line treatment of glycaemic control in patients with diabetes and HF, unless contra-indicated.	IIa	C	440 ,441

CLINICAL CASE HISTORY

TREATMENT HF_rEF



CLINICAL CASE HISTORY

PATIENT TREATMENT

- Tardyferon (Ferrous sulfate) 80 mg -1 tablet twice a day 3-4 months
- Perindopril 5 mg 1 tablet once a day

CLINICAL CASE HISTORY

SUMMARY AND RECOMMENDATIONS

- Regardless of the presence of symptoms, all patients with ID anemia and most patients with ID without anemia should be treated. The cause of ID also must be identified and addressed, especially in adults with new onset ID.
- The dose of oral iron depends on patient age, the estimated iron deficit, the rapidity with which it needs to be corrected, and side effects, which include metallic taste, and a number of gastrointestinal effects that generally correlate with dose. For the most part, all oral iron preparations are equally effective.
- True allergic reactions are exceedingly rare and vastly overestimated, largely due to experience with older products such as high molecular weight iron dextran (HMW ID), which is no longer used, and the practice of aggressively treating nonallergic infusion reactions with diphenhydramine and other therapies that convert the reaction to a more serious event. For individuals with asthma, inflammatory rheumatic conditions, or multiple drug allergies, generally limit premedication to a glucocorticoid alone.
- Effective treatment of ID results in resolution of symptoms, a modest reticulocytosis (peaking in 7 to 10 days), and normalization of the Hb level in 6-8 weeks. Causes for a lack of response include nonadherence to oral iron, ongoing blood loss, and incorrect initial diagnosis or the presence of additional diagnoses. Some of these additional diagnoses, such as celiac disease, may be especially important to evaluate.

CLINICAL CASE HISTORY

PROGNOSIS

For recovery:

- **Favorable** due to quick and efficient diagnosis and treatment of Iron Deficiency and its concomitant diseases

For life:

- With regular visits to the cardiologist and hematologist and adherence to treatment, her lifestyle should improve.

CONCLUSION

- The origins of anemia in heart failure are multifactorial
- Its pathways are complex and not well understood
- There is no single treatment that will suit all patients
- Treatment must be based on an understanding of the causes of anemia in each patient
- IV iron therapy is recommended for patients with HFrEF and absolute or functional ID in order to alleviate HF symptoms and improve exercise capacity and quality of life
- The role of anemia in developing of HF should be researched and recognized more to understand the target levels of Ferritin and Iron in patients with or without anemia and CHF to reduce mortality and improve quality of life

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THANK YOU FOR LISTENING !!

