Heme Myths!!

Thomas DeLoughery, MD MACP FAWM @bloodman
Oregon Health & Sciences University

GENERAL HEMATOLOGY
OHSU

DISCLOSURE

OHSU

Relevant Financial Relationship(s)

Speaker's Bureau – none

Author: UpToDate (Iron Tx)

CPD

Talk

- A potpourri of issues that commonly come up

OHSU
CPD

Pain Control

- “Doc can I stop my blood thinners as my hip is killing me since I can’t take motrin”

OHSU
CPD

NSAID and Anticoagulation

- Will raise risk of bleeding
  - Antiplatelet effect
  - GI toxicity
- Options for anticoagulated patients
  - DOAC/PPI plus
  - Celecoxib
  - Meloxicam
  - NSAIA (accepting risk of bleeding)

OHSU CPD

Co-administered OACs with NSAIDs and the risk of bleeding

Systematic review & meta-analysis
(PubMed, Embase, Cochrane Library, Web of Science)
Any study with a VKAs/DOACs & NSAIDs arm and a VKAs/DOACs alone arm or with a VKAs & NSAIDs arm and a DOACs & NSAIDs arm

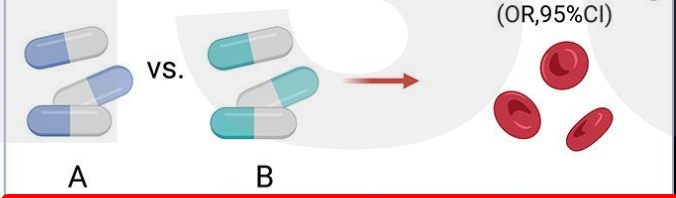
27 studies
(22 observational studies, 5 RCTs)

1,182,540 patients
(mean age: 59.3-83 years)

median follow-up:
0.5-14 years

Primary outcome: the risk of bleeding

Results



	Any bleeding	GI bleeding	Major bleeding
VKAs & NSAIDs vs. VKAs alone	1.55 [1.21-2.00]	2.66 [1.96-3.62]	1.55 [1.04-2.30]
DOACs & NSAIDs vs. DOACs alone	1.54 [1.33-1.80]	2.18 [1.02-4.69]	1.42 [0.84-2.40]
DOACs & NSAIDs vs. VKAs & NSAIDs	Risk of bleeding: 0.55 [0.34-0.90]		

Conclusions

- Co-administered OACs with NSAIDs significantly increased the risk of any bleeding and GI bleeding.
- Inconsistent results were observed regarding the risk of major bleeding.
- Without considering other confounding factors, DOACs were associated with a lower risk of bleeding compared to VKAs in AF and VTE patients.


OHSU

Macrocytosis – not always a harbinger of doom!

OHSU CPD

Macrocytosis

- RBC bigger than normal
- Not well standardized
- My worry point > 100 fl

OHSU CPD

Macrocytic Anemia

- Round
  - Membrane defects
- Oval
  - DNA synthetic defects
  - Smear with megaloblastic changes

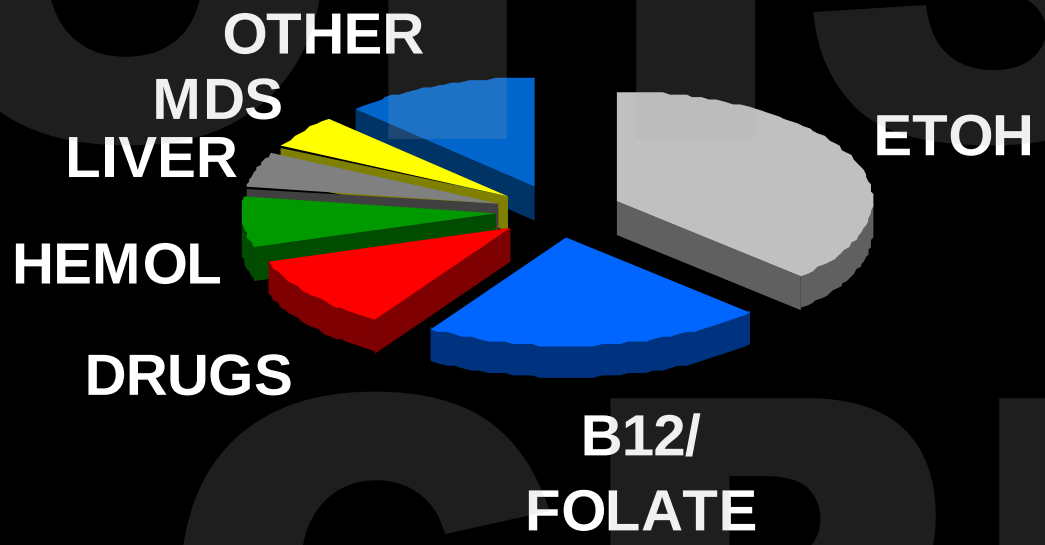
OHSU CPD

Macrocytosis

- Ovalomacrocytes
  - B_{12}/folate deficiency
  - Drugs: chemotherapy, AZT, anticonvulsants
  - Myelodysplasia
- Macrocyte
  - Liver disease
  - Hypothyroidism
  - Reticulocytosis
  - Alcohol
  - Pregnancy

OHSU CPD

CAUSES OF MACROCYTOSIS



OHSU CPD

Causes of Macrocytosis

- Broad differential
- Most macrocytosis not due to B_{12}/folate deficiency

- Lets run the other causes!

OHSU CPD

MDS

- Clonal bone marrow disease resulting in:
  - Ineffective production
  - Predisposition to leukemia
- More common in older patients

OHSU CPD

Clues to MDS

- Macrocytic anemia with other cell lines down
- Previous chemo or radiation therapy
- Nutrition normal
- Dx: genetics/marrow

OHSU CPD

Drugs

- Cytotoxic agents
  - Azathioprine
  - Methotrexate
- Sulfasalazine
- TMP-SMX
- Antivirals – d4T, lamivudine, valacylovir, zidovudine
- Anticonvulsants – phenytoin, valproic acid

OHSU
CPD

Pregnancy

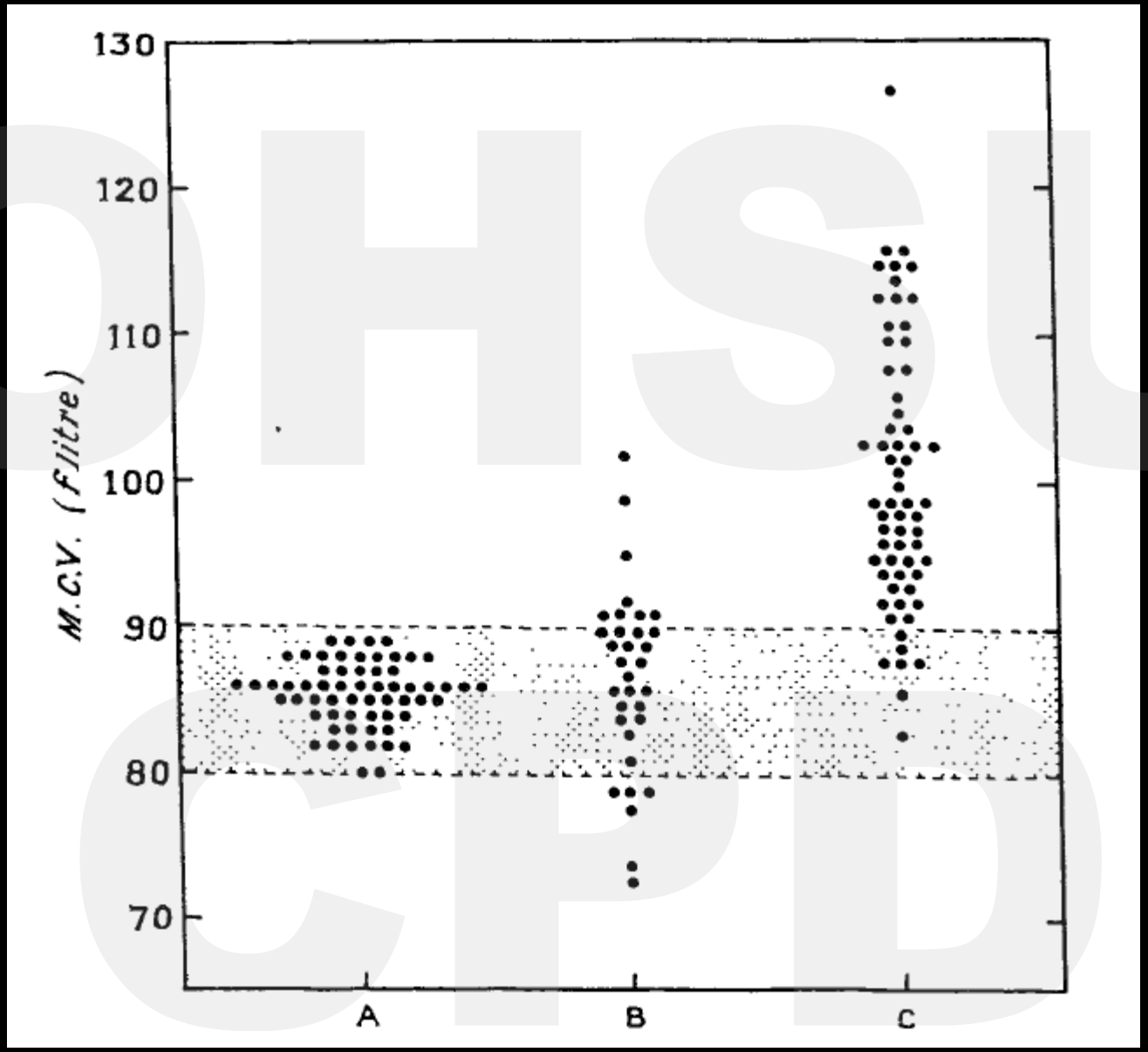
- Normally MCV can rise 4fl with pregnancy
  - Can be up to 20fl (100-110)
- Often masked by iron deficiency

OHSU CPD

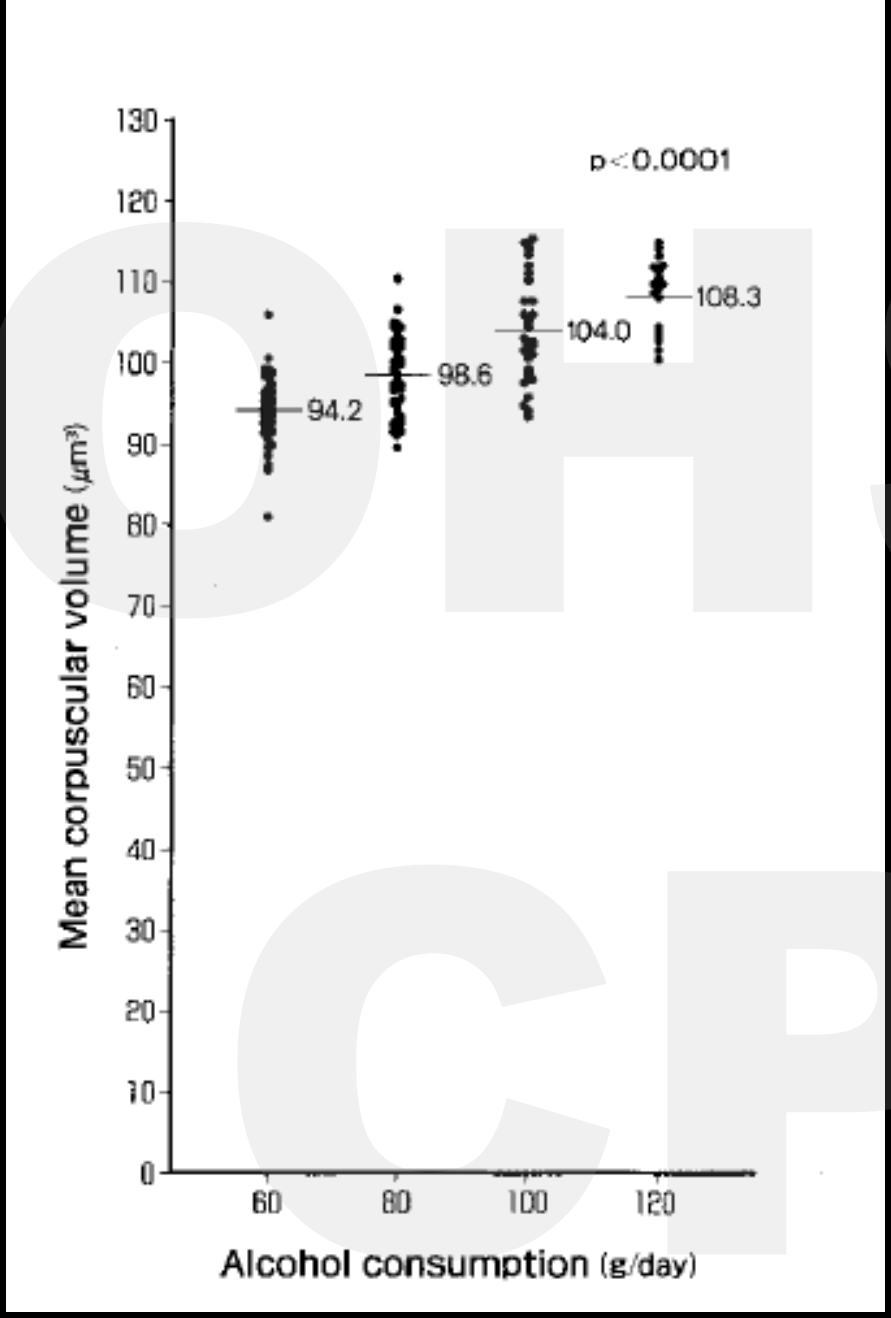
Alcohol

- Leads to rise in MCV
  - Abnormal lipid metabolism
  - Interference folate metabolism
    - Very high Hcy
- Can be as high as 120 fl
- Need good alcohol history

OHSU CPD



Lancet 1974



A Standard Drink in the US

= 18 mL or 14 g of alcohol

Beer	Wine	Liqueur	Spirit
(5% ABV)	(12% ABV)	(24% ABV)	(40% ABV; 80 proof)
12 oz (355 mL)	5 oz (~150 mL)	2.5 oz (~75 mL)	1.5 oz (~45 mL)

** ABV = Alcohol By Volume*

©Nutrientsreview.com

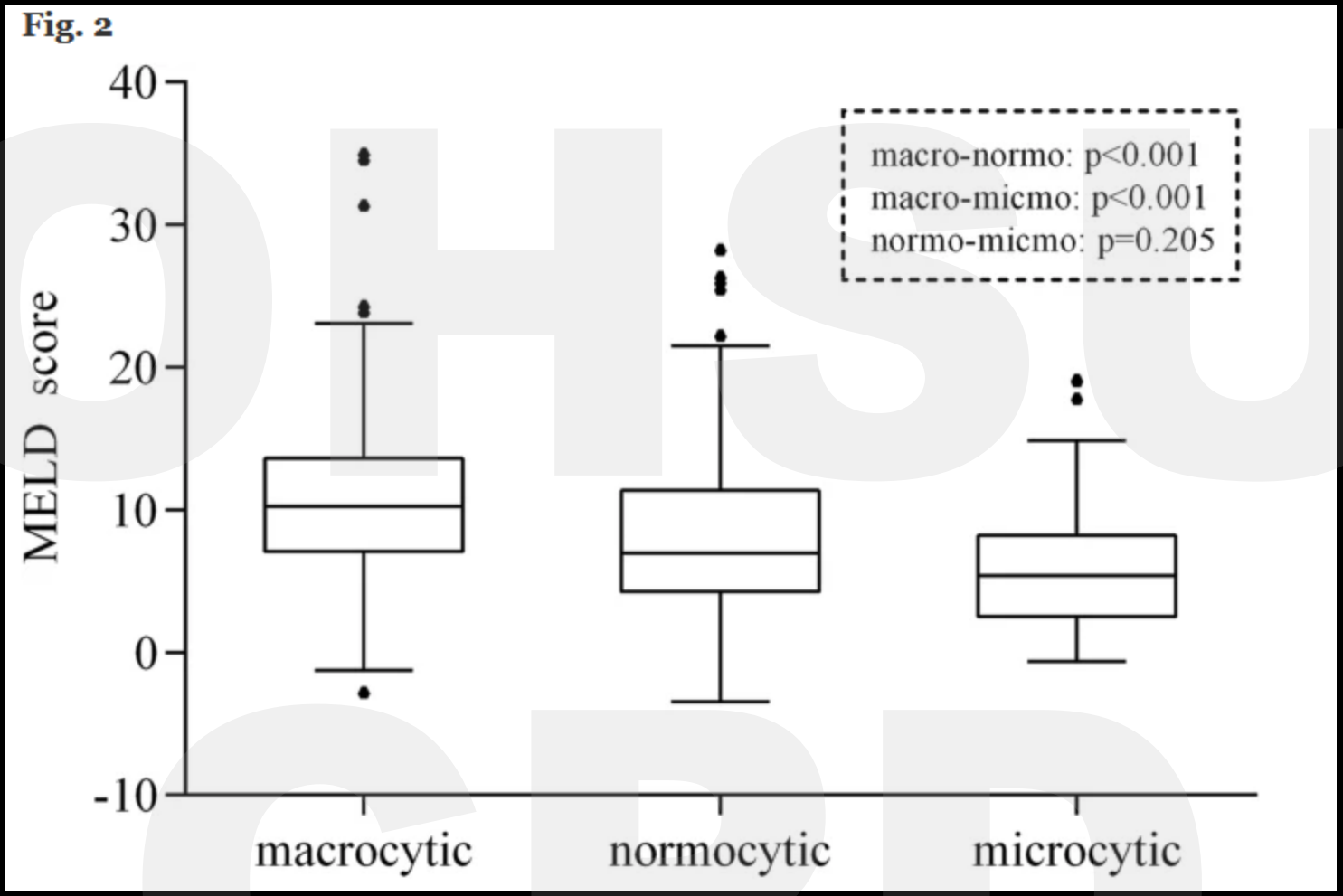
. (J Lab Clin Med 2001;138:332-7)

Liver Disease

- Independent of alcohol
- Abnormal lipids in membrane
- Related to severity of liver disease
- Can be masked by iron deficiency

OHSU CPD

Fig. 2

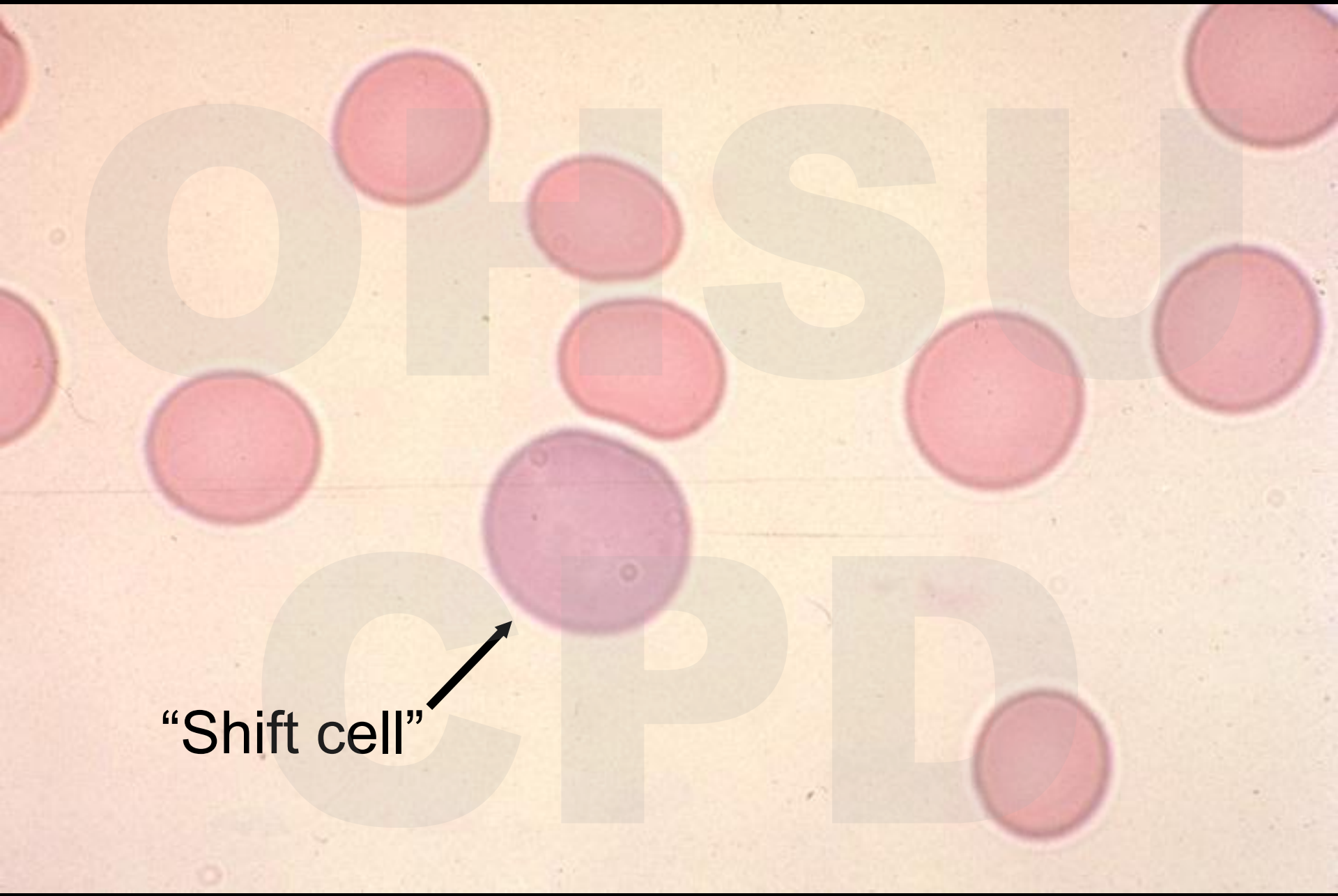


BMC Gastroenterology **18**, Article number: 161 (2018)

Reticulocytosis

- MCV of a reticulocyte is ~ 160 fl
- Brisk reticulocytoses can lead to high MCV

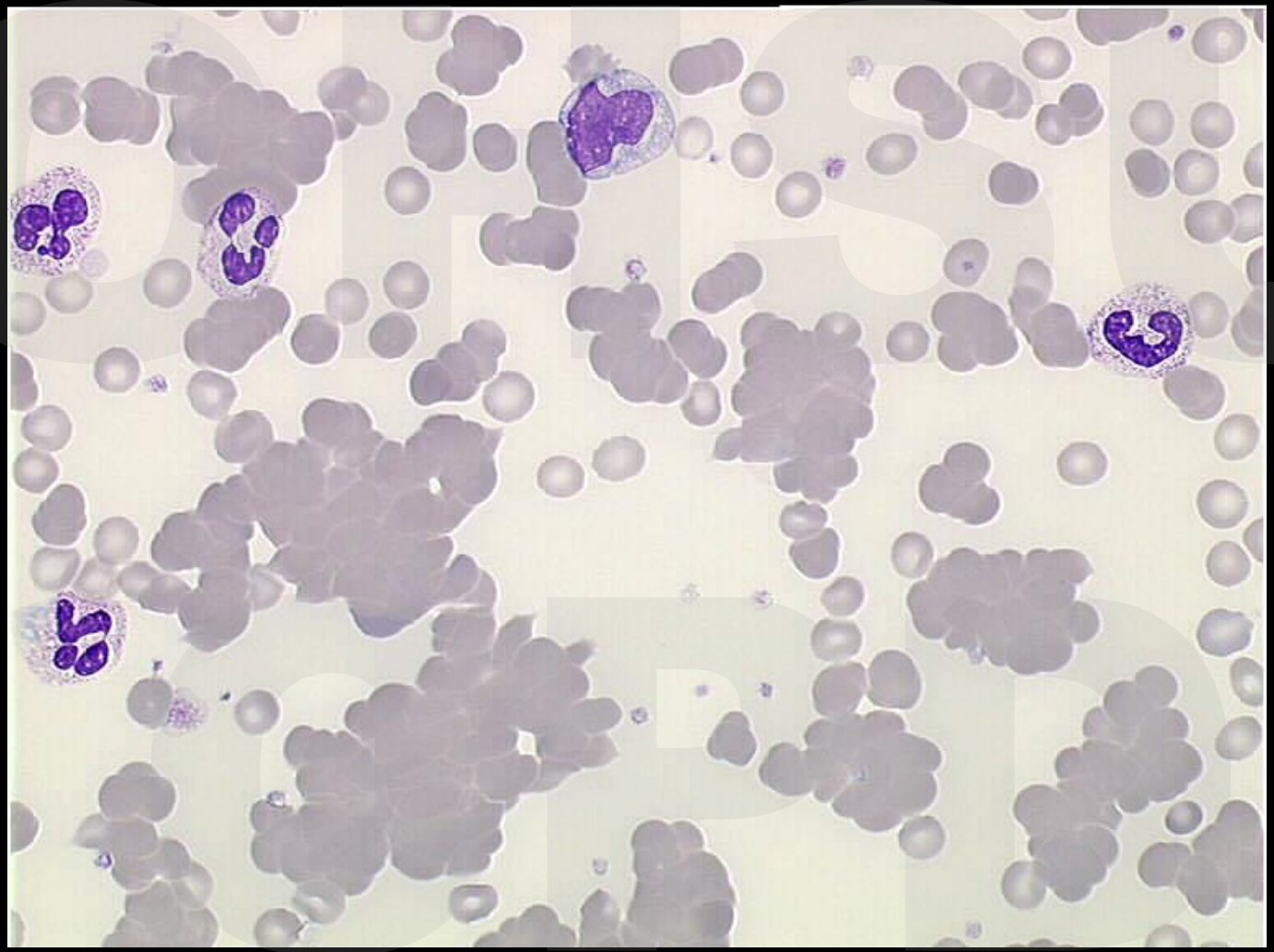
OHSU
CPD


"Shift cell"

Cold Agglutinins

- Spurious macrocytosis
- Red cells clumped together
- Often crazy MCVs (180 fl)

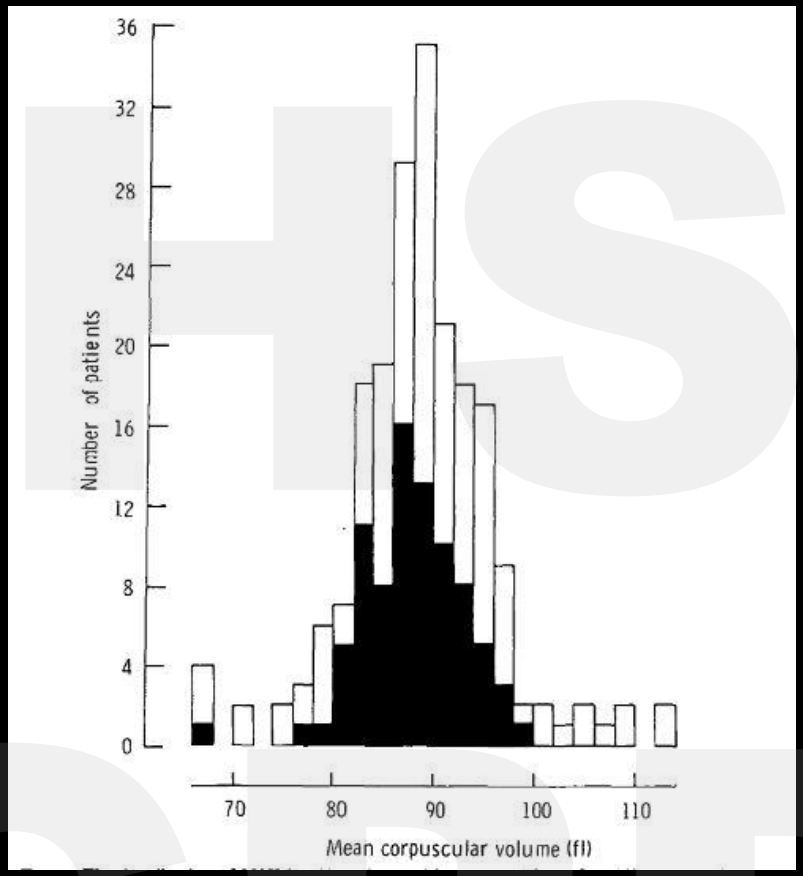
OHSU CPD



Thyroid Disease

- Usually mild macrocytosis (~ 100 fl)
- > 100 fl usually concomitant B12 deficiency

OHSU
CPD



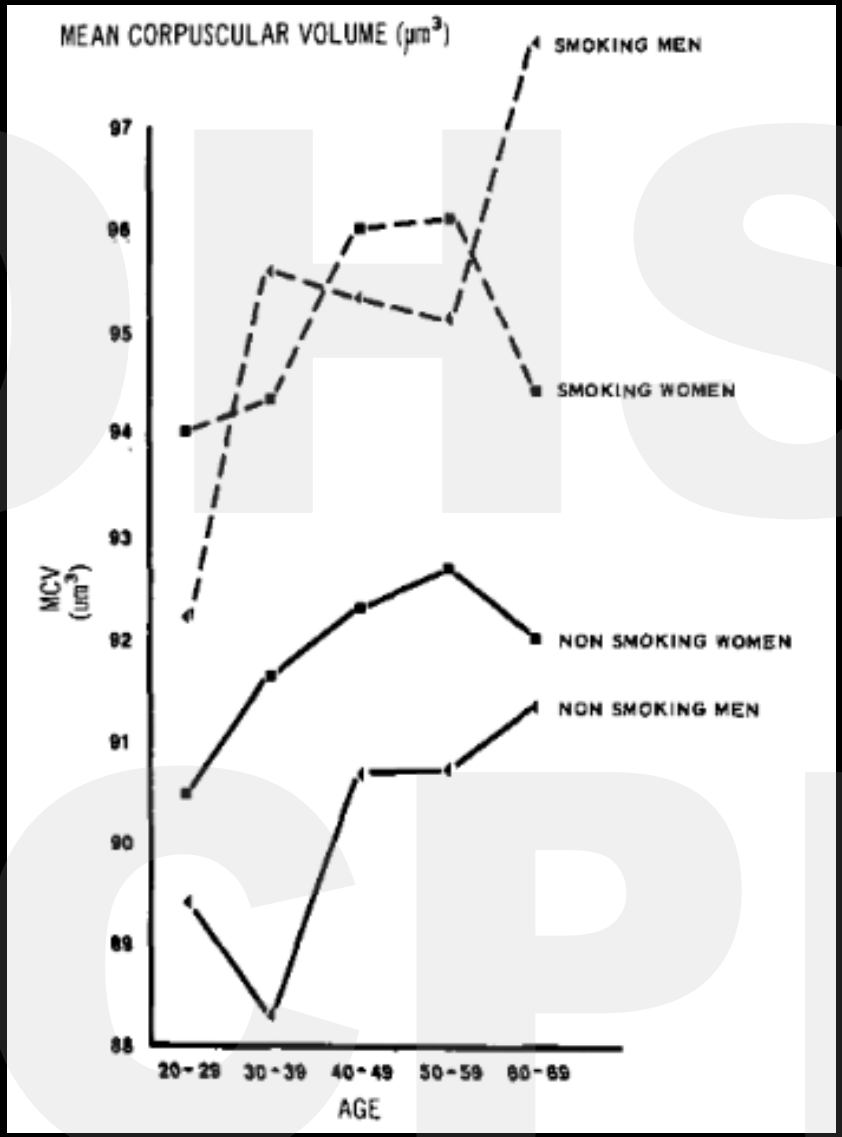
*** All patients MCV > 100 also had B_{12} deficiency**

QJM: 45:101, 1979

Smoking

- Smoking leads to marrow stress
- Aldehydes and other smoking toxins leading to RBC damage
- Rare > 100 fl

OHSU CPD

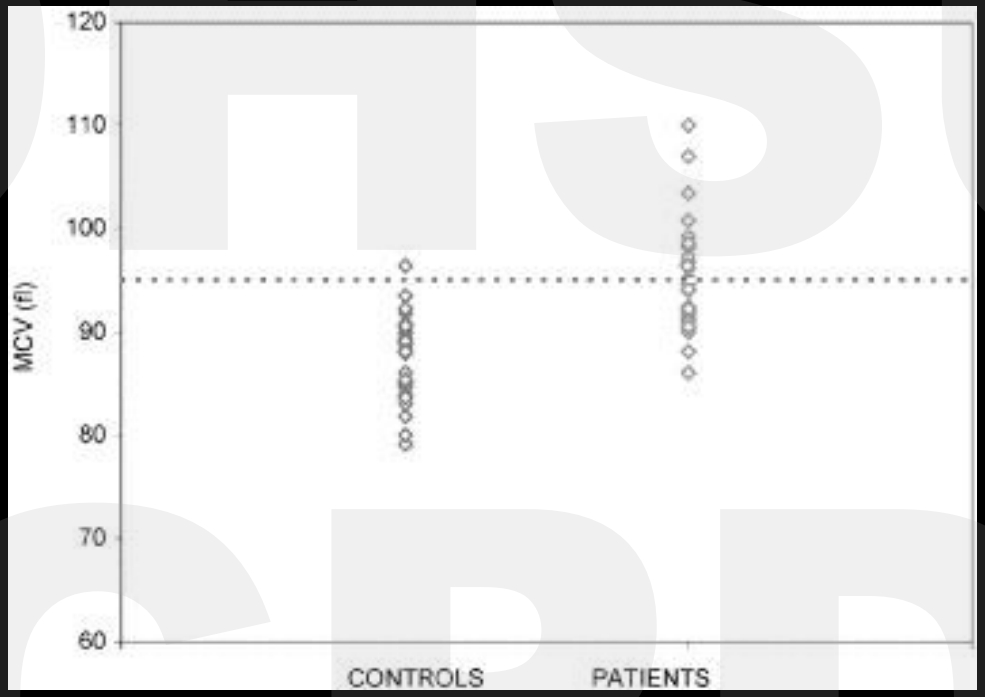


Am J Clin Path 63:35–44, 1975

COPD

- Strong association with hypoxic COPD and high MCV
- Increased reticulocytosis

OHSU
CPD



Resp Med 98:1117, 2004

MGUS

- 5% can have macrocytosis (100-109 fl)
- No relationship to size of monoclonal protein
- Not prognostic indicator

OHSU CPD


IN GOD WE TRUST
LIBERTY
2002
S

Copper Deficiency

- Increasing reports
- Severe anemia
- Neutropenia can be severe
- Marrow resembles MDS
- Seen in:
  - TPN
  - Bariatric surgery
  - Zinc toxicity
  - No obvious reason

OHSU CPD

Copper Deficiency

- Neuro defects
  - Ataxic and sensory loss
- Classic heme picture
  - Neutropenia
  - Anemia (often macrocytic)
  - Normal platelets

OHSU CPD

Diagnosis

- Copper level
- Therapy
  - Copper

OHSU CPD

Evaluation of Macrocytosis

- **Key Question!**
  - **Is the patient anemic?**

OHSU CPD

Benign Macrocytosis

- Most patients with macrocytosis and normal blood counts have no underlying hematological disease
- Can be familial

OHSU CPD

Benign Macrocytosis

- My work-up (not anemic)
  - History
  - Evaluate nutrients
    - MMA/Hcy/copper
  - Check TSH
  - Check reticulocyte count

OHSU CPD

Evaluation of Macrocytosis

- If anemic
- History
- MMA/Hcy/Copper
  - Older SPEP/Light chains
- TSH
- Retic count
- If worrisome ->marrow/genetics

OHSU CPD

Is Aspirin Safer than Warfarin?

- Aspirin often given to afib or DVT patients because it is perceived to be “safer”
- But is it???

OHSU CPD


FARBENFABRIKEN vorm. FRIEDR. BAYER & Co
250 GR
ELBERFELD.
ASPIRIN

BAYER
PHARMACEUTICAL PRODUCTS.

Send for samples and Literature to

FARBENFABRIKEN OF ELBERFELD CO.

40 STONE STREET, NEW YORK.

BAYER
PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

HEROIN

The Sedative for Coughs,

HEROIN HYDROCHLORIDE

Its water-soluble salt.

You will have call for them. Order a supply from your Jobber.

Write for literature to

FARBENFABRIKEN OF ELBERFELD CO.

40 Stone Street, New York,

SELLING AGENTS

The Treatment of Anemia.

By W. F. King, M.D.,
Columbus City, Ind.

During the past year I have been employing Ferro-Somatose in a number of selected cases, with gratifying results in every case. In all cases of anemia in which there is a pronounced loss of hemoglobin, in cases of weakness and emaciation, so often found in neurasthenics, and following the acute infectious diseases, Ferro-Somatose has proven the remedy par excellence, improving the appetite, increasing the number of red blood corpuscles, and producing a rapid and well marked increase in weight. The following cases are of interest:

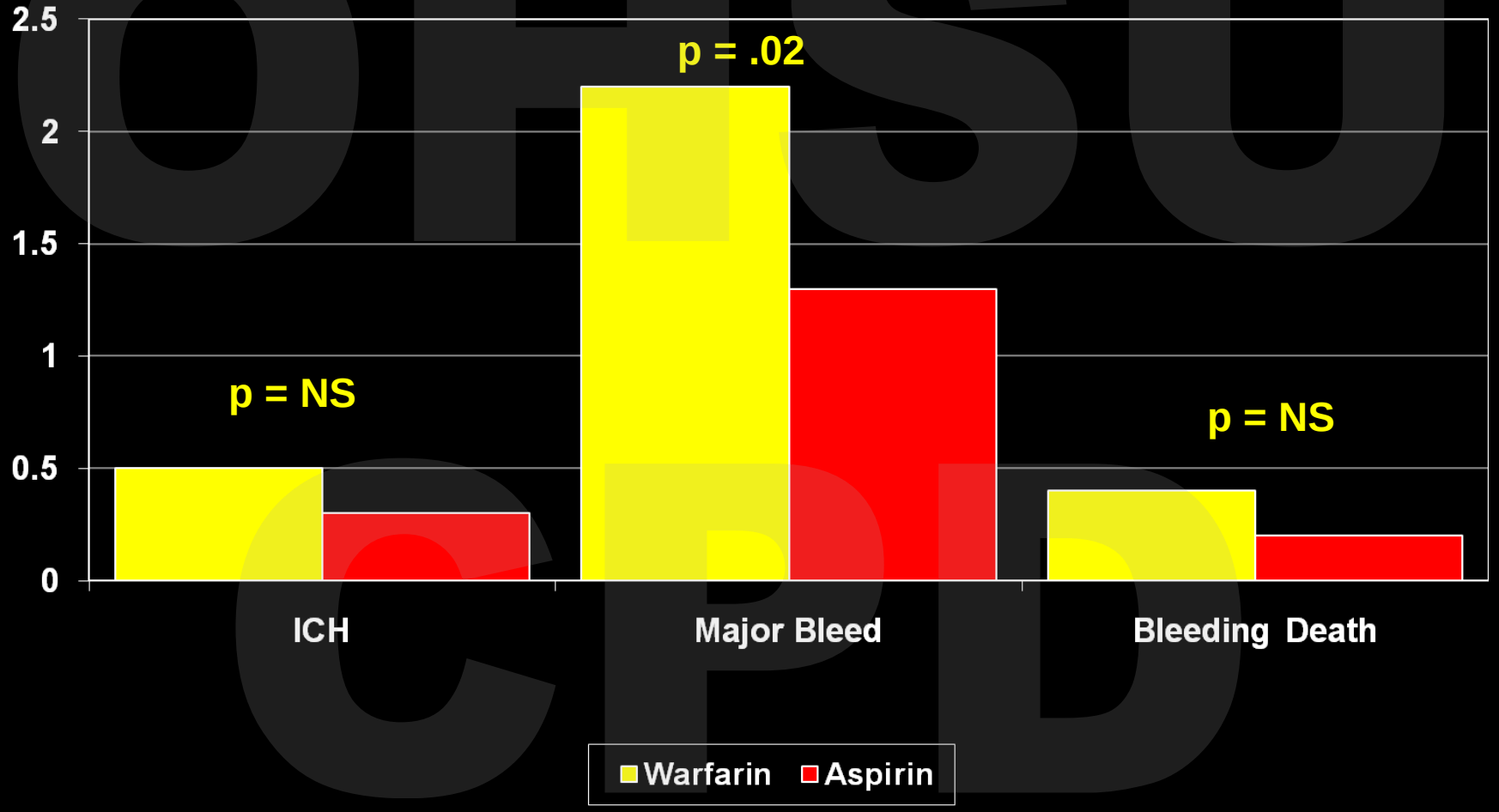
Summing up the experience of these five cases, Ferro-Somatose is certainly indicated in all cases of anemia, chlorosis, and in convalescence from acute infectious diseases. Care and judgment in selection of cases, with appropriate supplementary treatment, will be followed by gratifying results, and will give to Ferro-Somatose the first place in the list of chalybeate preparations.—*New Albany Medical Herald*, June, 1901.

Aspirin vs Warfarin

- No increase in ICH

OHSU
CPD

Warfarin vs Aspirin



OHSU CPD

BAFTA

- N = 973
- All over 75 year of age (mean 81.5)
- RCT
  - Warfarin 2-3 vs aspirin 81mg/day
  - f/u 2.7 years
- Lancet 2007; 370:493-503, 460-461

OHSU CPD

BAFTA: Bleeding Complications

End point	Warfarin	Aspirin	Hazard ratio (95% CI)
Major extracranial hemorrhage (%/yr)	1.4	1.6	0.87 (0.43–1.73)
All major hemorrhages (%/yr)	1.9	2.2	0.96 (0.53–1.75)

Mant JW et al. *Lancet* 2007; 370:493-503, 460-461.

OHSU CPD

Hazard Ratios For Bleeding Compared To Aspirin

Drug/combination	Adjusted hazard ratio	95% CI
Clopidogrel	1.33	1.11–1.59
VKA	1.23	0.94–1.61
Aspirin/clopidogrel	1.47	1.28–1.69
Aspirin/VKA	1.84	1.51–2.23
VKA/clopidogrel	3.52	2.42–5.11
VKA/clopidogrel/aspirin	4.05	3.08-5.33

Sørensen R et al. *Lancet* 2009; 374:1967-1974.

Aspirin vs Warfarin

- 52% reduction in ischemic stroke with warfarin
  - History of stroke ARR = 6%/yr
  - No history of stoke ARR = 1.2%/yr
  - Low risk of stroke ARR = 0.4%/yr
- 1.7 fold increase in hemorrhage
  - Absolute increase of 0.3%/yr

OHSU CPD

Aspirin and Stroke Severity

- Aspirin does not reduce risk of disabling stroke
  - 22-->13% (NS)
- Warfarin does reduce fatal stroke
  - 0.5-->0.2 events/yr

OHSU CPD

AHA Guidelines 2014

- **No** studies, with the exception of the SPAF (Stroke Prevention in Atrial Fibrillation)-1 trial, show benefit for aspirin alone in preventing stroke
- **Ineffective** in preventing strokes in those >75 years of age
- Did **not** prevent severe strokes
- Has **not** been studied in a population at low risk of AF
- **NOT** recommended

Aspirin vs Apixaban

- RCT
  - Aspirin 81-324mg
  - Apixaban 5mg bid
- More effective than aspirin
  - RR 0.45 (0.32-0.62)
- Same risk of bleeding
  - RR 1.13 (0.74-2.05)
  - Intracranial hemorrhage 0.85 (0.38-1.90)

OHSU CPD

ASA vs Rivaroxaban

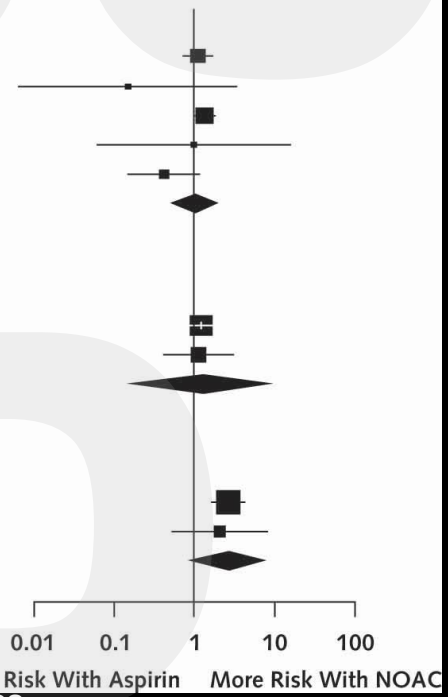
	Rivaroxaban 20mg (1107)	Rivaroxaban 10mg (1127)	Aspirin 100mg (1131)
Recurrent VTE	17 (1.5%)	13 (1.2%)	50 (4.4%)
Any Bleeding	196 (17.8%)	160 (14.2%)	143 (12.8%)
Major Bleeding	6 (0.5%)	5 (0.4%)	3 (0.3%)

N Engl J Med 2017; 376:1211-1222

OUSU CPD

Major Bleeding

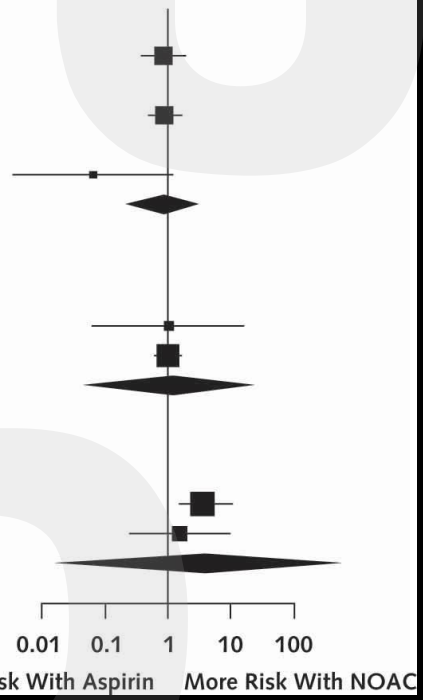
Study, Year (Reference)	Population	NOAC, *n* Events	NOAC, *n* Total	Aspirin, *n* Events	Aspirin, *n* Total	RR (95% CI)
Apixaban						
Connolly et al, 2011 (16)	AF (clinical)	44	2808	39	2791	1.12 (0.73–1.72)
Shoamanesh et al, 2020 (15)	AF (clinical) and recent ICH	0	21	1	9	0.15 (0.01–3.30)
Healey et al, 2024 (5)	AF (subclinical)	123	2015	90	1997	1.35 (1.04–1.76)
Geisler et al, 2024 (4)	Recent stroke	1	178	1	174	0.98 (0.06–15.51)
Kamel et al, 2024 (6)	Recent stroke	5	507	12	508	0.42 (0.15–1.18)
Overall			5529		5479	1.00 (0.51–1.98)
Heterogeneity: $I^2 = 40\%$; $\tau^2 = 0.1126$; $P = 0.155$						
Dabigatran						
Diener et al, 2019 (12)	Recent stroke	77	2695	64	2695	1.20 (0.87–1.67)
Chen et al, 2022 (14)	Recent stroke	8	188	7	187	1.14 (0.42–3.07)
Overall			2883		2882	1.20 (0.16–8.97)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 0.92$						
Rivaroxaban						
Hart et al, 2018 (13)	Recent stroke	62	3609	23	3604	2.69 (1.67–4.33)
Weitz et al, 2017 (17)	Venous thromboembolism	6	1107	3	1131	2.04 (0.51–8.15)
Overall			4716		4735	2.61 (0.89–7.68)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 0.71$						



Annals of Internal Medicine https://doi.org/10.7326/ANNALS-24-02132

ICH

Study, Year (Reference)	Population	NOAC, *n* Events	NOAC, *n* Total	Aspirin, *n* Events	Aspirin, *n* Total	RR (95% CI)
Apixaban						
Connolly et al, 2011 (16)	AF (clinical)	11	2808	13	2791	0.84 (0.38–1.87)
Shoamanesh et al, 2020 (15)	AF (clinical) and recent ICH	0	21	0	9	
Healey et al, 2024 (5)	AF (subclinical)	21	2015	24	1997	0.87 (0.48–1.55)
Geisler et al, 2024 (4)	Recent stroke	0	178	0	174	
Kamel et al, 2024 (6)	Recent stroke	0	507	7	508	0.07 (0.00–1.17)
Overall			5529		5479	0.80 (0.23–2.79)
Heterogeneity: $I^2 = 33\%$; $\tau^2 < 0.0001$; $P = 0.22$						
Dabigatran						
Chen et al, 2022 (14)	Recent stroke	1	188	1	187	0.99 (0.06–15.79)
Diener et al, 2019 (12)	Recent stroke	32	2695	32	2695	1.00 (0.61–1.63)
Overall			2883		2882	1.00 (0.04–22.41)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 1.00$						
Rivaroxaban						
Hart et al, 2018 (13)	Recent stroke	20	3609	5	3604	3.99 (1.50–10.63)
Weitz et al, 2017 (17)	Venous thromboembolism	3	1107	2	1131	1.53 (0.26–9.15)
Overall			4716		4735	3.20 (0.02–540.40)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 0.36$						



Annals of Internal Medicine https://doi.org/10.7326/ANNALS-24-02132

Aspirin: Bottom Line

- Limited to no effectiveness
- Not effective in older patients
- Not effective in preventing disabling strokes
- Less effective for DVT prevention 1° and 2 °
- Not the safer choice
- Not recommended!


RIP
Aspirin
for
Afib/DVT

Standard Heparin Is A Barbaric Relic Of An Ancient Era

- LMWH
  - Better outcomes in inpatients
  - Faster to therapeutic levels
  - Less heparin induced thrombocytopenia
  - Can use in patients who may get procedures

OHSU CPD

Meta-analysis of LMWH inpatient therapy

OHSU CPD

Recurrent DVT day 1-15

LMWH	SH	
3/365 (0.8)	12/371 (3.2%)	RR 76%

Recurrent DVT day 16 -90

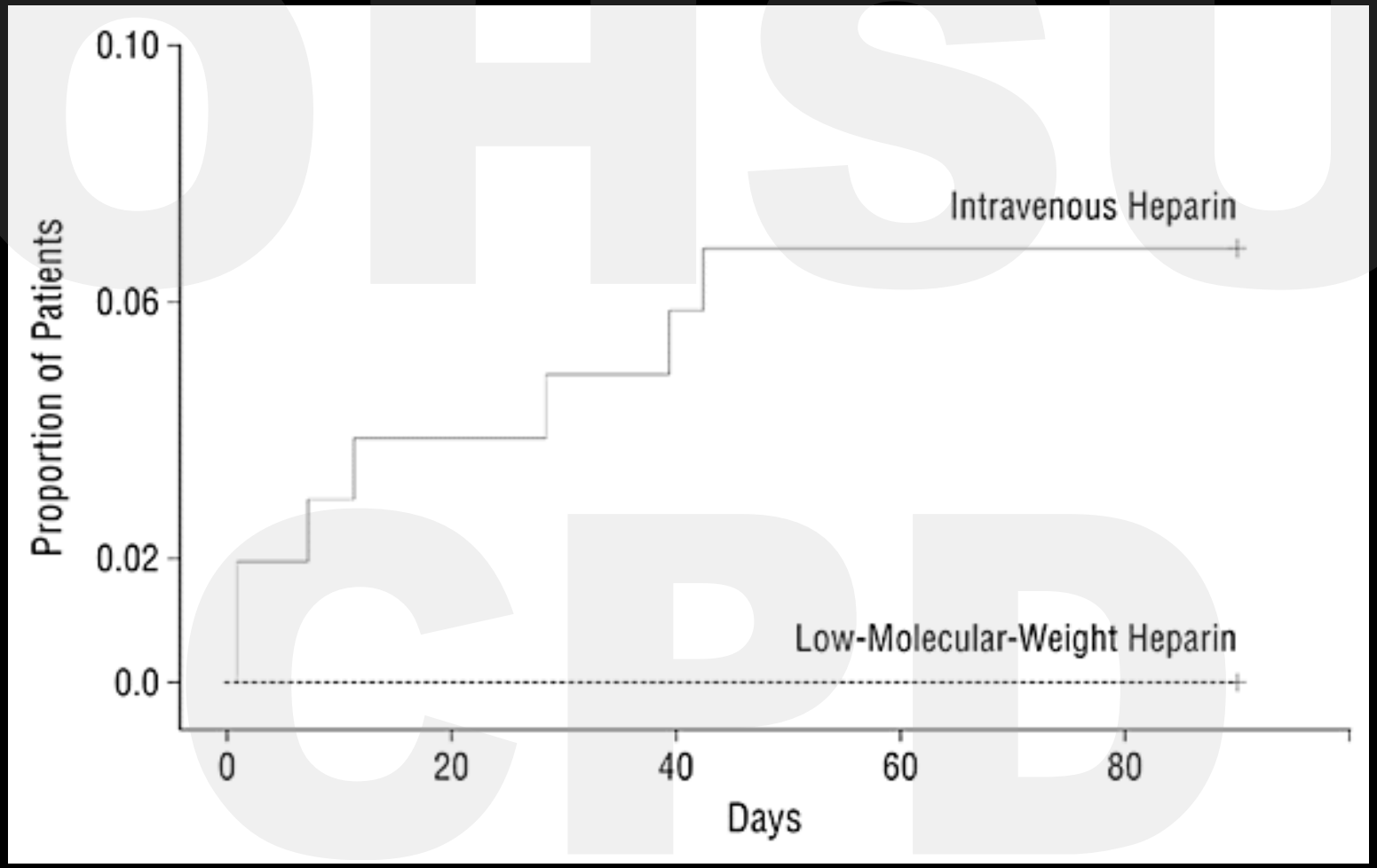
LMWH	SH	
7/365 (1.9%)	12/371 (3.2%)	RR 61%

Bleeding

LMWH	SH	
12/394 (3.0%)	27/402 (6.7%)	RR 58%

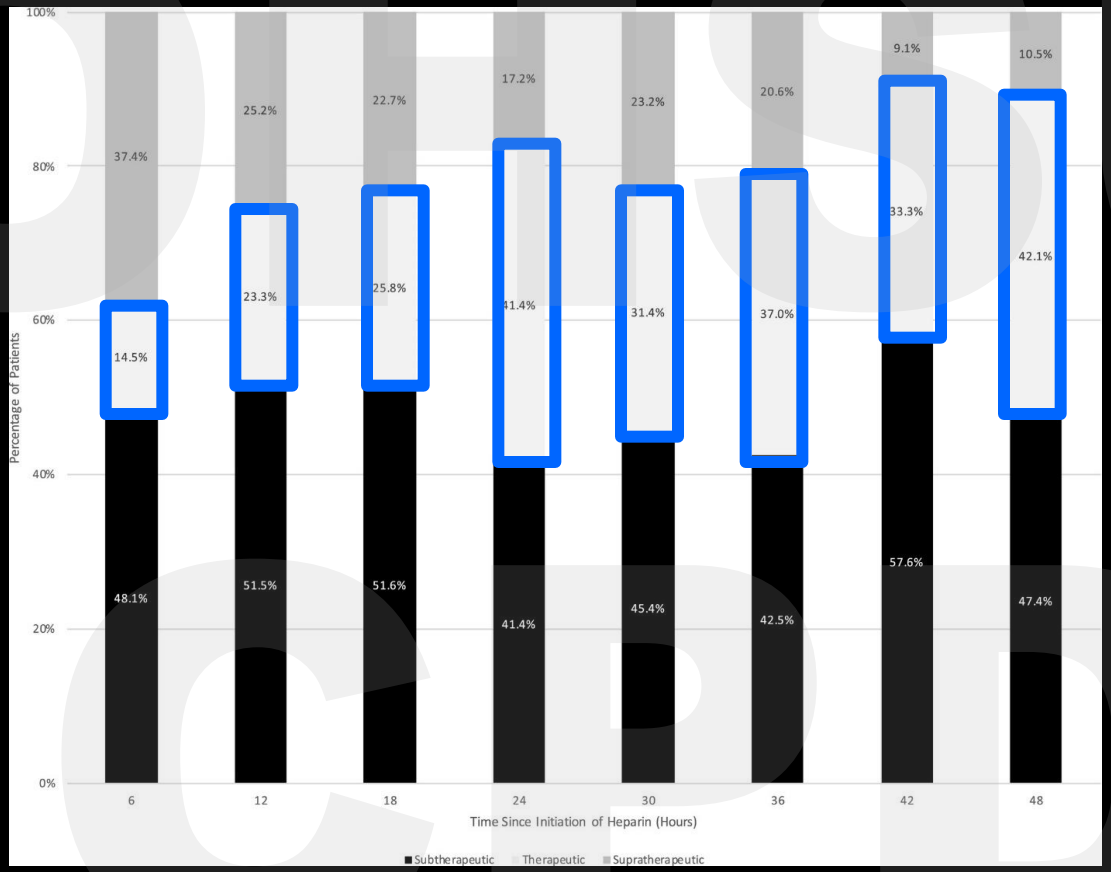
Am J Med. 1996 Mar;100(3):269-77

LMWH vs UFH: Therapy of Pulmonary Embolism



Arch Intern Med. 2000;160(2):229-236

Analysis of PTT in Patients With PE First 48 Hours of Anticoagulation With UFH



Academic Emergency Medicine, 27: 117-127, 2020

PERT Consortium Handbook of PE 2024

	Mortality	Acute recurrent VTE	Late recurrent VTE	Complications
Lensing et al. (1995)	Favors LMWH		Favors LMWH	Favors LMWH
Siragusa et al. (1996)	Favors LMWH	Favors LMWH	Favors LMWH	Favors LMWH
Gould et al. (1999)	Favors LMWH		Nonsignificant	Favors LMWH
Dolovich et al. (2000)	Favors LMWH		Nonsignificant	Nonsignificant
Quinlan et al. (2004)		Nonsignificant	Nonsignificant	Nonsignificant
Castellucci et al. (2014)			Favors LMWH	Nonsignificant
Robertson and Jones (2017)	Nonsignificant	Favors LMWH	Favors LMWH	Favors LMWH

Low molecular weight heparin is preferred due to an increasing body of evidence suggesting lower rates of thromboembolism recurrence and lower rates of hemorrhagic events in patients treated with low molecular weight heparin compared to unfractionated heparin

LMWH

- Can be used before procedures
- Can be used patients with renal issues
- No issues in pregnancy

OHSU CPD

Iron

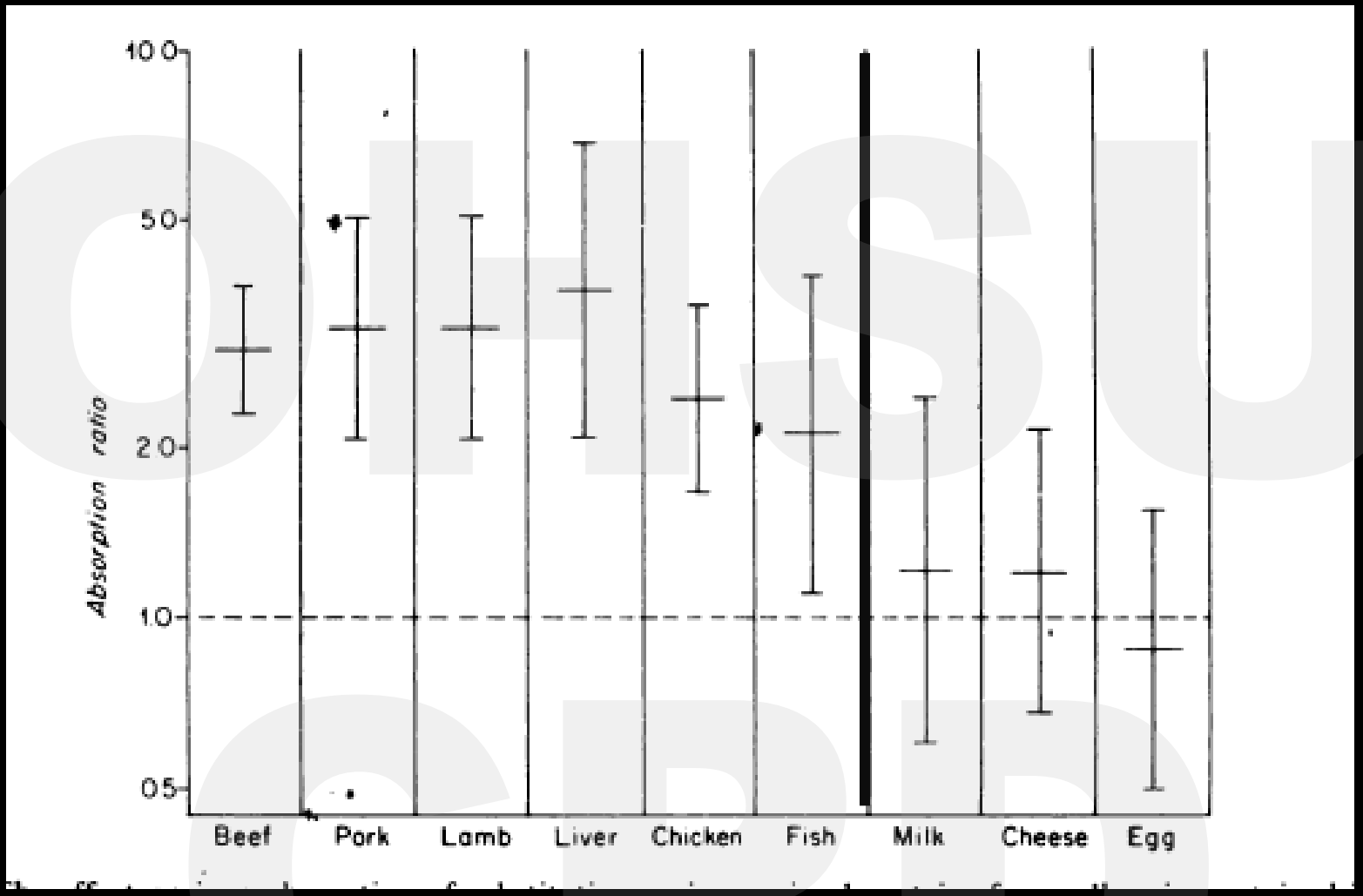
- TID? Every day? Every other day?

OHSU
CPD

Dietary Iron

- Heme iron 10x better absorbed than non-heme iron
- Meat protein improves iron absorption

OHSU CPD



Am J Clin Nutr **August**
1976 vol. 29 no. 8
859-867

Dietary Iron

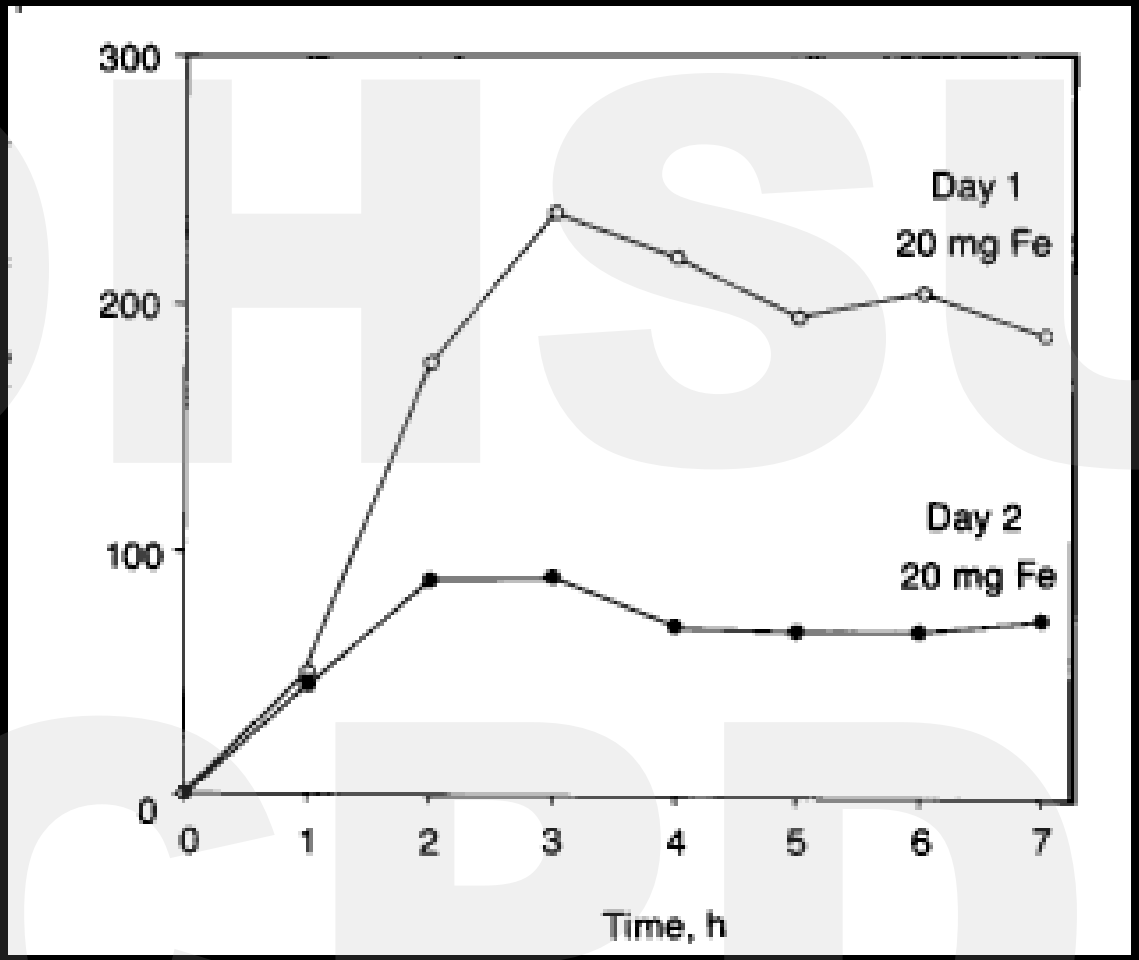
- Calcium, fiber can block iron absorption
  - Overcome by vitamin C
- Tea decreases 75-80%
- Coffee decreases 60% (5 oz!)

OHSU CPD

Oral Iron Pills

- Gut can only absorb a limited amount of iron
- Maxed out at ~ 10mg

OHSU CPD

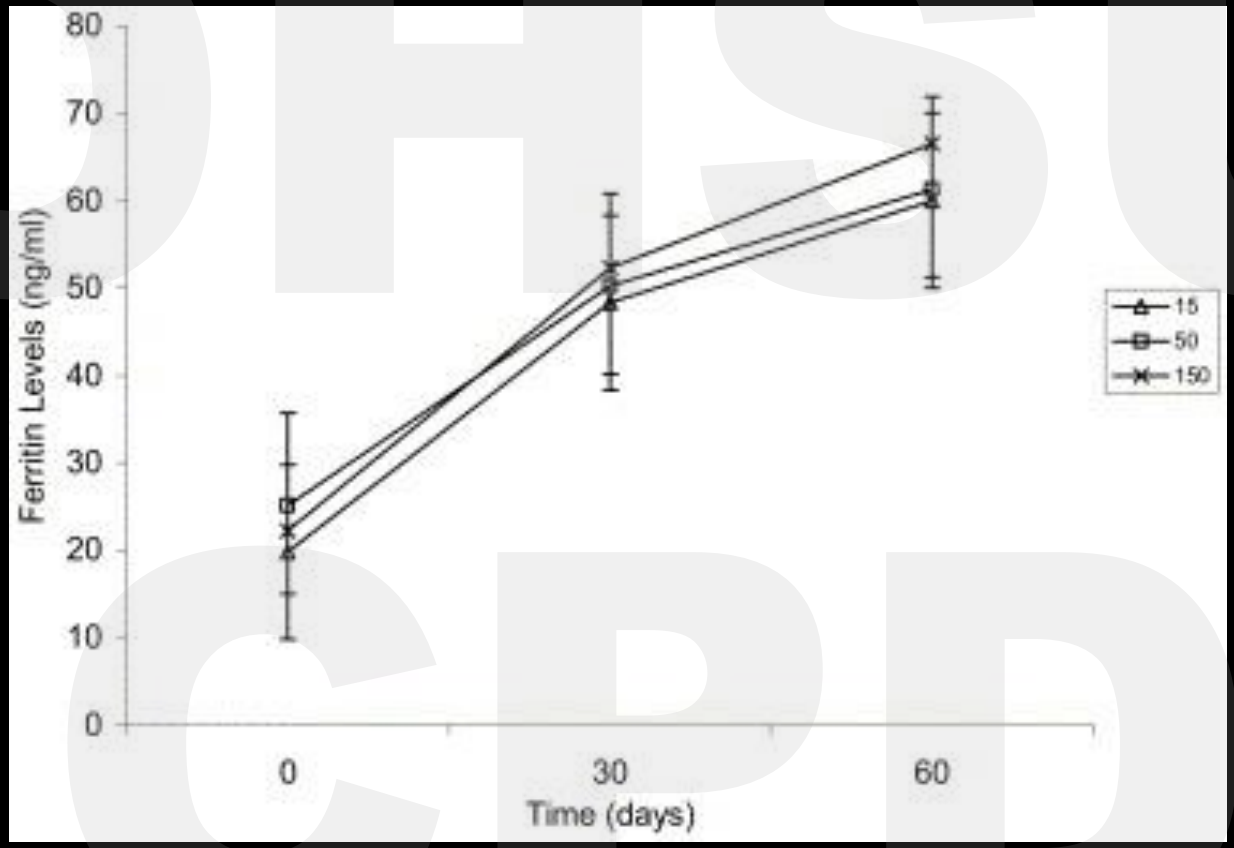


(*Arch Intern Med* 1987;147:489-491)

Hepcidin Response to Iron

OHSU CPD

15 vs 50 vs 150mg Oral Iron

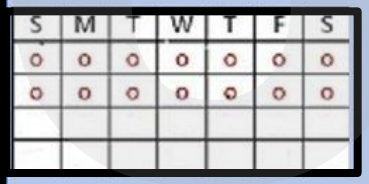


Am J Med. 2005 Oct;118(10):1142-7.

Does Alternate-Day Dosing of Oral Iron Therapy Improve Iron Absorption?

Allan S. Brett, MD, reviewing Stoffel NU et al. *Lancet Haematol* 2017 Oct 9

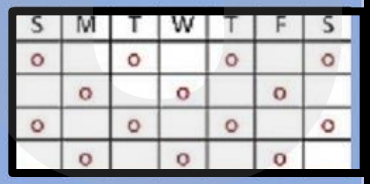
Daily Dosing 14 days



16%

131 mg

Alternate-Day Dosing 28 days



21%

175 mg

Fractional Absorption

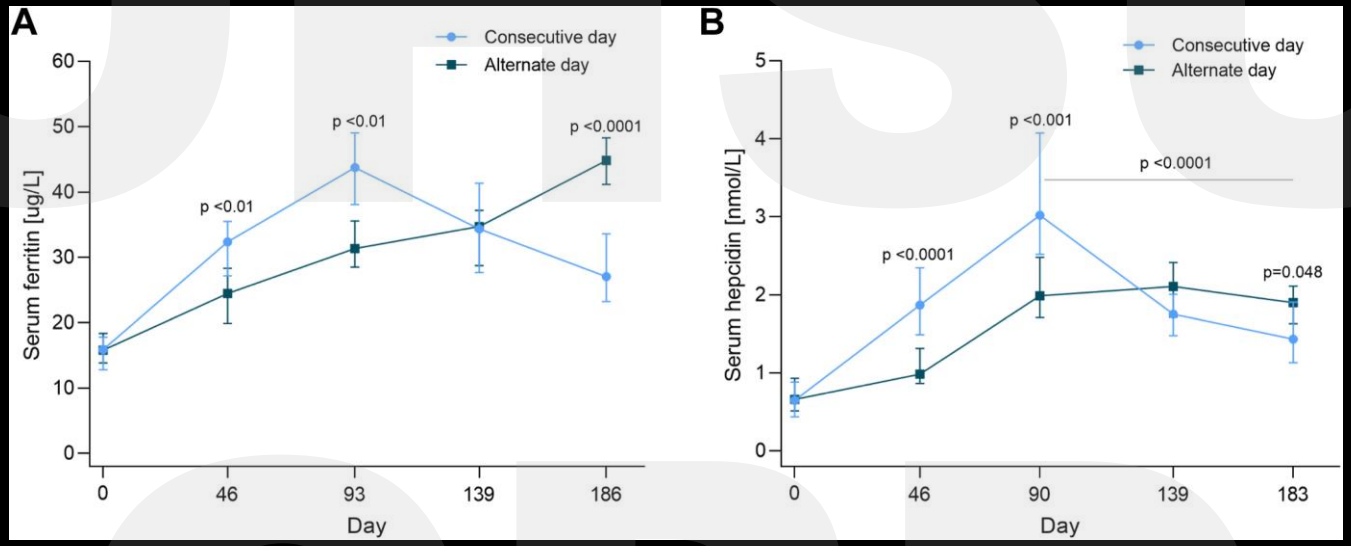
Total Absorption

Comment: Fractional absorption was better with alternate-day dosing, but total absorption would still have been better with daily dosing if that group had received 28 days of iron. Alternate-day dosing likely enhanced gastrointestinal tolerability.

NEJM Journal Watch

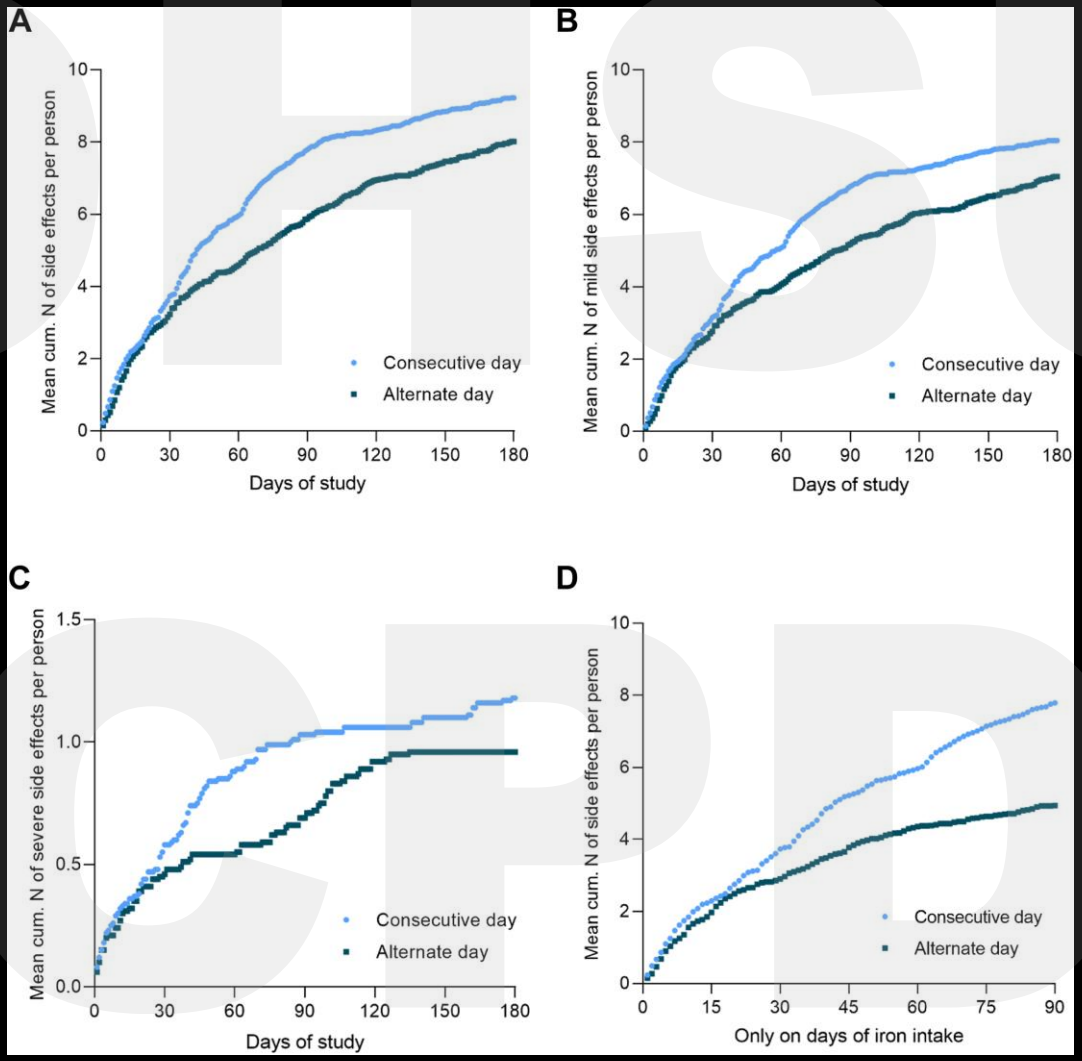
But 28 days of daily iron = 262 mg absorbed

Every day vs Every Other Day



eClinicalMedicine 2023 65DOI: (10.1016/j.eclinm.2023.102286)
Copyright © 2023 Terms and Conditions

Every day vs Every Other Day



eClinicalMedicine 2023 65DOI: (10.1016/j.eclinm.2023.102286)
Copyright © 2023 Terms and Conditions

Alternate Day Iron

- Summary of studies
- Ever day faster improvement
- Every other day better tolerated

OHSU CPD

Oral Iron Pills

- Years of studies have shown that the best iron preparation is….

OHSU
CPD

Oral Iron Pills

….the one that the patient can tolerate

- No consistent difference in any brand
- Many patients can't tolerate any pill on an empty stomach
  - Ok with meals

OHSU CPD

What I Do

- Cheapest iron pill
  - Ferrous sulfate
- Once a day with meals
  - Vitamin C 500
  - No tea or coffee for one hour after
- If intolerant can try lower dose

OHSU CPD

OHSU

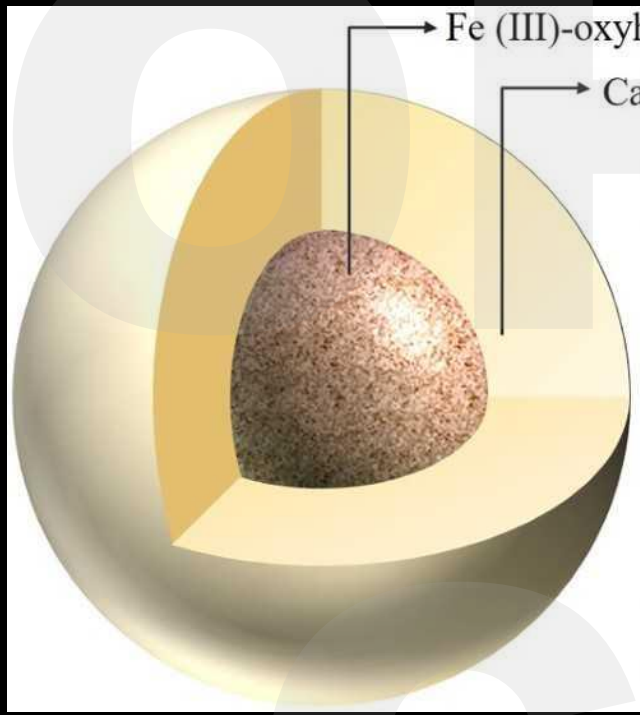
I am allergic to IV iron..

CPD

What is IV Iron

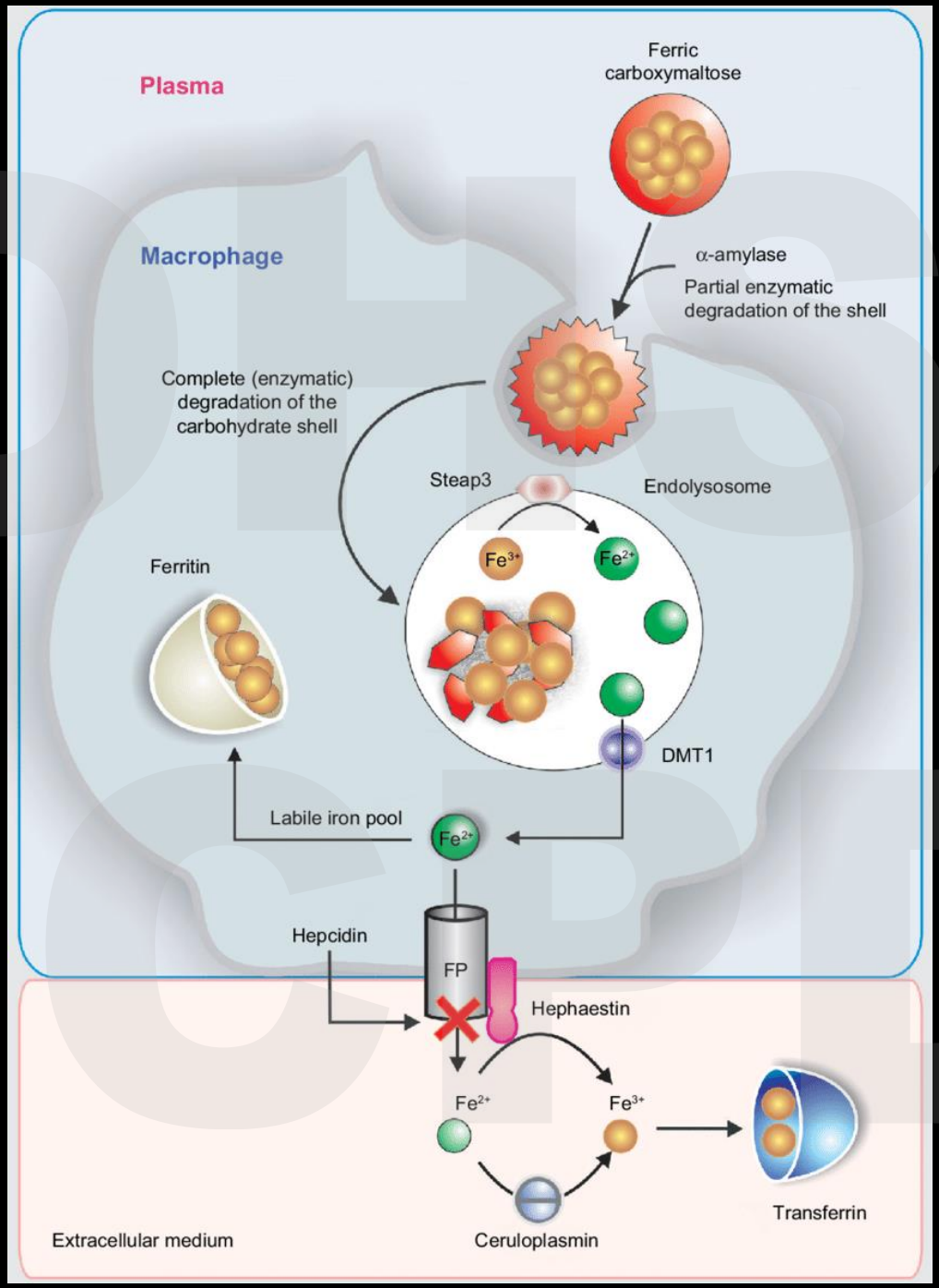
- Free iron very toxic
- IV iron preparation “coated” with carbohydrate
- Uptaken by macrophages to increase iron stores

OHSU CPD



Trade name	Carbohydrate shell
InFeD	Low molecular weight dextran
Ferrlecit	Gluconate
Venofer	Sucrose
Ferinject	Carboxymaltose
FeraHeme	Polyglucose sorbitol carboxymethyl ether
Monofer	Isomalto-oligosaccharides
Maltofer	Polymaltose

Nanomedicine . 2020 Jun;26:102178.


Plasma
Ferric carboxymaltose
Macrophage
α-amylase
Partial enzymatic degradation of the shell
Complete (enzymatic) degradation of the carbohydrate shell
Steap3
Endolysosome
Ferritin
Fe3+
Fe2+
DMT1
Labile iron pool
Fe2+
Hepcidin
FP
Hephaestin
Fe2+
Fe3+
Transferrin
Extracellular medium
Ceruloplasmin

IV Iron: Preparations

- Iron MW Iron Dextran: INFeD
- Iron Sucrose: Venofer
- Ferric Gluconate: Ferrlecit
- Ferumoxytol: FeraHeme
- Ferric Carboxymaltose: Injectafer
- Ferric Derisomaltose: Monoferric

OHSU CPD

Iron Salts

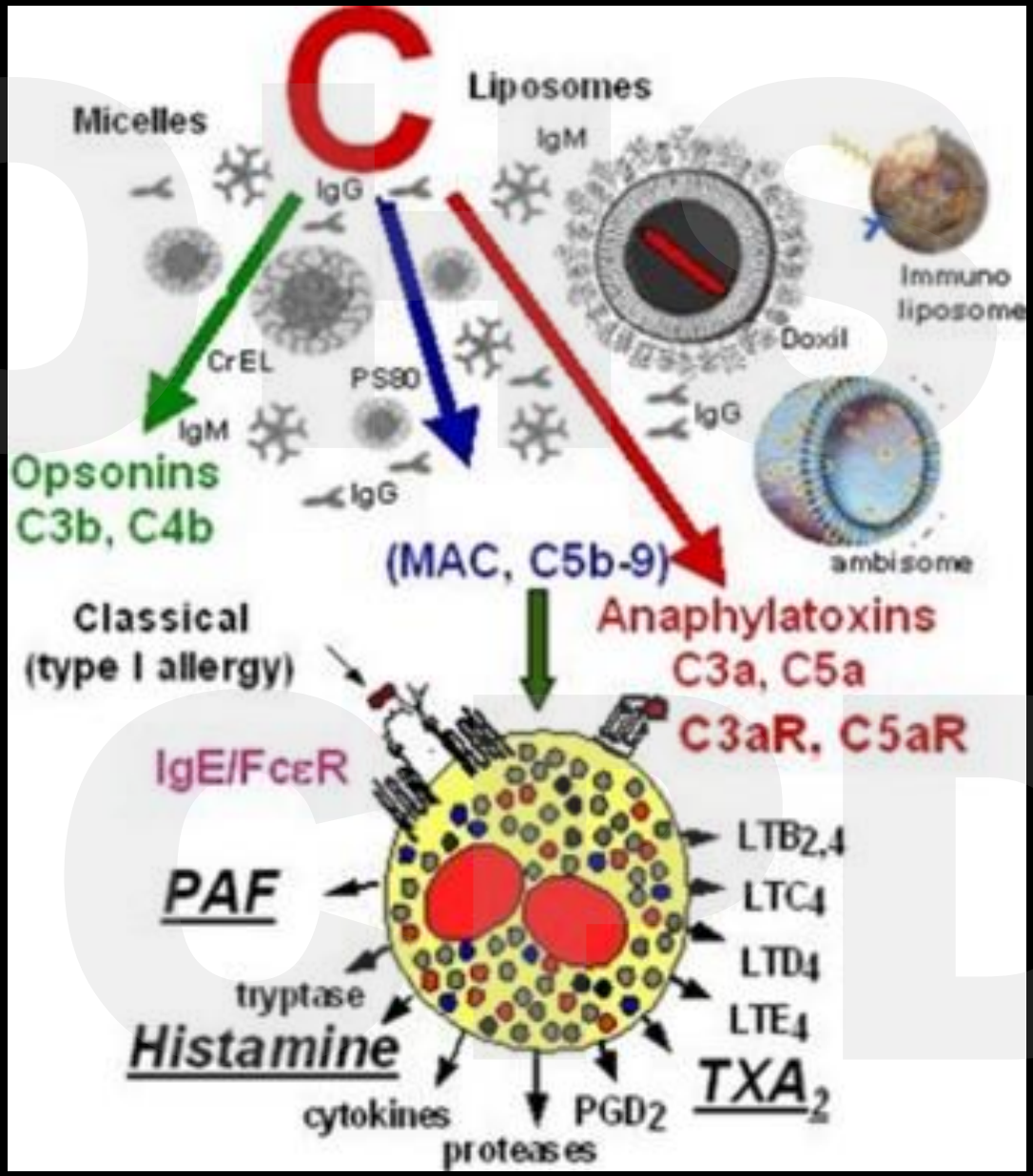
- Ferric Gluconate (Ferrlecit)
- Iron Sucrose (Venofer)
- Need multiple doses!
- Higher levels of labile iron
- Best for dialysis/EPO

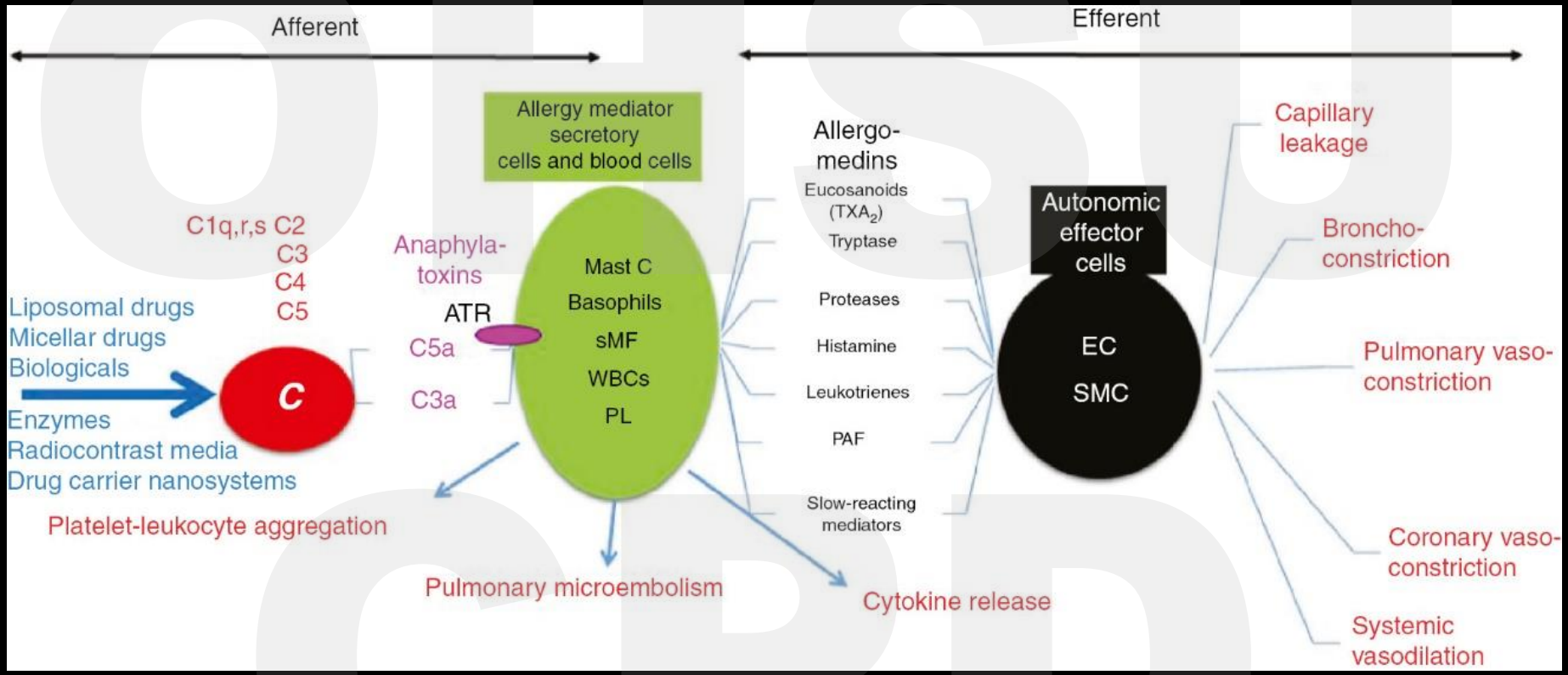
OHSU CPD

Reactions

- Complement mediated pseudo-allergy
- Drug nonspecifically activates complement
  - Similar to rituximab etc.
- True anaphylaxis very rare
  - Negative tryptase > 300 reactions

OHSU CPD

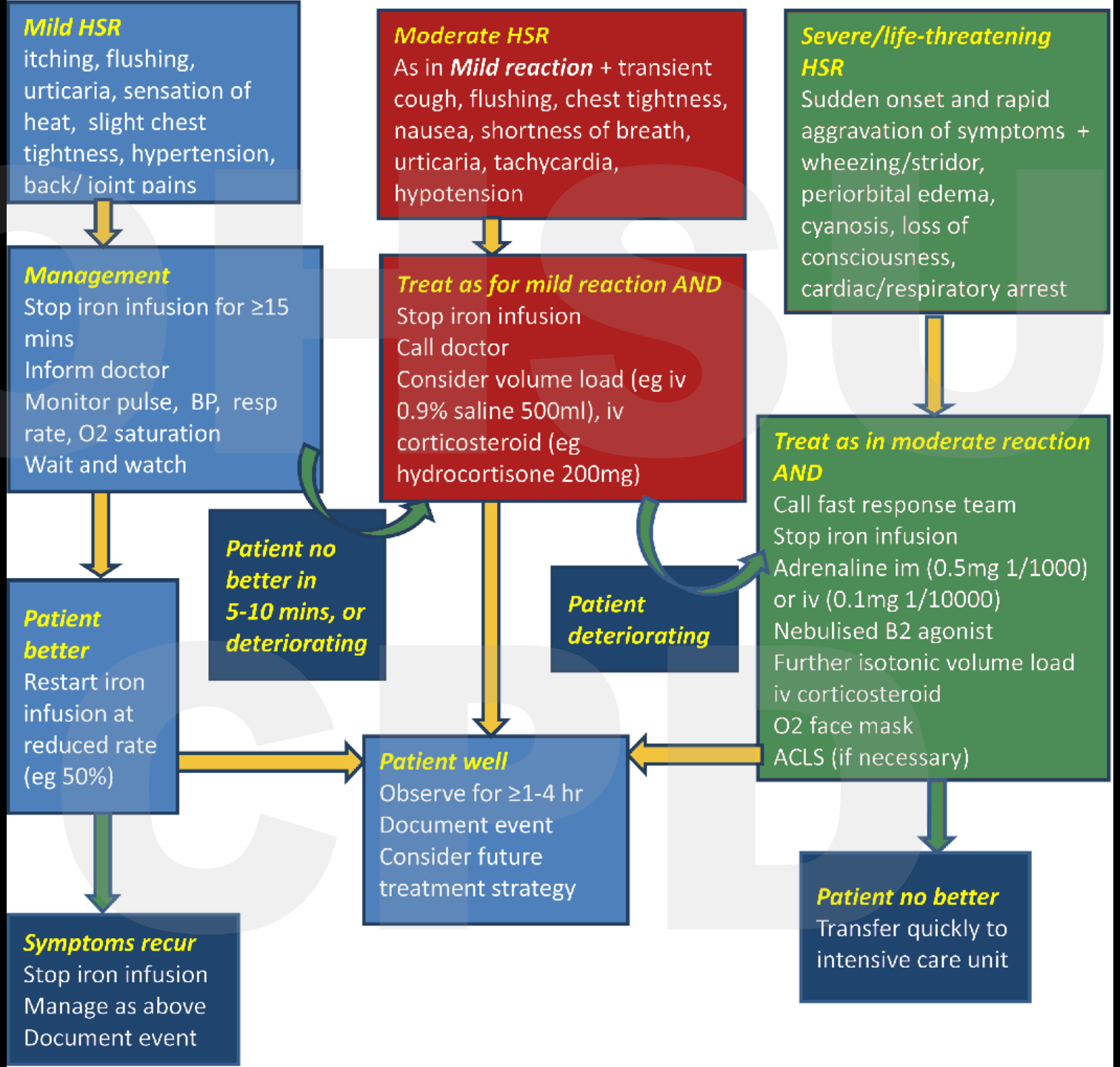

C
Micelles
IgG
CrEL
IgM
PS80
IgG
Opsonins
C3b, C4b
Liposomes
IgM
Doxil
Immuno
liposome
IgG
ambisome
(MAC, C5b-9)
Classical
(type I allergy)
IgE/FcεR
Anaphylatoxins
C3a, C5a
C3aR, C5aR
PAF
tryptase
Histamine
cytokines
proteases
PGD2
LTB2,4
LTC4
LTD4
LTE4
TXA2


Afferent
Efferent
Allergy mediator secretory cells and blood cells
Allergo-medins
Eucosanoids (TXA_2)
Tryptase
Proteases
Histamine
Leukotrienes
PAF
Slow-reacting mediators
Autonomic effector cells
EC
SMC
Capillary leakage
Broncho-constriction
Pulmonary vaso-constriction
Coronary vaso-constriction
Systemic vasodilation
C1q,r,s C2
C3
C4
C5
Liposomal drugs
Micellar drugs
Biologicals
C
Enzymes
Radiocontrast media
Drug carrier nanosystems
Anaphyla-toxins
ATR
C5a
C3a
Mast C
Basophils
sMF
WBCs
PL
Platelet-leukocyte aggregation
Pulmonary microembolism
Cytokine release

Implication

- No value test dose
- Premedication often doesn't help
  - Diphenhydramine makes things worse
- Treat as infusion reaction not allergy
- Studies show risk same with all iron preparations

OHSU CPD



Haematologica. 2014 Nov; 99(11): 1671–1676

Safety

- Minor infusion reactions common (~1-2%) but true anaphylaxis very rare
- Death rates (per 100,000 Medicare)
  - INFeD 0.8 (0-1.9)
  - Ferrlecit 6.3 (1.3 -1.4)
  - Venofer 6.6 (3.1-9)
  - FeraHeme 3.5 (0-7.8)

OHSU Data

- 35,737 infusions
- 77.5% women

- JAMA Network Open. 2022;5(3):e224488. doi:10.1001/jamanetworkopen.2022.4488

OHSU CPD

OHSU Data (Any Reaction %)

- LMW Iron Dextran 3.8
- Ferric Carboxymaltose 1.4
- Iron Sucrose 4.3
- Ferumoxytol 1.8

- Severe reactions: 1:15,000 infusions

OHSU CPD

OHSU Reactions

- Premedication no-value
  - Very confounded
- Test dose no value
- Allergy history predicted reactions

OHSU CPD

Infections

- RCT show no long term infection risk with IV iron
- Unease giving in acute infection but no data
  - Give when on ATB

OHSU CPD

Intravenous iron dosing and infection risk in hemodialysis patients: a pre-specified secondary analysis of the PIVOTAL trial

METHODS

Incident HD
Ferritin <400 µg/L
TSAT <30%

N=2141

IV iron sucrose

400 mg/mo
Unless ferritin:
>700 µg/L
or
TSAT ≥40%

Median: 264 mg/mo

Only administered
(**≤400 mg/mo**) if:
ferritin <200 µg/L
or
TSAT <20%

Median: 145 mg/mo

During infection
(investigator judgment)

RESULTS

Median follow-up 2.1 years

	Proactive high-dose		Reactive low-dose	
	46.5%	**HR: 0.98 *p*=0.80**	45.5%	Any infection (first event)
	29.6%	**HR: 0.99 *p*=0.92**	29.3%	Hospitalization for infection (first event)
	4.21%	**HR: 1.04 *p*=0.84**	3.91%	Death from infection (first event)

Risk of a first cardiovascular event was strongly associated with an infection-related event in the prior 30 days

HR: 2.83; *p*<0.0001

HR: 2.74; *p*=0.0006

CONCLUSION A proactive, higher dosing IV iron protocol did not affect infection incidence in a large HD population.

doi: 10.1681/ASN.2019090972

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Our Approach

- 1000mg of LMWID over one hour
- Test ferritin in one month
- Goal > 50ng/dl (100ng/dl)
- Monitor every 3-4 months

OHSU CPD

IV Iron Dosing

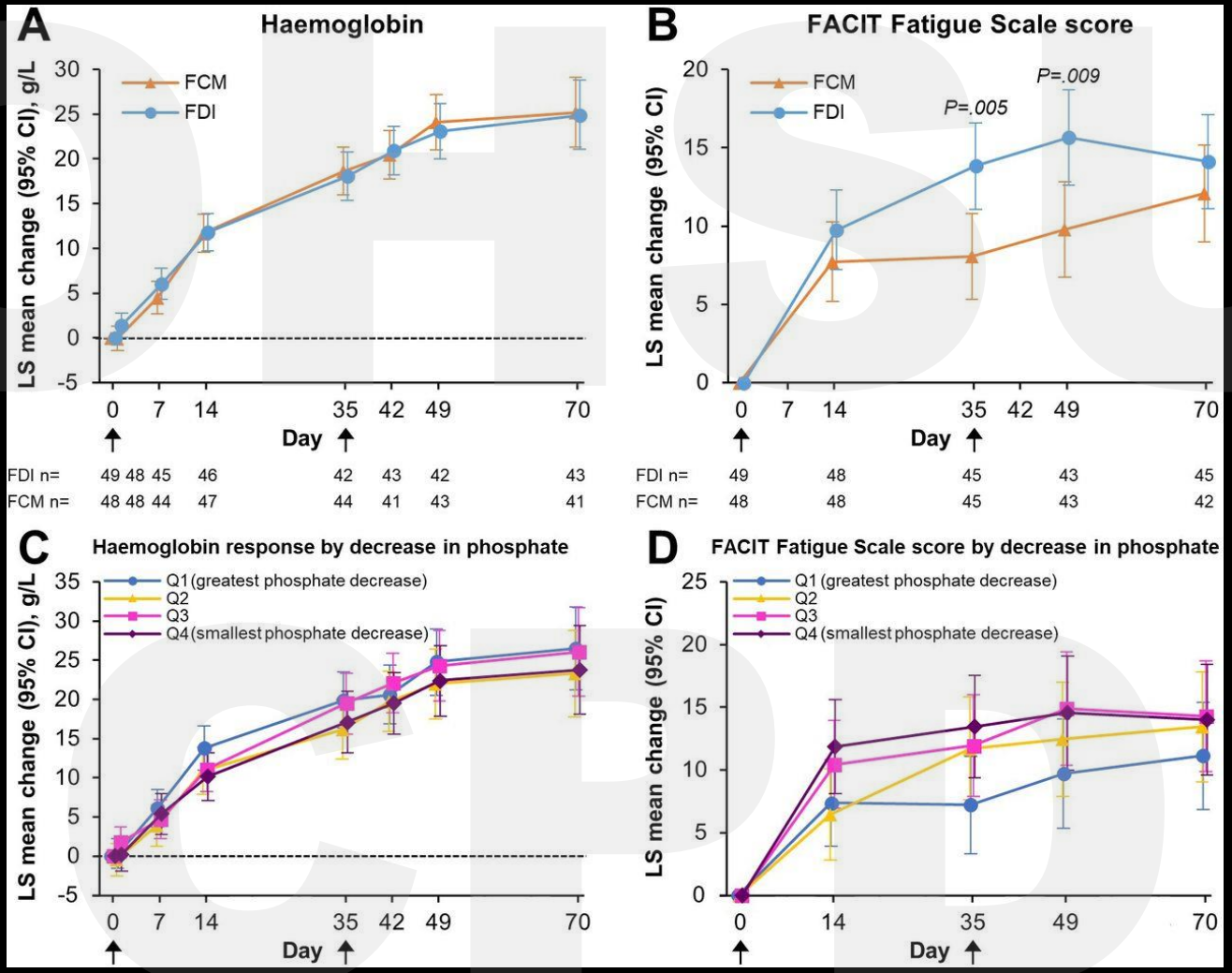
Formulation	Recommended Dose
LMW Iron dextran (InFed)	1000mg over 1 hr
Ferumoxytol (FeraHeme)	510 x 2 or 1020 over 15 min
Ferric carboxymaltose (Injectifer)	1000mg over 15 min or 750 mg x 2
Iron isomaltoside (Monoheme)	1-2000 mg over 15 min

Ferric Carboxymaltose

- High incidence hypophosphatemia
- <2.0 mg/dl: 50.8%: <1.3 mg/dl, 10.0%
- Associated with fatigue
- No longer first line therapy

OHSU CPD

Changes from baseline in haemoglobin and FACIT Fatigue Scale score, according to intravenous iron treatment (A, B), and by serum phosphate quartiles (C, D).



Heinz Zoller et al. Gut 2023;72:644-653

GUT


OHSU
CPD