Iron Deficiency Anaemia but Why?

Dr LAU Ching-wa
Specialist in Haematology
Blood Transfusion Service

3 Questions

- 1. Is anaemia incurable in my patient?
- 2. Is anaemia unavoidable in my bleeding patient?
- 3. Is transfusion improved clinical outcomes in this particular clinical scenario?

Iron **Distribution**

Total Body Iron ~ 50mg/kg BW

Blood Volume ~ 75ml/kg BW

Total Iron in RBC 1ml blood≈ 0.5mg elemental Iron

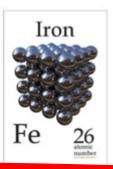
Myoglobin & Iron - containing **Enzymes**

Average Store ~10mg/kg

3000~ 4000mg 2200~ 2600mg

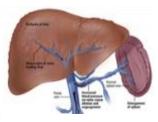
300~ 400mg 500~ 1000mg











Total Body Iron ~ 40mg/kg BW

2000~ 3000mg **Blood Volume** ~ 65ml/kg BW

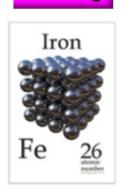
> 1300~ 1950mg

300~ 400mg 400~ 600mg

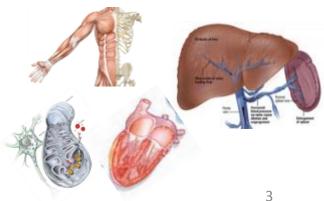
Average Store

5-10mg/kg

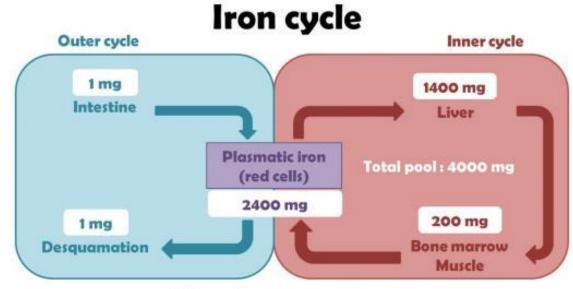








Iron Homeostasis



Absolute Iron Deficiency

- 1. Inadequate Iron Absorption
- 2. Blood Loss

(1ml blood≈0.5mg elemental Iron $\sqrt{1}$ g/dl Hb ≈200mg elemental Iron loss)

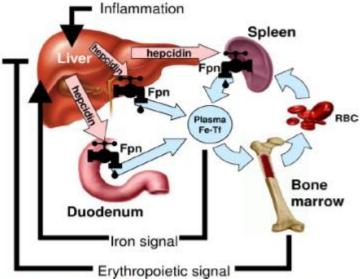


Figure 1. The role of hepcidin in Iron metabolism. Hepcidin-ferroportin interaction determines the flow of iron into plasma. Hepcidin concentration is in turn regulated by iron, erythropoietic activity, and inflammation.⁶

"Relative" Iron Deficiency

- → Fail to Mobilize Iron Store
- → Anaemia of Chronic Illness

Underdiagnosed Anaemia Being Screened During First-time Blood Donation (Aged 16~65)

Proportion of Chinese First Time Donor who Failed Pre-donation Hemoglobin Check (2016 & 2017)

	Men (Cut-off Hb < 13.0 g/dL)					Women (Cut-off Hb < 11.5 g/dL)					
Age Group	Total No. of New Donors	Overall Anaemia in Men, n (%)	Mild Anaemia (Hb 11.0- 12.9 g/dL)	Moderate Anaemia (Hb 8.0-10.9 g/dL)	Severe Anaemia (Hb < 8.0 g/dL)	Total No. of New Donors	Overall Anaemia in Women, n (%)	Mild Anaemia (Hb 11.0-11.4 g/dL)	Moderate Anaemia (Hb 8.0-10.9 g/dL)	Severe Anaemia (Hb < 8.0 g/dL)	Overall Anaemia ir Both Sexes
16-20	20069	1066 (5.3%)	1022 (5.1%)	43 (0.2%)	1 (0.0%)	27568	3379 (12.3%)	1542 (5.6%)	1789 (6.5%)	48 (0.2%)	4445 (9.3%)
21-30	10147	533 (5.3%)	515 (5.1%)	18 (0.2%)	0 (0.0%)	11316	1368 (12.1%)	626 (5.5%)	723 (6.4%)	19 (0.2%)	1901 (8.9%)
31-40	5309	262 (4.9%)	256 (4.8%)	6 (0.1%)	0 (0.0%)	8640	1199 (13.9%)	501 (5.8%)	675 (7.8%)	23 (0.3%)	1461 (10.5%)
41-50	3447	248 (7.2%)	238 (6.9%)	10 (0.3%)	0 (0.0%)	6475	1109 (17.1%)	422 (6.5%)	650 (10.0%)	37 (0.6%)	1357 (13.7%)
51-60	1874	158 (8.4%)	150 (8.0%)	8 (0.4%)	0 (0.0%)	3160	284 (9.0%)	155 (4.9%)	124 (3.9%)	5 (0.2%)	442 (8.8%)
61-65	93	11 (11.8%)	10 (10.8%)	1 (1.0%)	0 (0.0%)	116	10 (8.6%)	7 (6.0%)	3 (2.6%)	0 (0.0%)	21 (10.1%)
Total	40939	2281 (5.6%)	2194 (5.4%)	86 (0.2%)	1 (0.0%)	57312	7352 (12.8%)	3254 (5.7%)	3966 (6.9%)	132 (0.2%)	9633 (9.8%)

Another Study of Successful First-time Donors

Female: 32.4% have serum ferritin level below 30ng/ml & 19.6% have serum ferritin level below 15ng/ml (n=102). Male: 1% have serum ferritin level below 30ng/ml (n=104).

Remark:

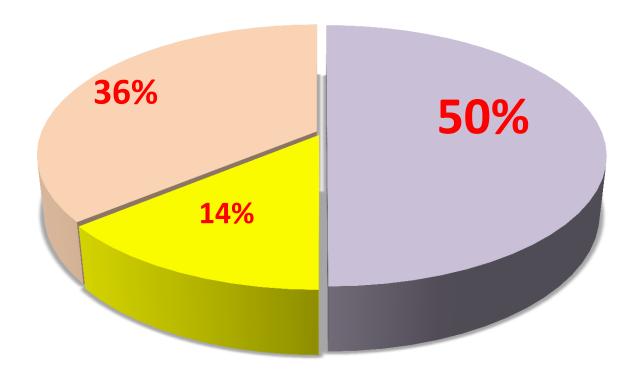
Projected Overall Underdiagnosed Anaemia in the Society (Aged 16~65)

Data projected from Proportion of Low Hb Deferral of New Blood Donors 2016 to 2017 and Population Census data in 2017

			Men					Women	omen Both Sexes			s			
Age group		Moderate Anaemia (Hb 8.0- 10.9 g/dL)	Severe Anaemia (Hb<8.0 g/dL)	Overall Anaemia in Men	Overall Anaemia in Men %	Anaemia	Moderate Anaemia (Hb 8.0- 10.9 g/dL)	Severe	Overall Anaemia in Women	Women	female &	Moderate (Hb 8 to 10.9g/dL)	(Hb<8	Overall Anaemia in both sexes	Overall Anaemia in both sexes %
16-20	8173	344	8	8525	5.3%	8373	9715	261	18349	12.3%	16547	10059	269	26874	8.7%
21-30	22306	780	0	23086	5.3%	27190	31403	825	59418	12.1%	49496	32182	825	82504	8.9%
31-40	22292	522	0	22815	4.9%	40306	54305	1850	96461	13.9%	62598	54827	1850	119276	10.3%
41-50	32797	1378	0	34175	7.2%	43732	67359	3834	114925	17.1%	76528	68737	3834	149100	13.0%
51-60	47345	2525	0	49870	8.4%	32751	26201	1056	60008	9.0%	80096	28726	1056	109879	8.7%
61-65	27839	2784	0	30623	11.8%	16016	6864	0	22879	8.6%	43854	9648	0	53502	10.2%
Total	160752	8333	8	169093	7.1%	168367	195846	7827	372040	12.7%	329120	204179	7835	541134	10.2%

A portion of the mild anaemia may be related to thalassemia. However, moderate and severe anaemia can seldom be explained by thalassemia.

Indications of Blood Transfusion in 2016



- Blood Loss (Gynecology 4%, GIB 20%, Elective operations 13%, Emergency operations 8%, Trauma 5%)
- Renal Insufficiency (Hemodialysis 7%, peritoneal dialysis and non-dialysis 7%)
- ➤ Marrow Failure 10%, Red Cell Disorders 6%, Hematological Malignancy 10%, some Oncological conditions 10%

Perpetuation of Iron Deficiency

Hospital Settings:

- Blood Transfusion as reflex response to treat Anaemia
- Pathological causes of Blood Loss managed
- Under-diagnosed Iron Deficiency in many chronic illness
 e.g. Chronic Renal Impairment, Chronic Heart Failure,
 Malignancy, Inflammatory Conditions...
- Blood Loss due to various procedures and blood taking
- Insufficient treatment to minimize Blood Loss
- Underlying Iron Deficiency seldom received

adequate treatment



GP/FM/SOPD Settings:

- Pathological causes of Blood Loss diagnosed and treated or referred to Hospital
- Underlying Iron Deficiency seldom received adequate treatment
- ●Insufficient treatment to control chronic Blood Loss (physiological or pathological)
- Anti-platelet or oral anticoagulation therapy may increase Blood Loss
- Acid suppressants inhibit Iron Absorption



- Inadequate Iron Intake
- Suboptimal Iron Absorption
- Helicobacter Pylori Infection
- Physiological Blood Loss
- Suboptimal Iron Supplement during pregnancy
- Blood Donation
- Poor Compliance to Iron Therapy





>80% of the male population & >90% of the female population below the recommended nutrient intake level for iron for adult

Centre for Food Safety of the Food and Environmental Hygiene Department 2014



The recommended nutrient intakes for iron based on varying dietary iron bio-availabilities

y weight							
		Recomi (mg/day	mended N /)	utrient l	ntake	100克· 質含量 克) 1	(#
		% Dieta	ry Iron Bio	o-availal	oility	(mg) v	alue
	15	12	10	5	肉類及家禽類	per 10	0 g
	[6.2] ^b	[7.7] ^b	[9.3] ^b	[18.6]	牛肉(熟)	Sala.	y .
	3.9	4.8	5.8	11.6	Beef(cooked) 羊肉(熟)	2. 6	
	4.2	5.3	6.3	12.6	Lamb(cooked)	1.9	3
	5.9	7.4	8.9	17.8	離肉 (熟) Pork(cooked)	1.8	1
					発肉 Chicken (熱) Chicken(cooked)	1. 2	(
	9.7	12.2	14.6	29.2		1. 6	a)
	12.5	15.7	18.8	37.6	聖某及種子類	A STATE OF THE PARTY OF THE PAR	ca Ca
	9.1	11.4	13.7	27.4	芝麻 Sesame	The same of the sa	.H.
					葵花子 sunflower	14.6	黄 (c
	9.3	11.7	14	28	seeds	6.8	(c)
	21.8	27.7	32.7	65.4	蕨果 Cashew nuts	6	±c,∦ Bea
T i	20.7	25.8	31	62	開心果 pistachio	4	雞べ
	19.6	24.5	29.4	58.8	杏仁 Almond	3. 7	(co
	7.5	9.4	11.3	22.6	合桃 Walnut	2.9	(coc
	10	12.5	15	30	花生 Peanut		(coc
		10	10 12.5	10 12.5 15	10 12.5 15 30		10 12.5 15 30 卷生 Peanut 1.6

*Based in part on a 1988 report from the FAO/WHO (8) and in part on new 起子能 Dried Goji requirements in menstruating women. Because of the very skewed distributerries ^bBio-availability of dietary iron during this period varies greatly.

Non-menstruating.

6.8

2.7

提子乾 Dried Raisins 2.6



八爪魚(熟) Octopus (cooked) 嫌 (熟) Oyster (cooked) 青口 (熟) Mussel

(cooked) 蜕(熟) clam (cooked)

耀頭水浸吞拿魚 tuna. canned in oil 1.5

豆麵

黃豆 (熟) soybean (cooked) 5.1 爲重 (熟) Lentils (cooked) 3.3 紅膜豆(熟) Red Kidney Bean (cooked) 2.9

雜心豆(熟) chickpea (cooked) 2.9 紅重(熟) Red Bean (cooked)

蜂豆 (熟) Green Bean (cooked) 1.8

硬豆腐 (未煮) Firm Tofu 2.7

積莱艇

木耳(乾) Dried Black Fungus 菠菜 (熟) spinach (cooked) 3.6 莧菜 (熟) Amaranth (cooked) 2.3 红菜頭 (熟) Beetroot (cooked)

100克食物鐵

質含量 (毫

克) Iron

(mg) Value per 100 g

9.5

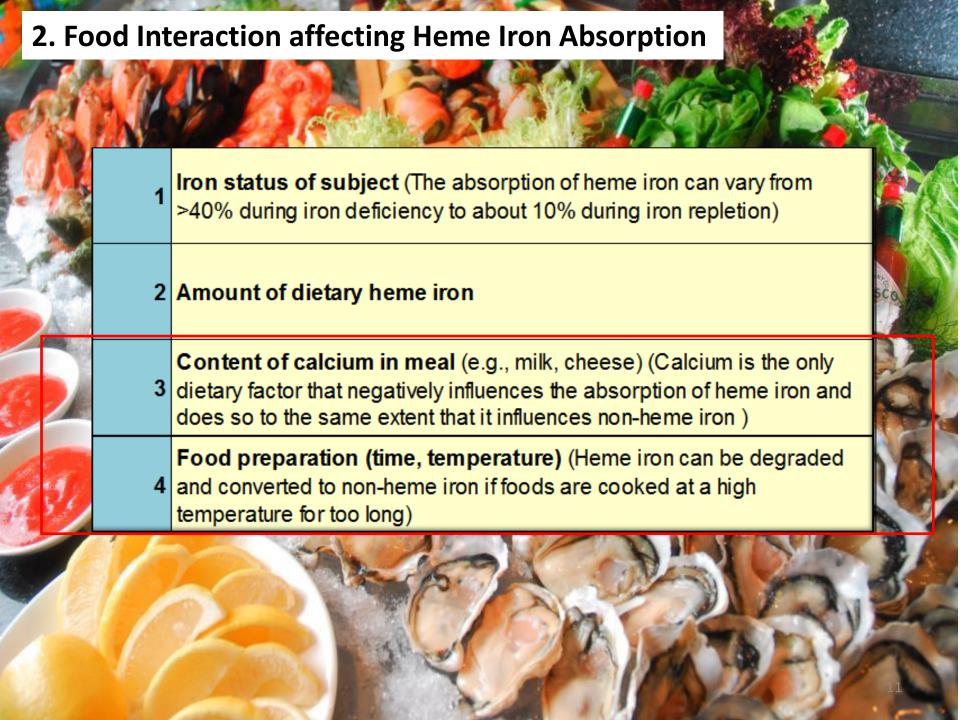
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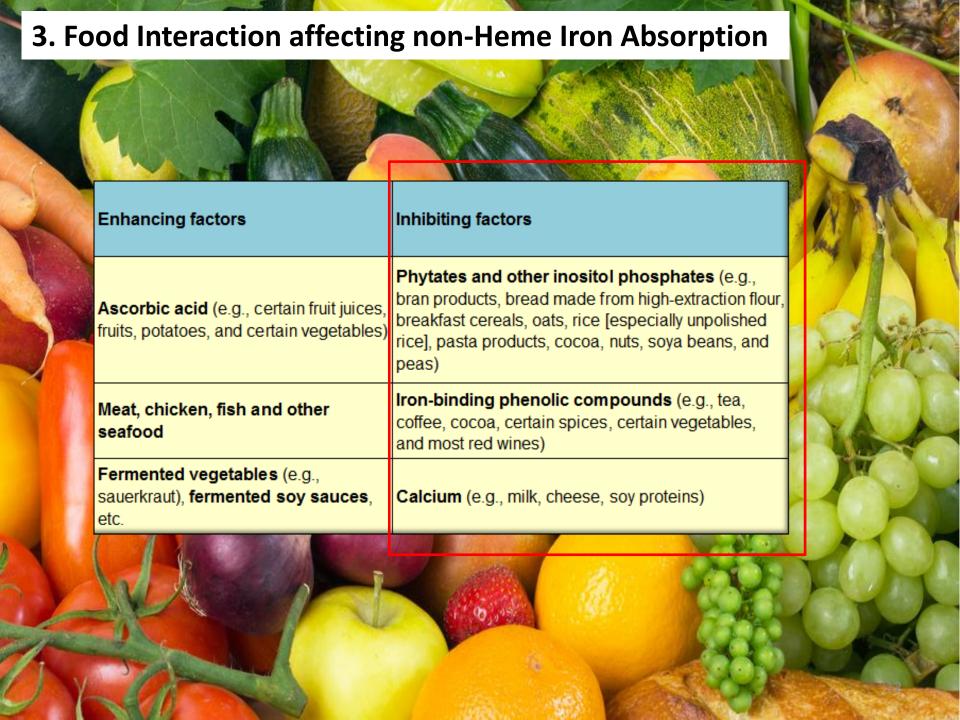
6.7

2.8

10

1.8





4. Helicobacter Pylori



- > 58.4% population is infected by H. Pylori
- > H. Pylori diminishes Iron Absorption from diet
- A number of meta-analyses confirmed the role of H. pylori eradication in improving Iron Deficiency Anaemia correction with appropriate Iron therapy

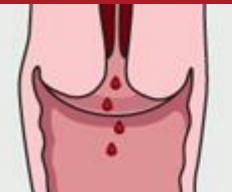


5. Physiological Blood Loss in Women

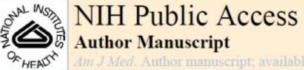
1 ml Blood= 0.5mg Elemental Iron \downarrow In 1g/dL Hb \approx 200mg Loss in Elemental Iron

Menorrhagia (>80ml/cycle) for 1 year→ > 500mg Loss in Elemental Iron / yr

Each Full Term Pregnancy Consumes ≈ 900mg Elemental Iron (WHO)



6. Improper Iron Supplement for Pregnancy





Published in final edited form as: Am J Med. 2008 November: 121(11): 943–948. doi:10.1016/j.amjmed.2008.07.012.

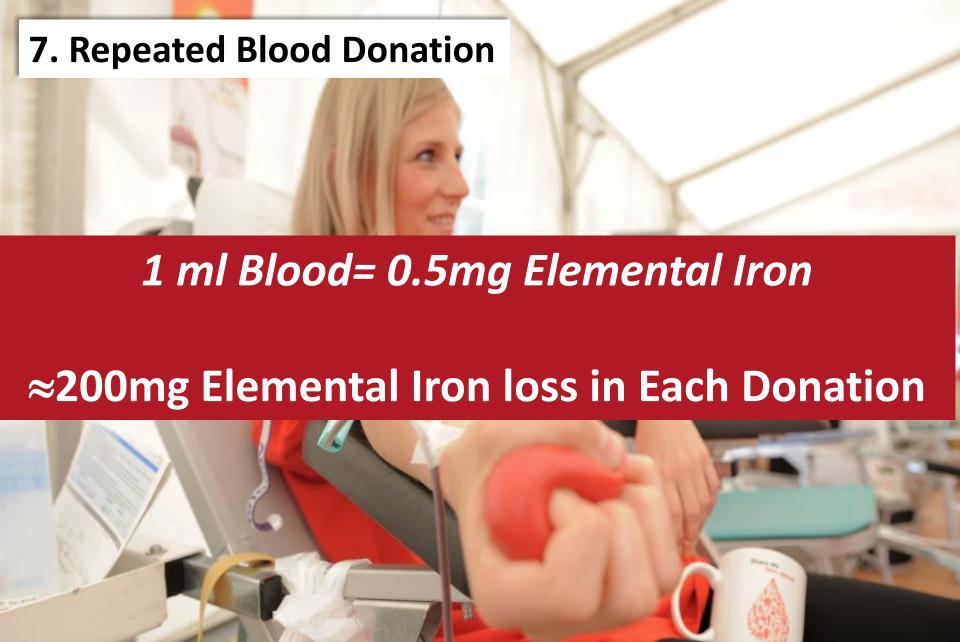
Individualized treatment for iron deficiency anemia in adults

Michael Alleyne, MDa,c, McDonald K. Horne, MDb, and Jeffery L. Miller, MDc,*

Multivitamin preparations should never be recommended as a sole therapy for iron deficient anemia, since the calcium, phosphorus and magnesium salts contained in iron-containing multivitamin pills impair absorption of elemental iron.



MINERALS		
Calcium (calcium carbonate)	250	mg
Magnesium (magnesium oxide)	50	mg
Iodine (potassium iodide)	0.15	mg
Iron (ferrous fumarate)	60	mg
Copper (cupric oxide)	2	mg
Zinc (zinc oxide)	25	mg
Chromium (chromium chloride)	25	mcg
Manganese (manganese sulfate)	5	mg
Molybdenum(sodium molybdte)	25	mcg
Selenium (sodium selenate)	25	mcg
THERAPEUTIC USE ONLY		



Perpetuation of Iron Deficiency

Hospital Settings:

- Blood Transfusion as reflex response to treat Anaemia
- Pathological causes of Blood Loss managed
- Under-diagnosed Iron Deficiency in many chronic illness
 e.g. Chronic Renal Impairment, Chronic Heart Failure,
- Malignancy, Inflammatory Conditions...
- Blood Loss due to various procedures and blood taking
- Insufficient treatment to minimize Blood Loss
- Underlying Iron Deficiency seldom received

adequate treatment

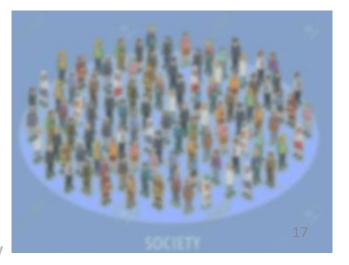


GP/FM/SOPD Settings:

- Pathological causes of Blood Loss diagnosed and treated or referred to Hospital
- Underlying Iron Deficiency seldom received adequate treatment
- Insufficient treatment to control chronic Blood Loss (physiological or pathological)
- Anti-platelet or oral anticoagulation therapy may increase Blood Loss
- Acid suppressants inhibit Iron Absorption



- •Inadequate Iron Intake
- Suboptimal Iron Absorption
- Helicobacter Pylori Infection
- Physiological Blood Loss
- Suboptimal Iron Supplement during pregnancy
- Blood Donation
- Poor Compliance to Iron Therapy



8. Drug Interaction affecting Iron Absorption

Clinical Data Analysis & Reporting System

Patient-Based Analysis

Data Source in (User Defined Query: Antacids, H2 Receptor

Antagonists or PPIs

Drug Dispensing Date Between 01/01/2017 and 31/12/2017)

3 1 3 1 3	,		
Institution Cluster	No. of Patient Headcount		
А	118594		
В	81754		
С	211878		
D	152885		
E	199999		
F	179179		
G	173743		
Grand Total:	1,118,032		

MEDICATIONS INHIBITING IRON ABSORPTION:

H2 receptor blockers, antacid medications, proton pump inhibitors; tetracyclines, quinolones; ACEI; levothyroxine; levodopa, carbidopa; cholestyramine and colestipol (bile acid sequestrant)

9. Anti-plaletet or oral anticoagulant may increase bleeding

Clinical Data Analysis & Reporting System

Patient-Based Analysis

Data Source in (

« Drug{Therapeutic Classification (BNF, Principal or Secondary) in (

Drug BNF: 2.9 ANTIPLATELET DRUGS

Drug BNF: 2.8.2 ORAL ANTICOAGULANTS)} »

Drug Dispensing Date Between 01/01/2017 and 31/12/2017)

	, , , , , , , , , , , , , , , , , , ,
Institution Cluster	No. of Patient Headcount
A	47645
В	36526
С	79987
D	57526
E	74886
F	64914
G	50320
Over all Tallet	411 804

Grand Iotal:

Perpetuation of Iron Deficiency

Hospital Settings:

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- Acid suppressants inhibit Iron Absorption

Iron Deficiency related to:

- Inadequate Iron Intake
- Suboptimal Iron Absorption
- Helicobacter Pylori Infection
- Physiological Blood Loss
- Suboptimal Iron Supplement during pregnancy
- Blood Donation
- Poor Compliance to Iron Therapy



10. Gastrointestinal Blood Loss

1 ml Blood= 0.5mg Elemental Iron

 \downarrow 1g/dL Hb \approx 200mg Loss in Elemental Iron

11. GIB received Blood Transfusion in 2016: Underlying Iron Deficiency is Insufficiently Treated

	GI neoplasms	Non-malignant Lower GIB	Non-malignant Upper GIB
Number of unique patients	3,604	3,161	5,612
Median age (range)	72 (3~105)	78 (0~106)	75 (0~105)
Number of transfusion episodes	5,377	5,870	9,789
Units of RC transfused	9,179	10,262	16,558
Episodes			
Pre-transfusion Hb absent	97 (1.8%)	14 (0.2%)	17 (0.2%)
Post-transfusion Hb absent	909 (16.9%)	305 (5.2%)	497 (5.1%)
Pre-transfusion Hb ≥8 g/dL	1,423 (26.5%)	1,429 (24.3%)	2,043 (20.9%)
Post transfusion Hb ≥ 10 g/dL	1,626 (30.2%)	1,602 (27.3%)	2,379 (24.3%)
Multiple units RC given	3,230 (60.1%)	3,521 (60.0%)	5,510 (56.3%)
Neither parenteral nor oral iron given	2,458 (68.2%)	2,352 (74.4%)	3,863 (68.8%)

OPTIMIZE HEMATOPOIESIS Neither parenteral nor oral iron in ~2/3 And Pillar MINIMIZE BLOOD LOSS

How often was iron deficiency managed in gastrointestinal bleeding?

Dr Ching-Wa LAU, Dr Jennifer Nga-Sze LEUNG, Dr Cheuk-Kwong LEE

Hong Kong Red Cross Blood Transfusion Service

3rd Pillar

OPTIMIZE
PATIENT-SPECIFIC
TOLERANCE TO
ANAEMIA

Post transfusion Hb ≥ 10 g/dL in 1/4 ~ 1/3

Multiple units RC given in ~2/3

Data from CDARDS

12. Gynecology Patients received Blood Transfusion in 2016: Underlying Iron Deficiency is Insufficiently Treated Bleeding Condition is Insufficiently Managed

Study Period between 01/01/2016 and 31/12/2016 Gynecology Patients Age \leq 60 (range 11~60), Non-operation related Admission (2,906 Transfusion Episodes of 5,889 units RC in 2,523 Unique Patients) Pre-Total Post-Post-Post-Post-Post-Post-Median 1 unit 2 units 3 units 4 units 5 units >5 units Transfusion transfusion transfusion transfusion transfusion transfusion transfusion Age RC RC RC RC RC RC Hb 7~8 Hb 8~9 Hb 9~10 Hb >10 Hb missing Hb **Episodes** Hb <7 < 7 77 777 525 77 1461 65 537 413 136 102 45 208 7~8 45 374 656 17 1047 287 179 52 411 114 8~9 45 148 117 266 3 43 76 85 51 9~10 44 23 16 0 0 0 0 4 21 5 39 ≥10 36 10 7 0 0 17 12 0 Pre-0 7 transfusion 46 16 50 10 0 0 0 76 17 26 15 11 Hb missing

2906

73

277

888

OPTIMIZE
HEMATOPOIESIS

3.2% GIVEN TRANEXAMIC ACID ALONE @ DISCHARGE

15.0% GIVEN IRON ALONE @ DISCHARGE

65.8% GIVEN IRON + TRANEXAMIC ACID @ DISCHARGE

UP TO 16.0% NOT GIVEN IRON OR TRANEXAMIC ACID @ DISCHARGE

OPTIMIZE
PATIENT-SPECIFIC
TOLERANCE TO
ANAEMIA

2/3 TRANSFUSED
WITH MULTIPLE UNITS

ALMOST 1/2 POST
TRANSFUSION
HB≥ 9G/DL

ALMOST 10% WITH NO
POST TRANSFUSION
HB CHECKED

937

448

283

Gaps in Managing Gynaecological Patients with Iron Deficiency Anaemia

Total

45

648

1623

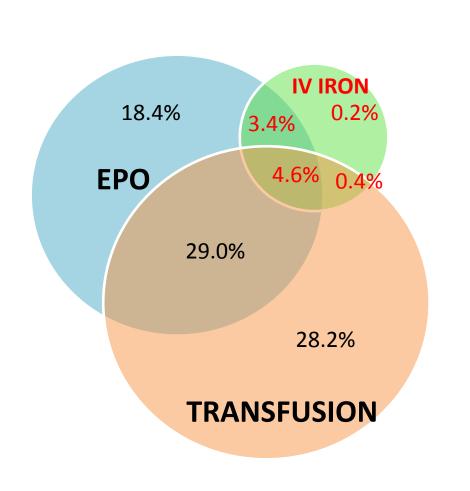
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Ching-Wa Lau¹, Wing-Cheong Leung², Nga-Sze Leung¹ and **Cheuk-Kwong Lee¹**, (1)Ho Transfusion Service, Hong Kong, Hong Kong, (2)Kwong Wah Hospital, Hong Kong, Hong



13. Anaemia Treatment in Hemodialysis: Underlying Iron Deficiency is Insufficiently Treated



	Hemodialysis Headcount	Parcantaga
No Treatment	683	15.9%
Transfusion Alone	1212	28.2%
EPO Alone	792	18.4%
IV Iron Alone	8	0.2%
EPO +IV Iron	147	3.4%
EPO+Transfusion	1248	29.0%
IV Iron+ Transfusion	16	0.4%
EPO+ IV Iron+ Transfusion	199	4.6%

N=4305

No Anaemia Treatment 15.9%

Data from CDARDS_2016



1 ml Blood= 0.5mg Elemental Iron \downarrow 1g/dL Hb \approx 200mg Loss in Elemental Iron

Anaemia is present in up to 90% of patients in the immediate postoperative period after major surgery.



15.Obstetric Patients undergoing Cesarean Section in 2016/17: Bleeding Condition is Insufficiently Managed

Hospital Code in (All Hospitals) AND Discharge Date between 01/10/2016 and 30/09/2017 AND Diagnosis Code (ICD9) in (74 CESAREAN SECTION AND REMOVAL OF FETUS)

Use of IV Transamin	Yes	No	Row Total
Institution Cluster	No. of Episodes	No. of Episodes	No. of Episodes
(Admission Date)	Headcounts	Headcounts	Headcounts
Α		872	872
В		966	966
С	19	2310	2329
D	5	903	908
E	43	1660	1703
F	13	1690	1703
G		1637	1637
Grand Total :	80	10038	10118

16. Obstetric Patients with PPH in 2016/17: Bleeding Condition is Insufficiently Managed

Hospital Code in (All Hospitals) AND
Discharge Date between 01/10/2016 and 30/09/2017 AND
Diagnosis Code (ICD9) in (666 POSTPARTUM HEMORRHAGE)

Use of IV Transamin	Yes	No	Row Total
Institution Cluster	No. of Episodes	No. of Episodes	No. of Episodes
(Admission Date)	Headcounts	Headcounts	Headcounts
Α	3	183	185
В	2	232	234
С	51	526	574
D	11	431	442
E	16	499	513
F	5	384	389
G		306	306
Grand Total:	88	2553	2635

Perpetuation of Iron Deficiency

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- Inadequate Iron Intake
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- Helicobacter Pylori Infection
- Physiological Blood Loss
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- Poor Compliance to Iron Therapy



Diagnosis

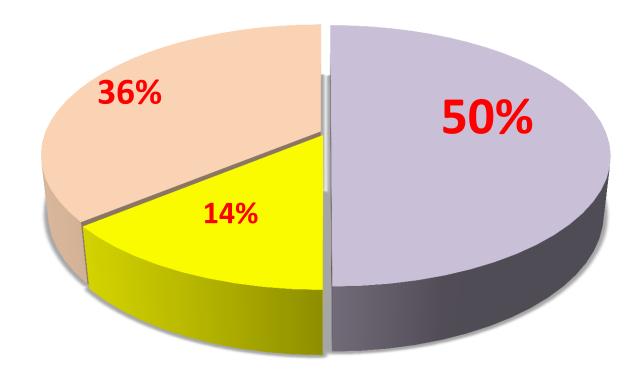
WHO Definitions of Anaemia in Adult					
(gm/dl)	Mild	Moderate	Severe		
Pregnant women	10.0-10.9	7.0-9.9	<7		
Non-pregnant women	11-11.9	8.0-10.9	<8		
Men	11.0-12.9	8.0-10.9	<8		

WHO Definitions of Iron Deficiency	Most global experts Definitions of Iron Deficiency			
<15 ng/ml	<30 ng/ml			
	Sensitivity 92%			
Positive predictive value 83%				
Ferritin 1ng/ml ≈ 8mg Iron Store				

TRANSFUSION ALTERNATIVES

- 1. Maximizing endogenous red cell production by TRANSFUSION ALTERNATIVES
- 2. Minimizing endogenous red cell loss by TRANSFUSION ALTERNATIVES and good surgical and anesthetic techniques
- 3. Safe and appropriate use of ALLOGENEIC BLOOD TRANSFUSION to improve patient clinical outcomes, not the number

Clinical Scenarios in which Benefits of Transfusion out-weight the Risks



- Blood Loss (Gynecology 4%, GIB 20%, Elective operations 13%, Emergency operations 8%, Trauma 5%)
- > Renal Insufficiency (Hemodialysis 7%, peritoneal dialysis and non-dialysis 7%)
- Marrow Failure 10%, Red Cell Disorders 6%, Hematological Malignancy 10%, some Oncological conditions 10%

Iron

Allogeneic red cell metabolized in a few weeks, the only thing left inside the patient is no more than 200mg of Elemental Iron



Every Unit of Red Cell ≈ 200mg Elemental Iron

Fe 26

GLOBAL BENCHMARK

Red Cell Use per 1,000 Population

