IRON DEFICENCY ANEMIA

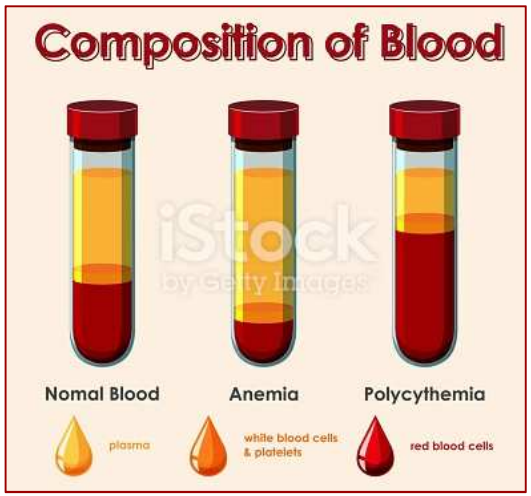
Do you suffer from
Iron Deficency Anemia (IDA)?

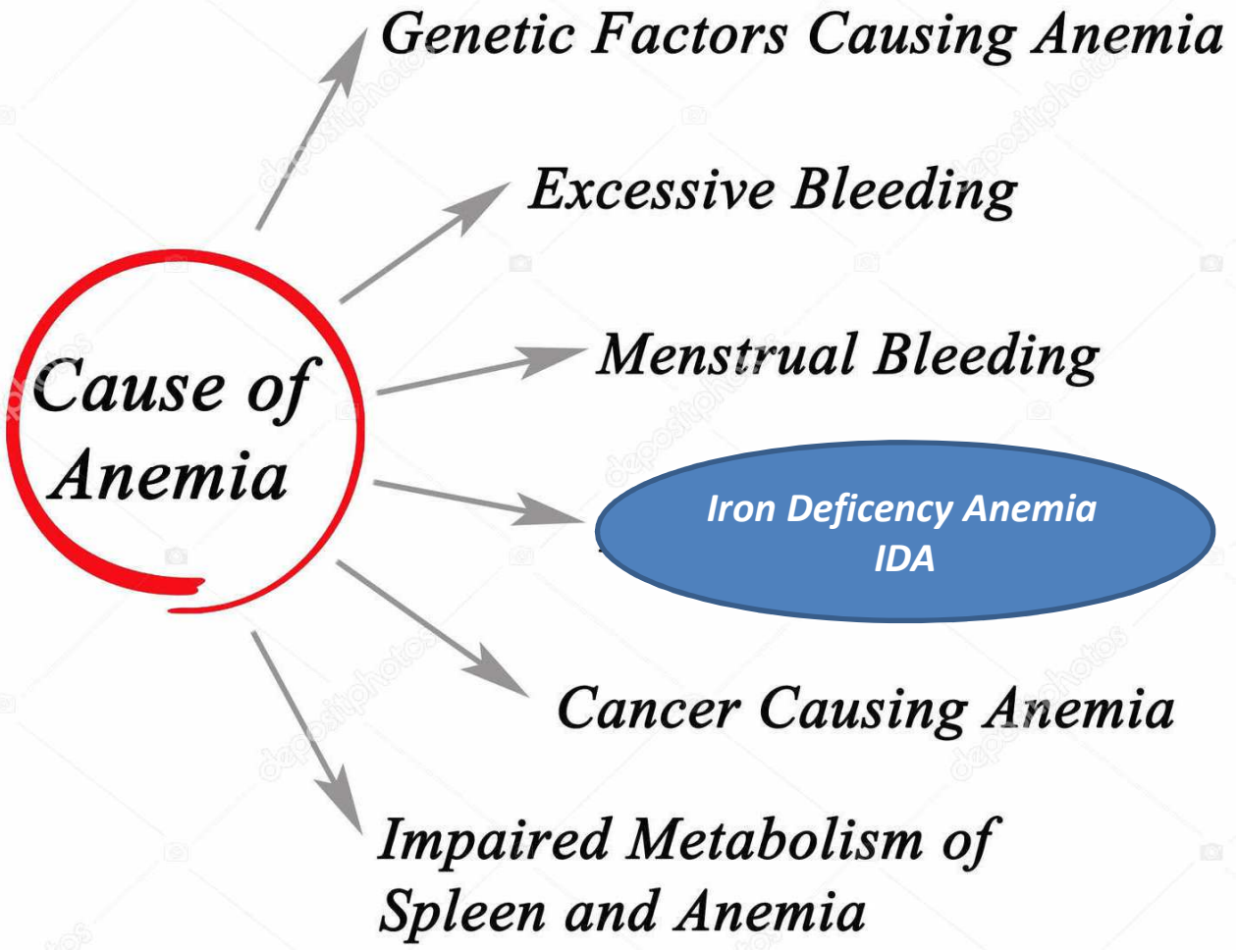
Would you like to increase your Serum Iron and your Ferritin by 50-70% in as little as 30 days?

With no side or adverse effects!

HERE IS HOW !

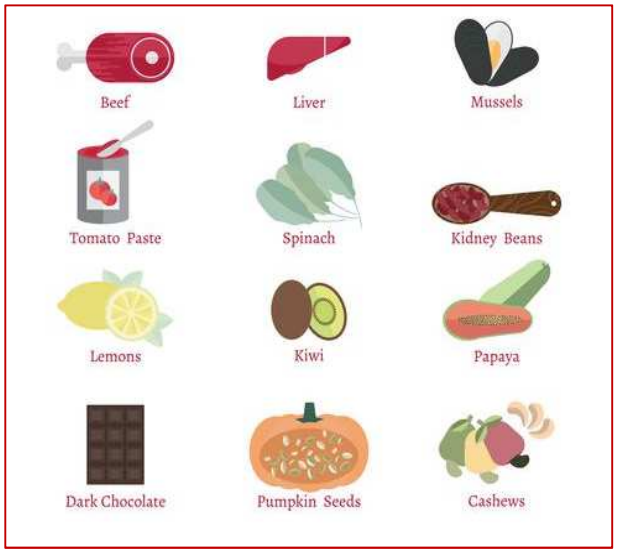
Causes of ANEMIA





IRON & FOODS

Generally, foods are **never deficient in iron!**



IRON in foods: **6-7 mg/1000 Kcal**
almost ubiquitous

MEAT/FISH: **40% heme**
60% non-heme

OTHER FOODS: **100% non-heme**

PROBLEM:

Iron is difficut to be absorbed: 1-2 mg out of 12-20 mg present in the daily diet

IRON ABSORPTION

DAILY DIET

Foods of plant origin, eggs and milk

Meat, fish

HEME IRON

NON-HEME IRON

Meat, fish and ascorbic acid

ACCELERATE ABSORPTION

+

Ca2+, Tannins, tea, wine and fibre make iron insoluble :

POOR ABSORPTION

-

DIRECT ABSORPTION

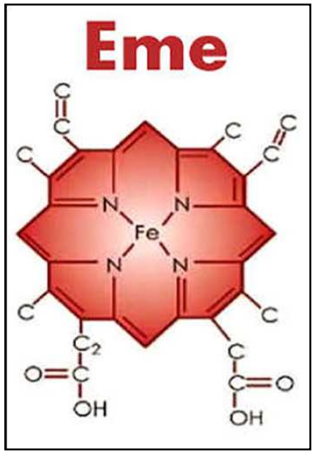
25%

LIMITED ABSORPTION

5%

Absorption level

HEME IRON



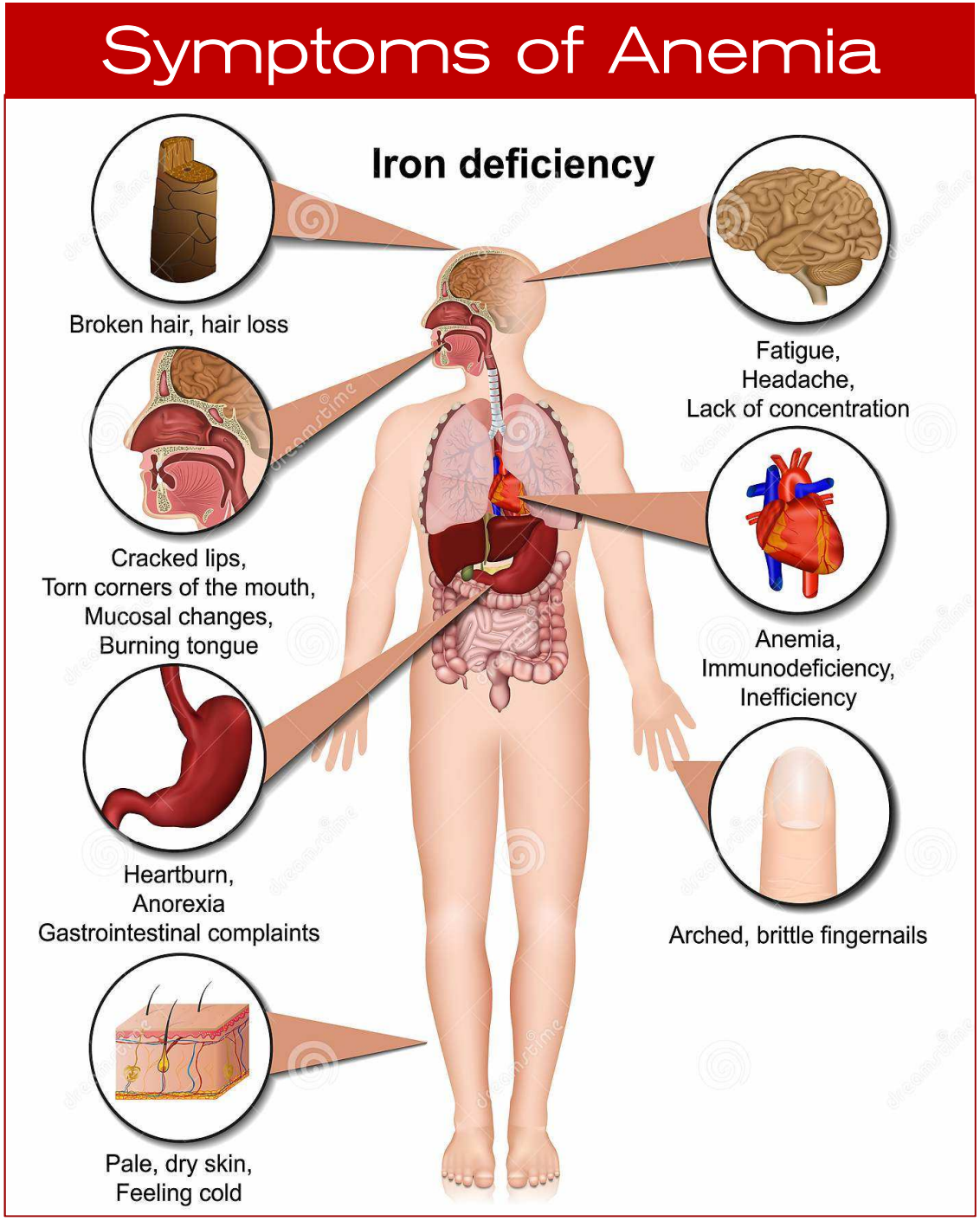
Absorbed at a level of 20%- 30%

NON HEME IRON

Absorbed at a level of 5%
(promoted by Citric, Lactic and Ascorbic acids)

Polyphenols and Tannins reduce absorption by 30%

Symptoms of Anemia



ORAL IRON SUPPLEMENTATION

Oral iron supplementation is by far the first and most frequent therapy.

Efficacy: very modest

Increase of iron parameters 10 – 30%

Results: very slow

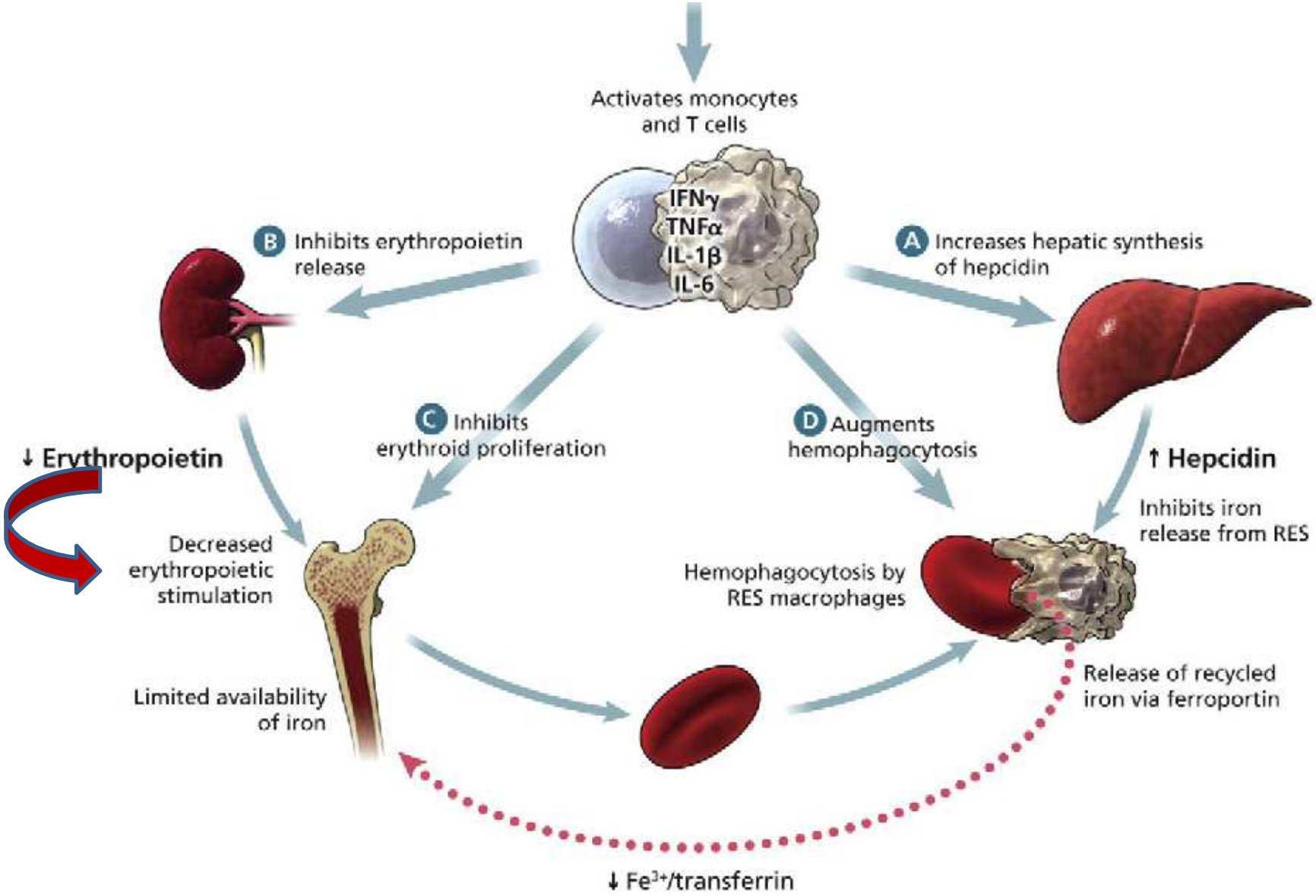
90- 120 days, in less than 50% of patients

PROBLEMS:

It dramatically increases oxygen free radicals within the gut, which induce or significantly aggravate inflammation by causing lipid peroxidation in the colon and by increasing pro inflammatory cytokines (*IL-1,IL-6, Gamma Inf., TNF-α, IL-3, IL-4.)* which lead to the reduction of erythropoiesis

Inflammatory stimulus: *infection, autoimmunity,cancer , iron supplementation*

Oral Iron Supplementation induces i**nflammation** which, on its turn, reduces Erythropoiesis



Other Common Adverse effects of oral iron

Oral iron therapy is also associated with many side effects such as :
constipation, diarrhoea, nausea, vomiting, abdominal pain, faintness

/ constipation

may obscure the diagnosis of continued gastrointestinal blood loss

Moreover, the *iron–enhanced oxidative stress* may lead to increase:

- **Mutagenesis**
- **Cell Death**
- **Ulceration**

Iron Oral therapy: failure in controlling Anemia in IBD patients

University Hospitals Birmingham NHS Foundation Trust

A recent study carried out at the University Hospital of Birmingham has shown that treatment with oral iron results in failure to control anaemia in 2 out of 3 IBD patients.

University Hospitals Birmingham NHS
NHS Foundation Trust

The failure to control anaemia in 2 out of 3 IBD patients is in part due to the side effects reported by over 50% of patients

JCC JOURNAL of CROHN'S and COLITIS

Journal of Crohn's and Colitis (2014) 8, 876–880

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

Iron treatment and inflammatory bowel disease: What happens in real practice?☆

Sebastian Lugg, Felicity Beal, Peter Nightingale, Neeraj Bhala, Tariq Iqbal*

Department of Gastroenterology, University Hospitals Birmingham, United Kingdom

Received 14 October 2013; received in revised form 8 January 2014; accepted 9 January 2014

KEYWORDS
Anaemia;
Inflammatory bowel disease;
Iron

Abstract

Background and aims: Iron deficiency anaemia (IDA), the most common extra-intestinal complication of inflammatory bowel disease (IBD), negatively impacts quality of life. We audited the recent practice of anaemia treatment in an unselected IBD population.
Methods: A questionnaire was distributed to adult IBD outpatients in a university hospital to assess the form and frequency of iron prescribed, duration of use, side effects, and completion of therapy. The efficacy of treatment was determined by the resolution of anaemia and change in haemoglobin from baseline.
Results: Of 87 IBD patients (60 patients with Crohn's disease, 25 with ulcerative colitis, 2 with microscopic colitis), 85 received various dosing regimens of iron tablets; 15 patients also received IV iron. Side effects were reported in 43 (51%) patients, with no clear relationship to dose prescribed and 26 (32%) patients were unable to complete the intended course. Only 36 (42%) patients completed the course of oral iron without side effects and in these patients, haemoglobin normalised in about 30%. Their median haemoglobin change was 12.5 (5.3–23.5) g/l. The median duration of treatment in those without side effects was 4.5 months, and in those with adverse effects was 2 months. Only one adverse effect was reported for IV iron.
Conclusions: Treatment with oral iron results in failure to control anaemia in 2 out of 3 IBD patients, which is likely in part to be due to the side effects reported by over half of patients. Patients failing to tolerate or adequately respond to therapy should be offered alternative treatment.

ALTERNATIVE to Oral Iron Therapy:

THE INTRAVENOUS ADMINISTRATION of iron preparations

but still serious side effects have been experienced:

- Hypersensivity reactions
- Tachycardia
- Strong Perspiration
- Worsening of Rheumatic Syndrome
- Myalgia
- Dysgeusia
- Iron Overload

How to fix the problem?

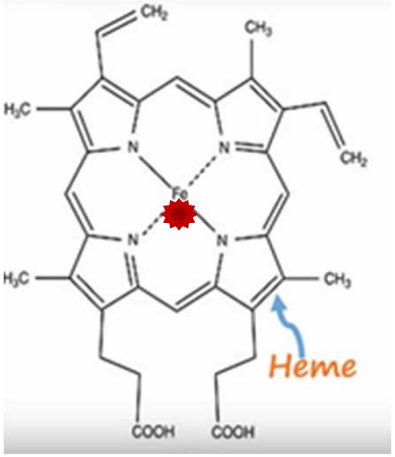
Here is the solution!

The first iron–free «Iron Fixative!»

Simple, fast, effective and…… fully safe

Introduction:The «Meat Factor»

it is well documented that **heme-iron** contained in meat is absorbed better than non-heme iron.



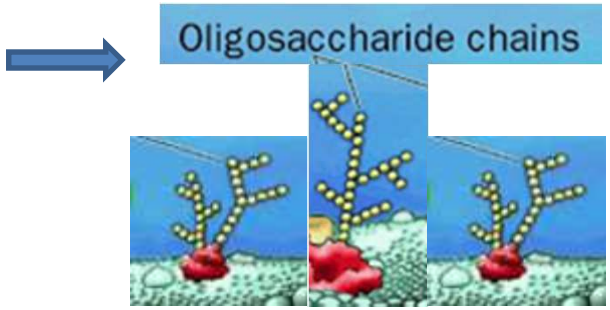
It has also been shown that meat promotes as well the absorption of non-heme iron contained in other foods

This "**Meat factor**", that promotes the absorption of non-heme iron, consists of certain carbohydrates present in the extra-cellular matrix of the muscular fibres of meat.

This has been demonstrated in vitro by using Caco-2 cells, which represent the gut mucosa.

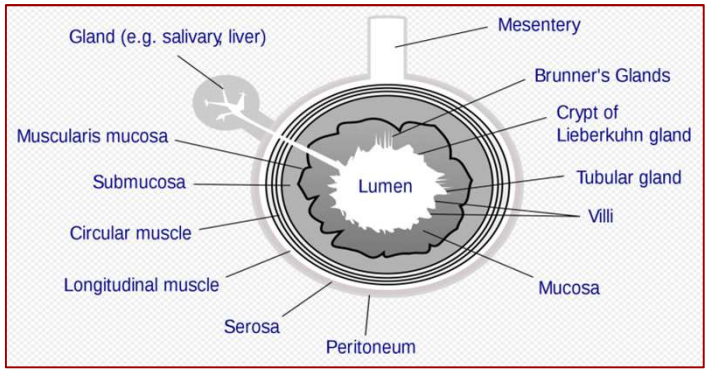
Discovery:
The « Fish Factor»

The main ingredient of IRON CATCH is a special type of "Fish Factor", made of *specific oligosaccharides* from fish cartilage, that is up to 5 times more active than *"Meat factor"* in *increasing the non–heme iron absorption from foods by the enterocytes*.



The location of iron absorption

Iron is absorbed **in the first part of intestine** (*duodenum and jejunum*), due to the action of proteins:



DMT1

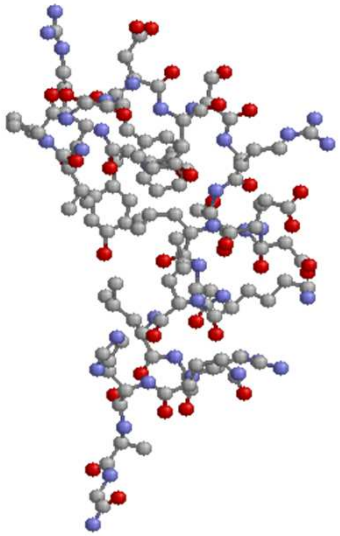
(Divalent Metal Transporter 1)

(*absorption*)

This protein binds **Fe^{2+}, Cu^{2+}** in the Lumen of the first part of intestine and **makes Fe^{2+} enter into the Enterocyte**

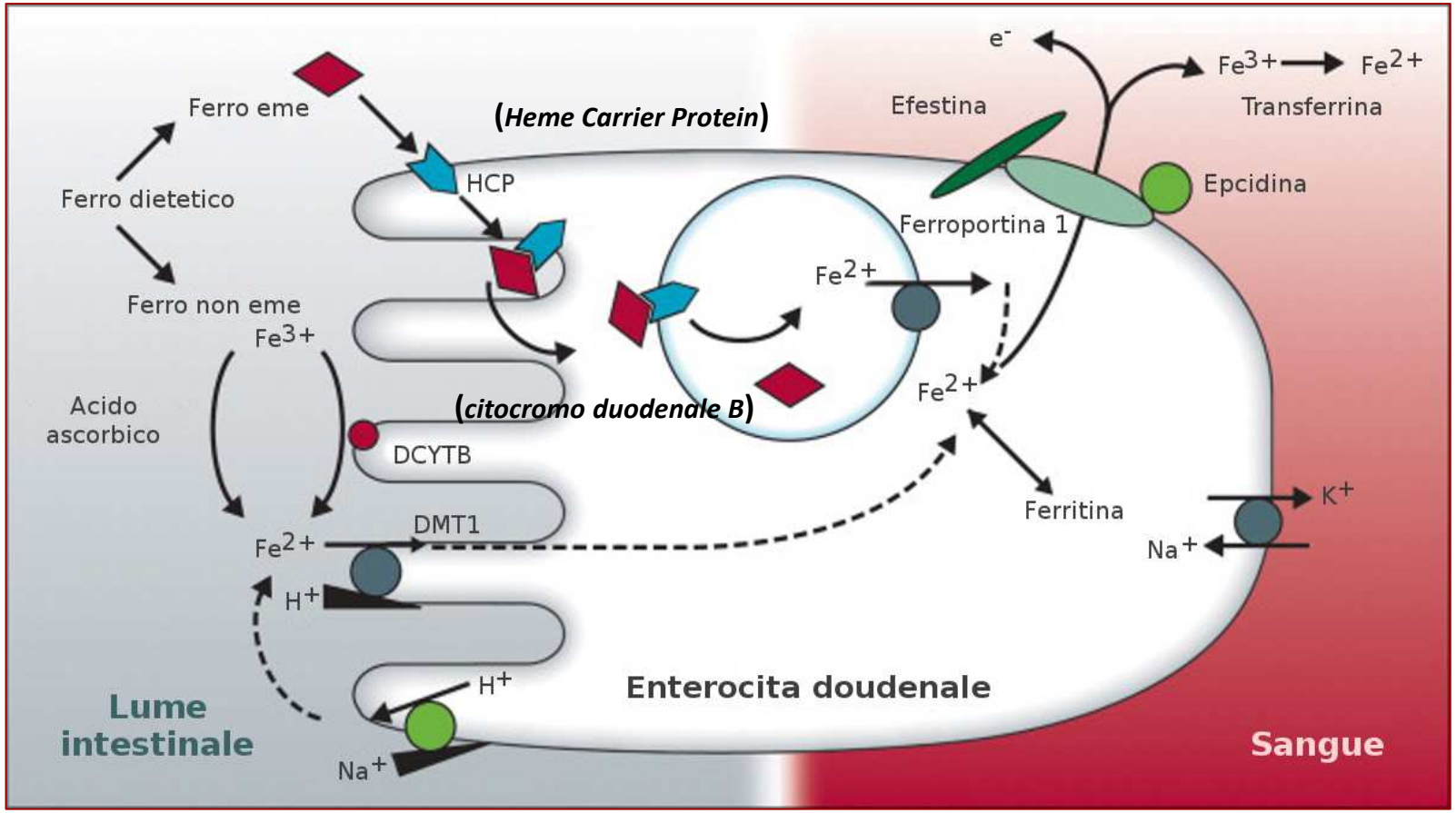
HEPHAESTIN (HEPH)
FERROPORTIN (IREG1 or Fpn)
(*passage from mucosa to blood)*

These proteins are **both oxydant;** by changing **Fe^{2+}** to **Fe^{3+}** allow **Fe^{3+}** to get out of the Enterocyte and **enter into the blood stream**, bound to **Transferrin**.



THE INTEGRITY OF THE MUCOSA IS FUNDAMENTAL

How Iron is absorbed into the blood stream



After entering into the Enterocyte through **DMT1, Fe^{2+}** must be oxydated to **Fe^{3+}** by **Hephaestin** and **Ferroportin-1,** which is the only "**exporter"** of iron into the **blood stream**, where **Fe^{3+}** binds to **Transferrin.** **Ferroportin** (*Fpn1*) is regulated by **Hepcidin**, a hormone produced by the liver; **Hepcidin reduces the iron-efflux activity of Fpn1** thereby reducing iron delivery to the blood plasma. Therefore, the interaction between **Fpn1** and **Hepcidin** controls the systemic iron.

When additional iron is not required by the organism, **Fe^{2+}** inside the enterocyte **binds** to Ferritin and is lost in the Intestinal Lumen when the cell desquamates.

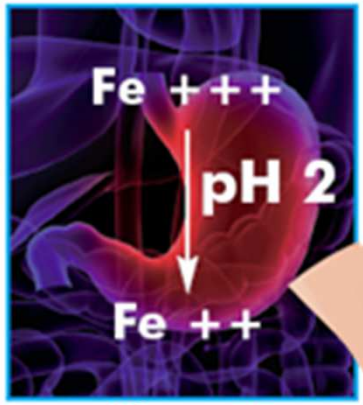
Iron absorption: «IRON CATCH Factor»

Fe 2+

Heme Fe: MEAT

Fe 3+

Non-Heme Fe:
MEAT
VEGETABLES



Absorption
~ 1 mg/die

Fish cartilage Glycosaminoglycans contain Oligosaccharides from fish extracellular matrix

3 to 5 times

through DMT1

INTESTINAL VILLUS

Facilitate Non-HEME Fe transport inside the intestinal mucosa by substituting the lacking "Heme frame"

highly enhances non-Heme iron absorption:

3 to 5 times more

Carbohydrate Fractions from Cooked Fish Promote Iron Uptake by Caco-2 Cells[1]

Eun Chul Huh, Arland Hotchkiss,* Janine Brouillette,* and Raymond P. Glahn[†2]

*Institute of Food Science, Cornell University, Ithaca, NY 14853; *U.S. Department of Agriculture/ARS, Eastern Regional Research Center, Wyndmoor, PA 19038; [†]U.S. Plant, Soil and Nutrition Laboratory, U.S. Department of Agriculture/ARS, Ithaca, NY 14853*

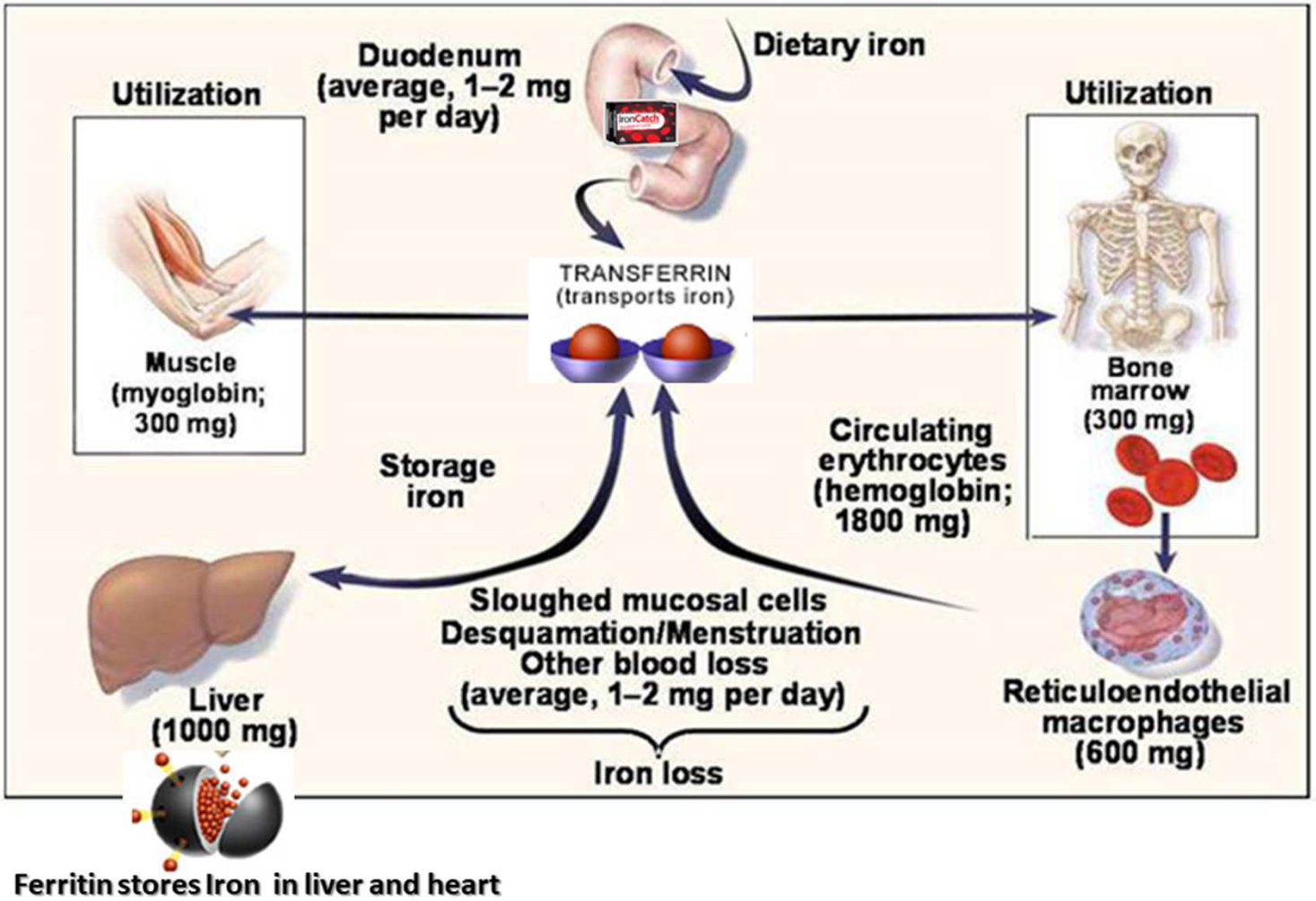
ABSTRACT The objective of this study was to isolate and characterize the meat factor(s) th… bioavailability using various analytical and in vitro cell culture techniques. Nonh… radiolabeled iron uptake or ferritin formation in Caco-2 cells. Fish t… as the muscle tissue of choice because of its low int… stomach (pH 2.0) was the primary factor … Subsequently, cooked fish sa… to release the fact… meat f… …for the …used Caco-2 cell iron …C18 reverse-phase HPLC were …peak." This observation coupled with protein …that the active fractions contained negligible amounts of …ly enriched with carbohydrates. Subsequent chromatography via high …atography with pulsed amperometric detection yielded 3 active peaks that in… …uptake 3.4- to 4.9-fold. Our results indicate that specific carbohydrates contribute to the …ffect of meat on iron uptake by the enterocyte. These carbohydrates may be oligosaccharides originating …rom glycosaminoglycans in the extracellular matrix of muscle tissue. J. Nutr. 134: 1681–1689, 2004.

Our results show that specific carbohydrates play a part in increasing the effect of meat on Fe captation by the enterocyte. These carbohydrates can be oligosaccharides originating from glycosaminoglycans in the extracellular matrix of muscle tissue.

KEY WORDS: • *meat factor* • *iron* • *in vitro digestion* • *Caco-2 cells* • *oligosaccharides*

Replenishment of Fe deposits

The *"Fish-Factor"* contained in IRON CATCH is able to form a complex with Fe^{2+}, which acts as *"Heme frame"* and makes iron enter into the enterocytes, through the DMT1, before being "exported" to blood as Fe^{3+} bound to Transferrin.



Clinical studies

Three clinical studies **were carried out:**

- **2 in *Italy***

and

- **1 in *Jordan***

on a total of **337 patients**

1st Study in ITALY

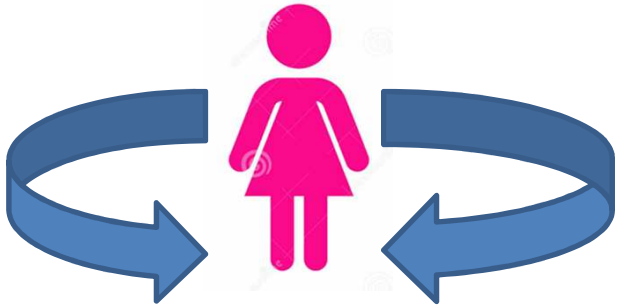
The study was carried out at the University Hospital "*Policlinico San Matteo*" of Pavia

OSPITALE DI S. MATTEO PAVIA

Fondazione IRCCS
Policlinico San Matteo

1st Study: enrolled patients

49 fertile women:

25 treated  **24 under placebo**

For each group, 2 sub- groups were planned:

With Plasma Iron <60mcg/dl

With Ferritin < 20 ng/ml

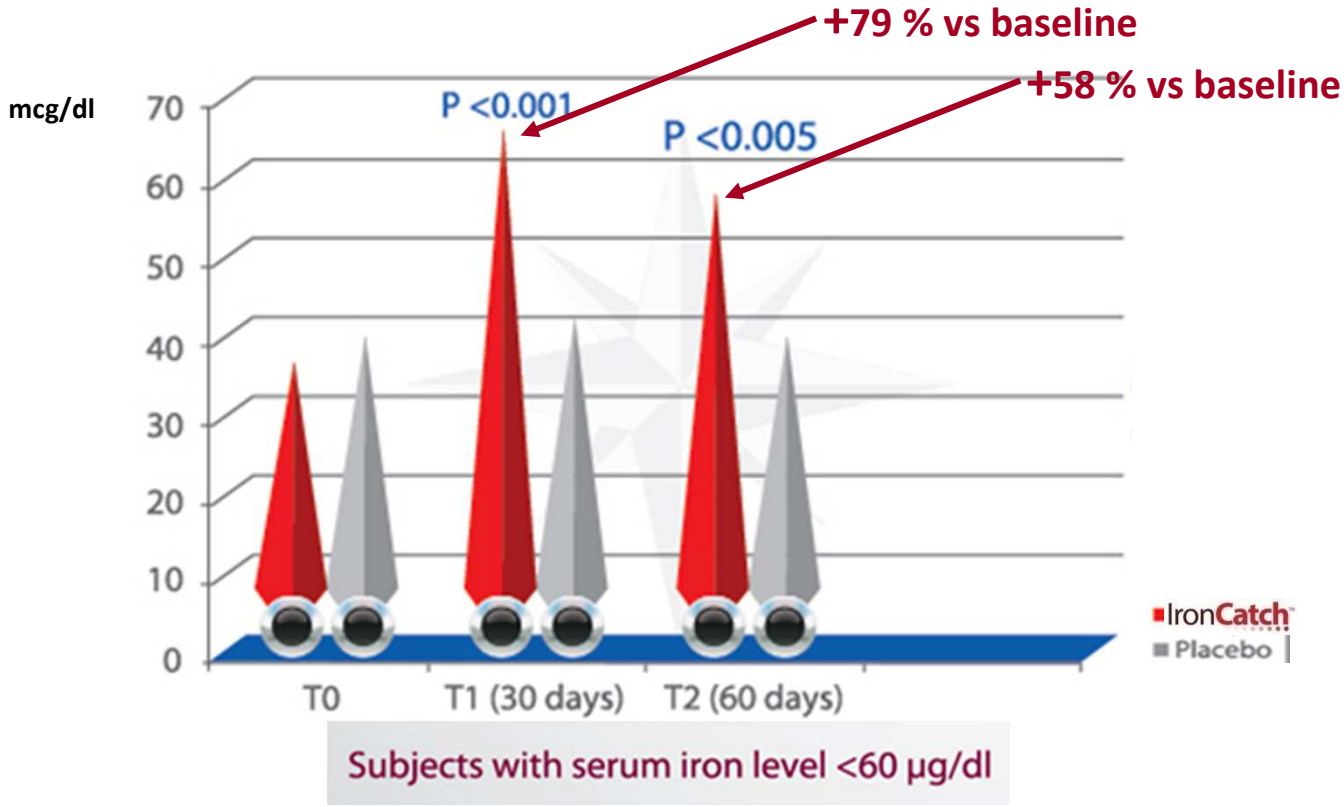
Treatment was carried out for 2 months with measurements at T0- T1 – T2

1st Study: results

SERUM IRON

Patients with serum iron < 60mcg/dl:

	T0	T1	%	T2	%
Serum Iron Mcg/dl	36,4± 9,8	65,3± 11,8	**+ 79**	57± 28,2	**+58**



Fondazione IRCCS
Policlinico San Matteo

1st Study: results

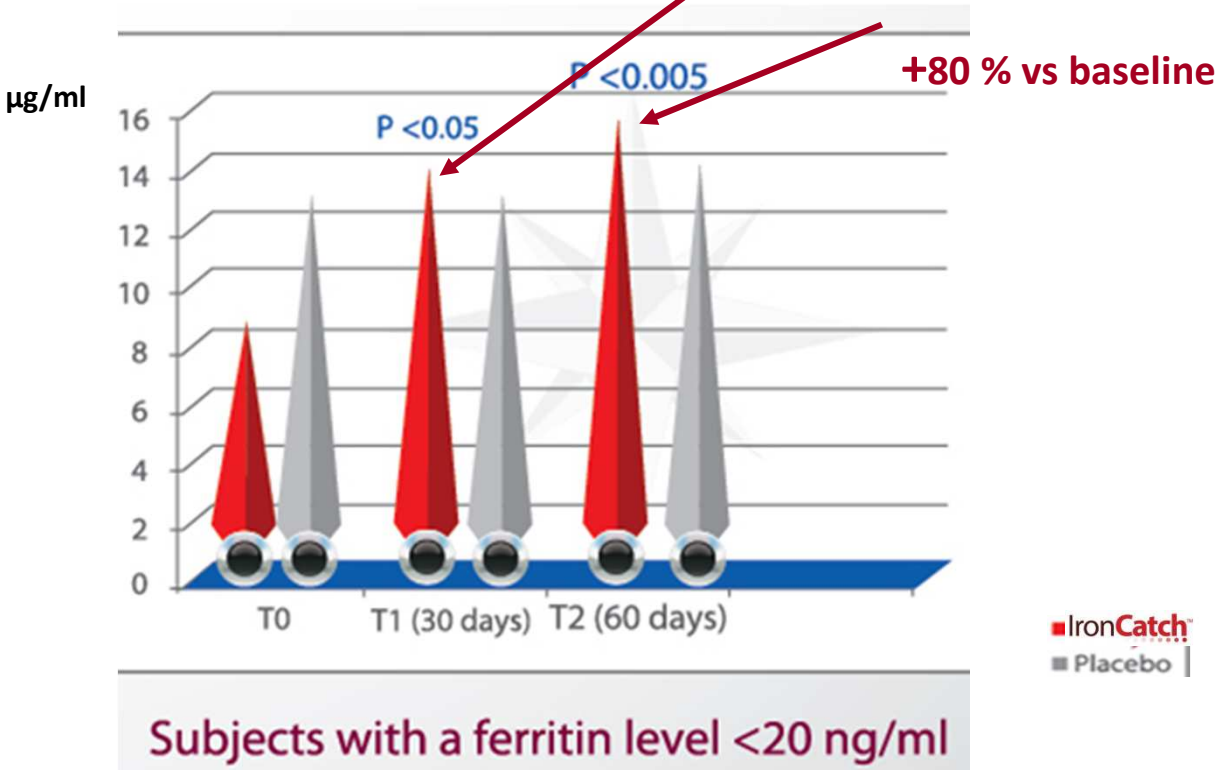
FERRITIN

Patients with Ferritin < 20ng/ml

	T0	T1	%	T2	%
Ferritin ng/ml	8,6± 4,4	13,9± 6,6	**+ 61**	15,5±10,5	**+80**

+61 % vs baseline

+80 % vs baseline



Fondazione IRCCS
Policlinico San Matteo

From the above data it is easy to conclude:

When Serum Iron is low,
it increases rapidly by 79% in just 30 days

When Ferritin is low,
it increases rapidly by 61% in 30 days and
by 80% in 60 days.

When *Sideremia* and *Ferritin are normal,*
they don't move significantly: no risk of overload !

The Placebo didn't cause any change in patients, neither for Serum Iron, nor for Ferritin.

Fondazione IRCCS
Policlinico San Matteo

Publication

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1: Minerva Med. 2006 Oct;97(5):385-390. Links

Effect of treatment with food supplement (containing: selected sea fish cartilage, vitamin C, vitamin E, folic acid, zinc, copper) in women with iron deficiency: double blind, randomized, placebo-controlled trial.

Rondanelli M, Opizzi A, Andreoni L, Trotti R.

Unita Endocrino-Nutrizionale, Azienda Servizi alla Persona, Istituzioni Assistenziali Riunite di Pavia, Pavia, Italy.

AIM: The term iron deficiency is used to indicate a condition in which the content of iron (Fe) in the organism is low, even before the consequent reduction in erythropoiesis comes about. This clinical situation is very frequent in patients in fertile age. The therapy commonly used (Fe salts) is often poorly tolerated. The use of a food supplement containing nutrients useful for improving the bioavailability of Fe and that is well tolerated can represent a valid alternative to iron therapy. METHODS: The present study examines 49 fertile women with iron deficiency, of normal weight and not undergoing estroprogestin treatment. The patients underwent 3 assessments: basal, after 30 and after 60 days to determine their complete

Related Links

- [Trace nutrients in total enteral nutrition: the basal status a [Minerva Gastroenterol Dietol. 1993]
- The effect of long-term calcium supplementation on indices of [Br J Nutr. 1996]
- Treatment for iron deficiency anaemia with a combined supplementatio [Eur J Clin Nutr. 1999]
- The impact of intensive serial plasmapheresis and iron supplementation or [Transfusion. 2003]
- Effect of intravenous ascorbic acid in hemodialysis patients w [Am J Kidney Dis. 2006]

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2nd Study in Italy

The 2nd study was carried out at the University Hospital "*Policlinico Sant'Orsola*" of Bologna

Policlinico
S.Orsola
Malpighi

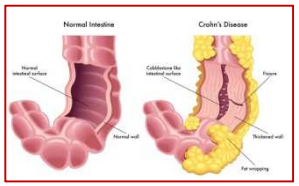
2nd Study: enrolled patients

25 patients

11 suffering from

CROHN'S DISEASE

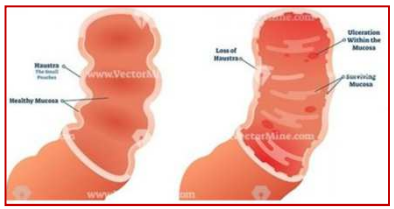
9♂ 2♀



14 suffering from

ULCERATIVE COLITIS

8♂ 6♀



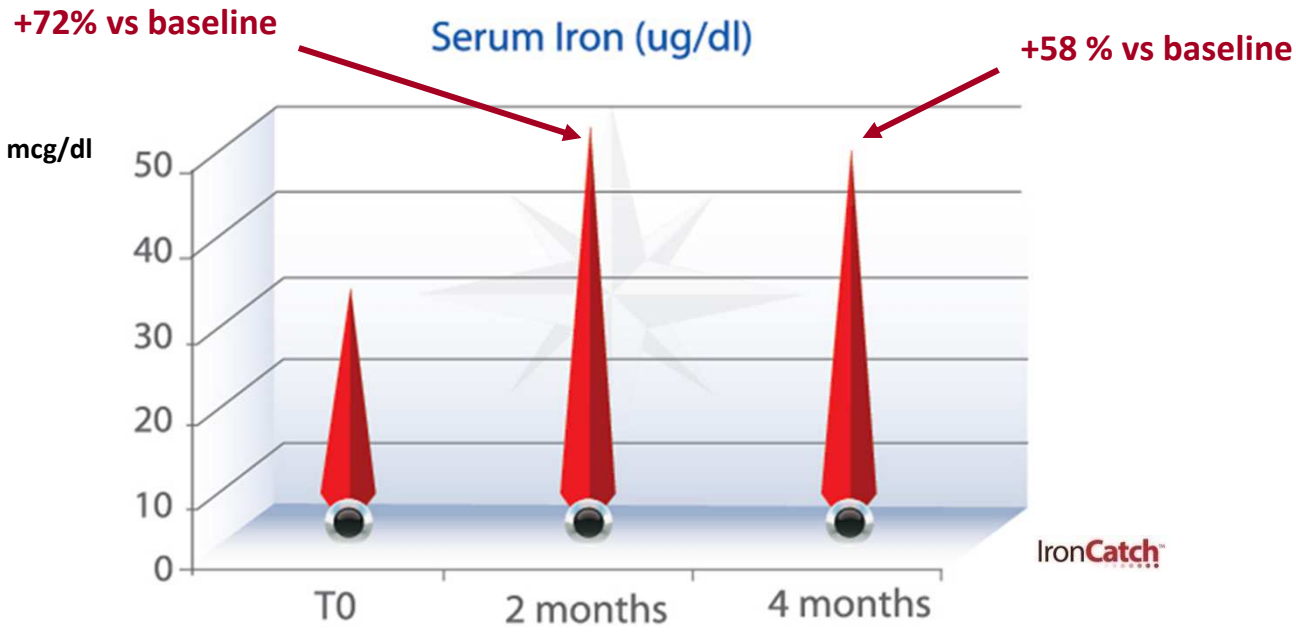
Treatment was carried out for 4 months with measurements at T0- T2 and T4

2nd Study: results

SERUM IRON

IDA Patients suffering from IBD :

	T0	T2	%	T4	%
Serum Iron mcg/dl	26,7± 13,6	46± 27,2	**+ 72**	44,5± 21	**+58**



2nd Study: results

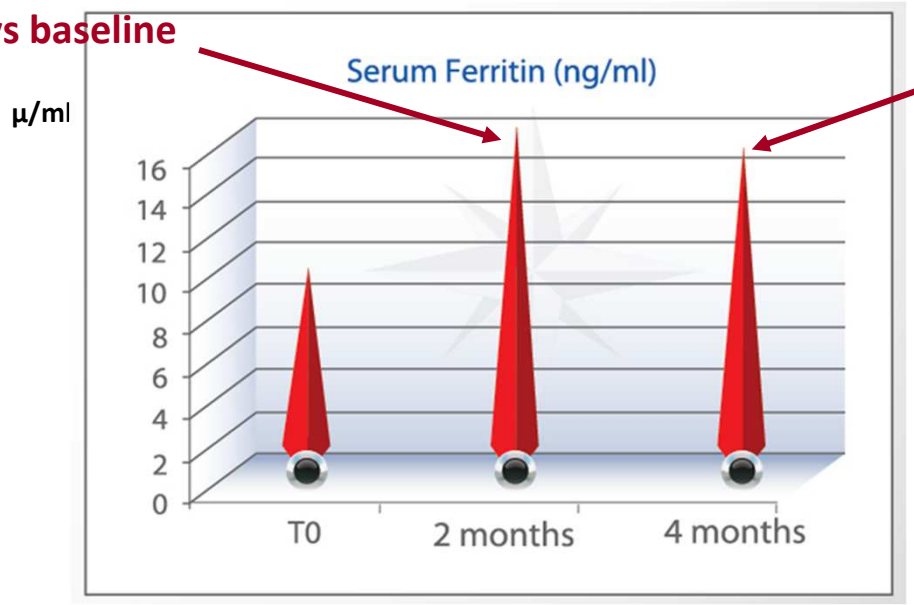
FERRITIN

IDA Patients suffering from IBD :

	T0	T2	%	T4	%
Serum Ferritin µ/ml	8,5± 6,8	14,5±20,5	**+ 70**	14,1± 10,3	**+66**

+70% vs baseline

+ 66 % vs baseline



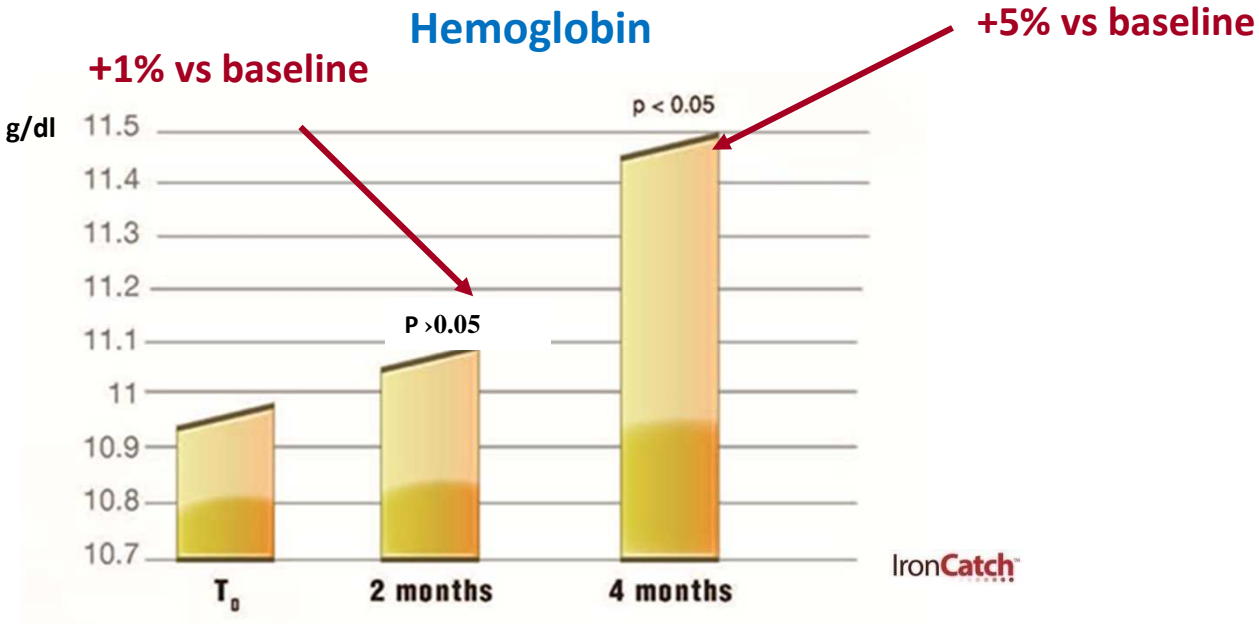
IronCatch

2nd Study: results

HEMOGLOBIN

IDA Patients suffering from IBD:

	T0	T2	%	T4	%
Hemoglobin g/dl	10,96 ± 0,90	11,07±1,02	**+ 1**	11,48± 0,94	**+ 5**



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wjg@wjgnet.com

World J Gastroenterol 2007 March 14; 13(10): 1575-1578
World Journal of Gastroenterology ISSN 1007-9327

RAPID COMMUNICATION

A new iron free treatment with oral fish cartilage polysaccharide for iron deficiency chronic anemia in inflammatory bowel diseases: A pilot study

Andrea Belluzzi, Giulia Roda, Francesca Tonon, Antonio Soleti, Alessandra Caponi, Anna Tuci, Aldo Roda, Enrico Roda

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Correspondence to: Belluzzi Andrea, MD, Ospedale S Orsola, UO Gastroenterologia Via Massarenti, 9-40138 Bologna, Italy. belluzzi@aosp.bo.it
Telephone: +39-51-6363873 Fax: +39-51-6363873
Received: 2006-11-12 Accepted: 2006-12-15

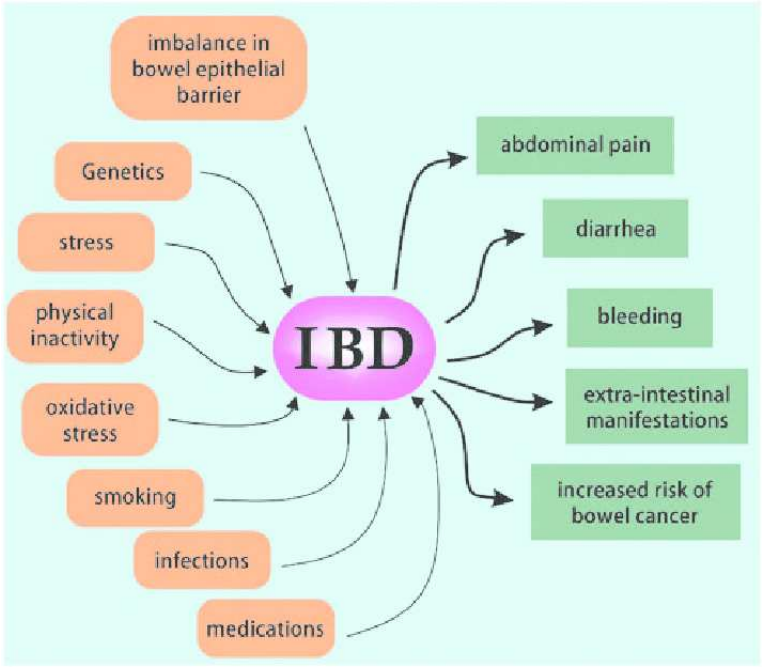
Key words: Ulcerative colitis; Crohn's disease; Anemia; Fish cartilage; Iron deficiency

Belluzzi A, Roda G, Tonon F, Soleti A, Caponi A, Tuci A, Roda A, Roda E. A new treatment with oral fish cartilage polysaccharide for iron deficiency chronic anemia in inflammatory bowel diseases: A pilot study. *World J Gastroenterol* 2007; 13(10): 1575-1578

http://www.wjgnet.com/1007-9327/13/1575.asp

From the above data it is easy to conclude:

Patients affected by IBD and IDA can easily increase in just 60 days:



Serum Iron by 72%

Serum Ferritin by 70%

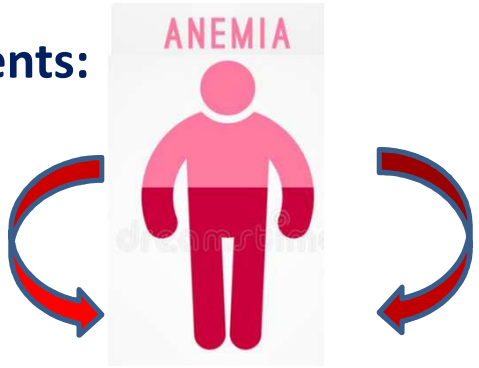
Hemoglobin by 5% in 120 days

No side effects were recorded !

3rd Study: in Jordan

It was carried out on

263 IDA patients:



201 women

and

64 men

Their level of Ferritin was evaluated after only 30 days of treatment with IRONCATH

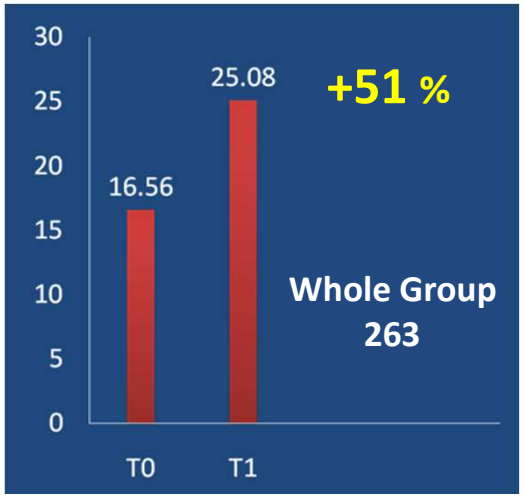
3rd Study: results

FERRITIN

Ferritin ng/ml	T0	T30	%
Men ♂	21,5	26,7	+24
Women ♀	7,2	12,5	+73
Total average	16,6	25,1	+ 51

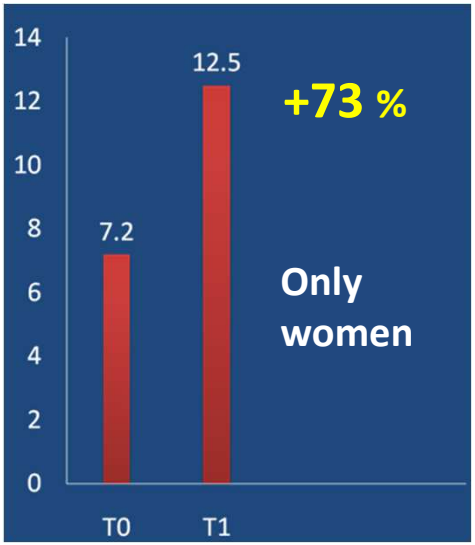
In men Ferritin increases less because the basal line is much higher than in women.

Ferritin ng/ml



IronCatch

Ferritin ng/ml



Conclusions from the three studies

The 3 studies taken into consideration were carried out in three different hospitals, of two different countries.

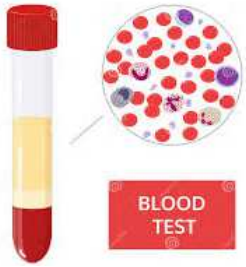
The three groups of patients were also different ones amongst each other :

At the Pavia Hospital patients were 50 fertile women, affected only by Iron Deficency Anemia (IDA)

At the Bologna Hospital patients were 17 men and 8 women affected by IBD and showing IDA

In the Jordan Study patients were numerous, 263 men and women, and the group was not homogeneous.

Final results from the three studies



Incredibly, in all the three studies, notwithstanding the various differences among the patient groups and the technicians making the iron measurements, the *final results* were quite *similar:*

- **Serum Iron increased in average between 58 and 79% in 30 days**
- **Ferritin increased in average between 61 and 70% in 30 days**

The results consolidated in 60- 120 days

NO ADVERSE EFFECT were recorded: fully safe!

Iron values in men increase less than in women because their baseline is higher

Subject with Normal Iron value didn't significantly vary:

No risk of overdose

The Product:

THE IRON-FREE SOLUTION

The most advanced, efficacious, fastest, easiest preparation for IDA

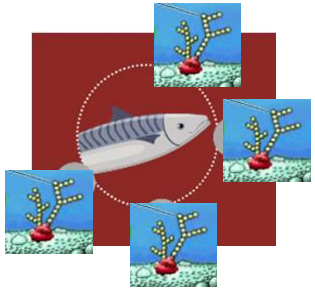
The therapy with *IRONCATCH* is 100% SAFE

- **No side or adverse effects**
- **Fast increase of iron in the body**
- **No contraindications**
- **No risk of overload**

Formulation strategy

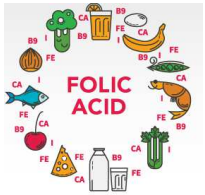
Iron-free

The **MAIN INGREDIENT**: «**FISH FACTOR** «
made of a special mix of **fish oligosaccarides**



The «**CATALIST COMPONENTS**»:

Vitamin C & E: **anti oxidants,**
help protect Fe^{2+} and facilitate iron absorption by the enterocytes



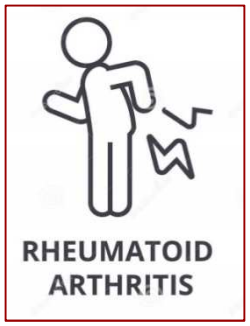
Folic acid: **necessary to prevent megaloblastic anemia and anomalies in the fetal nervous system during pregnancy**

Zn & Cu: **both contribute to the correct use of iron by the biological system.**
CU is essential for Fe absorption by enterocytes and after gastro-resection

Further Iron benefits in IDA : after only 1 week of treatment

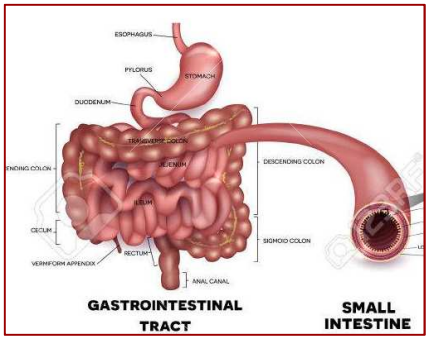
	Outcome	Significant benefit of iron supplementation demonstrated
Symptoms	Fatigue	✓
	Restless leg syndrome	✓
	Hair loss	✓
	Glossitis	✓
Quality of life measures	Impaired QoL	✓
	Impaired physical function	✓
	Impaired cognitive function	✓

Specially recommended when Iron Supplementaion is contraindicated like:

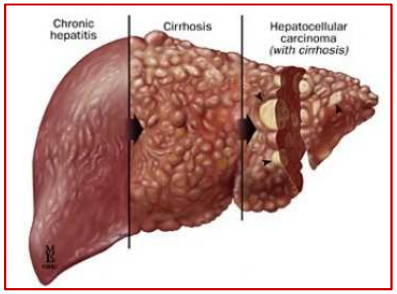


Stomach Ulcer

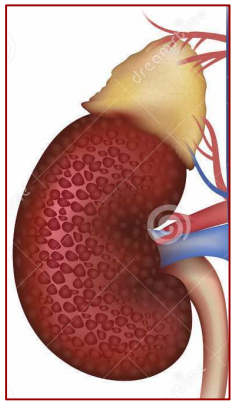
IBD



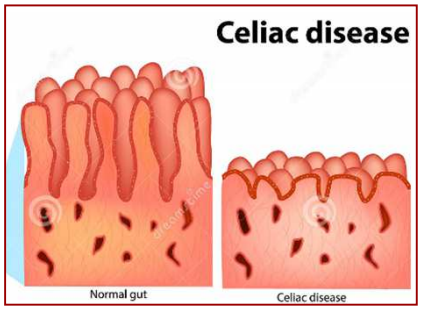
Gastro Resection (*also **CU** is needed*)



Serious Hepathopaties



Serious nephropathies



Anti Cancer Chemiotherapies

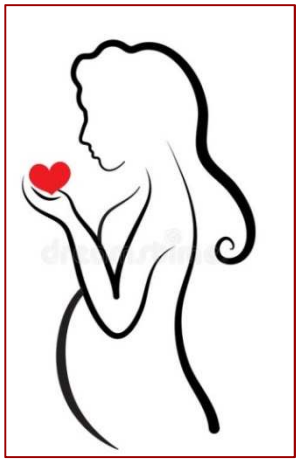
Further elective recommandation for:

Vegans and Vegetarians

Endurance sport

Lactation

Pregnancy

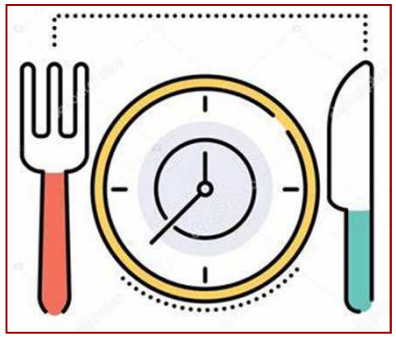


Junior formulation

Reduction of efficacy :

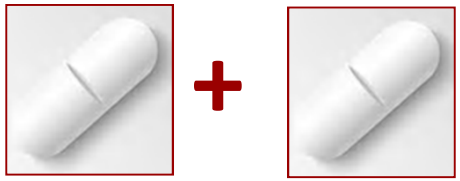
IRONCATCH is active in **acid environment**; therefore

if an **anti-acid Product** is administered during a **meal**



IRON CATCH in **that meal** would lose part of its **efficacy**

How to use it



2 tablets a day during main meals for
2 to **4** months, depending on the subjects

and

1 tablet daily for **maintenance.**

IRON CATH is for everybody and it is **essential for all those IDA patients** for **whom Oral Iron Therapy** is **contraindicated.**

Active no matter which the diet is!