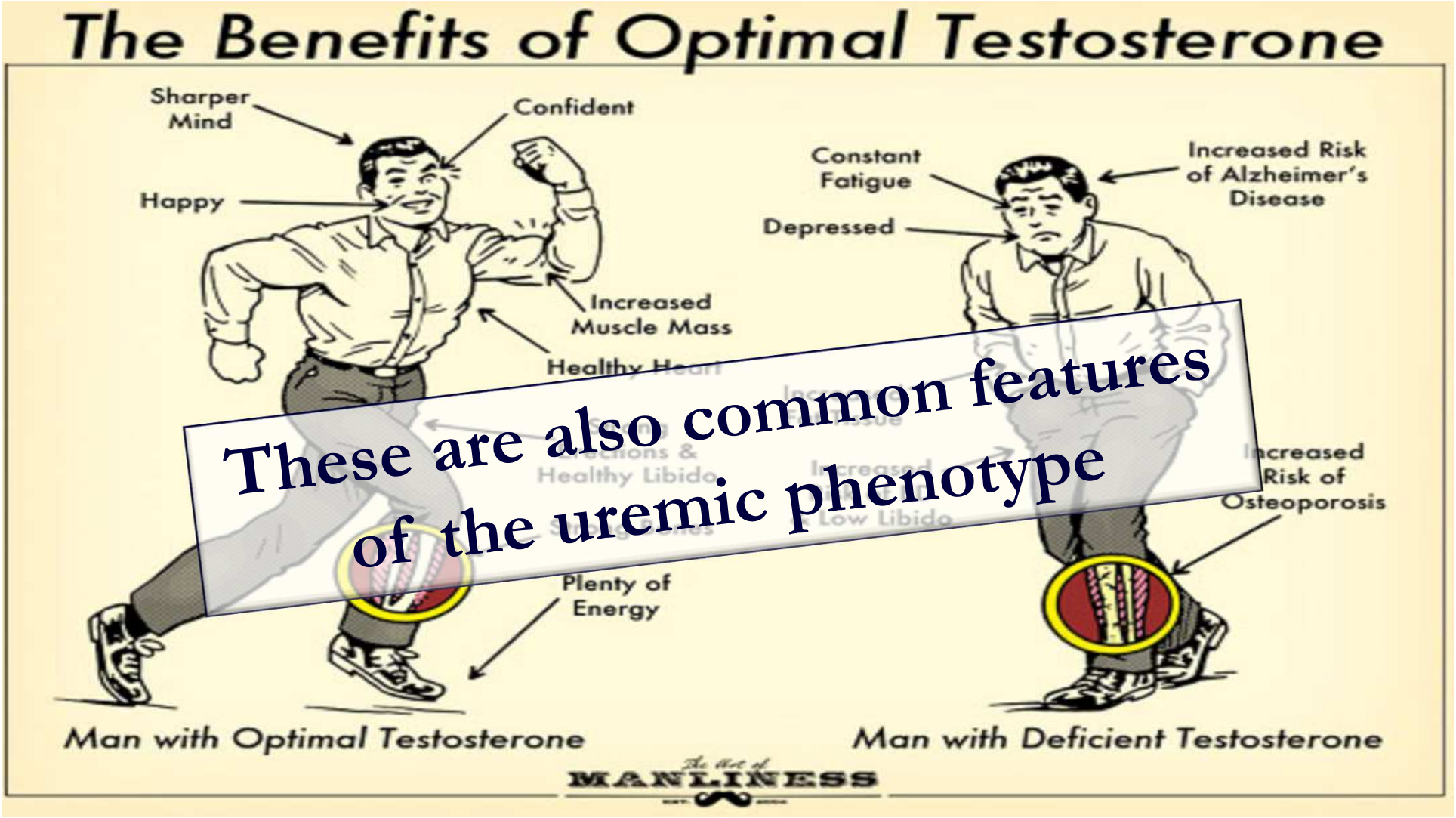
The Vulnerable Man

- Testosterone Deficiency in End Stage Renal Disease

Berliner DialyseSeminar

29. Berliner DialyseSeminar
02.-03.12.2016

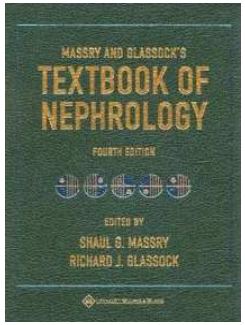


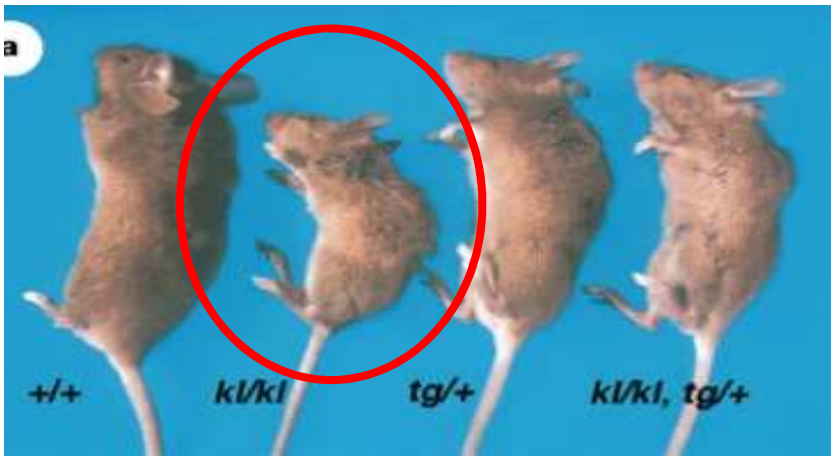
These are also common features of the uremic phenotype

Chronic Kidney Disease – a Clinical Condition with Klotho Deficiency

Mutant klotho mice

- shorter life span
- infertility
- skin atrophy
- vascular calcification
- hypogonadism
- sarcopenia
- osteoporosis





Biochem. J. (2014) **464**, 221–229 (Printed in Great Britain) doi:10.1042/BJ20140739

Testosterone increases renal anti-aging *klotho* gene expression via the androgen receptor-mediated pathway

Shih-Che Hsu*, Shih-Ming Huang*†, Shih-Hua Lin*‡, Shuk-Man Ka§, Ann Chen¶, Meng-Fu Shih** and Yu-Juei Hsu*‡[1]
*Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, R.O.C.
†Department of Biochemistry, National Defense Medical Center, Taipei, Taiwan, R.O.C.
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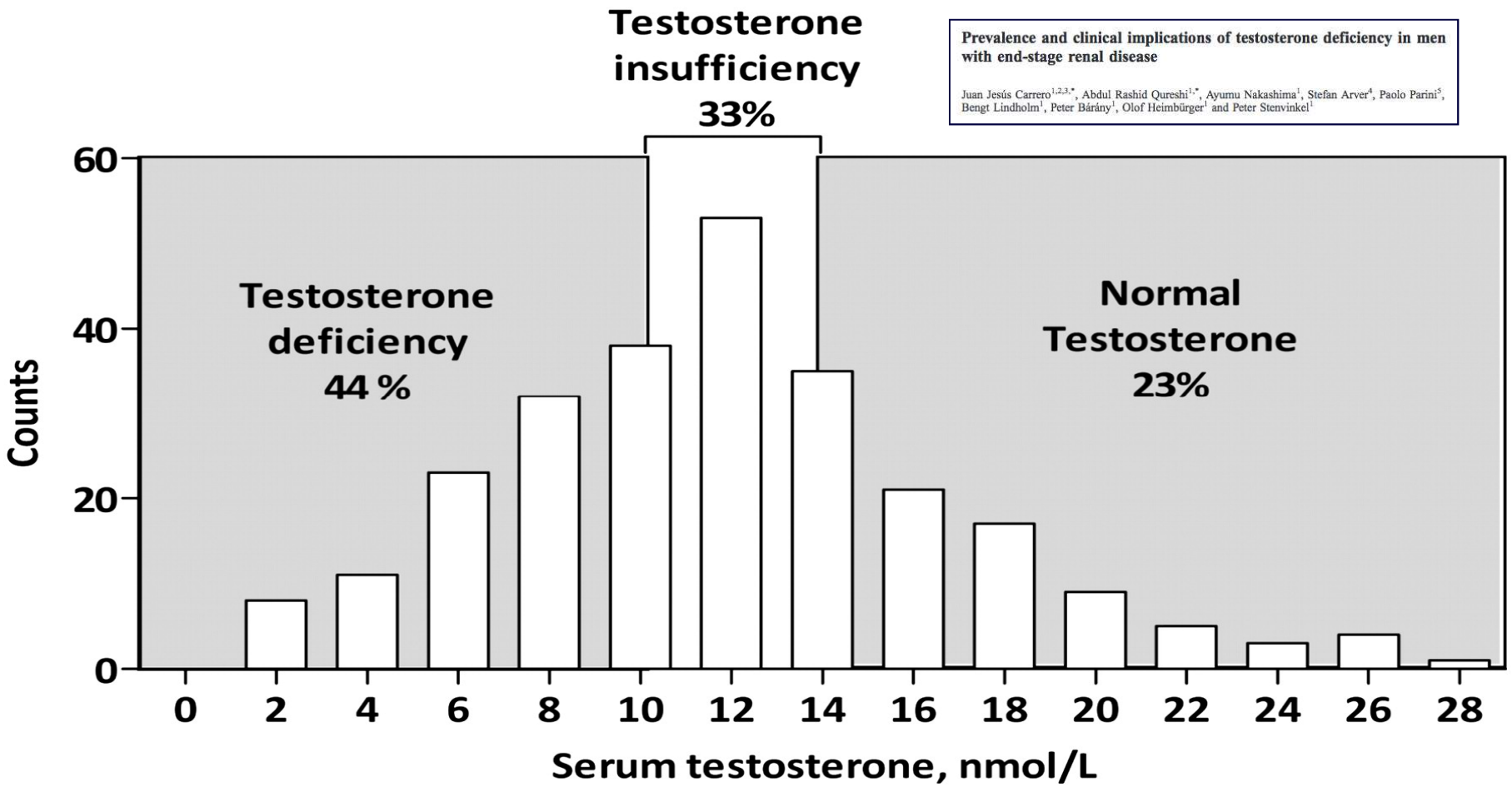
§Graduate Institute of Aerospace and Undersea Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.
¶Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.
**Department of Nephrology, Mackay Memorial Hospital, Taipei, Taiwan, R.O.C.

Testosterone Deficiency is a Common Feature of CKD

Prevalence and clinical implications of testosterone deficiency in men with end-stage renal disease

Juan Jesús Carrero[1,2,3,*], Abdul Rashid Qureshi[1,*], Ayumu Nakashima[1], Stefan Arver[4], Paolo Parini[5], Bengt Lindholm[1], Peter Bárány[1], Olof Heimbürger[1] and Peter Stenvinkel[1]



Causes of Low Testosterone Levels in CKD

- Prolactin-induced inhibition of gonadotropins
- Co-morbidities
  - Diabetes
  - Heart disease
  - Obesity
  - Old age
  - Rheumatoid flares
- Uremic bone disease (?)
- Proteinuria (?)

Prolactin Levels, Endothelial Dysfunction, and the Risk of Cardiovascular Events and Mortality in Patients with CKD

CJASN 2011

Juan Jesús Carrero,† John Kyriazis,* Alper Sonmez,‡ Ioannis Tzanakis,‡ Abdul Rashid Qureshi,* Peter Stenvinkel,* Mutlu Saglam,¶ Kostas Stylianou,** Halil Yaman,†† Abdullah Taslipinar,‡ Abdulgaffar Vural,‡‡ Mahmut Gok,‡‡ Mojdat Yenicesu,‡‡ Eugene Daphnis,** and Mahmut Ilker Yilmaz‡‡*

Hypogonadotropic Hypogonadism in Nephrotic Rats: Increased Sensitivity to Negative Feedback Effects of Testosterone

Allan R. Glass, Judith Beach, and Robert A. Vigersky

Metabolism 1985

Drugs Used by Nephrologist May Affect Testosterone Levels

Renin–angiotensin blockade reduces serum free testosterone in middle-aged men on haemodialysis and correlates with erythropoietin resistance

NDT 2005

Michael DeLong, Joy L. Logan, Kim-Chong Yong and Yeong-Hau H. Lien

Rosuvastatin decreases testosterone levels but not sexual function in men with type 2 diabetes

Ching Jung Hsieh [a,*], *Bin Huang* [b]

Diabetes Res 2016

Kidney & Blood Pressure Research

Kidney Blood Press Res 2016;41:1-8
DOI: 10.1159/000368541
Published online: January 08, 2016
Accepted: November 17, 2015

1423-0143/16/0411-0001$39.50/0
www.karger.com/kbr

Original Paper

Changes of Serum Total and Free Testosterone Concentrations in Male Chronic Hemodialysis Patients with Secondary Hyperparathyroidism in Response to Cinacalcet Treatment

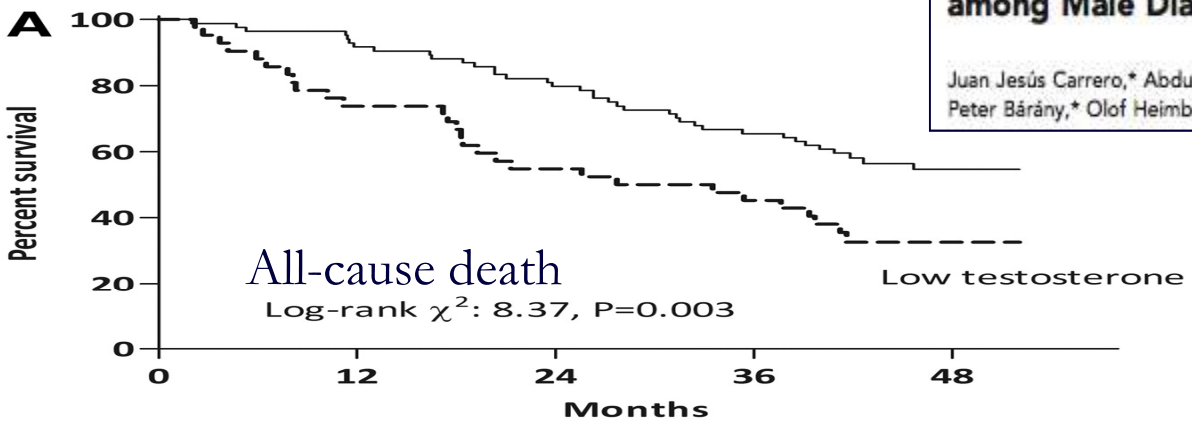
Piotr Kuczera Marcin Adamczak Andrzej Wiecek

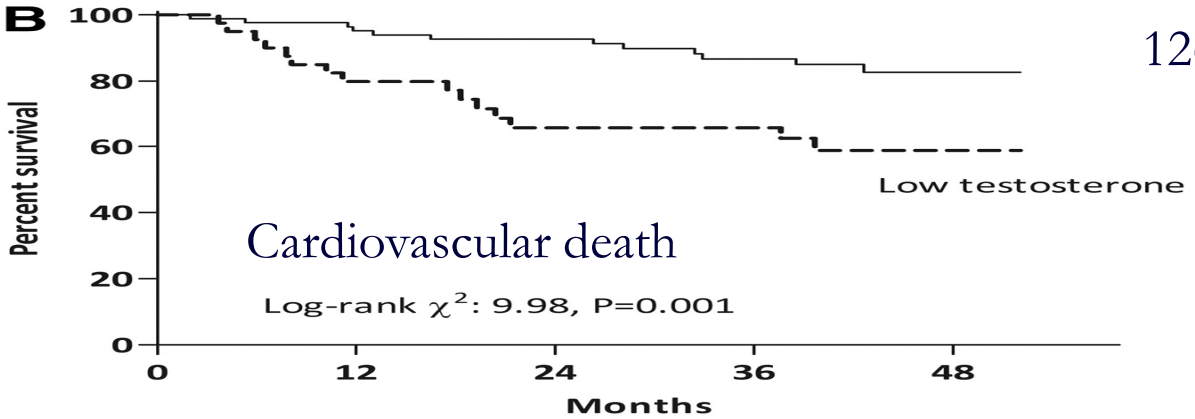
Low Testosterone Predicts Poor Outcome in CKD

Low Serum Testosterone Increases Mortality Risk among Male Dialysis Patients

Juan Jesús Carrero,* Abdul Rashid Qureshi,* Paolo Parini,† Stefan Arver,‡ Bengt Lindholm,* Peter Bárány,* Olof Heimbürger,* and Peter Stenvinkel*

JASN 2009





126 prevalent males on HD

Serum Testosterone Levels and Clinical Outcomes in Male Hemodialysis Patients

Aminu K. Bello, MD, PhD,[1] Peter Stenvinkel, MD, PhD,[2] Meng Lin, MSci,[1] Brenda Hemmelgarn, MD, PhD,[3] Ravi Thadhani, MD, MPH,[4] Scott Klarenbach, MD, MSci,[1] Christopher Chan, MD,[5] Deborah Zimmerman, MD,[6] George Cembrowski, MD, PhD,[1] Giovanni Strippoli, MD, PhD,[7] Juan-Jesus Carrero, PhD,[2] and Marcello Tonelli, MD, SM[1]

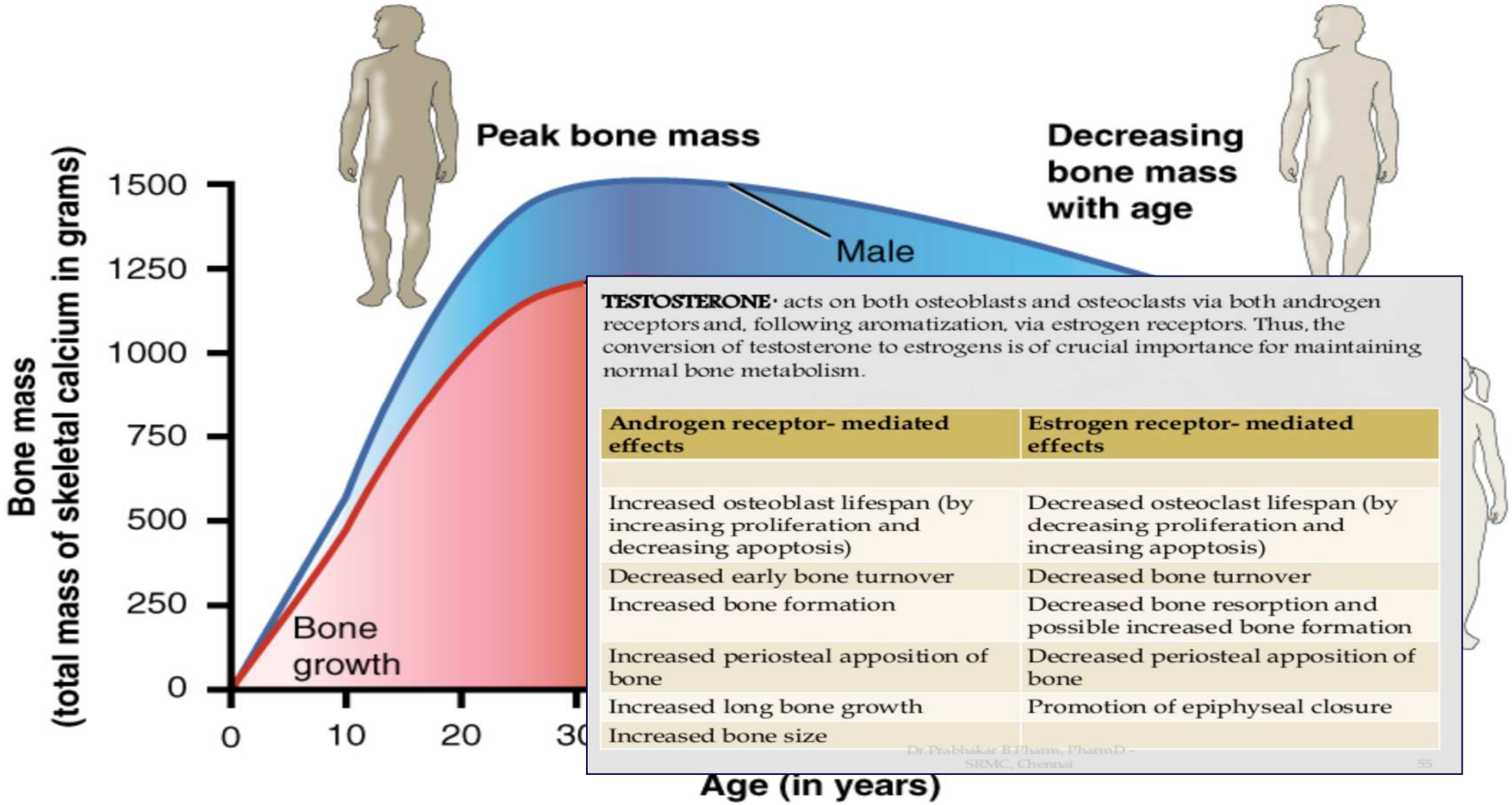
623 males

	Baseline Total Testosterone[a]			
	Normal (>346 ng/dL)	Borderline (231-346 ng/dL)	Low (<231 ng/dL)	*P* for Trend
Age <63 y[b]				<0.001
No. of patients	63	92	166	
No. of events	6	13	37	
Adjusted HR (95% CI)	1.00 (reference)	2.67 (0.96-7.44)	2.93 (1.10-7.78)	
Age ≥63 y[b]				0.1
No. of patients	40	85	177	
No. of events	14	25	71	
Adjusted HR (95% CI)	1.00 (reference)	0.97 (0.45-2.07)	1.03 (0.49-2.15)	

Am J Kidney Dis. 63(2):268-275.

Potential Beneficial Effects of Testosterone Supplementation on the Uremic Phenotype

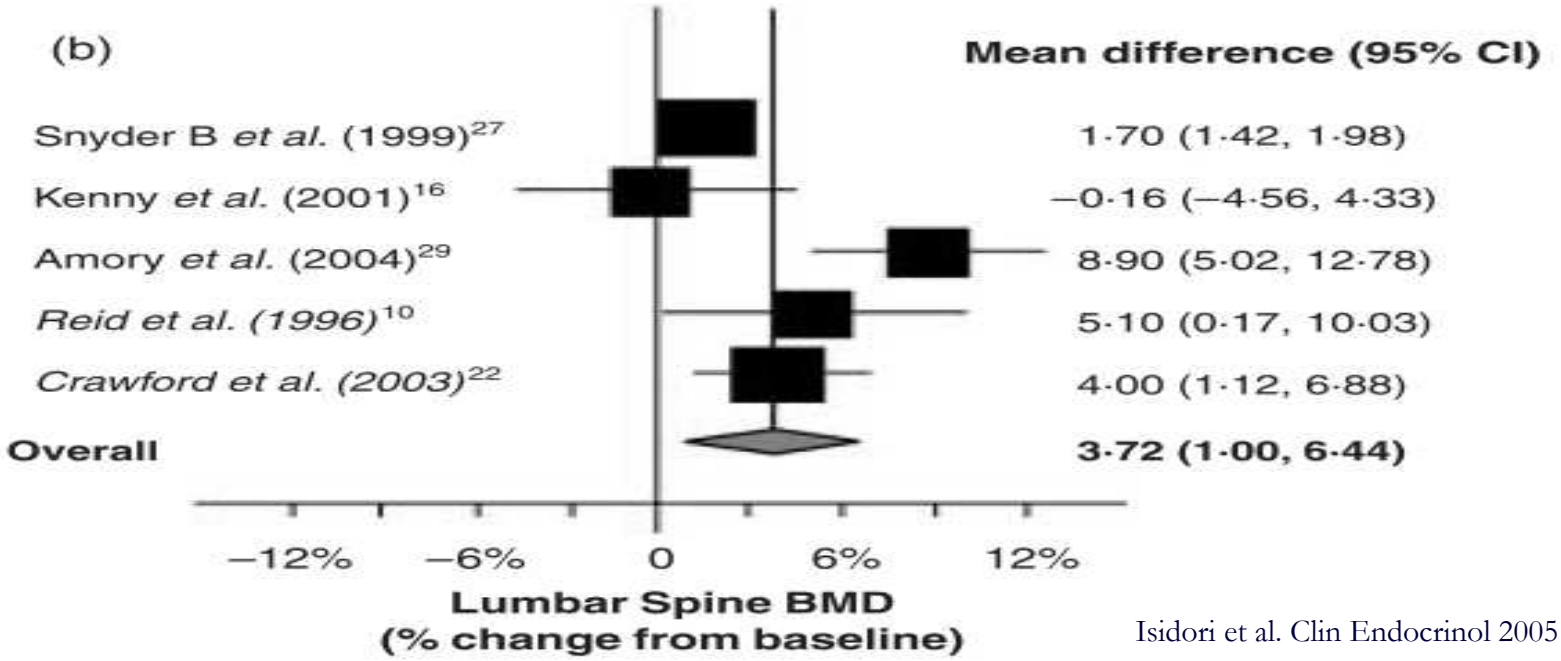
- Life quality
- Sexual functions including libido
- **Bone quality**
- Muscle strength
- Depression
- Insulin resistance
- Inflammation
- Oxidative stress
- Vascular function
- Anemia and iron utilization



TESTOSTERONE: acts on both osteoblasts and osteoclasts via both androgen receptors and, following aromatization, via estrogen receptors. Thus, the conversion of testosterone to estrogens is of crucial importance for maintaining normal bone metabolism.

Androgen receptor- mediated effects	Estrogen receptor- mediated effects
Increased osteoblast lifespan (by increasing proliferation and decreasing apoptosis)	Decreased osteoclast lifespan (by decreasing proliferation and increasing apoptosis)
Decreased early bone turnover	Decreased bone turnover
Increased bone formation	Decreased bone resorption and possible increased bone formation
Increased periosteal apposition of bone	Decreased periosteal apposition of bone
Increased long bone growth	Promotion of epiphyseal closure
Increased bone size	

Low Testosterone
- a Cause of Osteoporosis in Males



Isidori et al. Clin Endocrinol 2005

Effects of testosterone on bone density reported as % change from basal in lumbar spine

Hypogonadism is Associated with Vitamin-D Deficiency in Nonrenal Patients

VITAMIN D SYNTHESIS

Association of vitamin D status with serum androgen levels in men

E. Wehr*, S. Pilz*, B. O. Boehm†, W. März‡·§ and B. Obermayer-Pietsch*

Clin Endocrinol 2010

*Department of Internal Medicine, Division of Endocrinology and Nuclear Medicine, Medical University Graz, Graz, Austria, †Department of Internal Medicine, Division of Endocrinology and Diabetes, Ulm University, Ulm, ‡Department of Public Health, Social and Preventive Medicine, Mannheim Medical Faculty, University of Heidelberg, Mannheim and §Synlab Center of Laboratory Diagnostics, Heidelberg, Germany

European Journal of Endocrinology (2012) **166** 77–85 ISSN 0804-4643

CLINICAL STUDY

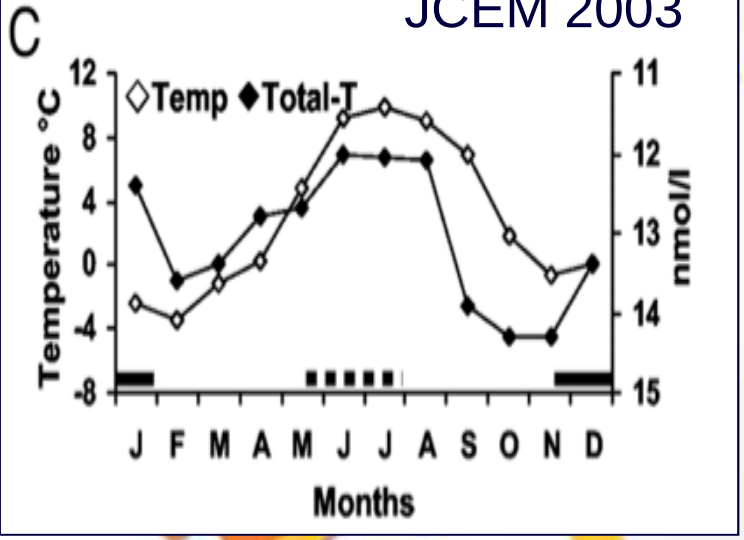
Association of hypogonadism with vitamin D status: the European Male Ageing Study

David M Lee, Abdelouahid Tajar, Stephen R Pye, Steven Boonen[1], Dirk Vanderschueren[2], Roger Bouillon[3], Terence W O'Neill, Gyorgy Bartfai[4], Felipe F Casanueva[5,6], Joseph D Finn[7], Gianni Forti[8], Aleksander Giwercman[9], Thang S Han[10], Ilpo T Huhtaniemi[11], Krzysztof Kula[12], Michael E J Lean[13], Neil Pendleton[14], Margus Punab[15] and Frederick C W Wu[7], the EMAS study group[†]

UNLIKELY LIKELY

VITAMIN D SYNTHESIS

JCEM 2003



UNLIKELY LIKELY

Potential Beneficial Effects of Testosterone Supplementation on the Uremic Phenotype

- Life quality
- Sexual functions including libido
- Bone quality
- Muscle strength
- Depression
- Insulin resistance
- Inflammation
- Oxidative stress
- Vascular function
- **Anemia and iron utilization**

ORIGINAL INVESTIGATION

Low Testosterone Levels and the Risk of Anemia in Older Men and Women

Luigi Ferrucci, MD, PhD; Marcello Maggio, MD; Stefania Bandinelli, MD; Shehzad Basaria, MD; Fulvio Lauretani, MD; Alessandro Ble, MD; Giorgio Valenti, MD; William B. Ershler, MD; Jack M. Guralnik, MD, PhD; Dan L. Longo, MD

Arch Intern Med. 2006;166:1380-1388

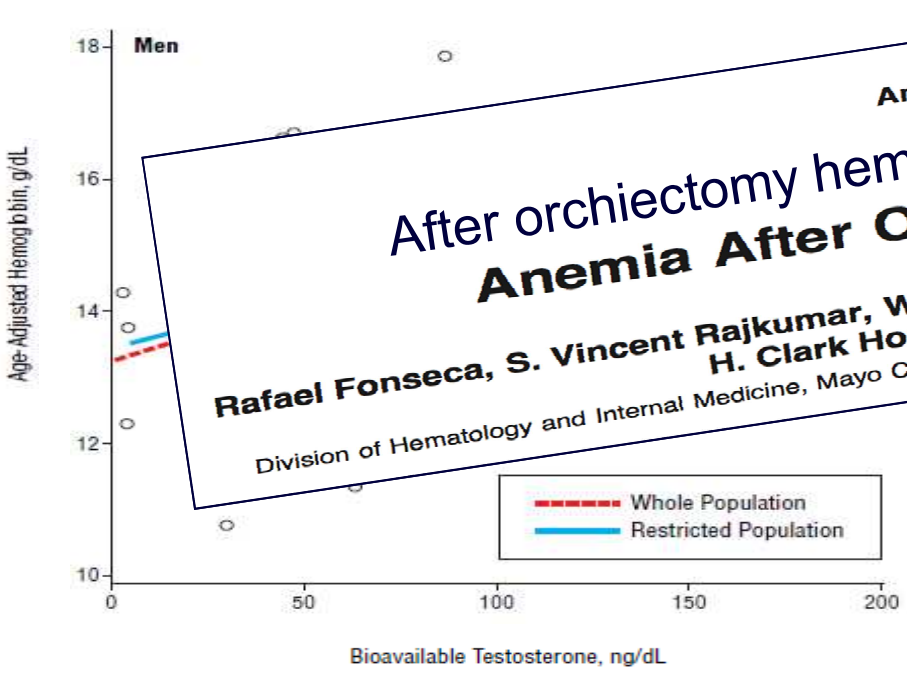
American Journal of Hematology 59:230–233 (1998)

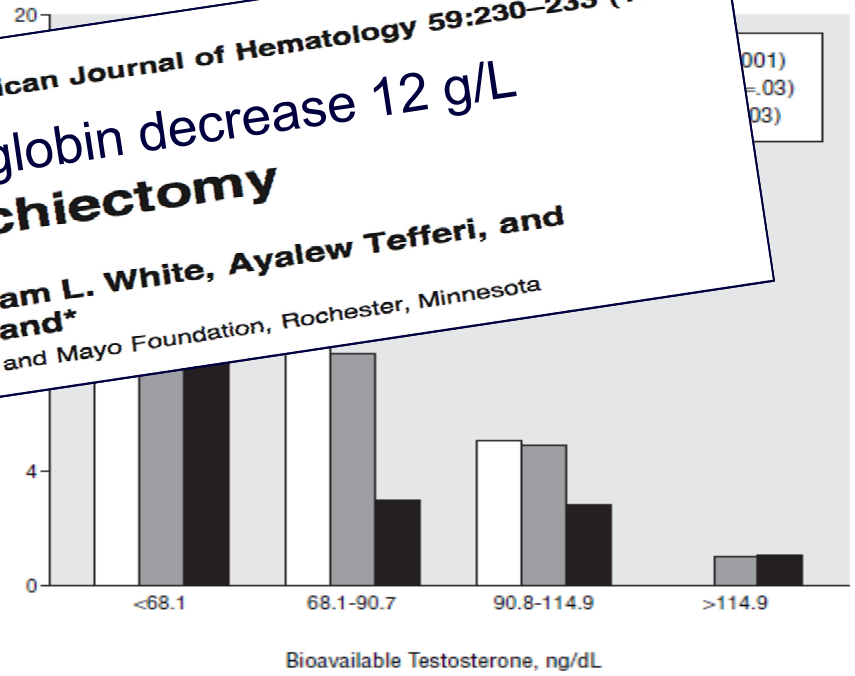
After orchiectomy hemoglobin decrease 12 g/L

Anemia After Orchiectomy

Rafael Fonseca, S. Vincent Rajkumar, William L. White, Ayalew Tefferi, and H. Clark Hoagland*

Division of Hematology and Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota





Hypothesis

- Endogenous testosterone levels are associated with hemoglobin levels in men with CKD.

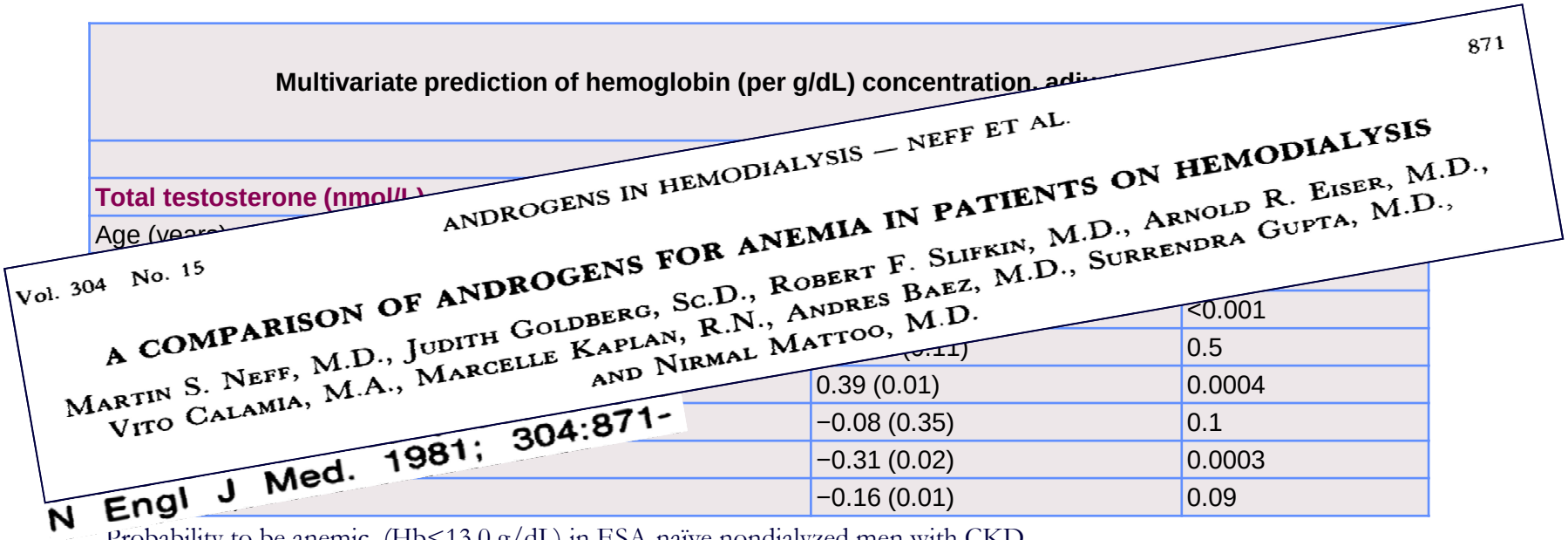
- Testosterone deficiency contributes to reduced ESA responsiveness in male HD patients.

Testosterone deficiency is a cause of anaemia and reduced responsiveness to erythropoiesis-stimulating agents in men with chronic kidney disease

NDT 2012

Juan Jesús Carrero[1,2,3,4], Peter Bárány[1], Mahmut Ilker Yilmaz[5], Abdul Rashid Qureshi[2], Alper Sonmez[6], Olof Heimbürger[1], Tanez Ozgurtas[7], Mujdat Yenicesu[5], Bengt Lindholm[2] and Peter Stenvinkel[1]

Testosterone vs. Hemoglobin in CKD 1-5 (I)


ANDROGENS IN HEMODIALYSIS — NEFF ET AL. 871

Vol. 304 No. 15

A COMPARISON OF ANDROGENS FOR ANEMIA IN PATIENTS ON HEMODIALYSIS

MARTIN S. NEFF, M.D., JUDITH GOLDBERG, SC.D., ROBERT F. SLIFKIN, M.D., ARNOLD R. EISER, M.D., VITO CALAMIA, M.A., MARCELLE KAPLAN, R.N., ANDRES BAEZ, M.D., SURRENDRA GUPTA, M.D., AND NIRMAL MATTOO, M.D.

N Engl J Med. 1981; 304:871-

Multivariate prediction of hemoglobin (per g/dL) concentration, adj		
Total testosterone (nmol/L)		
Age (years)		
		<0.001
	(0.11)	0.5
	0.39 (0.01)	0.0004
	−0.08 (0.35)	0.1
	−0.31 (0.02)	0.0003
	−0.16 (0.01)	0.09

Probability to be anemic (Hb<13.0 g/dL) in ESA-naïve nondialyzed men with CKD

	Odds Ratio	95% CI	P value
Testosterone deficiency <10 nmol/L	5.30	2.23-12.56	<0.0001

Adjusted for age, BMI, diabetes, CVD, eGFR, albumin, CRP, PTH

Testosterone vs. ESA Dose in HD-patients (II)

General characteristics of 126 ESA-treated prevalent male HD patients stratified according to median weekly ESA dose normalized per kg of body weight (IU/kg/week).

	ESA ≤ 121 IU/kg/week, $N = 63$	ESA > 121 IU/kg/week, $N = 63$	P-value
Age, years	64 (47–76)	62 (49–70)	0.4
Vintage, months	28 (10–58)	24 (17–54)	0.8
Davies comorbidity score, %			
Low	20	17	0.1
Middle	60	49	
High	19	33	
BMI, kg/m^2	25.4 (22.5–28.2)	22.3 (20.0–25.7)	<0.0001
s-Albumin, g/dL	3.5 (3.3–3.8)	3.5 (3.1–3.8)	0.4
CRP, mg/L	6.4 (2.5–17.0)	8.7 (3.4–27.7)	0.2
Haemoglobin, g/dL	12.1 (11.1–13.3)	12.3 (11.2–13.3)	0.2
Hypochromic RBC, %	0.8 (0.4–1.5)	2.6 (0.6–5.9)	<0.0001
Intravenous iron medication, %	76	63	0.2
SHBG, nmol/L	27 (19–42)	26 (20–38)	0.9
Total testosterone, nmol/L	11.0 (8.4–13.0)	8.0 (6.6–12.0)	0.04

Data are expressed as medians (interquartile ranges) or percentages.

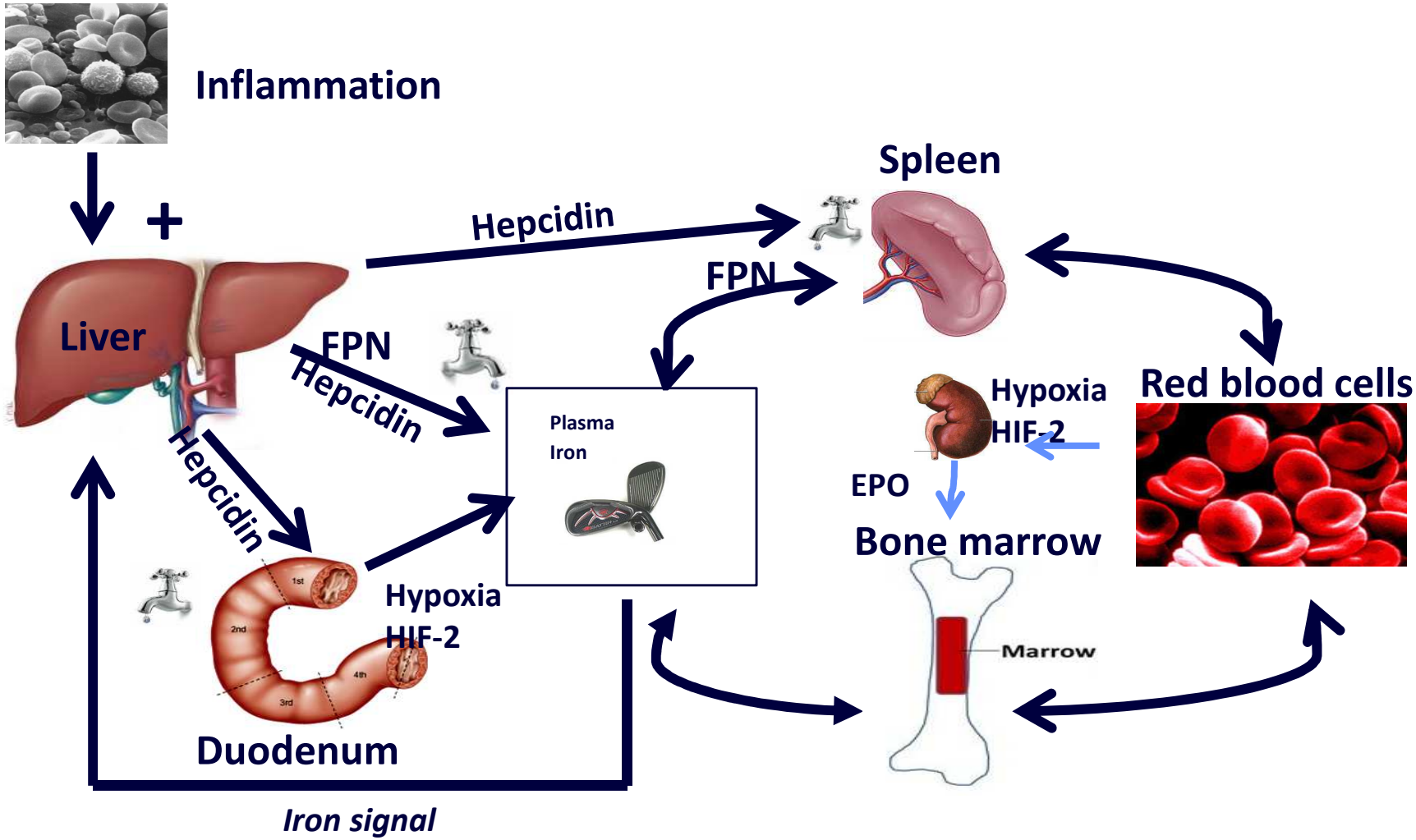
Testosterone vs. ESA Dose in HD-patients (III)

Model	Prediction of ESA dose (U/kg/week)	β (SE)	r^2	P-value
1	Total testosterone (in nmol/L)	−0.28 (2.3)	0.05	0.007
2	1 + Age (in years) and SHBG (in nmol/L)	−0.28 (2.5)	0.04	0.004
3	2 + Davies comorbidity score	−0.27 (2.4)	0.06	0.006
4	3 + CRP (in mg/L) and albumin (in g/L)	−0.26 (2.6)	0.06	0.02

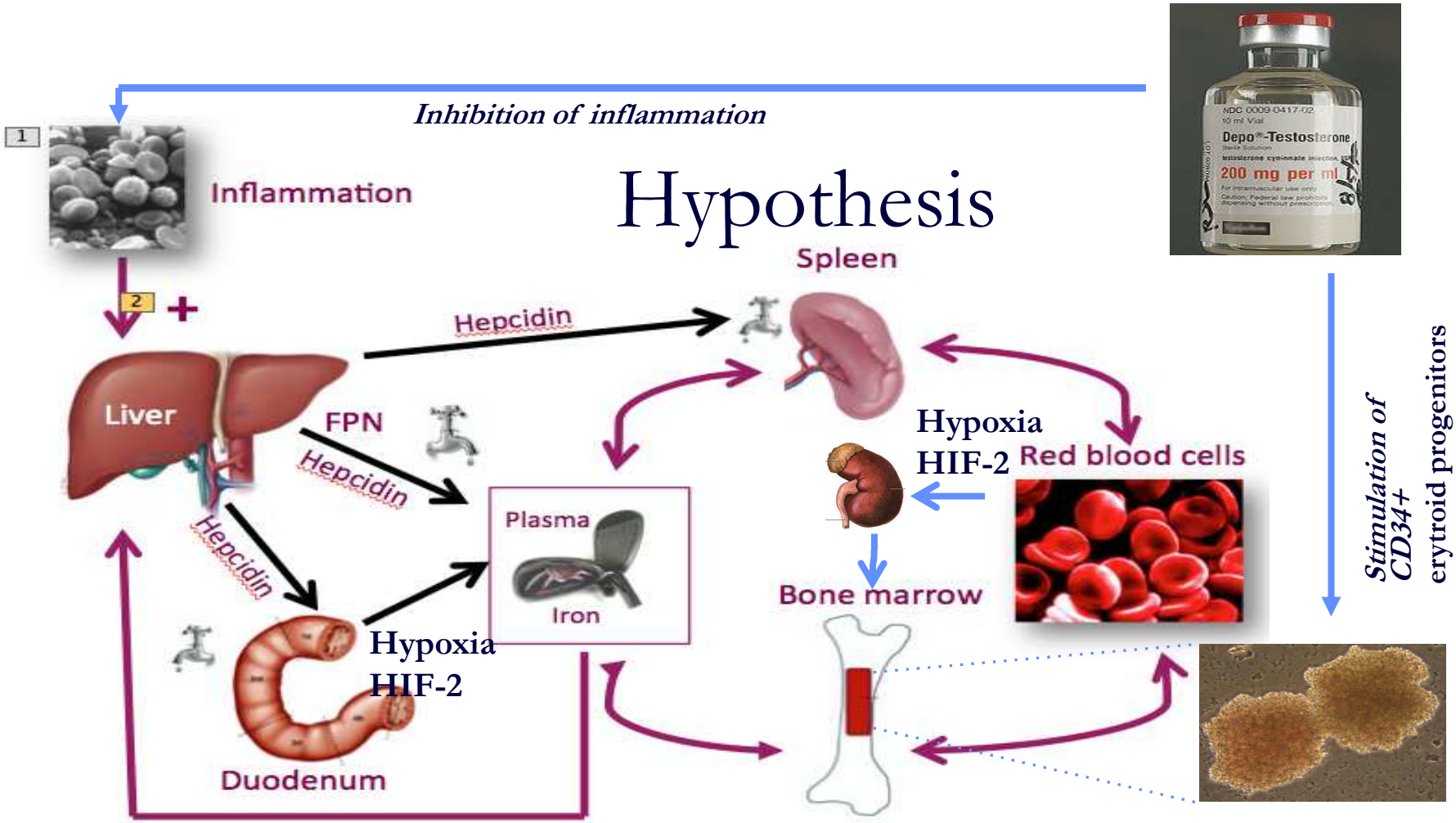
Probability to poor ESA responsiveness in ESA treated hemodialysis men.

	Odds Ratio	95% CI	P value
Testosterone deficiency <10 nmol/L	2.68	1.17-6.14	0.001

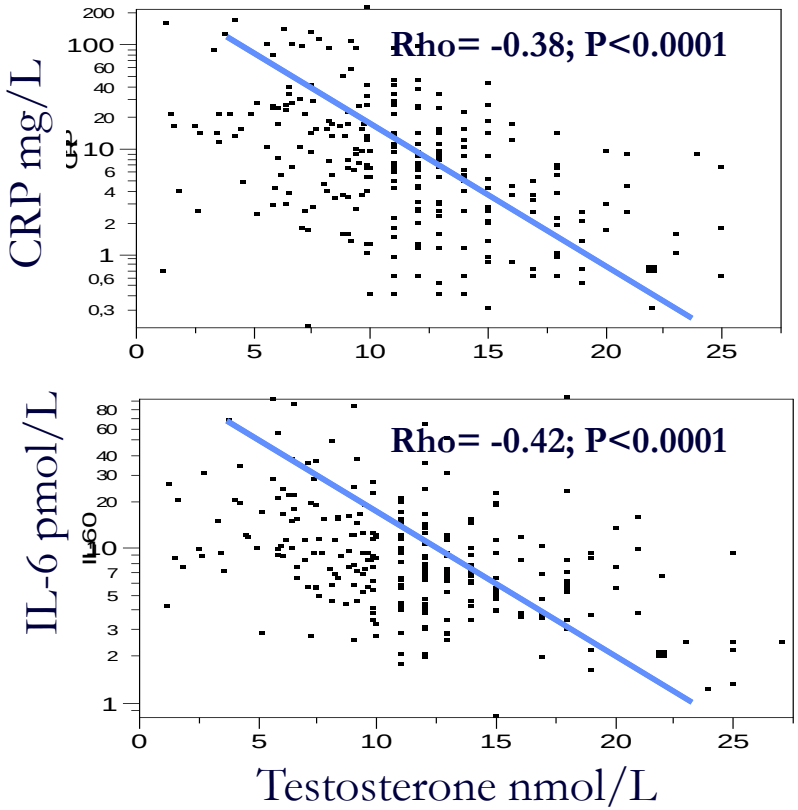
Adjusted for age, SHBG, co-morbidities, albumin, CRP


Inflammation
+
Liver
Hepcidin
Spleen
FPN
FPN
Hepcidin
Hepcidin
Plasma
Iron
Hypoxia
HIF-2
Red blood cells
EPO
Bone marrow
Hypoxia
HIF-2
Marrow
Duodenum
Iron signal

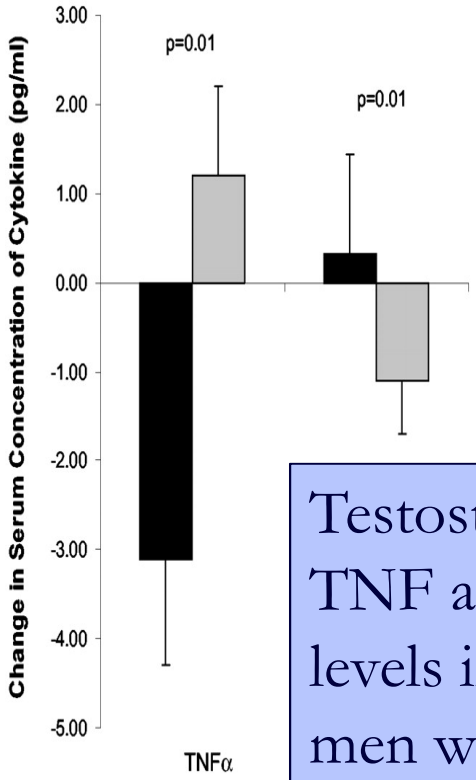
Hypothesis


Inhibition of inflammation
1
Inflammation
2
+
Spleen
Hepcidin
Liver
FPN
Hepcidin
Hepcidin
Plasma
Iron
Hypoxia
HIF-2
Duodenum
Hypoxia
HIF-2
Red blood cells
Bone marrow
Depo®-Testosterone
200 mg per ml
Stimulation of
CD34+
erytroid progenitors

Is Inflammation a Cause of Low Testosterone Levels in CKD?



Carrero et al. J Am Soc Nephrol. 2009 Mar;20(3):613-620



Testosterone decreased TNF and increased IL-10 levels in hypogonadal men with heart failure

Malkin et al. J Clin Endocrinol Metab. 2004;89:3313-8.

ORIGINAL ARTICLE

Endocrine Research

Testosterone Suppresses Hepcidin in Men: A Potential Mechanism for Testosterone-Induced Erythrocytosis

Eric Bachman, Rui Feng,* Thomas Travison,* Michelle Li, Gordana Olbina, Vaughn Ostland, Jagadish Ulloor, Anqi Zhang, Shehzad Basaria, Tomas Ganz, Mark Westerman, and Shalender Bhasin

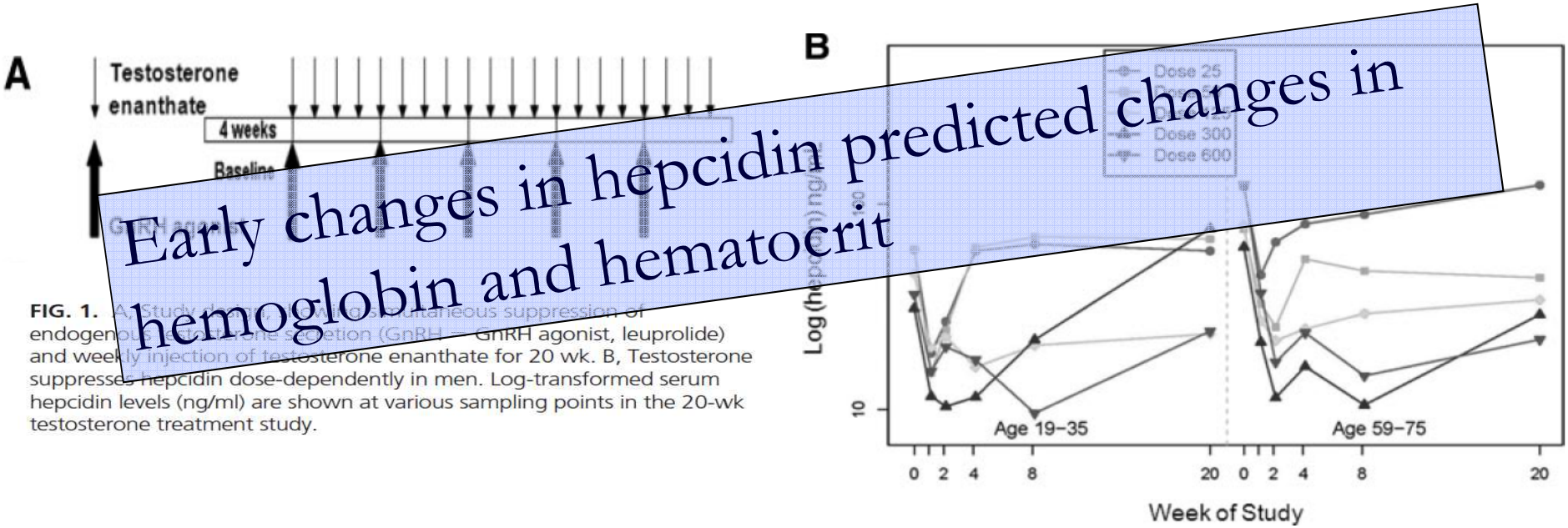
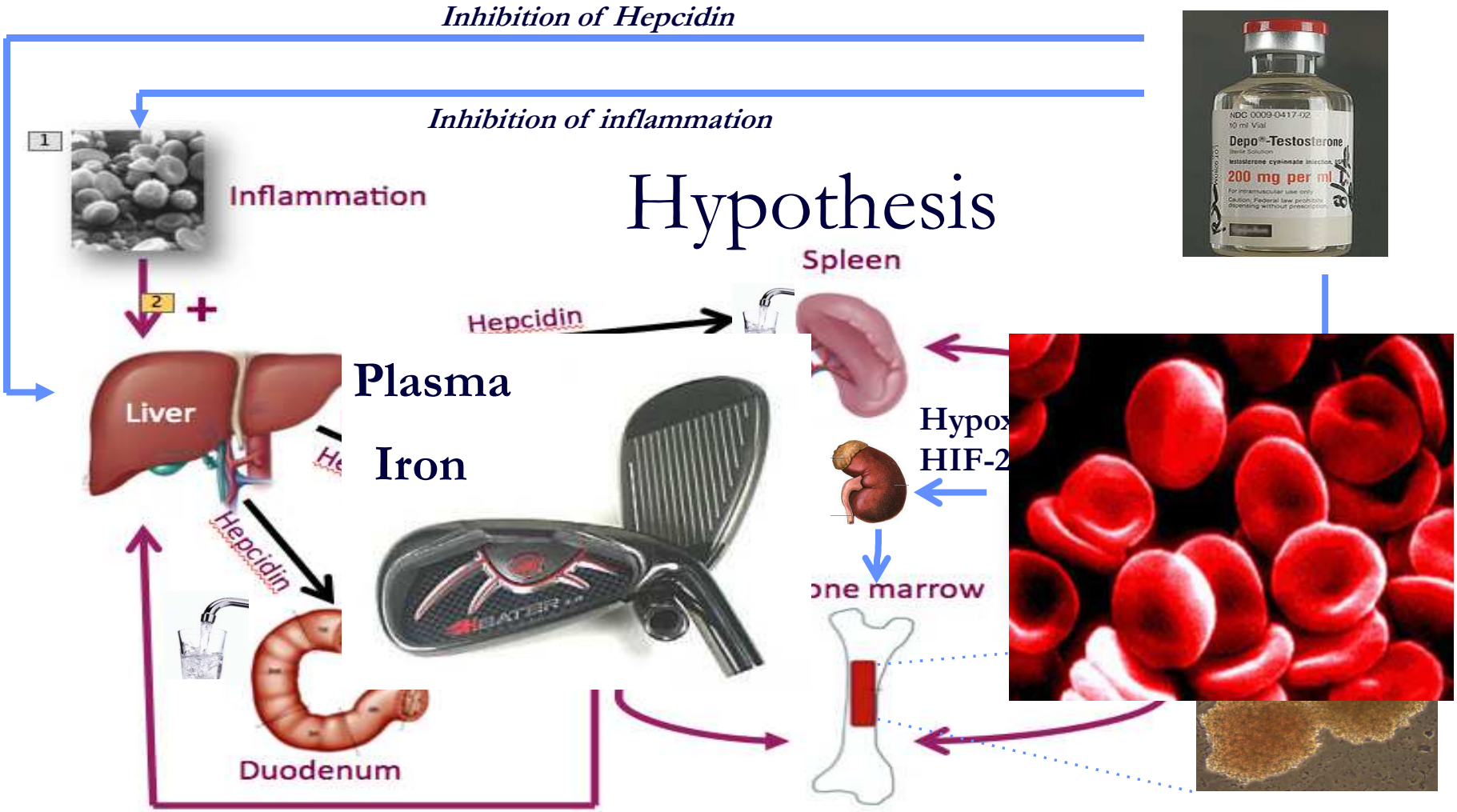


FIG. 1. A, Study design for the simultaneous suppression of endogenous testosterone secretion (GnRH agonist, leuprolide) and weekly injection of testosterone enanthate for 20 wk. B, Testosterone suppresses hepcidin dose-dependently in men. Log-transformed serum hepcidin levels (ng/ml) are shown at various sampling points in the 20-wk testosterone treatment study.

Early changes in hepcidin predicted changes in hemoglobin and hematocrit

J Clin Endocrinol Metab. 2010 Oct;95(10):4743-7

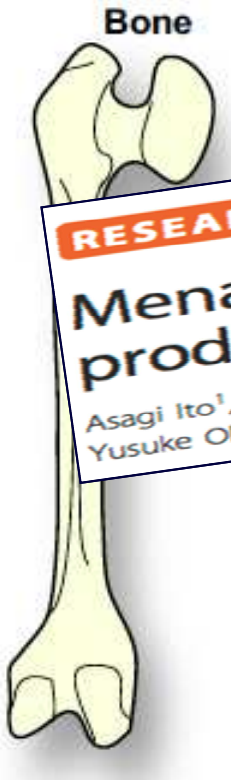

Inhibition of Hepcidin
Inhibition of inflammation
Hypothesis
1
Inflammation
2
+
Liver
Hepcidin
Spleen
Hepcidin
Plasma
Iron
Hypox
HIF-2
one marrow
Duodenum
Depo®-Testosterone
200 mg per ml

Endocrine Regulation of Male Fertility by the Skeleton

2011

Cell

Franck Oury,[1,6] Grzegorz Sumara,[1,6] Olga Sumara,[1] Mathieu Ferron,[1] Haixin Chang,[3] Charles E. Smith,[4] Louis Hermo,[4] Susan Suarez,[3] Bryan L. Roth,[5] Patricia Ducy,[2] and Gerard Karsenty[1,*]



Testis

RESEARCH

Open Access

Menaquinone-4 enhances testosterone production in rats and testis-derived tumor cells

Asagi Ito[1], Hitoshi Shirakawa[1*], Naofumi Takumi[1], Yoshihiko Minegishi[1], Ai Ohashi[1], Zakir H Howlader[1,2], Yusuke Ohsaki[1], Toshiro Sato[3], Tomoko Goto[1] and Michio Komai[1]

To be reproductive as a man you need strong bones

a

...ying cells in the **testicles** which increase synthesis of **testosterone**

DiaTest - Study Design

EudraCT-nr: 2011-005439-20

Population

- **Mal**
- **HD-**
- **ESA**
- **Test**
- **PSA**

Extra f

Safety aspects

- Prostata hypertrophy and cancer (check PSAs)
- Increasing hematocrit
- Sleep apnoea
- Volyme retention
- Liver toxicity

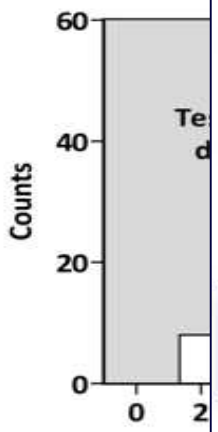
Week 36

Inflammation markers, SF36, MDRAS, ADAM, oxidative stress biomarkers, D-vitamin, PSA, DEXA, pqCT, handgrip, SGA, pulse wave velocity, bioimpedance, hepcidin

- **Primary end point:** Lower ESA dose requirements?
- **Secondary end points:** Improved muscle mass, better quality of life, better libido, less inflammation, less insulin resistance, better bone quality, better vascular function?

What did he say?

Testosterone Deficiency is a Common Feature of CKD



Drugs Used by Nephrologist May Affect Testosterone Levels

Renin–angio
in middle-ag
erythropoiet

Michael DeLong

The Effect of
Consulting fo

Giovanni Corona, M
Giulia De Vita, MD,
Mario Maggi, MD

Endogenous testosterone and ESA responsiveness in ESA-treated men undergoing hemodialysis.

Model	Prediction of ESA dose (U/kg/week)	β (SE)	r^2	P-value
1	Total testosterone (in nmol/L)	−0.28 (2.3)	0.05	0.007
2	1 + Age (in years) and SHBG (in nmol/L)	−0.28 (2.5)	0.04	0.004
3	2 + Davies comorbidity score	−0.27 (2.4)	0.06	0.006
4	3 + CRP (in mg/L) and albumin (in g/L)	−0.26 (2.6)	0.06	0.02
5	4 + hypochromic RBCs (≤1.1 versus > 1.1%)	−0.14 (2.9)	0.18	0.2

[1] Probability to poor ESA responsiveness (ESA wk/Kg<121) in ESA treated hemodialysis men.

	Odds Ratio	95% CI	P value
Testosterone deficiency <10 nmol/L [2]	2.68	1.17-6.14	0.001

[1] Adjusted for age, SHBG, co-morbidities, albumin, CRP


That's all Folks!


KAROLINSKA INSTITUTET
ANNO 1810
Karolinska
Institutet
“Art is I – Science is We”

Clin Exp Nephrol (2014) 18:499–506
DOI 10.1007/s10157-013-0840-6

ORIGINAL ARTICLE

Low serum testosterone is associated with atherosclerosis in postmenopausal women undergoing hemodialysis

Nobuaki Shiraki · Ayumu Nakashima · Shigehiro Doi · Juan Jesús Carrero · Naoko Sugiya · Toshinori Ueno · Peter Stenvinkel · Nobuoki Kohno · Takao Masaki

Biochem. J. (2014) **464**, 221–229 (Printed in Great Britain) doi:10.1042/BJ20140739

Testosterone increases renal anti-aging *klotho* gene expression via the androgen receptor-mediated pathway

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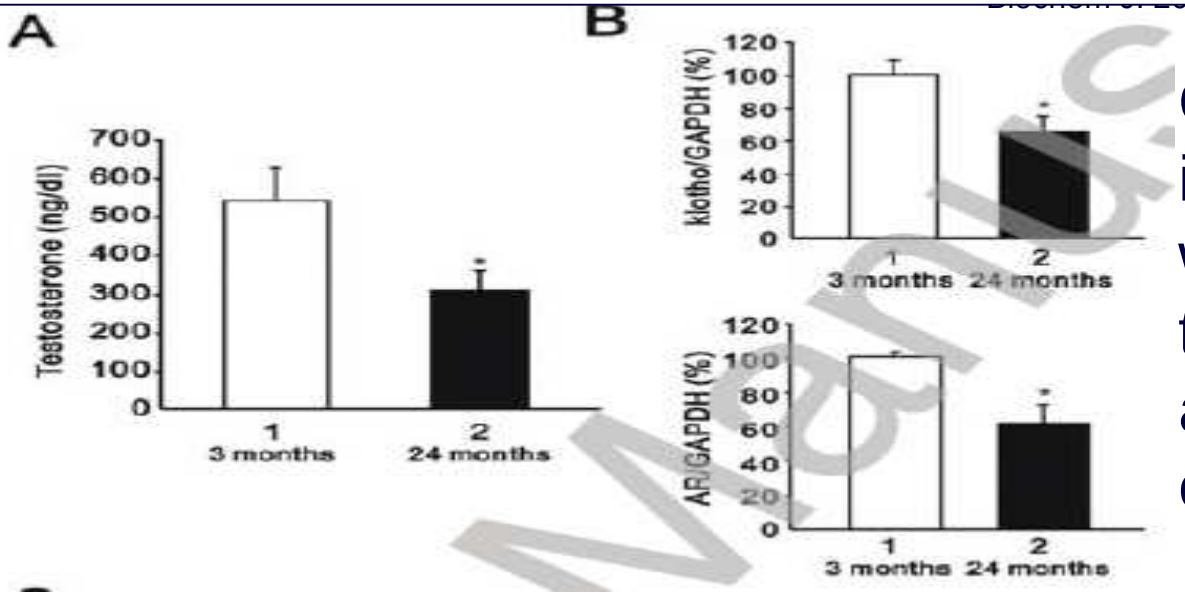
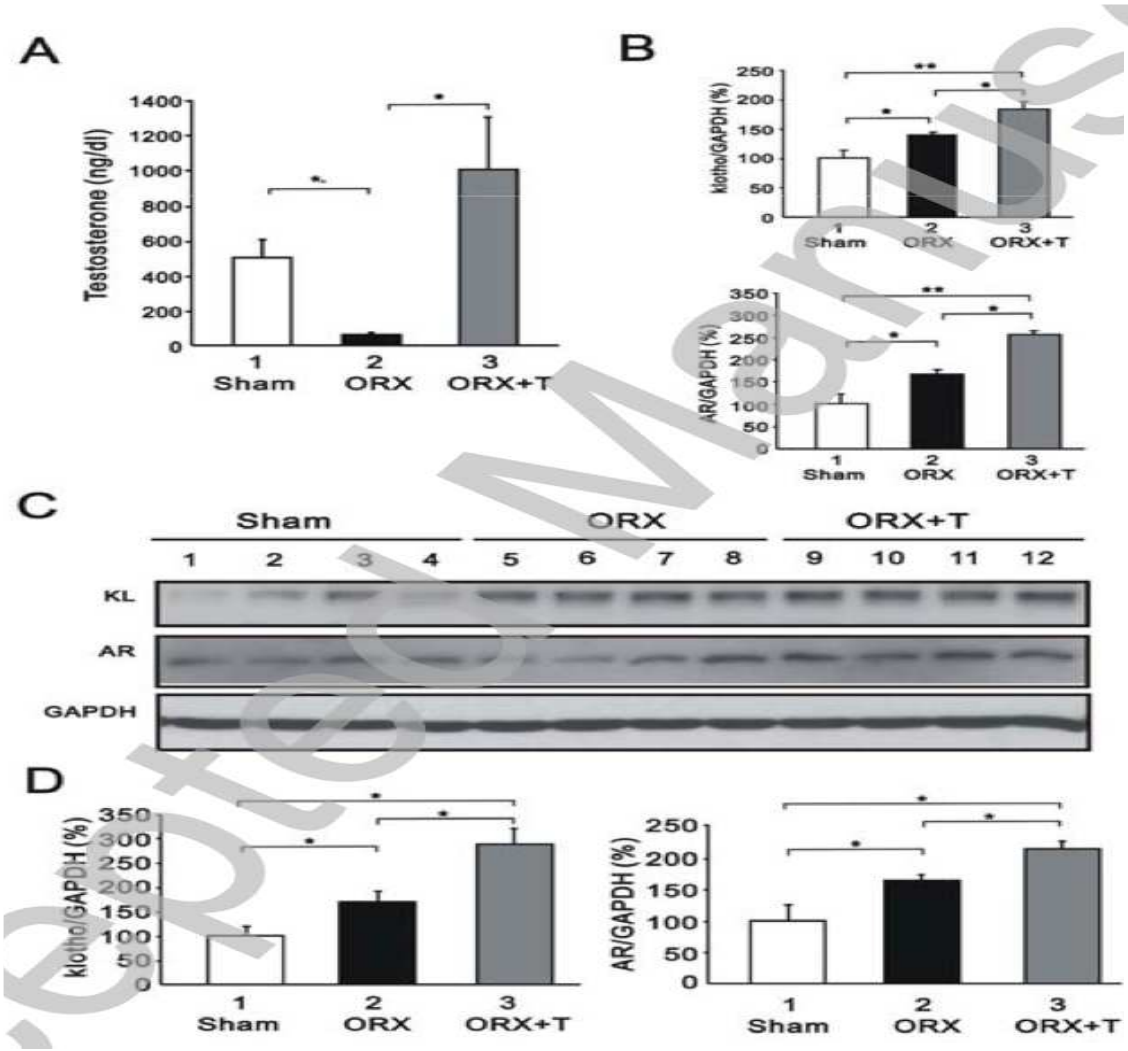
**Department of Nephrology, Mackay Memorial Hospital, Taipei, Taiwan, R.O.C.



Old age in mice is associated with lower testosterone and lower klotho expression



Testosterone up-regulates anti-aging klotho together with androgen receptor expression in the kidney *in vivo* and *in vitro* by recruiting androgen receptor onto the androgen response elements of the *klotho* promoter.

Biochemical Journal Immediate Publication. Published on 27 Aug 2014 as manuscript BJ20140739


BUFFALO BILL
BARRY WHITE
THE ULTIMATE COLLECTION
TIME

Testosterone is an Anabolic Hormone with Many Beneficial Effects on Men's Health

- Depression
- Poor concentration
- Excessive tiredness
- Lack of energy

- Reduced muscle mass and/or strength
- Increased body fat
- Osteoporosis
- Anemia

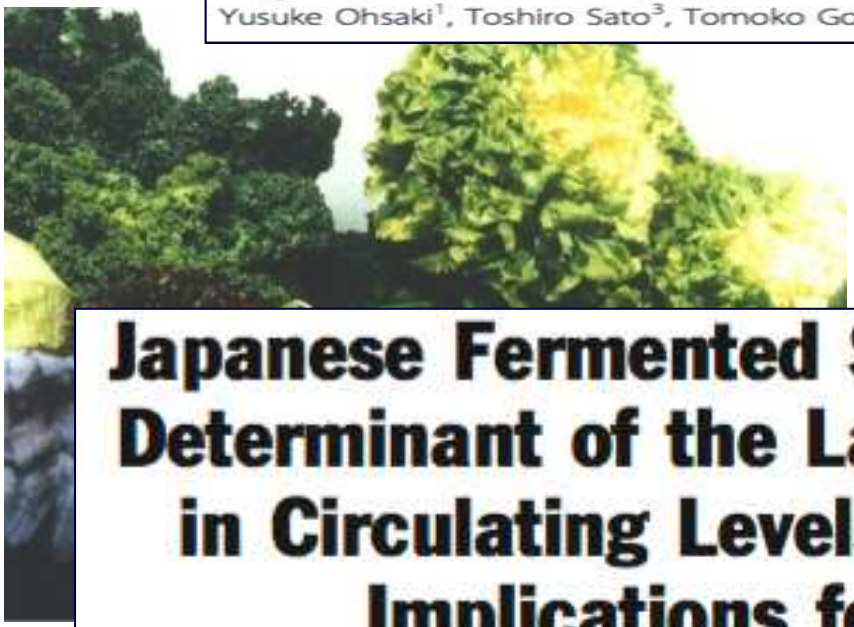
- Reduced libido
- Erectile dysfunction

Vitamin K Brist Vanligt hos Dialyspatienter

RESEARCH Open Ac

Menaquinone-4 enhances testosterone production in rats and testis-derived tumor cell

Asagi Ito[1], Hitoshi Shirakawa[1*], Naofumi Takumi[1], Yoshihiko Minegishi[1], Ai Ohashi[1], Zakir H Howlader[1,2], Yusuke Ohsaki[1], Toshiro Sato[3], Tomoko Goto[1] and Michio Komai[1]

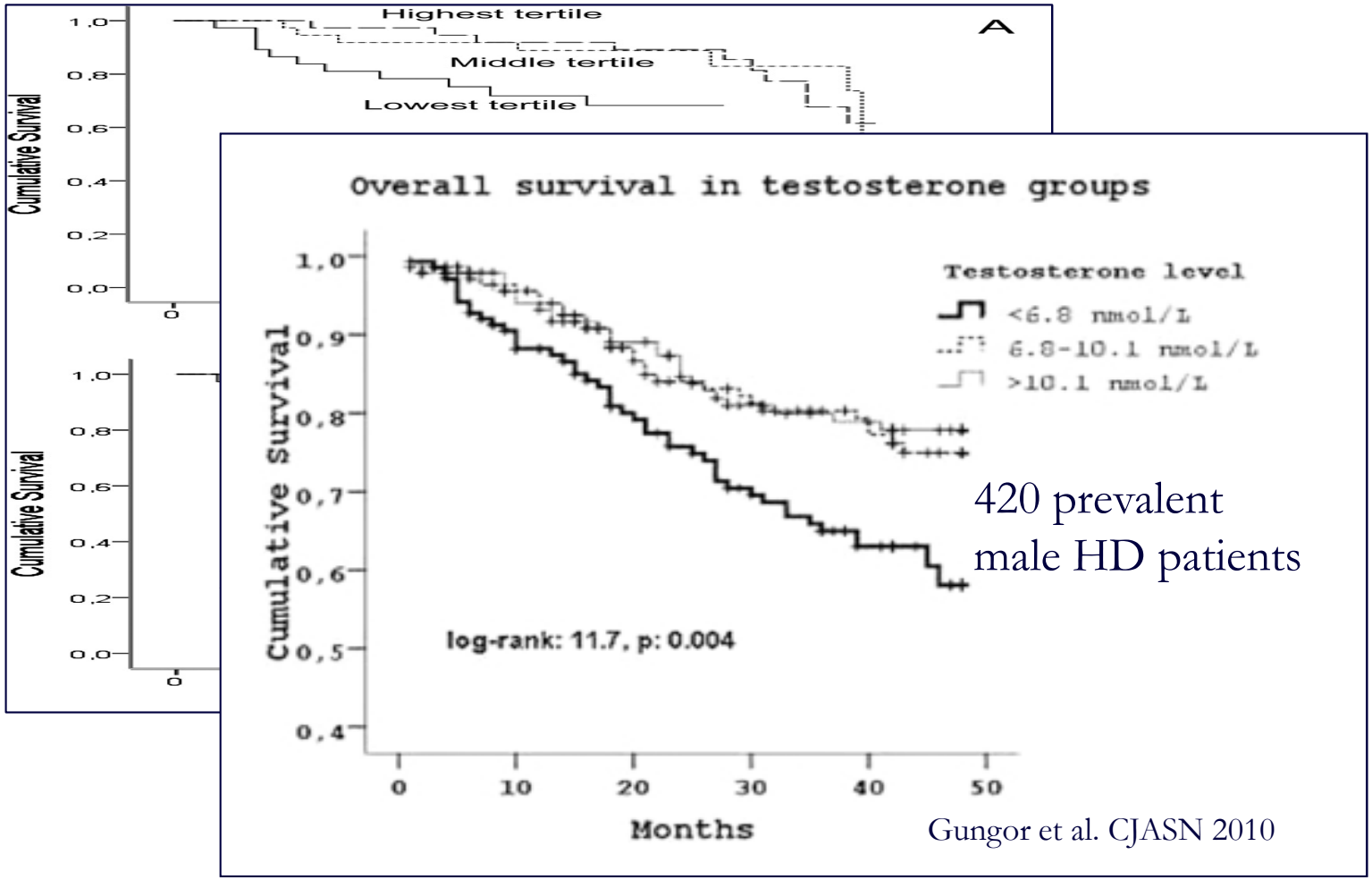


870 µg vitamin K2 per 100 gram natto.

Japanese Fermented Soybean Food as the Major Determinant of the Large Geographic Difference in Circulating Levels of Vitamin K2: Possible Implications for Hip-Fracture Risk

Potential Mechanisms by Which Testosterone Therapy may Result in Erytrocytosis

- Suppression of inflammation
- Hypoxia
- Stimulation of erytropoiesis
- Alterations in iron sensing
- **Direct suppression of hepcidin transcription**



420 prevalent male HD patients

Gungor et al. CJASN 2010

Clin Drug Investig (2016) 36:421–431
DOI 10.1007/s40261-016-0378-y

REVIEW ARTICLE

The Safety of Erythropoiesis-Stimulating Agents for the Treatment of Anemia Resulting from Chronic Kidney Disease

Nicolas Roberto Robles[1,2]

Side effects of ESA:

- Hypertension
- Cramps
- Access ”clotting”
- Stroke
- Risk for malignacies

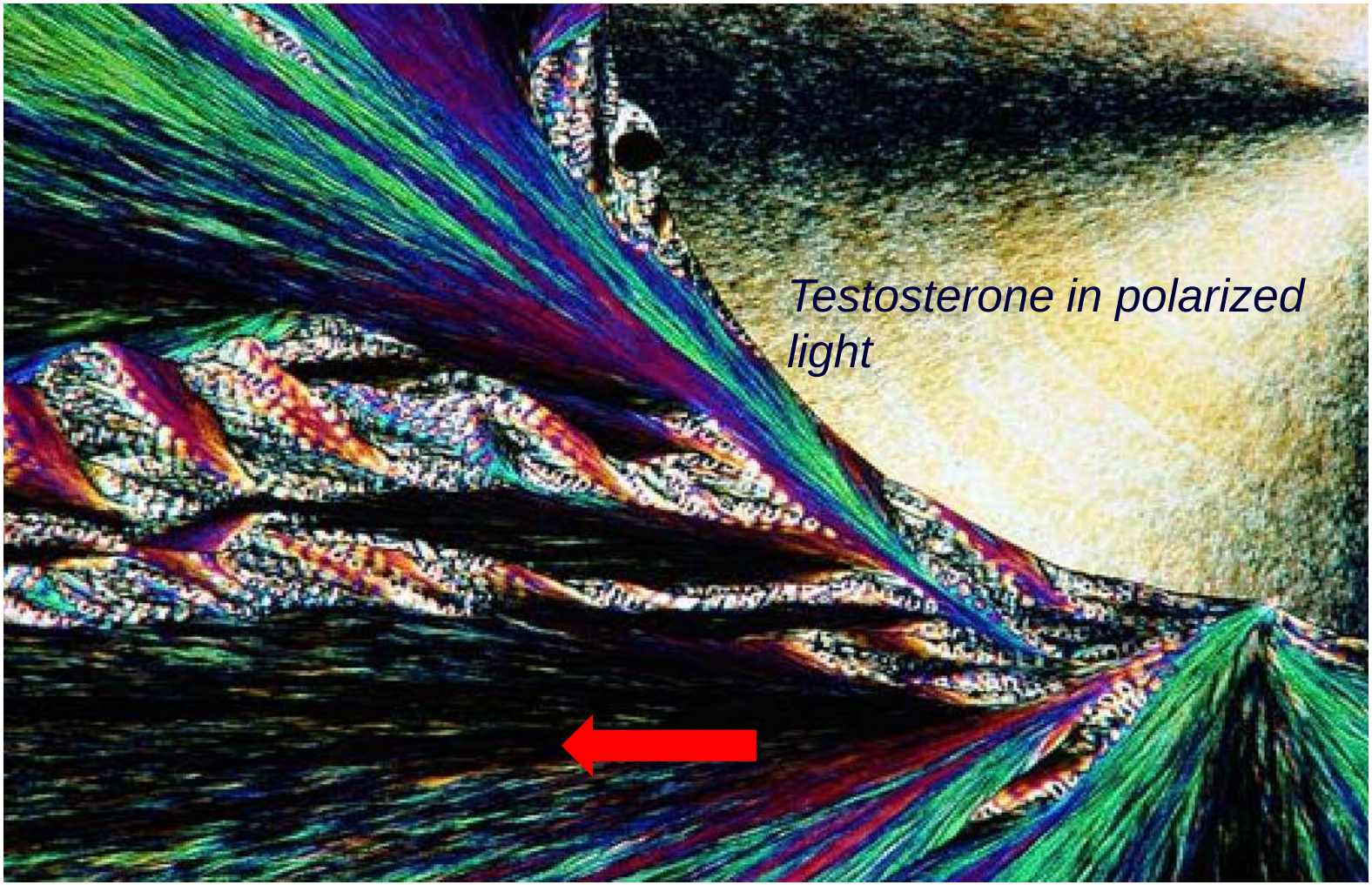
NDT Advance Access published July 21, 2016

Nephrol Dial Transplant (2016) 0: 1–6
doi: 10.1093/ndt/gfw268

Original Article

Association of erythropoiesis-stimulating agents and the incidence risk of cancer diagnosis among chronic dialysis patients: a nested case–control study

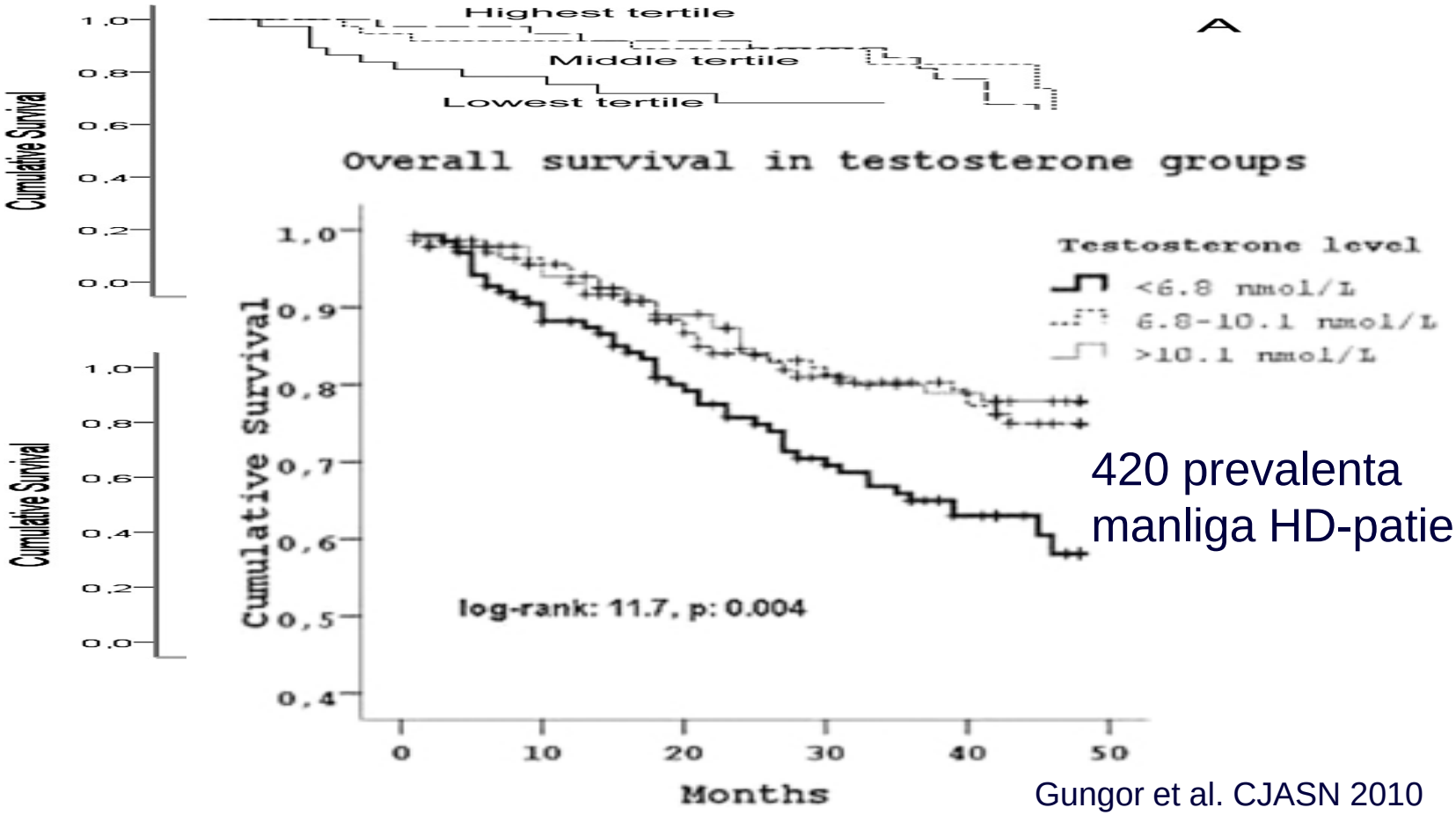
Émilie René[1], Hind H. Lazrak[1], Louis-Philippe Laurin[1,2,3], Naoual Elftouh[1], Michel Vallée[2,3] and Jean-Philippe Lafrance[1,2,3]


Testosterone in polarized light

Nettie Moore Lyrics

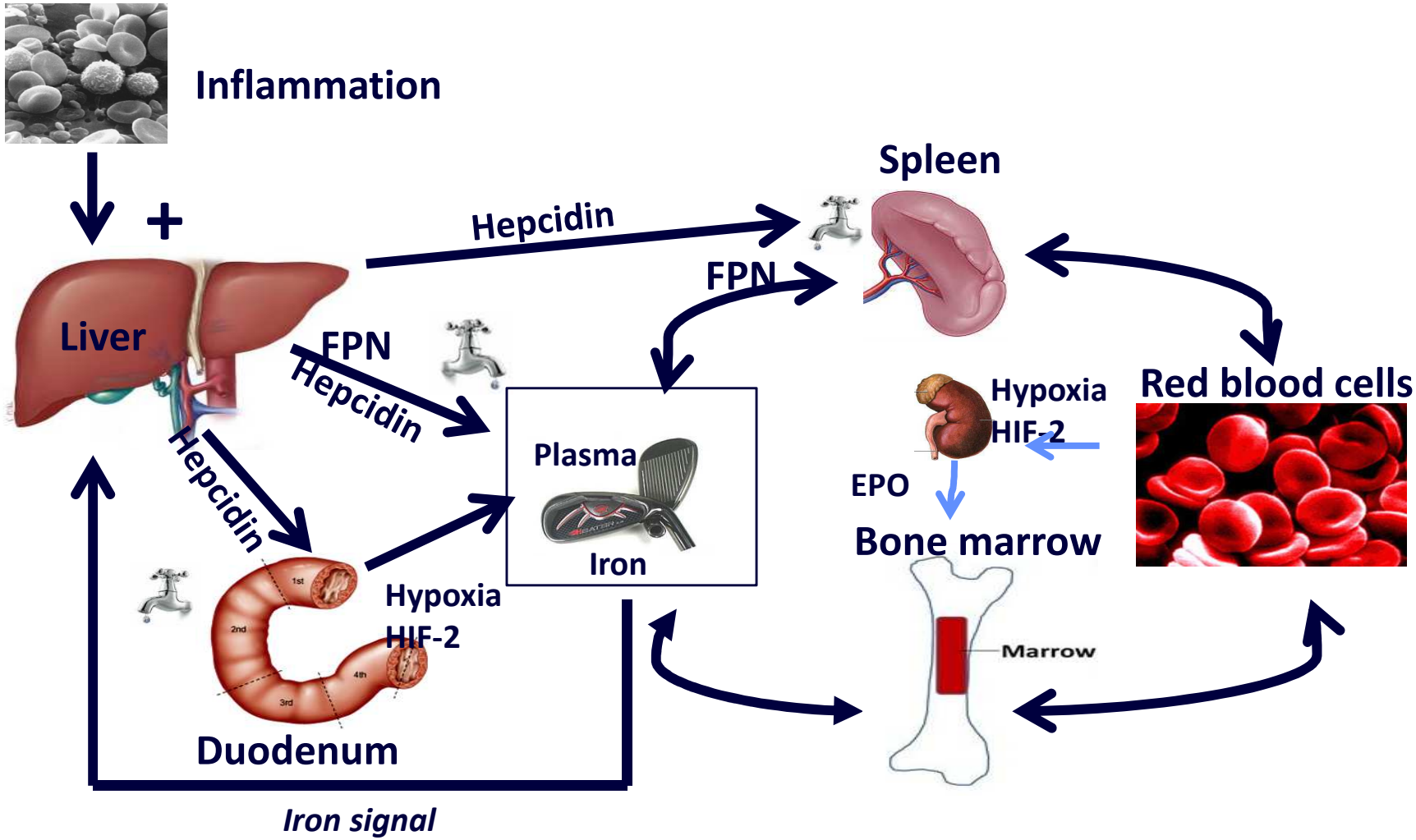
Bob Dylan

Well, the world of research has gone berserk
Too much paperwork
Albert's in the graveyard, Frankie's raising hell
I'm beginning to believe what the Scriptures tell

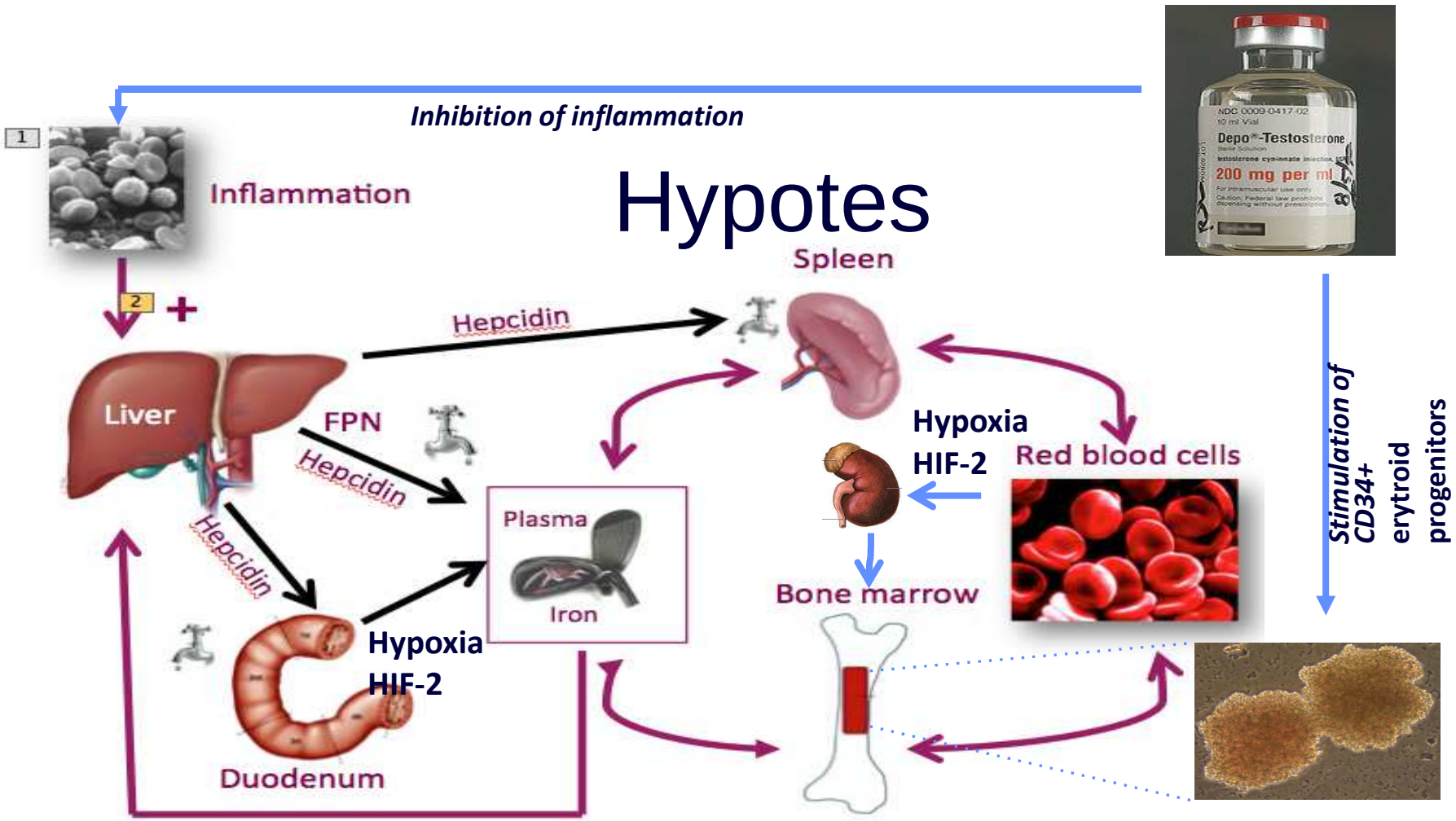


420 prevalenta manliga HD-patienter

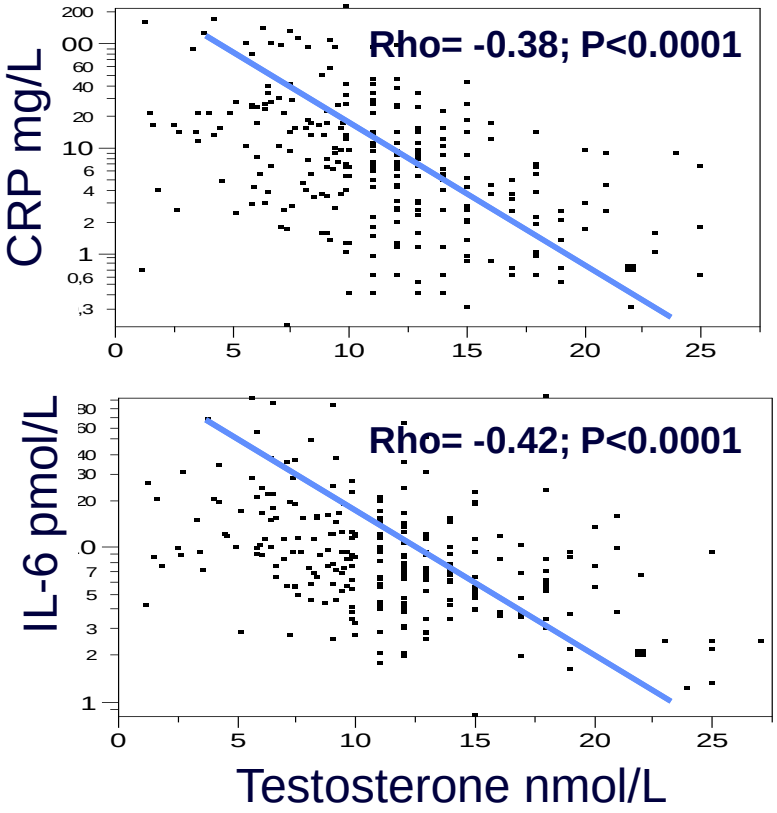
Gungor et al. CJASN 2010


Inflammation
+
Liver
Hepcidin
Spleen
FPN
FPN
Hepcidin
Hepcidin
Plasma
Iron
Hypoxia
HIF-2
Duodenum
Hypoxia
HIF-2
EPO
Bone marrow
Marrow
Red blood cells
Iron signal

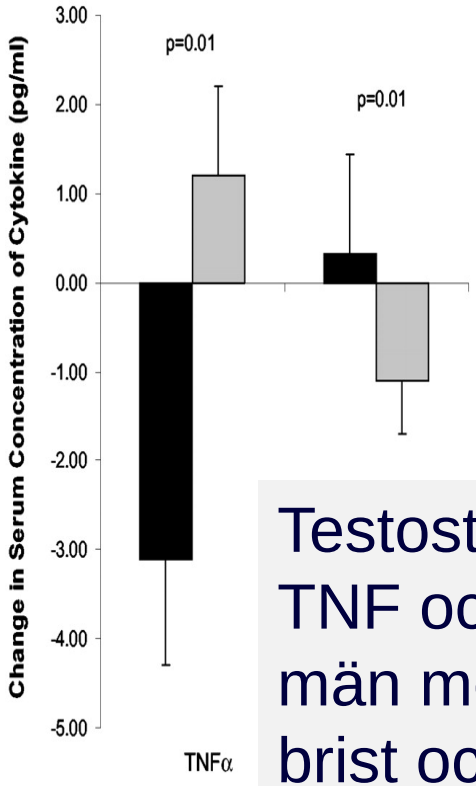
Hypotes


Inhibition of inflammation
1
Inflammation
2
+
Liver
Hepcidin
FPN
Hepcidin
Hepcidin
Plasma
Iron
Hypoxia
HIF-2
Duodenum
Spleen
Hypoxia
HIF-2
Red blood cells
Bone marrow
Stimulation of CD34+ erytroid progenitors
Depo®-Testosterone
200 mg per ml

Är Inflammation en Orsak till Låga Nivåer av Testosteron vid Kronisk Niursvikt?



Carrero et al. J Am Soc Nephrol. 2009 Mar;20(3):613-620



Testosteron minskar TNF och ökar IL-10 hos män med testosteron-brist och hjärtsvikt

Malkin et al. J Clin Endocrinol Metab. 2004;89:3313-8.

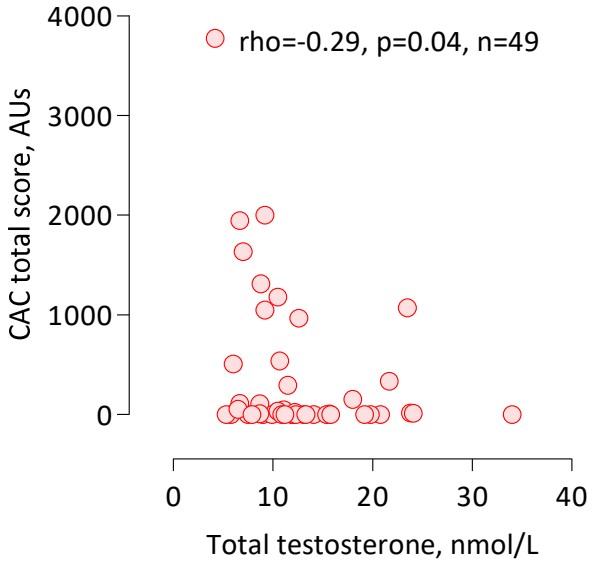
The Fountain of Youth – Can Nutritional and Pharmacological Interventions Extend Age?

Nutritional and life style interventions
• Caloric restriction (96)
• Red wine (121).
• Fish oil (omega 3) (106)
• Phosphate restriction (152)
• Physical exercise (104)
Pharmacological interventions
• *SIRT activation;* resveratrol (101)
• *Increased Klotho expression;* drugs that alter DNA hypermethylation (154), inhibition of NF-kB (81), PPAR-γ agonists (146), thyroid hormones (147), ACE-inhibition (148), D vitamin (155)
• *mTOR inhibition;* rapamycin (108), metformin (110), resveratrol (111)
• *Stabilizing telomeres;* statins (130), estrogens (131), telomerase reactivation (129), D-vitamin (132)
• *Limit DNA damage;* inhibition of NF-kB (135), anti-oxidants (136)
• *Phosphate-lowering:* phosphate binders (156), blocking of the intestinal phosphate transporter Npt2b (153)

Stenvinkel and Larsson. AJKD 2013

Tänkbara Gynnsamma Effekter av Testosteron hos Patienter med Kronisk Njursvikt

- Livskvalitet
- Sexualla funktioner (ökad lust)
- Kvalitet på benmassa
- Muskelstyrka
- Depression
- Insulinresistens
- Inflammation
- Oxidativ stress


rho=-0.29, p=0.04, n=49
CAC total score, AUs
4000
3000
2000
1000
0
0
10
20
30
40
Total testosterone, nmol/L

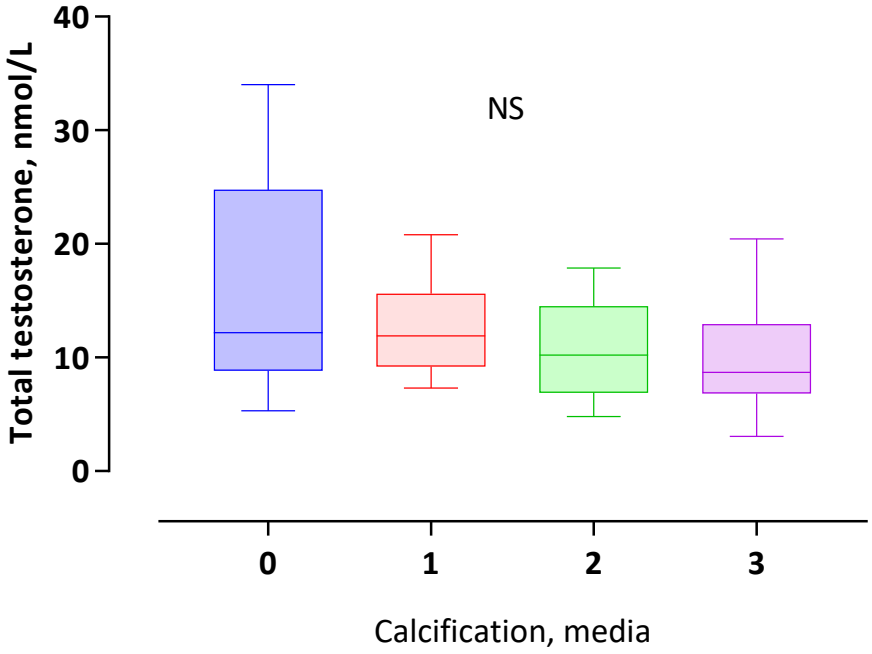
Testosteron vs. Hemoglobin vid CKD 1-5 (III)

Model	Prediction of ESA dose (U/kg/week)	β (SE)	r^2	P-value
1	Total testosterone (in nmol/L)	−0.28 (2.3)	0.05	0.007
2	1 + Age (in years) and SHBG (in nmol/L)	−0.28 (2.5)	0.04	0.004
3	2 + Davies comorbidity score	−0.27 (2.4)	0.06	0.006
4	3 + CRP (in mg/L) and albumin (in g/L)	−0.26 (2.6)	0.06	0.02

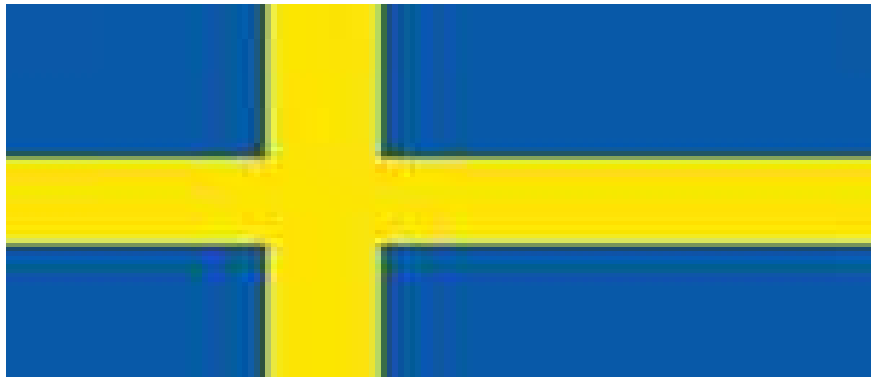
Ca 2.5 gånger ökad risk för låg ESA känslighet hos män som behandlas med HD

	Odds Ratio	95% CI	P value
Testosterone deficiency <10 nmol/L	2.68	1.17-6.14	0.001

Adjusted for age, SHBG, co-morbidities, albumin, CRP


Total testosterone, nmol/L
40
30
20
10
0
NS
0
1
2
3
Calcification, media

Methods: Cross-sectional study in……



….126 prevalent HD men

The median ESA equivalent dose was 10,000 (6,000–14, 750) U/week.

Age, years	63 (49–73)
Vintage, months	25 (14–55)
Davies comorbidity score, %	
Low	19
Middle	54
High	26
BMI, kg/m^2	24.6 (21.3–27.5)
s-Albumin, g/dL	3.5 (3.2–3.8)
CRP, mg/L	6.8 (2.9–21.0)
Haemoglobin, g/dL	12.2 (11.0–13.4)
Hypochromic RBC, %	1.1 (0.5–4.1)
Intravenous iron medication, %	69
SHBG, nmol/L	27 (20–39)
Total testosterone, nmol/L	10.0 (7.2–12.0)