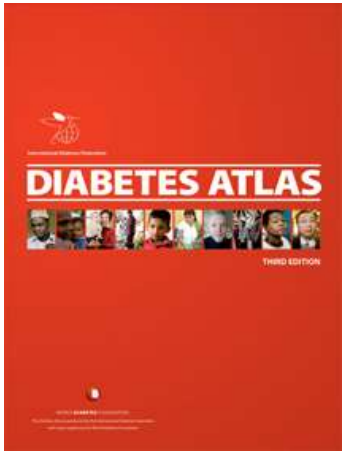
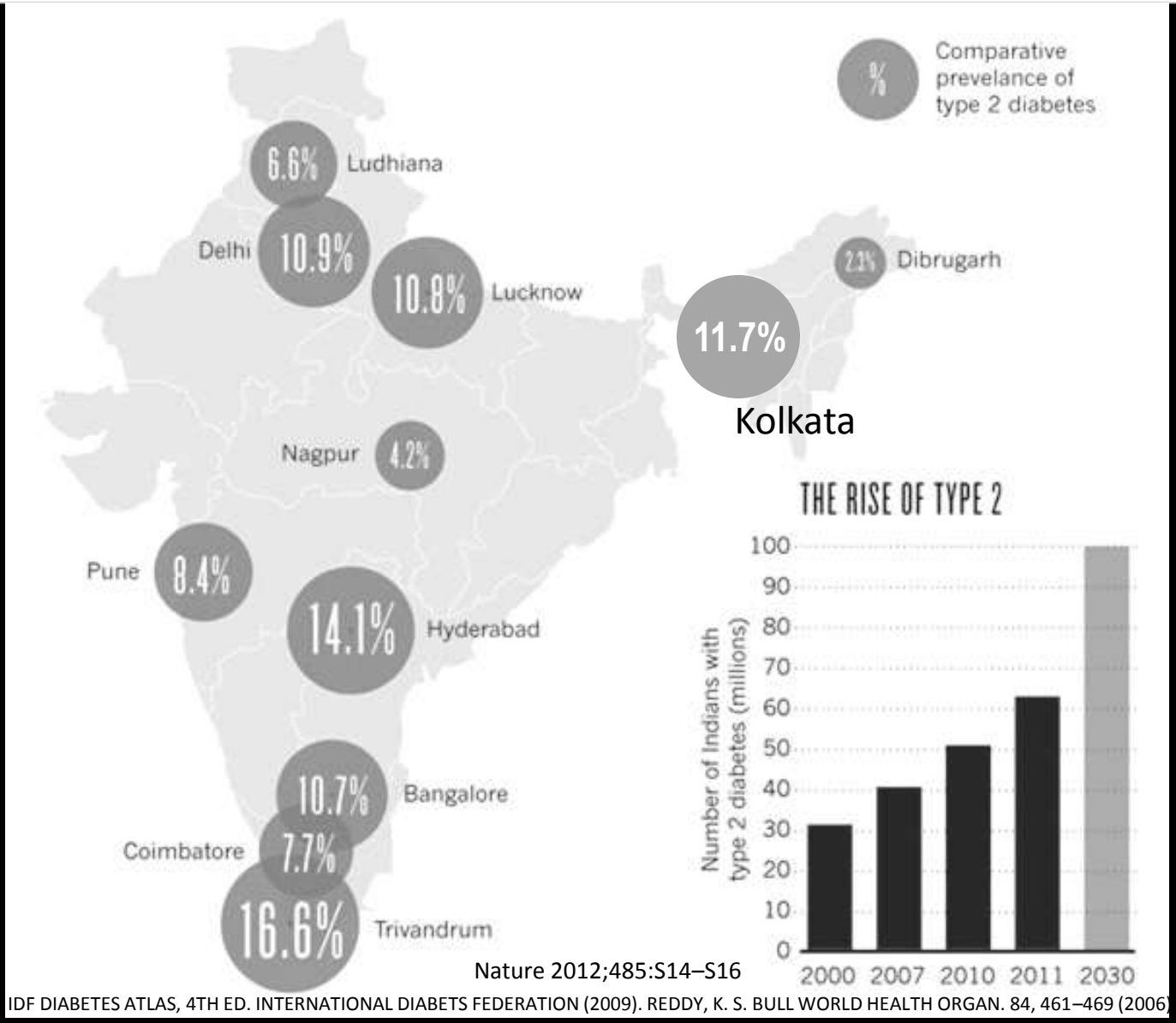


India is the "diabetes capital of the world"

Indian J Med Res 2007;125:217-230

Nature 17 may 2012;485:S14–S16

India's Diabetes Boom



Nature 2012;485:S14–S16

IDF DIABETES ATLAS, 4TH ED. INTERNATIONAL DIABETS FEDERATION (2009). REDDY, K. S. BULL WORLD HEALTH ORGAN. 84, 461–469 (2006)

Diabetic retinopathy (DR)

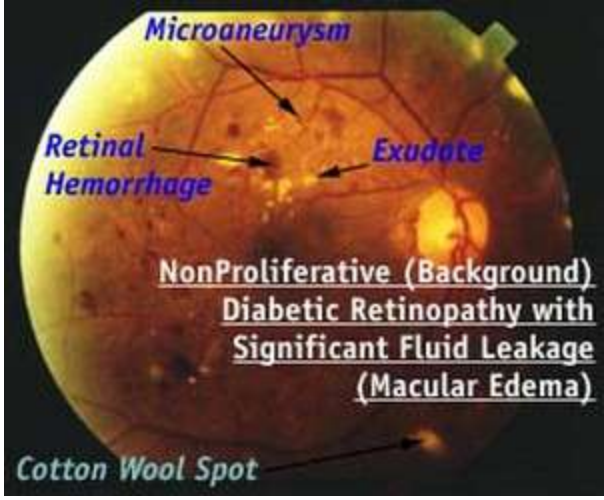
Diabetic retinopathy occurs in 87.5% of all persons having diabetes for >15 years

The severity of DR proportionately increased with longer duration of diabetes

PLoS ONE 6(11): e26747.

Diabetic retinopathy

Inside picture….



Retinal vascular microaneurysms, blot hemorrhages, cotton-wool spots, loss of retinal pericytes, increased vascular retinal permeability, alterations in regional blood flow, and abnormal retinal microvasculature, retinal hemorrhage

Vision loss

PLoS ONE 6(11): e26747.

AIIMS New Delhi Report

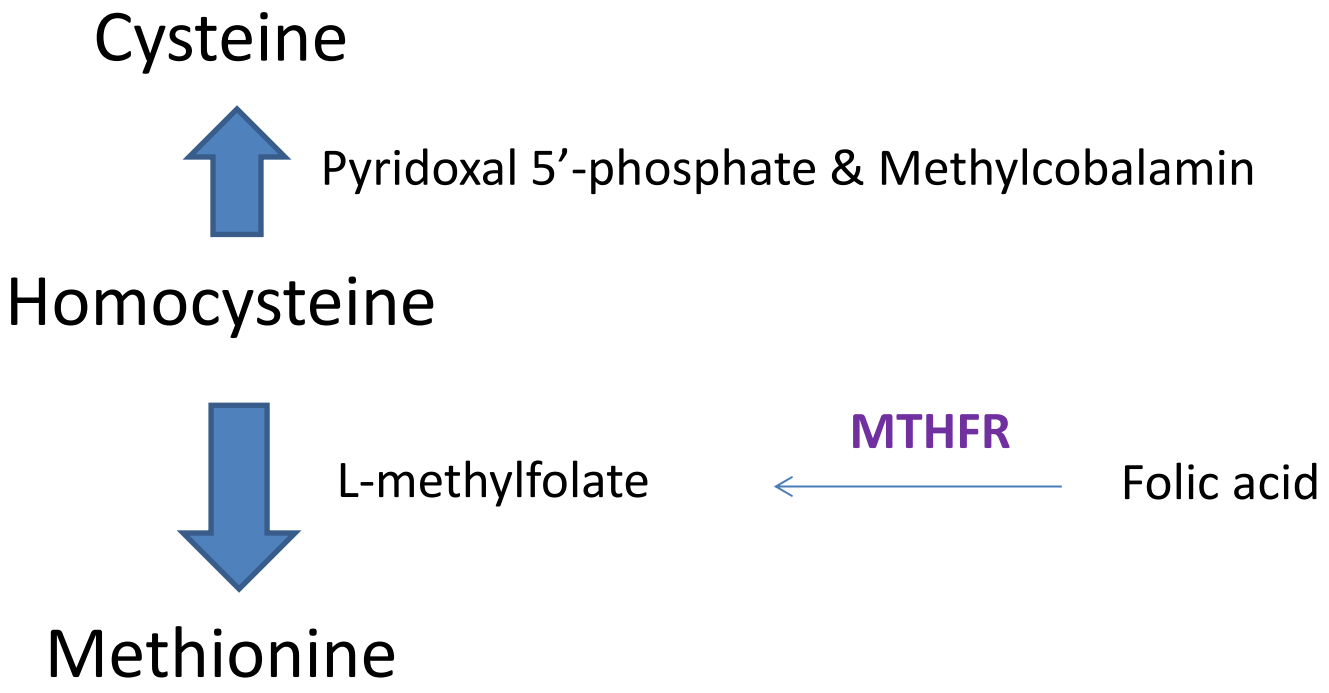
84% Indian population suffering from hyperhomocysteinemia

Hyperhomocysteinemia is an Independent risk factor in Diabetic retinopathy

Eye (Lond). 2004 May;18(5):460-5. Eur J Nutr 2002;41:68–77 PLoS ONE 6(11): e26747.

Hyperhomocysteinemia

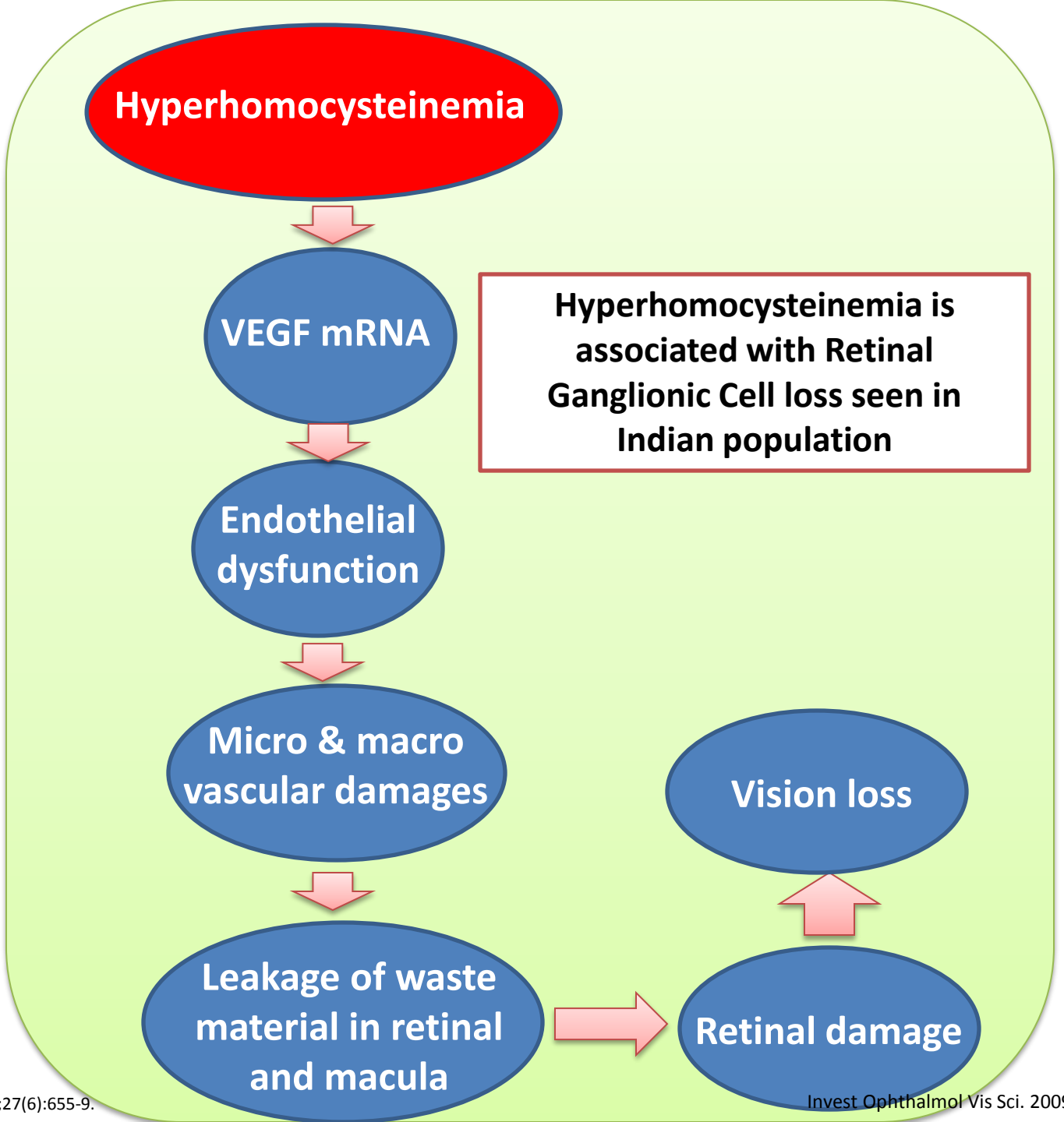
Elevated levels of Homocysteine concentration in blood is known as Hyperhomocysteinemia



Deficiency of L-methylfolate, Pyridoxal 5'-phosphate is the predominant cause of hyperhomocysteinemia

MTHFR: methylenetetrahydrofolate reductase

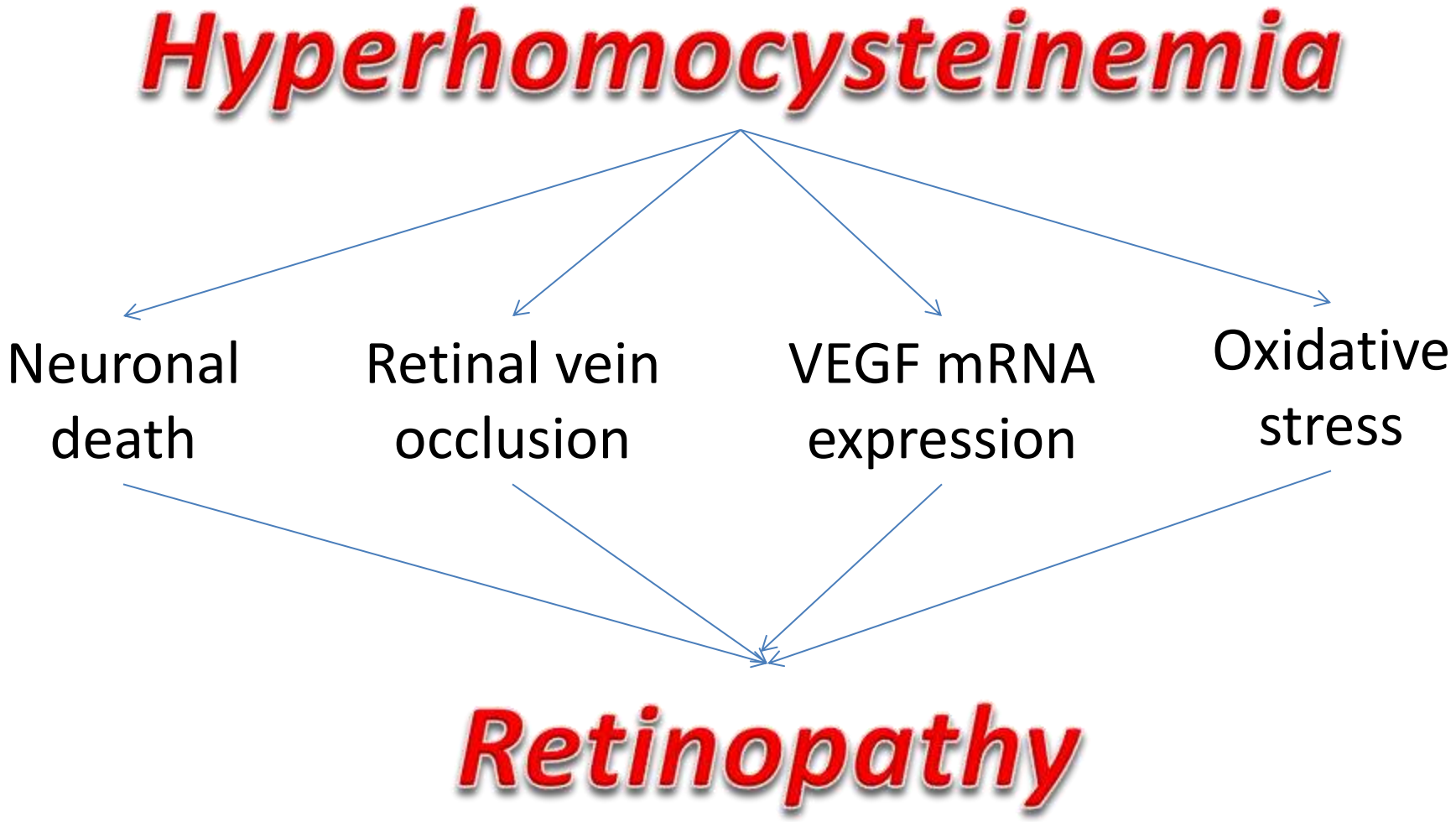
DIABETIC



RETINOPATHY

Diabetes Metab. 2001 Dec;27(6):655-9.

Invest Ophthalmol Vis Sci. 2009 Sep;50(9):4460-70.



Eur J Ophthalmol. 2008 Mar-Apr;18(2):226-32.

Elevated homocysteine increased steady state VEGF mRNA levels 4.4-fold

Diabetic retinopathy

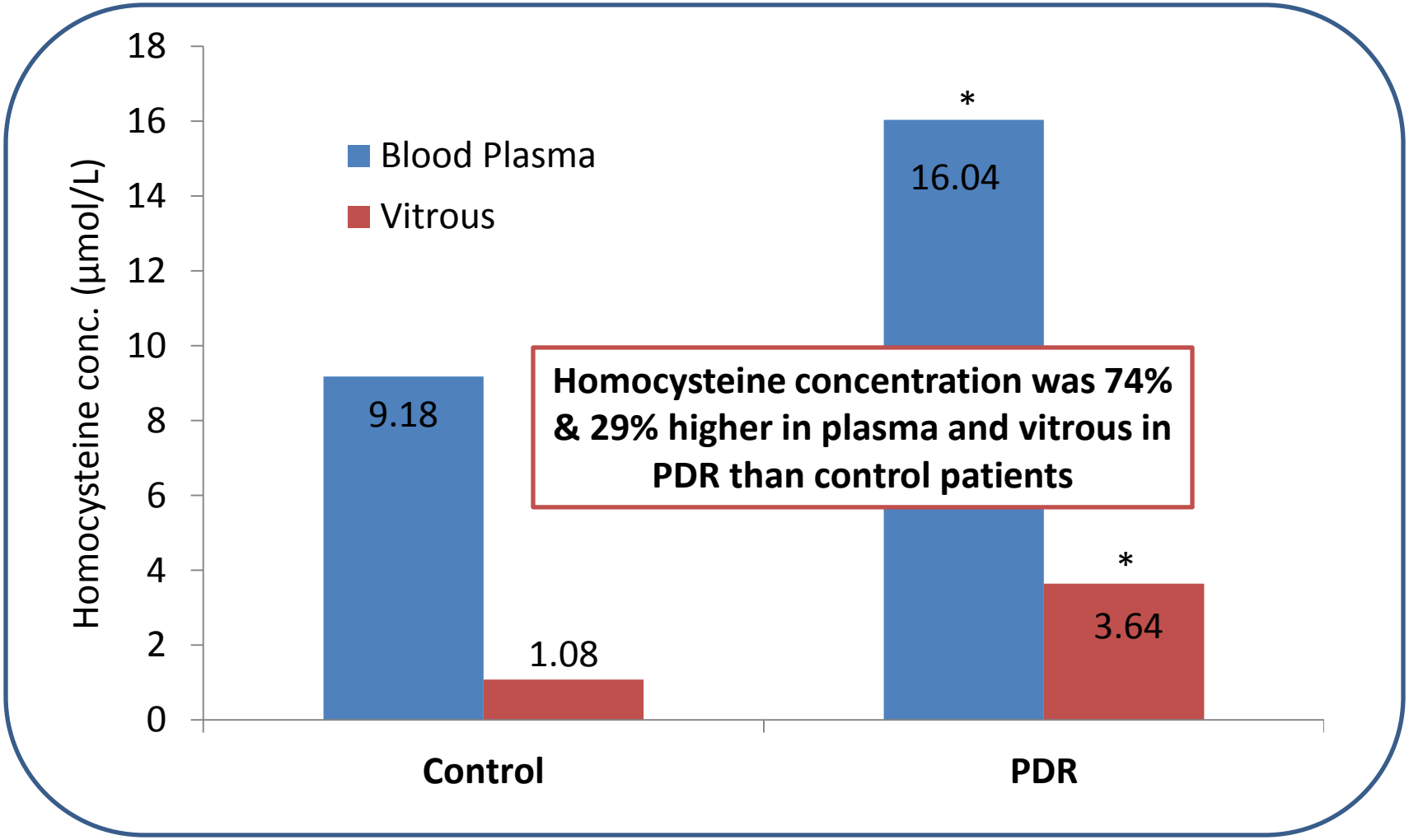
The Journal of Biological Chemistry 2004;279,14844-14852.

Plasma and vitreous homocysteine concentrations in patients with proliferative diabetic retinopathy

- 20 patients with PDR and 12 nondiabetic patients with nonproliferative ocular diseases
- Plasma and vitreous samples were obtained to measure

Retina. 2008 May;28(5):741-3.

Vitreous Hcy concentrations were elevated in patients with PDR probably due to breakdown of the blood-retina barrier



*P<0.001

Retina. 2008 May;28(5):741-3.

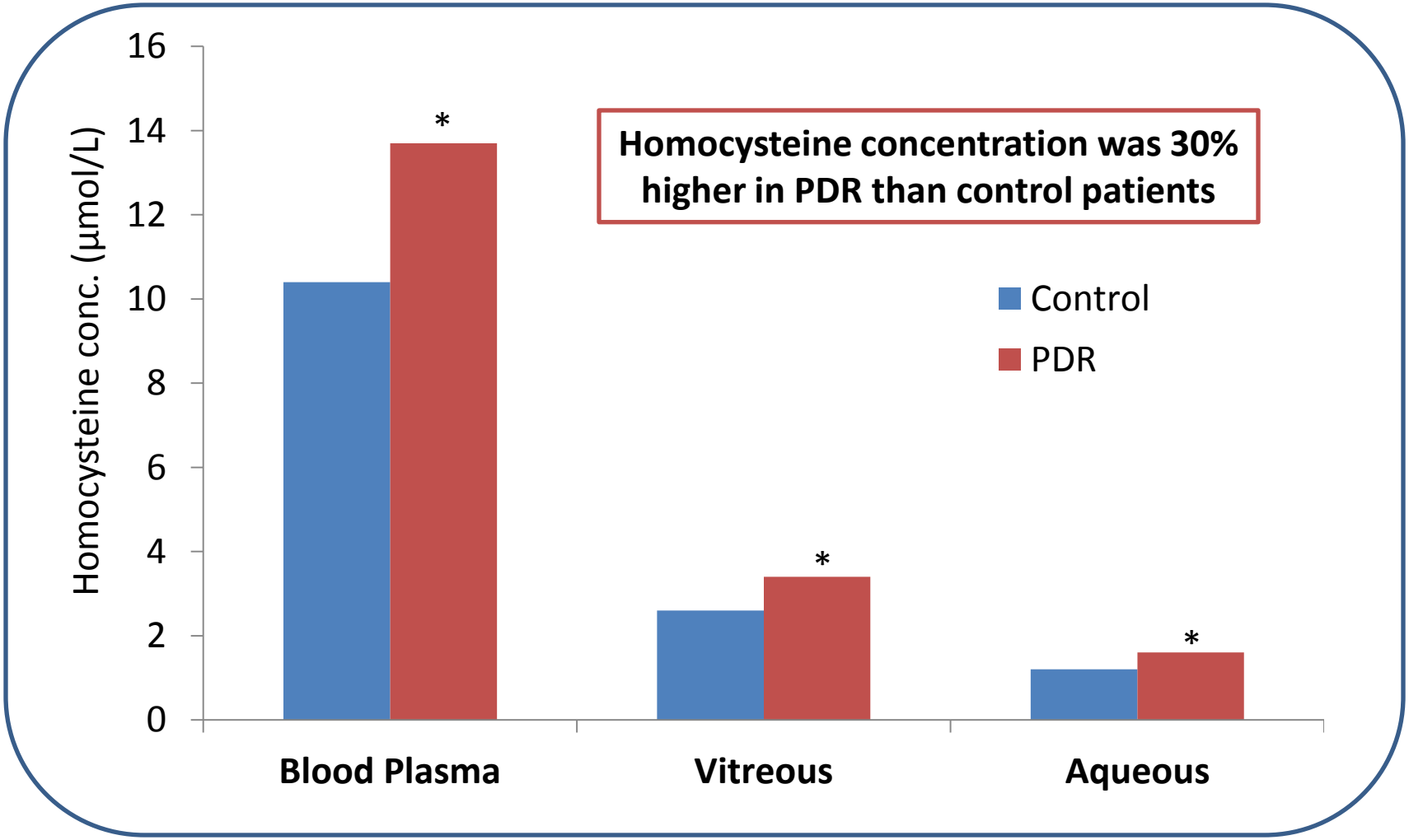
Plasma, aqueous and vitreous homocysteine levels in proliferative diabetic retinopathy (PDR)

- 20 eyes with PDR and 21 eyes of patients without diabetes mellitus were examined

- Blood plasma, aqueous and vitreous samples were collected during combined cataract and pars plana vitrectomy for homocysteine measurement

Br J Ophthalmol. 2012 May;96(5):704-7

British Journal of OPHTHALMOLOGY 2012



*P<0.001

Br J Ophthalmol. 2012 May;96(5):704-7

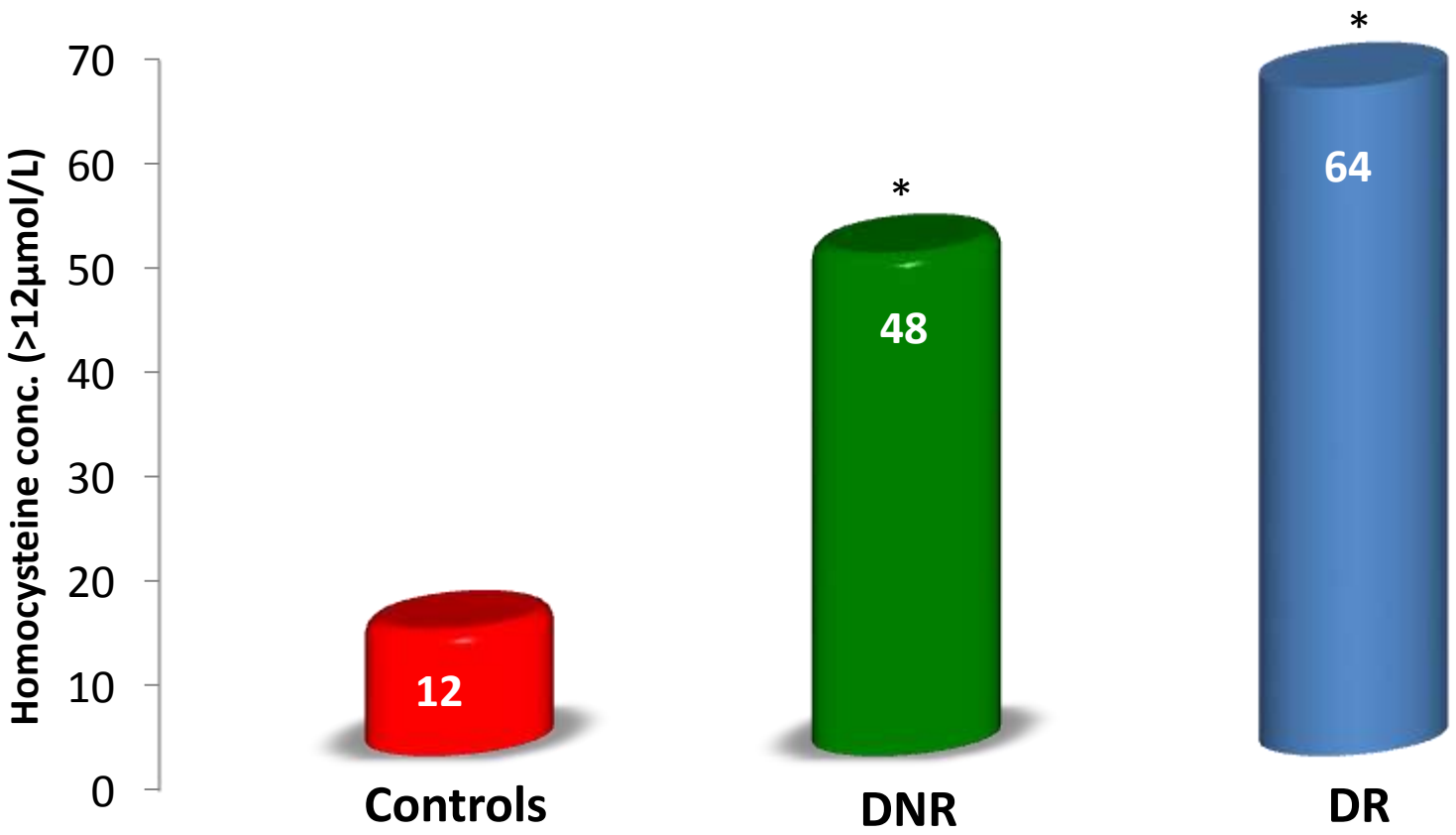
Status of B-vitamins and homocysteine in diabetic retinopathy: association with B-vitamin deficiency and hyperhomocysteinemia

- A cross-sectional case-control study
- 100 normal control subjects and 300 subjects with type-2 diabetes (T2D).
- Of the 300 subjects with T2DM, 200 had diabetic retinopathy (DR) and 100 did not (DNR).

PLoS ONE 6(11): e26747.

Contd..

% Prevalence of hyperhomocysteinemia with >12umol/L

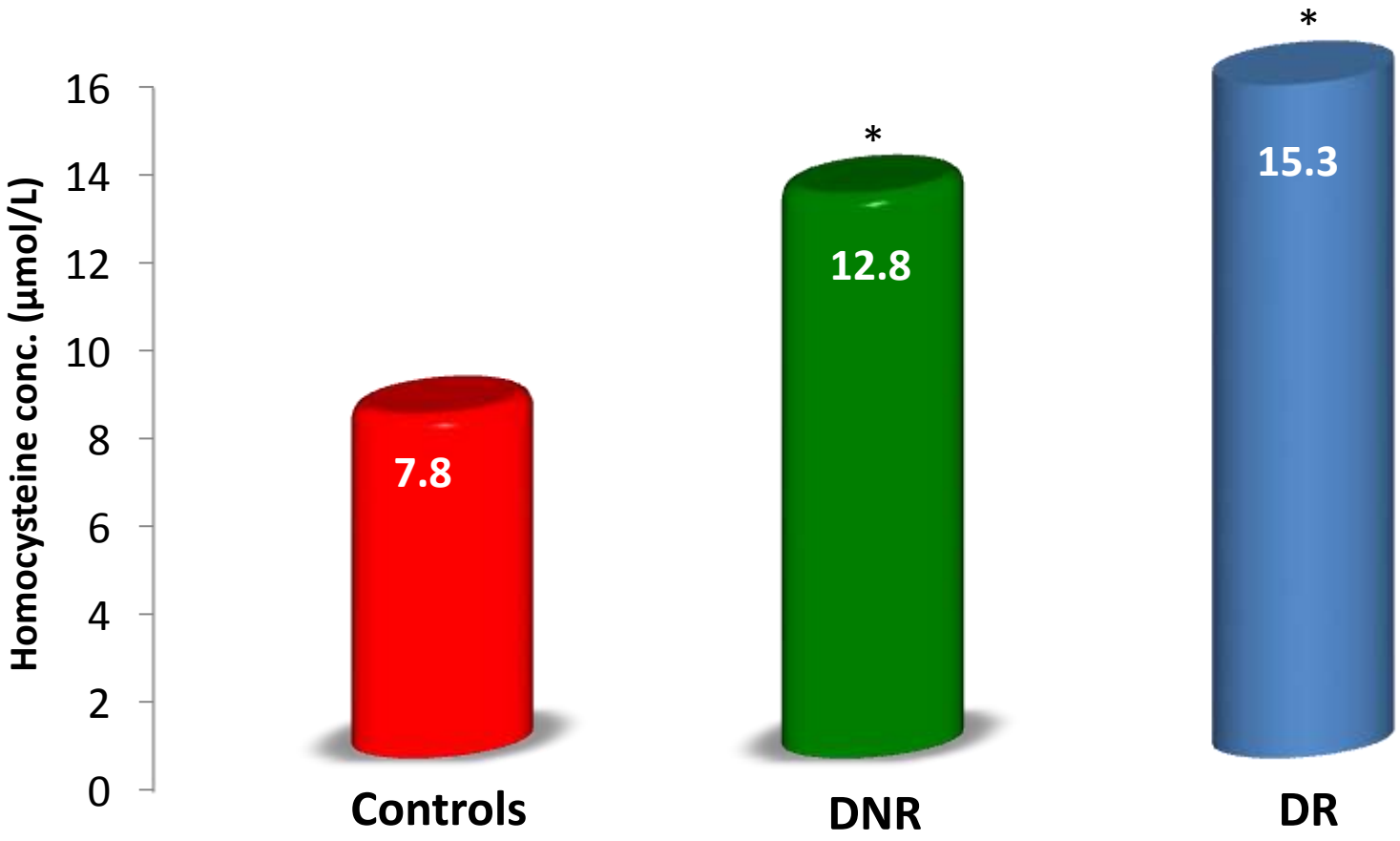


*P<0.05

PLoS ONE 6(11): e26747.

Contd..

Homocysteine concentration

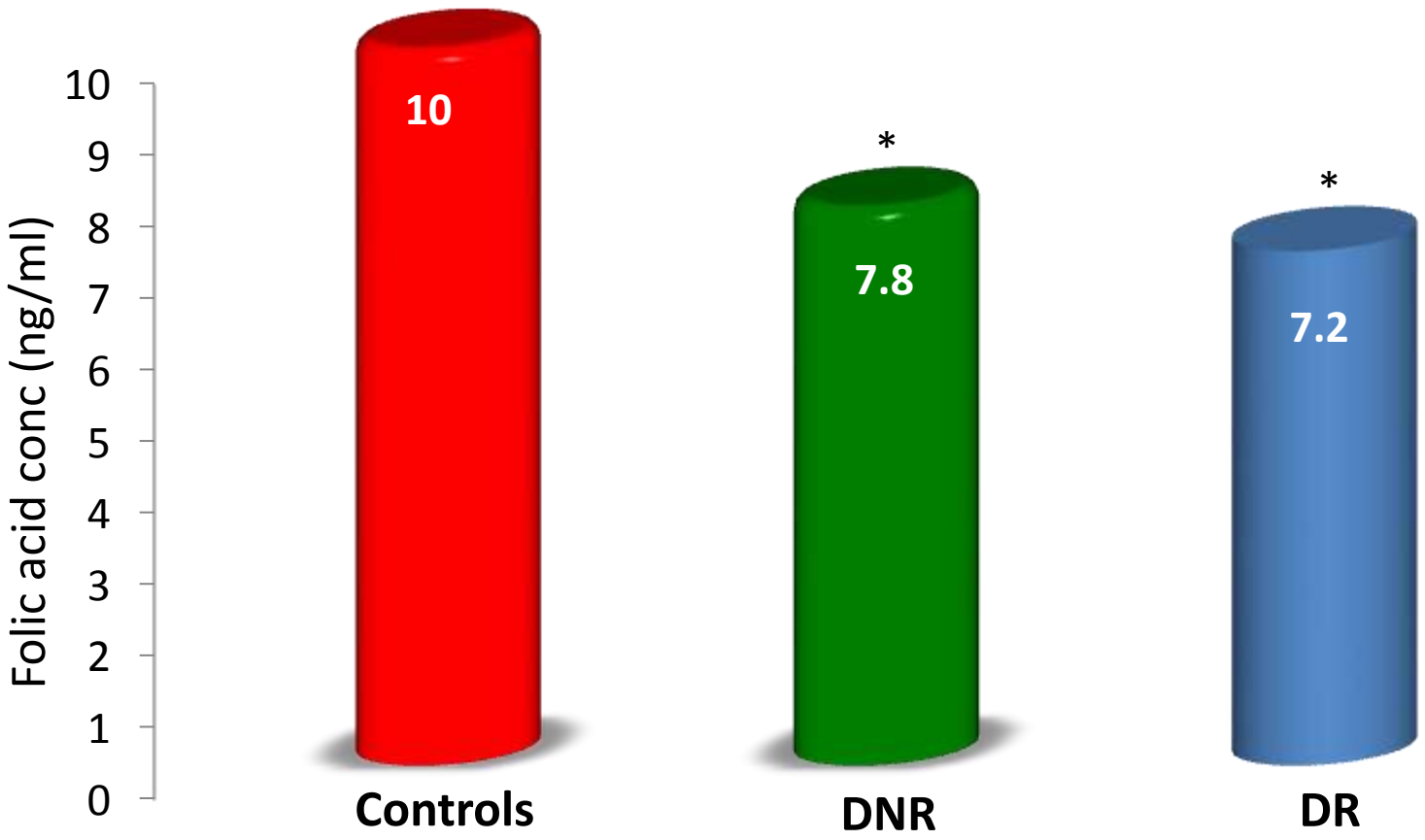


*P<0.05

PLoS ONE 6(11): e26747.

Contd..

Folic acid deficiency

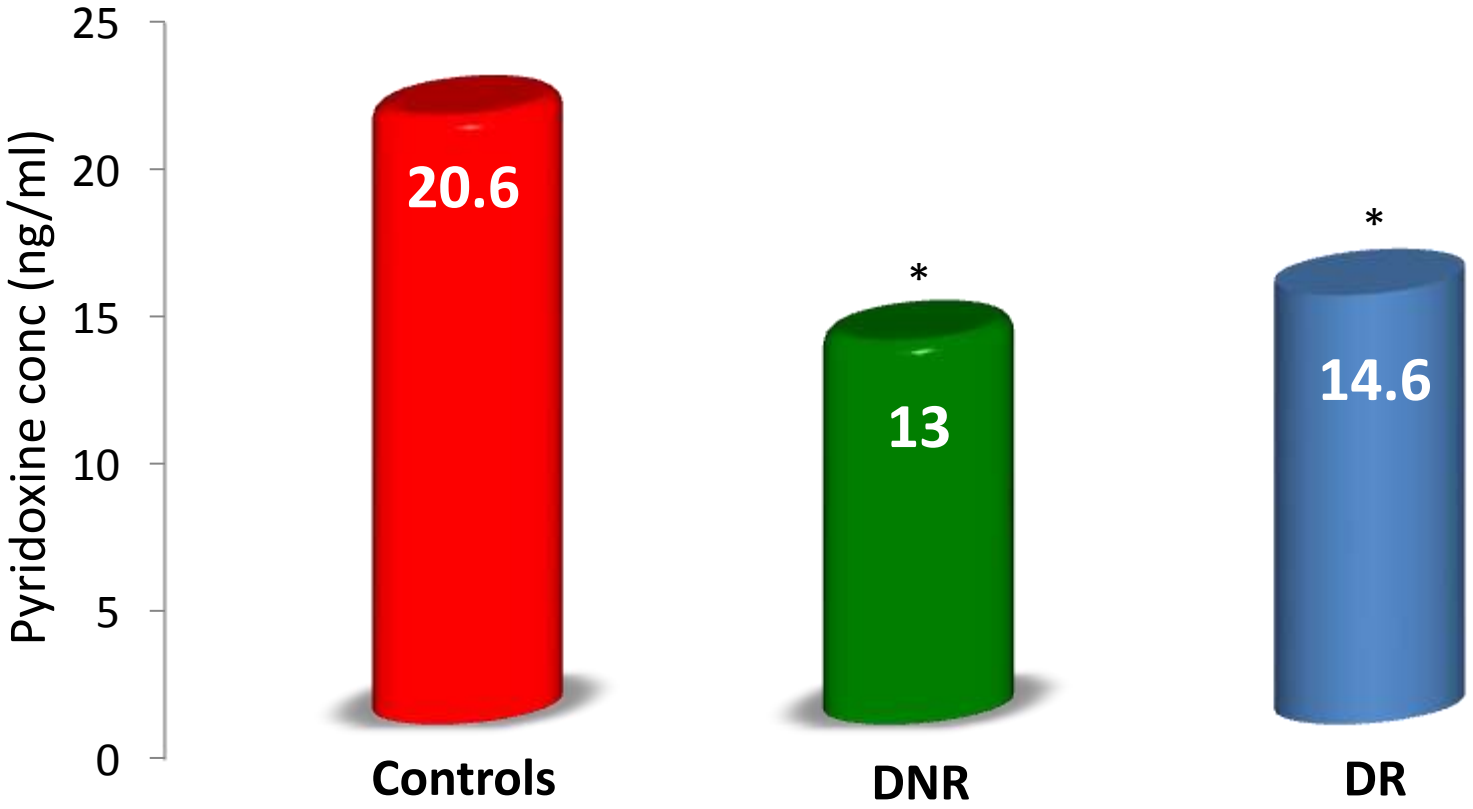


*P<0.05

PLoS ONE 6(11): e26747.

Contd..

Pyridoxine deficiency

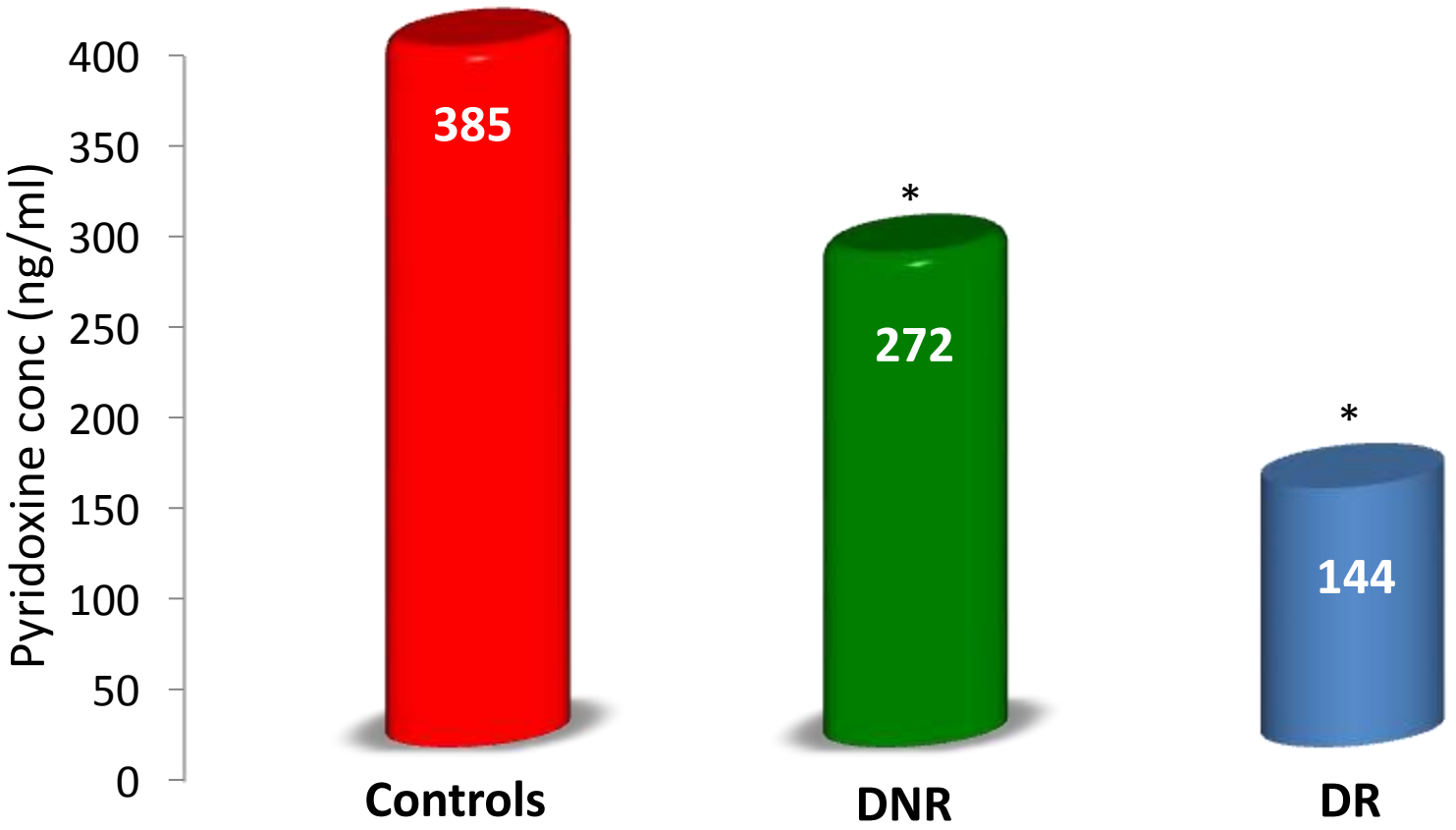


*P<0.05

PLoS ONE 6(11): e26747.

Contd..

Plasma vitamin B12 deficiency



P<0.05

PLoS ONE 6(11): e26747.

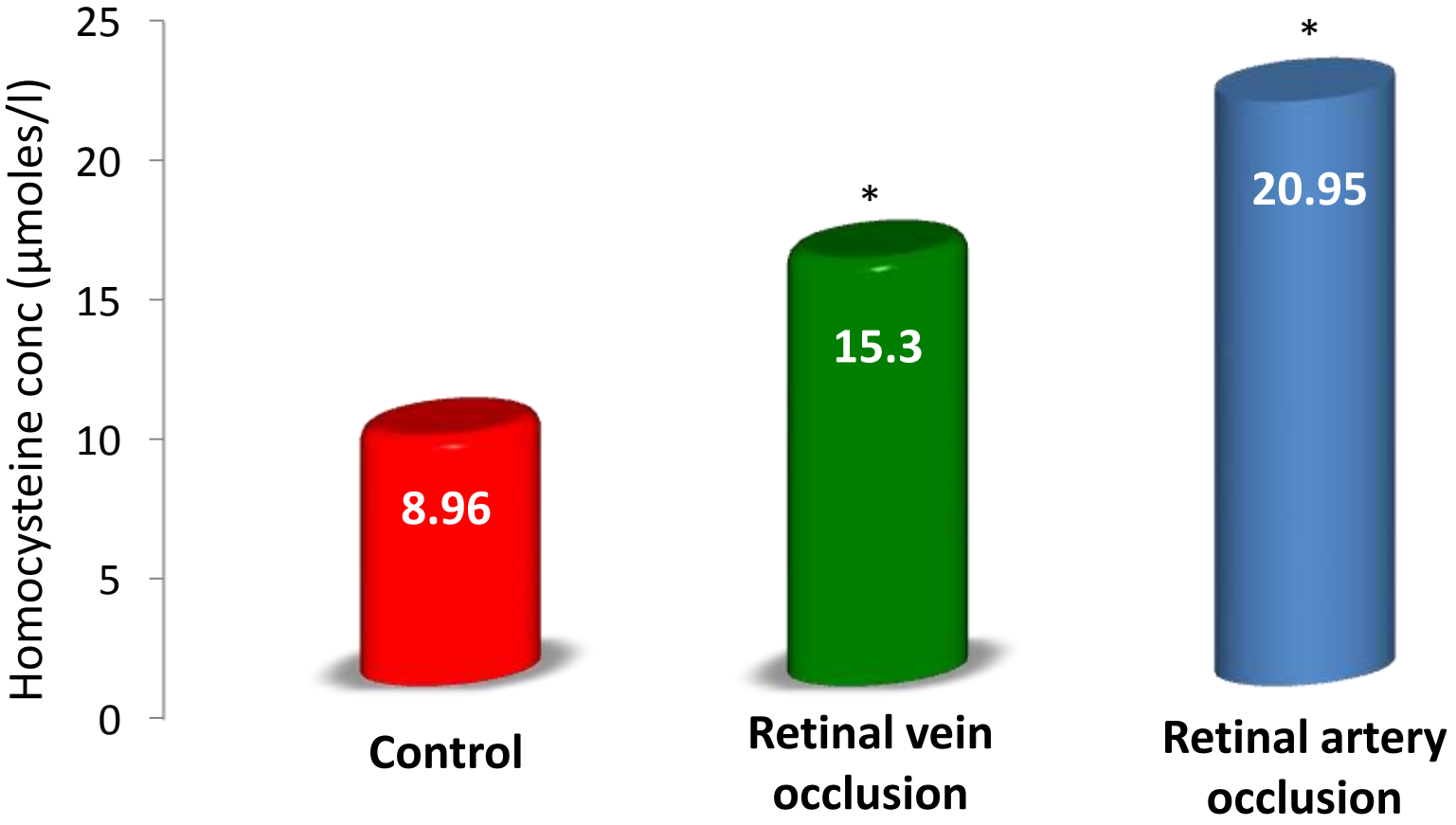
Hyperhomocysteinemia and retinal vascular occlusive disease

- Plasma total homocysteine was measured in 56 consecutive patients with recently diagnosed retinal vascular occlusive disease:

- 36 had central retinal vein occlusion, 12 branch retinal vein occlusion, and 8 retinal artery occlusion, and compared them with 59 age- and sex-matched healthy controls.

Eur J Ophthalmol. 2002 Nov-Dec;12(6):495-500

Homocysteine concentration



*P<0.001

Eur J Ophthalmol. 2002 Nov-Dec;12(6):495-500

Each 1 µmol/l increase in homocysteine was associated with a 7% increased odds of RVO

Conclusion

The data indicate that hyperhomocysteinemia & deficiency of B-vitamin could be an independent risk factor for DR.

Eur J Ophthalmol. 2002 Nov-Dec;12(6):495-500

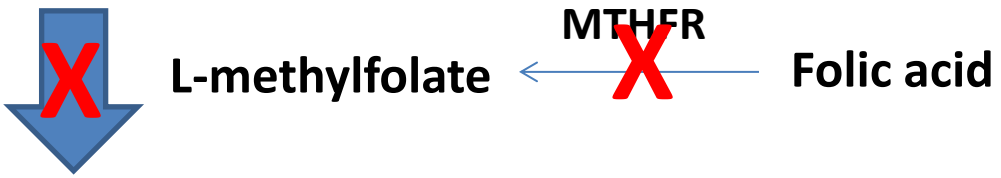
Regardless of dietary intake of B-vitamins,

MTHFR Polymorphism is a risk factor for Diabetic Retinopathy

Chin Med J 2003;116(1):145-147

MTHFR polymorphism

Homocysteine



Methionine

MTHFR Polymorphism leads to deficiency of active L-methylfolate concentration….causing Hyperhomocysteinemia

Prevalence of MTHFR Polymorphism

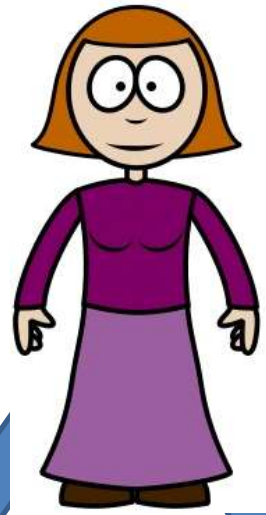
60%

Of the total population are having MTHFR genetic polymorphism

Rev Obstet Gynecol. 2011;4(2):52-59

There are two types of MTHFR genotypes, TT & CC

MTHFR **C** allele is physiologically protective and **T** allele is responsible for increased metabolic risk in Indian population



Mother

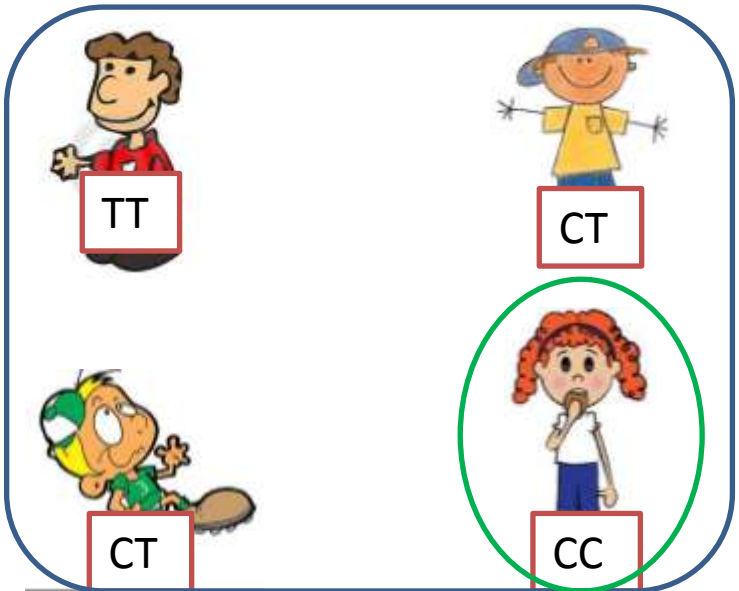
TT

CC

Father

TT

CC



MTHFR enzyme activity is reduced by 35% among the 677CT carriers and by 50% to 70% among 677TT carriers

Nat Genet. 1995 May;10(1):111-3.

BHU, Varanasi,
March 2012 Report

MTHFR Polymorphism in Uttar Pradesh

Ind J Hum Gen
Jan 2012 Report

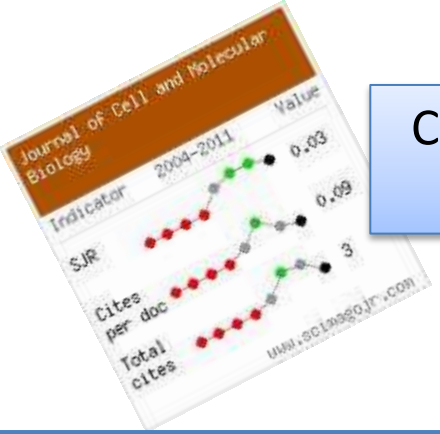
MTHFR Polymorphism is predominent in Uttar Pradesh

BHU Varanasi,
Feb 2012 Report

Homozygosity (TT) and heterozygosity (CT) for the MTHFR polymorphism

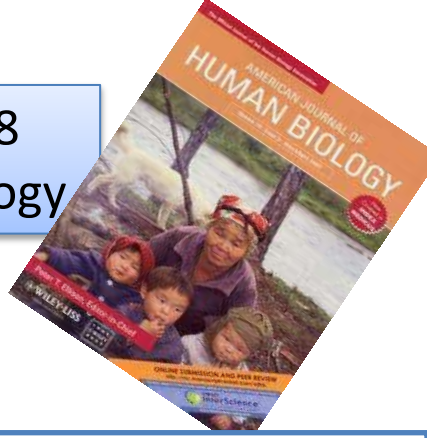
South Indian
Study 2004

MTHFR polymorphisms was found to be predominant among Tamilians



Caste study from Hum Mol Gen Lab Jun 2012

Delhi Study 2008 Dept of Anthropology



MTHFR polymorphisms was prevalent among Bramhin & Rajputs of Uttar Pradesh

MTHFR polymorphisms was prevalent among Ahirs & Jats of Haryana

Eastern Uttar Pradesh Report 2010

High MTHFR Polymorphism in Muslim population

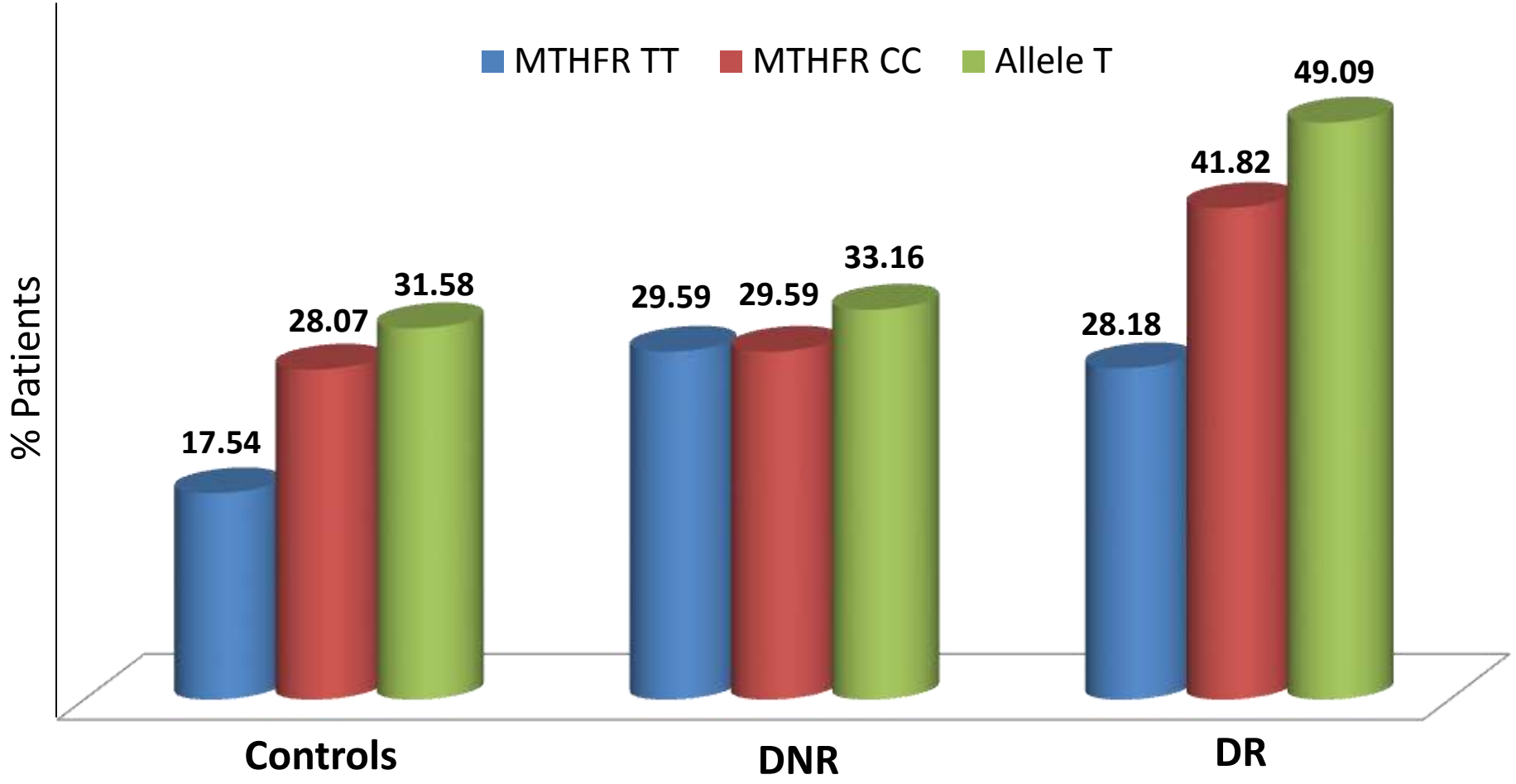
The relationship between MTHFR gene polymorphisms, plasma homocysteine levels and diabetic retinopathy in type 2 diabetes mellitus

Total of 208 patients with type 2 diabetes mellitus and 57 controls were recruited into the study.

MTHFR polymorphism is strongly associated with hyperhomocysteinemia and diabetic retinopathy

Chin Med J 2003;116(1):145-147

MTHFR polymorphism & DR



Chin Med J 2003;116(1):145-147

DIABETES RESEARCH AND CLINICAL PRACTICE 95 (2012) 110–118

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Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

An updated meta-analysis of methylenetetrahydrofolate reductase gene 677C/T polymorphism with diabetic nephropathy and diabetic retinopathy

An updated meta-analysis of methylenetetrahydrofolate reductase gene 677C/T polymorphism with diabetic nephropathy and diabetic retinopathy

A B S T R A C T

Studies investigating the association of methylenetetrahydrofolate reductase (MTHFR) gene 677C/T polymorphism with diabetic nephropathy and diabetic retinopathy have so far reported inconclusive results. We therefore aim to address this inconclusiveness by conducting a meta-analysis. Random-effects model was applied irrespective of between-study heterogeneity. Data and study quality were assessed in duplicate. A total of 7807 and 1599 subjects from 21 and 8 studies were analyzed for diabetic nephropathy and diabetic retinopathy, respectively. Carriers of 677TT genotype were 1.71 (95% confidence interval [95% CI]: 1.02–2.88; $P = 0.042$) and 2.89 (95% CI: 1.51–5.53; $P = 0.001$) times more likely to develop diabetic nephropathy separately relative to diabetic patients without nephropathy and nondiabetic controls. Likewise, this association was preserved for diabetic patients with retinopathy referring to those without (odds ratio [OR] = 1.86; 95% CI: 1.21–2.86; $P = 0.004$). Subgroup analyses showed that ethnicity was a possible confounder, especially in West Asians and Africans, and so were gender and duration of diabetes mellitus in diabetic nephropathy studies. Probability of publication bias was low across all comparisons as reflected by the funnel plot and corresponding test. Taken together, our results demonstrate that MTHFR gene 677TT genotype might confer a moderately augmented risk for diabetic nephropathy and diabetic retinopathy.

Diabetes Res Clin Pract. 2012 Jan;95(1):110-8.

…hence this arises the need of

Active supplementations of conventionally used vitamins…

Introducing

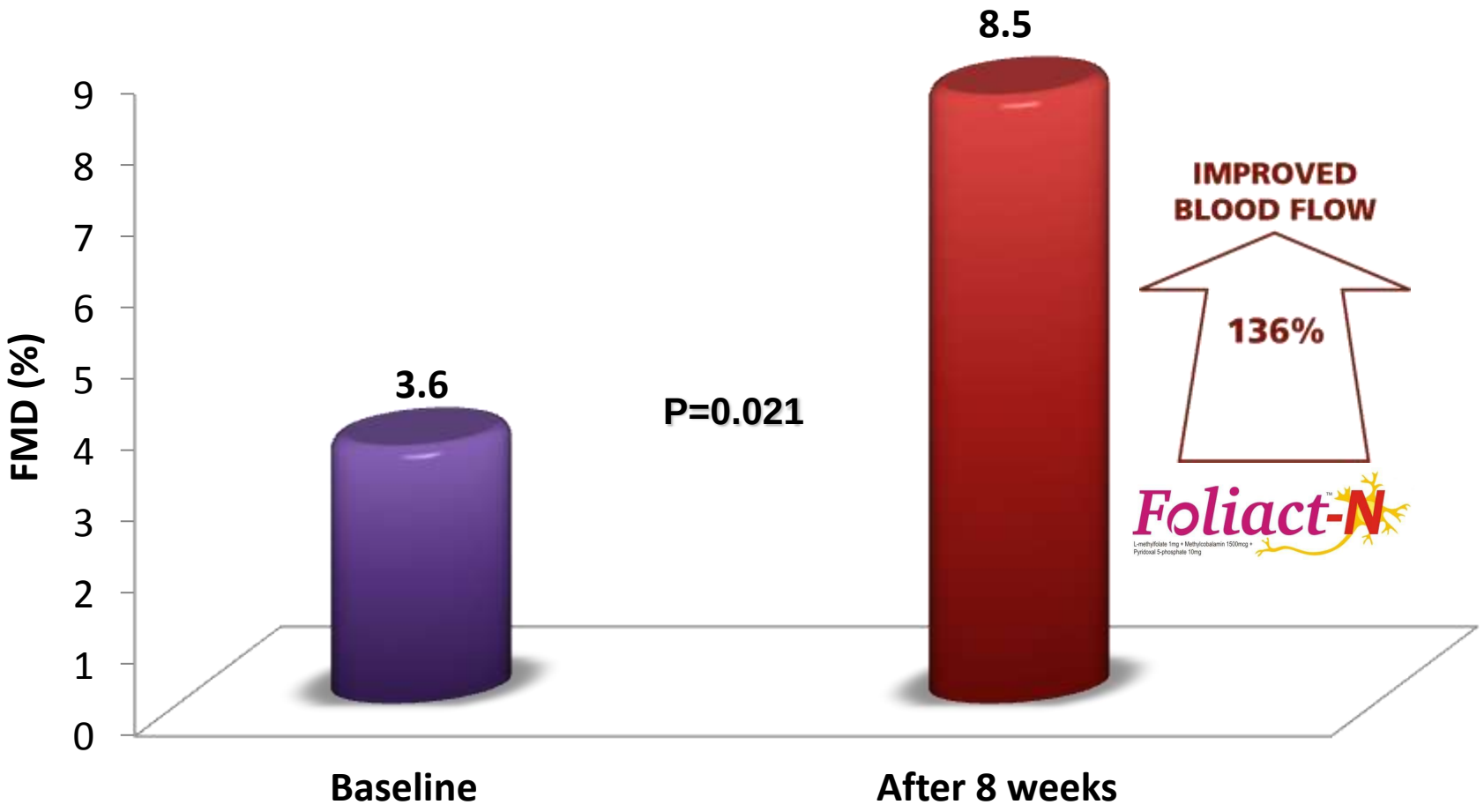
Triple combination of LMF + P5P + Methylcobalamin Improves Endothelial Function…

In a randomized, placebo-controlled, double-blind trial,

35 patients patients with endothelial dysfunction were randomized to Combination of LMF + P5P + Methylcobalamin or placebo for 8 weeks

Arterioscler Thromb Vasc Biol. 2006; 26: e43-e52

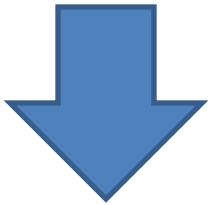
Triple combination significantly improved endothelial function by 136% at 8 weeks



FMD: flow mediated dialation

Arterioscler Thromb Vasc Biol. 2006; 26: e43-e52

Increasing retinal blood flow



Improving retinal function

How Foliact-N is different than conventional formulations ?

	Conventional formulations	Foliact-N	
Inactive	Folic acid	L-methylfolate	Active
	Vitamin B6	Pyridoxal 5'-Phosphate	
	Vitamin B12	Methylcobalamin	

Bypasses MTHFR polymorphism

Homocysteine

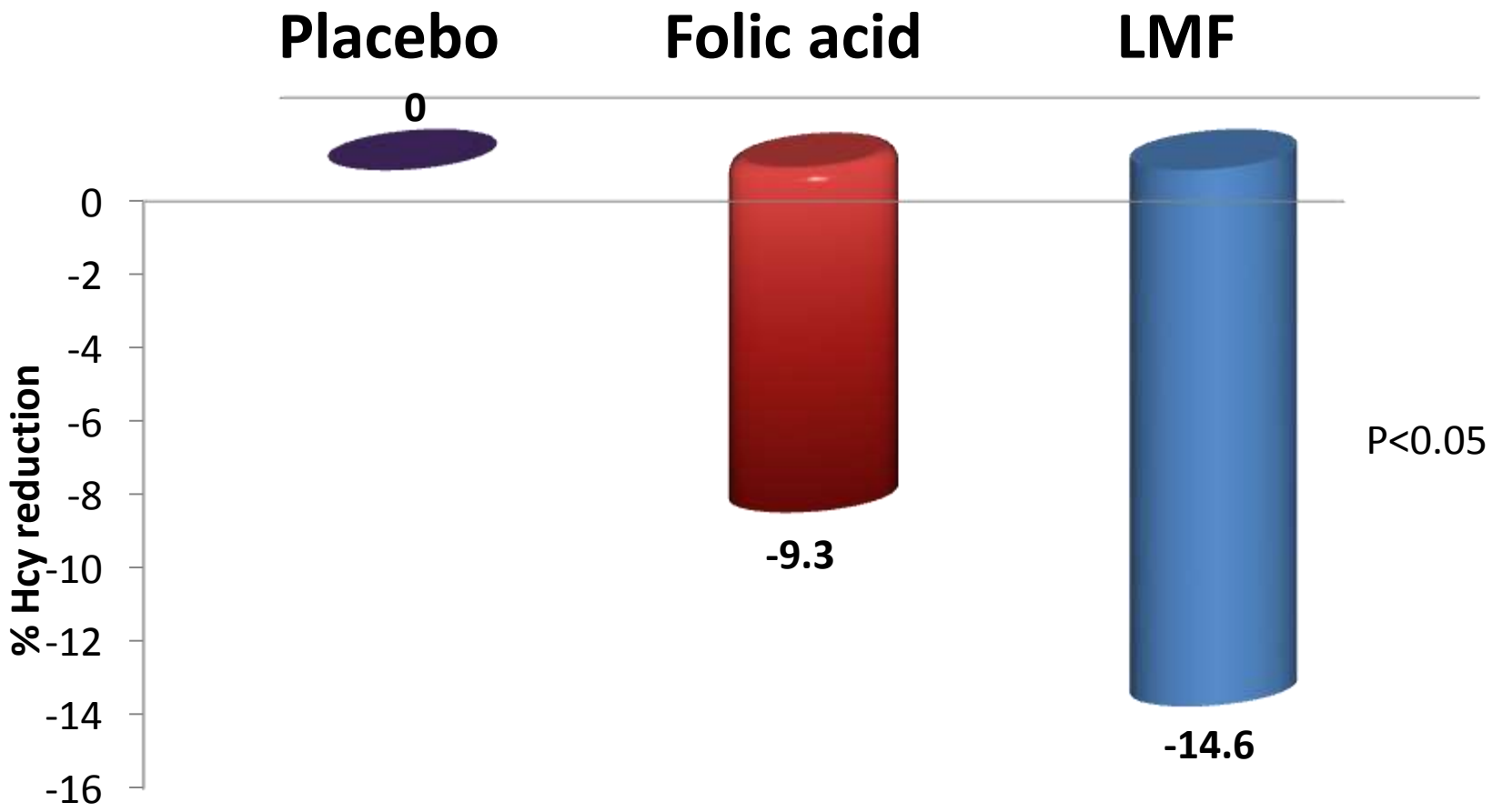
L-methylfolate

Methionine

Active L-methylfolate…..decreases homocysteine levels

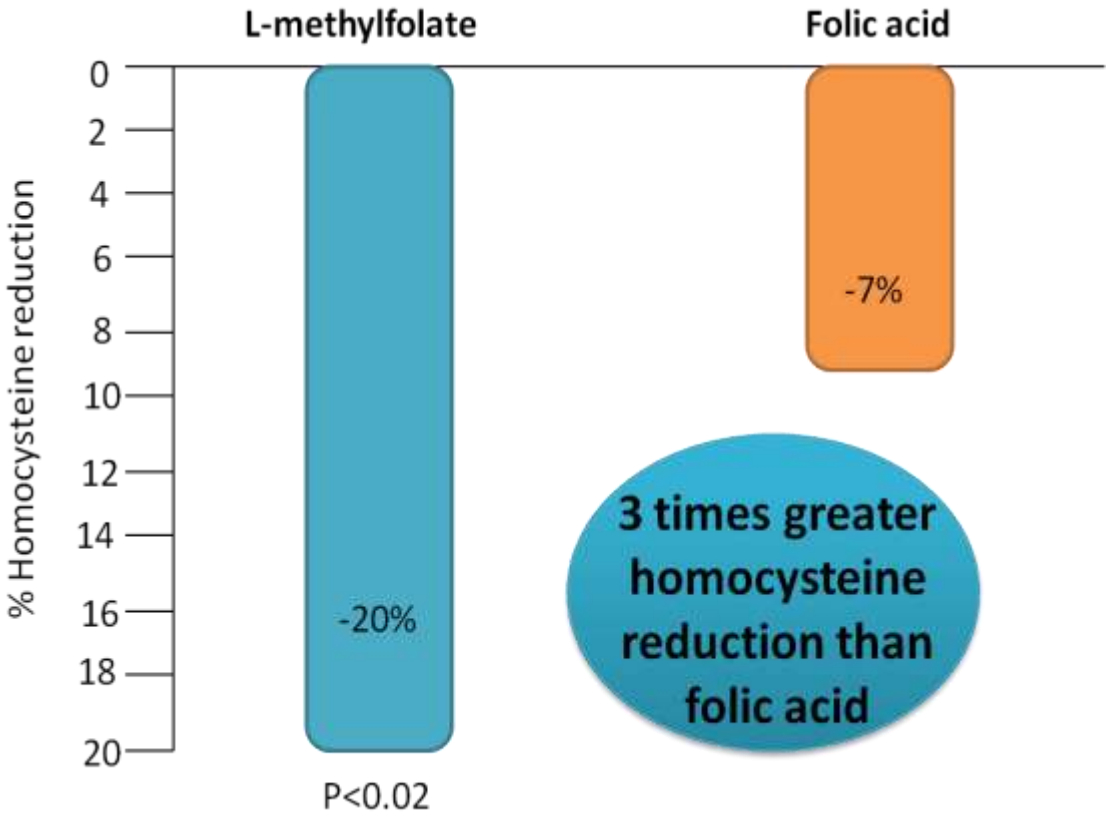
L-methylfolate vs folic acid

Homocysteine reduction after 24 weeks



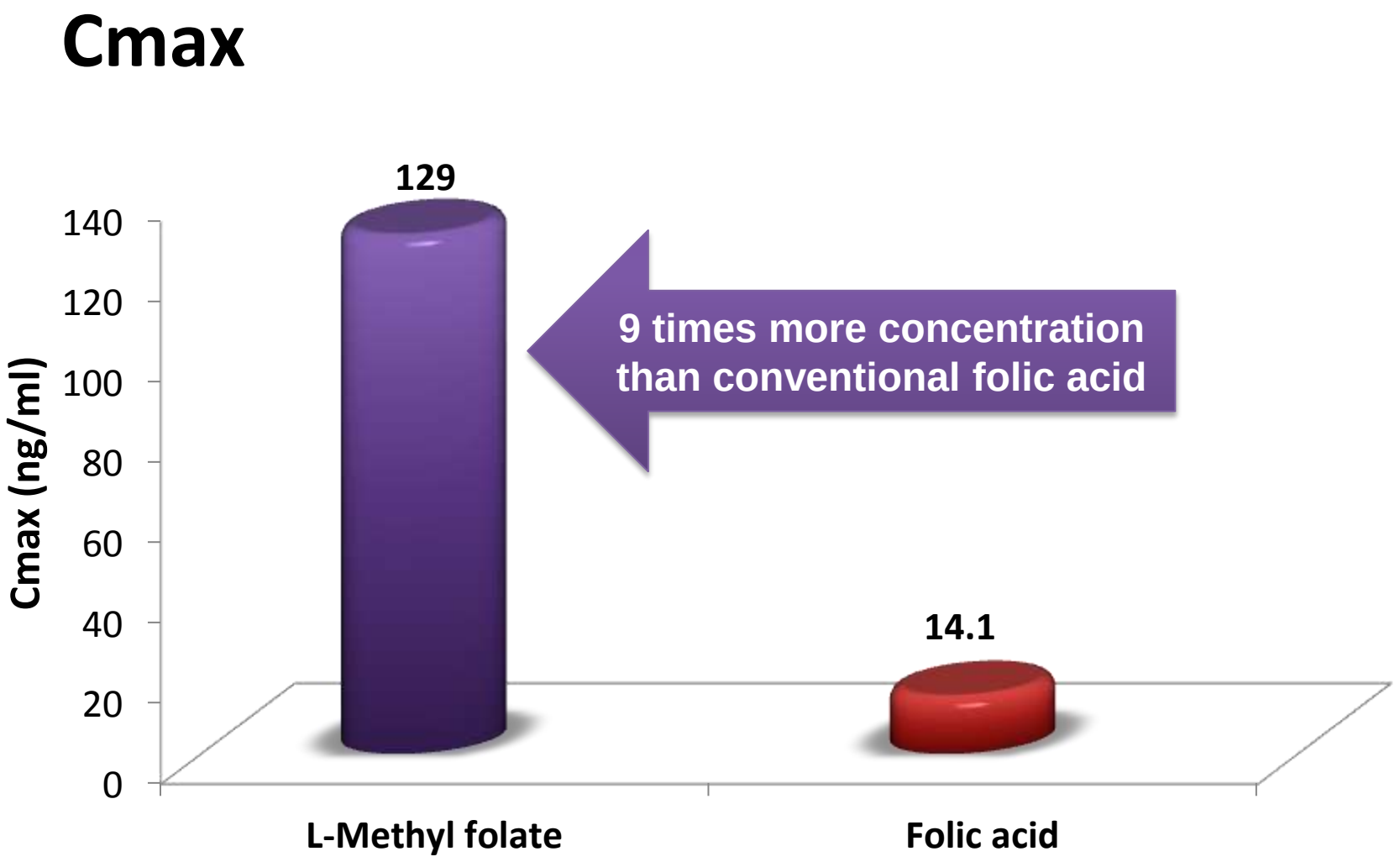
Am J Clin Nutr 2003;77:658–62

L-methylfolate vs folic acid



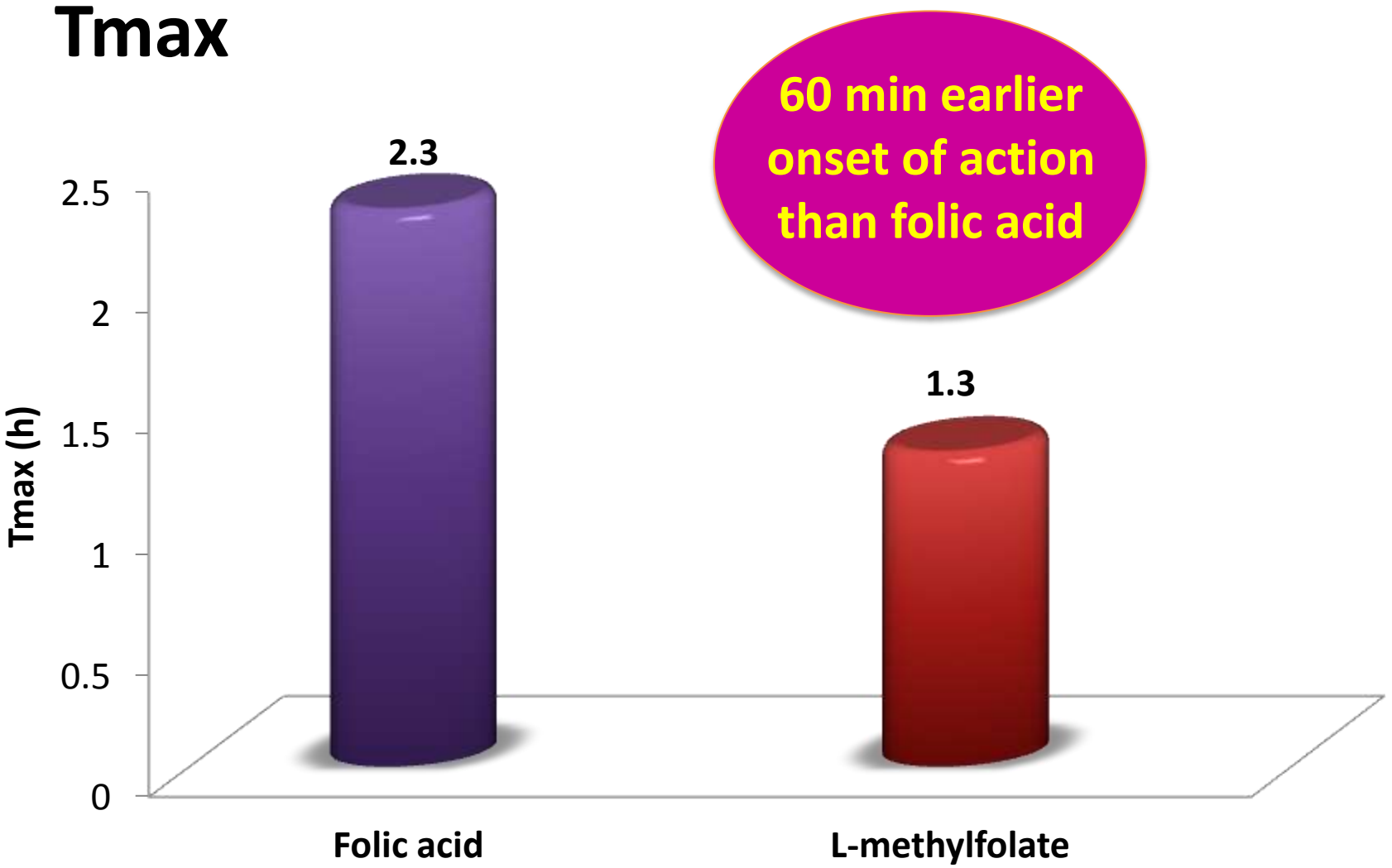
College of Medicine, Univ of South Alabama, submitted for Publication, data on file

L-methylfolate vs folic acid



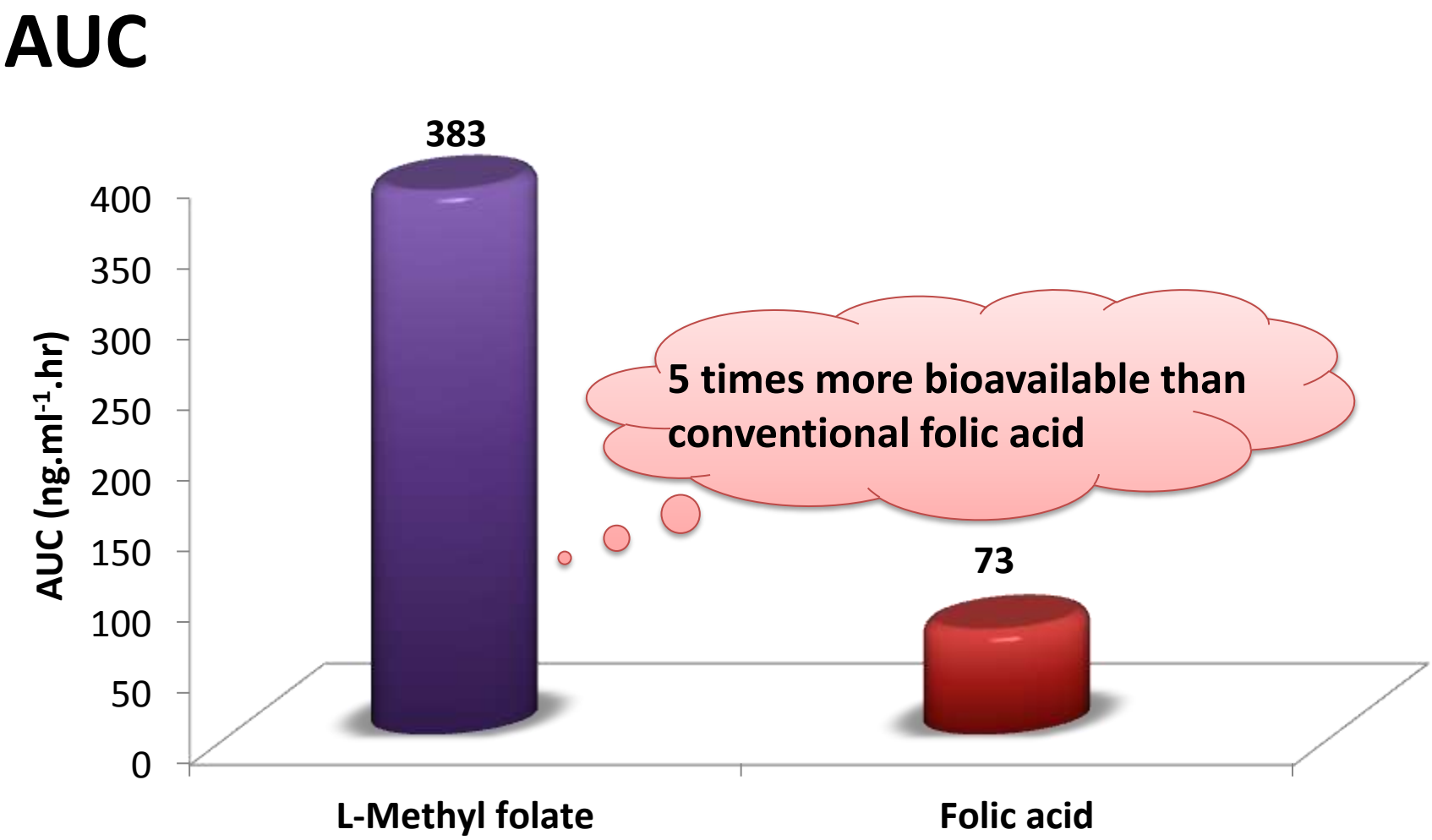
British Journal of Pharmacology 2004;141:825–830

L-methylfolate vs folic acid



British Journal of Pharmacology 2004;141:825–830

L-methylfolate vs folic acid



British Journal of Pharmacology 2004;141:825–830

Foliact-N Vs Other formulations

Conventional Preparation Folic Acid Vitamin B-6

Activation Steps

High T-max
Less Bioavailability
Less Cmax
Patients metabolism disorder

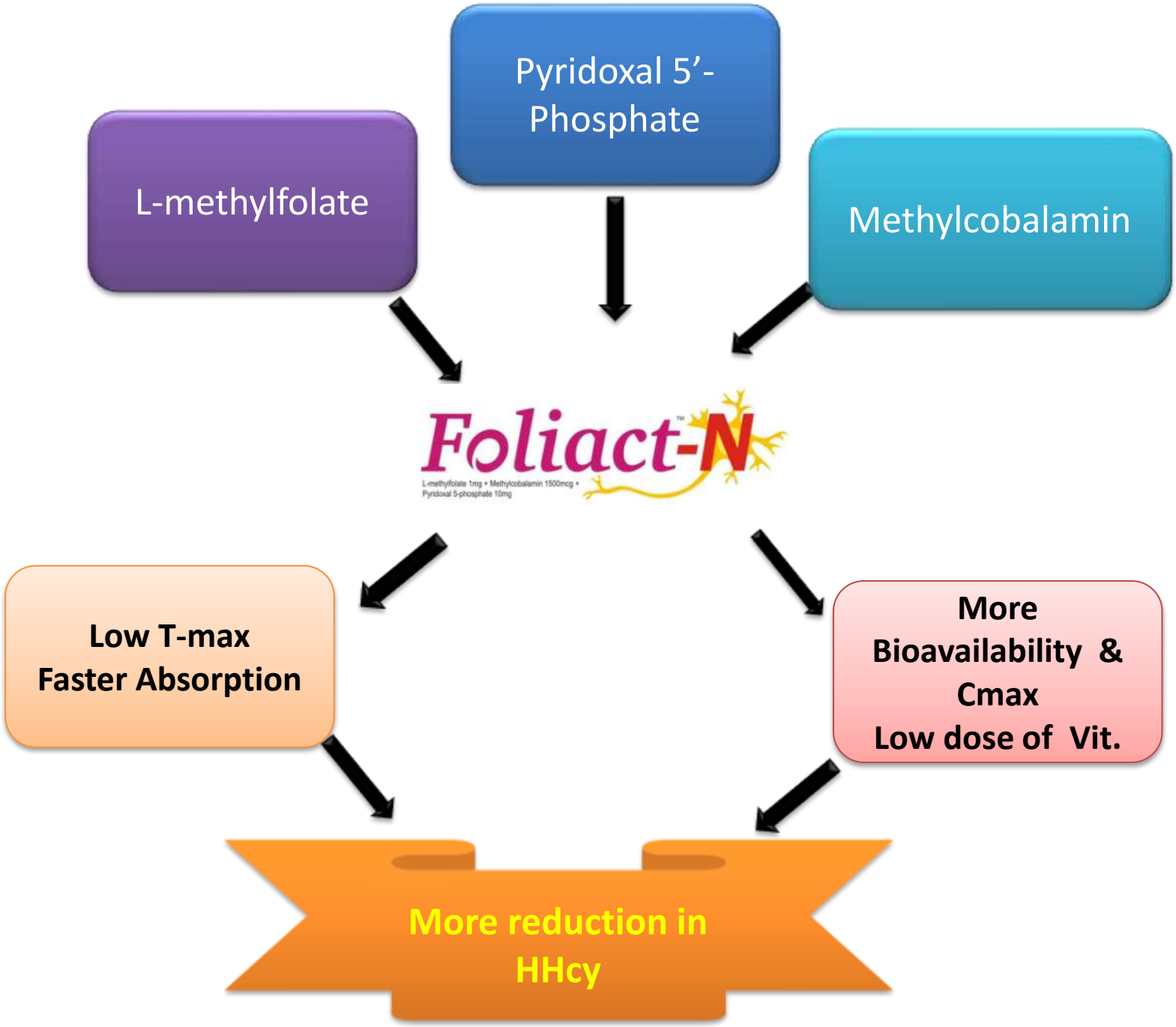
Results in less reduction in Hyperhomocysteinemia

Active metabolites for Folic Acid , Vit-6, 12 Are Essential

Foliact-N

P5P & Methylcobalamin

L-methylfolate


Pyridoxal 5'-Phosphate
L-methylfolate
Methylcobalamin
Foliact-N
L-methylfolate 1mg + Methylcobalamin 1500mcg + Pyridoxal 5-phosphate 10mg
Low T-max
Faster Absorption
More Bioavailability & Cmax
Low dose of Vit.
More reduction in HHcy

Indication & dosage

- For the prevention of diabetic retinopathy, venous occlusion
- One tablet OD