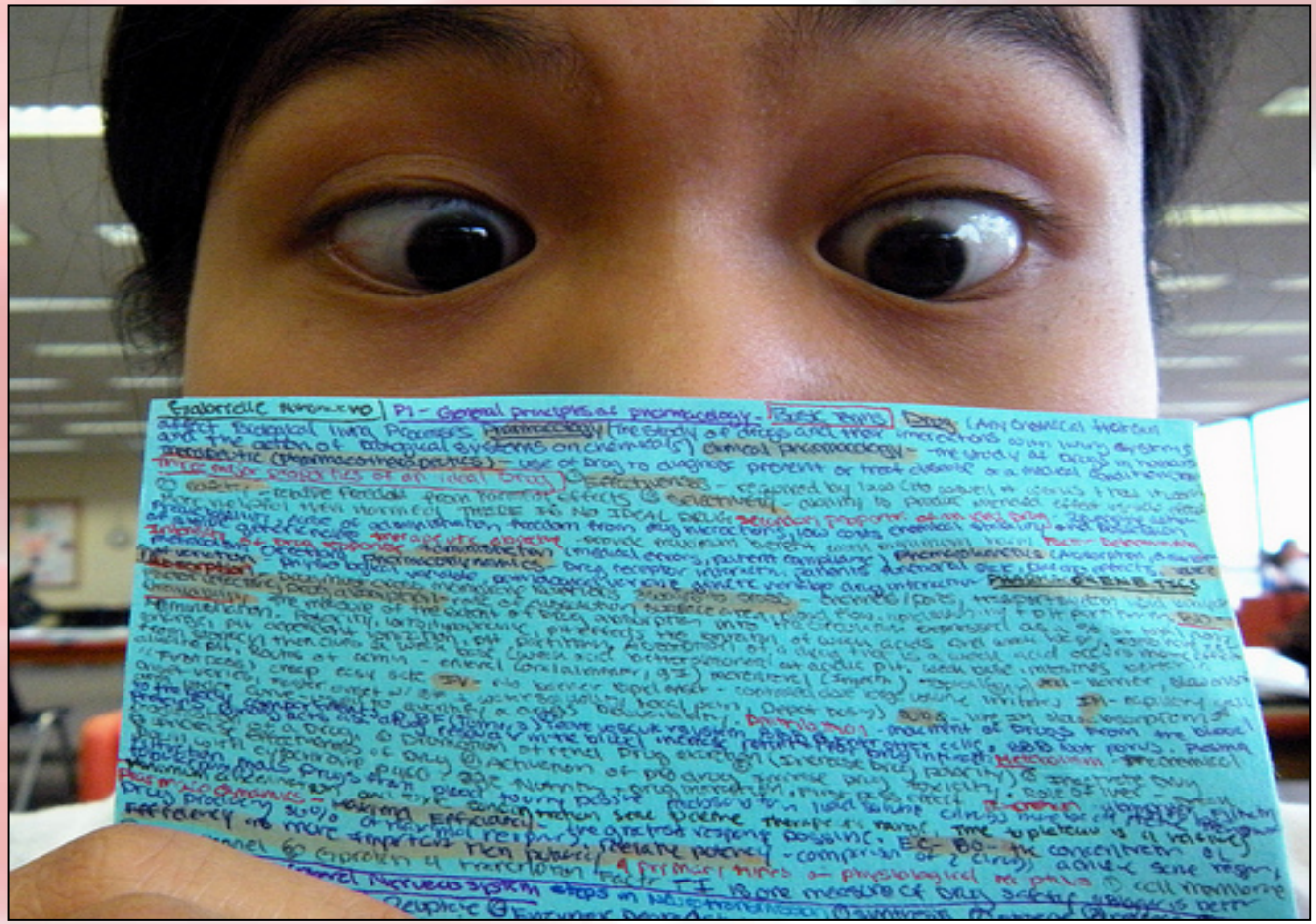
Déficit de vitamina B12 más allá de la anemia

Dra. **Belén** Alonso
Medicina Interna. Hospital Universitario de Gran Canaria Dr. Negrín

Objetivos:


WOMEN ON THE VERGE OF A NERVOUS BREAKDOWN
"Extravagantly stylish"
TIME OUT
a Pedro Almodóvar film
DVD
12

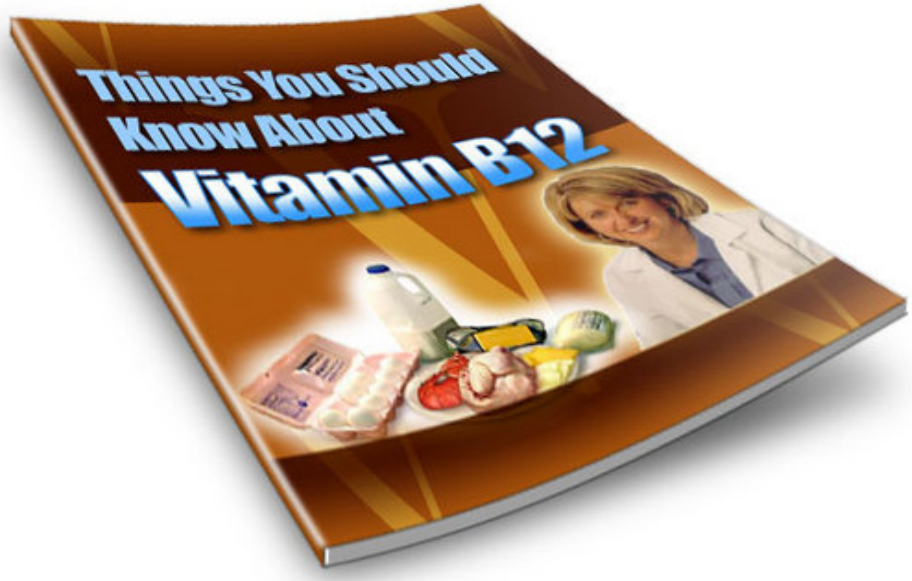
Objetivos:



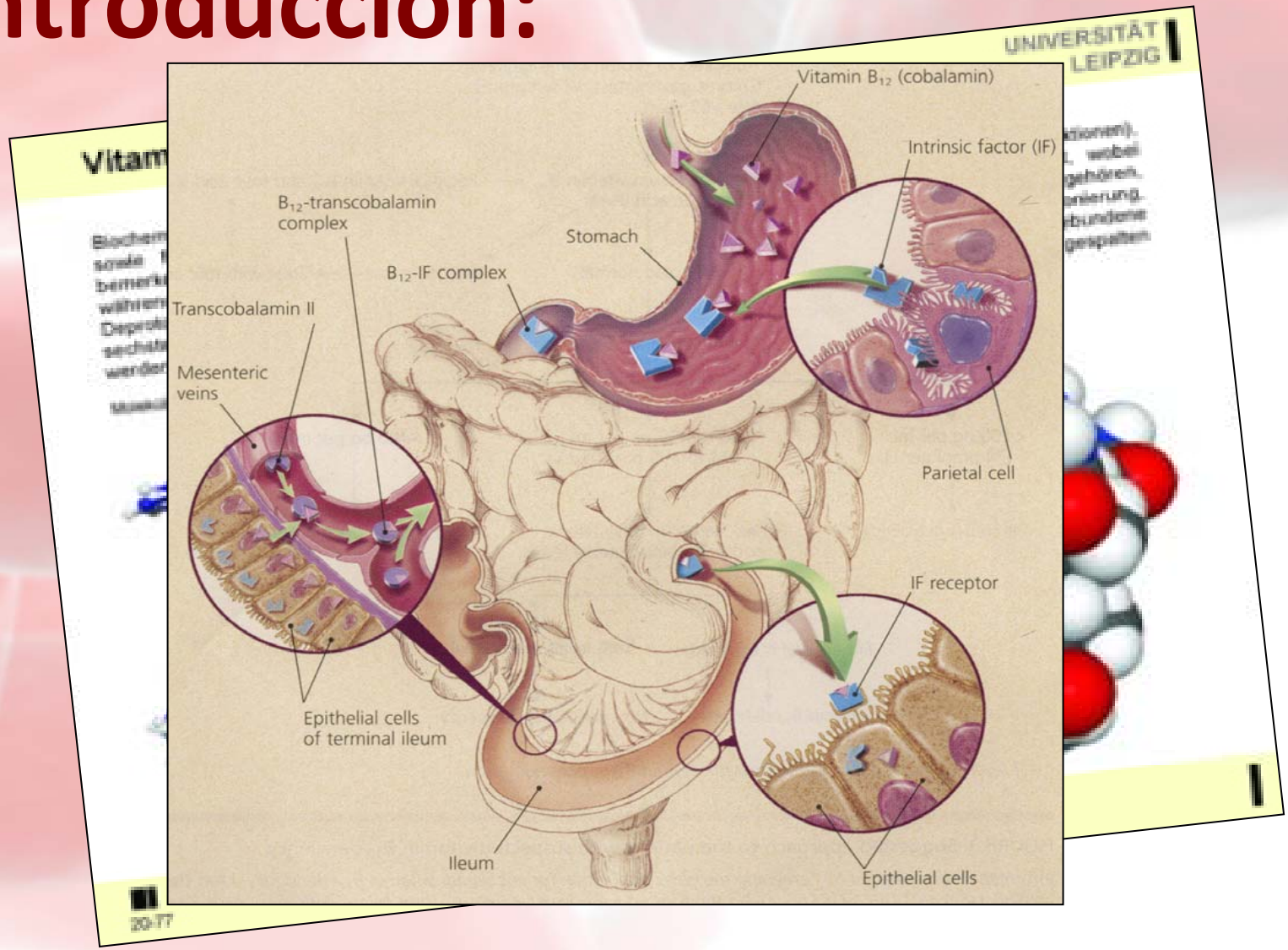
Objetivos:

“el abogado de los famosos”

Introducción:



Introducción:



Introducción:

Introducción:

	TOTAL
Anemia Hb 12.0/13.0g/dl	261/350 (74,5%)
Déf.VB12 (B12 en plasma < 200 pg/dL)	43/350 (12,2%)
Macrocitosis VCM > 101fl	8/350 (2,28 %)
Anemia + Def. Vit. B12	32/350 (9,1 %)
Anemia + Macrocitosis	6/350 (1,7 %)
Anemia + Macrocitosis + Déf. Vit. B12	2/350 (0,5 %)

Dra. B. Alonso. Tesis Doctoral. "Déficit de vitamina B12 en pacientes hospitalizados mayores de 60 años"

Introducción:

Introducción:

Tableau 4
Principales manifestations cliniques des carences en vitamine B12 [1,2,4,16,17,23,24,38] (*Clinical manifestations of cobalamin deficiencies*)

Manifestations hématologiques :
- fréquentes : macrocytose, hypersegmentation des neutrophiles, anémie macrocytaire
- rares : thrombopénie et neutropénie isolées, pancytopénie ;
- exceptionnelles : anémie hémolytique, tableau de peudomicroangiopathie thrombo

Manifestations neuropsychiatriques :
- fréquentes : polynévrites (surtout sensitives), ataxie, signe de Babinski ;
- classiques : sclérose combinée de la moelle ;
- rares : syndrome cérébelleux, atteintes des nerfs crâniens dont névrite optique, atr
- en cours d'étude : altérations des fonctions supérieures voire démences, accident
parkinsoniens, dépression, épilepsie, troubles du sommeil.

Manifestations digestives :
- classiques : glossite de Hunter, ictère et élévation des LDH et de la bilirubine (« a
- liens discutables : douleurs abdominales, dyspepsie, nausées et vomissements, d
- rares : ulcères cutanéo-muqueux rebelles et/ou récidivants.

Manifestations gynéco-obstétriques :
- discutables : atrophie de la muqueuse vaginale et infections chroniques vaginale
- en cours d'étude : hypofertilité et avortements à répétition (infertilité masculine)

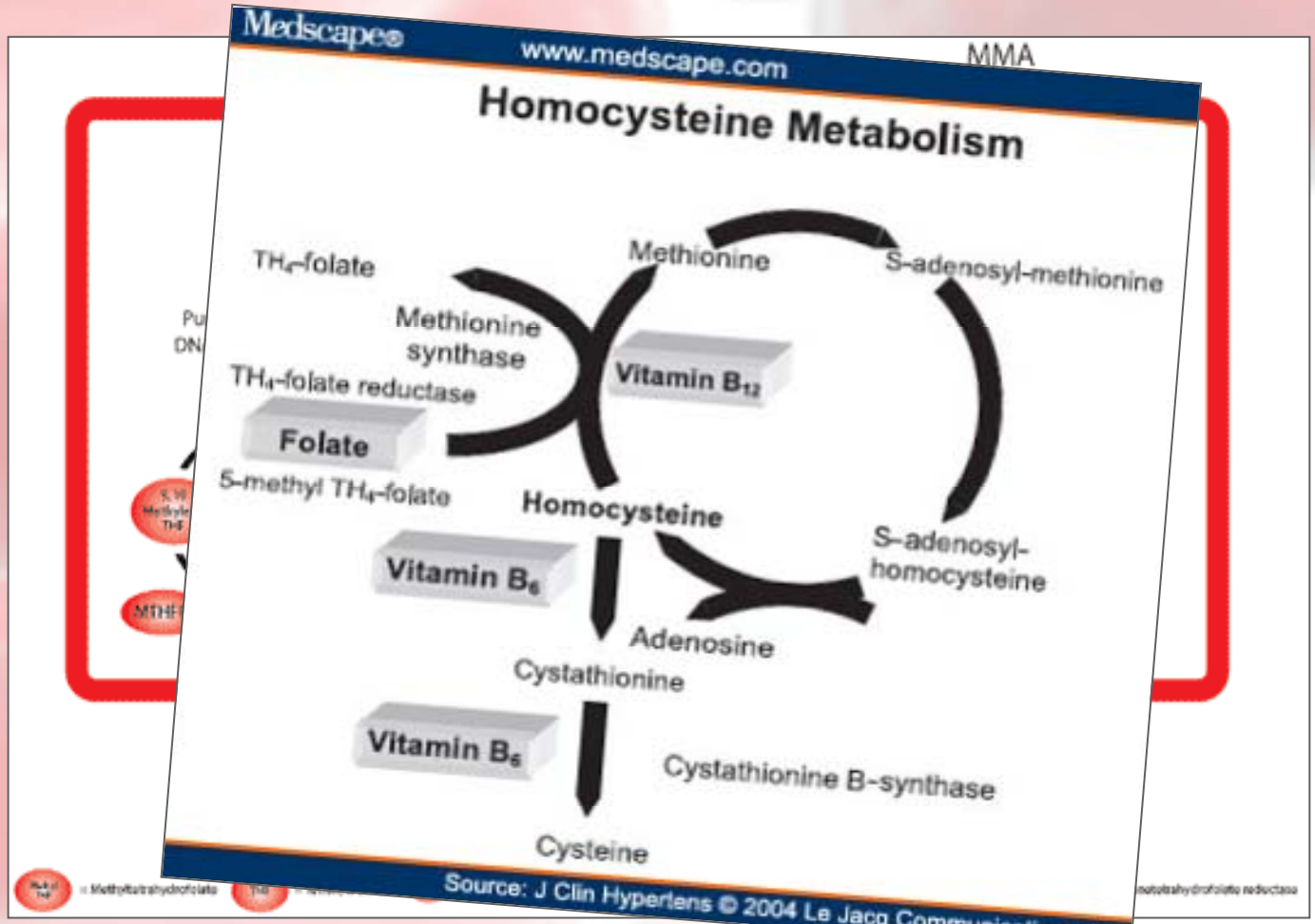
Autres :
- en cours d'étude : maladie thromboembolique veineuse et cardiopathies ischém

Table 1. Neurologic and Psychiatric Symptoms of Vitamin B_{12} Deficiency and Parkinson Disease (PD)

	Vitamin B_{12} Deficiency	PD
Autonomic		
Impotence, urinary or fecal incontinence	+	+
Orthostatic hypotension	+	+
Cerebral		
Dementia, memory loss, cognitive impairment	+	+*
Depression	+	+
Psychosis	+	+*
Myelopathic		
Subacute combined degeneration		
Ataxia	+	-
Spasticity	+	-
Lehrmitte sign (electric-shock–like sensations in the spine)	+	-
	+	+
Abnormal Gait†		
Spastic		
Shuffling	+	-
	-	+
Constitutional		
Fatigue	+	+

*Seen in PD or resulting from dopaminergic PD treatment), or both
†Note gait abnormalities do not always appear "typical" of textbook descriptions

Introducción:



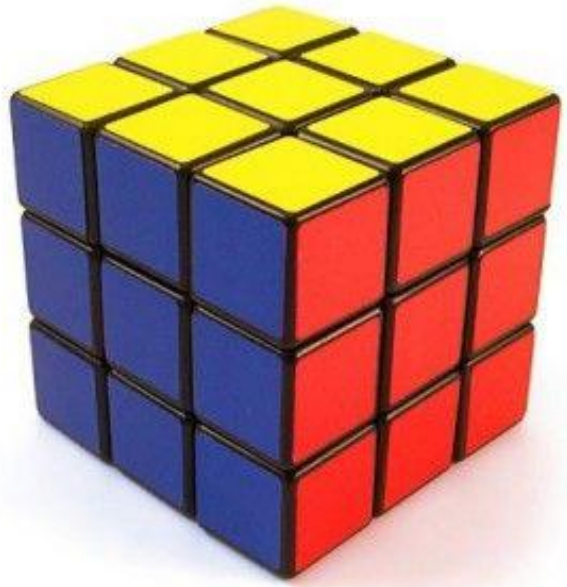
Introducción:

Homocisteína

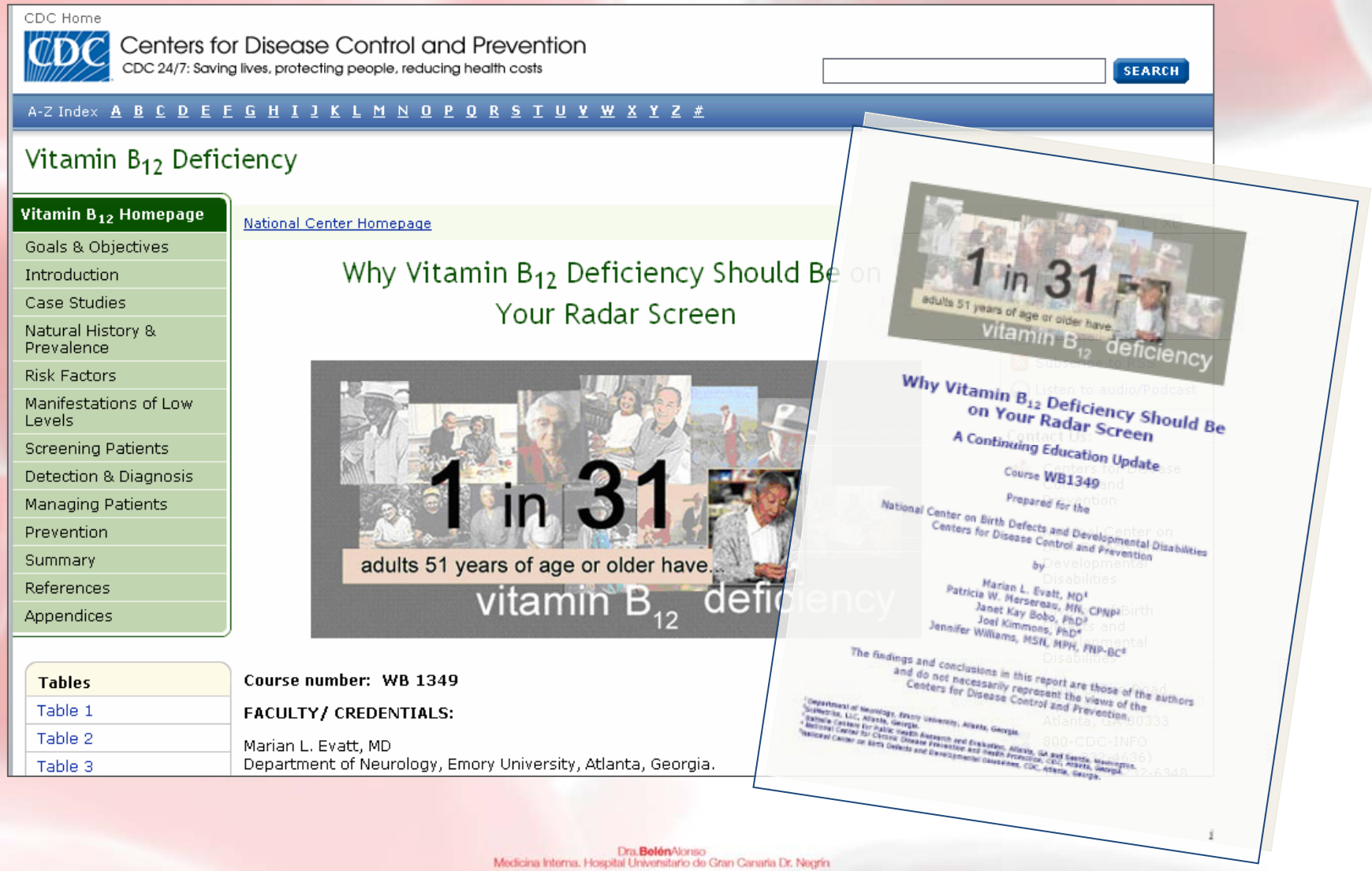
Metionina

MTHFR

Vitamina B12



Prevalencia:



Prevalencia:

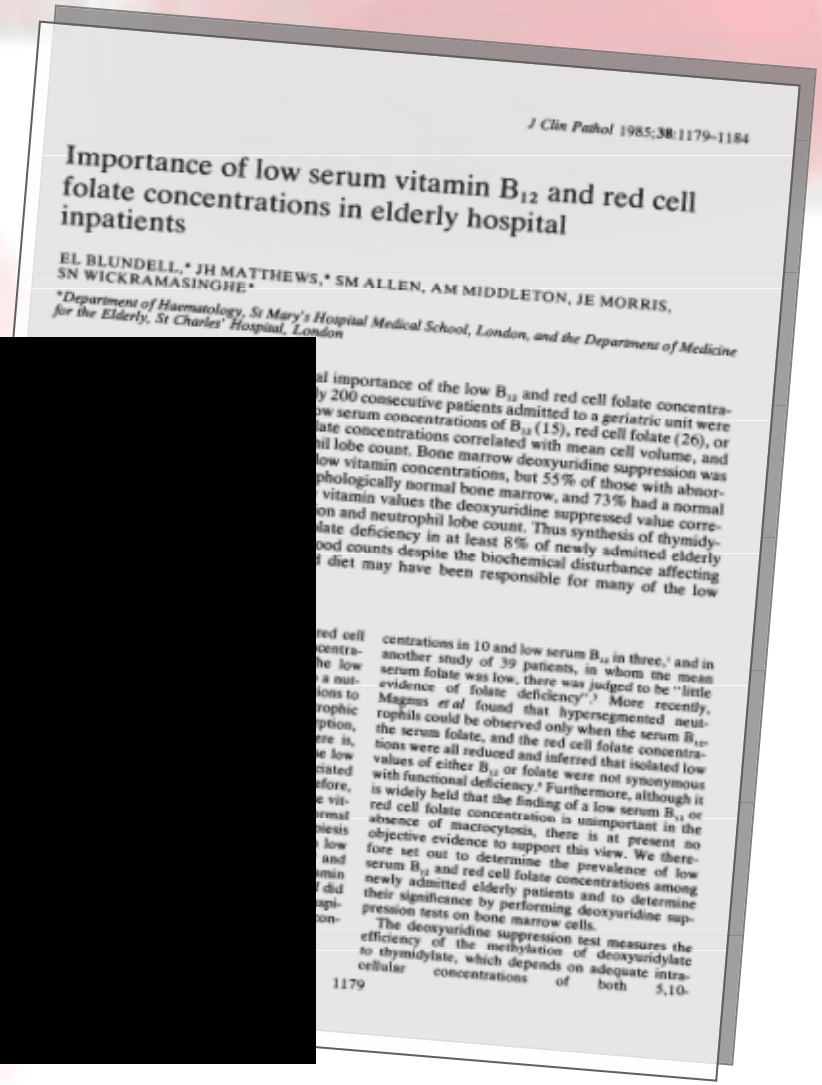
5

40

Prevalencia:

1985

200 pctes ingresados



J Clin Pathol 1985;38:1179–1184

Importance of low serum vitamin B_{12} and red cell folate concentrations in elderly hospital inpatients

EL BLUNDELL,* JH MATTHEWS,* SM ALLEN, AM MIDDLETON, JE MORRIS, SN WICKRAMASINGHE*

*Departments of Haematology, St Mary's Hospital Medical School, London, and the Department of Medicine for the Elderly, St Charles' Hospital, London

al importance of the low B_{12} and red cell folate concentra-
y 200 consecutive patients admitted to a geriatric unit were
w serum concentrations of B_{12} (15), red cell folate (26), or
late concentrations correlated with mean cell volume, and
il lobe count. Bone marrow deoxyuridine suppression was
low vitamin concentrations, but 55% of those with absor-
phologically normal bone marrow, and 73% had a normal
vitamin values the deoxyuridine suppressed value corre-
on and neutrophil lobe count. Thus synthesis of thymidy-
late deficiency in at least 8% of newly admitted elderly
ood counts despite the biochemical disturbance affecting
diet may have been responsible for many of the low

centrations in 10 and low serum B_{12} in three,[1] and in another study of 39 patients, in whom the mean serum folate was low, there was judged to be "little evidence of folate deficiency".[3] More recently, Magnus *et al* found that hypersegmented neutrophils could be observed only when the serum B_{12}, the serum folate, and the red cell folate concentrations were all reduced and inferred that isolated low values of either B_{12} or folate were not synonymous with functional deficiency.[4] Furthermore, although it is widely held that the finding of a low serum B_{12} or red cell folate concentration is unimportant in the absence of macrocytosis, there is at present no objective evidence to support this view. We therefore set out to determine the prevalence of low serum B_{12} and red cell folate concentrations among newly admitted elderly patients and to determine their significance by performing deoxyuridine suppression tests on bone marrow cells.

The deoxyuridine suppression test measures the efficiency of the methylation of deoxyuridylate to thymidylate, which depends on adequate intracellular concentrations of both 5,10-

23% défic

Etiología:

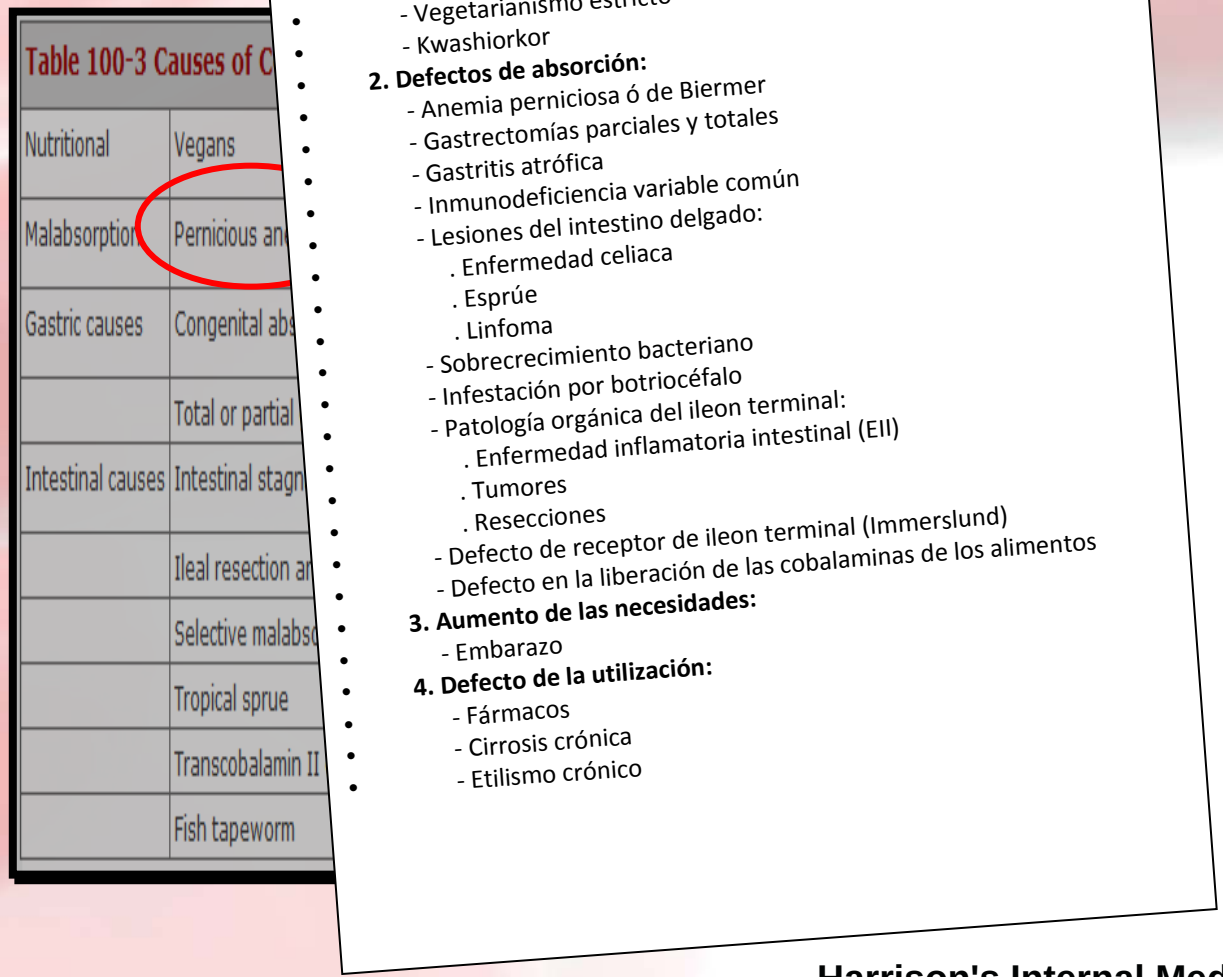


Table 100-3 Causes of C	
Nutritional	Vegans
Malabsorption	Pernicious an
Gastric causes	Congenital ab
	Total or partial
Intestinal causes	Intestinal stagn
	Ileal resection ar
	Selective malabs
	Tropical sprue
	Transcobalamin II
	Fish tapeworm

1. **Alteraciones dietéticas:**
   - Vegetarianismo estricto
   - Kwashiorkor
2. **Defectos de absorción:**
   - Anemia perniciosa ó de Biermer
   - Gastrectomías parciales y totales
   - Gastritis atrófica
   - Inmunodeficiencia variable común
   - Lesiones del intestino delgado:
     - . Enfermedad celiaca
     - . Esprúe
     - . Linfoma
   - Sobrecrecimiento bacteriano
   - Infestación por botriocéfalo
   - Patología orgánica del ileon terminal:
     - . Enfermedad inflamatoria intestinal (EII)
     - . Tumores
     - . Resecciones
   - Defecto de receptor de ileon terminal (Immerslund)
   - Defecto en la liberación de las cobalaminas de los alimentos
3. **Aumento de las necesidades:**
   - Embarazo
4. **Defecto de la utilización:**
   - Fármacos
   - Cirrosis crónica
   - Etilismo crónico

Harrison's Internal Medicine 17 edición

Diagnóstico:

Table 5. Tailored Diagnostic Approach for Vitamin B_{12} Deficiency

Problem	Goal	Suggested Tests
Patient with mild to severe hematologic or neurologic signs or symptoms, or both	Confirm suspected vitamin B_{12} deficiency	Serum B_{12}
Patient with hematologic or neurologic signs or symptoms, or both, unlikely due to vitamin B_{12} deficiency	Ensure if vitamin B_{12} deficiency exists, it is not missed	Serum B_{12} MMA* and Hcy†
Asymptomatic patient with condition known to cause vitamin B_{12} deficiency	Determine if vitamin B_{12} deficiency has developed yet	MMA (metabolic changes often precede low cobalamin levels)
Asymptomatic patient accidentally found to have low B_{12} level or high Hcy†	Determine if vitamin B_{12} deficiency exists	MMA

*MMA–methylmalonic acid
†Hcy–homocysteine

CDC 2010

Diagnóstico:

Table 1 Determinants of serum cobalamin levels.

''FALSE'' LOW VALUES[a]	''FALSE'' HIGH/NORMAL VALUES[b]
Folate deficiency	High Haptocorrin Levels:
Pregnancy[c]	Myeloproliferative disorders
Oral contraceptives[c]	Renal disease
Multiple myeloma[c]	Increased tissue release of Cbl
HIV infection[c]	Liver disease
Low haptocorrin levels	Low/absent transcobalamin
	Low affinity transcobalamin polymorphisms
	Inherited Disorders of Cbl metabolism
	Recent Cbl therapy
	Cobalamin analogues[d]:
	Nitrous oxide therapy
	High dose Vitamin C
	Intestinal bacterial overgrowth
	Assay methodological errors

Abbreviations: Cbl, cobalamin; HIV, human immunodeficiency virus-1.
[a] Indicates low Cbl levels in the absence of impaired Cbl supply to tissues.
[b] Indicates high or normal Cbl levels despite impaired Cbl supply to tissues.
[c] See text.
[d] Dependent on assay method.

Solomon L. Blood Reviews (2007) 21, 113–130

Tratamiento:

Due to	*Initial Cyanocobalamin*	*Maintenance Cyanocobalamin*
Pernicious anemia	Varies, not limited to: • 1 mg intramuscularly (IM) or subcutaneously (SQ) every (q) week x 8 **OR** • 1 mg IM or SQ x 7 in 1 month	• 1 mg IM or SQ q month **for life** **OR** • 1 mg–2 mg orally (PO) every day (QD) **for life**
Other food-bound B_{12} malabsorption problems	Varies, not limited to: • 1 mg IM or SQ q week x 8 **OR** • 1 mg IM or SQ x 7 in 1 month **OR** • 1 mg–2 mg PO QD	• 1 mg IM or SQ q month **possibly for life** **OR** • 650 µg–1 mg PO QD **possibly for life**

CDC 2010

Tratamiento:

La Colaboración Cochrane
Revisiones Cochrane

Buscar Revisiones
Advanced search

Explorar | Nuevas + Actualizadas | Otros idiomas

search & browse | por tema | listado completo de revis

Audio summaries | Evidence Aid summaries | Cochrane Me

- » Home
- » About us
- » Cochrane Reviews
- » News
- » Events
- » Training
- » Multimedia
- » Contact

Administración oral versus intramuscular de v
deficiencia de vitamina B12

Vidal-Alaball J, Butler C, Cannings-John R, Goringe A, Hood K, McC
McDowell I, Papaioannou A

Resumen en términos sencillos

Las dosis altas de vitamina B12 administradas por vía oral todos l
intramusculares

La deficiencia de vitamina B12 puede provocar anemia y complica
forma oral en la mayoría de los países. En esta revisión se incluy
un total de 108 participantes y realizaron un seguimiento de 93 d
derivadas de estos estudios limitados indican que las dosis alta
como la administración intramuscular para lograr respuestas he

Esta revisión debería citarse como: Vidal-Alaball J, Butler CC, C
Papaioannou A. Administración oral versus intramuscular de vita
(Revisión Cochrane traducida). En: , 2008 Número 4. Oxford: Up
(Traducida de , 2008 Issue 3. Chichester, UK: John Wiley & So

Editorial Group: Metabolic and Endocrine Disorders Group

Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency (Review)

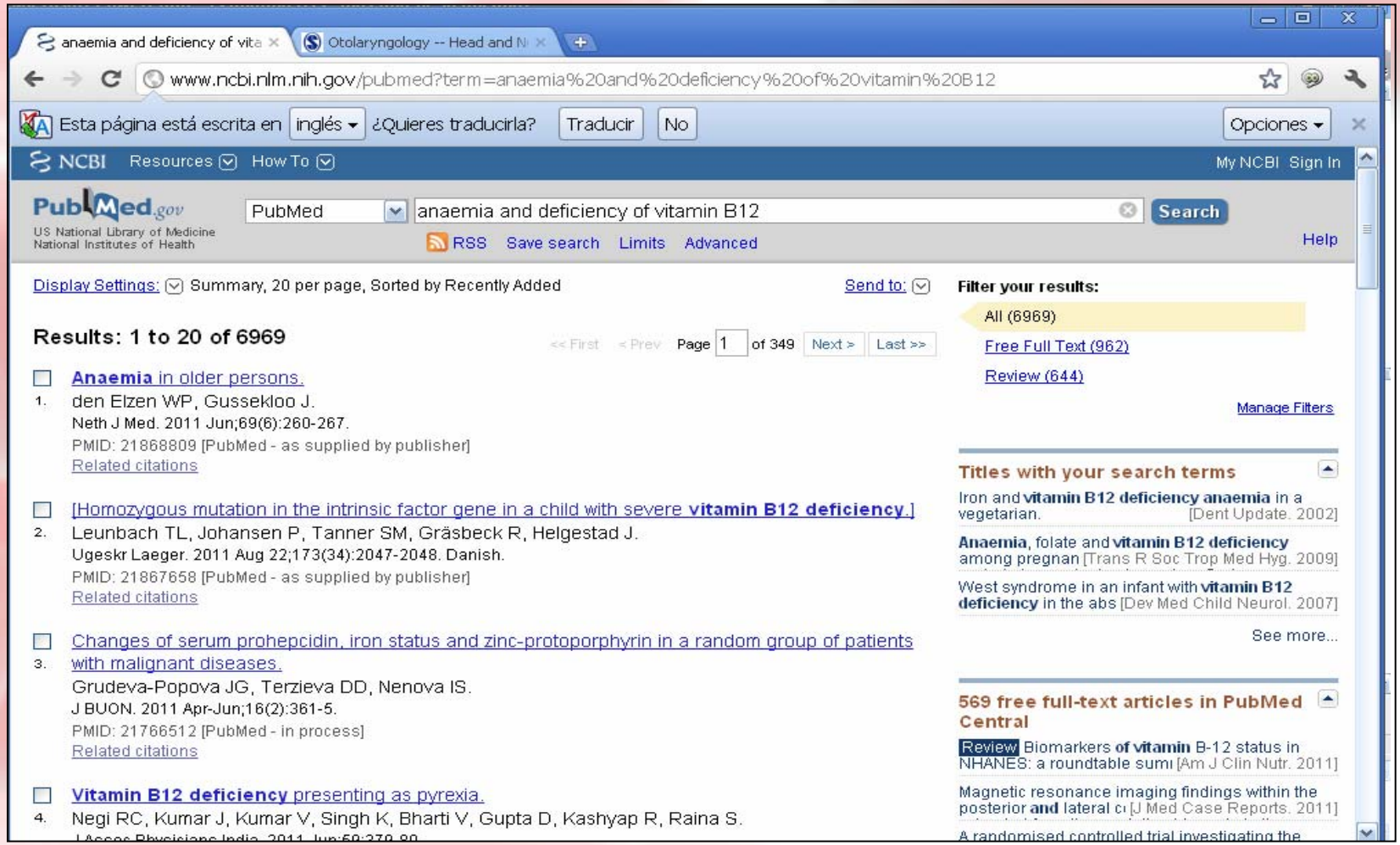
Vidal-Alaball J, Butler C, Cannings-John R, Goringe A, Hood K, McCaddon A, McDowell I, Papaioannou A

THE COCHRANE COLLABORATION®

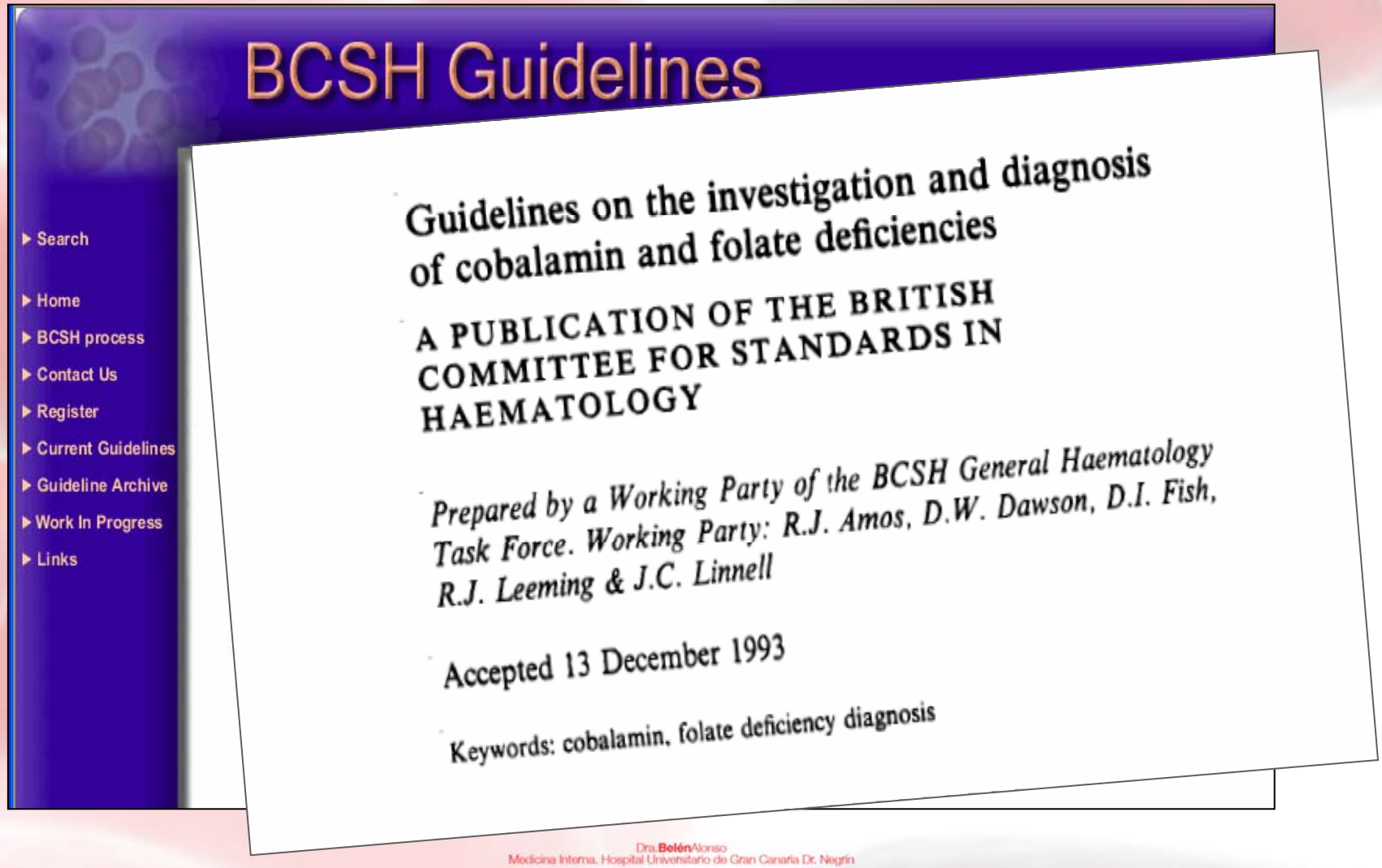
WILEY
Publishers Since 1807

Ella no baila sola…

Anemia – déficit VB12:



Anemia – déficit VB12:



Anemia – déficit VB12:

Table 2

Distribution of Types of Anemia in Persons Age 65 and Older, U.S.*
NHANES III, Phase II, 1991–94.

Anemia	Number in the United States	Type, %	All anemia, %
With nutrient deficiency			
Iron only	466,715	48.3	16.6
Folate only	181,471	18.8	6.4
B_{12} only	165,701	17.2	5.9
Folate and B_{12}	56,436	5.8	2.0
Iron with folate or B_{12} or both	95,221	9.9	3.4
Total	965,544	100.0	34.3
Without nutrient deficiencies			
Renal insufficiency only	229,686	12.4	8.2
ACI, no renal insufficiency	554,281	30.0	19.7
Renal insufficiency and ACI	120,169	6.5	4.3
Unexplained anemia	945,195	51.1	33.6
Total	1,849,331	100.0	65.7
Total, all anemia	2,814,000	NA	

ACI indicates anemia of chronic inflammation and NA indicates not applicable

*Note: This research was originally published in *Blood*. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood*. 2004;104:2263–2268. © The American Society of Hematology.[10]

NHANES III

Anemia – déficit VB12:

3 estudios

DEFICIT DE VITAMINA B12. ANALISIS DE FACTORES ETIOLÓGICOS Y FORMAS DE PRESENTACIÓN

B. Alonso[1], A. Conde[1], D. Fiallo[2], S. De La Iglesia[2], A. Gil[3], S. Suárez[1], P. Betancor[1]

[1]Medicina Interna, [2]Hematología. Complejo Hospitalario Dr. Negrín. Palmas de Gran Canaria (Las) (Las Palmas)

[3]Medicina Interna. Clínica de San Roque, S.A. Palmas de Gran Canaria (Las) (Las Palmas)

OBJETIVOS

Analizar la forma de presentación y frecuencia con que se realiza un estudio etiológico y sus resultados en una serie de pacientes con déficit de vitamina B12 ingresados en un Servicio de M. Interna.

MATERIAL Y MÉTODO

Se estudiaron 119 pacientes con diagnóstico de déficit de vitamina B12 (B12 < a 200 pg/ml). Se recogieron datos demográficos, antecedentes, tratamiento previo, motivo de ingreso, valores de hemoglobina, VCM, leucocitos, plaquetas, la presencia de anemia (definida por los criterios de la OMS). Se recogieron los estudios realizados para investigar la etiología del déficit. Se analizó la forma de presentación del déficit de vitamina B12, si se producía anemia o no y su relación con características clínicas o analíticas. También se analizó con qué frecuencia se realizaron estudios para determinar la etiología del déficit y si la realización del estudio se relacionó con características clínicas, con el grado del déficit vitamínico o con la presencia o intensidad de la anemia. Para evaluar la relación entre variables categóricas se utilizó el test de Chi-cuadrado y para la relación con variables continuas el test T- Student o U de Mann-Whitney.

RESULTADOS

51 eran varones (42,9%) y 68 mujeres (57,1%), con una edad media de 77,4 años. DE: 7,5 (rango de 60 a 94 años). Los principales diagnósticos de ingreso fueron: insuficiencia cardiaca, 45 (37,8%), infecciones, 55 (46,2%), accidente cerebrovascular, 9 (7,6%) y trombosis venosa profunda, 4 (3,4%). Tomaban metformina 28 pacientes (23,5%) y omeprazol 94 (79%). Presentaron anemia 83 pacientes (69,7%), siendo la hemoglobina media de 11,1 g/dl (rango: 6,7 a 16,4). Los varones tuvieron anemia con más frecuencia que las mujeres (80,4% vs 61,8%; p=0,029). Sin embargo, las mujeres tenían valores de vitamina B12 y la edad (p= 0,9).Presentaban

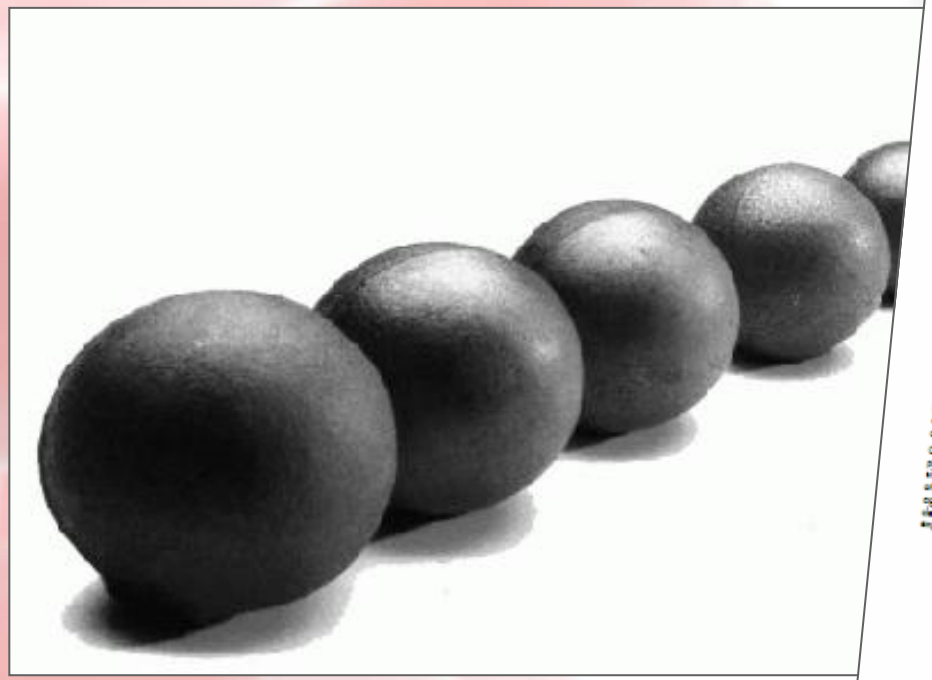
CONCLUSIONES

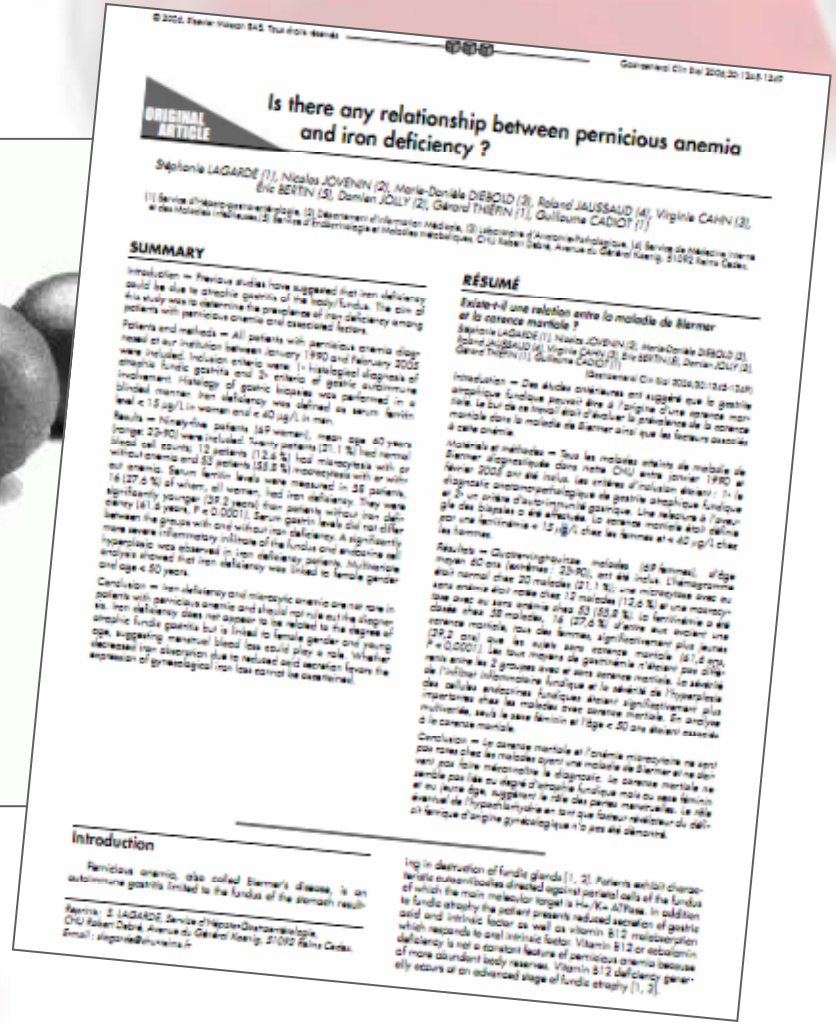
En nuestro estudio la anemia está presente casi en el 70% de los pacientes con déficit de vitamina B12. La

CONCLUSIONES

La prevalencia déficit de vitamina B12 en pacientes con anemia ferropénica es elevada, pudiendo oscilar entre uno de cada 5 a 10 pacientes. En presencia de anemia ferropénica se debe estudiar la posible coexistencia de déficit de vitamina B12, especialmente ante un ADE muy elevado. La microcitosis no excluye el déficit de B12 y de hecho es el hallazgo más frecuente.

Anemia – déficit VB12:





ORIGINAL ARTICLE

Is there any relationship between pernicious anemia and iron deficiency ?

Stéphanie LAGARDE (1), Nicolas JOVENIN (2), Marie-Danièle DIEBOLD (3), Roland JAUSSAUD (4), Virginie CAHN (3), Eric BERTIN (5), Damien JOLLY (2), Gérard THIÉRIN (1), Guillaume CADIOT (1)

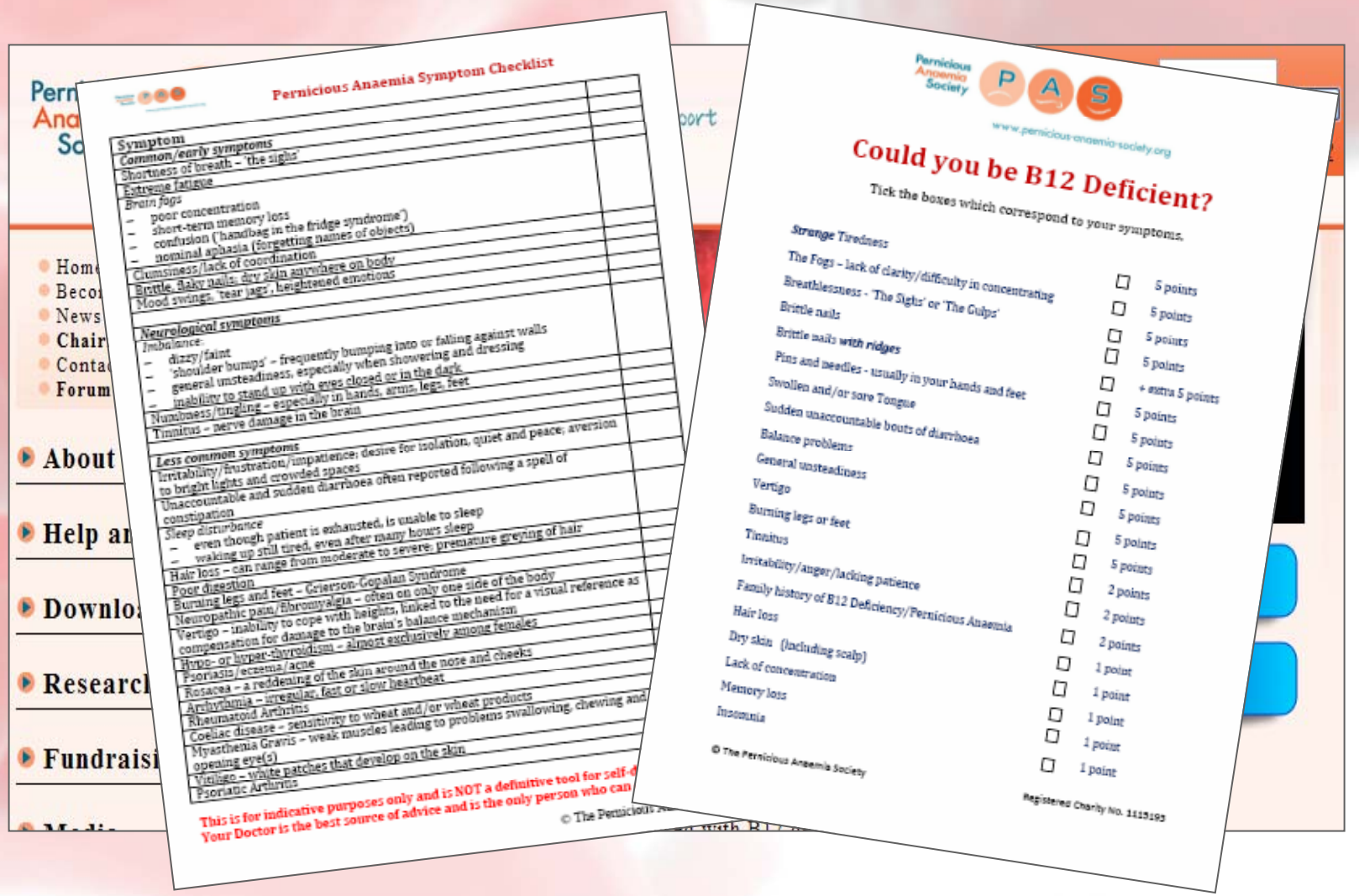
SUMMARY

RÉSUMÉ

Introduction

Pernicious anemia, also called Biermer's disease, is an autoimmune gastritis limited to the fundus of the stomach resulting in destruction of fundic glands [1, 2]. Patients exhibit characteristic autoantibodies directed against parietal cells of the fundus of which the main molecular target is H_+/K_+ ATPase. In addition to fundic atrophy the patient presents reduced secretion of gastric acid and intrinsic factor as well as vitamin B12 malabsorption which responds to oral intrinsic factor. Vitamin B12 or cobalamin deficiency is not a constant feature of pernicious anemia because of more abundant body reserves. Vitamin B12 deficiency generally occurs at an advanced stage of fundic atrophy [1, 3].

Anemia – déficit VB12:



Pernicious Anaemia Symptom Checklist

Symptom	
Common/early symptoms	
Shortness of breath – 'the sighs'	
Extreme fatigue	
Brain fogs	
– poor concentration	
– short-term memory loss	
– confusion ('handbag in the fridge syndrome')	
– nominal aphasia (forgetting names of objects)	
Clumsiness/lack of coordination	
Brittle, flaky nails; dry skin anywhere on body	
Mood swings, 'tear jags', heightened emotions	
Neurological symptoms	
Imbalance:	
– dizzy/faint	
– 'shoulder bumps' – frequently bumping into or falling against walls	
– general unsteadiness, especially when showering and dressing	
– inability to stand up with eyes closed or in the dark	
Numbness/tingling – especially in hands, arms, legs, feet	
Tinnitus – nerve damage in the brain	
Less common symptoms	
Irritability/frustration/impatience; desire for isolation, quiet and peace; aversion to bright lights and crowded spaces	
Unaccountable and sudden diarrhoea often reported following a spell of constipation	
Sleep disturbance	
– even though patient is exhausted, is unable to sleep	
– waking up still tired, even after many hours sleep	
Hair loss – can range from moderate to severe; premature greying of hair	
Poor digestion	
Burning legs and feet – Grierson-Gopalan Syndrome	
Neuropathic pain/fibromyalgia – often on only one side of the body	
Vertigo – inability to cope with heights, linked to the need for a visual reference as compensation for damage to the brain's balance mechanism	
Hypo- or hyper-thyroidism – almost exclusively among females	
Psoriasis/eczema/acne	
Rosacea – a reddening of the skin around the nose and cheeks	
Arrhythmia – irregular, fast or slow heartbeat	
Rheumatoid Arthritis	
Coeliac disease – sensitivity to wheat and/or wheat products	
Myasthenia Gravis – weak muscles leading to problems swallowing, chewing and opening eye(s)	
Vitiligo – white patches that develop on the skin	
Psoriatic Arthritis	

This is for indicative purposes only and is NOT a definitive tool for self-
Your Doctor is the best source of advice and is the only person who can

© The Pernicious

Pernicious Anaemia Society PAS

www.pernicious-anaemia-society.org

Could you be B12 Deficient?

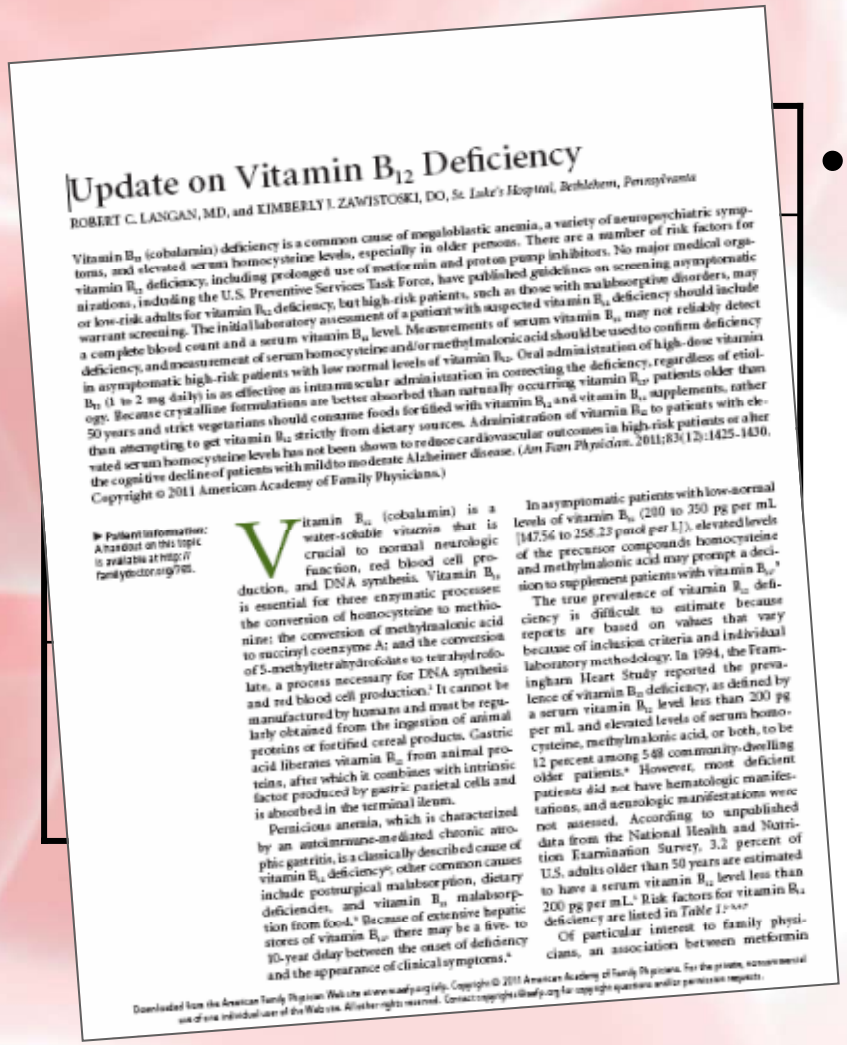
Tick the boxes which correspond to your symptoms.

Strange Tiredness	5 points
The Fogs – lack of clarity/difficulty in concentrating	5 points
Breathlessness - 'The Sighs' or 'The Gulps'	5 points
Brittle nails	5 points
Brittle nails *with ridges*	+ extra 5 points
Pins and needles - usually in your hands and feet	5 points
Swollen and/or sore Tongue	5 points
Sudden unaccountable bouts of diarrhoea	5 points
Balance problems	5 points
General unsteadiness	5 points
Vertigo	5 points
Burning legs or feet	5 points
Tinnitus	5 points
Irritability/anger/lacking patience	2 points
Family history of B12 Deficiency/Pernicious Anaemia	2 points
Hair loss	2 points
Dry skin (including scalp)	1 point
Lack of concentration	1 point
Memory loss	1 point
Insomnia	1 point
	1 point

© The Pernicious Anaemia Society

Registered Charity No. 1115193

Anemia – déficit VB12:



Update on Vitamin B_{12} Deficiency

ROBERT C. LANGAN, MD, and KIMBERLY J. ZAWISTOSKI, DO, *St. Luke's Hospital, Bethlehem, Pennsylvania*

Vitamin B_{12} (cobalamin) deficiency is a common cause of megaloblastic anemia, a variety of neuropsychiatric symptoms, and elevated serum homocysteine levels, especially in older persons. There are a number of risk factors for vitamin B_{12} deficiency, including prolonged use of metformin and proton pump inhibitors. No major medical organizations, including the U.S. Preventive Services Task Force, have published guidelines on screening asymptomatic or low-risk adults for vitamin B_{12} deficiency, but high-risk patients, such as those with malabsorptive disorders, may warrant screening. The initial laboratory assessment of a patient with suspected vitamin B_{12} deficiency should include a complete blood count and a serum vitamin B_{12} level. Measurements of serum vitamin B_{12} may not reliably detect deficiency, and measurement of serum homocysteine and/or methylmalonic acid should be used to confirm deficiency in asymptomatic high-risk patients with low normal levels of vitamin B_{12}. Oral administration of high-dose vitamin B_{12} (1 to 2 mg daily) is as effective as intramuscular administration in correcting the deficiency, regardless of etiology. Because crystalline formulations are better absorbed than naturally occurring vitamin B_{12}, patients older than 50 years and strict vegetarians should consume foods fortified with vitamin B_{12} and vitamin B_{12} supplements, rather than attempting to get vitamin B_{12} strictly from dietary sources. Administration of vitamin B_{12} to patients with elevated serum homocysteine levels has not been shown to reduce cardiovascular outcomes in high-risk patients or alter the cognitive decline of patients with mild to moderate Alzheimer disease. (*Am Fam Physician*. 2011;83(12):1425-1430. Copyright © 2011 American Academy of Family Physicians.)

▶ Patient information: A handout on this topic is available at http://familydoctor.org/785.

Vitamin B_{12} (cobalamin) is a water-soluble vitamin that is crucial to normal neurologic function, red blood cell production, and DNA synthesis. Vitamin B_{12} is essential for three enzymatic processes: the conversion of homocysteine to methionine; the conversion of methylmalonic acid to succinyl coenzyme A; and the conversion of 5-methyltetrahydrofolate to tetrahydrofolate, a process necessary for DNA synthesis and red blood cell production.[1] It cannot be manufactured by humans and must be regularly obtained from the ingestion of animal proteins or fortified cereal products. Gastric acid liberates vitamin B_{12} from animal proteins, after which it combines with intrinsic factor produced by gastric parietal cells and is absorbed in the terminal ileum.

Pernicious anemia, which is characterized by an autoimmune-mediated chronic atrophic gastritis, is a classically described cause of vitamin B_{12} deficiency[2]; other common causes include postsurgical malabsorption, dietary deficiencies, and vitamin B_{12} malabsorption from food.[3] Because of extensive hepatic stores of vitamin B_{12}, there may be a five- to 10-year delay between the onset of deficiency and the appearance of clinical symptoms.[4]

In asymptomatic patients with low-normal levels of vitamin B_{12} (200 to 350 pg per mL [147.56 to 258.23 pmol per L]), elevated levels of the precursor compounds homocysteine and methylmalonic acid may prompt a decision to supplement patients with vitamin B_{12}.[5]

The true prevalence of vitamin B_{12} deficiency is difficult to estimate because reports are based on values that vary because of inclusion criteria and individual laboratory methodology. In 1994, the Framingham Heart Study reported the prevalence of vitamin B_{12} deficiency, as defined by a serum vitamin B_{12} level less than 200 pg per mL and elevated levels of serum homocysteine, methylmalonic acid, or both, to be 12 percent among 548 community-dwelling older patients.[6] However, most deficient patients did not have hematologic manifestations, and neurologic manifestations were not assessed. According to unpublished data from the National Health and Nutrition Examination Survey, 3.2 percent of U.S. adults older than 50 years are estimated to have a serum vitamin B_{12} level less than 200 pg per mL.[6] Risk factors for vitamin B_{12} deficiency are listed in *Table 1*.[3,6,7]

Of particular interest to family physicians, an association between metformin

- Hasta un 30% de los pacientes con niveles normales de VB12 en suero tienen anemia y enfermedad neurológica.

***Am Fam Physician*. 2011;83(12):1425-1430**

Anemia – déficit VB12:

BMC Geriatrics

1949 -2009

25 estudios

21 OT

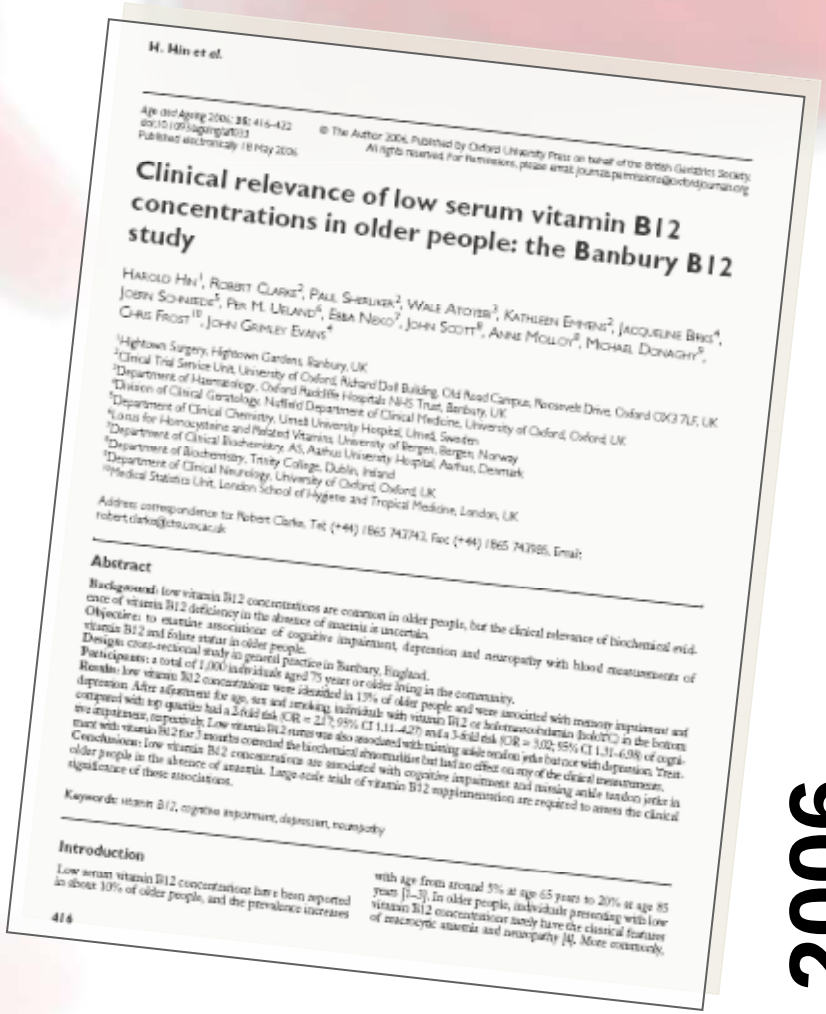
D. Cognitivo – déficit VB12:

1000 participantes

13 % déficit VB12

Asociación con deterioro cognitivo, depresión y neuropatía

3 casos de A. perniciosa



H. Min et al.

Age and Ageing 2006; 35: 416–422
doi:10.1093/ageing/afl033
Published electronically 18 May 2006

© The Author 2006. Published by Oxford University Press on behalf of the British Geriatrics Society. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org

Clinical relevance of low serum vitamin B12 concentrations in older people: the Banbury B12 study

HAROLD HIN[1], ROBERT CLARKE[2], PAUL SHERLIKER[2], WALID ATOYEBI[3], KATHLEEN EMMENS[2], JACQUELINE BIRD[4], JOERN SCHNEEDE[5], PER M. URLAND[6], EBBA NEXO[7], JOHN SCOTT[8], ANNE MOLLOY[9], MICHAEL DONAGHY[10], CHRIS FROST[10], JOHN GRIMLEY EVANS[4]

[1]Hightown Surgery, Hightown Gardens, Banbury, UK
[2]Clinical Trial Service Unit, University of Oxford, Richard Doll Building, Old Road Campus, Roosevelt Drive, Oxford OX3 7LF, UK
[3]Department of Haematology, Oxford Radcliffe Hospitals NHS Trust, Banbury, UK
[4]Division of Clinical Gerontology, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK
[5]Department of Clinical Chemistry, Umeå University Hospital, Umeå, Sweden
[6]Centre for Homocysteine and Related Vitamins, University of Bergen, Bergen, Norway
[7]Department of Clinical Biochemistry, AS, Aarhus University Hospital, Aarhus, Denmark
[8]Department of Biochemistry, Trinity College, Dublin, Ireland
[9]Department of Clinical Neurology, University of Oxford, Oxford, UK
[10]Medical Statistics Unit, London School of Hygiene and Tropical Medicine, London, UK

Address correspondence to: Robert Clarke, Tel: (+44) 1865 743743, Fax: (+44) 1865 743985, Email: robert.clarke@ctsu.ox.ac.uk

Abstract

Background: low vitamin B12 concentrations are common in older people, but the clinical relevance of biochemical evidence of vitamin B12 deficiency in the absence of anaemia is uncertain.
Objectives: to examine associations of cognitive impairment, depression and neuropathy with blood measurements of vitamin B12 and folate status in older people.
Design: cross-sectional study in general practice in Banbury, England.
Participants: a total of 1,000 individuals aged 75 years or older living in the community.
Results: low vitamin B12 concentrations were identified in 13% of older people and were associated with memory impairment and depression. After adjustment for age, sex and smoking, individuals with vitamin B12 or holotranscobalamin (holoTC) in the bottom quintile compared with top quintiles had a 2-fold risk (OR = 2.17; 95% CI 1.11–4.27) and a 3-fold risk (OR = 3.02; 95% CI 1.31–6.98) of cognitive impairment, respectively. Low vitamin B12 status was also associated with stinging ankle swollen ankle but not with depression. Treatment with vitamin B12 for 3 months corrected the biochemical abnormalities but had no effect on any of the clinical measurements.
Conclusions: low vitamin B12 concentrations are associated with cognitive impairment and stinging ankle tendon jerks in older people in the absence of anaemia. Large-scale trials of vitamin B12 supplementation are required to assess the clinical significance of these associations.

Keywords: vitamin B12, cognitive impairment, depression, neuropathy

Introduction

Low serum vitamin B12 concentrations have been reported in about 10% of older people, and the prevalence increases with age from around 5% at age 65 years to 20% at age 85 years [1–3]. In older people, individuals presenting with low vitamin B12 concentrations rarely have the classical features of macrocytic anaemia and neuropathy [4]. More commonly,

416

2006

D. Cognitivo – déficit VB12:

Table 3. Absolute risk and OR (95% CI) of cognitive impairment, depression, neuropathy and missing ankle tendon jerks by quartiles of vitamin status in participants with no history of prior treatment ($n = 830$)

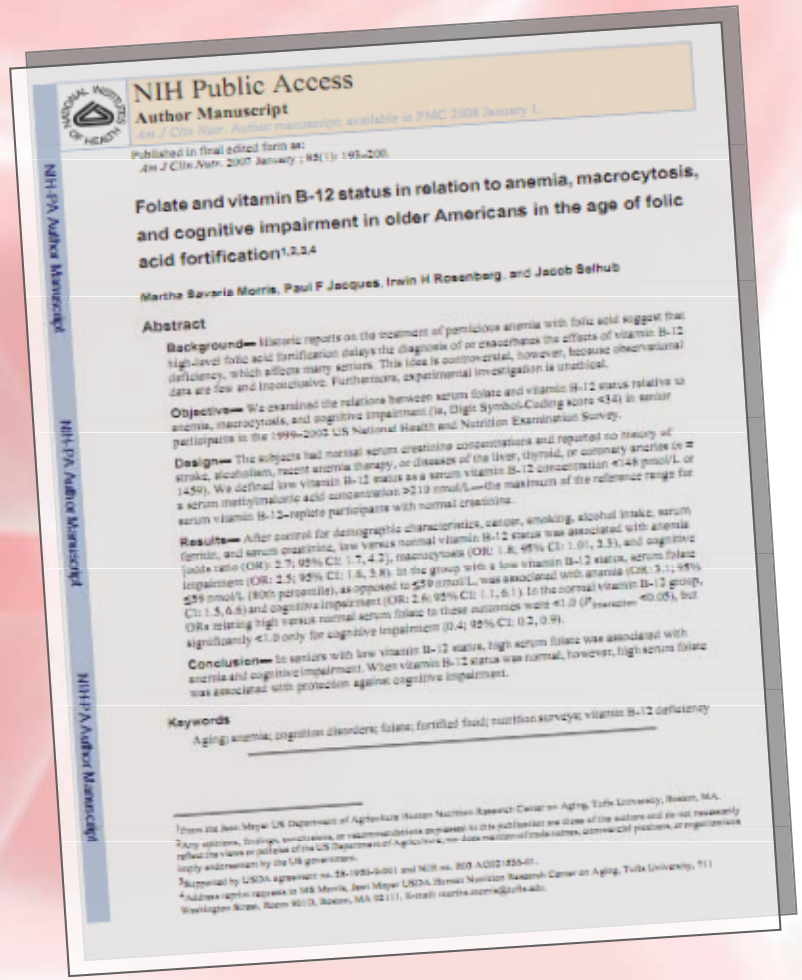
Quartiles of vitamin status		Mean level	Cognitive impairment (MMSE <22/30) ($n = 75$)		Depression (HAD-d >11) ($n = 62$)		Neuropathy[b] ($n = 30$)		Missing ankle tendon jerks ($n = 360$)	
			%	OR (95% CI)[a]	%	OR (95% CI)[a]	%	OR (95% CI)[a]	%	OR (95% CI)[a]
holoTC (pmol/l)	IV	122	3.8	1.0	4.7	1.0	2.9	1.0	35.1	1.0
	III	74	9.6	2.50 (1.06–5.88)	5.7	1.11 (0.47–2.67)	3.8	1.35 (0.46–3.96)	45.5	1.53 (1.03–2.26)
	II	53	10.5	2.62 (1.12–6.11)	9.8	2.02 (0.92–4.47)	3.4	1.15 (0.38–3.51)	42.5	1.35 (0.91–2.00)
	I	30	12.0	3.02 (1.21–6.98)	8.9	1.66 (0.74–3.71)	4.3	1.51 (0.52–4.38)	45.8	1.49 (1.00–2.21)
B12 (pmol/l)	IV	350	7.2	1.0	6.1	1.0	3.4	1.0	20.8	1.0
	III	240	7.3	0.99 (0.46–2.12)	9.3	1.47 (0.70–3.08)	3.9	1.21 (0.43–3.42)	44.4	1.46 (0.98–2.16)
	II	185	7.6	1.00 (0.47–2.12)	6.6	1.00 (0.45–2.20)	2.4	0.71 (0.22–2.29)	46.5	1.59 (1.07–2.36)
	I	125	13.9	2.17 (1.11–4.27)	7.1	1.00 (0.46–2.20)	4.8	1.52 (0.56–4.11)	42.5	1.30 (0.88–1.94)
Folate (nmol/l)	IV	55.3	2.9	1.0	5.2	1.0	2.4	1.0	39.4	1.0
	III	27.9	8.7	3.34 (1.27–8.60)	6.1	1.19 (0.51–2.74)	2.9	1.21 (0.36–4.02)	41.8	1.11 (0.75–1.65)
	II	18.6	14.4	5.34 (2.14–13.31)	10.4	2.07 (0.97–4.42)	4.3	1.81 (0.59–5.51)	42.7	1.09 (0.74–1.61)
	I	11.0	9.7	3.38 (1.31–8.70)	7.5	1.38 (0.62–3.08)	4.3	1.85 (0.61–3.64)	44.9	1.25 (0.85–1.85)
tHcy (µmol/l)	I	9.92	3.4	1.0	5.2	1.0	1.9	1.0	33.8	1.0
	II	12.69	7.7	2.35 (0.93–5.92)	6.1	1.04 (0.45–2.41)	2.4	1.34 (0.35–5.11)	43.4	1.47 (0.99–2.19)
	III	15.52	12.0	3.61 (1.50–8.68)	7.0	1.23 (0.54–2.79)	4.3	2.35 (0.70–7.84)	44.4	1.47 (0.99–2.19)
	IV	22.34	13.0	4.07 (1.70–9.75)	10.8	1.91 (0.89–4.09)	5.7	3.19 (0.99–10.27)	47.2	1.59 (1.06–2.37)
MMA (µmol/l)	I	0.18	4.4	1.0	5.6	1.0	2.9	1.0	32.6	1.0
	II	0.25	8.1	1.79 (0.60–3.41)	6.2	1.12 (0.49–2.58)	2.4	0.78 (0.23–2.60)	43.3	1.50 (1.00–2.23)
	III	0.32	7.2	1.43 (0.60–3.42)	7.0	1.19 (0.54–2.65)	5.2	1.78 (0.64–4.96)	44.4	1.55 (1.05–2.31)
	IV	0.68	16.4	3.67 (1.68–8.04)	10.3	1.72 (0.81–3.66)	3.9	1.27 (0.42–3.78)	48.6	1.76 (1.18–2.62)

CI, confidence interval; HAD-d, Hospital Anxiety and Depression Scale; holoTC, holotranscobalamin; MMA, methylmalonic acid; MMSE, Mini-Mental State Examination; tHcy, homocysteine.

[a]Adjusted for age, sex and smoking.

[b]Neuropathy was defined if they had more than two symptoms and more than two signs indicative of neuropathy.

D. Cognitivo – déficit VB12:



NIH Public Access
Author Manuscript
Am J Clin Nutr. Author manuscript; available in PMC 2008 January 1.

Published in final edited form as:
Am J Clin Nutr. 2007 January ; 85(1): 295–300.

Folate and vitamin B-12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification[1,2,3,4]

Martha Savaria Morris, Paul F Jacques, Irwin H Rosenberg, and Jacob Selhub

Abstract

Background— Historic reports on the treatment of pernicious anemia with folic acid suggest that high-level folic acid fortification delays the diagnosis of or exacerbates the effects of vitamin B-12 deficiency, which affects many seniors. This idea is controversial, however, because observational data are few and inconclusive. Furthermore, experimental investigation is unethical.

Objective— We examined the relations between serum folate and vitamin B-12 status relative to anemia, macrocytosis, and cognitive impairment (ie, Digit Symbol–Coding score <34) in senior participants in the 1999–2002 US National Health and Nutrition Examination Survey.

Design— The subjects had normal serum creatinine concentrations and reported no history of stroke, alcoholism, recent anemia therapy, or diseases of the liver, thyroid, or coronary arteries (n = 1459). We defined low vitamin B-12 status as a serum vitamin B-12 concentration <148 pmol/L or a serum methylmalonic acid concentration >210 nmol/L—the maximum of the reference range for serum vitamin B-12–replete participants with normal creatinine.

Results— After control for demographic characteristics, cancer, smoking, alcohol intake, serum ferritin, and serum creatinine, low versus normal vitamin B-12 status was associated with anemia [odds ratio (OR): 2.7; 95% CI: 1.7, 4.2], macrocytosis (OR: 1.8; 95% CI: 1.01, 3.3), and cognitive impairment (OR: 2.5; 95% CI: 1.6, 3.8). In the group with a low vitamin B-12 status, serum folate ≤59 nmol/L (80th percentile), as opposed to ≤59 nmol/L, was associated with anemia (OR: 3.1; 95% CI: 1.5, 6.5) and cognitive impairment (OR: 2.6; 95% CI: 1.1, 6.1). In the normal vitamin B-12 group, ORs relating high versus normal serum folate to these outcomes were <1.0 ($P_{interaction}$ <0.05), but significantly <1.0 only for cognitive impairment (0.4; 95% CI: 0.2, 0.9).

Conclusion— In seniors with low vitamin B-12 status, high serum folate was associated with anemia and cognitive impairment. When vitamin B-12 status was normal, however, high serum folate was associated with protection against cognitive impairment.

Keywords
Aging; anemia; cognition disorders; folate; fortified food; nutrition surveys; vitamin B-12 deficiency

[1] From the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging, Tufts University, Boston, MA.

[2] Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views or policies of the US Department of Agriculture, nor does mention of trade names, commercial products, or organizations imply endorsement by the US government.

[3] Supported by USDA agreement no. 58-1950-0-001 and NIH no. RO1 AG021326-01.

[4] Address reprint requests to MS Morris, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, 711 Washington Street, Room 9013, Boston, MA 02111. E-mail: martha.morris@tufts.edu.

The American Journal of
CLINICAL NUTRITION
A Publication of the American Society for Nutrition
NOVEMBER 2011 • VOLUME 94 • NUMBER 5 WWW.AJCN.ORG

EDITORIALS

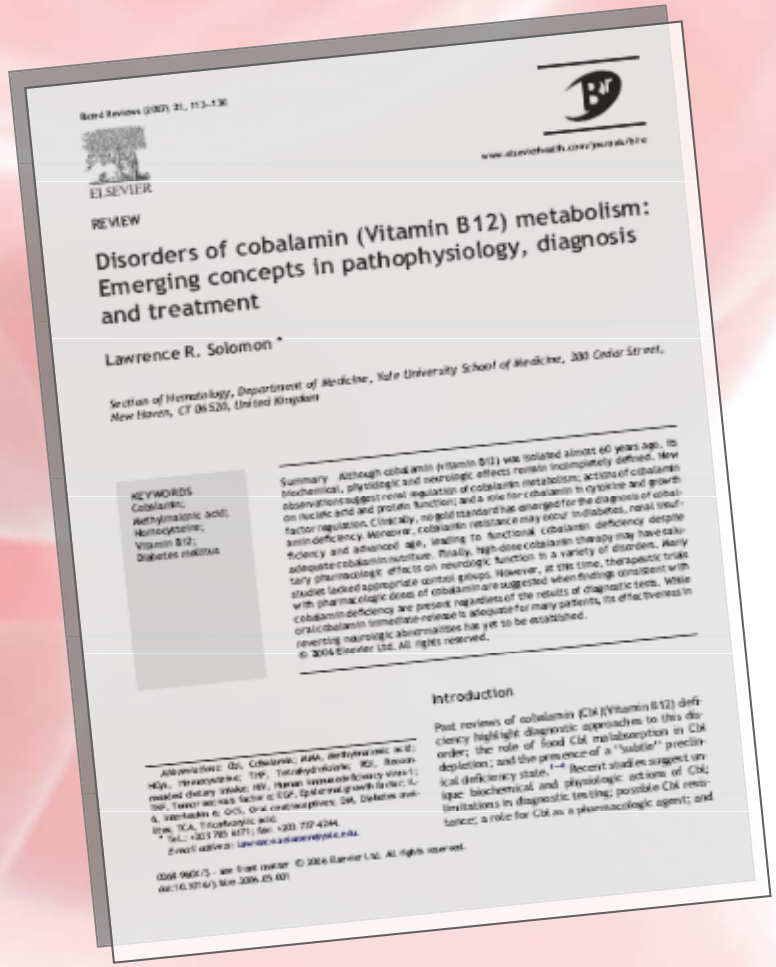
ORIGINAL RESEARCH COMMUNICATIONS

2007

↓VB12 + niveles altos de folato,

Anemia y deterioro cognitivo

Disfx inmunitaria – déficit VB12:



REVIEW

Disorders of cobalamin (Vitamin B12) metabolism: Emerging concepts in pathophysiology, diagnosis and treatment

Lawrence R. Solomon *

Section of Hematology, Department of Medicine, Yale University School of Medicine, 300 Cedar Street, New Haven, CT 06520, United Kingdom

2007

↑TBC en vegetarianos

Rpta inmune anómala a la vacuna antipneumocócica

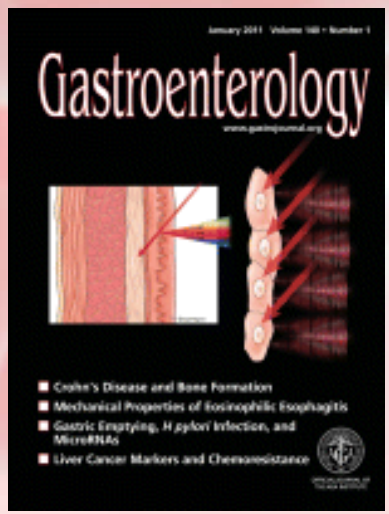
↓Linfocitos totales y CD8

Fx cadera – déficit VB12:

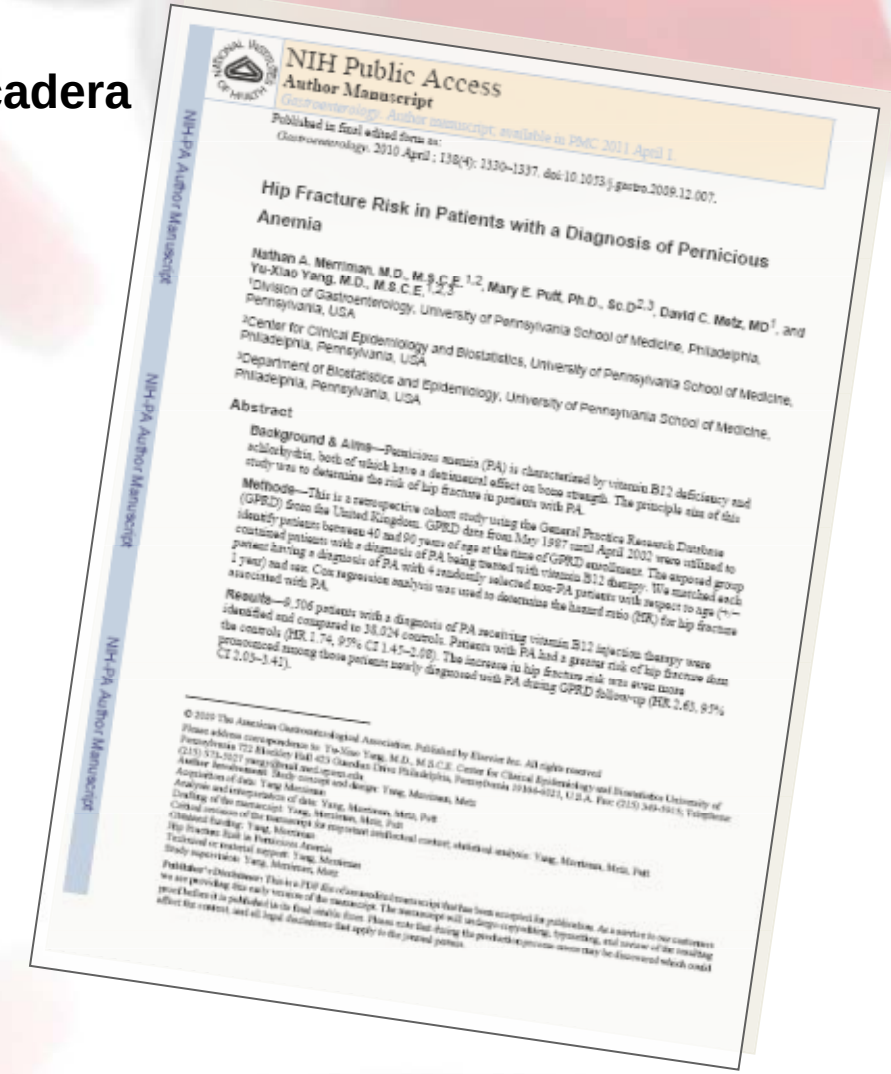
Pctes con AP, riesgo alto de Fx de cadera

Persiste riesgo a pesar de tto.

Aclorhidria crónica



2010


NIH Public Access
Author Manuscript
Gastroenterology. Author manuscript; available in PMC 2011 April 1.

Published in final edited form as:
Gastroenterology. 2010 April ; 138(4): 1330–1337. doi:10.1053/j.gastro.2009.12.007.

Hip Fracture Risk in Patients with a Diagnosis of Pernicious Anemia

Nathan A. Merriman, M.D., M.S.C.E.[1,2], Mary E. Putt, Ph.D., Sc.D[2,3], David C. Metz, MD[1], and Yu-Xiao Yang, M.D., M.S.C.E.[1,2,3]

[1]Division of Gastroenterology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

[2]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

[3]Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

Abstract

Background & Aims—Pernicious anemia (PA) is characterized by vitamin B12 deficiency and achlorhydria, both of which have a detrimental effect on bone strength. The principle aim of this study was to determine the risk of hip fracture in patients with PA.

Methods—This is a retrospective cohort study using the General Practice Research Database (GPRD) from the United Kingdom. GPRD data from May 1987 until April 2002 were utilized to identify patients between 40 and 90 years of age at the time of GPRD enrollment. The exposed group contained patients with a diagnosis of PA being treated with vitamin B12 therapy. We matched each patient having a diagnosis of PA with 4 randomly selected non-PA patients with respect to age (+/− 1 year) and sex. Cox regression analysis was used to determine the hazard ratio (HR) for hip fracture associated with PA.

Results—8,506 patients with a diagnosis of PA receiving vitamin B12 injection therapy were identified and compared to 38,024 controls. Patients with PA had a greater risk of hip fracture than the controls (HR 1.74, 95% CI 1.47–2.08). The increase in hip fracture risk was even more pronounced among those patients newly diagnosed with PA during GPRD follow-up (HR 2.65, 95% CI 2.03–3.42).

Please address correspondence to: Yu-Xiao Yang, M.D., M.S.C.E. Center for Clinical Epidemiology and Biostatistics University of Pennsylvania 722 Blockley Hall 423 Guardian Drive Philadelphia, Pennsylvania 19104-6021, U.S.A. Fax: (215) 349-5915; Telephone: (215) 573-5937 yangyx@mail.med.upenn.edu

Author Involvement: Study concept and design: Yang, Merriman, Metz
Acquisition of data: Yang Merriman
Analysis and interpretation of data: Yang, Merriman, Metz, Putt
Drafting of the manuscript: Yang, Merriman, Metz, Putt
Critical revision of the manuscript for important intellectual content: statistical analysis: Yang, Merriman, Metz, Putt
Obtained funding: Yang, Merriman
Study supervision: Yang, Merriman, Metz

Hip Fracture Risk in Patients with Pernicious Anemia
Technical or material support: Yang, Merriman

Osteporosis - déficit VB12:


ARTICLE IN PRESS

Archives of Gerontology and Geriatrics

Vitamin B_{12} and folic acid levels as therapeutic target in preserving bone mineral density (BMD) of older men

Ilkin Nahari[a,*], Ergun Bozoglu[a], Nuri Karadurmus[a], Ozdes Emer[b], Necmettin Kocak[c], Selim Kilic[c], Huseyin Deniz[a], Muhittin Serdar[a]

ABSTRACT

1. Introduction

2011

269 pctes > 65 años

Descenso de DMO, mayor pérdida ósea y riesgo de fx osteoporóticas

Osteporosis - déficit VB12:

Table 2
Subject's characteristics and femur bone mineral density values acco

	Vitamin B_{12} (pg/l)
	Group I <200
Number	65
Age (years)	76.6 ± 6.8
BMI (kg/m^2)	26.7 ± 3.9
Current alcohol intake (%)	1.6
Ever smoking (%)	12.5
Physical active[a] (%)	25.4
Femur total BMD (g/cm^2)	0.68 ± 0.13
Femur total T-score	−1.43 ± 0.88
Neck BMD (g/cm^2)	0.57 ± 0.13
Neck T-score	−1.94 ± 0.98

* One-way ANOVA test results.
** Chi-square test results.
[a] Engaging in 3 days or more of physical activity per week.

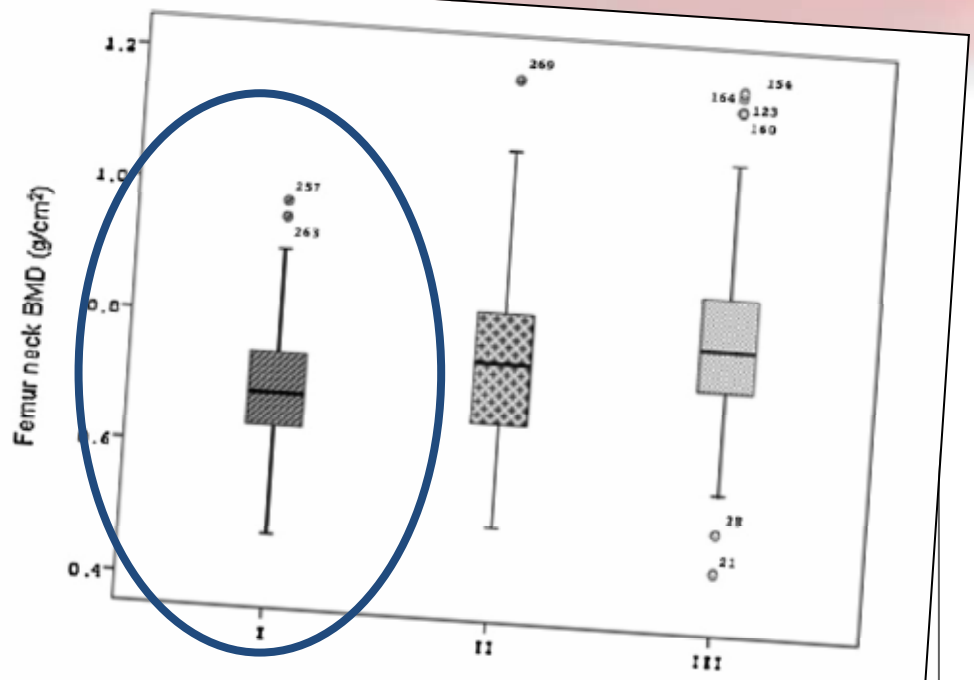


Fig. 1. Means of femur neck bone mineral density according to tertiles of serum vitamin B_{12} concentrations.

E. cardiovascular – déficit VB12:

niveles bajos de B12

hiperhomocisteinemia

E. cardiovascular – déficit VB12:

Eur J Nutr (2011) 50:97–106
DOI 10.1007/s00394-010-0119-6

ORIGINAL CONTRIBUTION

Is a low blood level of vitamin B12 a cardiovascular and diabetes risk factor? A systematic review of cohort studies

Sauri B. Rafnsson · Punnamaty Saravanan · Raj S. Bhopal · Chittaranjan S. Yajnik

Received: 15 February 2010 / Accepted: 11 June 2010 / Published online: 29 June 2010
© Springer-Verlag 2010

Abstract
Purpose To assess the prior hypothesis that low blood vitamin B12, partly through hyperhomocysteinemia and partly through direct effects, increases the risk of cardiovascular diseases and diabetes. As background, we also extracted all-cause mortality from the studies that met our criteria.
Methods A systematic review of prospective cohort studies identified through searching six electronic databases, screening of reference lists, and citation search. Included studies reported data on the association between vitamin B12 blood levels, or other appropriate surrogate biological markers e.g. holotranscobalamin or serum/urine methylmalonic acid, and fatal or non-fatal incident diabetes and cardiovascular events.
Results Seven studies were included. Studies differed regarding the population studied, length of follow-up, study outcomes, and data analysis—a narrative synthesis approach was performed to examine the results. Most studies met few of the quality assessment criteria which were adapted from the Scottish Intercollegiate Guidelines Network (SIGN). Only one high-quality study reported that low B12 increased the risk of incident cerebral ischaemia (RR = 1.76; 95% CI = 1.16–2.68). After controlling for homocysteine, the association persisted although weakened (RR = 1.57; 95% CI = 1.02–2.43), suggesting that the effects of low B12 were only partly mediated by homocysteine. In two studies, higher B12 levels were associated with a greater risk of total mortality (RR = 1.00; 95% CI = 1.00–1.00 and HR = 1.15; 95% CI = 1.08–1.22, respectively) and combined fatal and non-fatal coronary events (RR = 1.00; 95% CI = 1.00–1.00). No association between study outcomes and vitamin B12 levels was found in four other studies.
Conclusions Surprisingly, there is only very limited evidence that vitamin B12 deficiency predisposes to the risk of mortality and morbidity from either cardiovascular disease or diabetes in adults. Current data do not support vitamin B12 supplementation to reduce the risk of cardiovascular diseases or diabetes.

Keywords Vitamin B12 · Cardiovascular diseases · Diabetes mellitus type 2 · Cohort studies · Aetiology

S. B. Rafnsson (✉) · R. S. Bhopal
Public Health Sciences Section,
School of Clinical Sciences and Community Health
and Centre for Population Health Sciences,
University of Edinburgh, Teviot Place,
Edinburgh EH8 9AG, Scotland, UK
e-mail: S.B.Rafnsson@sms.ac.uk

P. Saravanan
Clinical Sciences Research Institute,
Warwick Medical School, CSR,
UHCW NHS Trust, Coventry CV2 2DX, UK

C. S. Yajnik
Diabetes Unit, KEM Hospital and Research Centre,
Rasta Peth, Pune, Maharashtra 411 011, India

Introduction

Vitamin B12 is an essential nutrient that functions as a coenzyme in two metabolic processes—the conversion of methylmalonyl-CoA to succinyl-CoA (by methylmalonyl CoA mutase—MCM) and the remethylation of homocysteine to methionine (by methionine synthase—MS) [1]. Remethylation of homocysteine happens in the cell cytosol and requires vitamin B12 as a cofactor in the presence of 5-methyltetrahydrofolate (from folic acid) [1–8]. However,

Springer

Año 2011

1ª Revisión

No datos concluyentes

E. cardiovascular – déficit VB12:

TABLE 4. Comorbidities With Folate and Vitamin B12 Deficiency and Combined Deficiency, by Age in Years

Comorbidity	20–29	30–39	40–49	50–59	60–69	70–79	80–89
Epilepsy	72	48	12	0	0	0	5
Peripheral neuropathy	0	12	72	12	36	20	0
Multiple sclerosis and/or demyelination	24	84	24	0	0	0	0
Migraine	12	60	24	0	0	0	0
Ischemic stroke	0	0	0	24	108	240	22
Hemorrhagic stroke	0	12	0	0	24	12	3
Cognitive impairment	0	0	0	0	12	30	6
Brain tumors	0	0	12	0	36	10	0
Parkinson disease or Parkinsonism	0	0	0	0	0	48	0

The Neurologist 2004; 10: 338-343.

Conclusiones:

- El déficit de vitamina B12 es frecuente.
- Existen diferencias geográficas.
- La concentración plasmática de VB12 puede no coincidir con la concentración tisular.
- No existen unos criterios diagnósticos para el diagnóstico de déficit de vitamina B12.
- Alta coexistencia con ferropenia.

Conclusiones:

- El déficit de VB12 no sólo se asocia con alteraciones hematológicas.
- La anemia perniciosa sólo explica el 10 % de las anemias por déficit de VB12.
- El tratamiento es sencillo y es barato, aunque no hay consenso en el mismo.

Piensa en mí…