

# B12 Deficiency with Neuro-Psychiatric Symptoms

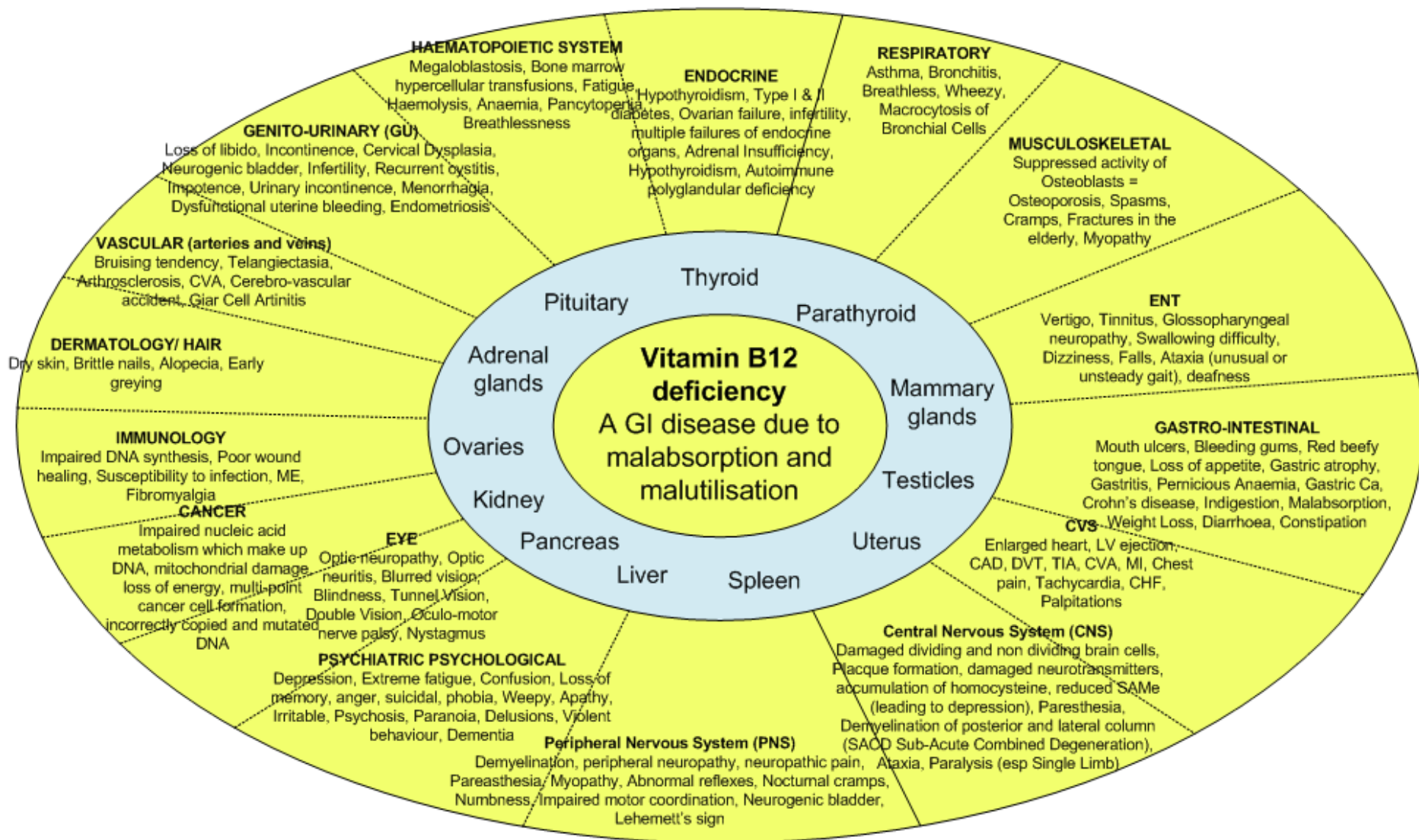
Serum B12 Level below 300ng/L with or without Anaemia or  
Macrocytosis

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# Vitamin B12 deficiency

Could we imagine the last of the vitamin B to be identified (1940) would possibly cause this much devastation to our body and mind?

A multi-system / polyglandular – multipoint syndrome



# Vitamin B12 Deficiency and Direct or Indirect Association with Diseases

- Vitamin B12 Deficiency causes:-
- Hematological
- Neuro – Psychiatric
- Gastro Intestinal
- Genito Urinary Disease
- If treatment is delayed – causes irreversible damage or fatality
- Cardiac Failure
- Exacerbation of Angina
- Asthma (exacerbation)
- Recurrent Anaemia/ Pancytopenia
- Gastric and other Cancers
- Athero Sclerosis / Stroke
- Cardio Vascular Disease
- Osteoporosis
- Post Viral Immune Deficiency Fatigue Syndrome (ME)
- Dementia
- Alzheimer's
- Optic Atrophy / Blindness
- Dysfunctional Uterine Bleeding
- Dysmenorrhoea
- Unexplained Diarrhoea / Colitis
- Recurrent Gastritis
- Pseudo Seizures
- Blackouts and Faints
- Subacute Combined Degeneration
- Single Limb Paralysis
- Multiple Sclerosis Like B12 Deficiency Syndrome
- Naturopathic Pain
- B12 Deficient Mother-Baby born with Neuro Muscular Damage
- Migraine Headaches
- Depression
- Tinnitus
- Vitiligo, Myxedema, Diabetes

# Vitamin B12 deficiency

## History

1849 (hundred and 57 years ago) the association between neuropsychiatric disorder and vitamin B12 deficiency was first described

### **Middle of the 19th century**

THOMAS ADDISON described the clinical picture

triad of:     anaemia  
              glossitis  
              paraesthesia of fingers and toes

Some years later ANTON BIERMAN described this condition as P.A. (Pernicious Anaemia)

1926 (80 years ago) PA was responsible for around 10,000 deaths each year in the US before the introduction of the liver diet

### **Early 20th century**

CARLOT presented natural history of the disease for 1200 patients. Only six were on a mission, the remainder usually survive between 1 and 3 years

### **A Truly Frightening Illness**

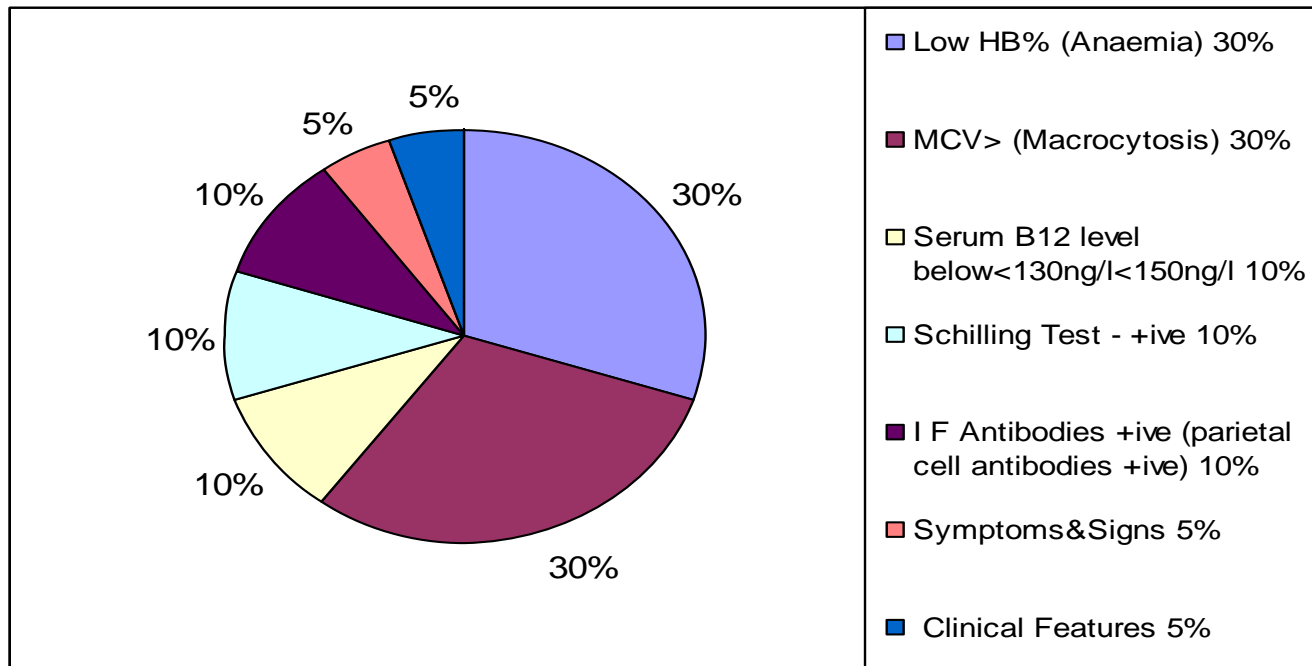
### **Late 1940s vitamin B12 isolated**

Which turned out to be the most active substance in medicine. Also the largest molecule so far identified, therefore identified an absorption problem from the GI tract to circulation

Though cobalamin deficiency turned out to be a GI disease, the patient suffering from cobalamin deficiency most often presented with anaemia and macrocytosis (IV stage) and accordingly cobalamin deficiency has until today being considered as a haematological disease and therefore the name Pernicious Anaemia and the diagnosis based on the Hb% and raised MCV.

**B12 Deficiency has been and still is synonymous with  
Pernicious Anaemia – Macrocytic Anaemia (P.A.)  
B12 Level Below <130<150ng/l (Stage IV)  
Therefore the Past and Present Diagnostic Criteria is based on:-**

**“The Addisonian Diagnostic Criteria”**



**Other Essential Tests**

**Urine Methyl Malonic acid**

**Plasma Homocystine estimation (Not as reliable as previously thought)**

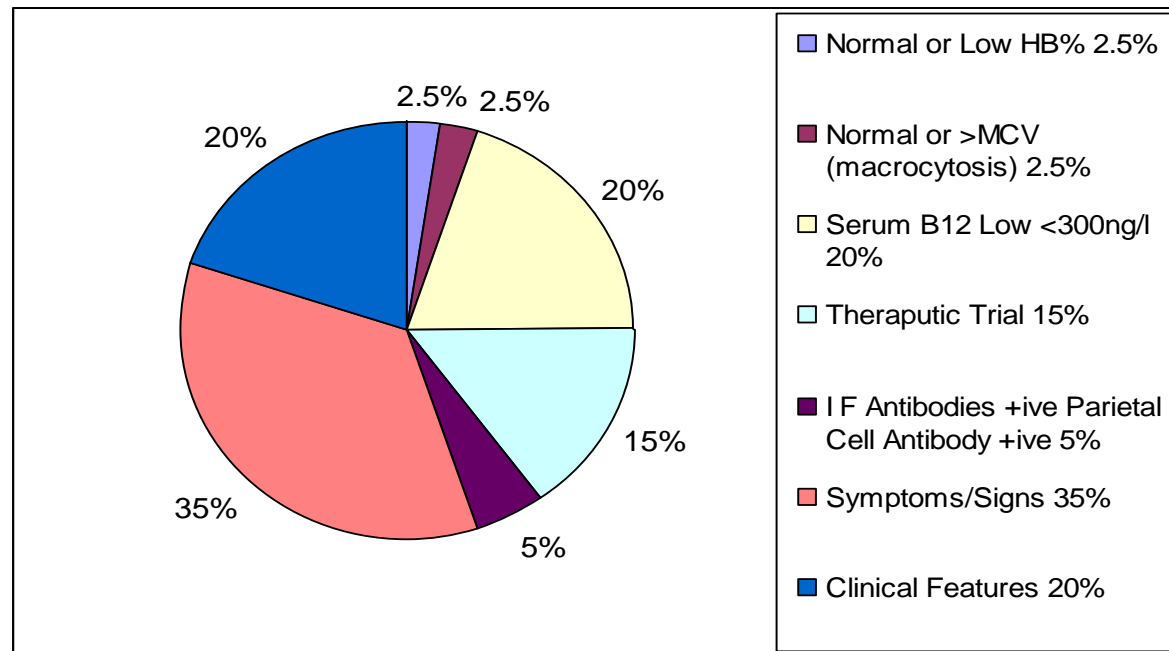
**Transcobalamin II estimation (clinical utility open to question)**

**Bone Marrow Examination**

**Schilling Test – of limited value, only reflects defective absorption**

# B12 Deficiency with Neuro-Psychiatric Symptoms Stages I II III Including Pernicious Anaemia Stage IV B12 Level Below <300ng/l

## “The Chandy Diagnostic Criteria “



Optional  
**Schilling Test**  
**Estimation of Urinary Methyl Malonic Acid**  
**Plasma Homocystine**  
**Transcobalamin II Estimation**  
**Bone Marrow Examination**

# Common Symptoms

Symptoms	Male	Female	Total
Tiredness	28	155	183
Lethargy	31	125	156
Depression	15	114	129
Dizzy (Faints)	16	99	115
Sleepy	17	66	83
Hair Loss	3	79	82
Pins and Needles	7	75	82
Headache	8	49	57
Loss of Memory	5	27	32
Gastric	6	22	28

# Seven Categories of B12 Deficiency

- Clinically significant B12 Deficiency (with moderate to severe Neuro-Psychiatric Symptoms) B12 level  $<200\text{ng/l}$  – with other related features(gastro-intestinal, Haem etc)
- Clinical B12 Deficiency (with mild to moderate Neuro-Psychiatric symptoms) B12 level  $<200 < 300\text{ng/l}$  with or without related features (gastro-intestinal, Haem etc)
- Subclinical Cobalamin Deficiency without signs or symptoms
- ‘Subtle Cobalamin Deficiency’ Subnormal/Normal B12 level with symptoms
- Functional Cobalamin Malabsorption
- Transient Cobalamin Deficiency
- Dietary B12 Deficiency-Vegetarians, Vegans, Poor Diet

# Four Stages of Vitamin B12 Deficiency

- I Serum B12 concentration low; no clinical or metabolic abnormalities. Low plasma level of holotranscobalamin II
  - II The plasma and cells stores B12 become depleted. Serum B12 is low with metabolic abnormalities
  - III Increased level of HCY and MMA and low holotranscobalamin II –low B12 level. Damaged metabolism, dU suppression is abnormal. Neuro-Psychiatric symptoms with mild haematological changes without anaemia
  - IV Clinical signs become recognisable (Addisonian criteria)
    - Macro Ovalocytosis
    - Elevated MCV or Erythrocytosis
    - Lowered haemoglobin
    - Patients presenting with the classical features of pernicious anaemia (PA) would therefore be expected to have progressed through stages I II & III over several years. Some vegans and patients with malabsorption of food cobalamin , may also progress through these stages. Sometimes over many years, but others may not progress beyond stage I or II. These considerations imply that there are many more individuals in stages I, II, & III of B12 Deficiency than in stage IV (PA).  
Low nutritional intake of Vitamin B12 may lead to negative balance and finally to functional deficiency when tissue stores of Vitamin B12 are depleted.
- Early Diagnosis (stage I & II) OF Vitamin B12 Deficiency seems to be useful because irreversible neurological damage may be prevented by cobalamin substitution.

# Irreversibility

**Irreversibility of Neuro-Psychiatric symptoms:** *Our study has shown that undue delay in diagnosing and treating of B12 Deficiency will inevitably lead to neuro-psychiatric symptoms becoming irreversible, if replacement therapy is not initiated early in the disease process.*

***Irreversible Neuro-Psychiatric symptoms:***

1. **Headaches, Memory Loss**
2. **Confusion, Depression**
3. **Weakness of Limbs, Paraesthesia**
4. **Loss of balance, Swaying to one side**
5. **Loss of sensation and power of limbs**
6. **Sub Acute combined degeneration of cord**
7. **Incontinence of bladder and bowel**
8. **Optic atrophy, Blindness**

**Symptoms resolved with treatment:** Neuro-Psychiatric symptoms of subjects presented at baseline were significantly improved over a period of time with treatment