During its early development the earth's atmosphere was, in chemical terms, a reducing environment and produced an abundance of ferrous iron which therefore became the form used in early biological molecules. Later, increasing amounts of oxygen became available, iron converted to the ferric form and organisms had to evolve various mechanisms to utilize it. Bacteria synthesise high-affinity chelating agents to extract iron from their surroundings; plant roots exude a substance which facilitates iron absorption; while mammals have evolved a specific "shuttle" protein – transferrin – in the upper intestinal tract. These mechanisms work well for bacteria, plants and many mammals, but humans appear to have difficulty in maintaining an adequate iron balance. Besides iron, erythropoiesis requires an adequate regular supply of other nutrients, notably folate and vitamin B12. The relative deficiency of these minerals and nutrients results in various forms of anaemia.

Anaemia, defined as a diminished capacity of the blood to carry oxygen, can be the result of a reduction in either the number of erythrocytes or the haemoglobin content, or in both combined. The symptoms and signs include tiredness, giddiness, headache, palpitations, angina, shortness of breath, oedema and pallor. The aetiological classification of anaemia is set out in Table 1. An important proportion of anaemias are deficiency anaemias, dependent directly or indirectly on nutritional deficiencies of iron, folate, and vitamin B12.

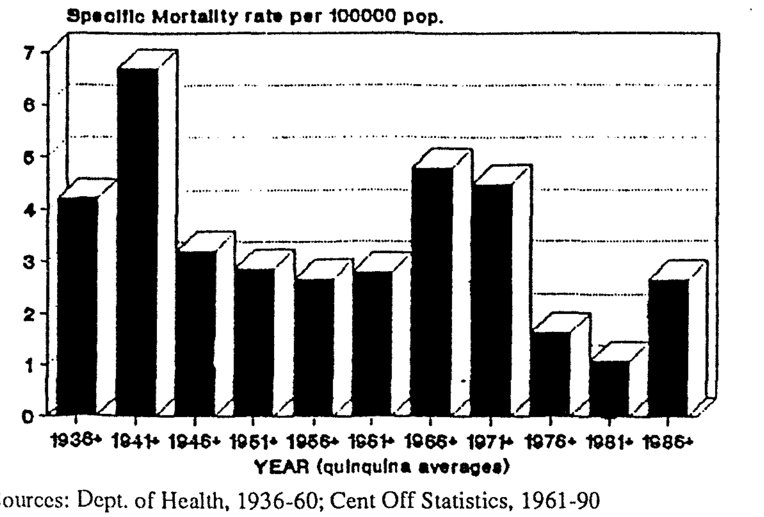
Nutritional anaemia is not a disease entity, it is rather a syndrome caused by malnutrition in its widest sense. WHO has defined it as "a condition in which the haemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency" (WHO, 1972). Anaemia is the end-result of severe nutrient deficiency of one or more hemopoietic factors, usually iron, less frequently folate or vitamin B12. Haemoglobin concentration, by which anaemia is diagnosed, is a relatively insensitive index of milder degrees of nutrient depletion, so that by the time a person becomes anaemic, there is already a marked degree of nutrient deficiency. The diagnosis of anaemia poses a number of problems, chief among them being the problem of defining what is "normal haemoglobin concentration". The norms below which anaemia or deficiency should be considered to exist are laid down in Table 2.

Nutritional anaemias are related to the social and economic circumstances of the population. They are thus an important problem in underdeveloped and developing countries, particularly in women of reproductive age and children. The proportion of women with a haemoglobin concentration below the norm is related to the GNP of the country/region. In Asia and Africa, regions with low GNP's, the

Table 1
The aetiological classification of anaemia

- ❑ Deficient production of erythrocytes
  - ◆ Iron deficiency
  - ◆ Cyanocobalamin (vit B12) deficiency
  - ◆ Folic acid deficiency
  - ◆ Myxedema
  - ◆ Ascorbic acid (vit C) deficiency
  - ◆ Disorders oferythropoiesis in the marrow
    - ◆ apalastic anaemia
    - ◆ malignant invasion
    - ◆ toxic effects of drugs, infection, uraemia
- ❑ Excessive loss of erythrocytes
  - ◆ Haemorrhage
  - ◆ Abnormal haemolysis
    - ◆ congenital defects (hereditary spherocytosis, thalassaemia, G6PD deficiency)
    - ◆ acquired causes

Figure 1 - SPECIFIC MORTALITY RATES FOR ANAEMIA



Sources: Dept. of Health, 1936-60; Cent Off Statistics, 1961-90

Table 2:
Diagnostic Criteria for Anaemia (WHO, 1972)

CHILDREN:	
6 months - 6 years	11.00 g/dl
6 - 14 years	12.0 g/dl
ADULTS:	
Males	13.0 g/dl
Females	
– non-pregnant	12.0 g/dl
– pregnant	11.0 g/dl

percentage of anaemic women was estimated at 58 and 40% respectively. In Latin America, with a moderate GNP, 17% of women were estimated to be anaemic. On the other hand, European countries were shown to have a incidence of anaemia amounting to 4-7%, while the USA and Australia has incidence rates of 6 and 5% respectively (WHO, 1979). There has been in the latter part of the twentieth century a marked improvement in the socio-economic and health status of the Maltese community. In 1952 it was commented that rickets was frequent enough in the Maltese population to justify enquiry, and efforts were initiated to supplement the diet of school children by the free distribution of milk. It was further commented that it was to be regretted that commercial propoganda focussed on the importance of vitamins and calcium, but neglected iron requirements – a mineral too often very badly needed by Maltese multiparous women and their offspring (Galea, 1954). The deficiency disorders remain a cause of population mortality (Figure 1).

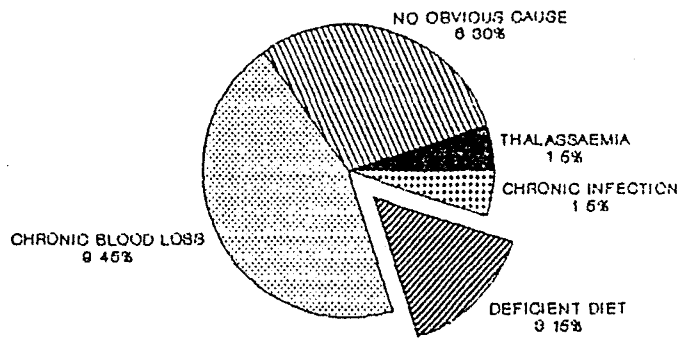
The social and health situation on the Maltese Islands improved in subsequent years. In the late 1960's a preliminary epidemiological study showed that the haemoglobin levels in both sexes fell within the normal range being above 12.8 g/dl in males and 12.2 g/dl in females (Fenech et al, 1970). The mean haemoglobin levels of 292 male donors were shown to approximate 14.0 g/dl, while in 41 female donors the level was lower at 12.7 g/dl (Schembri Wismayer and Gingell, 1970). Haemoglobin levels below 13 g/dl were found in 29.6% of adult males, while anaemia was identified in 2.9% of newborns who had a mean haemoglobin of 16.0 g/dl (sd 2.6) (Felice, 1975). Women of child bearing age were shown to have a mean haemoglobin level of 13.6 g/dl, a figure similar to those reported from other countries at the time:

United Kingdom	13.8 g/dl
Norway	14.1 g/dl
Canada	13.8 g/dl
Israel	12.4 - 12.8 g/dl

(Fenech, 1968).

The haemoglobin value did not appear to be markedly influenced by age, but there appeared to be a direct positive correlation between grand multiparity and haemoglobin level. The incidence of a low haemoglobin (under 12 g/dl) in the screened population was 6.2% in married women and 4.5% in unmarried women. The causes identified for the low haemoglobin in 20 patients are outlined in Figure 2 (Fenech, 1968). The mean haemoglobin level of 140 pregnant women was estimated at 11.56 g/dl (sd 3.92) at 24 weeks and 12.93 g/dl (sd 3.61) at 34 weeks gestation (Schranz, 1986).

Figure 2 - CAUSES OF ANAEMIA IN MALTESE FEMALES: 1966
Hb < 12 g/dl



Source: Fenech, 1968

Figure 3 - CAUSES OF PREGNANCY ANAEMIA: 1968 & 1990

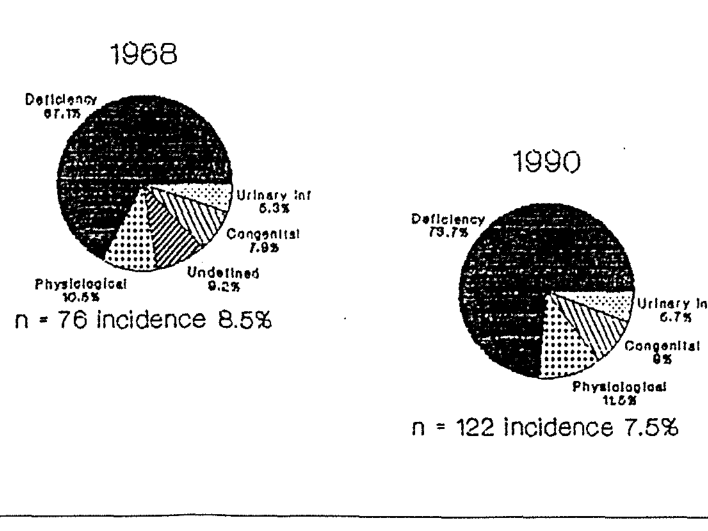
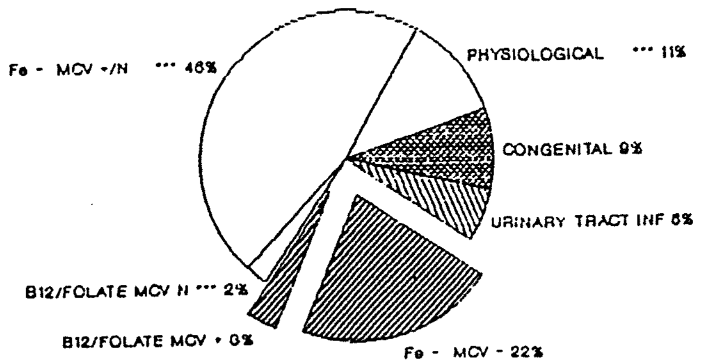


Figure 4 - PREGNANCY ANAEMIAS – REVISED DEFINITIONS
*(*** normal MCV: probably physiological)*



The incidence of anaemia in Maltese pregnant women, defined as a haemoglobin level of less than 11 g/dl, was estimated in 1968 to account for 8.5% of the screened population. About 40% of women were receiving haematological supplements at the time of screening. The incidence of anaemia appeared to be higher in women not receiving haematologicals than in women who received iron supplements (Table 3). Grand multipara had a significantly lower haemoglobin ($p<0.001$) and packed cell volume ($p<0.01$), than women of a lower parity. There was no association with maternal age (Benster, 1968). The causes of anaemia were identified to be caused by deficiency anaemias in 67.1% of cases (Figure 3), these being accounted for by iron deficiency in 56.6% and possible folic acid deficiency in 10.5%. It is well established that dietary iron is barely sufficient to meet the requirements of pregnancy, and deficiency is likely to occur if there is any additional predisposing factor. The anaemic pregnant patients were shown to have had a greater incidence of menorrhagia before pregnancy, gastro-intestinal disorders, haemorrhoids and bleeding gums. It was also found that the intake of meat was less frequent in anaemic patients (Benster et al., 1969). Higher figure were reported by Felice who found 25% of pregnant females to have a haemoglobin less than 11 g/dl (Felice, 1975). In 1990, the incidence of pregnancy anaemia in Maltese women was established at 7.2%, with nutritional anaemias accounting 73.7% of the patients with a low haemoglobin (Zammit, 1991). This high 1990 incidence of nutritional anaemias defined with the same criteria used in 1968 was reported irrespective of the high proportion of haematological and nutritional prescriptions used in the Maltese pregnant population. The Drug Use in Pregnancy Study in 1987 showed that 92% of women received iron supplements during their pregnancy, while a further 28% received nutritional supplements. The haematological supplements were generally prescribed by the second trimester (Savona-Ventura and Grech, 1990).

The incidence of a low pregnancy haemoglobin appears to have decreased during the twenty year period of the two surveys from 8.5% in 1968 to 7.2 % in 1990, though the difference was not statistically significant ($p>0.1$). The decrease was mainly in the number of patients with severe anaemia (Hb <10 g/dl) when the incidence fell from 2.7% to 1.8%. The incidence of a mild anaemia (Hb 10-11 g/dl) only decreased from 5.8% in 1968 to 5.4% in 1990. The causes for the anaemia showed little difference between the two study groups (Figure 3). Deficiency anaemias in 1968 accounted for 67.1% and 73.7% in 1990, while physiological anaemia of pregnancy accounted for 10.5% and 11.5% respectively. Congenital anaemias (mainly thalassaemia trait) accounted for 7.9% and 9.0% respectively, while urinary tract infection accounted for 5.3% and 5.7% respectively. There were 9.2% of cases in 1968 where the cause for the low haemoglobin was not identified, and this alone could have accounted for the differences noted. The reported incidences of pregnancy anaemia vary from one country to another depending on the social circumstances of the country. In developing countries, deficiency anaemia may account for up to 50% of pregnancies (Table 4).

Table 3:
Incidence of Pregnancy Anaemia by haematological use
(Benster, 1968)

Hb level	untreated	treated	TOTAL
<10 g/dl	3.25 %	1.75%	2.7 %
10 - 11 g/dl	7.5 %	3.5 %	5.8 %
< 11 g/dl (total)	10.75 %	5.25 %	8.5 %

Table 4:
Incidence of pregnancy anaemias (Hb<10 g/dl): 1953-1968
(Benster, 1968)

Malta		2.7%
United Kingdom:	London (East End)	9.0%
	Aberdeen	2.4%
Ireland (Dublin)		31.4%
USA (Louisiana: low income group)		20.0%
China (Hong Kong)		14.5%
Australia		3.0%
Israel (Jerusalem)		6.9%
S. Africa (Pretoria: Bantu)		2.0%
Trinidad		34.0 %
India (Vellore)		40.0%

Deficiency anaemias in the Maltese population appear to be a common problem during pregnancy, apparently accounting for 67-74% of all cases of anaemias. However in spite of the improvements in the social, economic and biological status of the population, and changes in the prescribing habits over the last twenty years, there has been little or no significant change in the incidence and type of pregnancy anaemia in Maltese pregnant women. These observations suggest that anaemias due to nutritional deficiencies are rare in the Maltese Islands, and deficiency anaemias are predisposed to by previous chronic blood loss. Furthermore the problem remains that the definitions used to identify deficiency anaemias in pregnancy must incorporate the physiological changes that are known to occur during pregnancy. A substantial proportion of cases defined as deficiency anaemias on the basis of a low ferritin, folic acid or vitamin B12 were shown to have normal mean corpuscular volumes suggesting these cases to be "physiological anaemias of pregnancy" caused by hypovolaemia.

These corrections would suggest that physiological anaemia of pregnancy may account for 59% of all cases with a haemoglobin less than 11 g/dl, while deficiency anaemias account for only 25% of cases (Figure 4)

In view of the data which suggests that less than a hundred women annually suffer from deficiency anaemia during pregnancy one must question the usefulness of routinely prescribing haematological supplementation to all women in a population with a good socio-economic status. These supplements should be reserved for women shown to have specific deficiency disorders, especially considering the gastro-intestinal side-effects of these drugs (Zammit and Savona-Ventura, 1992).

Congenital anaemias in the Maltese population are an important aspect of the problem. Beta-thalassaemia trait has been reported to occur in about 4% of the Maltese population, the prevalence being reportedly higher in Gozo than in Malta, and accounts for about 20% of anaemias in Malta (Vella, 1962; Cauchi, 1970; Felice, 1975), though recent studies in the pregnant female population suggest a prevalence of about 1% (Zammit et al, 1991). In addition the Maltese population has been found to have fatal haemoglobin varianta with an incidence of about 2% (Cauchi et al, 1969; Bannister et al, 1972; Felice, 1975), but these have no reported haematological significance since only heterozygous carriers have been described. Glucose-6-phosphate dehydrogenase deficiency has been shown to affect 2.7% of adult males and 1.9% of adult females (Cauchi and Grech, 1968). In infants partial deficiency accounted for 5.8% of males and 4.2% of females, while total deficiency was reported in only 1.5% and 0.4% respectively (Grech and Vicatou, 1973). In pregnancy Beta-thalassaemia was shown to be present in 17.8% of women having a haemoglobin less than 11 g/dl and in 8.8% of women with a haemoglobin less than 12 g/dl (Felice, 1975). The problems of thalassaemia and other congenital hemolytic disorders in pregnancy in Maltese pregnant patients have been previously reviewed (Grech et al, 1984; Savona-Ventura and Grech, 1991; Savona-Ventura, 1992; Kim, 1979).

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