

Pellagra

What is pellagra?^[1]

Pellagra results from the deficiency of niacin (vitamin B3). It was first described by Don Casal, a Spanish court physician in the 1700s, where thickened skin was noted in peasants. However, it was not until the 1900s that the cause and treatment of pellagra was determined.^[2]

Niacin can be derived from:

- Dietary sources: include nicotinic acid, nicotinamide and other biologically active derivatives. High bioavailability is in food products such as beans, milk and eggs. Flour is enriched with niacin and has an excellent bioavailability.
- Conversion of the amino acid tryptophan to niacin: an increased rate of turnover is seen in niacin deficiency states – eg, pregnancy and with the oral contraceptive pill – and conversion is inhibited by isoniazid.

Nicotinic acid and nicotinamide are precursors of two important co-enzymes: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP).

NAD and NADP are crucial to a number of oxidative and reductive reactions – eg, steroid formation, fatty acid synthesis, protein metabolism and DNA repair.

Absorption of vitamin B3^[1]

Both nicotinic acid and nicotinamide are absorbed from the stomach and small intestine. At low doses absorption depends on facilitated diffusion and at higher doses the absorption is passive. Some storage occurs in the liver.

Recommended dietary allowance (RDA)

Important information

The RDA is 13-19 NE/day for adults. NE is 'niacin equivalent', in which one NE = 1 mg niacin or 60 mg tryptophan. The RDA depends on age - see reference link for more information. ^[3]

How common is pellagra? (Epidemiology) ^[4]

- Consuming a balanced diet and fortification of commonly consumed foods renders vitamin B3 deficiency a rare occurrence in developed countries.
- Prior to food fortification with niacin, epidemics of pellagra were seen. However, sporadic cases are still occasionally seen.
- Niacin deficiency is seen in the following groups:
 - A focus on 'healthy eating', often without dietetic support, increases the risk of nutritionally restricted diets.
 - Vegan diet with inadequate wholegrain intake.
 - Diets based mainly on corn (low in tryptophan and niacin) - eg, China, Africa and India.
 - Alcoholics - usually deficient in other vitamins also.
 - Eating disorders - eg, anorexia nervosa. ^[5]
 - Hartnup's disease - congenital malabsorption of tryptophan from the intestine and kidney.
 - [Carcinoid syndrome](#) - tryptophan is increasingly converted to serotonin.

The incidence of pellagra in the countries of Africa and East Asia ranges from 5% to 35% (eg, Angola, Malawi, Tanzania or India). ^[1]

Pellagra symptoms (presentation) ^[1]

Classically described as '3 Ds':

- **D**ementia (altered cognition).
- **D**iarrhoea.

- **Dermatitis.**

Some add a fourth D - **Death.**

Early symptoms include:

- Loss of appetite.
- Generalised weakness.
- Irritability and aggression.
- Abdominal pain.
- Vomiting.

Continued deficiency leads to epithelial changes leading to:

- Stomatitis.
- Bright red glossitis.
- Vaginitis.
- Oesophagitis.
- Dermatitis - classically, a pigmented, scaly rash prominent in sun-exposed skin - eg, the back of the hand, called 'gauntlet of pellagra' or on the neck where it can form a ring called 'Casal's necklace'. The rash begins as itchy erythema and then looks similar to a tan and may vesiculate. [6] [7]

Other features include:

- Diarrhoea - due to a combination of proctitis and malabsorption.
- Dementia - may present as depression, followed by memory deficits and hallucinations or psychosis which may occur.
- Seizures.
- Paraesthesia - may occur.
- Malabsorption.

Diagnosis

After niacin has been processed it can be excreted in the urine. The products detected in the urine include nicotinic acid, niacin oxide and metabolites including 2-pyridone and 2-methyl nicotinamide.

The latter two metabolites can be measured to assess niacin deficiency (low levels will be present).

RBC levels of NAD/NADP can also be useful in the diagnosis.

Pellagra treatment and management

- Oral supplementation with nicotinamide is usually used.
- Nicotinamide is used in preference to nicotinic acid, as side-effects relating to vasodilatation are fewer - eg, flushing.^[8]
- Cutaneous lesions begin to resolve in 24-48 hours after starting treatment.

No toxic effects are seen with food sources of niacin.

Prognosis and prevention^[1] ^[4]

Pellagra is preventable and easily treatable when recognised, which has a large impact on patients given the associated morbidity and mortality.

Prompt diagnosis and treatment of cases lead to an excellent recovery.

Prevention involves adequate niacin intake and dietary advice to vulnerable groups, including pregnant women.

Further reading

- [Williams AC, Hill LJ](#); The 4 D's of Pellagra and Progress. *Int J Tryptophan Res.* 2020 Apr 16;13:1178646920910159. doi: 10.1177/1178646920910159. eCollection 2020.
- [Kapata N, Zumla A](#); Preventing pellagra during isoniazid preventive treatment. *Lancet Glob Health.* 2022 May;10(5):e600-e601. doi: 10.1016/S2214-109X(22)00163-2.

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