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Favism – brief history from the “abstain from beans” of Pythagoras to date

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*“...κύμων απέχεσθαι...”, “...kyamon apechehesthe...”
“...be far from the fava beans consumption...”
(part of Pythagorean consultations)*

Favism (fabismus, favismo, fabism) is a reaction to ingested fava plant; beans, pods and, most likely, foliage as well, or to inhalation of fava pollen. It is a hereditary abnormality of the red cell enzyme glucose-6-phosphate dehydrogenase (G6PD), resulting in its sudden destruction (hemolytic anemia and jaundice) following the intake of fava beans and other legumes as well as various drugs. Favism is common in Mediterranean, Africa and southern Asia. More than 400 genetic variants are recognized genetically.

Fava beans intake originated in the Near East in late Neolithic times, and after they are cultivated in ancient Egypt, Greece and Rome. Fava beans are mentioned several times in Homer Iliad (8th to 9th BC).^{1,2} The Greeks apparently associated the little black spot on the hilum with death and although the beans were sometimes offered in sacrifices to Apollo, the priest were strictly forbidden to eat or even to mention its name. Unlike the Egyptians and Greeks, the Romans had the fava beans in high esteem among legumes. The beans that mentioned Pythagoras (c. 570 to c. 495 BC) are fava beans (*vicia fava*, *vicia faba vulgaris*), which botanically are a large seeded vetch. They are well-adapted to the Mediterranean region because is very hardy to cold, grows vigorously during the cool wet months of winter, and present for centuries an unique and invaluable part of diet of the Mediterranean's basin living people. Its history is rife with superstition, prohibition, magic and fear.³⁻¹⁸

It is well known that for some people, fresh fava beans can be poisonous. Although common, favism as a genetically transmitted disease was recognized only at the turn of this century. It was fully explained just in the last decades.

Classic Greece doctors had seen through the importance of environment, natural elements and aliments for the right balance of organism. The presence of hemolytic anemia on individuals due to lack of the enzyme G6PD was known for many years. It is called favism meaning occurrence after consumption fava beans (Greek word “κύαμοι”, “kyamoi”, “κυαμισμός”, “kyamismos” - favismus). The observation that the consumption of fava beans

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causes various disturbances was the first observation of toxic hemolytic anemia and the rule "κυάμων απέχεσθαι", "*kyamon apechehesthe*" - "be far from the fava beans consumption" constitutes part of Pythagorean consultations.¹⁹⁻²⁹ This rule constricts a legume that is named Greek fava bean (*kyamos Hellenikos*, *vicia faba*, *Vica faba*) that already is cultivated and used in the Mediterranean by the Prehistoric season where at Theophrastus (372 to c.285 BC)³⁰ the word *kyamos* (*vicia faba*) characterizes the plant as well the kernel. Plynios (23 to 79 AD)^{31,32} and Dioscurides (40 to 90 AD)³³ separate the Greek fava bean from the fava Aegyptia reminding that the Pythagorean rule concerns only the Greek fava bean. Empedocles (495 to 435 BC)³⁴⁻³⁷ during the 5th century BC continues the Pythagorean teaching declaring that "δειλοί, πάνδειλοι, κυάμων από χειράς ἐχεσθαι", "*deiloi, pandeiloι kyamon apo cheiras echesthe*" - "unhappy, a lot of miseries, it is not touched upon fava beans". Kallimachos (310 to 240 BC) during the 3th century BC wrote "και κυάμων από χειράς ἐχεις, ανιόντος εδεστού, καγώ Πυθαγόρας ως ἐκέλευε" "*kai kyamon apo cheiras echeis, aniontos edestou, kago Pythagoras os ekeleve*" - I say also, as said also the Pythagoras, you do not touch upon fava beans, that is corroded food".³⁸ Pythagoras refused to walk through fields of fava beans and forbade his disciples to eat them. He is said to have met his death at the hands of the people of Crotonia in Ancient Italy.^{39,40} Pursued by them, Pythagoras die at the hands of his enemies because he would not flee across a bean field, he came to the edge of a bean field and, rather than set foot in it, was caught and killed as motioned by Artemidoros (1st century BC), Cicero (106 to 43 BC), Iamblichus (c. 245 to c. 325 AD), Diogenes Laertios (c. 3rd century AD), Pausanias (2nd century AD), Porphyry (234 to early 4th century AD) and Grigorios Nanzyanzynos (329 to 390 AD).^{20,41-46} Iamblichus tells of the time a group of Pythagoreans were being pursued by their enemies when they come across a field of favas in bloom. Rather than disobey the master's dictates and flee through the field, they were slaughtered, and when two were captured were questioned about their beliefs, they refused to answer. The husband chose death and the wife, a Spartan, bit off her tongue and spit it her captors to avoid spilling the beans.²³

The rejection of fava beans is also reported by philosophers of India constituting very probably prevention landed by the Greeks.

Whether the poisonings were the basis of Pythagoras' pronouncement or not, for many is not certain and this state of debate is well summed by Aristotle (384 to 322

BC) and Aulus Gellius (c. 125 to c. 180 AD), who say that Pythagoras proscribed fava beans either because they are like genitals (testicles), or because they resemble the gate of Hades, for they alone have no joints, since these two correlate well with traits connecting beans with human life and generation referred by other ancient writers, or again because they spoil, or because they resemble the batut of the universe, or believed that beans really meaning eggs and the eating of an egg is similar to eating the animal that comes from it, or because of oligarchy, for they are used or drawing lots.^{19,23}

Aristotle and Diogenes Laertios proposed that the Pythagoreans rejected fava beans because they are possibly poisonous and provoke flatulence, which can destroy mental peace by keeping one awake with a rumbling stomach.²⁰

The later sect known as the Orphics believed that Pythagoras had forbidden the eating of fava beans because they contain the souls of the dead. "Eating fava beans and gnawing on the heads of one's parent are one and the same," went one of their saying.

Herodotus (485 to 421 BC) reports that Egyptian priest consider beans to be unclean, while Pausanias and Porphyry note that they were forbidden for Orphics and the iniates at Eleusis and they were not to be touched including them in a list along with pomegranates, recently delivered women and dead bodies, showing a possible relationship with religious dogmas.^{35,44,45}

All the above testimonies emanate from who that are not doctors. The Hippocratic doctors cannot ignore the Pythagorean dietetics. However the prohibition of fava beans is not reported in their treatises.¹⁹ Around the turn of the century, physicians began to recognize the presence of favism after eating fresh fava beans and some people began to suffer a sudden illness that, in some cases, led rapidly to death. The cause seems obvious today, but it wasn't until 1904 when Clemens von Pirquet came up with the medical definition for allergies. Before this, it was difficult for doctors to get a handle on the concept that what might be fine for one person might be poison for another. The first modern report of favism (favismus, *kyamismos*) is found in a magazine of Lisbon where in 1843 Manuel Pereira de Mira Franco reported the case of individual who presented with jaundice each time where he ingested fava beans.⁴⁷ From 1856 the Sicilian Antonio Mina La Grua⁴⁸ but also other doctors as Di Pietra - Leone, Rizzo - Matera, Pietro Messina pointed out jaundice from different exhalations (possible by ethereal oil) of the fava beans flowers, inherited of this illness, and distinguished

this icterus from the jaundice of the malaria and confirmed the main role of fava beans. Giovanni Mule Bertolo (1900) observed the appearance of hemoglobinuria and proposed the term “favismus”, while the Sicilian patient Salvare Greco (his surname reminds his Greek origin but also his stigma) suffered from favismus as his grandfather from the part of his mother that from his experience and from the experience that he had inherited arranged itself in the cheque of Pythagoras for the not consumption of fava beans. In the threshold of the 20th century the doctors occupied that the pathophysiology of favismus was the haemolysis (destruction of red corpuscles) and in congress of Rome (1894) G. Montano reported hemoglobinuria (and no hematuria as it is previously believed) as the main symptom of the disease and distinguished the “decisive” reason, fava beans’) and the “predisposed” reason, idiosyncrasy.⁴⁹ Cases in Italy were also reported by Girotti 1899, Camillis 1901, and in Sardinia by Went 1899, and Steani 1904 as well. In Greece from 1895-1905 Doukas, Skavetzos, Kavvadias, Vellopoulos, Kontogeorgis, Tselios and other realised the illness in various regions of Greece (Continental and islander regions). Epidemiologic studies of Gasparrini in 1905 clarified the clinical picture, the familial character, the eclectic attack of young persons particularly male.⁵⁰⁻⁵²

A possible explanation of favism began to appear in the 1920’s, when scientists found that G6PD deficiency is actually a defence against malaria the main health problem in Greece and Southern Italy. It wasn’t until late 1940 that W. Boyd from Boston, noted that the British, in contrast to Mediterranean people, never developed favism after ingestion of fava beans suggesting a genetic difference as possible explanation. This information became more interesting during World War II, when treating malaria with quinine-based drugs resulted to reaction to the medicine in the same people did eating fava beans.⁵³⁻⁵⁷

Later, the complex explanation of illness became evident as American doctors after using antimalarial drugs (“favismus of Blacks”) related it with favismus of the Mediterranean origin. Later, lack of the enzyme G6PD was clarified as the cause of hemolysis. For years various substances of the fava beans were incriminate but also rarely other flowering plants for the challenge of hemolysis, were also described. It was observed that the syndrome was released mainly after consumption of fresh fava beans (likely smaller content dry or boiled fava beans, release after a simple contact with fruits or flowers even in a distance) and the substance may be transported even via breast feeding. The Greek work of Choremis, Doxiadis,

Kattamis, Stamatoyannopoulos, Fessas, Zannos-Mariolea and other on the subject and his extent in Greece with discovery of hot spots in various regions, while others gave elements for the nature and the inheritance of illness.⁵⁸⁻⁷² Later the physiologic polymorphism of the enzyme G6PD, was realized together with the existence of irregular molecules of the enzyme, the hereditary transfer. The Greek pediatricians realised the relation of lack with neonatal jaundice, the correlation with bone damages as the thalassemia, the co-incidence of illness in regions with malaria and also with other thalassemic syndromes and the selection advantage offered by lack of the enzyme in malaria infection in the heterozygous women but not in the hemizygotes men. The “Mediterranean phenotype” of the illness was realized and also the variants of the enzyme named after Greek regions or cities (Athens, Corinthus, Orhomenos, Lavadeia, Karditsa, Attica, Thessaly etc) became known. The condition is most common in males, only women who carry the gene from both sides of the family are susceptible and the condition is most severe among infants and children and the poison can be passed in mother’s milk.⁶⁶⁻⁷²

From all these it appears that even today it rather becomes acceptable that the compurgation of Pythagorean prohibition for the consumption of fava beans is valid and useful.

It is found that fava beans contain several chemical compounds that resemble those found in quinine. Fava beans are rich in two glycosidic compounds, vicine and convicine constituting some 2% of the dry weight. Upon ingestion, the glycosides are hydrolysed enzymatically to form pyrimidine aglycones, divicine and isouramil respectively. The proposed mechanism for the cause of favism is that the new compounds consequently undergo redox cycling and the process depletes reduced glutathione, leading to the formation of free radicals and hydrogen peroxide.

After decades of research it was proven that fava beans themselves also fight malaria with the same way as G6PD deficiency (reducing the amount of oxygen in the blood). In a theoretical basis when fava beans are consumed by people with G6PD deficiency who don’t suffer from favism (the vast majority of the population), the resistance to malaria is raised. In a theoretical basis even if fava beans are dangerous to a percentage of people, their benefits for the remainder of the population far outweigh their shortcoming. Additionally last years there are some informations that faba beans (*Vicia faba*) have lipid-lowering effects and may also be a good source of

antioxidants and chemopreventive factors.⁷³⁻⁹³

Is this the secret behind Pythagoras' puzzle? It's hard to say, 26 centuries later. One thing's for certain: He's not talking

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