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Favism - from the “avoid fava beans” of Pythagoras to the present

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“...κνάμων απέχεσθε...”, “...kyamon apechesthe...”
“...be far from the fava beans consumption...”
(Part of Pythagorean consultations)

Favism [fabismus, kyamismos (Greece) 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 to its sudden destruction (haemolytic anaemia and jaundice) following intake of fava beans, other legumes or various drugs. Favism is common in Mediterranean, Africa and Southern Asia. More than 400 genetic variants are recognized.

Fava beans intake originated in the Near East in late Neolithic times; they were afterwards cultivated in ancient Egypt, Greece and Rome. Fava beans are mentioned several times by Homer (8th to 9th BC). Greeks apparently associated the little black spot on the hilum with death and although the beans were sometimes offered in sacrifices to Apollo, it was forbidden to priests to eat or even mention their name. Unlike Egyptians and Greeks, the Romans highly respected fava beans among legumes. The beans Pythagoras is referring to are fava beans (*vicia fava*, *Vicia faba vulgaris*), which botanically are a large seeded vetch. They are well-adapted to the Mediterranean area because of being very hardy to cold. They grow

vigorously during the cool wet months of winter, and they constitute for centuries unique and invaluable part of diet in Mediterranean people. Their history is rife with superstition, prohibition, magic and fear.

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. The mechanism was explained only in the last decades.

Classic Greece doctors had seen through the importance of environment, natural elements and aliments for the right balance of organism. Haemolysis due to lack of the enzyme G6PD of red cells was known for many years. It is called favism meaning “occurrence after consumption of fava beans” (Greek word “κνάμοι”, “kyamoi”, “κναισμός”, “kyamismos” - favismus). The observation that the consumption of fava beans causes various disturbances was the first observation of toxic haemolytic anaemia and the rule “κνάμων απέχεσθαι”, “kyamon apechehesthe” - “be far from the fava beans consumption” was a Pythagorean consultation. This rule constricts a legume that is named Greek fava bean (*kyamos Hellenikos*, *vicia fava*, *Vicia faba*) that is cultivated and used in the Medi-

terranean already by the Prehistoric season where at Theophrastus the word *kyamos* (*vicia fava*) characterizes the plant as well the kernel. Plynio and Dioscurides distinct the Greek fava bean from fava Aegyptia reminding that the Pythagorean rule concerns only Greek fava bean. Empedocles during the 5th century BC continues Pythagorean teaching declaring that “δειλοί, πάνδειλοι, κυάμων από χείρας έχεσθαι”, “deiloi, pandeiloι kyamon apo cheiras echesthe” – “unhappy, a lot of miseries, it is not touched upon fava beans”. Kallimachos during the 3rd century BC wrote “και κυάμων από χείρας έχεις, ανιόντος εδεστού, καγώ Πυθαγόρας ως επέλενε” “kai kyamon apo cheiras echeis, aniontos edestou, kago Pythagoras os ekeleue” - I say also, as said also the Pythagoras, you do not touch upon fava beans, that is corroded food”. Pythagoras refused to walk through fields of fava beans and discouraged his disciples from eating them. He is said to have met his death in Crotonia in Ancient Italy. Pursued by them, Pythagoras died among 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 Iamblichus, Diogenes Laertios, Artemidoros, Porphyry, Pausanias, Cicero and Grigorios Nanzanzynos. 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.

Avoidance of fava beans is also advised by philosophers of India, probably landed by the Greeks.

Whether the basis of Pythagoras' pronouncement was poisoning or not, remains uncertain. This debate is well summed by Aristotle and Aulus Gellius, 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 for drawing lots.

Aristotle and Diogenes Laertios proposed that 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.

Orphics believed that Pythagoras had forbidden 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” was one of their saying.

Herodotus reports that Egyptian priests considered beans as unclean, while Pausanias and Porphyry note that they were forbidden by Orphics and the initiates at Eleusis. They also should not be touched including them in a list along with pomegranates, recently delivered women and dead bodies, showing a possible relationship with religious dogmas.

All the above testimonies emanate from authors are not doctors. The Hippocratic doctors cannot ignore the Pythagorean dietetics. However the prohibition of fava beans is not reported in their treatises. Around the turn of the 20th 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 is fine for one person may be poisonous 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 an individual who presented with jaundice each time where he ingested fava beans. From 1856 the Sicilian Antonio Mina La Grua 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, inheritance of this illness, distinguished this icterus from the jaundice of malaria and confirmed the main role of fava beans. Mule Bertolo observed the appearance of haemoglobinuria and proposed the term “favismus”, while the Sicilian patient Salvare Greco (his surname point to a 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 consultation of Pythagoras for the not consumption of fava beans. In the threshold of the 20th century doctors showed that

pathophysiology of favismus was haemolysis (destruction of red corpuscles). In a congress in Rome (1894) G. Montano reported haemoglobinuria (not haematuria as previously believed) as the main symptom of the disease and distinguished the “decisive” reason, fava beans”) and the “predisposed” reason, idiosyncrasy. 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. Epidemiologic studies of Gasparrini in 1905 clarified the clinical picture, the familial character, and the defective attack of young persons particularly male.

A possible explanation of favism began to appear in the 1920's, when scientists found that G6PD deficiency is actually a defence against malaria a major 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 genetic difference as a possible explanation. This information became more interesting during World War II, when treating malaria with quinine-based drugs resulted to reaction to the medicine similar to fava beans by the same people.

Later, the complex explanation of illness became evident as American doctors after using antimalarial drugs (“favismus of Blacks”) related it with Mediterranean favismus. Later, lack of the enzyme G6PD was clarified as the cause of haemolysis. For years various substances of the fava beans were incriminate but also rarely other legumes for the challenge of haemolysis, 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 discovered hot spots in various regions, while others gave elements for the nature and the inheritance of illness. Later polymorphisms of the enzyme G6PD were realized together with the existence of irregular molecules of the enzyme. The Greek paediatricians realised the relation of enzyme insufficiency with neonatal jaundice, the correlation with bone damages as thalassaemia, the co-incidence of

illness in regions with malaria, with other thalassaemic syndromes, and the selection advantage offered by lack of the enzyme in malaria infection in heterozygous women (but not in the hemizygotes men). The “Mediterranean phenotype” of the illness was realized and also sub-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, (women being susceptible only carry the gene from both sides of the family) and the condition is most severe among infants and children.

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

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 some people, their benefits for the rest of the population far outweigh their shortcoming. Additionally, in last years there exist some data that faba beans (*Vicia faba*) have lipid-lowering effects and may also be a good source of antioxidant and chemopreventive factors.

Is this the secret behind Pythagoras' puzzle? It's hard to say, 26 centuries later. Most probably, nobody definitively knows.

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