

AETIOLOGY THEORIES ABOUT PELLAGRA AT THE END OF THE NINETEENTH CENTURY AND EARLY TWENTIETH CENTURY IN THE VISION OF ROMANIAN DOCTORS

O. ANDREESCU¹ L. ROGOZEA¹

Abstract: *Pellagra is the prototype of the social disease from the late nineteenth and early twentieth century, affecting tens of thousands of people each year, particularly in rural areas. Trying to find a solution for this social plague, medical staff of that time, as V. Babeş, A. Babeş, I. Felix, D. Sergiu, I. Neagoe, have done original researches, with minimal material resources, regarding aetiology and treatment of pellagra. Proposals of prophylactic treatment consisting in domestic education lessons and attempts to improve the economic situation of the peasants were the results of aetiology researches.*

Key words: *Pellagra, social disease, corn.*

1. Introduction

Pellagra registered an impressive number of cases, especially in Spain, Italy, France and Romania. This explains the concern of numerous and important physicians from these countries to discover the pathogenesis of this disease.

Soon enough from the description of the first cases the link with corn consumption was made, and the maids theory (*Zea maidis* = corn) was formulated.

2. Pellagra in Romania

The first cases of pellagra, in the territory of present-day Romania, were described around the 1830's in Moldova, initially as isolated cases. But the number of sick increased rapidly, favoured by the fact that

Romania was a predominantly agricultural country, where maize cultivation was intensive, being considered the second largest corn exporter in the early twentieth century. In the same period the peasants' standard of living, their health and household education level, their material possibilities as well as religious beliefs created favourable conditions for the spreading of pellagra so that in the statistics made the early twentieth century the numbers exceeded several tens of thousands of sick people.

Because this condition affected the rural population (thus, in 1888, from 10626 of pellagrous statistically declared by Dr. D. Sergiu, most were farmers (7522) or workers (2132)), the number of physicians involved in the study of this disease as well as the material resources allocated to the

¹ University *Transilvania* of Braşov, Romania, Faculty of Medicine.

treatment of this disease were reduced compared to those attributed to other social diseases. In order to combat those, leagues and associations were founded which fought to eradicate them. However a few leading personalities of Romanian medicine from the early twentieth century tried, in line with international concerns, to establish the aetiology and seek therapeutic solutions. Among them were Prof. Dr. V. Babeş, A. Babeş, I. Felix, I. Neagoe and D. Sergiu.

The first records of these concerns are represented by two PhD theses written in 1836 (Dr. C. Varnav - "Rudimentum phziographiae Moldoviae", sustained in Budapest) and in 1858 (Dr. I. Teodori - "The Pellagra", sustained in Berlin) and later by the statistics and articles published in professional journals as well as by the lectures given regarding the pellagra theme [7], [11].

3. Studies regarding pellagra aetiology

On December 9, 1888 Superior Health Council of the country decided to appoint a permanent medical committee composed of the physicians Felix, Kalinderu, Stoicescu, Babes, Mina Minovici - for a complete study of the aetiology and means of combating pellagra in the country. At the first committee meeting from March 6, 1889 - it was decided that this would study the aetiology and prevention of pellagra (depending on what was found in our country and abroad) and that the study would begin by examining the aetiology of damaged corn in some places affected by pellagra through on-site investigations. Counties proposed for the study were Dâmboviţa, Dorohoiu, Tecuciu, Tritova and Vlasca [10].

The most sustained theory was the toxic-zeist one, theory that incriminated spoiled maize. Prof. Babes was the most important supporter of this theory, which he tried to support in many articles that he published,

containing the results of personal observations.

In the "Hospital" revue from 1900 he claimed that maize was a complete food, superior to potato and that zeist ideas must be rejected, as they are damaging both to the economy and scientific progress. In 1912 Dr. Babeş published along with Dr. V. Buşilă, a monograph concerning the research carried out in the Babeş Institute. They established that corn contains 9.65 [%] albumin, 3.8 [%] fat, 69.55 [%] carbohydrate, 1.455 [%] cellulose, 1.35 [%] ash etc.. Taking into account that a Romanian peasant consumed an average of 1300-1500 [g corn / day], equivalent to 4000 calories, the energy need was assured. However, pellagrous were considered denurtured, anaemic, their urine containing indicans and acetone, which meant the existence of a state of autophagic [1], [4].

In "Studies about pellagra" published in 1911, V. Babeş noted that in 1907 the number of pellagrous was increasing alarmingly, after foreign corn was introduced in 1907 in the country, mostly spoiled corn that was consumed especially by the poor. The same observation was made in 1918 during a meeting on 28 June. Following an order of the General Military Administration of 27 February 1918, the population received on the basis of a ration book for bread, bread made from spoiled corn mixed with flour. As a result, in May, after the period of Lent, there were several cases of pellagra in Bucharest. By making the connection with the date of enactment, Mr. Professor Babeş estimated the incubation period at about two months [2].

In the "Hospital" revue from 1903 Dr. Proca enunciated the idea of the existence of individual predisposition influenced by sex and age. This hypothesis was sustained by several authors from Italy but also from the country, who published the cases of new-born or breastfed children with

pellagrogen desquamation erythema and gastroduodenitis pellagra [10]. In contradiction to these were the authors who argued that in families with pellagra in our country, although the child started as early as the age of 10 to attend with their parents all their work and deprivation, living the same pellagrogen conditions, he did not exteriorize pellagra. This occurred much later, most commonly in adulthood. They concluded that these pellagrogen conditions must act for a long time, to consequently lead, in the presence of certain causes (illness, pregnancy, lack of milk and meat in the summer), to a paroxysm of nutritional imbalance [9].

In 1900 V. Babeş obtained a toxic substance from damaged corn, which he was able to neutralize through serum taken from convalescent pellagrous. This anti-toxic substance was in the blood of cured and convalescent pellagrous [8]. During his research, Prof. Sion isolated from damaged corn a toxic mould, which he entrusted to the Institute of Pathology and Bacteriology. There was researched the existence of a specific link between several fungi and microbes isolated from damaged corn, which came from corn stocks of the pellagrous, the "microbe" isolated by Prof. Sion, and pellagra (complement fixation, agglutination). For this the blood of 27 pellagrous was analyzed to investigate if blood along with these microbes or alcohol or ether extract from these microbes formed a specific system. They sought specific substances also in diarrhoeal manure typical to the pellagrous. The research was conducted together with Dr. Buşilă and Dr. A. Babeş (head of the Chemical Service). A specificity rapport was not found, but the authors continued to support the hypothesis about the aetiology of damaged corn arguing that not in all infectious diseases a complement fixation occurred [3].

These studies were also supported by

PhD doctorate students of Prof. Babeş in doctoral theses developed under his leadership; for instance Dr. Elena Manicatide in 1902 and Dr. Călinescu in 1912 with the thesis "The etiology of pellagra and antitryptic index in pellagra", showed that the antitryptic power of pellagrous was slightly lower than the normal average, which was not unimportant (compared to one drop of serum that neutralized 2 drops of 1% trypsin in healthy people, with pellagrous the ratio was reversed: two drops of serum were required to neutralize a drop of 1% trypsin) [5].

Incriminated in the genesis of pellagra were also different biological agents. In his inaugural thesis of 1890, Dr. Bocescu, under Professor Socol supervision, made cultures from saliva, blood and excrement from two patients with pellagra, highlighting in all cultures huge masses of coccus disposed in oodles, in chains or isolated in the form of monococcus or diplococcus [15]. Returning to this hypothesis in 1943 - Daniel Constantin and Ilie COSMULESCU argued that all biological agents - coccus, bacillus, aspergillus, protozoa, amoebas, filariidae - incriminated proved unimportant in this respect [6].

Following experimental treatment with atoxilol, and the conclusion that this product, particularly active in diseases caused by protozoa, had beneficial effects on pellagrous patients, professor Babeş admitted that even the transmission of pellagra may be due not only to toxic substances incurred in maize alteration by parasites, but also to parasites transmitted to predisposed organisms, either directly or by means of some insects or other organisms. That should be very small, to the limit of visibility even for the most powerful microscopes, however, results of treatment with arsenic encouraged further research in this regard [2].

Zeist toxicological hypothesis was also supported by other authors, among them Dr. Antoniu which fed different animals with corn damaged through greenery. After a few weeks hens thus fed had lost part of feathers, become sadder, were laying fewer, lighter eggs. Also dogs fed with damaged corn for several weeks developed an erythema on the dorsal part and their hair fell [15].

In 1926 Professor Mouriquand - delivered a lecture before Professor Cantacuzino and other staff of the university on "Nutritional Disorder". In it he discussed pellagra, considering studies of Babeş and Marinescu, but also the experimental pellagra, mentioning the experiments of Professor Cantacuzino and Dr. Nicolau that resulted in hair loss to rats nourished with corn, before they died. On that occasion he presented his personal experiment in which rats were fed with corn, hay and lemon juice (to prevent scurvy) - a perfectly balanced system, in which mice did not lose weight and did not have the hair loss. If, however, from this menu hay was removed, the pellagrous syndrome occurred - " Nutritional Disorder " – Prof. Mouriquand [9]. The author of this article argued that pellagra problem would have been caused by a deficiency to which an adjuvant cause was added (starvation, dietary imbalance, infections, alcohol). Also he presented the geographic spread of pellagra: countries where predominated corn consumption - frequent cases; countries where maize was missing - rare cases; poor regions, where less reconstituant aliments were eaten, very rare cases.

As early as 1900 Neagoe in the "Study on pellagra" [10] was making a link between poverty, abusive consumption of corn up to exclusivity, and pellagra, blaming also "ignorance and laziness" of Romanian peasant woman. He emphasized the fact that in the mountain area - where the lack of milk and various meats - fresh, smoked -was not present because there were plenty of pastures, even if corn of inferior quality and more

damaged than in the lowlands was consumed, pellagra was less present. By this observation, Neagoe raised the suspicion that not only damaged but also the good corn in excessive consumption had the same effect. In the lowlands, farmers even if they had a more substantial food - like eggs, milk, poultry - often preferred to sell it to others, such as townsmen, to meet their other needs. And when they were not sold, these foods were prohibited because of Lent. There were many who believed that for curing pellagra the intervention of both His Eminence the Metropolitan, by eliminating as much fasting as possible, and the Romanian state, by economic and cultural means [12].

Neusser noted that in regions where rotgut (spirits distilled made from corn) was consumed - Transylvania, Hungary - pellagra was rare. It was known that alcohol caused digestive, nervous and cutaneous disorders which were similar to pellagra. In Moldavia, where alcoholism was more spread and where slivovitz consumption was more popular than the consumption of plum brandy that was consumed in Walachia, the number of pellagrous was higher. The explanation is found in the digestive disorders determined by alcohol making digestion more difficult. Together with poor nutrition, alcoholism favoured the appearance of marasmus which made alcoholism to be considered one of the most energetic side causes of pellagra. On the other hand Dr. Neusser questioned that, if alcohol had such a big influence on pellagra, all alcoholics, even those less needy, should become pellagrous [15]. In the "Hospital" revue from 1940, in an article of Colonel Dr. N. Stroian and Major Dr. O. Aramă claimed that alcoholism occurred in the genesis of pellagra only to the extent that it caused lesions of the digestive tract, and the higher frequency of pellagra in the countryside and with the poor was explained by the fact that they drank and had nothing to eat [14].

The Medical School of Iasi presented, by Professor Danielopolu, its concept about the aetiology of pellagra: authors from this school found that abnormal fermentation on mayidic field, together with hyperacidity and enormous intestinal bacterial flora, favoured the appearance of toxins and super-toxins in the intestine of the pellagrous that determined the appearance of digestive disorders. These authors argued that acids, especially butyric acid, could intensify toxin action producing genuine hyper-toxins [11].

Starting also from gastrointestinal symptomatology, Dr. Petrescu, in 1904, considered dyspepsia as a predisposing factor for the occurrence of pellagra, and one of the aspects that might explain why not all those who fed on corn came down with pellagra. Likewise, he explained the role of alcohol as pellagrous factor through aggravation of dyspepsia or creating it [13]. Based on this conviction that dyspepsia opened the way for pellagra and accordingly on the conclusion that there was a manifest of hyperacidity to all pellagrous, he established for all patients, without exception, a high-dose treatment with alkali [12].

Dr. N Niculescu (Prof. Dr. Teodori) - supported the hypothesis that pellagra appeared to be a nervous disease, whose cause of development is the insufficient quality of food, especially albumin. If lacking in the nervous system this causes nervous disturbances. He considered this disease a nevrotime. Dr. Urbeanu connected nerve functional faults to the lack of potassium salts [15].

Other authors, starting from cutaneous manifestations, incriminated phenylalanine or lipid and pigmented substances that sensitize the skin at direct sunlight and in this way would condition the apparition of erythema (porphyrins) [6].

In accordance with the theory supported by Mouriquand, Randoin, Simmonnet -

which considered pellagra as multi-deficiency - in an article published in June 1938 in *Bullet. Mem. of Soc. Med. of Hosp. Bucharest - Claudian*, V. Runcan, A. Vrancea and L. Alexandrescu found an absence of vitamins A, B, C to patients with pellagra, managing to cure a case of spastic pellagrous paraplegia by administration of injectable vitamins. They were claims that pellagra resembled A avitaminosis (stomatitis, achilea, mucous colitis with bloody stools, skin dehydration, hyperkeratosis, hyperpigmentation, hypo-secretion of sweat) and C avitaminosis (gingivitis, stomatitis) [12].

Given the fact that internationally the lack of nicotinic acid was already considered as an etiologic factor, the research of Claudian, N. Gruia-Ionescu, P. Constantin showed that nicotinic acid from urine was present in the pellagrous. They maintained that the deficiency of nicotinic acid was not specific for the pellagrous urine or that it was not the only responsible for the appearance of pellagra. To it they also associated the deficiencies of A, B, C, D, E vitamins [14].

Dr. Coşmulescu linked pellagra to the fact that the most significant protein material, in terms of quantity, contained in the corn flour, the zein, did not contain amino acids indispensable for a good nutrition such as lysine, tryptophan. Under these circumstances zein was difficult to digest [6].

As a result of these studies therapeutic methods proposed were mostly of prophylactic purpose, trying to change the eating habits of farmers and raise their economic status and health. Due to the lack of material resources many of the projects remained at proposal stage. Therapeutic methods tested (auto-serum therapy, atoxyl, sodium anil-arsenilate, vitamins, alkalis, etc..) were considered as beneficial in the treatment of pellagra, but only nicotinic acid introduction in 1937 was the true therapeutic solution to the disease.

4. Conclusions

1. Pellagra is the prototype of the social disease in the late nineteenth and early twentieth century Romania affecting in several tens of thousands of individuals. Although the number of patients was very high, because they came mainly from rural areas, material resources invested in research and treatment were not significant. However, prestigious doctors and personalities of the time were involved in the study of pellagra.
2. Prestigious doctors and personalities of the time were involved in the study of pellagra like V. Babeş, A. Babeş, I. Felix, D. Sergiu, I. Neagoe etc.
3. There were PhD theses, and research studies in major university centres (Bucharest, Cluj, Iasi) which attempted not only to support the hypothesis most prevalent at international level: the zeist theory and the toxic-zeist one, but also to advance some original hypotheses.

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