Prions represent one of the contemporary dangers, which had threatening the medical world alongside AIDS, Ebola, aviary influenza etc. Being considering as spongiform encephalopathy agents, prions had been evidentiated by Stanley Prusiner in 1982 and named accordingly. They are cellular protein particles (Pr Pc) and do not contain nucleic acid.

Their multiplication is due to the stereo – chemical mechanisms than due to the genetic mechanisms. They had a long premonitory action and causes diseases to human being and animals, diseases being always lethargic.

In human being are known many more clinical forms as: Creutzfeldt – Jacob disease, Kuru disease, Alpert disease etc, with a slowly envolve, but with an inexorable final.

The concern of the dentist on disease cognition is higher especially in disease prophylaxis being no secure ways of fithing and neutralizing the agent.

Being a surgical specialty, dental medicine applies to some instruments and devices, which will be infested relationed with infested blood and tissues. That way the instrument can become vector on transmitting the spongiform encephalopathy agent. A part of oral tissues are wearers of this agent (gums, dental pulp, guinsy etc) and can contribute on transmitting the infection. It doesn't exist a specific treatment and neither usually ways of disinfection and sterilization, the agent being extremely resistant.


For the time being the prophylaxis remains the most secure method of control. Although it had been suggested some disinfection methods, it consider that burning is the most efficiently method of neutralize the agent from the instrument, hand pieces, connection hoses or from biological scraps. After having assessed the latest studies in literature and what has been happening in the Western medical practice, where diagnoses are more precise and the attention paid to the possibilities of certain illnesses to be spread is much better related to the real dangers to which every person is exposed, we have considered that the approach of the prion illness and their consequences would be an opportune scientific and very useful action from the point of view of the practitioner and not only.

In the contemporary mass-media there are articles about the 7 dangers which are threatening the world we are living in: a cosmic cataclysm (and nothing can oppose to it), war, environment pollution (stress included), hunger, diseases (degenerative diseases mainly) and insufficient medical care (the American literature describes in a series of really distressing statistics the fact that the number of iatrogenic illnesses has grown so much that it is more dangerous to go to a medical office than drive on the motorway.

Infections have always been a threat to the world and had a great impact, in history there were numerous cases of pandemic and epidemic infections, cholera, measles, which affected the ancient and medieval world. Nowadays, there have appeared other infectious diseases, widely described in medical literature (Ebola, AIDS, aviary influenza, so on) and lately, since the 1980’s to the present, there has been considerably discussed about spongiform encephalopathy (TSE)(1,32,61)

This is the topic of our approach, which aims to prove that the dentist can be very much involved, due to his activity, in taking and transmitting this infection (2,3,7,8).

There is a great number of diseases with infectious agents which are well described and which affect men, out of which more than 1400 infections come from animals. (5, 18) The pathogenic agents are diverse: microbes, viruses, so on. Lately, there has been discussed about subviral particles, which are protein particles carrying nucleic acids and which contradict everything that has been known about infections and the particles called prions (24, 25, 28).

Prions induce 12 types of diseases, all fatal, out of which 6 types affect animals and 6 affect...
men. Koch was the first who, by his postulates, established the manner to identify a pathogenic agent.

Thus:
- The pathogenic agent can be found in lesions and other cases of the disease;
- The pathogenic agent can be isolated from the infected host, be prepared and maintained in a pure culture;
- The pure pathogenic agent obtained in another host should be capable of producing infection;
- The pathogenic agent should be retrievable from the second host.

Research has proven that prions, these infectious protein particles do not abide by Koch’s postulates. They can be isolated but they cannot be maintained on a culture environment. They only develop in living organisms, under the very clear conditions, which cause the disease. Any infection with prions is fatal.

**Why should we talk about prions in dentistry?**

Firstly because prions exist and because any disease, which affects the oral and maxillofacial part, is of interest to us, as specialists, even more as these illnesses caused by prions interfere with the dental practice (4, 21, 36).

Then, because dentistry is a surgical discipline and in any surgery, the infection can spread easier and also because signs of the previously mentioned diseases could appear in the dental field. Likewise, there should be considered the fact that the dental procedures go beyond the epithelial barrier and enter the patient’s mesenchyme, thus the spreading of the infectious agent can be done quickly and without doubt (26, 30, 35, 44, 53).

Because dentistry is an instrumental discipline; in any technique there is used at least one instrument and the instrument could be the transmitting vector of the infectious agent (34, 35, 55).

Because it is a contemporary scourge and there should be mentioned that the highest degree of spreading has not been registered yet. Why? Because the incubation and prodromal stage last even to 20 and 30 years. Thus, it is expected that the highest impact will be in 20 - 30 years (9, 38, 61).

Last but not least, because in dentistry we use a lot of biological products, taken either from human or animal corpses. There aren’t any methods to highlight the prions in these products that we use: (membrane from calf dermis, lyophilized bone, pituitary hormones which are taken from corpses, so on). All the patients who are treated by this kind of therapy are in danger to suffer from a prion disease (9, 11, 17, 22, 23, 40).

**The etymology of prion**

It is a neologism created by a scholar, Stanley Prusiner, neurologist and Professor at the University of San Francisco, California, who introduced the term in molecular biology in 1982 and received the Nobel Prize for medicine due to this discovery (49, 50). The name comes from the notion of infectious protein or infectious protein particle.

**What are prions?**

We mentioned before that they are cellular protein particles. Actually, they are protein particles out of which the prions are developed. In the medical literature there is made a small confusion. Prusiner defined the prion as a pathological protein, but in literature, the name of prion is also attributed to the cellular particle, which comes from it. Prions (previously known as proteoverine, virinos, latent viruses) form a class of subviral infectious agents, of molecular weight between 27,000 – 30,000, unique in their way, resistant to all the inactivation processes which degrade the nucleic acids (warmth, UV rays, ionizing radiations). As they lack genome, they differ from all categories of infectious agents, which are known in the present, by the fact that they do not contain any type of nucleic acid (DNA or RNA) (6, 36, 37, 44).

**What is this protein called?**

It is a cellular protein particle PrPc, which exists in any mammal cell, situated on the outside of the cellular membrane and by certain mechanisms, which have been insufficiently studied and defined, are finally transformed into prionic protein, in short PrSc (Sc comes from scrapie, the protein being first noticed at the level...
of the sheep and goats brain, animals suffering from scrapie) (15, 50). The cellular protein particle (PrPc) can be noticed at the level of the central and peripheral nervous system, in the lymphatic system and at the level of the neuromuscular joints, as a protein situated at the surface of the of the cell, anchored by the cell membrane by a glycolipid anchor. Usually, this form is produced inside the brains of the mammals and it is harmless. The structural protein is a hydrophobe glycoprotein, of a molecular weight of 28KDa, including in its composition 208-220 amino acids, depending on the species. It has a NH2-terminal region, a central part and a COOH-terminal region. The NH2-terminal region contains 80-100 amino acids, a region made of five copies of an eight-repetition, but there are cases when this number is higher (for example in cows, where there are six of this copies). Numerous studies have shown that these repetitions have a high degree of conservation in animal series, which means they play an important role in the protein functioning. At the level of these repetitions there is a linking situs for the ions of some metals, especially for the copper ions and there is believed that the activity of this protein might depend on the presence of these ions (11, 18, 28, 39).

Usually, the protein – this protein particle – is synthesized in the cell, and the codes are given due to a gene from the 20 chromosome short arm, which changes the structure of this protein (58, 60, 62). From the ribosome, the particle moves through Golgi corpuscle and from there, it goes on its way up to the level of the cell membrane, where it has several functions (figure 1):

- It is either a receiver of a cell ligand;
- Or it takes part in the process of fixing the copper ions;
- Or it plays an antioxidant role.

This part is characterized by a special plasticity and by the presence of some helical structures, suggesting it is involved in the PrPc→PrPSc (11, 58) conversion. Under certain conditions it can take an altered shape, which represents the infectious agent involved in developing TSE. Out of reasons which are more or less known, its spacial representation changes (under the action of the cellular foldases), so that by folding and polymerization it changes from an alpha-helical structure into a beta-folding structure, abnormal, amyloid structure, which massively accumulates in the central nervous system. This is the process, which changes a normal protein into a pathological protein (figure 4) (44, 50, 51).

When it is installed at the level of the brains, this agent, by its very presence (the intimate mechanism is not yet known) changes the protein normal molecules into a great number of infectious copies, which are deposited at extracellular level as amyloid plaques or at intracellular level as prion fibrils or strains (aggregated by prions) (29,39, 51,52).

**What are the characteristics of the other pathological protein?**

It is identical from the pint of view of the composition. The difference comes from the point of view of the folded links. The change from the cellular protein to the pathological prion appears under certain conditions, either related to Ph, increase in temperature at that particular level, due to a more special protein and a neighbouring process (the simple presence of a pathological protein next to a normal one makes it change its structure as if it wanted to resemble the other, without changing the composition of amino acids). In other words, it is an isomer and this isomer has a particular molecular behavior. This protein places itself on the outside of the cell, on the membrane, but it does not remain single. Unlike the normal cell protein, it polymerizes, it gets closer to another identical
protein chain, and it forms strains and then a compact amyloid mass under the form of an amyloid plaque on the neural stroma. From this level, it affects, it inhibits the neural processes, so that at the level of the neuron, there are present certain phenomena of vacuolar degeneration, hence the name of spongiform encephalopathy, the brain looks spongious, with many empty parts. At the same time, it also generates astrocytosis and amyloidosis. Thus, vacuolar degeneration, amyloidosis and astrocytosis constitute a triad which establishes the diagnosis of the prion disease (18, 29, 36, 39, 41, 50).

As we have previously stated, prions do not contain nucleic acid, do not induce a specific immune reaction, as prions are immunogens. The prion diseases have a very slow evolution, they paradoxically appear in the absence of any immune reaction which could oppose the infection to spread. In the natural prion infections, we understand by the absence of any immune reaction the following aspects:

- Absence of specific antibody synthesis (anti-scrapie antibodies in the natural disease);
- Absence of a specific cellular reaction;
- Absence of any qualitative, quantitative or functional alteration of T and B lymphocytes;
- Absence of any changes at the level of the interleukins.

Some research undertaken in late clinical stages of the prion diseases have shown there are changes in some immunological constants, but they have always been non-specific, being interpreted on the basis of the major destruction of SNC and the strong relationship between SNC and the immune system (18, 39, 44, 50).

Fever does not appear, as the disease is extremely insidious. The prions are highly resistant to all known factors that disintegrate nucleic acids; therefore they cannot be destroyed by heat, ultraviolet radiations or by the antiseptics used in the current dentistry practice. Thus they are considered to be a danger.

There is an intra-cellular stage proper for the development of the prionic agent and an extra-cellular one for fixing it at the cell membrane.

It can be diffused, step by step, by nervous sheaths and by other parts, but it is not mandatory for the specific protein to travel from the peripheral receptor of the Gasser ganglion as it finds a certain protein to change, nearby, protein that, in its turn, changes another protein situated nearby, thus being diffused, step by step, all over that particular neuron which carries prions (17, 25, 27). This happens very often, as it diffuses 2 mm each month, as same as the prions, therefore the prodrome phase leads to prionic disease in 20-30 years of this disease. The prionic infection provokes spreading spongy cerebropathy that creates cerebral lesions, vacuolate degenerations, serious fatal diseases that evolve slowly causing death (25, 27, 42, 44).

**Which are the ways of transmission?**

The impossibility to locate an infectious agent, represented by nucleic acid, on the samples of patients with spongy cerebropathy, together with the extremely high resistance of this type of disease to treatments, usually leading to nucleous acid desintegration, creates the hypothesis of the infectious prionic protein. Stanley Prusiner was the first to come with the aforementioned hypothesis of the proteic etiology, particular to these diseases, in 1982 (44, 50). This states that PrPSc would act as a matrix in the normal conversion PrPC, in the PrPC related to the disease. Thus, the prionic protein disseminates itself by contact with the normal protein, determining the latter to change its initial position in space. These changes are produced in a chain reaction, which makes the newer infectious particles change, in their turn, the other normal prionic proteins they come in contact with. This hypothesis is also sustained by the fact that, in the absence of this normal protein, PrPSc is unable to determine the breakout of the disease (27, 38, 50, 54, 62). Although the present hypothesis could not initially explain the way in which a protein molecule could determine various biological properties, together with different forms of spongy cerebropathy. Later, it came into being the hypothesis that various forms of prionic disease would be caused by different shapes and/or the different level of glycozylation of the prionic protein (44).

Another hypothesis incriminates an infectious agent similar to viruses and called virino, whose copies would allow the development of the
neurodegenerative disease in different stages and, less often, characteristic change by mutation. This is an under viral infectious agent consisting of a small nucleic acid molecule, associated with a protein encoded by the host cell. Under the circumstances, it seems that virino is associated with the isoform scraper of the prionic protein (11).

However, the most circulating hypothesis is that PrPSc would be itself the main, or even the unique component of the infectious agent. This “protein only” hypothesis submitted by Griffith, in 1967, shows that the prion diffusion takes places by means of prPSc that faithfully replicates by recruiting endogeneous PrPSc in the absence of this form, it has been proved that PrPSc is unable to replicate and induce the disease. In order to become infectious, PrPSc must find the chemically similar molecules in the infested cell, so as to change their structure (11, 27, 62).

It can be genetically transmitted to human beings, by casual punctiform mutations located at the short arm level of the chromosome 20, together with the synthesis of the cellular protein gene. It can be transmitted to family, thus forming another type of family transmission to descendants. However, the one which is the most present in humans is transmitted by infections, aiming at food, used and non sterile devices, human or animal drug or other (hypophyseal hormones, insulin, transfusions). As there are no means for highlighting this particle, it can infest even the blood transfusion (31, 38, 62).

It is horizontally transmitted while eating. It seems that a very high incidence has been determined by animal feeding with infested meat flour. Also, it knows a vertical transplacental transmission and a iatrogenic one (34, 56, 60).

The dissemination is also possible by nervous means (ex: the way of the trigeminal nerve) or, as it happens in most cases, by lymphoid invasion after food ingestion, followed by neural invasion in two steps (34, 60).

From an epidemiological point of view, there is a sporadic, family form in the case of punctiform mutations. The disease appears at the same time with the specific genetic mutation due to the various mutation factors (27, 38, 58).

There is also the family form of transmission to descendants, the iatrogenic one transmitted by doctors by means of non-sterile devices and the epidemic form caused by infested food.

Clinical forms of prionic disorders in animals

Scrapie appears in sheep and goats. The manifestation of the clinical symptoms is very low. There are behavior changes to be noted. The animal becomes agitated, weird, cannot move properly or keep its balance, ataxia appears, skin disintegration, hair and wool fall, all of which are very important signs for the persons working in this environment. Animals usually die in 2 to 6 weeks, period in which they cannot be consumed (29).

Regarding the spongy cerebropathy in cattle, the same symptoms are manifested as in the case of scraper: anxiety, teeth grinding, stubbornness (it no longer responds to commands), mastication and mobility problems, paralysis, and death (29).

It is extremely important to mention that so far, a series of forms of prionic diseases were noted in humans such as the following: the Kreutzfeld – Jacob disease, the Gerstmann-Sträussler-Scheinker syndrome, the Kuru sickness, fatal familial insomnia and multiple sclerosis (1, 10, 19).

Clinical forms of prionic diseases in human beings

The Creutzfeld-Jacob disease can be clinically described by: myclonus, face spasms extended to the rest of the organism, sensibility disorders previously unknown to the patient, lack of psychical orientation and of movement coordination, paresis, paralysis, insomnia, madness gradually leading to schizophrenia, pneumonia as a complication, not as a direct cause of prions. Death inevitably occurs after 6 to 12 months from the outbreak of the disease.

In terms of paraclinical signs, the electroencephalogram is destructured and abnormal. In the cerebrospinal liquid, the protein 14-4-3 appears. NMR shows details related to the spongy aspect of the brain. In tonsillar and ganglionic biopsy, prions can be located in the respective lymphoid zone. However, cerebral biopsy (which, unfortunately, can only be seldom performed – as the cerebral tissue does not regenerate and death
can occur), presents vacuolation, amyloidosis and astrocytoma, the 3 anatomy pathological signs of the disease (10,13,30).

**The KURU sickness.** described for the first time in Papua New Guinea where 8000 cases were registered, is also called the laughing sickness (because in the first stages the patient unreasonably displays bursts of laughter). The outbreak and the dimension of the plague owed to the existence of cannibalism in the region, the dead being dismembered according to a sacred ritual. During the ceremony, men received "the lion’s share", i.e. the muscles, while women, children and the elderly (that were considered to belong to an inferior class), the internal organs and the brain, which were precisely the parts, infested by prions. The disease affected 90% of women, children, and the elderly, while male populations were usually not at risk (34, 39, 44).

Disease identification was carried out between 1950-1960, yet the habit of cannibalism, much more restrained nowadays, is still preserved. In the initial stage of the disease, patients have a violent behavior, they show lack of movement coordination, dysphagia, paralysis and death occurs in a year time from the outbreak of the disease.

The Kuru sickness can be divided in three stages: firstly, the patient can still move, secondly, he becomes sedentary as he stays seated and moves less, due to the difficulties and at last, the final stage when he/she is affected by paralysis.

**The Gerstmann-Sträussler-Scheinker syndrome** affects in a 1:10 scale per million, the persons aged between 20 and 60. The clinic symptoms are similar, mainly ataxy and madness (39, 44).

**The fatal familial insomnia** was described in 1979 by an Italian. He initially identified 2 women between 30 and 60 years old. The disease is autosomal, family transmissible and the proteic agent has been identified as the one in charge. Symptoms: continuous insomnia, hallucinations, madness, the patient becomes overweight and can no longer rest. The disease cannot be treated with sleeping pills and death occurs in 16 to 18 months; at autopsy, specific wounds are revealed in thalamus (the center that controls sleep) (34, 39).

**Alpert disease** appears in children of 1 to 5 years of age, i.e., in their period of growth, and is clinically defined by paraplegia and madness (34, 39).

### What are the dental symptoms of these prionic diseases?

The following symptoms are to be noted: coordination problems of the mandible and lingual and mandibular disorders, occlusive disorders, the patient having a central instability with all the efforts made by the dentist. Sometimes, the complete dentition makes impossible to induce the relation of centric occlusion. From now on, it is important to think of this prionic motivation. In pseudobulbar paralysis, dysphagia and disartria appear, the patient can no longer eat, has mastication and deglutition difficulties, problems to speak, facial parasthesias and he sometimes feels no taste (48).

Specialists have tried to locate prions at the level of oral tissues and they were highlighted at the level of gums and pulps (14, 21). In ill patients, prions are also located both in the oral cavity and the oral tissues. Dental pulp maceration from the infested animal was inoculated at the intraperitoneal level, thus infesting the host and causing its death. The prionic levels are higher at the level of gums, than at the level of pulps and they were also located in the Gasser and the tonsillar ganglion (12, 60). The tissues that contain prions are the following (14, 21, 30):

- In the trigeminal ganglion, where the trigeminal neuron stroma is located
- In the salivary glands,
- In the gingival fluid, the dental pulp of the tongue muscles and the tonsils.

What does this mean? It means that when an incision, depuration, or punction for anesthesia is performed, we come in contact with the infested prions.

The main infested categories are the medical devices, the water, and suction installations (45, 46, 55). When treating a patient who is likely to have prionic disease, it is recommended to work in a special room with a special suction source and, at the end of the procedure, all system must be disposed of.

The surgical, endodontical and proteic devices can be infected (5, 13, 47, 55). The aerosols produced by the turbine in a infected patient are inhaled by the doctor and are a possible threat to the personnel of that room (1, 7, 8, 13) so, mainly the surgeon and the helping personnel could be contaminated. The threat can also be
extended to the patient by means of the products used in tissue regeneration: animal products manufactured especially by freezing dry, dura mater substitute, frozen dry bone materials.

You can image the tragic situation of the organ transplant as there are no identification methods for prions (30, 40).

There is no specific treatment

Specialist tries the conversion inhibition of a protein into another by means of certain medicine but without success, so far.

Prevention, above all

This means taking all the necessary measures recommended by epidemiologists in the case of spreading infection, i.e. prior isolation and sacrifice of the potential infested animals, quarantine measures in the infested area (in Great Britain, all animals thought to be infested have been killed, that is 5.5 million cattle) (59).

In the case of patients, isolation and quarantine measures are imposed, especially regarding the contact with biological liquids and the infested tissues. In case of medical treatment, high protection of the personnel, space and devices is recommended, together with the use of already used instruments. The instruments and the protection material must be burnt out.

The dental treatments suppose the use of complex instruments such as: suction devices, in case the tubes are burnt out. The same procedure of burning out is to be applied for the active hand devices, such as the piece and the turbine. As a daily measure, it is recommended the immediate introduction of the used instruments in the washing and disinfection bath. Thus, the dry infested secretion on the device used sticks the prions to the surface of the device without the possibility of ever mechanically clean them or destroy them by means of ordinary disinfecting agents.

Another measure that could be used is double sterilization (16, 55, 57). At first, a sodium hydrate bath with a level of 40g per liter is used. The devices are boiled out, together with the respective solution, so that the action of sodium hydroxide and heat destroy the structure of proteic chain. The device is removed from this first bath, carefully washed and resterilized in several baths. In this way, we succeeded to avoid the transmission from one patient to another. However, the safest method is to burn out the devices used in surgery (22, 23, 26, 33, 57).

Medical experience in the field is in its earlier stage. So far, there are no cases of infested dentists due to patients or certified cases of disease spreading from one patient to another. However, the logics of antinfectious thought make us take into consideration these possible situations and the fact that we cannot deal with it.

The measures of use further adopted, with respect to the aforementioned data make possible the follow up of the devices, thus offering the possibility to suspect the entire patient chain, when a single patient shows signs of prionic disease. Each device is encoded and there is a designed person to keep track of them, i.e. be able to say that a specific instrument was used in surgery on a certain date, for a certain patient and then sterilized in the room x, to be used the next day on another patient, and so on and so forth. Thus, when a certain person of this chain is contaminated, the person in charge can tell exactly where the disease spread and who made a mistake. This fact only creates a tighter responsibility between us (33, 57).

Treaties and international conventions are to establish global measures to prevent this disease, which, as already mentioned, will have the maximum incidence in 20-30 years time (due to the period of prolonged incubation).

A very strict law already banished in France the use of cattle medical material. In the UK, there is a clear evidence of the mortal cases registered since 1980 (300 in all). Strict measures were imposed at a national level in developed countries, where special units follow the profilaxy and aim at eliminating the prionic disease.

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