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apropos

Prions

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What are prions?

Scientists only recently discovered protein particles which are the possible cause of three different types of disease in humans and animals: some which can be inherited, some transferred by infection, and some which occur "spontaneously" (i.e. neither through infection nor heredity). Most of these diseases are degenerative disorders of the central nervous system.

One of these diseases is the controversial mad cow disease (or BSE).

So called atypical "slow viruses" were originally thought to be responsible for the transmission of BSE; "atypical" because
– decades can pass before the disease breaks out;
– the victim exhibits no signs of inflammation or fever; and
– in all likelihood the victim's immune system is not impaired.

However, according the latest findings of medical science it is virtually certain that these illnesses are not caused by viruses, but by so-called prions. The term prion – an infectious protein particle – was coined in 1982 by Stanley B. Prusiner of the University of California in San Francisco. An essential difference between a prion and a virus is that the former lacks nucleic acids (= carriers of the genetic information needed for reproduction).

Prions are protein particles with a diameter of 4–6 nm (nanometres = millionths of a millimetre); viruses, by contrast, have a diameter of 10–450 nm. Prions lead to a change in shape in normal protein molecules. As these new cellular prion proteins cannot be broken down, they build up in the body, triggering processes which destroy body tissue. In contrast to viruses, prions are noted for their high resistance to heat and radiation, and are thus harder to inactivate.

Diseases caused by prions

All prion diseases identified thus far are fatal. They occur in both humans and animals. Typically the brain is affected, and in the final phase of the disease the brain tissue is often riddled with holes or displays spongiform inflammation. It appears to take many years or even decades before the symptoms develop.

The following prion diseases – often also described as spongiform encephalopathies – have been identified in humans and animals up to now:

In animals

– Scrapie in sheep, goats

This illness, the most widespread type of spongiform encephalopathy, was first identified over 200 years ago. The symptoms include uncoordinated movements, nervousness and intense itching, often causing the animals to scratch off their fleece.

In 1936 it was proven that the disease is transmissible. Since the prions can enter the grass through the afterbirth, the pastures on which afflicted sheep give birth are infectious for up to three years afterwards.

– FSE – feline spongiform encepholopathy

In the UK about 50 cases of this disease have been reported in domestic and Siamese cats. In all cases the animals had been fed with slaughterhouse scraps. The disease manifested itself in behavioural disorders and ended in death.

– CWD – chronic wasting disease – in elks, mule deer bucks

This disease has been under observation since 1967 in various types of deer in the USA and Canada. The clinical course of the disease is similar to that observed in cows and sheep and ends in death after about 6 months. The disease is probably transmitted via infected pastures, as up to now only those species of deer have been affected that feed direct from the ground in areas in which sheep suffering from scrapie have also grazed.

– TME – transmissible mink encephalopathy

This disease was observed for the first time in 1947 in US mink farms and can be traced to the use of feed containing the carcass scraps of cows and sheep afflicted with scrapie or Downer cow syndrome (now BSE). The disease is manifested in behavioural disorders and ends with the death of the mink after 3 to 8 weeks.

– BSE – bovine spongiform encephalopathy – mad cow disease

In the mid 1980s a major epidemic broke out among cattle. At first the animals became particularly aggressive, then began reeling about helplessly and finally collapsed and died. By early 1996 160,000 cows displaying such symptoms had to be destroyed. Autopsies of the carcasses revealed a sponge-like softening of the brain tissue. This change in the brain tissue was almost identical to that observed in sheep suffering from scrapie, an illness that has been rampant in the British Isles and Iceland for about 250 years. It was quickly ascertained how the disease had been transmitted from sheep to cattle: the carcasses of sheep that had suffered from scrapie had been processed to animal feed and mixed with the feed given to calves. In order to save energy, the prescribed temperature for thermal sterilisation of the feed was reduced in 1981 from 200 °C to 110 °C and the pressure was lowered as well. This change in processing meant that the prions were not destroyed, but could pass from the calves' stomachs into their lymph nodes and subsequently into the brain and bone marrow.

It is still not known for certain whether cattle can be infected directly by members of their own species suffering from BSE. The results of the first studies into this problem point to the possibility of transmission from cow to calf.

In humans

All prion-related diseases in humans share these symptoms: long incubation periods of up to 30 years and the progressive decline of the victim's mental and motor functions ending in death.

– Creutzfeldt-Jakob disease

The incidence of this disease is 1:1,000,000. 10–15 % of cases are hereditary. Sometimes persons are inoculated unintentionally (i.e. they are infected with prions) as a result of medical treatment. Previously, for example, children could be infected after being treated for dwarfism with growth hormones taken from the pituitary glands of deceased Creutzfeldt-Jakob sufferers. This is no longer a danger as now such hormone preparations are genetically engineered.

– GSS (Gerstmann-Sträussler-Scheinker) syndrome

Incidence <0.1:1,000,000. This disease is considered to be a form of Creutzfeldt-Jakob disease that occurs within families (hereditary genetic mutation). It begins with signs of damage to the cerebellum and ends fatally after several months or even years. The disease typically occurs in middle age.

– Lethal familial insomnia

The incidence of this disease is considerably lower than that of Creutzfeldt-Jakob disease. Symptoms: disturbed sleep together with disorders of the autonomic nervous system, followed by insomnia and mental deficiency. The cause of this disease is presumed to be an inherited genetic mutation.

– Kuru

This disease occurs only among certain tribes living in the highlands of Papua New Guinea. Infection probably occurred through ritual cannibalism, where in honour of the dead their brains were eaten by other tribe members (until 1958). Even though the practice of ritual cannibalism has since ceased and the disease is no longer spreading, about 2600 cases have still been registered since 1975.

How prion diseases are transmitted

It is about 15 years since the hypothesis was first put forward that infectious protein particles (prions) could cause certain degenerative illnesses in humans and animals. Being such a departure from conventional wisdom, the hypothesis was treated with deep scepticism and today is still the subject of intense debate. It is certainly unusual that protein particles without genetic material should be able to cause degenerative diseases of the brain.

If prion proteins come into contact with and attach themselves to normal proteins situated on the nerve cells, the host proteins alter their configuration and can adopt that of the prion proteins without changing their chemical composition. These newly created prion proteins can in turn attach themselves to normal proteins. In this way, all the normal protein particles gradually take on the structure of the prions. Once their configuration has been altered, the proteins can no longer be decomposed, but build up in the body where they have a cytotoxic effect on healthy tissue.

Scientists assume that the probability of a prion altering the conformation of a healthy protein is greater the more similarity there is between the two molecules.

Research into the field of prion diseases centres on the so-called prion protein (= PrP). Prion proteins consist of more than 250 chemical components and differ in more than 30 positions between humans and cattle and in 7 positions between sheep and cattle. This could explain the relatively easy transmission of scrapie within the sheep species and much rarer transmission of the disease to other animal species and humans. Position 129 of the some 250 chemical components making up the prion protein is thought to play a key role in the transmission of BSE to human beings. Three different amino acid combinations are possible in position 129, one of which is identical to the PrP found in cattle, making a change in the configuration as described above more likely.

Danger of infection through foodstuffs

Although numerous measures are taken to withdraw infected meat and other foodstuffs from circulation, consumers are palpably concerned.

As yet it has not been definitively proven that BSE can be transmitted to humans through the consumption of beef. March 1996 saw the first official discussion of a possible link between BSE and the Creutzfeldt-Jakob disease in humans. By mid-1996 11 patients had died of a variant of Creutzfeldt-Jakob disease that bears a striking similarity to BSE. While doctors assume that the victims were infected with the disease, it was discovered that all the victims had a certain combination of genes that might heighten their predisposition to the illness. However, no-one dares to assume the converse: that the new variant of Creutzfeldt-Jakob disease poses no danger to people who do not have this combination of genes.

The prevailing opinion in professional journals is that the probability of infection through foodstuffs is relatively low. Most attention has centred on cattle and foodstuffs derived from beef.

The highest concentration of prions are found in the brain, bone marrow and lymphatic tissue of the affected animals, while the concentration of prions in the muscular tissue is about $^{1}/_{1,000,000}$. Milk, milk products and gelatine, by contrast, are considered to be safe. The human intestine constitutes an additional barrier against infection through animal foodstuffs. It is assumed that the process of digestion reduces the chance of infection to 1 in a 100,000.

There is also no indication of any transmission of BSE from cattle to poultry or pigs, as a six–year experiment using BSE-contaminated feed has shown.

It does not even seem possible for humans to infect themselves from sheep carrying the scrapie prion, for in the 250 years since scrapie was first noted no increased incidence of Creutzfeldt-Jakob disease has been registered in the affected areas. In fact, the transmission from sheep to cattle did not occur until man decided to dispose of the carcasses of infected sheep by grinding them up and feeding them to herbivore cattle, thus severely meddling with the natural food chain.

Possible treatment

At present there is no possible treatment for prion diseases in humans.

In order to develop effective treatment it is first necessary to identify the precise transmission mechanism. The hypothesis that genetic disposition enhances the probability of infection first has to be corroborated by large-scale genetic analyses in humans and animals.

Once the mechanism has been identified, a mode of treatment could be developed. One possible therapy would be drugs which prevent the change in the conformation of healthy proteins to a pathogenic structure. Another possibility could be antigens to hinder the production of prion proteins in infected patients.

Tips for the underwriter

It is above all the Liability and Life/Health/Disability classes that could be challenged by prion diseases, e.g. either through potential loss scenarios or in the shape of increased demand for new insurance products such as a policy covering Creutzfeldt-Jakob disease.

Since a transmission of prion diseases from animals to humans is still considered unlikely, and since prion diseases in humans occur relatively seldom and there are no signs of any increase in their incidence, the consequences of these diseases for the Life, Health and Disability classes should remain rather limited.

Exposure is greatest in Liability insurance, where the following loss scenarios are possible in the Environmental Impairment and Product Liability sectors:

- infection of pastures and subsequent epidemics of the disease;
- infection through contaminated animal products such as fodder, foodstuffs, additives (e.g. gelatine), pharmaceuticals and cosmetics, provided transmission of the disease via such products has been proven.

It is not only the manufacturers of such products that are exposed, but also the catering industry and providers of analytical and quality-assurance services in the foodstuffs field.

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