What's new in Alzheimer disease?

Clinical scenario

"Hey, Doc, do you think we will have a preventive treatment for Alzheimer's in our lifetime?" a middle-aged man asks during a routine examination. It is one of those unusual days when things are on schedule and the waiting room is almost empty. You decide to take a moment to talk and ask him what is important to him about this question. You think perhaps he has a fear of getting dementia; from taking the family history, you know his mother has Alzheimer disease (AD). He tells you that he is a researcher and he is fascinated by the early but compelling evidence that AD and other neurodegenerative disorders that are referred to as *prionlike disorders* might be caused by protein misfolding. This has created the possibility of developing new prevention and treatment strategies.

Context

A prion is an abnormal protein that causes progressive protein misfolding in neurologic tissue in both humans and animals. The first known prion disease was scrapie in sheep. Prion diseases of humans are collectively referred to as *Creutzfeldt-Jakob disease (CJD)* and can be sporadic, genetic, or acquired. Acquired CJD is the most rare and the only infectious type; the prions can be transmitted either through dietary exposure (from bovine spongiform encephalopathy or mad cow disease) or from contamination (usually from medical procedures). Creutzfeldt-Jakob disease is a nationally notifiable disease and has a mortality rate of slightly more than 1 per million people per year.[1] There is now growing evidence that misfolded proteins are part of the underlying pathology in other neurodegenerative disorders, including AD, Parkinson disease, and amyotrophic lateral sclerosis (or Lou Gehrig disease), collectively referred to as *prionlike disorders*.[2] The good news is that there is progress in the areas of diagnosis, prevention, and treatment of prion and prionlike disorders.

Evidence

Currently, a definitive diagnosis of CJD requires neuropathic examination of brain tissue from a deceased patient. However, Canada's National Microbiology Laboratory has been working with an international consortium to detect disease-associated prion protein in the cerebrospinal fluid of CJD patients.[2] This means that we might soon be able to diagnose CJD (and one day possibly other protein misfolding disorders) in patients before death.

Much research is also being done in the area of the prevention and treatment of protein misfolding disorders. A recent study showed promising results of a vaccine to prevent the prion disorder called *chronic wasting disease* in deer and elks.[3] Drug development research that involves selective antibody targeting of misfolded proteins is also under way; this has been shown to inhibit prionlike proteins and neutralize their ability to cause cytotoxicity.[4]

The early evidence that protein misfolding might be the underlying mechanism for not only CJD but also other neurodegenerative disorders represents a scientific breakthrough. This has also raised new questions. Prion disease is known to have long, silent incubation periods, resistance to decontamination, and the potential for both zoonotic and health care–based transmissions.[1] Does the same apply for prionlike disorders? Currently, there is no strong evidence to suggest that health care–based transmission of protein misfolding disorders other than CJD occurs.[4]

Bottom line

Neil Cashman, one of Canada's foremost experts in neurodegenerative diseases has concluded: "A new era in diagnosis and treatment of propagated protein misfolding disorders is upon us, offering many opportunities to treat neurodegenerative diseases that were previously untreatable or poorly treatable."[4] Appreciating that dementia might arise from a number of different causes, recent evidence suggests that prevention or treatment of AD might indeed be possible within our lifetime.

La traduction en français de cet article se trouve à **www.cfp.ca** dans la table des matières du numéro **d'août 2015** à la **page e365.**

References

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CCDR Highlights summarize the latest evidence on infectious diseases from recent articles in the *Canada Communicable Disease Report*, a peer-reviewed online journal published by the Public Health Agency of Canada. This highlight was prepared by **Dr Patricia Huston**, a family physician, public health physician, and Editor-in-Chief of the *Canada Communicable Disease Report*.