Test for early detection of BSE, vCJD on horizon?

A new method for detecting abnormal prion proteins is being developed by a research team in Switzerland. The technique, protein misfolding cyclic amplification, could lead to a test for the early diagnosis of bovine spongiform encephalopathy (BSE) or new variant Creutzfeldt–Jakob (vCJD) disease long before any symptoms are visible. Existing tests for BSE are capable only of detecting the disease in cattle after death.

The replication of prion proteins associated with neurodegenerative diseases can take up to 40 years in vivo, but a team led by Dr. Claudio Soto of the Serono Pharmaceutical Research Institute in Geneva has been able to complete the process in a single day. "When an animal or a human being gets infected with the prion, this abnormal protein begins to replicate very slowly and transforms the host's normal protein into abnormal protein," says Soto. "So we thought, why can't we do the same thing in a test tube?"

The abnormal protein grows to form aggregates that remain clumped together for long periods. "The rate of growth depends on the number of units," says Soto. "So we tried letting them grow and then breaking them into little pieces, incubating them again to let them grow, and so on in a cyclical process."

The method is analogous to polymerase chain reaction (PCR), the cyclical technique commonly used to detect DNA by amplification. "You can't use conventional PCR here, because there is no DNA," he added. "We tried to create an amplification system like a PCR, but specially for proteins." Minute quantities of hamster brain tissue infected with scrapie were mixed with normal protein from the brain tissue of healthy hamsters, and ultrasound was used to break apart the prion aggregates (*Nature* 411:810-3). Detection of the resulting abnormal protein was performed by densitometric analysis.

The slow rate of replication has hampered investigation into the structural and infectious properties of abnormal prion proteins. Accelerating the conversion process will allow for in-vitro research aimed at understanding the molecular mechanisms of prion replication. Meanwhile, evidence of blood infectiveness remains circumstantial. Animals injected with large quantities of blood from infected animals have gone on to develop prion diseases, but Soto says there is no assurance that the prion is really present in blood "because none of the methods so far has been able to detect it there. Now, for the first time, we have the chance to examine if it really is there. We have some preliminary results in animals, which are positive. We also have blood from patients with CJD and nvCJD and we will be able to test this very quickly."

Although other neurodegenerative illnesses such as Alzheimer's and Parkinson's disease are not thought to be infectious, they share characteristics with prion diseases. "All these diseases are caused by changes in the shape of a normal protein, which then tends to aggregate, forming deposits in the brain," says Soto. "[This leads to] the death of neurons and brain damage. The molecular mechanisms are similar, so we believe this method could be applied to diagnose these diseases as well." — *Claudia Orellana*, Tübingen, Germany

Beware of DTC ads

With US spending on direct-to-consumer (DTC) advertising now surpassing $100 million a year for some drugs, American physicians are facing growing pressure to prescribe specific products. Will their Canadian counterparts also feel the heat? UBC's Therapeutics Initiative (TI) program thinks they will and is warning them to stand firm. Citing the antibalding drug finasteride as an example, TI program managers noted that 6 men have to be treated for 1 year for 1 man to be satisfied with his new appearance, and if treatment is stopped any benefit disappears within 6 to 12 months (**www.ti.ubc.ca/pages/letter.html**). They said that with MDs already receiving 10 requests for specific drugs from patients weekly, they must ensure that patients know the difference between advertising and a drug's known benefits, known harms and unknown risks. — *CMAJ*

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What do Homer Simpson and Winnie-the-Pooh have in common? Both were subjected to deep and meaningful research in past issues of *CMAJ*'s Holiday Review (*CMAJ* 1998;159[12]:1480-1; 2000;163[12]:1557-9). Our valiant researchers have also studied the impact of the way physicians wear their stethoscope — traditional or "cool" position — as well as the value of chicken soup in treating health problems. You too can contribute to this hallowed quest for scientific knowledge. Remember — very original research is what we are looking for. Dare to be different! Contact Dr. John Hoey (**john.hoey@cma.ca**); 800 663-7336 x2118. — *CMAJ*