

BREAKTHROUGH FOR HUNTINGTONS DISEASE

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Introduction

- What is Huntingtons Disease (HD)? – A husband's view
 - The decline of a wife and mother
 - Early and late symptoms
- A possible cure on the horizon
 - Human trial results
 - What is ASO?
- Latest news and way forward
- HASA's work with Roche SA

Through A Husband's Eyes

HD is a debilitating genetic neurological condition caused by toxic huntingtin protein. Currently no cure.



Gina in the late nineties
before HD

First Signs

- Could mistake for nervous twitches
- Occasional jerk of the torso in bed, and the fidgety wiggles of toes in sandals
- Gina kept busy and spoke less – was it apathy?



Birds migrating as the first signs of winter

HD Diagnosis

- Twitches and jerks got a little more frequent
- The neurologist's examination
- HD DNA Test
 - Pre-counselling session
 - Actual test
 - Results and post-counselling
- Positive diagnosis – a sad confirmation...
- ... but happy news would carry us...



Pregnancy and Motherhood

- Just over a week later... happy days, but it took a toll on Gina's body. By December 2001 when Shannon was born, Gina was displaying following symptoms:
 - Jerking/stiffening of the lower back and torso happened quite frequently.
 - Stiff-fingered hovering over an object before she grasped it.
 - A little two-step shuffle in her walk.
 - She seemed to be a second or two behind the conversation, and had a slightly bemused expression at times, as if what was said made no sense to her.
 - Her weight loss started becoming noticeable.
 - Choking on her food and drinks.

A Bitter Pill to Swallow

- Struggled with motherly chores
- Stressed her out, noticeable anxiety:
 - exasperated, short-breathed moans
 - anxious flicks of bony fingers at her hair at the back of neck



Gina in early 2003

The Gradual Affects

- Anger
- Bitterness
- Irrational attachment to Shannon
- Paranoia
- Illogical and selfish demands
- Unreflective so impossible to explain



Gina on a happy day

The Last Days at Home

- Down to under 40kg
- Percutaneous endoscopic gastrostomy (PEG)
 - Horrible device
 - Keep clean
 - Sore skin
 - Back pressure
 - Smell
 - Undignified
- Urinary Catheter and adult diapers
- Worsening moods / personality



At the End

- Her last years were spent in a frail care home where she needed total care with:
 - Chorea, including stiff flinching of legs and hands, and jerking of torso and neck.
 - Severely unstable gait, leading to a few falls, and eventually leading to inability to walk
 - Difficulty speaking, deteriorating continuously, to no audible speech at all towards the end
 - Short term memory loss
 - Emaciated body
 - The angry, irrational personality of the early and mid-term was replaced by what seemed a more peaceful apathy or resignation in the latter stages. As long as she had her TV and assortment of sweets and biscuits, she sat or lay quietly in her own unknown world.

Months before she died on
30th October 2009
(with speaker's mother and daughter)



A Possible Cure on the Horizon

- Shannon is 17 in December... and at risk.
- September 2014 announcement:
 - Ionis Pharmaceuticals of Carlsbad, California
 - test the safety and tolerability of
 - anti-sense oligonucleotide (ASO) medicine candidate called
 - IONIS-HTTRx in people for the first time



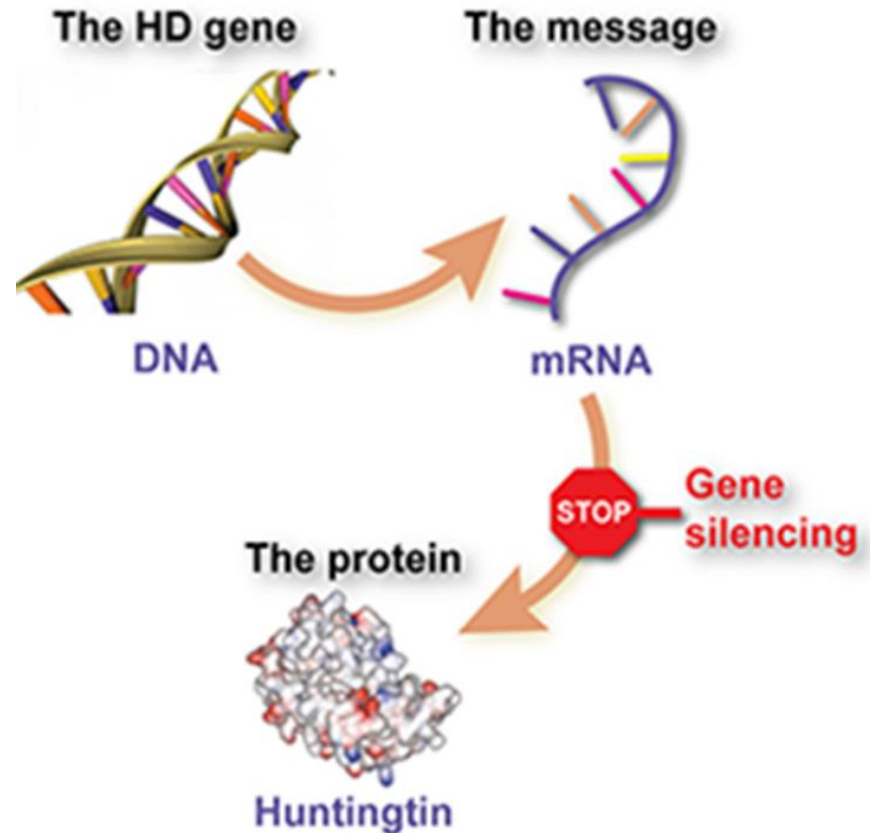
Trial and Results



- IONIS-HTTRx injected directly into cerebrospinal fluid (CSF) through a lumbar puncture
- Expected to diffuse into the brain
- December 2017 announcement and March 2018 published results:
 - Toxic protein decreased by up to 40% to 60% in CSF
 - Correlates to *55% to 80% lowering in the brain*
 - Well tolerated at all doses tested, with 100% of the 46 participants completing the study

What is ASO?

- Gene silencing
- ASO sticks to the mRNA message molecule, making the cell delete the message so the protein doesn't get made



Latest Greatest News

- American Academy of Neurology (AAN) Annual Meeting, April 2018: Participants with lower huntingtin levels also did **better on clinical exams** that test HD symptoms.
- Pharmaceutical giant, **Roche Pharmaceuticals**, has acquired the license to further develop IONIS-HTTRx. They have assembled an experienced international team tasked with the planning and coordinating of a global **Phase 3 clinical trial**
- August 2018: European Medicines Agency (EMA) granted **Priority Medicines** (PRIME) designation to IONIS-HTTRx (already Orphan Status)

HASA and Roche South Africa

- Working together to disseminate information to South African sufferers and to South African neurologists who have expressed interest in being part of trials.
- Roche South Africa has recently decided to support HASA with a grant for 2019. HASA will use this money to enhance its ability to disseminate information and support to the HD community in South Africa and Africa



A Final Snippet of Breakthrough Good News...

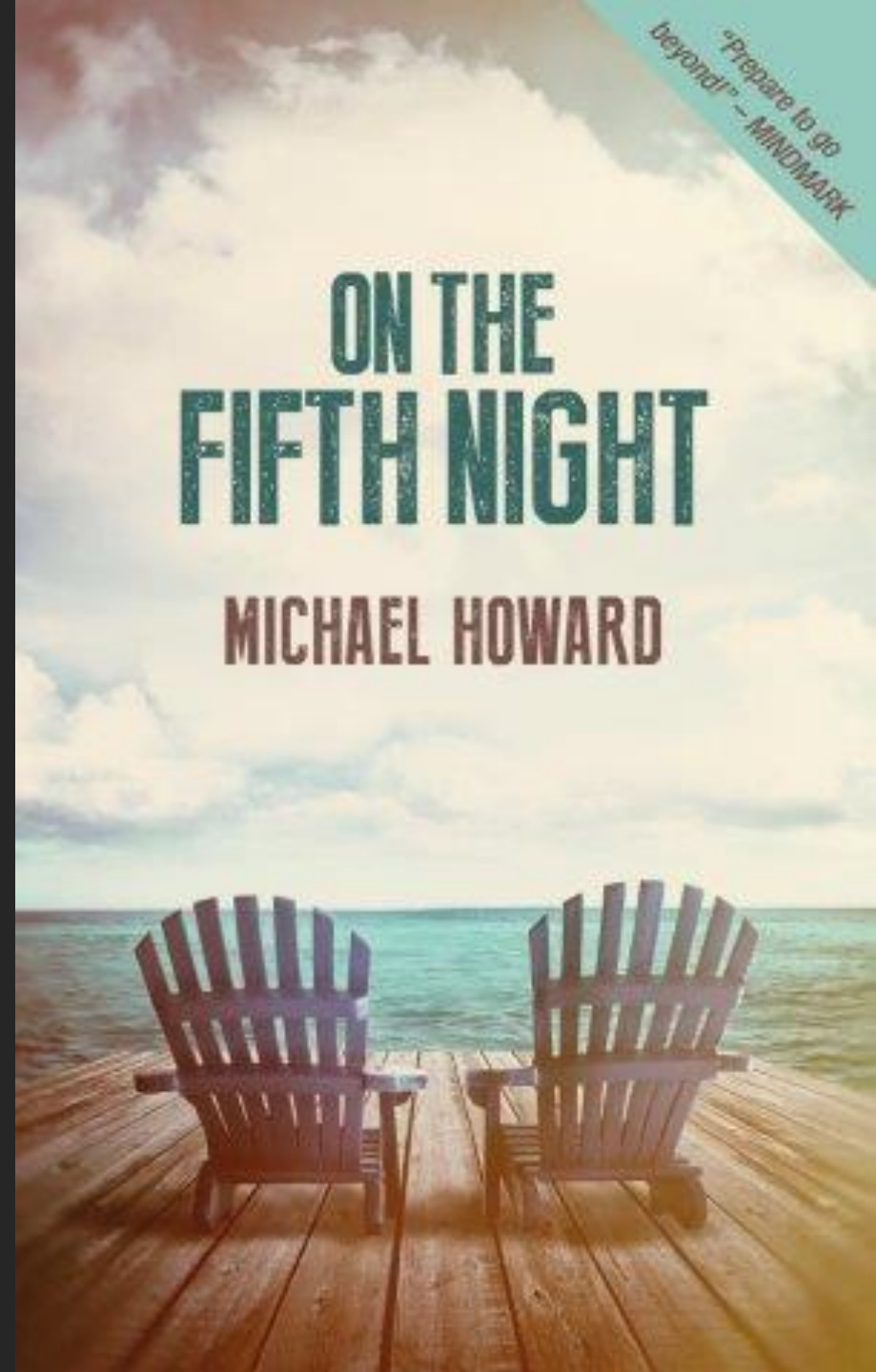
... this is a Spiritual Journey. We are spiritual beings, travelling fleetingly through this disordered realm.

The Benedictines say:

“Keep Death Daily Before Your Eyes.”

*Death is a delusion. See
for yourself.*

*Greta, Anne and Mark
make an unusual love
triangle. Greta is the late
wife who died of
Huntington's disease. And
Anne, the volatile second
wife, sees dead people.*



Conclusion

- HD Sucks but...
- Cures are on the way.
- Let us learn profoundly about ourselves through the disorders of our selves, our loved ones and our societies.
- Thanks. God Bless You All.

