Cure Discovered for Rett Syndrome:
A Review of the Disease and the
Recently Developed Cure

Name

Unit Project I
English 12 Section 35
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Introduction

This article reviews the symptoms, causes, and treatment options for Rett Syndrome (RS) and then focuses on the successful cure for the disease recently developed by Mohammed Taheriazar, MD at the University of North Carolina Medical Research Institute (UNCMRI). UNCMRI released the cure on September 15, 2005 after receiving FDA approval. The cure is a two-week drug treatment called “Bromocriptine-MT,” (named after Dr. Taheriazar) and it restores the health of patients of any age by causing the patient’s DNA to alter the amino acid base sequences in the MECP2 gene in order to return it to a non-mutated state. Scientists have known since 1999 that mutations of the MECP2 gene are the direct causes of the disease.\(^4\)

Considering that it has only been six years since the discovery of the link between MECP2 and RS, it is clear that the UNCMRI Rett Syndrome staff has been working non-stop to find the cure for the disease. Dr. Taheriazar gives all credit for the development of the cure to his wonderful staff of research assistants and to the National Institute of Health (NIH) because of the generous funding they have provided him in his efforts to find the cure.

Symptoms of the Disease

Rett Syndrome occurs most often in female children who undergo a normal growth-rate between birth and 6 months of age, followed by a subtle slowing in their growth-rate. Unless the MECP2 gene mutation is directly observed in the patient’s genes, doctors don’t offer RS as a diagnosis until the patient reaches between 6 and 18 months of age. Doctors must observe an abnormally slow developmental pattern to diagnose the disease. RS can be detected by any combination of behavioral, physiological, and neurophysiological symptoms (described below).

Both Dr. Bengt Hagberg, renowned expert on medical conditions, and the National Institute of Neurological Disorders and Stroke (NINDS) list the symptoms of RS as occurring in
four stages. The first stage of RS symptoms occurs between 6 months and 1.5 years, and is characterized by a decreased head growth-rate, a decline in eye contact, and delayed gross motor skills (e.g. sitting and crawling). A “rapid developmental regression” second stage of RS immediately follows the first.

Stage-two symptoms occur between ages 1 and 4, and last for weeks or months. Doctors name this stage “rapid regression” or “rapid destructive” because patients suddenly lose many of their mental and motor abilities. Approximately 15% of cases also experience seizures during stage two. In addition, during this stage patients lose purposeful use of their hands along with the capacity to communicate with others, and also begin to have difficulties breathing and sleeping. The electroencephalogram (EEG) analysis of a 6-year-old girl with stage II RS is pictured below. Notice the unusually high levels of brain activity in the patient, evident by the continuous and rapid wave oscillations in the left central leads.

Stage-three of RS begins between ages 2 and 10 and ranks as the peak of the disease. This stage is the critical period for determining the patient’s future outlook. Patients begin to gradually recover and regain some of their original abilities lost during stage-two such as alertness, attention span, and communication. The recovery process can, however, take years or decades.
The final stage of the disease (stage-four) can last for decades and usually occurs in patients age 10 and older. At this stage patients lose ambulation and become dependent on wheelchairs; this occurs even if they could previously walk. Patients also experience scoliosis and other skeletal distortions during this period. Nevertheless, physically disabled patients can still develop surprising communication abilities along with an “unexpected capacity to memorize.”

Causes of the Disease

Rett Syndrome is caused by mutations on the X chromosome, and in 80% of cases, on the MECP2 gene of the X chromosome. Further evidence for the genetic basis of RS was obtained after studies examining whether monozygotic (MZ) twins were concordant for RS revealed that there are at least 11 registered MZ pairs (International Rett Syndrome Association registry) in which both twins were infected with RS.\(^1\) Family studies have also shown that the probability of a mother having a second (non-twin) child with RS is only 0.4%. 1 in approximately 12,000 female newborns have the disease. It is important to note that less than 1 percent of patients inherited the disease, therefore random and sporadic mutations during spermatogenesis should be considered the underlying causes in 99% of cases.\(^4\) Table 1 lists the exclusion criteria for RS: \(^2, 6\)

<table>
<thead>
<tr>
<th>Rett Syndrome Exclusion Criteria:</th>
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<tbody>
<tr>
<td>Acquired neurological disorder resulting from severe infections or head trauma</td>
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<tr>
<td>Existence of identifiable metabolic or other heredodegenerative disorder</td>
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<tr>
<td>Organomegaly or other signs of storage disease</td>
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<tr>
<td>Evidence of perinatally acquired brain damage</td>
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<tr>
<td>Evidence of intrauterine growth retardation</td>
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<tr>
<td>Retinopathy or optic atrophy</td>
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<tr>
<td>Microcephaly at birth</td>
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Treatment of the Disease

Until the recently developed Bromocriptine-MT drug, attempts to treat the underlying causes of the disease “have failed to produce any substantive improvements, despite the use of multiple different preparations.” Life expectancy for patients has been a confounding 40 years old. Since clinicians haven’t discovered a cure until now, they’ve only been able to treat and make slight improvements of patients’ symptoms. Through physical therapy, doctors have helped stage III and IV patients to learn to walk again. Furthermore, counselors have used speech therapy to teach patients new communication skills or to relearn the ones they’ve lost. Lastly, doctors have been using pharmaceuticals to treat patients’ seizures and breathing difficulties. Table 2 lists some past pharmacological approaches to Rett Syndrome (p.109).

<table>
<thead>
<tr>
<th>Replacement</th>
<th>Dopamine agonists</th>
<th>Other aminergic agents</th>
<th>Antiepileptic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-dopa/carbidopa</td>
<td>Bromocriptine</td>
<td>Selegiline</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Tryptophan/tyrosine</td>
<td>Pergolide</td>
<td>Tetrabenzine</td>
<td>Sodium valproate</td>
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</tbody>
</table>

Between 1986 and 1990, Zappella and co-workers used the dopamine antagonist bromocriptine in a series of trials involving 12 girls with typical RS. Their results were promising and were the basis for Dr. Taheriazar’s development of the cure for RS. Specifically, Zappella et al. were unable to improve patients’ communication and mood for a significant amount of time, and they were unsuccessful at healing any of the motor problems associated with RS. In contrast, Dr. Taheriazar’s Bromocriptine-MT drug treats the disease at the gene level, which returns patients’ X chromosomes to a normal state. This enables their bodies to begin counteracting all of the effects of the disease, including speech, mood, and temperament problems, motor problems, scoliosis, etc.
Case Study: Candidate for Bromocriptine-MT

The remainder of this article discusses the story of Carolina, a 12 year old girl with Rett Syndrome who is looking forward to being treated next month with Bromocriptine-MT so that she can begin living a normal life. Carolina, the fourth child in her family, was born with RS and she’s suffered from the disease ever since. By the time she was 1 year old she gradually started losing interest in her toys and she was having a lot of problems just with sitting and crawling. Her parents were grief-stricken when they noticed these strange symptoms in their fourth child and immediately took Carolina to the emergency room. Doctors thought it would be a good idea to take a blood sample; after weeks of analysis they saw that Carolina had a mutated version of the MECP2 gene and diagnosed the unlucky girl with RS.

By her third birthday, Carolina could no longer play with her toys because she was constantly doing strange things with her hands, like clapping, wringing, and playing with her tongue. It turned out that these movements were common among RS patients and further confirmed the suspicion that she had RS. Her family became further depressed by this heartbreaking news and they were all worried that she would die soon. Once Carolina reached the third stage of RS at age 7, she began having seizures at least twice every month and could no longer walk or stand up on her own. Since she was also experiencing mental atrophy she would occasionally seem like she had no idea what was going on around her. The poor girl didn’t know what was wrong with her and would spend most of the time crying because she could no longer play games with her three siblings or her parents, or even walk in the garden in the backyard as she used to do every bright, Saturday morning.

When she turned 10 years old Carolina’s parents bought her a wheelchair to push her around in since it seemed that there was no longer any hope of her getting better. She also had
trouble speaking and could only communicate by pointing her eyes at the things that she wanted. Doctors tried to heal some of her symptoms through physical therapy and numerous drugs, but to no avail. It was becoming clear that Carolina was going to live a life very different from other children.

It’s so wonderful to know that Dr. Taheriazar discovered a cure for Rett Syndrome so that children will no longer have to go on living agonizing lives. It is also great to know that Carolina and her family can all rest assured that she will be cured as soon as she finishes the 2-week Bromocriptine-MT cycle. Bromocriptine-MT will restore Carolina’s walking abilities, mental capacity, language skills, and much more, so that she can once again be a happy child and member of her family. Her parents have already sent numerous letters of thanks to Dr. Taheriazar, his research staff, UNCMRI, and to countless other places so that everyone can know how truly good it feels to hear that one’s child will soon be cured of all of her mental and physical disabilities. Discoveries such as Bromocriptine-MT, and success stories like Carolina’s, give hope to all doctors and researchers in the medical field that they might some day find cures to debilitating diseases and return the joy into the lives of millions of people.
Cure Discovered for Rett Syndrome

References


Peer-Editing (Feeder 1B—Rosemary)
Very exhaustive analysis of Caitlin’s paper. Thank you!

Unit 1 Project

Content
- Causes: appropriate
- Progress: comprehensive
- Effects: detailed, and elaborated upon amidst the case study
- Treatment/Therapy: you have theorized a unique treatment option, one born out of your research. Nicely done.

Audience
- Diction & Terminology: appropriately elevated given “insider audience”
- Statistics & Studies: VERY appropriate

Style & Grammar
- Active Voice (throughout): well-done; very little passive voice
- Pathetic Voice (narrative section): appropriate (use of words and phrases like “unlucky,” “no longer,” “heartbreaking,” “poor,” etc.
- Odd & Improper Phrasing
  - “ranks as the peak of the disease”
  - The final stage of the disease (stage-four) can last for decades and usually occurs in patients age 10 and older.” Should be “usually begins in patients . . .”
  - “improvements of patients’ symptoms”
  - Etc.
- Verb tense
  - Some unnecessary shifts in verb tense (for example, bottom of p. 4)
- Punctuation
  - “disease, therefore random” should be “disease; therefore, random . . .”

The Numbers
- 5-7 sources: the first source you reference should be given a “1” (not a “4”)
- 4-6 pages: yes
- References page: yes

Other
- A very original, creative notion you worked with here, that you and your fictional peers have actually developed a cure. You obviously researched the disease enough to make your proffered treatment quite feasible. Thanks for an enjoyable read!

Score: 5.75