PRADER-WILLI SYNDROME

HOWARD WONG 3UU PER. 6

GENETICS SBS11QHG2 #24

PHYSIOLOGY

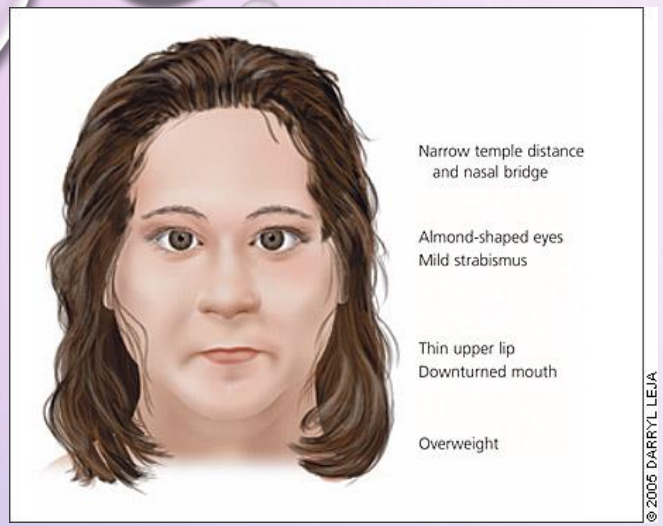

Fig. 1

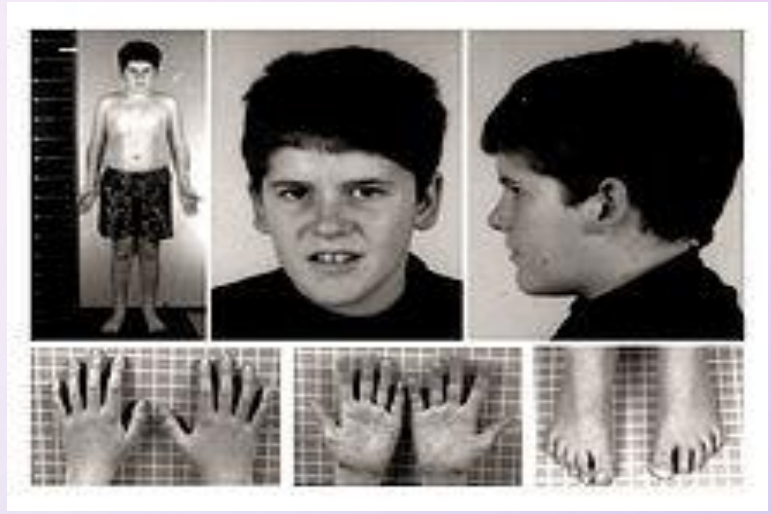

Fig. 2

- Prader-Willi Syndrome affects both the physical and mental state of a person, starting from birth until the rest of his/her life. Some affected parts of the body include the brain, hands and feet, stature and facial features.
- PWS has an onset between 2 to 5 years as doctors usually don't detect any physical or mental sypmtoms of PWS until a baby grows bigger and they are easier to spot.
- Also, PWS occurs in around 1 in 10,000 to 1 in 15,000 births. As there is no specific place that it is found most frequently in, Prader-Willi Syndrome can be found worldwide.
- There is a large range of symptoms for PWS, from hypogonadism (less functional gonads) to hypotonia (weak muscles) to hyperphagia (excessive eating). Other symptoms include narrow temples, thin upper lips, elongated faces, and a prominent nose. Physically, these patients look weak, obese and awkward in movement. Mentally, most PWS patients have mild learning disabilities with a few exceptions. (5% average to low average, 1-2% severe and mentally unstable. Patients outgrow some symptoms while others stay with them for their entire lives.
- PWS was discovered in 1956 by Andrea Prader and Heinrich Willi, (hence where the disease's name came from), Alexis Labhart, Andrew Ziegler, and Guido Fanconi.

MOLECULAR CAUSE

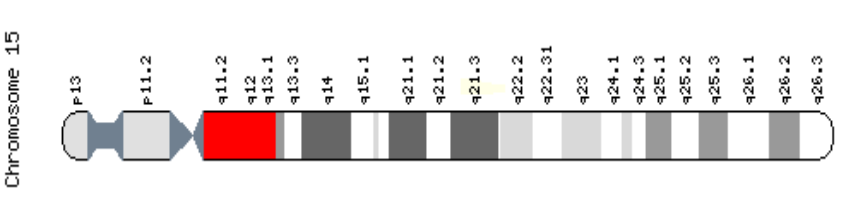

Fig. 3

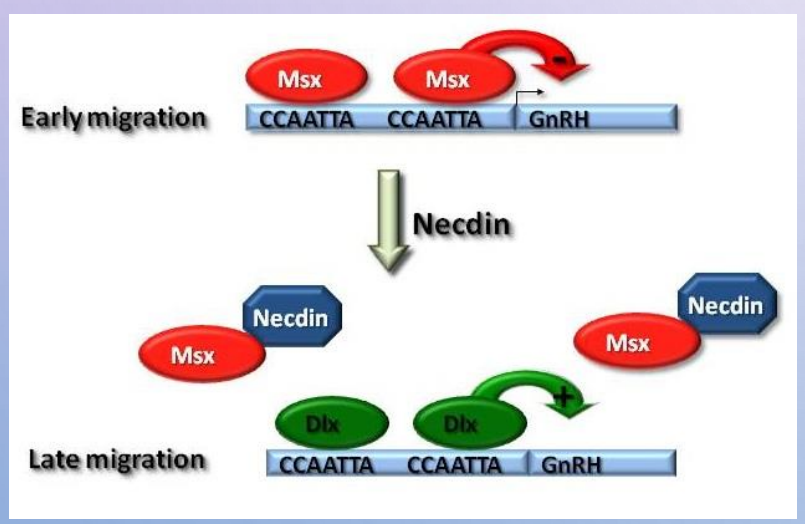

Fig. 4

- Prader-Willi Syndrome is a rare disease that comes from a deletion or inexpression of seven genes on chromosome 15 q11-13. About 70% of patients have a deletion on chromosome 15 (q11-13), 25% of patients have maternal uniparental disomy, and 5% of patients have problems or mutations dealing with imprinting genes and around 1% of patients get PWS from chromosomal abnormalities.
- Some of the genes and proteins that are deleted include SNRPN, necdin, and groups of snoRNAs; SNORD64, SNORD107, SNORD108, SNORD109, 29 SNORD116 and SNORD115. Necdin activates growth regulation and DNA-dependent transcription regulation. Small nucleolar RNAs guide chemical modifications of other RNAs. Small nuclear ribonucleoprotein-associated protein N plays a role in pre-mRNA processing.
- This is a spontaneous mutation as a PWS patient's parents and predecessors show no sign of having PWS before the patient him/herself.
- Siblings of PWS patients have <1% of getting PWS if the affected child has a gene deletion or uniparental disomy (as this all depends on randomness) , =< 50% if the affected child has a mutation of the imprinting control region (deletion inherited from father or mother is carrier), and =< 25% if a parental chromosomal translocation is present.

CURRENT TREATMENTS/DRAWBACKS

- Prader-Willi Syndrome was formerly diagnosed by clinical presentation. The traditional characteristics were hyperphagia, hypogonadism, hypotonia, short stature, obesity and mental disability. A person would go to a clinic to be checked on by a doctor who decided if any of their symptoms matched these. Then, he/she would diagnose the patient with Prader-Willi Syndrome. But, this kind of diagnostic seemed inefficient and had a lot of room for human error where the person might seem to have the syndrome but wasn't diagnosed with it or vice versa.
- One efficient diagnostic is genetic testing, which is one of the newest and most sophisticated technique to be used to test for genetic diseases and disorders. It involves directly examining the DNA of a patient and testing to see what problems it has to be able to classify it to a current genetic disorder. In the case of Prader-Willi Syndrome, a person is diagnosed with it if their genetic testing shows up that they have a deletion in chromosome 15. Genetic testing is recommended for infants and has been responsible for diagnosing more than 97% of cases dealing with Prader-Willi Syndrome.
- Other therapies for PWS include avoiding obesity, taking growth hormones, growing up in enhanced learning environments and undergoing therapies as babies to improve hypotonia, and speech/occupational therapy.. To avoid obesity, PWS patients should try to eat less, while their family, relatives and friends try helping them in the process, and they should exercise frequently. This will also help in preventing diabetes and sleeping disorders while helping Prader-Willi Syndrome patients build up their strength, stamina and overall physical health naturally. Growth hormones will help people improve their physical shape and body strength.
- Downfalls for avoiding obesity include the patient not obeying adults or their peers. Some patients might not exercise enough or even refuse to exercise at all, because of a lack of mental willpower, causing them to become increasing obese, which will lead to diabetes. Growth hormones also have negative side effects if too much of it is taken at a time. The risk of stroke increases in females and behavioral problems emerge from too much of an intake of hormones. The patients would then have to go through behavioral management, which causes more of a hassle to their recovery. There also might be chances that taking growth hormones could lead to sleep apnea.

PROPOSAL CURE/LIMITS

- The only problem with Prader-Willi Syndrome is that there is an absence of the paternal copy of chromosome 15 q11 to 13. So, genetic testing and genetic counseling should be done on a fetus to confirm if the disease is Prader-Willi Syndrome before any other measures are taken.
- If the test for Prader-Willi Syndrome is positive, immediate actions should be done to ensure the safety of the baby. Sections q11 to 13 from chromosome 15 should be replicated from the genes of the fatherto be genetically inserted into the constantly duplicating cells of the fetus through somatic gene therapy.
- This would require extreme care and accuracy to ensure that the genes are successfully inserted into the fetus. Soon, the fetus will also begin producing somatic cells that also contain the chromosome 15 q11 to 13 like a normal fetus would. This operation should be completed as early as possible since this will ensure that all the somatic cells in the fetus contain the missing chromosome sections. Finally, the patient should have mild to no sign of Prader-Willi Syndrome after their treatment and grow up like a normal person.
- Limitations include low success rates and high expenses. To successfully perform this operation, there would have to be precise insertions and as a result, anything can happen. Just a slight miscalculation would cause the whole treatment to fail and the patient would suffer even more than they should. Also, a patient might be missing more than just chromosome 15 q11 to 13, like the whole chromosome itself. Replacing a whole chromosome would be even harder than replacing a segment of it. Conducting tests also require a lot of hi-tech equipment which doesn’t come cheap. Considering all these factors, the success rate would be really low.

WORKS CITED LIST

References

- "Prader-willi Association (USA)." Prader-willi Association (USA). Prader-willi Syndrome Association (USA), 12 Nov. 2012. Web. 4 Mar. 2013. <Http://Www.Pwsausa.Org/Syndrome/Index.Htm>
- "Prader-willi Syndrome - Symptoms, Diagnosis, Treatment Of Prader-willi Syndrome - Ny Times Health Information ." Health News - The New York Times. The New York Times, 7 May 2012. Web. 4 Mar. 2013. <Http://Health.Nytimes.Com/Health/Guides/Disease/Prader-willi-syndrome/Overview.Html>
- "Prader–willi Syndrome - Wikipedia, The Free Encyclopedia." Wikipedia, The Free Encyclopedia. Wikipedia, 1 Mar. 2013. Web. 4 Mar. 2013. <Http://En.Wikipedia.Org/Wiki/Prader%e2%80%93willi_syndrome>

Images

- Slide 1 : Fig. 1 -> HTTP://WWW.AAFP.ORG/AFP/2005/0901/AFP20050901P827-F2.JPG
- Slide 1: Fig.2 -> HTTP://UPLOAD.WIKIMEDIA.ORG/WIKIPEDIA/COMMONS/THUMB/0/00/PWS.JPG/220PX-PWS.JPG
- Slide 2: Fig.3 -> HTTP://UPLOAD.WIKIMEDIA.ORG/WIKIPEDIA/COMMONS/2/24/ANGELMAN.PNG
- Slide 2: Fig.4 -> HTTP://REPRO.UCSD.EDU/FACULTY/MELLON/SITEASSETS/PUBLICATIONS/SLIDE14.JPG