Gene therapy dilemma: Would you tweak your child's genes if it might prolong life but leave her deaf?

Every time we decide to take a drug, we complete a personal risk benefit analysis. For example, will the pain relief promised by this ibuprofen or acetaminophen outweigh the chances of developing a stomachache?

And what if that calculus is a little more intense? Parents of children with a rare genetic disease may be choosing between prolonging their kid's life at the expensive of leaving him deaf according to the Wall Street Journal:

> Families in the drug trial must decide whether to permit the higher doses of cyclodextrin that research shows might arrest the disease. Hearing loss is one side effect. "Deaf or death, what are our options?" said Andrea Marella."We have to keep moving forward."

Andrea's son Andrew has Niemann-Pick disease type C (NPC), a very rare genetic disease that leads to faulty breakdown and movement of fats inside the cells of the body. As the fats build up, people with NPC experience unsteady movements, then dementia and ultimately death.

The drug, cyclodextrin, offers hope to relieve symptoms and prolong quality of life for NPC patients. But it is also likely to cause hearing loss by damaging the tiny hairs called cilia in the outer ear that help amplify sound. The chance of hearing loss is so likely that every child who gets the drug will probably experience at least some. But for the Marellas, the chance to have a few more years of healthy life with Andrew outweighs the risk of deafness.

These complex risk analyses are just one part of an expanding healthcare calculus. One that requires patients and healthcare systems to balance potential harm, potential benefit and cost. Andrew is part of a clinical trial so the medication and associated costs are covered. But in the majority of upcoming treatments genetic disorders, patients and providers will also have to think about costs.

Take for example the drug Glybera, arguably the first gene therapy to hit the market. It will cost $1 million, but cure people with the genetic disorder lipoprotein lipase (LPL) deficiency. The drug is a no-brainer for patients and for healthcare providers, because the costs of treating patients long term so outweighs the cost of the cure. But, insurance providers are still looking at weighs to spread those costs over several years.

More of these so-called orphan drugs are in the pipeline, potentially a lot more. And the costs of developing these treatments, many of which are designed to cure rare genetic disorders is something that insurers and drug companies need to start negotiating right away so patients will have access as soon as they are available, according to Nature:

> As gene therapies start to provide solutions for highly penetrant genetic diseases that had

> been intractable, the hand-wringing over their value and how government and private insurers around the globe will pay for them will likely begin… So far, pricing discussions for gene therapy has remained "under the radar" for many payers in the US, says Troyen Brennan [pharmacy benefit manager at CVS Caremark]. "I've not seen the national health insurers talking much about this, but they will be sooner or later."

How consumers and insurers will evaluate benefits and costs of these gene therapies will likely be an opaque and internal process as it is with other drugs. But there are many rare diseases with fairly straight forward genetic mutations at their root. We are rapidly moving toward the ability to cure them.

Additional Resources

- Alert for athletes and astronauts: Gene editing moving into clinics, results promising, Genetic Literacy Project
- Gene Therapy 3.0: Rise and fall and rise again of gene therapy–For real this time?, Genetic Literacy Project
- Gene therapies target rare diseases, Economic Times

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