

I'm A Human Pincushion And A Damn Lucky One



By *Josh Bloom* — February 21, 2018



Life is good. Photo: Esty [1]

Blaming your parents for your woes is both trite and whiny. No one wants to hear it. But the allergies and asthma that my brother and I got stuck with really are our parents' "fault." Two allergic parents -----> two very allergic sons.

I inherited what is called the "atopic triad" - a delightful combination of asthma, hay fever, and eczema. It isn't as much fun as it sounds. Atopy is the product of a screwed up immune system, and it occurs partly because my white blood cells make way too much of an antibody called IgE. While my ancestors 100,000 years ago may have benefited from a lot of IgE - its function is to fight off intestinal parasites - I don't need it. In the absence of parasites to fight, IgE finds other targets, like pollen, animal, dander, dust, and mold, and it is this mismatch that is responsible for the symptoms. With the exception of a meal at Chipotle, I rarely consume nematodes, but my stupid immune system doesn't realize this.

Fortunately, the pharmaceutical industry is coming out with some game-changing therapies that neutralize IgE and other allergy-causing proteins. It is unfortunate that I was born with these allergies, but I am lucky enough to have access to new biologics - drugs made from living organisms. Biologics are proteins, so they cannot be swallowed in pill form. Proteins are digested in the stomach and do not make it into the blood. So they have to be given by injection. I am taking two different ones.

I have never been so happy to have needles stuck in me. What a difference. Let's take a look at these drugs and see how they work.

ASTHMA

There are four biologics that are approved for moderate-to-severe asthma. They work in similar,

but subtly different ways.

- Xolair (omalizumab, Genentech, and Novartis) is a monoclonal antibody **(1)** that binds to IgE and removes it from the blood. The drug, which is given once or twice per month by subcutaneous injection, is approved for asthma that does not respond adequately to other medications, such as prednisone **(2)**. Xolair is also approved for an obscure condition called chronic idiopathic urticaria, chronic hives with no known cause. But, with any drug that modifies the immune system, there are always risks. Anaphylaxis occurs in about 1 in 1,000 people who get the injection. As a result, you have to sit for an hour or two in the doctor's office after the first few injections and also carry an epi-pen, since the anaphylaxis can occur at any time.
- Sinqair (reslizumab, Teva) is thought to work like Nucala - by inhibiting IL-5-mediated eosinophil production, although this has not been firmly established. It is given monthly by IV. Although it is effective in relieving asthma symptoms, the drug must be administered in a hospital or infusion center equipped to handle anaphylaxis.
- Nucala (mepolizumab, Glaxo-SmithKline) is also approved for asthma, but it works differently. As if we asthmatics don't have enough problems, there is another type of asthma that is caused by an infection-fighting white blood cell called eosinophils. Eosinophilic asthma results when these cells, which are not present in healthy lung tissue, infiltrate the airways, causing [multiple inflammatory responses](#) [2]. One of the key components of this response is interleukin-5 (IL-5). IL-5, a cytokine (2), which drives the production and maturation of eosinophils. Nucala, which is given by injection monthly, has been shown to reduce ER visits and hospitalizations for asthma as well as the dose of maintenance steroid (inhaled powders).
- Fasenra (benralizumab, AstraZeneca/Medimmune), which was approved in late 2017 is another drug for eosinophilic asthma. In Phase III clinical trials Fasenra cut the number of annual exacerbations by half, and half of the patients were able to cut their orally inhaled steroids (such as Advair) by 75%.

ATOPIC DERMATITIS

Talk about an unmet medical need. Eczema - commonly called atopic dermatitis (AD) **(3)** - can be much more than an annoyance. When it's severe it can ruin the lives of sufferers, some of whom have it over their entire bodies. Teens with eczema are more likely to [think about suicide](#) [3].

Until recently, the choice of therapies to treat the rash was poor. For severe eczema sufferers, it came down to steroids, either topical or systemic. Long-term steroid use, whether topical or (especially) systemic, carries with it a long list of side effects, some of which can be very serious.

This all changed in 2017 when Dupixent (dupilumab, Sanofi/Regeneron), the first-ever biological drug for atopic dermatitis was approved. Dupixent, which operates by a similar but different mechanism than the asthma medications, helps about 75% of people with severe AD after 6 months of bi-monthly injections. (With this one, you inject yourself after the first visit. A pre-loaded syringe arrives in a cold pack and you stick it in the fridge until it's time.)

Dupixent is an [interleukin-4 receptor \(IL-4R?\)](#) antagonist (blocker). When this receptor is blocked a number of cellular signals are interrupted, one of them being the production of IgE. If I haven't put you into an irreversible coma by now, take a look at the first drug, Xolair. It binds to IgE, taking it out of circulation. So, you might expect Dupixent to work for asthma. So do Sanofi and Regeneron. An October 2017 [press release](#) ^[5] noted that the drug was effective in reducing steroid use and also improving lung function. The companies are expecting FDA approval to expand the label to include asthma in mid-2018.

COST

New drugs are always expensive, and biologics usually more so.

Nucala costs about \$2,500 per month, roughly \$30,000 per year. Even with insurance, my monthly co-pay was \$375, which I would have happily paid. But that amount dropped by \$375 once I called the company's co-pay assistance program. It took about 5 minutes.

Dupixent costs \$37,000 per year. With insurance and help from the company, it also costs me nothing.

The bargain of a lifetime.

REPORT CARD

I have been taking Nucala for four months. My breathing is now normal and my lungs are clear. When I caught an upper respiratory infection last month I was able to avoid prednisone for the first time in ???

I have had two doses of Dupixent. The itching is about 75% less than before, and the full effect of the drug is not felt until 4 months.

Amazing.

NOTES:

(1) Monoclonal antibodies are clones (identical copies) of antibodies made from a single type of cell. They are generated in mice, isolated, and grown in cell cultures. Then these cells are converted into humanized monoclonal antibodies by genetic modification. This process forms hybrids that contain human and mouse proteins, which prevents the immune system from recognizing them as foreign pathogens. You cannot give mouse antibodies to a human.

(2) You do not want to have to take prednisone. It is terrible, but sometimes necessary. (See [Prednisone: Satan's Little Helper](#) ^[6].)

(3) The terms "atopic dermatitis" and eczema are often used interchangeably, but they are not identical. Eczema is a broader term that encompasses allergic skin inflammation from all sources,

including contact dermatitis - caused by an external irritant. "Atopic" means "away from from the skin," meaning that it is caused by something within the body. It usually occurs along with asthma and allergic rhinitis (hay fever).

Conflict of interest statement: My IRA contains some Regeneron Stock.

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[1] <https://www.etsy.com/listing/229058520/cactus-pincushion-crochet-cactus-green>

[2] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3990389/>

[3] <https://www.sciencedirect.com/science/article/pii/S0022202X15369074>

[4] https://en.wikipedia.org/wiki/Interleukin-4_receptor

[5] <http://investor.regeneron.com/releasedetail.cfm?releaseid=1046107>

[6] <https://www.acsh.org/news/2016/12/12/prednisone-satans-little-helper-10561>