Understanding Anti-Streptolysin O (ASO Titers)
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Anti-streptolysin O is an antibody reaction against streptococcal toxin left over in the body after a specific strep infection – generally Group A Beta-Hemolytic Strep.

1) ASO Titers (aka. levels) need to be compared to a baseline. It is the direction in which the markers are going (up or down) that is more important than overall absolute value.

Some individuals produce very high antibody levels while others do not. Some people may have an elevated baseline. Often there is not a previous test to compare values to, most of the time a doctor or laboratory will measure a known “upper limit of normal” for determining a suspected baseline value for ASO. If your test shows higher than the represented baseline value it is considered positive.

2) So this begs the question of what is the ULN for ASO? There are lots of studies here but what is important is that the studies have a very large range. For example in one study, kids not suspected of GABHS strep in the 5-10 year range, had

- 48% had titers below 100
- 6.8% had titers of 100
- 10.6% between 101-125
- 7.6% between 126-156,
- 22.1% between 157-195
- and 4.5% in 196-244

Unfortunately, even in this study, there didn't seem to be a second measurement taken within 1-2 weeks to look for rise or decline.

3) So "what level of response constitutes a positive?" Could a result of <100 still be an indication of a recent strep infection?

The answer appears to be yes, but only if you have a prior value done by the same lab, using the same technique. Most studies show that subjects will have a response 2-4x their baseline - this statistically could still fall within this "normal" range depending on the individual. So again, the importance is to look at trends and not absolute values.
4) What about falling titers? Does a high number indicate a current strep infection?
The answer seems to be no. There is just no good study about how fast ASO titers fall and what drives the rate of fall. Thus a single sample really gives no good indication of direction. Most studies agree that the rise is within a week of infection with a peak at 4 weeks, but there isn't a study of whether this peak remains if the initial infection goes untreated. So could someone with an untreated strep infection have a declining ASO titer? The answer appears to be yes.

For example, the most recent study by Kurlan [June 2008 - Pediatrics] has one subject that has positive throat cultures for 23 of 25 months but the ASO titers are falling within this entire time. What does this mean? No one knows.

5) Do all strains of strep produce an ASO response?
The best study I've found on this is Kaplan's 2003 paper "Immune Response to Group A streptococcal C5a Peptidase in Children: Implications for Vaccine Development." What this paper shows is that despite positive strep cultures on day 1, at a subsequent visit 4 weeks later,

- 46% of subjects presented no ASO rise,
- 55% presented no Anti-DNAseB rise,
- and 37% presented no rise of either ASO nor Anti-DNAseB

There also seems to be good research indicating that skin GABHS infections does not produce ASO response despite producing Streptolysin O.

What does this mean?
Does this mean that the test was bad? That some strains don't produce the streptolysin O protein? That some people don't mount a high immune response? That the individual is a strep carrier? That the strep was going on for some time and the ASO titers have already fallen? That skin GABHS infection differs from pharyngitis GABHS? The answer is that the scientific community doesn't know. There has been no careful study of the decline rate of ASO titers and the entire field of "strep carriers" is not at all clear.

So summarizing,

- A rising ASO titer (regardless of absolute value) is an indication of GABHS strep; however, you need a baseline to be sure it is rising.
- A falling ASO titer indicates that there was strep, but no one knows when.
A high ASO titer could be anything including that the titer is falling, rising, or just a high baseline. Statistically it is likely to be a falling titer.

Most will treat a titer of > 400 IU's as a falling titer (i.e., that there was once a strep infection sometime in the past). But the exact time of the infection is not known.

The interpretation of a low ASO titer is unclear. There could have been an infection and the titer has already fallen, the baseline for the person could be low, the individual may not respond with a strong immune response, the strain may not produce significant amounts of streptolysin O.

One final comment, Swedo does not require high ASO titers or even rising ASO titers to diagnose PANDAS. The titers are checked only when a positive strep culture is not available and you are retroactively looking for an indication of past infection. The flaw with using titers as an indication of prior strep infection is (as I stated above) that "low" values can still be associated with prior strep infections since the rate of ASO titer decline is not known, most people only have a single sample, and the ASO response is variable across individual and strep type.