This Week's Citation Classic®

Goodwin J S & Webb D R. Regulation of the immune response by prostaglandins. *Clin. Immunol. Immunopathol.* 15:106-22, 1980.
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This paper reviewed the evidence for a role for prostaglandin E (PGE) as an endogenous regulator of immune function. We concluded that PGE acted as a feedback inhibitor of T-cell proliferation and function, but that the available data on PGE in B-cell function was too conflicting to draw general conclusions. [The *SCI*® indicates that this paper has been cited in over 570 publications, making it the most-cited paper from this journal.]

Prostaglandins and the Immune Response

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In writing about my first *Citation Classic*,[1] I discussed my mentors in immunology, Ron Messner and Ralph Williams, and also other scientists whose ideas influenced mine. However, this present *Citation Classic* is a review article. Review articles are exercises in expressing complex concepts clearly on paper; in which case, my major influences were my sophomore high school English teacher, John Barrett, and also the Department of English at Amherst College, which forced all freshmen to write three essays a week for the entire year.

Little has been written about techniques for writing a good review. In academic circles review articles rank somewhere below Little League coaching on a CV. A popular definition for being over-the-hill is when the ratio of reviews to original papers published in a year exceeds one. By that standard, the entire field of geriatrics (my clinical specialty) is over-the-hill. Certainly, many reviews are terrible—long compilations of isolated facts with little attempt at interpretation. However, the power of a good review can be substantial.

When I was asked by Hugh Fudenburg to put together a critical review on the role of prostaglandins (PGs) in the immune response, the field was exploding with clearly conflicting observations. Among investigators of arachidonic acid metabolism, a common way of dealing with observations that conflict with one's own is to ignore them. Another too popular method, at least in private, is to simply state that one "doesn't believe" the other laboratory. This is silly. Many of the conflicting observations are published by very good investigators, with results on both sides of the conflict reproduced by other laboratories.

My way of dealing with the problem of how to discuss all the conflicting studies was to ask Dave Webb to coauthor the review. In just about any system that we had examined, his laboratory and mine had come up with different answers. He found that suppressive PGs were produced by adherent T cells; I thought they came from monocytes. I found that prostaglandin E directly inhibited T-cell proliferation; he showed it worked indirectly by inducing suppressor cells. He found profound effects of blocking PG production on antibody production *in vivo*; I found almost none. Here, clearly, was the perfect team to write a review on PGs and immunity. We agreed on almost nothing but that something important was going on. What we tried to do was to construct a paradigm into which would fit the greatest percentage of published observations relative to PGs and immunity, and then also clearly identify and discuss those observations that did not fit. Our assumption was, and still is, that reality will be best approximated when the paradigm developed can explain all or nearly all experimental observations. To ignore seemingly conflicting results for the sake of clarity in writing a review only serves to promote the continued existence of clearly unsatisfactory paradigms. Contradictory results can tell us something important if we are clever enough to figure out how to fit them together.

Over the past 10 years, the study of the role of arachidonic acid metabolites on immune function has continued to grow,[2-4] as have the number of conflicting observations. Sooner or later, some clever person is going to resolve the conflicts, making the task of future review writers much simpler but also perhaps less interesting.

1. **Goodwin J S.** Citation Classic. Commentary on *N. Engl. J. Med.* 297:963-8, 1977. (Cited 545 times.) *Current Contents/Life Sciences* 28(7):17, 18 February 1985.
2. **Goodwin J S,** ed. *Prostaglandins and immunity*. Boston, MA: Martinus Nijhoff, 1985. 209 p.
3. **Behrens T & Goodwin J S.** Control of the immune response by arachidonic acid metabolites. *Agent. Action.* 26:15-21, 1989.
4. **Hwang D.** Essential fatty acids and the immune response. *FASEB J.* 3:2052-61, 1989.

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