

## Staphylococcus-Related Glomerulonephritis and Poststreptococcal Glomerulonephritis: Why Defining “Post” Is Important in Understanding and Treating Infection-Related Glomerulonephritis

Richard J. Glassock, MD,<sup>1</sup> Anthony Alvarado, MD,<sup>2</sup> Jason Prosek, MD,<sup>2</sup> Courtney Hebert, MD,<sup>2</sup> Samir Parikh, MD,<sup>2</sup> Anjali Satoskar, MD,<sup>2</sup> Tibor Nadasdy, MD,<sup>2</sup> John Forman, MD,<sup>3</sup> Brad Rovin, MD,<sup>2</sup> and Lee A. Hebert, MD<sup>2</sup>

A spate of recent publications describes a newly recognized form of glomerulonephritis associated with active staphylococcal infection. The key kidney biopsy findings, glomerular immunoglobulin A (IgA) deposits dominant or codominant with IgG deposits, resemble those of IgA nephritis. Many authors describe this condition as “postinfectious” and have termed it “poststaphylococcal glomerulonephritis.” However, viewed through the prism of poststreptococcal glomerulonephritis, the prefix “post” in poststaphylococcal glomerulonephritis is historically incorrect, illogical, and misleading with regard to choosing therapy. There are numerous reports describing the use of high-dose steroids to treat poststaphylococcal glomerulonephritis. The decision to use steroid therapy suggests that the treating physician believed that the dominant problem was a post-infectious glomerulonephritis, not the infection itself. Unfortunately, steroid therapy in staphylococcus-related glomerulonephritis can precipitate severe staphylococcal sepsis and even death and provides no observable benefits. Poststreptococcal glomerulonephritis is an authentic postinfectious glomerulonephritis; post-staphylococcal glomerulonephritis is not. Making this distinction is important from the perspective of history, pathogenesis, and clinical management.

*Am J Kidney Dis.* ■(■):■-■. © 2015 by the National Kidney Foundation, Inc.

**INDEX WORDS:** Post-staphylococcal glomerulonephritis; post-infectious glomerulonephritis; latent period; kidney biopsy; renal disease; nosology; nomenclature; medical error; steroid treatment.

### The Domain of Postinfectious Glomerulonephritis

We suggest, based on evidence discussed in this article, that the domain of postinfectious glomerulonephritis should be occupied only by conditions that manifest all 3 of the following criteria: the glomerulonephritis is preceded by an infection that resolves with or without antimicrobial therapy; the infection is followed by a latent period, lasting more than several days and up to a few weeks, during which the patient returns to or toward his or her usual state of health; and the latent period ends with the acute onset of features of glomerulonephritis (specifically glomerular hematuria and proteinuria) and often some decrease in kidney function.

If one accepts this criteria-based diagnostic algorithm, poststreptococcal glomerulonephritis is the poster child for postinfectious glomerulonephritis. The pathogenesis of this paradigm is that a nephritogenic strain of  $\beta$ -hemolytic streptococcus causes an infection that usually is a pharyngitis, less commonly an impetigo or cellulitis. Early in the infection, and before there is an antibody response to the infection, antigens derived from the streptococcal organism enter the circulation and deposit in glomeruli. Later, as the antibody response to the streptococcal antigens flourishes, the infection becomes suppressed but the streptococcal antigens continue to enter the circulation. However,

now the streptococcal antigens combine with circulating antibodies to form immune complexes. When these circulating immune complexes achieve a certain molecular size, configuration, or charge, they deposit in glomeruli. In addition, the circulating antibodies can bind to the streptococcal antigens previously deposited in glomeruli. This leads to in situ immune complex formation. Together, the deposited circulating immune complexes and those formed in situ gradually accumulate to inflict a clinically significant glomerulonephritis days to weeks after the infection has cleared.<sup>1-3</sup> Local activation of the alternative complement pathway by the deposited streptococcal antigens also can be involved.<sup>1</sup>

From the <sup>1</sup>Geffen School of Medicine at UCLA, Los Angeles, CA; <sup>2</sup>Ohio State University Wexner Medical Center, Columbus, OH; and <sup>3</sup>Renal Division, Brigham and Women's Hospital, Boston, MA.

Received July 22, 2014. Accepted in revised form January 9, 2015.

Address correspondence to Lee A. Hebert, MD, Ohio State University Wexner Medical Center, Division of Nephrology, 395 W 12th Ave, Ground Fl, Columbus, OH 43210. E-mail: [lee.hebert@osumc.edu](mailto:lee.hebert@osumc.edu)

© 2015 by the National Kidney Foundation, Inc.

0272-6386

<http://dx.doi.org/10.1053/j.ajkd.2015.01.023>

It is not clear whether streptococci are the only organisms that can cause a postinfectious glomerulonephritis, as discussed later in this article. However, it is clear that staphylococcus-associated glomerulonephritis, now widely referred to as “post-infectious” or “poststaphylococcal” glomerulonephritis, does not belong in the domain of a postinfectious glomerulonephritis.

### History of the Term Postinfectious Glomerulonephritis

The precise origin of the term postinfectious glomerulonephritis is shrouded in the mists of history. However, as described in the excellent review by Rodriguez-Iturbe and Batsford,<sup>1</sup> 17th century physicians recognized that “edematous swelling and... dark and suppressed urine” was a “feared complication” of the convalescent period of “scarlet fever.”<sup>1(p1,094),4</sup> Further detail of the duration of the convalescent period, which later was referred to as the latent period, was provided by Wells<sup>5</sup> in 1806 and Bright<sup>4</sup> in 1836. The latent period now generally is regarded as about 1 to 4 weeks.<sup>6-9</sup> Some authors emphasized that the “preceding” or “prior”<sup>10</sup> infection often was a pharyngitis or impetigo that was so unremarkable that its existence had to be extracted by direct questioning of the patient.<sup>8</sup>

By the 1920s, multiple lines of evidence emerged indicating that a streptococcal infection, particularly as a pharyngitis or impetigo, was the most common infection type preceding the onset of acute glomerulonephritis.<sup>11</sup> However, the term poststreptococcal glomerulonephritis apparently was not used in publication until 1959, when David Earle and Robert Jennings described their concept of the natural history of “post streptococcal glomerulonephritis.”<sup>7</sup> It is clear that in their use of the prefix “post,” Earl and Jennings were acknowledging the historically puzzling circumstance of acute glomerulonephritis developing many days or weeks after a preceding infection had resolved. Like their predecessors, Earle and Jennings described the interval between the infection and the onset of glomerulonephritis to be “several weeks.”<sup>7</sup> Relevant to this discussion, in their landmark publication, the authors also described a case of glomerulonephritis associated with streptococcal endocarditis. However, they notably did not describe this condition as poststreptococcal glomerulonephritis.<sup>7</sup>

The notion that poststreptococcal glomerulonephritis generally is the product of a resolved infection is echoed in recent and authoritative reviews.<sup>1,12</sup> Also consistent with this idea is that antibiotic therapy does not reduce the occurrence of nephritis, although it reduces the development of acute rheumatic fever, another sequela of streptococcal pharyngitis.<sup>13,14</sup> Nevertheless, reports from the preantibiotic era document that streptococcus can cause acute glomerulonephritis during the course

of a severe subacute streptococcal infection (for example, case IV in Longcope et al<sup>11</sup>). So, the streptococcal infection need not fully resolve in order for an associated acute glomerulonephritis to emerge. Even so, the prior resolution of infection is the most consistent and intriguing feature of poststreptococcal glomerulonephritis.

### History of the Term Poststaphylococcal Glomerulonephritis

In the past several years, there have been at least 17 publications that have described an unusual form of glomerulonephritis that develops in people with a subacute or chronic infection with *Staphylococcus aureus* (most commonly methicillin resistant [MRSA]).<sup>15-32</sup> The remarkable feature of this glomerulonephritis is its resemblance to immunoglobulin A (IgA) nephritis in that the glomerular immune deposits usually consist of IgA that is either dominant or codominant with IgG and often accompanied by C3 deposition. In these recent publications, the rationale for naming this condition “post-infectious” or “poststaphylococcal” glomerulonephritis often was not stated. However, some authors required that at least 3 of the following criteria be present to merit the diagnosis of poststaphylococcal glomerulonephritis: the glomerulonephritis is preceded by an infection, likely staphylococcal in nature; serum C3 level is less than normal; kidney biopsy shows subepithelial humps in glomerular capillaries; glomerular IgA deposits in the mesangium and capillary walls are dominant or codominant with IgG; and a proliferative glomerulonephritis is present.

This definition can be faulted in a number of ways. First, to describe the glomerulonephritis as post-infectious because the glomerulonephritis develops after the infection prompts the question, What other form of infection-related glomerulonephritis can there be? Certainly there is no basis for a “preinfectious glomerulonephritis” (ie, the glomerulonephritis appears before the infection). Also, if staphylococcus-associated glomerulonephritis merits the term post-infectious glomerulonephritis, surely every form of infection-related glomerulonephritis warrants the use of “postinfectious.” For example, human immunodeficiency virus-associated nephropathy (HIVAN) would become “post-HIVAN,” endocarditis-related glomerulonephritis would become “postendocarditis glomerulonephritis,” and so on. In this context, it can be seen that the prefix “post” applied to staphylococcus-related glomerulonephritis is either illogical (there is no preinfection-related glomerulonephritis) or redundant (all forms of infection-related glomerulonephritis would need to have the prefix “post” added).

Download English Version:

<https://daneshyari.com/en/article/6157489>

Download Persian Version:

<https://daneshyari.com/article/6157489>

[Daneshyari.com](https://daneshyari.com)