This Week's Citation Classic

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Bruton O C. Agammaglobulinemia. *Pediatrics* 9:722-8, 1952.
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This paper presents observations over a four-year period on a four- to eight-year-old boy who had numerous serious infections and pneumococcal septicemia ten times. He was found to have no gamma globulin and when treated with gamma globulin his severe infections ceased. [The *SCI*® indicates that this paper has been cited in over 335 publications since 1961.]

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"After World War II, I was assigned to the Walter Reed Army Hospital to initiate a pediatric training program. It was there that I observed a four-year-old boy who had numerous infections and pneumococcal septicemia ten times. As chief of the service, with frequent rotation of interns and residents, it was necessary to assume personal responsibility for this very serious and most difficult medical problem. Essentially, I was on call to the boy around the clock. The onset of his attacks appeared quite suddenly; he often left home for school apparently well, only to have his teacher call to say that he was very ill with chills and fever. Fortunately, he always responded to penicillin and his blood culture was positive for pneumococci ten times. One can only speculate on the significance that penicillin was discovered the year he was born, and thus explain why someone had not discovered this condition previously. These patients probably just did not live long enough for their true deficiency to be recognized.

"It was obvious early on his second admission to the hospital in 1946 that he had a very unique disease, which many consultants and the literature were not helpful in solving. In the meantime, I could keep him alive with penicillin and give him pneumococcal vaccines in hopes of boosting these antibodies. There was no antibody increase with the pneumococcal vaccines used, and no response to several other bacterial vaccines given him.

"With repeated, very severe infections it was expected that his blood gamma globulin would be abnormally high; however, when this laboratory test became available, we found that just the opposite was true. He had no measurable gamma globulin in his blood serum according to the electrophoretic method used to determine it; thus, he had agammaglobulinemia.

"No gamma globulin—give him some. This I did and with very gratifying results. He no longer had the severe infections and/or septicemia with the administration of gamma globulin at monthly intervals. Treatment was continued for 14 months before I felt confident enough to publish these unique findings and was completely unprepared for the interest engendered by the report. It suggested many avenues for investigation, resulting in a flood of papers pertaining to the immune mechanism,[1] as well as an enlarging of the nomenclature of immunodeficiency diseases in man.

"Honors have been few as a result of this paper; however, a quote from Robert A. Good's introduction to the third workshop, 1967, on immunodeficiency diseases in man, is highly prized: 'Bruton's discovery of agammaglobulinemia in 1952 not only introduced a new concept of human disease, but opened a veritable Pandora's box for immunobiology.' This has proved to be true as any current general textbook of medicine or pediatrics will reveal.

"I believe my paper has become a *Citation Classic* because it opened for study a most important system in the human body, one which had been neglected for a long time."

1. Norman P S & Lichtenstein L M. Immune responses in man. (Harvey A M, Johns R J, McKusick V A, Owens A H & Ross R S, eds.) *The principles and practice of medicine*. New York: Appleton-Century-Crofts, 1980. p. 1073-9.