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Letter to the Editor

Humoral Immunity against *Bordetella pertussis*: Antibodies or B Cells?

Kirimanjeswara et al. (5) studied the role of B cells and antibodies in immunity to *Bordetella* by using murine infection models for *Bordetella bronchiseptica* and the human pathogens *B. pertussis* and *B. parapertussis*. They showed that although B cells are required for efficient clearance of all three *Bordetella* species, intraperitoneal injection of murine immune sera results in clearance of *B. bronchiseptica*, whereas the human pathogens persist. From these data and results of previously published studies which failed to show opsonic activity of human immune sera in vitro (7), they conclude that *Bordetella* species that are pathogenic for humans may have acquired the capacity to evade the human humoral immune response (5). The study by Kirimanjeswara and colleagues is a valuable contribution to the field. However, an alternative explanation for their results should not remain unmentioned.

Recently published studies have clearly shown that human immune sera efficiently induce leukocyte effector functions towards *B. pertussis* (6). *Bordetella*-specific immunoglobulin G (IgG) and IgA were shown to be capable of inducing phagocytosis, respiratory burst, and bacterial killing (2, 6). It was furthermore shown that *B. pertussis* is less efficiently cleared from mice deficient for IgG receptors (FcγR) (3, 4), which suggests that IgG is also crucial for the induction of leukocyte effector functions in vivo. Taken together, these data challenge the conclusion by Kirimanjeswara et al. that *Bordetella* species that are pathogenic for humans have acquired the capacity to evade humoral immune responses.

We feel that data from studies using the combination of inbred mouse strains and human pathogens should be interpreted with care. Their limited major histocompatibility complex repertoire may preclude the generation of a specific immune response of sufficient diversity, which is required for efficient host defense. Although Kirimanjeswara et al. showed that antibody titers and IgG subclass profiles did not differ between mice infected with murine *Bordetella* pathogens and those infected with human *Bordetella* pathogens (5), they did not document antibody specificities. Importantly, recent studies showed that not all *Bordetella*-specific antibodies trigger phagocyte effector functions; rather, opsonic activity of sera primarily depends on the presence of specific antibody subsets. Only pertactin-specific antibodies in human immune sera displayed opsonic activity and induced phagocytosis by human leukocytes (1). Although it remains to be established which *B. bronchiseptica*-specific antibodies (pertactin specific or others) display opsonic activity, documenting the specificity in addition to antibody titers in sera from mice seems mandatory for the interpretation of the results obtained by Kirimanjeswara et al. We look forward to sharing this information with them in the near future.

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Authors' Reply

We are in agreement with Drs. Rodriguez and van der Pol that antibodies are important in the clearance of *B. pertussis*, as demonstrated in our paper and previously by multiple groups. Our discussion focused on the observation that adoptively transferred antibodies clear *B. bronchiseptica*, but not *B. pertussis*, within 3 days, and we offer differential antigen recognition as one possible explanation. It is well-established that adoptively transferred antibodies require more than 1 week to clear *B. pertussis* from naive mice, and the contribution of different antigens is a topic of investigation in multiple laboratories.

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