Functional Indicators of Humoral and Cellular Immunity in Viral Infections *in Vivo*: A Comparative Analysis

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Experimental findings are presented characterizing the relative protective roles of humoral and cell-mediated immunity in classic and African swine plagues and supporting the notion of asymmetry of these two effector arms of immunity.

Key Words: *antiviral immunity; effectors of humoral and cellular immunity; immune response asymmetry*

Immunity in viral infections is usually evaluated on the basis of empirically chosen tests. It is common practice to resort to model virus-neutralizing reactions, even though they differ fundamentally in their immunological essence from what happens *in vivo* [4]. In reality, depending on the pathogenetic stereotype of a particular infection, effector reactions develop nonuniformly - a phenomenon sometimes referred to as "asymmetry in the effector arm of immunity." Experimental identification of the most important effector reaction is a difficult task [2] and, in our view, no adequate conceptual framework for doing this exists as yet.

The purpose of this study was to compare, in broad terms, the two arms - antibody- (humoral) and cell-mediated - of the immune response in classic and African swine plague (CSP and ASP). These two infections were selected because of their opposite immunological stereotypes: the main indicator of immunity in CSP is the activity of virus-neutralizing antibodies [1], whereas in ASP no virus neutralization occurs but prototypal cell-mediated reactions have been described, such as antibody-dependent cellular cytotoxicity (ADCC) and activity of cytotoxic T lymphocytes (CTL) [3,5,6].

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MATERIALS AND METHODS

Two- to four-month-old gilts belonging to a large-bodied breed of white swine were immunized with the virus of a live vaccine (LK vaccine developed at the All-Russian Institute of Veterinary Virology and Microbiology) against CSP or with an avirulent (FK) variant of the ASP virus. They were later challenged with the virulent Shi-Myn strain of the CSP virus in a dose of 1000 LD_{50} or the F-32 strain of the ASP virus in a dose of 10,000 LD_{50}. Characteristics of the virus strains and variants, the procedures for titration of the CSP virus based on the $CCID_{50}$ (median cell culture infective dose) in PK-15 cells and of the ASP virus based on the HAU_{50} (median hemagglutinating unit) in A cells of swine bone marrow, the neutralization reactions for the CSP virus, and the tests for ADCC and CTL directed against the ASP virus have been described previously [1,5,6]. In each group of gilts (7 to 20 animals per group), the response to the challenging dose was evaluated statistically by recording percentages of the animals protected from death, clinical manifestations of the disease, and viremia. Details of individual tests are given below.

RESULTS

Humoral immunity in gilts with CSP. Figure 1 summarizes the data on the reactions of animals given

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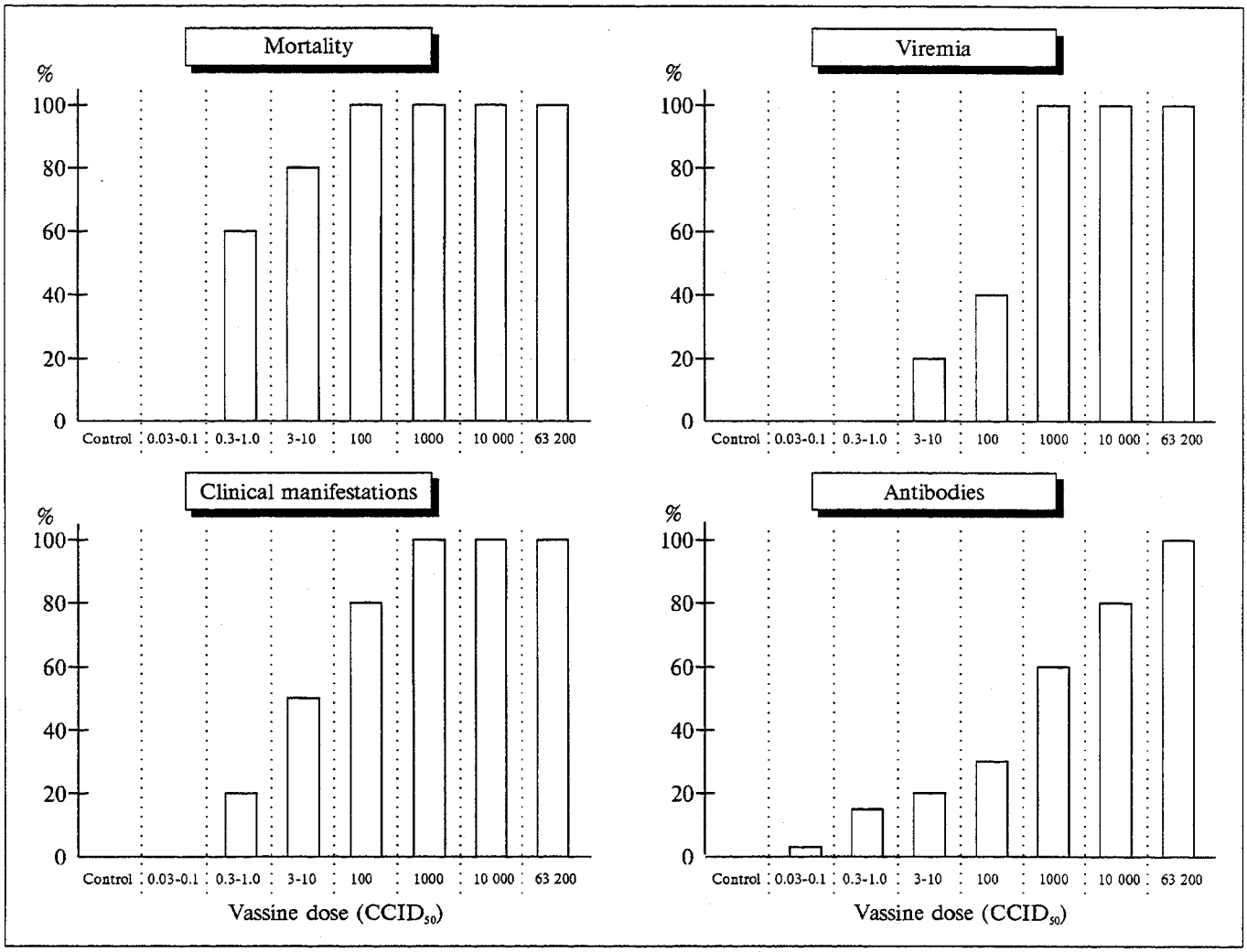

Fig. 1. Levels of virus–neutralizing antibodies and of the protection against death, clinical manifestations of disease, and viremia after challenge in gilts immunized with different doses of the vaccine virus.

the LK vaccine in various doses and challenged 14 days later. Antibody production was estimated on day 14 postimmunization, taking as 100% the antibody titer in the animals administered the highest dose of vaccine. Animals with a virus titer of ≥0.63 log $CCID_{50}$/ml blood were considered to have viremia. Animals with any deviations from normal (these ranged from a body temperature of ≥40°C to the typical symptom complex) in comparison with the control group were regarded as having clinically ma-

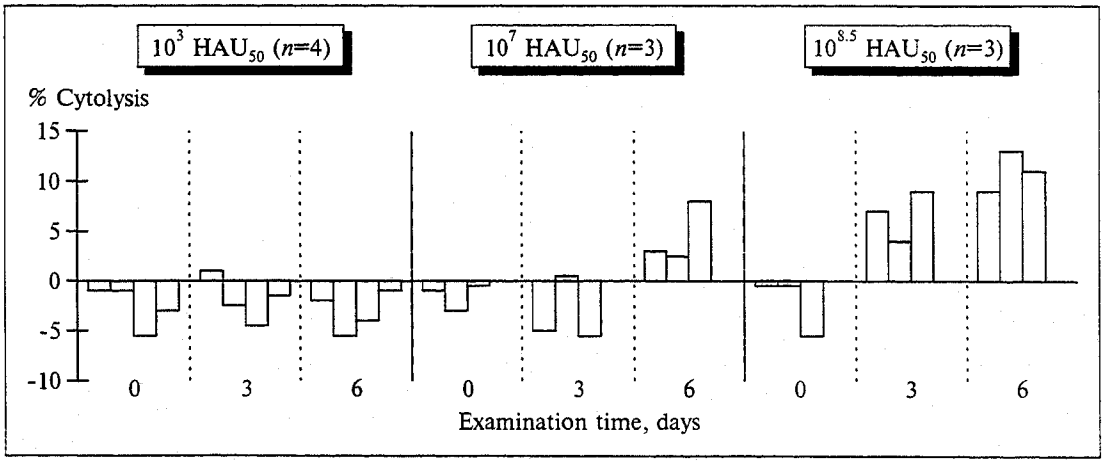

Fig. 2. Antibody activity in ADCC in gilts inoculated with the avirulent FK variant of the ASP virus in different doses.

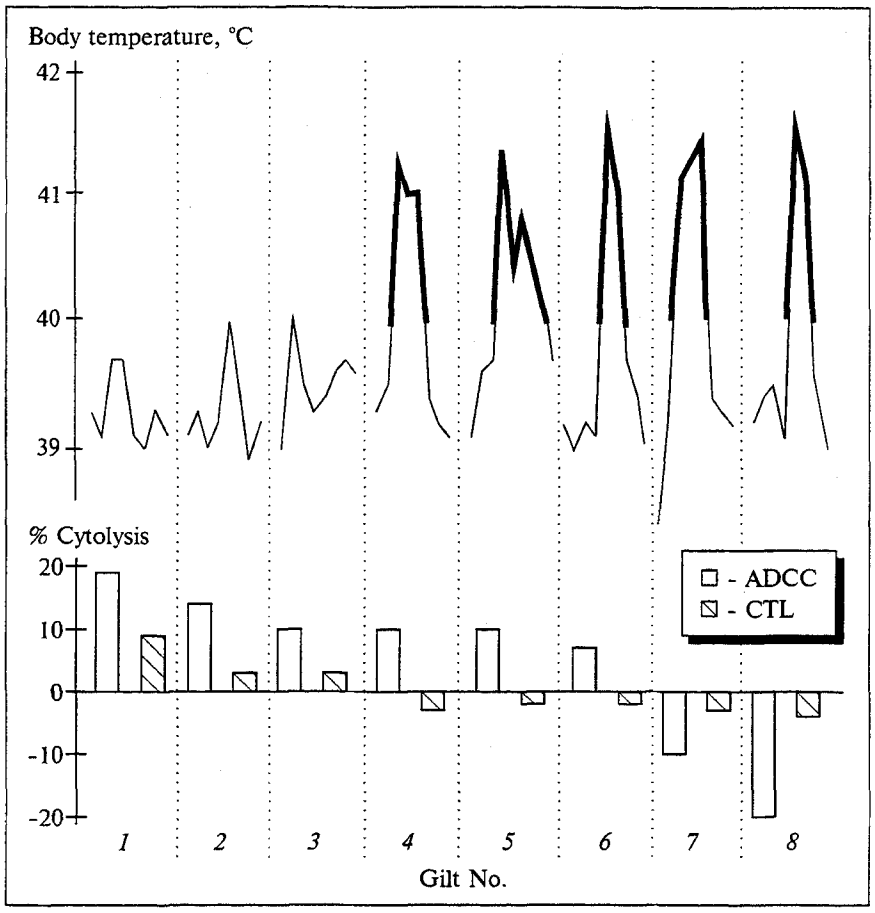

Fig. 3. Results of challenge depending on the specific activity of antibodies in ADCC and of cytotoxic T lymphocytes (CTL) in eight gilts with ASP.

nifest disease. For CSP, a strong positive correlation appears to exist between the resistance of animals to the infection and the level of humoral immunity, since the titers of virus-neutralizing antibodies directly depended on the dose of the inoculated vaccine virus ("replicating antigen"), a 100% level of protection being afforded to animals given this virus in a dose of 1000 $CCID_{50}$ or higher.

Cell-mediated immunity in gilts with ASP. As shown in Fig. 2, the formation of antibodies active in ADCC led to a dose-dependent response in animals inoculated with the avirulent FK variant of the ASP virus. A positive correlation was found between the level of specific cytolysis and the dose of virus. Data in Fig. 3 characterize the roles played by ADCC and CTL in protecting eight gilts with ASP. These animals, in which the level of specific cytolysis was determined on day 3 for ADCC and on day 6 for CTL, were selected to establish a gradient of immune states according to the activity of the tested effectors. It was found that the level of specific cytolysis ranged from 10-20% for ADCC and 3-10% for CTL in gilts Nos. 1, 2, and 3 to completely negative in gilts Nos. 7 and 8. Gilts Nos. 4, 5, 6, 7, and 8, in which CTL failed to display specific activity, responded to the challenge (on day 7) by developing a high-grade fever. The degree of resistance to infection directly correlated with the high levels of ADCC effectors and CTL.

Our comparative study of these two effector arms of the immune response in viral infections *in vivo* confirms, in general terms, the notion of their asymmetry. The results indicate the need for further research to identify and evaluate, on the one hand, the contribution of individual reactions to protective antiviral immunity *in vitro* and, on the other, the viral components responsible for their induction.

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