

Animal models for immune disorders include the following. A rodent model for multiple sclerosis, called experimental autoimmune encephalomyelitis (EAE) (79) involves injecting animals with myelin basic protein (80). A mouse model for rheumatoid arthritis involves injecting collagen (81). A mouse model for inflammatory bowel disease employs a strain of mice that naturally develops inflammation of the intestinal tract (82). Psoriasis (83) lupus (84) asthma (85) and other immune disorders also have well-characterized animal models.

b. Estimating human dose from animal studies

The most appropriate dose of a drug for humans can be derived from animal studies. The FDA provides guidance on converting effective doses from animal studies, to corresponding doses that are likely to be effective in human subjects (86). Two approaches with animals are in common use. The first is to arrive at the highest drug dose that is not toxic. This approach is commonly used for small molecule drugs for cancer. The second is to arrive at the dose of a drug that is optimally effective, as determined by tests sensitive to efficacy. With the information of the dose in hand, investigators then scale up the dose derived from animal studies, and then calculate a dose for first use in humans. Lowe et al. (87) Reigner and Blesch (88) Contrera et al. (89) and Sharma and McNeill (90) review methods for using animal studies to arrive at doses for humans. These methods include methods based on body surface area, and methods based on

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