Lymphocytic choriomeningitis virus (LCMV), a non-cytopathic infection of mice, has revealed the following findings that have helped us to understand basic immune mechanisms:

1. Neonatal tolerance, absence of immunity after intra-uterine or neonatal infection (Traub 1936, 1938). The comprehensive view and interpretation was made by Burnet (1949).
2. Immunity can cause disease (Rowe 1954; Hotchin 1962).
4. Immunity controls virus only partially, since virus survives at low levels (infection-immunity) (Rowe 1954; Volkert and Lundstedt 1968; Ciurea et al. 1999), but adoptive cytotherapy of virus-carriers (Oldstone et al. 1986) is possible by CD8+ T cells and/or CD4+ T cells plus neutralizing antibody-producing B cells (Volkert 1963; Planz et al. 1997).
5. Immune complexes in neonatal virus-carriers question B cell tolerance (Oldstone and Dixon 1967).
6. Cytotoxic T cells (CTLs) against virus-infected cells act comparably to allo-reactive CTLs (Oldstone and Dixon 1970; Marker and Volkert 1973).
7. CTLs cause lethal pathology in the form of T cell-mediated choriomeningitis (Cole et al. 1972).
8. T cells (Mims and Blanden 1972), (in particular CTLs, Doherty et al. 1976; Zinkernagel and Welsh 1976) also mediate anti-viral protection against LCMV, as had first been shown for ectromelia virus by R.V. Blanden.
9. MHC disease association of choriomeningitis (Oldstone et al. 1973; Zinkernagel et al. 1985) and of aggressive hepatitis (Leist et al. 1989).
11. Interferons induced by virus infections may have detrimental effects (Riviere et al. 1977), particularly during early life.

12. Natural killer (NK) cell responses early after systemic virus infection (Pfizenmaier et al. 1975; Welsh and Zinkernagel 1977).


14. Selective down-modulation of some viral transcripts during virus persistence in vitro and in vivo (Oldstone and Buchmeier 1982).

15. Immunosuppression by T cell-mediated anti-viral immunity indicates pathogenic mechanisms that may apply to HIV (Mims and Wainwright 1968; Silberman et al. 1978; Leist et al. 1988; Odermatt et al. 1991). This includes destruction of antigen presentation (althage et al. 1992; Borrow et al. 1995).

16. LCMV mutants that escape CTL activity may be selected (Pircher et al. 1990).

17. Viral antigen on cells strictly outside of lymphoid tissue, for example in pancreatic β-islet cells are immunologically ignored (Ohashi et al. 1991; Oldstone et al. 1991). In contrast to infection with LCMV, immunization with a vaccinia-recombinant expressing the LCMV-GP is not sufficient to cause disease, although it induces a potent, primed CTL response, Thus there is a high threshold for causing autoimmune disease (Ohashi et al. 1993).

18. Exhaustion of all available precursor T cells by virus that has spread throughout the lymphohemopoietic system, particularly LCMV-variants that replicate quickly and to high titers (Moskophidis et al. 1993).

19. Perforin is the key for efficient, rapid CD8+ T cell-dependent LCMV elimination (Kagi et al. 1994; Walsh et al. 1994).

20. Original antigenic sin at the CD8+ T cells level. CTL escape of mutant virus may still induce a CTL response against the original wild-type virus that is not active, however, against the mutant (Klenerman et al. 1998).

21. Natural antibodies that are secreted and present in normal serum without immunization influence the initial virus distribution after LCMV infection (Ochsenbein et al. 1999a).

22. LCMV can persist by selection of mutant virus that escapes neutralizing antibody responses (Ciurea et al. 2000) and CD4+ T helper cell responses (Ciurea et al. 2001).

23. Same open issues

a) Delay of neutralizing anti-LCMV responses? Neutralizing antibody responses against LCMV are vastly delayed (Rowe 1954; Hochin 1962). The delay suggests that viral antigen exhibiting the correct neutralizing epitope must still be available or even increase after day 50–100 at the time when neutralizing antibodies appear. CD8 elimination during the early phase of virus infection enhances generation of neutralizing antibody responses (Battegay et al. 1993; Planz et al. 1996). Both T cell-mediated general immunopathology and specific elimination of neutralizing antibody producing B cells may be involved.