TABLE 2. Mean generation time in vivo and in vitro of several bacterial species

Bacterial species	Animal, route, pretreatment[a]	Organ sampled	Mean generation time in vivo[b]	Mean generation time in vitro	Reference
Salmonella typhimurium	Mice, i.v.	Spleen	5–12 h (true)	0.5 h	9
Salmonella typhimurium	Mice, i.p.	Internal organs	7.8–11.4 h (net)	0.5 h	11
Salmonella typhimurium	Mucin-treated mice, i.p.	Carcass	23–24 min (net)	22 min	3
Listeria monocytogenes	Mice, i.v.	Liver, spleen	4.8–5.1 h (net)	1 h	8
Vibrio cholerae	Mice, p.o.	Upper bowel	2.6 h (net)	1.3 h	2
Leptospira icterohaemorrhagiae	Guinea pig, i.p.	Internal organs	7–11.6 h (net)	7–8 h[c]	6
Escherichia coli	Iron-treated rats, i.m.	Muscle	>60 min (true)	20 min	15
Escherichia coli	Mice, i.p.	Peritoneal wash	20 min (true)	28 min	13
Escherichia coli	Mice, lung	Lung	56 min (true)	28 min	13
Pseudomonas aeruginosa	Mice, i.p.	Peritoneal wash	33 min (true)	26 min	13
Haemophilus influenzae	Rats, i.v.	Blood	47 min (net)	28 min	17
Haemophilus influenzae	Asplenic rats, i.v.	Blood	34 min (net)	26 min	Present study

[a] i.v., Intravenous; i.p., intraperitoneal; p.o., oral; i.m., intramuscular.

[b] Net refers to calculations of mean generation time based upon number of bacteria recovered from animals, a net effect of replication and clearance; true refers to studies in which the mean generation time reflects replication only.

[c] Mean generation time for "broth-adapted" strain. The shortest generation time for freshly isolated virulent leptospira grown in the same medium was 17 to 21 h.

animal models, it is clear that in vivo replication need not be inefficient (compared to in vitro growth). Both host clearance of bacteria and limitation of nutrients or an environment necessary for optimal growth may limit the in vivo multiplication rate of bacteria. The extremely efficient in vivo multiplication of *H. influenzae* type b in asplenic rats despite fairly elaborate growth requirements suggests that the host clearance factors are more important than limitation of nutrients for this bacterial species.

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LITERATURE CITED

1. **Alexander, H. E.** 1965. The haemophilus group, p. 731. *In* R. J. Dubus and J. G. Hirsch (ed.), Bacterial and mycotic infections of man. Lippincott, Philadelphia.
2. **Baselski, V. S., R. A. Medina, and C. D. Parker.** 1978. Survival and multiplication of *Vibrio cholerae* in the upper bowel of infant mice. Infect. Immun. **22**:435–440.
3. **Berry, L. J., M. K. DeRopp, M. H. Fair, and E. M. Schur.** 1956. Dynamics of bacterial infections in mice under conditions known to alter survival time. J. Infect. Dis. **98**:198–207.
4. **Bivin, W. S., M. P. Crawford, and N. R. Brewer.** 1979. Morphophysiology, p. 81. *In* H. J. Baker, J. R. Lindsey, and S. H. Weisbroth (ed.), The laboratory rat, vol. 1. Biology and diseases. Academic Press, Inc., New York.
5. **Brock, T. D.** 1971. Microbial growth rates in nature. Bacteriol. Rev. **35**:39–58.
6. **Faine, S.** 1957. Virulence in leptospira. II. The growth *in vivo* of virulent *Leptospira icterohemorrhagiae*. Br. J. Exp. Pathol. **38**:8–14.
7. **Lowrance, B. L., and W. H. Traub.** 1969. Inactivation of the bactericidal activity of human serum by Liquoid (sodium polyanetholsulfonate). Appl. Microbiol. **17**:839–842.
8. **Mackaness, G. B.** 1962. Cellular resistance to infection. J. Exp. Med. **116**:381–406.
9. **Maw, J., and G. G. Meynell.** 1968. The true division and death rates of *Salmonella typhimurium* in the mouse spleen determined with superinfecting phage 22. Br. J. Exp. Pathol. **49**:597–613.
10. **Meynell, G. G.** 1959. Use of superinfecting phage for estimating the division rate of lysogenic bacteria in infected animals. J. Gen. Microbiol. **21**:421–437.
11. **Meynell, G. G., and E. W. Meynell.** 1958. The growth of micro-organisms *in vivo* with particular reference to the relation between dose and latent period. J. Hyg. **56**:323–346.
12. **Morris, J. G.** 1983. The metabolism, growth, and death of bacteria, p. 60–61. *In* G. Wilson and H. M. Dick (ed.), Topley and Wilson's principles of bacteriology, virology, and immunology, 7th ed. The Williams & Wilkins Co., Baltimore.
13. **Morris Hooke, A. M., D. O. Sordelli, M. C. Cerquetti, and A. G. Vogt.** 1985. Quantitative determination of bacterial replication in vivo. Infect. Immun. **49**:424–427.
14. **Moxon, E. R., J. F. Goldthorn, and A. D. Schwartz.** 1980. *Haemophilus influenzae* b infection in rats: effect of splenectomy on bloodstream and meningeal invasion after intravenous and intranasal inoculations. Infect. Immun. **27**:872–875.
15. **Polk, H. C., Jr., and A. A. Miles.** 1971. Enhancement of bacterial infection by ferric iron: kinetics, mechanisms, and surgical significance. Surgery **70**:71–77.
16. **Rubin, L. G., and E. R. Moxon.** 1983. Pathogenesis of bloodstream invasion with *Haemophilus influenzae* type b. Infect. Immun. **41**:280–284.
17. **Rubin, L. G., A. Zwahlen, and E. R. Moxon.** 1985. Role of intravascular replication in the pathogenesis of experimental bacteremia due to *Haemophilus influenzae* type b. J. Infect. Dis. **152**:307–314.
18. **Shaw, S., A. L. Smith, P. Anderson, and D. H. Smith.** 1976. The paradox of *Haemophilus influenzae* type b bacteremia in the presence of serum bactericidal activity. J. Clin. Invest. **58**:1019–1029.
19. **Shin, H. S., and M. M. Meyer.** 1968. The third component of the guinea pig complement system. II. Kinetic study of the reaction of EAC14, 2a with guinea pig C3. Biochemistry **7**:2997–3003.
20. **Zwahlen, A., J. A. Winkelstein, and E. R. Moxon.** 1983. Surface determinants of *Haemophilus influenzae* pathogenicity: comparative virulence of capsular transformants in normal and complement-depleted rats. J. Infect. Dis. **148**:385–394.