Chapter 1
DISTRIBUTIONS AND PREDISPOSITION: PEOPLE AND PIGS

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“As has been the subject of recent emphasis many times elsewhere, collaboration between immunology and epidemiology is the necessary basis for future progress in this area (the mechanisms of predisposition). Specifically, long-term studies of nutritional status and exposure-related variables are required together with measurement of parasite-specific humoral and cellular immune responses during periods of reinfection following drug treatment in patients of all ages and initial infection levels (Keymer \& Pagal, 1990)”

1. INTRODUCTION

The number of parasites a host carries is fundamental to our understanding of helminth parasite epidemiology. Worm burden is now known to influence the pathogenicity of the infection including effects upon nutritional status and cognitive function (see Chapters 3 and 4), to contribute to the regulation of infection and to impact upon the development of the most effective strategies for control (see Chapter 2). Three key epidemiological patterns which relate to worm burden have been described and studied intensively during the last two decades - these are (i) the frequency distribution of worms per host in a population, (ii) the relationship between host age and worm burden and (iii) the correlation
between worm burdens during periods of reinfection. Presently we have good empirical information to describe these patterns for *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm spp from a variety of geographical locations. The mechanisms which contribute to these observed patterns remain much more elusive and are likely to involve the interplay of exposure, acquired immunity and innate resistance. In this chapter we provide a historical perspective on the studies which have been undertaken to describe these patterns. We then assess the information available on the causative mechanisms behind reinfection and predisposition in humans and outline the difficulties inherent in the design of such studies. Finally we parallel the developments in humans with those in animal models and highlight the possibilities of using some new models which will be amenable to experimental manipulation of epidemiology, nutrition, immunology and genetics.

### 2. A HISTORICAL PERSPECTIVE ON AGGREGATION AND PREDISPOSITION IN HUMAN HELMINTH INFECTIONS

In his seminal work, 'A quantitative approach to parasitism', Crofton described the frequency distribution of parasites in a host population as clumped or overdispersed and best described mathematically by the negative binomial (Crofton, 1971). The pattern of overdispersion among helminth parasites within their hosts is now known to be widespread in both human and other animal hosts (see Anderson & May, 1979; Crompton, Keymer & Arnold, 1984; Shaw & Dobson, 1995). The first paper to detail this phenomenon and its significance in humans was that of Croll & Ghadirian (1981). They described endemic communities wherein most hosts harbour few or no parasites and the so-called 'wormy persons' carrying very heavy burdens. The worm burdens of *Ascaris lumbricoides*, *Trichuris trichiura* and the two species of hookworm, *Ancylostoma duodenale* and *Necator americanus* were counted after anthelmintic treatment of subjects from three Iranian villages and all distributions were overdispersed. Ironically, given later developments, in this study no significant correlation was found between pre-treatment and post-treatment worm burdens 12 months later.

Seeking an explanation for this observed frequency distribution (Figure 1.1) was to become one of the major concerns for parasite epidemiologists in